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A general theory of evolution based on energy efficiency: its implications for diseases

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Summary We propose a general theory of evolution based on energy efficiency. Life represents an emergent property of energy. The earth receives energy from cosmic sources such as the sun. Biologic life can be characterized by the conversion of available energy into complex systems. Direct energy converters such as photosynthetic microorganisms and plants transform light energy into high-energy phosphate bonds that fuel biochemical work. Indirect converters such as herbivores and carnivores predominantly feed off the food chain supplied by these direct converters. Improving energy efficiency confers competitive advantage in the contest among organisms for energy. We introduce a term, return on energy (ROE), as a measure of energy efficiency. We define ROE as a ratio of the amount of energy acquired by a system to the amount of energy consumed to generate that gain. Life–death cycling represents a tactic to sample the environment for innovations that allow increases in ROE to develop over generations rather than an individual lifespan. However, the variation–selection strategem of Darwinian evolution may define a particular tactic rather than an overarching biological paradigm. A theory of evolution based on competition for energy and driven by improvements in ROE both encompasses prior notions of evolution and portends post-Darwinian mechanisms. Such processes may involve the exchange of non-genetic traits that improve ROE, as exemplified by cognitive adaptations or memes. Under these circumstances, indefinite persistence may become favored over life–death cycling, as increases in ROE may then occur more efficiently within a single lifespan rather than over multiple generations. The key to this transition may involve novel methods to address the promotion of health and cognitive plasticity. We describe the implications of this theory for human diseases.

Introduction

In classical evolutionary theory, fitness is characterized by parameters such as survival and reproductive success. We believe that return on energy (ROE) represents the ultimate basis of competition during evolution. ROE is defined as a ratio of the amount of energy acquired and assimilated by a system per amount of energy consumed to generate that gain. ROE can be viewed as the *energy efficiency* of a trait, an organism, or a system.

Complex systems, including biologic living systems, may represent an emergent property of energy. Living systems may be seen as competing

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ultimately for energy by acquiring traits to increase ROE. This theory encompasses evolutionary strategies pursued thus far during natural history. It also includes evolutionary strategies that may emerge in the future which do not involve the variation–selection hallmarks of Darwinian evolution. The theory of ROE also carries implications for the here and now: we review its potential impact on conceptualizing and managing disease.

Living systems as an emergent property of energy

One useful way to describe a system is in terms of its energy content. The sun contributed mass to the earth and continues to shower it with energy. If we consider the earth as a system, the earth absorbs more energy than it emits [1]. Increases in energy content on earth can be said to be stored in forms such as heat, chemical bonds, or complexity. Defining living systems in this context is a highly subjective exercise. Schrodinger stated, ''It is by avoiding the rapid decay into the inert state of 'equilibrium' that an organism appears so enigmatic'' [2]. A complex system requires energy to sustain itself or to become more complex. We choose to define living systems as those entities possessing a property whereby the acquisition of energy enables the building of features that promote future acquisition of energy.

Direct energy converters such as photosynthetic microorganisms and plants transform light energy into high-energy phosphate bonds that fuel biochemical work. Other direct converters of energy may also reside at the interfaces with the earth's core. Ordinarily regarded as the end product of compressed dead biomass, even hydrocarbon deposits apparently harbor life. Indirect converters such as herbivores and carnivores feed off the food chain initiated by these direct converters of energy. In general, systems will also tend to form relationships with other systems to access new sources of energy.

Complexity theorists have observed that self-organization of lower order units to produce higher order occurs in nature [3,4]. Such phenomena can be attributed to an emergent property of energy. While temptation exists to ascribe intention or a sense of pursuit to the conversion of energy to higher order in a complex system, it may simply occur as a supply-side manifestation of energy and represent a passive consequence of a thermodynamic phenomenon. Complex systems, including biologic living systems, may occur as an emergent property of energy.

Evolutionary implications

Return on energy as the basis of evolution

Living systems compete for the acquisition of energy and, in concordance with this objective, the acquisition of traits that optimize ROE. The history of living systems and evolution chronicles the optimization of ROE through the aggregation of proximate traits. Consideration of the role of ROE may represent the best paradigm for understanding the historical path of evolution, explaining the current distribution of traits, and identifying a potential future trajectory of evolution. In essence, evolutionary history can be characterized by the emergence and proliferation of traits that directly or indirectly contribute to both present and future energy acquisition. Competition for energy and acquisition of traits that optimize ROE can explain proximate behaviors ranging from wealth generation to survival tactics to mating preferences. Trait acquisition can occur in many ways, including assimilating genes from the environment or innovating from scratch through mutations.

Thermodynamic calculations may determine the relative success of these pathways for innovations. Each trait incurs a current energetic cost and can potentially yield a stream of future energetic benefits. Depending on whether a trait represents a physical or a cognitive adaptation, those traits that improve ROE become preferentially distributed via either reproduction or communication to other systems. Energy represents the fundamental basis of competition among living systems and the ultimate source of natural selection. Elements of modern evolutionary theory can be reinterpreted in this framework.

Darwinian evolution and return on energy

Organisms compete for energy. To this end, features that improve ROE confers competitive advantage. Life–death cycling may represent a specific strategy that enables a set of systems to acquire traits that improve ROE. Fitness is determined by the inventory of genetic traits enhanced by sampling and recombination. Reproduction represents a process that enables variation. Speciation may amplify the variation by reproductively isolating the offspring of a common progenitor. Success in improving ROE replaces success in reproduction as a more general definition of the net present value of a particular future evolutionary path [5].

In similar fashion to how one views reproductive success, one regards the net present value of the future stream of energetic gains as determining the long-term success of a trait, organism, or system. A trait that has a positive effect on current ROE may even negatively impact ROE in the long run. For instance, a trait that improves the ROE of a metabolic pathway may temporarily increase the ROE of the system to which that pathway belongs, but such a trait may also produce dysfunctions such as obesity and diabetes. The development of these conditions can negatively affect health and mating prospects, which can then impair prospects for future gains in energy.

Darwinian evolution has heretofore proven formidable in improving ROE, but by no means does it represent the only way to this end. As noted previously, living systems can acquire features to enhance ROE through genetic innovations. In addition to resorting to mate selection, offspring production, and death, individuals can also acquire genes from other individuals through viral and plasmid exchange. Current trends also suggest that the human species has become motivated to engineer and otherwise manipulate genes in a novel manner. The next section discusses a more profound, emergent mechanism of trait acquisition.

Return on energy and the future of evolution

Darwinian concepts explain the types of evolutionary findings observed in recent natural history [5]. To explain how the components of extant organisms aggregated to form larger systems, a pre-Darwinian theory of evolution has been proposed [6]. This scheme proposes that these entities comprised energetic systems that organized based on contextual cues [6]. It also suggests that during the early days of evolution, communal sharing of innovation predominated over competition for resource assimilation [6].

As additional means to improve ROE emerge which do not involve variation, reproduction, and selection, a more general paradigm should account for all possible paths to achieve this improvement. A theory for the emergence of systems with improved ROE should encompass evolutionary strategies observed so far during natural history. It should also portend post-Darwinian processes that will not involve the variation—selection hallmarks of Darwinian evolution.

The evolutionary strategy that eventually proves most successful in improving ROE could look radically different than any current model. Improving ROE may involve the transmission of traits through ideas, or memes, rather than through the reproduction of physical codes [7,8]. The concept of a meme remains consistent with our theory. The storage of a meme or any type of information requires the consumption of energy by the system under consideration, whether that system constitutes a synaptic organization, ink on paper, or a magnetic memory medium [9]. One would expect release of that energy with the loss of information, and indeed, the erasure of information produces heat [9]. For species where cognitive function exists, the incremental benefit of acquiring a meme may be substantially more than that of a genetic innovation. In such situations, the acquisition of innovations through memes rather than genes may emerge as the more advantageous strategy for improving ROE.

Genetic traits generally disperse through related individuals over contiguous generations, and even then only downstream to subsequent generations. In contrast, memes can undergo vertical exchange in either direction, through related or unrelated individuals, even skipping generations. One can also distribute memes horizontally to related and unrelated individuals through multiple channels of communication. Unlike genetic traits, an individual can acquire memes during a single lifespan as adaptive needs change. The ability to acquire on demand suggests that by using memes rather than genetic traits, individuals can more actively influence the direction of their own evolution. Transmission of ideas also requires minimal gestation; the participating parties can reside in separate locales; and broadcast and reception of memes can occur at different times.

Life—death cycling may have represented an effective method for genetic adaptations to accrue, but it is not well suited for the accumulation of memes. With their unique cognitive abilities, humans may represent transitional forms in the shift from Darwinian evolution to non-Darwinian strategies employing directed innovation. In this setting, generational turnover due to the short duration of existence of any one individual hinders efficient accumulation and transmission of memes. Given the nature of ideas, a more effective strategy for accruing cognitive adaptations would involve having a single individual accumulate knowledge over an extended duration of existence. Longevity would increase the ability to accumulate memes and permit more extensive transmission of memes to other individuals. The strategy of indefinite persistence may ultimately supplant life—death cycling as the best way to improve energy efficiency. Indefinite lifespan may represent an emergent property of the competition for energy and the improvement of ROE.

Hierarchical considerations

Dawkins coined the phrase ''selfish genes'' to suggest that there are core units upon which natural selection acts [7]. Towards the larger end of the scale, the Gaia hypothesis views planets and ecosystems as living organisms undergoing their own evolution [10]. All entities in existence may occupy different levels in a hierarchy, even cultures [11], as Wilber has noted and codified in his notion of levels [12]. However, when considering improvements in ROE, no specific unit represents the target of selection. Indeed, improvement occurs at all points along physical, chemical, biologic, ecologic, social, and industrial scales. Choosing individuals, genes, or memes to serve as points of reference may reflect our anthropomorphic desire for self-understanding.

Individual activities that enhance ROE at lower scales of organization sum together and influence designs for enhancing ROE at higher scales of organization. A gene represents a biochemical molecule that competes for energy with other molecules. Its presence and behavior also affects the ROE of the organism that harbors it. Retinoic acid is another example of a molecule whose replication relies on indirect reproduction by larger systems within which it exists. These systems have come to depend on the function of retinoic acid in a larger context. Adenosine triphosphate (ATP) has succeeded as a biochemical entity because it functions as the currency of energy transfer among larger scale systems, including humans. Among non-biologic systems, machines exemplify units that have yet to seek energy or reproduce on their own, but achieve these objectives indirectly by serving utilitarian functions for humans.

The net energy efficiency associated with a particular unit essentially consists of two terms: a function of its own energy, and a function of the net energy gained by the overall system as a consequence of maintaining this unit. We can thus define the summation of the ROE of an individual and its contribution to the ROE of other orders of hierarchy as inclusive ROE, an extension of Hamilton's inclusive fitness [12]. Hamilton's inclusive fitness suggested that looking at the individual alone may fail to explain the evolutionary success of certain traits such as altruism which may prove detrimental to the individual. Only when the larger system is considered — the network of related kin in the case of altruism — does the teleology of such traits become clear. Similarly, consideration of the teleology of a trait with respect to ROE should include its contribution to other orders of hierarchy. Inclusive ROE may help explain the emergence and proliferation of a trait.

The concept of inclusive ROE helps explain why some traits that increase energy efficiency may not proliferate if it impairs the ROE of that larger system which intends to incorporate it. For example, a trait that increases metabolic efficiency may appear to increase ROE when considered in isolation, but if its emergence fails to coordinate with the needs of the larger organism, diseases such as obesity can arise, leading to decreased ROE for the organism in the long run. Conversely, a particular unit can operate at less than optimal ROE if the resultant increase in systemic ROE generated by its existence produces an overall net gain. In such cases, its value to the system exceeds its value unto itself.

Stochastic considerations may underlie the systemic advantages of diversity. The persistence of apparently suboptimal units may also hedge the larger system against potentially cataclysmic environmental change. Such events would incapacitate those entities that have become tailored to the current milieu [13]. When an organism dies, lower order components of that individual such as amino acids and carbohydrates can survive, redistribute into the environment, and subsequently participate in increasing the ROE of another individual. This phenomenon represents the basis of predator—prey relationships as well as that of nutrient cycling.

Medical implications

Evolutionary displacement

If energy efficiency contributes to success in competition, then appropriate linkages between availability and utilization of energy becomes critical. Light and temperature represent two of the fundamental cues for energy. Virtually all species use these cues as surrogates for ecologic opportunity and tailor their life-history strategies accordingly [15,16]. Various species use location of light, luminescence, movement of light, and day-length variations to customize a wide range of behaviors related to feeding, reproduction, and development [8]. Temperature alters many aspects of life-history strategies including growth rate, litter size, offspring sex ratio, final adult size, and lifespan [8]. Alterations of heat shock proteins in response to temperature suggest that rising temperatures can spur greater genomic instability and innovation

[15]. Given the adaptive integration of biologic function to cues of energy, diseases would arise when extant traits no longer effectively link availability and utilization of energy. Diseases that may be attributable to deviations from natural patterns of light and thermal cues are reviewed elsewhere [8,14,16,17]. We describe this loss of appropriate linkage between signal and response as the product of evolutionary displacement.

Many diseases may represent dysfunctions in the energetic system caused by evolutionary displacement. In the modern era, other proxies for energy such as sound, humidity, color variation, amount of movement in the visual field, and dietary patterns may have also become dissociated from their original functions. They may now subtly influence our core response strategies in an inappropriate fashion. For instance, dietary iodine may have once served as a surrogate for energy availability in the environment. The recent decoupling of this relationship through iodine supplementation may produce a source of modern thyroid disease [15]. Autonomic function plays an important role in energy regulation, but the system has become maladaptive in the context of modern environmental changes [18]. A myriad of conditions seen with aging, such as heart disease and cancer, may arise from inappropriate invocation of sympathetic activity [19].

Molecular pathways by which problems in energy can manifest in ailments have become increasingly apparent. Control processes such as glycosylation and methylation represent mechanisms whereby hydrocarbon moieties of energy can modulate the function of genes and proteins, enhancing the plasticity of responses within an individual lifespan. Each control layer further improves energy efficiency by adding a new degree of freedom to the available permutations of existence. Such controls may take on increasing prominence, given the rapid environmental remodeling induced by humans that may render many preexisting traits maladaptive. Subtle alteration of these processes may underlie many of the diseases that reflect evolutionary displacement, such as obesity [20].

Illegitimate signaling

Competition for energy comprises a major source of disease. Trauma and infection related to annexation of energy by predators or microbes can induce host dysfunctions. The need to protect host integrity against these appropriations has significantly influenced the development of many aspects of our current biology, including our autonomic and immune systems [18]. Substantial energy must be devoted to these maintenance functions; indeed, autoimmune diseases may epitomize a dysfunction of these mechanisms.

Competition for energy can also emerge in more subtle exchanges among individuals. Systems can co-opt preexisting signal—response relationships of other individuals and exploit them for asymmetric gain in energy. The exploitation of mating signals belonging to fireflies in the genus *Photinus* by predatory fireflies of the *Photuris* genus represents a classic example of this phenomenon [21].

Some diseases may occur as epiphenomena related to ''illegitimate signaling''. Infectious and neoplastic diseases exemplify this principle. Tumors and viruses use illegitimate signals to exploit preexisting host endocrine, cytokine, and autonomic pathways to promote their own survival and increase their energy [22]. Spatial distribution of cancers and viruses within the host may reflect an affinity for strategic locations that facilitate manipulation of a variety of host functions, including autonomic, endocrine, and cytokine regulation to misappropriate energy [22].

Illegitimate signaling can occur between individuals of a species, such as the alarm call of the Belding's Squirrel, and lead to transfer of energy [22]. Some types of communication among humans, such as misleading advertising and e-mail spam, may represent forms of illegitimate signaling to redistribute energy among individuals. Incentives for illegitimate signaling among humans may be rising in part due to the proliferation of communication technology and transportation that promote engagement of less related individuals, as compared to prior epochs when tribal kin-organizations reigned. An exploitation of our preexisting taste cues by illegitimate signalers may underlie our propensity towards obesity [17,22]. Agricultural crops, animal husbandry, and use of microbes for biotechnology represent another form of illegitimate signaling — manifestations of human hegemony over nature, enabled by the decoding and exploitation of pre-existing pathways in these species [22].

Autocatalysis

The ubiquity of death in nature has led to speculations that it represents a useful adaptation for evolution. Keeping an individual alive may not prove advantageous to the system as a whole if the persistence of that individual detracts from the fitness of the system of which it is a part. In the final evolutionary calculus, when the carrying cost of continued survival exceeds the residual unrealized fitness benefit, self-termination may become advantageous.

For instance, while it may be advantageous to evolve through reproduction, it is also advantageous for post-reproductive individuals to auto-catalyze and die rather than compete with resources with offspring. Weissman [23] first suggested that death represents an intentional process that enhances genetic fitness [24]. The development of inclusive fitness frameworks leads to further support for this proposal. These paradigms reveal the selfish benefits of altruistic behaviors, including self-termination, when one accounts for the additional fitness that accrues to related kin [14].

Lethal disease may reflect underlying programs of behavior. In an adaptive process known as phenoptosis, once these programs detect an unacceptable level of energy efficiency, they would facilitate the demise of the entity in question [8]. Such processes may operate in a fractal manner, exhibiting self-similarity at multiple scales, recapitulating schemes of operation at the cellular level (apoptosis), at the systemic level (autocatalysis) [8], and even at the level of cultural organizations [25]. This phenomenon has undergone extensive characterization in species such as salmonids and marsupials. Potential examples in humans include dysfunctions such as menopause, sepsis, and other methods of self-termination [8].

In this context, malignancies may represent renegade units that have evaded their autocatalytic duties and have assumed overly aggressive utilization patterns relative to the energy concerns of the greater system. In essence, cancer cells have subverted their own control systems to escape the certainty of apoptosis. While cancer currently kills hosts through its ill-fated attempt to acquire indefinite lifespan, the phenomenon may presage a future evolutionary trend [8]. Whether these units could one day successfully convey such traits to the greater host remains unknown. Science is currently consumed with harnessing the ability of stem cells to differentiate into terminal units, and to avert the regression of terminal units into immortal de-differentiated cells — that is, cancer. Ironically, harnessing the ability of terminal units to de-differentiate into immortal cells may represent a unique scientific opportunity to potentially alter the trajectory of human evolution [8].

Potential solutions

Examining the realm of strategies for improving ROE identifies several ways that our current incarnation may not represent the ideal vehicle for this process. Maladaptive processes have emerged as our environment has changed; we possess multiple vulnerabilities to illegitimate signalers; and the legacy strategies to improve ROE require life—death cycling. These maladaptive processes represent major impediments to the improvement of ROE because they interfere with health. Finding novel solutions to these maladaptive processes can contribute to improvements in ROE.

The first strategic step to this end may involve overhauling some of the conventional paradigms in medicine. We favor an integrated, systems-oriented approach to human diseases over the incumbent paradigm of hyper-specialization and academic fragmentation. We believe that a concerted effort to identify the fundamental precepts of disease may accelerate the development of solutions [18]. As has been postulated elsewhere [26], we assert that simple core rules may underlie the seemingly endless variety of medical conditions. Despite the long catalog of pathologies that can afflict humans, these conditions ultimately produce a much shorter list of nonspecific symptoms [18]. Autonomic dysfunctions induced by evolutionary displacement may constitute one of the central mechanisms that link many seemingly unrelated maladies [18].

Once identified, the best way to address evolutionary displacement may involve restoration of the natural relationship between signal and response, rather than creating dependency through the use of drugs that invariably produce tachyphylaxis. One embodiment would involve challenging the body with progressive entrainment until the proper relationship becomes once again restored. This so-called paradoxical approach may improve function by promoting the inherent strengths of the body, while avoiding the physiologic dependence typically associated with current pharmacologic intervention [27]. An alternative approach would involve restoring the full dynamic range of signals intended to be experienced by human response systems [8,28].

Finally, the early extinction of cognitive plasticity during adolescence limits our ability to acquire and distribute cognitive adaptations, which are more efficient methods than genes to accrue traits that improve ROE [16]. The decay of plasticity heightens our vulnerability to illegitimate signals that reduce the ability to improve ROE. Science itself may be an ongoing casualty of lost plasticity, as our legacy design may inhibit the creativity of human intellectual life [16]. Enhancing plasticity could represent a potential leverage point for solving many medical and social ills that afflict humanity, including aging, cancer, racism and war [16]. By helping individuals acquire memes more efficiently, and by helping scientists discover new ways to remodel our bodies and improve our physical health, interventions to improve the duration and quality of cognitive plasticity could emancipate humanity from our biologic legacy and improve our ability to compete for energy.

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