Biochemical Functions

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Function talk is a constant across different life sciences. From macro-evolution to genetics, functions are mentioned everywhere. For example, a limb's function is to allow movement and RNA polymerases' function is to transcribe DNA. Biochemistry is not immune from such a characterization; the biochemical world seems to be a chemical world embedded within biological processes. Specifically, biochemists commonly ascribe functions to biomolecules and classify them accordingly. This has been noticed in the recent philosophical literature on biochemical kinds. But while a lot has been written on biological and psychological functions, little has been said explicitly about biochemical fuctions. Here, I explore functional attribution to biochemical molecules. I argue that if we accept this attribution, then biochemical functions are constituted by chemical dispositional properties that causally contribute to selected biological processes. In section 2, I discuss the controversy concerning the characterization of biochemical functions. In section 3, I consider whether a biological or a chemical understanding of function can be applied to biochemical functions, illustrating the account with the example of vitamin B12. The result is that none of the theories on their own provides an adequate characterization. In section 4, I present an account of biochemical functions. In section 5, I assess this account taking into consideration common requirements for a theory of functions and an objection.

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1. Introduction

> The biochemical, for example, is not just the chemical aggregated. Biochemical entities may be individuated functionally in terms of their effects on the organism or the role that they play in a particular system.
>
> (Khalidi [2013], p. 200)

Function talk is a constant across different life sciences. From macro-evolution to genetics, functions are mentioned everywhere. For example, a limb's function is to allow movement and RNA polymerases' function is to transcribe DNA. Biochemistry is not immune from such a characterization. Specifically, biochemists commonly ascribe functions to biomolecules and classify them accordingly. This has been noticed in the recent philosophical literature on biochemical kinds. For instance, Slater ([2009]),Tobin ([2010]), Goodwin ([2011]), Bartol ([2016]), Havstad ([2018]), Kistler ([2018]), and Tahko ([2020], [2021]) mention that biochemical kinds are defined in terms of chemical composition and the function their instances exhibit in biological systems. Functional characterization is well spread in biochemistry and involves genes (Germain et al. [2014]) and kinds as vitamins (Combs [2012], p. 377; Carr and Maggini [2017]; Fang et al. [2017]). Proteins offer a common case study: they are defined in terms of the amino-acid chain that composes them and the function they play. The attribution of a functional property is not secondary, as proteins are classified into two varieties: fibrous proteins that mostly have a structural function; and globular proteins, such as enzymes or antibodies, that have a physiological function (Bartol [2016], p. 534). But while a lot has been written on biological and psychological functions, little has been said explicitly about biochemical functions. It is often assumed that biochemical functions are just biological functions (see Slater [2009]; Bartol [2016]), as those that can be identified following the principles of natural selection. Nevertheless, the important chemical compositional nature of biochemical kinds requires a deeper analysis of what biochemical functions are. The biochemical world seems to be a chemical world embedded within biological processes and this impacts the nature of biochemical functions as well.

In this article, I will explore the ontological consequences of accepting functional attribution to biochemical molecules, granted that scientific practice and the relevant literature seems to accept that this is the case.[1] Such analysis is important because biochemical kinds have recently caught the attention of philosophers interested in the unity and disunity of science, due to their representing 'kinds at the borders' (Kistler [2018]; Tahko [2020], [2021]). If, on the one hand, biochemical kinds have a structural-chemical nature, then, on the other, they also have a biological-functional one. Accordingly, understanding the nature of biochemical functions can inform such debates. Moreover, it can provide further clarity when considering functions in the biochemical context for different purposes. For instance, the ascription and understanding of biochemical functions can improve the explanation of the biosynthesis of some biochemical kinds and their necessary introduction via nutrition. Here, I will argue that if we accept such attribution as genuine, biochemical functions consist in causal dispositions to contribute to biological processes and manifest in specific circumstances because of the evolutionary history of the systems in which the molecule interacts. The proposed view has the benefit of being in dialogue with contemporary characterizations of functions while taking into account the peculiarity of biochemical functions, which cannot be simply identified as biological or chemical functions.

The structure of the article is as follows: In section 2, I will discuss the controversy over

[1] The conclusions are based on the conditional acceptance of genuine attribution of biochemical functions.

the characterization of biochemical functions and the relevance of this debate. In section 3, I will move to consider whether a biological or chemical view of function alone can be enough for biochemical characterization and I will illustrate my account using the example of vitamin B12. The conclusion of this analysis is that none of the theories mentioned seem adequate on their own to account for biochemical functions. Evolutionary accounts of function having a particular function aren't satisfactory either from a semantic or from an ontological point of view (Griffiths [2009]; Germain et al. [2014]; Garson [2018]), while the chemical approach does not capture the specificity of the contribution made within biological processes.[2] In section 4, I will present what I deem the most sensible way to understand biochemical functions. These functions consist of chemical dispositional properties that causally contribute to selected processes or traits within an organism. Their manifestation conditions are explicated in terms of actual chemical reactions, while the identification of the relevant chemical properties in the relevant context should be given in terms of evolutionary history. In section 5, I will assess this account, taking into consideration standard requirements for a theory of function. In conclusion, biochemical functions should be understood by considering jointly a causal dispositional view of functions and an evolutionary perspective.

2. Biochemical Kinds and Biochemical Functions

Biochemical kinds are characterized in terms of structure and function: they are some macro-molecules that play some roles or some functions within given contexts. A structural characterization of a biochemical kind will allow us to identify its chemical structure and composition (Slater [2009]), while the biological side is given by the functional aspect of these molecules. Nevertheless, what biochemical functions are is open to be debated. In the philosophical literature on biochemical kinds, functions are presented in relation to 'biological functions', while not expanding on which account of biological function is relevant and what the implications of such attribution could be. For instance, Slater ([2009], pp. 858–59]) in his article about monism or pluralism concerning macro-molecules writes that we can read these functions within the framework of the biological theories of function and with an holistic enterprise, even if he does not further specify how this could be done. A similar suggestion is presented by Bartol ([2016]) when he argues for the duality of biochemical kinds. He considers these kinds as presenting 'two joints': chemical in terms of structure and biological in terms of function. This is supported by the fact that, for Bartol ([2016]), biochemical functions are biological functions and so should be interpreted within a historical and evolutionary framework.[3] However, such his-

[2] I will refer to 'evolutionary accounts' of function to mean both backward-looking and forward-looking accounts of biological functions. I count as evolutionary all of those accounts that make a reference to maximizing Darwinian fitness of those bearing the traits with the relevant function either in the past or in the future. Accordingly, Bigelow and Pargetter's ([1989], pp. 189–91]) account also counts as evolutionary as they make explicit reference to maximizing Darwinian fitness in the future).

[3] This hypothesis is also presented, even if not discussed in detail, in (Slater [2009]; Tahko [2020]).

torical and evolutionary characterization does not pertain to the chemical, so biochemical kinds present a dual nature—according to Bartol ([2016]). The interplay (and potential tension) between the chemical-structural nature of biochemical kinds and the biological-functional nature is also present in (Havstad [2018]). Instead of contrasting the two approaches, she underlines that protein characterization is complex and involves the consideration of micro-structural properties, biological-functional properties, and aetiological properties. She reports that 'somehow, scientists are routinely and consistently individuating proteins according to some combination of their micro-structural and aetiological properties' (Havstad [2016], p. 739). Finally, in his works on biochemical kinds, Tahko ([2020], [2021]) discusses functions in the biochemical context as biological evolutionary functions that can be interpreted either with the aetiological theory or the with goal-directed dispositions one. While his account considers functions as dispositional properties, biochemical functions are still identified as biological ones. Leaving aside the concerns over what properties are relevant for kinds to be biochemical, let's focus on what are such functional properties. Little is said explicitly on how such attribution works and what biochemical functions are. Given the attribution of function to biochemical molecules and the important role that they play in interpreting the nature of biochemical kinds, we need then to explore what biochemical functions are.[4]

2.1. Vitamin B12 and its function

In order to evaluate how to interpret biochemical functions, granted that we accept their ascription as legitimate, I will focus on vitamins' function, not yet analysed in the philosophical literature.[5] This case is helpful because vitamins are complex chemical compounds characterized in terms of their chemical composition and the metabolic function they play within the organisms (as Combs [2012, 69]). Many of them come in forms of vitamers or vitamin families: different compounds that exhibit the same biochemical function. Often, vitamers are classified under the same kind, given that they share the same function and some common chemical composition and structure. Specifically, I will focus on the case of vitamin B12 because the ascription of function to these vitamins plays an important role in characterizing what these kinds are.[6] Vitamin B12 can be defined as 'the generic descriptor for all

[4] For instance, if we want to discuss functional monism or the prevalence of structural characterizations in biochemistry, as in Tobin ([2010]), Goodwin ([2011]), the importance of individuating such functions is evident.

[5] As pointed out by one of the anonymous reviewers, one could legitimately ask why not to focus on simpler case study, as oxygen O2. The choice of vitamin B12 is based on the fact that its complexity makes it a good case to characterize the biochemical properties. Specifically, vitamin B12's functions represent a case of multiple realization that allows us to appreciate the important functional characterization of its definition and identification: the different vitamers compounds are accumulated by having the same function. Furthermore, given the interest in considering aetiological characterization, this case study has features relevant for this purpose.

[6] Function ascription in the biochemistry of vitamins is common. Another example is the ascription of function to vitamin C: 'Vitamin C is actively accumulated into the epidermal and dermal cells via the two sodium-dependent vitamin C transporter (SVCT) isoforms 1 and 2 (27), suggesting that the vitamin has crucial *functions* within the skin' (Carr and Maggini [2017]; empahasis added). For more on functions and vitamins, see (Combs [2012]).

corrinoids (compounds containing the cobalt-centered corrin nucleus) exhibiting qualitatively the biological activity of cyanocobalamin' and it comes in four vitamers: cyanocobalamin, methylcobalamin, hydroxycobalaim, and adenosylcobalamin (Combs [2012], p. 377; Fang et al. [2017]). Combs ([2012], p. 377) identifies the 'biochemical functions of vitamin B12 as a coenzyme in the metabolism of propionate and the biosynthesis of methionine'. B12 vitamers are all characterized by a cobalt–corrin complex and by having a co-enzyme function in humans for various biochemical processes such as haematopoiesis, DNA and RNA production, neural metabolism, and carbohydrate, fat, and protein metabolism.[7] These chemical compounds are classified under the same category, B12 vitamin, because they display a combination of stable micro-structure, a cobalt–corrin complex, and physiological functions.[8] This might represent an instance of multiple constitution of the kind B12, where this kind is constituted by different chemical compounds that share some functional properties (Kistler [2018]).[9] For the purposes of this article, the most relevant implication of the multiple constitution of B12 vitamin is that different cobalamin compounds are classified as B12 because of the function they play in organisms. The chemical properties of being a cobalt–corrin complex are not enough to classify B12 as such, and classification practices consider the functional component as well, such as the role played in different physiological processes.

Moreover, B12 vitamins are considered an essential nutrient because they play a variety of different important functions in human physiology. However, an interesting feature of vitamin B12 is that its biosynthesis is confined to a few prokaryotic species, making its absorption possible only via nutrition (Combs [2012]; Rowley and Kendall [2019]). This implies that despite the necessary role that B12 vitamins have in human physiology, they are not synthesized or produced directly by humans but need to be introduced via dietary intake. Among the important functions of B12, one that has captured the attention of scientists is the function of vitamin B12 to contribute to the proliferation of erythroblasts during their differentiation (Koury and Ponka [2004]). But what does it mean that B12 has the function to contribute to haematopoiesis processes? In order to explore these issues, we need to understand what biochemical functions are.

3. Biological Functions and Chemical Functions

Some suggest that biochemical functions are biological functions as those conserved in evolution or those that will be conserved in evolution (Bartol [2016]; Havstad [2018]; Tahko [2020],

[7] Reference for chemical structure and function of vitamin B12 available here: <pubchem.ncbi.nlm.nih.gov/compound/Cobalamin>; see also (Combs [2012], chap. 17).

[8] The article does not aim to provide an analysis of biochemical kinds and of which properties are necessary and sufficient for a biochemical kind to be considered as such. Rather, it is relevant to consider that a functional characterization of such kind is often present, combined with a micro-structural one.

[9] For Kistler ([2018], p. 18), a kind is multiply constituted when there are two or more microscopic structures that obtain it; see also (Gillet [2013]).

[2021]). However, since biochemical kinds instances are complex chemical molecules or compounds, functional attribution within an evolutionary framework might not be as straightforward as it seems.[10] In this section, I will explore whether we should interpret biochemical functions as biological evolutionary functions. Having shown that such attribution is not straightforward, I will consider whether they can be considered chemical functions. As I will argue, neither the assumed evolutionary biological account nor the chemical one can be deemed satisfactory for biochemical functions.

3.1. Biological evolutionary functions

The philosophical literature on biochemical function often refers to 'biological theories' of function when considering the functional nature of biochemical molecules, specifically those that consider an evolutionary perspective on the topic (Bartol [2016]; Havstad [2018]; Tahko [2020], [2021]).[11] However, we can explore whether the role of biochemical functions can be interpreted or identified in an evolutionary way.[12] The discussion about biological functions in an evolutionary framework identifies three broad possible approaches: aetiological theories, the theory of biological advantage, and the theory of generalized selected effect. Here, I will explore if functional attribution to biochemical molecules can work following any of the aforementioned theories, and assuming that function ascription to B12 vitamins is genuine.

First, let us start by considering aetiological theories of function.[13] What is referred to as the 'strong aetiological theory' states that a trait's function is a difference-maker effect of such trait that contributed to the fitness of the ancestors and has been retained via natural selection because of these benefits (Neander [1991]; Davini [2021]). A trait can be defined as 'any detectable phenotypic property of an organism' (Valles [2013]) and so a biological function according to this theory is the function of a phenotypic property of the organism. However, B12 vitamins are not properly phenotypic properties of human beings, but rather chemical compounds that can only be absorbed via nutrition. B12 cannot be considered traits of organisms if we follow this definition of traits. Accordingly, the very identity of B12 vitamins rules out the strong aetiological theory so formulated in the first place, given that this theory assigns functions to traits and B12 are not traits. Consider Mitchell's ([1993], [2003]) definition, for

[10] Slater ([2009]) points out the difficulties of defining biochemical functions in an evolutionary sense.

[11] Bartol ([2016]) explicitly mentions evolutionary theories of function in reference to the function of proteins, suggesting that proteins could be considered historical entities. Tahko ([2020]) also discusses two evolutionary approaches to biological functions, the backward looking and the forward looking one.

[12] The literature on biological functions presents another approach: the causal theory of function. This will be discussed with the chemical view of functions and in section 4.

[13] It is possible to distinguish between the strong and the weak aetiological theory. In the section, I have discussed the strong aetiological theory, but a similar argument can be made for the weak version. This theory states that a trait T has the function of producing an effect of type E in organism O only if T satisfies the following: (i) T must have contributed to the fitness of O's ancestors by producing effects of type E; (ii) T must be hereditary (Buller [1998]). However, in humans, B12 vitamins are not hereditary traits nor are produced by hereditary traits. As a consequence, this theory would not accept B12 functions as such.

which a function is what allowed its bearer to be produced or reproduced in the ancestors of the population bearing that trait. B12 vitamins are bio-synthesized in nature only by prokaryotic single-celled organisms, as some bacteria and archaea. These organisms synthesize cobalamin compounds because they have cobalamin-dependent enzymes that need them as cofactors for various biological processes.[14] In these prokaryotic cells, the retention and production of B12 can be accounted for by natural selection, and so the action of B12 can be considered a proper function according to Mitchell's account. However, things are different if we consider the function that B12 vitamins play within human (or animal) haematopoiesis. Given their chemical nature as compounds and the fact that they can only be introduced in the body by nutrition, they can hardly be considered produced or reproduced as a direct result of the selection process in virtue of their haematopoietic role. Indeed, the reasons why mechanisms of production of B12 in prokaryotic organisms have been selected are not directly linked to the haematopoietic function B12 vitamins play in human beings.

If B12 do have functions, the aetiological theories are not the right place to look into. This does not come as an attack on the theories themselves though. Probably, the proponents of the aetiological theories would not ascribe the relevant function to B12 themselves, but rather to the biochemical processes in which B12 participate and for which B12 might even be necessary. Or they would not ascribe biological functions to biochemical molecules. Nevertheless, if we operate under the assumption that we are genuinely ascribing functions to biochemical molecules and compounds and that biochemical functions are evolutionary, then these theories cannot provide what is needed.

Another theory of function within the evolutionary framework is the theory of biological advantage according to which a function is a disposition to maximize the organism's fitness (Bigelow and Pargetter [1987]; Wouters [2003]). This theory also fails to capture B12 functions. B12 vitamins are not traits of an organism that can maximize an organism's reproductive fitness in the future. And, even more, it seems that B12 vitamins would still be difference makers in haematopoiesis even if this did not maximize the organism's fitness. This scenario is possible in the cases of dramatic environmental changes or more simply in cases in which there are anomalies in the quantity of B12 assumed. In the lack or excess of B12, these macromolecules would still play a role within haematopoiesis, even if this might have no impact on fitness or even a detrimental one. The difference vitamins are making is not interpreted by reference to maximizing fitness in the future and this rules out the theory of biological advantage.

Lastly, there is the theory of generalized selected effect. This theory does not rely on evolutionary selection mechanisms, but simply claims that a function is what allows its bearer to be retained within a process of selection. Specifically, 'the function of a trait consists in the activity that contributed to its bearer's differential reproduction, or differential retention, within

[14] 'Among the most prominent vitamin B12-dependent enzymes in bacteria and archaea are the methionine synthase isozyme MetH from enteric bacteria' (Rodionov et al. [2003]).

a population' (Garson [2017], p. 534). If we allow B12 vitamins to have undergone a process of selection, as general retention compared to other macro-molecules or compounds, then we might be tempted to accept the generalized selected effect theory. However, there is one main criticism that plagues the position: it allows too many things to count as function, it is too liberal. An example is the hard-rocks on the beach case proposed by Kingsbury ([2008]). Consider a rocky beach at the seaside. Due to hydraulic action and abrasion by water, a rock survives on the beach longer if it is harder because the environmental conditions will cause the lighter rocks to become sand sooner. In this case, we have a process of selection, erosion done by the sea, and a series of objects surviving selection, the hard-rocks. Following the generalized theory of selected effects, the hard rocks have the function 'hardness' that allows them to survive erosion. But is hardness a function of rocks? It seems not. To deal with these concerns, Garson ([2017], p. 536, [2019b], p. 42) adds the requirement that the entities being selected need to be part of a population, where a population has members that 'must engage in fitness-relevant interactions, whether competitive or cooperative' and rocks are not part of a population. This implies that rocks cannot be bearing a function in principle, because they are mere aggregates and the relative success of one rock does not depend on the chances of persistence of the others (Garson [2017], p. 537). What about B12 vitamins? Taken as chemical compounds themselves, B12 vitamins do not seem to constitute a population that engages in fitness-relevant interactions: one B12 compound is not in competition with other ones. This rules out the generalized theory as well. However, it is true that they do interact within organisms that undergo a process of selection and that have been (and are) in fitness competition with each other. This case illustrates the tension concerning biochemical functions that I will elucidate in section 4.

In conclusion, while we are intuitively inclined to think that the relevant activity of vitamin B12 is a function (as scientific practice considers it so), neither of the aforementioned accounts of function allow us to say as much. Surely, the assimilation and usage of B12 molecules by organisms can be accounted for by evolutionary history, but this does not give us a full story about what the function of B12 is. When we are at the micro-scale, functions do not seem to be identified in terms of evolutionary contributions, but rather as answers to the 'what-does-it-do questions' (Slater [2009]; Garson [2018]).

3.1.1 Two problems

The B12 case has allowed me to explore how to interpret (or not) the function ascription to some biochemical molecules if we follow an evolutionary account of functions. Trying to generalize, there are two main problems that we face if we consider biochemical functions from an evolutionary perspective, as identified by Garson ([2018]). These are the 'socio-linguistic argument' and the 'ontological argument'.

The 'socio-linguistic argument' is based on actual scientific and biological practice. This argument says that biologists do not attribute functions referring to selection, specially in 'proximal' questions in biology such as in molecular biology, physiology and biochemistry (see also Wouters [2003], p. 658; Griffiths [2009]). In these disciplines, functions of parts and processes are not identified in evolutionary terms, but rather they refer to causal contributions to given processes. As Griffiths ([2009], p. 15) writes: 'the identification of function in these biosciences seems to be a straightforward experimental matter. Ascriptions of function are confidently made by biologists who take organisms apart and examine their workings but do not test hypotheses about their evolution'. In the case of B12 vitamin, scientists are appealing to the current behaviour and causal effect of these molecules in the production of erythroblasts. Taken at face value, in biochemistry practitioners do not talk in terms of evolutionary functions. This might be a first source of problems in applying an evolutionary theory of functions in biochemistry (Germain et al. [2014]; Garson [2018]). However, despite the importance of analysing scientific practice when asking ontological questions, this argument cannot be considered conclusive. For instance, it is possible that an historical analysis is implicit or deemed irrelevant for practical reasons. And even if some biologists are committed to an evolutionary theory of function, they might still find more useful for their purposes to consider function as current behaviour.

This argument can then be complemented with an 'ontological argument' that focuses on the kind of entities that can or cannot bear an evolutionary function. For instance, functions can be attributed, as in the biochemical case, to items that do not take part in the evolutionary selection mechanism or do not have the relevant history. Accordingly, the evolutionary approaches to functions aforementioned are not appropriate to characterize biochemical functions because they wouldn't admit as functions those that are considered as such. This appears to be the case of B12 vitamins. It is at least debatable whether they had the relevant history of selection in virtue of their haematopoietic function in humans. First, they are not traits because they are not properly phenotypic properties of human beings (Valles [2013]). Second, their production is not a direct effect of evolutionary selection processes because of the role they play in human beings, but rather because they work as co-enzyme in some prokaryotes. Lastly, B12 vitamins do not constitute a population because, as non self-reproducing chemical compounds, they do not interact in a competitive or cooperative manner. An evolutionary explanation of the mechanisms synthesizing B12 in prokaryotes can be offered, however these are not related to the effects that these molecules have in human haematopoiesis.

3.2. Chemical functions

Despite functions in biochemistry often being associated with the biological component of their nature, there is also a form of function talk within organic chemistry. Here, I will explore whether chemical functions can help us in understanding biochemical ones.

Chemical functions are related to functional classifications of compounds in terms of functional groups. Functional groups are groups of atoms or bonds in a molecule that are responsible for some typical chemical reactions. The presence of the same functional group is also informative about the possible reactions that different compounds can undergo. These groups are called functional because they provide information about the specific role of compounds within a chemical reaction and the contributions provided to particular processes. Chemical functions, so interpreted, are then contributions to chemical reactions. This is in line with the causal theory of function for which a function is the causal role of an entity within a performed activity in a complex system or 'what an item does or is capable of doing' in a complex system (Wouters [2003, 636]; see also Cummins [1975]; Sterelny and Griffiths [1992]; Germain et al. [2014]). According to this theory, the ascription of a function amounts specifically to the identification of a property or a set of causal properties that contribute to given phenomena. This property or this special set of properties can be understood in terms of dispositional causal powers that are manifested within the right set of conditions and the right processes (Cummins [1975]; Tahko [2020]). Chemical functions are then dispositional properties that allow the compounds to contribute to given reactions. Moreover, the strict relation between functional groups and structural features, specifically the presence of specific atoms or bonds, seems to make them reducible: chemical functions correspond to a specific structure within the compound molecule. This analysis gives us a sense of chemical function, as the role that a given compound can play in virtue of the presence of a well-identifiable functional group.

Let us now consider the B12 case and biochemical functions. Can such a view of function be adequate? The attribution of these functions is often based on relevant activities of the entities under consideration, 'those likely to make a relevant difference' for a given phenomenon (Germain et al. [2014], p. 817). This is close to the aforementioned view of function. When we ascribe a function to cobalamin molecules, classifying them as B12 vitamins, we are associating them with a special set of causal properties (Griffiths [2009]). These causal properties are interpreted in terms of dispositions that can be manifested or not in different circumstances (Tahko [2021]). Accordingly, the disposition is explicated in terms of specific chemical bonds that happen between the molecules in the cobalamin compound and other molecules involved in erythropoiesis, and its manifestation can be expressed in terms of specific chemical reactions and given environmental conditions. As aforementioned in section 2.1, B12 vitamins have the disposition to contribute to the proliferation of erythroblasts during their differentiation (Koury and Ponka [2004]). This happens because vitamin B12 acts as a co-enzyme in the reaction involved in regenerating methionine, as required in normal erythropoiesis. Specifically, methylcobalamin (a vitamer of B12) takes part in 'the transfer of a methyl group from 5-methyl-THF to homocysteine via methylcobalamin, thereby regenerating methionine' (Koury and Ponka [2004], p. 109). In this sense, when we say that B12 vitamin has an haematopoietic function in humans we are referring to its dispositional property to react in a specific way during the regeneration of methionine required in erythropoiesis. Furthermore, this theory is compatible with the semantic and ontological considerations presented earlier in the article. First, it seems that scientists identify and classify biochemical functions in terms of causal contributions to a given environment and to given phenomena. In these 'micro-contexts', evolutionary considerations are often not present, while the consideration of causal action of these molecules is. Second, it satisfies the ontological requirement as well. Compounds, such as vitamins, can have chemical dispositional properties so we are ascribing to them properties that apt for their kind. Moreover, we can also provide a detailed story of the chemical reactions happening for the manifestation of such properties. Thus, we might be content in saying that we have found a functional framework for biochemical functions and their ascription.

Nevertheless, some dissatisfaction can still be present. Following Bartol's suggestion ([2016]), biochemical kinds seem to have a dual nature, a chemical and a biological one, and this affects the nature of biochemical functions as well. This is what makes them so interesting. At face value, biochemical kinds are not just chemical compounds, but those that have specific functions within biological systems, while a function is not taken as a definitional component of every chemical kind. Moreover, a mere chemical view of biochemical functions might be too restrictive. Biochemical functions do not only refer to the different functional groups the compounds have or to the presence of specific atoms and bonds, but they refer to a role within a given biological process or system. The haematopoietic function of B12 does not simply refer to the presence of a particular functional group or to the contribution to chemical processes or reactions, but to those chemical reactions that play a role within biological processes. *Prima facie*, this biochemical function ascription refers to a relevant activity or role of the molecule as one that is 'likely to make a relevant difference' for the given biological process under consideration (Germain et al. [2014], p. 817): B12 'makes a difference' for haematopoiesis. However, this difference-making is not within a chemical reaction only, but within those chemical reactions that operate in a biological process. B12 is not only a co-enzyme in the aforementioned reaction but also a vitamin and essential nutrient because of the role played in human physiology. The biological environment in which biochemical kinds operate provides a specific context to the phenomenon in consideration. This has made some philosophers–including Slater ([2009]), Bartol ([2016]), Havstad ([2018]) and Tahko ([2020], [2021])—to interpret biochemical functions as something more than chemical functions, and often they have seen them within an evolutionary or historical framework.

In the next section, I will argue that we can still retain biochemical functions as functions by proposing a combined account that embraces the dual nature of such kinds, the chemical and the biological one. The proposal is based on a causal account of functions *à la* Cummins ([1975]), as similar to the one used in cases of chemical functions, combined with an evolutionary perspective.

4. Biochemical Functions: A Unified Approach

Despite the chemical view of function is not adequate as it is, a causal theory of function still remains a valid starting point in our understanding of biochemical functions (Cummins [1975]; Wouters [2003]; Griffiths [2009]; Germain et al. [2014]). Together with the advantages aforementioned, this theory is invoked for cases like the ones considered here or for cases of 'proximal biology' (as in Wouters [2003]). A causal consideration of function is present in the mechanistic view and seems to case of molecular biology or biochemistry.[15] For instance, Griffiths ([2009], p. 15) and Germain et al. ([2014]) state that genetic functions do not refer to evolutionary functions, but rather to causal functions within biological systems. Here, I elaborate their suggestion by extending it to other biochemical cases and combining it with an evolutionary perspective. To do so, my analysis will be in two steps. First, I will endorse a specified version of the causal analysis that states that a biochemical function is a dispositional causal property of an entity involved in biological processes, that is those processes involved in the life of an organism and that have been evolutionary selected (Wouters [2003]). The view defended operates in the broad framework of the causal account of function, with the addition of the context and the details relevant for the biochemical context. Second, I will unify this account with an evolutionary approach. The view proposed has some novelty because it considers an application of the causal account of function to the biochemical domain in a precise way and dialogues with the previous literature on biochemical kinds. Moreover, it combines it with evolutionary considerations that allow the identification of those causal contributions relevant to the biological processes considered.

In the study of life, biologists divide the organism into different systems and subsystems that have specific capacities in maintaining the general phenomenon of life. In each of these systems and subsystems, the parts play a causal role, and this is what allows them to have functions. Such functions are causal dispositions, but, as stressed by Cummins ([1975]) and Germain et al. ([2014]), functions as dispositions are always contributions to something in a given context, and this context is the phenomenon of life of an organism. As a consequence, the relevant biochemical dispositions are those that causally contribute in biological processes and not any causal dispositional property of a given chemical molecule or compound. They are dispositions to bring out a specific effect within physiological processes and their causal contribution can happen independently from its being beneficial for the final survival or fitness of the organism.

[15] As suggested by an anonymous reviewer, the causal view of function has also been discussed in the mechanistic philosophy of science. According to these approaches, a component of a mechanism has a function when it makes a causal contribution to a system-level behaviour. This approach has been applied to biological functions as well and is in line with the view defended here. However, this approach is conditional on a mechanistic view, a commitment that goes beyond the scope of the article. Moreover, the account defended here gives a stronger role to the evolutionary component that we need to consider for biochemical functions. Further references references are Cummins ([1975]), Craver ([2001]).

The context of life makes it necessary to address a second point: why these molecules contribute to these specific processes in the way they do (Garson [2018, 2019a]). An answer can be given considering a modified aetiological account of functions.[16] In a nutshell, some entities play a specific causal role within an organism because they interact with parts or traits that have been directly selected. In the biochemical case, some specific molecules or compounds manifest some specific causal powers because they contribute to processes involving traits or components of an organism that have been evolutionarily selected in the ancestors. These functions are not straightforwardly evolutionary, as chemical molecules such as B12 do not have the right characteristics to be deemed as properly selected nor to be a trait or parts of a biological population themselves. Nevertheless, their action is within organisms that have undergone a process of selection and we can still consider an evolutionary perspective about them. This is because a given causal disposition counts as a function if the traits or processes that interact with it have been selected in the past when going into specific physiological processes (and not others) that involve this molecule. With Garson ([2019a]) and Griffiths ([2009]), I agree that there are no entirely ahistorical functions within biological organisms and in the life sciences: the context in which biochemical functions work is embedded in evolution. For functional attribution, one has to consider the evolutionary history of the organism under consideration.

This allows identifying not only the manifestation conditions of the dispositions (as in a standard causal theory of function) but also the relevant and adequate chemical dispositional properties that contribute to the processes within the biological organisms. Accordingly, the consideration of the evolutionary history of the processes to which the biochemical function contributes permits to have an account that selects only those contributions that are appropriate for the processes. From this, two main benefits follow: (i) it allows us to appreciate how, in this account, functions can be relational,[17] and (ii) it allows to identify those causal contributions in a non-arbitrary way (*contra* Tahko [2020]). First, different functions can be played by the same biochemical kind in different contexts and accordingly the functions are relative to given organisms.[18] The relativity of functions of biochemical kinds has been pointed out by Tahko ([2021], p. 33) as well, and seems to be a feature characterizing these phenomena. The consideration of the different evolutionary histories of the different processes identifies the relevant chemical dispositions. Moreover, the consideration of the different evolutionary histories of the relevant biological processes to which the functions contribute allows to answer a potential concern that is presented by Tahko ([2020]). Specifically, he is asking whether the various

[16] A further reference can be Kitcher's indirect theory of selection as presented by Wouters ([2003], p. 655): 'Functions are indirectly linked to selection if it is assumed that the function helps the organism to respond to selection pressures, but if it is left open whether or not the presence of the functional item is completely explicable in terms of selection'.

[17] I thank the anonymous reviewer for pointing out this aspect.

[18] The same biochemical molecule can have different biochemical functions in different biochemical processes and/or in a different organism. These phenomena of multiple determination have been discussed in the literature (Tobin [2010]; Goodwin [2011]; Bartol [2016]; Tahko [2020]).

biochemical functions and, accordingly, the relevant chemical dispositions, are just pragmatically selected according to the discipline that is inquiring into the function. If we consider the evolutionary history, then the individuation of the relevant dispositional properties is not discipline relative, but relative to the different evolutionary histories. In conclusion, an adequate view of biochemical functions needs to consider both the causal dispositional account to understand what these functions are and the evolutionary perspective to identify the adequate set of dispositional properties. This perspective is also important because it allows us to distinguish between biochemical kinds with positive biochemical functions from poisons or other dispositional properties that can be manifested within biological processes.[19]

Recall the B12 vitamin case. These vitamins have a series of functional dispositional properties. Such dispositional properties are manifested thanks to identifiable and specific biochemical reactions and the function, as explored in the previous section, is not directly evolutionary. Nevertheless, the haematopoietic function operated by B12 might be considered indirectly evolutionary or indirectly selected. Even if B12 is not selected for its haematopoietic role in humans, some traits interacting with them have been evolutionarily selected for their efficiency within humans' ancestors. Accordingly, the biochemical function of B12 is a set of dispositions to bring in a specific causal effect in the processes of haematopoiesis and erythroblasts proliferation that are a result of the process of selection. An approach that considers the evolutionary history permits the ascription of different functions to B12 vitamins in different organisms, as the same set of cobalamin compounds can have different dispositional properties that are manifested in different circumstances.[20] In bacteria, B12 manifests the set of dispositional properties relevant for a specific co-enzymatic action, while in human beings it manifests the set of dispositional properties relevant for other phenomena. The identification of these dispositional properties is not interest-relative, but rather is given by the different evolutionary of the processes in humans and bacterias to which vitamin B12 contributes.

In conclusion, in order to understand what biochemical functions are, we need to consider jointly a causal dispositional view of functions and an evolutionary perspective.[21] A biochemi-

[19] Specifically, we can identify poisons and distinguish them from vitamins or nutrients because the chemical dispositional properties of the first one do not interact with the process in the way it has been selected for. We can still allow poisons to have a biochemical function in that a given interaction chemical causal interaction with the organism is possible and happening, but then we might not deem them as nutrients or vitamins but as poisons. While both poisons and biochemical kinds can have biochemical functions, whether the chemical causal contributions are beneficial or not can be established only within an evolutionary framework. Moreover, we can include metabolic responses to poisons as biological processes to which biochemical kinds causally contribute. These processes have been selected in the past to interact in specific ways with the chemical molecules—that is to mitigate their poisoning effect. I thank the anonymous reviewer for suggesting the discussion on poisons.

[20] This can be accepted if biochemical kind ascription is given in terms of both composition and a set of functional properties, as the action of B12 compounds as co-enzymes. However, this article does not consider biochemical kind ascription itself.

[21] As suggested by an anonymous reviewer, this account is different from forms of pluralism in the literature. Pluralism usually refers to the usage of different accounts of function in different contexts (as Allen and Neal [2020]). In this case, instead, I am defending a view for which, if we want to understand properly the nature of biochemical functions, we need both approaches combined.

cal function consists in a specific set of dispositional properties that manifest in specific circumstances because of the evolutionary history of the traits or processes in which the biochemical molecule is involved. The manifestation of these dispositional properties can be identified with specific chemical reactions. The reason why such reactions happen in the way they do can be provided via the evolutionary history of the traits or features involved in the relevant subsystems. This approach captures the specificity of biochemical functions that are both chemical and biological and is explanatory adequate. This has some advantages compared to the two views in isolation. On the one hand, the causal account on its own does not identify the dispositional properties relative to the specific processes or might do that in a discipline-relative way (as pointed out by Tahko [2020]). On the other, a biological evolutionary account on its own is not adequate for the reasons mentioned in the previous sections. Moreover, the account presented here is compatible with the relativity of functions in terms of causal dispositional properties that are present but manifested in different environments. This allows the same molecules or compounds to have different functions within different biological organisms (as in Tahko [2020], [2021]) and to identify these properties in a non-arbitrary way.

5. Assessing The View

Having provided a possible way to retain biochemical functions, I will consider in this section whether this proposal is adequate and we can maintain biochemical functions as real functions. To do so, I will first assess if and how the theory satisfies three common desiderata for a theory of function (Nanay [2010]; Garson [2017]; Davini [2021]). Then, I will face a possible objection that is whether the theory allows too many entities to have a biochemical function.

5.1. Requirements

In the philosophical literature on functions, three requirements have been identified for a theory of function: (1) it should distinguish between function and lucky accident; (2) function ascription has to be explanatory; and (3) functions ought to be normative (Nanay [2010]; Garson [2017]; Davini [2021]). Let's consider them in order.

The first requirement states that a function should not be any role that an entity can play, but a given specific one. One example can be that the function of the limbs is to walk and not to allow us to wear skirts or trousers. A good theory of function should be able to discriminate the real functional role played by a given entity in a system from spurious or accidental functions. This requirement is satisfied because the theory constrains the function effects of a molecule or compound to those that contribute to the biological processes of an organism. Biochemical functions then are these specific dispositions and not any dispositional property of the considered biochemical kind: the organismal context constrains biochemical functions to a specific set of dispositional properties. For instance, B12 vitamins can take part in many chemical reactions, without these having a causal impact on the relevant biological processes. While, the haematopoietic function of B12 is so because it causally contributes to haematopoiesis, a biological process that has been selected to be so. The evolutionary component of the aforementioned theory constrains all the possible dispositional causal properties to those that are manifested in selected environments and the organisms under consideration. Furthermore, the same biochemical kind can have different functions in different organisms because of the different histories of selection of the processes in which they are involved. The causal dispositional account can help us in understanding what biochemical functions are, while the evolutionary component allows us to identify which of these properties are relevant in different organisms and environments.

Second, ascribing function should be explanatory. The explanatory power of function has two meanings. First, it helps to understand the behaviour or the contribution of a given trait or entity to processes or systems in the organism; second, function ascription can explain why a given trait, entity or feature exists. For instance, the function of sight for eyes explains the behaviour of eyes in a given organism and sight also explains why eyes have been selected.[22] Function ascription to biochemical molecules can be explanatory in the same way within the theory presented here. First, it illuminates some biochemical processes, such as vitamin functioning and vitamin biosynthesis. For instance, the function of B12 vitamins during haematopoiesis is explanatory because it helps the understanding of the proliferation of erythroblasts during their differentiation (Koury and Ponka [2004]). Second, the ascription of functions to B12 allows us to explain why it is synthetized by some prokaryotes and why it is necessary to introduce B12 in human diet. B12 is produced by some bacteria and archaea because the dispositional properties of B12 played a causal role as co-enzymes in the ancestors of these populations. Moreover, the theory presented allows explaining why B12 can be considered an essential nutrient: it has dispositional causal properties that play a role in some selected processes and are manifested in selected processes.

Let's now move to the last requirement, the normativity of function. This represents a more complicated issue, as normativity means that 'it is possible for something to have a function that it cannot perform' (Garson [2017], p. 1111). If the theory of function is normative, then the theory can account for a trait or entity to have a function that it is not capable of performing (see also Nanay [2010]). This condition is normally explicated with a theory of dysfunction, for which a trait is dysfunctioning when the trait fails to perform the role for which it has been retained in evolutionary processes. As Garson ([2017]) points out, it is more difficult to account for a theory of dysfunction if one accepts a causal theory of function, as this theory considers a function just any causal contribution to the process under consideration. What can we say about the amended theory defended here?

[22] This is normally done with an aetiological theory of function, as sight is the function of eyes because it is the behaviour of eyes in the ancestors of the organisms under consideration and eyes exist because sight caused them to be selected.

The first answer comes from the fact that it is not appropriate to ask how to make sense of biochemical 'dysfunctioning'. Biochemical molecules or compounds do not present what is normally called 'dysfunction', as they are not proper traits of an organism, but rather entities that contribute to biological processes, whether this is beneficial or not.[23] The specific dispositional properties are manifested whenever the chemical conditions are adequate, as their action is purely chemical. This can also happen when the action is not (or was not) beneficial for the organism. Thus, the scientific community speaks of biochemical alterations rather than dysfunction and they consist in chemical alterations of the molecules or when there is a lack or an excess of them. This does not exclude forms of dysfunctioning when considering the biological processes impacted by the biochemical alterations. However, such dysfunctioning does not lie at the level of the biochemical alterations, but at the level of the processes, cells or organs where the molecules act. Specifically, biochemical alterations can lead to the dysfunction of the relevant biological processes in a 'standard' evolutionary biological sense: the processes (or relevant biological entity) do not perform the role for which they have been selected in the past. For instance, we can have a dysfunction of erythroblasts due to an alteration, such as lack, of B12 vitamins (Koury and Ponka [2004]), but B12 vitamins do not display a dysfunction themselves.[24]

Nevertheless, recalling the dispositional and evolutionary components of the presented theory of function, the theory still allows for a form of normativity. There are cases in which the molecule or compound can have a function without manifesting or performing it in three ways. First, the manifestation conditions might be challenged in a way that the dispositional property is not manifested. For instance, there might be changes in the environment that prevent B12 to contribute to erythroblasts proliferation. Second, the trait or the cells with which the biochemical molecule or compound normally interacts can be damaged or are dysfunctioning for unrelated reasons. This latter dysfunction is understood within an aetiological theory of function, where the trait or cell is not performing the activities that were beneficial in the ancestors of the relevant population. Third, there might be some structural damage to the chemical structure of the macro-molecule that prevents the manifestation of the dispositional functional property.

In conclusion, the theory of functions presented here can allow for normativity thanks to

[23] Relevant to this, see the debate on finks and masks of dispositions in (Bird and Handfield [2007]; Choi [2012]).

[24] As pointed out an anonymous reviewers, misfolded proteins represent an interesting case of biochemical alterations. Misfolded proteins are those folded in a non-standard structure and are associated with different diseases, as degenerative ones (Reynaud, [2010]). In these cases, different chemical configurations can lead to the manifestation of different chemical dispositions and impact the processes to which the molecules contribute. The chemical contribution remains relevant to processes in a causal sense, and the possibility of such interaction is given by evolutionary history, but the process is then dysfunctioning in that it does not perform what it has been selected for. Specifically, in the case of misfolded proteins and degenerative diseases, it is the accumulation of such proteins (so an excess in quantity) that can lead to a detrimental chemical contribution to the relevant cellular process and prevent the functioning (of the process) in the way it has been evolutionary selected for. In this case, the 'dysfunction' is not of the protein *per se*, but of the process to which the proteins contribute due to an alteration in quantity of proteins.

the combination of a causal theory of function together with an evolutionary approach. This latter aetiological approach allows us to constrain the possible dispositional causal properties of a given biochemical kind to the only relevant ones for a given organism. It also gives the context for the manifestation or not of these properties. All things considered, we can retain this approach to biochemical functions as a valid account of functions.

5.2. Biochemical functions and biochemical kinds

Let's now move to consider a possible objection: the theory allows too much. Here we have defined biochemical function as a specific set of dispositional properties that manifest themselves in particular circumstances because of the evolutionary history of the traits or processes in which the biochemical molecule is involved. These dispositional properties are those that causally contribute to biological processes, where causal contribution is neutral as it can be beneficial or not. However, this position risks allowing for too many biochemical functions as 'causal contribution to biological processes' can imply that many different kinds have a biochemical function. For instance, zinc (Zn) is a chemical element, and thus a chemical kind, with atomic number 30 and a series of properties that have little to do with biological properties, such as being a brittle metal at room temperature. This element, however, is very important for many different biological processes. Zinc is defined as 'an essential trace element' necessary for 'the normal growth and the reproduction of all higher plants and animals, including humans. In addition, it plays a key role during physiological growth and fulfils an immune function. It is vital for the functionality of more than 300 enzymes, for the stabilization of DNA, and for gene expression' (Frassinetti et al. [2006]). When considered in the biological environment, it seems justified to accept that zinc has biochemical functions because this element has a series of dispositional properties that contribute to biological processes. Furthermore, some traits or processes interact with zinc and have been evolutionarily selected. This makes the function of zinc a biochemical function according to the present account. However, scepticism might rise in accepting zinc as having a biochemical function, as this can imply that any chemical element that satisfies the requirements can be considered a biochemical kind as well.

To answer this objection, I think it is important to distinguish between biochemical functions and biochemical kinds, as much as it is possible. Specifically, even if biochemical kinds need to have a biochemical function, having a biochemical function is not enough for a kind to be a biochemical one. As the zinc example shows, pure chemical kinds can also have a biochemical function, even if this does not make zinc necessarily a biochemical kind. The answer to this objection is a 'bite the bullet' strategy: many kinds can have a biochemical function if they satisfy the requirements. However, this does not imply necessarily that they are biochemical kinds.[25]

[25] As pointed an anonymous reviewer, we can ask if entities such as colours could have a biochemical function. I think that this would not be the case because a crucial component of the provided definition of biochemical functions is that they are constituted by chemical dispositional properties of chemical molecules or compounds:

This article does not have the aim nor the space to present a theory of biochemical kinds and the purpose is just to explore the theme of biochemical functions. Nevertheless, one way to develop an account of biochemical kinds can involve different structural and biological conditions as pointed out by Slater ([2009]).[26] For instance, a biochemical kind can be a chemical molecule or compound that displays a set of biochemical functions, and its existence is a direct or indirect effect of evolutionary pressure because it is bio-synthesized by organisms that have undergone a process of selection.[27] If we follow this possible definition, then zinc would not be a biochemical kind, even if it has a biochemical function. Alternatively, B12 vitamin would be a biochemical kind with different biochemical functions, because it is bio-synthesized by organisms, bacteria or archaea, and it plays different roles in relation to cells or traits that have been selected in these organisms or others. In conclusion, if some molecules play a role in biological processes we should not be afraid in accepting them as having a biochemical function, even if we might not accept them as instances of biochemical kinds.

6. Conclusion

In this article, I have argued that if we accept that function ascription to biochemical molecules is genuine, then we should interpret biochemical function as composed of chemical dispositional properties to causally contribute to biological processes within an organism. A biochemical function consists of a specific set of chemical dispositional properties that are relevant to chemical reactions in physiological processes. These dispositions are manifested in specific conditions because of the evolutionary history of the traits or processes in which the biochemical molecule is involved. This account is of relevance for the discussion on biochemical kinds and the philosophy of biochemistry because it discusses biochemical functions in their peculiarity and making reference to the positions already present in the literature. While the account presented is not entirely novel, as it is built in dialogue with the already existent debate, the application of these accounts to the biochemical domain represents a novel contribution. Function ascription in biochemistry is important both in the recent philosophical and scientific domain and an explicit clarification of what this entails is of value. Second, this account stresses the importance of evolutionary historical considerations in the identification of which chemical dispositional properties constitute the different biochemical functions. This allows the identification of the relevant functions and it is not easily seen with a simple causal contribution

such chemical dispositions need to be identifiable. The status of colours is metaphysically controversial, but even within a physicalist account of colours they refer to physical properties rather than chemical ones. Some physical properties, such as electromagnetic radiation, can have a function within biological processes, but this would require a specific analysis that goes beyond the scope of the article.

[26] This definition is a possible attempt to identify biochemical kinds and the author does not commit to it as a set of necessary and sufficient conditions. The purpose is only to identify some requirements that can allow distinguishing molecules or compounds playing a biochemical functions from biochemical kinds.

[27] This does not imply that these kinds are only bio-synthesized as a result of selection, as many biochemical kinds can also be synthesized artificially.

approach that might include all possible chemical contributions of a molecule. Moreover, the combination of a causal and historical approach is in line with the recent work in the literature that has underlined the role of historical theories of function (see Garson [2019a]).

To reach a clear account of what biochemical functions are, I have first presented what is the status of the controversy and what biochemical functions are taken to be in the debate. Then, I have considered whether the biochemical functions can be interpreted as either biological functions or chemical functions using the case of vitamin B12. Given the inadequacy of these views on their own, I have proposed a positive account for which we should consider both a causal theory of function together with an evolutionary approach. A causal theory of function offers us an account of what functions are, while an evolutionary perspective answers the question of why they are playing a particular role within the organism. Moreover, an evolutionary approach aids the identification of which chemical dispositional properties are relevant. Lastly, I have considered some requirements for which this approach to biochemical functions can be considered a genuine account of functions and a possible objection. The account presented respects the requirements, allowing us to retain biochemical functions as functions. Moreover, I have explored whether the theory might allow too much and I have concluded that we can answer this concern by separating biochemical kinds from biochemical functions.

In conclusion, biochemical kinds offer an interesting case study for all those philosophers that are interested in inter-level relations. Specifically, biochemical kinds have the peculiarity of being kinds at the borders, with a nature that is both chemical (offered by a structural characterization) and biological (offered by a functional one). However, little has been said in detail about what biochemical functions amount to. Here, I have tried to fill this gap and I have offered a theory of biochemical function that can be a starting point to build a bridge between the chemical world and the biological one. Moreover, it can also inform the discussion on the nature of biochemical kinds and inter-level relations.

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