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Universal biology and the statistical mechanics of early life

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All known life on the Earth exhibits at least two non-trivial common features: the canonical genetic code and biological homochirality, both of which emerged prior to the Last Universal Common Ancestor state. This article describes recent efforts to provide a narrative of this epoch using tools from statistical mechanics. During the emergence of self-replicating life far from equilibrium in a period of chemical evolution, minimal models of autocatalysis show that homochirality would have necessarily co-evolved along with the efficiency of early-life self-replicators. Dynamical system models of the evolution of the genetic code must explain its universality and its highly refined error-minimization properties. These have both been accounted for in a scenario where life arose from a collective, networked phase where there was no notion of species and perhaps even individuality itself. We show how this phase ultimately terminated during an event sometimes known as the Darwinian transition, leading to the present epoch of tree-like vertical descent of organismal lineages. These examples illustrate concrete examples of universal biology: the quest for a fundamental understanding of the basic properties of living systems, independent of precise instantiation in chemistry or other media.

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This article is part of the themed issue 'Re-conceptualizing the origins of life'.

1. Introduction

(a) Universal biology

Universal biology is the quest for a fundamental understanding of the basic properties of living systems, independent of their precise instantiation in chemistry or other media (e.g. [1]). Such a theory, if it in fact exists, would be the biological counterpart of the abstract theory of universal computation, due to Turing [2], von Neumann [3] and others. This theory established the foundation for practical computers, by showing, in principle, that universal computation was possible, and by describing, in general terms, the different components necessary for computation. The theory of universal computation has survived intact during the evolution of several different technologies from the relays, vacuum tubes and switches of the 1940s and 1950s up to the present day technology of massively complex integrated circuits. The basic architecture devised by von Neumann, and anticipated by Babbage, remains in use today [4].

In the historical development of computation, the abstract mathematical theory preceded the construction of actual working examples of computers. It is conceivable that this order could have been reversed; after all, mechanical devices to aid special computations have been available since the dawn of mathematics, including the abacus, slide rule, and in the nineteenth and twentieth century machines for calculating the solutions of differential equations, or the terms in complicated mathematical series. However, universal computers were only built when it was understood that such devices were logically allowed possibilities, although Babbage's Analytical Engine would have been the first Turing-complete computer (as its instruction set included conditional branching) if it had actually been built [4].

The central task of universal biology is, in some sense, the inverse of the development of universal computation. In computation, we start with the mathematical abstraction and build the instantiation. In biology, we start with the instantiation—many examples of living organisms—and our task is to establish the mathematical abstraction which they represent. The successful elucidation of a theory of universal biology from the examples of biology around us would answer the question of why it is that the phenomenon of life could exist, i.e. is a logically allowed possibility. Furthermore, universal biology would immediately shed light on the question of the ubiquity and inevitability of life, if it turned out that life is an inevitable consequence of the laws of physics, to be expected in any sufficiently complicated environment that is sufficiently far from equilibrium to enable multiple layers of hierarchical organization to exist, with numerous feedbacks between them. Our prejudice is that this is the case: life is one of the processes that allows planets to come to equilibrium.

If life is, in fact, a means to dissipate free energy, one would expect that the mechanisms behind all its universal properties involve free energy-driven non-equilibrium processes. One of these universal features of life is homochirality—the fact that all the chiral amino acids used by terrestrial biology are left handed (the sugars are right handed). The fact that this effect is not a mere enantiomeric excess is surprising and requires a detailed explanation. Our recent work [5] shows that homochirality emerges as a consequence of a rather general characteristic of life: autocatalysis/self-replication driven by an external source of energy. The consequence of the chiral symmetry breaking of biopolymers is that it is possible for them to make higher order structures, such as the supercoiling and packing of DNA, something that would be very difficult for racemic molecules.

This is not enough to define life in our opinion because one needs the dynamics associated with evolvability. A purely chemical process differs from a living system in that it does not store

information about its state in a medium that can then be replicated, with error, thus creating the conditions for evolvability.

Returning to the characteristic of life: the source of the driving free energy in the first self-replicating molecules or molecular complexes could be sunlight, voltage difference across a hydrothermal vent (for a recent review of the way in which the alkaline hydrothermal vent hypothesis relates to the functioning and evolution of the proton-motive force across a cell membrane, see [6]), or a constant influx of high free energy molecules. A theory of universal biology would not include the specific instantiation of the source of disequilibrium as it would jeopardize the universality of the theory, but one can infer the minimum free energy required for, for example, chiral symmetry breaking from such theory. Just as in the theory of universal computation, we ignore the thermodynamical cost of computation which would be relevant only if a particular manifestation of the universal Turing machine was the object of study. Yet the minimal thermodynamic cost of computation can be inferred from the theory [7].

In this article, we will review a specific problem that we have addressed from the viewpoint of universal biology, and present some new results. Up to now, we have built minimal dynamical system models to study two of the most perplexing features shared by all known life on the Earth: (i) the canonical genetic code [8] and (ii) biological homochirality [9]. Our work in both cases makes testable predictions. Our calculations on the evolution of the genetic code predict that life necessarily began in a collective, networked phase where there was no notion of species and perhaps even individuality itself [10,11]. In a new work presented here, we show how this phase would ultimately terminate, leading to the present epoch of tree-like vertical descent of organismal lineages. Even earlier, during the emergence of self-replicating life far from equilibrium in a period of chemical evolution, homochirality would have necessarily co-evolved along with the efficiency of early-life self-replicators. The mechanism that we have identified could be tested in the laboratory: it requires autocatalysis and that the system is driven far from equilibrium [5]. Owing to limitations on space, we will focus in this article on the genetic code, but refer the interested reader to a recent and complete discussion of the homochirality problem [12].

(b) Universal biology and astrobiology

The central concerns of astrobiology are three fundamental questions: (i) How does life begin and subsequently evolve? (ii) Does life exist elsewhere in the universe? (iii) What is the future of life on the Earth and beyond? Remarkably, despite their remoteness in space and time, such questions can be approached by studying terrestrial biology. Perhaps the clearest demonstration of this is the work of Woese & Fox [13] whose analysis of ribosomal RNA sequences showed that all life on the Earth is related, mapped out the evolutionary history of life on the Earth, and uncovered the existence of three domains of life (Bacteria, Eukaryota and the previously unrecognized Archaea) [14]. Woese and Fox not only discovered the Archaea but also pointed out a deep puzzle revealed by their work:

> The general eubacterial phenotype has been stable for at least 3 billion years—i.e. the apparent age of blue-green algae. The methanogenic phenotype seems to be at least this old in that branchings within the two urkingdoms are comparably deep. The time available to form each phenotype (from their common ancestor) is then short by comparison, which seems paradoxical in that the two phenotypes are so fundamentally different. We think that this ostensible paradox implies that the common ancestor in this case was not a prokaryote. It was a far simpler entity; it probably did not evolve at the 'slow' rate characteristic of prokaryotes; it did not possess many of the features possessed by prokaryotes, and so these evolved independently and differently in separate lines of descent.

We now know that geological and phylogenetic evidence suggests that life emerged and developed much of the complexity of contemporary organisms rapidly—in less than a billion

years or so. And as Woese and Fox were the first to point out [15], this requires a tempo and mode of evolution that must have been very different from conventional notions of vertical Darwinian evolution, one characterized by unusual rapidity and, they speculated, where early life had not yet developed the clear distinction between phenotype and genotype familiar today. To put a concrete and quantitative context to this general idea, we now turn to a discussion of the biological event that represents the most important evolutionary transition: the emergence of the genetic code. This event is synonymous with the emergence of species, as we will see, and remarkably can be modelled in a minimal way that is capable of making experimental predictions.

2. The evolution of the genetic code: a case study in universal biology

In order to illustrate how one can extract features of universal biology from contemporary biological data, we recount here a specific example from our own work, based upon what has been learned in the last decade or so from rather sophisticated analyses of the genetic code. To see further back in time than the root of the ribosomal tree of life, it is necessary to analyse the oldest relics of early life, evident not in molecules per se, but in the core mechanisms of cellular machinery. Whereas individual molecules reveal traces of their history, the interactions, dependencies and functions of molecules are expressed in the way that they come together to build the cell.

(a) The genetic code is special in two ways

The canonical genetic code is, of course, universal, with only a few exceptions now known, primarily in the nuclear code of ciliates [16], with other variations documented in the mitochondrial code or in the stop codons [17]. It is generally thought that the genetic code underwent large-scale evolution to its canonical form in an early epoch, followed by a period of minor adjustment and diversification [18]. However, an additional feature was noted shortly after the code table was empirically constructed. During the 1960s, Woese had noted that the structure of the genetic code of translation showed clear signs of being an evolved construct rather than a frozen accident. In particular, the structure of the code suggested that it was minimally sensitive to mutations or to translation errors [19]. Using Monte Carlo simulation of the error-minimizing properties of ensembles of synthetic genetic codes with the canonical degeneracy structure [20], it was shown definitively that the probability of a random code being less sensitive than the canonical genetic code was of order 1 in 10 million [21–25]. To make such estimates precise, molecular dynamics calculations of the end-to-end correlation functions of amino acids in water–pyridine mixtures were combined with advanced Monte Carlo simulations of the synthetic genetic codes [26]. Such analyses provide a strong argument that the canonical genetic code is not a ‘frozen accident’.

But the question remained as to how it was possible, in principle, for a genetic code to evolve, and avoid Crick’s dilemma that any variations to the genetic code would necessarily result in faulty translation and thus would be fatal [27]. Moreover, as Crick was perhaps the first to emphasize, the question of why the genetic code is universal had not been properly addressed by any of the verbal arguments that attempted to provide a narrative for how the different amino acids became incorporated into the code.

To address these points, Vetsigian, Woese and Goldenfeld (VWG) developed a mathematical theory for the dynamics of a genetic code, co-evolving with the proteins as organisms became more complex over evolutionary time [10]. This theory begins with the recognition that variations in the genetic code are fatal only if the code is a deterministic one (as it is today). However, early life would have used much less finely tuned cellular machinery, and would therefore not have required precision in the amino acid building proteins. Early translation would have been predominantly statistical, producing equivalence classes of amino acids to build proteins, and over evolutionary time refining these equivalence classes into the genetic code we have today. This scenario was tested in numerical experiments using digital life—artificial organisms

built from computer code that compete for environmental resources, possess primitive cellular translational machinery, and are able to evolve through plasticity of their genomes. The results of these computer experiments were rather striking: vertical Darwinian evolution was not sufficient to yield an outcome at long times that corresponded to the present state of life, with a universal genetic code that is minimally sensitive to errors. This mode of evolution certainly resulted in a refinement of the code, but one which was rather weak. Moreover, the process terminated quickly, leaving a community of early organisms with a patchwork of genetic codes, rather than a universal code, each of which was suboptimal at minimizing errors. Such fractured communities are not capable of explosive growth of genetic novelty, because the pools of innovation available to each sub-community are too small. VWG discovered that a very different situation arose if these digital organisms were strongly communal with mechanisms to exchange genetic material. Although ineffective at first, because of the lack of a universal genetic code, subcommunities that had sufficiently close genetic codes and whose translation machinery was sufficiently tolerant of error (more precisely, ambiguity) were able to take advantage of large pools of innovation, and eventually outcompeted the other subcommunities. In the end, the entire community had evolved to a state with a single, i.e. universal, genetic code, one which was optimal in terms of its ability to be insensitive to translation error or mutations. The conclusion from this analysis is that the rapid evolution of the early cell was driven by strongly collective dynamics, leading to a universal and optimal genetic code and a state capable of exploiting large pools of genetic innovation in order to survive in a wide variety of environments. This analysis was rather general: it required of life that it be capable of information processing, able to sense its environment and endowed with primitive genome dynamics that includes gene transfer and vertical evolution. Because this analysis focuses on the dynamical processes of evolution, rather than the specific molecules that instantiate these processes, we infer that all life that relies generally on information processing, innovation sharing and creation, and is on the path towards some separation between phenotype and genotype, necessarily will evolve explosively. As such, these results are powerful examples of universal biology, and they provide a framework that, in principle, resolves the puzzle that so preoccupied Woese and Fox in 1977.

(b) The genetic code and the three domains of life

Let us now discuss in more detail the phase diagram of life, as inferred from the numerical experiments on genetic code evolution. In the days before systematic genomic sequencing was a possibility, Woese and Fox applied an early technique that allowed them to compare the sequence of selected short segments of DNA from different organisms [13]. As they were after a way to classify all forms of life, their analysis was restricted to those genes shared by every cell, thus underlying the most essential features of biological systems. Eventually, they compared sequences of a ribosome subunit gene, the 16S rRNA found in prokaryotes, which revealed the astounding fact that life is separated into three main domains: Bacteria, Archaea and Eukaryota. This discovery had several paramount consequences across all areas of biology, two of which are particularly relevant for the remainder of the paper: (i) the fact that species can be operatively defined on the basis of similarities of the 16S rRNA and (ii) a minimalistic history of life, as represented in figure 1. The top of the figure shows that, at present day, life is divided into three domains. Going backward in time, the lineages of the Archaea and the Eukaryota coalesce. Further backwards, the two main lineages coalesce into the Last Universal Common Ancestor (LUCA) of all extant life. More about the major evolutionary transitions can be found in [28] and references therein.

The fact that extant life descended from a single ancestor is suggested by the properties shared by all organisms on the Earth, and the relatedness identified in the ribosomal tree. In fact, all life is based on the same nucleic acids, which provide a medium to store genetic information. The genetic code is almost the same across the three domains. Adenosine triphosphate (ATP) is the universal currency for chemical energy and is produced by an enzyme which is universally distributed: the ATP synthase. Likewise, much of the core metabolism was involved in the

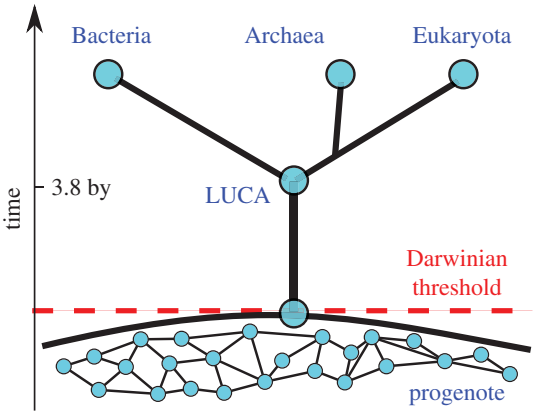

Figure 1. A (conjectured) brief sketch of the history of life. At present, life is divided into the three domains: Bacteria, Archaea and Eukaryota. Following the lineages of the three domains backward in time (solid lines), we find that they coalesce into the Last Universal Common Ancestor (LUCA), approximately 3.8 Gya. The dashed red line indicates the point in time where it is thought that the Darwinian transition occurred: before that, life was evolving in a communal way (progenote); after the Darwinian transition, life evolved as described by the Modern Synthesis. (Online version in colour.)

synthesis of fats, amino acids and sugars. Therefore, if on the one hand it is improbable that life descended from more than a single ancestor, it is clear, on the other, that that single ancestor should possess everything that is shared by extant life, not least the ribosome and the rest of the apparatus of genetic-code-driven protein synthesis.

Much of the evolution of LUCA has been clarified in light of the discovery that even distantly related organisms can directly exchange genetic material via horizontal gene transfer (HGT). Indeed, the past 20 years have seen an increased interest in the fact that (mostly) Bacteria and Archaea can perform HGT, by means of which they transfer genes conferring antibiotic resistance and the ability of metabolize alternative sources of carbon and energy. The role of HGT becomes, however, more controversial in the study of the evolution of early life, as it led to question the very foundation of the tree-like structure of the evolutionary relationship among species [29]. In fact, the key assumption for constructing phylogenetic trees is that similarities between genes (or genomes) allow one to infer the parent-to-offspring relationship among organisms. In this way, in a phylogenetic tree based on a gene that was horizontally transferred, two dissimilar species would appear closely related. A way to address this issue is to note that (at present time) HGT shapes mostly *accessories* part of the genomes, that is, genes that are not involved in vital organismal functions. By contrast, *core* genes such as the 16S rRNA evolve (slower) by vertical descent and are weakly, or not at all, affected by HGT. The reason is that core genes underwent strong coevolution and are thus much more interdependent on the rest of the genome. Therefore, transferring a core gene would most likely have lethal consequences for the recipient cell.

(c) The dynamical role of horizontal gene transfer

Woese proposed that 'in aboriginal cells all their cellular componentry could be altered and or displaced through external injection of genetic material' [15,30]. Therefore, the organisms did not carry a stable genealogical trace—there were no species—but evolution rather occurred as a communal phenomenon. This state of life, the *progenote*, is characterized by a high degree of HGT which shaped the totality of the genomes, and was therefore the main evolutionary driver up to a time where life organize itself into species. This point in time, termed by Woese the Darwinian threshold [30], denotes a transition in which evolution goes from being horizontally dominated to be vertically dominated, the latter simply being the conventional evolutionary theory described by the modern synthesis. The term 'Darwinian threshold or transition' is perhaps unfortunate, because one might erroneously infer that selection is not operating in the progenote phase.

Below, we provide a detailed analysis of this horizontal-to-vertical transition (or Darwinian transition) by means of a theoretical model and reduce its emergence to an interplay of evolutionary effects. More specifically, the following biological questions shall be discussed. Does life start evolving by vertical descent when it achieves a certain biological function? Did the frequency of HGT events decrease over time to allow life to organize itself into species? Does the progenote phase speed up and/or optimize evolution? Is the Darwinian transition a single-gene phenomenon or does it involve multiple genes or, even, the whole genome?

Owing to the infeasibility of carrying out an evolutionary experiment that exhibits a Darwinian transition, most investigators relied either on statistical inference methods, mostly analysing extant life, or theoretical models that reproduce (some conditions of) early life. These investigations can be conveniently classified into two types: those studying how HGT affects speed and optimality of evolution, and those studying how HGT alters the process of specie formations. In the first class, a notable study showed that the speed of HGT in evolving a population depends on the population size, suggesting an interplay between HGT and the intrinsic noise [31]. In the following work, HGT has been shown to accelerate the process of evolution and led the genetic code towards error-minimization [10].

The bibliography of the second class includes conventional population genetics models, the Eigen model and the Crow–Kimura model [32], extended to account for the effects of HGT [33]. These authors have shown that a high degree of HGT destabilizes speciation, in a way similar to an error-threshold transition [32]. A similar argument has been put forward to understand the role of HGT in triggering a Darwinian transition [34,35]. Both studies, although employing different models, concluded that a decrease in the rate of HGT is necessary to have vertical descent. In [34], it is argued that life evolved towards low rates of gene loss which rendered HGT events unfavourable. The first dynamical model that exhibits a Darwinian transition is presented in [35]. These authors identified a metastable behaviour due to selection-driven processes that becomes more prominent as the rate of HGT event decreases until it stabilizes speciation. Hence, the proposed scenario is that life evolved firewall mechanisms to 'protect' sensitive parts of genomes from horizontal injection of genetic material.

3. A model for the evolution of early life

We now construct a stochastic individual-level model of an evolving population that mimics the dynamics of early life. We show that an interplay of selection, mutation and HGT leads the population to cluster in genome space and subsequently evolve by vertical descent, following an initial phase where the population explores the genome space due to HGT and point mutations. We identify the transition between these two regimes as crossing a Darwinian threshold. The dynamics we find is generic, that is, occurs for general parameter values, provided that the genomes around which species are formed possess large enough fitness to avoid an error-threshold catastrophe. Importantly, entering the vertically dominated evolution phase does not require a decrease in the frequency of HGT events, in sharp contrast to what has been concluded in previous studies [34,35]. The interpretation of this result is that as cell designs increased in complexity and genomes became internally inter-dependent, a point in time was reached at which HGT becomes progressively less effective in improving the fitness of the fitter genomes, hence promoting the emergence of species and a vertically dominated mode of evolution.

In a second experiment, we analyse the evolution of a population in the presence of a fitness landscape that allows for equally good (or even better) variants of that gene. Moreover, we show that in the presence of HGT, the population fixates on a single allele, despite other equally good (or even better) variants of that gene existing, providing that the total population fitness is large enough to trigger vertical descent. This phenomenon is controlled by the strength of HGT.

Based on our results, we propose a short description of how early life evolved in the concluding remark, which supports the view of a single LUCA which evolved most of its cellular apparatus prior to lineage divergence.

(a) Model description

Evolution in early life features a high degree of HGT shaping the whole genome in addition to evolutionary drivers adopted in conventional population genetic theories. Our model starts from a population genetic theory extended so as to account for horizontal transfer of genetic fragments between organisms. Our model is similar to others analysed in previous works [31,33,35].

We consider a well-mixed population of N organisms, each organism carrying a circular genome of length L composed, for simplicity, by a sequence of two bases denoted as zero and one. Therefore, there are 2^L possible genomes which we index by the letter I. The whole set of genomes forms the genome space. Throughout the paper, the state of the system is fully specified by the genome abundances X_I (for all I), denoting the number of organisms possessing genome I divided by the total population size N. The population evolves stochastically in time due to the effects described below.

— *Reproduction*. Each organism replicates by binary fission with rate W_I, which depends on the corresponding genome I. The rate W_I is called the fitness of genome I.
— *Mutations*. During replication, each base of the offspring genome is subject to point mutations with probability μ. A point mutation changes (likewise) a zero into a one, or a one into a zero.
— *Selection*. A fitness landscape, $I \to W_I$, is assigned for each numerical experiment. As explained in more detail in the following, the fitness landscapes adopted here satisfy a similarity rule: the more similar two genomes, the more similar their fitness.
— *Competition/death*. Each organism dies with a rate proportional to the abundances of organisms with different genomes, weighted by their fitness. This way of modelling death is conventional in quasi-species theories [32], allowing, in our model, the total population size N to be conserved on average.
— *Horizontal gene transfer*. Each organism can offer a fragment of its genome to any other organism in the population. This process occurs with a rate constant h, that is independent of the genome. The transferred fragment has length given by a random uniformly drawn integer in the interval $[1, L]$, and overwrites the recipient genome preserving the position that the fragment occupied in the parent genome. This feature ensures that an HGT event increases similarity between organisms.

Each effect (reproduction with mutation, HGT and death) occurs with a rate given by the corresponding rate constant multiplied by the number of combinations that instantiate the effect. For example, the rate of occurrence of HGT events is equal to h times the number of organism pairs in the population. The set of final rates is then used to construct a Markov process, which we numerically simulate using a Gillespie algorithm [36].

(b) Detailed implementation of a model for early life

In this section, we give a detailed description of how we implemented the model we used for carrying out numerical simulations. As briefly explained in §3a, we consider a well-mixed population of N organisms, each organism carrying a circular binary genome of length L. Genomes are indexed by the letters I and J, and we denoted by I_l the lth bit of genome I. The genome abundance X_I indicates the number of organisms possessing genome I divided by the total population size N. To quantify the degree of similarity between two genomes, I and J, we adopt the Hamming distance d, defined as

$$d(I,J) = \sum_{l=1}^{L} \delta_{I_l,J_l}, \tag{3.1}$$

where δ is the Kronecker delta function.

Organisms are stochastically subject to three events: growth (with mutations), death and HGT. To each of these events corresponds a probability per unit of time that specifies its rate of occurrence. We use the Gillespie method [36] to simulate the stochastic population dynamics in accordance with the rates of occurrence.

We begin by defining the probability R_{IJ} that genome J mutates into genome I during growth. This is given by

$$R_{IJ} = (1-\mu)^{L-d(I,J)}\mu^{d(I,J)}, \tag{3.2}$$

where μ is the probability that a single base mutates during growth. We use this quantity to define rate of occurrence for the birth of genome I, which reads

$$\text{rate of birth of genome } I = \sum_J R_{IJ} W_J X_J, \tag{3.3}$$

where W_J is the fitness of genome J and $\sum_J$ is that we are summing over all possible genomes.

Throughout the paper, we use two fitness landscapes. In figure 2, we analyse the emergence of speciation using the following single-peak fitness landscape:

$$W_I = \exp\left(-d(I, 11\ldots1)\right). \tag{3.4}$$

In this case, the genome with all ones, $11\ldots1$, is the most fit genome, and all the others have a fitness that decays exponentially with the Hamming distance from the fittest genome. Note that the system is symmetric, that is, the dynamics are tantamount with respect to the choice of the fittest genome.

We adopt a similar definition for the double-peak fitness used to generate figure 3. In this case, two genomes have equal fitness: $11\ldots1$ and $00\ldots0$, whereas the fitness of all the other genomes depends on how distant they are from the two most fit genomes. In formulae, the fitness landscape reads

$$W_I = \tfrac{1}{2}\left(\exp\left(-d(I, 11\ldots1)\right) + \exp\left(-d(I, 00\ldots0)\right)\right). \tag{3.5}$$

To model death due to competition, we define a rate of occurrence that is proportional to the fitness of all genomes against which an organism I is competing. The fitnesses are weighted by their genomes abundances, that is

$$\text{rate of death of genome } I = X_I \sum_J W_J X_J. \tag{3.6}$$

In this way, we also ensure that the organism copy number is stochastically fluctuating around N, so that global extinction and exponential growth are avoided in the model.

Finally, we need to implement HGT. At any time, an organism donor I can copy a fragment of its genome and insert it anywhere into an organism acceptor J. Recall that genomes are circular. Because of this process, the genome J is altered and we denote with K the acceptor genome J after the HGT event. The rate of occurrence is defined by

$$\text{rate of HGT, a donor } I \text{ and an acceptor } J \text{ lead to newly born } K = hX_I X_J. \tag{3.7}$$

Thus, the rate of HGT scales quadratically with the genome abundances and is overall proportional to the constant h.

We conclude by noting that the dynamics described in the paper are generic: exploring the parameter value space does not lead to qualitatively different outcomes, but simply affects the timescales taken to observe the phenomena we have documented.

We conclude this section with several remarks. First, we are adopting the implicit assumption that the genome of an organism codifies a single biological function. In other words, each organism possesses a single gene. Second, the interplay between fitness and HGT is designed so as to increase organismal relatedness after an HGT event. In this way, HGT mimics the innovation-sharing protocol originally proposed by Woese [30], so that biological novelty can be laterally shared by organisms in a population. Finally, note that by virtue of the model being

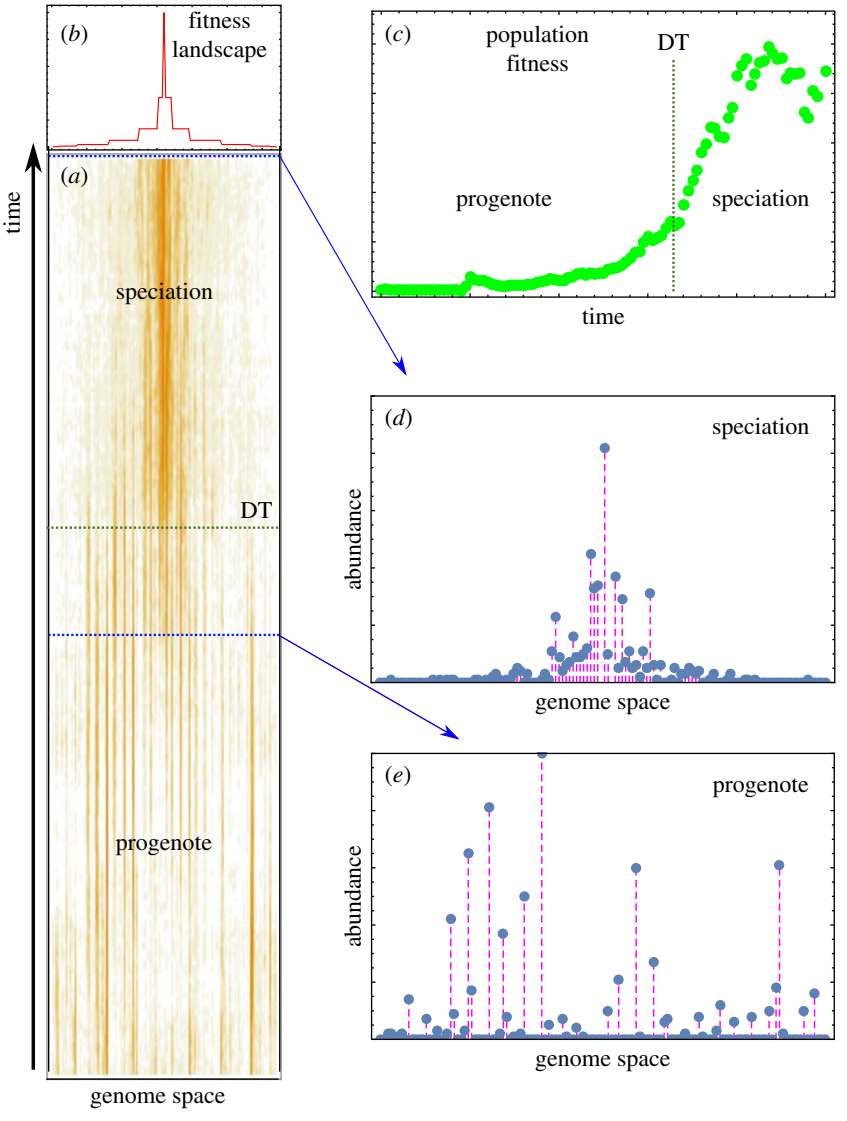

Figure 2. Single run dynamics obtained by stochastic simulations of $N = 10^4$ digital organisms, initialized with a random distribution in genome space. Each organism is characterized by a binary genome composed of $L = 7$ symbols, a mutation rate $\mu = 0.1$ and a HGT strength $h = 20$. (*a*) Genome abundances (displayed using a scale of brown) of a typical system dynamics. In the beginning, organisms populate almost uniformly the genome space until a certain point in time (DT), after which the system exhibits vertical descent around the fittest genome. (*b*) Fitness landscape is represented in two dimensions (see the electronic supplementary material). (*c*) The total population fitness (green dots), obtained from the run displayed in (*a*), is plotted versus time. The DT corresponds to the inflection point of the corresponding spline. (*d*,*e*) Snapshots of the genome abundances corresponding to the progenote phase and the phase where the system clusters around the most fit genome (speciation). (Online version in colour.)

inherently stochastic, evolutionary effects due to the intrinsic noise (such as the genetic drift) are automatically taken into account.

Next, we describe the results of two numerical experiments which differ in the choice of the fitness landscape. The first experiment aims to show how a population evolves in a progenote phase and subsequently exits due to the emergence of vertical descent (results in figure 2). In the second experiment (results in figure 3), we explore the influence of HGT on the sharing

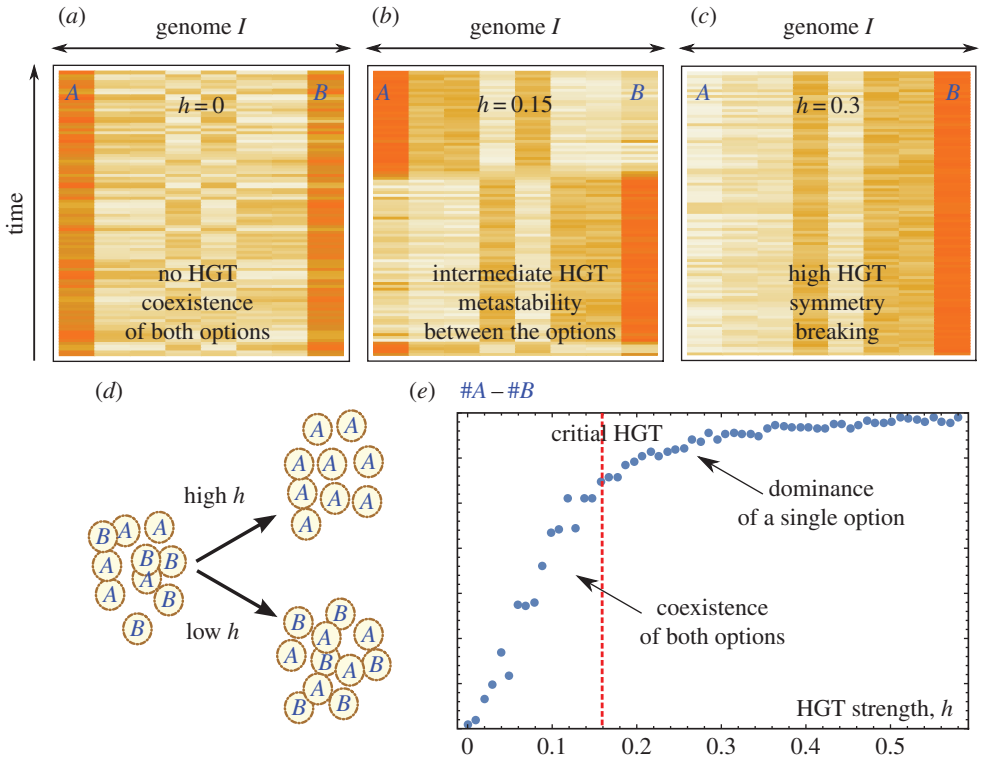

Figure 3. Stochastic simulation results of an interacting population of digital organisms evolving under a double-peak fitness landscape for various values of HGT strengths h. Genomes A and B have equal (high) fitness, whereas other genomes have low fitness (see the electronic supplementary material). Other parameter values are as in figure 2. (*a–c*) Asymptotic system dynamics when $h = 0$ (*a*), $h =$ medium (*b*), $h =$ high (*c*). Panel (*d*) summarizes this main effect. (*e*) The long-time difference between the number of individuals with genome A and those with genome B, displayed against the HGT strength h. The dashed red line corresponds to the critical HGT strength which separates two regimes: a linear increase and a nonlinear saturation. (Online version in colour.)

of biological novelty, showing that different long-term outcomes are possible, according to the strength of the HGT in play. This section is dedicated to discuss the simulation results and little is said about the implications that those results have for the biology.

(c) Transition from horizontally-to-vertically dominated evolution

Starting from the model defined in §3a, we construct a single-peak fitness landscape in the following way. One genome, $I = 11\ldots1$, corresponds to highest fitness. The fitness of all other genomes depends on how similar they are to the fittest genome, where the degree of similarity between two genomes is quantified by the number of bases that the two genomes have in common (i.e. the Hamming distance, see §3b). For example, let us consider an example of the pedagogical case of two-digit genomes. Suppose that $I = 11$ is the fittest genome; $I = 10$ and $I = 01$ are the most similar genomes to $I = 11$ (as they both have one base in common with $I = 11$), whereas $I = 00$ is the least similar genome to $I = 11$ having no bases in common. Therefore, we assign high fitness to $I = 11$, medium fitness to $I = 10$ and $I = 01$, and low fitness to $I = 00$. Fitness scales exponentially with respect to the number of bases that two genomes have in common.

The fitness landscape is shown in figure 2*b*. The horizontal axis representing the genome space is reordered so that the fittest genome is located in the middle of the axis, and neighbour genomes to the fittest genomes are placed according to their degree of similarity to the fittest genomes.

Thus, the least similar genomes to the fittest genome are at the extremes of the axis. In this way, the system can be conveniently represented in a planar figure. The horizontal axis in figure 2*a* is reordered in the same way.

Simulations are initialized by randomly distributing $N = 10^4$ organisms in genome space, each organism possessing a genome $L = 7$ symbols long. A typical simulation output is shown in figure 2*a*, where we have used a colour scale in brown to denote genome abundances. As shown in the figure, at early times the organisms explore the genome space for a transient period, necessary to evolve their fitness due to beneficial point mutation and HGT. After a specific time (green dots), the population settles around the fittest genome and evolves, from that time onwards, by vertical descent (thick brown vertical line). In this phase, a large fraction of the progeny maintains the genome inherited from their parents for the characteristic timescale of evolution.

The rate of evolution is displayed in figure 2*c*, showing the total population fitness, $W = \sum_I W_I X_I$, as a function of time. By interpolating the markers, we find two regimes with different concavity. This provides a quantitative way for defining the Darwinian transition for this numerical experiment. Initially, the fitness is concave up, indicating that the system is accelerating towards states of high fitness (i.e. the rate of change of fitness is increasing over time). After the transition, the fitness is concave down and reaches a plateau. The Darwinian threshold can be defined as the inflection point of the interpolated curve.

Although the behaviour shown in figure 2*a* occurs for a large range of parameter values, several restrictions are in order to observe speciation. A high mutation rate, a low fitness peak for the fittest genome, or a (very) high degree of HGT make the progenote phase proceed indefinitely without the system stabilizing around the fittest genome. For a high mutation rate, the system undergoes an error-threshold catastrophe [32], as too many mutations counter selection, thus impeding vertical descent.

(d) Horizontal gene transfer leads the system to symmetry breaking

We now investigate the effect of HGT in a situation where a gene admits two equally good alleles. For this purpose, we choose a fitness landscape with two peaks: two genomes, respectively, $I = 00\ldots0$ and $I = 11\ldots1$ have high fitness, whereas the fitness of the other genomes depends on the shortest distance between the genome and the fittest genomes. The same formula of the previous section is used. For example, considering $L = 3$, genome $I = 001$ is closer to $I = 000$ rather than $I = 111$, so the distance between $I = 001$ and $I = 000$ is used.

To investigate the effects of HGT, we run a simulation without HGT (i.e. $h = 0$) and show the long-time behaviour in figure 3*a*. In the absence of HGT, the system develops approximately equal abundances of both A and B; for low HGT strength (figure 3*b*), the two alleles do not coexist simultaneously, but a metastable behaviour is exhibited; for high HGT (figure 3*c*), the system becomes rich in a single allele.

4. Conclusion

In this paper, we have argued that it makes sense to consider models of living systems that are independent of the chemical substrate on which they are implemented. We have alluded to the two primary unifying features of all known life, the universality and near-optimal error-minimizing aspects of the genetic code and the presence of biological homochirality.

The characteristics of the genetic code, coupled with the rapidity by which the LUCA emerged, can all be accounted for, in principle, by assuming the existence of an earlier communal epoch of life in which HGT was rampant even among the components of core cellular functions such as the translation machinery [10]. Here, we have shown how this communal epoch would have come to a graceful end, without requiring any fine tuning or other extraneous mechanisms. Simply put, HGT ceases to be effective beyond a certain time, since there is nothing new to transfer. The resulting dynamics is then characterized purely by vertical evolution of the core cellular

functions, leading to the possibility to define species and lineages, and permitting the phylogeny and evolutionary trajectory of organisms to be tracked.

In summary, we have argued that those features, which are universal across all life on the Earth, are universal not because they are special to Earth systems, but because they are universal aspects of all living systems.

Data accessibility. This article has no supporting data.

Authors' contributions. All authors wrote the paper. N.G. and T.B. conceived and executed the study on the Darwinian transition. Computer simulations were programmed by T.B. All authors gave final approval for publication.

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References

1. Langton CG. 1989 *Artificial life: proceedings of an interdisciplinary workshop on the synthesis and simulation of living systems*. Reading, MA: Addison-Wesley Longman Publishing Co Inc.
2. Turing AM. 1937 On computable numbers, with an application to the Entscheidungsproblem. *Proc. Lond. Math. Soc.* **2**, 230–265. (doi:10.1112/plms/s2-42.1.230)
3. Von Neumann J. 1956 Probabilistic logics and the synthesis of reliable organisms from unreliable components. *Automata Stud.* **34**, 43–98. (doi:10.1515/9781400882618-003)
4. Von Neumann J 2012 *The computer and the brain*. New Haven, CT: Yale University Press. See forward by R. Kurzweil.
5. Jafarpour F, Biancalani T, Goldenfeld N. 2015 Noise-induced mechanism for biological homochirality of early life self-replicators. *Phys. Rev. Lett.* **115**, 158101. (doi:10.1103/PhysRevLett.115.158101)
6. Branscomb E, Biancalani T, Goldenfeld N, Russell M. 2017 Escapement mechanisms and the conversion of disequilibria; the engines of creation. *Phys. Rep.* **677**, 1–60. (doi:10.1016/j.physrep.2017.02.001)
7. Landauer R. 1961 Irreversibility and heat generation in the computing process. *IBM J. Res. Dev.* **5**, 183–191. (doi:10.1147/rd.53.0183)
8. Koonin EV, Novozhilov AS. 2009 Origin and evolution of the genetic code: the universal enigma. *IUBMB Life* **61**, 99–111. (doi:10.1002/iub.146)
9. Saito Y, Hyuga H. 2013 Homochirality: symmetry breaking in systems driven far from equilibrium. *Rev. Mod. Phys.* **85**, 603–621. (doi:10.1103/RevModPhys.85.603)
10. Vetsigian K, Woese C, Goldenfeld N. 2006 Collective evolution and the genetic code. *Proc. Natl Acad. Sci. USA* **103**, 10 696–10 701. (doi:10.1073/pnas.0603780103)
11. Goldenfeld N, Woese C. 2007 Biology's next revolution. *Nature* **445**, 369–369. (doi:10.1038/445369a)
12. Jafarpour F, Biancalani T, Goldenfeld N. 2017 Noise-induced symmetry breaking far from equilibrium and the emergence of biological homochirality. *Phys. Rev. E* **95**, 032407. (doi:10.1103/PhysRevE.95.032407)
13. Woese CR, Fox GE. 1977 Phylogenetic structure of the prokaryotic domain: the primary kingdoms. *Proc. Natl Acad. Sci. USA* **74**, 5088–5090. (doi:10.1073/pnas.74.11.5088)
14. Pace NR, Sapp J, Goldenfeld N. 2012 Phylogeny and beyond: scientific, historical, and conceptual significance of the first tree of life. *Proc. Natl Acad. Sci. USA* **109**, 1011–1018. (doi:10.1073/pnas.1109716109)
15. Woese CR, Fox GE. 1977 The concept of cellular evolution. *J. Mol. Evol.* **10**, 1–6. (doi:10.1007/BF01796132)
16. Swart EC, Serra V, Petroni G, Nowacki M. 2016 Genetic codes with no dedicated stop codon: context-dependent translation termination. *Cell* **166**, 691–702. (doi:10.1016/j.cell.2016.06.020)
17. Knight RD, Freeland SJ, Landweber LF. 2001 Rewiring the keyboard: evolvability of the genetic code. *Nat. Rev. Genet.* **2**, 49–58. (doi:10.1038/35047500)
18. Sengupta S, Higgs PG. 2015 Pathways of genetic code evolution in ancient and modern organisms. *J. Mol. Evol.* **80**, 229–243. (doi:10.1007/s00239-015-9686-8)

19. Woese CR. 1965 On the evolution of the genetic code. *Proc. Natl Acad. Sci. USA* **54**, 1546–1552. (doi:10.1073/pnas.54.6.1546)
20. Alff-Steinberger C. 1969 The genetic code and error transmission. *Proc. Natl Acad. Sci. USA* **64**, 584–591. (doi:10.1073/pnas.64.2.584)
21. Haig D, Hurst LD. 1991 A quantitative measure of error minimization in the genetic code. *J. Mol. Evol.* **33**, 412–417. (doi:10.1007/BF02103132)
22. Goldman N. 1993 Further results on error minimization in the genetic code. *J. Mol. Evol.* **37**, 662–664. (doi:10.1007/BF00182752)
23. Freeland SJ, Hurst LD. 1998 The genetic code is one in a million. *J. Mol. Evol.* **47**, 238–248. (doi:10.1007/PL00006381)
24. Ardell DH. 1998 On error minimization in a sequential origin of the standard genetic code. *J. Mol. Evol.* **47**, 1–13. (doi:10.1007/PL00006356)
25. Freeland SJ, Knight RD, Landweber LF, Hurst LD. 2000 Early fixation of an optimal genetic code. *Mol. Biol. Evol.* **17**, 511–518. (doi:10.1093/oxfordjournals.molbev.a026331)
26. Butler T, Goldenfeld N, Mathew D, Luthey-Schulten Z. 2009 Extreme genetic code optimality from a molecular dynamics calculation of amino acid polar requirement. *Phys. Rev. E* **79**, 060901. (doi:10.1103/PhysRevE.79.060901)
27. Crick FH. 1968 The origin of the genetic code. *J. Mol. Biol.* **38**, 367–379. (doi:10.1016/0022-2836(68)90392-6)
28. Szathmáry E. 2015 Toward major evolutionary transitions theory 2.0. *Proc. Natl Acad. Sci. USA* **112**, 10 104–10 111. (doi:10.1073/pnas.1421398112)
29. Doolittle WF. 2000 Uprooting the tree of life. *Sci. Am.* **282**, 90–95. (doi:10.1038/scientificamerican0200-90)
30. Woese CR. 2002 On the evolution of cells. *Proc. Natl Acad. Sci. USA* **99**, 8742–8747. (doi:10.1073/pnas.132266999)
31. Cohen E, Kessler DA, Levine H. 2005 Recombination dramatically speeds up evolution of finite populations. *Phys. Rev. Lett.* **94**, 098102. (doi:10.1103/PhysRevLett.94.098102)
32. Jain K, Krug J. 2007 Adaptation in simple and complex fitness landscapes. In *Structural approaches to sequence evolution* (eds U Bastolla, M Porto, HE Roman, M Vendruscolo), pp. 299–339. Berlin, Germany: Springer. (doi:10.1007/978-3-540-35306-5_14)
33. Park JM, Deem MW. 2007 Phase diagrams of quasispecies theory with recombination and horizontal gene transfer. *Phys. Rev. Lett.* **98**, 058101. (doi:10.1103/PhysRevLett.98.058101)
34. Vogan AA, Higgs PG. 2011 The advantages and disadvantages of horizontal gene transfer and the emergence of the first species. *Biol. Direct* **6**, 1. (doi:10.1186/1745-6150-6-1)
35. Arnoldt H, Strogatz SH, Timme M. 2015 Toward the Darwinian transition: switching between distributed and speciated states in a simple model of early life. *Phys. Rev. E* **92**, 052909. (doi:10.1103/PhysRevE.92.052909)
36. Gillespie DT. 1977 Exact stochastic simulation of coupled chemical reactions. *J. Phys. Chem.* **81**, 2340–2361. (doi:10.1021/j100540a008)