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On disagreements of theories of evolution

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ABSTRACT

Several theories of evolution have been developed since the initial work of Charles Darwin. Some are more gene-centric, while others argue for populations/species as the main units of selection. The overall picture is further complicated by the debates about the main driving forces behind the evolution processes. This has led to the formulation of Modern synthesis, Extended evolution synthesis, Selfish gene, Carcino-Evo, and Genome chaos theories, to name a few. While seen by many as contradicting and even mutually exclusive, I believe all these theories are in fact complementary. In this manuscript, I present arguments for looking at all of the above theories as various representations of an overarching motive that in fact makes them part of a fractal picture of evolutionary mechanisms and processes.

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Introduction

Confusion is a word we have invented for an order which is not understood. Henry Miller

Soon after Charles Darwin published his pivotal work 'On the Origin of Species' [1] various authors produced complementary evidence that resulted in the need for further development of the initial idea. Darwin himself worked on the expansion and improvement in the later editions of his original publication [2], trying to accommodate such new evidence. This coincided with Mendel's pivotal work [3] that was rediscovered some 35 years later [4]. By expansion of Mendel's theory, it became clear that genes can play a key role in the evolution of species. This initiated the debate about the specific role of the then newly discovered discriminant hereditary elements ('factors' in Mendel's terms) that were seen as determining individual organisms' properties in the large-timescale evolution processes. The concept that an organism by itself is not able to evolve (as it is born with a specific set of alleles that could not change during its lifetime) led to the idea that the smallest unit of evolution would be a population as a group of organisms that can exchange alleles and thus produce novel combinations that can, in turn, be subjected to selection.

As outlined by Bak et al. [5], in biology, Darwin's thoughts about evolution are always referred to as a theory, even though it is only a verbal characterization of some general observations rather than a mathematical expression of a general rule. When theories are expressed verbally, the confrontation with facts is cumbersome and leaves space for endless discussions among experts as to what constitutes the better description. The matter gets even more complicated as sometimes the experimental observation itself, without any condensation into more general principles, is viewed as a theory [5]. This leaves the debate open as to what exactly the Evolution theory consists of. The debate ensues as it is rooted in the fact that the evolutionary explanations are historical; they explain our observations on how populations or lineages change in particular ways (or remain the same) over time [6]. In general, these explanations are based on the observations of long-term (predominantly paleontological) changes in species. Still, they are limited by the fact that only partial evidence of these changes is available, and much is left to speculation about what the missing pieces might have been. With later discoveries, some of these missing pieces are gradually filled, but every so often that requires re-adjustment of the

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overall view of how the evolution of particular lineage(s) unfolded. All this leads to the current understanding that the evolutionary process is incredibly complex as its explanation requires integrating the internal (to the organism/population) and external (environmental) driving forces. This complexity makes it almost obligatory for a particular scholar to make a choice which of its multiple components to study.

Consequently, various approaches appeared to generalize or formalize the initial concept of Darwin so that they could expand together with the evolving understanding of what an individual/species is. One of the earlier such attempts was the so-called Modern Synthesis theory which refers to the early to mid-XX century formulation of evolutionary theory that harmonized classical Darwinian concept with a newer population-oriented view of Mendelian genetics [7]. Even as Modern synthesis tried to integrate existing knowledge it proved incapable of covering the entire spectrum of evidence getting accumulated. In evolutionary biology, it was therefore followed by the emergence of the Extended Evolutionary Synthesis (EES) [8]. The EES seeks to expand our understanding of evolution by considering additional mechanisms beyond just genes and selection. It recognizes that heredity is not solely determined by genes and acknowledges the role of epigenetics, cultural transmission, and other non-genetic factors in shaping evolution. For example, an explanation of the evolution of 'domestication syndrome' traits within the EES framework would include environmental variation (including the results of niche-constructing activities by the organisms themselves), and evolutionary changes to the genetic and epigenetic architecture, together with the developmental responses, as well as any extra-genetic channels of inheritance that result in changes in selection pressures [9]. The same authors noted, however, that these detailed dependency relations are easily disrupted. They are more sensitive to changes in background conditions and changes to values of *explanans* variables (i.e. in developmental processes) therefore making the resulting explanation more difficult to achieve. Conversely, the explanation provided by more traditional gene-centric theories is more stable because it enables inferences to more counterfactual situations without breaking the dependency relation.

The evolving context

Vermeij [10], further elaborated by Judson [11], argues that the history of life appears as an ecological arrow of time. In their view, the world's ecosystems have been restructured over time, as high-energy,

high-impact keystone species replace those with lower energetic needs and consequently a lighter impact on the environment. The relationship between high-energy and low-energy species appears asymmetric as high-energy species tend to have a higher impact on the ecological niches, thus exerting a higher effect on low-impact species. So, in their model, the pace of life increases over time although one can easily find exceptions and examples of ecological niches where such processes appear stalled [11–14].

Gould, on the other hand, has articulated an influential alternative framework – his model of 'passive diffusion from the left wall' [15]. He accepts that, in some sense, life's history is directional as the complexity of the most complex organism extant tends to increase over time. This trend is a consequence of life's simple origins, and of the fact that while there is no maximum bound on an organism's complexity, there is a lower one. In such circumstances, many specific histories of origin and extinction, each different from and often independent of one another, will tend to sum to a trend of increasing maxima. For each data point, a casual explanation can be found, but for the entire sequence no unified history can be devised [12]. This is further supported by the growing accumulation of data that demonstrate the omnipresence of horizontal gene transfer which cannot be dismissed as trivial in extent or limited to special categories of genes [16].

While trying to explain the observations from the paleontological record, Gould has arrived at the idea that evolution happens in a 'punctuated equilibrium' manner [17]. In this context, he advocated the crucial importance of the vagaries of a chaotic environment thus putting *species* as the main unit of evolution. Elaborating on the idea Buldyrev speculates that evolution goes as a punctuated equilibrium because an extinction of a stable species causes a gigantic extinction of many other species that have been well adapted to the environment the key species both inhabited and shaped [18]. Heng [19], working with (pre)malignant cells provided further evidence that the evolutionary processes happen in a 'punctuated equilibrium' manner at the cellular/tissue level in multicellular organisms. He further argued that these individual cell lineages with evolved properties meet all the criteria of being new species [20].

All these ideas are based on the concept that the *species* is something well-defined, which it is not [19,21] as no universal definition of species captures the multitude of mechanisms by which groups of organisms differentiate and diversify [22]. In an attempt to overcome this problem, Dawkins [23], for example, advocated a more gene-centric view of evolutionary

processes where genes are seen as selfish elements driving evolution through their struggle to self-replicate. It was recently shown, however, that most genetic sites experience varying selection, with an average effect close to zero, indicating little consistent selection pressure over different times and selection spread across many genomic regions [24]. This view has its further limitations as it can hardly accommodate most of the newest epigenetic modes and factors of inheritance even with the latest amendments to the concept [25]. As a result, the gene-centric view on the smallest unit of selection has difficulties explaining major events in evolution – sudden explosions in species diversity happening at various points in Earth's history, followed by prolonged periods of gradual evolution – that the 'punctuated equilibrium' concept accommodates better.

As the epigenetic drivers attracted more and more attention several researchers [19,26–28] used their studies of cancer cells and tissues to establish the importance of the 3D structures and overall genome organization in preserving and transmitting genetic information, thus making a strong case for the epigenetic principles of evolution [29]. As one can see, looking at the *explanans* and the *explanandum* from various scale perspectives produces different evolution theories. All of them struggle with the problem of scalability and below I will try to outline the main reasons for that.

Fractals as re-appearing patterns in the physical and biological realms

'A fractal ... exhibits self-similarity or pattern integrity—the retention of copies of itself on a hierarchy of scales' [30,31]. Such patterns are frequently observed in physical and biological realms [30] and have attracted the attention of many scholars, including evolutionary scientists. Gould himself seems to have considered the idea of the fractality of life and of the evolutionary forces that ensure its survivability. In his book [15] he states (p. 149): 'We live in a fractal world of "self-similarity," where local and limited cases may have the same structure as examples at the largest scale, I shall then argue that this particular case for the smallest of all fossils – single-celled creatures of the oceanic plankton – presents a structure and explanation identical with an appropriate account for the entire history of life'.

As one starts to elaborate further on the idea of fractality, inevitable expansions to processes at molecular, atomic, and sub-atomic levels ensue. To that end, England et al. [32,33] speculate that self-organization

is a natural phenomenon as complex systems can draw on energy from the environment, expending energy to temporarily decrease their own entropy. Kinetically stable behaviors of such systems are biased toward appearing to be finely tuned to the external drive, which means that they are a result of selection at molecular level. That also means that they are subject to evolutionary forces as the systems can change (evolve) in response to changes in the external driving force(s). This makes such systems meeting one of the crucial elements of the evolutionary definition of life [34,35].

Electrons within living matter, unlike electrons in plasmas, play a key role in building, sustaining, and shaping metastable and increasingly longer-lived macromolecular and higher-order structures. In the context of developing living matter, these structures act essentially as memories (old and/or continuously reproduced structures and behaviors) and ideas (new structures and behaviors), which allow for and facilitate the expansion of living matter in space and time utilizing biological evolution and self-organization [36]. This is also captured by the concept of self-organized criticality [5] where living matter tends to spontaneously achieve and maintain criticality, which is, incidentally, reflected in the fractal organization (a signature of a critical state) pervading all levels of biological organizational hierarchy [37]. Denton and his co-workers argue that even though numerous subcellular processes reflect the sculpting influence of natural selection, the core order at such scales necessarily reflects self-organization and physical law because it is this that directly determines the behavior and arrangement of atoms and molecules [38]. For example, any native protein structure exists in solution as a population of interconverting conformational states that are separated by energy barriers of varying heights. The latter defines the probabilities and thus rates of these state changes. The ones that happen on timescales of microseconds and slower usually correspond to large-scale (domain) motions within the protein structure. Such motions are relatively rare and might severely affect the main function of the protein concerned [39].

Similarly, the DNA sequences treated as sequences of letters have certain fractal properties [40]. At the molecular level, the geometrical packing of DNA in a cell resembles a self-similar structure with at least 6 levels of packing: a turn of the double helix (10bp), a nucleosome (200bp), a unit of 30nm fiber (6 nucleosomes), a loop domain (≈ 100 units of 30nm fiber), a turn of a metaphase chromosome (≈ 100 loop domains), a metaphase chromosome (≈ 100 turns).

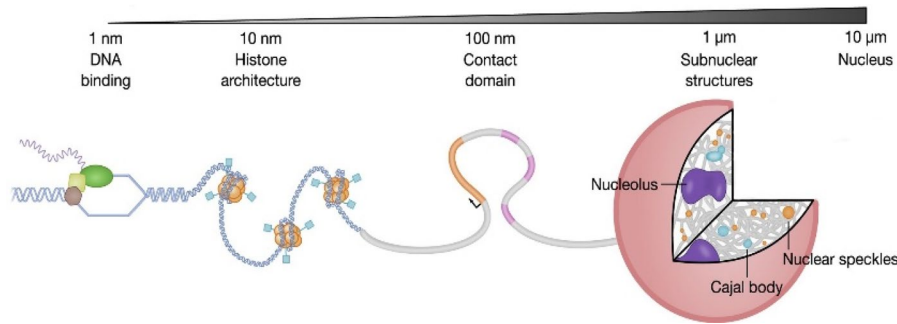


Figure 1. Scales of chromatin structure and organization. With modification from [39].

This structure however is not a rigorous fractal, because the packing of the units on different levels follows different organizational principles [18] over the five orders of magnitude of chromatin organization [41] (Figure 1).

Going one level higher, at the organellar level of organization within cells criticality and percolation are also key characteristics of mitochondria which have been shown to operate as systems in shifting critical states (i.e. close to chaotic behavior) that often undergo sharp phase transitions [42,43].

At the same scale, organizational properties of eukaryotic genomes affect cellular functions by nongenetic means through their physical and structural properties. That this leads to the recognition of fractality at play can be identified in the concept of Benett of the 'nucleotype' which describes those conditions of the nucleus that affect the phenotype independently of the informational content of the DNA [44]. The concept is based on the realization that genome size varies greatly between eukaryotes and shows many strikingly precise correlations with phenotypic characters, independent of information encoded in DNA. This is one of the pivotal works that emphasized the overall 3-D structure of the genome as possessing some critical functional significance, essential for development and evolution [45]. Others [46–48] also noted that besides its genetic roles, the genome affects cellular functions by nongenetic means through its physical and structural properties. We should note, however, that different authors paid attention to alternate aspects of these properties with Bustin and Misteli [46] focused on the mechanical forces genomes exert and their role as a scaffold for binding cellular components. Solovei, on the other hand, studied the effects of chromatin reorganization on the physical (optical) properties of the nucleus [47]. As was explained above, Heng [49,50] has greatly expanded the concept of the karyotype as a whole carrying essential information and thus playing crucial role in evolution. He and his colleagues identified both 3D organization

of the genome and the structural re-arrangements within the chromosomes as carriers of essential non-genic information that affects the outcomes of cell fate. Due to the spontaneous and radical re-arrangements of the entire genomes that are observed at the onset of cancerous development that seem to obey no specific rule they named their theory 'Genome Chaos theory'. What was apparently overlooked in that theory is that fractals play a significant role in describing chaotic systems [51]. Similar properties can be found in the organization patterns of prokaryotic cells where periodic oscillatory growth initiates suddenly when biofilms reach a critical size [52–54].

If we take the next level of organization as integrated multicellular structures (tissues), fractal patterns can be found to appear as these tissues evolve from normal to cancerous [55]. It is also demonstrated that in embryogenesis the evolution of cells to specific tissue types is guided by mechanical forces [56] thus bridging the molecular with cellular level interactions that result in fractal patterns. From the first cell fate bifurcation during blastulation to the complex symmetry breaking and tissue remodeling in gastrulation, mechanical cues appear critical in cell fate decisions and tissue patterning [56]. Recognition of these interactions between the physical forces (often exercised by specific molecules) and all levels of developmental biology analysis from transcription to morphogenesis results in initial attempts to explain in physical terms how the genome controls the dynamic behavior of each cell in a developing embryo [57].

As we go one more level up, when modeling living organisms, i.e. sexually reproducing populations composed of individuals represented by diploid genomes, similar behavior was observed - alleles of different activities complement each other fulfilling the environment requirements and populations evolve in the direction of a very restricted number of complementing haplotypes [58] thus presenting fractal patterns. At a larger scale, fractal connectivity can be identified

among the multiscale multispecies networks of landscape habitats [31].

All of the above is a demonstration of fractality that I argue underlies the evolution of every system, no matter its scale: from (sub)atomic, through molecular, cellular, tissue/organ, organism, population, to the planetary, galactical, and Universe as a whole.

However, to better understand why this is not already a universally accepted concept, we should remind ourselves that in the physical world that we inhabit, no perfect fractal is present as opposed to the purely mathematical abstraction. 'Strict fractal objects require infinite power-law scaling, which fails to address the limited range of scale invariance observed in nature' [59]. This can be easily understood as we consider the lower limits of structures we study (sub-atomic particles) and that at the largest possible scale (the Universe) the fractality is also broken [60,61]. This means that on both the smallest and largest cosmic scales, the Universe is not fractal-like at all and that only the intermediate scales have any chance of exhibiting fractal-like behavior [61,62]. This has a major implication on the use of the concept of fractality for the explanation of evolution – in the natural world fractals are always limited both to the upper and the lower ends.

There is one more major constraint on the use of fractals in evolution theories and it is that in fractals the fundamental characteristic of being differentiable is missing. Therefore, even in these intermediate scales it is a challenging problem to define operators on fractal sets [63] that could be considered driving forces for the evolutionary process at a given scale. This means that the evolutionary driver(s) can be identified but cannot be singled out at any scale. Some could appear of higher prevalence at smaller scales, while others – at higher, with all possible overlappings also at play in different time and space frameworks. Because of all this various authors that tend to focus their efforts on different scales have trouble achieving broad theoretical explanations that can cover multiple scales as difficulty arises in defining both the selection unit and major drivers [8,22,64–66] with these simultaneously appearing effects at different levels. My understanding is that all this complexity arises from the many imperfect fractals, discussed above, overlapping both in space and time, that underlie evolutionary processes at various scales. This has led to the idea of multilevel selection acting on organisms, populations, and species [67]. Attempts at defining them are omnipresent in evolution theory literature ultimately leading to the concept of 'interactors' [68–70].

Where does all this come from?

As highlighted by Biasuz et al. [57], over the past 25 years, technological breakthroughs in live imaging, sequencing, proteomics, and physical measurements have spurred a period of intense discovery of the parts that constitute the living matter, of their concentrations and localization in cells, and of their interactions. However, our brains simply cannot cope with the sheer volume of the data produced, which is further complicated by the fact that large volumes of data might be irrelevant to the processes studied. Furthermore, biology involves multiple layers of feedback that lie at the origin of unintuitive non-linear behaviors. For example, within tissues and cell lines, cells adopt different states of chromatin organization. Taken together, and embedded in the right environment, the genome, protein products, and the gene expression machinery act as a self-organized interactive information and materials processing system that not only reproduces a very complex system, and operates it during its lifecycle, but also thereby generates far more complex information – structure – than the genes alone can account for [71]. We are not yet sure how exactly this works as gaps remain in our understanding of how heterogeneity of chromatin states varies across populations dynamically [41]. This means that in biology processes are multiscale where the macroscopic properties of cells and tissues emerge from the mesoscopic properties of molecules or subcellular structures [57].

Examples of interaction at different levels could be seen with cases where nuclear genome doubling affects cytonuclear interactions because of all of the cascading scaling issues that can influence gene expression [72]. Many effects that were predicted and even supported by early studies of individual genes have not emerged as generalities as more genome-wide data is accumulated. Furthermore, perturbations to cytonuclear stoichiometry appear to be ameliorated by developmental, growth, and regulatory responses that stabilize at least some aspects of cytonuclear gene balance even upon allopolyploidy formation [73].

Because of all of the complexities described above, Biasuz et al. [57] pointed out that non-equilibrium features of biological tissues are often treated under a quasi-static approximation within certain limits on both timescale and spatial extension of observation. This greatly simplifies the theoretical analysis of biological processes but restricts the applicability of such analyses to small temporal and spatial scales [57].

Jost [74] takes an insightful approach to resolving this by postulating that the key feature of biological life is that a biological process is defined by its ability

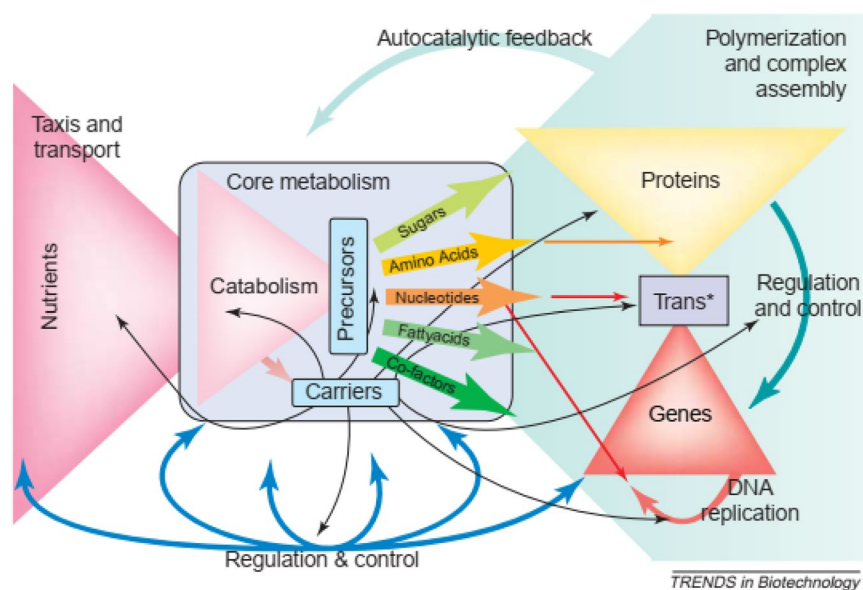


Figure 2. The nested bow-tie architectures of metabolism input a wide range of nutrients and produce a large variety of products and complex macromolecules using a relatively few intermediate common currencies. This architecture uses selective homogeneity at the knot to facilitate control, organization and management of the enormous heterogeneity in enzyme specificity, action and regulation, and in substrate size, flux and concentration. All modern technologies, from manufacturing to the power grid to the internet, are organized with bow ties. With permission and modification from Csete and Doyle [17].

to control and regulate other processes and maintains that ability over time. This can be detected in the functioning of a well-known motif at play in the architecture of complex systems, the so-called 'bow-tie' [75]. In general, this a functional system that can take into account a great diversity of inputs (fanning into the knot of the bow tie – Figure 2), process them with much smaller diversity in the protocols (the central part of the knot) to elaborate these inputs, and produce a wide diversity of outputs (fanning out of the bow tie) [71].

While resource efficient, its functioning is extremely difficult to dissect in detail as minor input(s) modifications can result in major changes in the outcome(s). This means that the same system (defined by the genetic information encoding for the functional units) will produce substantially different results in different environments. These environments could be different cell types, physiological conditions, developmental stages, etc. Lloyd [70], for example, emphasized the necessity of considering biological facts from the subcellular and allelic level up to the population level when evaluating the appropriateness and adequacy of population genetic models. When describing the biological objects involved in population genetic models, for which the parameters are specified or derived, they demonstrated that whether a model includes or omits parameters can have decisive consequences for its representational adequacy [70].

Providing further evidence of such complex machinery at work, Majérus [76] advocates that cells can be re-directed to produce either normal development or induce a conversion to malignant type based on the same genetic background, but subjected to different environments (stimuli). Having in mind the substantial work done by Heng [21,77] to provide evidence that these malignant cells are in fact new species, it becomes straightforward to conclude that ultimately, it's the interplay of all of the genetic and environmental factors that defines the evolution of any system.

And because the living systems are in fact non-equilibrium systems one should be reminded that the striking complexity that exists in both living and non-living systems is measured by their fractal dimension [78,79]. It is even argued that the phenomenon of consciousness may also have something to do with the interactions and collective self-organization of electronic states that are spread over, bind, and coordinate individual parts within and across scales into a multiscale self-conscious whole [37]. At the next level of societal organization online social networks have been proposed to display self-organizing criticality and the emergence of new functional properties and fractality.

As was already discussed [31], the value of the scaling exponent of the number-size relationship may vary widely, and the power-law scaling only holds over a finite range of time scales in real landscapes [80]. Adding to all this that most ecological patterns and

processes show scaling thresholds at which abrupt changes in scaling relationships occur, fractal fragmentation appears corresponding to shifts in underlying mechanisms [81]. This is also one of the reasons why the attempts to generalize based on a single (or a limited few) scale(s) bring so many exceptions that still make the appearance of unified evolution theory so difficult.

We should reflect on all of the above in the context of what was already discussed in brief – that there are no rigorous fractals in biology. First, in the physical world there are always lower and upper cutoffs of fractal behavior. This is due to the obvious fact that the physical particles (be it atoms or subatomic particles) are the smallest acting units thus also acting as the lower limit of fractality. At the upper limit, specific fractals are broken at the boundaries of a given environment to be replaced by the next fractal(s). Furthermore, it has been demonstrated that for hierarchical structures such as trees and lungs, in addition to the obvious lower and upper physical scale cutoffs, the branching pattern has a temporal dimension as it changes from one generation to the next [18]. As a result, it appears that biological networks are canonically ‘scale-free’ and are defined by the presence of long-range, power-law correlations arising from multi-fractal connectedness operating over multiple spatial and temporal scales [54]. Analyzed at any scale, self-organization is present at all levels of biology, which mirrors the ubiquity of self-organization in the non-biological world. In both worlds and at any scale self-organized systems that are supercritical (branching ratio >1) in limiting environments are driven back to critical-like states in limiting environments (branching ratio >1) are forced back to critical-like states (branching ratios ~ 1) which process provides a fractal-like template on which natural selection acts [59]. What makes this idea difficult to apply is that strict fractal objects have infinite power law scaling [82], which restricts the utility of the concept [83]. Such fractals fail when the limited range of scale invariance observed in nature need to be represented. Existing living systems display fractal-like behavior that typically spans only 0.5–2 orders of magnitude, although some examples span larger ranges [60].

Where does all this lead to?

A thorough study of the broad range of evolution theories that currently exist shows remarkable similarity with the development of mathematical theory that generates new mathematical theories that consider the initial theory in its different aspects. Turchin [84],

therefore, emphasized that each of these theories is in a certain sense simpler than the initial theory, just as the initial theory is simpler than reality, which it always considers in some certain aspect. The models are dismembered and a set of simpler models is isolated from the complex one [84]. Turchin made the insightful transition recognizing that it is not the ‘substance’ of the entities being described that matters, but their principles of organization.

As we analyzed various evolution theories that are seen by many as contradicting and even mutually exclusive, in the context of the discussion above we can see that all these theories are actually complementary. Here we presented how these theories are in fact various representations of an overarching motive that makes them part of a fractal picture of evolutionary mechanisms and processes.

The entire field of evolution theories is ripe for a breakthrough as fractality and non-linearity are becoming more and more adopted as concepts to be internalized [85]. The development of a unified theory (and its possible formalization) will require further collaborative efforts of biologists, mathematicians and philosophers and I sincerely hope this effort of mine can contribute to bringing them together to produce this much needed and long-expected outcome.

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Data availability statement

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