TOPICAL REVIEW

The concept of function in modern physiology

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Abstract An overview of the scientific literature shows that the concept of function is central in physiology. However, the concept itself is not defined by physiologists. On the other hand, the teleological, namely, the 'goal-directed' dimension of function, and its subsequent explanatory relevance, is a philosophical problem. Intuitively, the function of a trait in a system explains why this trait is present, but, in the early 1960s, Ernest Nagel and Carl Hempel have shown that this inference cannot be logically founded. However, they showed that self-regulated systems are teleological. According to the selectionist theories, the function of an item is its effect that has been selected by natural selection, a process that explains its presence. As they restrict the functional attribution of a trait to its past selective value and not its current properties, these theories are inconsistent with the concept of function in physiology. A more adequate one is the causal role theory, for which a function of a trait in a system is its causal contribution to the functional capacity of the system. However, this leaves unsolved the question of the 'surplus meaning' of the teleological dimension of function. The significance of considering organisms as 'purpose-like' (teleological) systems may reside not in its explanatory power but in its methodological fruitfulness in physiology. In this view, the teleological dimension of physiological functions is convergent to but not imported from, the teleological dimension of evolutionary biology.

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Function and physiology

In his introductory lecture of the 37th IUPS Congress hosted in 2013 by the Physiological Society, Sir Paul Nurse, citing the Oxford English Dictionary, referred to physiology as 'the branch of biology that deals with the normal functions of living organisms and their parts'. An overview of the scientific production and of the definitions of physiology given by the main physiological societies, shows that the concept of function is central in physiology. For example, the 2006 strategic plan of the American Physiological Society gives the following 'working definition of physiology' (APS, 2006): Physiology is the study of the function of organisms as integrated systems of molecules, cells, tissues, and organs, in health and disease'. A similar definition is found in Eckert's textbook (Eckert *et al.* 1988): 'animal physiology can be defined as the study of the function of animals and their constituent parts'. Interestingly, these definitions are not far from the initial one given in 1554 by the French physician Jean Fernel, who also referred to function to define physiology (Fernel, 1554): 'Physiology or discourse of human nature, which entirely

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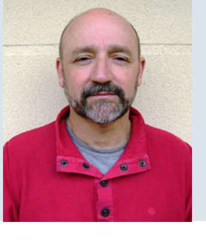

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explains the nature of healthy human being, all his faculties and his functions'. Analysis of the articles published in 2013 in *The Journal of Physiology* indicates that 22.8% of the articles have the word 'function' either in their title or abstract, a proportion higher than in 2003 (16.8%) and 1993 (10.4%). Similar percentage and increase in the last one or two decades are also found in other physiological publications, e.g. *The Journal of General Physiology*, *Experimental Physiology* and *The American Journal of Physiology, Regulatory, Integrative and Comparative Physiology*.

Taken together, these observations indicate that the concept of 'function' is fully relevant in current physiology, both to define this discipline and its specificity compared to other branches of biology, and in its scientific production. However, the concept itself is not defined by the physiologists themselves, who use it as a spontaneous conceptual tool for which meaning does not require an explicit definition. On the other hand, the concept of function is scientifically ambiguous due to its teleological, namely, 'goal-directed' dimension. When finality is no longer considered as scientifically valid, a teleological view of living organisms is thenceforth improper, a problem already stated more than a century ago by the German physiologist Emil Du Bois-Reymond (Du Bois-Reymond, 1882) when he pointed out the 'difficulty offered by the apparently teleological arrangement of nature [. . .] inconsistent with the mechanical view of nature'. Physiologists are hence in a rather troublesome position, as they refer in their practice to a concept that theoretical validity remains controversial. This uneasiness has been expressed by Knut Schmidt-Nielsen, saying (Schmidt-Nielsen, 1997): 'Examining how an animal copes with its environment often tends to show what is good for the animal. This may bring us uncomfortably close to explanations that suggest evidence of purpose, or teleology, and many biologists consider this scientifically improper'. One century before, Du Bois-Reymond, a fully materialist scientist, had expressed this epistemological discomfort in a more concise (and rather machist) formulation (Rothschuh, 1973): 'Teleology is a kind of woman no biologist is able to live about, but he is rather reluctant to be seen with her in public'.

Function and teleology

As 'function' remains largely used in physiology, functional attribution seems to hold a specific explicative value relevant for physiologists, despite its ambiguous scientific validity. The actual meaning of function is a philosophical problem, not purely speculative, as it has consequences in life science teaching. A recent survey in a French high school has indeed shown that finalist explanations are frequent in examination papers and that the majority of pupils has a teleological view of adaptation (Paulin & Simon, 2012), an observation that is probably not to be limited to French pupils. Intuitively, the explanatory content of functional attribution is that the function of item in a system explains why this item is present in this system. For example, saying that 'the function of the heart is to pump the blood in the vasculature' suggests that the fact that the heart pumps the blood is the reason why the heart is present in the body. However, if we refute a finalist explanation, explaining the existence of the heart by its effect does not seem logical, for the argumentation would be that the cause of the existence of an item should be its consequence.

In the early 1960s, two philosophers, Ernest Nagel and Carl Hempel, have analysed the structure of this teleological explanation trying to see if the presence of an item in a system could be logically deduced from its causal contribution to the behaviour of the system (Nagel, 1961; Hempel, 1965). They concluded that such an inference requires that the presence of this item is a necessary condition of the system behaviour, what Hempel (1965) has called the 'functional indispensability'. Unfortunately, the requisite of 'functional indispensability' is usually not satisfied, due to the functional redundancy that characterizes living organisms. Hence, as pointed out by Hempel, the explanatory and predictive value of this teleological argument is extremely weak.

Nagel also examined a second notion linked to teleology, what he called 'the fundamental point, the 'goal-directed' character of organic systems'. His conclusion is that self-regulated systems can be viewed as 'directively organised systems', and hence can be said as teleological systems without any finalism, the apparent goal being the self-maintenance of the system (Nagel, 1961). Hempel (1965) expressed a similar point of view about the teleological dimension of self-regulated systems, either biological or social ones. Such a teleological dimension, relevant for physiology, is convergent (though not strictly identical) to teleological thinking in evolutionary sciences independent from any finalism. Indeed, evolutionary biology often considers organisms as goal-directed evolutionary units, the evolutionary dynamics being driven by fitness optimization (Grafen, 2002; Day *et al.* 2003).

However, the fact that organic systems can be legitimately viewed as teleological systems due to their self-regulatory properties or to their fitness optimization leaves unsolved the question of the 'surplus meaning' of teleological statements, if any.

Function and natural selection

In a highly influential article on cause and effect in biology, Mayr (1961) has introduced the distinction between two different types of causality, proximate and ultimate causes. According to Mayr, proximate causation, related to 'how' questioning answered by functional analysis, is separated from ultimate causation, which deals with 'why' questioning answered by historical, evolutionary investigation. In Mayr's view, the apparent purposiveness of organisms is explained by the 'existence of complex codes of information in the DNA', and functional analysis deals with 'the decoding of the programmed information contained in the DNA code'. Acceptance of Mayr's dichotomy between proximate/ultimate causality has an important consequence on the concept of function. If the scientific respectability of teleological dimension is restricted to ultimate cause/evolutionary science ('teleonomy' in Mayr's terminology), the concept of function, with its 'teleological load', cannot be legitimately defined in reference to physiological concepts, and its definition should hence be imported from evolutionary biology into physiology, or its teleological dimension dismissed. However, this dichotomy between proximate/ultimate causation is now questioned and recent development in evolutionary sciences supports the idea of a more 'reciprocal conception of causation' (Laland *et al.* 2011).

In the 1970s has emerged a new theory, the aetiological selectionist theory of function. This theory and its several variants derive from the theory of selected effect, initially formulated by Wright (1973). According to Wright, the function of an item is the effect for which this item has been selected. Wright has named this definition the 'etiological' theory of function, as what defines the function of an item is the cause of the presence of the item: the presence of an item A, which has the effect E, is due to the fact that F, and hence A, has been selected. This definition seems to solve the logical problem of the explanation of the presence of an item by its effect. In contrast with the approach of Nagel and Hempel, Wright's solution is based on the historical dimension of his definition of function: functional attribution depends on the fact that the effect has been selected in the past. It is hence a 'backward-looking' theory of function (Buller, 1999*b*).

Though the selected-effect theory was not initially enunciated by Larry Wright in relation with biological functions, this definition has been applied to biology by several philosophers (Millikan, 1884, 1989; Neander, 1991, 1995, 2010; Griffiths, 1993; Godfrey-Smith, 1994; Buller, 1999*a*). Various formulations have been proposed by the authors that share a common core: the function of a trait is basically the effect of a trait that has been selected for its effect, in particular, when applied to living organisms, selected by natural selection. The selected effect is, in this case, its historical adaptive value, namely, the fact that this effect is an adaptation in response to natural selection.

The objective of these theories is to safeguard the logical validity of the aetiological functional explanation (the explanation of the existence of an item by its effect), which is ensured by the historical dimension of the selective pressure exerted on it (the item is here because it has been selected). They are especially attractive for they use the theory of natural selection to naturalize the teleological dimension of function (i.e. the 'purpose-like' appearance of living organisms) and to solve the logical problem of aetiological functional explanation (i.e. the fact that the cause of the presence of a trait is its effect; its functional consequence). The theory of natural selection is the 'conceptual glue' that links the aetiological and teleological dimensions of functional attribution. They can consequently be described as aetiological and teleological.

Despite their apparent consistency, these theories have a fundamental weakness. Indeed, the safeguard of the aetiological explanation requires that functional attribution in a current organism should be restricted to traits that have contributed to past selection of its ancestors. The requisite of the temporal dimension has been explicitly noted by Neander (1991): 'A trait is adaptive if it contributes to the fitness of the organism in its current environment, and it is an adaptation if it has evolved due to past contributions to fitness. Most traits are both (i.e., are adaptive adaptations), but some traits are only one or other of these. According to etiological theories traits with functions are necessarily adaptations, there are not necessarily adaptive'. Accordingly, current functional attribution to a current trait in a current organism should be exclusively based on the past contribution of this trait to past fitness. However, the importance of the distinction between the original and current adaptive significance, and the role of co-option of existing characters in evolution, are now clearly stated (Bateson & Laland, 2013). This is a major limitation to the aetiological–selectionist theories of function, which defines current function from past selection. Additionally, this definition, whether or not of any value in evolutionary biology, is clearly inconsistent with the conceptual use of function in physiology. Indeed, it is a diachronic approach of function, as the functional attribution is strictly dependent on the past contribution of a trait to the fitness of the organism, whereas the conceptual use of function in physiology is based, methodologically, on a synchronic functional analysis, namely, with no historical dimension required for functional attribution. Moreover, the selectionist theories define what a function is in exclusive reference to external causation (selective process) with no attention paid to internal causation in relation with organizational properties. This is, also, a conception opposite to what physiology is about, as well as far from how contemporary evolutionary biology conceives evolutionary processes (Pigliucci & Muller, 2010).

In 1975, Robert Cummins has proposed a definition of function based on a quite different view of function, the so-called causal role theory of function (Cummins, 1975). According to this theory, the effect of a given trait of a system is a function if the analysis of the system shows that the effect of this trait causally contributes to a higher-level distinctive functional capacity of the system. For example, we can say that the function of the heart is to pump the blood in the vasculature because the analysis of the cardiovascular system shows that the activity of the heart is one of the causes of blood flow. This theory focuses on the functional analysis of a living system, independently from its past history. Its epistemological dimension, close to the methodology of physiology, makes it attractive to account for the use of function in physiology. However, several objections have been done to the causal role theory (Millikan, 1884, 1989; Godfrey-Smith, 1994; Krohs, 2010). One of them is that this theory does not provide aetiological explanation. Cummins rebuts this objection by arguing that what functional analysis does – and should do – is to explain the contribution of a trait to the properties of a system, not to explain the presence of the trait. In other words, according to Cummins, the functional question 'What is it for?' is equivalent to the question 'How does it works?' and not to 'Why is it here?' Cummins does not deny that the theory of natural selection can account for the apparent teleology of living beings, but he convincingly asserts that any explanation based on this 'purpose-like' dimension, even naturalized by evolutionary theory, is a pseudo-explanation (what he calls 'neo-teleology') and argues for a definition of function logically independent of selection (Cummins, 2002). This does not mean that there is no relationship between physiology and evolutionary biology. Functionality is an operative concept both in functional attribution in physiology and fitness evaluation in evolutionary biology. However, current physiological function does not equate current fitness and, consequently, physiological function cannot be defined in reference to fitness. Adaptive significance may change, whereas function remains identical. In addition, functional attribution of a trait in a system may be done, and evaluation of its contribution to fitness may be putative or unsolved. For example, the function of the CFTR molecule is well characterized, as are the functional consequences associated with a large number of mutations of its gene (Sheppard & Welsh, 1999). However, this does not solve the question of the adaptive value of these mutants, about which several successive hypotheses about their fitness value have been proposed to explain their relatively high frequency in human populations (Poolman & Galvani, 2007; Lubinsky, 2013).

'What's the function? How can it help?'

Though highly convincing with regard to the notion of function in physiology, Cummins' conception is not fully satisfactory. Cummins (2002) argues that the 'What is it for' question can be reduced to the 'How does it work' question. The title of this section, which is actually a question asked during one of the sessions of the 2013 IUPS Congress in Birmingham, indicates that it is rather equivalent to the 'How can it help' question, obviously more teleological than Cummins' statement. The question is not whether it is legitimate or not to consider organic systems as 'goal-directed'. Nagel and Hempel have answered positively, on the basis that organisms are self-regulated systems. More recently, the organizational theory of function has extended this view. This theory is based on the idea that biological systems can be viewed as thermodynamically dissipative, self-maintained systems hierarchically organized (Mossio *et al.* 2010; Saborido, 2012). Such a pattern of organization accounts for the 'goal-directed' appearance of the system. The question is whether this teleological dimension significantly contributes to the concept of function. If we refute the aetiological selectionist theories of function as irrelevant, as least for physiology, it is hard to argue for a specific teleological explanatory power of functional attribution, for Hempel and Cummins have both developed strong arguments that the explanatory import of the teleological statement is weak, if not inexistent (Hempel, 1965; Cummins, 2002).

However, in his essay, Hempel has set forth the idea that the main interest of functional analysis does not reside in its explanatory but in its heuristic value, opposing the poverty of functionalism as an explicative doctrine to its fruitfulness as a programme for research (Hempel, 1965). In this view, postulating the teleological dimension of the system under investigation is fruitful because it legitimates a reverse engineering-based methodology of research. This teleological postulate does not step in the explanatory value of the functional attribution done by the physiologist, so there is no conflict between the teleological dimension of the system studied and the mechanistic explanation of its functioning. The French physiologist Claude Bernard had already noted this (Bernard, 1865): 'The physiologist is inclined to admit an harmonic and preestablished finality in the organised body [. . .] One should not conclude from this that the living machine should not be analysed as a gross one'. We can even say that it is because he postulates that the organized body is a living machine, hence a 'goal-directed' system, that the physiologist can analyse it as a machine. The idea that the significance of the teleological dimension of function in physiology resides in its methodological fruitfulness may explain why physiologists still use this term both in their scientific production and in the definition of their discipline, as the identity and specificity of the various fields of modern biology are defined more by their research programmes than by putative specific explanatory structures.

In conclusion, Nagel's and Hempel's work has shown that postulating a teleological dimension of biological systems under investigation, independently from their history, is scientifically acceptable and fruitful. Accordingly, the teleological dimension of physiological functions is convergent to, but not imported from, the teleological dimension of evolutionary biology. Indeed, functionality is an operative concept both in physiology and in evolutionary sciences: explaining the contribution of a trait to the properties of a system is closely related to evaluating its contribution to fitness. However, physiological function does not equate adaptive significance. It may seem paradoxical to argue for a definition of function logically autonomous from evolutionary processand to support the explanatory interaction between physiology and evolutionary biology. However, the paradox is only apparent, because this logical autonomy is necessary to go beyond the dichotomy between proximate and ultimate causation and to consider a 'reciprocal conception of causation' (Laland *et al.* 2011) between physiological and evolutionary processes.

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