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Understanding the relation between parts and whole in the biological realm. A metaphysical and epistemological analysis.

Macarena Alejandra Vidal Arenas

A dissertation submitted to the University of Bristol in accordance with the requirements for award of the degree of Doctor of Philosophy in the Faculty of Arts, Department of Philosophy.

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Abstract

This thesis explores the relationship between parts and wholes in the biological context. This topic is significant in philosophy and the sciences. Philosophical discussions have examined the nature of things, encompassing the evaluation of structures and organisations within various entities. In parallel, biological sciences often approach the analysis of biological entities by considering their composition of interconnected parts and wholes. Commonly biological entities are decomposed into parts to study biological systems. Still, the nature and the use of this relation between biological wholes and their parts have been taken for granted.

For this reason, the objective of this research will focus on analysing from an ontological and epistemological perspective regarding this topic. The ontological one addresses how the relation between parts and whole can be configured in the biological world, evaluating the central role of control and regulation action in configuring this relation, highlighting that this action not only constraint the interrelation, also they allow flexibility, context-sensitivity and new possibility of interaction. The epistemological dimension examines into how scientists acquire knowledge about the living world through these concepts of parts and wholes, highlighting their role in the organisation, classifications, explanations and communication of the living world and its diverse entities. By addressing these ontological and epistemological dimensions, this dissertation contributes to a more comprehensive understanding of the biological sciences' relationship between parts and wholes. The findings offer valuable insights into how our perception of the living world is shaped and how scientific knowledge is acquired within this framework.

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Author’s Declaration

I declare that the work in this dissertation was carried out in accordance with the requirements of the University's *Regulations and Code of Practice for Research Degree Programmes* and that it has not been submitted for any other academic award. Except where indicated by specific reference in the text, the work is the candidate’s own work. Work done in collaboration with, or with the assistance of, others, is indicated as such. Any views expressed in the dissertation are those of the author.

SIGNED: Macarena Vidal Arenas DATE: 20/07/2023

Dedicated to

Cristian and my parents,
for their unconditional support.

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Introduction

Almost everyone has a general idea of what is a whole or what is a part. Talking about parts composing something is a common expression to refer to diverse entities we perceive daily, and it is a common first approach to describing material objects. For instance, to think of our human body, we think of arms, hands, head or legs - in other words - in parts that compose it. Thus, describing objects in terms of parts and wholes is a common practice, but this distinction is not trivial in philosophy and science. This topic -parts and wholes- has been widely discussed in philosophy, particularly metaphysics. For example, when philosophers discuss how things are, they evaluate the structure and organisation of different features of them. Similarly, scientists implicitly appeal to parts and wholes when they study and explain phenomena in their particular sciences. For instance, when they claim that an atom is composed of subatomic particles and a cell is composed of organelles. This work is embedded in the philosophical discussion of part-whole relationships in biological sciences.

Regarding the philosophical discussion, metaphysicians have looked for a general definition of the relationship between parts and wholes, trying to answer questions about when and how composition occurs and what the nature of the relationship between parts and wholes may be (e.g., Lewis 1986; Varzi, 2014; Van Inwagen, 1990). Within this discussion, they have assessed if objects with parts exist (Cornell, 2018), what happens with objects with vague limits (Unger, 1980; Van Inwagen, 1990), or the nature of this vagueness (Hyde and Raffman, 2018; Merricks, 2001; Tahko, 2009). This metaphysical inquiry has been developed alongside investigations on concepts such as the identity of things, the persistence of entities over time and through change, and the distinction between accidental and essential properties of individuals. This work has contributed to developing our understanding of the nature of different entities and the implications of our thoughts about the material world. However, it is still unclear if a general response about the nature of material objects is even possible when we consider the vast diversity of existing things, which is especially relevant for dynamic and complex composite objects such as biological systems.

Thus, the evaluation of notions of composition, parts and wholes in the biological context is relevant for this metaphysical discussion because this science gives us cases of highly

dynamic and complex composite objects, which can adapt, reproduce and self-maintain. The field of biological sciences offers a unique setting where objects possess distinctive characteristics and provides an opportunity to examine the metaphysical assumptions that underpin current scientific as well as ontological implications. Additionally, it allows for investigating perceived challenges in defining and characterising scientific objects (see Guay and Pradeu, 2016). So, it is worth asking if this use implies an ontological commitment to conceiving the living world in a part-whole structure. Although in sciences such as biology reference to composite objects is widespread, in the metaphysical analysis of concepts such as composition, parts and wholes, philosophers have not paid much attention to the scientific knowledge attained about such objects (Ladyman, 2017).

In recent years, some philosophers have recognised that there is a gap between this metaphysical debate and the consideration of scientific knowledge as a source of analysis. Some philosophers have contributed to reducing this gap, addressing this issue in the scientific context (see Calosi and Graziani, 2014), and examining part-whole relationships in different sciences such as physics, chemistry, and biological sciences. Specifically, in the case of biological sciences, scholars (e.g., Kaiser, 2015; 2018a, and Jansen and Schulz, 2014) have studied the criteria to define when a biological element is part of the biological whole. Parallelly, Elselijn Kingma (2018) has studied the metaphysical relationship between the foetus/embryo assessing if the nature of this relation can be understood in terms of parts and whole. These inquiries show how the notions of part, whole and composition in the field of biology can be addressed with interesting philosophical questions. However, there are more aspects regarding part-whole relationships that can be assessed in the biological context.

Notwithstanding, these concepts are not only relevant to metaphysics reflection but also to epistemology. Life scientists often analyse biological systems in terms of wholes and parts when investigating some phenomena. Part-whole relations seem to have particular importance in the natural sciences because even though these relationships can also be established in physics and chemistry (e.g., molecules are formed by atoms), the characteristics of biological systems appear to be different from the non-living ones. Specifically, biological systems are characterised by being thermodynamically open, having a continuous exchange of energy and matter with their environment and presenting a complex multi-level organisation with highly interrelated and interdependent levels (Boi, 2017). All known life forms are structurally and organisationally amazingly complex, independent of whether one thinks of highly developed

multicellular organisms or simpler unicellular life forms like yeast or bacteria. Scientists use several strategies to approach biological phenomena, such as elaborating models, concepts and explanations. One particular process frequently used by biologists is to divide a system into parts and then analyse how these parts participate in the phenomenon's behaviour (Bechtel and Richardson, 2010).

This methodological principle has allowed scientists to give more detailed and comprehensive accounts of their studied phenomena. This methodological principle highlights a significant feature of scientific practice in biology – understanding living entities in terms of different levels of the biological organisation (e.g., cells are parts of tissues, tissues are parts of organs, organs are part of organisms and so on). Likewise, scientists also describe general biological entities that depend on their parts; mammals have arms, unlike birds with wings. Therefore, in these kinds of sciences, often the natural world is conceptualised in terms of entities made up of other more complex entities. When life scientists elaborate on these explanations, they implicitly employ a particular notion of composition, parts and wholes. Thus, analysing the idea of parts composing a whole is relevant to understanding 1) the nature of this relation in a biological context, 2) how the biological world is conceived and 3) the research strategies used in biological studies. Furthermore, the examination of the nature of this relation in the biological realm is also important for other theoretical discussions in the philosophy of biology, such as the concept of biological individuality or emergent properties. Because these discussions are closely linked to how biological entities are related in terms of parts and wholes.

The analysis of the epistemic implications of using these concepts in biological sciences is relevant to the development of the philosophy of science. Usually, this discipline does not pay sufficient tribute to the challenges scientists face when attempting to produce knowledge and understanding of an enormously complex world (Kampourakis and Uller, 2020). Indeed, some scientists can question why philosophers -who presumably do not have proper knowledge of scientific practice- analyse any activity related to science. Some specialists in science studies could also critique that philosophers of science are mostly ignorant of aspects of scientific activity, which they consider extremely important (see Barberousse, 2018). To reduce this possible lack of knowledge of scientific work, philosophers of sciences should engage more in practical issues of sciences. Recognising this issue, some philosophers have stressed the

relevance of understanding scientific reasoning on how scientific knowledge is and how it is produced through the explanations that scientists give (Rosenberg and McIntyre, 2020).

This shows that examining diverse scientific activities and how scientific knowledge is generated is becoming increasingly critical. This is especially true if we consider that scientists, in general, do not need to try to figure out what science is, what the difference is between an everyday explanation and a scientific one, how it is generated scientific knowledge to carry out their work or analyse how scientific is practised. Most of their understanding of science and its functioning comes from their peers, especially those who work on comparable issues using similar approaches (Kampourakis and Uller, 2020). They adopt an established way of working, following a specific modus operandi. Similarly, science students are taught fundamental techniques and guided on how to use them. Still, they are not provided with an explanation for selecting these methods or the reasoning behind their design (Grüne-Yanoff, 2014).

Considering the exposed above, fundamental philosophical issues about the relationship between parts and wholes within this scientific discipline still deserve to be addressed. Firstly, the ontological dimension is pertinent to examine the nature of the relation between parts and whole in biological objects. Secondly, from an epistemic perspective is relevant to know how scientists learn about this world through the notions of parts and wholes. So, this thesis has two main aims, each related to one of these dimensions. The first is evaluating the nature of relations between biological entities in terms of parts and whole. How is achieved and maintained the integration of elements in a biological whole, based on contemporary biological sciences. Secondly, the epistemological aim is to elucidate how scientists obtain knowledge about the living world through these concepts and problematic of the application of this metaphysical category of part/whole relation.

In the ontological dimension, I claim that biological entities are significant cases of studies to evaluate how the different biological elements are related in terms of parts and wholes. I stress that this relation is given under controlled circumstances, highlighting the role of *control* action in configuring this relation between parts and wholes in everchanging contexts like biological ones. This is not only due to its restrictive action but also because this action allows flexible, context-sensitive, and new possibilities of behaviour. Furthermore, these control processes are essential to examining the possibility of emergent properties. The detail of how these controls operate gives relevant antecedents to see how emergent phenomena can occur. About the epistemological dimension, biologists use notions of part, whole and

composition as organisational, classificatory, illustrative and narrative principles to understand the biological world. These notions allow us to visualise how the natural world is, being a helpful guide for scientists when deciding how to study a particular phenomenon. However, depending ontological assumptions considered about part/whole relations, this use can display limitations in giving an accurate idea about complexity of biological phenomena.

The philosophical analysis of the notions of parts and wholes from metaphysical and epistemological perspectives conducted in this thesis has four contributions. Firstly, analysing biological entities based on contemporaneous biological practice enriches the metaphysical discussion about parts and wholes. Reframing these classical philosophical questions in light of scientific knowledge, specifically from biological science, give philosophers rich and concrete examples of complex parts and wholes relationships that are sometimes difficult to elaborate on using abstract thinking.

Secondly, this examination of ideas of parts and whole in biology provides more antecedents to discuss central topics of the philosophy of biology, such as *biological individuality* and *emergence* concepts. In the case of *biological individuality*, philosophers of biology discuss what the best criteria to define biological individuality are and if it is possible that interactions between different biological organisms can result in new individuals. Concerning the *emergence* concept, the notions of parts and whole have a central importance because the issue to discuss is whether composite objects have emergent properties which cannot be reduced and accounted for in terms of their parts.

Thirdly, from an epistemic perspective, the examination of the use of parts and whole notions in different aspects of biological inquiry, including methodology, explanation, visual devices, and communication, contributes to enhancing our understanding of how scientists define the living world and how they apply the assumption of biological entities being composed of parts in their work. Additionally, clarifying how scientists apply this assumption in different ambits of their work contributes to enriching the understanding of philosophers about the scientific practice.

Fourthly, parallelly, this study also provides worthy information for scientists. Scientists do not analyse these assumptions that they use implicitly when studying a particular phenomenon. They are taken for granted. Therefore, philosophical reflection about this allows them to pay attention to these assumptions commonly overlooked in daily scientific work. A

detailed analysis of these assumptions or ideas established in scientific practice can help scientists to think critically about how they get this knowledge. Thus, this thesis contributes that scientists can develop an adequate understanding of their own scientific reasoning and work. Consequently, this understanding can benefit them to communicate or teach scientific content in a didactic and efficient way.

The plan of the thesis is as follows:

Chapter 1 consists of a critical review of metaphysical literature on the concepts of composition, part, and whole. This chapter will address issues such as what an object is, and how the sum of the whole is effectively more than its parts; Composition as Identity (CAI), And examination of the Special Composition Question (SCQ) and its different possible responses, namely universalist, nihilist, restrictive, and verbal dispute accounts. It is beneficial to take into account both these metaphysical questions and the problematic aspects that stand out within the metaphysical discussion. Additionally, it is argued the methodological decision of addressing this metaphysical issue, considering both biological theory and practice. In this manner, I can ensure that we have the relevant philosophical antecedents to questions related to composition and the nature of the relationship between the whole and its parts.

Chapter 2 evaluates the philosophical relevance of the analysis of notions of parts, and wholes in the biological realm, exanimating this classical philosophical issue regarding the nature of the relation between parts and whole can be relevant in philosophy of biology debates related to levels of organisation, emergence, self-organisation, elaboration of explanations and biological individuality. In order to argue the importance of this study in the biological realm, in this chapter, I will compare non-living and living entities.

Chapter 3 addresses the question *What tare conditions to configure the relation between the biological whole and its parts?* In this chapter I claim to rethink this relation, examining how a collection of elements interacts with each other to become an integrated unit despite environmental changes, from the challenges of synthetic biology. This is because these challenges can illustrate critical aspects of the composition relation from an experimental perspective in the work of design, modification, and assembly of synthetic biological entities. The attempt by synthetic biologists to effect designs provides us insights into how a collection of elements should interrelate to make up further biological objects. A great part of the work of

these practices is understanding how in the biological world the elements are interconnected in a coordinated way. I shall argue that a biological entity keeps a coordinated and unified behaviour and functions in variable contexts due to its communication, control actions. They sense and regulate as the system's elements interact with each other, allowing the system to keep itself stable against changes in its environment, allowing a flexible and context-sensitive behaviour. This chapter argues that a comprehensive ontological framework of this relation should pay attention to dynamic, temporal, and spatial aspects and not only focus on what components are, what they do, and how.

Chapter 4 is concerned with emergent properties. In the biological context, life scientists explicitly reference the emergence concept, to explain certain specific characteristics of the phenomenon they are studying. For this reason, this chapter shall carry out an examination considering the importance of control mechanisms in the configuration of the relation between parts and whole in a biological context; this chapter will address the following questions. 1) Could this relation between these types of wholes and their parts give room to emergent phenomena? 2) What type of emergent phenomena would they be? It is argued that emergent phenomena - both epistemic (e.g., patterns) and ontological (e.g., robustness) emergent properties - can occur in biological entities due to their specific organisation, performance, and control actions. Merely saying that its parts determine the property of a system, and their respective interactions is a problematic simplification when considering dynamic and open systems. The global constraints and control architecture and action are essential in how components interact in a flexible, context-sensitive and sometimes in novel ways. The chapter will present the possible conditions under which phenomena can occur.

Chapter 5 provides an epistemological analysis, forming a philosophical examination of scientific practice in the biological sciences. It develops a characterisation of the use of the *parts* and *whole* notions, examining the following questions. 1) In what ambits of scientific practice are these notions used? 2) What is the importance of these notions in studying the living world? 3) And what are the problematic aspects of this use? 4) How do these problematic aspects affect the communication of scientific content? The purpose of all this is to gain a more comprehensive view of relations between parts and wholes in the living world, increasing our understanding regarding how scientists define this world and also their work in ambits such as methodological elaboration of explanations and visual devices and communication of their findings. This thus contributes to the uncovering of scientific reasoning.

Chapter 1

Philosophical discussion on wholes, parts, and composite objects.

1.1 Introduction

The philosophical discussion surrounding composition, parts, and wholes has been a rich and extensive field of inquiry. Metaphysicians, in particular, have engaged in a quest to establish a comprehensive framework for these concepts. Delving into the realm of parts and wholes, philosophers have grappled with the fundamental question of whether a whole entity is more than a mere sum of its constituent parts. Additionally, the exploration of unity and identity probes the very nature of how these parts come together to form a cohesive and integrated whole. Philosophical inquiries have scrutinised whether a whole entity can be considered identical to its individual parts or if an additional unifying principle is necessary to truly comprehend their relationship. Work has also touched upon topics such as the persistence and

identity of objects over time, as well as the composition relation, unravelling how objects are made up of smaller components, and assessing the nature of the relation between these parts and the wholeness they compose. In this, philosophical debate on composite material objects, many metaphysicians have sought a general description of parts and wholes, trying to answer questions about when and how composition occurs and what the nature of the relationship between parts and wholes may be.

In the last thirty years, this metaphysical discussion has acquired relevance thanks to the work of Peter van Inwagen (1990), focusing on the question of how a plurality of objects composes a further object. There are three main answers to this question, viz.: restrictive, universalist and nihilist. Nevertheless, other philosophical accounts have argued such issues as that this is a verbal dispute (i.e., Hirsch, 2005) or that the formulation of this question is not appropriate to examine the composition problem (i.e., Sanford, 1993; Thomasson, 2007).

Considering these philosophical discussions, the main purpose of this chapter is to perform a critical review of metaphysical literature on the concepts of composition, part, and whole and to argue the relevance of carrying out a philosophical analysis of these concepts in the biological realm. In this way, I can ensure that we have the relevant philosophical antecedents for questions related to composition and the nature of the relationship between the whole and its parts, in order to then examine later these notions in the biological context.

To accomplish this objective, the following chapter will meticulously examine the philosophical discourse surrounding the concepts of parts, wholes, and composition. Specifically, the chapter will address the following main areas of debate. 1) The question of whether the whole can be considered to be merely the sum of its constituent parts, thereby exploring the nature of the relationship between parts and wholes. 2) An exploration of the metaphysical approach to composition, wherein composition is understood as identity. 3) Then, we shall enquire into studying material objects, focusing on if exist objects with parts. Moreover, this chapter will assess pertinent philosophical positions in detail, including universalism, nihilism, and restrictive views, to comprehensively examine their perspectives.

Additionally, it will analyse the problem of vagueness in the composition debate, questioning whether it may be construed as a merely verbal dispute. This section will carefully consider the challenges of vagueness and its implications for our understanding the relation of parts and wholes. Finally, this chapter will assess whether a definitive answer to the

composition question can be attained. It will explore the most appropriate approaches to evaluating the composition relation between different entities, aiming to shed light on the intricacies of this philosophical inquiry.

1.2 Philosophical discussions on composition, parts, and wholes.

One way of approaching the problem is to debate whether or not a whole is equal to the sum of its parts.

1.2.1 Is the whole the sum of its parts? or is the whole greater than the sum of its parts?

Frequently, the whole is defined by its parts. We can see this idea in statements such as "the whole is equal to the sum of its parts". When we make this claim, everyone has an idea as to what it means. However, there is no clarity on what such concepts as sum really mean, so the idea of a whole is still ambiguous. Hence, what these slogans mean is the main issue we need to clarify, in order to understand what the nature of the relation between parts and wholes is.

In metaphysics, when we describe an object as complex, we typically imply that it consists of multiple parts. Nevertheless, an essential query arises: are these entities merely the result of the sum of their individual components in a particular configuration? (Mumford, 2012). Perhaps, the idea that "the whole is the sum of its parts" is only a slogan to explain that a whole is the total parts and their respective activities together. The reference to the term "sum" gives a certain notion of unity. This means that the collection of entities or events are together in a particular way, as a whole. This seems redundant because the notion of wholeness is implicitly the same idea. This is simply another way of saying that a whole is a composite of its parts and so, it does not explain the main point in the discussion, namely, what is the nature relation of entities in terms of parts and whole?

We can find many cases where the whole is the aggregation of its parts; for example, a wall is the aggregation of hundreds of bricks. In this case, properties of the whole, such as shape, size or height, are perfectly explicable in terms of the parts and their specific arrangement. However, there are other kinds of wholes, where some properties are more

difficult to explain according to the arrangement alone. If we think of an electronic device, it has properties related to having a connection to the Internet, reproducing TV series, or playing music, among other examples. In these cases, it seems that not only the arrangement of parts is important, but so too is the specific activity that they carry out and how they interact with each other.

When it comes to piles of sand, the overall height and shape appear to be determined by the arrangement and composition of its individual parts. Consequently, the entirety of the heap can be viewed as the combination of its constituent elements, provided they are arranged correctly. When considering an electronic device, the characteristics and capabilities of the whole can be understood by examining the specific organisation, functions, and interactions among its various components. In this scenario, the whole is not only the sum of its parts but also encompasses the unique activities and interplay carried out by these parts. This is why philosophers occasionally make a distinction between integrated wholes and mere collections of elements (Mumford, 2012).

There are yet other kinds of wholes, where some properties are more difficult to explain according to the arrangement alone. For instance, biological wholes are composed of specialised parts, which play specific roles in the whole's functioning. They compose a whole not only by virtue of their particular features and specific location but also by how they interact. These parts are involved in crucial processes of the whole, playing specific roles in the structure and functioning of the whole.

Other cases are even more complicated to analyse because some properties or attributes of the whole cannot be explained in terms of its parts. Living beings serve as paradigmatic examples of this concept. The essence of life appears to reside within the entire organism and eludes identification within its individual components. To illustrate, a unicellular bacterium is live, yet if you isolate the macromolecules making up the bacterium, these constituents lack the attribute of being alive (Lobo, 2008). In these cases, it seems to be that the whole is greater than the sum of its parts. Therefore, the relationship between a biological whole and its components would differ significantly from that of a wall and its bricks.

The idea that “the whole is greater than the sum of its parts” is associated with the concept of emergence. The emergence concept is one philosophical context that discusses how a whole is related to its parts. The notions of composition, parts, and whole are central to

understanding this kind of property. The issue to define is whether composite objects have emergent properties that cannot be accounted for in terms of their parts. One of the main aims of the philosophical examination of the emergence concept is to define how to characterise emergent phenomena more precisely.

In a broad sense, emergence involves something *new* arising from something else, perhaps displaying independence or autonomy, in some degree, from that from which it emerged (Gibb, Hendry, and Lancaster 2019). For instance, although a thing is dependent on its parts (that is, it could not exist without them), it is also something new and different in relation to them (Gibb, Hendry, and Lancaster, 2019). So, a question that arises is how the relationship between a thing and its fundamental parts generates a novel property. Hence, to define the conditions under which emergence can occur, it becomes crucial to understand how the components are connected to the whole; what is the nature of this relation? What are the conditions under which a variety of elements can be integrated as a whole? Do these conditions of integration justify evaluating the possibility of an emergent phenomenon? This issue is relevant not only in metaphysics but also in the philosophy of biology. For this reason, the thesis will evaluate how parts and relations can be configured in the biological context and if the conditions of this configuration are sufficient to argue that an emergent phenomenon can occur.

1.2.2 Is the whole identical to its parts?

The concept of wholeness can also be expressed as "the whole is the same as its parts" or "the whole is, in some way, identical to its parts." These statements align with the idea of composition as identity (CAI), which argues that a whole is essentially indistinguishable from its constituent parts. CAI seeks to explain the close connection between parts and wholes by highlighting the inheritance of location and the unique composition of these entities (Cotnoir and Baxter, 2014). The notion of inheritance of location suggests that a whole occupies the same position as its parts. At the same time, the idea of the uniqueness of composition emphasises that any wholes with identical parts are identical themselves.

This thesis comes in a weak and a strong form. The weak form suggests that the composition is analogous to the identity relation, making it worthy of being categorised as a type of identity (see Lewis, 1991). In turn, the strong form claims that the composition relation

is strictly identical to the identity relation. Hence, the parts of a whole are literally (collectively) identical to the whole itself (Noonan and Curtis, 2022).

The strong version presents certain problematic aspects when examining the hybrid relationship of identity, which involves connecting pluralities and singular objects (e.g., the bricks = the wall). The classical identity relation defines the truth conditions for an identity statement as being true if and only if the terms "a" and "b" refer to the same thing. However, this explanation fails to apply to hybrid identity statements since plural terms do not have a single referent (Noonan and Curtis, 2022). Furthermore, adopting CAI would violate Leibniz's law, which states that if x = y, then any true statement about x must also be true about y, and vice versa (Forrest, 2016).

If we follow the strong proposal of CAI, then the wall is identical to the bricks, but a wall is a single object, whereas the bricks are many. Therefore, it appears that something is true for the bricks yet would not be necessarily true for the wall, which is a single object. The issue here is whether the same thing can be different numbers of things so that sameness is identity but not numerical identity. Some philosophers have argued that it is plausible to understand identity in a fashion that is not numerical. The philosopher Donald Baxter has argued that there many ways to say *composition as identity.* He, in his book "Identity in the Loose and Popular Sense" (1988), distinguishes between numerical identity (sameness in every respect) and qualitative identity (sameness in relevant respects). Baxter argues that when we speak of identity in everyday language, we are typically referring to a qualitative identity, which is a matter of sharing relevant properties or characteristics. This perspective aligns with the notion that "sameness is identity but not numerical identity," suggesting that identity is not solely based on numerical criteria but also involves shared qualities or characteristics.

If we consider identity in terms of properties and characteristics, what happens if the same parts can compose a different whole with other properties? Ross Cameron (2014) argues that CAI faces challenges in explaining how the same parts can simultaneously compose multiple wholes without introducing redundancy or violating the principle of identity. Imagine a car that is disassembled into its individual parts: the engine, wheels, chassis, seats, and so on. According to CAI, the vehicle and its components are identical, meaning they are the same entity. However, if we consider the parts individually, they can also compose other wholes. Similarly, the wheels, chassis, and seats can also be repurposed and incorporated into other vehicles or used in alternative contexts.

This example highlights the challenge that CAI faces in explaining how the same parts can simultaneously compose multiple wholes. If the car, its engine, and other components are identical, it becomes difficult to account for their simultaneous involvement in different compositions without either introducing redundancy (by positing multiple identical objects) or violating the principle of identity.

A fundamental aspect to clarify is what we understand as identity. Having clarity about what identity means is not only relevant at the moment when we consider that parts can compose different wholes, but also when we think in terms of the replacement of parts. If composition as identity were true, any change in the parts of an object would lead to a change in its identity, leading to a constant identity crisis. For example, according to this view, if a tree loses a leaf, it will cease to be the same tree. This does not align with our intuitive understanding of object persistence through time and across possible worlds.

If we accept that any change in any whole's part implies a change in the identity, then let us consider a series of objects where the difference between each successive object is exceedingly small. It becomes difficult to determine when a change in identity occurs. These objections challenge the notion of strict identity between objects and their parts. Hence, the question arises: at what point does the presence or absence of a part result in a different object?

Assuming that the identity of a whole is in all its parts (a six-pack of beer cans is its six beer cans) would give the floor to the problem of *mereological essentialism*. This essentialism refers to the view that an object's parts are essential to its identity. The problem would be if some part is lost or replaced. The whole would be another different composite object. Van Inwagen (1987) highlights this issue, arguing that mereological essentialism leads to an unacceptable consequence known as the "ship of Theseus" paradox. According to the paradox, if an object's parts are essential to its identity, then gradually replacing all its parts will result in a different thing altogether, which conflicts with our ordinary intuitions about identity. Additionally, if composition as identity were true, we would have to draw arbitrary lines to determine when an object becomes a different object due to the presence or absence of a part, which raises questions about the coherence of this view.

Another approach claims that when we talk about composition and identity it is also necessary to refer to unity. Philosopher Lynne Rudder Baker (1999) argues that an object's identity, cannot solely be based on its parts, as it also requires a unifying principle or a set of

organising relations. According to Baker, an object's identity is not exhausted by its parts but also includes the relational properties that bind those parts together. So, while Baker is correct in emphasising the importance of unity in understanding identity and composition, her insight also underscores the ongoing metaphysical challenge of establishing an entirely satisfactory account of the nature and source of this unity that binds parts into integrated wholes. This task is not easy at all, because before it is necessary to establish what are adequate characteristics should meet this principle. Additionally, it is possible or not to define a universal principle valid to any object, no matter how different they are (e.g., a table and a plant).

The problematic aspects of Composition as Identity (CAI) bring to light the importance of understanding how the relations between a whole and its parts can be configured. Before evaluating how parts are identical to the whole, it is necessary first to assess what are possibilities for configuring these relations. Then, we can define whether the identity of the whole is derived from the sum of its parts. In what cases does the mere aggregation of parts establish the identity of the whole, and in what cases does it not? Alternatively, we can investigate when it is essential to consider how the parts interact with one another in order to examine identity.

Exploring the configurations of relations between parts and wholes allows us to assess the specific conditions under which parts can be deemed identical to the whole and the nature of that identity. To provide a clearer perspective on composition, philosophers have examined questions such as: under what circumstances do two or more material objects compose a further object? What are the necessary and sufficient conditions for composition to occur? Is it possible to establish conditions valid for different entities such as a chair or an animal? The philosophical discussion about objects and the composition relation is analysed below.

1.3 Objects and the composition relation.

1.3.1 What an object is.

One task of metaphysics is to explain reality. To this end, metaphysicians carve reality into categories. Some things could fall under the category of contingent entity. Others fall under the event category, and so on. One question that philosophers might ponder is whether there is

a category under which everything falls. It seems hard to offer an informative account of such a category, where much is said about it, and it does not appear to enable categorisation or division at all. Some candidates for such a fully general category can be a thing, being, entity, item, and object (Rettler and Bailey, 2017).

The object category has been discussed widely in metaphysics. Philosophers attempt to explain what the nature of an object is, through the analysis of what an object is or what an object does. For this, one first approach can be to exemplify entities that we usually consider to be objects such as stones, chairs, tables, cars, laptops, or plants. Focusing on the object category, there is a great philosophical debate on the nature of objects, if they are composite or simple only, how simple objects compose a further object, or which things are simple objects. The philosophical discussion of these questions is what I shall explore in the following sections.

1.3.2 Composite objects.

Regarding composition, parts, and whole, many metaphysicians have sought a general account of these concepts. One philosophical analysis has been focused on mereology, which addresses logical and formal aspects of the relation between a whole and its parts (e.g., see Cotnoir and Varzi, 2021). Another is the philosophical examination of material composition. In this analysis, philosophers try to answer questions about when and how composition occurs and what the nature of the relationship between parts and wholes may be; these points have received much attention from philosophers (Cornell, 2018).

The composition concept refers to when some objects are the parts of another object: they compose that object, and that object is composite. So, the definition of the composition relation is expressed in terms of parts and wholes.

Understanding the fundamental characteristics of these objects has prompted a comprehensive discussion revolving around the question of the conditions under which a collection of objects come together to form a distinct entity. Individuals often possess pre-philosophical intuitions that guide their thinking when considering the nature of material objects. These intuitions arise from numerous instances that appear to be unequivocal cases of composition and those that clearly demonstrate non-composition. Given this, it is only natural

to inquire into what distinguishes these cases and to expect that there exists a definitive answer to this inquiry.

There are three potential responses to this inquiry in this philosophical framework, with the initial two being at the opposite and the final one more moderate approach. These responses can be categorized as follows: 1) universalist, 2) nihilist, and 3) restrictive. Universalism asserts that there are no instances where something is not composed, whereas nihilism claims that there are no instances where something is composed. Consequently, neither theory nor theory appeals to the existence of cut-off points. In turn, the restrictive view proposes that there are both simple and composite objects, this being a moderate answer to the SCQ, which is discussed below.

When analysing these answers, we encounter those who think that composite objects exist and have to explain the criteria to define when a plurality of x_s composes y. Hence, to argue that composition only occurs on certain occasions requires an explanation of criteria to define when two or more entities compose a further object. However, the reasons for determining the criteria for each of these occurrences are ill-defined. In the next sections, these views and their respective problematic aspects will be assessed extensively.

In recent years, the composition has attracted greater attention, thanks in large part to the work of Peter van Inwagen. He claims, in his book *Material Beings* (1990), that to understand what composition is, we should respond to the following question: in what circumstances do two or more material objects compose a further object? He called this the Special Composition Question (SCQ). In the next section, three possible answers to this question, namely universalist, nihilist, and restrictive are critically analysed.

1.3.2.1 The universalist view

The first possible answer is the universalist view, which can be expressed in the following way: The x_s compose a Y if and only if the x_s exist. This account claims that whenever you have two or more material objects, they always compose a further object (see Lewis, 1986; Armstrong, 1993). According to Lewis (1986), the part-whole relation obeys a principle of Unrestricted Composition. This principle claims that for any group of objects, there is a whole that they make up. Therefore, according to this view, for any group of things, there is something that

they compose. Regardless of the nature of objects, and the distance between them, if there exist two objects, they will compose a further one. Therefore, those who consider that composition always occur take the view that it is not necessary to set up the particular conditions *under which* composition occurs because it does not matter the condition or context, the composition relation will always occur.

One criticism that universalism faces relate to its seemingly arbitrary nature. If composition is unrestricted and any collection of objects can form a composite, it appears to allow for the existence of bizarre and counterintuitive entities. For example, that a laptop on a table has not composed an object. If these objects are located one over another, this is just circumstantial and is not a case of the composition of further objects. Hence, it raises concerns about the ontological implications and plausibility of universalism.

The universalist view is not a satisfactory answer to understand the material world. Universalism does not tell us is what kinds of objects there are. This account only tells us that composition always occurs. The nature of this relation, in what manner objects are related, and how parts form the whole is not specified. Then, how is possible to distinguish different objects?

Additionally, as to whether composition *always* happens, this position potentially entails an ontological commitment to accepting the existence of an indefinite number of objects. Some defenders of the universalist account such as Lewis (1986) claim that universalism is ontologically innocent. This means that universalism does not introduce any additional ontological commitments or entities beyond what is already accounted for in the objects' existence. According to Lewis, the ontological commitment of universalism is no different from the commitment already present in recognising the existence of individual objects.

Therefore, those who defend this view argue that the whole is not ontologically additional to all its parts, nor are the parts ontologically additional to the whole of which they are composed (Cameron, 2014). So, universalism emphasises the composition and arrangement of objects as a fundamental aspect of understanding the structure and complexity of the world without requiring any additional metaphysical assumptions.

Philosophers such as Byeong-uk Yi (1999) rebut this ontological innocence in, for example, his article entitled "Is Mereology Ontologically Innocent?", arguing that the concept of composition itself introduces ontological commitments. By positing that objects are composed of parts. Mereology implies a particular relationship between these parts and the resulting whole. This relational aspect of composition adds another layer of ontological commitment, as it requires the recognition of a distinct ontological category for composite objects.

This is an interesting point to examine. If we think of a sculpture, for example, made from marble, metal, and wood, according to the concept of composition, these individual parts combine to form a distinct artwork, a composite object. By considering the existence of the sculpture as a unified entity with its own aesthetic properties, we introduce ontological commitments. We attribute existence and specific characteristics to the statue that goes beyond the mere sum of its material parts. Then, by acknowledging the relationship of composition, we commit ourselves to recognising the existence of composite objects and their distinct properties or characteristics.

Therefore, in the event that, effectively, there is an ontological commitment, the universalist view would imply an ontological cost since we would have to accept the existence of an indefinite number of objects. In contrast, we can take it that the composition relation does not occur at all, and there would be no place for this ontological commitment. So, a nihilist view that claims that the composition would never happen and that there are only simple objects arranged y-wise would be ontologically more parsimonious because it implies fewer objects. At the same time, it eliminates the notion of parts and whole, whereby particular objects are parts of other objects. Thus, nihilism, to which I now turn, is also a more straightforward theory than universalism (Sider, 2013a). Regarding this nihilist account, I will talk in detail below.

1.3.2.2 Nihilist view: There are no composite objects.

The nihilist view argues that there is no such thing as a composite object made up of other objects. There are only simple objects. Therefore, the relationships between different entities should not be expressed in terms of parts and wholes. Composition never happens: two or more things never compose or add up to anything, so nothing has proper parts. This position is

contrary to common sense because if we think of a chair, we consider that this object has parts such as legs, a seat, and perhaps a backrest.

According to nihilists, there are fewer objects in the world than our common intuitions tell us. It is never the case that two objects or more compose a further object. Some advantages of nihilism, in comparison other two possible answers, are ontological parsimony and ideological simplicity (see Unger, 1980; Brenner, 2015a).

Philosophers such as Peter Unger (1979) reject the existence of composites. To argue for this position, Unger uses 'The Sorites Argument'. He claims that if there is a stone, it must be composed of a large number of atoms. There are many, but finite, atoms within the specific space region occupied by the stone. The net elimination of an atom from the stone would leave that number less of an atom even with the stone occupying the same spatial region. We follow by extracting two more atoms, and there still is a stone in that region. If we continue extracting atoms, we can have a stone consisting of zero atoms, which is absurd (Korman, 2020).

According to the above, where there are no such things as objects composed of other objects, then there are only simple objects. Composition never happens: two or more things never compose or add up to anything, and thus nothing has proper parts, neither chairs, stones, tables, plants, nor us, which goes against our pre-philosophical intuitions. To this objection, the nihilistic view states that chairs, tables, or plants are simples (no objects have parts) arranged to look like a composite object. Therefore, a chair is simples arranged chair-wise.

For van Inwagen (1990), a chair is "simples arranged chair-wise". There is no such thing as objects composed of other things. There are simple objects only. Therefore, the relationships between different non-living entities should not be in terms of parts and wholes. Real composition only occurs in the case of living beings. They have proper parts. Those parts must constitute a life. In his words:

> "the x_s compose y if and only if y is an organism and the activity of the x_s constitutes the life of y" (Van Inwagen, 1990. p.82).

In this way, to understand his answer, Van Inwagen (1990) highlights that it is necessary to understand the circumstances under which some entities constitute a life. However, van Inwagen's reference to the concept of 'life' is not precise. Analysing this sentence raises the question of what the individual life of a concrete organism is. Van Inwagen claims that is not

his job to define what life is. That is a task for biologists. This argument seems reasonable, yet it can result in a problematic scenario. If life's definition is an enterprise for biologists, this means that its definition is based on biologists' work. Then, the definition will be subject to review in the light of any new empirical evidence. Unfortunately, both philosophers and biologists have widely discussed the definition of life without achieving a satisfactory answer. The difficulty is due to disagreements about how abstract or specific definitions should be, differing compromises about what should be included in a definition, and even debates about the definitions' nature (Mariscal and Doolittle, 2020). Therefore, regardless of whether or not it is a task for this scholar or for biologists, this lack of definition keeps alive the doubt about what composite objects actually are.

This lack of precision gives rise to certain possible situations. For instance, if some non-living things show a functionality similar to that of living things, this principle of compositionality lacks a defined criterion. Whether we compare a living entity and a crystal, specific body shapes and structures are equally characteristic of living beings and crystals. Characteristics of the substance of the crystal depend on the atoms, molecules, or ions that make it up. The shape of the crystal is a direct consequence of its molecular structure, and its determination is dependent upon the forces exerted between the electrons and nuclei of the atoms involved (Harris, 2014).

Similarly, a living object depends upon the pattern of structure and principle of organisation regulating how the parts are combined. Both present growth processes (Harris, 2014). The crystals also grow in defined ways. The crystal's shape conforms to a precise and definite pattern. So, what is the difference between a non-living and a living object?

Van Inwagen's explanation of living individuality lacks a comprehensive description. As Wilson (1999) points out, van Inwagen's argument regarding the SCQ does not offer a robust set of criteria to differentiate living individuals from parts of longer-living individuals or groups of living individuals. Van Inwagen offers analogies to explain what makes something live but does not consider problematic cases, such as colonial siphonophores such as the Portuguese man-of-war. He does not explain how to define what constitutes the individual life or organism. Therefore, two central issues in van Inwagen's answer would not be clear. 1) Why would there not be non-living composite objects? 2) What is the composition relationship in living objects? Peter van Inwagen does not clearly argue why we should accept that only living

entities are composite objects and explain the nature of the relation between parts and whole in living entities.

Additionally, this nihilist view about material objects to describe some entities like chairs or tables often to appeal to a paraphrasing in compositional structure, namely chair is not an object, but they are "simples arranged chair-wise". Philosophers like Karen Bennett (2009) argues that the nihilist's proposed paraphrase scheme is not as straightforward as it is often portrayed. Bennett (2009) asserts that the paraphrase must be capable of explaining the mechanisms of molecular bonding and differentiating between unicellular and multicellular organisms. Additionally, she underscores that the nihilist must address a series of inquiries. For instance, how does the world need to be structured to accommodate simple entities organised in a table-wise manner despite the absence of actual tables? Similarly, how should the world be structured to encompass simple entities organised in complex-object-wise configurations despite there being no complex objects? Perhaps nihilist defenders claim that this is only a way to talk, but it is kept the doubt about why we refer to the material world in terms of objects that actually do not exist.

Jonathan Tallant (2014) analyses this issue by identifying a single question, structurally analogous to the SCQ. The question to answer would be slightly different from the SQC, namely, what are the circumstances under which some simples are arranged y-wise? He states that nihilists must give an answer to the "Special Arrangement Question" (SAQ). According to Tallant (2014), there is a question that nihilists must address, which is similar to the Special Composition Question (SCQ), but they are unable to provide a satisfactory answer. In response to this critique of nihilism, philosophers like Brenner (2015b) argue that it is unclear whether the nihilist is actually obligated to answer the SAQ. Additionally, regardless of whether or not the nihilist can or should answer the SAQ, non-nihilist perspectives would face the same challenge. Thus, even if the nihilist cannot respond to the SAQ, other viewpoints would be equally unable to do so.

In this scenario, is in question whether it is relevant to understand the different arrangements, how these are or what their main characteristics may be. Perhaps, for nihilists, these questions are not relevant because only simples are in existence. An arrangement can be given or not, but that is not important for a nihilist. If composite objects do not exist, it is not necessary to explain what the arrangements are that count as table-wise or chair-wise. They claim that material objects are simples. We can perceive something as a composite object

merely from a particular arrangement among simple, but that does not mean that composite objects exist.

Nevertheless, some questions arise from this position: why the idea of a sorting or an arrangement is different from a composition relation, or why some arrangements happened and not others? These doubts arise because there is no clear idea of what a composition relation should be. To say if something exists or not, first, we should have a defined idea about it. In other words, if nihilists argue that composition never occurs, what is the nature of that relation that does not exist? What are the characteristics of this relation? In this manner, it is clear for each position what it is debating. Perhaps understanding the arrangement among simples is key to catching why we consider some collections of entities to be a composite object, either if we consider composite objects or simples arranged y-wise, the main point is the arrangement among simples, to understand the entities of our daily experience. The arrangement may vary. They can be chair-wise, laptop-wise, or cell-wise. From these different arrangements, there arise distinct forms, structures, or properties. By analysing these arrangements, we can identify patterns and relationships, enabling us to classify and generate categories thereof them based on their specific arrangements.

For nihilists, the examination of the relation between parts and wholes can seem futile and useless because there is no such relation. However, whether or not we accept or not the possibility of this relation, still it is clear that we think in terms of objects composed of parts. Even if we do not accept their existence, the reference to those objects is compositional (an arrangement chair-wise). Then, this keeps alive the question of what it means when we talk about that. If the main objective is explaining the nature of reality, the idea of there being simples which can be established in arrangements in a such way that we can think in chairs, tables, cars, or houses does not say a great deal about why those arrangements are given and what the nature of these arrangements is.

If we accept the nihilist account that we just compositionally paraphrase and that this does not mean the existence of composite objects, it is a manner of speaking only and does not deserve any more attention. Some questions can arise; if how we describe the material world as relates to reality is only a way of talking, why do we use this compositional way to talk about reality? One possible explanation is that our use of compositional language reflects a deep-seated intuition or perception of the world, which would not imply that composite objects actually exist.

However, Bennet's (2009) argument, earlier, makes sense because when advocates of the nihilistic position appeal to this narrative, they do not adequately explain how different objects are. They provide a vague answer as to why we intuitively consider some objects to be composite. If the aim is to define how the material world is, the nihilist position would not be particularly informative on this point. Nevertheless, a nihilist defender can argue that the existence and nature of simples are enough to enable an understanding of the nature of material objects. They focus on the fact that material objects are simple, and we can perceive something akin to a composite object purely for a particular arrangement among simples, but that does not mean that composite objects exist. So, to understand the material world, we should focus on the nature of simple things.

While nihilists may not feel compelled to address questions of arrangement, there remains a crucial aspect within their viewpoint that demands further clarification: *the nature of simples*. If nihilists assert that only simples exist, they need to offer a clear understanding of what these simple objects entail. In doing so, they can provide an informative and compelling response to inquiries about material objects.

By thoroughly examining the characteristics and properties of simples, nihilists can shed light on the fundamental constituents of the material world. This entails identifying what simples are and elucidating how they interact, combine, or influence one another to give rise to the complexities we observe. A comprehensive understanding of simples becomes crucial for a coherent account of material objects in a nihilistic framework.

1.3.3 What are simples?

It is an interesting question to ask what an object has to be like in order to be a simple object. The evaluation of what is simple is not trivial, because, as Markosian (1998) claims, they are the basic building blocks that, when combined in various ways, can make up all other objects, so the nature of simples should have considerable bearing on the response to the SCQ. Having a defined idea of what simples are can help in understanding how two or more objects either compose a further one or are merely in a certain arrangement.

The inquiry regarding simples, aimed at achieving clarity, revolves around identifying the essential and mutually inclusive requirements for an object to be considered simple. One approach to defining simples is by stating that they lack proper divisions, as they are too minuscule to possess such divisions. Essentially, they lack spatial extension and exist as objects

of point-like size (Markosian, 1998; Carroll and Markosian, 2010). Although this notion appears plausible, if two points were capable of constituting a third object, that object would also be of point-size (Carroll and Markosian, 2010). Consequently, we could have point-size objects with parts.

Another alternative is the physical indivisibility view. This view claims that simples are objects that it is physically impossible to divide. One objection to this view is that for some object it may be the case that it is indivisible but has proper parts. Therefore, being indivisible does not imply that is mereologically simple (Carroll and Markosian, 2010). One alternative to this view is to consider simples as being metaphysically indivisible. In this case, although an object is physically indivisible it can be metaphysically divisible. This means that something is simple if and only if it is metaphysically impossible to divide it without first changing its intrinsic properties (Markosian, 1998). According to these conditions, a point could be a simple object, which would be metaphysically impossible to divide without first changing its size and shape (Markosian, 1998). Hence, this view would not be different to claiming the point-sized account, having the same disadvantages.

In turn, it is possible to propose that a simple is the fundamental particle of matter. If we accept this option, the definition of simples would depend on what physicists determine to be the minimum of matter. Therefore, there may end up not being any fundamental particles in the ultimate physics, so if the grounds to define simples is physics knowledge, this scenario would bring new challenges because it should analyse the concepts of quarks, space-time points, leptons, or the Higgs boson. For example, it is thought that leptons are considered indivisible particles with properties such as mass, charge, and spin. Nonetheless, some physicists have hypothesised that quarks and leptons have sub-components called preons, which are point particles (see Pati and Salam, 1974).

One problem with this view is that putative simples may turn out not to be any fundamental particles in the ultimate physics. Then, they would not be simples. Furthermore, it raises the question of who is to define whether simples are entities effectively having no proper parts, is it the physicists or the metaphysicians? (Carroll and Markosian, 2010). This is problematic in two respects. 1) If metaphysicians posit as simple entities that the physicist does not countenance, who is right? 2) If the physicist's theory defines what simples are, then it would not be necessary to appeal to a metaphysical position on the matter. Hence, we should expect physicists to establish the fundamental particular of matter, and then we shall know

what a simple object is. Accepting this could put us in the position where the metaphysical task of explaining how objects are is a useless examination and physics investigation will provide us with the answers to this issue. What, then, would be the place of metaphysics in this situation?

Other philosophers argue that simples are extended when an object is spatially continuous, and when the region it occupies is not part of some larger, spatially continuous entity (see Markosian, 1998; McDaniel, 2007). If each material object is identical to the spacetime region at which it is exactly located (see super-substantivalism view), then the region R wherein lies the extended simple S has a sub-region SR, where S would have a proper part located in this sub-region. Therefore, an extended simple would not be mereologically simple (Gilmore, 2018). Defenders of extended simples do resist the idea that the object is identical to the region where it is. For them, the object and particular region where such an object is located are mereologically disjoint (Markosian 1998; McDaniel 2007).

It can be seen that there is no agreement among the metaphysicians about what the simple object would be. If we consider this discussion together with the debate on composite objects, we have a situation where there is no clear idea about what the nature of material objects would be according to these approaches. My intention is not to answer what *is* a simple object, but rather to highlight this issue: in the analysis of the composition of material objects there are fundamental ideas that have not been clarified, such as what an object *is*. If the discussion on material composition has as its aim to gain a more complete understanding of reality, these responses are not informative enough to clarify how the material objects are.

If we refocus on the discussion of composite objects, the nihilist position thereon, where objects are simples only, does not provide an explanatory answer about the nature of material objects, because we do not yet know what simples are. Even so, a nihilist can argue that regardless of how simple they are, they alone exist. So, we cannot say anything about reality besides the existence of simples; we do not know what they are, but we do know that they exist. This answer is not satisfactory at all if the aim is to explain reality. Then, we must still allow room for doubt about what that existing entity is.

To claim that there are no composite objects, but rather simples arranged x-wise only, does not explain anything about what simple objects are, what lies in a particular arrangement, how this arrangement is to achieve that specificity to consider groups of simples such as a chair, a car, or a tree.

So far, we have seen that the position of universalism, where composition always occurs, runs counter to our intuitions and that we are at risk of accepting the existence of an indefinite number of objects. In turn, nihilism, where composition never occurs, is not explanatory enough to enable us to understand either the nature of simple objects or the arrangement that may exist between them, because this arrangement is different from a compositional relationship.

Of course, any metaphysical account inevitably claims to be necessary and valid universally, but, when we talk about material objects, is this goal possible? In the world, there is a great variety of objects, with different characteristics intuitively. We differentiate the simple objects from the composite, a piece of wood from a table. In turn, within these composite entities, we make distinctions between a table, an electronic device, or a living organism. When considering these aspects, it raises the question of why in this variety of objects common conditions of composition could be established. Besides, if there is no agreement on criteria to define when two or more material objects compose a further object, that does not imply that there are no composite objects. Perhaps, it could indicate that the approach to the composition problem is not appropriate. In the next section, I shall explore the possibility of different composition relationships.

1.3.3.3 Restrictive view: The Serial Response.

An alternative response to the SQC is the Serial Response. It proposes that the proper response to SQC is a string instance (see Silva, 2013; Carmichael, 2015). Accordingly, it could be that there is no general relation that any x must satisfy for it to be the case that there is an object composed of those x_s. Maybe the reality is that various "building elements" exist worldwide. For each type, there exists a unique relationship such that whenever some x of that type aligns in that specific relationship, then there is an object composed of those x_s.

On the one hand, an advantage of the Serial Response is its concurrence with the intuition that different factors must be involved in different cases of composition. Views such as universalism or nihilism fail to take account of the notion that whether some x_s compose something can depend a lot on what exactly the x_s are like. It is reasonable to assume that the way subatomic particles come together to compose an atom differs significantly from how molecules combine to create a rock or how cells contribute to the structure of a living body

(Carroll and Markosian, 2010). Conditions under which some simples make up a car do not appear to have anything significant in common with the circumstances under which some simples compose an animal or the planet Earth. Why should we consider that the conditions to compose a chair would be the same as those to compose a plant? Perhaps, the goal to provide an answer valid for all material objects regardless of their differences and specific characteristics is not the proper approach.

On the other hand, one of the main problems with moderate answers to the SCQ is that they must identify several relations that are linked to the concept of composition (Markosian, 2008). Besides, this view runs the risk of the possibility of genuine vagueness in the world. Accepting composition in some cases but not others lead to vague existence or arbitrariness.

In contrast, the universalist and nihilist positions have an advantage over the restrictive view: none of these answers has to indicate where the cut-off points will be between composition and non-composition cases, because neither of the answers considers that such points exist (Cornell, 2018). Universalism posits that there are no instances of non-composition, while nihilism argues that there are no instances of composition. Consequently, neither theory relies on the existence of cut-off points. In the forthcoming section, we shall inquire about vague boundaries and explore the intricate nature of limits.

1.4 Vagueness problem.

We start with the idea that vagueness arose from the impossibility of establishing cut-off limits and that to avoid vagueness objects should have clear limits. Philosophers have addressed how vagueness affects our understanding of the boundaries, of material objects and their identity (e.g., Merricks, 2001; Sider, 2003; Tahko, 2009; McDaniel, 2017;). One of the issues of this vague boundaries problem is to define what the nature of this vagueness is. This refers to whether all this talk about boundaries effectively reflects the structure of the world or simply the organising activity of our minds and is a matter of deep philosophical controversy. Is it a real ontological vagueness, or is it a mere question related to our language and our conceptual system? So, the vagueness issue has been assessed through different approaches such as the ontological, epistemic, or semantic.

Ontological vagueness refers to objects that have vague boundaries. These objects do not have a precise spatial/temporal beginning. Consequently, the concept of vagueness in composition pertains to whether there is a metaphysical boundary that defines the occurrence or non-occurrence of composition (Hyde and Raffman, 2018). One aspect to analyse is whether or not vague limits imply that the object does not exist. Philosophers such as Carmichael (2011) argue that vague composition does not mean that the existence of a composite object is vague. The vagueness in defining a clear cut-off does not imply that all putative entities that compose an object are in this vague margin. When considering rocks, which are candidates to compose Kilimanjaro, there are rocks in different zones of this volcano. Some rocks are on the summit, others in the penumbral region. The rock on the summit is definitely a part of Kilimanjaro, while the rock in the penumbral region is not definitely a part of it (Carmichael, 2011). Thus, while there may be uncertainty regarding the status of specific rocks, the overall existence of Kilimanjaro as a composite entity remains intact. The summit rock, which is undeniably part of the mountain, contributes to the existence of Kilimanjaro, even if the boundaries of its composition are not precisely delineated. Therefore, the possible vague boundary of a composite object is not a sufficient argument to conclude that there is no such composite object.

Other scholars argue that the world is not vague, so every plurality of objects always composes something or never does. There are other approaches to understand the vagueness, namely epistemic and semantic view. The epistemic view claims that the world is not vague, but that we are ignorant of the sharp edges that delimit objects. Hence, there are defined borders, but we cannot discover where those divisions lie (Williamson and Simons, 1992; Rescher, 2009). This view seems plausible, but if the issue of a vague border is sometimes related to a lack of knowledge, how can we know that we have enough knowledge to define the exact limit of the object? One answer is accepting that we never discover where the boundary is (see Fara, 2008). This viewpoint prompts a shift in focus from seeking definitive boundaries to acknowledging the inherent fuzziness and embracing the notion that our understanding is always subject to imprecision and limitations.

In its turn, the semantic approach posits that vagueness is a result of our words or concepts used to refer to objects. Unlike the epistemic conception of vagueness, borderline cases refer to instances where a predicate cannot be definitively classified as applicable or non-applicable. In this context, the term ‘definitely’ receives a semantic analysis as opposed to an

epistemic one (Hyde and Raffman, 2018). So, it is not possible to define boundaries exactly because words and concepts lack a sufficiently precise meaning. In this case, vagueness is a type of indeterminacy due to the use and constant changes in the particular use of a word by the speakers, which prevents the setting of sharp points of application and non-application of the word.

Other view is the *contextualist* approach. This approach. argues that determining an object's boundaries depends on the context and criteria used. Contextualists highlight the role of contextual factors, such as perspective, purposes, or composition criteria, in resolving vagueness and defining composite objects. One example of this is the Sider's account. In his book "Writing the Book of the World" (2013b), he argues that composition facts depend on the concepts and language we use to describe objects. Different contexts can give rise to different compositions, leading to context-dependent boundaries.

Similarly, Koslicki, in her book "The Structure of Objects" (2008), acknowledges the context-dependence of boundaries but suggests that this context-dependence is primarily grounded in the constitutive relations between parts. The precise boundaries of a composite object can vary depending on how its parts are organised and how they interact within a specific context. Different contexts may highlight different aspects of the object's constitution, leading to variations in boundaries.

If consider biological entities, boundaries are not fixed or absolute, but rather dynamic and context-dependent, similar to the perspective presented by Koslicki. The demarcation between one biological entity and another is frequently unclear, both spatially and temporally (Haber and Odenbaugh, 2009). We consider biological objects like organisms or species as often interacting and coexisting within complex ecosystems. These interactions blur the spatial boundaries between different entities. Organisms share habitats, resources, and genetic material through horizontal gene transfer processes. The interconnectivity and overlapping interactions challenge the idea of discrete and well-defined spatial boundaries between biological entities. Instead, boundaries become fuzzy as organisms engage in symbiotic relationships, competition, or niche sharing, constantly influencing and shaping one another.

Biological objects are intimately connected to their environments, and these interactions further contribute to the fuzziness of boundaries. Organisms adapt and respond to environmental cues, leading to phenotypic plasticity and trait variations. Moreover, environmental factors influence the distribution and behaviour of organisms, resulting in dynamic shifts in their boundaries (Begon and Townsend, 2021). The interconnectedness between organisms and their environment blurs the edges, as they are contingent on ecological factors and can change over time. Thus, examining the vagueness problem is crucial in understanding the complexities of living systems. The analysis of vagueness in the philosophy and theory of biology opens up avenues for exploring concepts such as species boundaries, individuality, and evolutionary transitions.

Indeed, the topic of vague limits has relevance in the philosophical examination of the biological world. The biological world is complicated and messy; this fact has led scholars to discuss issues such as where we draw the line between one species and another. Is there a precise moment when a new species emerges, or are there transitional forms that challenge our traditional taxonomic classifications?

The concept that the edges and boundaries of biological objects are often fuzzy and ill-defined has been a subject of interest for scholars in the fields of philosophy and biology. This is the case for Dupré. He, in his book “Processes of Life: Essays in the Philosophy of Biology” (2012), argues that biological entities, such as organisms or species, do not possess clear-cut boundaries but exist along a continuum. According to Dupré, this continuum perspective reflects biological phenomena's inherent variability and interconnectedness. Living systems exhibit complex interactions and dependencies and attempting to impose sharp limits on them can oversimplify their nature and hinder our understanding of their dynamics.

Similarly, Stuart Newman, a biologist and complexity theorist, has explored the issue of boundary fuzziness in the context of development and morphogenesis. In his research, Newman (2020) highlights that developmental processes involve gradual changes and transitions, making defining precise boundaries between different stages challenging. He emphasizes the importance of understanding the complex interactions and gradients that contribute to forming biological structures.

Andreas Weber, a biologist and philosopher, explores the interconnectedness of living systems in his book “Biology of Wonder: Aliveness, Feeling, and the Metamorphosis of Science” (2016). He proposes an “enlivenment” approach that emphasises life’s vibrant and participatory nature. According to Weber, living organisms are not passive objects but active participants in their environment. They actively shape and are shaped by their surroundings through their behaviour, metabolism, and ecological interactions. Weber challenges the notion of rigid boundaries in biology and instead proposes that boundaries between organisms and their environment are *porous*. Organisms are in constant communication and exchange with their surroundings, whether through chemical signalling, symbiotic relationships, or ecological interactions, engaging in these interactions through these *porous boundaries.*

These perspectives recognise biological objects’ complexity, interdependence, and continuous nature. They encourage an approach that considers dynamic interactions, spatial and temporal gradients, environmental influences, and contextual variability, leading to a deeper appreciation of life's interconnectedness and fluidity.

Boundaries in the biological realm can be understood at various levels, from the boundaries defining individual cells and organelles to those delineating tissues, organs, and the entire organism. These boundaries are intrinsically linked to the relations between the parts that make up these biological entities and their organization and interactions within specific contexts.

Considering these complex aspects of the biological world makes it more evident that it is necessary to have a clear idea about the nature of limits in any relevant discussion; in this way, we can establish the nature of this vagueness and the reasons for viewing a particular limit as vague. An ecosystem’s limits differ from those of a cell or a human body. The entities of the biological realm have boundaries with particular characteristics, which allow the flow of energy, information, and matter between organisms and their environment, emphasizing the interconnectedness and interdependence of living systems. Presumably, evaluating these boundaries in this realm cannot be the same as that applicable to entities like Kilimanjaro. Of course, the analysis can be made in a general way, assessing volcanoes and entities similar to a cell. Nevertheless, such an examination would not capture biological objects’ dynamic and interactive character.

These aspects of context-dependence perspective presented by Koslicki and their exemplification in the biological realm show that limit's existence is not independent. It has an ontological dependence on the object it is circumscribing. Hence, how a limit is will depend on what objects it is bordering. This ontological dependence on limits brings consequences such as vagueness, which may be due to the fact that one does not have a clear idea of what an object is. So, questions may arise as to whether a definition of these conditions is possible without a clear idea of what kind of object this is, its characteristics, and its behaviour. It seems to be that the consideration of the adequacy of a limit would depend on the specific characteristics of the object we are talking about. Then, if the existence of limits depends on the object's existence, is it possible to define those limits in a general and abstract way? Can they be valid for any object? If we think about the ontological status of a border, what does define it? Its existence is absolutely linked with the existence of the object.

Then, how can we make a difference in types of vagueness? How can we know if effectively this vagueness is a verbal, epistemic, or ontological issue? Answering this question seems challenging, especially if we want to examine material objects in general without making distinctions between them. Those who talk about the problem of vagueness refer to examples such as the mountain Kilimanjaro or a heap of sand. Why will that analysis be valid when considering a chair, a car, or a cell? The limit of Kilimanjaro is far from being in any way similar to a cell's limits (plasmatic membrane). The cell membrane has a specific structure and displays regeneration mechanisms through synthesising and recycling lipids and proteins, replacing damaged components. Therefore, the pretension to universality and generality can be problematic. How can we know that this possibility of vague limits is the same for every possible object existing in the world? So, the nature of vagueness may vary depending on the object under consideration, further complicating the task of identifying its underlying causes and implications. Agreeing with the contextualist view, determining whether an object is composite, or its boundaries are vague may depend on specific contextual considerations.

This issue is only relevant for the ontological view, because neither epistemic vagueness nor semantics questions the existence of composite objects; only the ontological account questions the existence of this type of object. Epistemic and semantic views discuss the difficulties of the subject of knowing or referring with a proper term to borders of material objects. Hence, in the case that we accept that ontological vagueness is possible, is this

possibility a sufficient condition to rule out the existence of all composite objects.? It seems that this is not entirely clear because the fact that an object has vague borders does not necessarily imply that the object does not exist. Even if we were to accept the possibility that vagueness can effectively exist in the material world (see Dummett, 1975; Horgan, 1994; Hudson, 2005; Lewis, 1986), that would not imply that the ontological vagueness applies to any particular object of the material world; the presence of vagueness in some instances does not mean that it extends universally to all things or that every composite object lacks clear boundaries. Recognising the existence of borderline cases of ontological vagueness does not undermine the existence of all composite objects.

Undoubtedly the problem of vagueness is central to the discussion of composite objects, mainly in defining what position is taken, namely a universalist, nihilist, or restrictive stance. However, there are other possibilities to address the SCQ. These are deflationary, arguing that this discussion is only a verbal dispute or a problem of the question's formulation.

1.5 Is SCQ a verbal dispute?

No doubt this debate can be analysed along many dimensions. One of these is by examining the formulation of the special composition question and its metaphysical relevance. Indeed, one way to respond would be to dismiss it altogether. This kind of response has been expressed by some philosophers, who have dismissed the SCQ for several reasons (Cornell, 2018). One of them argues that the composition issue is nothing more than a verbal dispute.

According to Hirsch (2005), the discussion regarding material composition is not truly about ontology but instead a mere disagreement in language. In other words, each viewpoint employs identical terms with different meanings, leading to confusion on the subject. Consequently, Hirsch suggests that both sides of the debate concur on all the facts, in some sense of 'fact', and simply disagree about the interpretation of truth conditions of certain *statements* like "there is a composite object."

Hirsch argues that when universalists state 'chairs exist', and nihilists counter 'chairs do not exist', both are expressing truths but with different interpretations of the term "exist." Additionally, he asserts that there are numerous ways to describe reality. Hence, there is no correct way to refer to reality.

However, it is possible that this composition discussion may be a verbal dispute because of a lack of a sufficiently precise meaning of our words or concepts used to refer to objects. However, it is crucial to define what a 'verbal dispute' is. Without an explicit criterion, we cannot explain if those who believe that 'there is a chair' is true and those who refute this, affirming that 'there are simples arranged as chair-wise' disagree on the meaning of these sentences or the ontological status of the object in question. Perhaps the sides in disagreement can disagree on both the meaning of terms and the facts; how then do we define the nature of disagreement? While I am open to the idea that this discussion about composition can be a verbal dispute arising from the lack of a sufficiently precise meaning of our words or concepts used to refer to objects, it is necessary to clarify the criteria to establish that a philosophical discussion is only a verbal dispute is.

Another possibility is that the possibility of vagueness is also generated by how this question is framed. If the question is about objects in general without a clear idea of what we are talking about, we can make a list of things we commonly consider objects, namely chairs, tables, cars, or laptops, so this is too general. Why will the analysis of compositional vagueness be valid for all these different objects? How do we distinguish for any object exiting whether the vagueness is ontological, epistemological, or verbal? It seems that it is easier to define this issue if we consider a specific type of object. In the next section, I shall question differently how the SCQ is formulated. Amie Thomasson (2007) and Sanford (1993) claim that the SCQ is *an unanswerable question.* I will discuss these accounts below.

1.6 Is the SCQ an unanswerable question?

The philosophers Sanford (1993) and Thomasson (2007) have argued that is difficult to answer because of the way in which the SCQ is formulated. Particularly, Sanford (1993) proposes that we would be better off replacing it with a multitude of structurally similar questions such as 'When is there some wall such that the bricks compose the wall'? The question asks how a brick, rather than x_s in general, can compose a table; and it asks how a brick can compose a wall rather than compose something or another y. According to this philosopher, asking questions in this way makes the issue of the material object's composition much more approachable.

So also, Thomasson (2007) argues that the SCQ is an unanswerable question, and the failure to find a uniform answer would not reflect on the issue of whether or not those objects exist, only reflecting the fact that the question cannot be answered.

Considering this argument, it is worthwhile to ask in what sense this question cannot be answered. Thomasson clarifies that these questions are unanswerable not in the sense that we are unable to find out the answer, but rather, because a closer examination is necessary. The formulation of the SCQ is too general, with the result that its possible responses do not give any information about how composition is. For this reason, we should not provide an answer put in the same terms as the question but instead replace the question by a more specific or better statement of it (Thomasson, 2009). She (2009) argues that if 'thing' and 'object' are understood in a general fashion, we cannot evaluate the truth-value of existence claims using general terms such as 'there is an object'.

It is not unreasonable to think that this impossibility of answering the SCQ satisfactorily is due to the question being formulated in general terms, seeking an answer for all existing objects. One can question why these problematic aspects would be valid for any object. If the key problematic aspect are limits and their existence depending on the object, we could address this issue with a clear idea about what object we are speaking about. Perhaps depending on what type of objects we are considering, this vagueness can be epistemic, linguistic, or ontological. Claiming that the SCQ is unanswerable reflects the inherent complexities and challenges involved in addressing the issue.

Sanford and Thomasson's proposal to replace general terms with more specific ones in the question of composition is indeed a valuable perspective from a philosophical standpoint. By focusing on particular types of objects, such as non-biological and biological entities, we can create a framework that allows for a more refined understanding of how a plurality of entities can compose an object. This approach facilitates the establishment of conditions that govern the composition of objects. This allows us to identify commonalities and patterns within these categories, leading to a more comprehensive understanding of the conditions by which the composition relation is given. By establishing these conditions, we can create a more precise framework for discussing and analysing composition.

By considering types of entities separately, we acknowledge the fundamental differences between these objects. Non-biological entities, such as physical artefacts,

presumably exhibit a different set of compositional conditions from those of biological ones, such as organisms. This differentiation enables us to tailor our understanding of composition to each type's specific characteristics and behaviours, avoiding the pitfall of applying a one-size-fits-all approach and taking into account the particularities of each type of object.

Now, does this reformulation ensure more satisfactory answers about composition relations? This is a valid question that warrants careful consideration. However, arriving at a definitive answer is not a straightforward task. One notable limitation of the proposed reformulation is its failure to meet the goal of universality, which is undeniably an essential aspect of any metaphysical analysis. General answers to this question do not say a great deal about how composite objects are or should be. At the same time, another objective of metaphysics is understanding material reality.

It would be necessary to establish which criteria the response should meet to be *satisfactory*. Composition is a complex philosophical topic with numerous interpretations and theories. Defining what constitutes *a satisfactory answer* requires establishing specific standards or principles by which the responses can be evaluated. Without clear criteria, assessing the adequacy and comprehensiveness of the provided answers becomes challenging. So, it is essential to determine the priorities and objectives of the metaphysical investigation. If the goal is to achieve a universal answer, this proposal put forward by these philosophers may be deemed inadequate. However, if the focus is on gaining a clearer understanding of the nature of the material world, this approach holds the potential to provide more informative insights. While the proposal of these philosophers may not address concerns of universality, it holds significant potential for shedding light on the nature of the material world and unravelling its intricacies.

Adopting a more specific framework makes identifying and analysing the relationships between entities within particular categories easier. This approach potentially allows for more informative answers that delve deeper into how composition relationships can be configured within those specific contexts. The reformulation might enable a more detailed exploration of the conditions under which entities combine to make up an object, what aspect are essential to understand how can be integrated. By focusing on specific types of objects, researchers can investigate the relevant characteristics, properties, and interactions that contribute to the occurrence of the composition relation within those categories.

Different metaphysical analyses attempt to arrive at answers that explain the nature of reality, how it is structured. With this in mind, each vision regarding composite objects should have to explain the reality with the existence or non-existence of composite objects. In this sense, I agree with Sanford and Thomasson when they propose that the question on composition should replace general terms with more specific ones. This does not mean analysing every single material object, but rather examining types of objects as non-living and living entities, for instances. In this way, it is easier to set up conditions under which a plurality of entities composes an object.

So, the reformulation of SCQ encourages us to consider the limitations of general responses and explore the particularities of composition relations within specific categories. By doing this, we stand a better chance of uncovering valuable insights into the nature of composite objects. While universality remains an important consideration, the reformulation serves as a reminder that a more targeted analysis can contribute to a richer metaphysical understanding of reality.

From what has been examined above, the different possible answers to SQC and their respective challenges (see Table 1.1) highlight the difficulty of addressing questions on the nature of the composition relation or defining what we are speaking of when we say that there is a relation between the parts and the whole. If we want to be informed about how it is possible a plurality of entities makes up an object, it is fundamental to know what that object or event is. When we have a clear idea as to the structure, organisation, and behaviour of the entity in question, we can identify circumstances or conditions that allow different elements to be integrated as a whole. Additionally, if we first understand how this is possible integration, we can study in what cases effectively the whole is or not the sum of its parts and whether its identity is due to parts that compose it.

Answers to Special Composition Question (SCQ)		
View		Challenges
Universalist	The composition relation always occurs.	Ontological commitment. We need to accept an infinite number of objects
Nihilist	The composition relation never occurs.	It does not explain what simple objects are.
Restrictive	Composition relations sometimes occur. A possible answer to the SQC is an instance of series. There are different types of composition relations.	Vagueness problem
Verbal dispute	The discussion about material composition is not truly about the fundamental nature of existence but rather a mere verbal dispute. Each viewpoint employs identical terminology with different interpretations, generating confusion on the matter.	It is not clear what are the criteria to define a verbal dispute
Unanswerable	The SCQ is an unanswerable question. The failure to find a uniform answer would not reflect on the issue of whether or not those objects exist, but only reflect the fact that the question cannot be answered.	It does not meet the universal criterion.

Table 1.1 Summary of possible answers to the SCQ

In this sense, the composition issue can be assessed according to types of entities, so that it is easier to set up conditions under which a plurality of entities composes an object. This concept aligns with the aforementioned approach of providing answers in a series-style format. In this approach, the conditions that are both necessary and sufficient by virtue of which some things compose another. This involves considering the categories to which these things belong and the specific relationships they must have to make up something. (see Silva 2013; Carmichael 2015). On this basis, I would like to examine how biological elements are

integrated in terms of parts and whole, and what are the conditions under which this relationship can be configured in the biological world.

Along with the above, I emphasise also that to evaluate diverse questions on how parts compose a whole, first, we should have a more comprehensive view of the diversity of objects that we commonly consider to be composite. The philosophical analysis of the composition relation should consider both non-complex and static objects such as chairs or heaps of sand and highly dynamic and complex objects, where the interrelation among the parts changes continuously. The sciences study these kinds of objects in detail; scientific knowledge can provide a broader perspective on composite objects. In the biological sciences, we have notable examples of complex and dynamic composite objects, which can be excellent case studies for the philosophical analysis of composition, part, and whole notions. Biological entities are complex and manifest a dynamic networking of interrelations among parts, depending on the environmental conditions. This is an exciting scenario to assess how this type of relationship can be configured. For this reason, one of the primary purposes here is to clarify how the parts of such biological entities, assuming that they have parts, are related to the wholes they compose, taking into account information both of theoretical biology and of biological practices.

Nonetheless, addressing this metaphysical issue from biological sciences can generate questions related to why such a metaphysical question as the nature of the relation between parts and whole should be informed by biological theory or practice, why we should consider this science's empirical work in examining this topic if it does not accomplish the universal pretension of metaphysical analysis. Science, as everyone knows, is fallible. So, why analyse this metaphysic topic in scientific contexts, specifically in the biological one? These questions will be answered in the next section.

1.7 Why analyse this metaphysical topic in the biological context?

In general, it is claimed that metaphysics issues are examined through a priori reasoning and conceptual analysis rather than empirical investigation. Metaphysical truths are independent of and not necessarily constrained by scientific theories. This discipline can inform and critique scientific theories rather than being subordinate to them.

Indeed, the relations between parts and wholes and composite objects are classic philosophical topics. These issues have been mainly analysed from a metaphysical perspective. However, it is also important to highlight that the study of parts and wholes is not the sole prerogative of philosophers. From a scientific perspective, biologists, ecologists, and systems theorists have also contributed significantly to understanding how individual components and their interactions contribute to the functioning and organisation of living systems. In the biological realm, reference to parts and whole is ubiquitous, but the nature of the relationship between a whole and its parts, in this field, has largely been taken for granted. This widespread reference to the relation between parts and whole links to one of the oldest philosophical discussions on this relationship.

These antecedents provide good reasons to consider contemporary biological theory and practice when analysing the configuration of relations between parts and whole and. The information that science provides on specific entities studied, and the practice thereof, presents to us entities with attributes or behaviour that might, by rational analysis, not be possible to conceive in such a level of detail, generating new possible scenarios to examine the nature of entities. I am not trying to argue that the metaphysical analysis of abstract entities is pointless. Indeed, it is essential to identify possible argumentative limitations of different positions on this topic. Instead, I highlight that scientific information - both as regards theory and practice - enriches the view that we can have regarding composition relations.

Metaphysical inquiries, by their nature, often involve speculative hypotheses about the fundamental nature of reality. These inquiries aim to uncover our living world's underlying principles and structures. While metaphysics traditionally deals with abstract and general concepts, the field of biology provides a fertile ground for testing and evaluating these metaphysical topics.

Whether we want to explain the difference between a table and a plant or how it should be addressed, this is something to be discovered through experience, not via a priori reflection. However, a metaphysician can argue that the analysis should be a priori and universal, whereby through rational examination only, it is possible to answer questions related to the nature of different entities. This examination requires acknowledging the limitations of the universal assertions and could embrace a more nuanced perspective that accounts for the inherent diversity and complexity of the objects in question.

Empirical findings and biological discoveries can challenge and inform metaphysical inquiries, helping to shape and refine metaphysical theories. Philosophers such as Ladyman and Ross (2007) argue that science provides us with some of the best-confirmed claims about reality, and some of these claims seem to be directly relevant to metaphysics. Indeed, they have defended naturalised metaphysics. This philosophical approach seeks to integrate metaphysics with scientific methods and concepts. It argues that metaphysics should be continuous and informed by scientific inquiry rather than being detached or separate from it. The naturalised metaphysics emphasis is that metaphysical analysis should be scientifically informed. Proponents of this approach argue that metaphysics should not be pursued independently of science but should be grounded in our scientific understanding of the world (e.g., Quine, 1969; Ladyman and Ross, 2007). Following this argumentative line, philosophers take the stance that our understanding of parts and wholes is significantly improved, examining how these concepts work in the best scientific theories (see Ladyman and Ross, 2007; Calosi and Graziani, 2014).

This seems a coherent proposal, but a question that arises in this discussion is what aspects of sciences should inform metaphysical analysis, theory or practice because it is one thing to consider successful scientific theories, which have been proven reliable, and the practice itself of scientific endeavour is another. While scientific practice provides valuable insights into the workings of scientific inquiry, it may not necessarily offer a reliable basis for drawing metaphysical conclusions.

On the other hand, theoretical knowledge is often more rigorous, refined, and subject to peer review, making it a more reliable source for metaphysical analysis. Additionally, scientific practice is highly contextual and subject to change. The methods, tools, and approaches employed in scientific research can vary across disciplines, time periods, and individual scientists. Relying solely on the specifics of scientific practice may lead to metaphysical conclusions contingent on those particular contexts, limiting their

generalisability. The contextual nature of scientific practice raises concerns about the extent to which metaphysical analysis can be derived from it. The practical aspects of scientific inquiry may not always provide a solid basis for drawing metaphysical conclusions, as contingent factors influence them and may lack the rigour and refinement of theoretical knowledge.

Against these limitations, we can recognise the importance for metaphysics of considering both scientific theory and practice. For instance, Nancy Cartwright (1983) suggests that metaphysical analysis should consider the contingencies and specificities of scientific practice. Similarly, Angela Potochnik (2017) argues that metaphysical theories should consider science's aims, values, and practices. She emphasises the need to align metaphysics with scientific inquiry's current goals and practices. Michael Friedman (2001) points out that scientific theories and practices are interdependent, and states that metaphysical analysis should consider the intertwined relationship between theories and the practical context in which they are developed. So also, Andreas Hüttemann (2021) claims that certain features of scientific practice are relatively stable (e.g., the elaboration explanations, methodology, and modelling) over a long time period. These stable features, he argues, can serve as a dependable foundation for drawing metaphysical inferences. So, from these activities of scientific practice, we can find a reliable basis for examining the metaphysical assumptions that underlie contemporary scientific work.

In addition, scientific inquiry, with its methods, experimental approaches, and empirical observations, can offer unique insights into the nature of reality that may not be fully captured by theoretical reflection. The contingencies, challenges, and unexpected findings in scientific practice can challenge prevalent metaphysical assumptions and prompt new lines of inquiry.

In this consideration of both theoretical and practical dimensions of science, it benefits to balance theory and practice when integrating metaphysics with scientific methods. While scientific practice can offer valuable insights, theoretical knowledge often provides a more rigorous and reliable source for metaphysical analysis. So, rather than leaving aside scientific practice due to the limitations it presents, it can be critically analysed. It would show us scenarios that a priori reasoning we cannot consider. Engaging with successful scientific theories while critically considering the limitations and contingencies of scientific practice can contribute to a more robust approach to metaphysics scientific informed.

Scientists do, indeed, make ontological assumptions about the nature of the entities that they study. Assumptions, which are essential in how scientists study phenomena. However, it seems necessary to identify reliable practices from non-reliable ones. This entails critically evaluating the methodologies, experimental approaches, and theoretical frameworks scientists employ. This way, we could ensure more adequate conditions for examining metaphysical assumptions by identifying reliable practices.

In the field of the biological sciences, philosophers such as Kaiser and Waters have made significant contributions by examining the metaphysical implications derived from the analysis of biologists' practices. Kaiser, in particular, has made notable strides in defining the concept of a biological part (Kaiser, 2018a) and studying genomic part-whole relations (Kaiser, 2018b)[1]. Her work involves analysing the metaphysical assumptions underlying the strategies of reasoning that biologists employ when they deconstruct the human genome into its parts.

By examining into the metaphysical foundations of biological practices, Kaiser sheds light on the conceptual frameworks that shape our understanding of biological entities. This line of inquiry helps uncover the implicit metaphysical assumptions inherent in biological research, allowing for a more nuanced comprehension of the philosophical underpinnings behind scientific investigations.

Similarly, Waters (2014) argues that metaphysical assumptions shape scientific explanations, and that metaphysics can inform scientific practice by providing conceptual frameworks and guiding research. Waters' perspective emphasises the importance of philosophical reflection about scientific pursuits. Metaphysics offers rich insights into understanding scientific methods and approaches to investigate complex phenomena based on a deeper understanding of the underlying metaphysical assumptions. Kaiser and Watters's investigations into the metaphysical underpinnings of biological practices exemplify the significance of considering philosophical perspectives in scientific research. In fact, in biological practice, there arise philosophical puzzles that require metaphysical scrutiny. For instance, questions about the nature of biological causation or the boundaries of biological

[1] Kaiser's work on part-whole relations has been focused on establishing when a biological element is part of a biological whole. This can be linked with the investigation covered by this thesis, but this study is about the configuration of all components into the whole. It does not analyse when one biological element is part of a specific whole.

individuality often require intelligent analysis. We can shed light on these puzzles by engaging in metaphysical inquiry and deepening our understanding of the underlying principles.

These antecedents provide good reasons to consider contemporary biological theory and practice when analysing the configuration of relations between parts and whole and. The information that science provides on specific entities studied, and the practice thereof, presents to us entities with attributes or behaviour that might, by rational analysis, not be possible to conceive in such a level of detail, generating new possible scenarios to examine the nature of entities. I am not trying to argue that the metaphysical analysis of abstract entities is pointless. Indeed, it is essential to identify possible argumentative limitations of different positions on this topic. Instead, I highlight that scientific information - both as regards theory and practice - enriches the view that we can have regarding composition relations.

Metaphysical inquiries, by their nature, often involve speculative hypotheses about the fundamental nature of reality. These inquiries aim to uncover our living world's underlying principles and structures. While metaphysics traditionally deals with abstract and general concepts, the field of biology provides a fertile ground for testing and evaluating these metaphysical topics.

Specifically, in the metaphysical discussion about parts and wholes, biological world presents an exciting scenario to assess how this type of relationship can be configured. Biological entities are complex and manifest a dynamic networking of interrelations among parts, depending on the environmental conditions. For this reason, one of the primary purposes here is to clarify how the parts of such biological entities, assuming that they have parts, are related to the wholes they compose in changing context.

1.8 Conclusions

In this chapter, I have carried out a critical review of the metaphysical debate on concepts of composition, part, and whole. I have evaluated the main antecedents of questions related to composition and the nature of the relation between the whole and its parts.

From my analysis, I can draw some conclusions; first, the philosophical discussion about material objects in the last 30 years has been focused on the SCQ. There are three main

answers to this question that do not explain clearly how different objects are and how they are related. Second, the universalist view manifests the risk of accepting infinite objects. Third, the nihilist view does not provide an informative answer because it does not explain clearly how simple objects are and their interrelations to each other, so the answer to what an object is would still be without a response. Fourth, the vagueness problem should be addressed with a clear idea about what thing we are discussing. In this manner, it is more approachable to evaluate whether the vagueness is ontological, epistemic, or a verbal dispute or confusion. Fifth, the possibility of ontological vagueness is not sufficient to rule out the existence of composite objects. Sixth, the question on the composition relation should use specific terms instead of general ones to make the examination feasible. In order to achieve a comprehensive picture of material reality, we have to have a clear idea of what entities exist and when and how they are related to each other. Finally, the philosophical analysis of composition, parts, and wholes should consider both non-complex and static objects, such as chairs or heaps of sand, and highly dynamic and complex objects, where the interrelation among parts changes constantly, as with biological entities.

Chapter 2

Parts and wholes in the biological world

2.1 Introduction

The opening chapter has introduced the classic philosophical discussion about the relation between parts, wholes, and composite objects' existence. While these profound questions have traditionally been examined through a metaphysical lens, it is crucial to recognise that the concept of composite objects extends beyond the realm of abstract analysis metaphysics. It finds a place in various scientific disciplines.

The reference to parts and wholes is pervasive within the biological realm, shaping our understanding of living organisms and their intricate structure and organisation. However, the nature of the relationship between a whole and its constituent parts has often been taken for granted or overlooked. This widespread reference to the relationship between parts and wholes immerses us in one of the oldest philosophical discussions, inviting us to examine the fundamental nature of this relationship more deeply. The biological sciences, in particular, provide remarkable instances of complex and dynamic composite objects that serve as

exceptional case studies for philosophical examination of composition, parts, and the concept of wholes.

In the first chapter, I have presented a compelling case for refraining from outright dismissing composite objects' existence. Furthermore, I propose that any philosophical exploration into the nature of the relation between parts and whole should encompass not only non-complex and static entities such as chairs or heaps of sand but also into the realm of highly dynamic, where the interactions between their parts constantly change. Detailed scrutiny of such things is the domain of scientific inquiry, offering a broader perspective from which to contemplate composite entities. One of the central objectives of this thesis is to examine biological entities in terms of parts and whole in order to understand how these relations can be configured in the biological world.

Before proceeding in that analysis, it is pertinent to argue that some questions can arise in relation to this aim. Among them are the basis of the importance of the notions of the parts and whole relation's study in the biological context, its significance and contribution to philosophy of biology and why this should be analysed separately from other composite objects.

To answer these questions properly, I shall develop a comprehensive literature review about central philosophy of biology debates related to concepts of parts and wholes biology such as levels of organisation, emergence, self-organisation, biological explanations, biological individuality and their respective connections with parts and whole concepts.

Finally, drawing from biological practice, it shall be clarified what constitutes a biological object and what types of biological things will be focused upon this investigation. In order to establish a solid foundation for understanding how it is possible the configuration of relation between parts and whole in context sensitive and dynamics entities like biological ones.

2.2 Importance of parts and whole concepts in philosophy of biology

The philosophical inquiry into the relation between parts and wholes and composite objects is not new. Indeed, they are classic philosophical topics being analysed from the metaphysical perspective. Nonetheless, philosophically studying, science enables us to ask about these topics. However, someone might wonder what the reasons for investigating the notions of composition, part and whole in the biological context are. Why should an abstract debate on the composition of material things have relevance for the philosophy of biology? Next, these questions shall be assessed to argue the importance of analysing the configuration of elements in terms of parts and whole due to its importance in philosophical debates related to levels of organisation, emergence, self-organisation, biological explanation and biological individuality.

2.2.1 Levels of organisation

The idea of levels of organisation in biology is applied by scientists like an organisational principle in the biological realm, having an importance both in how we understand this realm and how scientists investigate it. Biological entities at various levels, such as cells, tissues, organs, and organisms, can be viewed as wholes composed of specific parts interrelated in a particular way.

Biology recognises distinct ontological levels of organisation, such as molecules, cells, tissues, organs, organisms, populations, and ecosystems. So, these levels can be analysed from an ontological and descriptive perspectives. The ontological one refers to the idea that these levels represent entities with their own unique structures, properties, and functions. They are not merely conceptual constructs but represent objective levels of complexity and organisation in the natural world. Each level is characterised by specific organisational principles, processes, and properties (Miller and Spoolman, 2011).

Ontological levels represent a hierarchical organisation of living systems, and the corresponding levels of description reflect the need for diverse perspectives and methodologies to describe and explain the phenomena at each stratum adequately. Molecular biology, for instance, employs specialised concepts and techniques to elucidate the structure and behaviour

of molecules. At the same time, ecology draws upon distinct theoretical frameworks to study the intricate web of interactions between organisms and their environment.

Through local interactions and simple rules followed by individual organisms, complex collective behaviours such as nest building, foraging, and migration patterns are produced (Camazine, 2001). These phenomena can be seen in ant colonies and bee swarms.

At the same time, levels of organisation and levels of description and explanation are indispensable in biology. Different levels require different concepts, models, generalisations, and investigation methodologies to characterise properties, spatial-temporal scales, and causal processes operating at those levels.

In biological practice, the idea of the levels of organisation has many applications. For instance, inquiries at the molecular and cellular levels are crucial for developing targeted therapies (e.g., Athanasiou et al., 2018). Similarly, studies at the ecosystem level are vital for designing measures to preserve the biodiversity of different environments (Noss, 1990).

This topic is one of the central ones within the philosophy of biology. Philosophers have examined issues related to the nature of these levels, what constitutes a level of organisation, and how these levels can be defined and distinguished from one another (Eronen and Brooks, 2018). Are these levels adequate to understand the biological realm and its diversity, or do they generate misunderstood views about it? (See Eronen, 2015).

What is the causal relation between different levels (e.g., Craver and 2007)? For example, how do molecular-level processes give rise to and influence higher-level phenomena, such as cell behaviour or organ function? Conversely, how do higher-level structures and processes constrain and shape lower-level dynamics? What is the action of higher-level over lower level components?

Considering these philosophical issues, the study of part-whole relations is crucial for understanding how the components at one level of an organisation interact and integrate to make up the whole at a higher level, as well as how these interactions allow that higher level to have particular properties and behaviours. Also, this examination of the nature of the relation between parts and whole gives key antecedents to define if there are good reasons to accept the existence of levels of organisation.

Parallelly, the analysis of the nature of relations between parts and whole informs the development of appropriate levels of description and explanatory models for different phenomena. By understanding how parts interact to make up wholes, we can determine the most suitable level of description (e.g., molecular, cellular, organismal) and the corresponding theoretical frameworks or models needed to adequately explain the observed phenomena. At the same time how the whole structure constraint components interrelations[2].

2.2.2. Emergent properties

Studying how these relations are configured in the biological realm is crucial for metaphysical discussion pertaining to the part and whole concepts and composite objects and is relevant for investigations into the philosophy of biology. In discussions about emergent properties, for example, the notion of the composition relationship is a central issue. In the biological context, life scientists explicitly reference the emergence concept, to explain certain specific characteristics of the phenomenon studied. Understanding how it is possible to configure these relations is fundamental to defining the possibility or impossibility of emergent properties arising in the biological realm. Therefore, any analysis of notions of parts and wholes in the biological field should also examine emergence in the context of this discipline.

At the heart of the issue is whether the behaviour and properties observed at higher levels of biological organisation are entirely determined by and explainable in terms of the parts and processes at lower levels or whether an irreducible, novel causal efficacy emerges at these higher levels.

Reductionism, which has been the dominant view in modern science, holds that all properties and causal powers are ultimately reducible to and explainable by the fundamental physical constituents and laws. From this perspective, any apparent emergent biological property is simply an epistemically emergent pattern that arises due to the complexity and limitations of our ability to track all the causal interactions among physical components.

[2] Both dimensions of levels of organisations namely, ontological and descriptive will addressed in detail in Chapter 4 and 5.

However, others have argued for an ontological concept of emergence, which posits that genuine novel causal powers and irreducible laws govern the dynamics at higher levels of organisation. With its intricate web of non-linear interactions and context dependencies, the integrated whole can bring forth qualitatively new phenomena that are not predictable and reducible from the parts in isolation.

Considering these antecedents, the conditions required for integration to enable these emergent phenomena are crucial analysis points. Assessing the nature of integration, namely the conditions that determine how the individual components interact, cooperate, and organise themselves into a cohesive whole, it is possible to define whether the properties and behaviour of the whole are novel or not. In order to clarify these issues, Chapter 3 will define how it is possible to integrate. Later in Chapter 4, it is addressed if these conditions of integration of biological elements in terms of parts and whole are necessary and sufficient to occur emergent properties.

2.2.3. Self-organisation

Self-organisation is a fundamental concept observed and studied across various disciplines, from physics and chemistry to biology. It refers to ordered patterns, structures, or behaviours within a system solely due to the interactions among its components, without any external control or centralised coordination.

In physics, self-organisation is evident in phenomena such as the formation of convection cells in fluids, the emergence of coherent structures in turbulent flows, and the spontaneous magnetisation of ferromagnetic materials. In chemistry, self-organisation forms complex molecular structures, such as micelles and vesicles, through the self-assembly of molecules driven by intermolecular interactions (Bernardes, 1996).

This concept often is associated with concepts such as self-replication, self-reparation, and self-assembly (see Collier, 2003; Halatek, Brauns and Frey, 2018). Hence, the concept of self-organisation is frequently misunderstood, making it necessary to clarify between what can genuinely be considered self-organisation and what cannot.

Self-replication is deeply intertwined with self-organisation, from molecular interactions to cellular dynamics, regulatory networks, and morphogenetic processes (cite). The coordination and self-organisation components and processes are essential for self-replication to be carried out correctly in living systems. So, processes of self-organisation allow that self-replication occurs.

Self-repair refers to the ability of biological systems to detect and respond to damage or disruptions to their internal structure or functions. For instance, self-repair often involves regenerative processes, where specialised stem cells or progenitor cells can proliferate and differentiate to replace damaged or lost cells, facilitating tissue repair and regeneration (Krafts, 2010). Processes of self-organisation and self-reparation are related, but they do not imply the same. Self-repair is more specifically focused on the ability of a system to detect and rectify damage to its internal structure or functions. It is typically triggered in response to specific instances of damage.

Self-assembly is often considered a specific form of self-organisation, where the components have a predefined set of interactions or rules that govern their assembly, namely the interaction between elements is programmed into the early states (Collier, 2003). Contrarily, self-organisation can also occur in systems where the interactions among components are not limited to predefined rules.

Each of these concepts refers to organisational changes in a system, such that the later states have more apparent organisations than the earlier states. Additionally, these changes are not imposed by external agents or forces but rather arise from the components' interactions and dynamics within the system itself. Although these concepts are related, they should not be used in an interchangeable way. Some systems can self-replicate, but that does not mean that that system is self-organised (e.g., a machine designed to create copies of itself through a predefined process cannot be self-organised).

In the philosophy of biology, there is debate about the adequate requirements to consider a system as self-organised. One of the central aspects of self-organization is the idea of self-reference or circularity, where the system's behaviour is shaped by its own internal processes and dynamics rather than solely by external influences. Scholars such as Maturana and Varela (1991) and Rosen (1958) emphasise the idea of closure that the self-organised system displayed. Maturana and Varela propose that living systems are characterised by their

ability to self-produce and self-maintain through a network of internal processes, constituting themselves as distinct individuals or unities, emphasising the closure idea. Similarly, the theoretical biologist and philosopher Rosen developed the concept of 'relational biology' and the idea of 'complex dynamical systems' that exhibit self-referential or recursive behaviour. Both accounts focus on the self-reference aspect of self-organisation, but this self-reference is not the unique aspect of analysing self-organisation in the biological realm.

The philosopher Cliff Hooker (2011) highlights how the self-organisation processes allow systems to interact with the environment. He argues that the view about self-organisation in biological entities should focus on being dynamically open, having inputs and outputs, and involving interactive dynamic processes with their surroundings (Hooker, 2011). Biological systems, from individual cells to entire ecosystems, are fundamentally open and self-producing. They constantly interact with their surroundings, exchanging materials, energy, and information while maintaining and regenerating their organisation and structure. This point is interesting because it points out how self-organisation in biological systems is not only a question to understand self-reference processes but also how these processes can be triggered and configured by the system's interaction with its surroundings.

The exchange of materials, energy, and information with the surroundings is a source of perturbations, constraints, and opportunities that can initiate, shape, or redirect the self-organising dynamics within biological systems. Environmental cues, such as changes in temperature, nutrient availability, or the presence of signalling molecules, can act as catalysts or modulators of self-organisation, prompting the system to reorganise and adapt its internal processes accordingly.

Despite the debates around the concept, self-organisation is widely recognised as a fundamental principle in the study of complex systems, especially in biological entities. This concept helps explain how complex structures, patterns, and behaviours appear in living systems without the need for external control or centralised coordination.

Self-organisation profoundly relates to the metaphysical category of parts and wholes. Self-organisation processes highlight the different ways in which a whole's components can interact, considering the dynamic interactions that arise from the collective behaviour of parts within a whole system. All this is done without the need for external control. Self-organisation

processes make relevant the importance of understanding how it is possible to configure entities in terms of parts and wholes in dynamic entities.

2.2.4. Biological explanations

A proper explanation facilitates an understanding of why a particular phenomenon occurs. This understanding implies how and when a phenomenon happens. For instance, understanding how a seed germinates allows us to predict under what conditions this fact occurs or why the germination does not happen in a particular situation. This knowledge also allows for control of the germination process under different circumstances. In this task of understanding the living world and its entities, it is worth assessing in detail the role of the part, whole notions in elaborating biological explanations. In philosophy of biology a central issue is to evaluate how should scientists explain biological phenomena.

2.2.4.1 Part, whole notions and biological explanations.

We perceive the world as having rudimentary compositional relations, such as bricks composing a house, wheels and axles making up a car, and so on. Besides, we conceive of things in a compositional way, and also, explain them. We explain the motility of legs using the properties and relations of the muscles that compose them. This compositional perspective is common in both daily life and scientific practice.

These concepts play an essential role in elaborating methodological strategies and explanations. The biological sciences encompass a set of disciplines that study a variety of living things. Living entities are exposed to a changing environment, presenting adaptive processes and interacting and associating themselves with other systems or organisms in different ways. Studying the interactions between them and the environment and the processes involved in these interactions is a central issue for life scientists.

In the analysis of explanations, some philosophers of science who focus on the practices of biologists have highlighted that in biological sciences explain phenomena from a mechanistic perspective (Bechtel and Richardson, 2010). This view has had significant relevance in the philosophy of biology analysis. Indeed, a significant portion of the philosophical works concerning biological explanation revolves around causal and mechanistic traditions. Within biology (and the life sciences more generally there exists a longstanding

practice of elucidating a phenomenon by providing a detailed account of its underlying mechanism (see Bechtel, 2011; Craver and Tabery, 2019; Craver and Darden, 2013). So, phenomena of experimental biology are often explained in terms of the underlying mechanism responsible.

The methodological strategy of analysing and understanding a whole's behaviour by decomposing it into its parts is central to generating knowledge in the biological sciences. In the study of biological phenomena, biologists identify parts of a phenomenon and their respective roles in its functioning. One strategy frequently implemented by biologists is to divide a system into parts and then analyse how they participate in the phenomenon's behaviour (Bechtel and Richardson, 2010). The reference to parts and wholes also has importance in theorising the natural world. Scientists explain a biological phenomenon and refer to elements that compose a whole. Therefore, these relationships also play a central role in elaborating biological explanations. In this manner, scientists explain a phenomenon focusing on 1) identifying parts of the whole, 2) analysing their respective properties, and 3) organising elements and how they interact. All this serves to explain the functioning and behaviour of the whole. This can be seen in the scientific explanation of the specific cellular response to a stimulus through the signalling transduction process (see Figure 2.1). During this process, a cell has the ability to modify its behaviour through an interaction between a receptor and a ligand. The ligand (extracellular signal molecule) binds to the receptor (protein receptor) and triggers the production of other molecules within the cell. These molecules are crucial in relaying the signal from one location to another, for example, from the cell's plasma membrane to the nucleus. Frequently, a series of changes unfolds within the cell. These changes can affect the metabolism, gene expression or the shape and movement of the cell. This signal transduction pathway often acts as an amplifier, intensifying the cell's response to an external signal. The messenger molecules involved in this process can encompass amino acids, peptides, proteins, fatty acids, lipids, nucleosides, or nucleotides (Alberts et al., 2008). In this case, scientists identify every element involved and how these cellular elements interact with each other (e.g., receptor-ligand) to produce a response to a stimulus in a particular context.

It is in question whether this decomposition is accurate for studying dynamic phenomena. Can a decomposition strategy provide a comprehensive and adequate view of dynamic phenomena? In biology, interactions are context-dependent and are not only about

properties components and their organisation. When components interact and for how long is related to contextual requirements. A decomposition strategy can overlook this aspect.

Furthermore, the focus on breaking down living systems into smaller parts or components can lead to a reductionist approach, where biological phenomena can be completely explained by analysing the properties and interactions of their lower-level parts. This approach has been largely discussed in the philosophical analysis of biological explanations. Philosophers debate about the nature, relevance and accuracy of reductionist explanations in the biological realm (see Sarkar 1992; Kaiser, 2015).

How parts are defined and how they relate to the whole can be context-dependent. What may be considered a part in one context could be a whole in another, making the categorisation and organisation of biological phenomena challenging and potentially ambiguous. At the same time, an important matter of analysis is assessing how explanations should be elaborated, from parts to wholes or from the whole to its components. What approach would be more accurate to address a particular biological phenomenon? Is it only one approach, or is it better to have a pluralistic view in which many approaches are considered in order to account for the complexity of biological phenomena? If this is the case, what happens if approaches are incompatible?

Debates around part-whole relations in biological explanations highlight their fundamental importance for scientific practice. How parts are defined and related to the whole is not trivial, as the categorisation is often context-dependent and can shift depending on the phenomenon studied.

It is of sufficient importance that the links of each of these concepts to the relations between parts and the whole deserve to be treated separately and in detail. In Chapter 5, the use of these notions in the elaboration of explanations and their limitations or challenges when studying a given biological phenomenon will be evaluated.

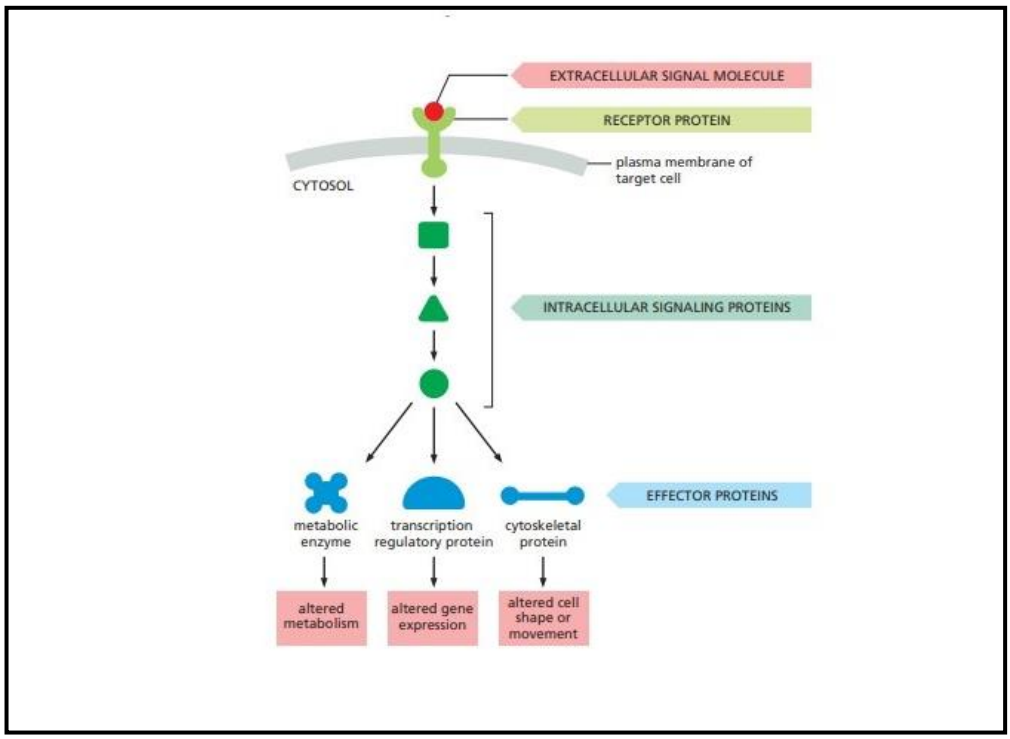

Figure 2.1 Image of a schematic signal transduction (Albert et al, 2008 p. 880)

2.4 Biological individual concept and parts-whole relations

The definition of when and how composition occurs is not an easy task because, in the biological world, there is a great variety of interactions between diverse biological entities. Specifically, this difficulty can be seen in the debate on biological individuality. Some cases of collective entities (e.g., bee colonies) or symbiotic interactions generate questions about individuality and composition. Sometimes these collective entities can be living individuals in their own right (e.g., a human is a collection of living cells). Others can be no more than an aggregation of a lower level of individuals (e.g., a school of fish) (Godfrey-Smith, 2015). Numerous instances can be found where groups of organisms make up colonies that exhibit interconnected causal relationships and specialised roles among their individual members. These cases raise the point of whether this collective entity or symbiotic union can be considered an individual. Therefore, the central question is whether two organisms can compose a biological individual, which is directly related to the debate on parts and wholes.

How are these concepts linked? Is the analysis of parts and whole relationships limited to discussing biological individuality?

The individualisation of different life forms is a fundamental issue that life scientists examine and is one of the most critical problems in defining an individual. This analysis involves decisions about the entities being investigated and the classificatory role of a biological individuality concept (Lidgard and Nyhart, 2017). For example, a problematic case of individuation is the aspen tree. The underground connections between this tree and other trees in the aspen grove create a network. These interconnected aspen trees share the same genetic makeup, challenging the conventional definition of distinct individuals based on spatial boundaries and genetic uniqueness (Lidgard and Nyhart, 2017).

Another problematic aspect is temporality. In this context, examining issues such as evolutive transitions from unicellular to multicellular and changes through reproductive, developmental, and morphogenetic stages over time is relevant, for instance, complex life cycles with "alternation of generations" (Godfrey-Smith, 2015; Love and Brigandt, 2017). A proper individuality concept should be able to explain issues such as new mechanisms of heredity (e.g., fission and sexual reproduction). New levels of biological individuality are formed from groups of species or the same species, the reproduction together of entities that previously reproduced independently, and the conflict between distinct genetic or cellular lineages in a composite individual, among others (Lidgard and Nyhart, 2017).

Cases such as chimerism, epistatic interactions in development (primarily interactions among genes), horizontal gene exchange symbiotic associations, or collective entities generate many questions about what entities can be considered to have biological individuality. Chimerism and mosaicism represent cases of intra-organism genetic heterogeneity, which make it a challenge to define what is a biological individual. At the same time, symbiosis (e.g., animals and bacteria) adds complexity to these matters, as it allows for the inclusion of organisms from diverse taxonomic groups within a putative individual (Love and Brigandt, 2017). Other cases are collective entities such as ant and bee colonies. Sometimes these collective entities can be living individuals in their own right (e.g., a human is a collection of living cells). In other cases, it can be no more than an aggregation of a lower level of individuals (e.g., a school of fish) (Godfrey-Smith, 2015). Some collective entities have a division of labour such as reproduction or feeding. There are numerous instances of communities of organisms characterised by intricate connections and specific roles among their members. In

certain cases, like that of an ant colony, most organisms cannot reproduce (Love and Brigandt, 2017). These cases have generated an intense discussion about what a biological individual is. This discussion focuses on establishing the most appropriate criteria for defining biological individuals and their properties.

Because of these problematic cases, some philosophers have proposed different individual accounts to cover all instances of biological individuals (Love and Brigandt, 2017). In this attempt to define an individual, philosophers of science and biologists propose different criteria, developing distinct perspectives such as evolutionary, ecological, genetic, or physiological, among others (Clarke, 2010; Pradeu, 2013; Santelices, 1999). These criteria evaluate aspects such as spatial and temporal continuity; spatial and temporal boundedness; indivisibility without losing character or function; integration of the immunological system; life cycles; autonomy, metabolic and physiological aspects; and capacity to undergo selection (Lidgard and Nyhart, 2017).

The self-organisation concept also has significant implications for understanding biological individuality. As discussed earlier, self-organising systems' self-referential exhibits a degree of cohesion, and integration that distinguishes them from mere collections of components. So, self-organised systems display integration and cohesion among their components, often considered a defining feature of individuals.

The above shows a variety of alternatives to approaching and understanding the notion of "biological individuality". From the perspectives described, identity and unity are common ideas linked to biological individuality. Identity involves distinguishing one instance of a class from another, typically by some persistent exclusive property (Lidgard and Nyhart, 2017). Unity refers to parts that compose the individual and are tightly cohesive.

In addition to these challenges, the biological individuality discussion has to figure out conceptual uncertainties due to the lack of definition of the "biological individual" and related terms (Pradeu, 2016). There is no clear idea of the meaning of the notion of a "biological individual" nor of associated terms such as 'organism', 'whole' 'parts', 'identity', 'unity', or 'cohesion', among others (see Santelices 1999; Clarke 2011; Lidgard and Nyhart, 2017; Wilson and Barker, 2019). Specifically on parts of a whole concept, a significant part of the discussion of biological individuality has been focused on under what criteria entities in interaction are

parts of a new whole. This link between these concepts deserves further analysis, which will be carried out in the upcoming section.

2.4.1 On the association between parts, whole, and biological individual concepts.

The conceptual association between these terms is especially relevant to my research because notions of 'parts' and 'wholes' are related to the idea of "biological individuality". The biological viewpoint regarding relationships between parts and wholes primarily depends on utilising biological theories and models to establish connections of inclusion and define the limits of biological individuals (see Godfrey-Smith, 2015; Guay and Pradeu, 2016; Pradeu, 2016; Molter, 2017). In this debate, it often is discussed what is considered a part or not, for example, whether a biological individual can be part of another biological individual. It can be seen in Holobiont analysis. Some biologists and philosophers argue that holobionts, collectives consisting of eukaryotic hosts and symbiotic microbes, can be considered individuals (Waters, 2018; Triviño and Suárez, 2020). Others, such as Douglas and Werren (2016), argue that a holobiont instead is an ecological community of organisms that encompasses a broad range of interactions (e.g., mutualism or parasitism), patterns of transmission (horizontal to vertical), and levels of fidelity among entities associated. Without a doubt, these cases of a superorganism, genetic chimeras, modular organisms (such as trees and corals), and symbiont consortia (such as holobionts) generate a question as to how parts are organised and behave in these kinds of living individuals.

This issue is central; even though these notions, namely, 'parts', 'whole' and 'biological individuality', are linked, they deserve their own examination. On the one hand, a separate evaluation can give us an idea about how these relationships can be instantiated and then let us see which of these instantiations would be the most appropriate when defining a biological individual. Suppose that the talk of parts and wholes in the biological world only relates to biological individuals. If we pay attention, we can note that we have three concepts: 'parts', 'whole', and 'biological individual', ideas for which there is no clear definition. In this case, the analysis would cause more confusion because we would be explaining concepts based on others that are not clear either.

Whether a colony should be considered a biological individual depends on the criteria accepted for defining individuality. This goes beyond the simple consideration of the

relationship between parts and the whole; it requires a more specific examination of the appropriate parameters to evaluate the *integrity* and *unity* of the entity. These parameters encompass various aspects such as *agency*, *autonomy*, *evolution*, or *immunology*. The point is, which of them is crucial in determining biological individuality? The debate surrounding biological individuality enquires into questions of unity and wholeness, but it also encompasses broader considerations related to evolution, autonomy, or agency. Thus, evaluating whether a colony qualifies as a biological individual involves exploring the intricate interplay of these factors.

Considering the earlier challenges regarding the definition of biological entities and individuals, it may be advisable to focus initially on examining non-problematic cases of an organism or biological individuality. By studying these cases, we can establish a foundation and better understand what constitutes a typical example of biological individuality. However, it is important to note that even within seemingly clear-cut cases, problems can arise. One of these is how we define non-problematic cases. We can specify an animal, such as a human or a tiger; these cases seem plausible cases of biological individuality. However, we encounter the presence of bacteria in their intestinal flora. Here, the question arises: do these bacteria form part of the animal or not? This example underscores the need to establish specific criteria for determining the inclusion or exclusion of entities within the scope of biological individuality. This has the problem of under what criteria we select cases. The selection of cases and establishing criteria for inclusion can pose challenges. Deciding whether certain entities are considered part of an organism or separate entities interacting with it requires careful analysis.

Studying different possible configurations of the relation between parts and whole in the biological world can contribute helpful information about this relation to decide which of these configurations is more appropriate to be considered biological individuality. In this sense, considering that one of the main things is to define how the *unity* and *integration* between different biological entities make up another one, it is essential to evaluate the integration conditions in the configuration of the relation of parts and wholes in the biological context. The analysis of these conditions clarifies what we are talking about when we refer to parts and whole in biology, giving more antecedents to define adequate criteria to assess individuality.

2.4.2 Are biological composite objects and biological individuality equivalent categories?

One could argue that when we refer to individuals, we refer to biological composite objects. We consider such individuals an ant, a cell, or a tiger. They undoubtedly are also biological composite objects. Hence there is a concurrence between these two categories. While there is some truth to that perspective, the crucial point is to recognise the potential problems that arise when we confine biological objects solely to the concept of an individual. What about entities studied by biologists that do not meet the criteria to be considered biological individuals? This raises the question of whether we should accept that any entity described by biologists automatically qualifies as an individual, thus adopting a flexible definition. Alternatively, we can reject this equivalence and acknowledge that while every biological individual is an entity, not every biological wholeness[3] necessarily qualifies as a biological individual. This distinction implies the need for specific and stricter criteria. By limiting our focus to organisms or biological individuals, we encounter limitations that hinder our analysis and provide a narrow perspective for understanding the configuration of this relationship within the biological world.

Suppose we pay attention only to a plurality of biological entities which make up an individual organism. The analysis would dismiss other kinds of entities. For example, in a colony of ants, a collection of ants composes a biological entity, namely a colony. Nevertheless, the colony is not considered an individual but a group of organisms. The composition relation analysis would cover single ants only, and the colony would not be assessed. Why should the study of the composition relationship be restricted to single ants and not the colony?

Ants exhibit eusocial behaviour, indicating that their society functions as a collaborative system where their roles determine their morphology (Camazine et al., 2003; Dorigo, Bonabeau and Theraulaz, 2000). In other words, they are so cooperative that some ants give up the ability to do specific tasks because doing so would not serve the colony (e.g., the Queen ant has the role of reproducing, begetting more ants for the colony).

Through these sophisticated interactions, ant colonies can perform many different tasks. Ants venture out of their nest, search for food, and return with it. They construct and maintain the nest, attend to the needs of the larvae, and relocate the pupae. Furthermore, ants engage in various additional activities (Gordon, 2010). Within an ant colony, a forager departs from the

[3] Biological wholeness and biological composite objects are used in an interchangeable way.

nest with the purpose of gathering food. The forager's task is established through interactions, as it is motivated to leave the nest by returning foragers. Subsequent interactions, such as encountering an alarmed ant, can alter the forager's mission and prompt it to return to the nest without food.

Ant colonies and other social insects exhibit sophisticated forms of advanced behaviour, encompassing tasks such as building intricate structures and coordinating collective defence and aggression in response to predator threats. (Camazine, 2001). According to other ant colony research, many collective behaviours in ant colonies result from self-organisation. Local interactions among ant workers follow simple rules from which emerge complex colony-level patterns (Bonabeau et al., 1997). To illustrate, consider an ant colony where the overall actions of the ants arise from the interconnectedness of individual ants through chemical trails (called pheromones). These trails, deposited by ants, serve to either attract or deter other ants (Tabony, 2006). The self-amplification of these chemical pathways contributes to the self-organisation of the ant population.

Recent research showcases the kinds of behavioural mechanisms that ant colonies apply to achieve social homeostasis in the face of disturbance. Specifically, ants adapt their spatial arrangement, movement patterns, and social behaviours (regardless of local density) in order to preserve important aspects of their spatial organisation and social interactions, even when faced with significant environmental changes (Modlmeier et al., 2019). When an ant engages in an action that affects another ant's position or duration in a specific location, it ultimately impacts the positions of all the other ants.

This sophisticated and specific behaviour makes ant colonies complex systems which can self-organise. The whole colony causes its own development, activity and reproduction. An ant colony generates another ant colony in addition to being able to respond to environmental disturbances.

Specifically, in the biological individual discussion, the issue is not to evaluate when a plurality of biological entities composes another biological entity, but instead, whether these entities make up a biological individual. A colony of ants, for example, compose another biological entity, namely a colony, but it is not necessarily an individual.

Biological composite objects and biological individuality are related concepts but are not necessarily equivalent. Each of them has its own particularities. Biological objects refer to

any living or non-living entities in the biological realm. This can include individual organisms, cells and tissues, organs, proteins, or biomolecules essential to performance and behaviour within an organism. They can be an ant colony or a complex system such as an ecosystem. While all biological individuals are biological objects, not all biological objects necessarily possess the same level of individuality required to be considered as an individual. For example, a single cell within a multicellular organism can be a biological object, but it does not display the same level of individuality as the entire organism itself.

In the biological context, there is considerable heterogeneity of life forms. There are viruses, bacteria, fungi, plants, insects, etc. At the same time, diverse bacteria, viruses, fungi, and so on exist within different biological entities. If we consider bacteria, there is heterogeneity in shape (e.g., streptococcus, bacillus, or spirillum), structure (e.g., gram-positive or gram-negative), or feeding (e.g., autotrophic, photoautotrophs, or heliobacteria). Many cases such as bacterial colonies, cellular slime moulds, mycelial fungi, and clonal plants, challenge the traditional idea of "organism". There are association systems, colonies and processes where it is also possible to assess the putative compositional relations. Some of these forms of life are not necessarily conceived of as organisms or individuals. These cases exemplify biological wholeness resulting from sophisticated associations between several different organisms.

In summary, even though the notions of part and whole have relevance in discussions of what biological individuals and organisms are, this does not mean that the analysis of these notions is restricted to biological individuals or organisms. First, there is no clarity about what we understand as a biological individual or organism. Secondly, the focus on entities that can be considered individuals or organisms would set aside other biological entities such as prions, organelles, enzymes, or systems. Once we have argued that the idea of biological individuality does not circumscribe a biological whole, we will examine how these entities are in depth.

2.5 Parts, wholes and composite objects in biology

Indeed, a general analysis of parts and wholes is not a simple task because a wide variety of things have been taken as wholes and parts. For example, Nagel (1952) distinguishes between some senses of "wholes" and "parts". Among these are: 1) The "whole" is used to describe something that has a spatial extension, and anything included within this spatial extent is referred to as a "part" of that whole; 2) Reference to denote a temporal period, where its parts

are the different temporal intervals within it; 3) Reference to any class, set, or collection of elements, the term “part” may indicate either a proper subclass of the initial set or any individual element belonging to that set; 4) The word “whole” may also indicate a pattern of relationships between specific objects or events, capable of being manifested in various instances with possible modifications; 5) The whole can be a process, wherein one of its parts represents a distinguishable phase of the larger encompassing process.; 6) The word “whole” may refer to any tangible object, and “part” refers to any of its properties. For example, the property of being cylindrical or malleable is considered a part of a given piece of copper wire.; 7) The whole can represent a system in which its spatial parts are interrelated in dynamic dependence, as seen in organic systems, for instance.

We can find some of these kinds of wholes and parts in the biological context. Biological wholes are objects with a spatial extension, as in the case of the human body. Also, they can be processes crucial in the survival and development of living entities. These processes are made up of many chemical reactions or other events that result in chemical transformation. Examples are signal transduction, metabolism, cell growth or response to stimuli. Biological wholes are also systems whose parts are involved in relations of dynamical dependence. The analysis of different composite biological entities will be presented below to identify the main aspects of the composition, parts, and whole notions in the biological field.

2.5.1 What biological objects are?

To assess this metaphysical topic in the biological context, firstly, we should have some idea about what a biological object is. This clarification is necessary because exploring metaphysical matters within fields like biology inevitably leads to the convergence of various concepts. When philosophers specialising in biology discuss identity, ontology, or processes, their interpretations may diverge significantly from those of a metaphysician (Ferner and Pradeu, 2017). So also, how scientists think of biological objects can differ from the traditional perspective of philosophers, necessitating a context-specific understanding. When investigating metaphysical topics within the domain of biology, it is vital to clarify what we are talking about. In this case, it is necessary to inquire what a biological object is. Recognising these distinctions can facilitate more meaningful and accurate discussions of the metaphysical assumptions in the biological context.

Of course, the diversity of entities in this realm is enormous. We have notable examples of complex and dynamic composite objects in the biological sciences, which can be excellent case studies for philosophical analysis of the composition, parts, and whole notions. Indeed, the biological sciences provide numerous notable examples of complex and dynamic composite objects that serve as excellent case studies for the philosophical analysis of the composition, parts, and whole notions. These examples offer rich insights into the intricate relationships and interplay between the whole and its components.

Considering that my research assesses the scientific practice in biology, I will consider any entity studied in biological sciences as a biological object. Biological things can range from biomolecules (e.g., DNA or RNA), prions, and cells to ecosystems. Therefore, when we talk about biological objects we are not limited to the idea of organisms or biological individuality.

One such example is the human body itself. The human body is composed of various organs, tissues, cells, and molecules, all functioning together in a highly coordinated manner. Each organ has its own specific structure and function, yet they work in harmony to maintain the overall health and well-being of the individual. This complex composition raises intriguing questions about how the various parts integrate and interact to give rise to the coherent and unified human body.

Similarly, ecosystems provide fascinating case studies for exploring the composition and dynamics of biological entities. An ecosystem comprises a multitude of organisms, ranging from plants and animals to microorganisms. All are interconnected through complex networks of energy flow and ecological interactions. Studying ecosystems allows us to examine how the diverse components come together to form a functioning ecological unit and how changes in one part can ripple through the entire system, affecting its stability and resilience.

Within the biological context, a wide range of composite objects can be observed, each exhibiting distinct characteristics, functioning, behaviour, and levels of complexity. Such biological entities include proteins, DNA molecules, cells, and ecosystems. Despite their differences, these entities share commonalities regarding their complex organised structures and involvement in various intricate processes.

While many of these biological objects are considered alive, it is essential to note that not all entities falling under the umbrella term “biological objects” possess the same status of being alive. For example, due to their unique characteristics, viruses have been subject to

debate regarding their classification as living or non-living entities. While they possess genetic material and exhibit some life-like properties when infecting host cells, viruses cannot independently carry out essential life processes.

For instance, there is the question, what is life? Both philosophers and biologists have widely discussed the definition of life without achieving a satisfactory answer. The difficulty is due to disagreements about how abstract or specific definitions should be, differing compromises about what should be included in a definition, and even debates about the definitions' nature (Mariscal and Doolittle, 2020).

In the realm of biology, certain biological entities exist in a grey area, where it remains uncertain whether they can be classified as living or non-living. These entities include prions, plasmids, organelles, endosymbionts, and reduced extracellular symbionts (Dupré and O'Malley, 2009). For instance, viruses, which consist of genetic material enclosed in a protein coat (Flint et al., 2020). The classification of viruses as living or non-living is a subject of intense debate, with some asserting that viruses are alive, others arguing that they are not, and a third group suggesting that they can only be considered living when inside an infected cell and are merely "seeds" otherwise (Forterre in 2010).

Other discussed entities include transposable elements, viroids, non-culturable microorganisms that presumably exist, organisms in a vegetative state, and prions (Postgate, 2000). These entities face similar challenges as they possess the capacity to undergo natural selection and exhibit biochemical complexity but lack specific properties typically associated with life. For instance, prions, which are protein products of living organisms, can induce conformational changes in other prions, facilitating cumulative evolution (Li et al., 2010). Despite this capability, they are seldom classified as "living" due to their limited activity in most environments and their relatively straightforward origin as misfolded versions of functional proteins.

Alternatively, philosophers of biology such as Dupré (2012) and Seibt (2024) argue that the focus shouldn't be on objects or static entities but on processes. This metaphysical processual view emphasises the primacy of processes over static substances. Following this position, biological wholeness is only a process; its parts are in each step of a particular process.

Nevertheless, biological practice routinely employs both entity and process concepts. Biologists describe entities like genes, cells, and organisms and processes like gene expression,

cell signalling, and metabolism. So, it raises the question of whether an exclusively substance or process ontology would fit with the biological realm's diverse nature. If we choose one of these possibilities, we can fail to properly understand the biological world because the focus would be on entities or processes and would dismiss the importance of the other. So, in the biological realm, we should consider all this gamut of diverse entities, whether objects or processes. Taking into account objects like cells and processes are carried out.

2.5.2 Non-biological versus biological wholes

Non-living wholes can be a heap of sand, a wall, a car, or an electronic device. Whereas the wholes, such as a heap of sand or a wall, are simple entities with attributes related to length, size, or shape, cars and electronic devices are more complex entities. They have specific characteristics with regard to a particular function. In these latter cases, the parts depend on each other functionally. In a mechanism, such as a car, one part, such as a wheel, piston, or steering rod, may be taken out and replaced by another like part without changing the nature of either the whole or any of the parts. Cars operate as functional wholes. Hence, substituting parts does not alter the nature of the whole because it works in the same way. In this case, we can see that the functioning of parts together is essential for defining the whole.

In contrast, if we consider an organ transplant in the human body, for example, a heart transplant, the replacement is more complex than a car component. Replace some parts of the human body, as in the case of a heart transplant, and many factors should be considered. Following a heart transplant, an essential concern is the potential rejection of the donor's heart by the recipient's body. It is crucial to consider this risk because the immune system may recognise the transplanted heart as foreign and initiate a rejection response, leading to potential harm to the organ. To mitigate this risk, individuals who undergo heart transplants are administered immunosuppressant medications, which help reduce the occurrence of organ rejection. As a result, the incidence of rejection continues to decrease over time. Hence, organ transplantation requires a meticulous matching process to ensure compatibility between the donor and recipient, considering factors such as blood type, tissue compatibility, and immunological factors. Additionally, the surgical procedure itself is complex and carries risks.

It can be seen that while in both cases, a component is replaced, the difference between replacing a piece of a car and transplanting an organ in the human body lies in the complexity of the systems involved.

As Nagel (1952) says, talking about something as a whole can imply many things. For this reason, there is an ambiguity around what that relationship between parts and wholes means. This lack of clarity is especially true in the biological realm, where a great variety of composite entities exist. These could be a protein, a cell, an ecosystem or an ant colony. Each one of these biological entities is different. All of them have organised complex functional structures. Each has particular characteristics, functioning, behaviour, and level of complexity. Complex processes that living entities carry out, such as metabolism, growth, death, reproduction, and adaptation, can also be composite entities.

Biological wholes are also systems whose parts are involved in relations of dynamical interdependence. A cell carries out processes of metabolism or synthesis of proteins and has a membrane as a border. An ecosystem is a system with a flow of matter and energy through interactions of different species with their environment through parasitism, depredation, or mutualism. Symbiotic associations are specialised interactions between diverse species, which could bring benefits in terms of reproduction, functioning, or adaptation. An ant colony is a highly structured association between ants, where each fulfils a specific function to maintain proper colony functioning. Biofilms, for instance, are a collective of one or more types of microorganisms (bacteria, fungi or, protists) that can grow on different surfaces. The analysis of these entities provides a broad view of how they are. In every one of these cases, the dynamic of interrelations of parts is crucial for understanding how these systems keep their structure and organisation in the face of constant environmental changes.

Indeed, I already have suggested that the philosophical examination of the relation between parts and whole should consider both non-complex and static objects, such as chairs or heaps of sand, and highly dynamic and complex objects, where the interrelation among the parts changes continuously. On this basis, I would like to examine the concepts of parts, whole, and composition in the biological context, defining the conditions under which the relation between parts and wholes can be configured and maintained in the biological realm. The enormous complexity of biological systems, the historical nature of all organisms, and the fact that organisms contain a historically evolved genetic program make them so different from non-living objects that generalisations derived from non-living things are, in most cases,

meaningless or trivial when applied to phenomena of life (Mayr, 1969). Is it possible to analyse living objects similarly to examining non-living things? Why should the relation of elements between parts and whole be the same in entities that are very different, such as a table and a cell?

The arrangement of parts in biological objects is vital in studying the biological sciences. From the understanding of this arrangement, we can define the configuration of this relation in this particular context. Biological scientists highlight that biological entities have specific organisation, dynamics, and processes, emphasising that one characteristic that differentiates living systems from physicochemical ones is the capability to self-produce and self-maintain through continuous exchanges of matter and energy with the environment (see Alberts et al., 2008; Cotgreave and Forseth, 2009; Lodish et al., 2008). This self-maintenance is accorded to the specific and sophisticated organisation of diverse biological elements which compose a biological entity.

a) Biological organisation

In biological entities, one key aspect is the organisation of different biological elements. Specific processes occur depending on the particular organisation and behaviour of these entities. The organisation's concept primarily pertains to allocating specific tasks and responsibilities within a system, known as functional roles or division of labour. At the same time, it encompasses the harmonious integration and coordination of these parts to form a unified whole. Additionally, organisation involves a crucial aspect of interdependence, where the functioning and existence of each component rely on its interconnectedness with others. This notion emphasises that organised parts' activity and survival depend on their mutual relationships. This principle is particularly evident in biological systems, where there is a tendency to sustain and safeguard the system by addressing and eliminating potentially harmful changes while preserving certain variations. For this reason, it is considered that biological entities manifest self-organisation.

In biology, self-organisation is crucial in various processes, including developing embryos, forming complex patterns in animal coats and skin pigmentation, and emerging collective behaviours in social insects and animal groups (Camazine, 2001). The self-organised

behaviour of biological systems is often attributed to genetic and environmental factors and the interactions among individual cells, organisms, or populations.

At the ecosystem level, self-organisation is exhibited in the interactions among different species, their environments, and the flow of energy and matter (Miller and Spoolman, 2011). This can allow the occurrence of complex food webs, nutrient cycles, and the self-organised formation of distinct ecological niches and habitats.

Understanding the fundamental modes of interaction within self-organising systems involves recognising negative and positive feedback mechanisms (Glass, 2005). Negative feedback, for instance, occurs when a slight disturbance applied to the system triggers a response that counters the disturbance. A negative feedback loop plays a crucial role in counteracting imposed changes in a system. In the case of the Krebs cycle, numerous enzymes are regulated through negative feedback, achieved by the allosteric binding of ATP. As ATP is both a by-product of the pathway and an indicator of the cell's energy level, its presence inhibits key enzymes such as citrate synthase, isocitrate dehydrogenase, and α-ketoglutarate dehydrogenase, which catalyse the first three reactions of the Krebs cycle. Consequently, this regulatory mechanism halts the Krebs cycle when the cell's energy level is deemed sufficient (Lehninger, Nelson, and Cox, 2004).

In contrast, positive feedback generally promotes changes in a system (Camazine, 2001). An illustration of this phenomenon can be observed in blood clotting. In this case, a critical step involves the creation of an enzyme known as thrombin, which not only contributes to the formation of the clot matrix but also expedites the generation of additional thrombin (Klabunde, 2011).

The self-organisation in biological systems differs in certain respects from that in physical systems. Firstly, the subunits of biological entities have greater complexity. For example, when the subunits are living organisms like fish or ants, there is a higher level of inherent complexity compared to physical systems where the components are inanimate entities like grains of sand or chemical reactants. Additionally, patterns are created solely through interactions governed by physical laws in chemical and physical systems (Camazine, 2001). For example, the hexagonal cells of moving fluid called Bénard convection cells obey physical laws related to forces governing the motion of molecules in a heated fluid (Rivier et al., 1984). In turn, in the biological context, entities obey both physical laws and . The

physiological and behavioural interactions among the living components are influenced by the genetically controlled properties of the elements.

Scientists have characterised self-organisation in different biological entities such as cells, insects' colonies or ecosystems. At the cellular and molecular level, self-organisation is evident in forming complex structures and patterns. For example, proteins fold into specific three-dimensional structures, or cytoskeletal components self-organise into intricate networks responsible for cell shape and motility. The particular interactions among biomolecules, such as hydrogen bonding and electrostatic forces, drive these processes.

At the ecosystem level, self-organisation implies the interactions among different species, their environments, and the flow of energy and matter. This can allow complex food webs, nutrient cycles, and the self-organised formation of distinct ecological niches and habitats.

b) Biological entities and their maintenance

The maintenance aspect is quite interesting in the biological world. Living systems possess a striking characteristic wherein their biological components engage in interactions and modifications, and create themselves to give rise to an autonomous, self-generated, and self-organised whole (Wolkenhauer and Muir, 2011). Living beings are self-sustaining systems that constantly generate their own chemical components. They use these components to build their organs and functional parts, ensuring the maintenance of their own organisation. (Moreno and Mossio, 2015). These entities are self-maintaining systems because they operate under a particular causal arrangement, where the actions of their individual components are essential for the continuity of the entire organisation through time (Saborido, 2014).

Biological entities present an organisation able to maintain itself. In this maintaining, metabolism plays a key role. This activity involves a series of procedures enabling entities to construct and replace their structures, undergo growth and reproduction, and respond to their surroundings. Metabolism refers to activities by which living beings continuously self-produce, self-repair, and maintain themselves (Moreno and Mossio, 2015). In other words, living beings constantly produce their own chemical components; with these components, they build their organs and functional parts (Moreno and Mossio, 2015). This autonomous self-

fabrication is, for many scientists, the feature that distinguishes life from non-life (see Rosen, 1991, Varela, Maturana, and Uribe, 1974). In the biological context, any activity, processes, and behaviour in these entities aid it to be self-maintaining.

To illustrate, cellular metabolism encompasses activities that build and sustain the cell, including tasks such as cell growth, duplicating the genome, and preparing for cell division. (Lehninger, Nelson and Cox, 2004). Typically, metabolism is associated with the cellular energy management system, which consists of catabolism, involving the release of energy, and anabolism, encompassing processes that utilise this energy to produce various cellular components like proteins and organelles. (Alberts et al., 2008).

At the same time, in the cell, not only is there a production of components, but there can also be degradation thereof. Protein complexes called the proteasome, for example, break down damaged, misfolded or otherwise obsolete proteins. These complexes play critical roles in protein quality control and other vital processes in the cell (Lehninger, Nelson and Cox, 2004). Also, the eukaryotic cell degrades long-lived, large, heterogeneous material through autophagy. Autophagy has two leading roles: 1) it takes cytosolic components to provide nutrients and energy during nutrient and/or energy deprivation periods; 2) it selectively removes cellular components, such as protein aggregates and dysfunctional or superfluous organelles, in order to respond to various cellular stresses, such as oxidative stress, organelle damage, or proteasome inhibition (Hoeller and Dikic, 2016).

Biological entities have a variety of interrelated elements, meaning they are interdependent. They participate in crucial processes, such as the generation or degradation of components, to maintain the organisation and good functioning of the biological entity, despite changes in the environmental conditions. Every biological element has a role which contributes to generating a complex web of mutual interactions, which, in turn, maintains the whole organisation and, consequently, the biological element itself.

One might think that talking about parts and wholes is limited to talking about composition. A primary idea is the question of what an entity is made of. Well, I say that an entity is made of its parts. A book is made of its pages. However, when we pay attention to biological objects, the question of what biological entities are *made of* is intimately related to the *activities of their parts.* This is because they produce their own parts and also eliminate parts. In a cell, for example, there are processes for synthesising proteins and degrading them.

In the biological context, the relationship between parts and wholes extends beyond the day-to-day idea of the composition we might have regarding other objects such as tables, chairs, or electronic devices. A biological whole is characterised by its constituent parts' interplay and coordinated activities. Recognising the integrated nature of biological systems enhances our understanding of their complexity and interactions among the elements. Biological entities are highly dynamic and interconnected, with numerous feedback loops and regulatory mechanisms. Each component within a biological system interacts with and influences others, contributing to the overall performance and behaviour of the system. These interactions can occur at various levels, from molecular and cellular interactions to interactions between organisms within ecosystems.

In the biological context, relations among entities are maintained over time. These are not random or arbitrary. These interactions' existence is not a trivial thing. Explaining the nature of these interrelations among different objects is essential to understanding how these various of entities are. Biological objects such as DNA, RNA, and ribosomes interact with each other and are not a simple non-specific arrangement. Still, they show sophisticated interrelations where these entities are integrated as a functional unity.

Therefore, the reasons why biological composite objects are worthy of examination separately from other composite things are: firstly, biological wholeness is self-regulated; secondly, these parts are involved in crucial processes of the whole, playing specific roles in the functioning and behaviour of the whole, generating and degrading its own components; thirdly, the characteristics of biological objects are not the result of the mere aggregation of the properties of the parts - the specific character and activity of the whole depend on the principle of self-organisation that regulates the interaction of parts; and fourthly, in biological objects, the interrelation between parts is crucial in the self-maintenance and self-organisation of the whole against the constant change of its environment.

Based on these characteristics of biological entities, we can see that the configuration of the relation between part and whole is given in changing conditions. So, to understand the nature of this relation in the biological realm, it is central to assess the conditions that allow biological elements to keep themselves integrated across time in different contexts.

Considering that biological scientists study these interactions: what entities, under what conditions are given, and how they are regulated. Scientific studies can provide helpful

information about the configuration between parts and whole, namely, how it is maintained or changed in response to internal and environmental conditions. In consequence, I shall examine this issue via synthetic biology, which characterises biological parts from an engineering approach, synthesising these parts and recomposing artificial biological entities such as genetic circuits or protocells. The synthetic biological work shows that the re-composition of an entity from standardised biological parts fails because these components display context-dependent interactions (Cameron, Bashor and Collins, 2014; Keasling, 2008), bringing several limitations and challenges. This approach will present many technical terms, which can be challenging to digest. However, examining these experimental limitations can show us - at least at a genetic and cellular complexity level - critical aspects of how a collection of biological elements can be interrelated in terms of parts and wholes in the living realm. By analysing the attempts of this discipline to design and construct new biological components, we can identify the possible conditions under which the interactions of a group of biological parts are maintained as a whole, despite frequent changes in their context. At the same time these limitations can say us what are critical aspects to evaluate the integration of biological entities in terms of parts and whole.

By assessing configuration conditions of relations between parts and whole, considering the work of synthetic biology, the investigation will focus on entities such as DNA, genomes, and cells. Even though I accept, as biological objects, the wide range of entities studied by biological scientists, this investigation shall centre on less complex components such as DNA, genomes, and cells. These entities play significant roles in biological processes, and their study provides valuable insights into fundamental aspects of life.

Cells, in particular, are widely recognised as the fundamental unit of life. They constitute the basis upon which all living beings are formed. This understanding arises from the fact that all living organisms, from simple single-celled bacteria to complex multicellular creatures like humans, are made up of cells. Cells serve as the fundamental units responsible for executing vital life processes. The consensus among scientists and a vast body of research in cell biology supports the perspective that cells play this crucial role. They display intricate molecular machinery, including DNA, RNA, proteins, and organelles, which work together to sustain life processes. The complexity of cells arises from the precise coordination and regulation of these molecular components. By studying cellular complexity, researchers can

uncover the underlying principles that govern cellular behaviour and understand how different cellular components contribute to overall performance.

Cells serve as a crucial nexus for de-compositional and re-compositional approaches to understanding life (O'Malley and Müller-Wille, 2010). De-compositional methods involve breaking down complex biological phenomena into their constituent parts, such as molecules, organelles, and cellular processes. Researchers can gain insights into the underlying mechanisms and functions within cells by studying individual components and their interactions. On the other hand, re-compositional approaches involve studying how these components come together and perform together. By paying attention to both de-compositional and re-compositional methods, researchers can effectively tackle the main objective of the thesis: that of understanding the configuration of parts and whole in the biological context.

Cells, as self-contained units, exhibit remarkable complexity and performance. They carry out vital processes such as metabolism, growth, and reproduction (Alberts et al., 2008). Scientists learn how organisms perform, evolve, and interact within their environments by examining cells. Cells, in particular, are considered the fundamental units of life, serving as the focal point for studying biological phenomena across various levels of analysis. Exploring these not-so-complex components enables researchers to unravel the intricate workings of living systems and deepen our knowledge of the biological realm's relations between parts and whole.

By focusing on entities such as DNA, promoters, plasmid, genomes, and cells, we can gain valuable insights into the configuration of parts and wholes within the biological realm. These entities play significant roles in biological processes, and their study contributes to our understanding of the fundamental aspects of life, paving the way for further exploration and discovery in the field of biology.

Additionally, studying these less complex biological entities within the biological realm can help us establish a foundation for understanding higher-scale biological phenomena. By unravelling the organisation and behaviour of DNA, genomes, and cells, we can explore the principles and patterns that govern the relationships between parts and wholes in more complex organisms and ecological systems.

The focus on biological objects rather than living ones is because, to date, what life *is* a question in debate. Therefore, this thesis will consider to be a biological object any object studied by biological practice.

It is necessary to assess the nature of the configuration of the relation between parts and whole in biology because a general view of concepts of parts and wholes may suggest a static or rigid view of objects. However, biological ones are constantly changing, adapting, and evolving. Thus, the dynamic nature of biological processes, including the constant exchange of matter, energy, and information, may be underrepresented, so it is necessary to examine how the conditions for this configuration between parts and whole can be maintained in dynamic circumstances.

2.6 Conclusions

In conclusion, the analysis conducted in this chapter yields several important insights. Firstly, examining metaphysical topics, such as parts and wholes, can significantly enrich our understanding of biological entities. By critically evaluating the metaphysical assumptions embedded within biological practice, we can uncover implicit views about the nature of these entities and their relationships. This, in turn, contributes to a more comprehensive understanding of the biological sciences. Secondly, the ideas of composition, parts, and wholes have significant implications for other key concepts in the philosophy of science and biology, such as levels of organisation, emergence, and biological individuality. The comprehensive understanding of under what conditions this relation can be configured in the biological context gives helpful antecedents to examine topics of interest in the philosophy of sciences and biology, namely levels of organisation, emergent properties, self-organisation, the elaboration of explanations and biological individuality. Thirdly, even though the this relation is linked with biological individuality concepts, the analysis of the notions of composition, parts, and wholes should not be limited solely to concepts of individual organisms, as there is no consensus on what entities should be considered biological individuals or organisms. Focusing only on organisms or biological individuals does not provide a comprehensive view of the possibilities of configuration of the relation between a biological whole and its parts in the living realm. Finally, complex biological entities exhibit a specific and flexible organisation, engaging in sophisticated interactions. Living wholes are relevant as study cases to assess the

composition relation because they are self-regulated and self-maintained through the production, degradation, and generation of their own components and specific responses to environmental changes. It becomes evident that the composition relation in the biological realm cannot be reduced to the mere aggregation of parts; it entails a deeper understanding of the dynamic interplay between elements to understand the configuration between parts and wholes. Studying biological practice reveals novel scenarios that offer valuable opportunities to explore the complex arrangements of the relations between parts and wholes.

This chapter has emphasised the importance of studying the relation between parts and whole in the context of biological entities. Through exploring biological practice, examining metaphysical assumptions, and considering various perspectives beyond individual organisms, we lay the groundwork for a more adequate understanding of the dynamics that underlie the behaviour and organisation of biological entities.

Chapter 3

Rethinking the relationship between parts and whole in Synthetic Biology.

3.1 Introduction

The previous chapter explored the concept of composition and its significance in the biological realm. Life scientists often analyse biological systems by considering the relationships between wholes and parts. For instance, biologists study how cells, tissues, and organs function together as a complete organism or how proteins and genes interact to carry out specific processes. These relationships between parts and wholes are crucial for understanding and explaining biological phenomena. However, it is noteworthy that these notions have been largely taken for granted within the biological field while receiving significant attention and debate in philosophy. Interestingly, as noted by Ladyman (2017), the philosophical discourse on composition has not been closely aligned with scientific knowledge of these objects.

Thus, this chapter aims to investigate the fundamental conditions that govern the relationships between biological entities in terms of their composition as parts and wholes. This investigation assumes greater significance when considering the intricate structures and

organisations that emerge in biological systems, which must adapt and sustain functionality despite environmental fluctuations.

To address this objective, the present chapter will examine the challenges encountered in synthetic biological practice. Synthetic biology, at its core, revolves around manipulating and assembling biological parts to create functional biological objects (Cameron, Bashor, and Collins, 2014). By comprehending the properties and behaviours of these individual parts, researchers can engineer them to collaborate synchronously, akin to assembling complex machinery from its components. Within the domain of synthetic biology, biological parts such as genes, proteins, and regulatory elements serve as building blocks that can be combined, modified, or re-engineered to construct synthetic biological systems exhibiting specific behaviours or performances. By exploring the limitations of experiments, we can gain insights into the crucial aspects of the relationship between the parts and the whole, particularly at the genetic and cellular complexity level.

To carry through this aim, firstly, I shall argue that a simple aggregation view on the composition relation is insufficient to give an understanding of the nature of this relationship in the biological world. Later, I will assess the main aspects of synthetic biological practices and their limitations. The analysis of the challenges of synthetic biology can illustrate key aspects of the composition relation because synthetic biology addresses this issue from an experimental perspective in its work of design, modification, and assembly of synthetic biological entities. The challenges of synthetic biology make us rethink —how integration is achieved and maintained in these systems. Compelled to expand our principles of integration, what are the principal aspects we must consider? What is the role of control and regulation in the configuration of relations in terms of parts and whole? this way, finally, I will argue that control and regulation actions make integration possible because they allow different processes to be carried out in time and place to correct errors and make possible a flexible and versatile performance of different components according to contextual conditions. Hence, we can understand integration as regulation-guided. This way, the integration can be stable against contextual changes due to control and regulation actions. They have restrictive roles and facilitate new possibilities of behaviour or performance.

3.2 Why rethink the composition relation from synthetic biology?

Intuitively, we can recognize that biological objects are much more complex than a mere set of elements arranged in a specific configuration. The reality of their composition is considerably more complex. Biological entities such as DNA, RNA, and ribosomes within cells exist not simply in an arbitrary arrangement but are intricately interconnected, functioning as an integrated unit. Therefore, a cursory analysis of the configuration of the cell's components reveals a striking difference from the assembly of a car or an electronic device. For example, various components, tools, designs, and instructions are needed to build a vehicle. It seems unreasonable to assume that the conditions required to create a car would be identical to those involved in forming a plant. The circumstances under which certain entities combine to make up a vehicle do not appear to share significant similarities with the conditions that govern the composition of bacteria, animals, or plants.

Even if all the necessary components for a car are present, a crucial distinction exists between the characteristics of a vehicle and those of a living cell. The functionality of a car relies on external control, such as a driver or an external control system, managing its parts, speed, and direction (Walde, 2010). Conversely, a living cell possesses inherent control over its own parts and functions. Within a living cell, all processes are regulated and orchestrated by the cell itself.

This disparity becomes particularly evident in the context of the development of synthetic biology[4]. Synthetic biology, as a field, aims to create and produce novel biological elements, including enzymes, genetic circuits, and cells, and even to modify existing biological systems (Keasling, 2008). A fundamental goal of synthetic biology is to characterise the constituent parts of these systems, synthesise them, and then reassemble them into an artificial

[4] Research practices such as synthetic biology display engaging scenarios to discuss philosophical topics. One area of exploration is re-examining concepts such as biological function and design, considering the advancements in systems and synthetic biology practices (Green, 2021). Another avenue for philosophical inquiry is the ethical analysis of the applications of synthetic biology products and technologies. Regarding the function concept, philosophers have delved into inquiries concerning how functions are defined and understood within the context of designing and constructing biological entities. In this context, functions are attributed to objects that arise from intentional design and human agency. Philosophers such as Krohs and Kroes (2009) have explored the challenges and implications of conceptualising the function notion in the context of engineered biological entities.

While acknowledging the philosophical interest in these issues, it is important to note that this thesis will not directly assess them. Specifically, the reference to a function or functional entity within this thesis will focus on discussing a biological entity's specific role and performance, in order to understand how biological elements are interconnected in a coordinated manner to make up a biological whole.

biological system. However, achieving this goal has proven to be far from simple. Its implementation presents numerous limitations and challenges.

Prima facie, one might think that following engineering principles, the knowledge provided by biological scientists, and good computational modelling would ensure the synthesis of biological objects. In principle, these scientists would have everything they needed to make a biological object successfully. They have well defined parts both in function and shape. They can predict the most suitable way to assemble components based on computational models. Thus, the configuration between parts and a biological whole would be given by the exhaustive characterisation and synthesis of the biological components and their assembly, guided by computer models.

However, by assessing into the goals and limitations of synthetic biology, we gain deeper insight into the nature of biological makeup. Synthetic biology's attempts to design and rebuild biological systems demonstrate that assembling biological entities is a highly complex process, not easily replicated through traditional engineering approaches. The challenges faced in achieving the goals of synthetic biology stress the intricate configuration of components within biological entities. Consequently, it becomes evident that the conditions and processes that govern the composition of biological entities differ significantly from those associated with artificial constructions such as vehicles or electronic devices.

Identifying and categorising car parts is crucial to knowing how components are assembled in the assembly process. All this is based on the instructions defined according to specific car designs. The design is central to assembling different elements to make up a particular object, with respective characteristics, because it provides instructions on how parts are placed and unified. However, is there something akin to a biological design for any life form in the biological world? This is an interesting question to analyse because when we think in the biological realm, there are no pre-established designs to follow.

The absence of pre-established designs in the biological realm makes this question particularly intriguing. Unlike human-made objects, biological entities do not adhere to blueprints or predetermined plans. Instead, the diverse characteristics observed in various life forms on Earth are the outcomes of intricate evolutionary processes. In the absence of a preconceived design, the development and ontogeny of living organisms rely on complex interactions between genetic information, environmental factors, and evolutionary pressures.

The blueprint for ontogeny emerges through a delicate interplay of genetic instructions, epigenetic modifications, and environmental cues, shaping the intricate development of an organism. This dynamic and evolution-driven nature of biological systems adds another layer of complexity to understanding how living entities come into existence and highlights the remarkable adaptability and diversity that arises through evolutionary processes.

Therefore, the conditions under which some entities make up a car do not appear to have anything significant in common with the circumstances under which other entities compose bacteria, animals, or plants. Why should we consider that the conditions to compose a car would be the same as those to compose a plant? Then, what conditions and processes make this configuration possible in the natural world? This is the question that we will try to answer through the analysis of the challenges and limitations of the practice of synthetic biology.

The difficulties of synthetic biology offer a unique experimental perspective on the relationship between biological objects. By evaluating this discipline's development and practice, we can gain insight into how biological entities are interrelated and how they come together to make up an object in the living realm. By analysing the challenges associated with synthetic biology, we can identify critical aspects that contribute to the composition relationship. Implicit assumptions about the composition relation are made when designing, creating, and manipulating biological entities, particularly with regard to the decisions made about which parts to use, how they are classified and positioned, and how they interact with other objects. A closer examination of synthetic biological research, including different approaches, objectives, and limitations, provides a valuable perspective on assessing the extent to which certain assumptions can aptly account for or, conversely, fail to encapsulate the nature of the configuration of biological elements in terms of parts and whole, allowing identity what would be the critical aspects of this configuration.

It is essential to analyse how a collection of entities that make up a biological entity work together as a whole, despite constant change. This analysis must consider how the unity of the whole's elements is possible, given that both internal and external conditions change, and in response, the interrelationships between elements also change. Going deeper into this question is crucial, as the mere assertion that the compositional relationship of an object "is not mere aggregation" does not sufficiently explain how this type of relationship operates in the biological world.

In the next section, I will expose an overview of what synthetic biology is and what constitutes its work in order to identify assumptions about composition relations and then explain its limitations and how they challenge these assumptions. Later, based on methodological strategies of synthetic biology scientists to face limitations, I shall argue that control and regulation activities are central to understanding not only how biological elements can perform in a specific way, keeping stability against perturbances, but also they are possible conditions for the integration of these elements, allowing the coordination, flexibility, versatility of this configuration of parts and whole.

3.3 Synthetic biology and its different practices and limitations.

Synthetic biology is a young research field that applies engineering principles to redesigning living systems or creating new entities featuring essential living characteristics. This research takes place across various levels of system complexity, spanning from individual functional modules within cells to complete cells, cellular communities, and tissues (Ivanov et al., 2021). From an engineering perspective, the idea of rational design is often promoted. This idea suggests that it is possible to assemble structures via replaceable and standardized components. Some synthetic biologists have adopted a similar vision in developing the synthesis of biological entities (Green, 2021). According to this perspective, the different layers of parts, devices, and modules of a computer, e.g., resistors, capacitors and transistors, integrated circuits and processors at higher levels, etc. are likened to biological molecules that interact through biochemical reactions, giving rise to biological devices and modules (Bölker, 2015).

Its origins can be traced back to the ground-breaking publication by Francois Jacob and Jacques Monod in 1961. Their study on the lac operon in E. coli provided crucial insights into the existence of regulatory circuits that govern a cell's response to its environment (Cameron, Bashor, and Collins, 2014). With the subsequent development of molecular cloning and polymerase chain reaction (PCR), genetic manipulation techniques became widely adopted in microbiology research, offering a powerful tool for engineering artificial gene regulation (Cameron, Bashor, and Collins, 2014). This technological advancement paved the way for effectively constructing synthetic gene networks in living cells, translating high-level functional specifications into the corresponding coding DNA sequences (Del Vecchio, Dy and Quian, 2016).

Simultaneously, researchers focused on enhancing computational tools that facilitated the sequencing of complete microbial genomes (Ideker et al., 2001; Jeong et al., 2000). As synthetic biology evolved, scientists began constructing simple genetic regulatory circuits, analogous to electrical circuits, to perform specific functions (Cameron, Bashor, and Collins, 2014; Del Vecchio, Dy and Quian, 2016). These circuits were further characterised using concise mathematical models (Cameron, Bashor, and Collins, 2014). To ensure the progress and standardization of synthetic biology investigations, researchers initiated international conferences to refine genetic systems engineering. By combining advances in molecular biology, genetic manipulation techniques, computational tools, and international collaboration, synthetic biology has grown into a multidisciplinary field that seeks to engineer living systems with precision and purpose.

This concise overview of the development and progress of synthetic biology makes it evident that the discipline has evolved in scope, goals, and aspirations, driven by advancements in theory, experimentation, and technology. Synthetic biologists have not only refined and perfected the tools, techniques, and predictive capabilities of design and construction but have also made significant contributions to our understanding of natural biological processes and their regulation, such as the DNA transcription process (Serrano, 2007; Mukherji and van Oudenaarden, 2009; Cameron, Bashor, and Collins, 2014; Green, 2021).

It may appear that with these remarkable technological advancements and the establishment of tools and mathematical models, synthetic biology has primarily sought to apply fundamental engineering concepts to design and to fabricate novel biological devices or systems with predictable behaviour. Consequently, the work of synthetic biology encompasses diverse practices that revolve around its core principles and methodologies.

The design and construction of synthetic biological objects form the focal point of an interdisciplinary community encompassing fields such as molecular biology, chemistry, physics, engineering, and computer science. However, this multidisciplinary nature presents a challenge in establishing a definitive and comprehensive definition that adequately encompasses all practices within synthetic biology. The term “synthetic biology” itself lacks a clear and universally accepted meaning (Schmidt, 2015). Theoretical and philosophical inquiries have therefore delved into questions surrounding the essence of this umbrella term and the existence of a common denominator. Despite the lack of absolute clarity, a

comprehensive understanding of synthetic biology's objectives, methodologies, challenges, and limitations can be obtained through a general analysis of its diverse practices.

By exploring synthetic biology's various approaches and techniques, we can discern common themes and recurring elements that underpin the discipline. While the specific manifestations of synthetic biology may differ across different scientific disciplines, the overarching goal of engineering and manipulating biological systems to achieve specific functions remains central.

In this way, although synthetic biology defies a singular and concise definition, it offers a comprehensive framework for understanding and investigating the design and construction of synthetic biological objects. By embracing the diverse range of practices within the field and examining their shared objectives and methodologies, we can develop a nuanced comprehension of synthetic biology's work and its challenges.

3.3.1 Synthetic Biology: approaches and methodology.

There is an interdisciplinary community working on the design and construction of synthetic biological objects. Many disciplines are involved in synthetic biology, such as molecular biology, chemistry, physics, engineering, and computer science. This interdisciplinarity brings with it the difficulty of establishing one definition that covers each of the practices appropriately.

It is crucial to consider various distinctions and classifications proposed by philosophers and researchers to better understand the work practices in synthesising biological entities. O'Malley (2009) and Deplazes (2009) have suggested different approaches within synthetic biology, each characterised by specific aims, methods, and constructs and differing positions on intellectual property and regulation.

O'Malley and colleagues (2008) categorised three approaches: *DNA-based device construction*, *genome-driven cell engineering*, and *protocell creation*. The main focus of *DNA-based device* construction is to design and implement distinct components in a modular manner, allowing for interchangeability and functionality. This method utilises gene synthesis and cellular techniques to fabricate DNA parts and combine them into larger functional systems. *Genome-driven cell engineering* operates at the whole genome level, employing both top-down

and bottom-up approaches. It involves minimal genome analysis, whole-genome synthesis, and the introduction of modified genomes into cells. Researchers break down design objectives into executable instructions, assembling smaller biological parts into larger devices and systems. *Protocell creation* aims to construct minimal cellular systems that approximate living cells. These systems, called semi-synthetic or minimal cells, consist of a limited number of components necessary for self-maintenance, self-reproduction, and evolution. The complexity of these cell-mimicking chemical systems has been progressively increasing over time.

Deplazes (2009) proposed additional categories, including *bioengineering* and *unnatural molecular biology*, which focus on the standardisation of biological parts and the artificial synthesis of DNA, respectively. The in-silico category refers to the computer science work designing biological entities.

While these classifications may not be exhaustive or universally agreed upon, they provide an overview of the aims and methodologies within synthetic biology. Understanding these categories helps to give a general picture of the field's interdisciplinary nature. With this foundation, we can research the design and assembly of synthetic biological devices, exploring how biological elements are configured to establish a composition relation, making a cohesive object. Next will be discussed how synthetic biological scientists carry out modelling, design, and assembly work in the construction of biological objects with different levels of complexity.

3.3.2 Design, modification, and creation of synthetic biological objects.

Most of the attempts of synthetic biological work are trying to create a synthetic biological object that is similar in shape, function, and behaviour to the original natural version. This aim is associated with the notion of *reverse engineering*, which involves comprehending the operations of a system in a backward manner through the examination of an existing system within its context (Green, 2021). This concept proves valuable in identifying general characteristics of system design, or *design principles,* that can be applied to new systems. There are also lines of investigation with a *forward engineering* notion. It involves the creation of novel synthetic biological entities with new functions, often by leveraging an established high-level model such as existing code or a living cell (Deplazes, 2009; Green, 2021).

So, the synthetic biological investigation has focused on two main dimensions in the last decade. 1) Efforts concentrated on discovering, creating, and characterising biological parts

and tools to develop these tasks. 2) Works dedicated to enhancing circuit complexity through the development of general approaches to combine available parts and modules to create more sophisticated systems (Purnick and Weiss, 2009). To carry out these objectives, the community of researchers has created a registry of standardised biological parts, in the form of the MIT' Registry of Standard Biological Parts (http://parts.mit.edu). The registry follows the standard of the "BioBricks" foundations in order to create, collect, and make publicly available standardised biological modules (O'Malley et al. 2008; Pade et al., 2015). Here, it is possible to find a significant number of parts and circuits, rapidly being added to. The building blocks in synthetic biology, referred to as *biological parts*, can be genetically encoded with specific biological functions in vivo. These functions can include a promoter sequence, an RNA aptamer, or a fluorescent protein (Wang, Wei and Smolke, 2013).

Standardisation, exemplified by initiatives such as the "BioBrick," presents an opportunity to establish compatibility among various biological parts and delineate engineers' assembly guidelines. By simplifying and standardizing the realm of biology, engineers can leverage pre-characterised parts to construct their own biological systems, bypassing the need for extensive research on each component or concerns about the intricacies of their assembly.

The concept of standardisation in synthetic biology aims to provide a framework that streamlines the design and construction processes, offering a repertoire of well-defined biological parts with known functionalities and characteristics. This allows engineers to focus on conceptualising and integrating these standardised parts rather than becoming entangled in characterising and assembling each component from scratch. Consequently, adopting standardised parts accelerates the development of new biological systems, facilitating the exploration of diverse functionalities and applications.

With established guidelines for part compatibility and assembly, engineers can confidently combine different standardized components to achieve specific biological functions, akin to assembling building blocks according to a predefined blueprint. This modular approach not only enhances the efficiency and reliability of the design process but also empowers engineers to create more complex and sophisticated biological systems by combining standardized parts in innovative ways.

Moreover, to produce a novel biological entity, synthetic biologists necessitate using biological devices. The concept refers to an abstract representation applied to physical

processes, facilitating the division of systems into essential functional components (Andrianantoandro et al., 2006). These devices represent biochemical reactions, which include transcription, translation, protein phosphorylation, allosteric regulation, ligand/receptor binding, and enzymatic reactions. Some devices may involve multiple reactants and products (for instance, a transcriptional device includes a regulated gene, transcription factors, promoter site, and RNA polymerase), while others may have only a few components (e.g., a protein phosphorylation device comprises a kinase and a substrate) (Andrianantoandro et al., 2006). Through the development of these devices, it becomes possible to determine: 1) the components necessary for synthesizing a particular biological object and 2) the types of devices that may be most suitable for specific biological activities and timeframes.

Within this framework, it is conceivable that biological systems can be designed and constructed akin to technical systems, particularly in electronics. This can be achieved by combining and integrating standardised and interchangeable modules, similar to how various components are assembled to create electronic devices. Synthetic biology relies on a collection of standardised components, such as amino acids, proteins, genes, circuits, and cells, which have undergone comprehensive characterisation. These standardised parts play a crucial role in achieving the synthetic biology objectives (Serrano, 2007). Furthermore, software modelling tools are crucial in assembling these parts to create novel biological functions.

The design and assembly of such other objects as a car, with the aim of a correct assembly working correctly and with predictable behaviour, is a relatively straightforward task. In vehicles, construction is possible along with defining diverse components, how they work together, and how the car will behave under various conditions.

From the abovementioned, it is possible to identify the following assumptions about making up a synthetic biological entity:

1) Standardisation: this assumption implies that by studying and understanding the individual standardised biological parts (e.g., promoters, coding sequences, terminators), we can predict and control the behaviour of the assembled synthetic biological object as a whole.

2) Modularity: A biological system, or synthetic constructs, can be divided into modular components or parts that can be combined and rearranged in different configurations to achieve desired functionalities. The synthetic biology framework relies on the assumption that

standardised biological parts can be treated as modular units that can be interchanged and assembled in various ways.

3) Compositionality: It suggests that the properties and behaviour of the whole synthetic biological object can be derived from the properties and interactions of its constituent parts. In other words, the characteristics of the assembled synthetic construct are the sum of the characteristics of the individual parts and their interactions within the system.

4) Engineering principles: The framework of synthetic biology assumes that living systems can be approached and manipulated using engineering principles, similar to how we design and construct non-living systems or machines. This assumption implies that biological systems can be rationally designed, optimized, and controlled for practical purposes. The activity of the whole is a product of the activity of its components.

Therefore, in an ideal scenario, the process of designing living systems for practical purposes would mirror the redesigning of a car to enhance its efficiency. Therefore, to achieve an adequate configuration between elements in terms of parts and whole would be enough, if we have the following requirements:

a) An appropriate design framework and robust mathematical and computational modelling, which can predict the behaviour of synthetic biological objects into the cell.
b) Access to a collection of standardised parts.
c) Assembly of the synthesised object with specific characteristics.
d) In the event that some part does not work, it can be replaced by a standardised similar part.

We can see that the main areas of work in synthetic biology are 1) design, 2) mathematical and computational modelling to predict operation and behaviour, 3) standardisation and categorisation of parts to ensure correct assembly, and 4) evaluation of synthesised objects in host entity (e.g., a cell). These areas involve work *in silico, in vitro,* and *in vivo* (see Figure 3.1).

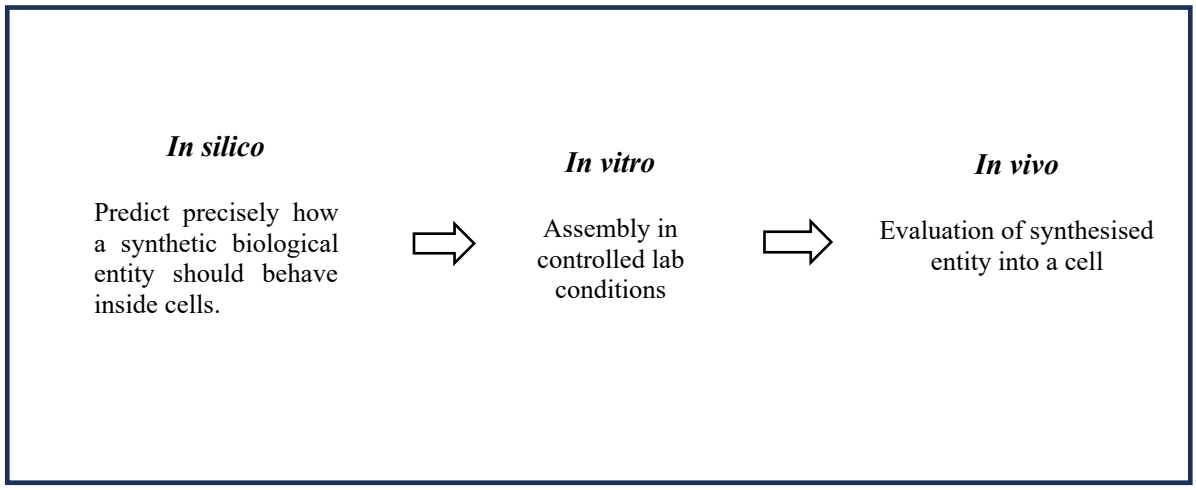

Figure 3.1. Schematic representation of different steps to synthesise a biological object.

Under this traditional engineering view, designing living systems for a practical purpose should be like redesigning a car to make it more efficient. We would have the parts, the right design, and good mathematical modelling to predict possible behaviours and create a new biological object with the corresponding characteristics. What could go wrong? The limitations that this practice faces do challenge the idea of the engineering view, as will be assessed in the upcoming section.

3.3.3. Limitations of synthetic biology practice.

Our knowledge is minimal regarding the diversity of life forms, including even the simplest. This limited knowledge of different life forms is, in significant part, due to the complexity and context-dependence that living entities display, these being important limitations for developing these aims of synthetic biology. So, the re-composition system failed because cellular components display complex and context-dependent functions.

What, though, are we talking about when we refer to context? Based on information in textbooks on Cellular and Molecular Biology and Cellular Physiology (e.g., Lodish et al., 2008; Sperelakis, 2012), in the cell, the context involves both internal and external conditions (see Table 3.1). Internal context pertains to fundamental biochemical mechanisms, including the management of DNA and RNA, levels of ATP, the production of proteins, and the regulation of cell cycle and division. Additionally, it encompasses specific processes like signalling pathways that play a vital role in the cell's interactions with the external environment. Within the cell, context also encompasses variations in physical conditions such as temperature and

osmolarity and dynamic changes in population density, diversity, and interplay. On the other hand, external context refers to the surroundings outside the cell, specifically the extracellular environment. Cells constantly interact with their surroundings, responding and adapting to changing conditions. These environmental factors, often challenging to precisely define and control, influence cellular behaviour and introduce unpredictability in engineered systems.

Internal conditions	***External conditions***
a) Genetic Information: Cells contain genetic material in DNA or RNA, which carries the instructions for cellular processes, growth, and reproduction. b) Metabolism: Cells have various metabolic pathways that enable them to obtain energy from nutrients, synthesise molecules, and carry out essential biochemical reactions. c) Organelles: Cells contain specialised organelles enclosed within membranes, including the nucleus, mitochondria, endoplasmic reticulum, Golgi apparatus, and others. These entities serve distinct purposes that actively participate in cellular processes. d) Cellular Components: Cells consist of various components, including proteins, carbohydrates, lipids, and nucleic acids, which play critical roles in cell structure, signalling, and regulation. e) pH and Ion Concentration: Maintaining proper cell pH levels and ion concentrations is vital for normal cellular function. Cells utilise ion channels and pumps to regulate the balance of ions across their membranes. f) Temperature: Cells have an optimal temperature range for their metabolic activities. Extreme temperatures can disrupt cellular processes and cause cell damage or death.	a) Nutrient Availability: Cells require a supply of nutrients, such as glucose, amino acids, vitamins, and minerals, to maintain their metabolic activities and support growth and repair. b) Oxygen Levels: Most cells require oxygen for energy production through aerobic respiration. Oxygen is obtained from the external environment or transported through the bloodstream to reach cells. c) pH and Ion Concentration: The extracellular environment also has specific pH levels and ion concentrations that can influence cell function. Variations in pH or ion balance can affect cellular processes and signalling. d) Temperature: The external temperature can affect cell function, especially for cells exposed to the external environment. Extreme temperatures can disrupt cellular processes and cause damage. e) Chemical Signals: Cell communication occurs via chemical signals, like hormones, growth factors, neurotransmitters, and cytokines, which can influence cell behaviour, differentiation, and proliferation. f) Mechanical Forces: Cells can be exposed to various mechanical forces, such as pressure, tension, or shear stress. These forces can impact cell shape, migration, and gene expression.

Table 3.1. Summary of main internal and external contextual conditions of a cell.

Taking into account these diverse contextual conditions, the question is whether the ideal engineering of constructing standardised and replaceable parts can account for the

complexity of biological entities. Biological systems pose unique challenges to this ideal engineering of standardisation and modular construction. Unlike engineered systems, living organisms exhibit a remarkable level of complexity and interdependence that cannot be easily reduced to interchangeable parts. The dynamic nature of biological entities, their ability to adapt and respond to changing environments, and the nuanced interplay between their components add layers of complexity that go beyond the traditional engineering paradigm. This issue will be addressed by examining how these characteristics of cells affect the three main areas of this multidisciplinary work, namely, design, assembly and prediction.

a) Design

One main task of the design of synthetic objects is the characterisation and standardisation of biological parts. This characterisation of biological parts also requires the predictable and reliable behaviour of synthetic cells in their environment (Bölker, 2015).

The characterisation of parts has presented a particularly challenging obstacle. In numerous instances, parts that were reasonably well characterised initially failed to demonstrate their expected performance when removed from the specific genetic or environmental context in which they were originally characterised, and they frequently failed to work correctly when placed into circuits with other parts (Cardinale and Arkin, 2012; Cameron, Bashor, and Collins, 2014).

While standardisation brings significant advantages, it also has its limitations. Biological objects possess inherent complexities that are not entirely captured by standardised parts alone. The dynamic nature of living organisms, their diverse and context-dependent interactions, and the influence of external factors introduce variables that can challenge the straightforward application of standardised components. Therefore, while standardisation is a valuable tool within the synthetic biology toolbox, it should be complemented by a deep understanding of the underlying biological principles to fully harness this discipline's potential.

This variety of coordinated interactions among a cell's elements evidences the intricate character of cellular networks. Recent scientific discoveries reveal that biological pathways are more complex than previously thought. Rather than following a straightforward path from one point to another, most pathways lack clear boundaries and often collaborate with multiple

pathways to accomplish different tasks. These tasks encompass genetic, metabolic, and signalling processes. Synthetic biologists face a significant challenge in creating a stable circuit within a complex network due to the multitude of interactions.

In this state of affairs, simplification, specification and standardisation facilitate the engineering of circuits or modules; this may not be advantageous, considering the host cell's complexity and context (Andrianantoandro et al., 2006). Attempting to design the activity of a synthesised module or circuit in isolation from the cellular context makes the definition of a module's or circuit's functioning and behaviour insufficient and limited. This situation challenging the assumptions related to engineer. Traditional notions from fields like computer engineering have espoused strict modularity and encapsulation as fundamental design principles. These principles allow components to be quickly composed plug-and-play while maintaining defined boundaries and interfaces. However, synthetic biology work limitations show a different scenario due to crosstalk between components and contextual effects.

b) Assembly

Ideally, when parts are assembled, those connections do not change when the module or circuit is integrated into a more complex network. Nevertheless, the parts can have multiple interactions with each other. This means that a particular molecule might participate in more than one pathway. So, the circuit's assembled components can begin to interact in relation to different paths unexpectedly.

Synthetic biologists and engineers encounter numerous challenges when attempting to assemble cellular circuits. The difficulty arises when a cellular circuit is designed, assembled in isolation, and inserted into a complex network of pathways. Predicting the circuit's behaviour within this intricate cellular network becomes challenging.

A major challenge in synthetic biology lies in developing standardised assembly methods that enable work across all levels of abstraction, including genes, pathways, and genomes. Equally important is understanding the intricate context dependencies that arise when different parts are physically juxtaposed (Ellis, Adie and Baldwin, 2011). Many synthetic devices are derived from naturally occurring systems. However, difficulty arises when attempting to construct modules using various wild-type devices, as these systems have been

optimised by evolution to operate specifically within their natural contexts. Consequently, when these modules are interconnected within an artificial context, their functionality may be compromised (Andrianantoandro et al., 2006).

The construction of synthetic genetic circuits often involves lengthy and ad hoc design processes, generating inconsistencies in predicting the performance and behaviour of created objects, particularly in less controlled environmental conditions. Context-dependence challenges assumptions of clear separability and modularity. Therefore, mechanisms for insulating and isolating parts from context influences become critical when integrated into larger systems.

b) Predictability

A significant challenge in this procedure involves the accurate prediction of the performance of simple devices in engineered cells, as well as the creation of systems that execute complex tasks with precision and reliability (Andrianantoandro et al., 2006). This limitation is due to various uncertainties. These uncertainties highlight the gaps in our current understanding of fundamental cellular properties. Issues such as random gene expression fluctuations, mutations, cell death, unpredictable external conditions, and complex interactions within cellular surroundings all contribute to the difficulty of effectively engineering individual cells with the same level of precision as designing specialised computers for specific tasks (Andrianantoandro et al., 2006).

Overall, lack of reliability, poor robustness, and the current incapability to anticipate potential behaviours of numerous interconnected genetic elements hinder progress in this area of investigation (Del Vecchio et al., 2018). Evidence of the challenge affected by the complexity of interconnections among the eukaryotic cell's elements is to be found in the difficulties of modular programming at the DNA level. Even though this modular programming is well established in synthetic biology, predicting its behaviour becomes more complex when we consider the panorama of layers of chromatin, alternative splicing, and post-translation modifications. This adds many different mechanisms for gene regulation over and above the basic transcriptional regulation programs used in bacteria and yeast (Ceroni and Ellis, 2018), and this only covers genetic pathways. The cellular scenario is more complex because metabolic and signal translation pathways are also carried out simultaneously. Biological

elements interact, leading to collective behaviours, modify, and create themselves to realise an autonomous self-fabricated, self-organised whole (Wolkenhauer and Muir, 2011).

The interaction network becomes more complex as each new component is introduced. Moreover, living cells may unpredictably alter their internal biochemistries to resist imposed changes (Elani, 2021). These characteristics present challenges in predicting the responses of re-engineered cells with novel functions. Changing circumstances make prediction a challenging task because they make it the case that the same gene circuit can have distinct behaviour in slightly different host cell strains (Endy, 2005).

The complexity of cellular pathways challenges both in terms of theoretical comprehension of the cell and in designing and synthesising intricate cellular circuits or entities. The vast number of components and dynamic regulatory processes operating within a cell's molecular machinery make it challenging to predict the precise outcome of engineering interventions with high certainty.

We might think that it is possible to categorise and characterise all possible contexts these synthetic biological objects can face, allowing us to preview different behaviours and connections among the devices' elements in each possible context. If we consider entities such as plants, they often face unfavourable conditions for their growth and development. Plants can live in diverse places with different meteorological conditions, and each one of these environments is constantly changing. To survive in these various environmental conditions, vegetal systems generate a response to the variety of inputs coming from their environment at the cellular level. Inputs might be humidity, dryness, heat, cold conditions, or pathogen attacks (e.g., viruses, bacteria, insects, or worms). Under these conditions, a plant cell generates a defence response (output). So, the cell produces a specific output for each input of dryness, cold, or pathogen attack. Then, from this perspective, we would expect that a plant, cell each time it faces the same stimulus/input, effects the same response/output.

Unfortunately, the issue is more complex. Research findings have demonstrated that the reaction of plant cells to the simultaneous presence of multiple stress conditions is distinct and unlike any other. This means that the response to inputs given simultaneously is not the sum of the responses that the plant cell makes separately to each input. The cell forms a new and unique response for two or more inputs. An example of this is when plants face both drought and heat stress simultaneously, their molecular response cannot be predicted merely

by studying their reactions to each stress individually (Rizhsky et al., 2002). The coexistence of different stress factors introduces considerable complexity. These combined stress responses are regulated by diverse signalling pathways, which may interact with and inhibit each other (Suzuki et al., 2014). This evidence shows that the behaviour and functioning of a vegetal system (vegetal cell) depend on the organisation of the whole network of interactions present in a specific space and at a specific time.

Although viewing the relationship between synthetic biological entities and their contexts in terms of input-output can be a convenient abstraction for design, the reality is that a biological perturbed system's response is undoubtedly dependent on its internal structure, i.e., it is embedded in the organisation of its self-maintaining metabolism (Bich and Moreno, 2016). So, the characterisation of the interaction of cells with the environment in input-output terms is limited and insufficient.

Regrettably, progress in biological engineering has been impeded by the inherent context-dependent nature of both basic parts and functional modules. Their intrinsic characteristics do not alone determine the salient properties of these components, which are instead also influenced by their interactions with surrounding parts and modules. In fact, the complexity observed in biological entities extends beyond their internal organisation and encompasses the intricate web of interactions they engage in with other living entities and their surrounding environment (Bölker, 2015). Unfortunately, the behaviour of individual parts and functional modules often defies predictability when operating within a complex cellular environment due to their dependence on context.

Based on the literature about the synthetic biology limitations, it is possible to characterise the limitations in different areas of synthetic work, namely design, assembly, and predictability (see Table 3.2). To sum up, considering the challenges and limitations faced in synthetic biological practice, it becomes apparent that the validity of the assumptions applied to design, assembly, and making predictions depends on the accuracy and completeness of the underlying biological knowledge and data used to construct the models and frameworks.

Limitations	Complexity	Context-dependence
Design	Synthetic parts and devices often fail to account for complexity.	Limited scope of standardisation.
Assembly	- Diversity of biochemical reactions. -Tedious ad-hoc assembly	-Synthetic circuit is not functional inside cell. -Tedious ad-hoc assembly.
Predictability	Many possible simultaneous interaction pathways.	Unpredictable behaviour of synthesised entity.

Table 3.2 Summary of main limitations in different synthetic biology practices.

3.3.4. How have synthetic biology scientists handled this complexity and context dependence?

The limitations encountered in synthetic biology research emphasise the significant role of host conditions in the performance and behaviour of biological parts. Host conditions refer to the cellular environment or organism in which synthetic biological components are engineered and operated. These host conditions can impact synthetic systems' efficiency, stability, and robustness, leading to unpredictable behaviours or limited performance. Several scholars have explored and emphasised the importance of understanding and optimising host conditions for successful synthetic biology applications (e.g., Kitney, 2009; Cardinale and Arkin, 2012; Freemont and Kitney, 2015).

Understanding and optimising host conditions is crucial for addressing limitations in synthetic biology. The behaviour of synthetic biological parts can be influenced by the contextual conditions already mentioned, namely cellular metabolism, protein degradation, transcriptional regulation, and interaction with endogenous cellular components. These inherent capacities of biological objects play a critical role in how their constituent elements are seamlessly integrated and coordinated, resulting in a cohesive whole.

These limitations show us an interesting scenario to evaluate.1) We have well-characterised parts (to ensure compatibility and interoperability) to assemble a whole (e.g., a genetic circuit or a promotor) performing a specific way. Then. It is introduced to a host biological entity (a bacteria), so this configuration of parts-whole is introduced to a new part/whole configuration (host). This new configuration displays a considerably greater number of elements interacting in different ways, carrying out different processes simultaneously.

So, not only this synthetic biological object should perform in the way the scientist wishes, but it should also integrate into this new configuration in such a way that in vitro performance is not altered. The main issue here is to characterize what makes something an integral whole composed of many parts. It is a challenge to ensure a scalable and reliable integration.

Indeed, researchers have been actively developing more sophisticated control designs and communication methods to overcome the limitations associated with host conditions in synthetic biology. Synthetic biology researchers work in mathematical modelling and novel feedback control strategies that enable more precise characterisation and regulation of synthetic circuits within the complex host environment (e.g., del Vecchio, Dy and Quian, 2016; Hsiao, Swaminathan and Murray, 2018; Qian and Del Vecchio, 2018; Boo). Scientists such as Del Vecchio Dy and Quian (2016) propose strategies and techniques for control design in synthetic biology, highlighting the need for rigorous characterisation and modelling of the synthetic devices, as well as the integration of control algorithms to optimise their performance.

Scientists in this field work on developing genetic tools, modular parts, and regulatory elements that enable precise control of cellular behaviour. Control designs have been expanded or directly implemented to enhance the reliability of synthetic genetic circuits in the presence of noise, decrease their susceptibility to genetic context variations, and improve their resilience when subjected to loading. Additionally, these control designs aim to ensure coordination across multiple cells within the synthetic system (Del Vecchio et al., 2018.).

Furthermore, via intercellular communication methods, scientists have researched ways to enhance the predictability and reliability of individual cells. Predictability and reliability can be achieved in two ways: statistically, by utilising a large group of independent cells, or by orchestrating the actions of individual cells (Andrianantoandro et al., 2006). By

employing intercellular communication, tasks can be coordinated among diverse cell populations, leading to the emergence of advanced and intricate behaviours (Andrianantoandro et al., 2006). Thus, the work in multicellular systems to achieve overall reliability in performing the complex tasks of a single cell can give better results.

Intercellular communication is fundamental in coordinating tasks across heterogeneous cell populations, thereby eliciting highly sophisticated behaviours. By leveraging communication mechanisms, synthetic systems can achieve enhanced coordination and collaboration among cells, improving overall reliability and performance when executing complex tasks (Yang et al., 2021). Consequently, the work in multicellular systems becomes paramount in attaining the desired level of reliability for the functioning of complex tasks, surpassing the limitations of isolated modelling, design, and assembly exercises that may prove insufficient in synthesising functional biological entities.

By applying these methodologies, researchers aim to achieve precise control over the functioning of synthetic devices, ensuring their desired performance and behaviour. This involves designing feedback loops, sensing mechanisms, and regulatory circuits that enable the system to respond and adapt to changing environmental conditions. Employing more elaborate control design methods, synthetic biology researchers strive to enhance the following areas:\

Reliability and predictability: These methods involve utilising mathematical models and control theory to accurately characterise the behaviour of the synthetic circuits within the host environment, making them less sensitive to variability within the host context (Del Vecchio, Dy and Quian, 2016). Researchers can optimise the system's performance and minimise unpredictability by gaining a deeper understanding of how the components interact and respond to various inputs.

Robustness to variability: Researchers are addressing this issue by developing control design methods that impart robustness to the system (Kumar and Hasty, 2023). Robust control strategies aim to ensure that the synthetic circuits exhibit desired behaviour and maintain performance despite variations in the host environment. By accounting for these variabilities and designing control systems that can adapt and compensate, researchers can improve the reliability of synthetic devices.

Characterisation of synthetic devices: Elaborate control design methods enable researchers to comprehensively characterise the behaviour of synthetic circuits, taking into

account both the intrinsic properties of the components and the influence of host conditions (Endy, 2005). This characterisation includes understanding synthetic devices' dynamic response, stability, sensitivity, and noise tolerance.

Feedback control strategies: Inspired by engineering control principles, researchers are developing advanced feedback control strategies to regulate and fine-tune synthetic devices. These strategies enable the system to monitor its behaviour continuously, compare it to desired specifications, and adjust accordingly (Qian and Del Vecchio, 2018). By integrating feedback control loops into synthetic circuits, researchers can enhance the system's ability to maintain desired behaviour despite external disturbances or fluctuations in host conditions.

Researchers have tried identifying and designing more robust control strategies that effectively orchestrate the assembled parts' behaviour and interactions by going into the dynamic interplay between biological components and the surrounding environment.

Synthetic biology scientists have recognised the need to carefully analyse and account for the intricate responses of biological objects to this complex and ever-changing context. They have acknowledged that a deeper understanding of control and regulation actions is crucial to achieving the integration of synthesised elements inside the host configuration performing the expected way.

Although computational modelling, considering control theory, has been helpful in improving the design and prediction of biological objects synthesised, there are still limitations. The efficiency of considering control and regulation action in reliability and performance prediction depends on what view about control is applied. For instance, the traditional control theory and engineering principles assume that environmental conditions and potential disturbances can be anticipated and accounted for in the design and implementation of control systems. This assumption works well in predictable and well-defined environments, where possible perturbations are known and can be modelled effectively. Their effectiveness diminishes notably in unstable conditions where unexpected pressures sporadically emerge (Whatcrare, 2012).

These limitations of synthetic biology stress the difficulties in integrating different elements performing in different ways simultaneously and how paying attention to control and regulation can improve this task. However, the improvements will depend on how control and regulation are conceptualised to moment to make computational models because our

understanding of many biological systems is still incomplete, and there may be unknown or poorly characterised components and interactions among them then an accurate mathematical representation can be challenging to develop when knowledge is incomplete. While control theory provides powerful mathematical frameworks, quantifying and formalising the multifaceted regulatory mechanisms in biological systems remains a significant challenge.

The efforts of synthetic biology scientists evidence how the configuration of elements in terms of parts and whole is not only a matter of having specialised biological parts in a specific arrangement; instead, but there are also more critical conditions that allow a relation that is stable and endures through time between parts and whole even though the complex interrelation among entities is context-dependant, which makes it variable. Thus, examining the limitations of synthetic biology practice provides us with the antecedents to define the essential conditions for what integration between the different elements can be kept across time.

3.4 Possible conditions of the relation between parts and wholes in changing contexts.

In composite objects such as chairs, tables, or cars, the configuration of elements in terms of parts and whole can be thought of as a group of things integrated in a specific way. This is an essentially correct view for composite objects such as bricks making up a wall or engine, fuel injector, wheels, seats, windows, and doors composing a car. However, this view appears overly simplistic regarding dynamic and complex composite objects such as biological entities, especially in light of the complexities discussed earlier. Hence, it is worth asking how biological entities can be related in terms of parts and wholes.

Undoubtedly, evolutionary processes play a central role in how different new life forms appear; among the living entities are many composite entities. These processes have allowed separate biological entities to become associated in terms of parts and whole, displaying a collective behaviour and performance. A paradigmatic example of this is the transition from unicellular to multicellular organisms. In a multicellular entity, individual cells work together in a coordinated manner and are either physically connected or positioned closely to facilitate strong interactions (Kaiser, 2001). So, evolutionary events have allowed that specific collection

of entities to become a further biological composite object - for example, mitochondria or chloroplasts uniting into the cell.

When entities are associated in such a way that they become a new biological entity, this displays a functioning and behaviour that is more complex. This transition involves creating fundamental connections among individuals and altering their roles as independent beings. The new entity in the living world means individuals engage in relationships that intrinsically bring about their transformation (Hernández and Vecchi, 2019). This means that one entity is a whole - mitochondria as free life- that becomes a part with a specific role in a whole - mitochondria as the cell's organelle.

This transition and transformation that some biological entities have undergone can establish such a relation of interdependence and coordination that the entities in interaction make up a new entity. The new entity is more complex and has sophisticated behaviour, given the specificity of labour. We can see this situation in lichens, which consist of the association between a fungus (mycobiont) and algae and/or cyanobacteria (photobionts). Within the lichen, there are optimal conditions for algae and/or cyanobacteria to carry out photosynthesis, through which sugars are generated that serve as food for the fungus. This symbiosis has allowed these organisms to colonize extensive areas. Scientists have distinguished numerous structural lichens from the simplest, where fungus and algae meet casually, to the most complex, where the mycobiont and the photobiont give rise to a lichen thallus. This structure is novel morphologically and more resistant, utterly different from either of the two organisms separately (Nash, 1996). In this last case, the symbiotic association relationship between these lineages (fungus and algae/cyanobacteria) gives rise to a new structure, namely, lichen thallus. In this interaction, parts (mycobiont and photobionts) cooperate to make up a new whole with its own structure and performance.

An association of simple entities does not mean the immediate composition of another being. It is not a question of an entity's members reuniting and interacting together to establish the existence of a new, more complex being. How different entities start to develop an interrelation such that they come to compose another biological object is a gradual process. In this, evolutionary conditions play a central role. Some evolutionary advantages in growth, feeding, or reproduction allowed that entity's collection to interact in a specific way to survive as a whole, unlike the previous free life forms.

One relevant point that both biologists and philosophers of biology can debate is the knowledge of when a collection of biological entities came to compose a new entity. The evolutionary process is gradual. Indeed, a major issue in the study of evolutionary events is defining the correct timescale over which to analyse the evolutionary process (Mestres and Arenas, 2017). This gradual nature of the process makes determining when there exists a new biological object challenging. Undoubtedly, this issue is philosophically relevant, especially in questions related to the definition of the organism and species concepts (see Clarke and Okasha, 2013).

However, regardless of this difficulty of establishing a defined moment at which a new biological entity is made up of entities that previously lived separately, many life forms have resulted from different evolutionary processes, and many of them are composite biological objects (e.g., eukaryotic cells, multicellular organisms, symbiotic associations as lichens). Evolutionary processes have played a central role in how biological entities organise and assemble with each other. The design of living entities has taken shape by the evolutionary processes that these entities undergo.

As a result of evolutionary processes, many different forms of life exist on the Earth, and they carry out specific processes related to feeding, development, reproduction, or survival. There are bacteria, fungi, plants, insects, mammals, and birds, being as the diversity of life is vast. Interestingly, even within each life form, there exists a remarkable variety of bacteria, fungi, plants, etc.

While an evolutionary perspective sheds light on how different biological entities can become integrated into a new whole, this perspective alone does not explain how the integration of these entities is maintained amidst constant environmental fluctuations. If we look at scientific practice, most of the efforts of both biologists and synthetic biology researchers are related to studying the different ways biological entities maintain the integrity and stability of their interrelation. Biologists and synthetic biology researchers strive to unravel the inner workings of these control and regulation actions through research and experimentation. By deciphering how different components interact, respond, and adapt within a system, scientists gain insights into the factors contributing to maintaining interrelationships despite environmental variability. Thus, we can better understand how biological elements can preserve interrelations in terms of parts and whole despite constant changes.

Therefore, in the next section, I shall argue the essential role of regulation and control in maintaining the integration of biological objects in terms of parts and whole. They are relevant not only in constraint and checking that a specific activity is carried out properly but also in allowing new performance possibilities, plasticity, and versatility.

3.5 Possible conditions of the biological integration: control and regulation.

The challenges of synthetic biology make us rethink —how integration is achieved and maintained in these systems. What are the principal aspects we must consider in the interrelation of biological parts in an integrated whole? If the control theory has been seen as of great help in improving the design and modelling, what would be the role of control and regulation in the configuration of relations in terms of parts and whole? What would be an accurate conceptualisation of control and regulation?

Indeed, synthetic biology, which aims to engineer novel biological systems by recombining natural parts, has exposed various limitations in our current frameworks for understanding how integration is achieved and robustly maintained in living systems. As researchers struggle to realise reliable, functional compositions such as genomic or transcriptional devices, it is compelling to re-evaluate how biological integration is.

As already we see above, the limitations of synthetic biology show the difficulties in integrating different elements performing in various ways simultaneously and how paying attention to control and regulation can improve this task. However, the improvements will depend on how control and regulation are conceptualised to moment to make computational models because our understanding of many biological systems is still incomplete, and there may be unknown or poorly characterised components and interactions among them then an accurate mathematical representation can be challenging to develop when knowledge is incomplete. While control theory provides powerful mathematical frameworks, quantifying and formalising the multifaceted regulatory mechanisms in biological systems remains a significant challenge. Hence, the effectiveness of this depends on the view about the control they apply in computational modelling. In previous sections was explained how, through control theory, synthetic biology scientists have counteracted, to some extent, the challenges that present the complexity and context-dependence of biological context. This highlights the importance of understanding the control action that defines how to configure the relationships

between the parts in different contextual conditions. The regulation ensures that the collective behaviours arising from the interactions of the components are precisely orchestrated and finely tuned. This approach aligns with the mechanistic view's emphasis on understanding biological phenomena by identifying the underlying components and the contribution to the phenomenon they produce.

Nonetheless, the mechanistic view's assumption of localised control mechanisms and linear causality oversimplifies the multifaceted nature of control. The properties of regulatory mechanisms like feedforward or feedback control, which are well-understood in isolation (Mangan and Alon 2003; Alon 2007), operate within large networks containing numerous overlapping mechanisms. This challenges the traditional mechanistic view that emphasises fixed structures and stable mechanisms. This underscores that control and regulation cannot be imposed simply or context-free, highlighting the complex and diverse nature of regulatory mechanisms within biological systems, where multiple feedback loops intertwine to enhance resilience, avoiding dependence on individual control elements (Whitacre, 2012).

Proponents of mechanistic explanations argue that network analyses ultimately depend on understanding the underlying mechanisms governing component interactions, suggesting that organisational patterns can be explained by integrating these mechanisms. However, how can the integration be given? New mechanistic inquiries have focused on examining the inner workings of individual biological mechanisms, often studying these under controlled and regularised conditions. Explanations about the integration of different mechanisms are not the main focus. They evaluate the control actions in isolated mechanisms, overlooking and failing to adequately recognise the significance of the distinctive features involved in how control operates within these systems (Bich and Bechtel, 2021). Indeed, philosophers such as Bich and Bechtel (2022) have often highlighted the simple conceptualisation of control as insufficient to explain how biological entities can be integrated and behave versatilely and adaptatively. Therefore, the mechanistic view would not be a proper framework to understand how the configuration between parts and whole is given in the biological realm. Its emphasis on components and *how they interact* can overlook the fundamental role of control and regulation as integrators that enable the harmonious and coordinated functioning of parts within a whole.

Contrary to strict modular decompositions, synthetic biology work suggests parts and wholes are more entangled and co-defined. This could support the philosophical view of process-oriented ontologies where parts/wholes are dynamically co-implicated. The *processual*

view emphasises the primacy of processes over static substances. In very general terms, this means that the existence of things is conditional on the existence of processes (see Seibt, 2022; Dupré and Nicholson, 2010). In this account, biological entities are not defined by immutable characteristics but are characterised by their dynamic processes, such as metabolism, growth, development, and evolution. These processes are central to understanding the nature and behaviour of organisms. It emphasises the contextual and relational nature of biological phenomena. Entities are conceived in terms of *what it 'does*.'

Nonetheless, the processual view has problems explaining the relationship of the processes with space and time (see Seibt, 2024), being essential in control and regulation activities. Regulation often crucially depends on the spatial positioning, localisation, and structuring of components across scales (e.g., gradients, compartments, and geometries). At the same time, temporal orchestration and coordinated timings are vital for regulatory dynamics, whether fast cycling feedback or developmental elongations.

Even though this view can more appropriately account for biological entities' dynamic, complex, and context-sensitive aspects, it emphasises their dynamic and changing nature; it can overlook the importance of structural and material factors in how biological processes are carried out. Regulatory dynamics are often tightly coupled to material constraints, forces, and physicochemical driving influences anchored in the spatiotemporal world in complex ways. For instance, specialised membrane proteins, like ion channels and transporters, determine the permeability and selectivity of the membrane. The structural features of membranes are essential for processes like cell signalling, nutrient uptake, and waste removal (Lodish et al., 2008).

Additionally, proponents of this view do not provide a convincing explanation of how the various material processes (e.g., genetic, physiologic, or metabolic) are related and combined (Seibt, 2024). This leaves the question of how integrating different processes is possible open.

Then, what would be the most appropriate ontological framework to understand the configuration of another part and whole in the biological context? What aspects would be having this ontology framework about the configuration of parts and whole? We can see that the mechanistic view tries to respond to *what* elements and *how* they interact. In the case of the processual view, the emphasis is on *what it does*. These views do not give a comprehensive picture of the nature of this configuration. Suppose a biological entity can remain stable against

contextual changes and adapt to them. In that case, it is essential to account for the when, where, and how long elements interact to understand the nature of the configuration between parts and the whole. To get an appropriate ontological framework of parts/whole configuration which considers all these aspects, it is necessary to pay attention to the role of control and regulation actions in facilitating the integration and coordination of multiple interactions occurring simultaneously within the biological entities.

The ideas associated with control and regulation are mostly restriction and limitation, checking how the mechanisms or processes are going on, ensuring stability, and maintaining homeostasis. However, the complexities involved in these re-engineered biological systems have forced us to reckon with our previous notions of how biological regulation and control actually work.

If we want to get a more accurate idea about control and regulation in the biological context, it is fundamental to shift the focus from identifying discrete "controllers" to understanding the provisioning of an integrative regulatory milieu that orchestrates diverse biomolecular processes into wholes while still allowing flexibility, plasticity, and selective response to disturbances. In this way, we can understand the integration in terms of regulation guided.

Understanding control as a restriction or constraint and regulation of how processes or mechanisms check that a specific activity is adequately done is a limited view. If control and regulation actions in biological entities are essential in responding to and adapting to environmental changes. In that case, we should focus on these aspects, considering them not from a restriction perspective but rather reframing our perspective from their role in allowing biological entities new performance possibilities, versatility, flexibility and selective capacity to respond to stimuli.

In scientific practice, biologists devote considerable efforts to understanding and analysing how control and regulation are given in the biological realm. Indeed, they study how the parts of biological wholes are configured in a changing environment with the above-mentioned characteristics. By paying attention to scientific information about maintaining the integrity and stability of the interconnected components within a biological system, we can understand how the control and regulation actions allow biological elements to be related in a stable, flexible and versatile way despite the ever-changing conditions.

a) Regulating interaction and keeping stability

Many processes are carried out in a cell, being essential to control and regulate them. Examples of crucial cellular processes are metabolism, photosynthesis (in plants, red and brown waterweeds, and some bacteria such as cyanobacteria), protein synthesis, cellular respiration, feeding, and cellular division (mitosis or meiosis). When and how these processes occur is not a random matter. Whether a gene is expressed, DNA is replicated, proteins or lipids are synthesised, or carbohydrates are metabolised, all are regulated in a sophisticated way. In any process executed in the cell, control activities verify each participating element's correct performance.

The car only functions appropriately if a driver or an external control system controls the car's parts, speed, direction change, etc. In the case of a living cell, the cell itself has control over all components and their respective performance (Walde, 2010). Non-living chemical processes occur depending on an available supply of free energy that is a matter of chance and independent of the processes it activates (Harris, 2004). In contrast to non-biological entities, a living object actively accumulates energy supplies. A process that illustrates this is the Krebs cycle. The physicochemical processes within this synthesise and store the substances which provide energy. The production of these substances is regulated; their release is in quantities appropriate to the needs of the total system for self-maintenance (Alberts et al., 2008). So, the processes are modified to adapt to changing external conditions, elaborating a response to these changes in a flexible way.

One example of this is the cell cycle regulation. This regulation involves a combination of intrinsic and extrinsic mechanisms that govern its progression. The cell cycle has different stages called G1 (cell increases in size), S (DNA synthesis), G2 (preparation to divide), and M (Mitosis) (Lehninger et al., 2004; Alberts et al., 2008). The process of cell division, whether starting or stopping, is initiated by external factors that impact the cell. These factors can range from something the death of a neighbouring cell to the release of growth-promoting hormones such as human growth hormone (HGH) (Lodish et al., 2008). Once the cycle has started, internal checkpoints regulate this. Checkpoints positioned after G1 and the initiation of G2 evaluate DNA integrity correspondingly before and after the S phase. We can see that interdependence is critical in coordinated behaviour and functioning and the specialisation of labour in elements that compose a biological object, such as a cell. Each of the cell's entities plays one or more defined roles. Some entities sense the environmental conditions. Others

transmit signals, and entities active or reprime the gene expression depending on the signal. Some entities check the proper development of processes, such as checkpoints at different cell division stages. If there are errors, entities such as ncRNAs repair them. Each process is highly regulated. Any action and interrelation among the cell's elements are active, repressed, or finalised according to specific conditions by other cells' entities. The systemic nature of biological regulation challenges the notion of clearly defined "regulator" and "regulated" components.

When these steps of regulation fail, this can have minimal effects or severe consequences for the cell. On the one hand, if multiple control actions govern a particular process, the failure of a single regulator may have minimal impact on that process. Alternatively, if a regulator is lacking or not working properly, it can have far-reaching consequences and potentially lead to cell death when numerous processes are impacted (Zampieri, Ganini and Melino, 2020). To illustrate this point, recall the DNA repair mechanisms and the regulatory action of checkpoints in cell division. If DNA repair fails, G2 checkpoints can detect DNA damage and abnormalities in spindle formation. In this scenario, the cell undergoes programmed cell death. Hence, the composite object - the cell - activates other control actions to disassemble the cell's components when it is impossible to maintain cellular conditions properly. Control and reparation are essential for the proper functioning of a cell. They allow response and stability in different contexts. Keep the integration of different components and their diverse performances.

To illustrate this, we seen processes such as DNA replication. During the replication, there are many repair and damage pathways. The process of DNA replication during cell division is susceptible to error. The rate at which DNA polymerase introduces inaccurate nucleotides while replicating is crucial in establishing the inherent mutation rate within an organism (Clancy, 2008). Consequently, DNA has mechanisms in place to repair and safeguard itself from damage. These mechanisms work diligently to eliminate or tolerate DNA damage, ensuring survival (Chatterjee and Walker, 2017). Besides errors by control mechanisms, the changing context can also be harmful to correct cellular performance. Biological entities manifest mechanisms which allow the repair of any damage to themselves that results from ordinary wear and tear. The environment can cause risky and harmful conditions. Skin cancer, a widely recognized instance of the connection between disease and DNA damage caused by environmental factors, can arise due to prolonged exposure to UV radiation from sunlight

(Clancy, 2008). However, it is important to note that hazardous conditions can also emerge internally. DNA can be adversely affected by oxidative damage resulting from metabolic by-products like free radicals. Studies suggest that a single cell may experience up to one million modifications in its DNA in a day (Lodish et al., 2008).

The preservation of cellular balance heavily relies on DNA repair and metabolic pathways. In regular cellular circumstances, DNA repair proteins play a crucial role in safeguarding the integrity of the genome, facing both external and internal sources of DNA damage. Cells initiate robust DNA damage response (DDR) pathways to effectively address DNA damage, ensuring sufficient time for specific DNA repair processes to eliminate the damage in a substrate-dependent manner physically (Chatterjee and Walker, 2017). This DDR is vital for maintaining the integrity of genetic material within cells, preventing mutations, and preserving overall genetic stability.

Therefore, control and regulation actions allow the coordination of the activities of different parts within a biological system. They ensure that various components and processes are synchronised and work together in a harmonised manner. This emphasises that the configuration of components is not only a question of *how it does, what it does* but also *where, when* and *for how long*. In this way, in multicellular organisms, control mechanisms regulate cell division, differentiation, and communication to maintain tissue organisation and overall organism development. Without these actions working properly, individual cells might undergo uncontrolled proliferation, leading to tumour formation and the disruption of tissue organisation. This phenomenon is well documented in cancer research, and one can find relevant references by searching for studies on the dysregulation of cell cycle control and its implications in cancer development (e.g., Dash and El-Deiry, 2004; Weber, 2007).

b) Context-sensitivity, flexibility and versatility

Cells' ability to respond in a specific way to diverse stimuli is crucial for adapting to different contexts. The context is not only related to particular conditions outside the entity—environmental context, for instance—but is also concerned with internal circumstances. This determines whether a response occurs and when it is carried out.

One process related to the response to external conditions is signalling transduction. Biologists define this process as the ability of a cell to change its behaviour in response to a

receptor-ligand interaction. Many specialised entities are involved in these kinds of processes. The process is initiated by cell surface receptors, which are proteins that interact with specific ligands. These receptors transmit signals to the inside of the cell. Typically, these proteins are found in the cell membrane and have two parts: an extracellular domain that binds to the ligand and an intracellular domain often chemically linked to a subsequent signalling pathway (Zubay, Parson and Vance, 1995). When a ligand binds to the receptor's extracellular region, it often causes a corresponding change in the cytoplasm, triggering a series of biochemical reactions known as signal cascades (Lehninger et al., 2004; Lodish et al., 2008).

Changes in metabolite levels can serve as indicators of internal conditions. The activity of metabolic enzymes can be influenced by fluctuations in metabolite levels, ranging from specific allosteric regulation to global transcriptional regulation (Lehninger et al., 2004). These changes can affect multiple metabolic pathways simultaneously and cannot selectively increase the flow of a specific metabolite. One example is the regulation of glucose metabolism. Glucose is a crucial energy source for cells, and its levels need to be tightly controlled to maintain cellular homeostasis. Different pathways are triggered depending on if glucose levels are high or low. The regulation of these pathways is not solely based on substrate concentrations. Instead, the flux through these pathways should be adjusted based on the current metabolic needs of the cell. This ensures that the cell's overall metabolic balance is maintained, allowing for the appropriate allocation of resources and energy (Wegner et al., 2015).

Cell components can also communicate amongst themselves. An example of this is the organelles' communication. Organelles within a cell must communicate and exchange information and metabolites (Soto-Heredero, Baixauli and Mittelbrunn, 2017). Recent investigations have evidenced intense crosstalk between organelles such as mitochondria and lysosomes (Soto-Heredero, Baixauli and Mittelbrunn, 2017; Todkar, Ilamathi and Germain, 2017). Due to this intense crosstalk between the organelles, one organelle's activity or stress status may affect another's. Direct physical interactions between mitochondria and the endolysosomal compartment have been observed as a swift method of communication between organelles. These interactions facilitate the exchange of lipids or other metabolites. Additionally, mitochondria-derived vesicles play a role in transporting superfluous mitochondrial proteins into the endolysosomal system, where they are either degraded or released into the extracellular space as exosomes. This communication is an additional quality

control mechanism for mitochondria and lysosomes, operating independently of autophagosome formation (Soto-Heredero, Baixauli and Mittelbrunn, 2017). We can see that the regulatory control architecture is not rigid but allows context-sensitive information processing that can dynamically alter the constraints and regulatory relations based on environmental inputs and state. So, control and regulation activities enable and facilitate various integrative processes in biological systems.

Additionally, these allow a selective response. Cells do not respond to just any signal or stimulus. Switch-off mechanisms exist to protect the cell from action against different conditions. Numerous signalling pathways are governed by "molecular switches" capable of deactivating a specific response if it proves detrimental to the desired cellular state (Lehninger et al., 2004). This may be achieved via several mechanisms. For example, it is commonly seen for ion channels that receptors may be desensitised to the ligand (Sperelakis and Kaneshiro, 2012). It is also possible to inhibit the information flow or stall the cellular response even after cellular detection of a given signal. The virtue of these mechanisms is ensuring that the cellular response is controlled.

Control and regulation not only play a central role in selective response to stimuli, but they also allow versatile behaviour or performances. In multicellular organisms, stem cells possess remarkable versatility. Through differentiation, they give rise to various specialised cell types. This process is tightly regulated by a complex network of transcription factors, signalling molecules, and epigenetic modifications (Orkin and Zon, 2008). Depending on the specific cues received from the surrounding microenvironment, stem cells can differentiate into diverse cell types, such as muscle cells, nerve cells, or blood cells, demonstrating their flexibility and adaptability.

This versatility and flexibility are not circumscribed to cells, we can see this control and regulation action in other biological systems. For example, epithelial tissues, such as skin and mucous membranes, demonstrate flexibility and versatility in the process of wound healing. This process involves a well-coordinated sequence of events, including inflammation, cell migration, proliferation, and tissue remodelling, regulated by various signalling molecules, growth factors, and extracellular matrix components (Gurtner et al., 2008). Likewise, ecosystems exhibit remarkable flexibility and versatility in response to disturbances or changes in environmental conditions. For instance, ecological succession, the process by which communities of organisms undergo sequential changes over time, exemplifies ecosystems'

flexibility and versatility. This process is regulated by various biotic and abiotic factors, such as competition, facilitation, disturbance regimes, and nutrient cycling, which collectively shape the composition and structure of the ecosystem over time. So, when a particular species population declines due to environmental stress, other species may fill the vacant ecological niche, ensuring the overall stability of the ecosystem. This process is regulated by factors such as competition (Folke et al., 2004).

This framework challenges notions of control and regulation, such as solely restrictive or constraining. Instead, it highlights their essential role in enabling functional versatility, selective response, and context-dependent adaptations. Therefore, control and regulation actions in biological entities should not be viewed solely on individual processes or mechanisms. Instead, we should consider their overarching role as integrative principles that orchestrate and harmonise the various interactions and processes occurring concurrently within the larger whole. This perspective expands the philosophical understanding of regulation beyond mere homeostasis and emphasises its contribution to adaptive behaviour.

The ontological framework about the configuration of parts and whole -both biology and synthetic biology work- should give a response not only to what (components), how (interact), or what they do but also to consider the spatial, temporal, and contextual factors.

The ontological framework in synthetic biology often focuses primarily on the ‘what’ (components) and ‘how’ (interactions). Existing modelling approaches in synthetic biology often focus on steady-state or simplified representations of biological systems. Nonetheless, the temporal and spatial aspects of component interactions, as well as their dynamics over time, are also important considerations. While these aspects may sometimes be considered secondary or supplementary, the discussed limitations above show that these aspects are crucial for a more comprehensive understanding and modelling of synthetic biological systems.

Hence, the initial focus on parts and whole may be on the components and their interactions, but this is insufficient. Whether it is wished for a comprehensive ontological framework or not, synthetic biology should aim to capture central integration conditions. For that, the framework of biological systems’ spatial, temporal, and contextual aspects enables more accurate modelling, simulation, and prediction of their behaviour (see Cooling et al., 2010; Jia and Schwille, 2019; Hardo and Bakshi, 2021).

Parallelly, this emphasis on the control and regulation dimensions of relation between a biological whole and its parts has particular relevance in philosophical discussions on emergent phenomena and downward causation, providing concrete evidence and examples to examine these philosophical topics. Considering this complexity and sophisticated relations between the whole's components, it is worth asking whether this relationship can display emergent properties. Indeed, the next chapter shall assess this possibility in the biological realm.

3.6 Conclusions

This chapter has highlighted the significance of control and regulation dimensions in understanding relations between parts and whole in the biological realm through examining synthetic biology work, its methodology, limitations and challenges.

Based on the analysis herein, several important conclusions can be drawn. First, this interdisciplinary research field provides an intriguing starting point for examining the composition relationship in biological objects. By analysing its objectives, methodologies, and challenges, we can gain an experimental perspective on how biological entities are interrelated and contribute to the composition of a whole. Evaluating the development and practice of synthetic biology offers valuable insights into critical aspects that influence the composition relationship. Second, the work in synthetic biology demonstrates that designing and assembling synthesised entities in isolation does not guarantee their behaviour and functioning in different contexts. Biological elements are not independent; they interact with each other and establish interrelationships based on specific conditions. The interactions between a collection of biological entities composing a whole are specialised and complex. Third, creating stable synthetic biological structures is challenging due to the ever-changing characteristics of living systems, the controlled temporal connections among individual components in a cell, and the exchange of molecules with the surrounding environment. Fourth, evolutionary events have played a significant role in allowing specific collections of entities to form composite biological objects, but this is not only perspective from which we can analyse how different biological entities are related in terms of parts and whole. Fifth, analysing this topic from synthetic biology perspective can give us valuable information about what key conditions are

under this compositional relation in given. Its limitations point out the importance of understand the conditions of the integration of different components, carrying out diverse processes in changing contexts. That way it necessary analyse what would be the proper ontological framework to understand the nature of this relation. The ontological framework, synthetic biology should aim to capture central integration conditions. Sixth, existing modelling approaches in synthetic biology often focus on steady-state or simplified representations of biological systems, addressing on the ‘what’ (components) and ‘how’ (interactions). Nonetheless, if we want account for the integration, the temporal and spatial aspects of component interactions, as well as their dynamics over time are also important considerations So, they should consider the 'when', where and for how long. Seventh, while the importance of control in the relationship between parts and the whole has been recognised in theoretical studies, synthetic biology offers valuable empirical insights that enhance our understanding of this relationship. By investigating how context can influence the behaviour and performance of parts, synthetic biology expands our knowledge of how conditions at the whole-system level affect the properties and dynamics of individual elements. Eighth, composite biological objects maintain structure and organisation despite constant environmental changes through sophisticated communication, control, and repair mechanisms. Control and regulation actions can detect and rectify errors, maintain proper balance, and prevent the propagation of perturbations throughout a biological whole. This contributes to the whole’s reliability and resilience, ensuring its adequate performance despite internal or external disturbances. Finally, in this realm, the organisation of complex biological entities is characterised by a specific and flexible arrangement of elements that engage in sophisticated interactions. The configuration of relation between parts and wholes entails dynamic relationships characterised by flexible behaviour. The elements within a whole act in a manner that preserves the composition relationship, adapting and adjusting as necessary.

Chapter 4

Relation between parts and whole and emergent properties in the biological realm.

4.1 Introduction

The concept of emergence holds significant importance in studying complex systems and for philosophical discussions surrounding the compatibility of mental causation and intentionality with physicalism (O'Connor, 2020). In this context, I aim to explore the relationship between a whole and its constituent parts, investigating how these parts interact and integrate to form a unified entity. This exploration is at the heart of the philosophical debate surrounding emergence.

The notion of composition, parts, and the whole is central to understanding emergent properties. The fundamental question is whether composite objects possess properties that emerge and cannot be explained solely in terms of their individual parts. In the previous chapter, I emphasised the role of control and regulation in shaping the relationship between

parts and the whole. Now, it is pertinent to inquire whether this role of regulation and control allows for the occurrence of emergent phenomena.

In the realm of biology, the emergence concept receives explicit mention as life scientists seek to explain specific characteristics of the phenomena they study. For example, ecological sciences delve into properties such as nutrient and energy flux patterns or resilience within communities and ecosystems (Konopka, 2009).

In this chapter, my primary aim is to analyse the concept of emergence within the biological context and define the nature of emergent phenomena. Specifically, I will examine these phenomena in biological systems and argue that their occurrence can be attributed to the unique organisation, performance, and control mechanisms inherent to such systems. In biological entities, emergent phenomena can occur. They can be epistemic (e.g., patterns), with it not being possible to predict a particular property or behaviour based on information about the whole's parts and its interactions. Additionally, there are ontological emergent phenomena like *robustness*. These are irreducible and have a global effect on an entity's parts through control and regulatory mechanisms. I shall argue that, based on these aspects, in biological entities ontological emergence can occur in a strong way.

In this chapter, I will assess and define the necessary conditions for the emergence of phenomena within the biological world, examining the hierarchical organisation, self-organisation, and control mechanisms prevalent in various types of biological systems, such as cells. Finally, it shall develop the reasons to accept the occurrence of emergent phenomena in the biological world.

4.2 Emergence in the sciences

The focus on the concept of emergence regained prominence in the 1970s when researchers found and developed complex non-linear systems encompassing both natural and artificial varieties (O'Connor, 2020). There is now a large recent body of literature developing accounts of emergence prompted by such systems. Indeed, philosophers analyse how emergent properties challenge reductionist approaches, ideas about causation, and explanations in different scientific domains.

With important scientific developments in disciplines such as quantum chemistry and molecular biochemistry, the popularity of the "emergentist" vision waned because the idea prevailed that it was enough to fully understand a "supposedly novel" behaviour or property with the knowledge delivered by these disciplines (see McLaughlin, 1992). The special attention to emergent phenomena in the scientific field is due, to a great extent, to the study of complex systems. These systems are often characterised as systems consisting of many elements that interact dynamically—a complex system that changes with time.

What reasons can we consider for complex systems displaying emergent properties? A complex whole is often dissected for analysis into ever more elementary parts and examined in terms of how they interact according to the given internal structure of the whole. It is challenging to show how particular component entities can give rise to certain specific relations. Although these relations are not random, the system's global behaviour is complicated to predict (Heylighen, Cilliers and Gershenson, 2017). The effects of such structures cannot be anticipated simply by knowing the components. Hence, examining the lower level is not enough to understand how the phenomenon is. It is also essential to analyse the structure at a higher level to understand the phenomenon.

Considering this, it seems that in these entities with complex effects, the phenomenon of emergence can occur. However, it is worth asking if this difficulty in predicting the behaviour of the whole from its parts might result merely from the methodological limitations when scientists study these entities. Would the non-possibility of prediction be enough to consider the possibility of the emergence phenomenon?

One of the issues that make this analysis complicated is that, firstly, the reference to the phenomenon of emergence occurs in various disciplines (e.g., physics, sociology or biology) and contexts. Each discipline brings its own perspective and nuances to the discussion, leading to diverse interpretations and definitions. Therefore, there is no unified vision of what emergence *is*. Generally, in science, a property is emergent if the parts of a complex system do not exhibit it on their own, and it is only possible at the collective level. In philosophy - as we already see above - the issue is more problematic, discussing whether a system's putative emergent property can be considered as such when it depends on the existence and action of its parts.

We can see that in science, the emergence concept is associated with the idea of new properties, patterns, or behaviours displayed at a collective level and not seen in the individual components. In turn, in philosophy, the debate is in what we define as *novel.* Under what conditions does a whole display a *new* property, behaviour, or pattern? Is this novelty present because is not possible to predict the property of behaviour? Is the new aspect an issue about whether or not the property is irreducible, or is it about whether the whole has a new causal power over its parts?

So, it is worth asking whether the phenomenon of emergence can occur in these systems, this being coherent under philosophical parameters. To address this question, I focus on the cell. The cell is an example of a complex biological whole, which - as I already highlighted in the previous chapter - displays sophisticated pathways and can respond to changes in the environment. However, despite its complexity, the reductionist view in cell biology has successfully provided detailed molecular explanations for many biological processes, contributing to significant advancements in our understanding of life. Why should we appeal to emergence to understand these entities? Considering these questions, I would like to discuss the possible conditions by virtue of which emergent properties can be given effect in this type of complex biological entity.

4.3 Conditions of the possibility of emergent phenomena in the cell.

In Chapter 3, I have highlighted the role of control and regulation in the configuration between parts and whole, allowing the biological entities to have the capacity to respond to a changing environment, maintaining the integrity of the system. So, in a biological object such as a cell, its parts are involved in different coordinated activities. This interrelation is not random but regulated through control mechanisms according to particular context conditions. This has been addressed in detail, emphasising the self-organisation and self-maintenance that these entities display. With this clearer idea about how the components of a biological system interact and how the system regulates these interactions, it is possible to evaluate the chance of emergent phenomena occurring in an entity such as a cell.

We need to define two main things to examine the possibility of the emergence phenomenon. Firstly, we should assess what we mean by emergent phenomena and identify the different types of emergences. Secondly, we need to understand the nature of control and

regulation in this context. Once these aspects are discussed within the philosophical context, we can evaluate whether the characteristics of these regulatory mechanisms create the conditions for the emergence phenomenon to occur.

4.3.1 Types of Emergence Phenomena.

What constitutes a genuinely new property, behaviour, or phenomenon? The concept of novelty is a central theme in the philosophical debate surrounding emergent properties. In the context of this discussion, some properties can be new in three main different ways: 1) predictability - a whole displays a new characteristic because cannot *predict* from its parts; 2) irreducibility - a novel property that possesses distinct characteristics that cannot be fully reduced to its constituent parts; 3) causal power, where the emergence of a novel property entails that the whole system exerts a causal influence on its constituent parts, often referred to as downward causation. This notion challenges traditional hierarchical views where causality flows solely from lower level components to higher level systems.

Which of these senses of novelty are valid to consider a phenomenon to be emergent? Well, an aspect to clarify this question is that there are different philosophical approaches to assessing emergence. In the literature, this concept is characterised in different ways. Scholars who have addressed the emergence topic generally concur that emergence theories can be categorised into two main groups, often referred to as *weak* and *strong* emergence. Weak emergence is often referred to as "epistemological emergence" in contrast to strong or “ontological” emergence (Bedau; 1997; Kim, 1999; Silberstein and McGeever, 1999; Clayton, 2006). Weak emergence is associated with the epistemic version of emergence; which states that a phenomenon is weakly emergent if it cannot be explained without crawling through the figurative lower level causal web of the underlying processes (Bedau, 1997). In turn, ontological emergence refers to the idea that emergent properties possess a distinct ontological status that cannot be fully reduced to the properties of the underlying components. Hence, it is related to the strong view because it emphasises that emergence is not irreducible and the whole has a new causal power over its parts.

While the specific labels and definitions may differ, this classification captures the overarching distinction in the field (see, Clayton, 2006; O’Connor, 2020). Considering and

accepting this division[5], we can decide what sense of novelty is adequate to apply and then define the possibility of the occurrence of emergent phenomena in the biological world, as well as determining if an ontological emergent phenomenon necessarily implies it is a strong one. The possibility of each of these options is analysed below.

4.3.1.1 Epistemic emergent properties.

From an *epistemological perspective*, an emergent phenomenon should not only be predicted from the system's elements. From *an ontological view*, the issue is not about predictability but irreducibility and causal power (Humphreys, 2016; O'Connor, 2020). Hence, an emergent phenomenon of a system is not reducible, and it affects the system's elements.

Epistemic emergence is a question of knowledge of the behaviour that can be gained regarding the whole from knowledge of the parts. In this type of emergence, the key issue is whether a property or behaviour can or cannot be predicted. Predictability refers to the extent to which the behaviour or properties of emergent phenomena can be anticipated or determined based on the behaviour or properties of their constituent parts. Therefore, if a property is non-predictable it can be considered emergent from an epistemic perspective because the emergent phenomenon would result from the limited ability to predict on the part of agents that study such systems (Humphreys, 2016). We can see that from this perspective, an emergent property is *novel* because the property is not displayed by the whole's components, it not being possible to predict the behaviour based on the parts alone.

Then, if we consider the aspect of predictability in the philosophical debate on emergent properties, we should see based on what kind of analysis the behaviour or property of the entity studied is not predictable. The examination of a whole can be on 1) components only. 2) components and their interactions 3) components, interactions, and context conditions.

If it is only based on the study of each component, presumably, this will be insufficient to predict the operation and behaviour of a complex biological whole. Someone might say that studying each part and their interactions would be enough. However, if the examined entity is as dynamic as cells, nothing indicates that the interactions that occur in an indicated space-time continue to be the same across time. Hence, paying attention to components and their respective

[5] Even though, within the literature regarding this debate, there more divisions, this analysis will focus on this categorisation, which has received more philosophical attention.

interactions and where they occur seems essential. This means specific locational and contextual conditions, organisational connectivity, and temporal contingencies (e.g., pH, Ca, Na concentrations, dispositions of macromolecules).

However, in this scenario, it can be claimed that predictability can be achieved if we have the necessary information on the complex entity, taking into account components, their interactions, and the circumstances in which these relations are carried out. By taking these factors into account, we can develop a more accurate prediction of its properties or behaviour. We can then predict the property or behaviour of the biological whole.

It is important to acknowledge that achieving predictability in complex entities, such as biological systems, is not as straightforward as suggested. While comprehensive information on the components, their interactions, and the surrounding circumstances can undoubtedly enhance our understanding, it does not guarantee accurate predictions of the system's properties or behaviour. Several inherent challenges and limitations undermine the notion of complete predictability in such systems.

As I have pointed out, biological pathways are not linear. In complex systems such as a cell, even a slight deviation in the starting conditions can result in substantial variations in the development of the entire system. If one cannot reach a satisfactory level of precision in knowledge of the initial conditions, it becomes impossible to predict the system’s behaviour. Hence, predicting such properties becomes increasingly complex, requiring an understanding of the system’s non-linear dynamics and the interplay between various elements. Thus, in non-linear wholes such as those in biology, small changes in the system’s initial conditions or parameters can lead to significant differences in the long-term behaviour of the system. This sensitivity to initial conditions makes long-term predictions in complex entities highly uncertain and difficult.

Biological wholes are subject to many internal and external factors that introduce significant uncertainty (as it was highlighted in Chapter 3). Internal factors, such as genetic variations and epigenetic modifications, contribute to the inherent variability observed within the cell. External factors, including environmental conditions and external stimuli, further amplify the complexity and unpredictability of these entities. Consequently, even with comprehensive knowledge of the components and their interactions, accurately accounting for

all these factors and their potential effects on the system's behaviour is a highly challenging task.

An example of an epistemic emergent property is *patterns*. These are the result of non-linear relationships that are unpredictable. *Patterns* can be related to spatial distribution, growth, and the flux of nutrients and energy. They can be related to behaviour, location, interconnectivity, or development. Simple non-linear interactions between large numbers of entities can lead to surprisingly complex patterns at the system level; often, unexpected *patterns* result even if detailed knowledge exists of the system's elements and their interactions (Camazine et al., 2003).

Patterns in biological systems cannot be predicted from a subset of parts and their interactions. To make a prediction, it is necessary to evaluate the whole system and the specific context in which certain system's conditions or self-organisation states sit. Does this mean that it is impossible to predict the behaviour and operation of a complex system at all? It does not. Simulation can be used to systematically study the rules governing components of boundary conditions under various network configuration parameters. The intricate nature of biological systems highlights the need for extensive parallel computation to predict global properties accurately. Computational modelling is a valuable tool for investigating complex entities, but it necessitates the consideration of numerous factors and variables in precise models and simulations. The complexity of the computational simulation closely resembles that of the entire system being simulated (Moreno, Ruiz-Mirazo and Barandiaran, 2011).

Computational models can simulate, for instance, gene regulatory networks to understand how genes are regulated under different conditions. Researchers can analyse how changes in these conditions impact gene expression patterns by incorporating several factors, such as transcription factors, DNA binding sites, and epigenetic modifications. These approaches acknowledge the complexity of the system and the need to capture the full range of factors that contribute to a particular behaviour.

Additionally, in this computational modelling and simulation, scientists apply probabilistic theory to make predictions (Groß et al., 2019). Probabilistic methods are often employed in computational modelling to capture and quantify uncertainty. Running simulations with varying inputs or parameters, scientists can obtain a range of possible outcomes and estimate the likelihood of different events or states. By incorporating uncertainty,

stochasticity, and probabilistic reasoning into models and simulations, researchers can make more robust predictions, quantify uncertainties, and gain deeper insights into complex systems.

Therefore, this possibility of making predictions does not necessarily dismiss the possibility of emergent phenomena occurring, for more than one reason. 1) To make accurate predictions about complex entities, scientists need to simulate almost the entire system and take into account many factors such as different context conditions. So, it is not an issue limited to components and specific interactions; rather, it is a matter of evaluating components' interactions occurring simultaneously with other interactions under specific circumstances. 2) There always exists the uncertainty of the accuracy of prediction. While comprehensive knowledge of the components, their interactions, and the surrounding circumstances undoubtedly enhance our understanding of complex biological systems, it does not guarantee complete predictability. Probabilistic models are also utilised to represent and analyse stochastic processes, where randomness and uncertainty are inherent.

This epistemic view of emergent phenomena is weak and relatively uncontroversial within pertinent philosophical discussions (Gibb, Hendry and Lancaster, 2019). This is due to it only referring to *the ability of cognitive agents* and their tools to predict the behaviour and functioning of the system studied. This type of emergent property within the metaphysical debate is considered less relevant because the main point is defining whether the property really exists regardless of the cognitive agent's capacity. Then, the most exciting questions in this discussion are: can emergent phenomena be a real property of a biological entity, or would emergent phenomena be limited to this epistemic sense only?

Philosophers of biology as Mossio, Bich, and Moreno (2013) have evaluated the concept of emergence in biological entities. Their proposed account of emergence sidesteps the epistemological issue and focuses instead on the ontological aspect. In their view, an emergent property is characterised by a unique set of relational properties that cannot be reduced to the constituent components of a property system. Whether the ontological irreducibility of a property is predictable or not does not alter its status as an emergent property, as the novelty arises from the novel relations among constituents (Mossio, Bich, and Moreno, 2013).

So, the crucial factor lies in determining whether these biological entities can exhibit a new property or behaviour that qualifies as an emergent phenomenon - a phenomenon which

is *a real* property, and it is not *novel* due to a lack of knowledge and abilities on the part of those who study a complex phenomenon.

Hence, in the next section, I shall evaluate this possibility of emergent phenomena from an ontological perspective, examining criteria such as irreducibility and causal power. The evaluation revolves around discerning the nature of this novelty—is it derived from new relations, as the authors contend, or does it stem from a new causal influence of the whole over its constituent parts? For this, I will consider the characteristics of biological systems already discussed, where parts' behaviour depends on both features of each element and the integrated whole of which these entities are part — this behaviour and interactions being controlled and regulated by sophisticated mechanisms.

4.3.1.2 Ontological emergent properties.

In the *ontological view,* the emergent phenomenon is not an issue of predictability. Rather, the issue is the possibility of the existence of an emergent property which cannot be reduced to the existence of its parts. If a property is ontological, irreducibility can be predictable or not. This does not change its condition of being an emergent property because the new relations affect a novel character among the constituents (Mossio, Bich and Moreno, 2013).

Recall that within the philosophical debate about emergence, the ontological account has been associated with the *strong* version of emergence, where an emergent property should be non-reducible and has *fundamental* higher level causal power over the parts; if the property accomplishes these requirements, it is a real property. On the other hand, *weak* emergence argues that emergent properties arise from the collective behaviour and interactions of lower level components without invoking new causal powers (Bedau, 1997).

a) Irreducibility in cells

To consider a global property as ontologically emergent, the existence of the property cannot be reducible to its parts only. Otherwise, if the reduction is possible, the components in isolation should function and behave the same as they do in their respective system. However, what

happens with entities such as cells, which - as we see in earlier analysis – can be seen to be self-organised and self-maintaining by the action of control mechanisms?

Within this context, some properties cannot be reduced to the elements involved by chains of interaction and reactions between elements, because the phenomenon involves a highly orchestrated, interlocking system of reactions, as seen in the synthetic biology work. The presence of numerous variables that interact in complex ways makes it impossible to simplify the behaviour by merely aggregating the properties of its individual components (Moreno, Ruiz-Mirazo and Barandiaran, 2011).

Properties of cell enzymes, for example, are not free but associated with different cell organelles such as membranes and cell walls. As a result of these interactions, the enzyme properties could be changed so that the behaviour of the free enzyme in solution would have little to do with that occurring under the structure of a multi-enzyme complex, free or bound to a membrane. Organelles can have positive or negative charges in such a way that the properties of these bound enzymes are qualitatively changed and display few similarities with those of the same enzyme in a free solution (Lehninger et al., 2004). It then appears challenging to conclude that the properties of an enzyme in a free solution are identical to those of the same enzyme in the living cell (Ricard, 2014). Hence, outside the system context, these elements do not interact in the same way and generate the same global properties. In the cell, every process is subject to context. Their functioning relies on the quantities of substrates and products present, as well as various factors within the cellular environment such as the local redox potential, osmolarity, porosity/viscosity/crowding, and temperature (Lehninger et al., 2004). Therefore, the specific structure of the organisation of a whole determines how and when particular interactions among parts occur in a biological system.

So also, the interconnection between different components of a biological pathway involved in signal transduction cannot be reduced. The behaviour of the pathway relies on a precise arrangement of proteins, enzymes, and signalling molecules, with specific activation and inhibition mechanisms. Disrupting even a single component or altering its regulation can have far-reaching consequences for the overall functioning of the pathway and its downstream effects within the system.

In this context, it is important to keep in mind that the philosophical discussion of the emergent phenomenon is not limited to irreducibility but also encompasses the causal effect of

the higher level on the lower level (downward causation). Thus, it seems essential to define what a *causal relation is,* in order to define whether or not it is possible to consider ontologically emergent phenomena and if they necessarily would accomplish this with the criteria of the *strong* perspective.

b) Causal power

Downward causation, also known as 'whole-part influence,' is often considered by many as the key characteristic distinguishing strong emergence from other forms of emergence. However, it also presents the most significant obstacle and point of contention in understanding and discussing strong emergence.

Analysing causality in the emergence debate is problematic because philosophers and scientists do not necessarily conceive this concept in the same way. In the context of biological entities, it is a hard task to establish causality because the relations are not linear. We might think of the causality in a situation like a stone impact and a window, breaking it. Hence, it is easy to define what is the cause, namely *the impact of a stone*. However, in the biological world, the situation is quite different. In linear relationships, changes in one variable are directly and proportionally related to changes in another variable. However, in non-linear relationships, the pattern of change between variables is more complex and can exhibit curves, thresholds, or other non-linear patterns. So, establishing causes in a similar way as the case of a stone impacting a window is presumably not possible.

Some examples of non-linear interactions can be seen in enzyme kinetics and gene expression. The relationship between enzyme activity and substrate concentration often follows a non-linear pattern. Initially, as substrate concentration increases, enzyme activity may increase rapidly, but as the substrate concentration approaches saturation, the rate of increase in enzyme activity slows down, eventually reaching a maximum plateau (Lehninger et al., 2004). The gene expression levels may respond differently to incremental changes in the stimulus, with threshold effects or non-linear amplification (Alberts et al., 2008).

No doubt, defining causal relations in this context is challenging. It is also necessary to examine if scientists talk about causes in the same way as philosophers do. In his book "Reduction and Emergence in Science and Philosophy," Gillett (2016a) examines the writings

of scientific emergentism. He points out that some scientists use the term *constraint* (see Freeman, 1999) or sometimes use the term *cause* (see Laughlin, 2005). However, even where these researchers use the notion of *cause*, it is charitable to interpret them as simply meaning "determine in some way" rather than using the term in the specific sense that philosophers assign to it.

The nature of causal relations lies at the heart of the ongoing debate surrounding emergence. An essential aspect of this debate involves clarifying the definition of causality itself. Questions arise about whether a more general and less stringent conception of causality is acceptable or if such a broad understanding would render the concept trivial and devoid of meaning.

This observation underscores the nuanced distinctions that exist between scientific and philosophical interpretations of causality. While scientists may employ causal language to describe relationships and constraints within complex systems, their usage might not align precisely with the more precise and rigorous understanding that philosophers bring to the concept.

Some scientists and philosophers of science argue that within biological systems, there exist various forms of causation, namely top-down, same-level, and bottom-up causation. So, the higher levels can possess their own causal effectiveness (see, e.g., Noble, 2008; Auletta, Ellis and Jaeger, 2008). Indeed, renowned biologists such as Humberto Matura, Francisco Varela (1975), and Robert Rosen (1991) have argued that biological systems display a special causal regime. This special regime will be addressed in the next section.

4.4 Biological causal regime.

Kim (1999) claims that emergent phenomena cannot possibly appeal to *physical closure*. This refers to the fact that the physical causes and interactions within the lower level are sufficient to explain all observed effects, challenging the possibility of emergent phenomena. Unlike this physical closure, some biologists and philosophers of biology have proposed the idea of *organisational closure*.

Organisational closure refers to the idea that certain systems, mainly living entities, possess a distinct organisational structure that enables them to maintain their identity and exhibit specific behaviours. Organisational closure suggests that the behaviour of a system is determined by the interactions and relationships among its components rather than being reducible to the properties and actions of its individual components.

Maturana and Varela (1991) put forth the concept of organisational closure, which sheds light on how a biological system maintains its integrity while remaining open to the flow of energy and materials. The biologists Maturana and Varela (1991) derived this notion from their extensive exploration of mathematical models of self-organising networks in the realms of cybernetics and cellular automata. It highlights the self-referential nature of living organisms, where the processes occurring within the system contribute to its own preservation and continuity. They define *organisational closure* as the intricate network of processes within a system, organised to enable it to self-produce (Maturana and Varela, 1975). However, the authors do not elaborate on how closure constitutes a causal regime that distinctly characterises a biological organisation.

In turn, Rosen's account of *closure* is based on a re-interpretation of the Aristotelian categories of causes, specifically focusing on the distinction between efficient cause and material cause. In his view, closure is primarily associated with efficient causes responsible for the dynamic processes and interactions within a system (Rosen, 1991). Efficient causes are associated with the mechanisms and processes that bring about change and produce specific effects. They involve the activities and behaviours of the system's components that contribute to the overall performance and organisation of the whole entity.

Nonetheless, one limitation of Rosen's account of closure is the lack of explicit guidance on identifying and understanding efficient causes within a biological system. While he emphasises the importance of efficient causes, he does not provide a clear framework or criteria for recognising and distinguishing these causes from other factors or entities within the system.

It is important to note that the concept of *organisational closure* has been subject to further development and refinement by subsequent scholars. Philosophers such as Mossio, Bich and Moreno (2013) have taken these ideas on *organisational closure* and have developed an account of the biological organisation. They provide a theoretical justification for emergent causation, asserting that the concept of emergent causal abilities can be consistently interpreted

as *constraints*. They maintain that the mutual relations between constraints depend on their involvement in the whole organisation. Within living systems, a subset of constraints is generated, which governs their internal processes and establishes a regime of closure constraints (Moreno & Mossio, 2015; Montévil and Mossio, 2015). This closure allows for specific developmental, metabolic, and adaptive processes, facilitating self-organisation, maintenance, and stability of the whole biological entity. The relationships between the elements of living systems produce and maintain each other through a network of mutual interactions. The whole system can collectively self-produce and self-maintain (Montévil and Mossio, 2015). In this account, an emergent closed organisation does not necessarily imply a strict causal relationship between the whole and its constituent parts in terms of upward or downward causation (Mossio, Bich and Moreno, 2013). Thus, causal relationships can be considered in many directions inside the regime's organisation, making the vertical perspective less relevant. This causal regime highlights how biological systems' elements are highly interconnected and mutually dependent and how the whole organisation controls its components through constraints.

Indeed, a way of understanding the causal power of higher-level properties in biology is to explain it in terms of *constraints* or *boundary conditions*. The idea is that the higher-level whole constrains the behaviour of lower-level elements that it comprises (e.g., Campbell, 1974; Emmeche, Køppe and Stiernfelt, 2000; Noble, 2008).

According to this scenario, is it worth asking what is the nature of these constraints in biological entities? In what directions do they exert an influence over part, vertically, horizontally or in many directions simultaneously? These constraints have a causal power and why constraints should have a causal power? All these questions shall be assessed below.

4.5 Constraints of biological entities

The constraint notion necessarily implies limitation. Crystal constraints, for instance, restrict what movements are possible among molecules. However, the control in biological systems seems to be more sophisticated. An example of this sophistication is the way eukaryotic cells compartmentalise, exerting spatial control over various essential boundary conditions that determine the environment in which their processes occur. These boundary conditions include

concentrations, contiguity, and permeability etc. (Lehninger et al., 2004). In order for the necessary boundary conditions to be present, and to avoid dispersion, the system relies on environmental scaffolds for spatial control, creating the required crowding for reactions to take place and achieving functional sufficiency (Bich, 2019). An effective control mechanism actively changes the rate of a specific event, reaction, or trajectory compared to unconstrained rates (e.g., catalysts) (Pattee, 1973). So, a constraint – in the biological context - is not limited to mere spatial control.

Some constraints imposed on neighbouring groups of cells, such as restricted spatial freedom, are evident constraints that originate from physical factors. These structural constraints can stop the growth and replication of cells due to overcrowding or insufficient food supply. However, *these* restrictions are not different from those present in growing crystals. As the group of cells expands, certain cell groups adapt their growth patterns depending on their positions within the group, rather than being solely influenced by external factors like the availability of food or space. In this case, the control constraint takes the form of a message or instruction that activates or deactivates specific genes within the individual cells (Pattee, 1972). Signalling transduction serves as an example of this phenomenon, as a cell can modify its behaviour in response to a receptor-ligand interaction. When it binds to the receptor, it triggers the production of additional molecules known as secondary messengers inside the cell. These secondary messengers then transmit the signal from one site to another, such as from the cell's outer membrane to the nucleus, leading to alterations in gene expression (Lehninger et al., 2004). Often, a cascade of changes takes place inside the cell, which results in a change in cellular functioning. The signal transduction pathway can amplify the cell's reaction to an external signal (Alberts et al, 2008).

As a result of constraints, the cell's components can interact, carrying out specific processes of synthesis, repair, and replacement of components of the system and generating its basic activities and behaviours. Biological organisms display a distinctive characteristic wherein the constraints and activities they restrict collectively maintain the conditions essential for a biological entity's survival (Bechtel and Bich, 2021). The system itself generates these multiple control mechanisms according to environmental conditions.

Undoubtedly, specific restrictions play a central role in controlling and regulating the interchanges between the various elements of the system. What, though, is the nature of these constraints? The constraint notion implies limitation. Complex systems are characterised by a

restricted range of possible states or reduced degrees of freedom options for changes in dynamics. This limitation confines the system's trajectories to sub-sets of the basic interactions (Hooker, 2013). Constraints, on the other hand, exert extra influence on the system, influencing its behaviour and contributing to its dynamic nature (Hooker, 2013; Winning and Bechtel, 2018). Therefore, they play a central role in the dynamics of the system.

In entities such as a cell, the constraints are flexible and variable. Such constraints do not *permanently* reduce the degrees of freedom—as the flexible restriction is changed, so too are the degrees of freedom left open in the controlled mechanisms (Bechtel and Bich, 2021). This flexibility allows that system to act on and change its own dynamical behaviour. Control mechanisms are also flexible insofar as they are sensitive to specific features of their medium and change their state accordingly. So, the reassociation between parts can produce a new interaction configuration between components and form new constraints in specific contexts. These control and regulation relations with other components' systems are complex, being established by a collective organisation requiring the whole system.

We can see that the interrelation among component elements is context-dependent. So, depending upon specific conditions, certain interactions are maintained or changed. Parts and their local interactions alone do not give a particular context. The organisation of a structured whole also determines how and when interactions occur. This determination is carried out through sophisticated control mechanisms that the same system generates. But this action provides sufficient reasons to accept the causal character of control activities and hence the occurrence of ontologically emergent property. To understand more comprehensively how the constraint action behaves, what is the direction of its influence and the possibility of emergent phenomena due to such activity, I shall analyse the hierarchical dimension of the biological realm.

4.5.1 Control actions and *hierarchy*.

Now, there is an important aspect of biological entities that has not yet been addressed to understand control and regulation processes: the idea of *hierarchy*. Based on what has already been discussed previously, we can see that hierarchical levels are part of the framework of the emergence discussion. We have a system divided into at least two levels: a "lower" level consisting of the parts, and a "higher" level, consisting of the whole system. The two levels

may be connected in the following two ways: 1) the parts of the system and their interactions on the lower level fully determine the behaviour of the entire system, or 2) otherwise, the higher level acts causally on the lower level, commonly called *downward causation*.

One central discussion is whether the ontological nature of a higher level is real or a heuristic construct for addressing complex phenomena. In the case that there does not exist such a thing as a higher level, the ontological emergence does not occur.

The ecologist Gleason (1926) rebuttals the idea of communities as real, cohesive wholes. For him, ecological communities are assemblages of species that coexist due to their individual ecological requirements and historical contingencies rather than as a result of any higher-level organising principles or processes. He argues that community boundaries are arbitrary and that communities exist on a continuum. Gleason's perspective highlights the difficulty in defining precise limits or boundaries of ecological communities.

But is this vagueness of ecological communities' limits enough to rule out the existence of them? This discussion recalls the debate about composite objects analysed in Chapter 1, where philosophers like Unger (1979) claim that there are no composite objects, only simple ones. So, a chair is arranged chair-wise. The central argument for ruling out the existence of composite objects is the vague boundaries. In this context, we can see that the issue is quite similar because contenders of higher level reality argue that the boundaries are not defined. Is the possibility of vagueness sufficient reason to rule out the existence of higher-level? As it was argued, there is a problem in defining what type of vagueness is (ontological, epistemological or verbal).

However, as it was argued, the nature of limits of boundaries depends on the object in question. The ontological, status of boundaries is not independent of the object of which they are borders. Biological systems are open, they flux of energy and matter. They change constantly through development or regeneration processes. A fix and static border is not accurate with the dynamic nature of biological entities.

Philosophers Jay Odenbaugh (2007) and Sterelny (2006) argue that we can accept the existence of communities or ecosystems despite vague boundaries. They recognise that the boundaries between communities or ecosystems may be blurred, transitional, or context-dependent in many cases, making delineating them as distinct wholes challenging. However, good reasons exist to accept ecological communities or ecosystems as a real whole.

Odenbaugh (2007) argues that some ecosystems have objective borders. He develops the case of a watershed. The boundaries of a watershed are delineated by the highest ridgelines surrounding the channels, meeting at the bottom where the accumulated water exits the watershed into larger water bodies like streams, rivers, or lakes. Within the confines of a watershed, the rates and patterns of nutrient cycling and energy flows tend to be distinct from the surrounding areas outside the drainage basin's borders.

Sterelny (2006) claims that community exists on a continuum, determined by the degree of internal regulation, boundary robustness, and emergent properties. This model suggests that the relationship between parts and wholes in ecological communities is rather a matter of degree, depending on the specific properties and dynamics of the community in question. Different communities may fall anywhere along this multi-dimensional space based on the degrees to which they exhibit these properties. The explanatory importance of treating it as a cohesive 'whole' depends on where it lies in this three-dimensional conceptual space.

These accounts, despite their differences, highlight how the boundaries should be analysed according to how the entity in question is and how it changes across time. The limits would not always have the same characteristics. Rigid notions of boundaries, which always require absolute precision or definiteness, potentially overlook biological systems' inherent fluidity and transformative processes.

Additionally, the attempt to resolve vagueness by appealing to lower-level entities introduces its own set of problems. If we accept that only lower-level entities are "real," we face the challenge of defining what constitutes the "lower level" in biological systems. This issue is particularly problematic because in the biological realm, what may be considered a lower level in one context can itself be a higher-level composite in another. This characteristic of biological organisation raises a fundamental question: How do we define the ultimate lowest level?

The problem becomes more acute as we consider potential candidates for this fundamental level. Would they be biomolecules like DNA or RNA? However, they are made up of atoms. So, would be this the proper lowest level? Additionally, there exist subatomic particles like protons or even entities like leptons. Hence, how do we define the lowest level? This dilemma remembers the philosophical problem of defining 'simples' (as discussed in Chapter 1), where there is no consensus on the criteria for identifying simple objects.

Moreover, this approach assumes that reducing biological phenomena to their smallest constituents will eliminate vagueness, but this assumption is questionable. Even at the quantum level, principles like the Heisenberg uncertainty principle introduce inherent indeterminacy. Thus, the strategy of appealing to a lower level to resolve vagueness in biology may be inadequate, as there is no consensus about the nature and definition of that level.

Regardless of this discussion, the hierarchical structure is an essential aspect of complex biological systems (Simon, 1962), the entities of one level being compounded into new entities at the next higher level (Mayr, 1982). This hierarchical arrangement is observable in biological systems, where cells join to form tissues, tissues assemble into organs, and organs come together to create functional systems. It is important to note that this hierarchical organisation is not limited to living organisms; it also exists in the non-living world—for instance, inanimate entities like elementary particles, atoms, molecules, and crystals. However, it is in living systems that hierarchical structure is remarkably significant. So, it is critical to analyse how biological hierarchy *is* in order to carry out a comprehensive examination of emergent phenomena.

The organisation of hierarchy in the biological context is a crucial aspect to consider. A prominent biologist, Howard Pattee (1973), defines the hierarchical organisation as a system encompassing multiple simultaneous activities involving structure and function. Pattee's work in theoretical biology, complex systems, and artificial life has provided valuable insights into hierarchical organisation. He distinguishes between structural and functional hierarchies (Pattee, 1969). *Structural hierarchies* are often characterised by graded sizes or the grouping of elements. For example, atoms, molecules, crystals, and solids can be identified as structural levels based on criteria of group and quantity. Each level consists of a larger collection of units from the lower level. Structural hierarchies exist in non-living and living matter (Pattee, 1972). In turn, *functional* or *control hierarchies* involve constraints. An example is the animal cell, which is constrained by external hormones (Pattee, 1973). This functional and control hierarchy is central to understanding the possibility of emergent phenomena occurring because it would explain how a higher level of control constrains the activity of components, generating new configurations and relationships between the elements constrained. For example, in a particular organism, the DNA sequences create a compilation of proteins, RNAs, and regulatory elements.

These regulatory elements enable the coordination of gene group expression (see Jacob et al., 1960). As a result, the genome functions like a database that can organise itself in response to signals from both the cell and the environment. However, the specific proteins and RNAs that will be produced, their timing, and their location are not entirely predetermined. Until triggered by transcription factors, DNA sequences remain inactive and unresponsive. Transcription factors are responsible for activating and deactivating genes, as well as other forms of epigenetic control. This control involves modifying the DNA region chemically and altering closely associated proteins at the gene's location (Jaenisch and Bird, 2003).

Consequently, epigenetic mechanisms appear to enable organisms to adjust gene expression in response to environmental changes. The combination of these mechanisms and cellular, tissue, and organ processes determines when and how they are utilised to regulate the genome. This is why multiple cell types can arise from the same genome; a heart cell, for instance, uses the identical core genome as other cells in the human body (Noble, 2008; Souza and do Amaral, 2019). Controls in cells may be executed by molecules, such as activators, repressors, or hormones, but the control value of these molecules is not an inherent chemical property.

One might argue that even though this functional or control hierarchy plays a central role in how lower level components carry out their respective activities, this does not necessarily mean that the whole acts over the parts, because control actions involve specific molecules or hormones that act to control a particular process. In other words, it is a *local* matter (e.g., the action of ligand or enzyme activity), so why consider it as an action of the whole over its parts? As such, the control exerted by these mechanisms seems to be localised rather than a global action of the entire entity over its constituent parts. Furthermore, even when considering kinetic and spatial control, the influence remains confined to specific regions or cellular compartments. Such localised control ensures that each individual process operates with precision and efficiency, without interference from unrelated elements. Therefore, the action of control and regulatory mechanisms is not a valid condition for what emergent phenomenon occurs in the biological context.

To respond to this objection, firstly, it is necessary to recognise that there is a vast variety of control and regulatory process occurring in the cell (see Bich et al., 2016). The control and regulation are not only generated by the *local* action of some molecules but rather, this activity is also controlled. Indeed, the control action can be of first and second order

(Aström et al., 2011). This means that not only is a process controlled, but also there is control of these mechanisms themselves. For example, in biological entities, the concept of second-order control can be observed in regulating physiological processes. Feedback loops involving hormones or neurotransmitters may not only modulate the primary process, such as glucose metabolism, but also adjust the sensitivity or response dynamics of the feedback system itself to maintain homeostasis.

As I have presented above, control in cells may be executed by molecules, such as enzymes or hormones. However, the control value of these molecules is not an inherent chemical property (Pattee, 1973). One of the most crucial control mechanisms is feedback loops, which can involve negative or positive feedback (Glass, 2005). A small perturbation applied to the system triggers a negative response that counteracts the perturbation in negative feedback. A single negative feedback loop performs the essential role of balancing changes imposed on a system. Many of the enzymes in the Krebs cycle are regulated by negative feedback, by the allosteric binding of ATP, which is a product of the pathway and an indicator of the cell's energy level. Also, the enzymes citrate synthase, isocitrate dehydrogenase, and α-ketoglutarate dehydrogenase catalyse high concentrations of ATP and inhibit the first three reactions of the Krebs cycle. This regulation stops this degradative cycle when the cell's energy level is good (Lehninger et al., 2004). The loop is generated because the output of the controlled process constitutes an input for the activity of the control constraint (Bich et al., 2016). Here, two loops' components of the controller and controlled system are coupled so that a particular state encompassing the two becomes stable and the system exhibits homeostasis around that state.

The local action is possible because it is found inside a specific configuration. Within cells, most enzymes engage in reactions where the reactants are produced through the combined influence of various constraints, including the membrane with its channels and pumps (Mossio, Bich and Moreno, 2013). These constraints are crucial in maintaining balance within the cell and regulating the interactions and relationships among different elements based on the specific context. This idea of constraint-based interactions implies that each component exists for the sake of the others, enabling the dynamic unit to achieve self-maintenance and self-regulation.

Are these actions of cellular control mechanisms sufficient to consider there to be *causal power*? According to some biologists and philosophers of science (see, e.g., Auletta,

Ellis and Jaeger, 2008; Maturana and Varela, 1991; Mossio, Bich and Moreno, 2013; Noble, 2008), these types of constraints have causal power in their own right. However, philosophers have their qualms about this, it being a profoundly problematic topic (see Section 4.2). Still, this conception, based on control mechanisms, seems to be more coherent than is sometimes assumed. Constraints and boundary conditions of a biological system (e.g., a cell) determine interactions among parts in terms of activation, silence, or change of frequency according to the system's requirements. This determination does not change component A's effect on component B. Instead, it determines the time at and duration for which this causal relationship occurs. Of course, it is possible that someone could accept the action of control and regulation, and at the same time can argue that this action does not necessarily indicate a causal character.

Although the causality aspect is relevant in the emergence analysis, my aim is not to elucidate a proper causal relation. Instead, I am interested in whether the whole's action on its parts - already examined in previous sections - is enough to make us accept that some global properties are emergent phenomena, regardless of whether the situation is considered causal or not[6]. In the upcoming section, I argue that there are good reasons to accept the occurrence of ontologically emergent phenomena due to the global action of control mechanisms on a biological whole's parts.

4.6 The possibility of ontological emergent properties. Control and regulation.

The action of control mechanisms can be considered not to be causal, but this does not imply that the effect or impact of the interrelation is less relevant. As we saw in Chapter 3, without the control and regulation action, a proper interrelation (being causal or not) between parts is rarely possible, and this is not limited to boundary conditions. The role is active, triggering or stopping an interaction.

Someone might accept that the effect of the whole is in terms of control and regulation but nonetheless argue that this action is a weak version of an ontologically emergent phenomenon because still there is a dependency on lower level component activities. As already mentioned above, strong emergence mostly is related to a *new causal power* of the whole over its parts. Well, here is an interesting discussion because is it really necessary to

[6] There is a largely philosophical debate on the nature of causal relations. The case of emergence has mainly discussed the possibility of downward causation. However, I will keep a neutral position regarding this, highlighting that biological entities' mechanisms of control exist and exert an effect on the activity of the entity's parts.

appeal to the causal dimension to accept a property as a strong version of emergence? This is an exceeding debate because, without a doubt, the causality idea is central to how entities are related to each other.

Even though we accept this globally controlled action over a whole's parts, there is an objection to considering it to be ontologically strong. This objection is styled 'collapse' by Taylor (2015)[7]. 'Collapse' refers to the fact that strongly emergent features can potentially be reducible ultimately to the underlying lower level features they depend on. This undermines the presumed causal novelty of strongly emergent characteristics in comparison to the base features. So, there would not have additional principles beyond those already implicit in the lower level rules. This is because all the information about the system, including its initial conditions and dynamics at the micro level, already encapsulates everything that can be known about it (Clayton and Davies, 2006).

Despite this, is every activity that occurs in the lower level only due to the conditions of this level? This can be true in some entities or systems (e.g., a system of gas particles). Nevertheless, biological beings are open systems; external constraints always operate on them. The internal controls defining a system are constantly disturbed by external ones. Can we evaluate these systems in the same way? It can be argued that even though we can recognise the difference between them in the degree of complexity and context conditions, still there exists the possibility these open biological entities "collapse". In other words, the response to environmental conditions of these systems is ultimately due to the actions of the whole's parts.

Hence, now it is relevant to assess if, effectively, the activity of lower level elements is due only to conditions of this level. Whether we accept those conditions depends exclusively on inherent parts' characteristics. So, it is correct to conclude that the conditions under which the different ways that parts' interrelations are given are due to the lower level.

However, in biological systems such as a cell, a relational network is organised such that its behaviour cannot be accounted for in terms of the inherent properties of these components. It is given by the coordination of several factors, for instance, constraints, activation, or deactivation of processes such as genetic expression, protein synthesis, or activation signalling pathways. So, this organisation involves various interconnected processes, such as metabolism, reproduction, and regulation, which work together to sustain the

[7] Similar objections have been stated by Kim (1999), Shoemaker (2007) and Van Cleve (1990),

organism's integrity and enable it to adapt to changing conditions. Indeed, at the core of organisational closure in biology are control and regulatory actions. They ensure that the various components and processes are carried out correctly, regardless of perturbations or changes in environmental conditions. Additionally, these actions allow the integration of different processes are carried out, defining when, where and for how long they occur. These aspects are not defining by intrinsic parts' properties Hence, the part's interrelations are conditioned to the whole's constraints and requirements.

In these types of entities, the self-organised, there is no central control. Global control acts depending on entities' requirements. These biological entities can regulate, amplify, activate, finish, and stabilise reactions or interactions among the system's components through control mechanisms. All this is in order to carry out self-organisation and self-maintenance processes. Therefore, looking at how control mechanisms affect the different biological systems processes is relevant to evaluating their performance and behaviour. Focusing on a given causal process as the phenomenon in question, marshalling the parts and operations that produce the phenomenon does not provide a comprehensive picture of the whole organisation and its maintenance.

This view takes a similar argumentative line to Santos's account (2015) on relational ontological emergence, which claims that even though every emergent property is instantiated by a specific kind of relational system, a cell, for instance, comprises various components, including the membrane, cytoskeleton, proteins, and nucleic acids, each possessing its own distinct properties, it is possible to consider emergent properties as ontological if we consider qualitatively transformative interactions between those constituents (i.e., the relationships between the components undergo qualitative changes that affect their properties), where the relational properties arise through such interactions. So, the putative emergent property does not derive form from the simple aggregation of lower level components and quantitative relations of their individual properties. It derives "…directly from the network of the transformative relations among the constituents" (Santos, 2015, p. 443).

I mostly agree with this account because an account for an emergent property depends on its components; it is possible to consider it as autonomous from an emergence basis because qualitatively lower level components can be transformed. Nevertheless, it is not completely clear how these network relations can transform components. This view can be complemented by taking into account the control action. Control mechanisms influence the coordination of

these relations between whole components. The regulation and control processes have already been described, specifically in the cell (e.g., feedback loops, pathway signalling, or repair mechanisms) allowing the network of transformative relations to be given. The organisation of a structured whole determines how and when interactions occur. This determination is carried out through sophisticated control mechanisms that the same system generates.

In biological objects, the various parts are engaged in coordinated activities. These parts not only contribute to the production of materials or the execution of specific functions within living entities, but also play a crucial role in creating conditions that enable other components to carry out their operations. This interplay of parts involves a complex network of interactions and control mechanisms that regulate different reactions and processes (Bechtel and Bich, 2021).

This is stronger than only considering properties not predictable or explained by lower level elements. Of course, this account does not attain the requirements of traditional *strong* emergence, where it is usually taken as emergent if there are new higher causal powers, powers that the lower level physical bases do not have (O'Connor, 2020), displaying a high level of autonomy as against its parts. Of course, in the cell, the control is carried out by the cells' components. However, the key aspect is that this component's activity is a specific way due to the whole configuration. The same elements in isolation and their interrelation would not necessarily be the same, so is not only an issue of the inherent characteristics of the parts. The control effect, causal or not, makes possible specific parts' activities. As was seen in the difficulties of synthetic biology, in numerous instances, parts that have been reasonably well characterised and design have shown that they do not guarantee how that parts interact and perform when removed from their original genetic or environmental context. When these parts were introduced into circuits alongside other components, they frequently failed to perform their intended functions accurately (Cameron, Bashor and Collins, 2014).

Additionally, someone can debate this idea, arguing that regardless of the importance and role of these types of mechanisms they are not causal, so this is not strong emergence at all, and therefore it is not possible that ontological emergent phenomena occur. Considering this position arise the question of why the causal power would be the definitory aspect to accept that the whole has a novel influence over its parts. By focusing only on the causal character in a strict sense (linear relation of cause and effect) we can dismiss relevant types of interactions between parts and whole and the whole and its parts. Whether the control action can or cannot

have causal power is another discussion. I consider that is reasonable to take the view that this action allows the occurrence of ontologically emergent properties because there is an effective and fundamental influence on the whole over its parts; this action is global and necessary for any type of part interaction possible. The *novelty* is given because these mechanisms allow new configurations between parts' interrelations, carrying out new processes and activating new pathways, bringing as a result new properties and behaviour in response to particular environmental conditions. The new configurations and interrelation between parts are achieved due to these control mechanisms, which sense any change in the context, activate processes, and regulate how they are carried out.

According to the assessment above, the high level displays an influence over the system's components, regardless of whether this determination has some causal power. The functioning and behaviour of a biological system depend on control and regulation mechanisms. In virtue of these, systems can sense and respond to perturbations and change inside the system and in its environment. Hence, control mechanisms are essential in producing the necessary components at the correct times and as needed, given external and internal conditions confronting the biological system. The behaviour of the parts is not the same in different wholes.

An example of this is gene expression. The cells of a multicellular organism are genetically homogenous, but the gene expression is not. Different genes are expressed in hepatic cells and heart cells. So, distinct proteins are synthesised because every cell type has its own requirements. Both hepatic cells and heart cells have similar components such as organelles, DNA molecules, and enzymatic complexes, but their functioning is different due to the context of each type of cell not being the same. The system's elements can do the work they do by virtue of how they are constrained. So, if a global property generates these control mechanisms on the system's elements and is irreducible, then it can be considered an emergent property.

Even though the control action on its elements is not accepted as *causal,* the control exerted by a biological system over the activity of its parts is a reasonable condition to define a phenomenon or property as emergent, regardless of whether it is a causal relationship. The global regulatory control architecture in biological systems is not rigid or static but exhibits remarkable context sensitivity and dynamic adaptability. This flexibility allows organisms to

process information from their environment and internal states and adjust their constraints and regulatory relationships to respond to context changes.

A property such as *robustness*[8] can be perfectly validly considered as emergent. A robust system can maintain its specific functionalities despite perturbations. Often, robustness is not an accidentally present, passive happening, but an evolved ability where the whole system actively responds to disturbances (Kitano, 2004).

In a robust entity, negative feedback is the principal mode of control that enables robust perturbation responses. This feedback contributes to the response to a wide range of stimuli, reducing its sensitivity to parameter variations and noise (Lehninger et al., 2004). In turn, positive feedback enhances robustness by intensifying the stimuli, often producing two stable states. As a result, the activation level of a subsequent pathway becomes easily distinguished from non-stimulated conditions. These distinct states can be sustained over time (Kitano, 2004). In this way, all biological systems rely on a specialised class of constraints that control processes related to specific variations induced by environmental perturbations and internal dynamics.

This property is emergent in an *ontological* sense because it is a real system feature. This status does not depend on the state of knowledge of cognitive agents or the degree of sophistication of the representational tools employed by agents. An emergent phenomenon such as *robustness* is irreducible to the activity of a set of the system's components. Besides, by control mechanisms such as feedback loops, the system's elements engage in new specific interactions to maintain stability against perturbations. This global property active control processes, senses and regulates how the system's elements interact with each other, allowing the system to keep stable against changes in its environment.

Some can say that this property is a higher level one but not is an emergent one, because can be reducible to whole elements and their respective interactions. However, a biological entity to achieve a robustness, it is not about a re-arrangement of components' interactions. Every process and new interactions are triggered by a global control and regulation action. The new interactions are not reducible to element properties. They are due to context-sensitivity,

[8] It is important to note that robustness does not imply remaining unchanged in response to diverse environmental stimuli. Instead, it entails maintaining the specific performance of the whole despite perturbations, often necessitating a flexible adjustment in the system's mode of operation (Kitano, 2004).

producing changes both quantitative and qualitative, is not a mere change in the arrangement of lower level's elements.

Some changes are:

Qualitative changes

1. Cellular signalling: Cells respond to various signals from their environment or other cells by activating or deactivating specific signalling pathways. These signalling events can lead to qualitative changes in gene expression, protein modifications, and cellular processes, such as cell migration, proliferation, or apoptosis.

2. Metabolic shifts: Depending on the availability of nutrients, energy sources, or environmental conditions, cells can switch between different metabolic pathways, such as glycolysis, oxidative phosphorylation, or fermentation. These metabolic shifts involve qualitative changes in the expression and activity of enzymes and the production of different metabolic intermediates.

Quantitative changes

1. Gene expression levels: Gene expression levels can change quantitatively in response to various stimuli or developmental stages. Cells can up-regulate or down-regulate the production of specific mRNAs and proteins, leading to quantitative changes in their molecular composition.

2. Metabolite concentrations: Metabolic processes involve the synthesis and breakdown of various metabolites, such as sugars, amino acids, and fatty acids. The concentrations of these metabolites can change quantitatively depending on cellular demand, nutrient availability, or environmental conditions.

3. Ion fluxes: Cells regulate the movement of ions (e.g., Na+, K+, Ca2+) across their membranes to maintain electrochemical gradients, membrane potentials, and cellular homeostasis. These ion fluxes can change quantitatively in response to various stimuli or during specific cellular processes (e.g., Berridge, Bootman and Roderick, 2003).

While individual biological components like genes, proteins, or metabolic pathways undoubtedly play crucial roles, the remarkable robustness of living systems cannot be solely attributed to any single entity. As an emergent property, robustness arises from coordinating and integrating myriad processes, feedback loops, and redundancies operating across multiple scales and hierarchical levels.

Cell stress response pathways represent an example of how robustness emerges from the coordinated action of multiple processes, feedback loops, and regulatory networks. Stress response pathways involve gene regulatory networks and signalling cascades that sense and respond to specific stressors, such as heat shock, oxidative stress, or nutrient deprivation (Dashek and Harrison, 2006). These pathways activate transcription factors that orchestrate the expression of stress-response genes, encoding proteins that protect cellular components, repair damage, or initiate adaptive responses.

Robust cellular functions rely on the concerted actions of gene regulatory networks, signalling cascades, and metabolic circuits that continuously sense, respond and adapt to fluctuations in the internal and external environments. These interconnected networks are replete with fail-safe mechanisms, such as genetic redundancies, alternative metabolic routes, and compensatory pathways, which collectively buffer the system against perturbations or failures in any single component.

Moreover, robustness manifests at higher levels of biological organisation, such as tissues and organs, where cellular populations exhibit remarkable collective behaviours. For instance, stem cell populations can replenish damaged or lost cells, while immune cells coordinate their responses to neutralise threats and maintain organismal homeostasis (Simons and Clever, 2011).

The robustness of the stress response does not arise from any single component or pathway alone. Instead, it emerges from the integration and coordination of multiple processes. As we already have seen earlier, integration and coordination are possible due to control and regulation actions. Indeed, different stress response pathways can crosstalk and influence each other’s activity, enabling cells to integrate information and coordinate response. In plant cells, the response to stress factors, for instance, the physiological processes, are regulated in a complex way by the crosstalk of several hormones (see Munné-Bosch and Müller, 2013).

Without global control activities operating at the whole level, individual components would function independently, lacking the necessary coordination and integration. Furthermore, they may not interact at the time and place required to respond to a particular stimulus. A control or regulatory action is necessary to trigger specific pathway interactions.

Indeed, the global control and regulation of a biological whole are responsible for orchestrating these regulatory responses, integrating information from different subsystems and modulating their activities to achieve the desired outcome at the level of the whole. By coordinating and regulating the activities of lower-level components in a cohesive manner, global control actions create the necessary conditions for the emergence of higher-level properties and behaviours that individual components alone could not produce. This global action is not only necessary, but also sufficient because it generates the essential possibility conditions, namely context-sensitivity, communication, reparation, coordination, integration, and new possibilities of interactions.

Without a global control action operating at the level of the whole, how do the individual components interact in a coordinated and integrated way in changing contexts? The coordination and integration are not a matter of component properties, but rather—as discussed in Chapter 3—they are an issue about when, where, and how long the interactions occur, that which depends on global regulatory activities.

Control and regulation integrate the activities of the lower-level components. Global control and regulation activities create the necessary conditions for the emergence of higher-level properties and behaviours; they do not depend on the capabilities of individual parts. Global control actions facilitate top-down regulation and integration, creating the necessary conditions for the emergence of higher-level properties and behaviours. By synchronising the actions of lower-level components, these actions enable the system to exhibit complex dynamics, adaptations, and functionalities that surpass the intrinsic capabilities of any individual part operating in isolation.

Hence, in complex biological systems, emergent phenomena can occur not only in epistemic terms (unpredictability) but also from an ontological perspective, where the whole's performance and behaviour are irreducible, and it exercises control activity on its components (see Table 4.1). Is this phenomenon limited to the cell? How widespread is the emergence phenomenon in the biological world? Firstly, this phenomenon - as I have conceptualised it -

occurs all the time in the cell. The parts' activity is context-dependent, so the control mechanisms are essential to generate a response and behaviour according to stimuli. Secondly, this capacity of control mechanisms is also displayed in other biological systems such as social insect societies. They also self-organise within a set of constraints (Bonabeau et al., 1997). Even though the global order in social insects can arise due to internal interactions among insects, it is equally relevant to consider external factors and constraints, all the more as the colony and its environment influence one another through interactions among internal and external factors (Bonabeau, 2001). Environmental factors acting as constraints or templates often play an essential role in determining the colony's displayed organisation (Bonabeau et al., 1997). An illustrative example can be the role of light. Darkness and daylight certainly influence activity patterns in most species of social insects and, for that matter, most animal species.

Ecological succession, for instance, is the process by which communities of organisms replace one another over time after a disturbance and display *robustness* in the face of perturbations (Turner et al., 1998; Walker and Del Moral, 2003). There are various processes involved in how succession in carried out. Among them are 1) pioneer species initiating the successional process by establishing themselves in disturbed or newly available habitats. 2)The presence of diverse seed banks, spores, and other propagules in the surrounding area in order to species recolonise. 3) Established species alter the environment's physical and chemical conditions, creating new niches and facilitating the establishment of later successional species (Walker and Del Moral, 2003).

In each of these processes, control and regulation activities guide the correct developments of them and their integration and coordination. For example, the control action integrates processes like soil formation, nutrient cycling, and the creation of microhabitats (White and Jentsch, 2004; Chang and Turner, 2019). It is also involved in the coordination of dispersal mechanisms, such as wind, water, or animal vectors, to ensure the availability of propagules at the right time and place (Chang and Turner, 2019).

Global control action in ecological succession lies in the integration and coordination of these processes, which can occur simultaneously, from the adaptations of individual species to the landscape-level dispersal of propagules. This integration ensures that the succession progresses in a proper way, allowing the establishment of resilient ecological communities after a disturbance.

To sum up, in biological entities, how parts are related to their whole and the whole to its parts make it possible that emergent phenomena can occur. Even though an emergent phenomenon is determined by the interaction of the system's parts, components' activities are mediated by highly sophisticated control systems, which can activate or deactivate reactions depending on particular contexts. Parts can relate to each other in ways not predicted by the properties of the parts but only by the specific whole system configuration that generates control mechanisms. So, some relevant properties of the system cannot be reduced to an aggregation of its parts. They are constrained to interact in a highly structured whole. I emphasise this point because saying merely that its parts determine the property of a system and their respective interactions is a problematic simplification when considering dynamic and open systems. Constraints and control systems are essential to how components interact in a flexible way. These tightly integrated and interconnected mechanisms enable cells to adapt, respond, and maintain functionality in a constantly changing environment.

Emergent phenomena in the biological realm	
Epistemological perspective	Emergent phenomena are not predictable from the parts' activities alone (e.g., growth patterns).
Ontological perspective	Phenomena (e.g., robustness) are irreducible to the activity of a set of components. The whole biological entity is able to control the activities of the entity's parts by the action of sophisticated mechanisms such as feedback loops, for instance.

Table 4.1. Summary of different types of emergent phenomena and their respective conditions.

So far, I have analysed the relation of biological entities in terms of parts and wholes and the possibility of emergent phenomena occurring. Now, it is pertinent to address the use of these notions in methodological and explanatory aspects of the biological sciences.

Several questions arise regarding this issue, such as how biologists use these notions to study biological phenomena. How widespread is the use of these notions? What types of living phenomena are explained through these notions? Does the reference to parts and wholes

necessarily imply a reductive explanation? What are the limitations of this use? What is the importance of these notions at the moment to communicate biological sciences content? In Chapter 5, I shall continue my investigation by addressing these questions in order to gain a more comprehensive view of relations between parts and wholes in the living world.

4.6 Conclusions

From my analysis, I can draw the following conclusions: First, in complex biological entities, the elements are organised in a particular and flexible fashion, participating in sophisticated interactions. Second, composite biological objects maintain their structure and organisation against constant environmental changes through sophisticated communication, control, and repair mechanisms. These multiple control mechanisms are generated by the system itself, according to the environmental conditions. Third, in the living world, talking about the composition relation refers to a dynamic relation, which has a flexible behaviour. The same whole's elements perform in such a way as to preserve the composition relation through the sophisticated mechanisms already mentioned. Fourth, these control mechanisms act as boundary conditions and constraints, which are not limited to merely reducing degrees of freedom of the dynamic trajectories of parts. They actively regulate the different activities of elements' biological systems. Fifth, constraints and control systems within complex biological systems facilitate flexible interactions among their components. These constraints shape the interrelations among elements and are heavily influenced by contextual circumstances. The behaviour and performance of these biological entities are intricately tied to their environment, highlighting the crucial role of contextual factors in shaping the dynamics and capabilities of biological systems. Control and regulation mechanisms in cells are highly dynamic and context dependent. They respond to various internal and external cues, such as environmental changes, stressors, or developmental signals. Finally, in complex biological systems, emergent ontological phenomena can occur. The whole's performance and behaviour are irreducible and exercise a control action on its components' activities. *Ontological* emergence, such as *robustness*, exemplify how the behaviour and performance of the entire system exert control over its components, whereby at the moment that there occurs some perturbation, sophisticated

mechanisms are activated to generate a response to perturbation. Regardless of whether the control action of the whole accomplishes the *strong* account's requirements, still, these phenomena can be considered *ontological*.

The examination made in this chapter highlights that understanding the relation of biological elements - between parts and whole - from the action of control mechanisms provides us with a reasonable framework on which to base acceptance that the biological realm can see the occurrence of ontologically emergent phenomena, which are given by coordinated relation configurations of the biological whole.

Chapter 5

Usage of parts, whole, and composition notions in biological sciences: Scope and limits.

5.1 Introduction

Our initial pre-intuitions about the entities surrounding us are in terms of objects composed of parts. It seems to be a basic and generalised assumption that we know how different entities are. Likewise, references to the composition idea are widely spread in biological sciences. Life scientists often analyse biological systems in terms of wholes and parts. Cell motility is examined by analysing the characteristics and interconnections of the molecules constituting the cells. The explanation behind the blood-cleansing function of kidneys is elucidated by understanding the properties and relationships among the cells that form these vital organs (Gillet, 2016b). So, these kinds of relations play an essential role in studying biological phenomena and developing explanations. However, as a basic assumption, this idea has largely

not been explicated. Hence, there needs to be more clarity - what does it mean that biological objects are composed of parts?

This generalised reference not only generates questions on the nature of the relation between a whole and its parts but also asks us how biologists use these notions at present to study biological phenomena. This chapter's primary interest is clarifying how these notions are used. What importance has the use of these notions in scientific practice? What is its role in the construction of biological knowledge? If the application of these concepts is varied, what are problematic consequences that these usages can bring?

Scientific research often expresses knowledge heavily contextualised within a particular system of interest, with its attendant methods, techniques, theories, and scientific questions guiding the spoken content of the concept. Therefore, detailing on the basis of what assumptions a phenomenon is studied helps to understand this context in methodological decisions, explanation elaboration and representation of the entities or processes investigated.

Considering all these aspects, this chapter's main aim is to characterise different uses of these notions in diverse areas of the scientific world, arguing that their usage has mainly *an organisational role*. The reference to these notions influences how we think about the living world and how life scientists' study, explain, represent, and communicate about different phenomena that occur.

All this is to define the relevance of this analysis and the role of parts and whole concepts in the scientific task of making sense of how the biological world is. It is unsurprising that scientists often reference parts and whole when they explain how biological phenomena are. However, it is necessary to examine the role in the different areas of scientific work so we can identify the possible problematic aspects that display this use. Then, we will evaluate how these problematic aspects of applying concepts of part and whole can create difficulties when communicating scientific information.

To carry out this task, I will evaluate what in ambits of the biological practice notions such as parts, whole and composition play a relevant role. This way, the chapter will focus on responding to two main questions. 1) In what domains of the scientific practice are these notions used? 2) What is the role and importance of part, whole, and composition notions in

producing knowledge about the living world? and 3) what are the challenges that can present this use?

This chapter will have the following structure: firstly, it will develop an overview of the scientific usage of parts, whole and composition notions in studying the living world. Then, it will make a detailed examination of the use of these notions and their respective difficulties in different ambits of scientific practice, namely, methodology, elaboration of explanations, representation strategies, and communication of findings. Finally, the characterisation of the usage of these notions in each ambit will be defined, offering the claim that this characterisation contributes to the philosophical understanding of scientific practice by examining basic assumptions about the living world.

5.2 Studying the living world in terms of *parts* and *whole*.

When we analyse the aims of science, we can think about issues such as description, classification, prediction, and explanation of a phenomenon. The sciences provide different approaches to the study of an entity or phenomenon. Each science studies phenomena based on diverse theoretical frameworks. Human beings, for instance, can be examined in terms of molecules, tissues, and organs, as living creatures, and as social individuals. Correspondingly, the field of philosophy of science delves into the philosophical assumptions, fundamental principles, and consequences of scientific pursuits (Hofmann and Holm, 2015). It also evaluates the diversity of methods in different sciences and how these methods achieve scientific aims (e.g., the understanding of a particular phenomenon) and what tools are available to meet these aims (Kampourakis and Uller, 2020).

Scientific activity has specific goals to achieve. Among them are 1) explaining a particular phenomenon (e.g., how ATP is produced in the cell); 2) defining the suitable research methodology (e.g., selecting and setting up experiments); 3) making predictions; and 4) designing new experiments to test those predictions.

In their investigations, scientists organise and analyse collected information to offer a possible explanation for a phenomenon. This is done with accuracy and is replicated so that empirical data will prove that the results are reliable and valid. Through experiments, observations, descriptions, comparisons, modelling, and theoretical studies, scientists address

their hypotheses regarding a specific phenomenon. The construction of scientific knowledge is relevant to analyse how information is acquired, compared and integrated. Actual scientific activity affects the structure of explanations within a scientific context, besides examining what characteristics of that context are most relevant in studying a particular phenomenon.

There are, within this context, some basic assumptions about entities and how they are studied. These assumptions help define parameters and criteria to the study specific phenomena of each scientific discipline. Of course, scientists do not analyse those assumptions. They are taken for granted. Their primary focus is on conducting research and advancing knowledge within the established boundaries of their discipline.

Here is where philosophical reflection can play a crucial role. By stepping back and examining the underlying assumptions, ideas, and conceptual frameworks that shape scientific practice, we can gain a deeper understanding of how scientific knowledge is constructed and what limitations or biases may be inherent in the process.

Philosophical analysis can scrutinise the ontological, epistemological, and methodological assumptions that scientists take for granted, questioning the very nature of the entities being studied, how knowledge is acquired, and the methods employed in scientific inquiry. This critical examination can potentially reveal blind spots, inconsistencies, or oversimplifications that may hinder our understanding of phenomena.

Among these basic assumptions is that *entities can be composed of parts*. Kauffmann, (1971), Wimsatt (1974), Bechtel and Richardson, (2010) have examined the common reference to this idea. They emphasise that a typical biological strategy is diving a system into parts and referring to it in terms of parts composing a whole. These notions are commonly applied in describing different objects in everyday and scientific contexts. Hence, it is worth a philosophical examination about the usage of concepts like parts and whole in the biological scientific practice, because these concepts play an essential role in elaborating methodological strategies and explanations. Questions such as how are they used in the biological sciences? Where are these notions applied? What is the importance of using these notions in knowledge generation about biological entities? What are their roles in biological thought?[9] What would be the problematic aspects of applying this assumption?

[9] This is not an attempt to claim that the usage of the composition relation notion is exclusive to the biological sciences. Of course, reference to visualising an entity as composed of parts is standard in other sciences. The

Science is a body of knowledge and a way of knowing. We should pay attention to scientists' ways of working to get a clearer idea of how they address their inquiries. Understanding the scientific conception of the living world is helpful. It is relevant in the attempt to make sense of the explanatory strategies, concepts, ways of reasoning, approaches to discovery, and problem-solving for biological phenomena by modern life science researchers.

The living world is diverse. Many life forms differ in physical features, size, anatomy, behaviour, and habitats. Hence, one of the central tasks of the biological sciences is to study and understand this living world. We can intuit that studying living entities involves researching complex structures and processes. To give explanations concerning these processes, it is necessary to analyse the diversity of interactions and relations between different living entities.

Biological scientists study the different life forms, their life cycles, and the different processes they carry out. Due to the living world's complexity and diverse phenomena, scientific enterprise calls for different approaches or methods. Under the biological sciences umbrella, diverse disciplines have their own research topics. Some of these are ecology studies, the interaction between living beings and the environment in which they live. Physiology deals with the functions and activities of life or living matter (such as organs, tissues, or cells) and the physical and chemical phenomena involved. Genetics refers to the study of genes and their roles in inheritance. Anatomy studies the structure and shape of such entities' bodies as plants and animals. Anatomy deals with the structural organisation of living entities, identifying parts and describing the structure and spatial organisation of the organisms studied (e.g., the muscles and bones of the human body). Likewise, histology studies the microscopic anatomy of biological tissues. In this way, biologists examine the size, shape, and structure of animals, plants, and microorganisms and their constituent parts' relationships—the arrangement of the parts of a plant or an animal, with a focus on the spatial disposition of parts.

reference is broad, for instance, in chemistry or psychology. In chemistry, for example, molecules such as H_2O are understood based on their components, namely hydrogen and oxygen atoms in this example. The interest of this chapter is in analysing in what dimensions of scientific practice the relation between parts and whole is used to get knowledge, examining this idea's role in the scientific understanding of biological entities.

As the living realm is vast and heterogeneous, in this study of different life forms, biologists categorise the living world on different levels. We usually consider biological systems to be layered: molecules, membranes, organelles, cells, tissues, organs, organisms, and communities. This organisation seems to give a coherent framework for thinking about the living world and interactions between diverse life forms.

5.2.1 Organisation of the Living World.

In the biological sciences, textbooks begin by highlighting the considerable diversity of life forms and how they are organised. So, we have things assembled with things to form new, more complex things, displaying a hierarchical order. The living world is presented as having levels of organisation, described in these terms:

> To enhance their understanding of nature, scientists classify matter into levels of organisation from atoms to the biosphere. Ecologists focus on organisms, populations, communities, ecosystems, and the biosphere (Miller and Spoolman, 2011, p.52)

Each level would be composed as follows:

> The term population include groups of individuals of anyone kind of organism. Likewise, community […] includes all the populations occupying a given area. The community and the non-living environment function together as an ecological system or ecosystem (Odum and Barret, 1971, p.5).

Firstly, this reference to levels of organisation is a helpful way to visualise the natural world and our own bodies. Subatomic particles compose atoms, which compose molecules; cells compose tissues, organs, and organisms; interbreeding organisms compose populations, and so on.

These descriptions highlight that a specific way to conceive the biological world is throughout levels of organisation hierarchy. These levels of organisation hierarchy are nested. This means that each level is made up of groups of lower level units. In this manner, populations are composed of groups of organisms. A community consists of a population group and so forth, indicating a hierarchical structure of levels of organisation based on part-whole relations. This hierarchical structure entails wholes at a particular level which serve as parts at subsequent

levels, including all higher levels (Wimsatt, 1994). Furthermore, parts within the same level collectively contribute to forming higher level entities.

In this way, the living world is presented as nested compositional hierarchies. Most things studied in biology consist of parts or components, and those parts themselves also consist of parts (Eronen, 2021). We can see clearly reference to parts of whole and composition notions. These notions explain how these levels are and how they are connected.

Understanding biological systems in terms of parts at various levels of organisation and providing some sort of guide to study the diverse biological phenomena, scientists pay attention to the phenomena characterising each level of organisation under study. So, cell biologists study the cell's structure, behaviour, and functioning. Population ecologists investigate how and why populations change over time.

If we consider a discipline such as ecology, its textbooks frequently explain that this discipline studies the interaction between living beings and the environment in which they live. They analyse how organisms interact with other organisms and their non-living (abiotic) environment, namely soil, water, other forms of matter, and energy (Miller and Spoolman, 2011). Examining this, ecologists seek to explain issues such as interactions, interrelationships, behaviours and adaptation of organisms, and the movement of materials and energy through communities or the development of ecosystems. To carry out this study, scientists distinguish different levels of organisation hierarchy.

This view plays a crucial role in how ecologists investigate and explain their object of study. Each level they refer to presents a specific structure, organisation, and functioning. So, scientists study how organisms of the same species work together in populations to survive and grow. In turn, they also analyse how populations of diverse species interact with each other in a community. At the same time, ecologists generally study structural and functional relationships between the population or community levels and the physical and chemical environment. They also study ecosystems as a whole, that is, the communities within their environment, the flows of matter and energy, and the balances of the chemical elements in that complex system explaining the increase in the degree of complexity at each level of the organisation hierarchy. Ecosystems can be small, like the tide pools found near the rocky shores of many oceans, or very large, like the Amazon rainforest.

Another aspect of how biologists describe these levels is that they depend on one another. Scientists present them as interdependent and integrated. This interdependence and integration refer to the fact that an individual organism, for instance, cannot survive over an extended period without the support of its population, just as an organ cannot survive as a self-perpetuating independently without the larger organism. Likewise, a community is reliant on the continuous cycling of materials and the flow of energy within the ecosystem (Odum and Barret, 1971; Miller and Spoolman, 2011).

Unlike bacteria or a tiger, communities and ecosystems do not have clear boundaries. They are not isolated from one another. Winds, for instance, can blow pollen from a forest into grassland (Miller and Spoolnman, 2011). Community and ecosystem are abstraction, a unit from which ecologists can study how organisms interact with other organisms' living (biotic) environment, defining trophic structures or spatial and temporal dynamics between them; so also, the relationship between these organisms with their non-living (abiotic) environment, such as soil, water, other forms of matter, and energy from the sun. An ecosystem is an ecological unit based on which ecologists investigate how interactions occur between living beings and their physical environment. Its delimitation depends on the ecologist who studies it, who defines its size in a way that makes sense to solve the questions of interest to themself. So, one ecologist may study how light, and temperature affect oaks, while another assesses how energy flows in the rainforest.

These aspects show how the living world is complex and messy. Its division into different levels of complexity has been crucial in the conception of the living world. It simplifies the world, structuring it into levels. So, this conception of the natural realm in terms of parts and wholes allows for characterising and visualising the diversity and interconnection of different life forms in an approachable way.

Also, the aspects mentioned evidence several conceptual difficulties around the idea of levels of organisation. What is the ontological status of these levels - abstract things or real concrete entities? Based on what is seen above, they can be both abstract (e.g., an ecosystem or community) or concrete (e.g., cells or organs). Additionally, at times, it signifies the relationships of composition between natural elements, while in other instances, it denotes abstract dependencies or dynamics occurring at various scales or descriptive levels (Brooks et al., 2021). Hence, though the concept of 'levels' has become widely accepted in biology, there

are considerable differences not only in conceptions of the levels but also in applications of the concept of hierarchy to a living thing.

From a philosophical point of view, this is problematic (see Brooks, DiFrisco and Wimsatt, 2021, Eronen; 2021; Eronen and Brooks, 2018) because, within these vast differences in the interpretations of its meaning and how the concept is applied to study the natural world, none of the proposed accounts has been widely accepted (Eronen and Brooks, 2018).

Some accounts have claimed a deflationary view of this concept using other concepts such as scale or composition. Where scale refers to the arrangement of things based on some property (such as size) that can be quantitatively measured in those things. (see Eronen, 2015). By sharing some properties, the idea of composition and scale would be more harmonious than the idea of levels, where a level can have components very different from each other (e.g., cellular levels are composed of proteins and DNA organelles). Nonetheless, does this resolve the polysemantic problem? If we use a concept as 'scale', would we not find ourselves again with the fact that the concept is applied under different criteria according to the requirements of the specific scientific investigation? It is possible to argue that specifying the scale property avoids confusion. However, the same thing can be said about levels if it is explicit in what senses the level concept is applied.

This observation highlights the fundamental nature of the problem at hand. It emphasises that the interpretation and application of scientific concepts, particularly those with multiple meanings, are intrinsically linked to scientific inquiries' specific context and goals. Diverse criteria and interpretations arise because scientists attempt to address the complexities and intricacies of the natural world from different angles and disciplinary perspectives.

While this inherent polysemy can be seen as a challenge, it also reflects scientific practice's dynamic and evolving nature. Science is a continually advancing enterprise that adapts to new discoveries, technologies, and conceptual frameworks. The flexibility in interpreting and applying concepts allows for a more comprehensive understanding of the natural world and promotes interdisciplinary collaborations incorporating diverse perspectives.

In this discussion, I think that idea of level should not be ruled out. The implementation of some concept of level or hierarchy has been indispensable to understanding and visualising the natural world. There is no doubt about the important heuristic role that levels of organisation play in biological sciences. The levels of organisation concept serve as an organisational

principle that aids in imparting basic knowledge of biology to novice scientists early in their training. Having a specific idea of organisation makes it more straightforward to define what phenomenon to study and how to address it, making the complexity of the living world more approachable.

Nevertheless, recognising this utility does not mean dismissing the limitations or conceptual confusion of different uses of this concept. Accepting the pragmatic role of levels of organisation means constantly re-evaluating their utility and limitations. We should be open to refining, adapting, or even discarding this concept if better alternatives appear. By explicitly addressing the pragmatic role of levels of organisation, we can enhance the understanding of their purpose and limitations. This can contribute to developing frameworks that better capture the complexities of the natural world.

5.3 Usage of parts, whole and composition notions in scientific practice ambits

5.3.1 Methodological ambit

Scientific knowledge is based on observation and/or experiment: from statements knowable based on observation, scientists' reason to their conclusions using a methodology or body of strategies. A significant part of scientific practice consists of properly examining and polishing the methods to research a particular phenomenon.

A central methodological strategy is picking a research unit. Having a defined unit is critical to deciding what aspects to study and how. Delineating the phenomenon is crucial in defining the researcher's questions and setting the experimental procedure. The units can be concrete entities such as a bacterium or enzyme or abstract ones such as communities or ecosystems. In both cases, the definition of these types of units and what its components are allows one to decide what particular aspect(s) to study, for example, how specific proteins are distributed in the cell membrane or the abundance of a species in a community.

Thus, firstly we should have an accurate idea about how the entity or phenomenon is studied. For that, its characterisation is crucial. If we think of cell biologists, they have dedicated a lot of time to characterising the different types of cells, establishing their general

features and fundamental differences between different cell types. So, the general idea about cells is of an entity consisting of a cytoplasm enclosed within a membrane, which contains various biomolecules such as proteins and nucleic acids (Pollard et al., 2017). So, these notions, parts and whole, guide the characterisation of a research unit.

In the biological sciences, disciplines such as molecular biology use particular methods to study the fundamental molecular components of cells, such as proteins, DNA, and RNA. Certain techniques within the realm of cell biology are concerned with tasks such as isolating cells of various types from tissues, cultivating cells outside the organism, cell disruption, and extracting organelles and macromolecules in their pure form. These methods are indispensable in the study of protein structure, function, and interactions (Lehninger et al., 2004). The methods mentioned are currently used by tens of thousands of scientists daily.

In textbooks of cellular biology, for instance, it is highlighted that a crucial point to understanding how a cell works, before developing how a cell works and what and how cellular processes occur, an essential prerequisite is attaining an accurate idea of the structural organisation of this biological entity (see Alberts et al., 2008). Once having identified what the cell's components are, scientists focus on what these components *are* and what they do in the cell. This means specific positions, movements, dynamics, and interactions with each other.

Through the development of the light microscope the examination of some structural details of individual tissues and single cells became possible. One example of this is the advance of the electron microscope, and methods for preparing ultra-thin sections of tissues, creating a new dimension to the study of morphology —that involving cellular structures in detail. (Lehninger et al., 2004). Electron microscopy has progressively unveiled the nature of the cellular structures found in plants and animals.

Biologists have developed methods to separate and extract cells from tissues to gather extensive information about the cells (Alberts et al., 2008). This involves subjecting cells to various techniques such as osmotic shock, ultrasonic vibration, passage through a small orifice, or blending. These methods break multiple cell membranes, including the plasma membrane and endoplasmic reticulum, which then quickly reseal to form small, enclosed vesicles. However, if executed carefully, these disruption procedures preserve the integrity of organelles such as nuclei, mitochondria, the Golgi apparatus, lysosomes, and peroxisomes. The resulting suspension of cells, known as a homogenate or extract, becomes a dense mixture containing

different membrane-enclosed organelles, each characterised by unique size, charge, and density. By carefully selecting the homogenisation medium for each organelle through trial and error, the various components, including vesicles derived from the endoplasmic reticulum, called microsomes, maintain most of their original biochemical properties (Lehninger et al., 2004).

One example of this exhaustive scientific analysis is protein studies. Most proteins in the cell work as part of complexes with other proteins. A viable approach is determining its specific interactions with other proteins to characterise an unknown protein's biological role. Co-immunoprecipitation is a technique employed to identify proteins that form strong associations with one another. This method makes it possible to discover novel binding partners, assess binding affinities, analyse binding kinetics, and gain insights into the functional role of the target protein (Phizicky and Fields, 1995). These researches show the importance for scientists to gain a clear idea about the structure of phenomenon, what types of components of biological entities have, in what places are located, how they are organised and interact amongst themselves. They are crucial to start to understand what a cell is and what activities are carried out. Scientists can more readily analyse the system or formulate questions of the same once they understand the types.

To study the biological research unit comprehensively, scientists decompose it into parts to investigate what activities (and how) these parts carry out in the whole. While literal decomposition has been an effective approach in biological research for identifying the function of a component (such as isolating an enzyme through fractionation), it can also disrupt the component's operation when it is dependent on coordinated interactions with other components. The actual effects of being part of a particular organisation only become apparent when observing the differences in behaviour between the original system and the isolated component, thereby defining the role of the organised setting in determining the component's function. Consequently, in biological research, the decomposition process frequently adopts a conceptual perspective rather than a literal one. This entails describing the components' function and examining how their performance is interconnected with other operations within the mechanism, representing a theoretical endeavour (Bechtel, 2007).

Whether decomposition can be performed in a laboratory or is a conceptual exercise, the main point to highlight is that a system decomposed into parts is essential in how the system is investigated. This exercise to decompose into parts helps to investigate the specific role of

different system components. It is helpful to differentiate and detail under what conditions diverse components perform in a particular way and interact.

Nonetheless, this methodology displays challenges. As already was seen in previous chapters of this thesis (Chapters 3 and 4, specifically) biological entities are dynamic and context sensitive. As philosopher of science William Wimsatt argues, decomposition can be problematic when there are strong interactions and non-linear relationships between the parts (Wimsatt, 2007). In entities like biological ones, which exhibit complex forms of interactions with its environment, is difficult or even impossible to separate components from its environment without altering these interrelations.

If we consider such a different biological discipline as ecology and the study of an ecological community, we have that one of the main objectives of community ecologists is to know the community composition and structure. To carry out this task, they study the number of species and their abundance in a given place and time, as well as how they are distributed, and under what circumstances this distribution changes over time. In this way, scientists can define the diverse factors that can modify the composition and structure of a biological community.

This work for understanding the part-whole organisation (in some form or other) of biological systems is the baseline to examine critical processes related to metabolism, growth, or reproduction. These notions help to articulate a specific investigation of a biological phenomenon.

The whole investigated can be a cell, where the cell's components share the intracellular space. This space has the cell membrane as a boundary, so cellular components are delimited. Nevertheless, other biological entities are without a defined boundary, as in an ecosystem. In an ecosystem, communities of different species interact with one another and their non-living environment of soil, water, and other forms of matter and energy, mainly from the sun (Miller and Spoolman, 2011). In this case, the whole is given by sharing a defined and specific location with a defined barrier but by the interaction and reactions of different entities involved.

How to evaluate the components' whole and their specific interactions can be studied depend on the inquiry type. However, these notions make it possible to delimit what things are investigated regardless of the differences in research aims. Scientists in each discipline define

under which parameters the phenomenon is studied based on which aspects are to be explained. They try to do work which is coherent under these parameters. In this establishment of parameters, the notions of *whole* and *parts* play a central role in how a study unit (the whole) is chosen and delimited to characterise it.

5.3.2 Explanatory ambit

5.3.2.1 Part, whole and composition notions in biological explanations.

Philosophers such as Kauffman (1971), Wimsatt (1974, 1976), and Bechtel and Richardson (2010) have highlighted and analysed an explanatory compositional strategy, particularly in biology. Kauffman (1971) claims that typical explanations in biology exhibit how parts and processes articulate together to cause the system to do some particular thing. In his article "Articulation of Parts Explanation in Biology and the Rational Search for Them", he points out that when biologists study an organism, depending on their scientific inquiry objective, it may be seen as doing infinitely many things and may be decomposed into parts and processes in infinitely many ways. So, they may decompose it into parts in different ways for different descriptions of what the organism is doing. Wimsatt (1976) also acknowledges that this aligns more closely with the language commonly used by biologists, particularly in the context of uncovering and explaining mechanisms.

Kauffman (1971) and Wimsatt (1986) hold the perspective that *a theoretical unit* serves as a guiding principle in studying a biological system. This entity can be broken down into its constituent parts and processes, explaining how these components and processes interconnect to generate the observed behaviour of the system. A complementary line of investigation is the work of Bechtel and Richardson (2010). In their analysis of the strategies of scientists to make mechanistic models, they address how a phenomenon is decomposed into parts in the biological sciences.

As the philosophers mentioned above have pointed out, scientists elaborate explanations based on the parts' activities in a part-whole fashion, this being especially visible in the elaboration of mechanistic explanations.

5.3.2.2 Causal-Mechanistic Explanations.

Some central aspects of the mechanistic view are: (a) Mechanisms are composed of parts. (b) The components of a mechanism participate in interactions, operations, or activities. (c) These interactions can produce a change or a particular behaviour or functioning of the mechanism. (d) These relations are given in a specific organisation within a particular space and time.

Therefore, an adequate explanation of the functioning or behaviour of the mechanism studied will depend on 1) identifying the parts of the system; 2) what type or types of interrelations among these parts are considered; 3) specifying the spatial organisation of the components. Moreover, in turn, there is the temporal sequence of operations or activities that these parts perform in succession until the mechanism is given is finished (Bechtel, 2011).

The system's behaviour as a whole can be broken down into organised interactions among the activities of the parts. Following the decomposition process, it is essential to reconstruct the mechanism under study. This involves conceptually reassembling the various components and operations into a coherent and organized arrangement that constitutes the mechanism. Additionally, further tasks are involved, such as understanding how multiple operations are coordinated in real time and exploring the interactions between the mechanism and its surrounding environment (Bechtel and Abrahamsen, 2013). Hence, this new mechanistic approach refers to at least two areas of analysis, namely the methodological (parts identification) and the explanatory (how parts are interrelated) (Fazekas & Kertész, 2011).

Mechanistic models successfully explain insofar as they accurately represent spatial, temporal, and causal relations among the system of interest's components as they pertain to producing the phenomenon explained. The very point of the mechanistic approach is to account for a phenomenon by understanding the mechanism responsible for these processes. Nonetheless, carrying out this decomposition strategy presents challenges. One of these is that a mechanistic explanation emphasises the component parts and their operations within the mechanism and can only be identified by taking the mechanism apart, literally or conceptually. However, the scenario is more complex if we consider that many biological system reaction pathways are non-linear.

Frequently, in a mechanistic view, there is an assumption of a sequential arrangement of the activities of the mechanism. As an example, consider the sequential explanation of

protein synthesis. It begins with the initiation of transcription by RNA polymerase, converting DNA into mRNA. The subsequent steps involve the transport of mRNA into the cytoplasm and pairing amino acids by tRNA with codons on the mRNA. Finally, the protein takes shape through its specific folding process. So, mechanistic explanations can account for events like this sequential pathway in terms of a whole (the mechanism) and its parts performing in their respective organised ways.

While mechanistic accounts commonly acknowledge the significance of parts organisation in the functioning of studied phenomena, they generally fail to address the specific forms of non-linear organisation found in living systems and the challenges that biologists face when attempting to comprehend the consequences of such intricate organisation (Bechtel, 2011). Although this sequential pathway is relevant to the appropriate functioning of a cell, there are also crucial non-linear pathways if considering mainly the relationships executed sequentially.

An example is the Krebs or the Citric Acid Cycle (see Figure 5.2). In this metabolic pathway the total degradation of organic matter occurs to transform it into inorganic matter, obtaining energy directly through the production of ATP molecules or reoxidation of the reduced coenzymes in the transport chain of electrons of the inner mitochondrial membrane (Lehninger et al., 2004). Thus, these pathways provide a significant basis for explaining how living organisms can maintain themselves as enduring, active individuals.

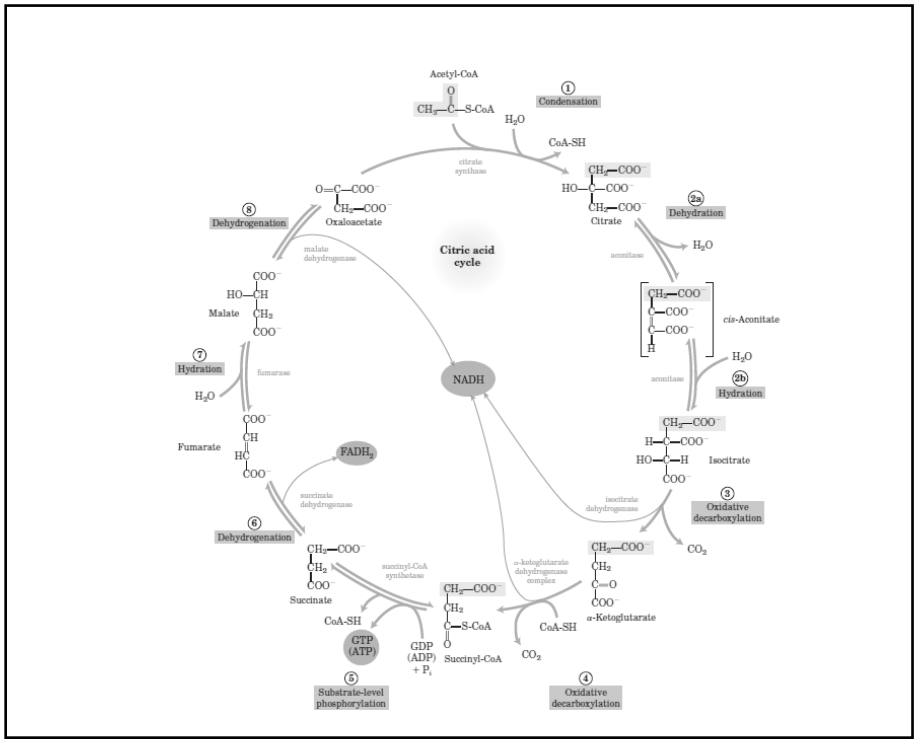

Figure 5.1. Diagram of Critic Acid Cycle or Krebs Cycle (Lehninger et al., 2004, p.624).

Undoubtedly, this scenario means a challenge for scientific practice. How are we to delimitate a mechanism correctly if many essential non-linear pathways are carried out simultaneously? How do scientists define the beginning and end of a process? The difficulty that these types of pathways display is highly complex, characterising precisely how the mechanism's parts and the operation of these parts are organised in order to understand the dynamic of the mechanism's interactions.

Given these challenges, the question arises as to whether this mechanistic perspective effectively represents biological work, as mechanistic philosophers postulate. Biologists utilise a range of causal concepts, including *pathways*, *cascades*, and *processes*, to elucidate their phenomena. However, prevailing philosophical perspectives often restrict the interpretation of these concepts exclusively to the framework of mechanisms. By equating these concepts with the notion of mechanism, it remains uncertain whether these interpretations adequately capture the diverse array of causal structures in biology.

The philosopher Lauren Ross (2022) argues that mechanisms and pathway concepts possess distinct characteristics and are associated with different strategies of causal inquiry. This suggests that the understanding and utilisation of these causal concepts in biology may extend beyond a strict mechanistic framework. It implies nuances and variations in how

biologists conceptualise and investigate causality, which a narrow focus on mechanisms alone may not fully capture. These differences between pathways, cascades, and mechanisms show that biologists apply a series of alternative approaches, such as network or dynamical systems theories, to capture many biological phenomena's dynamic and non-linear nature, not being limited to the mechanistic view.

Explaining the activity of a target object involves appealing to the action of some of its spatiotemporal parts. Not all parts are equally relevant, in any case. Hence, an essential scientific task is defining what parts are relevant to investigate. Glennan (2002) argues the relevance is according to the contribution to the phenomenon. Hence, components are relevant if they make a difference to the occurrence or characteristics of the phenomenon through their causal roles and interactions. However, in non-linear networks, this definition takes work. The causal properties of the parts are themselves non-linearly dependent on the whole network (Mitchell, 2009). Determining causal relevance is not always straightforward, especially in complex biological systems with complex causal networks, feedback loops, and non-linear interactions. Furthermore, how the relevance is defined can be context dependent. So, what counts as relevant may vary depending on the specific explanatory goals.

Even though mechanistic explanations are widely used to explain biological systems and represent a significant advance in providing essential insights into the explanatory pursuits of biologists, these explanations are not sufficient to explain causal relations in non-linear interactions in a space-time context which is profoundly changing.

For this reason, in recent decades, the scientific community has attempted multidisciplinary research projects. An example of this effort is the work of systems biology, which brings together disciplines such as biology, mathematics, and bioinformatics to account for the complexity of interactions in biological systems. The work of systems biology is motivated by the need for a theoretical framework more appropriate for investigating the dynamics and arrangement of numerous interconnected elements (Boogerd et al. 2007; Kitano 2001)[10].

[10] This collaboration presents difficulties. There is a need to improve how this integration between different disciplines with specific theoretical frameworks can be possible.

Such challenges show that these heuristic strategies are fallible. It is an exercise of trial and error. Scientists can begin by investigating a phenomenon composed of a set of elements and their respective interactions. However, sometimes, more than this is needed to explain the phenomenon's behaviour, it being a more complex organisation with more entities and interactions involved than it was considered to be initially. This highlights that the use of notions is a primary idea to guide how to address complex phenomena.

5.2.2.3 Explanations and Part/whole relation. Beyond mechanistic view.

Biological explanations and use of parts/whole ideas are not circumscribed to mechanistic view only. There are more types of explanations, where these notions are applied. Rasmus Winther (2006) expands the analysis by addressing mechanistic explanations and explanations elaborated in disciplines such as comparative morphology, where the predominant structural perspective rarely appeals to mechanisms. The composition relation reference is not only found in mechanistic explanations, in fields of anatomy or morphology, but this notion also plays a significant role in defining structure and organisation.

Winther (2006) claims that there is a style of biological theorising – compositional biology – based on the notion of parts and wholes and their respective functions and capacities. He examines disciplines such as comparative morphology, functional morphology, and developmental biology to provide an in-depth analysis of the importance of parts in biology. Winther (2011) claims that the explanations made in these biological disciplines are part-whole explanations.

When an element is part of a particular whole, the study target will define what the whole is. Each experimental system will comprise its own descriptions, guided by specific investigative questions and interests, even concerning general structures such as molecules, cells, and tissues. According to Winther (2006), providing a definitive definition of parts is impossible. Different frameworks exist for categorising different types of parts. Parts can be classified as structures, processes, mechanisms, or functions depending on the perspective. The specific framework used to partition the perspective determines which parts are considered relevant and whether certain aspects, such as particular mechanisms, should be considered parts within a relationship or interaction between parts.

Hence, a scientist may analyse intestinal flora as part of the human body or not, depending on a given context, such as a disease or immunosuppression condition. In this way, we have characterised what microorganisms are in the intestinal flora and in what zones of the human gastrointestinal tract they can be found and how they participate in crucial digestive processes. Enzymes produced by intestinal bacteria are essential in the metabolism of several vitamins.

An example is the synthesis of vitamin K, a necessary cofactor in producing prothrombin and other blood clotting factors (Gorbach, 1996). The approach differs if scientists want to learn how intestinal flora interact with the immune system and evaluate what microorganisms can produce certain diseases. Therefore, the decomposing of a system is not a one-size-fits-all task: it depends on the principles used.

In this manner, it can be unclear how the explanations derived from this diversity of criteria may be compatible when referring to the same entity, in this case, intestinal flora. Indeed, these philosophers - Kauffman (1971), Wimsatt (1974), Winther (2006) - point out that antagonistic and complementary representational sets of parts can be generated for the same system. Although it is a valid concern, it is essential to note that different criteria and explanations do not necessarily imply incompatibility or incoherence. While there may be different perspectives on the intestinal flora's nature and role, scientific inquiry aims to achieve a coherent and comprehensive understanding of the system. Researchers strive to integrate various perspectives and evidence to develop a more nuanced and complete understanding.

Undoubtedly, there is always the risk of a particular methodology not being entirely adequate for the study of a phenomenon, and for that reason, it is fundamental to make ever more efforts in collaborative work between scientists of different disciplines and philosophers of science to examine these challenges and actively engage in dialogue and critical analysis to develop frameworks that promote compatibility.Now, coming back to the uses of these notions in explaining biological phenomena, what do these philosophical analyses tell us about scientific practice? In these disciplines such as comparative morphology, functional morphology or developmental biology, it seems evident that the role of the notions of part, whole, and composition is establishing the organisation and structure of living forms. This definition of organisation and structure is fundamental to studying diverse life forms, making comparisons, evaluating performances with respect to their morphology, or examining their changes across time.

As the philosophers mentioned above have pointed out, scientists elaborate explanations based on the parts' activities in a part-whole manner. In this way, scientists can establish the phenomenon and its components. Now, the criteria to do it are variables. The research question(s) direct what thing is studied and how. Regardless of the difference in criteria, thinking of a phenomenon studied in parts and wholes is a central guide to delimitating the phenomenon, so later to define structural characteristics to make comparative studies or to assess how components are organised and under what conditions they interact.

Some might think that any approach to a phenomenon from the analysis components of a unit of study implies a reductive explanatory stance. The next section will examine this issue, and it will be argued that the study of parts' activities does not imply a reductionistic view.

5.3.2.3 Does addressing the activities of the parts imply a reductionist perspective?

Prima facie, it makes sense that examining the individual parts' activities to comprehend an entire mechanism is categorised as reductive analysis. Nevertheless, in pursuing decomposition, researchers generally do not presume that understanding the lower level components alone will fully elucidate the phenomena —at a minimum, they acknowledge the crucial role played by the organisation of these components and the conditions under which this organisation takes place.

Now, does necessarily this analysis of parts' activities within a whole imply a reductive perspective? To address this issue, it is necessary to distinguish between methodological and explanatory dimensions because one is how a phenomenon is studied and the other is what aspects of the phenomenon are explained from the data obtained. From a methodological perspective, the reductionistic strategy would consist in researching the behaviour of more fundamental components. From an explanatory view, explaining the system's behaviour would make reference only to factors at a lower level than the phenomenon.

The idea of the nested whole-parts relationship of living entities immediately suggests a reductionist research strategy: breaking the whole apart and studying its parts. So, within scientific practice, the reductionistic strategy would include researching the behaviour of more

fundamental system components studied to explain the system's behaviour, referencing only factors at a lower level than the phenomenon.

To address this difficulty, some scientists design their investigations to focus on understanding a biological system, which examines the functioning of the whole and its parts and how they participate in the network of interrelated processes that form them as systems. Systems biology is the field responsible for undertaking this task through a collaborative approach between numerous scientific disciplines such as biology, computer science, engineering, bioinformatics, physics, and more. The goal is to predict how these systems evolve over time and in different circumstances.

Considering the researcher's question, it is vital to examine what whole and its respective parts will be investigated. This aspect is relevant to both methodological strategies and the elaboration of explanations. The main point is how the phenomenon studied is addressed; what information from parts will be considered to explain the performance or behaviour of a whole? What do scientists want to explain based on that information? We consider in vitro experimental observations gained with isolated parts, through which it is possible to define how components interact with others in controlled circumstances. These studies do not ensure that the interactions would be the same in another context. Applying this useful strategy does not mean scientists desire to explain the entire phenomenon based on it. Indeed, scientists contrast in vitro examinations with in vivo conditions, which are changing, and evaluate how to incorporate these circumstances into laboratory experiments (see, e.g., Ghaemmaghami and Oas, 2001; LeRoux, Lakshmanan and Daily, 2009; Mamo et al., 2007; Sobańska et al., 2021).

Looking into the explanatory dimension, the reduction models typically assume that the reductive explanation is causal, where the interaction of its constituent parts explains a higher level feature. In the philosophical discussion, there is still no complete agreement about what exactly it means that an explanation is reductive (Brigandt and Love, 2022). According to William Wimsatt (1976), an early explanatory reduction model posits that reduction involves providing a causal explanation for an individual event rather than a generality. This explanation entails a "compositional redescription" of a higher-level state of affairs by focusing on its components (Brigandt and Love, 2022). Following a similar view but making a more detailed analysis, Hüttemann and Love (2011) have argued that reductive explanations have at least two significant facets. The first is composition (e.g., a heart is composed of myocardial cells and

other cellular entities). The second facet involves causation. The higher level entities are caused or determined by lower level entities; these causal relations are explained by three aspects, which are intrinsicality (intrinsic characteristics of the system present in each part of it), fundamentality (it appeals to a set of fundamental properties within the whole's parts), and temporality (the property of a whole at a particular time is explained based on the properties of its parts at an earlier time). In this fashion, the biological sciences are a mixture of compositional and causal claims. In turn, Kaiser (2011) emphasises the isolation facet of reductive explanations. She claims that explanations account for a phenomenon with regard to compositional dimension and properties and interactions of the components of the lower level, as well as that these kinds of explanations focus on internal factors and thus ignore or simplify the environment of a system. This isolation aspect is fundamental to consider in reduction analysis because it emphasises the point that causal relations between elements are given due to intrinsic characteristics of parts and pays little attention to context conditions.

According to these accounts, generally, it is accepted that in a reductive approach, a phenomenon is explained through the properties and interactions of entities that belong to a lower level. For example, from this perspective, the human brain can be explained through molecular components, which interact with each other according to the inherent characteristics of those components. Taking into account these characteristics of reductive explanations shows that a study of parts activity does not necessarily appeal to the reductionist view, depending on what factors are considered or not.

In biological sciences, mentioning notions of parts and whole serves to examine the system's structural arrangement (spatial relationships between entities) and understand biological systems' operational behaviour. This involves explaining the alterations occurring within different components and analysing the overall effects of processes on the biological entity (Brigandt, Green and O'Malley, 2017). The dynamics of the whole and components are studied, along with their specific arrangement and how this arrangement changes depending on particular circumstances. All these are crucial aspects studied by scientists in different investigations, such as the effect of climate change on ecosystems (Grimm et al., 2013) or the study of signalling cascade activation in the cell (Alberts et al., 2008). Therefore, the information obtained from activities of the parts of a biological whole is not necessarily used from a reductive perspective. According to specific research objectives, the information can be considered from a reductive or holistic stance. All these perspectives share, however, a

commitment to understanding how parts of a whole are organised (in some form or other) in the study of biological phenomena. This commitment can give the idea that is most relevant the study of parts and their characteristics than other factors like context-sensitivity, dynamics and non-linear relations of parts.

5.3.3 Representational ambit

In other forms of knowledge acquisition, science produces conceptual representations of different aspects of reality. *Representations* are diverse. They include thermometer readings, flow charts, verbal descriptions, photographs, X-ray images, digital imagery, equations, models, and theories (Frigg and Nguyen, 2021). In biological sciences, various representation methods are utilised to illustrate biological ideas, concepts, or phenomena. These modes of representation include animations, lifelike drawings, diagrams, graphs, charts, tables, equations, and linguistic input and output. Each form of representation presents a unique and precise approach to communicating biological information (Tsui and Treagust, 2013).

A significant feature of scientific practice in biology is that biological objects are represented as being constituted of a specific collection of parts located at different levels of the organisation. For instance, cells are said to consist of a cell membrane surrounding the cytoplasm containing organelles (Jansen and Schulz, 2014).

Within all these different representations, images are fundamental in biologists' work to obtain a visual representation of a phenomenon. Through visual representation, biologists have, for instance, explained how blood circulation occurs in our body. Visual representations are external depictions where certain spatial relationships within the image are interpreted, allowing them to convey meaningful information (Perini, 2013).

5.3.3.1 Diagrams

Figures identified as diagrams have a visibly simple and spare form (Perini, 2013). Three essential types of diagrams in biology are pictorial, compositional, and schematic (Perini, 2013). A compositional diagram represents a biological whole and its components. They are built out of discrete atomic characters showing their spatial relation. Examples of biological

diagrams can mean an entity such as a cell or a biological process such as enzymatic activity. Through these diagrams (see Figure 5.3), the scientist illustrates how a cell is, showing its components and how they are organised.

Cells display differences, but research has demonstrated that most cells have basic structural components in common. These components encompass fluidic layers that envelop the cell and its compartments, along with filament networks responsible for preserving the cell's form and aiding in the organisation of its contents (Boal, 2001). Additionally, there are significant resemblances in the chemical makeup of these structural elements among various cells. The numerous shared chemical and structural characteristics among cells encourage us to search for overarching architectures and components. Cytologists and cell biologists aim to develop abstract and general knowledge about cells, focusing on identifying the types of structures that are commonly found rather than examining each individual instance of a cell (Bechtel and Bollhagen, 2019). Scientists utilise cell diagrams to represent various organelles found within cells visually. These diagrams typically feature a limited number of instances for each organelle type, using suggestive icons to depict their shapes. While these diagrams effectively convey the presence and typical location of organelles, they inadvertently create the false impression that the majority of the cell's space is empty (Bechtel and Bollhagen, 2019. So, cell biologists frequently generate diagrams that leave out details. Through cellular diagrams, it is possible to gain an idea of the main characteristics and elements, organisation, and structure, representing both components of a system and their ubiquity in the cell simultaneously.

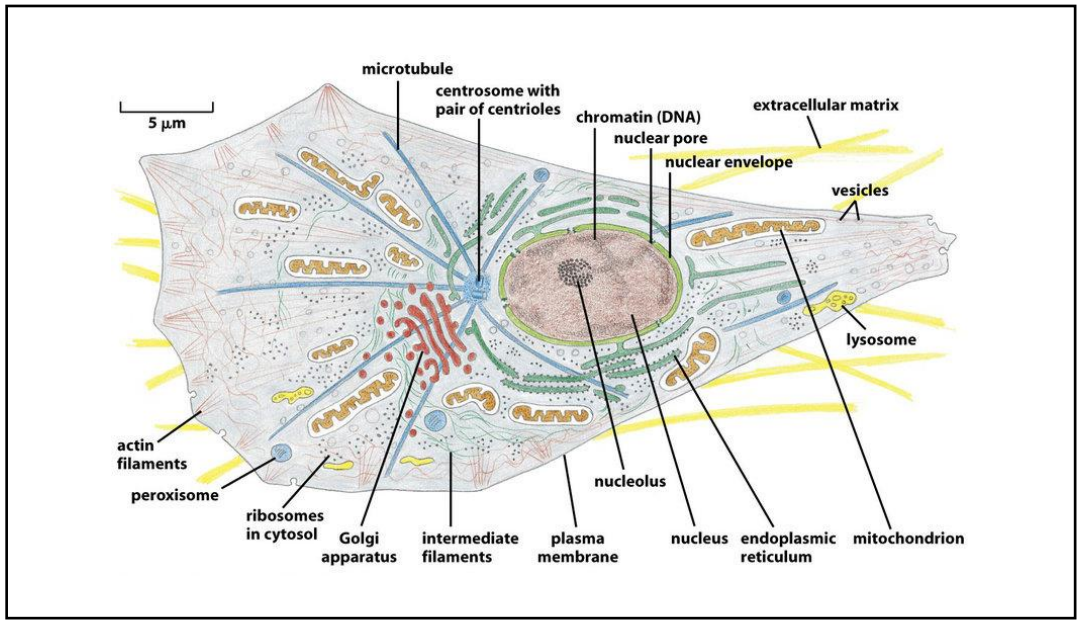

Figure 5.2. Cell diagram of a typical animal cell, showing its different components and respective compartmentalization into many different organelles (Alberts et al., 2008, p. 27).

This representation is not only relevant in the knowledge of a particular entity or processes, but also makes it possible to draw comparisons with other phenomena, identifying similarities and differences in aspects such as types of components, structure, and components' organisation and behaviour. When diagrams of animal and plant cells, for instance, are examined, it is possible to see that both cells have a cell membrane, but the plant cell also has a cell wall. In this manner, diagrams illustrate similarities and differences between the entities studied.

In ecology, food webs are diagrams that represent the complex network of feeding relationships within an ecosystem. They illustrate the transfer of energy and nutrients from producers (such as plants) to consumers (herbivores, carnivores, and decomposers).

These diagrams illustrate the variety and complex relationships between different organisms in an ecosystem. Each arrow represents the transfer of energy from one level to the next through the process of consumption. Food webs help ecologists understand the flow of energy and matter and the potential impacts of disturbances or changes within the ecosystem.

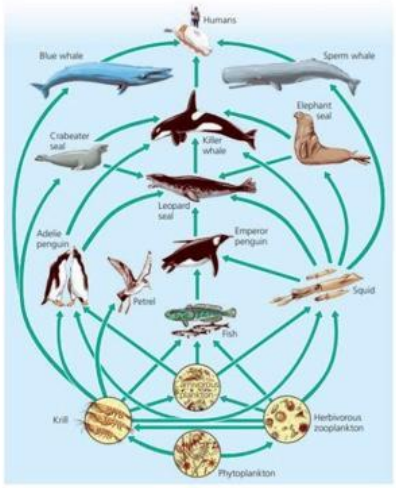

Figure 5.3. Diagram of the Antarctic food web (Miller and Spoolman, 2011).

The diagram of Figure 5.4. illustrates the relationship of feeding between different species of the Antarctic ecosystem. There are producers like phytoplankton. Primary consumers such as krill and copepods. Secondary consumers are squid, fish, and emperor penguins. Tertiary consumers (Killer whales) and Leopard seals, which are top predators. The diagram visually represents the complex feeding relationships and energy flows within the Antarctic marine ecosystem. It helps scientists and researchers understand the connections between different organisms, from primary producers to top predators, and how they are interconnected through the food web. In this case, this food web highlights the importance of krill as a key species, forming a crucial link between phytoplankton and higher trophic levels. Many Antarctic predators, such as whales, seals, and penguins, heavily rely on krill as their primary food source.

How are these diagrams designed? Again, return to the idea that the primary way to visualise and conceive objects, in general, is through parts that compose the entity in question. When complex systems and entities are studied on such a massive scale, as an ecosystem, and microscopic scale as biomolecules and cells, the representation and visualisation are a significant and essential part of life scientists' work. This is in order to make it more feasible to examine the phenomenon. The idea of a whole composed of specific components that display dynamic interrelation is central to understanding biological entities and processes. The delineation of the target studied will be analysed as a whole, and from there, scientists will

define components and respective interactions and assert their importance in the behaviour or performance that scientists wish to illustrate.

We can see that diagrams are symbolic representations of entities and phenomena, which try to show how they are and how they perform more straightforwardly and precisely. Diagrams are handy for thinking about dynamic phenomena— patterns of change over time (Sheredos et al., 2013). A diagram illustrates a whole (e.g., energy flow in an ecosystem) with particular elements representing different entities involved and their interrelations. Diagrams represent the organisation, structure of the phenomenon studied, helping to obtain a clearer idea of how certain biological entities perform and behave.

5.3.3.2 Models

Scientists, to represent the phenomenon investigated, make use of models. Models are simplified representations of more complex systems that help researchers structure the knowledge they acquire. Models perform various functions, from theoretical prediction to science education (Frigg and Hartmann, 2020). Models can represent some aspect of the world, some element of our theories about the world, or both simultaneously (Peck, 2004). Some examples of this are the billiard ball model of a gas, the Bohr model of the atom, and the Lotka–Volterra model of predator-prey interaction (Frigg and Hartmann, 2020). Therefore, a model can be either a concrete or an abstract object.

It must be kept in mind that models are not designed to replicate the natural world precisely but to depict a simplified version of it. These models play multiple roles, such as testing hypotheses, generating fresh insights, enhancing understanding, proposing and interpreting experiments, tracing cause-and-effect relationships, consolidating knowledge, and inspiring innovative approaches (Brodland, 2015). It is worth pointing out that these idealisations and abstractions can introduce ontological assumptions that may not accurately represent the complexities of the real world (McMullin, 1985; Morrison, 1999). A simplification and an abstraction imply that some aspects of a phenomenon are not taken into account to focus on aspects that scientists want to represent and explain. This strategy can give the erroneous idea that only entities or activities described or represented exist, delivering an incomplete view of the phenomenon.

When life scientists study the living world, they often take it as a starting point, designing and applying experiments and observations in order to understand how it is. However, this world is complex, and often it is necessary to appeal to models, which allow researchers to abstract away from the complex causal processes in nature to examine a particular phenomenon of the living world. Models, thus, are typically more straightforward, more tractable objects of study (Parke and Plutynski, 2020).

Models can be *mathematical*, *computational*, or *material* (also known as concrete or physical). The main distinction among these types lies in their composition. *Mathematical models* consist of mathematical structures and equations, focusing on specific factors or conditions to explore a phenomenon. The utilisation of mathematical equations aids in predicting the response of a biological system (Fisher, 2008).

Computational models are made of mathematics, algorithms, and sets of instructions and are typically studied on computers. In general, the goal of a computational model is to replicate the behaviour of the system it parallels and to do so based on actual, known properties of the system's components. Models produce these interactions using mathematical relationships and computational algorithms (Brodland, 2015), designing a reconfigurable network of interacting components. They can help suggest new experiments and provide a fast-track method to pre-test them. Network modelling and computational simulations in systems biology allow the study of larger integrated systems (Gross and Green, 2017). Dynamic modelling helps examine and predict changes in the vast number of interacting components and multiple feedback loops in specific circumstances.

Mathematical models, especially, have a long and successful track record in service of these ends in evolutionary biology and ecology (see Kingsland, 1995; McIntosh, 1986; Provine, 2001). Computational models are helpful in the study of complex biological systems with huge networks of interactions (e.g., signalling pathways models). Particularly when components are organised in feedback loops and non-linear functions characterise individual operations, cell biologists turn to computational models to understand their behaviour (Bechtel and Bollhagen, 2019).

So, as well, cell biologists turn to computational models to understand their behaviour when components are organised into feedback loops, and non-linear functions characterise the individual operations. In systems biology, computational modelling is vital in its investigation of the dynamics of complex biological systems. Here, the development of models has in the main established specific properties of a dynamic network of interactions between the system's components. Inference from models allows us to construct a general view of biological phenomena without assessing every case. The elaboration of models is useful both to represent a particular phenomenon and to make predictions.

The relevance of having notions such as *parts* and *whole* in mathematical and computational models can seem to be unclear because they are abstract devices. These models do not take into account detail regarding the structure and specific position of every system component. Mathematical models and material models exhibit significant differences, not only in their abstract versus concrete nature but also in terms of their respective applications when concluding the natural world. One example of this is mathematical models that focus on modelling approaches for cellular pathways, which do not incorporate molecular specifics like the precise positioning of molecules within the cell or the intricate three-dimensional structure of proteins (Fisher, 2008).

Nevertheless, when scientists investigate a complex system, the idea of an entity composed of parts is a basic view to conceive of the systems studied and a relevant assumption to develop a model. The development of many of these models is based on the abstraction of a system composed of parts and under what parameters these parts interact. This is a primary starting point for elaborate models to predict the behaviour of a complex phenomenon.

This point is crucial because, depending on assumptions about how the relation between parts and the whole, the model will be developed. So, the occurrence of these models depends on what assumptions are applied. As we see in Chapter 3, the scope and limitations of predictions of the behaviour of synthesised entities in the synthetic biology modelling depend on ontological assumptions from the designed model. For example, applying traditional assumptions about control in the elaboration of computational modelling is not adequate to predict the behaviour of synthesised objects inside the biological hosts.

In the case of *material models,* which are physical constructs (Parke and Plutynski, 2020), the design and construction of *material models*, the importance of the idea of *parts composing a whole,* seems more evident. We can see this in models that represent the structure of a biological entity (e.g., anatomic models of the human body). These models in biology can be abstract and partial representations highlighting certain structural and organisational features of physical entities. Indeed, an essential part of scientists' work is identifying the structure and organisation of their studied entities; the elaboration of structural models is fundamental. This can be seen in the research efforts that revealed additional details about the DNA molecule, such as its fundamental chemical constituents and the ways in which they are joined (Pray, 2008).

One of the most relevant and influential investigations in molecular biology was carried out by Watson and Crick and published in 1953. Watson and Crick's study revealed that the structure of DNA consists of two elongated helical strands entwined together, forming a double helix. Constructing a model depicting these properties played a crucial role in their research. Using cardboard cut-outs, symbolising the four bases' different chemical components and other nucleotide subunits, Watson and Crick manipulated molecules on their desktops, akin to solving a puzzle. The complementary bases fit together in the following way: A with T and C with G. Each pair is held together by hydrogen bonds.

In this manner, the DNA model illustrates the different parts that compose this macromolecule, its structure, and its organisation. Based on this model, it is possible to achieve a clearer idea of how DNA strands are located and composed of monomers called nucleotides; these are often referred to as bases because their structures contain cyclic organic bases (Lodish et al., 2008). It is simpler to comprehend that the DNA double helix exhibits an anti-parallel arrangement, wherein the 5' end of one strand aligns with the 3' end of its complementary strand (and vice versa). Each nucleotide is made up of a nitrogenous base linked to a pentose by a chemical bond called a covalent bond, and this pentose, in turn, is connected to a phosphate group, also by a covalent bond. Four nitrogenous bases are displayed in the double strand: 2 purines, adenine and guanine, and two pyrimidines, cytosine and thymine. Adenine binds to thymine and cytosine to guanine. For their helical structure to remain stable, these chains are linked by a chemical bond called the hydrogen bond. On the outside of each chain are sugars, specifically pentoses (see Figure 5.5). Each pentose, in turn, is attached to a phosphate group (Nelson and Cox, 2008). Watson and Crick's model suggests that variations in the sequence of

nitrogenous bases can find expression in the sequence of amino acids that make up proteins (Nelson and Cox, 2008). Through this DNA double helix model one can gather an idea of how this biomolecule is, illustrating what is the spatial relation between DNA's components and the global structural organisation of this biomolecule.

The development of material models implies trial and error processes to achieve a satisfactory result. In the case, the DNA model, for instance, started from an erroneous understanding of how the different elements in thymine and guanine (specifically, the carbon, nitrogen, hydrogen, and oxygen rings) were configured. Watson only decided to create fresh cardboard cut-outs of the two bases to explore the impact of atomic configuration after receiving a suggestion from American scientist Jerry Donohue (Pray, 2008). The work carried out by different scientists in achieving a satisfactory model shows the importance of the elaboration of models in scientific practice. Among these are investigations made by Rosalind Franklin and Raymond Gosling (1953) with X-rays, which help elucidate the DNA structure (double-stranded molecule). This molecule twists at regular intervals to form a helix. So, the elaboration of this model by scientists was an exercise of polishing theoretical assumptions on DNA composition and structure with experimental findings about it. This DNA model - widely accepted - has been central to understanding how it is possible for DNA to be replicated. This model elaboration illustrates how the basic assumption of *parts composing a whole* underlies choices related to visualisation strategies and the representation of biological data through diagrams or models.

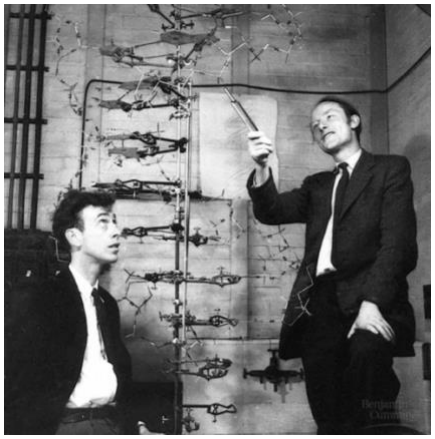

Figure 5.4. Metal model used by James Watson and Francis Crick (Barrington, 1953)

5.3.4 Communicational ambit

In the above sections, we can see the role of the notions of parts and whole in dimensions such as methodology and elaboration of explanations and models, having a heuristic role because their use allows us to address complex biological systems and obtain knowledge about them and their functioning. Nevertheless, this usefulness can also be seen when scientists communicate their findings or teach how the living world is. Hence, a comprehensive analysis of scientific practice examines how scientists get knowledge about the living world and how this knowledge is communicated.

Among essential aspects of scientific knowledge is the transmission of itself. Scientific work involves designing a methodology to respond to a research question, collect and interpret data, and elaborate explanations about a phenomenon. However, part of the job is also to disseminate and report on the results of the scientists' research. A fundamental goal of science is to transmit knowledge about scientific facts.

In the communication of science, the exchange of knowledge, explanatory dialogue, discussion of what has been discussed, suggestions for improvement, and deep conversation that helps to understand scientific knowledge are essential. This communicational dimension of scientific practice, prima facie, might seem foreign to the analysis of characterisation, where

methodology and elaboration of explanation are the main areas to consider. However, scientific practice also consists of the findings being made known to peers and the general public.

The sciences help us to understand the world and inform citizens' daily lives. One central issue of understanding scientific reasoning is to carry out what is necessary to produce captivating stories for general audiences if scholars wish to provide and engage a broad audience with their investigations and findings. Understanding the scientific content implies 1) obtaining specific information about the phenomenon studied (e.g., statistical data, descriptions, factors involved) and 2) knowing how that information was obtained.

The main goal of communicating scientific data and findings is to deliver precise information about a specific phenomenon. In this task, it is crucial how the scientific content is provided. Therefore, it is worth examining ways of communicating and sharing results with other scientists or the general public. Thus, the first central aspect is to ponder the type of audience. This audience can have a scientific background or not. To analyse the communication of scientific information, firstly, we consider an audience with a scientific background, such as the researcher's peers, and, later, the general public or students. Secondly, what is the purpose for which they wish to communicate? Already having an idea about this central communicative task of scientific practice, it will be possible to assess the relevance of parts/whole relation this area.

Scientific audiences. In the construction of scientific knowledge, the communication of findings is in the first instance among peers. Scientific activity is not solitary. It is collaborative work (De Ridder, 2019), allowing them to set up research parameters and refine experiments, hypotheses, and explanations or help each other gather data.

Scientists will discuss methodological issues such as investigation question(s), experimental design, and data analysis with peers. This community is primarily circumscribed to scholars of the same discipline. Findings are shared with colleagues who are engaged in the same study area. New scientific information on a phenomenon is presented and mainly shared with colleagues.

Even though there may be an assumption of shared foundational biological knowledge among scientific peers, the particular ways of conceptualising, representing, and investigating

biological phenomena can vary significantly. This is the case of the metaphysical category of parts and wholes. In previous sections, we have seen that these concepts' methodological, explanatory, and representational application depends on specific framework inquiries specific to each discipline. What is the whole and what are the whole's parts vary according to the phenomenon studied. These diverse criteria and interpretations arise due to attempting to address the complexities and intricacies of the natural world from different angles and disciplinary perspectives.

Different scientific disciplines may conceptualise part/whole relations differently, leading to challenges in interdisciplinary communication. The notion of parts and wholes can be understood and applied differently across various disciplines, which poses a significant challenge for interdisciplinary collaboration and effective communication of scientific content. Bridging these conceptual gaps requires efforts to establish common ground and shared terminology.

It is essential to address the challenges posed by varied understandings of parts and wholes to promote interdisciplinary education and training for scientists, researchers, and science communicators. This can involve specialised programs or courses that expose individuals to different disciplinary perspectives, encourage critical thinking about ontological assumptions, and provide training in effective communication across disciplinary boundaries. Philosophical reflection can contribute to identifying potential problems in different applications of these ontological categories.

We can see that several challenges exist in communicating biological sciences properly to peers in the field, especially when the interpretation and application of scientific concepts. This is particularly true when consider those with multiple uses and meanings, are linked to scientific inquiries' specific context and goals. When a concept has different interpretations or applications across disciplines or contexts, there is a risk of misunderstandings or misinterpretations, particularly when communicating to non-expert audiences unfamiliar with the nuances.

Non-scientific audiences. How the information is given is crucial in communicating scientific findings, taking into account that themes addressed by scientists take time to

understand. This is due to the reference to complex phenomena, where entities, mostly known, carry out sophisticated operations. The former presents coherent storytelling between a variety of different elements, which presumably are unknown to the audience. All elements and aspects of the phenomenon must fit together sensibly in order to describe and explain it correctly.

Firstly, it is clear that one of the difficulties of disseminating scientific content is its specific language, which can be a challenge for the general public. Much of the science being communicated has minimal connection to everyday experiences. It is challenging to incorporate information that the audience can misunderstand or dismiss.

In addition, there are social and cultural aspects about communicating scientific information. The philosopher Helen Longino (1990) has highlighted, that the communication and reception of scientific content are shaped by social and cultural contexts. So, at the moment to communicate scientific findings, the ontological assumptions underlying scientific theories and models may be received differently by diverse audiences, leading to varying interpretations and potential misunderstandings.

These social and cultural considerations in science communication apply to various fields, including biology, where certain foundational concepts can be particularly challenging to deliver. We already have seen that it is a generalised assumption that biological entities have parts. So, an important point to consider is how common ideas in science align with the intuitions of the general public, especially when scientists apply these concepts to study particular phenomena.

Therefore, clarifying certain basic assumptions about the phenomenon being studied is also essential when communicating and teaching information about them to non-specialised audiences. This is especially important when we consider that these assumptions can be a starting point for the scientific community, where there is generally no discussion about it. Making explicit the role of assumptions is also helpful for a listener (student or non-scientific audience) to obtain a more comprehensive understanding of what ‘being scientific’ and thinking scientifically actually is.

How, then, can information about the biological world be made more understandable and accessible to non-expert audiences? Considering the words we use to describe and perceive

the world around us, such as the names we assign to observable qualities like colours, shapes, and textures, these terms are easily comprehensible as they directly correspond to our experiences. Similarly, we have words that describe specific objects possessing these qualities, such as tables, chairs, cars, clocks, mountains, trees, dogs, and cats. These terms also have shared meanings that we can agree upon.

In this context, metaphysical concepts such as parts and wholes play a fundamental role in structuring scientific communication within the scientific community and in the context of the general public. These concepts shape the way we conceptualise, describe, and explain biological phenomena, influencing the language and frameworks used in scientific discourse.

In our daily experience, we describe objects in term of *parts* and *whole*. We can understand this by observing things such as cars or houses. So, we can explain observable objects like a house or a vehicle in terms of parts. We think a house is based on its walls, roof, windows, or doors. Similarly, we can obtain an idea about biological entities, such as cells or ecological communities, in terms of the parts that compose them. Therefore, presenting and explaining a piece of detailed information about a biological entity or phenomenon in terms of part and whole is helpful as a starting point to help audiences engage with the information given.

These concepts a helpful guide, when scholars are presenting the scientific content, because it is possible to define what it talks about. What are the central aspects that the audience should pay attention to? What happens with the phenomenon in question in the circumstances studied? In the presentation of a scenario, these notions help to establish a baseline to structure what it wants to communicate. In this fashion, it is a practical guide to articulate storytelling as regards information that will be delivered.

The biologist Randy Olson (2013) has emphasised the importance of storytelling in scientific communication with accessible language in order to engage non-experts' audiences. In the case of parts and wholes, notions contribute to articulating the narrative regarding a phenomenon. The narrative establishes a sense of coherence among diverse elements that might seem disconnected but require logical integration (Morgan and Wise, 2017). In this way, these notions help establish essential reference points to give a primary structure to the narrative. With reference points, it is possible to define what we are talking about and its main

characteristics (shape, structure or behaviour), helping to present a phenomenon and its main characteristics, organisation and behaviour. This makes it possible to compare phenomena or the same entity under different environmental circumstances (e.g., plant cells in drought or non-drought).

Using these concepts in the communications ambit helps bridge the gap between scientific and everyday language. The general public may not be familiar with scientific language or technical terminology. Science communicators can employ part-whole analogies and metaphors grounded in everyday experiences, making complex biological concepts more relatable and accessible.

In scientific communications, the language and terminology used often reflect the metaphysical assumptions about part-whole relations. Terms like 'structure,' 'system,' 'component,' and 'interaction' are prevalent in scientific discourse, reflecting the emphasis on understanding the relationships between parts and wholes.

This importance in the communicational narrative of the scientific content has its challenges because, as we have seen in previous sections, in biological phenomena, determining what constitutes a 'part' or a 'whole' is often a decision researchers make based on their specific research questions, methodological constraints, and theoretical frameworks. How we decompose or analyse wholes into parts is not always principled and can be influenced by pragmatic factors like our purposes, perspectives, or conceptual frameworks. Different decompositions of the same whole can yield different analyses. For instance, a molecular biologist may focus on individual proteins or genes as the primary units of study. At the same time, an ecologist might consider entire ecosystems or populations as the relevant wholes. Previous sections have discussed these limitations of decomposition strategies in studying dynamic phenomena. So, scientists should explain these limitations in order to communicate, specifying how decomposition can address some aspects of a phenomenon. Still, for others, like dynamics, its effectiveness is limited.

When these notions have different applications, they can be imprecise or ambiguous. Hence, there is a heightened risk of miscommunication and misinterpretation within the scientific community and when communicating with broader audiences. Therefore, communicating scientific concepts with multiple applications requires clear and explicit

explanations of the specific context, goals, and interpretations used to mitigate misunderstandings. This can be challenging when communicating to general audiences with varying levels of scientific literacy. Otherwise, if the different applications of scientific concepts are not communicated effectively, it may contribute to public confusion, scepticism, or mistrust, particularly when different interpretations or applications seem contradictory or conflicting.

Explicating the characteristics of scientific inquiry and applied reasoning can help contextualise uncertainties and limitations. Using precise language and avoiding exaggerated or definitive claims can maintain scientific transparency. Acknowledging limitations and uncertainties can foster trust and credibility with both peers and general audiences.

5.3.4.1 Role of visual tools in the scientific communication

Visual representations, such as diagrams and models (analysed in 5.5.3.1 and 5.3.3.2 sections), frequently employ part-whole notions, depicting complex systems as assemblages of interconnected components. Visual tools are didactic devices that transmit information about a particular phenomenon in communicating scientific content. Communication experts, such as Jean Trumbo (1999), have studied how effective visual aids, such as diagrams, illustrations, graphs, and animations, can significantly enhance the communication of scientific information. Visual representations can help simplify complex concepts, highlight key relationships, and make abstract ideas more concrete and relatable.

Biologists extensively utilise diagrams to present, assess, and modify their explanations of natural phenomena and their underlying processes (Sheredos et al., 2013). Diagrams illustrate how scientists conceive of or interpret a particular entity or process. They are a fantastic graphic tool for communicating new findings, allowing peers to evaluate interpretations about the investigated phenomenon (Frankel and DePace, 2012). Besides, it helps teach biological phenomena to students or any who are not an expert audience. Visual tools such as models and diagrams are fundamental in communicating and understanding the relationships between organisms in the domain of biology.

This ontological category of parts/whole is important in representing the living world and its entities. Analogies and visual representations that draw upon familiar examples of part-whole relationships, such as the workings of a machine or the structure of a building, can help make abstract scientific ideas more accessible and relatable. However, applying part-whole metaphors in widespread science communication can also pose challenges. The oversimplification of part-whole relationships may lead to misconceptions or distortions of scientific information delivered.

Therefore, the metaphysical concepts of parts and wholes play a crucial role in structuring scientific communication within the scientific community and in popular science contexts. These concepts provide organisational frameworks and serve as sources of metaphors and analogies to facilitate understanding. However, their use must be accompanied by careful consideration of potential oversimplifications, misleading analogies, and the need to maintain scientific accuracy while effectively engaging diverse audiences.

The importance of this in biological practice is clear. Still, an interesting issue to assess is whether this importance is circumscribed to a heuristic role only or if this reference to biological entities structured in terms of parts and whole is a real characteristic of these entities. Some might believe that reference to parts and wholes in biology is primarily a heuristic approach, a valuable framework or tool for understanding and explaining complex biological phenomena. Hence, dividing biological entities into components or parts and examining their interactions and relationships provides a practical and effective way to study and understand the complexities of living systems. The emphasis on the parts and the whole is considered a methodological strategy rather than a fundamental ontological characteristic of biological entities. Conversely, some could argue that the reference to parts and wholes in biology reflects a genuine ontological feature of biological entities. The human body, for instance, effectively has organs such as the lungs or kidneys. So, the parts and wholes framework is considered to capture a real characteristic of biological entities and their complexity.

Nevertheless, does this necessarily mean that recognising the heuristic role of ideas of parts and whole rules out the possibility of achieving accuracy about biological reality? It is worth noting that these perspectives are not necessarily mutually exclusive. Scientists may adopt a heuristic approach, recognising that their models and conceptual frameworks are pragmatic tools for investigation while also aiming to align these models as closely as possible

with the actual structure of the biological world. In practice, scientific research often involves a combination of heuristic and realistic approaches, as scientists strive to balance conceptual simplicity and accurate representation of the complex part-whole relationships in nature.

The way in which we obtain knowledge about the world is through specific methodologies using particular concepts. These methodologies and conceptual frameworks can be perfected or changed. Perhaps the pretension to achieve universal truths is not accomplished due to this variety of scientific strategies, but that does not mean that scientific investigations fail to provide reliable information about phenomena. The reference to parts and wholes in biology may go beyond a mere heuristic role and reflect a genuine characteristic of these entities, for instance, when and how particular genes are expressed or under what conditions a particular protein is synthesised.

Another interesting aspect is whether there might be another way to study these phenomena. To give an answer, first, we should recognise the idea of parts and whole from a cognitive view: that our mental representations and processes are shaped by the fundamental notion of entities existing in relation to part and whole. Psychological studies (Tversky and Hemenway, 1984) have demonstrated that parts significantly impact human cognition. These studies reveal that parts are distinct from other attributes of concepts and have a prominent role in the description and differentiation of concepts.

By recognising the significance of parts and wholes in human thought, we better understand how we perceive, categorise, and differentiate concepts. This understanding extends beyond simply recognising attributes and suggests that the relationship between parts and wholes is fundamental to our cognitive architecture. Of course, this analysis chapter is of an epistemological nature and not a psychological one. However, it is worth addressing this dimension to define how fundamental this idea of parts and wholes is. If this idea is crucial in how we have thought about the world, replacing it when we seek to study biological phenomena seems difficult. This is general and not restricted to the biological domain. It is so fundamental in our daily thought about the world that exploring this relationship by highlighting the use of these notions makes it more cognitively accessible and not only contributes to our theoretical understanding of human cognition but also has practical implications in fields such as science education, scientific design, and communication of scientific findings. So, the relevance is both for scientists and for individuals who are being informed about specific scientific data (e.g., colleagues, students and the general public.

5.4. Characterisation of the usage.

This particular view of *a whole composed of parts* in the study of the living world is key in two main areas of scientific practices. One of these relates to the specific way in which we think about this complex world. This view has influenced how study by scientists explains and represents different phenomena.

In this heuristic role, based on the examination made in previous sections, we can establish that the organisational aspect is central to studying the living world and its entities. This organisational labour - depending on the ambit of scientific practice being applied - can also have a role which is classificatory, illustrative, and narrative. These roles will be explained below.

Organisation. The reference to these notions helps in organising the living world's entities and the relations between them. This organisation has special importance in two dimensions. There is a practical one, where this principle has relevance in methodology, explanations, and diagrams/models' elaboration. Its central role is organising the diverse life forms and their respective interactions in terms of parts and wholes, facilitating a criterion to classify, design illustrative devices, and narrate in an organised way how the biological world is.

Classification. From a biological point of view, classifying is nothing more than ordering living beings into groups based on characteristics they have in common. Biologists deal with the diversity of life forms. This diversity requires classification. The best criteria to classify the different life forms have been a topic of debate both for theoretical biologists and for philosophers of biology. Regardless of this discussion, there is no doubt that the type of parts of an entity and how they are organised are criteria that are applied widely by biologists to classify the different parts of life. This can be seen in the distinction between prokaryotic and eukaryotic cells. This classification is central in biology, which is based on the components of each cell, that is, the presence or not of plasmatic and nuclear membranes or what type of organelles they have. In morphological studies, the classification of biological organisms considers their anatomic characteristics.

Illustrative. This idea is central to the generation of visual tools. These can be diagrams or models. They are vital in scientific work because they help in the investigation itself and in presenting to peers or the general public the findings of specific research.

Narrative. Presenting a phenomenon in terms of a basic idea of parts and whole is a guide for the structure of storytelling about a phenomenon. What is the phenomenon? What do researchers want to say about it? What are the main aspects that they want to highlight?

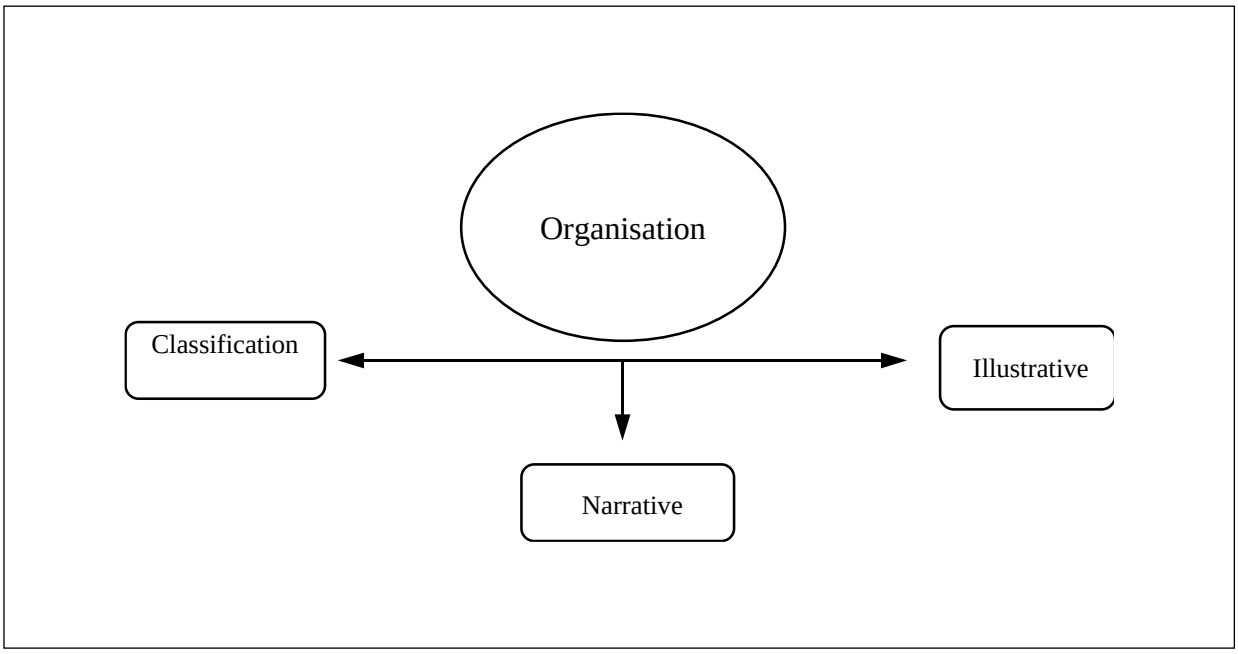

Figure 5.5. Schematic representation of different roles of notions of part, whole, and composition in scientific practice in the biological context.

To sum up, these notions are a guide to address a specific phenomenon because they offer an organisational principle that allows the classification of different life forms and the interactions between them. It is a guide in the design of many visual tools such as diagrams and models. Likewise, this conception of biological entities composed of parts is a narrative starting point to explain how different biological entities and phenomena occur (see Figure 5.6).

What do these philosophical analyses tell us about scientific practice? As the philosophers mentioned above have pointed out, there is a common strategy for breaking down

a phenomenon into parts—scientists elaborate explanations based on the parts' activities in a part-whole manner. This assumption is not exclusive to the biological sciences. This is a widespread assumption about how objects are. Anyone can imagine an entity as having parts. However, this chapter has detailed what is important in developing the study of biological entities. The relevance of analysing these terms lies in how biological entities and phenomena are conceived and characterised, establishing preliminary ideas regarding the phenomenon studied in terms of shape, size, structure, and organisation.

These introductory notions make it possible to define essential aspects of scientific practice related to methodological, explanatory, and representational issues about the phenomenon studied. Likewise, it also helps us clarify how and why the living world is presented to us. Having an idea about how this living world is conceived allows us to understand why biological phenomena are studied, classified, and explained in a certain way. This clarification enables us to understand scientific reasoning and practice better. This understanding of scientific work can significantly help with that specific scientific data or explanation, or a phenomenon making sense to non-expert audiences.

Besides characterising the use, problematic aspects in each dimension were also identified. Explicating these difficult aspects of this use in scientific practice and its consequences in science communication contributes to prompt efforts to develop more effective ways of conveying complex biological concepts and findings. This can lead to better understanding and dissemination of scientific knowledge within the scientific community and the broader public.

5.5 Conclusions

This chapter has examined and characterised the usage of notions *parts* and *whole* in different areas of scientific practice in biology. Their use and importance in ambits such as methodology, explanatory, representational and communicational have been evaluated.

From this analysis, it is possible to conclude, first, this widespread assumption of *entities composing parts is important* in scientific practice, namely methodology, modelling, elaboration of explanations, and visual representations. The role played by these notions in the scientific practice of the biological sciences has particular relevance in 1) how to conceive of the living world and its entities, 2) how to investigate different life forms and their interactions, 3) how to explain and represent the different phenomena that occur in this world, 4) how they communicate scientific information about this world. Second, the reference to parts and whole is an organising principle. It is a guide to define the methodology for starting to investigate a phenomenon to figure out how that particular biological phenomenon is, how to classify the different life forms and their interrelations. It is a helpful guide in the design of representational devices such as diagrams and models. At the same time, this organisational idea of how the living world and entities are and the interaction among them makes it possible to structure coherently the narrative at the moment to communicate scientific information to audiences. Finally, these notions are central to the organisation of the living world, allowing classification and visualisation of biological entities and their interactions. In these aspects, its importance lies in the construction of scientific knowledge about biological entities and phenomena. At the same time, how the phenomenon is delimited, characterised, classified, and visualised is relevant to understanding scientific knowledge production and scientific information about the phenomenon in question.

This chapter has highlighted that it is worth examining how scientists investigate, explain and illustrate their findings. The characterisation made contributes to this examination of scientific practice. It provides a clearer idea about aspects underlying choices of methodology, visualisation strategies, the representation of biological data through diagrams or models, and how the living world is presented to different audiences.

Applying these notions has limitations because the ontological assumptions underlying the ideas of parts and whole can vary depending on the aim of the inquiry, bringing as consequences potential misunderstood about biological phenomena when scientists communicate their findings.

Conclusions

This thesis has analysed the notions of part, whole within the biological realm. It has offered a comprehensive exploration of these concepts from both metaphysical and epistemological perspectives while considering implicit notions regarding the interconnectedness of wholes and their constituent parts in biological practice. This research has developed two primary objectives: first, to assessing conditions under which biological elements configure the relationships between parts and wholes in an integrated way; second, to thoroughly examine and characterise the utilisation of these notions within the biological practice, identifying its usefulness and problematics aspects of this use.

Starting with a critical review of metaphysical literature, by examining relevant philosophical antecedents, the thesis has established a foundation for addressing questions related to composition and the relationship between parts and wholes, arguing that there are insufficient reasons to rule out the existence of composite objects and highlighting that biological entities are exemplary case studies to evaluate the relation between parts and whole. Additionally, is argued the methodological decision to analyse this metaphysics topic from biological theory and practice, highlighting the importance of reframing classical philosophical questions in light of scientific knowledge, specifically from the field of biology.

Chapter 2 is a literature review about the philosophical relevance of analysing these notions in philosophy of biology topics such as levels of organisation, emergence, self-organisation, elaboration of explanations and biological individuality. It was argued what would be a biological object and why these biological entities should be analysed separately from non-biological objects.

Later, Chapter 3, it is highlighted the role of control and regulation actions in the question of how biological entities configure a relation between parts and whole, making up an integrated unit. By examining the challenges and insights provided by synthetic biology, this thesis explored the coordination, communication, control actions that contribute to a

biological entity's unified behaviour and functionality in variable contexts. From this examination, which aspects would have a comprehensive ontological framework on the relationship of the parts as a whole in the biological context was developed.

The concept of emergent properties took centre stage in Chapter 4, particularly within the context of complex systems and debates surrounding mental causation and physicalism. The examination emphasised the significance of composition, parts, and whole notions in understanding and defining emergent properties in biological entities. Control activities and the configuration of the relationship between parts and whole were explored to shed light on the occurrence of emergent phenomena. It was argued that emergent phenomena can occur, both epistemically and ontologically. The epistemic is due to the non-linear interactions that make it difficult to predict some biological entity's behaviours or properties from analysis of parts alone. In turn, ontological emergence can occur because of the action of control mechanisms. While components may have inherent characteristics that cause them to interact with specific counterparts, the specifics of when, how, and for how long they interact are not solely determined by these individual features. Instead, they are contingent upon the overall arrangement of the system. Control and regulation actions and various constraints, such as spatial and kinetic factors, play a crucial role in shaping these interactions. Regardless, if the action of control and regulation mechanisms is not accepted as causal, this does not imply dismissing their global effect on the whole's parts. This effect gives rise to novel configurations, distinct behaviours, improved performance, and novel responses against specific environmental conditions. The whole's performance and behaviour are irreducible and exercise a control action upon its components' activities.

Finally, has it further provided an epistemological analysis of scientific practice in the biological sciences. Considering both the importance and problematic aspects of their application. Talking about *parts composing something* is a common expression that refers to a large variety of entities that we perceive daily. It is a common first approach to explaining how different material things *are*. Scientists also use this everyday approach to start their investigations of some phenomena. In the biological sciences, it is not a different story. These notions are fundamental in the development of methodologies, elaboration of explanations, and designs, and creation of diagrams and models, as well as communicating scientific findings. Therefore, these notions provide a framework for analysing complex systems and objects, enabling us to acquire knowledge about their composition, behaviour, and interconnections.

This philosophical analysis of fundamental notions from both metaphysical and epistemological perspectives offers valuable contributions in several key areas. These contributions can be observed in the following domains:

a) Specific Discussion about Parts and Wholes: The analysis improves our understanding of the relationship between parts and wholes, considering both metaphysical and epistemic perspectives. By addressing these perspectives, the thesis offers insights into the nature of relationships within biological entities, the emergent properties, and the role of these concepts in the biological context.

b) Metaphysics: as has already been argued, analysing biological entities based on contemporaneous biological practice enriches the metaphysical perspective about how reality can be, reframing these classical philosophical questions considering scientific knowledge. So, this practice offers a unique opportunity to examine and scrutinise metaphysical accounts in light of empirical evidence. This evaluation process helps refine, revise, or potentially even reject metaphysical ideas that fail to align with the empirical evidence.

c) Philosophy of Sciences and Philosophy of Biology: This examination is beneficial for philosophers of science and particularly for philosophy of biology. This is due to that the analysis of how the configuration of relations between parts and whole is - considering biological contemporary practice - is relevant in other philosophical debates concerning sciences, such as the emergence and downward causation concepts, and also in topics of philosophy of biology, such as the idea of *biological individuality*.

At the same time, from an epistemic perspective, the exposed it throughout this thesis contributes to updating the philosophers' view about sciences, their reasoning, and their different practices. Philosophers of sciences have much to gain from engaging with contemporary scientific practice. The ever-evolving nature of scientific progress challenges and reshapes philosophical perspectives. The evaluation developed in this thesis enriches their philosophical understanding of current scientific work and provides them with real-world examples to ponder and incorporate into their theoretical frameworks.

d) Sciences: this investigation can also have repercussions outside the philosophical domain. Gaining a more comprehensive understanding of scientific reasoning at present to study biological phenomena is relevant not only for the philosophy of biology but also for scientists themselves. This is due to making explicit scientific reasoning regarding widespread and tacitly used notions. The importance of philosophically examining diverse scientific activities in the generation of knowledge is evident in today's scientific landscape.

Philosophical work often is considered intricate, distant, and sometimes without applicability to practical matters. Even some scientists do not know what the philosophy of science is. This philosophical analysis of contemporary scientific practice can usefully generate instances of dialogue between philosophers and scientists to reflect on their daily work. Engaging in a conversation between philosophers and scientists can create a fertile ground for reflecting on this. Through dialogue with scientists, philosophers can gain insights into cutting-edge research, emerging technologies, and novel discoveries. Parallelly, by exploring the underlying philosophical underpinnings of scientific methodologies, scientists can gain a deeper understanding of the conceptual frameworks that shape their research. Such reflection can lead to a more critical and self-aware scientific approach, enabling scientists to refine their methodologies, question assumptions, and address potential biases. Philosophical reflection upon biological practice can offer conceptual clarity, critical analysis, and ethical considerations that can inform scientific decision-making. These can contribute to discussions on the implications of scientific advancements, the social and ethical consequences of research, and the responsible use of scientific knowledge.

e) General Public: Eventually, this reflection of scientific practice by philosophers and scientists can help to develop effective ways to engage with the public beyond the academic field. People are not informed or learning about science as a 'tabula rasa', which must be filled with information. These people already have certain assumptions about how the world is and works. At the same time, they have intuitions about what scientific work is. Often, these assumptions or intuitions may be incomplete or wrong, which can bring, as an unfortunate result, a lack of understanding about the explanations that scientists are presenting to us or scepticism regarding them. In this scenario, it becomes crucial to explicitly convey how scientific practice truly operates and how it represents the world. This involves explaining the reasoning behind specific investigations and acknowledging the inherent limitations of

research. By doing so, we can foster a more profound understanding among the general audience about the nature of scientific practice and the intricacies of scientific phenomena.

The public can develop a more nuanced appreciation of scientific endeavours and findings through enhanced communication. It allows them to grasp the significance of research outcomes and the process that leads to those conclusions. Furthermore, this transparency can help dispel misconceptions and build trust between the scientific community and the broader society, promoting a more informed and receptive public attitude towards science.

Glossary

Assembly Refers to constructing or building biological systems or components from individual parts or modules. It involves arranging and combining various genetic elements, such as DNA sequences, proteins, or other biomolecules, to create functional biological entities with specific functions or properties. DNA assembly methods include restriction enzyme digestion and ligation and polymerase chain reaction (PCR).

ATP molecules ATP (adenosine triphosphate) is the primary energy currency. It involves numerous cellular processes, including energy transfer, metabolism, and signal transduction. ATP is composed of an adenosine molecule and three phosphate groups. The high-energy bonds between the phosphate groups store energy, which can be released by breaking these bonds through hydrolysis. When this energy is released can be utilised by the cell to drive various biochemical reactions.

Biological devices The concept of "biological devices" refers to engineered biological systems designed to perform specific functions or tasks. These devices are created by manipulating and reprogramming the genetic material of organisms, such as bacteria or yeast, to produce desired outputs or behaviours.

Biological pathways Refer to a series of interconnected biochemical reactions and interactions within a cell or organism to accomplish a specific biological function. These pathways involve the coordinated activity of molecules such as enzymes, proteins, and metabolites, which work together to carry out various cellular processes and physiological functions. Biological pathways are crucial in numerous biological processes, including metabolism, signal transduction, gene expression, and cellular communication.

Cell cycle refers to the series of events that occur in a cell's life, involving its growth, replication of genetic material, and division into two daughter cells. It is a highly regulated process that ensures the accurate transmission of genetic information from one generation of cells to the next.

Co-immunoprecipitation Co-immunoprecipitation is a technique used in molecular biology to study protein-protein interactions. This technique allows researchers to identify and characterise protein complexes and study protein-protein interactions in a physiological context. It involves the precipitation of a target protein and its associated interacting proteins from a complex mixture using specific antibodies.

Computational modelling and design: Computational modelling involves using mathematical and computational tools to model the behaviour of biological systems and predict the outcomes of genetic circuits. Computational models can simulate the dynamics of genetic networks, analyse their stability, optimize their performance, and guide the design process.

Modelling techniques include ordinary differential equations (ODEs), stochastic simulations, and Boolean networks, among others.

CRISR-based technologies Refer to a revolutionary set of genetic engineering and gene editing tools. CRISPR stands for "Clustered Regularly Interspaced Short Palindromic Repeats," which are a unique feature found in the genomes of certain bacteria. These repeats are associated with a group of proteins known as CRISPR-associated (Cas) proteins. The CRISPR-Cas system in bacteria is a natural defence mechanism against viral infections. It allows the bacteria to capture snippets of viral DNA during an infection and store them within its own genome. These stored DNA fragments act as a molecular memory that can be used to identify and target the virus if it invades again in the future. Researchers harnessed this natural bacterial defence system and turned it into a powerful tool for precise and efficient gene editing in a wide range of organisms, including plants, animals, and even humans.

DNA synthesis Synthetic biology relies on the ability to synthesise DNA sequences and assemble them into functional genetic constructs. DNA synthesis involves chemically synthesizing short DNA fragments, called oligonucleotides, and then stitching them together to create larger DNA sequences.

Electron microscopy: Electron microscopy is an imaging technique used to visualise the ultrastructure of biological samples at a high resolution. Unlike optical microscopy, which uses visible light, electron microscopy employs a beam of electrons to generate images. Electron microscopy provides detailed information about the morphology, organisation, and subcellular structures of cells and tissues, allowing researchers to observe fine details that are not visible using other imaging techniques.

Feedback loops Feedback loops refer to a system or process in which the output or result of that system influences or feeds back into its operation. Feedback loops can be positive or negative, depending on how they affect the system.

Genetic circuits Genetic circuits are the central building blocks of synthetic biology. They are designed to control the flow of genetic information within a cell and can be engineered to perform specific functions. Genetic circuits consist of interconnected DNA segments that encode regulatory elements such as promoters, transcription factors, and terminators. These elements interact to control the expression of genes and produce desired biological outputs.

Genetic engineering Genetic engineering consists of modifying and optimising biological systems. Genetic engineering techniques enable the precise manipulation of genetic material, allowing the insertion, deletion, or modification of genes to achieve specific objectives. Tools such as CRISPR-Cas9 have revolutionized genetic engineering by enabling targeted genome editing with high precision and efficiency.

Golgi apparatus The Golgi apparatus, also called the Golgi complex or Golgi body, is an organelle in eukaryotic cells. It comprises a sequence of flattened sacs enclosed by membranes known as cisternae. The main functions of the Golgi apparatus include altering, organising, and packaging proteins and lipids for transportation to their designated locations within the cell or for release outside the cell.

Host organism Synthetic biology often involves choosing a host organism suitable for the desired application. Host organisms can be bacteria, yeast, plants, or even mammalian cells.

Selecting an appropriate host involves considering factors such as genetic tractability, scalability, biosafety, and compatibility with the intended function.

Hydrogen bond It is a type of chemical bond that occurs between a hydrogen atom and an electronegative atom (such as oxygen, nitrogen, or fluorine) in a different molecule or within the same molecule. Although hydrogen bonds are weaker than covalent or ionic bonds, they are still significant and contribute to various important biological and chemical phenomena.

Krebs cycle The Krebs cycle, also known as the citric acid cycle or tricarboxylic acid cycle (TCA cycle), is a central metabolic pathway occurring within the cells of living organisms, including animals, plants, and microorganisms. It is a series of biochemical reactions that occurs in the mitochondria, the powerhouse of the cell.

Lysosomes Lysosomes are membrane-bound organelles containing various enzymes. They are responsible for digesting and recycling cellular waste materials, such as old cell components, macromolecules, and invading bacteria or viruses. Lysosomes break down these substances into simpler compounds that can be reused by the cell.

Methodological Reductionism This approach is used in science to take something to pieces in order to understand its components and determine how they function.

Mitochondria Mitochondria are organelles found in eukaryotic cells responsible for energy production. They generate adenosine triphosphate (ATP), the primary energy currency used by cells. Mitochondria have their own DNA and a double membrane structure.

Modular design This design allows the construction of complex genetic systems by combining these standardized parts in a plug-and-play manner. This approach promotes interoperability, reproducibility, and scalability in synthetic biology.

Modular programming Refers to designing and constructing biological systems using modular components or modules. Modular programming aims to create standardized, interchangeable biological parts or modules that can be assembled like building blocks to construct more complex biological systems. These modules often consist of DNA sequences encoding specific functionalities, such as protein production, sensing, or signalling.

Module Refers to functional units or components that can be assembled and interconnected to create complex biological systems. These modules are often designed to perform specific tasks or functions within a larger biological system.

Nuclei In biology, nuclei (singular: nucleus) are membrane-bound organelles in eukaryotic cells. They are typically spherical or oval-shaped and contain the cell's genetic material, including DNA. Nuclei play a crucial role in regulating gene expression and controlling cell functions.

Ontological Reductionism Refers to the idea that a system is ‘nothing but’ its components and that there is no more to say once the components have been analysed and described.

Peroxisomes Peroxisomes are tiny organelles enclosed by membranes, which play a crucial role in diverse metabolic functions. These organelles house enzymes that facilitate reactions responsible for breaking down fatty acids, neutralising toxic compounds, and creating particular lipids.

Prions It is a class of proteins that can cause infectious diseases in living organisms, including humans and animals. Unlike typical infectious agents such as viruses or bacteria, prions do not contain genetic material like DNA or RNA. Instead, they are misfolded versions of a normal cellular protein called the prion protein (PrP). The misfolding of the PrP protein leads to a conformational change, resulting in an abnormal three-dimensional structure. This misfolded protein can convert other normal PrP proteins into the same misfolded conformation, leading to a chain reaction within the body. This self-propagation process makes prions unique and highly concerning from a biological standpoint.

Resilience It is the capacity to adapt, maintain functionality, and regain stability after facing disruptive events or changing circumstances. Resilience involves absorbing shocks, adapting to new conditions, and returning to a balanced state or functioning.

Robustness Refers to the degree of stability, strength, and resistance to perturbations or variations in a system. A robust system or organism is characterised by its ability to withstand disturbances, uncertainties, or external influences without significant loss or degradation of its function or performance. Robustness implies reliability, durability, and resistance to disruptions, making the system less susceptible to failure or breakdown under change.

Symbiosis Refers to a close and long-term ecological interaction between two different biological organisms from different species. It is a mutually beneficial relationship where the organisms depend on each other for survival, growth, and reproduction. Symbiotic relationships can take various forms, including mutualism, where both organisms benefit; commensalism, where one organism benefits while the other is unaffected; and parasitism, where one organism benefits at the expense of the other. Symbiotic interactions are widespread in nature and can occur between various organisms, including plants, animals, and microorganisms.

Synthesis protein The synthesis of proteins refers to the process by which cells build proteins using the genetic information encoded in DNA. Proteins are essential molecules that perform various functions in living organisms, such as enzymatic activity, structural support, transport of molecules, and signalling.

Systemic approach This approach states that a system cannot be comprehensively understood by breaking it down into its individual parts and examining their isolated properties. Instead, it is crucial to consider the components within the context of the entire system. Systemic approaches prioritize circular causality rather than linear causality.

Systems biology This field encompasses experimental, analytical, and modelling techniques that aim to elucidate how complex interactions give rise to biological properties. Primarily reliant on integrating data from functional genomics methods, systems biology focuses on the dynamic modelling and analysis of extensive networks, such as gene regulatory networks or metabolic networks.

Standardisation It is a fundamental principle in synthetic biology. It involves developing standardized biological parts, such as promoters, coding sequences, and terminators, that can be easily combined and reused in various genetic circuits and organisms.

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