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Review

Extended physics as a theoretical framework for systems biology?

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ABSTRACT

In this essay we examine whether a theoretical and conceptual framework for systems biology could be built from the Bailly and Longo (2008, 2009) proposal. These authors aim to understand life as a coherent critical structure, and propose to develop an extended physical approach of evolution, as a diffusion of biomass in a space of complexity. Their attempt leads to a simple mathematical reconstruction of Gould's assumption (1989) concerning the bacterial world as a "left wall of least complexity" that we will examine. Extended physical systems are characterized by their constructive properties. Time is acting and new properties emerge by their history that can open the list of their initial properties. This conceptual and theoretical framework is nothing more than a philosophical assumption, but as such it provides a new and exciting approach concerning the evolution of life, and the transition between physics and biology.

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1. Introduction

Research concerning life necessarily deals with complexity. Biological systems cannot obviously be reduced to very few components, like genes. The conception of the gene as a simple causal agent is based in the superposition of three assumptions: (1) a stretch of DNA determines which protein is made; (2) a stretch of DNA is the origin of an inheritable phenotype characteristic; (3) "once genetic information has passed into protein it cannot get out again" (Crick, 1958). This notion is invalid because not all eukaryotic DNA codes for proteins, and DNA does nothing by itself. The egg machinery enables the DNA to be used to make proteins (Noble, 2008). Various molecular elements of living organisms (lipids, methyl and other epigenetic groups, etc.) are not coded for by DNA sequences. Thus, on one hand the gene is the causal agent, but on the other one it is the cell, or the tissue (Atlan and Koppel, 1997, Atlan, 1999).

As mentioned by Westerhoff et al. (2009) simple paradigms at work in classical physics (like the principle of minimum potential energy in mechanics, or in quantum mechanics) are of no use in theoretical biology. Living organisms are open thermodynamical systems that function at a non-equilibrium steady-sate (Nicolis and Prigogine, 1989). To maintain this state, they need a metabolic activity that requires 14 proteins that cannot be disentangled from the activity of more than three hundred gene products. This number is too large for a simple bottom-up explanation (Westerhoff et al., 2009). Thus, new strategies are being proposed to explain biological phenomena. One of them proposes to generate hypotheses at a top-down level (as an example: Barabasi and Albert, 1999; Jeong et al., 2001) and replace them by more precise forms of the hypotheses "in a bottom-up" fashion (Westerhoff et al., 2009) before testing them. Another one proposes to simultaneously introduce

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assumptions at different levels of biological organization (Noble, 2002, 2006 pp. 71–73, Soto et al., 2004; Lesne and Victor, 2006). The "virtual heart", a computer reconstruction of the heart developed by Noble involves three levels: electrical excitation, blood vessels and muscle fibres (Noble, 2002, p. 76). These multi-level approaches deeply change the structure of scientific explanation. In contradiction with the so-called Occam's razor requirement[1] rather than characterizing a system in terms of its physical constraints, physical and biological parameters are often coupled.

Could it be possible to find a conceptual and a theoretical framework to systemic approaches that will avoid statements such as: "science is either physics or stamp collecting" (Rutherford, quoted by Westerhoff et al., 2009)? We will not attempt to answer this question. We will focus, instead, on the example of evolution, a process described by Gould (1996) as not completely governed by natural selection. According to him, neutral and random mutations occur at the lowest level (Kimura, 1968). At the highest level, massive extinctions are not due to adaptative struggles between individuals and/or species (Raup, 1994). Instead, massive extinctions result from accidental and catastrophic changes in environmental conditions. In contrast, the salient feature of life involves the stability of its bacterial mode, "physically constrained" from the starting point due to the chemistry of life and self-organization. Gould calls this symmetry breaking between simple physics and biology "the left wall of complexity" (1996). Gould's view emphasizes the tree of life with its maximum number of branches, and not the tiny right tail in the curve of evolution through a space of complexity. In other words, humans are just an accident and the bacterium the rule.

This paper will examine whether this description of evolution as the diffusion of biomass through a space of complexity could be fully explained by theoretical science by means of a new hypothesis positing that biological properties are nothing but extended physical ones, in the logical sense of the term (Bailly and Longo, 2008, 2009). This explanation is highly incompatible with the characterization of the natural world as essentially determined at the physical level. This view of evolution is founded on the use of a new observable: "anti-entropy", that constitutes an extension to classical statistical mechanics, where scales can be decoupled, and where "positive" and "negative" entropy are defined by the use of simple distributions of probabilities. Anti-entropy is analysed in a perspective partially inspired from the "principle of order by order" proposed by Schrödinger, and in connection with a new diffusion equation of biomass through a "space of complexity" that is neither a normal physical phase space, nor the abstract Hilbert's space of quantum mechanics (2009). This explanation leads to a simple mathematical reconstruction of Gould's complexity curve of biomass (1989). This view of evolution remains speculative; however, philosophy doesn't have to deal only with empirical statements or nomological propositions. In spite of the fact that "the space of complexity" is yet to be verified, it provides a new and exciting approach for a philosopher. Philosophy is not science, even if there is no scientific assumption that can be said to be philosophically free.

2. A problem coming from "what is life"?

As a starting point, we will use Schrödinger's informal and clever remarks as presented in his short text: What is life? (1944). On the one hand, he rejects the division between physics and biology and of a multilayered approach in natural sciences but, on the other, he strongly criticizes what he calls the "naïve approach of the physicist". Life is nothing alien to physics: "we must therefore not be discouraged by the difficulty of interpreting it by the ordinary laws of physics" (1944). However, life requires special attention.

First of all, statistic laws of physics and physical chemistry are inaccurate "within a probable relative error of the order of $1/\sqrt{n}$", if (n) is the number of molecules or of elements covered by the law. Thus, these laws apply only to very large populations of elements. After considering mitosis and meiosis mechanisms and crossing-over laws, Schrödinger assumes that the gene is nothing but a large molecule consisting of a rather short number of atoms. Delbrück's model concerning gene stability and mutations was not in contradiction with such an assumption. The final conclusion was that genes and gene actions are outside of ordinary statistic laws of physics, if not of quantum mechanics.

The Austrian physicist predicted that the remarkable stability of both genes and genetic recombination mechanisms require a specific chemical structure, i.e., an "aperiodic" one-dimensional crystal that conforms to the Heitler–London's forces. This was not a simple assertion founded on Delbruck's speculations; it must be understood as a physical assumption based on a theoretical distinction between the physics of gases and the chemistry of crystals. In a way, for Schrödinger, life is just a "clockwork", but with a "very big grain of salt" (1944). Indeed, a clockwork is not a simple mechanical phenomenon. He argued that the regular pace of the clock must be secured by a comparatively weak spring, "that overcomes the small disturbances by heat motion" (1944). Thus, the clock's motion actually obeys a non-linear dynamic and differential equation. However, a living system is not a mere clockwork. Something must be added in order to make it alive, to work and to function. The chromosomal crystal, if it exists, must contain in its aperiodic structure a "code script" that "under suitable conditions" controls the development of the organism "into a black cock or a speckled hen", as an "architect's plan and a builder's craft in one" (1944, p. 23).

It should be noted that Schrödinger didn't simply assume that a biological function was present in a physical structure, as Mayr (1961), Jacob (1970) or Monod (1970) did. Instead, he tried to provide the physical conditions that could explain its emergence. This approach led him to develop a special principle. Schrödinger argued that life cannot be explained by the mere use of negative entropy: "to put it briefly, we witness the event that existing order displays the power of maintaining itself and of producing orderly events" (1944, p. 82). Thus, the biological organization is not only maintained by "extracting order" from the environment, as a simple open thermodynamic system far from equilibrium. Organization and evolution are coming from nothing but "a stream of order" "governing atoms". This stream of order is not merely what Prigogine called later a "dissipative structure" (1979, 1989). Schrödinger did not have the conceptual equipment to formulate more explicitly this strange assumption. Let's simply draw a double conclusion. In Schrödinger's views the "principle of order by order" is a dynamical one. Life is not an association of atoms. Additionally, this "stream of order" is not fully explained by the natural selection principle.

3. Life as the diffusion of the biomass

Before examining what life is from Bailly–Longo's standpoint, we will introduce a preliminary remark. Current views on the origins of life assume that life had one or many historical origins, and it evolved from pre-existing non living physical systems. Thus, this view led to a research program to find the chemical and physical conditions that could explain the emergence of life. One way to address this question is to investigate how life started with prebiotic elements, passed to the step of functional molecules

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[1] Hypotheses should not be multiplied beyond necessity (Entia non sunt multiplicanda praeter necessitatem).