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Theoretical principles for biology: Organization

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A B S T R A C T

In the search of a theory of biological organisms, we propose to adopt organization as a theoretical principle. Organization constitutes an overarching hypothesis that frames the intelligibility of biological objects, by characterizing their relevant aspects. After a succinct historical survey on the understanding of organization in the organicist tradition, we offer a specific characterization in terms of closure of constraints. We then discuss some implications of the adoption of organization as a principle and, in particular, we focus on how it fosters an original approach to biological stability, as well as and its interplay with variation.

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"The physiologist and the physician must never forget that the living being comprises an organism and an individuality. […] Indeed, when we wish to ascribe to a physiological quality its value ad true significance, we must always refer to this whole and draw our final conclusions only in relation to its effects in the whole."

Claude Bernard, 1865/1984, quoted and translated by Wolfe, 2010.

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1. Introduction

For the past five decades, most of biological research has been framed on the hypothesis that biological organisms are essentially determined by genetic information,[1] and the molecular mechanisms through which such information is expressed. This hypothesis – which we refer to here as genocentrism – acknowledges of course that a variety of causal factors (e.g. physical, environmental …) concur in enabling the development and functioning of biological organisms. Yet, among these factors, genetic ones would have a special status, insofar as they determine the *distinctive* features of biological phenomena. In particular, protein synthesis, (and thereby biological functions) results from the expression of genetic information. According to a genocentric perspective, therefore, what makes biological systems specific with respect to other natural systems is ultimately the fact that they would be the result of the expression of genetic information.

Understood in this way, genocentrism carries on a form of explanatory reductionism insofar as biological phenomena are assumed to be adequately explained[2] by appealing to genetic information. In particular, the concept of organism loses centrality in biological sciences (Laubichler, 2000) because of its supposed derivability from genes: organisms would be, under adequate conditions, the *result* of the expression of genetic information through development.

The research program framed on genocentrism has undergone a spectacular development, remarkably represented by the Human Genome Project, which was declared complete in 2003. Recently, however, experimental evidence is increasingly challenging the idea that genetic information determines biological functions: in particular, gene expression is subject to massive variability, which suggests that DNA *under*determines functional proteins and, in the end, the very organization of the organism. Far from being mere "noise", variation is increasingly conceived as an inherent dimension of gene expression (Lestas et al., 2010; Dueck et al., 2016). Moreover, experimental biology shows not only that gene expression is variable, but even inherently stochastic (Raj and van Oudenaarden, 2008; Kupiec and Sonigo, 2000).[3]

As a matter of fact, the accumulation of experimental evidence at odds with genocentrism has induced a progressive renewal of interest in more integrative accounts, which aim at complementing genes with other determinants of biological phenomena. A main example of this trend is Systems Biology (Kitano, 2002) that elaborates mathematical and computational models on large, multiscale molecular networks, whose dynamics cannot be determined by genetic information and which, in turn, control the activity of genetic templates.

In the search for integrative accounts, a specific theoretical option consists in claiming that the relevant level of description at which Biology should be framed is that of the organism: the alternative to genocentrism would therefore be *organicism* (Gilbert and Sarkar, 2000; Ruiz-Mirazo et al., 2000; Soto and Sonnenschein, 2005). From an organicist perspective, organisms are the main object of biological science because they are the systems that underlie biological phenomena and – crucially – they cannot be reduced to more fundamental biological entities (such as the genes or other inert components of the organism).

The elaboration of a theory of biological organisms requires dealing with their distinctive complexity, which in turn requires taking into account a number of dimensions, including individuation (see Clarke, 2011; Miquel and Hwang, 2016), agency (Barandiaran et al., 2009; Arnellos and Moreno, 2015; Soto et al., 2008, 2016), regulation (Bich et al., 2015), adaptivity (Di Paolo, 2005), historicity (Ruiz-Mirazo and Moreno, 2012; Longo and Montévil, 2011, 2014), … and cognition (Thompson, 2007). In this paper and in Montévil et al. (2016a), we take a theoretical step toward a Biology of Organisms by arguing that organisms are governed by two theoretical principles: *organization* and *variation*. All biological organisms, in all their diversity and richness of forms and kinds, meet two general principles without exceptions: they are organized, and their organization undergoes variation.

As theoretical principles, organization and variation constitute overarching hypotheses that frame the intelligibility of the objects within the biological domain. Taken together, they characterize the relevant aspects of biological objects, that are measurable observables, relations and changes. To better grasp their nature, a relevant comparison can be made with the role of space and time in Physics, ever since Newton and Kant. One may consider space and time as "conditions of possibility" for constructing physical knowledge; in more modern terms, positing *a priori* the phase space (i.e. the list of pertinent observables and parameters) allows us to spell out a complete determination of the intended processes in physical theories, by equations or evolution functions. Analogously, the ambitious aim of this work is to single-out the principles to be posited as *a priori* conceptual tools for the intelligibility of ontogenesis.

In the general discussion of Montévil et al. (2016a), we further elaborate on the status of organization and variation as theoretical principles. One important implication of this strategy is that, although the two principles are supposed to lay the foundations of a biology of organisms, their domain of application is not necessarily restricted to the latter. Indeed, the set of systems that comply with the two principles – and can therefore be taken, by definition, as *biological* systems – is presumably larger than that of organisms. For instance, it has been recently argued (Nunes-Neto et al., 2014) that ecosystems might be described as organized systems by appealing to the same organization principle we are presenting herein. Accordingly, if they were shown to comply with both the organization and variation principles, ecosystems might be conceived of as biological systems, although not necessarily as organisms (Moreno and Mossio, 2015). In other words, we submit that biology is the science of systems meeting the principles of organization and variation, organisms being a specific, particularly relevant, class of biological systems. In the general discussion of Montévil et al. (2016a), we further elaborate on the status of organization and variation as theoretical principles.

To characterize each principle, as well as their mutual relations, we elaborated in two distinct papers: the present one deals with organization, while Montévil et al. (2016a) explores variation. Within our framework, the two principles are closely related, and each one is involved in the biological realization of the other. On the

[1] Note that we do not aim to discuss the notion of genetic information here; see Perret & Longo (2016) and Longo et al. (2012a) for a critical analysis.

[2] The notion of "theoretical determination" should not be confused with "determinism". Determinism corresponds to the assumption that the perfect knowledge of a given situation at a given time entails its future descriptions. Theoretical determination is the framework for understanding the changes of the intended object, and this framework can be non deterministic, as is the case in quantum mechanics, for example. Genocentrism rather corresponds to an assumption of "completeness" of the DNA as a code for development.

[3] This perspective broadened theoretical determination proper to genocentrism, although it mostly continued to attribute a central role to genes in ontogenesis. In short, "stochastic gene expression" is an increasingly relevant perspective, which modifies the role of randomness in molecular biology, as this moves from "noise" to a form of "functional randomness", while preserving the genocentric perspective. In Montévil et al. (2016a), we further discuss this issue and show how our analysis of organismal constraints may also propose a tentative understanding of the role of genome and the way its stochastic expression is canalized within and by the organism.