On the feasibility of a nonadaptive–nonsequential abiogenesis. An alternative to the Oparin-Haldane model

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Abstract

The emergence of life from non-living matter remains one of the most profound unresolved questions in natural philosophy. The Oparin-Haldane model assumes a gradualist evolution, where adaptive precursors are obligated. Yet, for more than a century, all experimental efforts have failed to achieve abiogenesis. May it be that this view is paradoxical in explaining how living matter arises without preexisting coordinated and complex structures, since these are assumed to be already the product of selection well before living forms could control inheritability. In Oparin-Haldane's model, adaptive changes in molecules are largely decoupled from abiogenesis. Here, instead, I elaborate on the possibility of a nonadaptive-nonsequential model, in which life-grade complexity emerges spontaneously, ungoverned by natural selection, through contingent coalescence under excess capabilities. The Price equation, as a mathematical tool, can help assisting our thinking on the evolvability of selection itself. Selection is best understood as the non-null covariance between a trait value and its fitness, a quantity that itself evolves. Prior to abiogenesis, this covariance should be effectively zero, then selection begins to govern the number of feasible interactions among the primaeval components. By releasing abiogenesis from gradualist idealisations, this model may provide a new theoretical foundation for interrogating life's origins.

Keywords: origins of life, nonadaptive abiogenesis, dissipative structures, Price equation, molecular bricolage, Oparin-Haldane hypothesis, gradualism, evolutionism, spontaneity

Introduction

Two opposed philosophical views have tried to give answer to the problematic of the origins of life. For a detailed account on the historical confrontation among vitalistic and materialistic arguments on the feasibility of this mysterious phenomenon (life emerging from inert matter), I suggest the first chapters of Oparin's *Origins of Life on the Earth* [1]. This is not an exhaustive review either. Instead, the purpose of this brief piece is to give, I hope, a new perspective on why all our efforts to observe a material abiogenesis have failed to this day, and what might be an alternative way forward to pose this never-ending question to nature.

L. Pasteur first demonstrated that *generatio aequivoca*, or spontaneus generation of life, was impossible *de facto* – reproduction of living matter required an "egg" with instructions [2–5]. After some intense debate, the experiments were certainly replicated, and the question solved [6]. The "*omnis cellula e cellula*" by R.L.C. Virchow [7] rendered a new meaning, and remained as a paradigmatic principle of biological reproduction (or the "*inmortality of the protoplasm*" [8]) until our days. However, although Pasteur's discovery filled an important gap in knowledge, an intriguing question emerged: whence do living things arise, if not from inert matter? [9, 10]

Besides a subtle margin for vitalistic responses –*à la* "life is eternal" [11]–, many experimentalists in that era confronted the question seriously. The general materialist answer was that evolutionism, not spontaneity, led to abiogenesis [4, 8, 12–15]. They believed that only a gradual chemical evolution could explain this apparent decrease of entropy, or the gradual accumulation of information of an isolated system [16–18]. In the words of A.I. Oparin: "(...) *these polymers, which were already capable of forming poly-molecular systems, were, of course, simpler than living protoplasm. Only later, due to the prolonged evolution of these systems, their interaction with the environment, and natural selection, did the types of organization that characterize living beings appear.*" [14], pg. 230. It is further argued that the "*the substances that we produce artificially are not exactly the ones which can be isolated from living organisms*, reasoning that "*if such substances were formed now in some place on Earth, (...) they would be eaten, one after another*" [19]. J.B.S. Haldane shared a similar view [16, 20], and, taken together, these reasonable speculations were the best explanation available at the time.

Here I argue, however, that this generalised response reflected a false dichotomy, i.e. spontaneous emergence of life could not be accepted as a valid materialist explanation. This was probably due to a reluctance toward the semantics of "spontaneity" [4]. In addition, I argue that this historical contingency profoundly impacted every theoretical (e.g. the Oparin-Haldane hypothesis [16, 21, 22]) and experimental (see the below section) attempt to tackle the question. Hence, we are nowhere close to replicate abiogenesis. This standard abiogenesis model requires the chemical compounds to evolve sequentially, with *necessary* steps inferred from modern-day biology (which led to the recurrent and confusing debate on "who–first" [23–28]).

Could we do better with alternative models to help new experiments shed light on this unsolved, yet fundamental problem? In this piece, I show how we could better trace the appearance of life in any given system using a formalism derived of the Price equation, just by changing this adaptive–sequential model of abiogenesis to a nonadaptive–nonsequential. This is possible since, in the latter model, selection starts to be controlled when an alive system arises, not before, contrary to the classical model.

No abiogenesis yet?

Before detailing a potential new course of action, I will further justify the need for it by examining the main achievements and failures of prebiotic chemistry and synthetic biology, which are the two main fields attempting to give a mechanistic answer to a material abiogenesis.

The famous triumphs in this regard are found on the side of prebiotic chemistry. If we keep the watchmaker's traditional metaphor, these would correspond to alchemists trying to exactly reproduce the gears and other small parts of this rare clock (i.e. life). The most celebrated are undoubtedly the Miller-Urey experiments. They demonstrated that sudden changes of potential in a recreated Earth's prebiotic environment can produce amino acids within a brownish organic solution with acquired complexity [29]. Many more related experiments have been conducted, for example, to form nucleobases [30]. However, the production of some well-known parts of the clock does not grant us any new knowledge on how to build it, provided that the prebiotic conditions are correctly assessed [31]. These same arguments extend to the other classic experimentalists, like J. Oró (purines from hydrogen cyanide [32]), or C. Ponamperuma (adenine synthesis and Urey-Miller extensions [33]). After these initial excitements, efforts in this field have moved in multiple directions, providing many solutions to produce interesting chemicals, but, unfortunately, unsuccessful in generating abiogenic reactions [34–43]. This may be partly due to the prevailing framework, in which abiogenesis is not expected to occur in a short period of time, but rather through a slow adaptive evolution lasting millions of years, involving molecules that are not possible to generate in the current biosphere [19]. As a result, attempts to observe an abiogenic reaction from inert materials in a laboratory setting are often met with pessimism [44].

What if we just search for the parts of the clock that produce its characteristic "tic-tac"? Abiogenesis is often conceptualised as a slow generation of first replicators. We generally acknowledge that the first replicator was probably a RNA autocatalyst, maybe similar to a ribozyme [45, 46]. In a nutshell, the hypothesis is that a ferric impactor led to a reduced environment in which RNA could be formed on a proper geological time [47]. We indeed achieved RNA oligomerisation catalysed by olivine in reduced, alkaline environments [48], but self-reproduction of RNA is still not achieved without human engineering [49–51]. However, we know that replicators of other nature are possible [52], although the ability to storage substantial information on them is absent, so that variability in offspring chemical populations is contingent on kinetics [53], as aperiodic crystals growing. In fact, these are *trivial* replicators, since their information cannot change the character value in which it is encoded [54, 55]. To this day, all efforts to arrange a sequential chemical evolution leading to the emergence of life have failed.

Now a brief note on synthetic biologists, that would rather be proper watchmakers, or better said, engineers who dissect and try to recreate the clock's "tic-tac" by understanding the relationship among the elements of the most sophisticated *rolex*, or modern-day life. That the construction of a synthetic life can ultimately lead to a natural answer is debatable [56], but it might, in theory, generate new knowledge about the necessary biological interactions and functions, without assuming certain prebiotic conditions. Maybe, if we understand a cell better, we could improve our definition of life to search for its emergence [57]. Unfortunately, the obtained knowledge is more related to the maintenance and stability of modern-day cells [58]. The questions quickly morphed into "how many functions we can alter or delete from this modern cell without compromising its long term viability?", although there are some exceptions [59]. However, we are left with models like the "minimal cell" [60–62], way too much complex to be accounted for the question of abiogenesis [63].

Finally, the following questions are frequently confounded in published literature: (i) how

life emerges (in general), and (ii) historical origins of life on Earth. While (ii) is contingent to the local chemistry and the historical events (impactors, change in orbit, etc.), (i) should be addressed with general principles. General principles that would be dependent on an observational or empirical definition of life. However, they should be attainable theoretically, and, by definition, experimentally.

This piece is focused on question (i). While question (ii) is interesting, it is more related to a "molecular paleontology", or the historical record of evolution on Earth. Scientists working on question (i) are more intrigued on how inert matter can, all of a sudden, behave as living matter (in any given condition). But the latter has nothing to do with the abiogenesis model of preference, as the inert-living interface is also a problem found in the Oparin-Haldane view.

Here it is provided what I believe a novel synthesis towards the resolution of problem (i). As I am more certain that, at least, this proposal is still to be experimentally contested, I wanted to elaborate on some principia towards the design of future experiments.

Evolvability of the trait-fitness covariates

Part of the difficulty in answering this question may lurk in the fact that we have not clearly defined what we are looking for. The watchmaker's view on abiogenesis requires selection in the first steps of living "purpose" (rupture of symmetries, like enrichment of L-molecules in the amino acid pool), to surpass the imposed threshold of chance. That is usually the argument since selection is the only distinctive feature of living matter that we know of that can govern over such an unfeasible thermodynamic fate, which regime of possibility is determined by a Boltzmann distribution that includes both state functions, energy and entropy [17, 64, 65].

An interpretation of the latter is that the amount of selection should be fairly high and constant at any time during biological evolution, including first gradualist reactions – as depicted by Oparin and Haldane, by many works [28, 66], and even in divulgation, for example, in the third chapter of Dawkins' *Selfish Gene* [67]. But, an intriguing question that remains fairly unexplored is: how selection itself has evolved? Does it make sense to think in adaptive terms in the advent of biological evolution itself? To help our thinking, we could make use of the Price equation to establish a new model in which selection is zero before the emergence of life [68]. The Price equation [69] is often expressed as

$$\Delta\bar{z} = \mathrm{Cov}(w, z) + \mathbb{E}(w\Delta z') \tag{1}$$

Where $\Delta\bar{z}$ is the change in the average value of the trait z across generations and can be approximated with the sum of two terms. The first term, $\mathrm{Cov}(w, z)$, is just the covariance between fitness w, and the trait value z, representing the effect of natural selection (i.e. memory of traits that worked better/worse). The second, $\mathbb{E}(w\Delta z')$, is the expected value of the within-group changes in the trait z, and it is weighted by fitness w to impact the number of descendants on the next generation. This reflect neutral variation. Although eq. (1) is commonly used to assess selection among conflicting organizational levels [70], it provides a simple mathematical description of any adaptive population, and is therefore most suitable to help a hypothesis on the origins of natural selection. However, these equations are just correlative (not causal). A more proper way to causally isolate the selection would be to remove the influence of fitness w from the second term [68],

$$\Delta\bar{z} = \mathrm{Cov}\left(\frac{w}{\bar{w}}, z'\right) + \bar{\delta} \tag{2}$$

Where the first term is now the covariance between the relative fitness and a given trait, and $\bar{\delta}$ is the average transmission bias. Although this equation is still just a mathematical tool, it helps to trace, quantitatively, the infinitesimal appearance of the selection, that is, the inheritability of the trait's value fitness,

$$\lim_{t \to t_1^+} \mathrm{Cov}\left(\frac{w}{\bar{w}}, z'\right) > 0, \quad \text{where } t_1 \text{ is the first occurrence of selection} \tag{3}$$

However, spontaneous rupture of chemical symmetries could fulfil the condition of eq. (3) [52, 71]. As fixing a threshold for "life" is inherently subjective, and this is a problem when defining the origins of it, we first need to extract a quantitative property which is probably unique to life; one that is shared from the first to the last consensually recognized organism. Let this shared property be not merely the inheritability of a trait, but the *control* over this information-enrichment process, so that living systems keep optimizing the amount of selection until equilibrium. The latter is axiomatic, yet justified since every living being observed uses a channel for the inheritance of its traits. It is, thus, an empirical definition of life. Here, the total accumulated change in the covariance between fitness w and a trait z remains finite over time

$$\int_{t_1}^{\infty} \left| \frac{d}{dt} \mathrm{Cov}\left(\frac{w}{\bar{w}}, z'\right) \right| dt < \infty$$

This implies that the rate of change of covariance decays as time approaches infinite, where the trait will be –theoretically– perfectly fitted to an invariant context. We do not need to assume any function for the evolution of selection, so we can introduce the limit with an equilibrium value W such that

$$\int_{t_1}^{\infty} \left| \frac{d}{dt} \mathrm{Cov}\left(\frac{w}{\bar{w}}, z'\right) \right| dt < \infty, \quad \text{with} \quad \lim_{t \to \infty} \mathrm{Cov}\left(\frac{w}{\bar{w}}, z'\right) = W, \quad W > 0 \tag{4}$$

Where W represents the maximum optimal value for the covariance between a given trait and its associated fitness for an invariant context. However, such equilibrium remains unattainable in practice, as the context to which they must adapt remains in perpetual change. Consider a catastrophic perturbation, where the continuity of selection is impossible (ie. life's extinction due to meteorite impact). One may interpret the trait's value extinction ($\Delta\bar{z}$) as an infinite decrease in fitness (w). Thus, W is a perturbable theoretical fitness goal, and this perturbation is extricated from the variability on transmission bias ($\bar{\delta}$)

Conceptually this is a clear epistemic rule to search for: a point in time at which eq. (4) first holds, but still continues to hold for all subsequent moments in any given chemical system, provided the integrity of the living system is maintained ($W > 0$). Should W fall to zero and remain so in a given system, the statistical trace of prior selection would disappear entirely. In Table 1, a simple syllogism with these premises is proposed to account for the emergence and evolvability of natural selection.

	logical value
premise 1	$\mathrm{Cov}\left(\frac{w}{\bar{w}}, z'\right)$ is ≈0 and uncontrolled in abiotic systems
premise 2	$\mathrm{Cov}\left(\frac{w}{\bar{w}}, z'\right)$ in current organisms tends to equilibrium (W)
conclusion	$\mathrm{Cov}\left(\frac{w}{\bar{w}}, z'\right)$ changed from ≈0 (abiogenesis) to W

Table 1: Syllogism of null selection. The syllogism may be reversed for the transmission bias ($\bar{\delta}$), which interpretation is that trait inheritability (or fidelity copy) had a maximum noise value prior to the origins of life.

In practice, however, hinting the first instance of selection (eq. 3) could be an extremely difficult task, because many relative measures (e.g. fitness) are hard to quantify. Instead, the channel for inheritance that allows the approximation to W is not defined yet, and can be a much easier proxy for increasing selection. A way to determine wherever this channel is enabled is estimating the regression slope h between parental character value z and its offspring z', which is the standard measure of heritability in quantitative genetics, is defined as

$$h = \frac{\mathrm{Cov}(z', z)}{\mathrm{Var}(z)}, \tag{5}$$

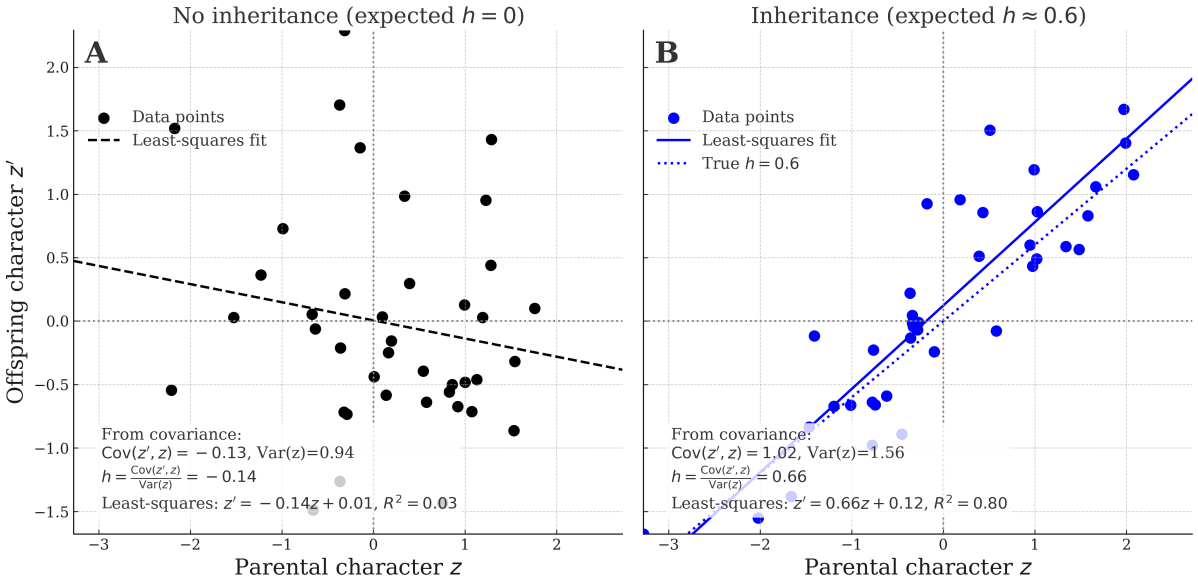

Figure 1: Two mock examples where h values indicate the expected behavior within an inert (A) and a living (B) system. Both examples consist of a population of parental character values (z), and a population of offspring character values (z'). In (A), effective covariance between z and z' is 0, because negative inheritance does not retain a biological sense. This is expected in prebiotic processes, since they are not controlled by the living machinery. In (B), parental trait z predicts trait z' in the offspring. Variance in z and z' (variability in the information transmission) can be caused either by transmission bias δ or by changes in relative fitness $w/\bar{w}$.

and captures whether offspring traits z' statistically resemble parental traits z. This definition does not involve fitness w directly, but rather formalizes the existence, and the reliability, of the inheritance channel for the examined character. In contrast, the causal form of the Price equation (eq. 2) isolates the effect of selection as the alignment between relative fitness and offspring traits. Thus, when $\bar{h}$ is higher than 0 (eq. 5), it is allowing for offspring traits z' to have statistical memory of the parental traits z. This in turn makes it possible for z' to covary with relative fitness in the causal form of the Price equation (eq. 2), thereby establishing the first conditions under which natural selection can operate (Table 1). On the other hand, when $\bar{h} = 0$, the system does not have any statistical memory, and thus inheritance is forbidden. An example is shown in Figure 1.

Thus we expect an increase in h distributions over time, in which inheritability beings to be further controlled by the incipient living form, as populations begins to purify unfaithful replication of traits. Figure 2 shows two mock distributions of h for the above example regressions. Nevertheless, that z' is more or less invariant to z does not give us any direct insight about the fitness of z', nor its selective coefficient, because changes in average h can

be also due to transmission bias δ besides to fitness changes. To test whether transmission bias is affecting h fluctuations, the environment of the interrogated chemical system should suffer a change, and be controlled by an experiment in which environment does not change. The expected deviance on h caused by transmission bias δ will be exposed by the control experiment, and be different than that caused by the loss-of-fitness Δw, that will be exposed by particular environmental changes.

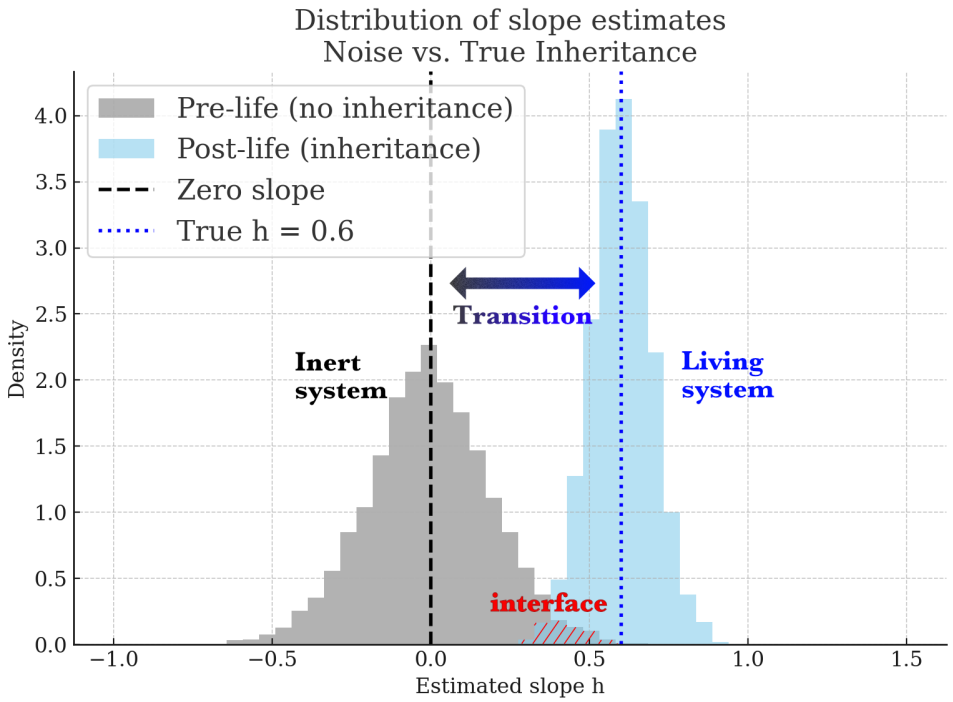

Figure 2: Mock h distributions for the examples shown in Figure 1. Values are just for illustration purposes and they do not retain biological significance. Interface regions where h values could be part of both distributions may exist. In this way, it is shown that the Price equation can be a good mathematical tool to trace abiogenic products, assuming that abiogenesis requires no prior adaptive selection of molecules.

Another way to put it is that, in a purely inert system (e.g. a prebiotic environment), any fluctuation in $\bar{h}$ can only come from transmission bias δ (chemical instability, symmetry ruptures, unexpected disruptive events, etc.).

Coupling of adaptive selection and abiogenesis

Another major difference is found when comparing the nonadaptive–nonsequential and the adaptive–sequential models. In the Oparin–Haldane's view, the emergence of selection and the emergence of life remains uncoupled in time. Oparin clearly stated that adaptive selection occurred in non-living molecules, but also that the first "living thing" is not a poly-molecule, but an slime: "*with certain reservations we can even consider that piece of organic slime (...) as being the first organism*" [19]. J.B.S. Haldane, contrary to A. I. Oparin, recognised that "*the first living, or half-living things were probably large molecules synthesised under the sun's radiation*" [20]. This is an important discrepancy [72] that has been largely neglected in posterior literature. However, Haldane also acknowledged: "*clearly we are in doubt as the proper criterion to life*" [20].

For the sake of clarity, we can consider this classical scenario depicted by both scientists, and imagined by many [28]. A pool of compounds, of distinct nature and stages of aggregation, populate an ocean sterile of life. The pace and causes for the compounds to aggregate are uncertain.

In an adaptive-sequential model (Oparin-Haldane), molecules would suffer selection when, over time, certain molecules are slowly formed prevalently over others. That is to say, they are suffering adaptive selection, without being considered life forms. Under this model, the trick of tracing the trait-fitness covariance won't be useful to hint abiogenic reactions, since adaptive changes are expected within non-living compounds.

However, at the time of elaboration of the Oparin-Haldane narrative, neutral forces of evolution were largely neglected, maybe with exception of the Fisher-Wright models in population genetics [73, 74]. Now, we do acknowledge that a substantial portion from the vast amount of variation found in the largely purified genomes of today, is due to random sampling processes, not adaptation [75, 76]. It is sensible to think that the generation of variability in non-living compounds, which are not purified, was not directed by any adaptive forces (memory of traits that worked better, or eq. 4), because there were, by definition, no available channels of inheritance to allow for selection (eq. 5, Figs. 1& 2). That is to say, variability in the pool of compounds will be determined, contingently, by the local chemistry and the events disturbing that chemistry. This concept is very similar to Prigogine's *historical element* [17], in which the past states of molecules determine their present state, acquiring a probabilistic, or historical character. Thus, under the nonadaptive–nonsequential model, the first occurrence of selection occurs at the time of the first abiogenic reaction (or the origin of life), but this is forbidden in an adaptive–sequential model.

The latter, however, it is just a description and does not say anything about the validity of the models. However, Oparin–Haldane reactions will remain untraceable, unless defined by other feature that is shared by all known life forms (empirically), obviously besides the maintenance of adaptive selection.

The problem of spontaneous complexity

A problem, in appearance, with the above is, how the emergence of life-grade complexity can be attained in absence of selection? Could teleonomic principles be acquired by chance, all of a sudden? [77]. The history of this issue is indeed tortuous [78]. Instead, I invite the reader to think of that characteristic annoying tangle of wires and cords occurring with any vintage computer hardware. This process, surely, occurs due to the remarkable probability for the disordered state to exist, without precluding any adaptive advantage or increase in fitness of this particular computer's character.

This is a common premise in the so-called Constructive Neutral Evolution [79]. The latter is a model in which, at any level (genetic or not), complexity can be attained without an adaptive response [80]. There is some evidence that these processes are common in biological systems, specifically, regarding the over-complicated kinetoplastid regulation of a protist and gene scrambling, among others [79, 81]. It was formulated for biological systems with "excess capacities"; we here invoke it as a way to understand arbitrary (nonadaptive) coalescence under conditions of free energy excess [64]. Furthermore, molecules of high complexity can be attained abiotically [82]. Other examples of CNE in other hierarchical levels might be found within the Major Evolutionary Transitions, which are discrete events on evolution history [83]. One notable case is the taming of plastids by Eukarya. Whether these processes were adaptive

afterwards, and not neutral, it is reasonable to assume that the encounter leading to a first endosymbiosis of *Cyanobacteria* was serendipitous [84], and thus nonadaptive.

These findings are therefore of much help to allow a syllogism for unprecedented spontaneous complexity (Table 2), meaning there is no earlier instance with chemical complexity equal to or exceeding it, but that it could be exceeded spontaneously, in absence of adaptive selection.

This interpretation is in line with the Prigogine's *Theory of Dissipative Structures*, in which the "order through fluctuations" is a mechanism (not reducible to the equilibrium principle) leading to "inhomogeneous spontaneities" [85].

	logical value
Premise 1	Any process that exhibits *unprecedented complexity* can occur *spontaneously* (i.e. without adaptive guidance).
Premise 2	Abiogenesis exhibits unprecedented complexity.
Conclusion	Therefore, *abiogenesis can be spontaneous*.

Table 2: Syllogism of unprecedented spontaneous complexity

A nonadaptive–nonsequential model of abiogenesis

The combination of previous syllogisms' conclusions grants a novel nonselective view of abiogenesis, in which life-grade complexity is attainable nonadaptatively, but where nonadaptativeness' rupture is forced in abiogenesis. The latter is granted because of the hazardous establishment of the inheritability channel (Fig. 2), where parental traits begins to control inheritability of traits over noise (Fig. 1), thus hinting the advent of adaptive evolution (eq. 4). This model allows for broader views of life's emergence, where the sequential evolution of the "clock parts" may be violated.

This view rejects the intuition that chemical systems achieve life-grade complexity in a slow sequential fashion, and that this process is adaptive and necessary, i.e.: the conditions, the parts, and their change over time were the ones meant to be to achieve abiogenesis, and no others. In such model, gradual evolution and assembly of parts is paradoxical (Fig. 3). Acquisition of parts are –by definition– not slow gradual events, but discrete transitions towards complexity. The features of coalescent structures are achieved contingently (before selection), so evolution would eventually purify any of the nonadaptive traits z that may be required to achieve abiogenesis, since –again, by definition– they were acquired before life begun and they may carry a great cost on fitness w. In addition, gradualism does not account for dramatic global changes, in which sudden increase on chemical complexity may have been favoured. Maybe the best historical example is the sudden condensation of water vapour to form barren oceans ($\approx$0.1 Myr in Mars, $\approx$1.5 Myr in Earth) over (initially) oceans of magma [86, 87]. Furthermore, each one process involved in the formation of the oceans could have occurred more than once, or even periodically, because Earth's accretion time is longer than the time required for the formation of its oceans [86].

Two recent contributions not only strongly support the experimental validity of this model's narrative, they also constitute the most notable developments toward the resolution of the challenge in recent years [88, 89]. I briefly summarize the main findings chronologically (by publication date). The first experiments show that a variety of semihollow structures, with different morphologies and thickness, were achieved spontaneously in a Miller-Urey experiment [88]. The latter consist of silicon-enriched HCN polymers, a kind of compartment not present in

modern-day biology. Instead, the second experiments show how photo-RAFTs, or reversible addition–fragmentation chain transfers driven by light pulses, lead to the polymerization-induced self-assembly (PISA) of some components, selected *ad hoc* [89]. These, importantly, are not based on modern-day biological parts, but they spontaneously form micelles that "self-reproduce". Although molecular changes that occur in these micelles over time are the result of contingency rather than selection, as they have no possibly enabled inheritance channel and thus they follow the nonadaptive regime (Fig. 1), this could be an interesting result to be falsified by the latter model.

Altogether, these reasons could be a sufficient explanation of why we are failing so far: we might be exploring a very narrow spectrum of the chemical possibilities [78].

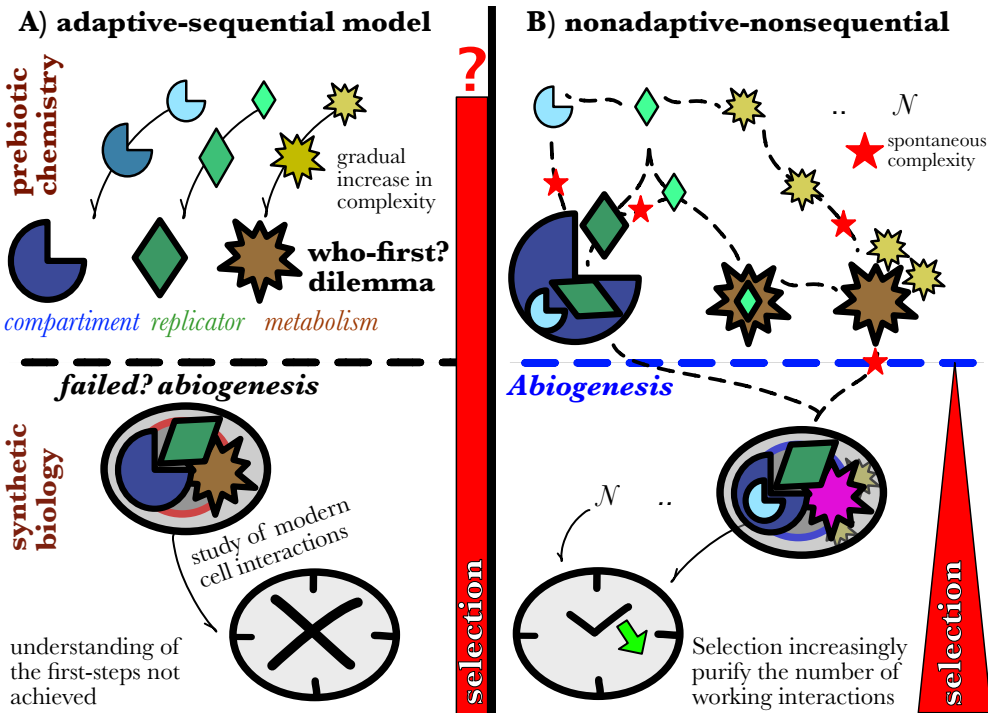

Figure 3: Trying to replicate abiogenesis with a sequential evolution has been failing for one-and-a-half centuries (A). Prebiotic chemistry and synthetic biology remain decoupled, as the link between them correspond to the unresolved question. Origin of selection has been a matter of debate in the sequential–adaptive model, but is intuitively time-bounded to the competition of molecules that slowly generate complexity within a primeval broth, as narrated in many works [28, 66], with the clearest account in the third chapter of Dawkins' *Selfish Gene* [67]. We can render an alternative model where nonadaptive traits drive contingent emergences of complexity (B). Global changes, like condensation reactions, could be important in producing spontaneous changes in complexity (red stars). Several different ways may be equivalent to generate abiogenesis. Importantly, in this model modern-day cells may have lost some nonadaptive traits that could be key to achieve a particular abiogenesis, as modern-day cellular life has a suboptimal fitness and their genomes have been increasingly been pruned by purifying selection. The number of allowed interactions between the primeval parts also decay over time, as they begin to be controlled by abiogenic products to perpetuate the "tic-tac" of the clocks, but not before. In (B), the primaeval component "brown star" might be required for a certain number of abiogenic reactions, but it is never found in modern life forms, as they remain largely purified.

Other recent study has also pointed out the fundamental historical limitations of sequential models, particularly in the context of the RNA-world hypotheses [90]. While this perspective presented a compelling view of the field, it adheres to a concept similar to the Jacob's "molec-

ular bricolage" [91]. Here, the coalescence of molecular components remains excessively constrained by biochemical architectures akin to extant life (eg. the need of a protein coding system). In addition, they invoke selection to facilitate the assembly of parts, whose chemistry is necessarily similar to that of modern life. A truly generalist model for abiogenesis must not rely on strict biochemical continuity with known life. This may, nonetheless, be a legitimate model for abiogenesis on Earth. Here I propose a different one, in which conditions for coalescence of the parts are most varied when selection is null (possible interactions are maximal because they are uncontrolled by selection in prebiotic conditions), and that this list of conditions must be not limited to Earth's prebiotic environment. Possible interactions between parts on the successful populations would be rapidly constrained by selection, explaining for example the *post-hoc* generality of the genetic code. But, importantly, in the nonsequential–nonadaptive model, the achievement of a rudimentary code is not necessarily time-placed at the very same occurrence of abiogenesis, as there could be other ways to control inheritability of fitness and fulfil eq. (4) [92]. I provide a succint comparative for these three models of abiogenesis (Table 3).

Feature	**Nonadaptive-Nonsequential**	**Molecular Bricolage (Seelig & Chen, 2025)**	**Sequential (Oparin-Haldane)**
Abiogenesis definition	$\lim_{t\to t_1^+} \mathrm{Cov}\left(\frac{w}{\bar{w}}, z'\right) > 0$, tending to W	Not defined in the coalescence of modular parts	Gradual chemical evolution leading to self-replication
Selection timestamp	When fitness-trait covariance begins to be controlled (abiogenesis)	Selection follows from modular assembly, but not defined *per se*	Selection in prebiotic reactions, evolvability of selection not defined
Formalism	Derived from the Price's equation	Absent	Absent
Generality	It relies on premises, but it can be tested (and be wrong) in any chemical or computational system	Assumes necessity of code and modern-day parts	Assumes necessity of Earth-like conditions, modern-day parts, and adaptive-sequential evolution
Experimental Feasibility	Testable experimentally and computationally, as long as we can measure the complexity and the fitness-trait covariate of the systems over time	Experimentally testable for limited conditions on chemical systems	Relies on historical plausibility rather than experimental validation, testability is narrow

Table 3: Comparison of three abiogenesis models.

But how could the nonadaptive-nonsequential model be tested?

Under this model, abiogenesis can be abstracted as a rare, mineral, spontaneous (favourable), and complexifying reaction; and, once it occurs, the abiogenic products are forced to store information of the outcomes of the interaction between their characters and the environment, in order to permeate it more efficiently. Let us consider, once more, the classical Oparin-Haldane example [19, 20], where UV radiation and other abiotic processes will ensure a concoction of different chemicals within the primaeval oceans, and the former will act upon the latter with certain periodicity (e.g. day-night cycle). In this scenario, a falsification of a nonadaptive–nonsequential model is easy to design, as it just requires monitoring the relevant parental character values z over time (e.g. half-life of an amphiphile, aromaticity, molecular weight, etc.), and to stipulate the measurements of the offspring character values z' (i.e. change in the selected parental character values). If the model is accurate, the origin and maintenance of very simple life forms will be observable starting as soon as (i) z and z' begin to correlate, (ii) this correlation is governed, thus maintained (Fig. 1), and (iii) with the appropriate control design, once h distributions are shown adaptive (Fig. 2). On the other hand, if each one abiogenic reaction requires a slow adaptive selection prior to its occurrence, this model would be useless.

It could be argued that all this model does is to impose a very low complexity threshold for the origin of life. For example, it may be feasible for a group of very simple replicators without a proper isolation from the environment to fulfil the conditions of the model. A counterargument is that our picture of what life is is heavily biased by the observation of a gargantuan sample of diverse and complex life forms that have evolved over billions of years. Hence, it seems more conservative to rely on a model that is able to trace inheritance and selection mechanisms coupled to the origin of life, than to rely on our impression of what life should be, an impression based on the description of present-day cellular biology.

In spite the above consideration, we could trace the origins of the exemplified spontaneous system, and that of many others. Should some efforts be directed in pondering how to screen each one coalescence-prone condition?

In this line of action, R. Hazen argued that mineral evolution and its reactions are inherently governed by a regime of chance [78]. He proposed a semi-quantitative estimate of the feasible prebiotic reactions leading to the origins of life on Earth-like planets, calculated with time and surface areas for mineral reactions. His result, an upper limit of 2×10^{53} serendipitous abiogenesis "experiments", is the number of distinct mineral-surface reactions that could have taken place on the Hadean Earth. This number is way beyond of any human laboratory setting, insofar these consist of nonadaptive–nonsequential reactions that we have to test by combinatorics. However, reaching abiogenesis might be inevitable over planetary timescales in Earth-sized natural laboratories [78]. Despite being a simplistic demonstration, we may consider it a good proxy for the upper limit of uncontrolled reactions needed to achieve abiogenesis (in Earth-like planets). Hazen further expressed: "*strategies exist to increase the likelihood of observing improbable chemical reactions in the laboratory. One can work backwards from modern biochemistry to focus on key molecular species and their products. New approaches in combinatorial chemistry, coupled with computational chemistry, hold the promise of quickly narrowing the search.*" [78]. I agree with this, even if it is stated in the likes of the adaptive–sequential model. The more interesting question is whether we can use the nonsequential–nonadaptive model to further delimit the regime of chance; i.e. to investigate only the reactions where chemical systems increase their trait-fitness covariates spontaneously, and acquire the ability to control them over time.

Brute-force computational chemistry does not seem practical to screen such large quantity of

reactions. Indeed, if we consider all the physicochemical combinatorics needed, it is a daunting computational task. Instead, we could limit the combinatorics to the chemical compounds and conditions (reaction experiments) that fulfil the premises of the model. First, we already acknowledged that the control over the inheritance of characters is definitory of life (syllogism of null selection), as shown in Figure 1. Therefore, we should subtract a value corresponding to the number of reactions not able to generate such spontaneous control of inheritability, and that should be represented by the majority of the mineral reactions, n, which denotes the orders of magnitude excluded. Thus, $2 \times 10^{53-n}$ is a substantially smaller subset where only abiogenic reactions are found. Second, and under the nonsequential model of abiogenesis, we would only need to screen reactions that are not sequential (syllogism of unprecedented spontaneous complexity). We can extract again a theoretical value for all the conditions leading to compound-simplification reactions, c (c is subtracted only to the list of abiogenic reactions, and represents likewise orders of magnitude). We now have that only $2\times10^{((53-n)-c)}$ abiogenesis experiments are needed to assess for Earth-like conditions, which, although unknown, should be an insignificant proportion of reactions to test. But, while determining c could be simpler (screening the enthalpy of reactants and that of the products), methods to infer n are a seemingly unfeasible task; how can we estimate the magnitude and nature of that one parameter? A good alternative strategy could be predicting the less likely abiogenic reactions and disregarding them, thus treating n as a pseudo-proxy of the true parameter.

A compatible idea has been recently reviewed by Barlett *et al.* [93]. They propose to examine the increase in information processing over time, using the internal complexity of the system as an indicator. In fact, this effect could be best captured by quantifying Cov $\left(\frac{w}{\bar{w}}, z'\right)$ over time, as this provides a quantitative proxy to assess whether selection has emerged and inheritability is controlled (Fig. 2). In relation to this, some authors investigated how to search for group selection on chemical systems [71, 94]. One recent attempt to do this is promising [95], but this still remains a theoretical and logistical challenge. Finally, although I have not disclosed any efforts on how "computational life" might help falsify or not any model of abiogenesis, self-replicating programs have been running a lot lately. Recently, we have some examples of how the choice of the programming language – extended brainfuck, SUBLEQ, or Forth (family of languages) – does exert a defining outcome on the rise of computational "self-replicators" [96]. These kind of conclusions could be more useful to solve natural questions if matched correctly with what we know so far about evolvability and inheritability of biochemical traits [97].

Finally, I do not claim for the validity of this model. For the Oparin-Haldane hypothesis to be a truer model of nature, we should observe that any abiogenic reaction requires an uncertain number of very slow chemical reactions, and to prove that these were directed by adaptive selection. Instead, for the nonsequential–nonadaptive model to be a truer model of nature, we should observe that any abiogenesis can be achieved spontaneously from precursors, and that the reactions needed were undirected by adaptive selection. In the future, it could be that we find that some chemical systems only develop Oparin-Haldane-like abiogenesis, while others are successful in nonsequential-nonadaptive abiogenic reactions. Including the nonsequential–nonadaptive is thus helpful (1) as a null, (2) to test more kind of questions (or chemical reactions) that were prevented in the Oparin-Haldane view, and (3) to quantitatively trace inheritability of parental characters z as the first instance of selection, and thus abiogenic reactions.

In the end, the quest might still be to figure out the material rules of this elusive *generatio aequivoca* to occur, or the very phenomenon long deemed impossible by the most gravous materialists of old. What an irony!

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