

**The Open Texture of Functions:
A Framework for Analyzing Functional Concepts in Molecular Biology**

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Abstract

In recent times, the exponential growth of sequenced genomes and structural knowledge of proteins, as well as the development of computational tools and controlled vocabularies to deal with this growth, has fueled a demand for conceptual clarification regarding the concept of function in molecular biology. In this article, we will attempt to develop an account of function fit to deal with the conceptual/philosophical problems in that domain, but which can be extended to other areas of biology. To provide this account, we will argue for three theses: (1) some authors have confused metatheoretical issues (about the meaning and application criteria of terms) with metaphysical ones (about teleology); this led them to (2) look for explicit definitions of “function”, in terms of necessary and sufficient criteria of application, in order to make the concept of function eliminable; however, (3) if one leaves metaphysical worries aside and focuses on functional attribution practices, it is more adequate to say that the concept of function has an open texture. That is, that a multiplicity of application criteria is available, none of which is sufficient nor necessary to attribute a function to a trait, and which only in concert form a clear picture. We distinguish this thesis from some usual forms of pluralism. Finally, we will illustrate this account with a historical reconstruction of the ascription of a water transport function to aquaporins.

1. Introduction

In recent times, molecular biologists and biochemists have expressed concerns about the diversity and validity of functional attributions (e.g. see Doolittle, Brunet, Linquist & Gregory, 2014; Greenspan, 2011). These were driven by a series of factors, two important ones being the exponential growth of sequenced genomes and structural knowledge of proteins, and the existence of subcommunities working on different model organisms, which had begun to employ terminology that did not match their peers'. Both led to the creation of computational tools, such as Gene Ontology (<https://geneontology.org>, GO hereafter) which attempt to provide a controlled taxonomy of functional vocabulary to facilitate communication among specialists in different organisms (Ashburner et al., 2000; see Leonelli, 2016, for some philosophical discussion surrounding this tool).

The development of these tools was not exempt from conceptual/philosophical debates; for instance, Thomas (2017) argues that among GO's three sub-ontologies (Molecular Function, Cellular Component and Biological Role) only annotations in the third count as genuine biological function attributions—and not the first, despite its name. Others have also carried out philosophical investigations of other controversies in molecular biology—e.g. Guttinger and Love (in press) examine the ones surrounding the ENCODE project.

Since there seems to be a demand for conceptual clarification in these areas, in this article, we will attempt to elaborate an account of function fit to deal with the conceptual/philosophical problems in those debates—we expect, however, our account to have wider applicability. Very briefly, we will argue (very much in line with Guttinger and Love, op. cit.), and then show via historical examples, that the concept of function has an *open texture*. That is, that there is no *definition* (in the sense of a set of necessary and sufficient conditions for the application of a concept) of function at play in molecular biology, but rather that functional attributions are carried out by considering a wide and heterogeneous array of evidence, taken from different sources, which only together forms a clearer picture.

The idea that there exist different criteria for determining functional concepts has been pointed out before by proponents of various forms of pluralism. However, as we will show, our position differs from those pluralisms because we posit that these different criteria serve for operationalizing a single concept; that is, they constitute different types of relevant evidence for the ascription of one and the same function. In this sense, though we share that there exist a plurality of determination/operationalization methods of function, we are *monists* regarding the number of concepts there are (see section 7 for more on this).

To achieve our goals, we will first delve into a series of meta-philosophical discussions, which we think will help clarify the type of project we are embarked on, as well as the historical roots it has in the philosophy of science. In particular, we will link the idea of the concept of function having open texture with the logical empiricist early project, and its subsequent abandonment, of searching for definitions of theoretical concepts. One of the reasons this will be illuminating is that, much like in this historical case, a lot of confusion has emerged from the conflation of metaphysical issues (e.g., those surrounding the “naturalization” of teleology) with metatheoretical ones (those surrounding the meaning and/or application criteria of concepts).

Going forward, the plan will be as follows. The next two sections will contain these meta-philosophical considerations. In section 2, we intend to show that the classical accounts of functional language are *eliminativist*, and that the main motivation behind this eliminativism is that they tended to confuse metaphysical issues (surrounding teleology) with metatheoretical ones. That is, that the search for explicit definitions as a way of specifying meaning relates to the goal of being able to replace any occurrence of apparently teleological terms with other non-problematic language. In section 3, we draw an analogy between the above and the early attempts by logical empiricists to define theoretical concepts. Our goal in this section will be to introduce the idea of the concept of function having an *open texture*, as the logical empiricists came to realize regarding theoretical concepts.

Since ours is a point about the way that scientific practice works, the way to argue for it will be via examples. We present two case studies. The first and preliminary one (section 4) is a historical case from the field of ethology and is about the way that a reproductive function (attracting conspecific females) was assigned to male cricket songs. We mostly follow the work done by Olmos (in 2018a and 2018b). By first presenting a case from a different field, we hope to show that our account has some plausibility outside of the area that specifically interests us. The second and main case study (section 5), examines the way in which a water transport function was assigned to a family of proteins in the MIP family, which ended in a Nobel prize. In section 6, we turn to contemporary molecular biology and make some remarks about the way in which functional attribution works in this area today. We will present (at least part of) the contemporary methods/toolkit for assigning functions in that area, which, once again, act jointly to produce functional attributions. Finally, in sections 7 and 8, we consider some possible objections and present our conclusions.

2. Meta-Analytical Remarks: Conceptual Analysis, Eliminativism and Teleology

Discussions around the concept of function in biology have a long history in the philosophical literature, with some long-standing disagreements that persist until the present day. Perhaps one of the reasons for this impasse has to do with the fact that not all approaches have the same objectives. Thus, it will be useful to begin by stating some meta-analytical points about what our project involves and what our general goals are.

A classical paper by Millikan (1989, pp. 290-291) distinguishes between three different types of analysis that one can attempt, which she calls descriptive definition (more commonly referred to as conceptual analysis), theoretical definition and stipulative definition.

Conceptual analysis involves providing some kind of description (more on which kind below) of the way a term is used by some community. As Neander (1991, p. 170) usefully puts it: “[conceptual analysis] involves trying to describe the criteria of application that the members of the linguistic community generally have (implicitly or explicitly) in mind when they use the term.” Note that those criteria might be implicit, and that members of the community in question need not be entirely conscious of them in order to apply them—in the same way we are not always conscious of grammatical rules when we speak. Therefore, a

conceptual analysis of functions proceeds not by examining what scientists *say* when asked what functions are, but rather by looking at how they apply that concept in their functional attribution practices.

Theoretical definition, according to Millikan, is the kind of thing one provides when one says that water is H₂O or that gold is the element with atomic number 79. This is not intended to be a reconstruction of the way people in general or chemists in particular use those terms (though they may, and in the second case do, use them that way). Rather, they intend to be contingent empirical claims about the way the world is, which were true (if they are so) before modern chemistry emerged.¹

Stipulative definition has received less attention. Though it is clear that nobody is attempting to give a *purely* stipulative account of functions, as if we were inventing a new term, the analysis in question might have some stipulative *component*. Garson (2016, pp. 9-10) and Brunnander (2011) link this idea to the notion of explication (see Carnap, 1950), according to which the task (or at least one possible task) of philosophy is to replace vague and inexact concepts with more precise ones. Note that, according to Carnap, two of the requisites for an adequate explication are that (i) clear cases of (non-)application of the original term be preserved as such, and (ii) doubtful or borderline cases are decided one way or the other; so, explications have both descriptive and stipulative components. Carnap also requires that (iii) the explication should be fruitful for achieving some conceptual/philosophical goal—in our case, this relates to decoupling the issue of teleology from the issue of empirical meaning/applicability, and to clarify how functional terms have this last characteristic.

In light of this distinction, we should make clear that our goal here is of the first and third kinds. We are attempting to do a form of conceptual analysis, or more precisely, to explicate the concept of function (moving forward, we continue to speak of conceptual analysis since that is the terminology most authors use, but the reader should keep in mind that it can have some stipulative component). There are various reasons why we think this can be fruitful. More generally, to cite Neander again, “it would be futile trying to do conceptual analysis if we didn’t have any use for it; but we do. We need it to clarify thought and communication, which are the time-honored reasons for engaging in the activity.” (1991, p. 172). We hope to show that an analysis of the concept of function, as it is used in molecular biology, can be helpful in alleviating concerns related to teleology, as well as enriching the philosophical debate with the study of a case from a different area.

At this point, we must expand on what we understand by an adequate conceptual analysis. Many times, conceptual analysis of a term is equated to providing a *definition* for it (as Millikan’s chosen terminology exemplifies). One important point is that definitions (in the technical philosophical sense, not in popular use) must provide both necessary and sufficient

¹ She takes her variant of the etiological account to be providing this. One may wonder why this would count as a type of definition. We would simply prefer to call it theorization. The idea that scientific laws (or law-like statements, if one prefers) are not definitions also has a long history in the discipline (see Nagel, 1961, pp. 169-193; Moulines, 1962). However, this is beside the point here, and we will not discuss it any further.

conditions for the application of the defined term (the *definiendum*).² This is usually expressed syntactically via the idea that definitions should be written as biconditionals, where one part contains the *definiendum* and the other the *definiens*. Therefore, all cases in which one would be willing to assert the *definiendum* must also be cases in which one could assert the *definiens*, and vice-versa. In syntactic terms, one should be able to replace each occurrence of the *definiendum* in a sentence with its *definiens*, and vice-versa (as is the case with the sides of true biconditionals). It is in this sense that explicitly defined concepts are eliminable.³ Note that this elimination is a matter of principle, not of actual usage. One could wish to keep defined terms, e.g., for practical or pragmatic reasons (see Chen, 2022).

The idea that an adequate analysis of function requires finding necessary and sufficient conditions for its application is very important because it configures the way in which philosophical argumentation in the area works. The way to argue that a definition is inadequate is to show that it either overgenerates (the *definiens* applies to more cases than the *definiendum*) or undergenerates (the reverse). In Garson's terms:

[W]e should also think about what kind of project we are engaged in when constructing a theory of function. (...) Philosophical analyses have traditionally been thought of as conceptual analyses, that is, as attempts to set out what most people have in mind, either implicitly or explicitly, when they use a term. (...) In principle, the way to discredit a conceptual analysis is pretty simple: one devises a counterexample, real or imagined, in which we would intuitively apply the term in ways forbidden by the analysis (or in which we would intuitively refrain from applying the term in ways licensed by the analysis). (Garson, 2016, p. 8)⁴

Supporters of different accounts of function have lengthily argued this way, by both accusing other approaches and defending their own of both overgenerating—e.g., vestigial traits for the etiological account (Griffiths, 1993; Wouters, 2005), “promiscuity” (like assigning the heart the function of making noise) for the systemic one (Millikan, 1989; Wouters 2005)—and undergenerating—e.g., the case of exaptations, where current use does not match what the trait was selected for (Caponi, 2020).⁵

² Neander (1991, p. 171) argues that Millikan's theoretical definitions are not exempt from this requirement, at least to the point that they are definitions, and based on the examples that Millikan herself gives. Also, interestingly, in that paper Neander argues that the requirement of finding necessary and sufficient conditions is too strong, but she then goes on to defend the etiological approach as if it were providing both (in the way described below).

³ Millikan (1989, p. 288) takes her analysis of function to be a recursive definition, not an explicit one. However, recursively defined terms are also eliminable if one iterates the application of the definition until the base clause is reached.

⁴ Curiously, Garson (2016) labels his project as one of conceptual analysis, but in a later work (2019) he claims to be giving a theoretical definition. In any case, he seems to believe that conceptual analysis (done right, within the context of a specialist community) and theoretical definition will tend to coincide, so perhaps this does not make much of a difference for him.

⁵ Exaptations would actually be a case of both over- and undergeneration at the same time, since the function that is attributed is not the one that the trait currently has.

Our hypothesis is that the reason philosophers have sought analyses in terms of sufficient and necessary conditions relates to another criterion for an adequate analysis: the “naturalization” of teleology. Many times, this criterion is implicit, but at others it is not. To provide just a few examples, Wright (1973) claims that:

Now it seems to me that the notion of an organ having a function—both in everyday conversation and in biology—has no strong theological commitments. Specifically, it seems to me consistent, appropriate, and even common for an atheist to say that the function of the kidney is elimination of metabolic waste (...). Accordingly, the final major aim of this analysis will be to make sense of natural functions, both as functions in the same sense as consciously contrived ones, and as functions independent of any theological presuppositions—that is, independent of conscious purpose (p. 143)

More recent approaches, such as the organizational approach (introduced by Mossio, Saborido, & Moreno, 2009), also make similar claims:

Since the second half of the 20th century, the discussion around the concept of function has become a classic within the philosophy of science and, especially, within the philosophy of biology. One of the main reasons for this interest lies in the fact that functional explanations seem to entail a teleological dimension that can hardly be accommodated within a classic scheme of “scientific explanation”, which represents a real challenge for a naturalistic perspective in science and philosophy. This teleological character, commonly accepted when we refer to artifacts or organizations that are designed by human beings to fulfill certain purposes, is more problematic when we deal with biological systems. From a naturalistic point of view, it does not seem easy to preserve this teleological dimension for the explanations of Biology. (Saborido, Mossio, & Moreno, 2010, pp. 31-32, our translation)

The worry is that functional *explanations*, which explain the presence of a trait from its function, seem to be appealing to final causes. And this is problematic for two reasons. More generally, because pre-Darwinian (and some not very scientifically serious post-Darwinian) authors equate final causes with the conscious intentions of a God—hence Wright’s reference to atheism. The other, more technical one, is that if one thinks of final causes as efficient causes, maybe because one believes that (all/functional) explanations should be (efficiently) causal, then the problem is of backwards causation—i.e. functional explanations explain the presence of a trait from its (posterior) effects (see Garson, 2019, pp. 16-17).

We believe the two requirements we alluded to in this section are related because if one is able to provide a definition of function in non-teleological sounding terms (e.g. {past organisms, effects, reproductive success, ...} or {capacity of a system, parts of the system, causal interactions between the parts, ...}) then one can be sure that each apparition of “function” can be replaced with a description using only these terms—since, as we saw above, defined terms are eliminable—and thus the appearance of teleology disappears. This connection has been noted sometimes, for example Nagel asserted that:

“[A] function of item *i* in system *S* and environment *E* is *F*, presupposes [his own account of function, not important here] (...) *If [my] view of biological functions is correct, functional statements, as well as the presuppositions of functional ascriptions, can also be rendered without using functional concepts.*” (Nagel, 1979, p. 314, our emphasis)

In other words, most past and present accounts are implicitly or explicitly *eliminativist* of functions and functional language⁶. Even if they do not see themselves as such, the type of analysis being sought, as evidenced by the type of argumentation that has surrounded them, shows that they are.

Note, however, that the project of reconstructing the actual criteria of application of functional terms is, at least in principle, independent from the issue of teleology. At least grant us that one can embark on the first type of project without putting concerns of the second type as desiderata for an adequate analysis—in any case, conclusions about teleology can be consequences of the analysis. Once one leaves metaphysical worries aside and centers on metatheoretical ones, we will argue that there is no reason to expect an adequate conceptual analysis of a technical scientific term (like “function”) to provide necessary and sufficient conditions for its application. The next section proceeds through an analogy between debates around function and the early attempt by logical empiricists to eliminate theoretical terms through definitions. We will hold that, as they came to realize about theoretical concepts in general, the concept of function has an open texture. As we saw in this section, this will have methodological consequences on how discussions around accounts of function should carry on in the future.

3. Open Texture

In this section, we take a brief detour through an analogy, which we believe will be illuminating, between the search for explicit definitions of functional concepts in the philosophy of biology and the early attempt by the logical empiricists to define theoretical concepts.

Much like (in our hypothesis) philosophers of biology sought explicit definitions of function to deal with the problem of teleology, the logical empiricists, influenced by the empiricist (in this case epistemological instead of metaphysical) *dictum* that there should be nothing in knowledge that was not in experience, initially considered that theoretical concepts (those that did not refer to directly observable entities) should be defined on the basis of observational concepts. Again, like in the biological case, their original intention was to show

⁶ It is important to make the following clarification. Throughout this section, we have been discussing the possibility of elimination of functional concepts. Later on, we will critique this eliminativist stance. However, it is also possible to engage in a different discussion, which involves the elimination of the *terms* used to name such concepts. It could be argued that these terms imply agency or anthropomorphism (in a similar sense to how the notion of 'natural *selection*' might be considered inadequate, as Darwin himself noted, for suggesting an anthropomorphizing and reification of nature). We will not address this issue in this work, as it is (relatively independent) of our main objective. We thank the anonymous reviewer for this observation.

that theoretical concepts were eliminable and that scientific laws/statements containing them, like “ $F = ma$ ” or “gold is the element with the atomic number 79”, could be reformulated without the suspicious terms. Hempel (1958) contains a thorough history of these elimination attempts. A short summary (of the relevant parts) would be something like the following.

Their first idea was that statements linking theoretical and observational vocabularies (which they called correspondence rules or interpretative statements) were, as said, definitions. That is, they had the logical form: T_1 if and only if (O_1, \dots, O_n) , where T_1 is a statement containing only theoretical terms, and O_1, \dots, O_n contain only observational ones. More specifically, their proposal was that these were *operational* definitions. That is, the right part of the biconditional contained another conditional, that linked some (observational) condition to another (observational) effect. One example of this type of operational definition would be “ x has temperature y if and only if (if I touch x with a thermometer, then the thermometer marks y)”.

There are several problems with this idea. The first (and not so important for us, because we do not presuppose that a definition of function must be operational in this sense) is that, since conditionals with false antecedents are true, everything that we do not touch with a thermometer has every possible temperature. The second and more serious one is that when they attempted to look for these types of definitions in actual theories, they could not find them. One reason, continuing with our example, is that there are usually multiple ways of operationalizing theoretical concepts—e.g., there are objects whose temperature cannot be measured with a thermometer (e.g. the Sun) but are measured in other ways.

Carnap’s solution to these problems consisted in switching the elements of the definition around, by putting the condition as an antecedent to the biconditional. In the case of temperature, this would read “if I touch x with a thermometer then (x has temperature y if and only if the thermometer marks y)”. Statements with this form are called bilateral reduction statements, and Hempel notes various things about them. The first is that these are not, strictly speaking, definitions, because they do not provide sufficient and necessary conditions of application of the theoretical term. Hence, they do not allow the elimination of theoretical terms from scientific discourse. More importantly:

[Since these bilateral statements offer] merely partial specifications of meaning, this approach treats theoretical concepts as “open”; and the provision for a set of different, and mutually supplementary, reduction sentences for a given term reflects the availability, for most theoretical terms, of different criteria of application pertaining to different contexts. (Hempel, 1965, p. 52)

In other words, if one leaves aside (epistemological) preconceptions of how theoretical terms should apply to experience, one can give a more adequate account of how real scientific practice works. In that practice, scientists use multiple determination/operationalization criteria for the same concept, each of which works within some range of values or

circumstances. Furthermore, the idea that they are “open” entails that one can always find more reductive statements that extend the range of applicability of the theory in question.⁷

Once again, we do not presuppose that the application criteria of the concept of function need to be rendered as bilateral reduction statements (and neither would Hempel, since he later on weakens these conditions even more, by allowing statements that connect theoretical and observational concepts to take any logical form). But there is a valuable lesson to be learned here, which we believe does apply to our case. Our position is that, much like in the case of theoretical terms, the concept of function has many application criteria associated with it. Even if one does not take an operationalist stance, one has to recognize that, in real biological practice, biologists ascribe functions to traits through a range of considerations from different sources. Though some application criteria may be more important than others in some contexts, there is no single privileged criterion under which all functional attributions are made. Moreover, new criteria can always be proposed. Ignoring or downplaying this heterogeneity of criteria because of some metaphysical/epistemological preconception will only lead one to perform inadequate conceptual analyses.

Guttinger and Love (in press) take a similar position.⁸ Their interest, like ours, lies in clarifying the actual methods of application of functional terms to cases (also, like us, taken from molecular biology—though they look at cases taken from genomics, while we will focus on more traditional ascriptions of functions to particular proteins). In their words:

(1) Methods do not flow directly from theory. Theories of biological function are insufficient guides to experimental practice. Finding ‘the’ correct theory of biological function does not provide a trustworthy guide to solve the FICV [Functional Identification, Characterization, and Validation] problem. (2) Focusing on methodological practices, we discover a complex landscape of proxy-measures being used in functional genomics. There is a toolkit of proxies that are applied to assess how genomes work. These proxies are dynamic and cannot be classified neatly along the lines of different functional concepts. (3) These proxies have a life of their own, recombining in novel and unexpected ways. This expansion and reassortment of the proxy toolkit in experimental practice is observable within ENCODE and gives birth

⁷ The idea of open texture comes from Waismann (MacKinnon, Waismann, & Kneale, 1945), who, in that text, is discussing MacKinnon’s criticism, according to which a fundamental presupposition of empiricism is that “there is no more to the content of a statement than the total evidence which would warrant its assertion” (p. 119). This relates to the idea that one can give a complete conceptual analysis—a necessary and sufficient list of application criteria—for a concept in terms of an operational definition. According to Waismann, this is not an assumption of empiricism, since it recognizes that “we can never exclude altogether the possibility of some unforeseen situation arising in which we shall have to modify our definition. Try as we may, no concept is limited in such a way that there is no room for any doubt. We introduce a concept and limit it in some directions; (...). This suffices for our present needs, and we do not probe any farther. We tend to overlook the fact that there are always other directions in which the concept has not been defined.” (pp. 122-123)

⁸ We are not sure if it is identical to ours. Specifically, we are not sure if their idea of proxy measures lines up neatly with what we call criteria of determination/operationalization. They do seem to have a similar spirit, though.

to new forms of data and theoretical tensions that have largely been overlooked in the ENCODE controversy. (Guttinger & Love, in press, pp. 3-4)

Of course, we must support our position beyond a mere analogy with the logical empiricists,⁹ and we do so in the only way we can, via examples.

4. Preliminary Case Study: Male Cricket Songs

The above meta-philosophical digression on the explicit definability of theoretical terms is not a mere logical technicism. Instead, we consider that the eliminationist spirit behind the attempts to define functional concepts constituted an obstacle to the realization of an adequate conceptual analysis of these concepts. If one approaches the question of functional attribution leaving aside metaphysical prejudices, then one can see that previous conclusions regarding the open texture theoretical terms in general also apply to the case of functional concepts.

In this section, we briefly summarize the variety of evidence that was used for the ascription of a reproductive function (attracting conspecific females) to male cricket calling songs, compiled by Richard Alexander in several works (Alexander, 1958, 1960, 1961, 1962, 1967) and systematized and put in a philosophical context by Olmos (2018a, 2018b). This will serve as a model for the subsequent treatment of functional attribution in biochemistry and molecular biology.

The trait in question consists of a sound (identifiable by a particular sequence of chirps) that male crickets produce, in absence of other organisms in the vicinity, by rubbing their forewings (or tegmina) together, in a process called “stridulation”. The relevant evidence for attributing a reproductive function to this trait can be divided in four groups: (i) proximate effects, (ii) biological role/process, (iii) comparative evidence and (iv) natural selection evidence.¹⁰

Proximate effect evidence mainly shows that the trait has the attributed function as an effect. In the case of the crickets, this includes observational studies, e.g.:

⁹ The claim that functional concepts are open-textured does not necessarily imply that they are theoretical concepts—that is, concepts that gain empirical applicability within the framework of a scientific theory. While this point could be defended (and has been defended, for example, by Ginnobili, 2011), it is not our intention to do so in this work. Our appeal to logical empiricism is weaker, as we only aim to highlight the similarities between the eliminativist spirit of early empiricism regarding theoretical terms and the current eliminativist approach that dominates the discussion of functional attribution in the philosophy of biology. Moreover, we believe it is possible to adopt the insights gained by logical empiricists regarding the application of concepts and their open texture, independent of their conception of theory. In conclusion, the arguments presented in this work do not rely on the existence of a scientific theory in which functional concepts are fundamental concepts. The reader should also keep in mind the important role of tacit knowledge, particularly with regard to the application of scientific concepts. Authors like Thomas Kuhn have argued this point even in areas where scientific theories are presented explicitly, such as in the case of classical mechanics (Kuhn, 1970).

¹⁰ Olmos uses a different categorization, namely: (i) observational, (ii) experimental, (iii) comparative and (iv) evolutionary. For various reasons (e.g., some pieces of evidence would fall into more than one category in this taxonomy) we prefer our own.

If a culture of field crickets containing several adult males and females is kept under observation, it is soon noted that some sort of sound is being produced by one or more of the males almost continually. A few distinct types of sounds gradually become apparent to the observer, as do the situations in which they are produced. Eventually one becomes able to describe relative positions of different individuals in the culture and the types of activity in which they are engaged without looking at them solely by the types of sounds being produced by the males. (Alexander, 1958, p. 104)

as well as experimental evidence. For example, both Alexander (1960, 1967) and Olmos (2018a) mention a wide variety of experiments in relation to these songs.¹¹ For instance, experiments showed that female crickets could be attracted to calling songs coming from a speakerphone, in absence of a male. Conversely, if a cricket's stridulating mechanism is disabled (e.g. its wings are tied together) females stop searching for that male. This aims to establish whether the trait is sufficient and/or necessary (under some normal conditions) for the effect to take place. Of course, that the presence of the trait is sufficient and/or necessary for an effect to take place does not mean that this effect is its function, since traits can have many effects that are not functions. For example, the possession of a heart may be both sufficient and necessary for a beating noise to be produced in an organism (necessary not in the sense that nothing else *could* produce it, but that, in absence of a heart, the noise is not *actually* produced). Nevertheless, knowing whether it is so constitutes non-conclusive but important evidence that this effect is/could be the function of the trait. For instance, if the tying the crickets' wings did not preclude females from approaching, that would not mean that attracting females is not the function of the song, since the male crickets could have many overlapping ways of achieving that effect. But the fact that it does preclude them adds one piece to a (more complicated) puzzle that needs to be pieced.

As just noted, proximate effect evidence is not enough, by itself, to identify proper biological functions, since traits can have multiple effects that are not functions. In the crickets' case, for example, the song also has these other effects:

(...) there is evidence that under different circumstances the calling sound of male crickets can (a) attract predators (...); (b) attract females (...); (c) act as a locomotor depressant (at high intensities) for females; (d) cause aggressive chirping and other aggressive actions; (e) stimulate calling by other males; (f) inhibit calling by other males; and (g) cause other males to move away (Alexander, 1967, p. 499)

The rest of the criteria serve to choose, among the proximate effects, which count as functions (e.g., (b)) and which do not (e.g., (a)). Biological role evidence puts effects into context by looking at them within an understanding of the lifecycle of the organism. As Olmos (2018a, p. 60) notes, in the case of the crickets, whole sequences of behaviors, both antecedent and following the calling sound, were registered together with it. These sequences of behaviors can be represented graphically as ethograms like the one in Fig. 1.

¹¹ We will not recapitulate all of them here, the interested reader can check those sources.

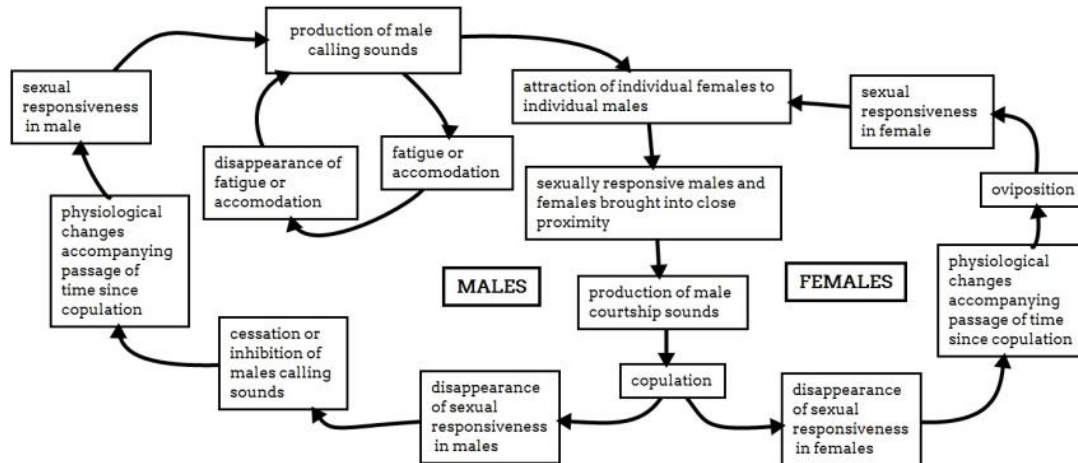


Fig 1. Ethogram representing a sequence of behaviors in crickets. Notice that the production of the calling sounds by the males is on the top left. Taken from Olmos (2018b, p. 100), who in turn elaborates it from data found in Alexander (1962).

Olmos (2018a, p. 66) assimilates the production of this ethogram to an instance of a bottom-up systemic analysis, where the “*explanandum*” capacity¹² is sought, parting from the known activity of one of its components instead of the other way around.

The third type of evidence is comparative. This kind of evidence seems aimed at legitimizing the attributed function itself, by showing that it is not a unique or *ad hoc* function postulated only to account for a specific trait of a specific species. Rather, there seems to be some shared repertoire of acceptable functions that one can appeal to (more on the idea of function repertoires/taxonomies in the next sections).

Alexander cites a very wide variety of traits with communicative functions in a wide variety of (sometimes very distantly related) animals, which act as a way of legitimizing the particular attribution to the calling song. For example, he mentions phenomena as different as acoustic mating signals in birds, chemical signals in social insects and odorous signals in mice. The author also presents comparative evidence in organisms that are phylogenetically closer to the crickets as well as evidence of calling signals specifically in other arthropods (see Alexander, 1967, pp. 508-511 for more examples). As Olmos (2018a, p. 62) recognizes, Alexander mentions both homologous (e.g., grasshopper calling songs) and analogous (e.g., patterns of light emittance in some *Coleoptera*) traits in his comparisons. Additionally, the author also looks at other kinds of acoustic signals and their functions in the crickets themselves, which he summarizes as “(a) calling (pair-forming); (b) aggressive; (c) courtship; (d) courtship interruption; (e) postcopulatory (pair-maintaining); (f) ‘recognition’” (Alexander, 1967, p. 499).

¹² See Olmos, Roffé, & Ginnobili (2020) for some criticisms of this terminology.

Finally, we come to natural selection. As Olmos notes (2018a, p. 63) the places where Alexander appeals to selective considerations (e.g., Alexander, 1962), he *presupposes* that the song above has a calling function. Instead, his focus is to speculate on how the calling song might have evolved from other sounds the crickets make, particularly the courtship song. He first draws on some comparative evidence to argue that the courtship song was present before the calling song (e.g., the fact that in all orthopterans where the female mounts the male there is—sometimes soundless—vibration of the wings by the male in close proximity), to then formulate a selective hypothesis:

I believe that there was selection for increased rhythmicity, intensity, and duration in the original courtship song (once or many times, it makes little difference) because these characteristics enhanced the courtship function itself, through increasing consistency, range, and redundancy. Eventually, through just this kind of change, this song must have become operative at such distances that it was sometimes advantageous (i.e., in some instances or in some species) for the male to be triggered into stridulation without contact with the female, and sometimes advantageous for the female to be attracted by hearing the sound when she was not otherwise in contact with the male. In this way the calling function, in the approximate form that it assumes today, could have evolved. (Alexander, 1962, p. 452)

Note that the author is more careful in his choice of language here, using qualificatives such as “I believe” and “could have evolved”. Previously he had also stated that the question of how other songs evolved from the courtship song was “the most difficult question of all” and that the evidence could only point to “some rather convincing indications” (Alexander, 1962, p. 451).

We can conclude, following Olmos, that:

[Natural selection evidence] could be said to be indirect, in the sense that it requires a previously established functional attribution, to only then formulate an evolutionary explanation to account for it. Here, the evolutionary explanation could operate by reinforcing the functional attribution, insofar as it presupposes it and offers a plausible explanation of its origin. (Olmos, 2018a, p. 63, our translation)

What can be extracted from this case study is that functional attribution appeals to heterogeneous evidence, and that in the practice of functional attribution, none of the different sources of evidence, by itself, provides necessary and sufficient conditions for it. Moreover, we believe that these results can be extended to functional attributions in other areas of biology. The next section purports to show that the same heterogeneity of the relevant evidence in functional attribution can also be found in other areas, as distant as biochemistry and molecular biology. We insist that this point may seem anomalous only if considered from the perspective of the traditional approaches to function, which tend to privilege one specific type of evidence over the others. However, the absence of necessary and sufficient conditions for the application of technical scientific concepts, as we saw in the previous section, is to be expected if one approaches functional biology as a typical area of science.

5. Main Case Study: Aquaporin Function Attribution to MIP Channels

One major research goal within molecular biology is the attribution of functions to genes and gene products. In this section, we will review the history of the ascription of a water permeation function (also known as an aquaporin function) to genes and the proteins encoded by them, which belong to the MIP (for membrane intrinsic protein) family. Throughout this examination, we will once again highlight the heterogeneous sources of evidence that were used in this ascription, as well as the insufficiency of each taken separately. With this, we aim to show that a second case study, from a very different area of study, supports our account of functional attribution.

In the beginning of the 90s a growing family of homologous proteins from quite diverse organisms was reported (Baker & Saier, 1990; Pao et al., 1991; Sandal & Marcker, 1988) These proteins were (i) the major intrinsic protein from bovine lens fiber junction membranes, also known as MIP26 (for major intrinsic protein of 26kDa), (ii) the *Escherichia coli* glycerol facilitator (GLP), (iii) a tonoplast intrinsic protein (TIP) located at the protein storage vacuolar membranes of plant seeds, (v) the 'Big Brain' (BIB) neurogenic protein of *Drosophila*, (iv) the plant-nodulin-26 (NOD) from the peribacteroid membrane of soybean/Rhizobium root nodules, and (vi) a partially sequenced protein from *Streptomyces coelicolor* that could also be a glycerol facilitator. All these proteins had a high degree of sequence similarity, and hence were grouped as members of the same protein family, despite being present in wildly different organisms (from bacteria to plants and animals).

Analyzing the aminoacidic sequence, all these proteins seemed to be integral membrane proteins with six transmembrane helical segments; protein sequence alignment and phylogenetic trees were also determined. However, the different organ/body part localizations of these proteins (cow's eyes, plant root nodules and seeds, fly's brains, bacterial inner membranes, etc.) caused confusion about their proper function. If similarity of sequence points to similarity of function, it is difficult to see which function needs to be performed in these very different contexts.

Even though, at first, it could be thought that different members of the family perform different functions, functional analogies were then observed, for example between lens syncytium and legume root nodules (Baker & Saier, 1990); and, considering the homology of all these proteins to the glycerol facilitator, a small molecule transport function was proposed. The tridimensional structure (predicted from the primary sequence, though not "observed" yet) suggested that they were embedded in membranes and that they could form channels to facilitate the passage of molecules from one side of the membrane to the other, because of the predicted structure's general similarity with other known proteins involved in transport. Additional evidence to support that these proteins have some kind of participation in fluid transport was that expression of some of them in pea plants was induced after water deprivation (Guerrero, Jones, & Mullet, 1990). So, it was proposed, for example, that MIP26, present in lens fiber cells, was a channel through which these cells may absorb interstitial fluid (Gorin, Yancey, Cline, Revel, & Horwitz, 1984), and that TIP was a small

metabolites channel in charge of moving these molecules between the storage vacuoles and cytoplasm of seed storage tissues (Johnson, Hofte, & Chrispeels, 1990). Note that, in this initial ascriptions, part of the function was common among the members of the family—i.e., acting as channels—but another was not—different molecules were thought to be transported in each case.

Here, in these diverse initial attributions, there seem to be multiple sources of evidence acting in concert. The ubiquity and range of these proteins seemed to point, at first glance, to some function that is very basic to life, and hence to some version of the protein that was present in an ancestor of all these organisms. We already see some comparative/evolutionary reasoning at play: the ubiquity and wide range of a (putative/primary) homology points to some—for now unknown—function, since it is considered unlikely that a DNA sequence or its product will either arise independently or be preserved for so long and in so many different lineages unless it is present in ancestor, with stabilizing selection is acting against its modification. Structural knowledge, together with previously ascribed functions to similar structures, suggested channels. Experimental evidence (e.g., pattern of expression in water deprivation contexts) seemed to support this idea, while organ location suggested the molecule that was being transported. Note, however, that each of these functional ascriptions were taken as very tentative, not established ones. In other words, these lines of evidence were, in accordance with our account, not taken by the relevant communities as sufficient for functional attribution.

In a separate and completely independent line of research, the hematologist Peter Agre and his co-workers were developing a method to isolate the Rh molecule from red cells, and a small protein kept appearing in the tests as a contaminant. Different results pointed to the possibility of being in the presence of an undiscovered molecule. Agre's group cloned the cDNA of the 28 kDa protein and obtained a 269-amino acid polypeptide, which was abundant in mammalian red cells but also in renal proximal tubules (Denker, Smith, Kuhajda, & Agre, 1988). This protein was named CHIP28 and was detected to be similar to the major intrinsic protein of the bovine lens MIP26, indicating that it could be part of the MIP family (Preston & Agre, 1991). Thus, Agre and his team knew that the protein could be a channel with fluid transport capabilities.

In a conversation that Agre had with John Parker a possible function was proposed: water transport. In an interview with Claudia Dreyfus for *The New York Times* (Dreifus, 2009) Peter Agre says:

Then in 1991, I visited John Parker (he died in 1993). He'd been my hematology professor at the University of North Carolina. He said, "boy, this thing is found in red cells, kidney tubes, plant tissues; have you considered it might be the long-sought water channel?" It was his suggestion that caused me to change the direction of my research. What my lab team was able subsequently to prove was that 28K formed these little tubes inside many cells and that water passed through them. With that, more than 100 years of scientific controversy was ended.

What Parker referred to with the “long-sought water channel” were some investigations from the 60s within a third and also independent line of research, in the biophysics and physiology communities (revised in Alleva, Chara, & Amodeo, 2012). To explain this idea, consider that water can pass through the lipidic walls (membranes) of cells via osmosis. By that time, it was known that some biological membranes, such as frog skin or red blood cell membranes, have a higher water permeability than expected for water crossing biological membranes directly through the lipid bilayers (Dainty & House, 1966; Rich, Sha’afi, Romualdez, & Solomon, 1968; Ussing, 1965). This biophysical measurement suggested the existence of pores for water permeation located in those membranes. These pores were thought to be proteins, since Macey and Farmer’s experiments showed that sulfhydryl reagents reduced osmotic water permeability in red cells (Macey & Farmer, 1970). During the following years, there was a period of intense biophysical research in this area, and different kinds of experimental approximations supported the hypothesis of the presence of protein channels allowing the transport of water through biological membranes. However, the isolation and identification of those pores with a water permeation function was not yet available.

One may see this third line of research as performing a kind of systemic analysis in the opposite direction to the other two, i.e., in a top-down way. The first and second lines of research came upon a ubiquitous protein (or protein family) and were trying to establish its function—in systemic analysis’ terms, the relevant capacity of the organisms to which the protein’s activity contributed. In contrast, these biophysicists and physiologists knew that a particular function (or capacity) had to be taking place, but they did not know how it was implemented in actual organism’s cells.

Agre’s identification of the MIP family members with CHIP28, along with his encountering the biophysical experiments from the ‘60s, paved the way for the hypothesis of MIP proteins as water channels. Agre and Preston designed an elegant experiment to test if CHIP28 was able to show water transport function (Preston, Carroll, Guggino, & Agre, 1992). They injected *Xenopus laevis* oocytes with CHIP28 cRNA to induce over-expression of the corresponding protein. This technique was already known and widely used for the study of proteins with an ion channel function, but it was the first time it was applied to evaluate water transport. In this case, the oocytes expressing CHIP28 were submitted to an osmotic challenge and a dramatic swelling, followed by their rupture, was observed, while the control oocytes failed to swell. Therefore, Agre and Preston concluded that CHIP28 was the much sought after water pore, after which they renamed it AQP1. This experiment paved the way for looking at whether other proteins in the MIP family exhibited this behavior as well.

Two years later, Agre, Chrispeels and Sasaki sent a letter to the Letters to the Editor section of American Journal of Physiology (Agre, Sasaki, & Chrispeels, 1993):

A large family of integral membrane proteins related to major intrinsic protein of mammalian lens, MIP26, has been identified in diverse organisms (3). The structure of these proteins suggests that they may be channels, but the physiological functions of most are undefined. Our laboratories have discovered three new proteins related to MIP26, and each protein facilitates rapid and selective movement of water in the

direction of an osmotic gradient. These three proteins are the first known molecular water channels; therefore, we proposed the name aquaporins (AQP).

This work ended with a Nobel Prize for Agre due to the “discovery of water channels”.

Note that it was only after these experiments were performed that the function of the MIP family was considered firmly established. Once again, it is worth pausing to evaluate the number of elements that were present in this functional ascription. Consider the role of the experiment, which the biochemistry community sometimes takes as the decisive element in the attribution. We propose a thought experiment: suppose that, in the 1950s (before any of the other lines of research had begun), a team of hematologists found a novel protein as a contaminant and, for whatever reason, decided to make the experiment just mentioned. Would it have been possible to establish that water transport was the function of the molecule knowing only this? The answer is, of course, no. What Agre and Preston’s experiment shows is that the protein actually has the effect of transporting water. But firstly, the fact that a trait has an effect does not mean that the effect is its function. They could have been proteins that facilitated the creation/transport of water channels to the cell walls, or—even if it was known that they were located at the cell walls—water transport could have been a side-effect of a different function (e.g. acting as a receptor of some kind), or—even if it was known that they are channels—they could have been channels for other things, with water being accidentally transported,¹³ and so on. To add to this, before the 60s, it was thought that water channels were unnecessary for cells since water can pass directly through the cell wall. Moreover, if we imagine that no other similar proteins had been discovered yet, it would have been dubious to ascribe an important novel function to a single protein, found only once.

What these considerations highlight is the fact that the experiment was decisive only because there already existed a large body of heterogeneous evidence pointing in the same direction beforehand. Comparative-evolutionary evidence suggested that the proteins were ubiquitous and that the function had to be very basic to life, comparative-structural knowledge suggested that the protein acted as a channel, water transport at a rapid pace (i.e. through some kind of pore) was a known capacity of cells, etc. Only in this wider context can an experiment showing the proximal effect of a structure have the significance it did. Agre’s merit was more in synthesizing different lines of research into a single, definite, direction than in performing the actual confirmatory experiment.

Note that what we just proposed is not merely an abstract thought experiment. The life science community faces these kinds of problems all the time. Novel structures with unknown functions are constantly found, discussions around whether an effect observed in the laboratory is an actual biological function are omnipresent, etc. In the next section, we

¹³ In fact, they *do* transport other things, which are relevant for the survival of the cell (see, for example, Gomes et al., 2009, for a revision of this idea). The fact that Agre, Chrispeels and Sasaki decided to name the proteins “aquaporins” had the effect of biasing later research. This is a nice example of the importance of naming in biology.

will (very briefly) review some ways in which functional attribution works in biochemistry today.

6. Functional Attribution in Biochemistry Today

Over the last 20 years there has been an exponential accumulation of sequenced genomes and structural knowledge about proteins, accompanied by an immense influx of accessible biological data. This has led to an explosion of data in the field, and computational tools such as GO (Gene Ontology), UniProt, BLAST (Basic Local Alignment Search Tool), PDB (Protein Data Bank), among others, have emerged. These tools aim to establish a controlled and standardized vocabulary for naming and establishing genes products and their functions, thereby facilitating cross-disciplinary communication and analysis. The methodological and theoretical toolkit available to ascribe a function to a single gene or gene product today is vastly more complex than the one present at the moment of the aquaporin case, but the rationale of the work within the biosciences is not radically different.

When a gene or gene product is investigated to understand its function usually a workflow or pipeline for functional attribution is deployed. This workflow can be best interpreted as a series of applicable heuristics rather than a strict recipe to be followed. It can begin with sequencing a gene or entire genome, followed by BLASTing the sequence (i.e. aligning it to members of an enormous database of known sequences and ranking them by degree of coincidence) to check for similarity with other known sequences. If a significant portion of the sequence is similar to other known genes, the degree of similarity and occurrence of mutations in key areas can be established. If similarity is high, and key mutations are not present, GO can be referenced to see the function of the similar gene. It can then be assumed that the gene performs the same function without repeating all the relevant experiments. This functional attribution relies primarily on comparative evidence, implicitly incorporating evidence from the original attributions.

Alternatively, if there is no similarity with known sequences or there is variation at key locations, several other heuristics can be adopted. These include gene knockout (or knockdown) using techniques like CRISPR-Cas9 editing (i.e., seeing what known biological process are affected when the gene is not present, a way of determining the proximate and distal effects of the gene), as well as tools to determine/predict the structural and topological location of the gene's products, such as subcellular localization assays, structural resolution techniques such as X-ray crystallography, cryo-EM, NMR, AlphaFold prediction, among others. Additionally, other techniques—which, again, provide evidence from multiple and heterogeneous lines—can be deployed, such as mutating the new sequence in putative key functional domains to resemble known relatives and studying the resulting effects experimentally, performing computational studies such as quantum or classical molecular dynamics simulations, and carrying out evolutionary studies such as synteny analysis, gain and loss assessments, etc.

Due to reasons of space, we cannot extend too much on what each of these techniques does in detail. What is important for our purposes here is that much like in our two historical cases, contemporary biological practice also treats the concept of function as one with an open texture. That is, functional attribution is carried out through the accumulation of evidence from different sources that point in some direction, none of which is considered sufficient and/or necessary by itself.

7. Responses to possible objections

In this section we consider some objections that could be raised against us, with the intention of clarifying our position.

This is just a form of pluralism, similar to others already present in the literature

Yes and no. We agree with the core idea of the pluralists that there is more than one criterion used to identify functions in biological practice. That is, like them, we are pluralists regarding the existence of multiple operationalization criteria for functions. There are, however, some differences between our position and theirs.

The first is that we do not believe that a multiplicity of operationalization criteria for a concept entails the existence of multiple different concepts. In that sense, regarding the existence of function concepts, we are *monists*. We believe there is one concept of biological function, not many. When one performs a kind of systemic analysis to situate the behavior of a cricket in its life cycle and then uses evolutionary/comparative evidence to look at other related (or even non-related) species, one is simply using joint evidence to determine *the* function of the calling song. It would be misleading to describe the situation as using one type of evidence to attribute a function-type-1 to the calling song and using another to attribute a function-type-2.¹⁴

Note that these points are independent of the distinction of between-discipline and within-discipline pluralism (Garson, 2018). We agree with within-discipline pluralists that a heterogeneity of criteria and evidence are used in functional attributions, even within a single field. Both our case studies show that, within two different disciplines, the concept of function is operationalized in many different ways—e.g. molecular biologists used top-down and bottom-up systemic approaches, comparative evidence, proximate effect evidence, etc. to attribute a water transport function to aquaporins. What both cases also show is that this heterogeneous evidence was used to determine *the* function of the trait in question. If a plurality of function-concepts existed, then biologists could have concluded that aquaporins have the proximate-effect-function of transporting glycerol, the evolutionary-function of

¹⁴ This is not to say that a trait cannot have more than one function, it only means that when one says “the/a function of x is y” one always *means the same* by “function” in that sentence.

regulating water in the cells, and so on. Instead, what we find is that those lines of evidence were used *jointly* in a *single* functional ascription.

Another, perhaps more subtle but no less important, difference is how we view the field of the philosophy of functional biology, what its main tasks are, and how we should carry on from here. A lot of work and energy has been poured into debates over whether certain philosophical accounts over- or under-generate (e.g. is the systemic account too “promiscuous” in assigning functions? Does the etiological account have problems with exaptations? etc.) Merely stating that within some disciplines more than one of these accounts is used does not automatically solve those issues. Above, we cited Garson (2016) himself saying that the way to argue in the field is by showing cases of over- or under-determination. Our perspective implies a change in focus. The thesis of the open texture specifically allows us to stop worrying about these alleged counterexamples to philosophical accounts and nudges us to look more into additional case studies, to see in which different and interesting ways the concept of function is being operationalized. We found that, for example, comparative evidence (which almost no-one was talking about) is very frequently used as evidence for functional ascriptions.

Operationalization criteria, by themselves, do not specify the meaning of the term. Only definitions can do that

Meaning is a complex phenomenon, and we cannot get into complicated discussions around this notion here. The easiest response is that we agree with Neander (1991, pp. 170-171) when she characterizes her objective as “a search for the criteria of application that people generally have in mind when they use the term under analysis, and discuss the merits of such a search, leaving the issue of meaning aside.” As we said in section 2, we believe the project of providing conceptual analyses in this sense is worthwhile even if it is not connected with the project of establishing the meaning of the terms being analyzed.

A second response would be that we do have paradigmatic cases of meaningful terms which we *know* are not explicitly definable: primitive terms in axiomatized theories. The case is interesting because what one does with these terms is, precisely, to give (as axioms) some criteria of application, which do not suffice to eliminate the terms in question from every statement containing them. It is not surprising that logical empiricists, who tended to view empirical theories as axiomatizable entities, took this position about theoretical terms, which they tended to view as primitives in those theories. However, one does not need to go that far in the case of functions. Though some have argued that there is something like a theory of functions (Ginnobili, 2011), here we only intend to show the objector that she is wrong in claiming that every meaningful term has to be definable.

We downplay [your preferred] account or type of evidence

For instance, in the cases we looked at, evidence from natural selection (both past selection and present-day fitness) did not play a significant role in performing the functional attributions in question. We acknowledge that there may be other cases where these (or other) types of evidence might play a more significant role. Functional biology is enormous, and it is possible that functional concepts are applied somewhat differently in different areas. If we want to have a (meta)empirically informed conception, all we can do is study how these concepts are applied in particular areas. More than defending a particular set of application criteria as the only existing ones, our objective is to shift the way in which the discussion is carried on going forward.

Also note that we do accept that, even in the functional attributions we examined, natural selection does ultimately *explain* how the relevant populations acquired the functional items in question. But, as we said in section 2, we are in the business of reconstructing the criteria of *application* of the term (i.e. the way in which functions are attributed to traits), not of proposing an *explanation* of the existence of traits that are already recognized as functional—that is a worthwhile endeavor, but it is a logically posterior one.

To emphasize, it is true that once a functional attribution is made, the question of how the population came to historically acquire (in the sense of an efficient cause) that functional trait can remain open. And there is a sense in which the explanation will only be complete (or at least more complete) once we have answered this question. In contemporary biology, natural selection is the most common answer to the acquisition of functions. However, the fact that natural selection is part of a (more) complete explanation does not imply that etiological approaches are right in claiming that functional attribution is equivalent to (and replaceable by) the selectionist explanation of the origin of the functional trait. The most that can be conceded to the etiological approach is that the selective history is one piece of evidence (and usually not the most important one, nor the only one provided by evolutionary biology) that supports functional attribution.

We confuse the definition of the term with the evidence in favor of that definition

Some people would recognize that a multiplicity of criteria is used to attribute functions to traits, but would view those criteria as providing (defeasible) evidence for a single definition or conceptual core of the notion—see, e.g., Garson (2016, p. 7),

Our response would be that, at least in the cases we analyzed, there seems to be no criterion that is more important or preferential to others when attributing functions. Instead, we see all the operationalization criteria acting in concert, each providing additional evidence that, only together, forms a clear picture.

The fact that some pieces of evidence can seem decisive at certain points, like Agre's experiment with the oocytes, is an artifact of not seeing the context in which those pieces of evidence appeared. That context usually includes some robust background knowledge into which a missing piece is inserted. Once again, our conclusions here follow from an analysis

of historical case studies. It may be the case that in other fields (or even in the same field, at other times) some lines of evidence are considered to be more important than others. We would be happy if someone were to argue for this, and if the discussion was reoriented in this direction.

8. Conclusions

In this paper, we have developed a novel account of the concept of biological function for molecular biology, but which we believe to be applicable outside this domain, as we have shown with our preliminary example. According to this account, the concept of function is not explicitly definable by a set of necessary and/or sufficient criteria, but rather has an open texture.

As we explained, the idea that many—if not the most important—scientific concepts do not have explicit definitions in this sense, nor do they need them, is not new in the philosophy of science. The logical empiricists had already argued that theoretical concepts have no definitions, but rather their application criteria can be specified via “bilateral reduction statements”, which only provide partial specifications of meaning. While we are not advocating a return to the logical empiricist philosophy of science, which has many known problems, our account does take inspiration from this tradition and thus has deep roots in the history of the discipline.

Our hope going forward is that more studies looking at the rich and varied ways in which historical or contemporary functional attributions have been carried out in different domains, instead of spending so much attention on abstract discussions over whether a particular account or criterion over/under-generates in some way.

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References

- Agre, P., Sasaki, S., & Chrispeels, M. (1993). Aquaporins: a family of water channel proteins. *American Journal of Physiology*, 263, F461. <https://doi.org/0.1152/ajprenal.1993.265.3.F461>.
- Alexander, R. D. (1958). Sound production and communication in insects. *Animal Behaviour*, 6(3/4), 252. doi: 10.1016/0003-3472(58)90086-1

- Alexander, R. D. (1960). Sound communication in Orthoptera and Cicadidae. In W. E. Lanyon & W. N. Tavolga (Eds.), *Animal Sounds and Communication* (Vol. 7, pp. 38–92). American Institute of Biological Sciences.
- Alexander, R. D. (1961). Aggressiveness, Territoriality, and Sexual Behavior in Field Crickets (Orthoptera: Gryllidae). *Behaviour*, *17*(2/3), 130–223.
- Alexander, R. D. (1962). Evolutionary Change in Cricket Acoustical Communication. *Evolution*, *16*(4), 443–467. doi: 10.1111/j.1558-5646.1962.tb03236.x
- Alexander, R. D. (1967). Acoustical Communication in Arthropods. *Annual Review of Entomology*, *12*, 495–526. doi: 10.1146/annurev.en.12.010167.002431
- Alleva, K., Chara, O., & Amodeo, G. (2012). Aquaporins: Another piece in the osmotic puzzle. *FEBS Letters*. *586*(19), 2991–2999. doi: 10.1016/j.febslet.2012.06.013
- Ashburner, M., Ball, C. A., Blake, J. A., Botstein, D., Butler, H., Cherry, J. M., ... Sherlock, G. (2000). Gene Ontology: Tool for the unification of biology. *Nature Genetics*, *25*(1), 25–29. doi: 10.1038/75556
- Baker, M., & Saier, M. H. . (1990). Letter to the Editor: A Common Ancestor for Bovine Lens Fiber Major Intrinsic Protein, Soybean Noclulin-26 Protein, and E. coli Glycerol Facilitator. *Cell*, *60*(2), 185–186. doi: 10.1016/0092-8674(90)90731-s
- Brunnander, B. (2011). Philosophy and default descriptivism: The functions debate. *Metaphilosophy*, *42*(4), 417–430. doi: 10.1111/j.1467-9973.2011.01701.x
- Caponi, G. (2020). The Darwinian Naturalization of Teleology. In L. Baravalle & L. Zaterka (Eds.) *Life and Evolution: Latin American Essays on the History and Philosophy of Biology* (pp. 121–142). Springer, Cham. doi: 10.1007/978-3-030-39589-6_8
- Carnap, R. (1950). *Logical Foundations of Probability*. Chicago: University of Chicago Press.
- Chen, B. (2022). On Biological Function: A Critical Examination of Eliminativism. *Transversal: International Journal for the Historiography of Science*, *13*. doi: 10.24117/2526-2270.2022.i13.02
- Dainty, J., & House, C. R. (1966). An examination of the evidence for membrane pores in frog skin. *The Journal of Physiology*, *185*(1), 172–84.
- Denker, B. M., Smith, B. L., Kuhajda, F. P., & Agre, P. (1988). Identification, purification, and partial characterization of a novel M(r) 28,000 integral membrane protein from erythrocytes and renal tubules. *Journal of Biological Chemistry*, *263*(30), 15634–15642. doi: 10.1016/s0021-9258(19)37635-5
- Doolittle, W. F. (2018). We simply cannot go on being so vague about ‘function.’ *Genome Biology*, *19*(1), 223. doi: 10.1186/s13059-018-1600-4

- Doolittle, W. F., Brunet, T. D. P., Linquist, S., & Gregory, T. R. (2014). Distinguishing between “function” and “effect” in genome biology. *Genome Biology and Evolution*, 6(5), 1234–1237. doi: 10.1093/gbe/evu098
- Dreifus, C. (2009). Using a Leadership Role to Put a Human Face on Science. *The New York Times*. Retrieved from <https://www.nytimes.com/2009/01/27/science/27agre.html>
- Garson, J. (2016). *A Critical Overview of Biological Functions*. Dordrecht: Springer.
- Garson, J. (2018). How to Be a Function Pluralist. *The British Journal for the Philosophy of Science*, 69(4), 1101–1122. doi: 10.1093/bjps/axx007
- Garson, J. (2019). *What Biological Functions Are and Why They Matter*. Cambridge: Cambridge University Press. doi: 10.1017/9781108560764
- Ginnobili, S. (2011). Función como concepto teórico. *Scientiae Studia*, 9(4), 847–880.
- Gomes, D., Agasse, A., Thiébaud, P., Delrot, S., Gerós, H., & Chaumont, F. (2009). Aquaporins are multifunctional water and solute transporters highly divergent in living organisms. *Biochimica et Biophysica Acta - Biomembranes*. Elsevier B.V. doi: 10.1016/j.bbamem.2009.03.009
- Gorin, M. B., Yancey, S. B., Cline, J., Revel, J. P., & Horwitz, J. (1984). The major intrinsic protein (MIP) of the bovine lens fiber membrane: Characterization and structure based on cDNA cloning. *Cell*, 39(1), 49–59. doi: 10.1016/0092-8674(84)90190-9
- Greenspan, N. S. (2011). Attributing functions to genes and gene products. *Trends in Biochemical Sciences*, 36(6), 293–297. doi: 10.1016/j.tibs.2010.12.005
- Griffiths, P.E. (1993). Functional analysis and proper functions. *British Journal for the Philosophy of Science* 44, 409–422.
- Guerrero, F. D., Jones, J. T., & Mullet, J. E. (1990). Turgor-responsive gene transcription and RNA levels increase rapidly when pea shoots are wilted. Sequence and expression of three inducible genes. *Plant Molecular Biology*, 15(1), 11–26. doi: 10.1007/BF00017720
- Guttinger, S., & Love, A. C. (in press). modENCODE and the elaboration of functional genomic methodology. In C. Donohue & A. C. Love (Eds.), *Perspectives on the Human Genome Project and Genomics*. Minneapolis: University of Minnesota Press.
- Hempel, C. G. (1958). The Theoretician’s Dilemma. In H. Feigl, M. Scriven, & G. Maxwell (Eds.), *Minnesota Studies in the Philosophy of Science* (Vol. 2). Minneapolis: University of Minnesota Press.
- Johnson, K. D., Hofte, H., & Chrispeels, M. J. (1990). An Intrinsic Tonoplast Protein of Protein Storage Vacuoles in Seeds is Structurally Related to a Bacterial Solute Transporter (GlpF), 2(6), 525–532.

- Kuhn, T. S. (1970). Postscript—1969. In *The Structure of Scientific Revolutions* (2nd ed., pp. 174–210). Chicago: University of Chicago Press.
- Leonelli, S. (2016). *Data-Centric Biology: A Philosophical Study*. Chicago: University of Chicago Press.
- Macey, R. L., & Farmer, R. E. L. (1970). Inhibition of water and solute permeability in human red cells. *BBA - Biomembranes*, 211(1), 104–106. doi: 10.1016/0005-2736(70)90130-6
- MacKinnon, D. M., Waismann, F., & Kneale, W. C. (1945). Symposium: Verifiability. *Aristotelian Society Supplementary Volume*, 19(1), 101–164. doi: 10.1093/aristoteliansupp/19.1.101
- Millikan, R. G. (1989). In Defense of Proper Functions. *Philosophy of Science*, 56(2), 288–302.
- Mossio, M., Saborido, C., & Moreno, A. (2009). An Organizational Account of Biological Functions. *British Journal for the Philosophy of Science*, 60(4), 813–841. doi: 10.1093/bjps/axp036
- Moulines, C. U. (1982), *Exploraciones metacientíficas*. Madrid: Alianza Editorial.
- Nagel, E. (1961). *The structure of science*. New York: Harcourt.
- Nagel, E. (1979). Teleology revisited. In *Teleology Revisited and Other Essays in the Philosophy and History of Science* (pp. 275–316). New York: Columbia University Press,.
- Neander, K. (1991). Functions as Selected Effects: The Conceptual Analyst's Defense. *Philosophy of Science*, 58(2), 168–184.
- Olmos, A. S. (2018a). *El concepto de función y la explicación funcional de la neuroetología*. Buenos Aires: Teseo Press. Retrieved from <https://www.teseopress.com/elconceptodefucion/>
- Olmos, A. S. (2018b). La heterogeneidad de criterios para la atribución funcional. Estudio de un caso. *Ludus vitalis*, 26(50), 51–76.
- Olmos, A. S., Roffé, A. J., & Ginnobili, S. (2020). Systemic Analysis and Functional Explanation: Structure and Limitations. In L. Baravalle & L. Zaterka (Eds.), *Life and Evolution: Latin American Essays on the History and Philosophy of Biology* (pp. 209–229).
- Preston, G. M., & Agre, P. (1991). Isolation of the cDNA for erythrocyte integral membrane protein of 28 kilodaltons: member of an ancient channel family. *Proceedings of the National Academy of Sciences of the United States of America*, 88(24), 11110–11114.

- Preston, G. M., Carroll, T. P., Guggino, W. B., & Agre, P. (1992). Appearance of Water Channels in *Xenopus* Oocytes Expressing Red Cell CHIP28 Protein, *Science*, 256(5055), 385–387. <https://doi.org/10.1126/science.256.5055.385>
- Pao, G. M., Wu, L. F., Johnson, K. D., Höfte, H., Chrispeels, M. J., Sweet, G., ... Saier, M. H. (1991). Evolution of the MIP family of integral membrane transport proteins. *Molecular Microbiology*, 5(1), 33–37.
- Rich, G. T., Sha'afi, I., Romualdez, a, & Solomon, a K. (1968). Effect of osmolality on the hydraulic permeability coefficient of red cells. *The Journal of General Physiology*, 52(6), 941–954. doi: 10.1085/jgp.52.6.941
- Saborido, C., Mossio, M., & Moreno, A. (2010). La Dimensión Teleológica Del Concepto de Función Biológica Desde la Perspectiva Organizacional. *Teorema: International Journal of Philosophy*, 29(3), 31–56.
- Sandal, N. N., & Marcker, K. A. (1988). Soybean noduline 26 is homologous to the major insittrinsic protein of the bovine lens fiber membrane. *Nucleic Acids Research*, 16(19), 9347. doi: 10.1093/nar/16.19.9347.
- Thomas, P. D. (2017). The Gene Ontology and the Meaning of Biological Function. *Methods in Molecular Biology (Clifton, N.J.)*, 1446, 15–24. doi: 10.1007/978-1-4939-3743-1_2
- Ussing, H. (1965). Transport of electrolytes and water across epithelia. In *Harvey Lecture 1964* (pp. 1–30).
- Wouters, A. G. (2005). The Function Debate in Philosophy. *Acta Biotheoretica*, 53(2), 123–151.
- Wright, L. (1973). Functions. *Philosophical Review*, 82(2), 139–168. doi: 10.2307/2183766