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Emergence in Complex Physiological Processes: The Case of Vitamin B12 Functions in Erythropoiesis

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Abstract: In this paper, we will explore the relation between molecular structure and functions displayed by biochemical molecules in complex physiological processes by using tools from the philosophy of science and the philosophy of scientific practice. We will argue that biochemical functions are weakly emergent from molecular structure by using an account of weak. In order to explore this thesis, we will consider the role of vitamin B12 in contributing to the process of erythropoiesis. The structure of the paper is the following: First, we will consider biochemical functions and why they cannot be easily reduced to their chemical realisers. We will suggest weak emergence as an alternative while also accounting for the relevance of the context, in our case, systemic and organisational. The paper will conclude by considering (1) how the usage of tools from the philosophy of science, such as weak emergence, can aid our understanding of the relations between the components of complex phenomena, such as erythropoiesis, and (2) how the philosophy of scientific practice sheds light on the explanatory role of processes that are dynamically stabilised and the different levels of organisation implied.

Keywords: biochemical functions; weak emergence; robustness

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1. Introduction

Biological and life scientists use the concept of function in reference to a variety of structures and processes that concern living organisms. And even more so, it is noted that one of the differences between the living and the inanimate is that biological systems display functions, but how these functions arise from physical-chemical components is still the object of discussion and seems to lack scientific explanation. This question becomes even more complicated to answer if we consider functional ascription to entities such as biochemical molecules, which operate as a key link between chemical processes in organisms and biological processes.

Biochemical molecules, such as vitamins, proteins, or nucleic acids, are commonly ascribed functions, however, they are chemical compounds and not the standard target for functional ascription [1–4]. This opens questions on the relation between the structure that these molecules display and their (attribution of) functionality. Specifically, one can ask whether it is possible to reduce the functionality of these molecules to their chemical structure or not. In this paper, we will explore the relationship between molecular structure and functions displayed by biochemical molecules in complex physiological processes by using tools from the philosophy of science. We will argue that biochemical functions are weakly emergent from molecular structure by using the account of weak emergence suggested by Franklin and Knox [5] and Bellazzi [6]. According to this account, a given phenomenon can be considered weakly emergent if it is novel and robust. Novelty implies that the postulation of the phenomenon allows for novel explanations compared to only postulating the entities from which it emerges. Robustness implies that the phenomenon is stable within given perturbations, which we will consider in terms of multiple realisability [6–8].

In order to explore this thesis, we will consider the role of vitamin B12 in contributing to the process of erythropoiesis. The structure of the paper is the following: First, we will consider the status of the controversy and why the biochemical functions of vitamin B12 cannot be easily reduced to their chemical realisers. Mostly this is because of the relevance of the evolutionary history of erythropoiesis, which is relevant to identifying which chemical properties of the molecules are contributing to the process. Given that reduction is not feasible, we will suggest weak emergence as an alternative to reductionism, as in the account mentioned above. While building up on Franklin and Knox [5] and Bellazzi [6], we will also present a novel contribution to this account by considering the relevance of the context, in our case evolutionary, to weak emergence. The paper will conclude by considering how the use of tools from the philosophy of science, such as weak emergence, can aid our understanding of the relations between the components of complex phenomena, such as erythropoiesis. We will also specify how the philosophy of scientific practice sheds light on the explanatory role of processes that are dynamically stabilised and the levels of organisation that are present in such processes.

2. Biochemical Functions: Erythropoiesis and Vitamin B12

Vitamin B12 is a vitamin functional for different life and physiological processes, among which erythropoiesis, the renovation of red blood cell. This vitamin comes in four forms: vitamers of cobalamin-compounds: cyanocobalamin, methylcobalamin, hydroxycobalaim, and adenosylcobalamin. This characterisation of vitamin B12 shows that this kind is not characterised only by structural chemical properties but also by the function that these groups of compounds display: it is a functional kind, like "acid". Vitamins are not defined by their composition (alone), but by the behaviour they display in given physiological and biochemical processes [9]. Given the core role that the functional properties play for this kind, it is then important to ask: What does it mean that this vitamin has a function? How does it relate to its structural components?

Functional ascription at the molecular scale has been the object of discussion in recent literature (see [10,11]). This is because, while on the one hand, functions are regularly ascribed at the molecular scale, on the other, there is tension regarding whether evolutionary or etiological views of functions can be applied to such cases because of both "socio-linguistic arguments" and "ontological arguments" (as in [4,12]). The first wants to underline that scientists do not ascribe functionality to molecules by thinking of evolutionary-selected functions. The second instead focuses on whether molecules can be the right ontological target of evolutionary selection. These considerations can lead instead to using a chemical view of function for biochemical molecules, akin to the causal theory of functions [13]. The shortcoming of this approach is that biomolecules seem to have functionality in terms of their contribution to specific biological processes rather than having a different chemical reactivity profile. A way to keep together the considerations while accepting genuine functional ascription to molecules can be found in Bellazzi [4], according to whom a correct analysis of functions in biochemical systems needs to comprise both their chemical and biological characterisation. This can be conducted by identifying which chemical components of the molecule contribute to the process under consideration, via which chemical reactions, and how this contribution is process-specific. This offers us the following account of biochemical functionality:

BC-function: Biochemical functions are associated with a set of chemical properties that lead to a specific effect within biological processes. These biological processes are a product of evolution, and, as such, the relevant chemical properties are indirectly evolutionally selected [4].

This account of function, while it individuates a specific realization basis for biochemical functions, does not reduce such functions to their chemical components, as the individuation of them is not specific enough to analyze the contribution that biochemical molecules make. This view accordingly builds on a casual contribution view of functions a-la-Cummins [13], for which a function is a causal contribution to a given process.

However, this view is also different from it as it adds and specifies that the evolutionary context is the one picking up the relevant chemical processes for the biological process (and not the interest of the scientists)[1]. Moreover, this account of functions is compatible with the organizational account of functions, which has proved successful in the analysis of other cases of relations between different parts of given systems [14,15]. According to an organizational account of functions, functions have to be understood as inherently related to the idea of the self-maintenance of biological systems. This view works well with the proposed account of functions, as biochemical functions are seen as specific causal contributions to an organizational system or process that are contributing to life. In this sense, a biochemical function can be seen as realized by those chemical properties of the molecule that contribute to a higher or organizational process that maintains life. At the same time, this account does not want to present a unique view of functionality and can be seen as compatible with forms of function pluralism, for which we can ascribe functions in different ways in different contexts (as in [11]). In this regard, the account is compatible with using a causal contribution view of functions in some contexts, a biochemical view of functions in others, and an etiological evolutionary view of functions for others as well.

Let us consider an example to make the case more precise: erythropoiesis[2]. Erythropoiesis is the process that produces new erythrocytes in order to allow for the renovation of red blood cells and the destruction of the old ones that are needed daily to keep blood healthy. In order for this process to proceed properly, different biochemical molecules are needed, and in particular, the role of folic acid, vitamin B12, and iron has been underlined. Specifically, vitamin B12 is needed for the proliferation of erythroblasts during differentiation. A lack of this vitamin can lead to severe dysfunction in erythropoiesis, which can result in erythroblast apoptosis and anemia. As a result of this brief overview of the considered physiological processes, we can notice that erythropoiesis is a complex process that requires the interaction of different components that need to be integrated for the process to continue appropriately. In this paper, we focus on the biochemical function of vitamin B12 in this process. Following the account aforementioned, the biochemical function of vitamin B12 (**BF-B12**) corresponds to the specific set of chemical dispositional properties that are manifested in "the transfer of a methyl group from 5-methyl-THF to homocysteine via methylcobalamin, thereby regenerating methionine" [16].

Accordingly, we can unpack B12 vitamin function as those chemical dispositional properties that react in a specific way during the regeneration of methionine required in erythropoiesis (following the account presented in [4]). The action of the chemical powers of **BF-B12** depends on the right biological context for their contribution and on the presence of the right process to which the molecules can contribute. This can be seen within the framework of an organisational account of function: the organisational process of erythropoiesis needs to be happening, also thanks to cell regulatory mechanisms and the action of various enzymes and co-factors, for the **BF-B12** to be realised. Given the organizational account of function that works well in this context, it is important to stress that this functional contribution relates to the well-functioning of a process that is *evolutionarily selected*. The role of evolutionary selection is important in identifying which processes and contributions of vitamin B12 result in functional erythropoiesis in a way that is beneficial to the self-maintenance of the organism.

This consideration rules out the possibility of fully reducing biochemical functions to their chemical realizers. This is so because the organizational and system considerations that pertain to the process of erythropoiesis are needed in order to identify the specific contribution that relates to the biochemical function. How can we then characterise the relationship between chemical components and the biochemical function realised in erythropoiesis, if not via a reductive strategy? An answer can be provided by weak emergence.

3. Weak Emergence of Biochemical Functions: Erythropoiesis and Vitamin B12

Emergence is a useful tool to characterise the relationship between dependent but different or autonomous components of a given system [17]. The discussion on this notion is wide in terms of conceptions, applications, and topics, and it is important to clarify where we stand in this regard. Emergence can firstly be characterised in terms of epistemic or ontological emergence, where the first (epistemic) refers to the relation between the entities or phenomena within theories and relations of explanations/computation and the second (ontological) regards some ontological or qualitative difference that the emergent entity has in comparison to the lower level. In the case of epistemic emergence, a given entity is considered emergent in relation to whether that emergent property or entity cannot be *derived*, *computed*, *or predicted* on the basis of the theories, laws, or postulated properties that realise them [18]. In the case of ontological emergence, instead, a given entity is considered emergent in relation to *whether that entity displays some novel or causally specific features that makes them qualitatively and ontologically* different from the lower-level [18,19]). In this paper, we are concerned with *ontological emergence*[3]. A second important distinction that one can draw within the sphere of ontological emergence is the difference between weak and strong emergence[4]. A given phenomenon is considered weakly emergent when it is "realised by the lower-level ones" in a genuine way, even if every token of the property of the emergent phenomenon is identical with *some* lower-level feature at the time considered [19]. A given phenomenon is instead considered strongly emergent when it is realised by the lower-level entities, but at least one token of the properties of the emergent phenomenon is novel compared to the lower-level at the time considered [19].

In this paper, we will consider ontological weak emergence and follow this characterisation: a given phenomenon can be considered weakly emergent if it is novel and robust [5,6]. Novelty implies that the postulation of the phenomenon allows for novel explanations compared to only postulating the entities from which it emerges. Robustness implies that the phenomenon is stable within given perturbations, which we will interpret in terms of multiple realisabilities. This account presents a combination of epistemic and ontological criteria in that it considers both the contribution that considering a given entity makes to explanations and the stability displayed. Moreover, it acknowledges the relevance of robustness, a feature of biological systems that plays a crucial role in the discussion in the biological sciences [7,21].

In detail, the defining properties of the phenomenon under consideration are considered emergent when they are characterised by two features:

- Novelty: "it is possible to identify the emergent property in a distinctive way[5] from the properties held by the lower-level entities, and the consideration of such a property improves explanations, leading to new ones" [6]; see also [22]). Novelty is a useful criterion to identify emergence as it captures the epistemic component that the postulation of emergent phenomena can bring. Specifically, it allows us to see that there are explanations that can be provided by applying emergent phenomena.
- Robustness: the emergent property displays stability within a certain range of perturbations and relatively to some lower-level properties, which we will interpret here in terms of multiple realisations [5,8]. While novelty is mostly epistemic, robustness is the ontological feature of this account. In this paper, robustness is interpreted in terms of multiple realisability, as in Boone [7] and Bellazzi [6], where a phenomenon can be considered multiply realisable when it can be realised by different lower-level entities.

Weak emergence, so formulated, can be a fruitful conceptual tool when considering the relations between chemical structure and biochemical functions. This view combines a form of dependence, allowing for the identification of the specific chemical components that contribute to the physiological processes, with the ontological autonomy and relevance of the functional contribution. This allows us to maintain the specificity of the biochemical functions while keeping them distinct from the chemical features from which they are realised. Moreover, as we will clarify in the next section, this account allows for good compatibility with scientific practice, as the weak emergence of biochemical functions in the right context can be an *explanans* for their stability and relevance in erythropoiesis. Specifically, it is legitimate to ask about the relationship between novelty and robustness and the weak emergence of the phenomenon. On the one hand, we can interpret novelty and robustness as our means to track and have access to the weak emergence of the phenomenon that we are considering. On the other hand, weak emergence represents the ontological reason or principle why the phenomenon displays novelty and robustness (see also [21]).

Let us now apply this account to the case study considered. As we said in the previous section, vitamin B12 has **BF-B12** in erythropoiesis, and this can be identified with the specific chemical properties of the vitamin B12 molecules that are responsible for the transfer of a methyl group from 5-methyl-THF to homocysteine via methylcobalamin. These properties are relevant because of the evolutionary history of erythropoiesis, which evolved in order to interact specifically with the chemical properties of given chemical compounds. Can **BF-B12** in erythropoiesis be considered weakly emergent?

The first step is to consider whether **BF-B12** in erythropoiesis satisfies **(a) novelty.** Novelty is defined as the capacity to lead to new explanations once the property is distinctively identified and it is possible to identify a distinctive causal profile of such property. This criterion is mostly epistemic and tells us that the postulation of the property considered provides more explanatory power than simply postulating the lower-level entity from which it emerges. In the case considered by this paper, it means that postulating **BF-B12** in erythropoiesis is more explanatorily powerful than considering the simple cobalamin as a chemical compound and its functional profile, i.e., its reactivity profile. We argue that this is the case for two reasons. The first is that, as we said, the consideration of the merely chemical properties of the compound is not specific enough to tell us which properties are contributing to erythropoiesis and thus does not give us enough explanatory power. Specifically, the reactivity profile of the various cobalamin compounds comprises a variety of reactions the molecules can undergo, and this differs from the more specific contribution vitamin B12 makes to erythropoiesis. In terms of explanations, the consideration of **BF-B12** as a biochemical function allows us to consider the specific functional role that the vitamin plays as a vitamin and not as a series of chemical compounds. This provides us with more specific explanations. Moreover, it allows us to see the contribution vitamins make to a specific physiological process. In a nutshell, considering BF-B12, it explains the functional role of the vitamin in a more specific and focused way than its chemical counterpart, thanks to the specificity of the function and its role in the context. The second reason for which the consideration of **BF-B12** is novel in this sense can be found in the multiple realisabilities that this function displays. As we said, multiple realisability can be defined as the capacity of a given type to be realized by different lower-level ones. Vitamin B12 can contribute to erythropoiesis in its four vitamers form; that is, four different chemical compounds can contribute to erythropoiesis thanks to specific relevant interactions. This allows the **BF-B12** in erythropoiesis to be multiplied by the four vitamers. Why would this matter for our explanations? The answer is that the consideration of **BF-B12** as such, compared to the chemical properties of each vitamer compound, allows us to consider the contribution of vitamin B12 to erythropoiesis while screening off chemical differences. Accordingly, the consideration of the biochemical function in itself (without considering the details of the realisers) can allow us to improve our explanatory power in terms of making a more direct and simpler explanation compared to the one that would consider each vitamer on its own (following a chemical explanation only) compared to a biochemical systemic one.

Moreover, the account of biochemical functions presented is compatible with an organisational view of functions (as in [15]). The analysis of the function from the point of view of the organizational system can boost our explanatory perspective as it allows the identification of the level of biochemical complexity that generates a particular physiological phenomenon, namely the regeneration of erythroblasts, and the contribution that B12 makes to this process. The introduction of **BF-B12** in erythropoiesis can thus be considered novel. Moreover, this novelty remains particularly interesting because it allows considering the explanatory role that biochemical functions have, despite their manifestation and causal role being, by definition, context-dependent. The context dependency of biochemical phenomena can be used either in favor of or against their ontological, that is, existent, status (as in [3,23]). In the account proposed, it is the fact that biochemical functions are context-dependent, that is, within an organizational systemic setting, that allows for their novelty to be explanatorily relevant.

Let us now turn to **(b) robustness**. The literature on robustness is wide in scope and relevance, as we can identify different kinds of robust behavior. Nevertheless, robustness can be seen as a useful "bridging notion" that allows for the integration of practical and theoretical aspects of a given phenomenon [24]. Generally, we can define robustness as the capacity of a given phenomenon to remain stable within given perturbations. This interpretation of robustness is well captured by the expression of Giuliani, for which robustness relates to the "die-hardness" of a phenomenon: this phenomenon can resist variations at the lower level [8]. In the context of biological cases, we find that an interesting application of this can be seen in terms of multiple realizability (as in [6,7]). In this case, a phenomenon is "hard to die" when there are different phenomena or things at the lower level that can realise it.

Let us unpack this further. Multiple realisations can be seen as having the same type of entity; in the case discussed, a given biochemical function is realised by different types of entities at the lower level, that is, the chemical properties of different cobalamin compounds [7,25]. Moreover, according to this understanding of multiple realisations, at the given time *t* every token of the property considered will be realised by some specific token features of the realising feature. For example, in a given instance of erythropoiesis, the contribution of **BF-B12** to erythropoiesis can be realized by a set of token molecules of cyanocobalamin (one of the vitamers of vitamin B12), and in another instance, it can be realized by instances of metyhlcobalamin. This makes the function **BF-B12** multiply realised, while maintaining the possibility that, in given instances, the token functions remain singularly realised.

Given the definition of robustness in terms of multiple realisability, the fact that **BF-B12** can be realized by different molecules while maintaining the efficiency and organizational stability of the process of erythropoiesis is sufficient ground for its robustness. Again, the multiple realisability and robustness of such functions can only be properly understood if we consider the organizational context around such functions, that is, the process of erythropoiesis and its evolutionary history. It is thanks to this organizational structure that the contribution that given chemical components bring to erythropoiesis can remain robust, despite being realized by different vitamins of vitamin B12.

In conclusion, while there is a relation between the chemical structure of vitamin B12 and its functional contribution, we have grounds to interpret such a relation in a non-reductive way, specifically by interpreting such functions as weakly emergent. **BF-B12** can display novelty because the postulation of biochemical functions understood as organizational and specific functions can improve our explanations of erythropoiesis. This is so because the notion of function used is causally specific and allows for the context and organizational dependence that these phenomena maintain. Moreover, **BF-B12** can display a form of robustness as well as stability, as the function is multiply realizable because vitamin B12 can be composed of four different vitamers. Accordingly, **BF-B12** is weakly emergent as it displays novelty and robustness within erythropoiesis.

4. Scientific Practice and Weak Emergences

Why is the consideration of weak emergences relevant for scientific practice, and what are the benefits that their consideration can bring?

As we said above (Section 3), novelty and robustness are our means to track the weak emergence of the phenomenon that we are considering. On the other side, weak emergence represents the ontological reason or principle why the phenomenon displays novelty and robustness. Emergence is, in a way, the feature through which we can both postulate the existence of something and its knowledgeability (as in [6]). So, when in scientific practice we are studying an emergent phenomenon, we can know that it is such because it displays novelty and robustness; we have epistemic access to its emergence thanks to its being novel and robust. But, from an ontological point of view, the phenomenon can display novelty and robustness because it is emergent and so existent in the first place[6].

Let us consider this more precisely. Novelty has been defined as what captures an epistemic dimension of scientific practice, allowing the identification and explanation of a new stable dynamic process, i.e., of a phenomenon that is context-dependent. The emergent property or phenomenon offers an *explanans* for these new dynamics. More precisely, the weak emergence of BF-B12 allows for explaining why vitamin B12 contributes to erythropoiesis in the specific way considered. However, this is also possible because the emergent property has an explanatory power by virtue of its stability, that is, its robustness: we are able to track the contribution of BF-B12 in a way that is stable and that "screens-off" the fact that these molecules are multiply realisable.

This suggests considering the role that robustness has in this account and its relevance for scientific practice. On the one hand, robustness is a feature of the phenomenon that indicates (epistemically) the presence of a weak emergent phenomenon; on the other, robustness is also an ontological feature of the phenomenon because it brings in multiple realisabilities. This is so because the emergent property can be understood independently from the system's constituent at the lower levels and can acquire a proper ontological status: it is something different from its realizers. In scientific practices, this allows the emergent entity to become an *explananda*, and an object that can then be identified, tracked, and explained.

We can notice that, thus, a weakly emergent phenomenon can be both an *explanandum*, as something that explains a specific contribution, and an *explananda*, by becoming a self-standing phenomenon and thus an object of scientific inquiry. This duality allows us to see that at the crossroads of functional accounts and robust explanations, there is an issue of philosophy in practice that regards how different levels of explanation are identified and inquired about. What, in fact, becomes relevant is accounting for, on the one hand, the specific causal contribution that the emergent entity has while, on the other hand, how much such entity can be explained once it is identified as a core contributor to the phenomenon. In the case considered, BF-B12 has a given causal specificity in erythropoiesis that is novel, allowing for better explanations, and remains robust; at the same time, the function of BF-B12 remains something to be explained in scientific practice, justifying its investigation in scientific terms. How can we then have something that is both *explanans* and *explanandum*?

As Giuliani wrote [8], one of the core features of biological systems is that they operate with different *levels of organisations* that are connected by specific nodes, such as, for instance, biochemical molecules. Moreover, this paradigm allows for the detection of a clear "signature of robustness", i.e., the ability of a system to keep different scales of response to environmental stimuli separated.

The consideration of different levels of explanation can allow us to see how emergent phenomena can play this double role in scientific practice. Erythropoiesis can be divided into "biochemical" and biological "level". The first is the system of biochemical reactions needed in the regeneration of methionine for erythroblasts. In this case, the emergence of BF-B12 allows us to explain (being an *explanans*) the contribution made by vitamin B12 thanks to its robustness and novelty. The second is the biological level, which allows us to see how the production of new erythroblasts contributes to the organism. At this level, the stability of BF-B12, given its robustness, allows it to be a target of the relevant evolutionary explanations that still need to be further investigated. This interplay allows us to see how, within given levels of organisation, we can see the relevance that weak emergence brings.

This is possible because the account of weak emergence used considers robustness, which allows us to identify the ability of a system to "keep separate different scales of response to environmental stimuli" (as in [8]). The robustness of BF-B12 represents a bridge between the two levels of explanation, the biochemical and the biological, and this can be further used within scientific practice.

This reflection can be further expanded by considering the relevance that robustness plays across other levels of organization. Robustness is the *explanandum* for inquires from an ontogenetic or phylogenetic point of view, and it is the *explanans* for evolvability or higher-level biological phenomena. In this sense, robustness is a target of natural selection and can be listed among the features that enable evolutionary change. This is an example that Huneman [26] labels with the term "explanatory reversibility" [24]: "Thus, with respect to evolution, robustness may be seen as an aspect to be explained by (*explanandum*) or as a feature that explains (*explanans*) evolutionary change and/or the particular evolutionary trajectories that are discovered in the history of life. Robustness as an *explanandum* connects with other evolutionary *explananda* such as complexity, modularity or evolvability". The context dependency (e.g., embodied topological features of the system) can be understood, in this sense, as the "invariance through continuous transformation" exhibited at the network level (Huneman, ibidem). This is something that we can apply to BF-B12, and it will allow us to further see the duality of *explanans* and *explanandum* that its weak emergence plays. Biochemical functions remain stable while changing the specific vitamer considered and while maintaining the contribution to the network involved in erythropoiesis. The function to be explained is no longer an attribute of a piece of matter but of that piece of matter (molecules) in a given network. This allows it to be something that explains a specific contribution but also something that has to be explained within the evolutionary history of the network of relations involved in erythropoiesis.

Concluding that weak emergence is so characterised allows us to see how the consideration of weakly emergent phenomena can contribute to scientific practice, specifically when there are different levels at play[7]. The consideration of biochemical functions provided framed them as fundamentally dependent on the network in which they operate. Network approaches allow us to account for biological regulation in terms/trough weak (but robust) emergent properties and allow us to link the components of our analysis. Giuliani wrote that this allows for the detection of a clear "signature of robustness", i.e., the ability of a system to keep different scales of response to environmental stimuli separated [24][8]. This offers two different sides of the explanation. On the one hand, the emergent phenomenon is a source of explanation for the biochemical level considered; on the other, the emergent phenomenon can become a target of explanations thanks to its robustness.

5. Conclusions

The characterisation of the relationship between structure and function in biochemical systems and molecules is still an object of discussion. This characterisation is even more relevant if we consider that biochemical functions operate as a key link between chemical processes in organisms and biological processes. In this paper, we have argued that the use of the philosophical tool of weak emergence can allow us to characterise the relation between structure and function in a way that is interesting for scientific practice as it considers the levels of organisations involved. Specifically, we have built up on an account of weak emergence (as in [5,6]) by considering how the context, in our case systemic and evolutionary, can allow us to frame weak emergence in a way that can aid the consideration of different levels in scientific practice. This is so because weak emergence can allow us to shed light on the different explanatory roles that are present in processes that are dynamically stabilised and the levels of organisation that are present in such processes. Specifically, we concluded by considering how the emergent phenomenon can be both explanatory and explained, thanks to the crucial role that it plays as the connecting link between biochemical and biological processes and its robustness.

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Notes

[1] For a more detailed analysis of the relation between this view of functionality and Cummins' account can be found in [4].

[2] The main reference for erythropoiesis is [16]. Moreover, parts of this section rely on the discussion on biochemical functions published in Bellazzi [4].

[3] As suggested by the reviewer, it is important to notice that sometimes weak emergence is referred to as epistemic emergence, while strong emergence refers to ontological emergence (as also in [18]). In this paper, we are considering ontological weak emergence, which considers the features of the emergent entity as qualitatively different from the lower-level, but still dependent on it and not presupposing any form of non-physicalism. Moreover, this account wants to be compatible with forms of epistemological or methodological reductionism, allowing for scientific research to advance in a way that allows a reductive methodology or explanation of the emergent features, without changing their ontological status (as in [5,6]).

[4] The distinction between weak and strong emergence can also be framed within epistemic contexts. For instance, Chalmers [20] defines weak emergence as the case in which the "high-level phenomenon arises from the low-level domain, but truths concerning that phenomenon are *unexpected* given the principles governing the low-level domain" and strong emergence as the case in which the "high-level phenomenon arises from the low-level domain, but truths concerning that phenomenon *are not deducible even in principle* from truths in the low-level domain".

[5] In a "distinctive way" indicates that the emergent property possesses a specific causal profile compared to the entities realising it, that is leading to specific effects.

[6] The difference between the epistemic and ontological aspect of our argument is important to underline why the characterisation of emergence proposed is not circular. Specifically, weak emergence is what makes the phenomena novel and robust in the moment in which we want to track them, but it is precisely the manifestation of these features that allows us to see that weak emergence is in place.

[7] As suggested by one of the reviewers, a further implication of this paper could impact how we can conceptualise the distinction and interplay between pragmatic systems biology and systems-theoretic biology. While this represents an interesting further development, it goes beyond the scope of this paper and remains to be explored in future work.

[8] Segue: For Giuliani, the biological way to robustness in an ever-changing environment is the presence of a network in which elements self-organize, by the only effect of their location in the network, in differentiated roles, so as to ensure both high sensitivity to environmental stimuli and the maintenance of an invariant structure.

References

1. Bartol, J. Biochemical kinds. *Br. J. Philos. Sci.* **2016**, 67. [CrossRef]
2. Havstad, J.C. Messy chemical kinds. *Br. J. Philos. Sci.* **2018**, 69. [CrossRef]
3. Tahko, T.E. Where do you get your protein? Or: Biochemical realization. *Br. J. Philos. Sci.* **2020**, 71. [CrossRef] [PubMed]
4. Bellazzi, F. Biochemical functions. *Br. J. Philos. Sci.* 2022; forthcoming.
5. Franklin, A.; Knox, E. Emergence without limits: The case of phonons. *Stud. Hist. Philos. Sci. Part B Stud. Hist. Philos. Mod. Phys.* **2018**, *64*, 68–78.
6. Bellazzi, F. The emergence of the postgenomic gene. *Eur. J. Philos. Sci.* **2022**, *12*, 17. [CrossRef] [PubMed]
7. Boone, W. Multiple realization and robustness. In *Biological Robustness: Emerging Perspectives from within the Life Sciences*; Springer: Cham, Switzerland, 2018; pp. 75–94.
8. Giuliani, A. The Robustness/Sensitivity Paradox: An Essay on the Importance of Phase Separation. In Biological Robustness: Emerging Perspectives from within the Life Sciences; 2018; pp. 163–173.
9. Thyssen, P. Are Acids Natural Kinds? *Found. Chem.* **2023**. *preprint*. [CrossRef]
10. Havstad, J.C.; Palazzo, A.F. Not Functional yet a Difference Maker: Junk DNA as a Case Study. *Biol. Philos.* **2022**, *37*, 29. [CrossRef]
11. Malaterre, C. What Are Ribozymes for? Arguing for Function Pluralism. In *Functions: From Organisms to Artefacts. History, Philosophy and Theory of the Life Sciences*; Gayon, J., de Ricqlès, A., Dussault, A.C., Eds.; Springer International Publishing: Cham, Switzerland, 2023; pp. 265–280.
12. Garson, J. There Are No Ahistorical Theories of Function. *Philos. Sci.* **2018**, *86*, 1146–1156. [CrossRef]
13. Cummins, R. Functional Analysis. *J. Philos.* **1975**, *72*, 741. [CrossRef]
14. Mossio, M.; Saborido, C.; Moreno, A. An organizational account of biological functions. *Br. J. Philos. Sci.* **2009**, 60. [CrossRef]
15. Bertolaso, M. On the structure of biological explanations: Beyond functional ascriptions in cancer research. *Epistemol. Riv. Ital. Di Filos. Della Sci.* **2013**, *1*, 112–130. [CrossRef]
16. Koury, M.J.; Ponka, P. New insights into erythropoiesis: The roles of folate, vitamin B12, and iron. *Annu. Rev. Nutr.* **2004**, *24*, 105–131. [CrossRef] [PubMed]
17. O'Connor, T. Emergent Properties. In *The Stanford Encyclopedia of Philosophy, Winter 2021 ed.*; Zalta, E.N., Ed.; Stanford University: Stanford, CA, USA, 2021. Available online: https://plato.stanford.edu/archives/win2021/entries/properties-emergent/ (accessed on 20 February 2024).

18. Gillett, C. The Varieties of Emergence. On Their Natures, Purposes, and Obligations. In *Reduction and Emergence in Science and Philosophy*; Cambridge University Press: Cambridge, UK, 2016; pp. 173–199.
19. Wilson, J. *Metaphysical Emergence*; Oxford University Press: New York, NY, USA, 2021.
20. Chalmers, D.J. Strong and weak emergence. In *The Re-Emergence of Emergence: The emergentist hypothesis from Science to Religion*; Clayton, P., Davies, P., Eds.; Oxford University Press: New York, NY, USA, 2006.
21. Eronen, M.I. Robustness and reality. *Synthese* **2015**, *192*, 3961–3977. [CrossRef]
22. Knox, E. Abstraction and its limits: Finding space for novel explanation. *Noûs* **2016**, *50*, 41–60.
23. Santos, G.; Vallejos, G.; Vecchi, D. A relational-constructionist account of protein macrostructure and function. *Found. Chem.* **2020**, *22*, 363–382. [CrossRef]
24. Bertolaso, M.; Serrelli, E.; Caianiello, S. Introduction: Issues About Robustness in the Practice of Biological Sciences. In *Biological Robustness: Emerging Perspectives from within the Life Sciences*; Springer: Cham, Switzerland, 2018; pp. 1–22.
25. Polger, T.W.; Shapiro, L.A. *The Multiple Realization Book*; Oxford University Press: New York, NY, USA, 2016.
26. Huneman, P. Robustness: The explanatory picture. In *Biological Robustness: Emerging Perspectives from within the Life Sciences*; Springer: Cham, Switzerland, 2018; pp. 95–121.

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