

In G.O.D. We Rust-The Beauty of UnIntelligent Design



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From Cells to Societies: A Dynamic Fractal

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Abstract

What if the standard random mutation-based view of the evolution of species and cancers is incomplete to the extent that it is an all-encompassing framework that misses a much bigger picture, the fundamental creative nature of nature. What if a reality of ongoing creation (GOD, General Open-System Dynamics) has been replaced with a stagnant dogma of accident driven evolution. If we reverse our current perspective, previously miraculous, improbable events may be scientifically understood from first principles that emerge by embracing a far from equilibrium thermodynamic perspective based on the work of Nobel laureate Ilya Prigogine.

Introduction

Man's understandings naturally start from the simple and move over time to the more complex. But, what is simple, what is complex, what is time, how and why is there change? An integration of physics and biology emerges after considering these terms from the perspective of far from equilibrium thermodynamics as developed by Nobel laureate Ilya Prigogine. The life's work of Nobel laureate Ilya Prigogine provides an alternative foundation for understanding physics and life. In his last book, *The End of Certainty*,¹ he fully embraces his earlier work (*From Being to Becoming*²) and concludes that flowing energy has a creative organizing capacity that is fully consistent with the Second Law of Thermodynamics (as extended by Prigogine for open systems). His perspective can now be extended to living systems, creating the "Physics of Life",³ the physical basis for a systems biology perspective.



Discussion

It is a well-established paradigm that the genetic transfer of information occurs through the transcription of DNA to RNA,⁴ followed by the translation of RNA into proteins which then integrate into life's concert of homeostatically regulated enzymatic activities, post translational modifications playing a central role⁵.

The broadly accepted hypothesis in the scientific community is that life and evolution are the result of an accumulation of improbable accidental events that have miraculously been retained by evolution. This line of thinking is a natural consequence of foundational physics based on a logical mathematical formalism of timeless equilibrium. A logical extension of this perspective leads to the conclusion that time is reversible.⁶ However

from this perspective, the appearance of irreversibility occurs in a time-biased fashion, at every instant, for unknown reasons. Thus there is a discrepancy between these conclusions and the everyday experiences of living organisms. We are guided by the arrow of time from birth till death. Random statistics cannot explain life since it is statistically too improbable to exist.

Prigogine's work explains how flowing energy can naturally organize matter to create flow-dependent structures that are thermodynamically stabilized by sufficient entropy production. Evolving complexity from this seminal thought provides a physical foundation for the emergence of life and evolution, driven by the creative nature of nature. Creativity can be thought of as solutions emerging from systemic complexity that better degrade thermodynamic potential. They emerge when a far from equilibrium systems are pushed to a flow-dependent critical point, at which time the system might spontaneously undergo a far from equilibrium phase space change to a higher level of spatial and temporal organization (negative entropy), or it might collapse to a lower level of organization, flow dependent or not.

What is a fractal and what is a dynamic fractal? The difference between a beautiful picture and life is time and adaptation. The fractal mathematics developed by Benoit Mandelbrot ⁷ creates beautiful complex pictures. Their algorithms generate repeating patterns independent of magnification used. With each cycle an element of time is created. Each reiteration can be visualized as a beautiful, flowing, sequence in a repetitive loop.



Unlike the generation of consistent patterns, life constantly must adapt to the environment that is constantly changed by adapting life. Therefore, algorithms for survival must constantly change. Feedback loops can create time dependent homeostasis. A system (a collection of molecules) is timeless when at equilibrium because entropy (disorder) is at a maximum and free energy (the ability to do anything) is at a minimum. Hence, everything is fully random and void of useful information (negative entropy). There is no change to manifest time.¹ In contrast, a network of localized inorganic, flow-dependent reactions, interacting, feeding and being fed by each other, can (must?) ultimately lead to the far from equilibrium phase change known as life.

Environmental conditions, from the sub-cellular to the planetary, create flow dependent structures that are in turn affected by their own creation, thus creating an adaptable dynamic fractal. Consequently, a complex landscape of evolving selective pressures maintains ongoing homeostatic ability with constant dynamic adaptability. Evolution of all complex systems, across scales of time and space, are driven by the flow of excess energy potential and the production of entropy.⁸ The flow of living systems is maintained by building complexity in concert with appropriate cellular damage prevention

(antioxidant) and recycling (autophagy) efforts. The energy flux of these processes are in constant dynamic free radical guided self adjustment to overcome the friction of life, excess free radicals i.e. entropy. Life and evolution must occur because they are driven by the flow of energy ^C. The conclusions that emerge from the joining biology with far from equilibrium thermodynamics shake the foundations of our universally accepted truths, while providing direction for the future.

It appears that the scientific establishment has failed to grasp the genetic consequences of life's most fundamental property, adaptability. Currently, the physical foundations of life are ironically embedded in a dead, equilibrium perspective of random statistics. However, the ability of flowing electrons to create statistically essentially impossible molecular distributions, such as those seen in Belousov–Zhabotinsky reaction, ^{sr} suggests a clear parallel with the metabolic redox processes of living systems. Redox reactions can account for emergence and evolution of life, as well as all manifestations of human consciousness and all of our societal structures (financial, political, religious, educational, etc.).^{ss} Thus, a more advanced perspective of humanity's place in the chemistry set of evolution needs to be developed and implemented for natural harmony. A new level of human consciousness must emerge to successfully integrate with the environment to become part of the future.

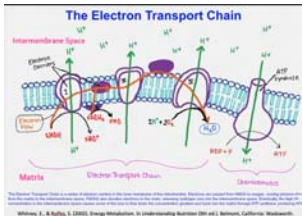


Flowing energy, in order to maintain the high level of adaptability characteristic of living systems, for now best exemplified by human beings, requires sophisticated feedback mechanisms in order to monitor the balance between negative entropy accumulation and entropy production. Human consciousness is the mechanism, but it needs a scientific foundation for guidance. Entropy exported by a flow-dependent system must be greater than the negative entropy retained in order to have thermodynamic stability. $dST_{(total)}/dt = dSE_{(exchange)}/dt + dSI_{(internal)}/dt$ Is there a common characteristic that can be monitored in order for the system achieve and remain stable? If so, what is its nature, and what are the biological manifestations by which homeostatic adaptability is accomplished?

The answer to these questions will integrate free radical-induced biochemical changes (homeostatic and/or damaging excess) with the intrinsic truth that in a human population everything is regulated by endocannabinoid activity^{sF} from conception to death. By definition, half the people will be above and half will be below average for any particular phenotype, for example forgetfulness, chosen because memory is intrinsically required for the required feedback necessary for homeostasis. How might forgetfulness be involved with evolutionary adaptability? Clearly, from the perspective of adaptation, there should be an advantage when incorrect information is replaced with updated new and presumably more correct information. The nature of all flow dependent structures will always reflect the sources that created, and feed them. Consequently, the harmony of exchanges between these structures with their environment must constantly adapt as the

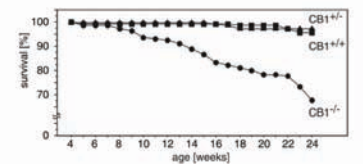
environment adapts to nature's ever unfolding creativity. The consequences in a population that results from a distribution of cannabinoid effects on memory will be reflected in the flow dependent structures (dissipative structures^{su}) that constitute ourselves and those that we create as complexity increases. Increasing complexity actually creates time, be it in cells or society.

Memory is intrinsically a fundamental asset to living systems because allows for responsive non-random behavior. As the complexity of organisms increases, the consequences of memory permeate the organism's negentropic hierarchy. Superficially, it may seem that a greater memory capacity would naturally be beneficial. However, with the complexities of human consciousness, forgetting has become essential for optimizing adaptability. Extrapolating the animal behavioral studies to people, those with lower levels of cannabinoid activity (both endogenous and consumed) will typically experience greater levels of stress because of their lower ability to sufficiently control free radical damage production that results from/in change. Psychologically and physiologically they are less likely to forget stresses from the past.



Cannabinoids protectively regulate damage-causing free radical generation by balancing dangerous carbohydrate promoted ATP production, produced by electron transport system for differentiated cellular functions, with protective recycling activity promoted when cells burn fats and recycle free radical damage components. A destructive phenotype emerges as positive feedback loop. These individuals may suffer from an inability to deal with current stress due to lower endocannabinoid activities. Stress permeates and regulates the flow-dependent complexities of life by the free radical induced changes in biological molecules that control critical flow patterns. Consequently, environmentally determined epigenetic changes institutionalize behavior. As will be explained below, the main theme of this manuscript is that life successfully transformations metabolic patterns into epigenetic patterns that increase the probability of creating supporting genetics.

Vertebrates with above average levels of cannabinoid activity for any phenotype under consideration will have different characteristics than those with lower levels. Profoundly, CB1 knockout mice that lack CB1 activity and cannot get “high,” die prematurely, and are too stressed to move about their cagest. Without sufficient cannabinoid activity, stressful memories are more effectively retained. A deficiency in forgetting results in an individual spending more conscious time looking backwards (remembering) because the past represents a known,



Mortality rate in offspring from heterozygous (CB1^{+/+} × CB1^{+/-}) matings. Note that more than 30% of all CB1 knockout mice under 24 weeks of age die of natural causes. In contrast, less than 5% of the heterozygous and wild-type litter mates die during the same time span. (Zimmer, 1999)

even if unpleasant. The past is safe because nothing is new so no adaptation is required. Some individuals with strong memories coupled with a fearful predisposition may represent individuals deficient in cannabinoid activity (BLPs = Backward Looking People). There are additional phenotypes that have been demonstrated in CB1 deficient mice.¹⁶

The more stressed an individual is, the greater the tendency to try to control the future stress from forgotten and unforgotten stresses of the past. In contrast, Forward Looking People (FLPs) may have a greater tendency to embrace the unknown because they are more optimistic and tend to be more relaxed because they more readily forget the stresses of the past. The optimistic FLP may be predisposed to taking more chances than a pessimistic BLP. Consequently, they may naturally be more accident-prone. Individuals with this phenotype are more likely to experiment with the unknown and maybe even dare to try cannabis. This simple possibility invalidates many epidemiological studies that assume a random distribution of whatever characteristic is being examined. These studies assume that there is an equal probability of cannabis use among sick versus healthy individuals, between those suffering pain and those not suffering pain, how foolish. It has already becoming quite clear that people with chronic conditions prefer to use cannabis-based treatments rather than more conventional pharmaceutical alternatives.¹⁷

Stress, and its avoidance, is a determinant of behavior, it's important to have a realistic definition of "stress." Thermodynamically stress may be viewed as any change to which a flow dependent homeostatic system must adapt, good or bad, for systemic survival. Homeostasis always requires continuous adjustments of flow. As within each individual, in a dynamic fractal-like manner, the collective consciousness of a population is intrinsically regulated by the balance between BLP and FLP activities. Relaxation is a multidimensional biological process facilitated by cannabinoids because of their ubiquitous homeostatic ability to regulate free radical activity. Cannabinoids are adaptogens.¹⁸ Without sufficient cannabinoid activity a person is naturally tend to look more fearful¹⁹ of the unknowns intrinsic in the future. They are driven to control the future by staying in the past. Their conservative nature emerges and provides a biological and philosophical rationale for becoming a political and religious aggregate of like-minded thinkers that provide social stability.

However, social stability must be balanced with progress since everything is always changing as the future unfolds. How to best optimize for a successful future?²⁰ A natural starting point would be to understand the nature of our creation so that we can become more harmonious and synergistic with it. Understanding the physics and biological manifestations of flowing energy seems to be logically mandated. With sufficient flow and evolving complexity, nonlinear rearrangements will occur as they always have in the past. From the perspective of the evolving human mind, what might we expect? The physical foundations of evolving biological systems will echo throughout a dynamic system's evolving complexity. Social systems,²¹ including education, politics, finances

and international interactions will spontaneously reorganize as the human brain evolves concurrently, as it always has, with increase cannabinoid activity. *Canna sapiens* will emerge from *Homo sapiens*, as a higher (more cannabinoid activity), less self-destructive nature normalizes.

How might the integration of far from equilibrium thermodynamic thinking affect our understanding of life and evolution? It is a well-established paradigm that the genetic transfer of information occurs from DNA to RNA, its subsequent translation into proteins integrate into life's concert of homeostatically regulated enzymatic activities. A broadly accepted thought in the scientific community is that life and evolution are the result of an accumulation of improbable accidental events miraculously retained by evolution. This line thinking is a natural consequence of foundational physics that is based on a logical mathematical formalism of timeless equilibrium (maximum entropy, minimum free energy). A logical extension naturally leads to the conclusion time that is reversible. Essentially, the appearance of irreversibility in our everyday world²⁰ occurs in a time-biased fashion at any instant for unknown reasons. There is a discrepancy between these conclusions and the everyday experiences of living organisms that are guided by of the arrow of time. Random, time independent statistics cannot explain life. It is too improbable to exist.

Before new biological concepts can be examined, the physical underpinnings of life must be considered. Prigogine provides a novel foundation that can be developed into a synergistic understanding of physics and life. Surprisingly, it appears that the scientific establishment has missed understanding the genetic consequences of life's most fundamental property, adaptability. Currently, the physical foundations of life are ironically embedded in a dead, equilibrium perspective of random statistics. The ability of flowing electrons to create a statistically impossible molecular distribution, as seen in the Belousov–Zhabotinsky reaction,¹⁰ provides a clear parallel with the metabolic redox processes of living systems.

Life and evolution are driven by the creative nature of nature. Creativity, solutions of systemic complexity that degrade potential, emerge when far from equilibrium systems are pushed to a flow dependent critical point whereby the system spontaneously undergoes a far from equilibrium phase change to a higher level of spatiotemporal organization (negative entropy). Conceptually, a network of localized, inorganic flow dependent reactions interacting, feeding and being fed by each other, ultimately move a system a sufficient distance from equilibrium and the far from equilibrium phase change of life emerges and is repeated throughout the evolution of species.

All Environmental conditions, both sub-cellular and planetary, create flow dependent structures that are in turn will be affected by systemic interactions resulting from their own creation thus creating a dynamic fractal. Consequently, a complex landscape of evolving, selective pressures maintains ongoing homeostatic ability with constant dynamic adaptability. Evolution of all systems, across scales of time and space, are driven

by excess energy potential but that is maintained by appropriate cellular prevention (antioxidant) and recycling (autophagy) efforts that are in constant engagement to overcome the consequences of the friction of life, free radicals. Life and evolution must occur, driven by the flow of energy, but shaped by free radicals. Consequently, below is a metabolic perspective on the evolution of species and cancers. Life's main energy sources, carbohydrates and lipids, are not functionally equivalent.^{22,23} Carbohydrates preferentially feed the efficient, but dangerous, electron transport system that promotes and supports differentiated cellular functions including nerve transmission, muscle contraction, and hormone production. Essentially, efficient energy production promoted by metabolizing carbohydrates through the electron transport system is the functional equivalent of a nuclear reactor that sometimes leaks radioactivity in a cell. Electron transport system in mitochondria provides efficient, clean energy in the form of ATP to drive cellular differentiation. But, imbalances can produce excess free radicals. A complex society in all of its manifestations can be built with sufficient energy availability. Similarly, so can the differentiated functions of cells can be performed. Unfortunately mitochondrial energy producing metabolism, like radiation represents the, produces free radicals under conditions of inappropriate mitochondrial input ²⁴, or restricted outflow. When excess free radicals are metabolically produced, cells will produce fat, through well-established pathways that range from whole body to subcellular, in order to reduce excess free radical production from excess carbohydrate catabolism. From an entropic perspective, both the intracellular and social recycling enhances negentropic activity. Their dialogue allows a state of health to emerge from living systems and their societies, mathematically known as an attractor.

A novel concept that emerges from the thermodynamic perspective is that there is an optimal state of health for each organism that can be represented as an attractor. In most humans, it is suggested that the health attractor is likely to represent the transition from youth to adulthood. Quite astonishingly, it seems that when a cell, or organism, sufficiently recycle free radical damaged cellular components (autophagy), the biochemistry moves towards that attractor, and thus helps to restore health.

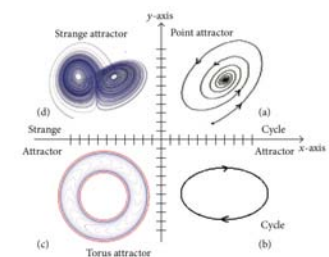


FIGURE 6: Different types of attractors constructed in 2-dimensional phase space; (a) point attractor, (b) limit cycle, (c) limit torus, and (d) strange attractor (after [29]).

In vertebrates, CB1/electron transport driven ATP production, and subsequent production of cellular biochemical and free radicals, is balanced by recycling free radical damaged cellular components driven by CB2 activity. Less electron transport driven energy and associated free radical production occurs when cells recycle. Additionally, since fat burning is promoted by CB2 activity,²⁵ it may also promote beta-oxidation dependent symmetrical stem cell expansion as occurs in embryonic stem cells.²⁶ In contrast, CB1 activity promotes electron transport system driven stem cell differentiation.²⁷ From metabolic perspective, a more differentiated cell is driven further from equilibrium because it is more negentropic than a less differentiated one. Functionally, different

circuits of metabolic pathways may expand or contract to modulate free radical induced damage production that occurs with electron transport activity. The prominent role of aerobic glycolysis and glutaminolysis are examples of energy-production-efficiency plasticity used as a buffering mechanism to homeostatically maintain safe steady states of free radical production that can be efficiently handled by steady-state levels of enzymes that reduce the negative consequences of excess free radicals.

Metabolic parameters describe common functional cellular states in healthy and cancer cells, the difference being their regulation. A senescent embryonic stem cell, like the initial zygote, is totipotent and has minimal energy requirements. It stably survives with minimal free radical induced perturbations by using fat as the dominant fuel source. Environmental factors can trigger either symmetrical cell division that produces two totipotent fat burning stem cells, or asymmetrical division that produces another stem cell (totipotent?) as well as one differentiated cell that has turned on the electron transport system to form the metabolic basis for further differentiation²⁸. Effectively these cells became adult stem cells prior to achieving their final differentiated state. They have not made the epithelial-mesenchymal transition to a higher level of differentiation. For example, these cells have not developed anchorage dependent differentiation functions. They may remain detached and mobile until a nourishing home is found that provides them with the needed developmental signals to settle down and start a colony that may be part of healthy growth and/or restoration, or it may be a sugar fueled cancer metastasis. In either case, a spectrum energy patterns fuel survival.

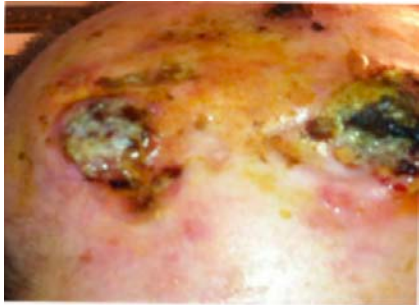
Free radicals drive progressive selection of survivable metabolic states in cells, a process that leads to the development of cancers. Cannabis as well as other herbal/nutritional options can promote the killing of these cells by forcing them to burn fat. AMPK activation controls the transition to fat burning. Is responsible for turning off the electron transport system and inhibiting the alternative safe energy source, the Warburg affect, aka aerobic glycolysis ^{FCaus}. Healthy cells can successfully make this metabolic transition. However cancer cells already producing excess free radicals and typically cannot successfully make the transition. They undergo apoptosis from the excess free radical production.

Unfortunately continued exposure to therapy induced excess free radical production in cancer cells can select for more survivable metabolic states that subsequently create their required genetic changes for long-term survival. A lethal feedback loop can amplify the metabolic/genetic catastrophe to produce more stable, death resistant, less differentiated, fat burning cancer cells. The disease worsens as the imbalance is amplified by free radical inducing treatments. The worst-case scenario seems to be coupling the protective properties of fat burning with the enhanced flow required to sustain cell division. This type



of cancer cell actually grows when treated, for example with radiation. The man's head in the picture below show the tumors that would grow when treated. He was irradiated over 100 times! Healthcare or Wealthcare?

These treatment resistant tumors still responded to cannabis extracts (topical and oral



consumption). All other treatments had failed to stop tumor growth. The images below show that otherwise drug and radiation resistant tumors were progressively destroyed, down to the bone, by what appeared to be a necrotic process.



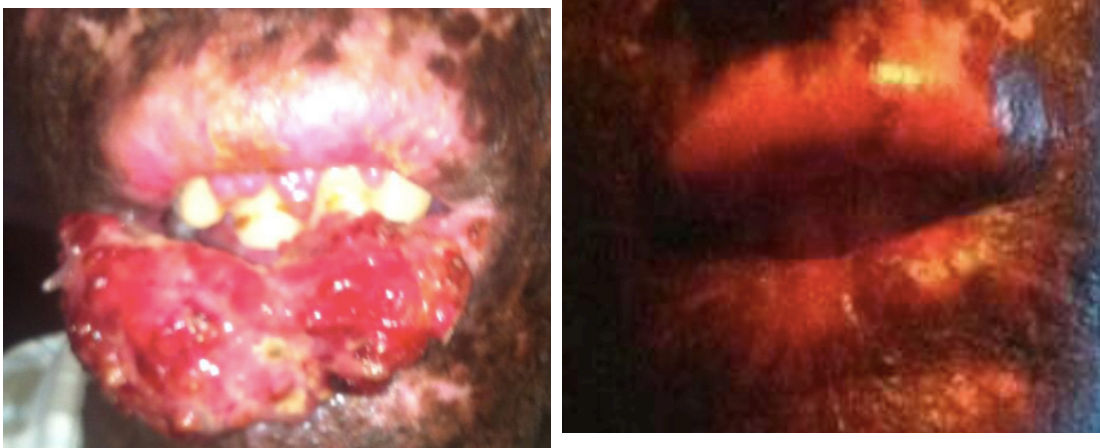
Patients have used excess free radicals to kill drug resistant cells using metabolic manipulation to reduce normal metabolic escape pathways, coupled with additional free radical overload with high dose intravenous vitamin C (interacts with iron in the blood to produce hydroxyl radicals, the Fenton reaction). For any cell, metabolic status will determine whether free radical stress will induce apoptotic or necrotic death. Plasticity of energy flow in vertebrate systems is emphasized by the presence of the CB1 receptor on mitochondria ³² and components of the electron transport system on the plasma membrane of human cells ³³. In essence, we as a species are exploring the possibility that the source of human regenerative capacity is implemented through the endocannabinoid system, possibly with significant neurological stimulation and guidance. We are just beginning the journey out of ignorance as the will Global Cannabis Awakening proceeds.

The main concept developed in this chapter is that survival of the fittest means survival of the most adaptable, not the strongest and not the smartest. Consequently, adaptability of a flow dependent system mandates that the constant adaptive interface between the system and its environment occur at the metabolic, not the genetic level. Metabolic imbalances promote excess free radical production that create epigenetic modifications, followed by focused genetic change on the genes and their controlling regions that are responsible for thermodynamic flow dependent survival. DNA damage and its repair provide a source of the changes that characterize evolution³⁴ (gene duplications, recombinational events, low fidelity error prone DNA polymerases that bypass damages stalled replication and transcription forks³⁵, replication/transcription conflicts²⁷, retroviral activation, etc. Consequently it seems that there are two pathways by which evolution advances, one random, and the other nonrandom. Directed change occurs by metabolically selecting/directing needed, nonrandom, free radical-promoted genetic change, by selecting metabolic states in a multi-gene fashion that promotes a systemic metabolic survival state. Metabolically directed is quasi-Lamarckian molecular evolution.

Statistically, the above perspective makes intrinsic sense. DNA is a complex molecule

unlikely to randomly form from its components. How is it that DNA is probably the most successful molecule in the universe? An estimated 50,000,000,000 tons exists on the planet Earth.³⁶ The answer found in the success of molecular cooperation driven by flowing energy and entropy production. Energy driving evolutionary change provides an easy to understand explanation for the evolution of life, species and similarly, cancer drug resistance and the genetic diversity of tumors. Potential important beneficial health consequences, especially with respect to cancer need to be considered. The existing scientific/medical framework has been unsuccessful in creating the desired health outcomes. Yet, a simple shift in perspective creates an entirely new reality when considering the causes and treatments of cancers.

The far from equilibrium approach to understanding life intrinsically leads to the all pervasive role of flowing energy in creating and sustaining life. Numerous reports coming from varying biological specialties are increasingly finding metabolic solutions for health concerns. An extreme example demonstrates the utility of a cannabis-driven metabolic approach. Multiple cancers result from genetic defects in a cell's ability to repair ultraviolet light induced mutagenic DNA damages. The patient below shows a multi-phenotypic reversal, in I year, by cannabis extracts of the genetic deficiency Xeroderma pigmentosum³⁷) that cause cancers. The cannabis-based treatment protocol eliminated pain and depression, while healing melanoma on the scalp, as well as tongue and lip cancers. Additionally, sight was restored (personal communication B. Radisic, J. Bowman).



Is there a connection between the lack of nucleotide excision repair seen in Xeroderma pigmentosum and the potential for cannabinoids to regulate free radical production and potentially associated base excision repair?³⁸ It is important to remember that when we are dealing with open systems we are focusing on dynamic not static processes. Consequently small perturbations can be amplified into macroscopic systemic changes (the well-known butterfly effect). The human body has approximately 15 trillion cells that every day suffer at least 30,000 oxidative base damages.³⁹ One damage, at one point

in time and in the wrong gene could kill a person if it amplifies through the system to create a lethal cancer. Common sense dictates that an extensive amount of life's organization must be devoted to protecting life from excess free radical damage and the organizational disruption that free radicals impose on cellular biochemical harmony. When flow dependent organization decreases below a thermodynamic critical point it leads to the systemic negentropic collapse, commonly known as apoptosis.

One of the most dramatic examples of metabolic adaptability in response to potential free radical damage is seen when a cell enters S-phase of the cell cycle. The electron transport system, after having efficiently provided the needed energy to build up a cell's negentropic potential during anabolic production during the G1 phase of the cell cycle, is shut down. The free radical modifications of cellular constituents become the multidimensional signaling elements of homeostasis. They form the feedback loop that directs cells to minimize the excess free radical production coming from the electron transport system. By significantly increasing use of the safer, but less efficient aerobic glycolysis process, a.k.a. the Warburg affect ⁴⁰. Evolution selected for S-phase energy not to be produced by the electron transport system when DNA is unwrapped and more susceptible to damage. Instead, replicating cells get their energy from anaerobic glycolysis and glutaminolysis^{41,42}.

What might the consequences metabolic flexibility be from a dynamic perspective? Imagine a population of cancer cells having a single mutation in the same gene. An unsynchronized population will be in all phases of the cell cycle. Those that cannot efficiently amplify free radical imbalances to cause apoptosis will survive any assault that kills by an apoptotic mechanism. Consequently, cells in S-phase will have a greater probability of surviving while simultaneously free radical induced damages and their repair will be focused on replicating and transcribed genes. Abnormally prolonged transcription of free radical stressed metabolic patterns will naturally select mutations that promote successful metabolic flow that is defined by transcription and enzymatic activity patterns. Thus, many cancers are characterized by increased energy flux through aerobic glycolysis and glutaminolysis pathways. They were probably initially nonrandomly metabolically selected for prior to becoming imbedded in genetics as a consequence of metabolically focused genetic change. Functional directed genetic change is a scientific version of creationism.

Similarly, glutaminolysis, driven by the MYC oncogene⁴³ provides an additional ATP source that maintains the carbohydrate driven differentiated state by supporting Krebs cycle intermediates. In contrast, as with aerobic glycolysis,³⁰ glutaminolysis⁴⁴ and AMPK activity seem mutually exclusive, again separating synthetic and differentiated pathways from those responsible for recycling of free radical damage to cellular components. An overview of metabolic options explains both the origins and treatment possibilities of cancers, as well as all diseases. The use of chemotherapy and radiation⁴⁵ simply selects for the surviving metabolic states that subsequently become institutionalized as genetics.

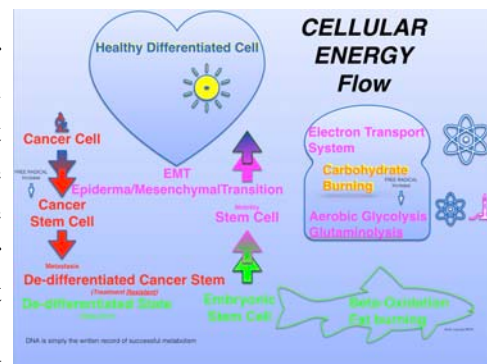
Shut down of cellular communication with the outside, while focusing on internal recycling. Autophagy moves the system to a lower level of communication with the environment while decreasing its internal entropy by reducing free radical damage associated molecular circuitry through recycling. Autophagy can become a cell's ultimate survival mechanism,⁴⁶ which is good when the cell survives, re-differentiates and rejoins the community of cells as a harmonious part of the greater structure. DNA is the record of metabolic success.

Adaptation requires that first a unique biochemical state is selected that is typically maintained by epigenetics synergistically with the metabolic adaptation from homeostatic post-translational modifications. Consequently, excess free radical damages, due to maintaining and expanding an original metabolic imbalance, are focused on transcriptionally active genes⁴⁷ that promote survival. Consequently, the damages themselves, the DNA nicks and single-stranded regions that are undergoing repair, can promote recombinational events, gene duplications, and mutations, providing new material for evolution.⁴⁸ For example, stalled DNA and RNA polymerase molecules can generate a variety of novel DNA outcomes.^{49, 50, 51} The significance of DNA architecture is emphasized by the fact there exists both global DNA repair as well as transcription-coupled repair.^{52,53} DNA repair systems operate in different environments, architecturally and biochemically. A variety of consequences, depending on circumstantial specifics, should be expected. For example DNA repair can trigger DNA strand breaks that trigger polyADP-ribose polymerase hyper-activation (Parp) that links DNA repair with NAD metabolism and necrotic cell death.⁵⁴

The above proposal clearly challenges conventional modern interpretations of molecular genetics and its role in evolutionary change. The evolution of species, and cancers for the most part is not the randomly created mutations on a genome wide level, but focus of mutational change where it's needed, the genes that are responsible for survival in any metabolic state. Add to that intellectual perturbation of corroborated, unpublished studies (personal communication YW Kow, Z Hatahet) that demonstrated the fat burning, drug/radiation resistant HL60 monocytic cells do not express base excision repair enzymes. In contrast, these repair enzymes were expressed in the drug sensitive parent cell line. (Melamede and Stubbs, unpublished results).

Conclusion

In conclusion, life is a natural endpoint after 1 billion years of energy driven chemical complexity evolving in the test tube planet Earth. We now have sufficient scientific foundation to understand the nature of that process so that human health and planetary



health may be best addressed for healthy survival. Each individual living organism is simply a flow dependent, quantized probe in adaptability (not good for the ego), adapting as the complexity of the chemical reaction moves into the future. Embracing adaptability facilitates movement into the future. Cannabinoid deficient BLPs currently run the world, unfortunately too often, driven by greed and power, a natural consequence of a more primitive state (no pun intended), naturally of FLPs. In contrast, the activist medical cannabis community that is leading the Cannabis Awakening successfully uses cannabis-based metabolic approaches (whether they know it or not) to control cancers, HIV and associated illnesses, dementia, dyslipidemia, Kaposi sarcoma, autoimmune diseases, pain, fibrotic illnesses etc. numerous age-related inflammatory based imbalances in body systems.

The concepts are simple. A state of health can only be achieved with a balance of damage production, with repair and prevention. For the first time we have a simple definition of health, it can be measure by moving the system further from equilibrium in a sustainable fashion. The complexity of an organism grows as it matures both by increasing the amount of matter as well as increasing its organization (negative entropy ⁵⁵). Aging and age-related illnesses promote a return to equilibrium. Death is a far from equilibrium phase change to a lower level of organization. It is encouraged to our ignorance. Once a human reaches adulthood they no longer move further from equilibrium by growing in size unless, for most people, they're just getting fat. A fat body is further from equilibrium. If burned, it would release more energy then a thinner body of equal weight. In terms of health promoting complexity a fat, unfit human is closer to equilibrium. Fat is simply an indication that the organism was consuming too many hydrates. In order to not burn them and generate excess free radicals, the cells turn carbohydrates into fat. The popular Ketogenic⁵⁶ and Paleo⁵⁷ diets promote cellular recycling, consistent with the increasing appreciation the metabolic underpinnings of so many conditions. A thin person is not necessarily metabolically healthy call they may suffer from a metabolic imbalance where the body is excessively burning fat to compensate for the excess free radical production, as would occur from inappropriate excess carbohydrate intake that leads to metabolic syndrome.

The entire planet is now undergoing a far from equilibrium phase change characterized by fluctuations of the intensive variables of the system that approach infinity. From a physicochemical perspective, these are measurable parameters that occur prior to a far from equilibrium phase change. Today we see supporting indications for this possibility on the global level in the form of fluctuating weather patterns, novel migrations of species including humans, inappropriate distributions of chemicals such as the plastic poisoning the oceans, and the nanoparticles that we eat and breathe, etc. The energy and associated information flow in the modern world is generating excess stress, and hence increasing our free radical load. Our ignorance regarding the physics of life keeps us supporting wealth-care instead healthcare.

Today “citizen scientists” all around the world are dramatically improving their health with a variety of cannabis-based preparations that contain highly variable biologically active landscapes. Typically people are treating themselves at home, often in the absence of medical oversight. Metabolically, every human is different, even twins. In order to most effectively use cannabis, each patient needs to develop a relationship based on self-experimentation so they can match their medical needs with the medicinal properties that different strains provide. As the godfather of cannabis, Dr. Mechoulam has stated, “cannabis is a treasure trove of pharmacologically active chemicals”.⁵⁸ Globally, cannabis activists are educating and people are successfully treating themselves for illnesses and conditions for which the healthcare system failed to provide any satisfying real health-promoting solutions. Autism promoted by vaccines, cancers metabolic syndrome and autoimmune diseases are all promoted by a toxic environment, toxic food and bad information promoted by healthcare, and society in general. They are recognizing fake medicine and fake science. They are demanding cannabis freedom for survival. Along with that freedom will come new concepts whose implementation will drive health and the genetics.

As more and more people recognize the harm that ignorant, corrupt, (collusion with the biomedical industry) governments are causing the people they are supposed to be helping, Only those that adapt and support a healthier, happier future for people and the planet will remain. The future will be one no longer of power, but of cooperation if we are to survive. Consequently, the increased cannabinoid activity in the human population will become embedded ultimately in the genetics that will stabilize, at least temporarily, until new adaptation is implemented.

Summary

Life is an adaptive negentropic flow dependent superconductor driven by the adaptive coherent flow of the adaptive redox potential that collaborate to manifest as time, distance from equilibrium, as complexity emerges. Life is a dynamic redox capacitor that stores evolving negentropic complexity.

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