The universal principles of self-organization and the unity of Nature and knowledge

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It is argued that diverse complex adaptive systems, such as proteins, cells, organisms, organizations, societies and ecosystems, all together constitute one developing, multiscale continuum-economy composed of interacting and interdependent adaptive organizational forms that co-exist and co-evolve at different spatiotemporal scales, forming a nested set of interdependent organizational hierarchies. When reconceptualized in equivalent terms of self-organizing adaptive networks of energy/matter/information exchanges, complex systems of different scales appear to exhibit universal scale-invariant patterns in their organization and dynamics, suggesting the self-similarity of spatiotemporal scales and fractal organization of the living matter continuum.

The self-organization of biomolecules into cells, cells into organisms and organisms into societies and ecosystems is presented here in terms of a universal scale-invariant organizational process driven by economy and assisted by memory and innovation. It is driven by economy as individual adaptive organizations compete and cooperate at every scale in their efforts to maximize the rate and efficiency of energy/matter/information extraction from their environments and the rate and efficiency of negative entropy production. Evolutionary memory, manifested as organizational structure balancing economic efficiency and adaptability, and innovation, manifested as stochastic generation of new organizational forms, facilitate economy-driven self-organization. Self-organization is proposed to be an ever-expanding process covering increasingly larger spatiotemporal scales through formation of interdependent organizational hierarchies. The process of self-organization blends Darwinian phases dominated by diversification, competition, and selection and organizational phases dominated by specialization, cooperation, and organization.

It is argued and illustrated that the self-similarity of spatiotemporal scales in the organization and dynamics of living matter can be exploited both for scientific discovery within specialized disciplines and the unification of individual sciences within one and the same conceptual framework of self-organization. This is achieved by 1) defining scale-invariant organizational concepts, patterns and measures; 2) reconceptualizing organizational phenomena of different scales in the same scale-invariant terms and 3) mapping the knowledge structures of different scales onto each other, using overlapping patterns for alignment, filling in missing parts, and re-structuring misaligned patterns on the assumption of spatiotemporal self-similarity of scales.

Keywords: self-organization; scale-invariant organization and dynamics; self-organizing fractal theory (SOFT); adaptation through organizational state transitions; innovation through stochasticity; structure as evolutionary memory; steady-state metastability; integration through moonlighting; inter-scale conceptual mapping; self-organization as cognition.

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Introduction

Descartes and Newton placed firm foundations for the emergence, development and success of modern sciences. The unsurpassed economic achievements of the Industrial Revolution ignited and fueled by Newtonian science have been matched by the increasing pressure of mechanistic instruction in professional training, education and in society at large. The mechanistic worldview and reductionism have rarely failed Western societies, economically speaking, and have eventually become unconscious operational defaults of the Western mind. We are compelled to interpret reality in mechanistic terms and to approach analysis of any phenomenon by taking it apart to ever-smaller pieces, studying pieces in isolation and deducing the underlying design. It is not surprising, therefore, that molecular and cell biology, where the greatest majority of studies are performed in the spirit of reverse engineering, came to be dominated by clockwork images of macromolecules, cells and organisms. “One of the acid tests of understanding an object is the ability to put it together from its component parts. Ultimately, molecular biologists will attempt to subject their understanding of cell structure and function to this sort of test by trying to synthesize a cell” [1].

Disconcertingly, even a cursory overview of accumulated research literature strongly suggests that familiar and appealing mechanistic concepts and interpretations have become manifestly inconsistent with experimental reality at all scales of biological organization, from macromolecules through sub-cellular organization and individual cells to whole organisms, thus suggesting a systemic crisis of the mechanistic paradigm and reductionism in life sciences [2-5]. The classico-mechanistic conceptualization, when applied to biological phenomena, appears to have evolved from an insufficient but convenient analogy to the mental block that precludes understanding and adequate modeling of living systems [5].

In the search for alternative conceptualizations of biological complexity, stochasticity as a general principle of differentiation and adaptation, and self-organization as a concept of emergence, were suggested as the core of an emerging interpretational framework promising to unite phenomena across different scales of biological organization, from molecules to societies [3,6,7]. The conceptual framework of self-organization was used to rationalize and explain a variety of otherwise paradoxical experimental observations pertaining to molecular motors and protein translocation [4], sub-cellular organization [2,6], stochasticity in gene expression, cell plasticity, organism development and other biological phenomena [3,8,9]. Expanding the paradigm of self-organization, such concepts as evolutionary memory, bounded stochasticity and adaptive plasticity were recently introduced to resolve a contradiction between the inherent ambiguity of molecular recognition and the apparent specificity and order observed in intracellular signaling and metabolic conversions [7].

Unlike mechanistic interpretations, emerging concepts of self-organization appear to be consistent with experimental reality at all scales of biological organization and are universally meaningful whether one speaks about biomolecules, sub-cellular structures, cells, organisms or social and business organizations, and whether one considers phylogenetic or ontogenetic time scales. In other words, the concepts of self-organization appear to be scale-invariant, suggesting that they may reflect certain universal attributes common to diverse complex phenomena taking place at different spatiotemporal scales. The universality of organizational patterns across scales of biological complexity becomes especially apparent when complex phenomena/systems of different scales, such as proteins, cells, organisms, ecosystems, organizations, societies and economies, are reconceptualized in equivalent terms of self-organizing adaptive networks of energy/matter/information exchanges [10-13].

It is argued in this essay that the apparent self-similarity of scales in biological (broadly defined) systems is a consequence of the unity and fractality of living matter, which exists and evolves in reality as one dynamic multiscale organization/continuum of intelligence composed of the interdependent and mutually defining/morphing adaptive organizational forms of energy/matter/information exchanges manifested as biomolecules, cells, organisms, ecosystems, organizations, societies and so forth. It is only the culturally acquired habit of misconceptualizing living matter in mechanistic terms that makes biomolecules, cells, organisms, ecosystems, organizations and societies *to appear* to the reductionist mind of the human observer as if they were isolated, self-defined, standardized and interchangeable systems of the mechanistic type, designed for some purpose, i.e. as parts of the Machine.

It is suggested that the development and expansion of the continuum of living matter proceeds through the process of self-organization driven by economic competition and facilitated by memory and stochasticity/innovation. The economic competition between alternative organizational forms is resolved to the common benefit of surviving competitors through cooperation, specialization, organization and formation of self-affine organizational hierarchies.

The arguments and discussion presented are intentionally kept qualitative and descriptive. However, references are made to the quantitative frameworks that are in place to step in. Fractality is qualitatively defined as similarity of the spatial and/or temporal organizational patterns reproduced again and again at different scales of space and/or time. Fractality is presented and used as a form of symmetry, i.e. as the invariance of a pattern/form in relation to scaling.

It is demonstrated that scale invariance of the organizational patterns underlying complex adaptive phenomena of different scales can be exploited for scientific discovery by 1) reconceptualizing diverse complex phenomena in the same conceptual terms of self-organization, 2) mapping the specific knowledge structures developed within specialized disciplines onto each other and 3) filling in the gaps in the aligned knowledge structures and re-structuring misaligned parts on the assumption of spatiotemporal self-similarity of scales.

The reconceptualization of biological and other phenomena within the framework of self-organization is unavoidably contrasted with familiar textbook images of the same phenomena, which, for the most part, are products of the mechanistic interpretation of living matter and which reside in our unconscious as unquestioned and often unquestionable defaults and assumptions. As the conventional and habitual tend to acquire the quality of faith and relative independence from reality with time, the experimental evidence inconsistent with conventional mechanistic interpretations but supporting the conceptualization of biological and other phenomena in terms of self-organization is reviewed throughout the essay.

Because, as it is argued further, economic development and competition are at the heart of all self-organizational phenomena, let us begin our inquiry into the nature and causes of self-organization with a discussion of an unconventional theory dealing with the emergence, organization and evolution of the economy at the cellular scale known as cellular metabolism.

Metabolism: recruitment for evolution of new function

To explain the emergence of novel metabolic functions in the course of biological evolution without invoking the questionable assumptions required by the textbook model of retrograde evolution [14], such as availability and stability of intermediates in the backwardly evolving metabolic pathway, Jensen proposed the recruitment model of metabolism in 1976 [15], which was later extended by O'Brien and Herschlag [16]. According to the recruitment model, primitive cells possessing limited genetic information produced a small number of metabolic enzymes-generalists. These metabolic generalists exhibited both substrate ambiguity and catalytic promiscuity, and were largely unregulated. Such a state of affairs would entail poorly organized production of a variety of metabolites generated through biochemically diverse but inefficient metabolic sequences/pathways, which included both enzymatic and non-enzymatic steps. It is useful to visualize metabolic organization in terms of a network of chemical transformations. However slow and inefficient, any sequence of chemical transformations represents a potential metabolic pathway or a unique path probabilistically realized within a complex network of interconnected and interdependent chemical transformations, where nodes are metabolites and links are chemical reactions connecting a pair of metabolites. In such a stochastic network of chemical transformations operating inside a host cell there is a fair chance that some fortuitous combination of sequential non-enzymatic and/or enzyme-mediated chemical reactions would give rise to a metabolite that is valuable for the host cell in terms of the host's competitive advantage. Competition among primitive cells would enforce recruitment of enzymes to those biochemical steps and/or pathways that happened to generate valuable products for their hosts. In other words, enzymes-generalists are recruited to improve on the already pre-existing but slow and inefficient pathways, rather than creating them *de novo*. Employing the recruited generalists in larger numbers can boost the volume of useful production. Employing specialists rather than generalists can increase the efficiency with which valuable products are generated. Relatively specific and thus more efficient enzymatic activities may therefore have emerged via duplication and divergence of genes coding for those enzyme-generalists that proved to be useful for their host cells. This route to specialization, likely accompanied by division of labor and organization, is facilitated by the fact that in many cases a desired activity and/or specificity is already present in an ancestral enzyme-generalist and requires only accentuation rather than creation *de novo*. Notice the conceptual parallels between the emergence of a specific enzymatic activity and the emergence of a specific metabolic pathway - both of them (an activity and a pathway) are recruited for function from large (but bounded) stochastic sets of activities and pathways, correspondingly, because both of them confer competitive advantage to the higher order systems of which they are integral parts. Overall, the competition for limited resources among primitive cells and the selective pressure for metabolic efficiency drive the evolution of cellular metabolism from unorganized generalists to organized and regulated specialists.

All the basic tenets of the recruitment model are well supported by a large and continuously growing body of experimental evidence summarized in a number of excellent reviews [15-18]. One gene – one enzyme – one substrate – one product, until recently a staunch dogma born from the clockwork image of the cell and the "lock-and-key" paradigm of protein science, is now considered as an oversimplification at best, even by researchers trained in the dogma. Despite the facts that convincing demonstration of low level alternative enzymatic activities and specificities is experimentally challenging and that their existence does not fit well in the conventional image of biological specificity, and thus has never been addressed in a systematic manner, an ever-increasing number of modern enzymes are being reported to exhibit more than one activity and/or specificity [16,17,19]. "Although enzyme specificity has long been considered the hallmark of biological processes, evidence presented in the past few years indicates that the possibility of protein promiscuity may have been seriously overlooked, simply because it was never routinely addressed." [20]

It is important to emphasize that the commonly overlooked promiscuity in interactions is a property shared by all proteins to a lesser or greater degree. Contrary to familiar "lock-and-key"-type conventional images, a protein molecule in solution, unlike the same molecule in a crystal structure, exists as a dynamic ensemble of inter-converting conformers, and even hydrophobic cores of tightly folded proteins behave more like liquid rather than solid [21-23]. Single molecule studies necessitated the introduction of such notions as static and dynamic disorders, the former to reflect the fact that any population of seemingly identical (isogenic) protein molecules is always composed of different individuals and the latter to indicate the fact that the properties of the same individual molecule change over time [24,25]. Because a group of isogenic protein molecules always represents a differentially populated spectrum of inter-converting conformers, promiscuity is to be expected, with the degree of promiscuity being only a matter of distribution and dynamics of pre-existing populations of different conformers [22]. Within this image of molecular recognition, a binding site is not a static and given entity, and its identity is not defined in the absence of bound ligand [26].

Now consider active sites of enzymes, which represent highly reactive and dynamic chemical environments packed with nucleophiles, electrophiles, acids, bases, metal ions and cofactors, and where the same functional groups can play different roles in different enzymatic reactions [16,17]. Keeping in mind the dynamic nature of proteins in solution, it is easy to see that both catalytic promiscuity and substrate ambiguity should be a rule rather than an exception. In other words, substrate and catalytic specificities of a population of isogenic enzyme molecules are balanced somewhere between the rigid order of near-absolute selectivity and the chaos of unselective promiscuity. Obviously, different enzymes are likely to exhibit different degrees of ambiguity with respect to their substrates and the types of reactions they catalyze. It is also easy to see how relatively minor interventions, such as mutations, binding of cofactor or auxiliary protein, posttranslational modifications and others, may readily bias and/or restrict conformational dynamics of an enzyme, thus leading to reversible or irreversible "specialization" of the enzyme, manifested as catalytic and/or substrate specificity. Indeed, mutational analyses and protein-engineering experiments demonstrate that a new enzymatic activity and/or specificity can often be generated by nothing more drastic than a point mutation, often outside the active site [19,27-30].

The current views on global organization of metabolism together with a recent proposal to treat metabolism in probabilistic terms support Jensen's model [18,31]. Modern analytical technologies based on mass spectrometry are revealing the unexpected richness and diversity of metabolites and, by inference, of biotransformations maintained within any given organism [31,32]. It is proposed that the production of major metabolites simply reflects a high probability of the corresponding conversions, while multiple and diverse micrometabolites are generated by low-probability background biotransformations. "…If a metabolite is capable of being produced at all, it will be: it is merely the quantity that is in question." [18].

Adaptation to environment through stochasticity

It is useful to consider the recruitment model of metabolism in the context of the relationship between the cell and its environment - something that the reductionist mindset habitually neglects. The loose structures of ancestral metabolic networks together with the great molecular and pathway diversities they generated were most likely highly advantageous for primitive cells. Unlike many modern cells, which are born into the relatively stable and often structured environments created and maintained by their parents, primitive cells, by all accounts, faced survival and competition within highly dynamic and unstable milieus. Metabolic flexibility and adaptability were (and are) probably more important than metabolic efficiency in dynamic environments. Of note, modern business management manuals emphasize that the winning management strategy for business organizations competing in dynamic and rapidly changing markets involves continuous maintenance and exercise of organizational flexibility and adaptation, even if they come at the expense of production efficiency [33]. It is also worth noting that the evolution from a loosely structured and inefficient but very pliable metabolic network of primitive cells to a highly organized, tightly regulated and more efficient metabolic organization of modern complex cells comes at the expense of flexibility, and thus is more likely to occur in parallel with stabilization of the cellular environment. It is thus reasonable to suggest that, in the course of evolution, cells are forced either to seek and populate relatively stable/predictable environmental niches or to stabilize/control their environments through their actions, or to pursue both strategies simultaneously. Because the environment is usually large and powerful and cells are small and weak, those cell populations that discovered and capitalized on the advantages of communication, cooperation and collective action had significant competitive advantages over the cells unable or unwilling to communicate and to cooperate. Yet more advantages could be achieved through proper organization and management of collective actions, through the creation, maintenance, and protection of a collective habitat, through division of labor, and through formation of multicellular organizations of specialized and cooperating cells within a protected habitat and so forth.

It should be pointed out that metabolic adaptation by means of gene duplication and divergence is a genetic mechanism that may be too slow under many circumstances. It is, therefore, most likely reserved for adaptation to relatively slow changing aspects of the environment. One of the mechanisms used to cope with rapid change is epigenetic regulation. Both the specificity of metabolic channeling and the overall efficiency of metabolism can be greatly enhanced through organization/regulation of promiscuous enzymes, without necessarily making enzymes more specific. Such well-known regulatory mechanisms as inhibition by end product and activation by substrate, for example, can minimize dissipative effects of catalytic and substrate promiscuity [15]. In addition, spatial organization and management of enzymatic activities by means of clustering, scaffolding and/or through microcompartmentation may improve both specificity and efficiency of metabolic conversions [34-37]. The advantage of such higher hierarchy organization/management/control lies in its flexibility. Triggered by an environmental change, a rapid relaxation of the organization/regulation of metabolic enzymes would transiently increase frequencies of alternative chemical reactions catalyzed by temporarily deregulated promiscuous enzymes, thus leading to higher biochemical diversities of the metabolites produced and the alternative pathways explored in a search for solutions to the problems caused by the environmental change. Novel environmental conditions would be eventually matched by a new organizational state of metabolic network, achieved through recruitment/accentuation of beneficial pathways chosen among competing alternatives. Following beneficial reorganization of enzymatic activities and/or pathways, the pressure for metabolic efficiency would drive stabilization of the novel organizational state by re-establishing appropriate organization/controls. It is fair to suggest, therefore, that the adaptability of the network of interacting and interdependent chemical transformations that constitutes metabolism is based and relies on stochasticity of individual enzymes, while the organization, control and management of metabolism serve to improve its efficiency, often at the expense of flexibility.

In conditions of relatively stable environments, the pressure for metabolic efficiency forces the cell to constrain the inherent stochasticity of its metabolic reactions by establishing the higher hierarchy organization/controls that channels intracellular fluxes of energy and matter along specific routes, thus ensuring efficient and competitive performance of cellular metabolism under given ambient conditions. However, upon environmental changes, the constraining influence of higher hierarchy organization/controls may need to be relaxed to allow the stochastic network of chemical transformations underlying metabolism to search for and to adopt alternative configurations that would be more adequate to new circumstances, promoting the survival and/or evolutionary success of the host.

Curiously, an analogous mechanism appears to underlie the adaptation of gene expression to environmental challenges in eukaryotes. As recently pointed out by Paldi [38], the molecules used in epigenetic control of gene expression are all key molecules of basic metabolism. For example, acetyl-CoA is used for acetylation, S-adenosyl-methionine is used for DNA and protein methylation and NAD^+ is used for poly-ADP-ribosylation of many nuclear proteins. Because intracellular concentrations of these metabolites reflect the metabolic state of the cell, Paldi argues that epigenetic modifications of chromatin are under the control of basic metabolism. In starving cells, for instance, which have high concentrations of acetyl-CoA and NAD$^+$ and lack methionine, the rate of epigenetic modifications promoting chromatin mobility increases, while the modifications stabilizing chromatin are suppressed. It is fair to suggest, therefore, that the relaxation of gene expression control by means of global de-stabilization of chromatin leads to an increased disorder in gene expression, due to the inherently stochastic nature of the latter [3,39], thus creating molecular and pathway diversities for self-organization and selection to work on. Successful adaptation of the cell to environmental challenge means normalization of metabolism, which is achieved through selection/accentuation of a novel configuration of active genes and pathways that is more adequate to new circumstances. Normalization of metabolism restores physiologically normal intracellular concentrations of metabolites, thus promoting the modifications that stabilize chromatin and establishing a novel pattern of epigenetic restrictions meant to stabilize and maintain a novel expression profile. Notice, that the mechanism is conceptually the same as the one described before for epigenetic regulation of metabolism – relaxation of higher hierarchy organization/controls, such as chromatin destabilization, is the first reaction in response to the failure/malfunction within the economy of the cell caused by environmental challenge. The relaxation of organization/controls is meant to increase disorder in the system by taking advantage of the inherently stochastic nature of gene expression. The increased disorder, which generates molecular and pathway diversities, is then followed by self-organization and the emergence of a novel gene expression profile that is more adequate to new circumstances. The novel gene expression profile is eventually stabilized by re-establishing higher hierarchy organization/controls. Again, adaptability is based on stochasticity, while organization and control promote efficiency.

The self-organizing fractal theory

In fact, the mechanism of adaptation comprising the local or global relaxation of pre-existing structure/order into a transient state of limited disorder which is then followed by self-organization and the emergence of a new organizational configuration can be found at different scales of organizational hierarchy, where it is routinely used by many seemingly disparate complex adaptive systems. Consider, for example, the business organization. One of the modern guidebooks on business management describes the so-called “bureaucratic trap” into which companies accustomed to competing successfully under stable or slowly changing market conditions are prone to fall. Pressed by competition and in pursuit of production efficiency, such companies tend to develop an excessively rigid and elaborate internal structure, which is embodied in rule-following culture, channeled communication, regimentation, schedules, planning milestones and production processes governed by fixed specifications, procedures and checkpoints. With time, as a rule, such companies become efficient but inflexible, failing to adapt to changing market conditions, missing business opportunities, and eventually loosing competition. The advice for managers of such companies is to loosen up the excessive organizational structure of their business by adding a bit of chaos to allow for and stimulate stochastic exploration of internal organizational configurations and external market opportunities in a search for the best match between the organizational structure of their company and the environment [33]. Thus, it appears that at the scale of business organizations, in the same way as at the molecular and cellular scales, organization and control serve efficiency (at the expense of flexibility), while adaptability relies on stochasticity/innovation.

One certainly may raise a brow – isn’t it just a far-stretched and fancy analogy? Is there any value in such comparisons, beyond fleeting amusement? What is really common between the cell and the business organization? The answer is: it depends. It depends on the choice of conceptualization. Perceiving phenomena as different may simply mean that the habitual conceptualization one uses for perception is focused on the appearances of the particular and thus is unable to reveal the universal, making phenomena appear more different and complex than they are in reality. If this is the case, introducing a more adequate conceptualization may resolve the complexity of appearances into the simplicity of underlying universal principles.

Both the cell and the business organization have been conceptualized as complex adaptive systems [2,3,40-42]. The protein molecule and the organism are also seen as complex adaptive systems [3,43,44]. The ecosystem and the biosphere are interpreted as complex adaptive systems [45,46]. Moreover, it was recently suggested that biomolecules, cells, organisms, ecosystems, business organizations and economies constitute a nested set of interdependent self-organizing networks of energy/matter/information exchanges that co-exist and co-evolve at different spatiotemporal scales [7,47]. On one spatiotemporal scale, biomolecules self-organize into cells. On another scale, cells self-organize into organisms and, on yet another scales, organisms self-organize into ecosystems and humans self-organize into organizations and societies and so forth (Fig. 1). In fact, it was also suggested that all of these systems/networks represent the interdependent parts of one integrated and hierarchically structured network of energy/matter/information exchanges, with the network itself organized as a spatiotemporal fractal. In other words, complex systems at different scales are proposed to be self-similar, exhibiting universal patterns in their organization and dynamics. It is only the habit of mechanistic (mis)conceptualization and reductionism that makes them appear as isolated, unrelated and independent phenomena of daunting complexity [47].

Notwithstanding the currently qualitative character of this theory of living matter, it certainly deserves deliberation because of its apparent power to simplify the complex, to explain paradoxes and to make a wide range of testable predictions, opening new vistas for rational thought and scientific discovery. As a bonus, it provides a whole new scientific method and demonstrates great potential as a universal and unifying theoretical framework. For, if the organizational dynamics of protein molecules, cells, organisms, business organizations, economies, ecosystems, and other complex adaptive systems are indeed self-similar and governed by the same self-organizational principles, then 1) by studying and understanding a part, one studies and understands any other part and the whole at the same time; 2) the chaos of fragmented and incoherent knowledge being generated by reductionist approaches and mechanistic interpretations within specialized and isolated disciplines can be readily restructured into one harmonious and self-consistent whole, simply by reconceptualizing and mapping the problems and knowledge of different disciplines onto each other, benefiting both the individual disciplines and the whole structure of knowledge at the same time, and 3) the theories pertaining to the experimentally intractable systems studied in climate science, ecology, sociology, economics, and other sciences can be verified by the experiments performed with appropriately chosen systems at convenient spatiotemporal scales.

Let us for the moment assume that the self-organizing fractal theory of living matter is correct and examine whether it is useful and efficient as a theoretical framework to structure and explain what is known and to predict the unknown. Perhaps what is even more important is to compare its performance as a paradigm of living matter with that of the conventional mechanistic conceptualization of living systems, which currently dominates and directs research and thought in the life sciences.

The organizational state transition as a universal mechanism of adaptation

A reasonable place to start is to formulate the universal mechanism of adaptation to environmental change in general conceptual terms and to look for its manifestations at different spatiotemporal scales. A universal response of diverse complex adaptive systems to environmental changes involves a transition from one metastable organizational state/configuration of the system to another. Let us call such transition the organizational state transition. The organizational state transition proceeds through the following three-step process – 1) a relaxation (local or global) of a pre-existing organizational configuration into a transient state of relative disorder by loosening higher hierarchy organization/controls followed by 2) economy-driven, memory- and stochasticity-assisted self-organization to a new and more productive (under given environmental conditions) organizational state/form and 3) stabilization of the new organizational state/form through re-establishment of higher hierarchy organization/controls.

Indeed, it is not difficult to see that many, and maybe all, seemingly disparate self-organizing complex systems of different natures and at different spatiotemporal scales use recurring organizational state transitions as a universal strategy to evolve and adapt to changes in their environments.

At the molecular scale, the conformational dynamics of protein molecules, including local or global unfolding and refolding, constitutes the critical and defining part of the relationship between proteins and their environment [21,22,48-50]. Experimental and theoretical studies indicate that the relaxation behavior of proteins does not follow simple exponential relaxation. Instead, the relaxation data are best approximated either by stretched exponential or by power law [21,51,52]. Nonexponential relaxation behavior is explained by the hierarchical structure of the constraints imposed on protein dynamics [52,53]. A new arrangement within one tier, which can be required, for example, for adaptation of protein structure in the course of allosteric transition or binding, often requires a relaxation of a higher hierarchy tier, which conceptually represents a higher hierarchy organization/control. In this way, protein structure is able to adapt through folding and refolding events taking place at different spatiotemporal scales. Pertinently, the physicists studying proteins suggest considering protein folding/structure as a general paradigm of biological complexity [43,50,52].

At the sub-cellular scale, as an alternative to the conventional textbook interpretation of glycolysis as a set of coupled biochemical reactions generating energy in the

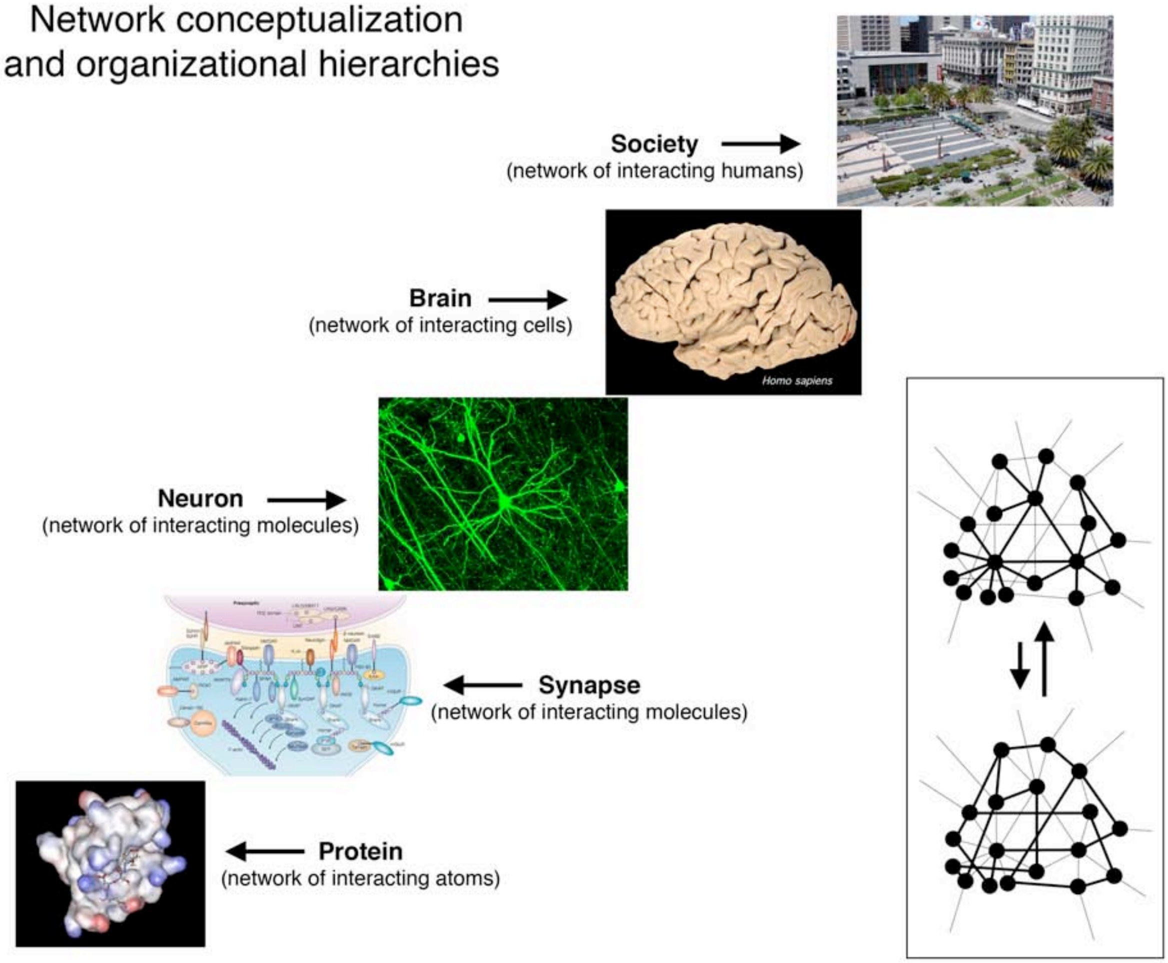

Figure 1. Network conceptualization and organizational hierarchies. Diverse complex adaptive systems, such as proteins, cells, organisms, ecosystems, organizations, and societies, all together constitute one developing, multiscale continuum-economy composed of interacting and interdependent adaptive organizational forms/networks that co-exist and co-evolve at different spatiotemporal scales, forming a nested set of interdependent organizational hierarchies. Whether we speak of a protein, a sub-cellular structure, a cell, an organism, an organization or an ecosystem, they all can be conceptualized as a metastable network, where links invariably represent exchanges of energy, matter and/or information between the corresponding constituent parts, be it atoms, molecules, cells or organisms. The links in such networks are of an inherently probabilistic and dynamic nature. The major fluxes of energy, matter and/or information of a given network configuration (shown as bold links) are always embedded in a sea of low probability exchanges (shown as dotted links). A switch to an alternative network configuration of a biological system in the course of adaptation and/or evolution necessarily requires and relies on adaptive plasticity of nodes able to find, establish, and maintain new links. In reality, for any given network configuration, the strengths of links or the frequencies of exchanges between nodes do not follow simply bimodal distributions - as shown here with bold and dotted links - but are usually described by heavy-tail distributions such as power law or log-normal, as has been demonstrated for such real-world systems as neuronal cortical circuits [54] as well as metabolic [55,56] and gene regulation networks [57]. In addition, real-world networks normally possess multiple metastable configurations characterized by different occupational probabilities, switching between them with different transition probabilities in the process of adaptation and/or evolution. See also Fig. 2.

Sources of the images shown: Society - Union Square, San Francisco; Brain – image of a human brain (credits to Todd Preuss, Yerkes Primate Research Center) is reproduced from Fig. 1 in Ref. [58]; Neuron - the pyramidal neuron “dow” is reproduced from Fig. 6(d) in Lee et al. [59]; Synapse - a schematic diagram of the PDZ protein organization at a mammalian excitatory synapse is adapted from Kim and Sheng [60] by permission from Macmillan Publishers Ltd: Nat. Rev. Neurosc. © 2004; Protein – a syntrophin PDZ domain complexed with its peptide ligand (PDB id. 2PDZ) was visualized using the WebLab™ ViewerLite 3.2 software. Network configurations in the inset are adapted from Ref. [61]. The figure as a whole is adapted from Ref. [7].

form of ATP inside a watery bag of organic materials in a spatiotemporally indiscriminating manner, the work of Colin Masters and other investigators suggests a new image of glycolysis emerging as a dynamic, flexible and efficient metabolic organization supplying energy differentially in accord with specific physiological demands that are continuously changing in space and time [34,62]. These investigators argue that the glycolytic sequence exists and functions as transiently immobilized enzymatic clusters associated with F-actin and other cytoskeleton scaffolds. Such an arrangement flexibly couples energy generation with the structural changes taking place in the course of a broad range of cellular adaptive responses. Additional complexity and flexibility comes from 1) the segmented nature of the glycolytic sequence, with individual segments able to function independently in response to specific metabolic demands; 2) the existence of multiple enzyme isoforms that differ in their binding properties to each other and/or to their scaffolds and 3) the existence of multiple isoforms of actin and other scaffolds. The adaptability of the glycolytic sequence, which has evolved to meet an enormous diversity of specific energy demands varying at multiple time and space scales within a multicellular organism, appears to rely on organizational state transitions involving recurring relaxations of pre-existing arrangements of the sequence into a transient state of relative disorder which are followed by re-assembly of the sequence into new configurations in response to specific energy demands and the pressure for metabolic efficiency.

At the cellular and organismal scales, Madlung and Comai recently suggested that the universal response of plant genomes to various types of internal and external stress involves a relaxation of epigenetic imprints, to a degree proportional to the degree of physiological impairment, followed by stochastic remodeling of affected genomes through expression and silencing of different genomic sequences as well as through DNA rearrangements and transpositions. The novel gene expression configurations that prove to be adaptive are then stabilized by re-establishing epigenetic restrictions [63].

At the scale of business firms and economy, in addition to the strategy of adaptation discussed above, which involves relaxation of the firm's organizational structure followed by stochastic exploration of the fit between the organization and its environment, consider the strategies embodied in the term "labour market flexibility", which are used by organizations to adapt their production and/or business routines/cycles to fluctuations and changes in their socio-economic environments. These strategies include temporary or fixed-term contracts, relaxation of hiring and firing regulations, reassignment of employees to different activities within the same organization, outsourcing, locational flexibility and others [64]. It is not difficult to see that most, and maybe all, of these strategies can be mapped onto their conceptual correlates in the economy of cellular metabolism viewed in the context of inherently flexible enzymatic activities and specificities and their management achieved through the dynamic organization and reorganization of enzymes into different metabolic clusters and/or routines in response to changing demands of adaptation, efficiency, and survival [34,35]. It is also worth mentioning the conclusions of modern organizational analysts suggesting that discontinuous transformation (i.e. organizational state transition) and creative destruction are the must-to-adopt strategies for any corporation aspiring to stay competitive and productive [65].

In the socio-politico-economical sphere, virtually all the revolutions known to humanity follow the same pattern. Old structure of socio-politico-economic relationships is destroyed or loosened, leading to a temporary chaos followed by the emergence of a novel organizational state achieved through the (self-)organizing activity of new leaders and institutions. The novel organizational state, which as a rule constitutes an economically advanced system of production governed by progressive political institutions, is then stabilized by establishing a novel system of behavioral norms, rules and values, reflected in the constitution, laws and regulations, and maintained through law enforcement, social conditioning, and education. The conceptual parallels between socio-political revolutions/reformations and the epigenetic mechanisms of metabolic adaptation are evident and deserve closer scrutiny. It is hardly coincidental that both organizational phenomena are often triggered by starvation or other major malfunctions or imbalances in the corresponding scale economies.

If one accepts the idea that biosphere and geosphere represent two intimately intertwined and interdependent aspects of one and the same planetary network of energy/matter/information exchanges, then biological extinctions, speciation bursts, and geophysical perturbations may simply represent the manifestation of periodic relaxations and reorganizations of an evolving planetary network of energy/matter/information exchanges responding to accumulation of internal stresses [45,66-69]. It is fair to suggest that the climate change we currently face, which appears to be unavoidable unless it is first understood in all its complexity and then acted upon in an informed and focused manner, will cause both global and local relaxations of socio-politico-economic organization followed at first by chaos and then by the re-emergence of a new order through the self-organizing activity of surviving individuals and organizations adapting to new geo-politico-socio-economic realities. Hurricane Katrina and its aftermath are a real-life example of local relaxations, illustrating likely future scenarios.

Last but not least, in harmony with Thomas Kuhn's interpretation outlined in his classic text "The Structure of Scientific Revolutions", scientific development itself can be thought of as the self-organization of a knowledge structure punctuated by local and global relaxations and reorganizations of this structure as knowledge grows and develops [70]. Transient relaxations are triggered by internal stress accumulating in the form of inconsistencies, contradictions, paradoxes and a growing misfit between the experimental reality and the dominating paradigms assumed to account for this reality. Relaxations are followed by restructuring of the affected domains of knowledge under the guidance of novel emerging paradigms. Transient relaxation into a state of relative interpretational disarray represents the crisis of an old form/paradigm. The emergence of a new and more productive structure of knowledge, achieved through reconceptualization and reorganization, represents the paradigm shift.

To summarize, the recurring organizational state transitions taking place at multiple spatiotemporal scales appear to constitute a universal mechanism/pattern underlying the adaptation and evolution of what can be conceptualized as complex adaptive systems co-existing and co-evolving at different spatiotemporal scales.

Concluding the discussion on state transitions, the following comments may be useful. First, the conceptualization of adaptational phenomena in terms of recurring organizational state transitions not only provides clear qualitative insights into the universal behavioral and response patterns shared by diverse complex systems, but also opens opportunities for quantitative analysis and modeling, as organizational state transitions can be readily captured within the mathematical framework of the network theory dealing with phase transitions and other types of organizational dynamics in complex networks [11,13,71-74]. Once captured with adequate mathematical descriptors, measures, and models, the dynamics of complex systems can be studied both analytically and in computer simulations, with the purpose of understanding, predicting, and controlling the behavior of complex systems (Fig. 2).

Second, organizational state transitions have obvious conceptual parallels in the physics of phase transitions, and the exploration of these parallels may potentially be very fruitful. Pertinently, the physics of phase transitions has by now crossed disciplinary borders, making its first successful in-roads in economics and establishing a novel research field termed econophysics. The concepts and techniques developed to study collective organizational phenomena taking place during phase transitions in non-living matter are already proving to be useful for the understanding and modeling of complex economic phenomena [75,76].

Third, there is a large and continuously growing collection of currently fragmented and disconnected research data in molecular and cellular biology that is inconsistent with and/or directly challenges a wide range of conventional notions and interpretations based on the mechanistic conception of living matter. One of the attempts at synthesis of such data into a meaningful alternative picture can be found in the "controversial" book recently published by Gerald Pollack, in which he provides an impressive in scope and insight-stimulating discussion of the experimental evidence contradicting the conventional image of cellular physiology [77]. It is hardly coincidental that as an alternative to traditional interpretations failing to explain multiple aspects of experimental reality, Pollack suggests the phase transition as a universal concept accounting for a wide range of basic processes in cellular physiology.

Indulging in prophesying, it thus seems very likely that biology, reconceptualized in terms of self-organizing networks and organizational state transitions, together with the network theory and the theory of critical phenomena (phase transitions), will become a winning self-fertilizing combination, for it brings together the theoretical muscles of mathematics and physics, the power of computer analysis and simulation and the enormous diversity of experimentally tractable systems of biology. Experimental biology may become the ultimate test-bed for theories, computational analyses, and simulations of a wide range of complex phenomena of different natures. In addition, as surprising as it may seem, economics, sociology, and other sciences are bound to make critical contributions to the theory of complex adaptive matter, for, as it is argued here and elsewhere [47], economics and sociology is but biology of a grand scale.

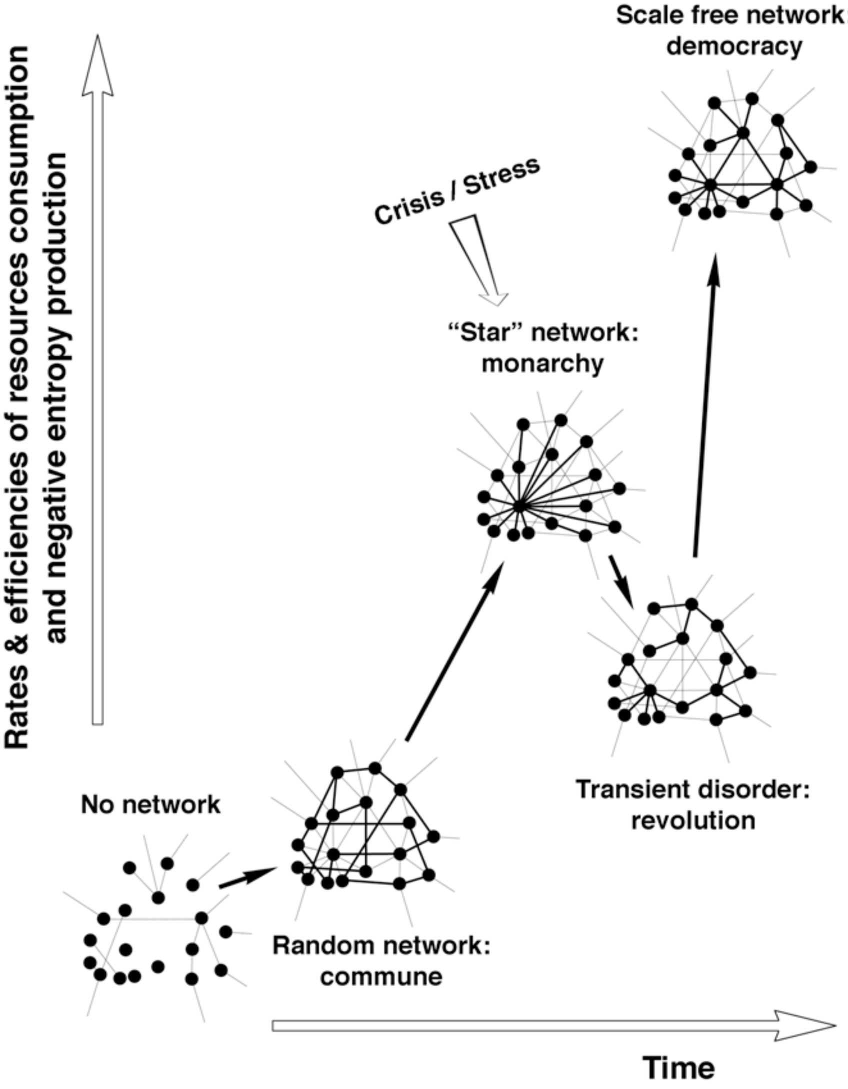

Figure 2. Adaptation/evolution through organizational state transitions. A typical trajectory of organizational development is shown as evolution of a network. The evolutionary trajectory comprises a series of transitions between different network types/classes. The network types shown are known to possess different systemic properties that are specific to a particular organization (type/class) of network but which are independent of the natures of nodes and links [11,13]. Such systemic properties are often scale-invariant, being shared by diverse complex adaptive systems operating at different spatiotemporal scales. Black arrows indicate transitions between different organizational states of an evolving network. Solid links indicate stable/frequent exchanges of energy/matter/information between individuals/nodes. Dotted links indicate weak ties/exchanges. The development of an organizational form starts with no discernable network of stable exchanges maintained between the largely competing but occasionally cooperating individuals/nodes. Due to the pressure of economic competition, a primitive cooperative commune, approximated as a random network, emerges as a first organizational form. Competition between different communes leads with time to the emergence of the monarchy-type organizational form characterized by centralized management/organization of collective activities. Next, in this particular scenario, either due to external or internal competition/stress, the "star" network experiences a localized and transient disorganization, which eventually gives way to the emergence of an organizational form characterized by power-law distribution of organizing influence, modeled as a scale-free network. Notice that the presented organizational trajectory as a whole can be scale invariant. For example, the part/domain of the "star" network, which was disorganized due to crisis/stress, is likely to recover by following the same organizational pattern locally – no organization, commune, monarchy, democracy – but on another spatiotemporal scale.

In reality, of course, the organizational dynamics is much more complex. Exchanges are probabilistic, the strengths of links/exchanges do not follow bimodal distribution, as shown, but often obey log-normal or power law distributions (see Fig. 1), organizational transitions are contextual, i.e. defined by the environment and defining the environment at the same time, transitions are reversible to a certain degree. Networks/organizations can grow or shrink, fragment or merge with other organizations, and so forth. Yet, the first attempts to formalize organizational dynamics and evolution in quantitative terms using graph-theoretical measures and models convincingly demonstrate that relatively simple network approximations can adequately capture much of the relevant complexity in computer simulations, given the development, choice and application of appropriate network measures and models [72,74].

Self-organization through stochasticity, competition, specialization and cooperation

Recruitment models of self-organization

The recruitment model of metabolism bears an uncanny conceptual resemblance to a number of self-organizational models that were put forward at different times within different disciplines to describe the emergence and evolution of different complex adaptive systems, suggesting that essentially the same organizational pattern is reproduced again and again on different spatiotemporal scales.

Consider the response threshold models of division of labor in social insects [78,79]. These models assume that individual insects in a swarm begin to perform a particular task only when a corresponding stimulus from their environment exceeds a certain value. The response threshold varies among members of the group, and individuals with the lowest response thresholds are recruited to the task first. By performing the task, the recruits diminish the stimulus, and thus reduce the probability that other individuals will be recruited to the same task. Because individual insects in the swarm have different thresholds to distinct environmental stimuli, an ensuing division of labor occurs in a self-organized fashion, benefiting both the group as a whole and the individual members as its parts.

At the scale of the organism, a reconceptualization of cell differentiation and organism development in terms of self-organization and stochasticity was recently put forward as an alternative to the conventional concepts of program and design, as the latter became manifestly inconsistent with the experimental reality of stochasticity in gene expression and cell plasticity [3]. Within this new model, the developing organism is viewed as a growing community of interacting expression profiles represented by individual cells. Due to the inherently stochastic nature of gene expression, individual expression profiles spontaneously diverge, thus continuously generating a great variety of individual behaviors/phenotypes among genetically identical cells. Each individual cell, in very much the same sense as described for social insects, has its individual thresholds to respond to distinct environmental stimuli by expression of responsive genes. Cell differentiation thus proceeds in a self-organizing manner through specialization, division of labor and cooperation within a community of the interdependent expression profiles interacting with each other and with their environment. Within a growing organism, useful expression profiles are awarded (likely through appropriate allocation of resources), become dissociable from physical identities of the cells providing them and are maintained and evolve as a metastable system of interdependent and interacting virtual functions sustained by the flow of physical cells passing through the structure of the organism. Individual cells pursue and achieve their prosperity by assisting/boosting the prosperity of specific cellular organizations/tissues they belong to. The organism is conceptually equivalent to the business organization, viewed as a metastable and evolving network of interacting virtual functions [2].

At the scale of humans and their organizations, perhaps one of the earliest theoretical treatments of and praises for self-organization can be found in “An Inquiry into the Nature and Causes of the Wealth of Nations”, the 1776 classic work of the founder of the modern economic theory, Adam Smith. Urging to leave the regulation of economy to free market and competition, Smith essentially argues that the best formula for economic progress and wealth generation is the self-organization of productive activity of citizens pursuing their own self-interests in the conditions of the free market economy. It may be not perfect, but it is better than any of alternatives. He also suggests that the primary source of production efficiency is division of labor accompanied by specialization and proper organization. Inherently stochastic individual activities and inventiveness are brought to bear on production of what is in demand within and outside a given socio-economic system. The competition for economic efficiency necessitates specialization, division of labor, and organization. An “invisible hand” of the free market magically organizes and structures the whole of evolving economy in such a way as to maximize inventiveness, industrious effort, and productive activity of its participants, thus maximizing wealth generation to the common benefit of all [80].

Since the “invisible hand” of the free market is a conceptual equivalent of self-organization, it is reasonable to suggest that whatever scale we choose to consider – the protein molecule as self-organization of atoms [50], the cell as self-organization of molecules [2,6], the organism as self-organization of cells [3], the social swarm as self-organization of insects [79], the business organization as self-organization of humans [42], the economy as self-organization of individuals and their organizations [80,81] and so forth - it is the forces of economic competition that underlie and drive the self-organization of all scale-specific organizations-economies. Independent of scale, it appears that self-organization universally involves such phenomena as innovation, embodied in the notions of stochasticity, choice, and individual self-expression, as well as the competition, specialization, cooperation, and organization of scale-specific complex adaptive agents, be it biomolecules, cells, organisms, humans, organizations, ecosystems or others. The universal phenomena underlying self-organization come as pairs of opposites - competition and cooperation, stochasticity/freedom and organization. The mechanism by which such pairs of opposites are reconciled to the common benefit of all participants appears to be the formation of adaptive organizational hierarchies. To illustrate this latter conjecture, let us formulate the process of self-organization in general conceptual terms.

Self-organization: a general model

Consider a large population of common descent individuals placed to survive in a complex environment. Each individual is endowed with a unique, broad, but bounded spectrum of abilities/behaviors, with partial overlap (due to their common descent) between individual spectra. The individuals are inherently stochastic in the sense that, unless organized and regulated, they are likely to be engaged in different, uncoordinated, and, often, competing activities at any given time.

The individuals compete to survive, by survival meaning the maintenance of their internal individual structures/organizations, and succeed, by success meaning an increase in the rates and efficiencies of energy/matter/information consumption and wealth generation. Individual success may lead to the improvement and/or sophistication of internal individual structures/organizations as well as the growth and/or replication of successful structures/organizations and, thus, the proliferation of successful individuals/structures. At the moment, let us broadly define “wealth” as negative entropy and “wealth generation” as production of negative entropy. The complex environment is characterized by a heterogeneous spectrum of usable resources of energy/matter/information. Some of these resources are more usable and/or more abundant than others.

During a certain phase of self-organization, let us call it the “Darwinian phase”, individuals compete for available resources by trying to find an economically optimal match between their unique spectrum of abilities, the competitive pressures associated with different resources and their individual capacity for increasing their fitness through improvement/adaptation of their own internal organization. As a result, Darwinian competition improves individual fitness, promotes diversification of individual activities, and maximizes aggregate resource consumption from the environment. However, this Darwinian phase is unlikely to last long, for cooperation and organization inevitably emerge and flourish, due to the pressure of competition. As pointed out by Adam Smith, the formation of a cohesive group of cooperating individuals allows for a dramatic increase in their collective resource consumption and wealth generation, which can be achieved through specialization, division of labor and organization. The formation of protein folding nuclei, the scaffolding and/or microcompartmentation of metabolic enzymes inside the cell, the emergence of the first primitive cells, the emergence of the first multicellular organisms or business organizations are but a few examples of the emergence of cooperatives driven by economic competition at the respective spatiotemporal scales. Following the emergence of cooperatives, the intensity of Darwinian competition is transferred to the inter-group scale. Competition between individuals within the same group is necessarily suppressed and constrained by the organization of relationships within a given group and by the competition between different groups. The organization of individuals into groups through cooperation, division of labor and organization is unavoidable, because it represents an economically advantageous strategy in the competition with unattached individuals and other organized groups (Fig. 3).

The emergence of competing cooperatives and the transfer of the intensity of Darwinian struggle to a larger spatiotemporal scale, from the inter-individual to inter-group level, signify the formation of the 1st tier in a growing organizational hierarchy. Now the groups themselves can be considered as the 1st tier individuals. With respect to their individual activities/behaviors, the groups are stochastic and adaptive within the bounds set by their individual organizational structures. The purposes, however, remain the same, i.e. to survive and to succeed. The Darwinian phase commences and repeats itself on a larger spatiotemporal scale. Winners are selected on the basis of their fitness. To be fit means to possess an efficient and adequate (with respect to given environmental circumstances) internal organization of energy/matter/information exchanges, i.e. an efficient internal economy. However, because the environment is heterogeneous and complex, there may be as many winners as there are environmental niches to be discovered and exploited. Competition between groups is accompanied, therefore, by divergence and specialization of individual groups trying to discover and to exploit all sources of energy/matter/information available in their environment (Fig. 4). Notice that for any given group all other groups it cooperates or competes with are simply aspects of its environment. Once again, Darwinian competition improves the individual fitness/organization/economy, promotes specialization,

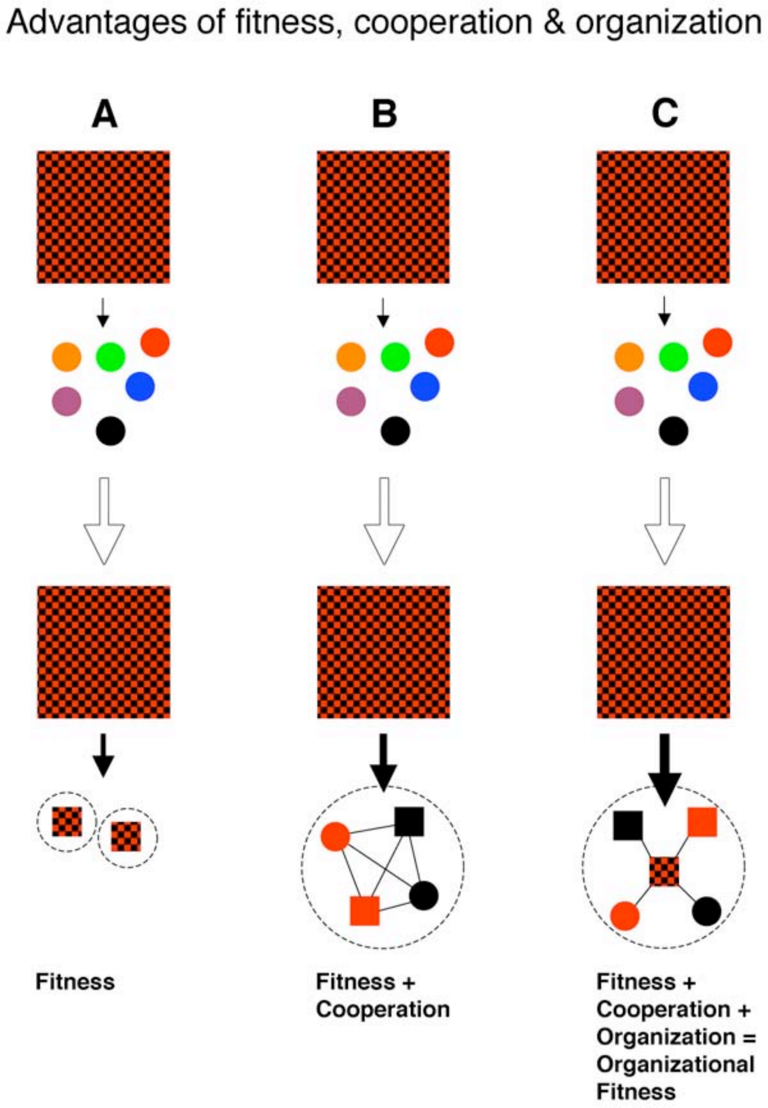

Figure 3. The advantages of fitness, cooperation and organization are illustrated by three possible scenarios of group evolution, shown as schematics. Partially heterogeneous individuals (small colored circles) are placed to compete for limited resources in a heterogeneous environment (large patterned square). Different colors, shapes, and patterns symbolize different aspects of individuals and their environment. The resemblance between an individual and its environment symbolizes individual fitness. A better match between an individual and its environment results in a higher rate of resource consumption by the individual. White arrows indicate the direction of time. Black solid arrows symbolize the relative success of a group measured as the in-flow rate of resources into the group, with the arrow's size being proportional to the rate of resource consumption from the environment. *Scenario A* illustrates the advantage of individual fitness: only those individuals who managed to adapt to the environment survived natural selection. *Scenario B* illustrates the advantages of fitness plus cooperation: the survived individuals may not be as fit individually as the winners in scenario A, but as a cohesive community of cooperators they consume resources faster, thanks to the specialization of individuals and the establishment of cooperative exchanges (shown as links) between specialized individuals. *Scenario C* illustrates the advantages of fitness plus cooperation plus adequate management/organization/economy: resources can be extracted and consumed still faster if individual fitness and cooperation are complemented by adequate management/organization/economy.

Notice, please, that the emergent organizations/cooperatives (circled by dotted lines) can be considered as "individuals" of a higher organizational hierarchy. Following the formation of organizations/cooperatives, competition for resources between unattached individuals and between groups of individuals that differ in their organization will continue, inevitably leading to 1) improvement of the internal organizations/economies of individual groups (organizational fitness), 2) the emergence of communities made of specialized and cooperating groups (fitness plus cooperation), and 3) the emergence and subsequent improvement of the management/organization/economy of the communities of groups (fitness plus cooperation plus organization). In other words, both the arguments presented and the organizational dynamics shown are scale-invariant. See also Figure 4.

and maximizes the aggregate consumption of resources from the environment. Once again, Darwinian phase is resolved through the emergence of cooperation between individual specialized groups followed by their further specialization and by the organization of previously independent groups into competing domains/communities made of cooperating groups. The formation of competing domains and the shift of Darwinian struggle to a yet larger spatiotemporal scale signify the emergence of the 2nd tier within the expanding organizational hierarchy. Integrating diverse groups/activities into diverse organizational configurations, individual domains/communities of groups emerge as stochastic and adaptive individuals of the 2nd tier. The formation of higher order tiers at ever-increasing spatiotemporal scales is driven by the same forces and follows the same organizational patterns, thus leading to continuous expansion of nested organizational hierarchies over increasingly large spatiotemporal scales. As a result, resources are consumed from the environment and wealth/negative entropy is generated at ever-increasing rates with ever-improving efficiencies.

An important but unappreciated consequence of such an organizational process is the emergence and development of an increasingly precise and detailed spatiotemporal representation of the environment, which co-evolves with the environment and is reflected/coded in the increasingly precise and detailed spatiotemporal structure of energy/matter/information exchanges maintained and evolving within the expanding organizational continuum.

In addition to hierarchical growth upward through integration, groups that by their nature can grow in size, either by reproduction of their members or by accepting new members from outside or by a combination thereof, often employ another mechanism to the same end - the formation of hierarchy downward, through fragmentation and specialization. If one of the groups, for example, succeeds in competition with others, meaning a group accumulates wealth at a relatively high rate, its internal organization will tend to be preserved overall, serving as a framework proven to be successful. This framework will constitute the highest organizational hierarchy within this group. The new members of the group, either born within or accepted from outside, will pursue increasing fragmentation and specialization of individual activities within the constraints of the parental framework with the aim of improving the overall economic efficiency of the parental organizational configuration, thus further increasing energy/matter/information consumption and wealth generation by the group as a whole. What was done before by individuals A, B, C and D will be performed, upon wealth accumulation, by guilds "A", "B", "C" and "D" with sub-specializations developing within each of the guilds. However, the original structure of the relationships between A, B, C and D will be preserved as long as it supports and promotes overall competitiveness of the group. The extent of the division of labor and the degree of complexity within a given group will be defined by the rates and efficiencies of resource consumption and wealth generation within this group. As noticed by Adam Smith - "… separation of [different trades and employments] is generally carried furthest in those countries which enjoy the highest degree of industry and improvement; what is the work of one man in a rude state of society, being generally that of several in an improved one." [80].

Many complex self-organizing systems employ both mechanisms simultaneously. If successful, the formation of a cooperative domain made of groups of individuals, for example, would lead to increasing amounts of energy/matter/information flowing into the cooperative domain. Certain groups and/or individuals, due to their special positions and/or roles within the organizational structure of this successful domain, may acquire privileged access to the collectively generated resources and use them to increase their own complexity by building their individual hierarchies through the fragmentation-specialization mechanism. This fact underscores a critical significance of the resource distribution problem within successful cooperatives, which is outside the scope of our discussion and is addressed in general qualitative terms elsewhere [47].

Either of the two mechanisms or their combination leads to the same overall result, however - the emergence and development of a growing hierarchical network of interdependent organizations that co-exist and co-evolve on different spatiotemporal scales. It seems appropriate to call such a process self-organization. Self-organization does include Darwinian evolution as its integral part, but goes beyond the random variation and selection principle. In addition to Darwinian evolution, self-organization, being essentially an economy-driven organizational process, encompasses cooperation, specialization, organizational forms, hierarchies, spatiotemporal scales, inter- and within-scale interdependencies and relationships as well as other phenomena, such as adaptive plasticity, memory, and intelligence [7,47].

Efficiency and adaptability

Let us return to the 1st tier individuals, i.e. groups in our model, and consider the dynamics of the internal organization of energy/matter/information exchanges within a given group. Once established and proven as an

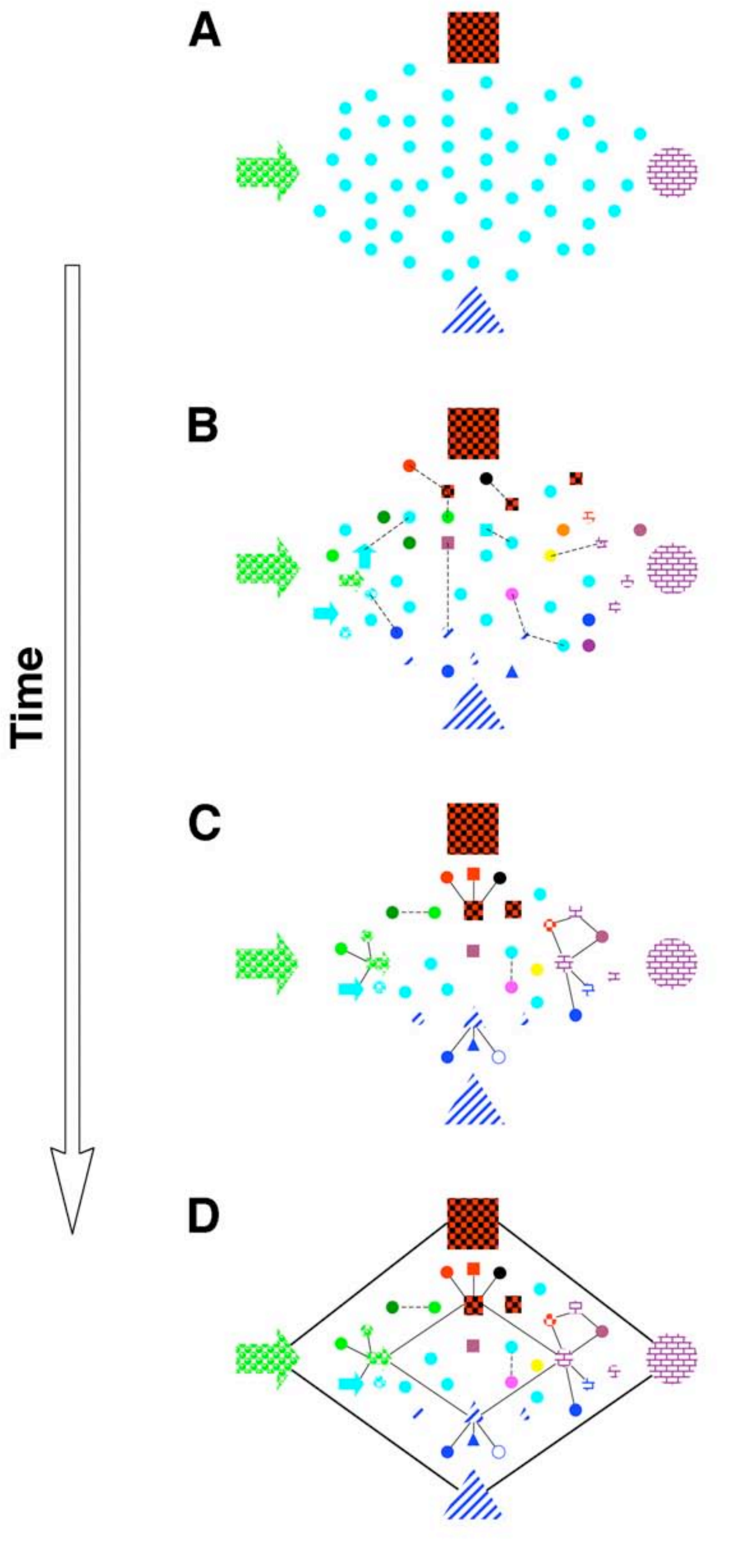

Figure 4. Schematics of self-organization. *A)* A group of individuals (small circles) is placed to compete for resources in a heterogeneous environment. Four different niches/aspects of the environment are shown as the large Arrow, Square, Circle and Triangle. The colors and patterns characterizing each of the niches symbolize different aspects of the corresponding environmental niches (they can be thought of as niches within niches). *B)* Individuals compete for resources, adapt to their immediate environments through stochastic diversification and occasionally cooperate through mutually profitable stochastic exchanges of energy/matter/information (dotted links). The resemblance of an individual to its environmental niche symbolizes the fitness of the individual. A better match between an individual and its environment results in a relatively higher rate of resource consumption from the environment. *C)* Economic competition in conditions of limited resources leads to the establishment of frequent/stable exchanges (solid links) within emerging groups/cooperatives of specialized individuals, followed by selection of the most competitive organizational forms/networks of individuals (see also Figure 3 and discussion in the text). *D)* Given the existence of a spatiotemporal relationship between environmental niches (shown as thick links between Arrow, Square, Circle and Triangle), those cooperatives/groups/organizations that managed to discover such a relationship and establish a matching structure of energy/matter/information exchanges among themselves to their common benefit (shown as links between niche-specific groups) are likely to prevail over other groups (not shown) that failed either to cooperate or to perceive/discover the existence of the spatiotemporal relationship between environmental niches.

Notice please how the economic competition between complex adaptive systems at multiple spatiotemporal scales enforces 1) the organizational self-similarity of scales and 2) the emergence of an increasingly precise representation of the environment, which emerges and evolves in the form of nested organizations/structures, i.e. individuals, groups, and communities of groups, operating at multiple spatiotemporal scales in an interdependent and co-defining/co-morphing manner (see discussion in the text). Notice that both the argument presented and the organizational dynamics shown are scale-invariant.

economically attractive arrangement for participating individuals, the internal organization of exchanges within a given group restrains stochasticity of individual behaviors/activities, channeling the otherwise stochastic exchanges of energy/matter/information along the routes proven to be useful for the group as a whole. The internal organization of a group emerges as a specific spatiotemporal network/configuration of the energy/matter/information exchanges maintained between individual members of the group. The structure of this network is "extracted" from a vast pool of all possible configurations that can be potentially realized among the same stochastic individuals. It is important to stress that a particular configuration is extracted in a statistical sense, meaning that, upon organization, certain pathways of energy/matter/information exchanges become probabilistically preferred in the system. The exchanges unsanctioned or unsupported by a given organizational configuration do occur but with much lower frequencies/probabilities. In other words, alternative configurations or organizational states always lurk in the background as unrealized potentialities (Fig. 1, inset).

In conditions of competition, a successful group growing in size, either through multiplication of its members or by attracting other individuals from outside, is likely to capitalize on the group's economic success by improving economic efficiency of an already existing and proven configuration/framework rather than experimenting with alternative configurations. A great increase in economic efficiency can be achieved through the fragmentation-specialization mechanism discussed above, i.e. by growing organizational hierarchy downward. Improved economic efficiency allows for further organizational growth, which, in turn, allows for further fragmentation, specialization and improvement of economic efficiency. However, employing such a strategy to increase the efficiency of a given network configuration comes at a price. First, it tends to progressively limit the freedom of individual expression as organizational complexity increases, thus suppressing both the emergence of innovations and their diffusion/adoption. Second, it compromises the ability of a system to sample alternative and potentially better configurations, thus decreasing the chances to ever change/improve the overall organizational structure of the system. Third, a group caught in a "bureaucratic trap" becomes less perceptive to changes in its environment. It looses its adaptability and, sooner or later, competition with others, thus endangering its own existence during environmental changes. It is tempting to call such a strategy the "dinosaur's strategy". They grow fast and powerful, they have no competitors except their own kind, they may prevail temporarily, but eventually they die off or fragment en masse, failing to recognize and adapt to environmental changes, which they often provoke themselves.

Within a hierarchical system, the organization of higher hierarchies constrains organizational dynamics at lower hierarchies. It is thus of no surprise that the initial response of many complex systems to external or internal stresses includes relaxation of organizational hierarchies, often in proportion to the degree of impairment of the economy of the system upon stress. Organizational relaxation provides an opportunity to sample a much larger spectrum of alternative configurations of energy/matter/information exchanges available for the system in the search for an adequate response to the stress. Upon organizational relaxation, the adaptability of the system is increased at the expense of efficiency.

To appreciate the relationship between economic efficiency and organizational/structural adaptability from the evolutionary perspective, let us imagine three individual domains each made of several cooperating groups and consider their competition in the context of the self-organizational model outlined above. Suppose that the only difference between these three domains is the way in which they are organized. Let one of these domains be organized as an extremely efficient, clockwork-like complex machine - all fluxes of energy/matter/information are tight and exactly specified, no dissipation or alternative choices are allowed. Suppose the second domain has almost no structure - its internal fluxes of energy/matter/information are chaotic and unpredictable. The third domain is characterized by semi-structured organization of energy/matter/information fluxes both between its groups and within its individual groups. In conditions of competition in a dynamic environment, the clockwork domain, which has the most efficient organization with respect to given environmental conditions, may have a temporary advantage. However, it is 1) highly sensitive to random breakdowns or malfunctioning within its structure, being prone to cascading failures due to the high interdependence of its components connected by tight linkages and 2) likely to loose its efficiency under different environmental conditions. The semi-structured domain, albeit less efficient than the machine-like domain under certain environmental conditions, is adaptive and tolerates random failures and stress well. While the group(s) affected by failure or underperformance may temporarily undergo relaxations and reorganizations within the semi-structured domain, unaffected groups have a relative freedom to compensate for temporarily non-functional group(s) through organizational restructuring and adaptation of unaffected parts, thus maintaining the overall performance of the domain, minimizing overall damages, finding new and better solutions, and adapting to environmental changes. The unstructured domain, undoubtedly the superior one in terms of plasticity, is likely to lose the economic competition to the semi-structured domain due to its poor economic efficiency in most environmental conditions.

It can be concluded, therefore, that within each of the organizational hierarchies in our model of self-organization, evolutionary competition selects at the end of the day not the most economically efficient configurations/organizations, i.e. the fittest, but the organizations that are in harmony with their environments, i.e. the organizations/configurations that keep on chasing an optimal balance between economic efficiency and organizational flexibility in conditions of continuously changing environments. The dynamics of biological structures/organizations are driven by eternal conflict between two opposites, economic efficiency and organizational adaptability. Too much of a specific order/structure compromises adaptability, while too much plasticity compromises economic efficiency. It should be pointed out that the balance between economic efficiency and adaptability is dynamic and context-dependent. It tends to shift towards efficiency in stable environments and towards organizational plasticity in dynamic environments. This may explain the universal compulsion of biological systems to influence, stabilize, and control their environments. Embodied in the concept of homeostasis, this universal compulsion is manifested in different forms at different, and maybe all, scales of biological organization. Controlled and stable environments provide competitive advantage, for they allow for and are conducive to the development of complex and efficient internal organizations-economies. Notice, please, that no machines, however sophisticated they may be, are concerned with homeostasis or feel compelled to control their environments, including other machines.

Steady-state metastability and integration through moonlighting

Another apparently scale-invariant feature of the continuum-economy of living matter is the steady-state metastable character of its constituents. Tom Misteli, who was the first to apply the concept of self-organization to describe sub-cellular dynamics, pointed out steady-state metastability as a universal property of sub-nuclear and sub-cellular structures, describing them as dynamic macromolecular organizations maintained by the flux of their resident components continuously entering and leaving sub-cellular structures/organizations [6]. In addition to nuclear compartments such as nucleoli, Cajal bodies, promyelocytic leukemia bodies, splicing factor compartments and others, it has been shown that euchromatin, heterochromatin, the cytoskeleton, the Golgi complex, as well as the macromolecular complexes mediating basic biological processes such as DNA replication and repair machineries, transcription apparatus, and others, are maintained and function as steady-state dynamic macromolecular organizations feeding on the flow of their resident components that enter, participate in, and leave the corresponding structures/organizations with different recruitment probabilities, residence times, and turnover rates [2,82,83]. Remarkably enough, even elongation factors were found in a dynamic and rapid exchange between two molecular pools, the elongation factors transiently associated with elongating complexes and the freely mobile nucleoplasmic pool of factor molecules [84]. Counterintuitive from the mechanistic design perspective, the flexible and dynamic integration of functions, achieved through a constant exchange of shared (moonlighting) molecular components among diverse macromolecular structures/compartments, was suggested to have evolved to ensure both the efficient performance and the adaptability of the cell as a whole, endowing the cell with such advantageous organizational attributes as structural and communicational integration, functional self-organization on demand, just-in-time problem-solving, redesign, and others [2].

While being poorly compatible with conventional mechanistic conceptions, the emerging image of the dynamic cell bears an unmistakable resemblance to the human-scale economy and its constituents, social and business organizations. The business (or social) organization can be thought of as an evolving network of interacting and interdependent functions, which is manifested at any given moment as a network of psycho-socio-economic relationships/transactions maintained between concrete human individuals performing functions. Individuals may come and go, as they usually do; what remains and lives is a metastable and continuously evolving organization of specialized functions. The physical identities of individuals representing different functions may not be preserved on the time scales characteristic of long-lived business organizations and social institutions. Different specialized occupations within long-lived organizations and institutions are typically characterized by different turnover rates, which tend to be higher for simple functions and lower for more complex ones, given relatively stable environmental conditions and satisfactory economic performance of the organization.

Significantly, a similar pattern of steady-state metastability has been observed and linked to overall economic performance on the scale of the whole economy as well. The studies of organizational scholars suggest that change in the economy as well as overall performance of an economic system are driven more by entries and exits of firms than by adaptations of individual companies [85,86]. As an example, of the one hundred largest American companies making the first Forbes 100 list in 1917, sixty-one companies ceased to exist seventy years later and only 18 remained on the list of the top 100 firms by 1987. Of these 18, only two companies performed better than the averages. The same pattern emerged from an examination of the Standard & Poor's (S&P) 500. Of the five hundred companies that started in the S&P 500 in 1957, only seventy-four remained on the list through 1997. Of these seventy-four, only twelve outperformed the S&P 500 index itself over 1957-1998 [65,81]. Interestingly, the average turnover rates in the S&P 500 group appeared to accelerate over time, from about 1.5% per year in the 1920's and 1930's to about 10% in 1998. Of note, evolutionary ecologists, such as Geerat J. Vermeij, argue that natural ecosystems are organized for high productivity and diversity while pointing out the conceptual parallels between economic development and evolution of ecosystems. Analyzing trends in the fossil records, they suggest that ecosystem diversity and productivity are increasing over macroevolutionary time and that the increase in ecosystem productivity is associated with an increase in turnover of living matter [87].

Perhaps, it may be useful to picture any given economy as a large evolving organization. The development of such an organization-economy is driven both by the internal dynamics of competing and cooperating businesses and institutions within the economy and by external relationships/transactions with the environment, including other economies. Much in the same way as the network of relationships/transactions between individual humans within a given business organization is a manifestation of an organizational network of interdependent and interacting functions evolving and performing as a whole, the interacting and interdependent social and business organizations within a given economy constitute a network of interdependent and interacting functions, which evolves and performs as one integrated whole, but on a larger spatiotemporal scale. Individual functions at both scales may be and are often invented and performed by physically different individuals/organizations.

To summarize, it is hardly coincidental that conceptually the same organizational pattern accounts for experimental reality whether we consider the organization and dynamics of molecules within the cell [2,6], of cells within the organism [3], of human individuals within the organization [47] or of organizations within the economy [86,88]. It is fair, therefore, to suggest that steady-state metastability may represent a universal dynamic organizational pattern conserved across different scales of (biological) organizational hierarchy, from sub-cellular structures to ecosystems and societies.

Another promising candidate for a scale invariant pattern is the dynamic integration of functions achieved through a continuous exchange of "moonlighting" components between different organizations within the same scale economy. Conspicuous at the sub-cellular scale, such an integrative strategy may not be as apparent at other scales of organizational hierarchy simply because it has either never been looked at systematically, as it is counterintuitive from the habitual mechanistic standpoint and from the conventional engineering design perspective, or it has not yet been adopted at every scale. Migratory and pollinator species as integrators of ecosystems, migrating cells, viruses and molecular species within and between cells and organisms are at least compatible with the idea of the dynamic integration through moonlighting being a scale invariant pattern. Although, in the human-scale economy, organized systematic exchanges of moonlighting employees across different organizations and/or between different departments within the same organization do not appear to be a prominent strategy at present, it does not mean that such exchanges will not become commonplace in the future. In fact, organizational analysts studying the behavior, evolution, and economic performance of organizations argue that the institutionalization of such exchanges may represent a winning strategy that enhances organizational adaptability and competitiveness in complex dynamic environments [41,89]. Comprised of about two hundred companies routinely exchanging personnel and intellectual property, the Toyota Production System with its remarkable combination of large-scale integration, high performance, and resilience to potentially devastating disasters, such as the Aisin crisis, for example, was cited as one of the real-world examples of emerging superior organizational strategies [71].

It is worth reiterating that, at the cellular scale, the steady-state metastability of sub-cellular structures/organizations and the continuous exchange of their shared (moonlighting) components allow the cell to efficiently perform as one integrated whole of immense complexity, on the one hand, and, on the other hand, to remain responsive and sensitive to the constantly changing opportunities and challenges in ambiguous and unpredictable dynamic environments [2]. Perhaps, business managers, organizational theorists, economists and policy analysts, on one side, and molecular and cell biologists, on the other side, may profit admirably from collaborations aimed at learning how Nature has already solved, at the molecular and cellular scales, the organizational challenges we currently face at the human scale of organizational reality, instead of reinventing the bicycle by the slow process of trial and error (see *Inter-scale conceptual mapping*).

Conceptual revisions

The reinterpretation of biological organization and dynamics within the conceptual framework of self-organization bears too many ramifications to be explored by any single author or even listed within the confines of a single paper. Let us, therefore, restrict our discussion by considering only a few more examples illustrating the explanatory and predictive powers of the new conceptualization.

Take, for example, the concept of function. According to conventional views, which are based on the unconscious belief in the adequacy of such mechanistic concepts in biology as "design" and "reverse engineering", function is an attribute assigned to the part by the design of the whole, and thus can be understood by studying isolated parts and inferring the design of the whole. Quite differently, the paradigm of self-organization stipulates that any novel function emerges at first as a serendipitous invention of the part and is then preserved as a function as long as it provides selective advantage to and/or secures the existence of the whole, helping the whole to endure and to prosper. In other words, any novel function is at first selected to exist, because it provides competitive advantage to the whole, and any existing function is then maintained by all available means, either because it still provides competitive advantage or because it transformed, at some moment in the past, from being simply advantageous to being essential as competition caught up. Any function is normally maintained through recruitment of available part(s) to perform the function, most likely by means of appropriate allocation of resources within the organization of the whole.

To illustrate this latter conjecture, let us recall the recruitment model of metabolism. Within the self-organizational paradigm, the function of an enzyme, and of any protein to this end, is not inbuilt into and inseparable from the enzyme, but emerges as a compromise between the capabilities of the part and the needs of the whole, a larger scale system, such as the cell. A particular enzyme/protein is recruited to perform a required function because it is an appropriate candidate for this function under given conditions. This situation is adequately described using the social metaphor of hiring an appropriate candidate for the vacant position representing a certain function within a complex business organization: a trained specialist would be preferable in most cases but simply an available candidate with a "good fit" to the organization could be a viable (and in some cases even advantageous) alternative as well. In the same way, if there is no "appropriately trained" candidate-specialist around, the needed function in the cell/organism may simply be performed by a suitable candidate that is available, albeit maybe less efficiently. Indeed, the fact that the deletion of the gene for beta-galactosidase followed by appropriate selection results in the appearance of new beta-galactosidase activity supports the notion that function is not an inherent attribute of the part, but is defined by the needs of the whole [90,91]. Also, the problems caused by the lack of "appropriately trained" candidate(s) for a given function can be solved through reorganization of the system. As an example, the absence of myoglobin, which performs an essential function of intracellular oxygen transport, was compensated for in myoglobin knockout mice by higher densities of capillaries and increased blood oxygen-carrying capacity, which presumably allowed the knockout mice to rely on purely diffusion-based mechanisms for oxygen transport [92,93]. Quite differently, the mechanistic mindset assumes that the properties of the part, such as the physico-chemical composition and three-dimensional structure of a protein for example, specify its function within a larger scale system, much like the physical structure of a gear determines its function within a clockwork mechanism [5].

It is fair to suggest that while the recruitment to an existing function is a question of finding the best fit between the needs of the whole and the capabilities of available parts, the emergence of new functions is driven by the inventive activity of individual parts. A fortuitous activity of an individual part that happened to confer a competitive advantage to the whole may come to be supported through appropriate (re)allocation of resources within the whole, thus emerging as a new function. It is likely to be maintained and supported as long as it makes the whole more competitive. Notice that often, and maybe always, a function is the activity that mediates a specific form of energy/matter/information exchange or transformation. As such, it does not necessarily have to be performed by its initial inventor all the time. In other words, once emerged, function is dissociable from the physical part performing it and becomes a virtual entity, a need of the whole. One may think of any organization, be it the cell, the ecosystem or the business organization, as a system of interacting virtual functions that can be and are often performed by physically different real parts at different times during the lifespan of the whole, which is normally much longer than the typical lifespan of individual parts. What exists and evolves as a whole is a particular organization of energy/matter/information exchanges, i.e. an organizational form, which is actualized at any given moment by the concrete physical entities-individuals engaged in exchanges of energy/matter/information among themselves and with their environment. These physical entities/individuals may come and go, while the organizational form lives and evolves. It should be pointed out that the entities/individuals passing through the virtual organizational form are endowed with their individual sets of choices and activities/behaviors, which are defined and bounded by individual internal structures encompassing their individual memories/histories, and that it is the individual choices and actions at the scale of the parts that renders the organizational whole alive, intelligent, and adaptive on the scale of the whole.

As an example, the concept of recruitment for evolution of new functions makes the surprising discovery of so-called moonlighting proteins, which perform more than one function in the cell and/or in the organism, less surprising and even expected in hindsight. If a protein, be it enzyme or not, through its serendipitous activity happens to be useful for a larger scale system, be it the cell or the organism, by "useful" meaning providing selective advantage to the host cell/organism as a whole, it would only be prudent to allocate additional resources in support of such useful activity, which can be achieved by boosting expression of and/or duplicating the useful gene, for example. As a next, but optional step, the new activity may be subject to economic optimization through genetic and/or epigenetic mechanisms. It may thus be speculated that evolutionarily older proteins are more likely to have multiple functions, simply because they have had more evolutionary time and opportunities "to invent" new functions while operating within relatively loosely organized ancient hosts, as compared to evolutionarily younger proteins "born" more recently into the complex and highly regulated organizational environment of modern cells and organisms. Also, since self-organization is driven by economic competition, evolutionarily older proteins are more likely than younger ones to be intimately involved in cellular economy, i.e. metabolism. Perhaps, this may explain why at least 7 out of 10 glycolytic enzymes and at least 7 out of 8 enzymes of the tricarboxilic cycle moonlight or are suspected to, and why glyceraldehyde-3-phosphate dehydrogenase (GAPDH), the product of one of the ancient genes existing for millions of years, has at least 10 confirmed non-enzymatic moonlighting activities [94]. It is tempting to speculate that the products of so-called "house-keeping" genes may, therefore, constitute the least flexible part or, in other words, the "skeleton" of functional organization of the cell/organism.

After all, the belief that reverse engineering, reductionism, and mechanistic interpretations are adequate and sufficient means to provide us with the designs and, thus, with the understanding of biological systems is only an illusion of the mechanistic mindset, simply because no such designs appear to exist according to experimental reality. An ecosystem, an organism, a cell, and a macromolecule, each on its own spatiotemporal scale, survive and excel as best as they can. They represent transient organizational forms that emerge, evolve, and vanish within one integrated multiscale economy of living matter, where they interact with, shape and, at the same time, are being shaped by other organizational forms. The ecosystem, the organism, the cell and the macromolecule, each on its own scale, are adaptive and flexible organizations that can exist and perform in multiple configurations, achieving the same ends in different and potentially innumerable ways. And each of their many configurations and developmental trajectories represents a unique "design" in the conventional sense of the word. The multiplicity of protein folding pathways, remarkable insensitivity of protein folding to mutations, alternative pathways for synthesis of the same metabolites, suppressor mutations and the apparently normal phenotypes of mice missing presumably essential genes are but a few examples of the organizational flexibility of living matter.

It was recently suggested that what is erroneously perceived and interpreted as "design" (due to the habit of mechanistic conceptualization) is, in fact, memory [7]. The concept of evolutionary memory, which was recently added to the expanding conceptual framework of self-organization in order to replace the notion of design, is equivalent to the concept of biological structure, the latter meaning a spectrum of alternative configurations of energy/matter/information exchanges available to a given system, be it a biomolecule, a sub-cellular organization, a cell, an organism or an organization. Such an expanded notion of biological structure stipulates that any given biological structure represents a bounded set of alternative configurations of energy/matter/information exchanges and that any given actualization of biological structure is the outcome of a unique, context-dependent developmental trajectory. Any actualized biological structure, therefore, is a unique organization of energy/matter/information exchanges that embodies the ontogenetic memory of its own development and the phylogenetic memory of the evolution of the set. Unlike design, evolutionary memory, in the same way as the "real" memory studied in neuropsychology [95], is contextual and flexible. It does rely on the past, but accommodates to the present and remains open to alternative futures [7].

Because any given biological organization performs its function within the economy of a larger organizational scale and is forced by evolutionary competition to balance efficiency and adaptive plasticity, the pressure for efficiency tends to narrow the configurational space available for a biological organization, while the pressure for adaptive plasticity tends to expand its spectrum of permitted configurations, with both trends active at both ontogenetic and phylogenetic time scales. As one of the consequences, a prolonged life in a controlled and stable environment, a natural desire and an aim of any biological organization, would inevitably lead with time to a narrowing of the configurational space available for a successful biological organization and to a decreased adaptability/plasticity at all interdependent scales of organizational hierarchy. Considering ontogenetic time scales, this inevitable outcome has an obvious import for understanding of such conspicuously ubiquitous biological phenomena as aging and degeneration, which are manifested as a progressive loss of plasticity/adaptability at all organizational scales within an ageing organism, from global physiology through individual organs down to individual cells and molecules. Considering phylogenetic time scales, this inevitable outcome raises questions about the consequences of environmental stabilization for human health. The reconceptualization of health, aging and degeneration as economy-driven, multiscale organizational phenomena may prove to be much more fruitful in both theoretical and practical terms than the conventional theories of health and aging locked within the conceptual box of the mechanistic "tear-and-wear" interpretations.

To summarize, the systematic conceptual revisions of conventional mechanistic interpretations of biological (and non-biological) organization and dynamics within the framework of self-organization are likely to bring about a wealth of unexpected revelations and discoveries. The conceptual framework of self-organization provides a fresh perspective on biology and on the world in general, suggesting new and promising directions for scientific inquiry while at the same time clearly marking inadequate interpretations and those avenues of research that are likely to be fruitless and wasteful. Moreover, because the self-organizing fractal theory stipulates the self-similarity of scales as a universal form of symmetry pervading all living matter, capitalizing on such symmetry naturally suggests a new approach to scientific discovery. As is further argued, the reconceptualization of adaptive complex phenomena/systems within the framework of self-organization followed by mutual mapping and co-alignment of the organizational patterns uncovered at different spatiotemporal scales can be used as a scientific discovery method and, simultaneously, as a way to unite specialized scientific disciplines within one and the same interpretational framework/paradigm.

Inter-scale conceptual mapping as a scientific method

To illustrate how reconceptualization of available knowledge followed by mutual alignment and complementation of the knowledge structures pertaining to different spatiotemporal scales can be used as a practical discovery method, let us consider the conceptual parallels between cellular metabolism and the human-scale economy.

In his work "The Wealth of Nations", Adam Smith makes an insightful observation that the extent of the division of labor is limited by the size of the market. It reaches a greater degree in a wealthier society in comparison to a poorer one and is promoted by a high density of population found in towns but not in scattered small villages. He also emphasizes the critical importance of efficient transport and communication systems both for wealth generation and for the degree of the division of labor. Smith points out that the first civilized societies with a developed division of labor emerged and thrived on sea-coasts and on the banks of navigatable rivers, i.e. in environments where humans could make use of "water-carriages", which were at the time the only economically efficient means of transportation able to support relatively high rates of trading exchange. Mapping these patterns on the biology of the cell prompts one to hypothesize that it is the sizes of internal and external markets for the products of individual cells that allow for and support the complexity of modern cells in multicellular organisms. The paradoxically enormous macromolecular densities inside modern cells, estimated to be up to 200-300 mg/ml of protein alone [96], and even the very existence of cells as such begin to make much more sense in the economic context of self-organization, for a high density of macromolecules means a large internal market and the relative ease and efficiency of intermolecular exchanges of energy/matter/information. A large market and efficient exchanges are conducive to and promote division of labor, economic efficiency and wealth generation, thus providing competitive advantage to the cell as a whole. Of note, the same logic applies at the scale of the whole organism (and up), of course – this may explain why organisms are so densely packed with cells (as cities with people) and why internal fractal-like systems of energy/matter/information distribution and exchange have necessarily evolved/emerged as a common, if not universal, organizational feature of organism physiology [97]. It also becomes reasonable to suggest that the development and maintenance of such a complex molecular economy as the one observed inside the cell pre-suppose the existence of an active and economically efficient system of intracellular transport and exchange, which is most likely organized as a fractal. The intracellular exchange/distribution systems of individual cells should also be necessarily coupled - structurally and functionally - to a larger scale organization of energy/matter/information transport and exchange, i.e. to the circulation system of the organism.

It should be pointed out that the textbook image of the cell as a well-mixed watery bag of enzymes and other organic materials is not really supportive in regard to these speculations. But since the conventional image is not consistent with experimental reality either, so much worse for the image. Even a cursory review of the existing research literature makes a strong case for the existence of a highly organized intracellular circulation system. The intracellular circulation has been invoked in a multitude of experimental and theoretical studies performed independently by a variety of investigators, who invariably came to the same conclusion while pursuing their own research interests and lines of inquiry. A few examples may suffice. West and colleagues, in their efforts to explain allometric scaling in biology, namely the three-quarter power-law relationship between the standard metabolic rate of a species and the species's body mass, which appears to hold from proteins to elephants, proposed a generalized theory of fractal organization of biological organisms. Their theory, which provides an elegant explanation of allometric scaling, remarkable in its generality and its ramifications for biology, directly demands the existence of an intracellular distributive system of energy/matter coupled to organismal circulation, and predicts that this intracellular system is organized as a fractal, due to the pressure for economic efficiency [97]. Coulson put forward the flow theory of metabolism in order to resolve the paradox created by conventional biochemistry between the large (up to three orders of magnitude) differences in basal metabolic rates observed between small and large mammals and the apparent absence of significant differences in their metabolic enzymes and the circulating nutrient concentrations measured within the same animals [98-100]. The flow theory directly implies the existence of a highly developed intracellular organization and intracellular circulation. Wheatley and Clegg refined and expanded Coulson's ideas to the cell internum, suggesting the microtrabecular lattice discovered by Porter with the help of high-voltage electron microscopy as a possible physical correlate of the cytomatrix organization [100-102]. Hochachka pointed out that conventional diffusion-based and concentration-driven models of metabolic regulation predict major changes in concentrations of metabolic pathway intermediates upon the transition from low- to high-work rates in the cell. These predictions, however, are in stark contradiction with the experimental reality indicating that over 60 metabolites tested at different loci and in different pathways remain remarkably homeostatic upon such transition. Noticing that this paradox is a product of the inadequate assumptions implied in the conventional "watery bag" image of the cell, and that this paradox cannot be resolved without changing those assumptions and the image itself, Hochachka made a sound case for an intracellular convection system, presenting a wealth of experimental evidence that suggest or implies its existence [93].

To summarize, the predictions derived from an inter-scale conceptual mapping of a human-scale economy onto cell physiology and the experimental reality of cell physiology are consistent with each other, while both of them defy the conventional image of the cell built on mechanistic interpretations and reductionist reasoning.

It is evident that even a brief and coarse-grained comparison of human-scale economy and cellular metabolism, when both phenomena are reconceptualized in the equivalent terms of economy-driven self-organization, allows for a productive re-evaluation and restructuring of experimental and theoretical knowledge pertaining to cell physiology, using the structure of the relatively well-understood organizational patterns in human-scale economy both as a structural template and as a "relevance filter", i.e. as a paradigm. Even though in this particular illustration a larger scale phenomenon, the economy, was used to assist reconceptualization and restructuring of a smaller scale phenomenon, i.e. cell physiology, and only two scales were considered, it should be pointed out that, generally speaking, the inter-scale conceptual mapping is an intrinsically scale-free process, where a successful organizational form of knowledge structure may propagate both ways, up and down the scale. In other words, the scale-invariant organizational concepts, patterns, and measures discovered at or appropriated from one scale can be used to organize the knowledge structures at many other scales in a mutually molding manner, using the principles of parsimony and self-consistency as selective constraints applied across and within individual scales. It can be shown, for example, that the organizational patterns outlined for evolution of cellular metabolism at the beginning of our discussion have their counterparts in economic, social, ecological, and even psychological phenomena. Vice versa, certain organizational patterns discovered by organizational ecologists, sociologists, economists, and psychologists within their respective disciplines are likely to provide deep insights into the organization and functioning of the cell and organism when used as templates to structure the experimental reality in molecular, cellular, and organismal biology/physiology. The conceptual framework of self-organization provides a common language for communication and exchange of knowledge and methodology across borders of specialized disciplines, thus transforming the whole of human knowledge into one integrated dynamic medium, where alternative organizational forms of knowledge emerge, compete, and cooperate, exerting their morphing influence across and within different spatiotemporal scales.

It is fair to suggest that, as a scientific method, inter-scale conceptual mapping demonstrates an apparent potential to bring about a rapid progress in and a mutual enrichment of numerous fields of scientific inquiry, while at the same time establishing conceptual consistency across different spatiotemporal scales and across different disciplines. It is worth reiterating that inter-scale mapping is not limited to qualitative comparisons (even though it does provide an immediate opportunity of grasping the essence of many seemingly disparate complex adaptive phenomena to anyone who is well-versed in at least one of the specialized fields dealing with self-organized complexity). Applying the quantitative frameworks of graph theory, statistical physics, percolation theory, fractal analysis and the theory of phase transitions to a variety of organizational phenomena, the emerging multidisciplinary science of networks rapidly learns to capture the biological and non-biological complexity with ever-increasing precision and depth, using quantitative descriptors, measures and models amenable to comparative analysis [11,13,71-74].

In conclusion, it should be pointed out that, in reality, the emergence of such a scientific method appears to be unavoidable and is already under way, albeit perhaps in an unconscious, unformulated and unfocused form at present. The rapidly growing interdisciplinary popularity of such universal concepts as networks, fractals, self-organized criticality, self-organization, phase transition, percolation, and others, as well as of the models, measures, and methods associated with these concepts, can be viewed as a manifestation of the fortuitous discovery of scale-invariant organizational concepts, patterns and measures followed by increasingly successful attempts of applying them to an increasingly wider range of complex phenomena. This activity, in turn, promotes the slow and difficult process of reconceptualization, a process that is slowed and resisted by the powerful influence of the organizational forms/structures - the proponents of the mechanistic paradigm - that reside both in our unconscious and in our society and institutions. It is fair to suggest that the focused search for scale-invariant concepts and patterns combined with the qualitative and quantitative co-alignment of knowledge structures pertaining to different disciplines and scales, through collective cooperative efforts of experts and specialists, may dramatically accelerate the positive changes gradually taking place both in our unconscious and in our society, to the common benefit, and perhaps survival, of all.

The big picture

The classico-mechanistic conceptualization and reductionism embodied in the Newtonian-Cartesian paradigm of the world gave an incredible power of comprehension to the societies that were first to adopt them as an organizational form structuring their knowledge and experience of objective reality. The Scientific and Industrial Revolutions, which brought explosive economic growth and great political and military power to early adopters of the Newtonian-Cartesian paradigm - thus ensuring the rapid worldwide expansion and the influence of both the adopters and the paradigm - are the clearest proofs of the advantage in looking at the world through the conceptual glasses of the mechanistic framework.

As a mental organizational form, mechanistic conceptualization and reductionism proved to be remarkably advantageous in practical terms for the rapid and efficient generation of wealth, and thus were fixed and preserved in the mental dimension of Western societies as a successful conceptual framework. Part of the wealth generated with the help of the mechanistic paradigm was/is used for the further development of sciences, which was/is pursued largely through the fragmentation-specialization mechanism, without challenging the parental framework itself. Classical physics became regarded, and deservingly so, as the mother of rational science, the standard to align with and the example to copy. The other disciplines followed suit. In economics, for example, the appropriation of concepts and methodologies from mathematics and physics by Marginalists, such as Walras, Jevons and Pareto, was meant to bring the quantitative rigor of "hard" sciences to the traditionally "soft" and speculative theories of their predecessors, social philosophers such as Adam Smith, in an effort to turn economics into a "real" science [81]. The same trend, to a larger or smaller degree, affected virtually every specialized domain of rational inquiry, including molecular and cell biology.

However, even though today we live surrounded by the wonders created with the help of the classico-mechanistic paradigm and reductionism, including, among myriads of others, modern research technologies that generate a wealth of data and computer technologies that process and analyze the information being generated, it is becoming clear that for a certain class of phenomena/systems the classico-mechanistic paradigm excels at generating information, but fails at meaningful structuring of the information it generates so successfully. The failure of the mechanistic framework to structure the experimental reality of certain phenomena into self-consistent and unambiguous images is leading to a paradoxical situation when increasing amounts of experimental data bring about increasing confusion rather than better understanding. The phenomena/systems in question, therefore, have been appropriately termed "complex". Pertinently, complex phenomena are common to those domains of human activity and knowledge where problems are piling up with no solutions in sight. Consider, as examples, climate change, local and global socio-political and socio-economic problems and conflicts, ecological and environmental crises, stagnation in sciences and arts, degradation of mental and physical health.

In their essence, complex systems/phenomena defying the mechanistic interpretational paradigm represent collective organizational phenomena, in which multiple adaptive agents interact with each other, following local decisions and rules, and in which the coordination and organization of individual activities give rise to the emergence of global properties and characteristic patterns at the scale of collective behavior. Collective behavior is observed, measured, and interpreted as one whole by the human observer, who then calls it the "complex system" with emergent properties. Proteins, cells, organisms, ecosystems, organizations, societies and economies are but a few examples of such collective organizational phenomena.

Although the classico-mechanistic object and the complex living system are different in many aspects, it is worth emphasizing two of them. Namely, the relative strengths of external versus internal couplings of an object/system and the organizational dynamics of the internal couplings maintained between constituents of the object/system. Generally speaking, internal couplings, meaning exchanges of energy/matter/information, between the constituents of a classico-mechanistic object are exceedingly strong in comparison with the external couplings of the object to its environment, so that the internal organizational state of the classico-mechanistic object is largely independent from the environment in a wide range of environmental conditions. The classico-mechanistic object is uncoupled from and thus insensitive to its environment. On contrast, the internal organizational state of a living system is sensitive to and is often modified by fluxes of energy, matter or information through which the living system is coupled to its environment. The strengths of external couplings maintained between constituents of a living system and the environment may be or may grow comparable with that of the internal couplings maintained within the system. In addition, the organization of internal couplings, i.e. the organizational state of the living system, tends to change along with a changing environment, being a reflection of the environment in a certain sense. The living system is coupled to and to a large extent defined by its environment, co-evolving together with the environment. In fact, the definition of what constitutes environment and what constitute the living system is ambiguous and relative, as living systems may fragment, on the one hand, and exert a strong controlling influence over or even absorb their environments in the course of adaptation and evolution, on the other hand.

At any given time, the network of internal couplings maintained between individual constituents of a living system has a statistically preferred but modifiable, i.e. adaptive, organization, which is manifested as the spatiotemporal structure of the living system (Fig. 1, inset). The structure of the living system carries both phylogenetic and ontogenetic memories of the previous encounters between the system (evolving as a spatiotemporal organizational form) and the environment. Conceptually, *any biological structure is a memory.* Because living systems continuously influence each other through exchange of energy/matter/information, their individual organizational states and behaviors may become coordinated and organized, giving rise to metastable collective macro-states and macro-behaviors, which then emerge and exist as complex adaptive systems at larger spatiotemporal scales. The strong environmental coupling of living systems, their context-dependency, and the memory-based adaptability of their internal structures/organizations may explain why mechanistic conceptualization and reductionism are so appropriate and efficient when dealing with classico-mechanistic objects and are so misleading and confusing when applied to living organizations.

Perhaps, the closest analogy to living systems in physics is critical phenomena taking place during phase transitions in non-living matter. A non-living system, such as water vapor or ferromagnet, is said to become critical when it approaches organizational state transition, from gas to liquid or from the non-magnetic to magnetic phase, as examples [103]. Notably, the strength of internal couplings between constituents of a system needs to be tuned so as to become not too strong and not too weak for critical phenomena to emerge. In physical systems, such tuning is usually achieved by adjusting some external parameter, such as pressure or temperature. Remarkably, the prominent features of critical phenomena, such as cooperative behavior, long-range correlations, non-linearity, large variability and fluctuations, sensitivity, instability, choice, fractal organization, self-similarity of scales, power laws and even memory effects, are highly characteristic of living systems and very uncommon and often antithetical to machines and conventional engineering. It appears, therefore, that living systems continuously maintain themselves in the state of self-organized criticality [66]. In this regard, it is important to point out that conventional mathematical tools, such as differential calculus and Gaussian statistics, which are routinely used in the field of conventional engineering and, by analogy and habit, in biology interpreted in mechanistic terms, are inappropriate for quantitative descriptions of the fractal organization and dynamics of critical systems, where fluctuations are scale-free, response functions are nondifferentiable and the mean and variance are meaningless. An obvious implication being that, in many, and perhaps most, cases, conventional mathematical tools and methods are inappropriate for quantification and modeling of biological organization and dynamics. As was pointed out on a number of occasions, fractal analysis, fractal statistics as well as scaling techniques from statistical physics may need to be used instead of conventional math and statistics in order to capture biology in quantitative terms [104-106].

Experimental evidence of the fractality and criticality of living matter is, meanwhile, abundant and continues to accumulate at increasing rates, converging from different lines of scientific inquiry to one and the same general conclusion. As early as 1972, Benoit Mandelbrot, who pioneered the application of fractal analysis to spatiotemporal organization of natural objects and systems, pointed out the abundance of fractals in nature and showed that the lung's bronchial trees, vasculatures and botanic trees as well as the variation of prices in stock and commodity exchanges are organized as fractals [104]. Since then, in biology, a variety of other organ systems, such as the nervous system, bowel, biliary ducts, renal calyces, and others, were found to contain fractal-like structures [107]. At the cellular scale, neurons [108], dendritic arborizations [109] and sub-cellular organization [110] were found to exhibit fractal properties.

The application of fractal analysis to physiological time series revealed that such outputs of human physiology as heartbeat, gait, brain activity, and others show self-similarity in their fluctuations at different time scales, suggesting criticality and fractal organization of the systems generating such signals/outputs. Notably, the disruption of the fractal organization of physiologic time series was linked to pathology, aging, and degeneration [107,111]. Long-range correlations in the time series characterizing protein structure fluctuations are consistent with the idea of fractal organization of proteins [21,51,112-114]. Fluctuation behaviors of economic indicators, protein structures and organs are characterized by remarkably similar statistical patterns, implying similarities in the organization and dynamics of the corresponding systems.

Perhaps the most abundant evidence of the fractal organization of living matter, which spans many spatiotemporal scales in a continuous and self-consistent manner from individual channel molecules through individual synapses, individual neurons and local neuronal circuits to the large-scale organization of the brain, has been amassed in neurobiology. The topological analysis of brain functional networks, based on the wavelet decomposition of magnetoencephalographic recordings followed by network formalization and analysis, has revealed the fractal organization of the brain [115]. The conclusions of large-scale analyses of the brain are well consistent with and echo the results and conclusions of studies of spatiotemporal synchronous neural activity in acute and organotypic cortex slices, which suggested self-organized criticality and fractal organization of the local neuronal networks responsible for spontaneous synchronized activity patterns in superficial cortical layers [116]. The gating of ion channels [117,118], vesicular exocytosis [119], spike trains [120] and local amplitude fluctuations of the human electro- and magnetoencephalograms [121] were found to exhibit fractal (self-similar) behavior in time. Notably, the breakdown of fractality in theta oscillations in patients with major depressive disorder indicates that the fractal organization of neuronal activity may represent a salient feature of the healthy human brain [122].

To explain Kleiber's law, i.e. the scaling of standard metabolic rate as three-quarter power of body mass in biology, West and colleagues suggested fractality as a universal geometrical principle underlying the organization of physiological systems mediating distribution and exchange of energy and matter within biological organisms [97]. The theoretical models of West et al. harmoniously weave together evolutionary theory, economic optimization of energy/matter exchanges between internal and external environments, and fractal geometry into a universal organizational principle that may hold over many, and maybe all, scales of biological organizational hierarchy [97,123,124].

Significantly, fractal organization is not exclusively specific for what is traditionally regarded as biological systems, but is found ubiquitously in nature. Applying graph theoretical approaches to analysis of metabolic networks, Ravasz et al. revealed their hierarchical organization and suggested that hierarchical modularity may represent a generic architecture of many biological and non-biological scale-free networks [125]. Song et al. showed that many scale-free hierarchical networks, such as, for example, the World Wide Web, social networks, protein interaction, and metabolic networks have fractal organization [126]. Power-law distributions, a symptom of self-organized complexity, are a conspicuously common natural pattern [127]. The sizes of earthquakes [128], intensities of solar flares [129], number of species in biological taxa [130], city population sizes [131], personal wealth [131] as well as fluctuations of financial market indices, growth domestic products, business firm sizes and other economic and social indicators [76] are all well approximated by power-law distributions. Since power-law distributions naturally emerge from the self-similarity of scales, the ubiquity of power laws in nature is consistent with the image of the living matter continuum maintained as a spatiotemporal (multi)fractal.

Altogether, the self-similarity of organizational patterns at different spatiotemporal scales, which has been either experimentally demonstrated or indirectly deduced for a remarkably wide spectrum of complex adaptive systems and organizational phenomena, ranging from molecules to economies and ecologies, supports the self-organizing fractal theory of living matter and may explain the apparent efficacy with which inter-scale conceptual mapping reveals the universal scale-invariant structural and dynamic patterns shared by different self-organizing phenomena/systems.

Unquestionably, the mechanistic way of thinking and reductionism have become our unconscious operational defaults for very good reasons. Adherence to the mechanistic paradigm is a well-meant and rational consequence of its unsurpassed and glamorous success in explaining and predicting the experimental reality of classico-mechanistic objects. The mechanistic paradigm and reductionism brought about and support the economic prosperity and well-being of a great number of people. They are here to stay and be celebrated as one of the greatest achievements of human intelligence, and deservingly so. However, their very success and power, if misused and unchecked, are likely to lead to the worst assault on reason, plunging the whole of collective rationality into a state of delusion. Imagine an individual who invented a mental heuristic that happened to be useful for solving a number of related problems. Among rational people this person would be considered as naïve at best if he or she insisted that this one method is applicable to *all* problems, just because it generates a lot of data and some of the data may even be interpreted as relevant to the problems the method is applied to. Whether at the scale of individual rationality or at the scale of collective rationality, indulgence in wishful thinking in the face of an apparent misfit between theory and experimental reality is counterproductive and is bound to spell a disaster. It is a state of denial, which must be overcome by the willful efforts of considering alternative solutions, approaches, and frameworks. The Newtonian-Cartesian paradigm is a founding framework of modern sciences, but it would be irrational to believe that it is a final and all-embracing one. Ironically, such belief turns the mechanistic paradigm into a form of religion itself. And in the same way as the success and power of institutionalized religion were misused in the past, leading to the medieval atrocities and crimes against humanity done in the name of God and causing a widespread intellectual and economic stagnation, the success and power of the Newtonian-Cartesian paradigm, its institutionalization and the blind adherence to the mechanistic worldview can be easily misused, setting off the modern equivalent of the Dark Ages in the name of scientific and technological progress.

Summary and conclusions

It is suggested that living matter exists as one developing multiscale continuum-economy of energy/matter/information exchanges organized as a spatiotemporal fractal. The continuum-economy of living matter is composed of the interdependent and mutually defining/molding adaptive organizational forms/networks of energy/matter/information exchanges. These adaptive organizational forms/networks co-exist and co-evolve together at different spatiotemporal scales and are manifested as such familiar organizational phenomena as biomolecules, cells, organisms, ecosystems, organizations, societies and so forth.

The self-organization of biomolecules into cells, cells into organisms and organisms into societies and ecosystems proceeds through a scale-invariant organizational process driven by economy and facilitated by memory and stochasticity/innovation. It is driven by economy as individual constituents of living matter at every scale compete and cooperate in their efforts to maximize the rate and efficiency of energy/matter/information extraction from their environments and the rate and efficiency of negative entropy production. It is facilitated by evolutionary memory, where memory is defined as a bounded set of spatiotemporal configurations of the energy/matter/information exchanges maintained between individual constituents of a given biological organization. The spatial aspect of memory approximates the conventional notion of (biological) structure/organization, while the spatiotemporal aspect of memory approximates the conventional notions of (biological) development and behavior.

The notions of "development" and "behavior" are likely to be conceptually synonymous, describing the same process but referring to vastly different spatiotemporal scales. Ontogenetic development is a recall of a phylogenetic memory in a new environmental context. Biological behavior is a recall of an ontogenetic memory in a new environmental context. Each memory recall ends up either sustaining and reinforcing an old idea/form/context or creating a new idea/form/context. The persistence of a given memory/structure/idea and its success in terms of its influence on the environment are defined by the economic performance of this memory/structure/idea and by its contribution to the persistence and success of a larger-scale biological organization of which this memory/structure/idea is a constituent.

Stochasticity, individual self-expression, innovation and choice, being different aspects/expressions/names of one and the same activity, facilitate the exploration and discovery of new organizational forms and patterns by generating diversity of alternative forms - individuals, ideas, behaviors and structures - that compete and cooperate with each other to survive and prevail. *Each newborn individual is a seed of a new idea.*

The process of self-organization blends Darwinian phases dominated by diversification, competition, and selection, and organizational phases dominated by specialization, cooperation, and organization. Darwinian phases create and improve parts. Organizational phases create wholes. The economic competition among different organizational forms at every spatiotemporal scale of the ever-evolving and dynamic continuum of living matter enforces scale-specific organizations to continuously balance organizational adaptability and economic efficiency, thus ensuring the conservation of adaptive plasticity, perceptiveness, criticality and organizational structure/memory across all scales of biological organizational hierarchy. Self-organization, as life itself, is an ever-expanding process covering increasingly larger spatiotemporal scales through the formation of interdependent organizational hierarchies.

The adaptation of biological organization to environmental changes and/or to internal stresses/crises in the course of evolution is achieved by means of recurring organizational state transitions. An organizational state transition proceeds through local or global relaxation of pre-existing organizational structure into a transient state of relative disorder, which is followed by local or global self-organization and the emergence of a new organizational structure that matches the environment better than its predecessor. Organizational state transitions are triggered by a misfit/disharmony between a given biological organization and its environment, which is manifested and/or perceived as a failure of or a deficiency within the internal economy of the organization. Adaptation means a restoration or an improvement of the match between the biological organization and its environment, with a better match corresponding to a higher rate and/or to an improved efficiency of energy/matter/information exchanges between the biological organization and its environment.

In a certain sense, any biological organization is a reflection, crude or refined, of its environment. Since living matter represents a hierarchical set of nested self-organizing forms/networks of energy/matter/information exchanges, which are manifested as societies, ecosystems, organisms, organs, cells, and molecules, and because different complex systems constitute each other's environments, they are all forced by economic competition either to mimic their environments to an increasingly precise degree and/or to shape their environments after their own image, thus unwittingly establishing and maintaining self-similarity of scales within the living matter continuum. The organizational forms/systems that fail to do so are selected against, loosing economic competition with others, and vanishing in the course of self-organization/evolution of living matter. From the mechanistic point of view, this may explain why and how the spatiotemporal self-similarity of scales is established and maintained within the continuum-economy of living matter. From the metaphysical point of view, self-similarity of scales ensures continuous self-awareness of living matter expanding over multiple spatiotemporal scales.

Self-similarity of biological organization and dynamics across different spatiotemporal scales represents a form of symmetry pervading all living matter. This symmetry can be exploited both for scientific discovery within specialized disciplines and for the unification of sciences within one and the same conceptual framework by 1) finding and defining scale-invariant organizational concepts, patterns, and measures; 2) reconceptualizing the organizational phenomena of different scales in the same scale-invariant terms and 3) mapping knowledge structures pertaining to the phenomena/systems of different scales onto each other, using overlapping patterns for alignment, filling in missing parts and re-structuring misaligned patterns on the assumption of spatiotemporal self-similarity of scales. By its very nature, such inter-scale/inter-disciplinary mapping inevitably leads to the mutually informing and mutually molding unification of specialized disciplines within one and the same conceptual framework and, thus, to the emergence of one integrated global knowledge/image of objective reality shaped by the collective contributions from individual sciences and guided by the principles of parsimony, self-consistency and self-similarity applied within and across different disciplines and scales. Indeed, it appears that the whole is in every one of its parts, but the parts can only know the whole when they create it together.

Self-organization is creation of knowable reality.
Creation of knowable reality is cognition.

Acknowledgments

To the memory of Kurakina Taisia Vasilievna.

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