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The Complexity-based Explanatory Strategy, Biological Levels, and the Origin of Life[1]

Abstract

A long-standing debate on the causality of levels in biological explanations has divided philosophers into two camps. The reductionist camp insists on the causal primacy of lower, molecular levels, while the critics point out the inescapable shifting, reciprocity, and circularity of levels across biological explanations. We argue, however, that many explanations in biology do not exclusively draw their explanatory power from detailed insights into inter-level interactions; they predominantly require identifying the adequate levels of biological complexity to be explained. Moreover, the main explanatory strategies grounding both theoretical and experimental approaches to one of the central debates in contemporary biology, i.e., on the origin of life, are primarily and sometimes exclusively driven by issues concerning the levels of biochemical complexity, and these only subsequently frame more substantial and detailed accounts of inter-level biochemical interactions.

1. Introduction

1.1. Causal interactions, levels, and complexity in biological explanations

Based on their analysis of relevant cases across biology, a number of authors[2] [3] hold the view that detailed explanations of phenomena at various biological scales, including the molecular scale, do not unequivocally support the classical reductionist view of a fixed upwards hierarchy of causal powers and entities. Generally speaking, the more closely we probe the levels of life and the more detailed our explanations become, the less support we find for the reductionist approach. This is apparent in molecular processes, the explanations of which require causal reciprocity between the various levels of DNA bases, chromatin, proteins, and cellular structure to account for desired experimental outcomes and relevant phenomena.[4] Accordingly, biological entities are identified at multiple levels (organism, tissue, cells, and molecular networks) as causally relevant, and reductionism in its various forms is, at best, an account of practices in isolated biological contexts for specialized purposes.[5]

An alternative view wary of reductionism is that there is no coherent theory driving biology whatsoever; all we get are isolated practices to manipulate particular organisms and their properties.[6]

Thus, the *causal reciprocity*[7], *circularity*[8] and *shifting*[9] of levels are typical of explanations across biology - this includes the level of molecular properties relevant for living processes that reductionists have tried to deem causally basic. Put otherwise, the causal hierarchy in explanations of biological entities and their interactions is typically context-laden. And when such explanations are integrated, the various aspects of these explanations can causally parse,

prioritize, and order levels differently while jointly providing relevant insights.[10] This is revelatory of the incommensurability of complementary explanations, to paraphrase Wimsatt[11]. It is very hard to argue against this point, but even if it weren't, joining in this debate is not our main goal.

As a general anti-reductionist viewpoint has become prevalent in philosophy of biology, the real philosophical challenge is to provide an overarching and coherent account of biological explanations and inter-level interactions and entities that realize them, within a mechanistic[12] or instrumentalist paradigm[13] or within a particular understanding of causation[14]. Ontological and metaphysical implications are also of interest.

Yet orthogonal to the explanations proffered by the proponents of the two sides in the debate on reduction is a class of biological explanations set up in a way that does not rely on the details of inter-level causal relations and whose explanatory power is predicated on inter-level interactions playing a side role, or even no explanatory role whatsoever. A central focus of those developing such explanations is the level of complexity of biological entities[15], where the explanatory power and plausibility depend on identifying an adequate extent of complexity. We will now turn to such cases.

2. The complexity-based explanatory strategy in biology

When formulating explanations where the inter-level causal connections are not the main concern, it is crucial to identify the adequate level of complexity and only secondarily to identify or develop models of exact structures of inter-level interactions. Moreover, the level of complexity of entities rather than their causal status and causal powers primarily determines

whether they should be deemed the main building blocks of life on which explanatory power rests. We are interested in the nature of the justification characterizing this type of explanatory strategy. How much we can know in biology if we hold the explanatory aspect of inter-level causation to be secondary?

In fact, the complexity-based aspect of explanations is visible across various areas of biology. In metabolomics, for example, analysis has been guided by identifying structural features of metabolic processes[16]. The explanations identify these complex units, and only later do they fill in the details of interactions within them. In microbiological research, especially in the study of archea, superorganisms, not individual bacteria, are identified as the basic units of inheritance and metabolic processes because of the ubiquitous lateral gene transfer among the units[17]. The study of inheritance and metabolism is predicated on the choice of a level of complexity at which analysis will be undertaken. In genetics, discovery of cis-regulators has already extended genetic explanations beyond the identification of a specific kind of molecule to a wider biochemical context, while the discovery of metylation as a key regulatory mechanism, the role of chromatin in transcription, and the importance of interactions between the DNA-complex and protein make the choice of the right level of complexity as a framework for analysis paramount in genetics.

In some cases, however, the level of complexity becomes a central issue, not just an aspect (albeit important) of explanations. The explanatory power in such cases does not, nor can it depend on the details surrounding the inter-level interactions. Rather, it frames the way they are conceptualized. In what follows, we focus on the use of complexity-based explanatory strategies in a central issue in contemporary biology, the question of the origin of life. In this area, debate and inquiry are driven by the issues of the complexity of biological levels to a far

greater extent than in the cases mentioned above. As will quickly become apparent, the evidence used in various theories of the origin of life hangs on the issue of the proper characterization of the complexity of biological levels – only secondarily resting on detailed accounts of interactions across the levels.

The issue of the minimal complexity that characterizes life frames two main and opposed approaches to the question of the origin of life. The RNA-first theory postulates an ancient molecule similar to RNA as the first specialized molecule to perform the basic biological functions of biological control and inheritance. The other theory views life as a complex metabolic system whose origin can be traced to suitable biochemical processes which gather simpler organic molecules in a specific way. Both theories depend on the adequate identification of relevant levels of complexity (proteins, specialized molecules, their co-evolution, or gradually evolving molecular units). Problematically, one has to start by identifying the relevant level (or levels) based on very general and somewhat scarce insights into the level's inner biochemical workings, and only then suggest the details of the relevant biochemical interactions. In other words, the issue of inter-level interactions (of keen interest to those involved in the debate on reduction) becomes part of the picture at a later stage.

Moreover, the addition of the molecular and biochemical states to create the new level of complexity is not thermodynamically equivalent to the addition of the individual interactions carried out by individual entities. It may be implausible, thermodynamically speaking, to search for exact biochemical interactions as the mark of life before identifying the levels of complexity that may realize them. Even experiments addressing the origin of life start with dilemmas over complexity, while the questions of whether complexity, adaption, and biochemical control are

distributed across the biochemical network or localized in some basic elements are only subsequently addressed.

Although the molecules that seem to be the basic elements of living forms are ubiquitous, both theory and experiments must initially address a relentless march of complexity in evolution. Our characterization of life when inquiring about its origins requires a complexity-based explanatory strategy. In many ways, this is the primary question about life and figuring out the reduction dilemma that preoccupies philosophers will depend on it – insofar as our understanding of life goes. Thus, the relevance of explanations based on causal interactions across biological levels depends on what sort of complexity generates life and which levels are recognized as holding together in the first place. This sort of insight must be deepened with the knowledge of biochemical details, but they can be neither initiated by nor reduced to them.

3. The origin of life: biological levels and their complexity

The general approach to the question of the origin of life in biology has not been driven by the interaction-based aspects of life but has preceded it. This is also true of other, more refined questions stemming from the initial question posed by various, often contradictory, theories. Whether answers to such questions are satisfactory depends on how adequately we identify the level of complexity relevant for the phenomenon of life, as a certain level of complexity is indispensable for its origin. And this identification of relevant level of complexity only later frames inquiry into the details on a multitude of interactions across biological levels and their fine structure. What we think of living forms in terms of their complexity will imply the kind of

interactions we seek to account for them and their origin. Thus, one way or another, we start with interaction-neutral questions on biological entities and their structure.

This methodological framework escapes the reductionist-minded philosophical accounts of biology: it stands in stark contrast to the kinds of explanations that reductionists put at the forefront of their accounts of biology wherein analysis of molecular properties and processes is deemed explanatorily basic. In a nutshell, whether we think that the search for the origin of life is a search for a particular specialized molecule or for particular chemical environments and chemical networks, the issue of the complexity of levels necessarily frames the debate and the kind of biochemical stories that will be supplied by either side.

4. Theories of the origin of life and its complexity

4.1 The RNA-first theory of the origin of life and the complexity of life

This section looks at two major theories of the origin of life, the RNA-first and metabolism-first theories. The former was devised to pin down a specialized molecule that marked the beginning of life and the latter to discover the biochemical environment that started life.

The RNA-first theory of life suggests a molecule similar to RNA was the first specialized molecule to perform the basic biological functions.[18] Its further evolution by natural selection produced more complex life. This theory deals successfully with the challenge of explaining two crucial marks of life as it currently exists: 1) the evolution of enzymes that catalyze living processes, and 2) the unit of heredity, its structure and mechanisms[19]. The complex network of

enzymes evolved from the RNA-like molecule, the argument goes, and DNA is only an end result of the evolution of a primordial hereditary unit.

It is obvious that the exposition of the RNA-first theory of the origin of life depends on a fairly detailed explanation of the interactions of the specialized molecule that enabled it to perform the double biological function in the first place while also enabling the evolution of other molecules. The epistemic status of this dependence is nowhere near the explanations of interactions in molecular biology that would make it a show-case for the reductionist insistence on the primacy of molecular interactions, despite the possible reductionist motivations of the creators of the theory.

There is a starting and motivating assumption, albeit reticent and semi-explicit, of minimal complexity characterizing life in the form of a specialized molecule which can perform key biological functions that we see today.[20] Thus, the chosen level of complexity is confined to the molecules that can self-replicate without proteins. Such a specialized molecule is chosen as the biochemical complex starting life as we know it, and RNA happens to fit the bill. The actual RNA properties provide adequate support, at least initially, for a general level of the theory. In fact, the claim is that something similar to RNA, not necessarily the exact molecule of RNA we see today, emerged. Whether it represented an appropriate level of complexity is another question, but the specialized-molecule-first theory inevitably starts with the choice of a complexity level it deems adequate. This choice is based on a very general idea of the details of relevant biochemical mechanisms – an exciting but tenuous analogy – with the RNA mechanisms isolated from DNA and the rest of our biochemical machinery. In effect, the first step is taken before the biochemical details are filled in.

The critique of the theory stems from the epistemic (methodological and conceptual) primacy of the issue of the adequate (plausible and probable) level of chemical complexity of early forms of life, given the structure of RNA-like molecular processes. In fact, the plausibility of the RNA-first theory hangs on the structure of the former, rather than on the details of a suitable molecular structure. Thus, although the structure of the postulated RNA-like molecule is less complex than that of the DNA molecule, it is too complex to be simply and *ad hoc* deemed the first step in the evolution of life, the step that by virtue of its primacy does not require inquiry further in the past. The molecular constituents of RNA are monomers assembled into more complex polymers. These entities and the processes characterizing them and their formation are already complex and life-like (in terms of self-replication) and thus require substantial explanation if they are to be the first step in the formation of the RNA-like molecule. This requirement is not a nagging appeal to go ever further back in the history of life to find a plausible scenario for the formation of what may be the first functioning living unit. Rather, it exposes the following crucial problem with the initial RNA-first suggestion: « As a random event without a highly structured chemical context, this sequence has a forbiddingly low probability and the process lacks a plausible chemical explanation, despite considerable effort to supply one » [21]. In fact, the realization that the stages preceding the formation of RNA or an RNA-like molecule are integral to the explanation of the origin of life was raised early on by those who thought RNA was one of the first stages of the emergence of life.[22]

Identification of the nature of complexity of life prior to the RNA-first phase, if there was such a phase, has to be an integral part of the theory and must be characterized in biochemical terms. The theory's plausibility hangs on identifying and accounting for relevant levels of complexity. Postulating the solutions within the RNA-first framework without addressing this

more general question does not provide the full or perhaps even the main part of the answer. Thus, concerns about complexity frame the issue, leading to divergent theoretical and experimental approaches and arguments.

4.2 The biochemical context and the context of the cell

The idea that living forms generate their own environment was first articulated by Varela and Maturana[23]. They argued that the *autopoietic* aspect of life is as important as units of inheritance and the function of enzymes. Thus, for instance, the evolution of the cell cannot be properly understood if we do not take into account that metabolic processes constantly arrange an immediate and an ever more extended environment in a way that benefits the cell. This on its own suggests that the origin of life must be a quest for autopoietic biochemical environments, not simply a search for a particular kind of molecule. Life is a system of particular complexity, and its origin should be explained accordingly by identifying suitable candidate chemical processes which can con-join suitable organic molecules in a suitably complex way. The guiding idea is to identify the basic level or levels of the complex biochemical environments characterizing life and fill in the biochemical details of origin accordingly.

Following this lead, the metabolism-first theory of the origin of life suggests metabolic processes encapsulated in a protomembrane could have occurred in porous rocks close to the volcanic vents at the bottom of the ocean.[24] Such places provided needed energy, deposits of organic gels filled with suitable organic molecules in rocks, and a metabolic network where interactions and selection could take place. This type of network could generate its own constituents – the core characteristic of a living system. Natural selection then refined this

recursive network by favouring particular chemical pathways. Such self-catalytic processes occurring in initial metabolic networks are now well known and well studied in organic chemistry and are always extended to be a part of a larger biochemical context: « Even in deep core of metabolism … we do not see the cycle in isolation » [25].

This approach views the inter-level interactions and the chemical pathways as framed by two structural features of metabolic networks, namely, chemical self-catalysis and recursion. Thus, we are seeking a proto-metabolic system when we are looking for the initial seat of life, i.e. a specific chemical network that could favourably join organic molecules, rather than a particular fairly complex kind of a molecule, the kind assumed in the early version of the RNA-first theory to randomly pop up from unidentified chemical processes. The initial living system emerges as a complex unit, whose complexity is enabled by more or less regular chemical processes of autocatalysis in certain chemical systems. This particular level and kind of complexity is identified as the mark of life.

4.3 Conclusion

The initial general task of explaining the emergence of the complex molecules that characterize life is inevitably tied to the notion of adequate biochemical complexity. The story of interactions should fill in the details but *the initial explanatory target is the jump in biochemical complexity characterizing the emergence of life* that can be explained in numerous ways, e.g. with the RNA-first sort of theory or with the metabolism-first theory. Identifying the right level (or levels) of complexity that characterizes the emergence of life hangs over any attempt to explain the origin of life at the level of detailed molecular interactions. This exposes the weakness in early

instances of the RNA-first theory, a weakness addressed theoretically and experimentally by both the proponents and the critics of the theory. Based on the available knowledge of biochemistry, today's life biologists opt for different and often opposed levels of complexity at which life emerged, all developing ideas that substantiate the biochemical details within their proposed framework. But explanations in terms of biochemical details can go only so far in explaining the origin of life, especially if they espouse a narrow level of biochemical complexity. For example, the early RNA-first theory was confined to a single stage, the origin of which required further explanation.

Thus, we inevitably start by choosing a level of complexity, or a stratification of complexity, that our theory will address, i.e., a level deemed relevant, and go on to provide general reasons for its selection. Is it the level of proteins, the specialized molecules emerging initially without proteins, the co-evolution of the two, or the level of more basic molecular units that evolved in a way that conjoined a number of processes? When we consider such options, we realize that the knowledge of detailed interactions is scarce. Yet such considerations are the groundwork for the more detailed biochemical models and experimental approaches. They are, in fact, hypotheses to be probed. They concern not only the right level of complexity but also the nature of complexity: whether we want the level of substantial metabolism with diverse elements or specialized molecules constituting a "thin" metabolic system.

5. Thermodynamics and the complexity of life

We can go even deeper and ask a question about the proper level of complexity of living forms in terms of thermodynamic processes. How does life emerge, thermodynamically speaking, and

what does this tell us about the nature of its complexity and interactions across biological levels? In very general terms, then, « what is needed … is an extension of ordinary thermodynamics so that it can apply to systems maintained far from equilibrium by the flow of energy »[26].

In a thermodynamic system, we are trying to understand, based on the available assumptions, the statistical mechanical prediction of the next most probable state in the development of the system, i.e., the one with the maximum entropy that the system will produce.[27] The so-called maximum-entropy distribution includes all possible combinations of those states not excluded by the information about the system we have at the time. Every other outcome that decreases entropy will necessarily be biased. This is true of thermodynamic systems and their configuration of individual states. But it is also true of systems that involve currents, whether physical or biophysical, as the maximum-entropy principle is consistent with the feedback mechanisms that produce currents in biochemical systems.[28] Thus, the system will develop towards the state of maximum-entropy carrying along, as it were, the current flows that characterize it.

In practical terms, this means the occurrence of metabolic systems characterized by feedback thermodynamic cycles is exactly what we would expect in the course of the evolution of complex organic systems on the earth, and, thus, it is exactly what we should seek as a mark of life. It is, in fact, a thermodynamic mark of life. A reductive citric acid cycling is one example; it characterizes the biochemistry of living systems and, as such, has been examined in detail.[29] More generally put, metabolism is a basic structural feature of ecosystems, but the realization of these structures is achieved by different biochemical processes which are essentially ordinary thermodynamic systems, the existence of which accords with the predictions of maximum-entropy distribution. Such a specific complexity of living forms as a consequence

of thermodynamic properties is the level which should be the target of the search for the origin of life.

There are certainly limitations to this approach. An analysis in terms of thermodynamics is fairly abstract and often too tenuously connected to the living systems when they are examined experimentally. At a minimum, however, we can conclude that how states add up to create a new level of complexity is, thermodynamically speaking, not equivalent to simply parsing them into individual interactions and entities in isolation from the context to achieve certain purposes, as in molecular biology. Indeed, it may be impossible to avoid identifying the levels of complexity as the mark of life prior to the search for the exact biochemical interactions that may realize them, irrespective of whether or not we subscribe to the specialized-molecule-first or metabolism first account.

6. The basic assumptions in the experimental approaches to the origin of life

What about the experimental side of the question on the origin of life? Aren't experiments predicated on the understanding of particular interactions to start with and doesn't the issue of complexity inevitably retreat into the background once the experimental work begins?

Experiments differ to a great extent in their justification and their assessment of the biochemical plausibility of the questions they address. Thus, a number of experiments[30] motivated by the RNA-first theory aim to provide a particular mechanism of control and kind of molecule that can perform postulated functions. Their daunting task is to proffer a plausible chemical explanation of the occurrence of the already complex RNA-like molecule. These experiments are really responding to the aforementioned challenge of the critics who say such a

specialized molecule is so complex that the approach to it must supply a plausible chemical story of its origin. Thus, the issue they address is a particular level of complexity, specifically the functional and chemical complexity of an RNA-like molecule. In that sense, the concern about complexity is the basic methodological framework, framing the search for relevant biochemical interactions in experiments addressing the RNA-first theory. The debate itself, irrespective of who wins or loses, is conceptually and methodologically guided by such a framework. This is even more obvious in the experiments motivated by the theory of life originating at the ocean vents; it even appears in the early experiments addressing the origin of life.

The experiments that test the processes deemed relevant by the metabolism-first theory look into the chemical processes responsible for the coding mechanisms.[31] They are based on the presupposition that such mechanisms can be a result of an entire molecular network with a number of intermediaries, rather than a specialized molecule such as RNA: « In this experimental setting, networks of small and randomly synthesized amino acids and single RNA units aid each others' formation, assembly into strings and evolution of catalytic capacity. Both types of molecules grow long together »[32]. Again, the parsing of the relevant biochemistry is led by the issue of complexity of levels, not by concerns about immediate chemical interactions across levels. In fact, « [c]omplexity, adaptation and control are distributed in such networks, rather than concentrated in one molecular species or reaction type »[33].

Even the Urey-Miller experimental design, the first in a string of experiments addressing the origin of life, was an exercise in the emergence of complexity, only later seeking detailed accounts of interactions. It intended to identify potentially basic (inorganic) and complex (amino-acids) building blocks and determine whether the former could emerge from the latter. Whether complexity, adaptation, and control are distributed across the biochemical network at

each particular stage or localized in some basic elements is really neutral to the question addressed by the original experiment.

7. How simple can the basic level of life be?

The molecules that seem to be the basic elements of living forms are ubiquitous. But this fact on its own may be neither an answer to any of the questions on the origin of life, nor very informative in that respect. It simply tells us that such a molecular level of complexity may not be sufficient to explain the origin of life despite the attempts to identify the molecule that can perform the basic living functions in the RNA-first theories. The relentless march of complexity in evolution, probably a gradual process of many smaller transitions[34] is a phenomenon that must be addressed. The question that cannot be bypassed by this or any other theory is how likely it is that such molecules will assemble into a kind of complex system that characterizes living forms. Life begins when a certain level of complexity is reached, and the key question is what sort of level it is. Hence, explaining the origin of life requires a complexity-based explanatory strategy.

Life can be sorted out by the extent of complexity, starting with the gathering of crystals into polymers. Alternatively, we might try to identify various levels of the basic unit of life, the cell, in terms of their complexity. One suggestion is to characterize the stages in the complexity of cells as the formation of the ur-cell, proto-cell and the living cells that exist currently. The quantitative measure of complexity will understandably vary from one issue in biology to another and from one area of biology to another. But could there be a general criterion of complexity in biology? Some biologists (Maynard-Smith & Szathmary 1997) are skeptical of addressing complexity in a precise manner. Yet as we have seen, we cannot really start asking

questions about the origin of life without dwelling on the nature of complexity, so it is worthwhile investigating various ideas of measuring complexity. In general, the number of parts may be a good provisional measure across biology,[35] and computer simulations[36] can go a long way to determining the relevant parameters. This groundwork may yet pave the way for a satisfying account of the origin of life.

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Notes

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[2] Wimsatt 2000, 2007; Kitcher 1984, Dupre 1995, 2012; Thompson 2007; Perović & Miquel 2011.

[3] See Perović (2014) for a detailed summary of some of these accounts and arguments.

[4] See: Lesne 2007, 2008; Hüttemann & Love 2011; Perović & Miquel 2011; Wimsatt 2000, 2007.

[5] Hüttemann & Love 2011.

[6] Waters 2004.

[7] Perović & Miquel 2011.

[8] Thompson 2007.

[9] Wimsatt 2000.

[10] Perović 2014; Wimsatt 2007.

[11] Wimsatt 2007: 163.

[12] Machamer, Darden, & Craver 2000.

[13] Waters 2004.

[14] Woodward 2010.

[15] We defined this issue previously in terms of heterogeneity and homogeneity of entities.

[16] Mashego et al. 2007.

[17] Dupré & O'Malley 2007; Wilson & Sober 1989.

[18] Orgel & Crick 1993; Orgel 1986.

[19] Pace & Marsh 1985; Cech 1985.

[20] Orgel 1986.

[21] Trefil, Morowitz, & Smith 2009, online edition (available at https://www.americanscientist.org/article/the-origin-of-life).

[22] Orgel 1986: 146.

[23] Varela and Maturana 1991.

[24] Trefil, Morowitz, & Smith 2009, online edition.

[25] Ibide.

[26] Ibide.

[27] Jaynes 1957.

[28] Morowitz & Smith 2007.

[29] Ibide; Russell & Hall 1997.

[30] Powner, Gerland & Sutherland 2009; Hanczyc, Fujikawa, & Szostak 2003.

[31] Russell & Hall 1997.

[32] Trefil, Morowitz, & Smith 2009.

[33] Ibide.

[34] Maynard-Smith & Szathmary 1997.

[35] Stuart Kauffman kindly suggested this to the author in an elaborate form that will be developed in a different paper.

[36] See www.biota.org.