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9. Examining specific life-origin models for plausibility

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Abstract: All models of life-origin, whether Protometabolism-First or pre-RNA / RNA World early informational self-replicative models, encounter the same dead-end: no naturalistic mechanism exists to steer objects and events toward eventual functionality. No insight, motive, foresight or impetus exists to integrate physicochemical reactions into a cooperative, organized, pragmatic effort. Inanimate nature cannot pursue the goal of homeostasis; it cannot scheme to locally and temporarily circumvent the 2nd Law. This deadlock affects all naturalistic models involving hypercycles, composomes and chemotons. It precludes all spontaneous geochemical, hydrothermal, eutectic, and photochemical scenarios. It affects the Lipid, Peptide and Zinc World models. It pertains to Co-evolution and all other code-origin models. No plausible hypothetical scenario exists that can convert chance and/or necessity into an organized protometabolic scheme. In this paper the general principles of previous chapters are applied to the best specific models of life origin in the literature. Tibor Ganti's chemoton model and the pre-RNA and RNA World models receive more attention, as they are the most well-developed and preferred scenarios.

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Introduction: Every life-origin model encounters the same great impasse

Every naturalistic hypothetical path seems to lead to the same dead-end. More accurately stated, no “paths” exist in the first place within inanimate physicodynamic reaction space that would lead to any spontaneous protometabolic schema. “Paths” presuppose directionality and goal. Not even evolutionary selection manifests directionality or pursues a goal. Paths to pragmatism exist only in the minds of theorists, not in inanimate nature. The inanimate physical world is constrained, not controlled. Cross-reactive, resource-consuming, spontaneous biochemical reactions prevail, not metabolic “success.” Only agency pursues paths to function. Life and its attributes must be presupposed in order to actually generate any hypothetical scheme of life-origin.

To avoid redundancy, we shall avoid reviewing here the general principles established in all of the other chapters of this anthology. Instead, we shall simply examine all of the leading abiogenic scenarios that exist in the literature. These begin with Miller-Urey amino acid syntheses and synthetic routes from inorganic gases to organic molecules that would hopefully polymerize. Miller’s publication in 1953 [1] was originally thought to solve the life-origin mystery. Life-origin investigators learned very quickly that the formation of amino acids from electrical sparks was a long way from explaining abiogenesis [2].

Jeffrey Bada’s group recently found in some of Stanley Miller’s old spark-discharge vials from 1958 amino acids that had never been reported. The addition of H_2S gas apparently increased the yield of amino acids. “A total of 23 amino acids and 4 amines, including 7 organosulfur compounds, were detected in these samples.” [3]. Not all of these amino acids were relevant to life, and they were not homochiral.

Life-origin models proceed from Dyson’s “Garbage Can” model all the way up through self-replicative, auto-catalytic informational modes in sophisticated vesicles. It is beyond the scope of this one short chapter to critique in detail each model. But we can legitimately classify them into groups requiring common pre-assumptions. Those pre-assumptions often have no basis in observational fact. They also strain rational credibility at every turn. Not one prediction fulfillment has ever occurred independent of artificial selection that steers events, controls and regulates outcomes. The leading hypotheses are rarely, if ever, falsifiable, disqualifying them as scientific theories.

1. Cairns-Smith's clay life

In a class all its own was Cairns-Smith's "clay life" [4]. This was far from the first model of early abiogenesis. But we begin with it because it was clearly unique, intriguing and utterly inanimate. Cairns-Smith examined clay matrix crystals and considered them to provide a possible self-replicative pro-life scaffolding upon which living systems could be built [4-8]. Cairns-Smith, Ingram and Walker [7] addressed formose production by minerals. But Cairns-Smith explored more generally primitive "genes," "genetic takeover" from those primitive genes, and finally an imagined primitive metabolism.

Cairns-Smith deserves much credit for realizing that the key to any info-genesis scenario, whether in clay crystals or any other matrix, would not be found in their highly self-ordered crystalline state, but rather in their crystal *irregularities*. To this day, many otherwise brilliant investigators are still thoroughly confused as to the relation between information and order. Order and information are antithetical [9]. Without uncertainty (almost nonexistent in highly ordered states), no hope of information generation and recordation is possible in any physical medium. Cairns-Smith was wise enough to realize that any potential genetic information that could be "taken over" from clay crystals would have to be found in the irregularities of those crystals, not in their high order or regular structure.

What Cairns-Smith could not explain was how happenstantial uncertainty (random crystal irregularities) could write meaningful, functional Prescriptive Information (PI) (Chapter 1, sections 3 and 4). To this day the question remains, "Take-over of what?!" What would be the basis for assuming that randomly distributed clay crystal irregularities could generate Functional Information (FI) [10-14], whether mere Descriptive Information (DI) or the much more difficult to explain Prescriptive Information (PI) [15-18]? The notion makes no more sense than expecting a random number generator to write a sophisticated computational program.

Many other problems existed with the clay life model. The crystal irregularities were buried in inaccessible layers. The crystal irregularities, even if they had meaning, could not be "read." The number of such irregularities would be insufficient to retain the amount of information required by life. In addition, no satisfactory mechanism of genetic takeover was ever proposed. The information would have to be translated from inaccessible clay crystal irregularities into nucleotide sequences. No theoretical means of code bijection (one-to-one correspondence between "languages") exists. The automaticity of crystal formation was thought to mimic genetic replication. But crystallization provided no Turing tape readability with which to covey instructions to future generations. No mechanism of heritability of irregularities was provided by the model. No replicative genetic system existed to maintain and propagate any PI that might arise. The clay remained as dead and as when the model was first imagined. And the clay contained no meaningful or functional PI to replicate, let alone be "taken over."

An important lesson from Cairns-Smith's work at the time was how plausible and convincing a case could be made for a totally hypothetical scenario that had no real basis in fact. After reading the thoroughly entertaining and popular book *Seven Clues to the Origin of Life* [4], the transition from mere clay to life seemed not only possible, but likely. Some had such vivid imaginations and were operating under such a naturalistic metaphysical imperative as to brazenly call the transition "inevitable." The same history has been repeated a hundred times. Fads move through the life-origin scientific community almost as though it were a seasonal fashion show. Science fiction quickly gains scientific respectability when materialistic metaphysical presuppositions trump sound scientific principles. We become "true believers," all in the name of science, in scenarios with little more than superstition to support them.

2. Silicone and boron-based life

Early on astrobiologists toyed with the idea of life forms that might not use carbon as their main "backbone." Both non-layered silicone and boron were considered.

Interest in silicon [19-22] did not last long because silicon polymers cannot gain sufficient length for adequate information retention. Silicon also forms bonds with other elements that would interfere with silicon-silicon chain formation. Silicon also lacks the relatively easily-broken-and-rejoined covalent-like bonds enjoyed by carbon, hydrogen, and oxygen in organic compounds [23]. Says Trevors and Abel,

> Silicon bonds are too rigid and irreversible for cellular metabolic recycling of structural, enzymatic, regulatory, and informational biopolymers. Silicon is too insoluble in an aqueous environment. Sand, a typical silicon compound, is a good example. No organisms could have been produced except in an aqueous environment [24-26]. Carbon, unlike silicon, is amenable with the help of catalysts to dehydration synthesis even in an aqueous environment. Yet carbon-based organisms do not dissolve in ponds, rivers, and oceans. Carbon chains are unique. Finally, silicon chains lack the ability of carbon chains to establish a lipoprotein-like connection between different kinds of biomolecules.

> Lipids have a different solubility and serve different functions from proteins. Both are needed for life as we know it. Carbon-carbon bonds provide both kinds of branching using the same basic building blocks. Lipoprotein molecules can cooperate to contribute to cellular survival through such functions as membrane formation. Silicone oxide can form layers, but lacks the unique properties of lipoprotein needed for semi-permeable membranes, active transport, secretion, and excretion. [23, pg..]

Silicon was also of interest because it can serve as a surface adsorbent and catalyst for proper alignment and polymerization of polyadenosines and polyuradine [20, 27-41]. But polyadenosines and polyuradines, like the monotonous clay crystals to which they adsorb, contain almost no Shannon uncertainty. Without Shannon uncertainty, no opportunity exists for instructions to be instantiated into any medium. Clay-adsorbed homopolymers could not possibly be the source of highly informational genetic instructions [23].

A side issue related to silicon dioxide and silica carbonate is that such minerals display filamentous-looking features that have called supposedly ancient microfossils into question [42, 43]. Patterns suggesting fossilized filamentous bacteria (e.g. cyanobacterial) can form independent of life. Scientists have trouble telling what is or was alive on Earth. Microscopic structures uncovered in the roughly 3.5-billion-year-old Apex Chert formation in western Australia were originally described as the oldest microbial fossils. These structures were thought to be blue-green algae embedded in a silica-loaded rock. The branching structures were always suspect. University of Kansas geospectroscopist Craig Marshall and his colleagues determined that these structures might not be carbon-based after all [44], but rather a series of fractures filled with quartz and iron-rich hematite. The signature for hematite is very similar to that of carbon. The case has grown stronger that these microstructures are not ancient microfossils of cyanobacteria they were originally thought to be.

The notion of boron life did not receive serious attention for very long. Insufficient boron seems to exist in the cosmos to support life on any planet. Large quantities of boron compounds would be needed to provide enough diversity from which the environment could have “selected” accidental algorithmic metabolic function. The only problem is that no one has ever observed a nontrivial algorithm arise accidently. Borate minerals, however, can stabilize ribose [45]. The instability of ribose constitutes a major problem for the RNA World model.

Neither silicon nor boron provides the replicative potential of carbon biopolymers. In addition, both silicon and boron fail to provide the peculiar secondary and tertiary folding versatility needed to catalyze and support life. The unique lock-and-key binding fits that are so important to carbon biochemistry are not provided by boron or silicon molecules. In short, silicon and boron life-origin models face way too many serious hurdles to provide plausibility. No empirical evidence exists for any form of life other than carbon-chemistry life.

3. Geochemical self-organization models

Many geochemical models have been published suggesting how a very early protometabolism could have "self-organized." The main problem with all of them is that no basis for formal organization exists except in the mind of the theorist. Every investigator mentally constructs the needed and desired biochemical pathways to metabolic success with no basis within inanimate nature for such cooperative integration of tasks Relentless progress up multiple foothills towards the mountain peak of pragmatic success is imagined. Little possibility is allowed for the effect of gravity back down any of those foothills, let alone the mountain top.

Wächtershäuser explored the "Iron-Sulfur-World" [46-48] in which complex organic molecules were formed from the catalysis and energy release of the redox system FeS + H2SFeS2 + H2. Alpermann, et al [49] have adapted Wächtershäuser's model using vesicles to achieve the needed compartmentalization. They call their initial prebiotic unit "Polymersomes." In April of 2011, Wächtershäuser's model of a precursor to the RNA World hypothesis was updated by Frederick Kundell [50]. Kundell suggested a cubic pyrite crystal edge serving as a catalytic surface for the production of a condensed ribose, and potentially a proto-nucleic acid. Martin, Russell and Hall have worked in the same area for over two decades, concentrating on serpentinization of ultramafic crust, iron monosulphide bubbles and hydrothermal vents [51-57].

Many others have investigated hydrothermal vents [51, 58, 59]. In one of the most recent [60], Lane argues that the first donor was hydrogen and the first acceptor CO2. Martin, Russell, et al [51] had previously noted striking parallels between the chemistry of the H(2)-CO(2) redox couple present in hydrothermal systems and the core energy metabolic reactions of some modern prokaryotic autotrophs. Lane points out that "synthesis of ATP by chemiosmosis today involves generation of an ion gradient by means of vectorial electron transfer from a donor to an acceptor." [60].

Recently a Zinc World has been suggested [61]. "ZnS surfaces (1) used the solar radiation to drive carbon dioxide reduction, yielding the building blocks for the first biopolymers, (2) served as templates for the synthesis of longer biopolymers from simpler building blocks, and (3) prevented the first biopolymers from photo-dissociation, by absorbing from them the excess radiation."[61] This was believed to be powered by UV-rich solar radiation at photosynthetically active porous edifices made of precipitated zinc sulfide (ZnS). Similar conditions are found around deep-sea hydrothermal vents.

Among the many problems with hydrothermal vent models is that homochirality and the polymers themselves break down at high temperatures. An aqueous environment is no friend of "dehydration synthesis." The removal of a molecule of H_2O to form each peptide bond is rather difficult in an environment of water molecules! RNA bases and even some of the essential amino acid monomers are degraded in hot aqueous environments. Other problems include dilution factors and lack of containment in compartments. Thus along with heat's advantages (e.g., speeding up reaction rates) comes a slew of problems. This has led some to postulate a cold origin of life where denaturization and other breakdowns would not occur.

Various eutectic ice approaches have been tried [62-68]. The main problem with eutectic ice environments is that the reaction rates are slowed to a snail's pace. No sophisticated enzyme catalysts exist yet in any type of envisioned protocell, whether peptide first or pre-RNA world models. In order for any macroevolutionary scenario to even seem plausible at cold temperatures, huge phase spaces of varying polymers and efficient enzymatic catalysis would have been required. Neither were available. And time was limited since earth's cooling.

Eshenmoser pursued the chemical etiology of nucleic acid structure [69-71]. Rode suggested a salt-induced peptide formation reaction in connection with adsorption processes on clay minerals as the source of a possible Peptide World [72]. Carney and Gazit have further explored peptide assemblies that "possess the ability to bind and stabilize ribonucleotides in a sequence dependent manner." [73]

Many other geochemical models explore hypothetical chemolithoautotrophic pathways [74-81] [82]. Many geochemical models arise out of astrobiological research programs sponsored by NASA grants. In all these geochemical models, no naturalistic basis is ever presented for inanimate nature's *pursuit* of any potential functional pathway. Teleology is of course disallowed by any naturalistic model. Yet without pursuit of formal function, not even the naturalistic version of teleology, teleonomy, is ever observed to arise spontaneously.

4. Protometabolism First models

Most prebiotic molecular evolution models involve organic components and are many and varied [83-140]. As Fry points out [141], autotrophy versus heterotrophy and "soup" versus hydrothermal vent environments remain the major dividing theoretical camps [2, 47].

Freeman Dyson proposed an initial "Garbage Can model" in 1982 [142, 143]. The Dyson model in 1982 was not specific about the nature of the proposed inorganic reactions and catalysts [144]. No experimental basis is provided for high discrimination factors between similar molecules (e.g., amino acids). As Anet points out, the high discrimination factors are far more difficult to achieve than mere catalysis [144, pg. 655]. Dyson's oligopeptides contained around a five-monomer active site in twenty-monomer strings. But the non-active-site monomer sequences are critical to folding and function.

von Kiedrowski [136, 137, 145] demonstrated a self-replicating hexadeoxy nucleotide [145]. Short double helix templates can self-replicate easily. The two strands separate with a certain probability to form templates. Szathmary points out that longer strands can serve as templates too, but do not replicate "because the two strands do not separate spontaneously; intervention is required."[146, pg. 32].

Lifson refutes theories of self-organization that fail to incorporate natural selection [90]. But what exactly is the prebiotic mechanism of selection for function at the level of monomer sequence formation? Biopolymers form with rigid covalent bonds prior to any folding. Selection occurs at the phenotypic level, not at the genetic level of polymer formation [147]. Even in Peptide and Protein Worlds, sequencing would have determined minimum-free-energy folding space. Some have argued that sequences of at least 80-100 mers are necessary for any substantial selective catalysis [148].

Differential autocatalytic doubling is seen as a substitute for informational genetic replication and the basis for natural selection in protometabolism first models. Constrained geochemical conditions are actually seen as advantageous by some in limiting the possibilities of early protolife development [48, 149, 150]. This would reduce the likelihood of cross reactions and metabolic dead-ends. This more deterministic hypothesis resembles Dean Kenyan's "biochemical predestination" model of life origin [151] which Kenyan himself eventually disowned.

Protometabolism First models such as Robert Shapiro's [152] are seen as more probable by metabolists than Information First genetic models. The extreme improbability of RNA world scenarios is the reason. But others such as

Leslie Orgel have challenged this [144, 153, 154]. Plausibility is perhaps just as lacking for protometabolism first models as replication-first models.

4.1 Composomes

The naturalistic dream upon which all macroevolutionary theory is founded is a "self-reproducing and evolving proto-metabolic network." Given all of the many biochemical problems with RNA World models, many investigators have returned to previously-abandoned Metabolism First models [53, 56, 143, 146, 152, 155-159]. The self-replication and ligation of peptides has received some attention [160, 161]. But the catalytic properties of peptides is well known to be little more than those of ribozymes—extremely poor compared to proteins.

Lancet, Segre and Shenhav have championed "composomes" [162], Graded Autocatalytic Replication Domains (GARD) [163], and Lipid World models [164]. Progress was limited with these models. Composomes are theoretical Metabolism First protocellular entities. Early on they are believed to have found themselves contained within lipid vesicles or micelles. They are not seen as full-fledged living systems. But they example one of the simplest conceivable models of protolife. Compositional "genomes" (assemblies of varying molecular species) are thought by some to be able to propagate evolvable chemical and structural information.

Catalytic organic amphiphiles within vesicles provide what Lancet's group calls "compositional information." [163, 165-167]. Lancet's protocells are able to propagate without polynucleotides. Irregularities that arise in the envisioned catalytic networks are considered to be mutations [167].

It has never been clear exactly how "compositional information" is read, or exactly how this three-dimensional composition organizes and instructs a protometabolism. The model resembles the old imaginative protoplasm gel theory of life. The devil is in the details of any model. Detail is sorely lacking in the composome model. The problem with a non-digital means of analog replication is that the fidelity of information quickly deteriorates.[168-171]. The units of replication and selection need to be discrete. Nevertheless, Sterelny and Griffiths [172, 173], Lancet and Shenhav [167], and Pohorille [174] argue for analog instructions playing the major role.

Autocatalytic amphiphilic assemblies are hypothesized to co-evolve along with their surroundings. Auto- or perhaps mutually-catalytic "metabolic networks" are envisioned. They are "devoid of sequence-based biopolymers, yet could exhibit transfer of chemical information" with the hope that they might also undergo selection and evolution without a genetic apparatus [162]. They are viewed as rudimentary "compositional genomes." The chemical composition of the environment would have theoretically governed the chemical repertoire generated within molecular assemblies in these compositional protocells. Segre et al's "lipid world" includes evolutionary genetic membranes that do not require protein or RNA enzyme catalysis (Segre, Ben-Eli, Deamer, et al., 2001).

The compounds generated within the composomes would have then altered the chemical composition of the environment. This is called the environment exchange polymer graded autocatalysis replication domain (EE-GARD) model [162]. In the computer models of composome evolution, early stage composomes disappeared, while others emerged.

EE-GARD is of course not the only non-genetic Metabolism-First life-origin model. Many models throughout recent decades have been proposed. Freeman Dyson's two-step model attempted to bridge the gap and provide transition from garbage-can Metabolism First to more template–directed informational genetic models [143]. Yarus posits a more contemporary two-step model [175]. Many of these models emphasized a three-dimensional physicochemical and structural concept of information as opposed to the linear digital PI messaging found in all known current life. Eshenmoser [71], Russell, Martin and Hall [51, 55, 176] Shapiro [177, 178], Kauffman [179, 180], de Duve [150], Wachtershauser [48], Morowitz [181], Deamer [182], Pohorille [174] and Lindhal [183] models provide specific chemical detail. Wong [184, 185], Guamaeres [159, 186] and Di Giulio [187, 188] offer models that attempt to link early protometabolism to code development. But, as we shall see below, virtually all Metabolism First models lack organizational motive, ability and naturalistic explanation.

4.2 Compartmentalization

Compartmentalization becomes a major issue early on in life-origin research. Most life-origin models today incorporate some form of an early micelle, vesicle, or pseudo membrane.

Pier Luigi Luisi [189-194] and David Deamer [182, 195-204] have been leaders in primordial membrane research. The problem is that most primordial pseudo membranes that would keep needed protometabolites in the compartment also keep toxic metabolites in with them. In addition, needed nutrients are kept out without highly selective active transport mechanisms. The simple bilipid layers of vesicle models lack this sophistication. Simple but serious osmotic problems even exist with bilipid vesicular pseudomembranes. Active transport and highly specific differentiations are necessary in channels to exclude cross-reacting factors, yet provide needed metabolites. Even Wächtershäuser's "surface metabolist" model requires a water-resistant pseudomembrane on pyrite crystal surfaces [47]. Mansy et al have done some of the most recent and impressive work on protomembranes [205-208].

The latest RNA World models of life origin all require a membrane of sorts that can expand and divide. This pseudomembrane encircles an RNA replicase ribozyme [209]. An additional ribozyme is thought to have formed within this vesicle that catalyzed the synthesis of essential membrane-genome relationship factors [193].

4.3 The problem of sequencing

It is only recently that the origin-of-life scientific community has been candid in acknowledging the problem of co-polymer sequencing. Perhaps the Origin of Life Prize was instrumental in stimulating previously neglected discussion and research into gene emergence (www.lifeorigin.org). A co-polymer is a polymer consisting of two or more different monomers. This is distinguished from homopolymers where all monomers are identical. It is much easier to form homopolymers under prebiotic conditions than co-polymers. As Pier Luigi Luisi point out, "the kinetics and thermodynamics attending the synthesis of copolymers poses stringent constraints for the biogenesis and growth of specific sequences." [210] Luisi goes on to say that although co-oligopeptide chains can be produced by prebiotic reactions, "It is not possible by the bottom up approach to find the conditions for the synthesis of our actual proteins—lysozyme, chymotrypsin or the like, . . ." [210] Sequencing is critical in proteins and nucleic acid. But of course the sequencing of amino acids to form proteins stems back to the prescriptive codon sequencing and editing of DNA and mRNA. The chemical bonds between nucleotides are all identical. The chemical bonds between amino acids are also identical. The problem of sequencing, especially the prescriptive sequencing of nucleotides will not be solved by any physical law [9, 15, 18, 211]. The same is true of the formal Hamming block-coding and codon table used to reduce noise pollution in the Shannon channel.

4.4 Hypercyles

Few concepts are more important to any protometabolic scheme than Eigen and Schuster's original notion of hypercycles [212-226]. Hypercycles have been proposed as a source of spontaneous naturalistic self-organization [215, 218, 219, 225]. Biochemical cycles act as catalysts. Hypercycle theory is based on positive and negative feedback constraints [48, 162, 174, 227-230]. These mere circular constraints are typically confused with formal controls. These deterministic cycles of interaction are envisioned to give rise spontaneously to pragmatic pathways, networks, and finally integrated metabolic processes. The key word is "envisioned." An imaginative human mind can envision extraordinary creativity through natural process without any empirical or prediction fulfilling confirmation. Actual experimental observation of physicodynamic interactions say otherwise. Eigen was able to *engineer* a hypercycle of cooperating RNAs that catalyzed each others' replication [231]. But engineering always involves formal controls. Wächtershäuser attributes what he considers to be non-genetic memory to the branching products feeding back into the cycle.

The reason Eigen's hypercycles are so appealing is that the simpler chemical cycles obviate the need for protein enzymes and even ribozymes. The cycle itself provides catalysis. Hypercycles are envisioned to provide fuel for a bottom-up theory of self-organization and life origin, all from purely chemical "systems." A cyclic process sign is used to replace equality in mass-balance equations. Once again, mere cyclical constraints are confused with formally programmed feedback controls needed to organize any bona fide pragmatic system (e.g., metabolism).

Blomberg, the head of NASA's Astrobiology program at the time, reminded us of the Eigen-Schuster "error theshold,"

> There is a limitation of size due to the accuracy, which can be called the Eigen Schuster error threshold [217, 232]. If the size of a replicating macromolecule becomes too large, then there will be too many errors, and no systematic reproduction. This leads to a dilemma, sometimes called the Eigen dilemma: it was necessary to have a high accuracy to obtain long, functionally active macromolecules. But to achieve high accuracy, long active controlling macromolecules were needed. There are many chicken and egg problems of that kind for this stage that obscures a direct step by step development. [233]

4.5 Tibor Ganti's well-developed chemoton model

Perhaps the most well-developed, comprehensive Protometabolism-First model published by any one author is Tibor Ganti's "chemoton theory" [86, 87, 146, 234-237]. Tibor Ganti's chemoton model is a hypercycle take-off. Ganti envisioned interconnected autocatalytic, or at least mutually catalytic [223], Eigen-Schuster type hypercycles [213-219] in well-organized elementary units of life called "chemotons." [87, 234, 236, 237]

Ganti's basic idea is that stoichiometric cycles act as catalysts. No proteins exist yet, and therefore no linear digital prescription is needed. He uses a cyclic process sign to replace equality in mass-balance equations [238]. The cycles do the work of enzymes and ribozymes. It's a bottom-up theory that is very appealing to those faithfully committed to purely materialistic metaphysical presuppositions. The model depicts a transition directly from chemicals to living "systems" without any formal controls.

Chemotons have three self-producing (autocatalytic) stoichiometric subsystems that are coupled to one another: autocatalytic metabolism, a genetic polymer, and a membrane. The key to life is "fluid automata," complex systems of chemical reactions in fluid phase that function like machines. They have no solid parts. But they can be regulated.

Ganti's models are quite different from Lancet, Segre and Shenhav's composomes discussed earlier. Ganti recognizes and even emphasizes the need for cybernetic controls. "Chemical reactions as building blocks can be assembled into regulated and program-controlled chemical automata without including any solid components." Ganti realizes that true organization is essential for life to exist. The chemoton model's "organizational principles must be present in every living being." Ganti calls his chemical cycles and networks "cycle stoichiometry." Ganti sees a direct link between genetic cybernetics and computer science. "Program control must control a functional system and enzymatic regulation must also regulate a functional system."[146, pg xii] "Chemoton theory is concerned primarily with this machinery aspect."

Says Ganti, "A chemoton is the simplest chemical machine which shows the generally accepted characteristics of life." [146] The first problem with this is that no such machine exists. The simplest living organism is a cell containing multiple operating systems, hundreds if not thousands of programs, multiple layers and dimensions of Prescriptive Information (PI), and huge numbers of molecular nanocomputers all cooperating in one concerted integrative effort [239, 240]. The second problem is that "the generally accepted characteristics of life" depend upon who is defining life. No two scientists' definitions of life seem to be the same. Life-origin science has a long history of defining-down life to something far less than life in order to make our models "work for us." [241]

Ganti repeatedly refers to his chemotons as not only "interconnected systems of chemical reactions," but as "organized regulated processes." "Organizational principles must be present in every living being," [146, pg 1]. The question of exactly how chance and or necessity could sense, obey or pursue a formal "organizational principle" is never addressed. Until this missing essential piece of the puzzle is supplied, the model falls apart as a supposedly naturalistic explanation.

Ganti envisioned his fluid automata chemotons to have two parts: an operating part—the automaton; and a controlling part—the genetic programs

[146, pg. 13]. Regarding the controlling part, Ganti makes a stunning admission: "Of course, *the sequence of signs is not material* [italics mine]. But neither is it independent of material, since the sign is carried by some material substance." [146, pg 13] In other words, Ganti regards the information found in the sequence of signs as nonmaterial even though that sequence is instantiated into a physical medium of monomeric sequence. It is surprising to this author that much of the supposedly controversial material presented in *The First Gene* Ganti himself would probably have had to agree with.

What in nature for Ganti could possibly be "not material" (not mass/energy)? Naturalistic science is physicalistic. Reality tends to be defined solely in terms of mass/energy. When Ganti talks about non-material representational sign syntax, does he believe in some sort of non-material "super nature"? Ganti would probably assure us of his commitment to a naturalistic worldview. The whole point of naturalistic life-origin science is to avoid nonphysical explanations of what is claimed to be a purely physical reality. But is his cybernetic model tenable under the naturalistic metaphysical imperative? Representationalism is a little hard to explain from a physicalist perspective. So are the mathematics and reason upon which the scientific method relies. To argue logically for physicalism is to deny physicalism. There is nothing physical about the exercise of logic theory.

What does Ganti's word "program" mean? Programming requires purposeful logic-gate settings. Exactly how are programs instantiated into this liquid chemoton's physicality? What is the basic unit of selection and instruction in this liquid? By what chemical mechanism did this programming arise? Can we cite any examples of chemical reactions in liquid phase, especially, programming and optimizing algorithms? Says Ganti, "The living system is a program-controlled cybernetic system." [146, pg 12] Ganti continues, "Cybernetics itself originated from the study of the regulated and controlled operation of living systems, and program control is already familiar from the genetic program." [146 pg 12]

Says Ganti, "Chemical reactions as building blocks can be assembled into regulated and program-controlled chemical automata without including any solid components." [146, pg xiv]. But what is the nature of this mysterious liquid program? Is it a liquid crystal? How could programmed information be instantiated into a liquid OR highly ordered solid structure? And what exactly *does* the "regulating" of these chemical reactions? What sort of magic cybernetic liquid crystal is this?

There is no basis for logic theory, quantification, decision theory, scientific debate, computation, computer science, controlled experimentation, or engineering within the physicalist world view. But we ought not be too hard on Ganti for acknowledging the reality of representational signs in the cybernetics of life. The sequence of physically instantiated “signs” (“physical symbol vehicles;” tokens) is everything when it comes to the message of messenger molecules.

The most serious problem with Ganti’s model is that he is unable to generate a basis for “programming” OR “organization” from mere physicodynamics. Interconnected hypercycles are even more constrained than individual cycles. Constraints are not controls. Constraints cannot steer events toward pragmatic goals.

Ganti’s chemotons are assumed to be already evolved prior to the appearance of catalytic RNA’s [146, pg vii]. So RNA linear digital prescription cannot explain Ganti’s acknowledged need for programming and organization in the forming of chemotons. RNA was supposedly assembled only later by substrates already present in the chemoton [146, pg vii]. This notion alone does not explain how the particular functional sequencing of “signs” [actually tokens—“physical symbol vehicles” in a Material Symbol System (MSS) [242, 243]] was achieved.

Exons, the protein-coding regions of eukaryotic DNA, were found to contain a seemingly random statistical distribution of the four nucleotides. Weiss et al. reported that “Protein sequences can be regarded as slightly edited random strings.” [244]. These facts led this author to originally surmise that nucleotide sequencing in highly informational strands must be physicodynamically indeterminate not only in exons, but probably in the very first informational single-stranded, non-templated RNAs. All of the 3’5’ phosphodiester bonds are the same between coding nucleotides. With a seemingly random nucleotide frequency of distribution, one would expect no physicodynamic “preference” in sequencing. But the recent finds of extensive highly-functional regulatory microRNAs in non-coding introns raises new questions. Introns contain a great deal of redundant order. They were once thought to represent non-informational junk DNA. For configurable switch-settings to have cybernetic function, the switch must exhibit near equal physicodynamic opportunity to be flipped either way. “Off” must be just as feasible as “On” from the standpoint of natural law’s influence on the physical switch. If the laws of physics in any way militate against “Off” (e.g., the force of gravity favored the down position of the switch knob on a vertical switch board), the switch setting becomes less significant algorithmically. To whatever degree the switch-setting is forced by physicochemical necessity, its Shannon uncertainty drops. Shannon uncertainty is nothing more than a probability function. Its ability to instantiate *prescriptive information* nose-dives with increasing physicodynamic determinism. Maximum information retention at that switch is realized only if "On" and "Off" are equally possible from the standpoint of physics and chemistry.

Constraints and physical laws are normally poisonous to control unless configurable switches are specifically designed to be physicodynamically inert. This is exactly the case with the coding regions of DNA. Protein coding sequences are non-ordered by "necessity" (law). Weiss et al found that proteins are "slightly edited random strings." [244] The 1% nonrandom factors were thought to arise out of secondary structure requirements and low complexity regions.

Very recent work has also shown that up to 120 mer cyclic homopolymers of RNA can form spontaneously in heated aqueous environments. No catalysts or templates are required. Oligomerization of 3′, 5′-cGMP to ~25-nucleotide-long RNA molecules, and of 3′,5′-cAMP to 4- to 8-nucleotide-long molecules were achieved [245]. The authors hoped that this research might explain the first genetic polymers. But they failed to address how such high redundancy could instantiate much Shannon uncertainty, let alone PI. Highly ordered strings should have a very low information-retaining ability. Programming with highly redundant, intron-like sequences would have to be very simple and limited. Perhaps the information requirements for regulation are minimal, with only short segments needing specificity, and the bulk of the redundancy going into basic noncritical carrier structure of the active sites. But with the discovery of so many highly functional, yet highly-ordered microRNAs, it does raise the question of whether ordered strings, not just seemingly random strings, can be used to prescribe function. Functional sequencing can include repeated selection of the same nucleotides in monomeric sequencing (syntax). Order in a sentence or programming string is not necessarily from physicodynamic causation. In a linguistic string, for example, some letters have a high frequency of arbitrary re-use. Morse code assigns the shortest symbols to represent the most frequently used letters ("." represents and "e"). "Freedom" from physicochemical law exists in the coding regions of DNA to program biopolymeric messenger molecules. This programming freedom includes frequent re-use of the same nucleotide in microRNA prescriptions. The situation is a little like a programmer re-using redundant modules, or an engineer using many highly-ordered components to manufacture a sophisticated product.

Also surprising, if not shocking, is the discovery that the negative complementary strand of coding DNA that is physicodynamically base-paired can simultaneously prescribe regulatory function independent of the positive strand's prescriptive function. Both PI sets are sequence dependent. Clearly some formal factors are transcending what seems to be the purely physicodynamic base-pairing to prescribe multiple unrelated formal functions with each complementary strand. It is a false conclusion that these formal functions were prescribed by base-pairing itself. Purely physicodynamic base-pairing is incapable of programming any formal function. The programming is so formally sophisticated that it prescribes and organizes even physicodynamics to accomplish computational cybernetic goals. The evidence only continues to mount for the Formalism > Physicality (F > P) Principle presented in Chapter 12.

The existence of Ganti's initial PI is just presupposed rather than explained by his model. Ganti repeatedly acknowledges the need for programming and organization, but provides no naturalistic model for either formalism.

Ganti is right that, "A living being is a controlled system." [146, Pg. 13] But Ganti thoroughly confuses circular physicodynamic constraints with formal organizational *controls* needed to generate "usefulness." [246] Constraints and Laws cannot possibly generate cybernetics. We should never confuse mere order with algorithmic programming. Ganti says, "A strictly defined order exists in our television set, radio, or computer." [146, pg. 19] Physicodynamic order (e.g., redundant crystalline structure or oscillations) doesn't make television sets. Says a peer reviewer of this paper, "Actors collecting the necessary and defined resources using processes to act on them through formal cybernetic and algorithm organization make televisions. The televisions, in turn, run electronics which are taking incoming analog or digital inputs and converting them to audio-visual displays through algorithm organization."

Ganti pursues order in his liquid automatons in an effort to explain programming, organization and the beginnings of cellular cybernetics. He looks for "forced coupling between the forced trajectories so that the solution is capable of operating as an automaton with a given function." [146, pg 19] Neither cause-and-effect ordering (necessity) nor oscillating (redundant) chemical reactions can explain phenomena such as chemotaxis. Chemotaxis requires freedom from forced constraint and law. Genetic programming is similar to computer programming wherein degrees of user freedom are programmed into the software. The user gets to choose from among real options. No trajectory is forced. No highly ordered oscillation allows a bacterium to avoid noxious stimuli. Logic gates require programming freedom, not fixed order.

Could circular constraints ever generate formal regulatory control and organization of protometabolism? Many publications have argued that this is possible. But they are all purely theoretical with no observational or prediction fulfilling support. The circular intertwined diagrams of Tibor Ganti certainly look plausible at first glance [146, 236, 237]. Upon more careful, critical analysis however, they are merely *self-constraining* feedbacks, not formally selfcontrolling feedbacks. No choice contingency is involved. No steering or selective programming in pursuit of formal utility is achieved by purely chemical positive or negative circular cause-and-effect constraints. Minimal uncertainty is involved in circular constraint, and therefore almost no Prescriptive Information (PI) is required. Indeed, PI control is nearly impossible. Any feedback is forced in a circular cause-and-effect deterministic chain. Increased production of reactant A will always lead to increased feedback production of reactant A_1 or B in cases of positive self-constrained feedback. The opposite is true in cases of negatively self-constrained feedback No opportunity exists for formal *"regulation"* of anything. The product ratios are forced by the relative constraints irrespective of any formal need or desired utility. No fine-tuning in pursuit of function optimization is possible or even desired by a self-constrained cycle. The term "feedback *mechanism*" is an illusion. Only unimaginative redundant, cyclical, physicodynamic determinism prevails without regard to mechanistic (machine like) pragmatic benefit. Sophisticated machines don't spontaneously generate any more than life spontaneously generates.

Ganti's model of life-origin was doomed from the start for two major reasons: 1) his failure to understand the difference between "constraints" and "controls," and 2) his confusion of physicodynamic laws with the arbitrary cybernetic rules of life's programming.

Controlled paths can be paths with purposefully preset switches. *Preset switches are formal decision-node choice commitments*. They are logic gates. And they must be freely set to either open or closed positions with programming intent. Neither coin flips at each decision node (fair or weighted) nor physicodynamic laws will achieve sophisticated algorithmic function. Life is algorithmic and dependent upon linear digital prescription using a material symbol system (MSS) [243].

Ganti's notion of cybernetics is nothing more than physicodynamic coupling—cause-and-effect chemical reactions interconnected by forced stoichiometric connections between three auto-catalytic cycles. The three cycles are unable to function without each other. Their cooperation together forms an interdependent super system, a model which, if it actually existed, Michael Behe might claim exemplifies "irreducible complexity" [247].

In addition, "If A, then B" reactions are constrained, not formally controlled to achieve desired function. Such cycles of constraint, even if they lead to positive or negative feedback, are not true examples of formal control, regulation, pragmatic organization, or true systems. Cycle stoichiometry would have to be steered by controls, not mere reaction constraints, to achieve formal integration and final metabolic function. Only by highly selective catalysis and formal regulation of the cyclic pathway can stoichiometry produce any desired useful work.

Ganti considers an oscillatory chemical reaction a chemical automaton (p 19) because of his sometimes loose definition of "cybernetic." At other times, he more accurately defines "cybernetic." A major problem with Ganti's model is that he shifts back and forth between the two definitions of cybernetic within his model. Mere oscillation is not cybernetic, at least not to the degree we could draw any analogies with sophisticated machine generation or function. A pendulum swing doesn't do very much "useful work." A reviewer counter argued that crystal oscillators can be used in computers to provide input function for circuitry timing. "Crystal oscillation provides useful work—timing input function—which allows all dependent circuits to be coordinated." But the key to this contention is "can be used" (by agents). A hill does not become a simple machine (an inclined plane) until an agent decides to use that hill as the means to achieve a desired function. The hill itself does not perform useful work. The hill just exists in a formally neutral sense. A hill is not "an inclined plane" until that hill is used by human agents to do useful work—to achieve a desired purpose—to accomplish formal utility. A hill is not a simple machine merely because the hill exists. The hill can be used by us to increase the efficiency of raising a heavy object to a higher altitude against the force of gravity. The choice and act of an agent rolling a heavy object up the hill, rather than lifting it, alone makes the hill a simple machine. The wind can blow a tumble weed up the hill, but no *functional work* is accomplished. The inanimate environment does not value the tumble weed winding up at a higher altitude. No formal goal is pursued, and no utility accomplished, in seeming opposition to nature's relentless trend towards disorganization and loss of sophisticated utility.

Ganti talks about "successive chemical transformations involving organic acids in biological oxidation." [146, pg xi]. Ganti did not seem to concern himself with the prevailing serious problem of how interminably-long biochemical reactions take without sophisticated enzymes with remarkable rate constants (10^7 to 10^8 times the acceleration rate). Szathmary, in critiquing Ganti's model, seems to believe that a non-enzymatic chemoton would be impossible [146, pg 41]. Over a hundred reaction steps would be required for the simplest chemoton. Two thirds of these reactions have been shown in the literature to be infeasible in a prebiotic environment [146, pg 41]. Even if sophisticated protein enzymes had been available from the start, how would a hundred different chemoton reactions all be integrated into a unified and coherent pragmatic system in a prebiotic environment?

More problems with Ganti's model are listed by Stegmann [248]. The Krebs Cycle, like a biopolymer, can be viewed as an "ordered [sequenced] set." Stegmann [248] asks which factors determine the identity and the sequence of the elements of this 8-tuple? "In the Krebs cycle, each reaction product becomes the substrate of the subsequent reaction." Oxalacetate (O) accepts an acetyl residue, producing citrate (C). The C next becomes the substrate for the reaction that produces isocitrate (I). The sequence of the 8-tuple $\langle O, C, I, G, ... \rangle$ is a direct result of "If A, then B" reactions. Thus says Stegmann, "the order [the sequence] is not determined by the properties of a molecule present before the reactions occur. It is not even necessary that the set of substrates is present before the cycle starts, because the substrates are produced as the cycle unfolds."

Where is this chemoton *unit of life* in observational nature? Chemotons as elementary units of life have never been observed. No prediction fulfillment has ever been realized of spontaneously forming chemotons coming to life. For all of the tens of millions of life forms that exist on earth, one would expect to be able to identify innumerable examples of spontaneously generated chemoton units from which all these organisms supposedly arose originally. And we would also expect to be able to vivisect organisms down to their simplest chemoton units of life for study. But any attempt to reduce life down to its imagined sub cellular chemoton level invariably kills that life.

Glass et al. [249] identified 382 of the 482 *Mycoplasma genitalium* protein-coding genes as essential, plus five sets of disrupted genes that encode proteins with potentially redundant essential functions, such as phosphate transport. Genes encoding proteins of unknown function constituted 28% of the essential protein-coding genes set. It remains to be seen how many peptides, polypeptides, and small RNAs are essential for regulation in this Mycoplasma in order for it to be alive. This is the simplest form of life known. It cannot be reduced to a smaller living chemoton unit. Just because we *say* life is reducible to only five criteria does not make it so in objective reality.

Says Ganti, "Thinking in a suitable abstract chemical state space" (a cycle stoichiometry state space), "It is possible to *design* fluid chemical automata in a similar way to that used by mechanical *engineers* when *planning* mechanical automata or by electrical *engineers* when *designing* a radio or a computer. *The same method is used* and *the work can be done at the desk.*" [Italics mine] [146, pg 23] Ganti goes on to point out that, "The author has *designed* several 'chemical machines'" [146, pg 23]. We might ask in response to this argument, "Are these contentions supposed to provide support for a prebiotic naturalistic spontaneous generation of a chemoton?!

The primary problem with the chemoton model is that the reaction chain always branches into innumerable “wild goose chases.” Controls, not mere constraints, are needed at every fork in the road to achieve computational success. Ganti’s main figure of the minimum chemoton (Fig 1.1) in *Principles of Life* is telling. It depicts a non-existent abstract scenario featuring careful, deliberate exclusions of the innumerable dead-end branches, cross-reactions, and negative feedbacks that shatter hypercyclic dreams. In addition, Fig. 1.1 in his book does not show the rapid consumption of valuable resources by both the “right” and the “wrong” paths that could be taken. There is no right or wrong path in a purely physicalistic reality. Whatever cause-and-effect determinism militates is “right,” whether it produces any functional benefit or not. No basis exists for “correct” (computationally successful) switch-settings within Monod’s chance or necessity (Monod, 1972). Freedom of selecting each fork in the road of the potential reaction network is essential to generate formal function. In the absence of choice-with-intent, we simply do not observe three conceptually complex autocatalytic cycles simultaneously integrating themselves into a protometabolism. Algorithmic programming is required to couple them appropriately to achieve unified and coherent holistic function. Ganti just presupposes—blindly believes—all this spontaneous cooperation. No observational support exists in the history of human experience for such spontaneous pragmatic self-organization.

Says Ganti, “It is also a splendid recognition that living systems are complicated fluid machines consisting of invisible wheels in an imaginary field. But if this is true, then those claiming that such a machine could not be developed by itself are probably correct.” [146, pg 24] One wonders how “machines consisting of invisible wheels in an imaginary field” would be any more respectable a scientific hypothesis than vitalism.

Ganti continues, “Obviously, a constructor was needed who designed the controlling program first, but also planned the controlled machine. Who was the constructor who designed these congenial machines and who was the chemist who realized these plans?” Somehow Ganti’s model does not seem to be measuring up to the plausible naturalistic model it is claimed to be.

Biochemical products of cycle stoichiometry can occur spontaneously. But these products are not directed toward or integrated into any desired or needed task. The reactions just happen without regard for any pragmatism. They are not programmed or organized into any process. “A cell is not a bag of enzymes.”

Contrary to the current preferred scenario, the environment doesn’t “co-evolve” with physicodynamics towards ever increasing spontaneous functionality. The inanimate environment could care less whether anything “functions" or whether "useful" products are produced. No basis exists for the environment preferring them. The only way hundreds, if not thousands, of co-evolution steps could progress towards an organized protometabolism is via Freudian "wish-fulfillment" in our minds, not in a physical inanimate environment. Not only would all available resources be consumed in the militated automaticity of Ganti's first few coupled reactions, but the products would cross-react and lead to biochemical dead-ends. The number of cycles and cycle couplings would have to far exceed by orders of magnitude the number of current-life enzymes needed to accomplish just the reductive citric acid cycle alone.

Like Stuart Kauffman, Ganti asks many of "the right questions" which others run from: "Living systems are program-controlled chemical machines. So where is the program?" [146 pg 30]. Ganti answers by saying that in self-regulating chemical processes, reaction networks are regulated by feedback. He views feedback as being the precursor or primordial program itself. But what exactly is feedback in the case of Ganti's chemoton model? The forced or "necessary" products of chemical reactions become substrates and/or catalysts for more automatic cycles of the same constrained process. Autocatalysis and self-replication are self-ordering phenomena of physicochemical necessity, not formal programming freedom. They are like the redundant oscillation of a pendulum, or one full revolution of a tornado or hurricane. Ganti senses something is wrong with his attempted equating of controls with constraints: "However, for program control, external intervention is necessary which regulates, via external information, the operation of the machine." What external information might that be? Could it be Prescriptive Information (PI)? What would be the source of PI a prebiotic naturalistic environment? Mere stoichiometric cycles cannot generate formal PI *or* organization.

Programming is something much more than mere auto-catalysis. No programming whatsoever is required for trivial autocatalysis. "Automaticity" is not synonymous with "program." The automaticity of trivial autocatalysis relies solely on cause-and-effect forces, self-ordering, and the laws of nature. Programming, on the other hand, relies upon *freedom from* that order and necessity. Algorithmic programs are possible only because the programmer can make real choices at each successive decision node. Switch-settings must not be physicodynamically determined by interlocking chemical reactions! Programming decisions require freedom from physicochemical determinism.

Ganti keeps presupposing "process" in his model. He pre-assumes that natural events are progressing relentlessly toward ever-improving functionality. No natural mechanism is provided for such a preference. Then he repeatedly argues that he has logically proven his thesis. According to Ganti, a clear unambiguous answer has been given to the question of the genesis of life (Ganti, 2003, pg. 41):

> Is it possible to *prepare a plan*—a metabolic *map*—of a chemoton in which, compounds present in the primordial atmosphere can be substituted for the letters in the *abstract* reactions? If so, then this will represent a credible *pathway* for the genesis of life which is *not based on chance*. [146 pg 39, italics mine].

The problem is that it would not be based on physical determinism either. Preparing a plan is formal, not physical [15, 211, 250, 251]. Ganti is right that chance cannot explain abstract plans and maps, as he calls them. But neither can the fixed invariant laws of nature. Ganti continues: "If such a *design* can be realized, this will show that the spontaneous genesis of life cannot be regarded as an accidental improbable miracle, but as a process directed by the laws of nature . . ." Ganti simply does not understand, or refuses to acknowledge, that fixed law precludes the very programming freedom and organization which his model requires. *Physicodynamic determinism locks logic gates into a fixed position and destroys all hope of formal programming of utility [250].*

The fixed laws of nature cannot "prepare a plan." The laws of nature cannot "map" out a journey through a maze, "represent" in "abstract" terms, or "design" a single engineering function. All of the latter accomplishments are formal and algorithmic. They are phenomena arising from a different category entirely from redundant natural law. Natural law cannot program anything. Ganti continues to reason from within a certain internal inconsistency:

> The chemoton model can be used to design program-controlled proliferating fluid automata which form spontaneously [!] and show properties characteristic of living systems in an exact and concrete manner if the necessary data are known, just as an engineer designs his machines and instruments [!]. ([146, pg 41], exclamation marks mine)

Ganti is first saying that his abstract, human-crafted model can be used to design program-controlled fluid automata. He is describing obvious engineering functions here. Both his model and the program-controlled fluid automata designed by his model are algorithmic. Neither chance nor necessity could produce any of these objects. Under no circumstances would they be expected to form spontaneously in nature. Even if they did, they would display none of the properties or characteristics of living systems, which are invariably algorithmic to an extraordinary degree. Spontaneous events have almost nothing in common with how "an engineer designs his machines and instruments." An engineer designs through an integrated succession of purposeful decision-node choice commitments. Each and every choice is made with intent to achieve a desired function. The function comes into existence only upon implementation and halting of the finished program. The initial program may not be ideal. But it must produce the basic computational function to even be considered a program.

But Ganti is right to emphasize "the property of specially organized systems."

Ganti is correct when he says, "Life itself is the continuous organized functioning of the system, which can only be maintained at the price of continuous performance of work" [146, pg. 72]. But his correctness is realized only within the context of proper definitions of "organized" and "work." "Organized" is always algorithmic, never self-ordered. An algorithm is a stepwise procedure governed by purposeful programming choices. Organization cannot arise from law-like self-ordering phenomena. "Work" is always defined by utility relevant to some need, desire, or goal. Life is cybernetic. All known living organisms manifest the ability to harness, transduce, store, and call up when needed chemical energy for the work of staying alive. As Ganti points out, organisms must maintain themselves permanently far from equilibrium. This requires the constant expenditure of captured and algorithmically-transduced energy.

Where is the empirical support for this chemoton pipe dream? Ganti repeatedly argues in effect, "See, no miracle is needed." But in the absence of empirical support for spontaneous programming, faith in miracles is exactly what is being presented as though it were a scientific model. Even spontaneous multiple couplings of organic autocatalytic cycles has not been empirically supported, especially in prebiotic environments.

Can bona fide "systems" exist without control and regulation? Undeniable life is empirically unknown without the essential ingredient of highly fine-tuned metabolism made possible only by highly organized systems of sophisticated enzymes. The fine-tuning cannot be so easily dismissed from the "necessary and sufficient" definition of empirical life. But it is all-too-easily dismissed from Ganti's abstract model of life. The efficiency of regulation may well be the most significant component of life. It is the key to homeostasis in a constantly changing, hostile environment. The primordial environment was far more hostile than it is today. Abstract theoretical models of life all-too-easily escape the checks and balances of empirical accountability and predictability which are so crucial to science. Ganti's model dangerously departs from scientific empirical accountability. We have abandoned observable biological categories in favor of purely metaphysical mental constructions. Life and its criteria have now become philosophic and psychological abstractions. As in theoretical physics, all sorts of "realities" can be deduced in such a fantasy world that have no connection with "the real world."

Antirealists no doubt recoil at the notion "objective reality." We tend to be obsessed with our "epistemological problem." This often leads to committing a non-sequitur. We fallaciously conclude that because we cannot know inside our minds that objective reality exists outside of our minds, that objective reality doesn't exist, or cannot exist, or doesn't matter. Objective reality will have the last laugh over our dying anthropocentric and solipsistic brains and minds.

Near the end of his long career, the esteemed Leslie Orgel saw little hope of any kind of Metabolism First model being successful: "In my opinion, there is no basis in known chemistry for the belief that long sequences of reactions can organize spontaneously---and every reason to believe that they cannot."

Metabolism First models have no purely physicodynamically steered pathway from self-ordered or random molecular assemblies toward the Aristotelian "final" state of true organization and metabolic pragmatic benefit. In fact, "efficient" causation of formal function and organization cannot even be explained from physicodynamics alone. Molecular assemblies can spontaneously self-order. But they do not self-organize into bona fide function-valuing and function-pursuing systems. Thus it is not surprising that only computer models exist of composomal evolution with no empirical realizations of spontaneous metabolism arising within a truly "natural" nature. Computer models almost always have smuggled-in hidden experimenter teleology to make the computer model work for the investigator. The supposed evolution model invariably is found to exhibit "directed evolution," which is NO evolution at all. "Directed evolution" is a self-contradiction. If the supposed evolution is directed, it is not evolutionary. If it is evolutionary, it cannot be directed. The whole point of evolutionary theory is to obviate the necessity of any artificial steering. So-called "natural process" must be free of any hint of teleology. Simply renaming "teleology" to the more naturalistic-sounding "teleonomy" doesn't help. If the process is directed or engineered in any way, it is not "natural." No more "natural process" mechanism is provided in the literature for "teleonomy" than for "teleology."

Non-genetic Metabolism First models require constantly re-inventing the wheel from scratch with each new generation. No means exist of preserving and propagating any already hard-won organizational and pragmatic advances. But, no basis was ever provided for any *initial* metabolic organizational success, either. It was just blindly believed because such faith was required for any materialistic model to get off the ground. We conveniently imagine spontaneous self-organization of formal metabolic integration and success in the first place. From there it is an easy matter to further imagine a relentless uphill refinement of metabolism. Optimization is firmly believed to occur in the complete absence of any goals or purposeful steering. Finally, the process is of course proclaimed to be "inevitable," all in the name of science! Anyone who might raise an eyebrow of educated skepticism about this scenario is immediately labeled a "vitalist" or "religionist." No possibility of practicing quality skeptical science is entertained.

The inability of mere "chance and necessity" to optimize, and the lack of evolvability of self-sustaining autocatalytic networks presents serious, if not fatal, problems for all protometabolism-first models [252].

5. Self-replicative, auto-catalytic, informational models.

Protometabolism First models depend upon physicodynamic coupling of circular constraints. The presumed constancy of these integrated cycles is envisioned to eliminate the need for both enzymes and the replication of genetic instructions. From Protometabolism First models we move to self-replicative, auto-catalytic, informational models. As we consider these models, it is wise to keep in mind what Kovac et al warned: "A system of self-replication has to consist of both replicators and replicants." [253]

5.1 RNA World

RNA World theories initially envisioned free-standing RNA oligomers folding into ribozymes that spontaneously acquire both catalytic and information-retaining functions. Primordial ribozymes are best thought of as single strands of RNA folded back onto themselves with a considerable degree of base-pairing stems and loops—bulge, internal, hairpin, multi-loops with branches, etc. This folding is determined by the sequencing of ribonucleotides. Ribozyme sequencing does not provide DNA-like, coded, codonic prescription of amino acid sequencing. For an RNA World to get off the ground, ribonucleotide sequencing must be such that when the single strand folds back onto itself, base-pairing causes a secondary structure to form that will fold into a tertiary structure that is self-replicative.

RNA chemists quickly encountered many serious road bocks to any natural RNA World model. Ribonucleotide oligermization did not occur spontaneously, especially in aqueous environments. Ribose was difficult to form and was unstable. An RNA World model "assumes a large prebiotic source of D-ribose. The problem of obtaining a homochiral population of pure D-ribose is daunting. But even prior to that dilemma are problems with any ribose. The generally accepted prebiotic synthesis of ribose, the formose reaction, yields numerous sugars without any selectivity. Even if there were a selective synthesis specifically of ribose, there is still the problem of stability. Sugars are known to be unstable in strong acid or base, . . ." [254]. "These results suggest that the backbone of the first genetic material could not have contained ribose or other sugars because of their instability." [254].

Pyrimidine ribonucleotides have been synthetized in the presence of phosphate using a precursor of both ribose and nucleobases [255, 256]. But a plausible prebiotic synthesis of purines is still lacking. Ribonucleotides are difficult to activate. No basis for functional sequencing existed. Cytosine was extremely difficult to make, even by highly intelligent chemists [257, 258]. Even Gerald Joyce and Leslie Orgel became skeptical of the RNA World [259, pg. 213]. Says Orgel,

> I believe that it is very unlikely that RNA did arise prebiotically on the primitive earth. Ribonucleotides are such complicated molecules that they are not likely to have formed in sufficient amounts and with sufficient purity on the primitive earth to permit the formation of even the simplest self-replicating RNA molecule. [260 pg. 213]

As Fry points out [141], even as recently as in the 3rd Edition of *The RNA World* [148], Joyce and Orgel still refer to the RNA World model as "the prebiotic chemist's nightmare."

Nevertheless, adherence to the RNA World [261-264] and early information models still prevails in many circles [265-279]. It has become impossible to deny the essential role of informational biopolymers. All Protometabolism First models suffer primarily from a lack of heritable mutability and retained progress. Open-ended evolution (OEE) requires separation of genotypic and phenotypic functions [242, 280, 281]. Even early Information First models are all plagued with a need for molecular evolution to improve the genetic material symbol system's functional token sequencing. Yet no basis for selection for phenotypic function exists at the point of genetic polymerization [147, 282].

A self-replicative ribozyme has been a lot harder to design and engineer than RNA chemists originally supposed. Some advancements in ribozyme engineering have occurred, however [283]. But artificially engineered self-replicative ribozymes usually catalyze only self-replication of that one ribozyme [284]. Paul and Joyce successfully engineered a self-replicating ligase ribozyme [285, 286]. The authors explain, "A self-replicating molecule directs the covalent assembly of component molecules to form a product that is of identical composition to the parent." Note that the "component molecules" are just presupposed rather than explained. "When the newly formed product also is able to direct the assembly of product molecules, the self-replicating system can be termed autocatalytic." Paul and Joyce designed "a self-replicating system based on a ribozyme that catalyzes the assembly of additional copies of itself through an RNA-catalyzed RNA ligation reaction. The R3C ligase ribozyme was redesigned so that it would ligate two substrates to generate an exact copy of itself, which then would behave in a similar manner."[285] The problem with this ribozyme for life-origin specialists is its lack of prebiotic plausibility. Would it have formed spontaneously under harsh conditions with limited component resources, with no steering and regulatory controls, and no enzyme catalysis? As admitted by the authors, a "rational design approach" was used to create this sophisticated molecule. This hardly provides evidence for a stochastic ensemble arising in a prebiotic world with all of the attributes of this ribozyme. In addition, the authors admit, "Exponential growth was limited, however, because newly formed ribozyme molecules had greater difficulty forming a productive complex with the two substrates. Further optimization of the system may lead to the sustained exponential growth of ribozymes that undergo self-replication." [285]. Notice that only "further optimization" "may" lead to sustained exponential growth of this ribozyme. What would be the naturalistic impetus for pursuing functional optimization? The environment doesn't care whether anything functions. And if further optimization did somehow continue, most all resources in the environment would be consumed in the massive self-replication of this one ribozyme. What resources would be left for all of the hundreds, if not thousands, of other needed ribozymes to form? Ribozymes are very poor catalysts compared to proteins. Any protometabolism would require a large number of ribozymes in the same place and time. What would organize all these reactions into a productive protometabolic effort? What would prevent all of the many cross-reactions? [287].

Ma and Yu suggested that two RNA synthesis ribozymes may be integrated into one RNA molecule, as two functional domains which could catalyze the copy of each other. Thus the RNA molecule could self-replicate and be referred to as "intra-molecular replicase" [288]. Ribozymes that function as RNA polymerases have been humanly engineered [283, 285, 287]. But no catalytic polymerases have been found among natural ribozymes, and no protometabolism is organized by self-catalyzed, self-replicative ribozymes.

Anet [144] differs with Shapiro, Dyson, Kauffman, de Duve, Wachtershauser, Morowitz, Deamer, Lancet, Lindhal, Guamaeres, and Russell, all of whom promote models of early spontaneous protometabolism. Anet likes instead Nicholas Hud's molecular midwives, intercalations and base-stacking as a source of functional nucleic acid molecules [289-293]. But it is not at all clear how intercalations and base-stacking arranges varying monomers into prescriptive strings using a linear digital symbol system. The model purports to provide a source of new untemplated information, but mere Shannon uncertainty is erroneously equated with "information." Certainly no basis is provided for the generation of Prescriptive Information (PI). Even Shannon uncertainty would be compromised by a tendency toward self-ordering.

More recent RNA World models all include vesicle containment [205, 294-296]. Yarus and Janas found that membrane-binding RNAs coat artificial phospholipid membranes relatively uniformly, except for a frequent tendency to concentrate at bends and membrane junctions. Yarus calls RNA protocells "ribocytes" [297, 298].

The biggest problem with bilipid vesicle pseudo-membranes is their lack of highly specific active transport tunnels and mechanisms to control the "ingestion" of needed metabolites, the rejection of deleterious molecules from entry into the protocell, and the excretion of toxic waste products from the vesicle. Some slight progress has been made with osmotic factors which can actually promote vesicle division [253, 299, 300]. But Kovac et al remind us that "logical possibility does not equal thermodynamic feasibility." [253].

No natural basis exists for optimization of ribozymes' primary structure, either, so as to yield pragmatic folds and three-dimensional shapes. Ribozymes are in a sense nothing more than combinatorial composomes. There is no reason a composome can't exist as a folded linear digital biopolymer. Prior to folding, ribozymes are combinatorial strings of "alphabetical characters" or token sequences. The fact that they start out as linearly arranged prior to folding does not disqualify them from being composomes. The alphabet consists of four possible "letter" or token options. Only one of four nucleotide options can be selected at each locus in the string. In the absence of selection in a materialistic world, the monomeric component would either be 1) random, 2) ordered to some degree by physicochemical law-like tendencies, or 3) ordered to some degree by unequal availability of each base in a given environment. Some bases like cytosine would have been extremely rare in a prebiotic environment. So any spontaneously forming composomal string of ribonucleotides would be considerably ordered by a greater abundance of some nucleotide options over others. This would greatly reduce the Shannon uncertainty and information potential of any string formation. If there were no physicodynamic preferences for any one base over another from the base-4 alphabet, and all nucleotides were equally available in the prebiotic environment, each potential selection at each locus would represent two bits of Shannon uncertainty.

No folding takes place until the ribonucleotide string is already polymerized with rigidly formed 3'5' phosphodiester bonds. The sequencing determines via thermodynamics the particular secondary and tertiary folding that eventually produces a functional ribozyme.

Natural selection is only eliminative, not constructive [239, 240]. Empirical evidence and prediction fulfillment are both sorely lacking in support of the contention that random variation (noise) can generate good new ideas, implementations, designs or engineering from which the environment could "select." This is true of RNA stochastic ensembles and any early RNA analogs forming in a pre-RNA world. It is all the more true of the derivation of current life's universal linear digital symbol system. These tokens represent and prescribe future primary structure (sequencing), folding, secondary and tertiary structure (three-dimensional catalysts, machines and nanocomputers), and the eventual molecular interactions between them (e.g., protein-protein interactions).

Natural selection does nothing more than *eliminate* second-rate phenotypic organisms arising from inferior programming [147]. Evolution contributes nothing to new programming [15, 250]. Duplication plus variation (random noise) has never been shown to generate a single new nontrivial program. A mechanism for programming potential new function using a linear digital material symbol system exists nowhere in the environmental selection paradigm. Natural selection has never been observed to prescribe a single new superior genome or metabolome from mere noise "variation." Instead of a natural process mechanism for spontaneous programming of genetic and genomic Prescriptive Information (PI), blind belief in the amazing, mystical powers of "variation" of duplications is propagated. Optimism still exists, however, that one day the prebiotic self-organization of an RNA World will be worked out [45, 63, 301-305]. But the RNA World remains to this day entirely imaginative [306]. Even if it ever existed, Blomberg, head of NASA's Astrobiology program at the time, admitted, "The RNA world may have been a great achievement, but it could hardly provide, in a direct way, the functions that were necessary for the final steps to the first organisms." [233]

5.2 Pre-RNA World and RNA World analogs

The Pre-RNA World model [133, 254, 307-313] arose out of necessity because spontaneous RNA chemistry in a prebiotic environment proved to be unrealistic. "Ribose is difficult to form selectively, and the addition of nucleobases to ribose is inefficient in the case of purines and does not occur at all in the case of the canonical pyrimidines."[256] Thus pre-RNA World models began to arise in which RNA analogs, alternative RNA-like molecules with backbones different from ribose-phosphate, and possibly even peptides, serve primarily as catalysts. The backbone of RNA analogs is made up phosphate-bonded non-ribose sugars [69, 71].

Early on, Orgel and Joyce realized the seriousness of problems with initial RNA chemistry in a prebiotic environment [314, 315]. They also investigated simpler nucleic acid polymers. Examples of specific RNA analogs are (L)-a-threofuranosyl oligonucleotides and TNAs [316]. These molecules have threose rather than ribose in their sugar-phosphate backbones and yet retain many of the properties of RNA including the ability to pair up in double helices. Anastasi, et al reviewed recent experimental work on the assembly of potential RNA precursors [303]. Powner, Gerland and Sutherland investigated the synthesis of activated pyrimidine ribonucleotides under plausible prebiotic conditions [256]. House discussed possible roles for dihydrouracils in the pre-RNA world [312]. Matray and Gryaznov investigated the synthesis and properties of RNA analogs-oligoribonucleotide N3'-->P5' phosphoramidates. [317] Kolb found many of the properties of urazole to make it a good potential precursor to uracil and guanazole a potential precursor to cytosine in a pre-RNA world [313].

Nielson investigated peptide nucleic acids (PNAs) using an amide rather than ribose backbone [318, 319]. Diederichsen investigated alternating D- and L- alanyl peptide nucleic acids (ANAs) [320].

Iris Fry [141] describes models such as Cairns-Smith's and de Duve's as "Preparatory metabolism" models. Both Cairns-Smith and de Duve find the prebiotic emergence of RNA implausible. But they both believe correctly that a genetic polymer is essential for open-ended evolution (OEE). Says Howard Pattee, "Separate description and construction components are necessary for complex systems that can adapt and evolve." [321, pg 261]. Fry argues that other models should also be considered "preparatory" rather than Metabolism First [141]. As usual, no explanation is provided as to how inanimate nature would go about "preparing" for eventual metabolic success. Failure to explain how so-called "natural process" physicodynamics could anticipate and pursue formal function impedes virtually all models of life origin, whether Protometabolic First or Information/Replication First. Appealing to a preRNA World does not solve this problem either. No motive or basis exists for selection of cooperative organization over disorganization. Only investigator minds imagine inanimate nature incorporating urazole and its ribosides, peptide RNA analogs, group II introns and other self-replicative ribozymes into auto-catalytic schemes. Nature does not scheme. All code-origin models are plagued by the same lack of environmental pursuit of pragmatism of any kind. Inanimate nature does not value or pursue "usefulness." Unaided physicodynamic constraints and laws do not generate controls that steer interactions toward formal function.

Even Pre-RNA World chemistry proved to be far more unrealistic than originally envisioned [152, 177, 178, 257, 258, 322-324]. Leslie Orgel was the premier life-origin investigator of the late twentieth and early twenty-first century. Orgel could find no basis for a Protometabolic World of self-organization:

> In my opinion, there is no basis in known chemistry for the belief that long sequences of reactions can organize spontaneously---and every reason to believe that they cannot. [155]

Thus Orgel had little choice but to hypothesize a simpler RNA analog scenario that could eventually evolve into an RNA World. He believed there had to have been alternate polymers, perhaps RNA analogs, in a preRNA World. But his optimism only seemed to wane near the end of his illustrious career. And opponents of the RNA World are no more impressed with the plausibility of useful RNA analog formation than that of RNA. It has been argued by opponents of the preRNA and RNA World that the spontaneous formation and self-organization of RNA analogs such as TNA, PNA, ANA and urazole in a prebiotic environment is not significantly more plausible than the RNA World model [150, 178, 303, 325]. In addition, it has not been established that any of these alternative backbones could provide the extensive Shannon uncertainty and Prescriptive Information (PI) potential provided by current life nucleic acids [15, 16, 18, 318, 326]. Nevertheless, adherence to the Pre-RNA World model remains strong in many circles [133, 175, 264, 311, 313, 327-331].

6. Early photosynthetic models

The earliest photosynthetic cells are thought to have been almost certainly anoxygenic. Oxygenic photosynthesis and the subsequent rise of atmospheric oxygen supposedly occurred around 2.4 billion years ago [332]. Complex biosynthetic pathways of carbon fixation would have been needed involving new photosynthetic cofactors, electron carriers, and pigments [141]. Endosymbiosis is thought to have played a role [333-337]. Schopf states,

> Fossil evidence of photosynthesis, documented in Precambrian sediments by microbially laminated stromatolites, cyanobacterial microscopic fossils, and carbon isotopic data consistent with the presence of Rubisco-mediated CO_2-fixation, extends from the present to ~3,500 million years ago. Such

> data, however, do not resolve time of origin of O2-producing photoautotrophy from its anoxygenic, bacterial, evolutionary precursor. Though it is well established that Earth's ecosystem has been based on autotrophy since its very early stages, the time of origin of oxygenic photosynthesis, more than 2,450 million years ago, has yet to be established.[338]

Grenfell et al [339] point out that the Sun was originally shining 20-25% less brightly than today. They maintain that earth would have been an ice ball without greenhouse-like conditions to warm the atmosphere. They thus conclude that greenhouse gases must have been present on early Earth to warm the planet. Argue Grenfell et al.:

> Evidence from the geological record indicates an abundance of the greenhouse gas CO(2). CH(4) was probably present as well; and, in this regard, methanogenic bacteria, which belong to a diverse group of anaerobic prokaryotes that ferment CO(2) plus H(2) to CH(4), may have contributed to modification of the early atmosphere. Molecular oxygen was not present, as is indicated by the study of rocks from that era, which contain iron carbonate rather than iron oxide. [339]

Mulkidjanian and Galperin believe that life started within photosynthesizing ZnS compartments [61, 340]. They contend that life could have evolved under the conditions of elevated levels of Zn2+ ions, byproducts of the ZnS-mediated photosynthesis. UV-rich solar radiation set the stage for a Zinc World. They envision precipitated zinc sulfide (ZnS) providing photosynthetically active porous edifices similar to what is found near deep-sea hydrothermal vents. They cite as evidence the roles of Zn2+ ions and possibly manganese sulfide in modern organisms, particularly in RNA and protein structures:

> Under the high pressure of the primeval, carbon dioxide-dominated atmosphere ZnS could precipitate at the surface of the first continents, within reach of solar light. It is suggested that the ZnS surfaces (1) used the solar radiation to drive carbon dioxide reduction, yielding the building blocks for the first biopolymers, (2) served as templates for the synthesis of longer biopolymers from simpler building blocks, and (3) prevented the first biopolymers from photo-dissociation, by absorbing from them the excess radiation. In addition, the UV light may have favoured the selective enrichment of photostable, RNA-like polymers. [61]

Baltscheffsky investigated stepwise molecular evolution of bacterial photosynthetic energy conversion [98]. Various other embryonic Photosynthetic models have been proposed [341-363]. All of them require considerable organization and pathway integration to be able to harness, transduce, store, and call up when needed energy in a usable form. Even if this organization were to spontaneously generate, innumerable mechanisms would have to simultaneously arise that could accomplish something creative using the transduced stored energy. Even the simplest protometabolism would had to have been masterfully organized to meet homeostatic metabolic needs necessary for life.

7. Code-origin Models

Much work has been done trying to elucidate how genetic code arose naturalistically [159, 184-186, 188, 298, 364-391]. Di Giulio, Wong, Yarus, Schimmel and Guimaraes have probably been the leading code-origin theorists. The conceptually ideal nature of genetic code [392-398], however, is difficult to explain working only with after-the-fact differential survival and reproduction of the best already-programmed organisms. Genetic programming must not only preceed, but prescribe the existence of any organism. This is not just true for the fittest organisms, but for any living organism. No basis exists within the metaphysical belief system of naturalism for selection of coded instructions prior to the realization of phenotypic superiority [147].

The Code Co-evolution Model of code origin was first proposed by Wong [387, 388] and updated 30 years later [184]. Wong's model suggested that genetic code co-evolved with biosynthetic pathways of AA. "Amino acid biosynthesis and hydrophobicity were important factors in shaping the genetic code, as the primitive code co-evolved with new varieties of amino acids generated by the expanding pathways of biosynthesis." [390] Ronneberg concluded that Wong's code co-evolution theory cannot adequately explain the structure of the genetic code [379]. Wong countered with a defense of his model [389, 390]. Others have entertained variations of Wong's approach that differ in important respects [368, 399] [159, 186, 400]. Lahav suggested a unique co-evolution of enzymes and ribozymes [128]. Guimaraes has published probably the most recently updated code origin model [159, 186, 400-402].

Yockey [403, pg 4-5] shows that the Central Dogma—the one-way-only flow of Prescriptive Information (PI) from the codon alphabet of 64 (or 61) block codes to the amino acid alphabet of 20—is a mathematical property arising from the redundancy (poorly termed "degeneracy") of the genetic code, not just a physicodynamic property of nucleic acids and amino acids per se. It is a mathematical impossibility for PI to flow in the opposite direction as is required by many code-origin models that propose slow growth of the code table over long periods of time. The PI in the redundant codon table had to have been there first. When told only that a pair of tossed die generated a total of 7, there is no way to recover the information of whether the two die showed a 1 and 6, 2 and 5, 3 and 4, 4 and 3, 5 and 2, or 6 and 1. Detailed information is permanently lost in the totaling of the two die. One cannot determine from knowing only the amino acid, without the codon table, which of the 1, 2, 3, 4 or 6 codons that prescribed that amino acid. Such information is crucial with many genetic diseases and with cancer mutations.

The genetic code is ideally arranged to minimize the effect of genetic noise in the Shannon channel [392, 395-397, 403, pg 104-107]. This optimal coding requires the additional information that would not have existed if the code were slowly constructed through evolution from amino acids to codons. Naturalistic code-origin models seem to consistently ignore this reality. The devil is in the details of which codon prescribed which amino acid in each unique situation. Some genetic diseases are caused by a point mutation of one of the three nucleotides in a codon even though the amino acid prescribed is unaffected!

8. Composome, Chemoton and RNA evolution would have been extremely limited.

Composomes, chemotons and ribozymes do NOT have separate description and construction components. The two components are one in the same. Sequencing directly determines structure and catalytic ability. This creates real problems for any abiogenic evolutionary model that hopes to maintain its optimized self-replicative sequencing, folds, structure and function while simultaneously mutating to a different sequence that is optimized for some other metabolic function other than self-replication. When the "genome" changes, the phenotypic "organism" itself changes in an immediate and direct way. The odds of the primary structure (sequencing) being the same for both optimized self-replicative function and a separate sophisticated metabolic function are miniscule at best. Any move towards an improved new metabolic function will simultaneously compromise the ribozyme's or protocell's hoped-for (never once observed) spontaneous self-replicative function.

Another unanswered question for RNA World advocates is, "What correlation exists between highly-optimized, error-free self-replication of sequences, and highly optimized metabolic function? How could one sequence simultaneously be optimized for both important functions? The reason ribozymes receive so much attention in life-origin science is their ability to simultaneously serve as catalysts and information-retaining linear digital strings. Their catalytic function and information retention depends upon their particular sequence of ribonucleotides. But in ribozymes, the exact same sequence that would be optimized for catalysis of self-replication is also the "heritable" sequence. For the heritable sequence to mutate necessarily involves the deoptimization of the already optimized catalytic sequence and function. In ribozymes the two sequences are one in the same with shared functions. Progress in one area compromises progress in another. No selection pressure for either function takes place upon polymerization of ribonucleotides with rigid bonds. The environment has no goal or desire to optimize either function, let alone organize both together into an integrated homeostatic metabolic scheme with accurate self-replication. The Functional Information (FI) [10-14] found in ribozyme's primary-structure sequencing would be largely limited to the sequencing that prescribes folding into that particular ribozyme. The ribonucleotide sequencing would first and foremost have to be optimized for self-replication. Simultaneous optimization of this same sequence for contribution to any holistic metabolic scheme would be almost impossible. Even in a protocell, hundreds if not thousands of metabolic functions other than the self-replication function would be needed to organize anything close to life.

Recently even Szathmáry's group has argued effectively that composomes cannot evolve [252]. Compositional "genomes" (assemblies of varying molecular species) are thought by some to be able to propagate evolvable chemical and structural information [162-165]. Szathmary's group calls these macromolecular aggregates "ensemble replicators." They are thought to be able to replicate three-dimensional structures that would support the idea of composome evolution. Vasas, Szathmáry and Santos found in a 2010 PNAS paper entitled "Lack of evolvability in self-sustaining autocatalytic networks constrains metabolism-first scenarios for the origin of life,"

> In sharp contrast with template-dependent replication dynamics, we demonstrate here that replication of compositional information is so inaccurate that fitter compositional genomes cannot be maintained by selection and, therefore, the system lacks evolvability (i.e., it cannot substantially depart from the asymptotic steady-state solution already built-in in the dynamical equations). We conclude that this fundamental limitation of ensemble replicators cautions against metabolism-first theories of the origin of life, although ancient metabolic systems could have provided a stable habitat within which polymer replicators later evolved. [252, pg. 1470]

Thus three-dimensional composomes cannot evolve. Composomes lack the dichotomization of genome from phenotype needed for evolution to occur

[404-408]. A buffer zone must exist between genome and phenotype to allow for the simultaneous existence of genetic drift and a relatively stable phenotypic life simultaneously.

Any mutation of an oligoribonucleotide sequence in the RNA World would tend to produce a much more immediate phenotypic change than seen with current organism DNA mutations. And that mutation would be almost certainly be far more deleterious to the already accidentally and barely achieved self-replicative function. Any movement towards a beneficial new metabolic function would be de-optimizing to the self-replicative function.

But even before that, no reason or mechanism was ever provided for how the sequencing was achieved that would produce self-replicative function. How did an inanimate nature pursue optimization of self-replicative sequencing in the first place?

The primary structure (the sequencing) is "written in stone" with rigid 3'5' phosphodiester bonds before any prescriptive function could be realized. And the environment has no desire or preference for replication over non-replication. No basis exists for selection for potential self-replicative function. Either a stochastic ensemble against all odds just happens to form that has self-replicative catalytic ability, or it doesn't. The finest RNA chemists in the world have had an extremely difficult time purposefully engineering ribozymes to auto-catalyze [62, 294]. The statistical prohibitiveness of a stochastic ensemble achieving this function cannot be circumvented in the absence of a selection mechanism or experimenter engineering.

But suppose by some miracle a primary structure stochastic ensemble formed spontaneously which catalyzed self-replication. Any mutation would not only not pursue a new function, it would compromise and de-optimize the already-existing self-replicative function. Self-replication would be sacrificed at the expense of selection for almost any other metabolic function.

Virtually all Protometabolism First and RNA World models lack organizational motive, ability and naturalistic explanation. No reason is provided from these purely physicodynamic interactions as to why inanimate nature would pursue the goal of formal integration and function.

The self-replicative optimization was itself already problematic because it would consume all resources in the mass production of the same self-replicator oligoribonucleotide sequence. Selfish auto-catalytic self-replications would completely exhaust the phase space resources so that none of the other scores (if not hundreds) of essential protometabolic contributors could have formed at the same place and time.

The vast combinatorial and structural phase space needed for other spontaneous stochastic evolutions of functions would be completely consumed before any "search" could begin. But of course *there is no search*. Environments don't search for anything. Evolution has no goal, especially not prebiotic evolution (for which there is zero observational evidence, or even plausible rational support). Function first has to exist for it to be secondarily preferred. The environment has no preference for function over non-function. Evolution is nothing more than elimination of lesser quality already-living organisms [239, 240].

The difficulty with which most of these needed organic contributors are chemically produced, their short-lived stability in most prebiotic environments, the innumerable cross reactions that occur, the exclusivity of left-handed amino acids and right-handed sugars with no straight forward means of homochiral production, are just a few of the many problems with Metabolism First models.

Rocha describes natural selection as a "statistical bias on the rates of reproduction of populations of individuals," but acknowledges that "this is as far as (statistical) dynamics can take us to describe this process" [243, pg. 11]. No reason is provided as to why a statistical bias might exist that would favor formal organization. No contrast is drawn between mere physicodynamic constraints and formal controls, between fixed laws and the arbitrary formal rules needed to generate formal pragmatic systems. Choices, not constraints—and rules, not laws—are needed to organize any formal utility. Until science fully acknowledges this objective reality, progress in life-origin studies will continue to encounter immovable road blocks.

Literal genetic algorithms, not figurative ones, prescribe and control life. Nucleotides function in an objective, not just a subjective human symbolic capacity. The particular symbol selection at each decision node of nucleotide polymerization is isolated from physicodynamic causation by a *dynamic discontinuity* [242, 243, 409]. The nonphysical instructions are physically instantiated into material symbol systems using physical symbol vehicles. The programming is fundamentally formal, not physical. "Semantic/semiotic/bioengineering function requires dynamically inert, resortable, physical symbol vehicles that *represent* time-independent, non-dynamic "meaning (e.g., codons)." [9] Physicodynamics cannot participate in representationalism. The latter is purely formal, not physical. No empirical or rational basis exists for granting to physics or chemistry such non-dynamic capabilities of functional sequencing. Neither chance nor necessity (fixed law) can program configurable switches to integrate circuits, write coded instructions, or organize formal utility.

The bottom line is that no naturalistic basis exists for optimization of ribozymes' primary structure. The environment is blind to isolated function.

The notion of molecular evolution has nothing to work with as a basis for selection other than self-replication. But self-replicative function is very different from metabolic function. No reason exists for a sequence optimized for self-replication to also be simultaneously optimized for hundreds of other metabolic catalytic functions needed for a protometabolism to organize. Even if all the individual ribozyme catalytic metabolic functions somehow got optimized at the same time as the self-replicative function, nothing would exist in a prebiotic environment to organize a living system. We would have nothing but a vesicle or micelle that was a "bag of ribozymes." If a "bag of enzymes" does not constitute a living cell, a "bag of ribozymes" certainly wouldn't. The capabilities of ribozymes are extremely limited with only minimally effective rate constants and sophistication compared to proteins.

A recent paper in The Quarterly Review of Biology shows that almost all of the very few supposedly "helpful" adaptive mutations involve either the loss or the modification of existing function [410]. It was already well-known that most mutations are outrightly deleterious. What is significant about this study is that it shows even the rare supposedly "beneficial" mutations degrade the genome. Genetic research seems to be consistently showing information decay from mutations, not improvement in the quality of sophisticated prescription [279].

Systems biology [411-417] has risen to the forefront as investigators have discovered ever more amazing degrees of metabolic organization and control. No basis exists for organization or control in a chance-and-necessity-only materialistic worldview. This problem is just as real, if not more acute, in primordial systems biology [418, 419].

Biosemiosis—communication within and between cells, is now firmly entrenched in our understanding of life. This includes the molecular biological level [420-424] [15, 326, 406-408, 425-449]. Communication of meaningful/functional messages is impossible without arbitrary selection of symbols or programming choices.

9. Panspermia

It has never been clear to this author why any astrobiologist would think that panspermia would help solve the life-origin problem on earth. The age of the cosmos is only three times that of the earth. How could the statistical prohibitiveness of spontaneous generation of life on earth possibly be helped significantly by multiplying that ridiculously low probability by a mere factor of 3?

Problems exist with the notion of panspermia from other solar systems. For a rock or ET spacecraft to overcome the gravity of an average source planet, it would need an escape velocity equivalent to around 16,000 mph. An asteroid hit would be required. In addition, any rock coming from around 40 light years away would take around a million years to get here. DNA would be destroyed by radiation even in spores. The temperature in space is nearly absolute zero. No nutrients or oxygen would exist during the trip. Entry into the earth's atmosphere would cook the rock. The impact of whatever superheated meteriorite was left wouldn't help much.

Recently Hoover [450] has claimed to have found microfossils in carbonaceous chondritic meteriorites. This is not the first time he has made this claim [451]. The astrobiological scientific community remains skeptical. Carbonaceous chondrites are meteorites that are thought to have formed in the early solar system. The metals in these meteorites are found as silicates, oxides and sulfides rather than in their free form. They can also contain considerable amounts of carbon and organic compounds, especially if they have never been heated to more than 50 degrees C. They are important because they seem to have formed in oxygen-rich environments, and many of them contain minerals that appear to have been exposed to water. Different kinds of carbonaceous chondrites have formed depending upon the planet and region of the early solar system from which they originated.

Hoover attempted to rule out contamination of his samples, but Brasier argues: "In terms of syngenicity, these samples have been sitting around in laboratories for between 205 and 73 years. It is well known that microbial contaminants can penetrate deep into such rocks, even during storage." [452]

Morphology is not very reliable in identifying such microfossils. In addition to filamentous bacteria varying a great deal in morphology, electron microscopy introduces many artifacts. Brasier [452] argues that such filamentous structures can form abiotically as ambient inclusion trails (AITs). These AITs greatly resemble cyanobacterial microfossils, and have compositions similar to those described by Hoover that are enriched in carbon, sulphur and silica-rich minerals in their filament margins. NASA itself is cautious about supporting Hoover's claims. Carbon enrichment is a major component of all the meteorites that Hoover studied. The evidence for life in Hoover's samples is probably no better than that for the Martian meteorite ALH840001.

After over 40 years of trying to detect an intelligent message from outer space, the Search for Extraterrestrial Intelligence (SETI) has come up empty handed.

For a discussion of the metaphysical notion of multiverse, see Chapter 11, Section 5.

10. Conclusions:

No evasion of the facts is any longer possible. The reality of Prescriptive Information's control of life is undeniable [281, 453-460]. The many recently discovered additional layers and dimensions of PI only make explaining the derivation of PI all the more daunting a task. The roles of micro RNAs, peptides and small polypeptides, in addition to regulatory proteins, have proven linear digital regulation of function within bona fide formal molecular biological systems. Even linear digital controls of development are now quite apparent.

Any kind of organization requires programming for potential function, arrangement of components, control and regulation of events prior to the existence of any pursued biofunction. But of course no prebiotic chemical system is capable of pursuing eventual function.

Eigen/Schuster hypercycle models and Ganti chemoton/stoichiometric models excite naturalistic explanatory hope. The reason is that they provide a vivid illusion of control and self-organization. In reality, no such formal control or organization is provided by mere constraints. Both positive and negative feedback circular constraints occur that affect reaction products deterministically. But no formally integrative and fine-tuned system of regulation and sophisticated function arises from circular physicodynamic constraints.

Any evolution of improved metabolic function would compromise its self-replicative function, as the two would almost always have two widely different optimized structures. Similarly, the molecular evolution of any new metabolically functional structure would compromise its self-replicative structure. Ribozymes, like any other composome, cannot evolve much without progressive loss of their already-optimized auto-catalytic tertiary structure. Not even the auto-catalytic function of ribozymes has ever been observed to occur without extensive human engineering. As mentioned above, so-called "directed evolution" is a nonsense term that violates the evolutionary requirement of being non-teleological.

In Leslie Orgel's last paper, entitled "The implausibility of metabolic cycles on the prebiotic earth" [153], Orgel emphasized that ". . . , solutions offered by supporters of geneticist or metabolist scenarios that are dependent on "if pigs could fly" hypothetical chemistry are unlikely to help."

Nobel laureate biologist George Wald stated without hesitancy that "one has only to contemplate the magnitude of [the] task to concede that the spontaneous generation of a living organism is impossible." [461]

References

1. Miller, S.L. 1953, A production of amino acids under possible primitive earth conditions, Science 117, (3046) 528-529.
2. Morowitz, H.J. 1999, The theory of biochemical organization, metabolic pathways, and evolution, Complexity, 4, 39-53.
3. Parker, E.T.; Cleaves, H.J.; Dworkin, J.P.; Glavin, D.P.; Callahan, M.; Aubrey, A.; Lazcano, A.; Bada, J.L. 2011, Primordial synthesis of amines and amino acids in a 1958 Miller H2S-rich spark discharge experiment, Proceedings of the National Academy of Sciences.
4. Cairns-Smith, A.G. 1990, *Seven Clues to the Origin of Life*. Canto ed., Cambridge University Press: Cambridge.
5. Cairns-Smith, A.G. 1966, The origin of life and the nature of the primitive gene, J Theor Biol, 10, (1) 53-88.
6. Cairns-Smith, A.G. 1977, Takeover mechanisms and early biochemical evolution, Biosystems, 9, (2-3) 105-109.
7. Cairns-Smith, A.G.; Ingram, P.; Walker, G.L. 1972, Formose production by minerals: possible relevance to the origin of life, J Theor Biol, 35, (3) 601-604.
8. Cairns-Smith, A.G.; Walker, G.L. 1974, Primitive metabolism, Curr Mod Biol, 5, (4) 173-186.
9. Abel, D.L.; Trevors, J.T. 2005, Three subsets of sequence complexity and their relevance to biopolymeric information., Theoretical Biology and Medical Modeling, 2, 29 Open access at http://www.tbiomed.com/content/2/1/29.
10. Teller, C.; Willner, I. 2010, Functional nucleic acid nanostructures and DNA machines, Curr Opin Biotechnol, 21, (4) 376-91.
11. McIntosh, A.C. 2010, Information And Entropy – Top-down Or Bottom-up Development In Living Systems?, International Journal of Design & Nature and Ecodynamics, 4, (4) 351-385.
12. Hazen, R.M.; Griffin, P.L.; Carothers, J.M.; Szostak, J.W. 2007, Functional information and the emergence of biocomplexity, Proc Natl Acad Sci U S A, 104 Suppl 1, 8574-81.
13. Carothers, J.M.; Oestreich, S.C.; Davis, J.H.; Szostak, J.W. 2004, Informational complexity and functional activity of RNA structures, J Am Chem Soc, 126, (16) 5130-7.
14. Szostak, J.W. 2003, Functional information: Molecular messages, Nature, 423, (6941) 689.
15. Abel, D.L. 2009, The biosemiosis of prescriptive information, Semiotica, 2009, (174) 1-19.
16. Abel, D.L. Prescriptive Information (PI) [Scirus Topic Page]. http://www.scitopics.com/Prescriptive_Information_PI.html (Last accessed September, 2011).
17. Abel, D.L. 2011, Moving 'far from equilibrium' in a prebitoic environment: The role of Maxwell's Demon in life origin. In *Genesis - In the Beginning: Precursors of Life, Chemical Models and Early Biological Evolution* Seckbach, J.Gordon, R., Eds. Springer: Dordrecht.
18. Abel, D.L.; Trevors, J.T. 2007, More than Metaphor: Genomes are Objective Sign Systems. In *BioSemiotic Research Trends*, Barbieri, M., Ed. Nova Science Publishers: New York, pp 1-15
19. Mann, S.; Perry, C.C. 1986, Structural aspects of biogenic silica. In *Silicon Biochemistry; CIBA Foundation Symposium 121*, Joyn Wiley & Sons: Sussex, UK, pp 40-58.
20. Trevors, J.T. 1997, Bacterial evolution and silicon, Antonie Van Leeuwenhoek, 71, (3) 271-276.
21. Williams, R.J.P. 1986, Introduction to silicon chemistry and biochemistry. In *Silicon Biochemistry: CIBA Foundation Symposium 121*, John Wiley & Sons: Sussex, UK, pp 24-39.
22. Vysotskii, Z.Z.; Danilov, V.I.; Strelko, V.V. 1967, [Properties of polysilicic acid gels and conditions of the origin and development of life], Usp Sovrem Biol, 63, (3) 362-79.
23. Trevors, J.T.; Abel, D.L. 2004, Chance and necessity do not explain the origin of life, Cell Biology International, 28, 729-739.
24. Ball, P. 2004, Water, water, everywhere?, Nature, 427, 19-20.
25. Good, W. 1973, The role of water in the origin of life and its function in the primitive gene, J Theor Biol, 39, (2) 249-276.
26. Papagiannis, M.D. 1992, What makes a planet habitable, and how to search for habitable planets in other solar systems, J Br Interplanet Soc, 45, (6) 227-230.
27. Burton, F.G.; Lohrmann, R.; Orgel, L.E. 1974, On the possible role of crystals in the origins of life. VII. The adsorption and polymerization of phosphoramidates by montmorillonite clay, J Mol Evol, 3, (2) 141-150.
28. Ertem, G.; Ferris, J.P. 1998, Formation of RNA oligomers on montmorillonite: site of catalysis, Orig Life Evol Biosph, 28, (4-6) 485-499.
29. Ertem, G.; Ferris, J.P. 2000, Sequence- and regio-selectivity in the montmorillonite-catalyzed synthesis of RNA, Orig Life Evol Biosph, 30, (5) 411-422.
30. Ferris, J.P.; Huang, C.H.; Hagan, W.J., Jr. 1988, Montmorillonite: a multifunctional mineral catalyst for the prebiological formation of phosphate esters, Orig Life Evol Biosph, 18, (1-2) 121-133.
31. Ferris, J.P.; Ertem, G.; Agarwal, V. 1989, Mineral catalysis of the formation of dimers of 5'-AMP in aqueous solution: the possible role of montmorillonite clays in the prebiotic synthesis of RNA, Orig Life Evol Biosph, 19, (2) 165-178.

32. Ferris, J.P.; Ertem, G. 1992, Oligomerization of ribonucleotides on montmorillonite: reaction of the 5'-phosphorimidazolide of adenosine, Science, 257, (5075) 1387-1389.
33. Friebele, E.; Shimoyama, A.; Hare, P.E.; Ponnamperuma, C. 1981, Adsorption of amino acid entantiomers by Na-montmorillonite, Orig Life, 11, (1-2) 173-184.
34. Miyakawa, S.; Ferris, J.P. 2003, Sequence- and regioselectivity in the montmorillonite-catalyzed synthesis of RNA, J Am Chem Soc, 125, (27) 8202-8208.
35. Paecht-Horowitz, M.; Eirich, F.R. 1988, The polymerization of amino acid adenylates on sodium-montmorillonite with preadsorbed polypeptides, Orig Life Evol Biosph, 18, (4) 359-387.
36. Ding, P.Z.; Kawamura, K.; Ferris, J.P. 1996, Oligomerization of uridine phosphorimidazolides on montmorillonite: a model for the prebiotic synthesis of RNA on minerals, Orig Life Evol Biosph, 26, (2) 151-171.
37. Ertem, G.; Ferris, J.P. 1996, Synthesis of RNA oligomers on heterogeneous templates, Nature, 379, (6562) 238-240.
38. Friebele, E.; Shimoyama, A.; Ponnamperuma, C. 1980, Adsorption of protein and non-protein amino acids on a clay mineral: a possible role of selection in chemical evolution, J Mol Evol, 16, (3-4) 269-278.
39. Huang, W.; Ferris, J.P. 2003, Synthesis of 35-40 mers of RNA oligomers from unblocked monomers. A simple approach to the RNA world, Chem Commun (Camb), 12, 1458-1459.
40. Kawamura, K.; Ferris, J.P. 1999, Clay catalysis of oligonucleotide formation: kinetics of the reaction of the 5'-phosphorimidazolides of nucleotides with the non-basic heterocycles uracil and hypoxanthine, Orig Life Evol Biosph, 29, (6) 563-591.
41. Ferris, J.P.; Hill, A.R., Jr.; Liu, R.; Orgel, L.E. 1996, Synthesis of long prebiotic oligomers on mineral surfaces, Nature, 381, (6577) 59-61.
42. Kerr, R.A. 2003, Geochemistry. Minerals cooked up in the laboratory call ancient microfossils into question, Science, 302, (5648) 1134.
43. Garcia-Ruiz, J.M.; Hyde, S.T.; Carnerup, A.M.; Christy, A.G.; Van Kranendonk, M.J.; Welham, N.J. 2003, Self-assembled silica-carbonate structures and detection of ancient microfossils, Science, 302, (5648) 1194-7.
44. Javaux, E.J.; Marshall, C.P.; Bekker, A. 2010, Organic-walled microfossils in 3.2-billion-year-old shallow-marine siliciclastic deposits, Nature, 463, (7283) 934-8.
45. Ricardo, A.; Carrigan, M.A.; Olcott, A.N.; Benner, S.A. 2004, Borate Minerals Stabilize Ribose, Science, 303, (5655) 196-.
46. Wächtershäuser, G. 1988, Before enzymes and templates: theory of surface metabolism, Microbiol Rev, 52, (4) 452-84.
47. Wächtershäuser, G. 1992, Groundworks for an evolutionary biochemistry: the iron-sulphur world, Prog Biophys Mol Biol, 58, (2) 85-201.
48. Wächtershäuser, G. 2007, On the Chemistry and Evolution of the Pioneer Organism, Chemistry & Biodiversity, 4, (4) 584-602.
49. Alpermann, T.; Rüdel, K.; Rüger, R.; Steiniger, F.; Nietzsche, S.; Filiz, V.; Förster, S.; Fahr, A.; Weigand, W. 2011, Polymersomes Containing Iron Sulfide (FeS) as Primordial Cell Model, Origins of Life and Evolution of Biospheres, 41, (2) 103-119.
50. Kundell, F.A. 2011, A suggested pioneer organism for the wachtershauser origin of life hypothesis, Orig Life Evol Biosph, 41, (2) 175-98.
51. Martin, W.; Baross, J.; Kelley, D.; Russell, M.J. 2008, Hydrothermal vents and the origin of life, Nat Rev Microbiol, 6, (11) 805-14.
52. Martin, W.; Russell, M.J. 2003, On the origins of cells: a hypothesis for the evolutionary transitions from abiotic geochemistry to chemoautotrophic prokaryotes, and from prokaryotes to nucleated cells, Philos Trans R Soc Lond B Biol Sci, 358, (1429) 59-83; discussion 83-85.
53. Russell, M.J. 2003, Geochemistry. The importance of being alkaline, Science, 302, (5645) 580-1.
54. Russell, M.J.; Hall, A.J. 1997, The emergence of life from iron monosulphide bubbles at a submarine hydrothermal redox and pH front., Journal Geological Society London,, 154, 377-402.
55. Russell, M.J.; Hall, A.J.; Martin, W. 2010, Serpentinization as a source of energy at the origin of life, Geobiology, 8, (5) 355-71.
56. Russell, M.J.; Martin, W. 2004, The rocky roots of the acetyl-CoA pathway, Trends in biochemical sciences, 29, (7) 358-63.
57. Russell, R.; Zhuang, X.; Babcock, H.P.; Millett, I.S.; Doniach, S.; Chu, S.; Herschlag, D. 2002, Exploring the folding landscape of a structured RNA, PNAS, 99, (1) 155-160.
58. Fox, S.W. 1995, Thermal synthesis of amino acids and the origin of life, Geochim Cosmochim Acta, 59, (6) 1213-4.
59. MacLeod, G.; McKeown, C.; Hall, A.J.; Russell, M.J. 1994, Hydrothermal and oceanic pH conditions of possible relevance to the origin of life, Orig Life Evol Biosph, 24, (1) 19-41.

60. Lane, N.; Allen, J.F.; Martin, W. 2010, How did LUCA make a living? Chemiosmosis in the origin of life, Bioessays, 32, (4) 271-80.
61. Mulkidjanian, A.Y. 2009, On the origin of life in the zinc world: 1. Photosynthesizing, porous edifices built of hydrothermally precipitated zinc sulfide as cradles of life on Earth, Biol Direct, 4, 26.
62. Attwater, J.; Wochner, A.; Pinheiro, V.B.; Coulson, A.; Holliger, P. 2010, Ice as a protocellular medium for RNA replication, Nature Communications, 1, (1 September).
63. Kanavarioti, A.; Monnard, P.A.; Deamer, D.W. 2001, Eutectic phases in ice facilitate nonenzymatic nucleic acid synthesis, Astrobiology, 1, (3) 271-81.
64. Miyakawa, S.; Cleaves, H.J.; Miller, S.L. 2002, The cold origin of life: B. Implications based on pyrimidines and purines produced from frozen ammonium cyanide solutions, Orig Life Evol Biosph, 32, (3) 209-18.
65. Miyakawa, S.; Cleaves, H.J.; Miller, S.L. 2002, The cold origin of life: A. Implications based on the hydrolytic stabilities of hydrogen cyanide and formamide, Orig Life Evol Biosph, 32, (3) 195-208.
66. Monnard, P.A.; Apel, C.L.; Kanavarioti, A.; Deamer, D.W. 2002, Influence of ionic inorganic solutes on self-assembly and polymerization processes related to early forms of life: implications for a prebiotic aqueous medium, Astrobiology, 2, (2) 139-52.
67. Monnard, P.A.; Kanavarioti, A.; Deamer, D.W. 2003, Eutectic phase polymerization of activated ribonucleotide mixtures yields quasi-equimolar incorporation of purine and pyrimidine nucleobases, J Am Chem Soc, 125, (45) 13734-40.
68. Orgel, L.E. 2004, Prebiotic adenine revisited: eutectics and photochemistry, Origins of life and evolution of the biosphere, 34, (4) 361-9.
69. Eschenmoser, A. 1999, Chemical etiology of nucleic acid structure, Science, 284, (5423) 2118-24.
70. Eschenmoser, A. 2007, On a Hypothetical Generational Relationship between HCN and Constituents of the Reductive Citric Acid Cycle, Chemistry & Biodiversity, 4, (4) 554-573.
71. Eschenmoser, A. 2007, The search for the chemistry of life's origin, Tetrahedron, 63, 12821-12844.
72. Rode, B.M. 1999, Peptides and the origin of life, Peptides, 20, (6) 773-86.
73. Carny, O.; Gazit, E. 2011, Creating prebiotic sanctuary: self-assembling supramolecular Peptide structures bind and stabilize RNA, Orig Life Evol Biosph, 41, (2) 121-32.
74. Hoenigsberg, H.F. 2007, From geochemistry and biochemistry to prebiotic evolution...we necessarily enter into Ganti's fluid automata, Genet Mol Res, 6, (2) 258-73.
75. Bender Christopher, J. 2009, Chemical Evolution and Biomimetic Chemistry. In *Chemical Evolution II: From the Origins of Life to Modern Society*, American Chemical Society: Washington DC, pp 313-331.
76. de Souza-Barros, F.; Vieyra, A. 2007, Mineral interface in extreme habitats: a niche for primitive molecular evolution for the appearance of different forms of life on earth, Comp Biochem Physiol C Toxicol Pharmacol, 146, (1-2) 10-21.
77. Huber, C.; Wachtershauser, G. 1998, Peptides by activation of amino acids with CO on (Ni,Fe)S surfaces: implications for the origin of life [see comments], Science, 281, (5377) 670-2.
78. Lazard, D.; Lahav, N.; Orenberg, J.B. 1987, The biogeochemical cycle of the adsorbed template. I: Formation of the template, Orig Life Evol Biosph, 17, (2) 135-48.
79. Lazard, D.; Lahav, N.; Orenberg, J.B. 1988, The biogeochemical cycle of the adsorbed template. II: Selective adsorption of mononucleotides on adsorbed polynucleotide templates, Orig Life Evol Biosph, 18, (4) 347-57.
80. Mojzsis, S.; Krishnamurthy, R.; Arrhenius, G. 1999, Before RNA and After: Geophysical and Geochemical Constraints on Molecular Evolution. In *The RNA World*, 2nd ed.; Mojzsis, S.; Krishnamurthy, R.Arrhenius, G., Eds. Cold Spring Harbor Laboratory Press.
81. Nutman, A.P.; Clark, R.L.F.; Bennett, V.C.; Wright, D.; Norman, M.D. 2010, ≥3700 Ma pre-metamorphic dolomite formed by microbial mediation in the Isua supracrustal belt (W. Greenland): Simple evidence for early life? , PreCambrian Research, 183, (4, 15 December) 725-737.
82. Marakushev, S.A.; Belonogovaa, O.g.V. 2009, The parageneses thermodynamic analysis of chemoautotrophic CO2 fixation archaic cycle components, their stability and self-organization in hydrothermal systems, Journal of Theoretical Biology, 257, (4, 21 April) 588-597
83. Bartsev, S.I.; Mezhevikin, V.V. 2005, Pre-biotic stage of life origin under non-photosynthetic conditions, Advances in space research, 35, (9) 1643-7.
84. Chernavskii, D.S.; Chernavskaya, N.M. 1975, Some theoretical aspects of the problem of life origin, J Theor Biol, 50, (1) 13-23.
85. Edwards, M.R. 1996, Metabolite channeling in the origin of life, J Theor Biol, 179, (4) 313-22.
86. Gánti, T. 1979, *A theory of biochemical supersystems and its application to problems of natural and artificial biogenesis*. University Park Press: Baltimore.
87. Gánti, T. 2003, *Chemoton theory*. Kluwer Academic/Plenum Publishers: New York.
88. Goldstein, J. 2003, The construction of emergent order, or, how to resist the temptation of hylozoism, Nonlinear dynamics, psychology, and life sciences, 7, (4) 295-314.

89. Kasting, J.F. 1990, Impacts and the origin of life, Earth Miner Sci, 59, (4) 37-42.
90. Lifson, S. 1997, On the crucial stages in the origin of animate matter, J Mol Evol, 44, (1) 1-8.
91. Miyakawa, S.; Yamanashi, H.; Kobayashi, K.; Cleaves, H.J.; Miller, S.L. 2002, Prebiotic synthesis from CO atmospheres: Implications for the origins of life, PNAS, 99, (23) 14628-14631.
92. Sowerby, S.J.; Petersen, G.B. 2002, Life before RNA, Astrobiology, 2, (3) 231-9.
93. Sylvester-Bradley, P.C. 1976, Evolutionary oscillation in prebiology: igneous activity and the origins of life, Orig Life, 7, (1) 9-18.
94. Trevors, J.T. 2011, Origin of microbial life: Nano- and molecular events, thermodynamics/entropy, quantum mechanisms and genetic instructions, J Microbiol Methods, 84, (3) 492-5.
95. Acevedo, O.L.; Orgel, L.E. 1987, Non-enzymatic transcription of an oligodeoxynucleotide 14 residues long, J Mol Biol, 197, (2) 187-93.
96. Baaske, P.; Weinert, F.M.; Duhr, S.; Lemke, K.H.; Russell, M.J.; Braun, D. 2007, Extreme accumulation of nucleotides in simulated hydrothermal pore systems, Proc Natl Acad Sci U S A, 104, (22) 9346-51.
97. Baltscheffsky, H. 1975, Protein structure and the molecular evolution of biological energy conversion, Biosystems, 6, (4) 217-23.
98. Baltscheffsky, H. 1981, Stepwise molecular evolution of bacterial photosynthetic energy conversion, Biosystems, 14, (1) 49-56.
99. Bartel, D.P. 1999, Creation and evolution of new ribozymes, Biol Bull, 196, (3) 322-3.
100. Joyce, G.F. 2002, Molecular evolution: booting up life, Nature, 420, (6913) 278-9.
101. Joyce, G.F.; Orgel, L.E. 1998, The origins of life--a status report, Am Biol Teach, 60, (1) 10-2.
102. Jukes, T.H. 1987, Transitions, transversions, and the molecular evolutionary clock, J Mol Evol, 26, (1-2) 87-98.
103. Jukes, T.H. 2000, The neutral theory of molecular evolution, Genetics, 154, (3) 956-8.
104. Jukes, T.H.; Kimura, M. 1984, Evolutionary constraints and the neutral theory, J Mol Evol, 21, (1) 90-2.
105. Kauffman, S.A. 1992, Applied molecular evolution, J Theor Biol, 157, (1) 1-7.
106. Kauffman, S.A.; Macready, W.G. 1995, Search strategies for applied molecular evolution, J Theor Biol, 173, (4) 427-40.
107. Kimura, M. 1969, The rate of molecular evolution considered from the standpoint of population genetics, Proc Natl Acad Sci U S A, 63, (4) 1181-8.
108. Kimura, M. 1983, *Neutral Theory of Molecular Evolution.* Cambridge University Press: N.Y., N.Y.
109. Lahav, N. 1985, The synthesis of primitive 'living' forms: definitions, goals, strategies and evolution synthesizers, Orig Life Evol Biosph, 16, (2) 129-49.
110. Miller, S.L.; Lazcano, A. 1995, The origin of life -- Did it occur at high temperatures?, Journal of Molecular Evolution, 41, 689-692.
111. Nei, M.; Niimura, Y.; Nozawa, M. 2008, The evolution of animal chemosensory receptor gene repertoires: roles of chance and necessity, Nat Rev Genet, 9, (12) 951-63.
112. Nei, M.; Suzuki, Y.; Nozawa, M. 2010, The Neutral Theory of Molecular Evolution in the Genomic Era, Annual Review of Genomics and Human Genetics, 11, (1) 265-289.
113. Oehlenschlager, F.; Eigen, M. 1997, 30 years later--a new approach to Sol Spiegelman's and Leslie Orgel's in vitro evolutionary studies. Dedicated to Leslie Orgel on the occasion of his 70th birthday, Orig Life Evol Biosph, 27, (5-6) 437-57.
114. Pennisi, E. 2001, MOLECULAR EVOLUTION: Genome Duplications: The Stuff of Evolution?, Science, 294, (5551) 2458-2460.
115. Perlovsky, L. 2002, Statistical limitations on molecular evolution., J Biomol Struct Dyn, Jun;19, (6) 1031-44.
116. Wahl, L.M.; Krakauer, D.C. 2000, Models of experimental evolution: the role of genetic chance and selective necessity, Genetics, 156, (3) 1437-48.
117. Weiner, A.M. 1999, Molecular evolution: aminoacyl-tRNA synthetases on the loose, Curr Biol, 9, (22) R842-4.
118. White, D.H. 1980, A theory for the origin of a self-replicating chemical system. I: Natural selection of the autogen from short, random oligomers, Journal of molecular evolution, 16, (2) 121-47.
119. White, D.H.; Raab, M.S. 1982, A theory for the origin of a self-replicating chemical system. II. Computer simulation of the autogen, Journal of molecular evolution, 18, (3) 207-16.
120. Wright, M.C.; Joyce, G.F. 1997, Continuous in vitro evolution of catalytic function, Science, 276, (5312) 614-7.
121. Yoshiya Ikawa, K.T., Shigeyoshi Matsumura, Shota Atsumi, and Tan Inoue 2003, Putative intermediary stages for the molecular evolution from a ribozyme to a catalytic RNP, Nucleic Acids Res., March 1; 31, 1488-1496.
122. Zeldovich, K.B.; Shakhnovich, E.I. 2008, Understanding Protein Evolution: From Protein Physics to Darwinian Selection, Annual Review of Physical Chemistry, 59, (1) 105-127.
123. Küppers, B. 1975, The general principles of selection and evolution at the molecular level, Prog Biophys Mol Biol, 30, (1) 1-22.
124. Küppers, B. 1979, Towards an experimental analysis of molecular self-organization and precellular Darwinian evolution, Naturwissenschaften, 66, (5) 228-43.

125. Küppers, B.-O. 1990, *Information and the Origin of Life*. MIT Press: Cambridge, MA.
126. Kurakin, A. 2006, Self-organization versus Watchmaker: molecular motors and protein translocation., Biosystems 84, (1) 15-23.
127. Kurakin, A. 2010, Order without design, Theoretical Biology and Medical Modelling, 7, (1) 12.
128. Lahav, N. 1991, Prebiotic co-evolution of self-replication and translation or RNA world?, J Theor Biol, 151, (4) 531-539.
129. Lahav, N. 1993, The RNA-world and co-evolution hypotheses and the origin of life: implications, research strategies and perspectives, Orig Life Evol Biosph, 23, (5-6) 329-44.
130. Lahav, N. 1999, *Biogenesis: Theories of Life's Origin*. Oxford University Press: Oxford.
131. Lahav, N.; Chang, S. 1982, The possible role of soluble salts in chemical evolution, J Mol Evol, 19, (1) 36-46.
132. Lazcano, A. 2010, Historical Development of Origins Research, Cold Spring Harbor Perspectives in Biology, -.
133. Lazcano, A.; Miller, S.L. 1996, The origin and early evolution of life: prebiotic chemistry, the pre-RNA world, and time, Cell, 85, (6) 793-8.
134. Lifson, S.; Lifson, H. 1999, A model of prebiotic replication: survival of the fittest versus extinction of the unfittest, J Theor Biol, 199, (4) 425-33.
135. Lifson, S.; Lifson, H. 2001, Coexistence and Darwinian selection among replicators: response to the preceding paper by Scheuring and Szathmary, J Theor Biol, 212, (1) 107-9.
136. Kiedrowski von, G. 1996, Origins of life. Primordial soup or crepes?, Nature, 381, (6577) 20-1.
137. Kiedrowski von, G. 2001, Chemistry: a way to the roots of biology, Chembiochem, 2, (7-8) 597-8.
138. Miller, S.L. 1997, Peptide nucleic acids and prebiotic chemistry [news] [see comments], Nat Struct Biol, 4, (3) 167-9.
139. Miller, S.L. 1998, The endogenous synthesis of organic compounds. In *The Molecular Origins of Life*, Brack, A., Ed. Oxford University Press: Oxford, U.K., pp 59-85.
140. Miller, S.L.; Schopf, J.W.; Lazcano, A. 1997, Oparin's "Origin of Life": sixty years later, J Mol Evol, 44, (4) 351-3.
141. Fry, I. 2011, The role of natural selection in the origin of life, OLEB, 41, 3-16.
142. Dyson, F., 1999, Life in the Universe: Is Life Digital or Analog? In *Life in the Universe: Is Life Digital or Analog?*, NASA Goddard Space Flight Center Colloquiem, Greenbelt, MD, 1999; Greenbelt, MD,
143. Dyson, F.J. 1998, *Origins of Life*. 2nd ed., Cambridge University Press: Cambridge.
144. Anet, F.A. 2004, The place of metabolism in the origin of life, Curr Opin Chem Biol, 8, (6) 654-9.
145. Kiedrowski von, G. 1986, A self-replicating hexadeoxy nucleotide, Angewandte Chemie Inernational Edition in English, 25, 932-935.
146. Gánti, T. 2003, *The Principles of Life*. Oxford University Press: Oxford, UK.
147. Abel, D.L. 2009, The GS (Genetic Selection) Principle, Frontiers in Bioscience, 14, (January 1) 2959-2969 Open access at http://www.bioscience.org/2009/v14/af/3426/fulltext.htm.
148. Gesteland, R.F.; Cech, T.R.; Atkins, J.F. 2006, *The RNA World*. 3 ed., Cold Spring Harbor Laboratory Press: Cold Spring Harbor.
149. Smith, E.; Morowitz, H.J. 2004, Universality in intermediary metabolism, Proc Natl Acad Sci USA, 101, 13168-13173.
150. de Duve, C. 2005, *Singularities landmarks on the pathways of life*. Cambridge Univ. Press: Cambridge, UK.
151. Kenyon, D.H.; Steinman, G. 1969, *Biochemical Predestination*. McGraw-Hill Book Co.: New York.
152. Shapiro, R. 2000, A replicator was not involved in the origin of life, IUBMB Life, 49, (3) 173-176.
153. Orgel, L.E. 2008, The implausibility of metabolic cycles on prebiotic earth, PLoS biology, 6, 5-13.
154. Pross, A. 2004, Causation and the origin of life. Metabolism or replication first?, Orig Life Evol Biosph, 34, (3) 307-21.
155. Orgel, L.E. 1998, The origin of life--a review of facts and speculations, Trends Biochem Sci, 23, (12) 491-5.
156. Dyson, F.J. 1982, A model for the origin of life, J Mol Evol, 18, (5) 344-50.
157. Orgel, L.E. 2000, Self-organizing biochemical cycles, Proc Natl Acad Sci U S A, 97, (23) 12503-7.
158. de Duve, C. 2007, Chance and necessity revisited, Cell Mol Life Sci, 64, (24) 3149-58.
159. Guimaraes, R.C. 2010, Metabolic Basis for the Self-Referential Genetic Code, Origins of life and evolution of the biosphere.
160. Lee, D.H.; Granja, J.R.; Martinez, J.A.; Severin, K.; Ghadri, M.R. 1996, A self-replicating peptide, Nature, 382, (6591) 525-8.
161. Isaac, R.; Chmielewski, J. 2002, Approaching exponential growth with a self-replicating peptide, J Am Chem Soc, 124, 6808-6809.
162. Shenhav, B.; Oz, A.; Lancet, D. 2007, Coevolution of compositional protocells and their environment, Philos Trans R Soc Lond B Biol Sci, 362, (1486) 1813-9.
163. Segre, D.; Lancet, D.; Kedem, O.; Pilpel, Y. 1998, Graded autocatalysis replication domain (GARD): kinetic analysis of self-replication in mutually catalytic sets, Orig Life Evol Biosph, 28, (4-6) 501-14.

164. Segre, D.; Ben-Eli, D.; Deamer, D.W.; Lancet, D. 2001, The lipid world, Orig Life Evol Biosph, 31, (1-2) 119-45.
165. Segre, D.; Ben-Eli, D.; Lancet, D. 2000, Compositional genomes: prebiotic information transfer in mutually catalytic noncovalent assemblies, Proc Natl Acad Sci U S A, 97, (8) 4112-7.
166. Segre, D.; Lancet, D. 2000, Composing Life, EMBO Rep, 1, (3) 217-222.
167. Lancet, D.; Shenhav, B. 2009, Compositional lipid protocells: reproduction without polynucleotides. In *Protocells: Bridging Nonliving and Living Matter*, Rasmussen, S.; Bedau , M. A.; Chen, L.; Deamer, D.; Krakauer, D. C.; Packard, N. H.Stadler, P. F., Eds. MIT Press: Cambridge, MA.
168. Maynard Smith, J. 1998, The units of selection, Novartis Found Symp, 213, 203-11.
169. Maynard Smith, J. 1999, The 1999 Crafoord Prize Lectures. The idea of information in biology, Q Rev Biol, 74, (4) 395-400.
170. Maynard Smith, J. 2000, The concept of information in biology, Philosophy of Science, 67, (June) 177-194 (entire issue is an excellent discussion).
171. Dawkins, R. 1995, *River out of eden : a Darwinian view of life*. Basic Books: New York, NY.
172. Sterelny, K.; Smith, K.; Dickison, M. 1996, The extended replicator, Biology and Philosophy, 11, 377-403.
173. Sterelny, K.; Griffiths, P.E. 1999, *Sex and Death*. Univ of Chicago Press: Chicago.
174. Pohorille, A. 2009, Early ancestors of existing cells. In *Protocells: Bridging Non-living and Living Matter*, Rasmussen, S.; Bedau , M. A.; Chen, L.; Deamer, D.; Krakauer, D. C.; Packard, N. H.Stadler, P. F., Eds. MIT Press: Cambridge, pp 563-581.
175. Yarus, M. 2011, Getting past the RNA world: the initial darwinian ancestor, Cold Spring Harb Perspect Biol, 3, (4).
176. Mielke, R.E.; Russell, M.J.; Wilson, P.R.; McGlynn, S.E.; Coleman, M.; Kidd, R.; Kanik, I. 2010, Design, fabrication, and test of a hydrothermal reactor for origin-of-life experiments, Astrobiology, 10, (8) 799-810.
177. Shapiro, R. 2006, Small molecule interactions were central to the origin of life, Quarterly Review of Biology, 81, 105-125.
178. Shapiro, R. 2007, A simpler origin of life, Scientific American, Feb 12.
179. Kauffman, S.A. 2010, On emergence, OLEB, 40, (4-5) 381-383.
180. Kauffman, S. 2007, Question 1: origin of life and the living state, Orig Life Evol Biosph, 37, (4-5) 315-22.
181. Morowitz, H.J.; Srinivasan, V.; Smith, E. 2010, Ligand field theory and the origin of life as an emergent feature of the periodic table of elements, Biol Bull, 219, (1) 1-6.
182. Deamer, D.; Szostak, J.W. 2010, The Origins of Life. Cold Spring Harbor Press: Cold Spring Harbor, NY.
183. Lindahl, P.A. 2004, Stepwise evolution of nonliving to living chemical systems, OLEB, 34, 371-389.
184. Wong, J.T. 2005, Coevolution theory of the genetic code at age thirty, Bioessays, 27, (4) 416-25.
185. Wong, J.T. 2007, Question 6: coevolution theory of the genetic code: a proven theory, Orig Life Evol Biosph, 37, (4-5) 403-8.
186. Guimaraes, R.C. 2004, The Genetic Code as a Self-Referential and Functional System, International Conference on Computation, Communications and Control Technologies, 7, 160-165.
187. Di Giulio, M. 2005, The origin of the genetic code: theories and their relationships, a review, Bio Systems, 80, (2) 175-84.
188. Di Giulio, M. 2008, An extension of the coevolution theory of the origin of the genetic code, Biol Direct, 3, 37.
189. Luisi, P.L.; Ferri, F.; Stano, P. 2006, Approaches to semi-synthetic minimal cells: a review, Naturwissenschaften, 93, 1-13.
190. Luisi, P.L. 2006, *The Emergence of Life: From chemical Origins to Synthetic Biology*. Cambridge Univ. Press: Cambridge.
191. Luisi, P.L.; Rasi, P.S.; Mavelli, F. 2004, A possible route to prebiotic vesicle reproduction, Artif Life, 10, (3) 297-308.
192. Luisi, P.L. 2002, Toward the engineering of minimal living cells, Anat Rec, 268, (3) 208-14.
193. Szostak, J.W.; Bartel, D.P.; Luisi, P.L. 2001, Synthesizing life, Nature, 409, (3, Jan 18) 387-90.
194. Fischer, A.; Oberholzer, T.; Luisi, P.L. 2000, Giant vesicles as models to study the interactions between membranes and proteins, Biochim Biophys Acta, 1467, (1) 177-88.
195. Deamer, D.W. 2010, Origin of life just got closer: Life After the synthetic cell, Nature Struc Biol, 465, (27 May).
196. Deamer, D. 2010, Introduction to Definition of Life Section, Astrobiology, 10, (10) 1001-1002.
197. Rasmussen, S.; Bedau, M.A.; Liaohai, C.; Deamer, D.; Krakauer, D.C.; Packard, N.H.; Stadler, P.F. 2008, *Protocells: Bridging Nonliving and Living Matter*. MIT Press: Cambridge.
198. Deamer, D.W. 2008, Origins of life: How leaky were primitive cells?, Nature, 454, (7200) 37-38.
199. Deamer, D.; Pohorille, A. 2008, Session 34. Synthetic Cells and Life's Origins, Astrobiology, 8, (2) 453-455.
200. Monnard, P.A.; Deamer, D.W. 2003, Preparation of vesicles from nonphospholipid amphiphiles, Methods Enzymol, 372, 133-51.

201. Pohorille, A.; Deamer, D. 2002, Artificial cells: prospects for biotechnology, Trends Biotechnol, 20, (3) 123-8.
202. Monnard, P.; Deamer, D. 2002, Membrane self-assembly processes: Steps toward the first cellular life., Anat Rec, 268, (3) 196-207.
203. Deamer, D.; Dworkin, J.P.; Sandford, S.A.; Bernstein, M.P.; Allamandola, L.J. 2002, The first cell membranes, Astrobiology, 2, (4) 371-81.
204. Apel, C.L.; Deamer, D.W.; Mautner, M.N. 2002, Self-assembled vesicles of monocarboxylic acids and alcohols: conditions for stability and for the encapsulation of biopolymers, Biochim Biophys Acta, 1559, (1) 1-9.
205. Mansy, S.S. 2010, Membrane Transport in Primitive Cells, Cold Spring Harbor Perspectives in Biology, -.
206. Mansy, S.S.; Schrum, J.P.; Krishnamurthy, M.; Tobe, S.; Treco, D.A.; Szostak, J.W. 2008, Template-directed synthesis of a genetic polymer in a model protocell, Nature, 454, (7200) 122-5.
207. Mansy, S.S.; Szostak, J.W. 2008, Thermostability of model protocell membranes, Proc Natl Acad Sci U S A, 105, (36) 13351-5.
208. Mansy, S.S.; Szostak, J.W. 2009, Reconstructing the Emergence of Cellular Life through the Synthesis of Model Protocells, Cold Spring Harb Symp Quant Biol.
209. Chen, I.A.; Roberts, R.W.; Szostak, J.W. 2004, The emergence of competition between model protocells., Science, 305, 1474-1476.
210. Luisi, P.L. 2007, The problem of macromolecular sequences: the forgotten stumbling block, Orig Life Evol Biosph, 37, (4-5) 363-5.
211. Abel, D.L. 2007, Complexity, self-organization, and emergence at the edge of chaos in life-origin models, Journal of the Washington Academy of Sciences, 93, (4) 1-20.
212. Cronhjort, M.B. 1995, Hypercycles versus parasites in the origin of life: model dependence in spatial hypercycle systems, Orig Life Evol Biosph, 25, (1-3) 227-33.
213. Eigen, M. 1971, Self-organization of matter and the evolution of biological macromolecules, Naturwissenschaften, 58, (In German) 465-523.
214. Eigen, M.; Biebricher, C.K.; Gebinoga, M.; Gardiner, W.C. 1991, The hypercycle. Coupling of RNA and protein biosynthesis in the infection cycle of an RNA bacteriophage, Biochemistry, 30, (46) 11005-18.
215. Eigen, M.; Gardiner, W.C., Jr.; Schuster, P. 1980, Hypercycles and compartments. Compartments assists--but do not replace--hypercyclic organization of early genetic information, J Theor Biol, 85, (3) 407-411.
216. Eigen, M.; Schuster, P. 1977, The hypercycle. A principle of natural self-organization. Part A: Emergence of the hypercycle, Naturwissenschaften, 64, (11) 541-65.
218. Eigen, M.; Schuster, P. 1981, Comments on "growth of a hypercycle" by King (1981), Biosystems, 13, (4) 235.
219. Eigen, M.; Schuster, P.; Sigmund, K.; Wolff, R. 1980, Elementary step dynamics of catalytic hypercycles, Biosystems, 13, (1-2) 1-22.
220. Hecht, R.; Happel, R.; Schuster, P.; Stadler, P.F. 1997, Autocatalytic networks with intermediates. I: Irreversible reactions, Math Biosci, 140, (1) 33-74.
221. Igamberdiev, A.U. 1999, Foundations of metabolic organization: coherence as a basis of computational properties in metabolic networks, Bio Systems, 50, (1) 1-16.
222. Kaneko, K. 2003, Recursiveness, switching, and fluctuations in a replicating catalytic network, Phys Rev E Stat Nonlin Soft Matter Phys, 68, (3 Pt 1) 031909.
223. Lee, D.H.; Severin, K.; Yokobayashi, Y.; Ghadiri, M.R. 1997, Emergence of symbiosis in peptide self-replication through a hypercyclic network [published erratum appears in Nature 1998 Jul 2;394(6688):101], Nature, 390, (6660) 591-4.
224. Scheuring, I.; Czaran, T.; Szabo, P.; Karolyi, G.; Toroczkai, Z. 2003, Spatial models of prebiotic evolution: soup before pizza?, Orig Life Evol Biosph, 33, (4-5) 319-55.
225. Smith, J.M. 1979, Hypercycles and the origin of life, Nature, 280, (5722) 445-446.
226. Tsokolov, S. 2010, A Theory of Circular Organization and Negative Feedback: Defining Life in a Cybernetic Context, Astrobiology, 10, (10) 1031-1042.
227. Morowitz, H.J. 1992, *Beginnings of cellular life*. Yale University Press: New Haven.
228. New, M.; Pohorille, A. 2000, An inherited efficiences model of non-genomic evolution, Simulat Pract Theor, 8, 99-108.
229. Shenhav, B.; Segre, D.; Lancet, D. 2003, Mesobiotic emergence: molecular and ensemble complexity in early evolution Adv. Complex Syst, 6, (15-35).
230. Smith, E.; Morowitz, H.J.; Copley, S. 2009, Core metabolismas a self-organized system. In *Protocells: Bridging Living and Non-Living Matter*, Rasmussen, S.; Bedau , M. A.; Chen, L.; Deamer, D.; Krakauer, D. C.; Packard, N. H.Stadler, P. F., Eds. MIT Press: Cambridge, pp 433-460.
231. Eigen, M. 1992, *(with Winkler-Oswatitsch, R.), Steps Toward Life: A Perspective on Evolution*. Oxford University Press: Oxford, UK.
232. Swetina, J.; Schuster, P. 1982, Self-replication with errors. A model for polynucleotide replication, Biophysical chemistry, 16, (4) 329-45.

233. Blomberg, C. 1997, On the appearance of function and organisation in the origin of life, J Theor Biol, 187, (4) 541-54.
234. Gánti, T. 1975, Organization of chemical reactions into dividing and metabolizing units: the chemotons, Biosystems, 7, (1) 15-21.
235. Gánti, T. 1980, On the organizational basis of the evolution, Acta Biol, 31, (4) 449-59.
236. Gánti, T. 1997, Biogenesis itself, J Theor Biol, 187, (4) 583-93.
237. Gánti, T. 2002, On the early evolutionary origin of biological periodicity, Cell Biol Int, 26, (8) 729-35.
238. Abel, D.L.; Trevors, J.T. 2006, Self-Organization vs. Self-Ordering events in life-origin models, Physics of Life Reviews, 3, 211-228.
239. Johnson, D.E. 2010, *Probability's Nature and Nature's Probability (A call to scientific integrity)*. Booksurge Publishing: Charleston, S.C.
240. Johnson, D.E. 2010, *Programming of Life*. Big Mac Publishers: Sylacauga, Alabama.
241. Abel, D.L. 2000 To what degree can we reduce "life" without "loss of life"?, Workshop on Life: a satellite meeting before the Millenial World Meeting of University Professors, Modena, Italy,
242. Rocha, L.M. 2000, Syntactic autonomy: or why there is no autonomy without symbols and how self-organizing systems might evolve them, Annals of the New York Academy of Sciences, 207-223.
243. Rocha, L.M. 2001, Evolution with material symbol systems, Biosystems, 60, 95-121.
244. Weiss, O.; Jimenez-Montano, M.A.; Herzel, H. 2000, Information content of protein sequences, J Theor Biol, 206, (3) 379-86.
245. Costanzo, G.; Pino, S.; Ciciriello, F.; Di Mauro, E. 2009, RNA: Processing and Catalysis: Generation of Long RNA Chains in Water, J. Biol. Chem., 284, 33206-33216.
246. Abel, D.L. 2010, Constraints vs. Controls, Open Cybernetics and Systemics Journal, 4, 14-27 Open Access at http://www.bentham.org/open/tocsj/articles/V004/14TOCSJ.pdf.
247. Behe, M.J. 1996, *Darwin's Black Box*. Simon & Shuster: The Free Press: New York.
248. Stegmann, U.E. 2005, Genetic Information as Instructional Content, Phil of Sci, 72, 425-443.
249. Glass, J.I.; Assad-Garcia, N.; Alperovich, N.; Yooseph, S.; Lewis, M.R.; Maruf, M.; Hutchison, C.A., III; Smith, H.O.; Venter, J.C. 2006, Essential genes of a minimal bacterium, PNAS, 0510013103.
250. Abel, D.L. 2008, 'The Cybernetic Cut': Progressing from description to prescription in systems theory, The Open Cybernetics and Systemics Journal, 2, 234-244 Open access at www.bentham.org/open/tocsj/articles/V002/252TOCSJ.pdf
251. Abel, D.L. 2009, The capabilities of chaos and complexity, Int. J. Mol. Sci., 10, (Special Issue on Life Origin) 247-291 Open access at http://mdpi.com/1422-0067/10/1/247
252. Vasas, V.; Szathmáry, E.; Santos, M. 2010, Lack of evolvability in self-sustaining autocatalytic networks constrains metabolism-first scenarios for the origin of life, Proceedings of the National Academy of Sciences, 107, (4) 1470-1475.
253. Kovac, L.; Nosek, J.; Tomaska, L. 2003, An overlooked riddle of life's origins: energy-dependent nucleic acid unzipping, J Mol Evol, 57 Suppl 1, S182-9.
254. Larralde, R.; Robertson, M.P.; Miller, S.L. 1995, Rates of decomposition of ribose and other sugars: implications for chemical evolution, Proc Natl Acad Sci U S A, 92, (18) 8158-60.
255. Szostak, J.W. 2009, Origins of life: Systems chemistry on early Earth, Nature, 459, (7244) 171-2.
256. Powner, M.W.; Gerland, B.; Sutherland, J.D. 2009, Synthesis of activated pyrimidine ribonucleotides in prebiotically plausible conditions, Nature, 459, (7244) 239-42.
257. Shapiro, R. 1999, Prebiotic cytosine synthesis: a critical analysis and implications for the origin of life, Proc Natl Acad Sci U S A, 96, (8) 4396-4401.
258. Shapiro, R. 2002, Comments on `Concentration by Evaporation and the Prebiotic Synthesis of Cytosine', Origins Life Evol Biosph, 32, (3) 275-278.
259. Joyce, G.F.; Orgel, L.E. 1999, Prospects for understanding the origin of the RNA World. In *The RNA World*, Second ed.; Gesteland, R. F.; Cech, T. R.Atkins, J. F., Eds. Cold Spring Harbor Laboratory Press: Cold Spring Harbor, NY, pp 49-78.
260. Orgel, L. 2003, Some consequences of the RNA world hypothesis., Orig Life Evol Biosph, 33, (2) 211-8.
261. Lehman, N.; Jukes, T.H. 1988, Genetic code development by stop codon takeover, J Theor Biol, 135, (2) 203-14.
262. Lehmann, J. 2000, Physico-chemical constraints connected with the coding properties of the genetic system, J Theor Biol, 202, (2) 129-44.
263. Lehmann, J.; Riedo, B.; Dietler, G. 2004, Folding of small RNAs displaying the GNC base-pattern: implications for the self-organization of the genetic system, J Theor Biol, 227, (3) 381-95.
264. Lehmann, K.; Schmidt, U. 2003, Group II introns: structure and catalytic versatility of large natural ribozymes, Crit Rev Biochem Mol Biol, 38, (3) 249-303.
265. Szathmary, E. 1999, The origin of the genetic code: amino acids as cofactors in an RNA world, Trends Genet, 15, (6) 223-9.
266. Szathmary, E. 2000, The evolution of replicators, Philos Trans R Soc Lond B Biol Sci, 355, (1403) 1669-76.

267. Szathmary, E. 2001, Biological information, kin selection, and evolutionary transitions, Theoretical Population Biology, 59, 11-14.
268. Szathmary, E. 2003, Why are there four letters in the genetic alphabet?, Nat Rev Genet, 4, (12) 995-1001.
269. Szathmary, E. 2006, The origin of replicators and reproducers, Philos Trans R Soc Lond B Biol Sci, 361, (1474) 1761-76.
270. Szathmary, E. 2007, Coevolution of metabolic networks and membranes: the scenario of progressive sequestration, Philos Trans R Soc Lond B Biol Sci, 362, (1486) 1781-7.
271. Szathmary, E.; Demeter, L. 1987, Group selection of early replicators and the origin of life, J Theor Biol, 128, (4) 463-86.
272. Szathmary, E.; Gladkih, I. 1989, Sub-exponential growth and coexistence of non-enzymatically replicating templates, J Theor Biol, 138, (1) 55-8.
273. Szathmáry, E.; Jordan, F.; Pal, C. 2001, Can genes explain biological complexity?, Science, 292, 1315-1316.
274. Szathmary, E.; Maynard Smith, J. 1997, From replicators to reproducers: the first major transitions leading to life, J Theor Biol, 187, (4) 555-71.
275. Szathmary, E.; Santos, M.; Fernando, C. 2005, Evolutionary potential and requirements for minimal protocells, Top Curr Chem, 259, 167-211.
276. Szathmary, E.; Smith, J.M. 1995, The major evolutionary transitions, Nature, 374, (6519) 227-32.
277. Szathmary, E.; Zintzaras, E. 1992, A statistical test of hypotheses on the organization and origin of the genetic code, J Mol Evol, 35, (3) 185-9.
278. Ycas, M. 1999, Codons and hypercycles, Orig Life Evol Biosph, 29, (1) 95-108.
279. Zintzaras, E.; Santos, M.; Szathmary, E. 2002, "Living" Under the Challenge of Information Decay: The Stochastic Corrector Model vs. Hypercycles, J Theor Biol, 217, (2) 167-181.
280. Ruiz-Mirazo, K.; Pereto, J.; Moreno, A. 2004, A universal definition of life: autonomy and open-ended evolution, Orig Life Evol Biosph, 34, (3) 323-46.
281. Ruiz-Mirazo, K.; Umerez, J.; Moreno, A. 2008, Enabling conditions for 'open-ended evolution', Biol Phil, 23, (1) 67-85.
282. Abel, D.L. The GS (Genetic Selection) Principle [Scirus Topic Page]. http://www.scitopics.com/The_GS_Principle_The_Genetic_Selection_Principle.html (Last accessed September, 2011).
283. Johnston, W.K.; Unrau, P.J.; Lawrence, M.S.; Glasner, M.E.; Bartel, D.P. 2001, RNA-catalyzed RNA polymerization: accurate and general RNA-templated primer extension, Science, 292, (5520) 1319-25.
284. Bartel, D.P.; Szostak, J.W. 1993, Isolation of new ribozymes from a large pool of random sequences, Science, 261, (5127) 1411-8.
285. Paul, N.; Joyce, G.F. 2002, Inaugural Article: A self-replicating ligase ribozyme, PNAS, 99, (20) 12733-12740.
286. Paul, N.; Joyce, G.F. 2003, Self-replication, Curr Biol, 13, (2) R46.
287. Zaher, H.S.; Unrau, P.J. 2007, Selection of an improved RNA polymerase ribozyme with superior extension and fidelity, RNA, 13, (7) 1017-26.
288. Ma, W.; Yu, C. 2006, Intramolecular RNA replicase: possibly the first self-replicating molecule in the RNA world, Orig Life Evol Biosph, 36, (4) 413-20.
289. Hud, N.V.; Anet, F.A. 2000, Intercalation-mediated synthesis and replication: a new approach to the origin of life, J Theor Biol, 205, (4) 543-62.
290. Hud, N.V.; Jain, S.S.; Li, X.; Lynn, D.G. 2007, Addressing the problems of base pairing and strand cyclization in template-directed synthesis: a case for the utility and necessity of 'molecular midwives' and reversible backbone linkages for the origin of proto-RNA, Chem Biodivers, 4, (4) 768-83.
291. Hud, N.V.; Lynn, D.G. 2004, From life's origins to a synthetic biology, Curr Opin Chem Biol, 8, (6) 627-8.
292. Hud, N.V.; Plavec, J. 2003, A unified model for the origin of DNA sequence-directed curvature, Biopolymers, 69, (1) 144-58.
293. Hud, N.V.; Polak, M. 2001, DNA-cation interactions: The major and minor grooves are flexible ionophores, Curr Opin Struct Biol, 11, (3) 293-301.
294. Cheng, L.K.L.; Unrau, P.J. 2010, Closing the Circle: Replicating RNA with RNA, Cold Spring Harb Perspect Biol.
295. Engelhart, A.E.; Hud, N.V. 2010, Primitive Genetic Polymers, Cold Spring Harbor Perspectives in Biology, -.
296. Schrum, J.P.; Zhu, T.F.; Szostak, J.W. 2010, The Origins of Cellular Life, Cold Spring Harbor Perspectives in Biology, 2, (9) -.
297. JANAS, T.; YARUS, M. 2003, Visualization of membrane RNAs, RNA, 9, (11) 1353-1361.
298. Yarus, M. 2002, PRIMORDIAL GENETICS: Phenotype of the Ribocyte, Annu Rev Genet, 36, 125-51.
299. Macia, J.; Sole, R.V. 2007, Protocell self-reproduction in a spatially extended metabolism-vesicle system, J Theor Biol, 245, (3) 400-10.
300. Chen, I.A. 2006, GE Prize-winning essay. The emergence of cells during the origin of life, Science, 314, (5805) 1558-9.

301. Klussmann, M.; Blackmond Donna, G. 2009, Origin of Homochirality. In *Chemical Evolution II: From the Origins of Life to Modern Society*, American Chemical Society: Washington DC, pp 133-145.
302. Klussmann, M.; Iwamura, H.; Mathew, S.P.; Wells, D.H., Jr.; Pandya, U.; Armstrong, A.; Blackmond, D.G. 2006, Thermodynamic control of asymmetric amplification in amino acid catalysis, Nature, 441, (7093) 621-3.
303. Anastasi, C.; Buchet, F.F.; Crowe, M.A.; Parkes, A.L.; Powner, M.W.; Smith, J.M.; Sutherland, J.D. 2007, RNA: prebiotic product, or biotic invention?, Chem Biodivers, 4, (4) 721-39.
304. Pino, S.; Ciciriello, F.; Costanzo, G.; Di Mauro, E. 2008, Nonenzymatic RNA ligation in water, JBC, 283, 36494-36503.
305. Breslow, R.; Cheng, Z.L. 2009, On the origin of terrestrial homochirality for nucleosides and amino acids, Proc Natl Acad Sci U S A, 106, (23) 9144-6.
306. Wu, M.; Higgs, P.G. 2009, Origin of self-replicating biopolymers: autocatalytic feedback can jump-start the RNA world, J Mol Evol, 69, (5) 541-54.
307. Kamioka, S.; Ajami, D.; Rebek, J., Jr. 2010, Autocatalysis and organocatalysis with synthetic structures, Proc Natl Acad Sci U S A, 107, (2) 541-4.
308. Spitzer, J.; Poolman, B. 2009, The role of biomacromolecular crowding, ionic strength, and physicochemical gradients in the complexities of life's emergence, Microbiol Mol Biol Rev, 73, (2) 371-88.
309. Cairns-Smith, A.G. 2008, Chemistry and the missing era of evolution, Chemistry, 14, (13) 3830-9.
310. Strasdeit, H. 2005, New studies on the Murchison meteorite shed light on the pre-RNA world, Chembiochem, 6, (5) 801-3.
311. Dworkin, J.P.; Lazcano, A.; Miller, S.L. 2003, The roads to and from the RNA world, J Theor Biol, 222, (1) 127-34.
312. House, C.H.; Miller, S.L. 1996, Hydrolysis of dihydrouridine and related compounds, Biochemistry, 35, (1) 315-20.
313. Kolb, V.M.; Dworkin, J.P.; Miller, S.L. 1994, Alternative bases in the RNA world: the prebiotic synthesis of urazole and its ribosides, J Mol Evol, 38, 549-57.
314. Joyce, G.F.; Inoue, T.; Orgel, L.E. 1984, Non-enzymatic template-directed synthesis on RNA random copolymers. Poly(C, U) templates, J Mol Biol, 176, (2) 279-306.
315. Joyce, G.F.; Orgel, L. 2006, Progress toward understanding the origin of the RNA world. In *RNA World*, 3rd ed.; Gesteland, R.; Cech, T.Atkins, J. F., Eds. Cold Spring Harbor Laboratory: Cold Spring Harbor, pp 23-56.
316. Schoning, K.; Scholz, P.; Guntha, S.; Wu, X.; Krishnamurthy, R.; Eschenmoser, A. 2000, Chemical etiology of nucleic acid structure: the alpha-threofuranosyl-(3'-->2') oligonucleotide system, Science, 290, (5495) 1347-51.
317. Matray, T.J.; Gryaznov, S.M. 1999, Synthesis and properties of RNA analogs-oligoribonucleotide N3'-->P5' phosphoramidates. In Vol. 27, pp 3976-3985.
318. Nielsen, P. 2009, Peptide nucleic acids as prebiotic and abiotic genetic material. In *Protocells: Bridging Nonliving and Living Matter*, Rasmussen, S.; Bedau , M. A.; Chen, L.; Deamer, D.; Krakauer, D. C.; Packard, N. H.Stadler, P. F., Eds. MIT Press: Cambridge.
319. Nielsen, P.E. 1993, Peptide nucleic acid (PNA): a model structure for the primordial genetic material?, Orig Life Evol Biosph, 23, (5-6) 323-7.
320. Diederichsen, U. 1996, Pairing properties of alanyl peptide nucleic acids containing an amino acid backbone with alternating configuration, Angew Chem Int Ed Engl, 35, 445-448.
321. Pattee, H.H. 1977, Dynamic and linguistic modes of complex systems, Int. J. General Systems, 3, 259-266.
322. Shapiro, R. 1984, The improbability of prebiotic nucleic acid synthesis, Orig Life, 14, (1-4) 565-570.
323. Shapiro, R. 1987, *Origins : A Skeptic's Guide to the Creation of Life on Earth*. Bantam: New York.
324. Shapiro, R. 1988, Prebiotic ribose synthesis: a critical analysis, Orig Life Evol Biosph, 18, (1-2) 71-85.
325. Orgel, L.E. 2004, Prebiotic chemistry and the origin of the RNA world, Critical reviews in biochemistry and molecular biology, 39, (2) 99-123.
326. Abel, D.L.; Trevors, J.T. 2006, More than metaphor: Genomes are objective sign systems, Journal of BioSemiotics, 1, (2) 253-267.
327. Kamioka, S.; Ajami, D.; Rebek, J. 2009, Autocatalysis and organocatalysis with synthetic structures, Proceedings of the National Academy of Sciences,
328. Perry, R.S.; Kolb, V.M. 2004, On the applicability of Darwinian principles to chemical evolution that led to life, International Journal of Astrobiology, 3, 45-53.
329. Rodin, S.; Ohno, S.; Rodin, A. 1993, Transfer RNAs with complementary anticodons: could they reflect early evolution of discriminative genetic code adaptors?, Proc Natl Acad Sci U S A, 90, (10) 4723-7.
330. Schuster, P. 1984, Polynucleotide evolution, hypercycles and the origin of the genetic code, Adv Space Res, 4, (12) 143-151.
331. Stadler, B.M.; Stadler, P.F.; Schuster, P. 2000, Dynamics of autocatalytic replicator networks based on higher-order ligation reactions, Bull Math Biol, 62, (6) 1061-86.

332. Hohmann-Marriott, M.F.; Blankenship, R.E. 2010, Evolution of Photosynthesis, Annu Rev Plant Biol.
333. Margulis, L. 1981, *Symbiosis in Cell Evolution: Life and Its Environment on the Early Earth*. W.H. Freeman: San Francisco, CA.
334. Palmer, J.D. 1997, Organelle Genomes--Going, Going, Gone!, Science, 275, (5301) 790-.
335. Fukui, S.; Fukatsu, T.; Ikegami, T.; Shimada, M. 2007, Endosymbiosis as a compact ecosystem with material cycling: parasitism or mutualism?, Journal of theoretical biology, 246, (4) 746-54.
336. Kutschera, U.; Niklas, K.J. 2008, Macroevolution via secondary endosymbiosis: a Neo-Goldschmidtian view of unicellular hopeful monsters and Darwin's primordial intermediate form, Theory Biosci, 127, (3) 277-89.
337. Kleine, T.; Maier, U.G.; Leister, D. 2009, DNA Transfer from Organelles to the Nucleus: The Idiosyncratic Genetics of Endosymbiosis, Annual Review of Plant Biology, 60, (1) 115-138.
338. Schopf, W.J. 2011, The paleobiological record of photosynthesis, Photosynth Res, 107, (1) 87-101.
339. Grenfell, J.L.; Rauer, H.; Selsis, F.; Kaltenegger, L.; Beichman, C.; Danchi, W.; Eiroa, C.; Fridlund, M.; Henning, T.; Herbst, T.; Lammer, H.; Leger, A.; Liseau, R.; Lunine, J.; Paresce, F.; Penny, A.; Quirrenbach, A.; Rottgering, H.; Schneider, J.; Stam, D.; Tinetti, G.; White, G.J. 2010, Co-evolution of atmospheres, life, and climate, Astrobiology, 10, (1) 77-88.
340. Mulkidjanian, A.Y.; Galperin, M.Y. 2009, On the origin of life in the zinc world. 2. Validation of the hypothesis on the photosynthesizing zinc sulfide edifices as cradles of life on Earth, Biol Direct, 4, 27.
341. Blankenship, R.E.; Hartman, H. 1998, The origin and evolution of oxygenic photosynthesis, Trends Biochem Sci, 23, (3) 94-97.
342. Broda, E. 1975, The begginning of photosynthesis, Orig Life, 6, (1-2) 247-51.
343. Buick, R. 1992, The antiquity of oxygenic photosynthesis: evidence from stromatolites in sulphate-deficient Archaean lakes, Science, 255, (5040) 74-7.
344. Castresana, J.; Saraste, M. 1995, Evolution of energetic metabolism: the respiration-early hypothesis, Trends Biochem Sci, 20, (11) 443-448.
345. Hartman, H. 1998, Photosynthesis and the origin of life, Orig Life Evol Biosph, 28, (4-6) 515-21.
346. Jennings, R.C.; Belgio, E.; Casazza, A.P.; Garlaschi, F.M.; Zucchelli, G. 2007, Entropy consumption in primary photosynthesis, Biochim Biophys Acta, 1767, (10) 1194-7; discussion 1198-9.
347. Gupta, R.S.; Mukhtar, T.; Singh, B. 1999, Evolutionary relationships among photosynthetic prokaryotes (Heliobacterium chlorum, Chloroflexus aurantiacus, cyanobacteria, Chlorobium tepidum and proteobacteria): implications regarding the origin of photosynthesis, Mol Microbiol, 32, (5) 893-906.
348. Margulis, L.; Obar, R. 1985, Heliobacterium and the origin of chrysoplasts, Biosystems, 17, (4) 317-25.
349. Morowitz, H.J.; Heinz, B.; Deamer, D.W. 1988, The chemical logic of a minimum protocell, Orig Life Evol Biosph, 18, (3) 281-7.
350. Sundstrom, V. 2008, Femtobiology, Annual Review of Physical Chemistry, 59, (1) 53-77.
351. Suzuki, J.Y.; Bauer, C.E. 1995, A prokaryotic origin for light-dependent chlorophyll biosynthesis of plants, Proc Natl Acad Sci U S A, 92, (9) 3749-53.
352. Tamulis, A.; Tamulis, V.; Graja, A. 2006, Quantum mechanical modeling of self-assembly and photoinduced electron transfer in PNA-based artificial living organisms, J Nanosci Nanotechnol, 6, (4) 965-73.
353. Volkov, A.G.; Gugeshashvili, M.I.; Deamer, D.W. 1995, Energy conversion at liquid/liquid interfaces: artificial photosynthetic systems, Electrochim Acta, 40, (18) 2849-68.
354. Xiong, J.; Fischer, W.M.; Inoue, K.; Nakahara, M.; Bauer, C.E. 2000, Molecular evidence for the early evolution of photosynthesis, Science, 289, (5485) 1724-30.
355. Ham, M.-H.; Choi, J.H.; Boghossian, A.A.; Jeng, E.S.; Graff, R.A.; Heller, D.A.; Chang, A.C.; Mattis, A.; Bayburt, T.H.; Grinkova, Y.V.; Zeiger, A.S.; Van Vliet, K.J.; Hobbie, E.K.; Sligar, S.G.; Wraight, C.A.; Strano, M.S. 2010, Photoelectrochemical complexes for solar energy conversion that chemically and autonomously regenerate, Nat Chem, advance online publication.
356. Foyer, C.H.; Bloom, A.J.; Queval, G.; Noctor, G. 2009, Photorespiratory Metabolism: Genes, Mutants, Energetics, and Redox Signaling, Annual Review of Plant Biology, 60, (1) 455-484.
357. Trevors, J.T. 2002, The subsurface origin of microbial life on the Earth, Res Microbiol, 153, (8) 487-91.
358. Leebens-Mack, J.; DePamphilis, C. 2002, Power analysis of tests for loss of selective constraint in cave crayfish and nonphotosynthetic plant lineages, Molecular biology and evolution, 19, (8) 1292-302.
359. Dismukes, G.C.; Klimov, V.V.; Baranov, S.V.; Kozlov, Y.N.; DasGupta, J.; Tyryshkin, A. 2001, The origin of atmospheric oxygen on Earth: The innovation of oxygenic photosynthesis, Proc. Natl. Acad. Sci. USA, February 27; 98, (2170-2175).
360. Cavalier-Smith, T. 2001, Obcells as proto-organisms: membrane heredity, lithophosphorylation, and the origins of the genetic code, the first cells, and photosynthesis, J Mol Evol, 53, (4-5) 555-95.
361. Pereto, J.G.; Velasco, A.M.; Becerra, A.; Lazcano, A. 1999, Comparative biochemistry of CO2 fixation and the evolution of autotrophy, Int Microbiol, 2, (1) 3-10.
362. Fridlyand, L.E.; Scheibe, R. 1999, Regulation of the Calvin cycle for CO2 fixation as an example for general control mechanisms in metabolic cycles, Bio Systems, 51, (2) 79-93.

363. Volkov, A.G.; Deamer, D.W. 1997, Redox chemistry at liquid/liquid interfaces, Prog Colloid Polym Sci, 103, 21-8.
364. Crick, F.H.C. 1968, The Origin of the Genetic Code, J. Mol. Biol, 38, 367-379.
365. Di Giulio, M. 1997, On the origin of the genetic code, J Theor Biol, 187, (4) 573-581.
366. Di Giulio, M. 2000, Genetic code origin and the strength of natural selection, J Theor Biol, 205, (4) 659-661.
367. Di Giulio, M. 2001, The Non-universality of the Genetic Code: the Universal Ancestor was a Progenote, Journal of Theoretical Biology, 209, (3, April) 345-349.
368. Di Giulio, M. 2001, A blind empiricism against the coevolution theory of the origin of the genetic code, J Mol Evol, 53, (6) 724-732.
369. Di Giulio, M. 2002, Genetic code origin: are the pathways of type Glu-tRNA(Gln) --> Gln-tRNA(Gln) molecular fossils or not?, J Mol Evol, 55, (5) 616-622.
370. Di Giulio, M. 2003, The early phases of genetic code origin: conjectures on the evolution of coded catalysis., Orig Life Evol Biosph, 33, (4-5) 479-489.
371. Di Giulio, M.; Medugno, M. 1998, The historical factor: the biosynthetic relationships between amino acids and their physicochemical properties in the origin of the genetic code, J Mol Evol, 46, (6) 615-621.
372. Di Giulio, M.; Medugno, M. 1999, Physicochemical optimization in the genetic code origin as the number of codified amino acids increases, J Mol Evol, 49, (1) 1-10.
373. Di Giulio, M.; Medugno, M. 2000, The robust statistical bases of the coevolution theory of genetic code origin, J Mol Evol, 50, (3) 258-263.
374. Di Giulio, M.; Medugno, M. 2001, The level and landscape of optimization in the origin of the genetic code, J Mol Evol, 52, (4) 372-382.
375. Higgs, P.G.; Pudritz, R.E. 2009, A Thermodynamic Basis for Prebiotic Amino Acid Synthesis and the Nature of the First Genetic Code, Astrobiology, 9, (5) 483-490.
376. Ikehara, K. 2002, Origins of gene, genetic code, protein and life: comprehensive view of life systems from a GNC-SNS primitive genetic code hypothesis., J Biosci, 27, (2) 165-86.
377. Legiewicz, M.; Yarus, M. 2005, A More Complex Isoleucine Aptamer with a Cognate Triplet, J. Biol. Chem., 280, (20) 19815-19822.
378. Ribas de Pouplana, L.; Turner, R.J.; Steer, B.A.; Schimmel, P. 1998, Genetic code origins: tRNAs older than their synthetases?, Proc Natl Acad Sci U S A, 95, (19) 11295-11300.
379. Ronneberg, T.A.; Landweber, L.F.; Freeland, S.J. 2000, Testing a biosynthetic theory of the genetic code: Fact or artifact?, PNAS, 97, (25) 13690-13695.
380. Sanchez, R.; Grau, R. 2006, A novel algebraic structure of the genetic code over the galois field of four DNA bases, Acta biotheoretica, 54, (1) 27-42.
381. Schimmel, P.; Ribas de Pouplana, L. 1999, Genetic code origins: experiments confirm phylogenetic predictions and may explain a puzzle [published erratum appears in Proc Natl Acad Sci U S A 1999 May 11;96(10):5890], Proc Natl Acad Sci U S A, 96, (2) 327-328.
382. Seligmann, H.; Amzallag, G.N. 2002, Chemical interactions between amino acid and RNA: multiplicity of the levels of specificity explains origin of the genetic code, Naturwissenschaften, 89, (12) 542-551.
383. Yarus, M.; Christian, E.L. 1989, Genetic code origins, Nature, 342, (6248) 349-350.
384. Schultz, D.W.; Yarus, M. 1996, On malleability in the genetic code, J Mol Evol, 42, (5) 597-601.
385. Yarus, M. 1991, An RNA-amino acid complex and the origin of the genetic code, New Biol, 3, (2) 183-9.
386. Yarus, M.; Schultz, D.W. 1997, Further comments on codon reassignment. Response, J Mol Evol, 45, (1) 3-6.
387. Wong, J.T. 1975, A co-evolution theory of the genetic code, Proc Natl Acad Sci U S A, 72, (5) 1909-1912.
388. Wong, J.T. 1976, The evolution of a universal genetic code, Proc Natl Acad Sci U S A, 73, (7) 2336-40.
389. Wong, J.T. 1980, Role of minimization of chemical distances between amino acids in the evolution of the genetic code, Proc Natl Acad Sci U S A, 77, (2) 1083-6.
390. Wong, J.T. 1988, Evolution of the genetic code, Microbiol Sci, 5, (6) 174-181.
391. Wong, J.T. 1991, Origin of genetically encoded protein synthesis: a model based on selection for RNA peptidation, Orig Life Evol Biosph, 21, (3) 165-76.
392. Labouygues, J.M.; Figureau, A. 1984, The logic of the genetic code: synonyms and optimality against effects of mutations, Orig Life, 14, (1-4) 685-692.
393. Szathmary, E. 1991, Four letters in the genetic alphabet: a frozen evolutionary optimum?, Proc R Soc Lond B Biol Sci, 245, (1313) 91-9.
394. Szathmary, E. 1992, What is the optimum size for the genetic alphabet?, Proc Natl Acad Sci U S A, 89, (7) 2614-8.
395. Bradley, D. 2002, Informatics. The genome chose its alphabet with care, Science, 297, (5588) 1789-1791.
396. Freeland, S.J.; Hurst, L.D. 1998, The genetic code is one in a million, Journal of Molecular Evolution, 47, 238-248.
397. Itzkovitz, S.; Alon, U. 2007, The genetic code is nearly optimal for allowing additional information within protein-coding sequences, Genome Res, 17, (4) 405-12.

398. Segal, E.; Fondufe-Mittendorf, Y.; Chen, L.; Thastrom, A.; Field, Y.; Moore, I.K.; Wang, J.P.; Widom, J. 2006, A genomic code for nucleosome positioning, Nature, 442, (7104) 772-8.
399. Di Giulio, M. 2004, The coevolution theory of the origin of the genetic code, Physics of Life Reviews.
400. Guimaraes, R.C. 2001, Two punctuation systems in the genetic code. In *First steps in the origin of life in the universe*, Chela-Flores, J.; Owen, T.Raulin, F., Eds. Kluwer Acad. Publ: Dordrecht, NL.
401. Farias, S.T.; Moreira, C.H.; Guimaraes, R.C. 2007, Structure of the genetic code suggested by the hydropathy correlation between anticodons and amino acid residues, Orig Life Evol Biosph, 37, (1) 83-103.
402. Guimaraes, R.C.; Moreira, C.H.; de Farias, S.T. 2008, A self-referential model for the formation of the genetic code, Theory Biosci, 127, (3) 249-70.
403. Yockey, H.P. 1992, *Information Theory and Molecular Biology*. Cambridge University Press: Cambridge.
404. Pattee, H.H. 2001, The physics of symbols: bridging the epistemic cut, Biosystems, 60, (1-3) 5-21.
405. Pattee, H.H. 2001, Irreducible and complementary semiotic forms, Semiotica, 134, 341-358.
406. Pattee, H.H. 2005, The physics and metaphysics of Biosemiotics, Journal of Biosemiotics, 1, 303-324.
407. Pattee, H.H. 2007, The necessity of biosemiotics: Matter-symbol complementarity. In *Introduction to Biosemiotics: The New Biological Synthesis*, Springer: Dordrecht, The Netherlands, pp 115-132.
408. Pattee, H.H.; Kull, K. 2009, A biosemiotic conversation: Between physics and semiotics, Sign Systems Studies 37, (1/2).
409. Rocha, L.M. 1998, Selected self-organization and the semiotics of evolutionary systems. In *Evolutionary Systems: Biological and Epistemological Perspectives on Selection and Self-Organization*, Salthe, S.; van de Vijver, G.Delpos, M., Eds. Kluwer: The Netherlands, pp 341-358.
410. Behe, M. 2010, Experimental Evolution, Loss-of-Function Mutations, and "The First Rule of Adaptive Evolution", The Quarterly Review of Biology, 85, (4 December).
411. Sun, W.; Julie Li, Y.-S.; Huang, H.-D.; Shyy, J.Y.-J.; Chien, S. 2010, microRNA: A Master Regulator of Cellular Processes for Bioengineering Systems, Annual Review of Biomedical Engineering, 12, (1) 1-27.
412. Sun, L.; Becskei, A. 2010, Systems biology: The cost of feedback control, Nature, 467, (7312) 163-164.
413. Cotterell, J.; Sharpe, J. 2010, An atlas of gene regulatory networks reveals multiple three-gene mechanisms for interpreting morphogen gradients, Molecular Systems Biology, 6, (425).
414. Chuang, H.-Y.; Hofree, M.; Ideker, T. 2010, A Decade of Systems Biology, Annual Review of Cell and Developmental Biology, 26, (1) 721-744.
415. Buchanan, M.; Caldarelli, G.; De Los Rios, P.; Rao, F.; Vendruscolo, M. 2010, Networks in Cell Biology. Cambridge University Press: Cambridge.
416. Ferrell, J. 2009, Q&A: Systems biology, Journal of Biology, 8, (1) 2.
417. Danesi, M. 2005, Modeling systems theory, Journal of Biosemiotics, 1, 213-225.
418. Krishnamurthy, L.; Nadeau, J.; Ozsoyoglu, G.; Ozsoyoglu, M.; Schaeffer, G.; Tasan, M.; Xu, W. 2003, Pathways database system: an integrated system for biological pathways, Bioinformatics, 19, (8) 930-937.
419. Kuhn, H. 1972, Self-organization of molecular systems and evolution of the genetic apparatus, Angew Chem Int Ed Engl, 11, (9) 798-820.
420. Kull, K. 1993, Semiotic paradigm in theoretical biology. In *Lectures in Theoretical Biology: The second Stage*, Kull, K.Tiivel, T., Eds. Estonian Academy of Sciences: Tallinn, pp 52-62.
421. Kull, K. 1998, Organism as a self-reading text: Anticipation and semiosis, International Journal of Computing Anticipatory Systems, 1, 93-104.
422. Kull, K. 1999, Biosemiotics in the twentieth century: A view from biology., Semiotica, 127, 385-414.
423. Kull, K. 2005, A brief history of biosemiotics, Journal of Biosemiotics, 1, 1-36.
424. Kull, K. 2006, Biosemiotics and biophysics--The fundamental approaches to the study of life. In *Introduction to Biosemiotics: The New Biological Synthesis*, Barbieri, M., Ed. Springer-Verlag New York, Inc. : Dordrecht, The Netherlands; Secaucus, NJ, USA
425. Artmann, S. 2005, Biosemiotics as a structural science, Journal of Biosemiotics, 1, 247-285.
426. Barbieri, M. 2005, Life is 'artifact-making', Journal of Biosemiotics, 1, 113-142.
427. Barbieri, M. 2006, Is the Cell a Semiotic System? In *Introduction to Biosemiotics: The New Biological Synthesis*, Barbieri, M., Ed. Springer-Verlag New York, Inc. : Secaucus, NJ, USA
428. Barbieri, M. 2006, Introduction to Biosemiotics: The New Biological Synthesis. Springer-Verlag Dordrecht, The Netherlands.
429. Barbieri, M. 2007, Has biosemiotics come of age? In *Introduction to Biosemiotics: The New Biological Synthesis*, Barbieri, M., Ed. Springer: Dorcrecht, The Netherlands, pp 101-114.
430. Barbieri, M. 2007, Is the cell a semiotics system? In *Introduction to Biosemiotics: The New Biological Synthesis*, Barbieri, M., Ed. Springer: Dordrecht, The Netherlands, pp 179-208.
431. Barbieri, M. 2007, BioSemiotic Research Trends Nova Science Publishers, Inc.: New York.
432. Barbieri, M. 2007, The Codes of Life: The Rules of Macroevolution (Biosemiotics). Springer: Dordrecht, The Netherlands.
433. Barbieri, M. 2008, Biosemiotics: a new understanding of life, Naturwissenschaften, 95, 577-599.

434. Barbieri, M. 2008, Cosmos and History: Life is semiosis; The biosemiotic view of nature, The Journal of Natural and Social Philosophy, 4, (1-2) 29-51.
435. Battail, G. 2005, Genetics as a communication process involving error-correcting codes, Journal of Biosemiotics, 1, 143-193.
436. Chang, H.-l. 2005, Natural history or natural systems? Encoding the textual sign, Journal of Biosemiotics, 1, 227-245.
437. Deely, J. 1992, Semiotics and biosemiotics: are sign-science and life-science coextensive? In *Biosemiotics: The Semiotic Web 1991*, Sebeok, T. A.Umiker-Sebeok, J., Eds. Mouton de Gruyter: Berlin/N.Y., pp 46-75.
438. Emmeche, C. 1999, The Sarkar challenge to biosemiotics: Is there any information in a cell?, Semiotica, 127, 273-293.
439. Favareau, D. 2006, The Evolutionary History of Biosemiotics. In *Introduction to Biosemiotics: The New Biological Synthesis*, Barbieri, M., Ed. Springer-Verlag New York, Inc. : Dordrecht, The Netherlands; Secaucus, NJ, USA pp 1-68.
440. Florkin, M. 1974, Concepts of molecular biosemiotics and of molecular evolution. In *Comprehensive Biochemistry*, Florkin, M.Stoltz, E. H., Eds. Elsevier: Amsterdam, pp 1-124.
441. Hoffmeyer, J. 1997, Biosemiotics: Towards a new synthesis in biology, European Journal for Semiotic Studies, 9, 355-376.
442. Hoffmeyer, J. 2006, Semiotic scaffolding of living systems. In *Introduction to Biosemiotics: The New Biological Synthesis*, Barbieri, M., Ed. Springer-Verlag New York, Inc. : Dordrecht, The Netherlands; Secaucus, NJ, USA pp 149-166.
443. Hoffmeyer, J.; Emmeche, C. 2005, Code-Duality and the Semiotics of Nature, Journal of Biosemiotics, 1, 37-91.
444. Jämsä, T. 2006, Semiosis in evolution. In *Introduction to Biosemiotics: The New Biological Synthesis*, Barbieri, M., Ed. Springer-Verlag New York, Inc. : Dordrecht, The Netherlands; Secaucus, NJ, USA
445. Kawade, Y. 1996, Molecular biosemiotics: molecules carry out semiosis in living systmes, Semiotica, 111, 195-215.
446. Nöth, W. 2005, Semiotics for biologists, Journal of Biosemiotics, 1, 195-211.
447. Salthe, S.N. 2006, What is the scope of biosemiotics? Information in living systems. . In *Introduction to Biosemiotics: The New Biological Synthesis* Barbieri, M., Ed. Springer-Verlag New York, Inc.: Dordrecht, The Netherlands; Secaucus, NJ, USA
448. Sharov, A. 1992, Biosemiotics. A functional-evolutionary approach to the analysis of the sense of evolution. In *Biosemiotics: The Semiotic Web 1991*, Sebeok, T. A.Umiker-Sebeok, J., Eds. Mouton de Gruyter: Berlin, pp 345-373.
449. Vehkavaara, T. 1998, Extended concept of knowledge for evolutionary epistemology and for biosemiotics. In *Emergence, Complexity, Hierarchy, Organization. Selected and edited papers from Echo III*, Farre, G. L.Oksala, T., Eds. Espoo: Helsinki, pp 207-216.
450. Hoover, R.B. 2011, Fossils of Cyanobacteria in CI1 Carbonaceous Meteorites NASA/Marshall Space Flight Center Journal of Cosmology, 13, (March).
451. Hoover, R.B. 1997, Meteorites, microfossils and exobiology. . In *Instruments, Methods, and Missions for the Investigation of Extraterrestrial Microorganisms SPIE, 3111*, Hoover, R. B., Ed. pp 115–136.
452. Brasier, M.D. 2011, Life in CI1 Carbonaceous Chondrites?, Journal of Cosmology, 13, (March).
453. Ruiz-Mirazo, K.; Moreno, A. 2006, On the origins of information and its relevance for biological complexity, Biological Theory, 1, (3) 227-229.
454. Ruiz-Mirazo, K.; Moreno, A.; Moran, F. 1998, Merging the Energetic and the Relational-Constructive Logic of Life. . In *Artificial Life VI*, Adami, C.; R., B.; Kitano, H.Taylor, C., Eds. MIT Bradford Books: Cambridge MA, pp 448-451.
455. Konopka, A.K. 1994, Sequences and Codes: Fundamentals of Biomolecular Cryptology. In *Biocomputing: Informatics and Genome Projects*, Smith, D., Ed. Academic Press: San Diego, pp 119-174.
456. Konopka, A.K. 1997, Theoretical Molecular Biology. In *Encyclopedia of Molecular Biology and Molecular Medicine*, Meyers, R. A., Ed. VCH Publishers: Weinheim, Vol. 6, pp 37-53.
457. Konopka, A.K. 2001, Towards understanding life itself, Comput Chem, 25, (4) 313-5.
458. Konopka, A.K. 2003, Systems biology: aspects related to genomics. In *Nature Encyclopidia of the Human Genome*, Cooper, D. N., Ed. Nature Publishing Group Reference: London, Vol. 5, pp 459-465.
459. Konopka, A.K. 2003, Information theories in molecular biology and genomics. In *Nature Encyclopedia of teh Human Genome*, Cooper, D. N., Ed. Nature Publishing Group Reference: London, Vol. 3, pp 464-469.
460. Konopka, A.K. 2003, Sequence complexity and composition. In *Nature Encyclopedia of the Human Genome. Vol. 5.*, Cooper, D. N., Ed. Nature Publishing Group Reference: London, pp 217-224.
461. Wald, G. 1954, The Origin of Life, Scientific American, 191 44-53.

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10. What Might Be a Protocell's Minimal "Genome?"

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Abstract. The origin of life's biggest mystery is the origin of the genome which contains the information to cybernetically control all aspects of cellular life today. Without formal control, no life would exist. The genetics-first and metabolism-first models will be examined, each having characteristics that strain scientific credibility. Major physical science limitations and the formidable information science problems are examined. These problems usually result in over-simplifications in speculative scenarios. More serious are the 11 peer-reviewed scientific null hypotheses that require falsification before any of the naturalistic scenarios can be considered as serious science. Assuming the problems can be resolved, the requirements for a minimal "genome" can be discussed in the areas of initial generation of programmed controls, replication of the genome and needed components that make it useful, regulation of "life's" processes, and evolvability. Life is an intersection of the physical sciences of chemistry and physics and the nonphysical formalism of information science. Each domain must be investigated using that domain's principles. Yet most scientists have been attempting to use physical science to explain life's nonphysical information domain, a practice that has no scientific justification.

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Introduction: Pseudo-Scientific Speculations or Science?

A hundred years ago, the title's question wouldn't have been needed since a cell was thought to be bag of plasm [1] originating in a "warm little pond" [2]. Fifty years ago, protein and DNA structures had been determined so science "knew" the secrets of the genome. With the Miller/Urey [3] synthesis, many thought that the origin of life explanation was near. Fifteen years ago, it started to be realized that "junk DNA" was a misnomer. Five years ago, epigenetic control systems largely determined by non-coding DNA began to be discovered. As new knowledge of functional complexity is revealed, we realize that our knowledge of that complexity has been increasing exponentially, with no end in sight. As one layer is pealed back, a new level of functional complexity is exposed. Rather than getting simpler, the more we know, the more we know we don't know! "As sequencing and other new technologies spew forth data, the complexity of biology has seemed to grow by orders of Magnitude" [4]. There seems to be an exponential increase in knowledge, with the target of understanding the origin receding ever faster.

The origin of life (OOL) is unknown and is obscured by the lack of knowledge of the prebiotic conditions that existed as life "developed." "Most of the (bio)chemical processes found within all the living organisms are well understood at the molecular level, whereas the origin of life remains one of the most vexing issues in chemistry, biology, and philosophy" [5]. "The origin of life remains one of the humankind's last great unanswered questions, as well as one of the most experimentally challenging research areas" [6]. Any speculation inevitably involves science as we don't know it. It is metaphysically presumed that since life obviously exists, there must have been a time when non-life developed into life through natural mechanisms. It is also presumed (with no substantiating reasons) that Pasteur's Law of Biogenesis, all life is from life ("Omne vivum ex vivo" [7]), must not have been applicable during life's formation from inanimate material. Pasteur's warning that "Spontaneous generation is a dream" ("La génération spontanée est une chimère" [8]) is perhaps appropriate to consider with the various speculations. It is important to realize that "we don't yet know, but the answers will be coming" isn't a scientific statement, but rather expresses faith in naturalism-of-the-gaps, which is no more scientific than the god-of-the-gaps explanation that most scientists would dismiss out-of-hand.

Speculation on a particular aspect of life may not prove fruitful since all known life is a carefully-orchestrated cybernetic system [9-12]. Without consideration of the origin of cybernetic processes, they are "systems and processes that interact with themselves and produce themselves from themselves" [13]. Michael Polanyi argued that life is not reducible to physical and chemical principles, but rather that, "the information content of a biological whole exceeds that of the sum of its parts" [14]. "A whole exists when it acts like a whole, when it produces combined effects that the parts cannot produce alone" [15]. "Understanding the origin of life requires knowledge not only of the origin of biological molecules such as amino acids, nucleotides and their polymers, but also the manner in which those molecules are integrated into the organized systems that characterize cellular life" [16].

It should be noted that speculation is important within science, since that is the way that new lines of thought are proposed in order to test scenarios for possibility and feasibility [17]. While the dream of becoming a Nobel laureate may encourage wide dissemination of a speculation, it seems appropriate to warn about spreading such speculations outside the scientific community. The public too often views a scientist's speculation as validated science, so that the speculative nature is overlooked. The public may value a scientist's view in much the same way that a movie star's endorsement of a product is seen as important. There seems to be a wide-spread belief in chemical predestination, even though its chief promoter [18] has repudiated its possibility. For example, when signs of water on Mars were discovered, the media proclaimed that there must be life then. Our collective preoccupation with the Search for Extraterrestrial Intelligence [19] illustrates the belief in the inevitability of life.

1. Overview

The approach of this essay will be to consider scenarios for developing the minimal replication and control information ("proto-genome") for a protocell, since even "protolife" would require self-replication and control ability. Note that the ability to use the "genomic" information for functionality is also critical. Metabolic cycles [20], homochirality [21-24], cell membranes [25-26], and other required components will not be the primary thrust, even though all are indirectly controlled by today's genome. An excellent review of the organic chemistry for biomolecular origin is available [27]. Each proponent's scenario will be briefly highlighted, with the primary arguments against the scenario coming from proponents of an alternative scenario, typically as quotes. Finally, we'll examine principles that are almost universally ignored in OOL scenarios, but are in critical need of scientific explanation.

1.1 RNA (Genetics) First Scenarios

A ribosome, "a molecular fossil" [28], can join amino acids without additional enzymes except for those that are imbedded in the ribosome itself to make it a ribozyme (enzymes needed to manufacture tRNAs presumably developed later). "An appeal of the RNA world hypothesis is that it solves the 'chicken and egg' problem; it shows that in an earlier, simplified biota the genotype/replicator and phenotype/catalyst could have been one and the same molecule" [29] (but the RNA/enzyme of a ribozyme is another chicken/egg problem). "RNA appears well suited to have served as the first replicative polymer on this planet" [30]. The origin of the RNA World by stringing together optimistic extrapolations of prebiotic chemistry achievements and experimenter-directed RNA "evolution" (a misnomer) has been described as "the 'Molecular Biologists' Dream ... [and] the prebiotic chemist's nightmare" [31]. An excellent review [32] describes the potential and problems of the RNA world. The "difficulties in nucleobase ribosylation can be overcome with directing, blocking, and activating groups on the nucleobase and ribose … These molecular interventions are synthetically ingenious, but serve to emphasize the enormous difficulties that must be overcome if ribonucleosides are to be efficiently produced by nucleobase ribosylation under prebiotically plausible conditions. This impasse has led many scientists to abandon the idea that a RNA "genome" might have assembled abiotically, and has prompted a search for potential pre-RNA informational molecules" [33]. It has been pointed out that "what is essential, therefore, is a reasonably detailed description, hopefully supported by experimental evidence, of how an evolvable family of cycles might operate. The scheme should not make unreasonable demands on the efficiency and specificity of the various external and internally generated catalysts that are supposed to be involved. Without such a description, acceptance of the possibility of complex non-enzymatic cyclic organizations that are capable of evolution can only be based on faith, a notoriously dangerous route to scientific progress” [20]. The experimenter-directed “side products would have amounted to a fatal and committed step in the synthesis of a nascent proto-RNA. This problem illustrates a difficulty in non-enzymatic polymerization that must be taken into account when considering how the nature of the synthetic routes to and structural identities of early genetic polymers: irreversible linkages are adaptive for an informational polymer only when mechanisms exist to make them conditionally reversible [34].

“No physical law need be broken for spontaneous RNA formation to happen, but the chances against it are so immense, that the suggestion implies that the non-living world had an innate desire to generate RNA

There is no reason to presume that an indifferent nature would not combine units at random, producing an immense variety of hybrid short, terminated chains, rather than the much longer one of uniform backbone geometry needed to support replicator and catalytic functions” [35]. “The RNA molecule is too complex, requiring assembly first of the monomeric constituents of RNA, then assembly of strings of monomers into polymers. As a random event without a highly structured chemical context, this sequence has a forbiddingly low probability and the process lacks a plausible chemical explanation, despite considerable effort to supply one” [36]. “It has been challenging to identify possible prebiotic chemistry that might have created RNA. Organic molecules, given energy, have a well-known propensity to form multiple products, sometimes referred to collectively as ‘tar’ or ‘tholin.’ These mixtures appear to be unsuited to support Darwinian processes, and certainly have never been observed to spontaneously yield a homochiral genetic polymer. To date, proposed solutions to this challenge either involve too much direct human intervention to satisfy many in the community, or generate molecules that are unreactive ‘dead ends’ under standard conditions of temperature and pressure” [27].

Some [27, 33] believe that inorganic crystals or clay served as a template for the original RNA. The “replication of clay ‘information’ has remained hypothetical, and transfer of replicated clay properties to nucleic acids even more so” [29]. Crystals contain a very small quantity of information in their regular structures, so that any significant information would have to be in irregularities. How would inanimate nature produce those irregularities to serve as templates for functional information in replicative polymers?

"The reaction system... is a purified reconstituted system in which all of the components and their concentrations are defined. The number of components is amazingly large, yet this is one of the simplest encapsulated systems for carrying out protein translation and RNA replication. With regard to the origin of life, the first living systems would have had functionally identical translation and replication systems, but they must have been simpler and contained machinery for nutrient transport. The complexity of our system implies that extant translation machinery has become highly sophisticated during the evolutionary process" [16].

1.2 Metabolism-First Scenarios

Metabolism-first scenarios involve development of a self-replicating, self-sustaining chemical system that is able to capture energy and that is contained within a protocell [24] or geothermal vent [38-39]. Perhaps energy transfer used an "osmosis first" paradigm [40, 26]. Unlike RNA first, there is no nucleotide genome to control replication or component construction so that selection would have favored "not the best replicator, but the reaction that sucked in fuel the quickest, denying energy to other chemical processes" [41]. The "bag of chemicals" (composome) presumably would grow until it reaches a size that enables it to divide, with each "daughter" inheriting about half the chemical contents. "The origin of life was marked when a rare few protocells happened to have the ability to capture energy from the environment to initiate catalyzed heterotrophic growth directed by heritable genetic information in the polymers ... The origin of life occurred when a subset of these molecules was captured in a compartment and could interact with one another to produce the properties we associate with the living state" [39]. There have been simulations [42-43] in which the composomes "undergo mutation-like compositional changes" that are claimed to illustrate evolution, but these have never been experimentally observed.

Although metabolism-first avoids the infeasibility of forming functional RNA by chance, "replication of compositional information is so inaccurate that fitter compositional genomes cannot be maintained by selection and, therefore, the system lacks evolvability (i.e., it cannot substantially depart from the asymptotic steady-state solution already built-in in the dynamical equations). We conclude that this fundamental limitation of ensemble replicators cautions against metabolism-first theories of the origin of life" [44]. Concerning the chemical cycles required, "These are chemically very difficult reactions ... One needs, therefore, to postulate highly specific catalysts for these reactions. It is likely that such catalysts could be constructed by a skilled synthetic chemist, but questionable that they could be found among naturally occurring minerals or prebiotic organic molecules…The lack of a supporting background in chemistry is even more evident in proposals that metabolic cycles can evolve to 'life-like' complexity. The most serious challenge to proponents of metabolic cycle theories—the problems presented by the lack of specificity of most non-enzymatic catalysts—has, in general, not been appreciated. If it has, it has been ignored. Theories of the origin of life based on metabolic cycles cannot be justified by the inadequacy of competing theories: they must stand on their own" [20].

2. Major Unresolved Difficulties

Nearly all scenarios presented as science during this author's education using the American Chemical Society's "From Molecules to Man" have been shown to be incorrect by today's science. Scientists need to use much caution during speculative dreaming about mechanisms that can be considered as explanations for the observations that are currently available. Some of the major difficulties requiring scientific explanation will be highlighted in this section

2.1 Physical Science Limitations

What natural interactions produced homochilarity, α-linkage only amino acids, and non-enzymatic peptide bonds and other dehydration reactions in aqueous solutions to produce proteins and RNAs? What physical laws could integrate biochemical pathways and cycles into a formal protometabolic scheme? How did the enzymes required to level life's 10^{19} range of uncatalyzed reactions [45] spontaneously polymerize and self-assemble?

2.2 Formidable Information Science Problems

"Biological information is not a substance ... biological information is not identical to genes or to DNA (any more than the words on this page are identical to the printers ink visible to the eye of the reader). Information, whether biological or cultural, is not a part of the world of substance" [46]. "All the equations of physics taken together cannot describe, much less explain, living systems. Indeed, the laws of physics do not even contain any hints regarding cybernetic processes or feedback control" [10]. The argument for abiogenesis "simply says it happened. As such, it is nothing more than blind belief. Science must provide rational theoretical mechanism, empirical support, prediction fulfillment, or some combination of these three. If none of these three are available, science should reconsider that molecular evolution of genetic cybernetics is a proven fact and press forward with new research approaches which are not obvious at this time" [47]. "The challenge for an undirected origin of such a cybernetic complex interacting computer system is the need to demonstrate that the rules, laws, and theories that govern electronic computing systems and information don't apply to the even more complex digital information systems that are in living organisms. Laws of chemistry and physics, which follow exact statistical, thermodynamic, and spatial laws, are totally inadequate for generating complex functional information or those systems that process that information using prescriptive algorithmic information" [48].

It is important to realize that data generated by regular fluctuations (such as seasons or light/dark cycles) have extremely low information content, offering no explanation for life's functional information. Communication of information requires that both sender and receiver know the arbitrary protocol determined by rules, not law. A functioning protocell would have needed formal organization, not redundant order. Organization requires control, which requires formalism as a reality [Chapt 1]. Each protein is currently the result of the execution of a real computer program running on the genetic operating system. How did inanimate nature write those programs and operating systems? The genome would be useless without the processing systems needed to carry out its prescriptive instructions.

2.3 Over-Simplification of Information Requirements

"Whatever the source of life (which is scientifically unknowable), the alphabet involved with the origin of life, by the necessary conditions of information theory, had to be at least as symbolically complex as the current codon alphabet. If intermediate alphabets existed (as some have speculated), each predecessor also would be required to be at least as complex as its successor, or Shannon's Channel Capacity [49] would be exceeded for information transfer between the probability space of alphabets with differing Shannon capacity. Therefore, life's original alphabet must have used a coding system at least as symbolically complex as the current codon alphabet. There has been no feasible natural explanation proposed to produce such an alphabet since chance or physicality cannot produce functional information or a coding system, let alone a system as complex as that in life" [50]. Coded information has never been observed to originate from physicality. "Due to the abstract character of function and sign systems [semiotics -- symbols and their meaning], life is not a subsystem of natural laws. This suggests that our reason is limited in respect to solving the problem of the origin of life and that we are left accepting life as an axiom... Life express[es] both function and sign systems, which indicates that it is not a subsystem of the [physical] universe, since chance and necessity cannot explain sign systems, meaning, purpose, and goals" [51]. "The reductionist approach has been to regard information as arising out of matter and energy. Coded information systems such as DNA are regarded as accidental in terms of the origin of life and that these then led to the evolution of all life forms as a process of increasing complexity by natural selection operating on mutations on these first forms of life" [52]. "From the information perspective, the genetic system is a pre-existing operating system of unknown origin that supports the storage and execution of a wide variety of specific genetic programs (the genome applications), each program being stored in DNA. DNA is a storage medium, not a computer, that specifies all information needed to support the growth, metabolism, parts manufacturing, etc. for a specific organism via gene subprograms" [50].

There are many features in current life that are extremely difficult to envision as arising from a protocell. The smallest genome (though not autonomous) found so far is in "the psyllid symbiont Carsonella ruddii, which consists of a circular chromosome of 159,662 base pairs... The genome has a high coding density (97%) with many overlapping genes and reduced gene length" [53]. “The origin and evolution of overlapping genes are still unknown” [54]. Since they are prevalent in the simplest known genome, a big question is how and why did overlapping genes arise? Recently, sub-coded information [55] and a second genetic code [56] characterizing alternative splicing have been discovered. Various transcribed RNAs are mixed and matched and spliced into mRNAs for specifying protein construction and other controls. MicroRNAs regulate large networks of genes by acting as master control switches [57]. Tiny polypeptides (with 11-32 amino acids) can function as "micro-protein" gene expression regulators [58]. Were these features required initially, or by what interactions of nature did they arise later?

Scientists are investigating “the organization of information in genomes and the functional roles that non-protein coding RNAs play in the life of the cell. The most significant challenges can be summarized by two points: a) each cell makes hundreds of thousands of different RNAs and a large percent of these are cleaved into shorter functional RNAs demonstrating that each region of the genome is likely to be multifunctional and b) the identification of the functional regions of a genome is difficult because not only are there many of them but because the functional RNAs can be created by taking sequences that are not near each other in the genome and joining them together in an RNA molecule. The order of these sequences that are joined together need not be sequential. The central mystery is what controls the temporal and coordinated expression of these RNAs” [59]. "It is very difficult to wrap your head around how big the genome is and how complicated ... It's very confusing and intimidating ... The coding parts of genes come in pieces, like beads on a string, and by splicing out different beads, or exons, after RNA copies are made, a single gene can potentially code for tens of thousands of different proteins, although the average is about five ... It's the way in which genes are switched on and off, though, that has turned out to be really mind-boggling, with layer after layer of complexity emerging" [60]. When and how did these features arise? Were any present in the first life?

2.4 Scientific Hypotheses Requiring Falsification

In addition to falsifying Shannon Capacity Theorem [49] if a proposed original information system isn’t as complex as today’s codon-based system, the following testable null hypotheses (proposed in peer-reviewed papers) may require falsification. No scenario should be accepted as science if it violates one or more of these unfalsified null hypotheses [60-61, 11-12].

#1 Stochastic ensembles of physical units cannot program algorithmic/cybernetic function.

#2 Dynamically-ordered sequences of individual physical units (physicality patterned by natural law causation) cannot program algorithmic/cybernetic function.

#3 Statistically weighted means (e.g., increased availability of certain units in the polymerization environment) giving rise to patterned (compressible) sequences of units cannot program algorithmic/cybernetic function.

#4 Computationally successful configurable switches cannot be set by chance, necessity, or any combination of the two, even over large periods of time.

#5 Self-ordering phenomena cannot generate cybernetic organization.

#6 Randomness cannot generate cybernetic organization.

#7 PI (prescriptive information [12]) cannot be generated from/by the chance and necessity of inanimate physicodynamics.

#8 PI cannot be generated independent of formal choice contingency.

#9 Formal algorithmic optimization, and the conceptual organization that results, cannot be generated independent of PI.

#10 Physicodynamics cannot spontaneously traverse The Cybernetic Cut [11]: physicodynamics alone cannot organize itself into formally functional systems requiring algorithmic optimization computational halting, and circuit integration.

3. Could a Protocell Live and Reproduce Without a "Genome?"

Assuming that the problems highlighted in the previous sections can be overcome (including falsifications of 2.4), this section will discuss the key topic of this essay. The protocell will be assumed to have an appropriate boundary (membrane, microtubule, etc.) that separates the "living" protocell from its environment. This section will highlight what would be required of a “proto-genome,” without regard as to whether such a “genome” is feasible (not operationally falsified). “There seems to be little general agreement as to how the molecular apparatus needed to implement genetics within a cell could have come about. In fact, there seems to be nothing but puzzlement on such questions with virtually no chemically founded suggestions being made at all” [63]. We will be examining the functional requirements of the proto-genome, as opposed to hypothetical implementations. A proto-genome may have little resemblance to today’s DNA-based genome since it will be assumed that life’s origin didn’t involve DNA. Consequently, we will be attempting to examine life as we don’t know it, an exercise that should always be accompanied by healthy scientific skepticism.

It is important to realize that John von Neumann proposed and proved the requirements for a self-replicating automaton long before the discovery of DNA’s information [64]. A self-reproducing system must contain the necessary components of any computer system, as well as the program for its own construction with the hardware needed to accomplish that construction.

3.1 Replication Requirements

A mechanism is needed to divide the protocell into two approximately equal daughters with each daughter being capable of growth and eventual division for exponential population potential. The “proto-genome” with its processing system must replicate itself, along with all cellular controls (functional information and senders/receivers/processors) into each daughter. Unless the “proto-genome” has replisome capabilities included in the “proto-genome” rather than a separate enzyme, the self-contained capability is required to duplicate all other needed components for “life” with high fidelity. Each daughter also needs a replicated (or split) cell boundary.

Science knows that the current replication hardware and software requires all the components to be fully functional for replication to occur at all. All known errors during replication result in a decrease of both Shannon and functional information [65], usually producing a cell that is no longer able to reproduce. Reliable replication is fundamental to life, a characteristic lacking in composomes [44].

3.2 Control Requirements

Controlled chemical metabolic networks are needed that can selectively admit "fuel" (redox, heat, photons, etc.) into the cell and process the "fuel" to harness the energy for growth, reproduction, manufacturing of needed components that can't migrate in, and other useful work. Both sender and receiver of the each control signal are needed, along with knowledge of the protocol rules for correct communication. The manufacturing control for needed cellular components would probably require enzymatic functionality for polymerization, along with producing homochiral components. In addition, control is required for cell division. Without control, organization (as opposed to self-ordering) is impossible, and functionality would disintegrate, with "tar" a likely result.

Cellular control is a cybernetic process, so all of the requirements of the first eight chapters need instantiation into the protocell. While the proto-genome may contain the control instructions, those instructions must be read by other components (unless the proto-genome has expanded capabilities so that it can read itself), and communicated reliably (using "agreed upon" arbitrary protocols between sender and receiver, source and destination) to the components effecting the control operations. This is not an easily-dismissed prerequisite since control in known life is critical to make the chemical components "alive." In addition, mere physicodynamic constraints cannot generate formal biological controls [66].

3.3 Evolvability Requirements

The system would have to be capable of accurate duplication, but capable of gradual changes that would permit evolution to life-as-we-know-it. A robust information structure that can be self-maintained (including error-correction), such as in a long genetic polymer, would be required. The feasibility of formation of such a polymer has yet to be shown with any prebiotic mixture proposed to date. The enzyme- and template-independent 120-mer polymers recently generated in water at high temperatures [67] are non-informational homopolymers similar to those adsorbed onto montmorillonite clay surfaces [68]. The aqueous polymers are also cyclic and require some experimenter engineering to achieve 120 mer length.

The proto-genome would also need to be able to effect highly accurate duplication of the entire proto-cell, with only an occasional "error" that could produce a very similar proto-cell, still possessing all three of the requirements in section 3. The proto-genome, along with all the proto-cell components, would need to have a feasible path to eventually produce cells with the functional complexity of today's life. It does little good to speculate a "simple" initial system unless there are feasible scenarios that can traverse from the proposed initial system to life as we know it, including coded information and other features highlighted previously. For example, one could envision dipping a finger into a bottle of ink and flicking the ink toward a white sheet would eventually produce a pattern that looks like an English letter. That would not explain the formal rules and meaningful syntax of letters that you are currently observing in this book, however.

4. Conclusions

While scenarios for the first cell can be envisioned purely from physicality, a "proto-genome" introduces cybernetic aspects that can have no origination from inanimate material. In particular, organization, prescriptive information, and control require traversing The Cybernetic Cut on a one-way CS (Configurable Switch) Bridge [11] that allows traffic only from formalism to physicality. Just as formalism needs recognition as reality, it is also critical to recognize the limits of physical science, such as physics and chemistry, whose spontaneous inanimate mass/energy interaction behavior is constrained by laws, not formal controls. Initial starting constraints chosen by an experimenter become controls for an experiment, but those chosen constraints are instantiations into physicality of nonphysical formalisms.

Life is an intersection of physical science and information science. Both domains are critical for any life to exist, and each must be investigated using that domain's principles. Yet most scientists have been attempting to use physical science to explain life's information domain, a practice that has no scientific justification. Since the chemistry and physics of life are controlled by prescriptive information (not just constrained by laws), biology is really an information science, not a physical science.

References

1. Haeckel E 2004, The Evolution of Man, Translation (original 1911), p49.
2. Darwin C 1871, http://darwin-online.org.uk/content/frameset?viewtype=side&itemID=F1452.3&pageseq=30
3. Miller SL 1953, "Production of Amino Acids Under Possible Primitive Earth Conditions," Science: 117, p528.
4. Hayden E 2010, "Human Genome at Ten: Life is Complicated," Nature 464, 3/31/10, p664-667.
5. Stochel G, Brindell M, Macyk W, Stasicka W, & Szacilowski K 2009, Bioinorganic Photochemistry (West Sussex, England: John Wiley & Sons,), p109.
6. Miller SL & Cleaves HJ 2007, "Prebiotic Chemistry on the Primitive Earth" in Isidore Rigoutsos and Gregroy Stephanopoulos, eds., Systems Biology Volume 1: Genomics (New York: Oxford University Press), 3.
7. Encyclopaedia Britannica 1902, 10th Edition.
8. Pasteur L 1862, http://www.pasteur.fr/ip/easysite/go/03b-00000j-0e7/institut-pasteur/histoire/
9. Corning P & Kline S 2000, "Thermodynamics, Information and Life Revisited, Part I: to Be or Entropy," Systems Research, 4/7/00, p273-295.
10. Corning P 2005, Holistic Darwinism, p330.
11. Abel DL 2008, "The 'Cybernetic Cut': Progressing from Description to Prescription in Systems Theory," The Open Cybernetics and Systemics Journal (2), p252-262.
12. Abel DL 2009, "The Biosemiosis of Prescriptive Information," Semiotica, 1/4/09, p1-19.
13. Kauffman L 2007, CYBCON discusstion group 18, 9/20/07, p15.
14. Polanyi M, Quote originally at Michael Polanyi Center site, now at nostalgia.wikipedia.org/wiki/Michael_Polanyi
15. Corning P 2002, "The Re-emergence of 'Emergence': A Venerable Concept in Search of a Theory," Complexity 7(6), p18-30.
16. Ichihashi N, Matsuura T, Kita H, SunamiT, Suzuki H, & Yomo T 2010, "Constructing Partial Models of Cells," Cold Spring Harb Perspect Biol, 4/28/10, 2:a004945.
17. Abel DL 2009, "The Universal Plausibility Metric (UPM) & Principle (UPP)," Theoretical Biology and Medical Modelling, 12/3/09, 6:27.
18. Kenyon D 1969, Biochemical Predestination.
19. SETI Website, setiathome.ssl.berkeley.edu/
20. Orgel L 2008, "The Implausibility of Metabolic Cycles on the Prebiotic Earth," PLoS Biol 6(1), e18.
21. Toxvaerd S 2009, "Origin of Homochirality in Biosystems," Int. J. Mol. Sci., 3/18/09, p1290-1299.
22. Blackmond D 2010, "The Origin of Biological Homochirality," Cold Spring Harb Perspect Biol, 3/10/10, 2:a002147.
23. Lee T & Lin Y 2010, "The Origin of Life and the Crystallization of Aspartic Acid in Water," Crystal Growth & Design 10 (4), p1652-1660.
24. Chown M 2010, "Did Exploding Stars Shatter Life's Mirror?," New Scientist, 5/19/10.
25. Mansy S 2010, "Membrane Transport in Primitive Cells," Cold Spring Harb Perspect Biol, 4/21/10 doi: 10.1101/cshperspect.a002188.
26. Lane N, Allen J, & Martin W 2010, "How Did LUCA Make a Living? Chemiosmosis in the Origin of Life," BioEssays 32, p271–280.
27. Benner S, Kim H, Kim M, & Ricardo A 2010, "Planetary Organic Chemistry and the Origins of Biomolecules," Cold Spring Harb Perspect Biol, 6/1/10.
28. Johnson D & Wang L 2010, "Imprints of the Genetic Code in the Ribosome," The Scripps Research Institute, 3/18/10.

29. Yarus M 2010, "Getting Past the RNA World: The Initial Darwinian Ancestor," 4/21/10, Cold Spring Harb Perspect Biol doi: 10.1101.
30. Cheng L & Unrau P 2010, "Closing the Circle: Replicating RNA with RNA," Cold Spring Harb Perspect Biol, 6/16/10, doi: 10.1101/cshperspect.a002204.
31. Joyce G & Orgel L 1999, "Prospects for Understanding the Origin of the RNA World," in The RNAWorld, 2nd ed., p49–77.
32. Orgel L 2004, "Prebiotic Chemistry and the Origin of the RNA World," Crit.l Rev. in Biochemistry and Molecular Biology: 39, p99–123.
33. Sutherland J 2010, "Ribonucleotides," Cold Spring Harb Perspect Biol, 3/10/10, 2:a005439.
34. Engelhart A & Hud N 2010, "Primitive Genetic Polymers," Cold Spring Harb Perspect Biol, 5/12/10, doi: 10.1101/cshperspect.a002196.
35. Shapiro R 2007, "A Simpler Origin for Life," Scientific American, 2/12/07.
36. Trefil J, Morowitz H, Smith E 2009, "The Origin of Life," American Scientist 97(2), 3-4/09, p206-210.
37. Hazen R & Sverjensky D 2010, "Mineral Surfaces, Geochemical Complexities, and the Origins of Life," Cold Spring Harb Perspect Biol, 4/14/10, 2:a002162.
38. Schrum J, Zhu T, & Szostak J 2010, 5/19/10, "The Origins of Cellular Life," Cold Spring Harb Perspect Biol doi: 10.1101/cshperspect.a002212.
39. Deamer D & Weber A 2010, "Bioenergetics and Life's Origins," Cold Spring Harb Perspect Biol, 1/13/10, 2:a004929.
40. Luisi, P, Ferri F, et al. 2006, "Approaches to semi-synthetic minimal cells: a review," Naturwissenschaften 93, p1-13.
41. Russell M 2009, as reported by John Whitfield in "Nascence man," Nature 459, 5/21/09.
42. Segre D, Ben-Eli D, & Lancet D 2000, "Compositional Genomes: Prebiotic Information Transfer in Mutually Catalytic Noncovalent Assemblies," PNAS 97 (8), 4/11/00, p4112–4117.
43. Shenhav B, Oz A, & Lancet D 2007, "Coevolution of Compositional Protocells and Their Environment," Phil. Trans. R. Soc. B 362, p1813-1819.
44. Vasas V, Szathmáry E, & Santos M 2010, "Lack of Evolvability in Self-sustaining Autocatalytic Networks Constrains Metabolism-first Scenarios for the Origin of Life," PNAS, 2/11/10, www.pnas.org/content/107/4/1470.
45. Lad C, Williams N, & Wolfenden R 2003, "The Rate of Yydrolysis of Phosphomonoester Dianions and the Exceptional Catalytic Proficiencies of Protein and Inositol Phosphatases," PNAS: 100 (10), 5/13/03, p5607-5610.
46. Hoffmeyer J & Emmeche C 2005, "Code-Duality and the Semiotics of Nature," J. Biosemiotics (1), p37-64.
47. Trevors JT & Abel DL 2004, "Chance and Necessity Do Not Explain the Origin of Life," Cell Biology International: 28, p729-739.
48. Johnson DE 2009/2010, Probability's Nature and Nature's Probability: A Call to Scientific Integrity, p48.
49. Shannon C 1948, "A Mathematical Theory of Communication," Bell System Technical Journal: 27, July & October, p379-423 & 623-656.
50. Johnson DE 2010, Programming of Life, p37&49.
51. Voie A 2006, "Biological Function and the Genetic Code are Interdependent," Chaos, Solitons and Fractals: 28(4), p1000-1004.
52. McIntosh A 2009, "Entropy, Free Energy and Information in Living Systems," International Journal of Design & Nature and Ecodynamics 4 (4), p351-385.
53. Nakabachi A, Yamashita A, Toh H, Ishikawa H, Dunbar H, Moran N, & Hattori M 2006, "The 160-Kilobase Genome of the Bacterial Endosymbiont Carsonella," Science: 314 (5797), 10/13/06, p267.
54. Veeramachaneni V, Makalowski1 W, Galdzicki M, Sood R, & Makalowska I 2004, "Mammalian Overlapping Genes: The Comparative Perspective," Genome Res.: 14, p280-286.

55. Cannarozzi G, Schraudolph N, Faty M, von Rohr P, Friberg M, Roth A, Gonnet P, Gonnet G, & Barral Y 2010, “Role for Codon Order in Translation Dynamics,” Cell 141, 4/16/10, p355-367.
56. Barash Y, Calarco J, Gao W, Pan Q, Wang X, Shai O, Blencowe B, & Frey B 2010, “Deciphering the Splicing Code,” Nature, 5/6/10, p53-9.
57. Lieberman J 2010, “Master of the Cell,” The Scientist, 4/1/10, p42.
58. Kondo T, Plaza S, Zanet S, Benrabah E, Valenti P, Hashimoto Y, Kobayashi S, Payre F, Kageyama Y 2010, “Small Peptides Switch the Transcriptional Activity of Shavenbaby During Drosophila Embryogenesis,” Science 329, 7/16/10, p336-339.
59. Gingeras T, www.desdeelexilio.com/2010/06/28/epigenetica- entrevista-a-thomas-gingeras/
60. Le Page M 2010, "Genome at 10: A Dizzying Journey into Complexity," New Scientist, 6/16/10.
61. Abel D & Trevors J 2005, "Three subsets of sequence complexity and their relevance to biopolymeric information," Theoretical Biology and Medical Modelling, 8/11/05, 2:29.
62. Abel D & Trevors J 2006, "Self-Organization vs Self-Ordering Events in Life-Origin Models," Physics of Life Reviews (3), p211-228.
63. Yana K, Fanga G, Bhardwaja N, Alexandera R, & Gersteinb M 2010,“Comparing Genomes to Computer Operating Systems in Terms of the Topology and Evolution of Their Regulatory Control Networks,” www.pnas.org/cgi/doi/10.1073/pnas.0914771107.
64. von Neumann J, Theory of Self-Reproducing Automata, 1966.
65. Abel DL 2009, "The GS (genetic selection) Principle," Frontiers in Bioscience (14), 1/1/09, p2959-2969.
66. Abel, DL 2010, “Constraints vs. Controls,” Open Cybernetics and Systemics Journal, 4, p14-27.
67. Costanzo G, Pino S, Ciciriello F, Di Mauro E 2009, “RNA: Processing and Catalysis: Generation of Long RNA Chains in Water,” J. Biol. Chem., 284, p33206-33216.
68. Ferris JP 2002, “Montmorillonite Catalysis of 30-50 Mer Oligonucleotides: Laboratory Demonstration of Potential Steps in the Origin of the RNA World,” Origins of Life and Evolution .

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Chapter 11: The Universal Plausibility Metric (UPM) & Principle (UPP)*

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Abstract: Mere possibility is not an adequate basis for asserting scientific plausibility. A precisely defined universal bound is needed beyond which the assertion of *plausibility,* particularly in life-origin models, can be considered operationally falsified. But can something so seemingly relative and subjective as plausibility ever be quantified? Amazingly, the answer is, "Yes." A method of objectively measuring the plausibility of any chance hypothesis (The Universal Plausibility Metric [UPM]) is presented. A numerical inequality is also provided whereby any chance hypothesis can be definitively falsified when its UPM metric of ξ is < 1 (The Universal Plausibility Principle [UPP]). Both UPM and UPP pre-exist and are independent of any experimental design and data set. No low-probability hypothetical plausibility assertion should survive peer-review without subjection to the UPP inequality standard of formal falsification ($\xi < 1$).

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Introduction: The seemingly subjective liquidity of "plausibility"

Are there any *objective* standards that could be applied to evaluate the seemingly subjective notion of *plausibility*? Can something so psychologically relative as plausibility ever be quantified?

Our skepticism about defining a precise, objective Universal Plausibility Metric (UPM) stems from a healthy realization of our finiteness [1], subjectivity [2], presuppositional biases [3, 4], and epistemological problem [5]. We are rightly wary of absolutism. The very nature of probability theory emphasizes gray-scales more than the black and white extremes of p = 0 or 1.0. Our problem is that extremely low probabilities can only asymptotically approach impossibility. An extremely unlikely event's probability always remains at least slightly > 0. No matter how many orders of magnitude is the negative exponent of an event's probability, that event or scenario technically cannot be considered impossible. Not even a Universal Probability Bound [6-8] seems to establish absolute theoretical impossibility. The fanatical pursuit of absoluteness by finite subjective knowers is considered counterproductive in post modern science. Open-mindedness to all possibilities is encouraged [9].

But at some point our reluctance to exclude *any* possibility becomes stultifying to operational science [10]. Falsification is critical to narrowing down the list of serious possibilities [11]. Almost all hypotheses are possible. Only a few of them wind up being helpful and scientifically productive. Just because a hypothesis is possible should not grant that hypothesis scientific respectability. More attention to the concept of "infeasibility" has been suggested [12]. Millions of dollars in astrobiology grant money have been wasted on scenarios that are possible, but plausibly bankrupt. The question for scientific methodology should *not* be, "Is this scenario possible?" The question should be, "Is this possibility a *plausible* scientific hypothesis?" One chance in 10^{200} is theoretically possible, but given maximum cosmic probabilistic resources, such a possibility is hardly plausible. With funding resources rapidly drying up, science needs a foundational principle by which to falsify a myriad of theoretical possibilities that are not worthy of serious scientific consideration and modeling.

Proving a theory is considered technically unachievable [11]. Few bench scientists realize that falsification has also been shown by philosophers of science to be at best technically suspect [13]. Nevertheless, operational science has no choice but to proceed primarily by a process of elimination through practical falsification of competing models and theories.

Which model or theory best corresponds to the data? [14 (pg. 32-98)] [8]. Which model or theory best predicts future interactions? Answering these questions is made easier by eliminating implausible possibilities from the list of theoretical possibilities. Great care must be taken at this point, especially given the many non-intuitive aspects of scientifically addressable reality. But operational science must proceed on the basis of best-thus-far tentative knowledge. The human epistemological problem is quite real. But we cannot allow it to paralyze scientific inquiry.

If it is true that we cannot *know* anything for certain, then we have all the more reason to proceed on the basis of the greatest "*plausibility* of belief" [15-19]. If human mental constructions cannot be equated with objective reality, we are all the more justified in pursuing the greatest likelihood of correspondence of our knowledge to the object of that knowledge—presumed ontological being itself. Can we prove that objectivity exists outside of our minds? No. Does that establish that objectivity does not exist outside of our minds? No again. Science makes its best progress based on the axioms that 1) an objective reality independent of our minds does exist, and 2) scientists' collective knowledge can progressively correspond to that objective reality. The human epistemological problem is kept in its proper place through a) double-blind studies, b) groups of independent investigators all repeating the same experiment, c) prediction fulfillments, and d) the application of pristine logic (taking linguistic fuzziness into account), and e) the competition of various human ideas for best correspondence to repeated independent observations.

The physical law equations and the deductive system of mathematical rules that govern the manipulations of those equations are all formally absolute. But the axioms from which formal logic theory flows, and the decision of when to consider mathematical equations universal "laws" are not absolute. Acceptance of mathematical axioms is hypothetico-deductively relative. Acceptance of physical laws is inductively relative. The *pursuit* of correspondence between presumed objective reality and our knowledge of objective reality is laudable in science. But not even the axioms of mathematics or the laws of physics can be viewed as absolute. Science of necessity proceeds tentatively on the basis of best-thus-far subjective knowledge. At some admittedly relative point, the scientific community agrees by consensus to declare certain formal equations to be reliable descriptors and predictors of future physicodynamic interactions. Eventually the correspondence level between our knowledge and our repeated observations of presumed objective reality is considered *adequate* to make a tentative *commitment* to the veracity of an axiom or universal law until they are proven otherwise.

The same standard should apply in falsifying ridiculously implausible life-origin assertions. Combinatorial imaginings and hypothetical scenarios can be endlessly argued simply on the grounds that they are theoretically possible. But there is a point beyond which arguing the plausibility of an absurdly low probability becomes *operationally* counterproductive. That point can actually be quantified for universal application to all fields of science, not just astrobiology. Quantification of a Universal *Plausibility* Metric (UPM) and application of the Universal *Plausibility* Principle (UPP) inequality test to that specific UPM provides for definitive, unequivocal falsification of scientifically unhelpful and functionally useless hypotheses. When the UPP is violated, declaring falsification of that highly implausible notion is just as justified as the firm commitment we make to any mathematical axiom or physical "law" of motion.

1. Universal Probability Bounds

"Statistical prohibitiveness" in probability theory and the physical sciences has remained a nebulous concept for far too long. The importance of probabilistic resources as a context for consideration of extremely low probabilities has been previously emphasized [20 (pg. 13-17)] [6-8, 21]. Statistical prohibitiveness cannot be established by an exceedingly low probability alone [6]. Rejection regions and probability bounds need to be established independent of (preferably prior to) experimentation in any experimental design. But the setting of these zones and bounds is all too relative and variable from one experimental design to the next. In the end, however, probability is not the critical issue. The plausibility of hypotheses is the real issue. Even more important is the question of whether we can ever operationally falsify a preposterous but theoretically possible hypothesis.

The Universal Probability Bound (UPB) [6, 7] quantifies the maximum cosmic probabilistic resources (Ω, upper case omega) as the context of evaluation of any extremely low probability event. Ω corresponds to the maximum number of possible probabilistic trials (quantum transitions or physicochemical interactions) that could have occurred in cosmic history. The value of Ω is calculated by taking the product of three factors:

1) The number of seconds that have elapsed since the Big Bang (10^{17}) assumes a cosmic age of around 14 billion years. 60 sec/min X 60 min/hr X 24 hrs/day X 365 days per year X 14 billion years = 4.4×10^{17} seconds since the Big Bang.

2) The number of possible quantum events/transitions per second is derived from the amount of time it takes for light to traverse the minimum unit of distance. The minimum unit of distance (a quantum of space) is Planck length (10^{-33} centimeters). The minimum amount of

> time required for light to traverse the Plank length is Plank time (10^{-43} seconds) [6, 7, 8, pg 215-217]. Thus a maximum of 10^{43} quantum transitions can take place per second. Since 10^{17} seconds have elapsed since the Big Bang, the number of possible quantum transitions since the Big Bang would be 10^{43} x 10^{17} = 10^{60}.
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> 3) Sir Arthur Eddington's estimate of the number of protons, neutrons and electrons in the observable cosmos (10^{80}) [22] has been widely respected throughout the scientific literature for decades.
>
> Some estimates of the total number of elementary particles have been slightly higher. The Universe is 95 billion light years (30 gigaparsecs) across. We can convert this to cubic centimeters using the equation for the volume of a sphere (5 x 10^{86} cc). If we multiply this times 500 particles (100 neutrinos and 400 photons) per cc, we would get 2.5 x 10^{89} elementary particles in the visible universe.
>
> A Universal [6, 7]Probability Bound could therefore be calculated by the product of these three factors: 10^{17} x 10^{43} x 10^{80} = 10^{140}
>
> If the highest estimate of the number of elementary particles in the Universe is used (e.g., 10^{89}), the UPB would be 10^{149}.

The UPB's discussed above are *the highest calculated universal probability bounds ever published by many orders of magnitude* [7, 8]. They are the most permissive of (favorable to) extremely low-probability plausibility assertions in print [6] [8 (pg. 216-217)]. All other proposed metrics of probabilistic resources are far less permissive of low-probability chance-hypothesis plausibility assertions. Emile Borel's limit of cosmic probabilistic resources was only 10^{50} [23 (pg. 28-30)]. Borel based this probability bound in part on the product of the number of observable stars (10^{9}) times the number of possible human observations that could be made on those stars (10^{20}). Physicist Bret Van de Sande at the University of Pittsburgh calculates a UPB of 2.6 X 10^{92} [8, 24]. Cryptographers tend to use the figure of 10^{94} computational steps as the resource limit to any cryptosystem's decryption [25]. MIT's Seth Lloyd has calculated that the universe could not have performed more than 10^{120} bit operations in its history [26].

Here we must point out that a discussion of the number of cybernetic or cryptographic "operations" is totally inappropriate in determining a prebiotic UPB. Probabilistic combinatorics has nothing to do with "operations." Operations involve choice contingency [27-29]. Bits are "Yes/No" question *opportunities* [30 (pg. 66)], each of which could potentially reduce the total number of combinatorial possibilities (2^{NH} possible biopolymers: see Appendix 1) by half. But of course asking the right question and getting an answer is not a spontaneous physicochemical phenomenon describable by mere probabilistic uncertainty measures [31-33]. Any binary "operation" involves a bona fide decision node [34-36]. An operation is a *formal choice-based function.* Shannon uncertainty measures do not apply to specific choices [37-39]. Bits measure only the number of non-distinct, generic, *potential* binary choices, not actual specific choices [37]. Inanimate nature cannot ask questions, get answers, and exercise choice contingency at decision nodes in response to those answers. Inanimate nature cannot optimize algorithms, compute, pursue formal function, or program configurable switches to achieve integration and shortcuts to formal utility [28]. Cybernetic operations therefore have no bearing whatever in determining universal probability bounds for chance hypotheses.

Agreement on a sensible UPB in advance of (or at least totally independent of) any specific hypothesis, suggested scenario, or theory of mechanism is critical to experimental design. No known empirical or rational considerations exist to preclude acceptance of the above UPB. The only exceptions in print seem to come from investigators who argue that the above UPB is *too permissive* of the chance hypothesis [8, 12]. Faddish acceptance prevails of hypothetical scenarios of extremely low probability simply because they are in vogue and are theoretically possible. Not only a UPB is needed, but a fixed universal mathematical standard of *plausibility* is needed. This is especially true for complex hypothetical scenarios involving joint and/or conditional probabilities. Many imaginative hypothetical scenarios propose constellations of highly cooperative events that are theorized to self-organize into holistic formal schemes. Whether joint, conditional or independent, multiple probabilities must be factored into an overall *plausibility* metric. In addition, a universal plausibility bound is needed to eliminate overly imaginative fantasies from consideration for the best inference to causation.

2. The Universal Plausibility Metric (UPM)

To be able to definitively falsify ridiculously implausible hypotheses, we need first a Universal *Plausibility* Metric (UPM) to assign a numerical plausibility value to each proposed hypothetical scenario. Second, a Universal *Plausibility* Principle (UPP) inequality is needed as plausibility bound of this measurement for falsification evaluation. We need a cut-off point beyond which no extremely low probability scenario can be considered a "*scientifical-*

ly respectable" possibility. What is needed more than a probability bound is a *plausibility* bound. Any "possibility" that exceeds the ability of its probabilistic resources to generate should immediately be considered a "*functional non-possibility*," and therefore an implausible scenario. While it may not be a theoretically absolute impossibility, if it exceeds its probabilistic resources, it is a gross understatement to declare that such a proposed scenario is simply not worth the expenditure of serious scientific consideration, pursuit, and resources. Every field of scientific investigation, not just biophysics and life-origin science, needs the application of the same independent test of credibility to judge the plausibility of its hypothetical events and scenarios. The application of this standard should be an integral component of the scientific method itself for all fields of scientific inquiry.

To arrive at the UPM, we begin with the maximum available probabilistic resources discussed above (Ω, upper case Omega) [6, 7]. But Ω could be considered from a quantum or a classical molecular/chemical perspective. Thus this paper proposes that the Ω quantification be broken down first according to the Level (L) or perspective of physicodynamic analysis (${}^{L}\Omega$), where the perspective at the quantum level is represented by the superscript "q" (${}^{q}\Omega$) and the perspective at the classical level is represented by "c" (${}^{c}\Omega$). Each represents the maximum probabilistic resources available at each level of physical activity being evaluated, with the total number of quantum transitions being much larger than the total number of "ordinary" chemical reactions since the Big Bang.

Second, the maximum probabilistic resources ${}^{L}\Omega$ (${}^{q}\Omega$ for the quantum level and ${}^{c}\Omega$ for classical molecular/chemical level) can be broken down even further according to the astronomical subset being addressed using the general subscript "A" for Astronomical: ${}^{L}\Omega_A$ (representing both ${}^{q}\Omega_A$ and ${}^{c}\Omega_A$). The maximum probabilistic resources can then be measured for each of the four different specific environments of each ${}^{L}\Omega$, where the general subscript A is specifically enumerated with "u" for universe, "g" for our galaxy, "s" for our solar system, and "e" for earth:

Universe	${}^{L}\Omega_u$	
Galaxy	${}^{L}\Omega_g$	
Solar System	${}^{L}\Omega_s$	
Earth	${}^{L}\Omega_e$	(${}^{L}\Omega_e$ excludes meteorite and panspermia inoculations)

To include meteorite and panspermia inoculations in the earth metrics, we use the Solar System metrics ${}^{L}\Omega_s$ (${}^{q}\Omega_s$ and ${}^{c}\Omega_s$).

As examples, for quantification of the maximum probabilistic resources at the quantum level for the astronomical subset of our galactic phase space, we would use the ${}^{q}\Omega_{g}$ metric. For quantification of the maximum probabilistic resources at the ordinary classical molecular/chemical reaction level in our solar system, we would use the ${}^{c}\Omega_{s}$ metric.

The most permissive UPM possible would employ the probabilistic resources symbolized by ${}^{q}\Omega_{u}$ where both the quantum level perspective and the entire universe are considered.

The sub division between the ${}^{L}\Omega_{A}$ for the quantum perspective (quantified by ${}^{q}\Omega_{A}$) and that for the classical molecular/chemical perspective (quantified by ${}^{c}\Omega_{A}$), however, is often not as clear and precise as we might wish. Crossovers frequently occur. This is particularly true where quantum events have direct bearing on "ordinary" chemical reactions in the "everyday" classical world. If we are going to err in evaluating the plausibility of any hypothetical scenario, let us err in favor of maximizing the probabilistic resources of ${}^{L}\Omega_{A}$. In cases where quantum factors seem to directly affect chemical reactions, we would want to use the four quantum level metrics of ${}^{q}\Omega_{A}$ (${}^{q}\Omega_{u}$ ${}^{q}\Omega_{g}$, ${}^{q}\Omega_{s}$ and ${}^{q}\Omega_{e}$) to preserve the plausibility of the lowest-probability explanations.

3. Quantification of the Universal *Plausibility* Metric (UPM)

We keep italicizing plausibility because of prior experience with readers confusing the UPM with a probability measure. The UPM is *not* a probability measure. It is a plausibility measure. The computed Universal Plausibility Metric (UPM) objectively quantifies the level of plausibility of any chance hypothesis or theory. The UPM employs the symbol ξ (Xi, pronounced *zai* in American English, s*ai* in UK English, *ksi* in modern Greek) to represent the computed UPM according to the following equation:

$$\xi = \frac{f\,{}^{L}\Omega_{A}}{\omega} \qquad \text{Equation 1}$$

where *f* represents the number of *functional* objects/events/scenarios that are known to occur out of all possible combinations (lower case omega, ω) (e.g., the number [*f*] of functional protein family members of varying sequence known to occur out of sequence space [ω]), and ${}^{L}\Omega_{A}$ (upper case Omega, Ω) represents the total probabilistic resources for any particular probabilistic context. The "L" superscript context of Ω describes which perspective of analysis, whether quantum (q) or a classical (c), and the "A" subscript context of Ω enumerates which subset of astronomical phase space is being evaluated: "u" for universe, "g" for our galaxy, "s" for our solar system, and "e" for earth. Note that the basic generic UPM (ξ) equation's form remains constant despite changes in the variables of levels of perspective (L: whether q or c) and astronomic subsets (A: whether u, g, s, or e).

The calculations of probabilistic resources in ${}^{L}\Omega_{A}$ can be found in Appendix 2. Note that the upper and lower case omega symbols used in this equation are *case sensitive* and each represents a completely different phase space.

The UPM from both the quantum (${}^{q}\Omega_{A}$) and classical molecular/chemical (${}^{c}\Omega_{A}$) perspectives/levels can be quantified by Equation 1. This equation incorporates *the number of possible transitions or physical interactions that could have occurred since the Big Bang.* Maximum quantum-perspective probabilistic resources ${}^{q}\Omega_{u}$ were enumerated above in the discussion of a UPB [6, 7] [8 (pg. 215-217)]. Here we use basically the same approach with slight modifications to the factored probabilistic resources that comprise Ω.

Let us address the quantum level perspective (q) first for the entire universe (u) followed by three astronomical subsets: our galaxy (g), our solar system (s) and earth (e).

Since approximately 10^{17} seconds have elapsed since the Big Bang, we factor that total time into the following calculations of quantum perspective probabilistic resource measures. Note that the difference between the age of the earth and the age of the cosmos is only a factor of 3. A factor of 3 is rather negligible at the high order of magnitude of 10^{17} seconds since the Big Bang (versus age of the earth). Thus, 10^{17} seconds is used for all three astronomical subsets:

${}^{q}\Omega_{u}$ = Universe = 10^{43} trans/sec X 10^{17} secs X 10^{80} protons, neutrons & electrons = 10^{140}

${}^{q}\Omega_{g}$ = Galaxy = 10^{43} X 10^{17} X 10^{67} = 10^{127}

${}^{q}\Omega_{s}$ = Solar System = 10^{43} X 10^{17} X 10^{57} = 10^{117}

${}^{q}\Omega_{e}$ = Earth = 10^{43} X 10^{17} X 10^{42} = 10^{102}

These above limits of probabilistic resources exist within the only known universe that we can repeatedly observe—the only universe that is scientifically addressable. Wild metaphysical claims of an infinite number of cosmoses may be fine for cosmological imagination, religious belief, or superstition. But such conjecturing has no place in hard science. Such claims cannot be empirically investigated, and they certainly cannot be falsified. They violate Ockham's (Occam's) Razor [40]. No prediction fulfillments are realizable.

They are therefore nothing more than blind beliefs that are totally inappropriate in peer-reviewed scientific literature. Such cosmological conjectures are far closer to metaphysical or philosophic enterprises than they are to bench science.

From a more classical perspective at the level of ordinary molecular/chemical reactions, we will again provide metrics first for the entire universe (u) followed by three astronomical subsets, our galaxy (g), our solar system (s) and earth (e).

The classical molecular/chemical perspective makes two primary changes from the quantum perspective. With the classical perspective, *the number of atoms* rather than the number of protons, neutrons and electrons is used. In addition, *the total number of classical chemical reactions that could have taken place since the Big Bang* is used rather than transitions related to cubic light-Planck's. The shortest time any transition requires before a chemical reaction can take place is 10 femtoseconds [41-46]. A femtosecond is 10^{-15} seconds. Complete chemical reactions, however, rarely take place faster than the picosecond range (10^{-12} secs). Most biochemical reactions, even with highly sophisticated enzymatic catalysis, take place no faster than the nano (10^{-9}) and usually the micro (10^{-6}) range. To be exceedingly generous (perhaps overly permissive of the capabilities of the chance hypothesis), we shall use 100 femtoseconds as the shortest chemical reaction time. 100 femtoseconds is 10^{-13} seconds. Thus 10^{13} simple and fastest chemical reactions could conceivably take place per second in the best of theoretical pipe-dream scenarios. The four ${}^{c}\Omega_{A}$ measures are as follows:

$${}^{c}\Omega_{u} = \text{Universe} = 10^{13} \text{ reactions/sec} \times 10^{17} \text{ secs} \times 10^{78} \text{ atoms} = 10^{108}$$

$${}^{c}\Omega_{g} = \text{Galaxy} = 10^{13} \times 10^{17} \times 10^{66} = 10^{96}$$

$${}^{c}\Omega_{s} = \text{Solar System} = 10^{13} \times 10^{17} \times 10^{55} = 10^{85}$$

$${}^{c}\Omega_{e} = \text{Earth} = 10^{13} \times 10^{17} \times 10^{40} = 10^{70}$$

Remember that ${}^{L}\Omega_{e}$ excludes meteorite and panspermia inoculations. To include meteorite and panspermia inoculations, we use the metric for our solar system ${}^{c}\Omega_{S}$.

These maximum metrics of the limit of probabilistic resources are based on the best-thus-far estimates of a large body of collective scientific investigations. We can expect slight variations up or down of our best guesses of the number of elementary particles in the universe, for example. But the basic formula presented as the Universal Plausibility Metric (PM) will never change. The Universal *Plausibility* Principle (UPP) inequality presented below is also immutable and worthy of law-like status. It affords the ability to objectively once and for all falsify not just highly improbable, but ridiculously implausible scenarios. Slight adjustments to the factors that contribute to the value of each ${}^{L}\Omega_{A}$ are straightforward and easy for the scientific community to update through time.

Most chemical reactions take longer by many orders of magnitude than what these exceedingly liberal maximum probabilistic resources allow. Biochemical reactions can take years to occur in the absence of highly sophisticated protein enzymes not present in a prebiotic environment. Even humanly engineered ribozymes rarely catalyze reactions by an enhancement rate of more than 10^5[47-51]. Thus the use of the fastest rate known for any complete chemical reaction (100 femtoseconds) seems to be the most liberal/forgiving probability bound that could possibly be incorporated into the classical chemical probabilistic resource perspective ${}^{c}\Omega_{A}$. For this reason, we should be all the more ruthless in applying the UPP test of falsification presented below to seemingly "far-out" metaphysical hypotheses that have no place in responsible science.

4. Falsification using The Universal Plausibility Principle (UPP)

The Universal Plausibility Principle (UPP) states that *definitive operational falsification* of any chance hypothesis is provided by the inequality of:

$$\xi < 1 \qquad \text{Inequality 1}$$

This definitive operational falsification holds for hypotheses, theories, models, or scenarios at any level of perspective (q or c) and for any astronomical subset (u, g, s, and e). The UPP inequality's falsification is valid whether the hypothesized event is singular or compound, independent or conditional. Great care must be taken, however, to eliminate errors in the calculation of complex probabilities. Every aspect of the hypothesized scenario must have its probabilistic components factored into the one probability (p) that is used in the UPM (See equation 2 below). Many such combinatorial possibilities are joint or conditional. It is not sufficient to factor only the probabilities of each reactant's formation, for example, while omitting the probabilistic aspects of each reactant being presented at the same place and time, becoming available in the required reaction order, or being able to react at all (activated vs. not activated). Other factors must be included in the calculation of probabilities: optical isomers, non-peptide bond formation, many non-biological amino acids that also react [8]. The exact calculation of such probabilities is often not straightforward. But in many cases it becomes readily apparent that whatever the exact multi-factored calculation, the probability "*p*" of the entire scenario easily crosses the plausibility bound provided by the UPP inequality. This provides a definitive objective standard of falsification. When $\xi < 1$, immediately the notion should be considered "not a *scientifically plausible* possibility." A ξ value < 1 should serve as an unequivocal operational falsification of that hypothesis. The hypothetical scenario or theory generating that ξ metric should be excluded from the differential list of possible causes. The hypothetical notion should be declared to be outside the bounds of scientific respectability. It should be flatly rejected as the equivalent of superstition.

f / ω in Equation 1 is in effect the probability of a particular *functional* event or object occurring out of all possible combinations. Take for example an RNA-World model. 23 different functional ribozymes in the same family might arise out of 10^{15} stochastic ensembles of 50-mer RNAs. This would reduce to a probability *p* of roughly 10^{-14} of getting a stochastic ensemble that manifested some degree of that ribozyme family's function.

Thus f / ω in Equation 1 reduces to the equivalent of a probability *p*:

$$\text{UPM} = \xi = p\, {}^{c}\Omega_{e} \qquad \text{Equation 2}$$

where "*p*" represents an extremely low probability of any chance hypothesis that is *asserted to be plausible* given ${}^{L}\Omega_{A}$ probabilistic resources, in this particular case ${}^{c}\Omega_{e}$ probabilistic resources.

As examples of attempts to falsify, suppose we have three different chance hypotheses, each with its own low probability (*p*), all being evaluated from the quantum perspective at the astronomical level of the entire universe (${}^{q}\Omega_{u}$). Given the three different probabilities (p) provided below, the applied UPP inequality for each $\xi = p\, {}^{q}\Omega_{u}$ of each hypothetical scenario would establish definitive operational falsification for one of these three hypothetical scenarios, and fail to falsify two others:

$p = 10^{-140} \text{ X } 10^{140} = 10^{0} = 1$ giving a ξ which is NOT < 1, so NOT falsified

$p = 10^{-130} \text{ X } 10^{140} = 10^{10}$ giving a $\xi > 1$, so NOT falsified

$p = 3.7 \text{ x } 10^{-151} \text{ X } 10^{140} = 3.7 \text{ x } 10^{-11}$ giving a $\xi < 1$, so Falsified

Let us quantify an example of the use of the UPM and UPP to attempt falsification of a chance hypothetical scenario:

Suppose 10^3 *biofunctional* polymeric sequences of monomers (f) exist out of 10^{17} possible sequences in sequence space (ω) all of the same number (N) of monomers. That would correspond to one chance in 10^{14} of getting a functional sequence by chance ($p = 10^3/10^{17} = 1/10^{14} = 10^{-14}$ of getting a functional sequence). If we were measuring the UPM from the perspective of a classical chemical view on earth over the last 5 billion years (${}^c\Omega_e = 10^{70}$), we would use the following UPM equation (#1 above) with substituted values:

$$\xi = \frac{f\,{}^c\Omega_e}{\omega} = \frac{10^3 x 10^{70}}{10^{17}}$$

$$\xi = \frac{10^{73}}{10^{17}} = 10^{56}$$

Since $\xi > 1$, this particular chance hypothesis is shown unequivocally to be plausible and worthy of further scientific investigation.

As one of the reviewers of this manuscript has pointed out, however, we might find the sequence space ω, and therefore the probability space f/ω, to be radically different for abiogenesis than for general physico-chemical reactions. The sequence space ω must include factors such as heterochirality, unwanted non-peptide-bond formation, and the large number of non-biological amino acids present in any prebiotic environment [8, 12]. This greatly increases ω, and would tend to substantially reduce the probability p of naturalistic abiogenesis. Spontaneously biofunctional stochastic ensemble formation was found to be only 1 in 10^{64} when TEM-1 β-lactamase's working domain of around 150 amino acids was used as a model [52]. Function was related to the hydropathic signature necessary for proper folding (tertiary structure). The ability to confer any relative degree of beta-lactam penicillin-like antibiotic resistance to bacteria was considered to define "biofunctional" in this study. Axe further measured the probability of a random 150-residue primary structure producing *any* short protein, despite many allowable monomeric substitutions, to be 10^{-74}. This probability is an example of a scientifically determined p that should be incorporated into any determination of the UPM in abiogenesis models.

5. Don't multiverse models undermine The UPP?

Multiverse models imagine that our universe is only one of perhaps countless parallel universes [53-55]. Appeals to the Multiverse worldview are becoming more popular in life-origin research as the statistical prohibitiveness of spontaneous generation becomes more incontrovertible in a finite universe [56-58]. The term "notion," however, is more appropriate to refer to multiverse speculation than "theory." The idea of multiple parallel universes cannot legitimately qualify as a testable scientific hypothesis, let alone a mature theory. Entertaining multiverse "thought experiments" almost immediately takes us beyond the domain of responsible science into the realm of pure metaphysical belief and conjecture. The dogma is literally "beyond physics and astronomy," the very meaning of the word "metaphysical."

The notion of multiverse has no observational support, let alone repeated observations. Empirical justification is completely lacking. It has no testability: no falsification potential exists. If provides no prediction fulfillments. The non-parsimonious construct of multiverse grossly violates the principle of Ockham's (Occam's) Razor [40]. No logical inference seems apparent to support the strained belief other than a perceived need to rationalize what we know is statistically prohibitive in the only universe that we *do* experience. Multiverse fantasies tend to constitute a back-door fire escape for when our models hit insurmountable roadblocks in the observable cosmos. When none of the facts fit our favorite model, we conveniently create imaginary extra universes that are more accommodating. This is not science. Science is interested in falsification within the only universe that science can address. Science cannot operate within mysticism, blind belief, or superstition. A multiverse may be fine for theoretical metaphysical models. But no justification exists for inclusion of this "dream world" in the sciences of physics and astronomy.

It could be argued that multiverse notions arose only in response to the severe time and space constraints arising out of Hawking, Ellis and Penrose's singularity theorems [59-61]. Solutions in general relativity involve singularities wherein matter is compressed to a point in space and light rays originate from a curvature. These theorems place severe limits on time and space since the Big Bang. Many of the prior assumptions of limitless time and sample space in naturalistic models were eliminated by the demonstration that time and space in the cosmos are quite finite, not infinite. For instance, we only have 10^{17}-10^{18} seconds at most to work with in any responsible cosmological universe model since the Big Bang. Glansdorff makes the point, "Conjectures about emergence of life in an infinite multiverse should not confuse probability with possibility." [62]

Even if multiple physical cosmoses existed, it is a logically sound deduction that linear digital genetic instructions using a representational material symbol system (MSS) [63] cannot be programmed by the chance and/or fixed laws of physicodynamics [27-29, 32, 33, 36-39, 64, 65]. This fact is not only true of the physical universe, but would be just as true in any imagined physical multiverse. Physicality cannot generate nonphysical Prescriptive Information (PI) [29]. Physicodynamics cannot practice formalisms (The Cybernetic Cut) [27, 34]. Constraints cannot exercise formal control unless those constraints are themselves chosen to achieve formal function [28, 66]. Environmental selection cannot select at the genetic level of arbitrary symbol sequencing (e.g., the polymerization of nucleotides and codons). (The GS Principle [Genetic Selection Principle]) [36, 64]. Polymeric syntax (sequencing; primary structure) prescribes future (potential; not-yet-existent) folding and formal function of small RNAs and even DNA. Symbol systems and configurable switch-settings can only be programmed with choice contingency, not chance contingency or fixed law, if nontrivial coordination and formal organization are expected [29, 38]. The all-important determinative sequencing of monomers is completed with rigid covalent bonds before any transcription, translation, or three-dimensional folding begins. Thus, imagining multiple physical universes or infinite time does not solve the problem of the origin of *formal* (nonphysical) biocybernetics and biosemiosis using a linear digital representational symbol system. The source of Prescriptive Information (PI) [29, 35] in a metaphysically presupposed material-only world is closely related to the problem of gene emergence from physicodynamics alone. The latter hurdles remain the number-one enigmas of life-origin research [67].

The main subconscious motivation behind multiverse conjecture seems to be, “Multiverse models can do anything we want them to do to make our models work for us.” We can argue Multiverse models ad infinitum because their potential is limitless. The notion of Multiverse has great appeal because it can explain everything (and therefore nothing). Multiverse models are beyond scientific critique, falsification, and prediction fulfillment verification. They are purely metaphysical.

Multiverse imaginings, therefore, offer no scientific threat whatever to the universality of the UPM and UPP in the only cosmic reality that science knows and investigates.

6. Conclusions

Mere possibility is not an adequate basis for asserting scientific plausibility. Indeed, the practical need exists in science to narrow down lists of possibilities on the basis of objectively quantifiable plausibility.

A numerically defined Universal *Plausibility* Metric (UPM $= \xi$) has been provided in this paper. A numerical inequality of $\xi < 1$ establishes definitive operational falsification of any chance hypothesis (The Universal Plausibility Principle [UPP]). Both UPM and UPP pre-exist and are independent of any experimental design and data set. No low-probability plausibility assertion should survive peer-review without subjection to the UPP inequality standard of formal falsification ($\xi < 1$).

The use of the UPM and application of the UPP inequality to each specific UPM will promote clarity, efficiency and decisiveness in all fields of scientific methodology by allowing operational falsification of ridiculously implausible plausibility assertions. The UPP is especially important in astrobiology and all areas of life-origin research where mere theoretical possibility is often equated erroneously with plausibility. The application of The Universal Plausibility Principle (UPP) precludes the inclusion in scientific literature of wild metaphysical conjectures that conveniently ignore or illegitimately inflate probabilistic resources to beyond the limits of observational science. The UPM and UPP together prevent rapidly shrinking funding and labor resources from being wasted on preposterous notions that have no legitimate place in science. At best, notions with $\xi < 1$ should be considered not only operationally falsified hypotheses, but bad metaphysics on a plane equivalent to blind faith and superstition.

7. Appendix 1

2^{NH} is the "practical" number (high probability group), measured in bits, rather than the erroneous theoretical n^N as is usually published, of all possible biopolymeric sequences that could form, where

N = the number of loci in the string (or monomers in polymer)
n = the number of possible alphabetical symbols that could be used at each locus (4 nucleotides, 64 codons, or 20 amino acids)
H = the Shannon uncertainty at each locus

For a 100 mer biopolymeric primary structure, the number of sequence combinations is actually only 2.69×10^{-6} of the theoretically possible and more intuitive measure of n^N sequences. The reason derives from the Shannon-McMillan-Breiman Theorem [68-71] which is explained in detail by Yockey [72, pg 73-76].

8. Appendix 2

For best estimates of the number of atoms, protons, neutrons and electrons in the universe and its astronomical subsets, see [73].

Simple arithmetic is needed for many of these calculations. For example, the mass of our galaxy is estimated to be around 10^{12} solar masses. The mass of "normal matter" in our galaxy is around 10^{11} solar masses. The mass of the sun is about 2×10^{30} kg. The mass of our solar system is surprisingly not much more than the mass of the sun, still about 2×10^{30} kg. (The Sun contains 99.85% of all the matter in the Solar System, and the planets contain only 0.136% of the mass of the solar system.) The mass of a proton or neutron is 1.7×10^{-27} kg. Thus the number of protons & neutrons in our solar system is around $2 \times 10^{30} / 1.7 \times 10^{-27} = 1.2 \times 10^{57}$. The number of electrons is about half of that, or 0.6×10^{57}. The number of protons, neutrons and electrons in our solar system is therefore around 1.8×10^{57}. The number of protons, neutrons and electrons in our galaxy is around 1.8×10^{68}. We have crudely estimated a total of 100 protons, neutrons and electrons on average per atom. All of these estimates will of course vary some through time as consensus evolves. But adjustments to ${}^{L}\Omega_{A}$ are easily updated with absolutely no change in the Universal Plausibility Metric (UPM) equation or the Universal Plausibility Principle (UPP) inequality. Definitive operational falsification still holds when $\xi < 1$.

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References:

1. Emmeche, C. 2000, Closure, function, emergence, semiosis, and life: the same idea? Reflections on the concrete and the abstract in theoretical biology, Ann N Y Acad Sci, 901, 187-97.
2. Baghramian, M. 2004, *Relativism*. Routledge: London
3. Balasubramanian, P. 1984, *The concept of presupposition: a study*. Radhakrishnan Institute for Advanced Study in Philosophy, University of Madras: [Madras].
4. Beaver, D.I. 2001, *Presupposition and assertion in dynamic semantics*. CSLI Publications; FoLLI: Stanford, Calif.
5. Bohr, N. 1949, Discussion with Einstein on epistemological problems in atomic physics. In *Albert Einstein: Philosopher-Scientist*, Schilpp, P. A., Ed. Library of Living Philosophers: Evanston, IL.
6. Dembski, W. 1998, *The Design Inference: Eliminating Chance Through Small Probabilities*. Cambridge University Press: Cambridge.
7. Dembski, W.A. 2002, *No Free Lunch*. Rowman and Littlefield: New York.
8. Meyer, S.C. 2009, *Signature in the Cell*. Harper Collins: New York.
9. Kuhn, T.S. 1970, *The Structure of Scientific Revolutions*. 2nd 1970 ed., The University of Chicago Press: Chicago.
10. Sokal, A.; Bricmont, J. 1998, *Fashionable Nonsense*. Picador: New York, NY.
11. Popper, K.R. 1972, *The logic of scientific discovery*. 6th impression revised. ed., Hutchinson: London.
12. Johnson, D.E. 2010, *Probability's Nature and Nature's Probability (A call to scientific integrity)*. Booksurge Publishing: Charleston, S.C.
13. Slife, B.; Williams, R. 1995, Science and Human Behavior. In *What's Behind the Research? Discovering Hidden Assumptions in the Behavioral Sciences* Slife, B.Williams, R., Eds. SAGE Publications: Thousand Oaks, CA, Vol. 167–204.
14. Lipton, P. 1991, *Inference to the Best Explanation*. Routledge: New York.
15. Press, S.J.; Tanur, J.M. 2001, *The Subjectivity of Scientists and the Bayesian Approach*. John Wiley & Sons: New York.
16. Congdon, P. 2001, *Bayesian Statistical Modeling*. John Wiley and Sons: New York.
17. Bandemer, H. 1992, *Modeling uncertain data*. 1st ed., Akademie Verlag: Berlin.
18. Corfield, D.; Williamson, J. 2001, Foundations of Bayesianism. Kluwer Academic Publishers: Dorcrecht, p 428.
19. Slonim, N.; Friedman, N.; Tishby, N. 2006, Multivariate Information Bottleneck, Neural Comput., 18, (8) 1739-1789.
20. Fisher, R.A. 1935, *The Design of Experiments*. Hafner: New York.
21. Fisher, R.A. 1956, *Statistical Methods and Statistical Inference*. Oliver and Boyd: Edinburgh.
22. Eddington, A. 1928, *The Nature of the Physical World*. Macmillan: New York.
23. Borel, E. 1962, *Probabilities and Life*. Dover: New York.
24. van de Sande, B. 2006 Measuring complexity in dynamical systems, RAPID II, Biola University, May.
25. Dam, K.W.; Lin, H.S. 1996, Cryptography's Role in Securing the Information Society. National Academy Press: Washington, D.C.
26. Lloyd, S. 2002, Computational capacity of the universe, Phys Rev Lett, 88, 237901-8.
27. Abel, D.L. 2008, 'The Cybernetic Cut': Progressing from description to prescription in systems theory, The Open Cybernetics and Systemics Journal, 2, 234-244 Open access at www.bentham.org/open/tocsj/articles/V002/252TOCSJ.pdf
28. Abel, D.L. 2009, The capabilities of chaos and complexity, Int. J. Mol. Sci., 10, (Special Issue on Life Origin) 247-291 Open access at http://mdpi.com/1422-0067/10/1/247
29. Abel, D.L. 2009, The biosemiosis of prescriptive information, Semiotica, 2009, (174) 1-19.
30. Adami, C. 1998, *Introduction to Artificial Life*. Springer/Telos: New York.
31. Abel, D.L. 2002, Is Life Reducible to Complexity? In *Fundamentals of Life*, Palyi, G.; Zucchi, C.Caglioti, L., Eds. Elsevier: Paris, pp 57-72.
32. Abel, D.L. 2006 Life origin: The role of complexity at the edge of chaos, Washington Science 2006, Headquarters of the National Science Foundation, Arlington, VA
33. Abel, D.L. 2007, Complexity, self-organization, and emergence at the edge of chaos in life-origin models, Journal of the Washington Academy of Sciences, 93, (4) 1-20.
34. Abel, D.L. The Cybernetic Cut [Scirus Topic Page]. http://www.scitopics.com/The_Cybernetic_Cut.html (Last accessed May, 2011).
35. Abel, D.L. Prescriptive Information (PI) [Scirus Topic Page]. http://www.scitopics.com/Prescriptive_Information_PI.html (Last accessed May, 2011).
36. Abel, D.L. 2009, The GS (Genetic Selection) Principle, Frontiers in Bioscience, 14, (January 1) 2959-2969 Open access at http://www.bioscience.org/2009/v14/af/3426/fulltext.htm.

37. Abel, D.L.; Trevors, J.T. 2005, Three subsets of sequence complexity and their relevance to biopolymeric information., Theoretical Biology and Medical Modeling, 2, 29 Open access at http://www.tbiomed.com/content/2/1/29.
38. Abel, D.L.; Trevors, J.T. 2006, Self-Organization vs. Self-Ordering events in life-origin models, Physics of Life Reviews, 3, 211-228.
39. Abel, D.L.; Trevors, J.T. 2007, More than Metaphor: Genomes are Objective Sign Systems. In *BioSemiotic Research Trends*, Barbieri, M., Ed. Nova Science Publishers: New York, pp 1-15
40. Vitányi, P.M.B.; Li, M. 2000, Minimum Description Length Induction, Bayesianism and Kolmogorov Complexity, IEEE Transactions on Information Theory, 46, (2) 446 - 464.
41. Zewail, A.H. 1990, The Birth of Molecules, Scientific American December, 40-46.
42. Zewail, A.H. 1999, The Nobel Prize in Chemistry. For his studies of the transition states of chemical reactions using femtosecond spectroscopy: Press Release. In.
43. Xia, T.; Becker, H.-C.; Wan, C.; Frankel, A.; Roberts, R.W.; Zewail, A.H. 2003, The RNA-protein complex: Direct probing of the interfacial recognition dynamics and its correlation with biological functions, PNAS, 1433099100.
44. Sundstrom, V. 2008, Femtobiology, Annual Review of Physical Chemistry, 59, (1) 53-77.
45. Schwartz, S.D.; Schramm, V.L. 2009, Enzymatic transition states and dynamic motion in barrier crossing, Nat Chem Biol, 5, (8) 551-558.
46. Pedersen, S.; Herek, J.L.; Zewail, A.H. 1994, The Validity of the "Diradical" Hypothesis: Direct Femtoscond Studies of the Transition-State Structures, Science, 266, (5189) 1359-1364.
47. Wiegand, T.W.; Janssen, R.C.; Eaton, B.E. 1997, Selection of RNA amide synthases, Chem Biol, 4, (9) 675-83.
48. Emilsson, G.M.; Nakamura, S.; Roth, A.; Breaker, R.R. 2003, Ribozyme speed limits, RNA, 9, (8) 907-18.
49. Robertson, M.P.; Ellington, A.D. 2000, Design and optimization of effector-activated ribozyme ligases, Nucleic Acids Res, 28, (8) 1751-9.
50. Hammann, C.; Lilley, D.M. 2002, Folding and activity of the hammerhead ribozyme, Chembiochem, 3, (8) 690-700.
51. Breaker, R.R.; Emilsson, G.M.; Lazarev, D.; Nakamura, S.; Puskarz, I.J.; Roth, A.; Sudarsan, N. 2003, A common speed limit for RNA-cleaving ribozymes and deoxyribozymes, Rna, 9, (8) 949-57.
52. Axe, D.D. 2004, Estimating the prevalence of protein sequences adopting functional enzyme folds, J Mol Biol, 341, (5) 1295-315.
53. Barrau, A. 2007, Physics in the multiverse. In CERN Courier, Vol. December.
54. Carr, B. 2007, Universe or Multiverse? Cambridge University Press: Cambridge.
55. Garriga, J.; Vilenkin, A. 2008, Prediction and explanation in the multiverse. In Phys.Rev.D 77:043526,2008.
56. Axelsson, S. 2003, Perspectives on handedness, life and physics, Med Hypotheses, 61, (2) 267-74.
57. Koonin, E.V. 2007, The Biological Big Bang model for the major transitions in evolution, Biol Direct, 2, 21.
58. Koonin, E.V. 2007, The cosmological model of eternal inflation and the transition from chance to biological evolution in the history of life, Biol Direct, 2, 15.
59. Hawking, S.; Ellis, G.F.R. 1973, *The Large Scale Structure of Space-Time*. Cambridge University Press. : Cambridge.
60. Hawking, S. 1988, *A Brief History of Time*. Bantam Books: New York.
61. Hawking, S.; Penrose, R. 1996, *The Nature of Space and Time*. Princeton U. Press: Princeton, N.J.
62. Glansdorff, N.; Xu, Y.; Labedan, B. 2009, The origin of life and the last universal common ancestor: do we need a change of perspective?, Res Microbiol, 160, (7) 522-8.
63. Rocha, L.M. 2001, Evolution with material symbol systems, Biosystems, 60, 95-121.
64. Abel, D.L. The GS (Genetic Selection) Principle [Scirus Topic Page]. http://www.scitopics.com/The_GS_Principle_The_Genetic_Selection_Principle.html (Last accessed May, 2011).
65. Abel, D.L.; Trevors, J.T. 2006, More than metaphor: Genomes are objective sign systems, Journal of BioSemiotics, 1, (2) 253-267.
66. Abel, D.L. 2010, Constraints vs. Controls, Open Cybernetics and Systemics Journal, 4, 14-27 Open Access at http://www.bentham.org/open/tocsj/articles/V004/14TOCSJ.pdf.
67. Origin of Life Science Foundation, I. Origin of Life Prize. http://www.lifeorigin.org
68. Shannon, C. 1948, Part I and II: A mathematical theory of communication, The Bell System Technical Journal, XXVII, (3 July) 379-423.
69. McMillan 1953, The basic theorems of information theory, Ann. Math. Stat., 24, 196-219.
70. Breiman, L. 1957, The individual ergodic theorem of information theory, Ann. Math. Stat., 28, 808-811 [Correction in **31**:809-810].
71. Kinchin, I. 1958, The concept of entropy in probabililty theory. Also, On the foundamental theorems of information theory. In *Mathematical Foundations of Information Theory*, Dover Publications, Inc. : New York.

72. Yockey, H.P. 1992, *Information Theory and Molecular Biology*. Cambridge University Press: Cambridge.
73. Allen, A.N. 2000, *Astrophysical Quantities*. Springer-Verlag: New York.

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Chapter 12: The Formalism > Physicality (F > P) Principle *

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ABSTRACT: The F > P Principle states that "Formalism not only describes, but preceded, prescribed, organized, and continues to govern and predict Physicality." The F > P Principle is an axiom that defines the ontological primacy of formalism in a presumed objective reality that transcends both human epistemology, our sensation of physicality, and physicality itself. The F > P Principle works hand in hand with the Law of Physicodynamic Incompleteness, which states that physicochemical interactions are inadequate to explain the mathematical and formal nature of physical law relationships. Physicodynamics cannot generate formal processes and procedures leading to nontrivial function. Chance, necessity and mere constraints cannot steer, program or optimize algorithmic/computational success to provide desired nontrivial utility. As a major corollary, physicodynamics cannot explain or generate life. Life is invariably cybernetic. The F > P Principle denies the notion of unity of Prescriptive Information (PI) with mass/energy. The F > P Principle distinguishes instantiation of formal choices into physicality from physicality itself. The arbitrary setting of configurable switches and the selection of symbols in any Material Symbol System (MSS) is physicodynamically indeterminate—decoupled from physicochemical determinism.

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Introduction: The reality of nonphysical formalism

Both the physicodynamic force relationships of classical physics and quantum statistical reality conform to mathematical description. The prescriptive mathematical formulae known as "natural laws" are formal, not physical. Why do these mathematical expressions work so well not only to describe, but to predict future physicodynamic interactions? Eugene Wigner [10], Hamming [11], Steiner [12], and Einstein [13] all published on the "unreasonable" effectiveness of formal mathematics to describe and predict physical interactions. Einstein asked, "How is it possible that mathematics, a product of human thought that is independent of experience, fits so excellently the objects of physical reality?" [13] Mathematics is the ultimate expression of formal logic. Numerical representation and quantification are highly prized in science. Quantification permits by far the best modeling of physicality. But quantification is formal, not physical. The rational rules of mathematics, logic theory, and the scientific method are also all formal, not physical. Together they provide for reliable prediction of physical events.

Relationships in nature tend to stay constant despite varying local initial conditions. This constancy is defined by numerical constants. We value laws and the constants they employ because they are invariant in nature (excepting quantum decoherence, for the moment). Invariance is the key to prediction. Despite the variables, universal mathematical relationships exist that tell us how forces and physical objects will interact. The preciseness of quantification in force relationships minimizes subjective factors, objectifying our understanding of physical reality. Most advances in science have resulted from the formal manipulation of these numerical representations. In short, nonphysical formalism is the glue that holds all forms of scientific investigation together.

Other formalisms include logic theory, language, and cybernetics. None of these formalisms can be explained by physicality alone within a materialistic, physicalistic, naturalistic worldview. Naturalism looks for derivation of everything though mass/energy interactions and through chance- and-necessity causation. But chance contingency does not explain computational programming, or any other form of nontrivial utility. Logic gates cannot be set to open-or-closed functionality by redundant fixed law, either. If logic gates were set by law, they would all be set to the same position. Logic would be impossible. Binary programs would consist either of all "1's," or of all "0's." No uncertainty would exist, and therefore no Prescriptive Information potential. There would be no freedom of purposeful choice from among real options. Programming of any kind requires choice contingency, not forced law, and not mere chance contingency.

In the case of evolution, we refer to choice contingency as "selection pressure." But as has been covered many times in this anthology, selection pressure cannot steer events towards *eventual* utility. Evolution cannot pursue *potential* function at the decision-node programming level where organization originates. Evolution cannot work at the genetic/genomic/epigenetic/ epigenomic programming level where the phenomenon of regulation and control originates (The Genetic Selection [GS] Principle [5]).

At the level of consciousness, choice contingency in the intuitive sense is undeniably real. Certainly at the level of human cognition, no one doubts the reality of purposeful choice. In addition, one cannot even argue for the worldview of a strict physicalistic determinism without employing formal choice contingency in the logical argument itself. Any defense of physicalism is therefore self-contradictory. There will be no escape in logical or scientific debate from the reality of choice contingency. 95% of the practice of physics, (the study of physicodynamics), consists of formal nonphysical mathematics and logic theory. The other 5% consists of observation which cannot be reduced to mass/energy either. Why do mathematics and logic theory serve us so well in the pursuit of scientific knowledge? And why should a fundamentally chaotic, irrational and non-formal physicality be so wonderfully able to be modeled by rational and mathematical formalism? Could it be that physicality has its roots in, and arose out of, a formalism even more fundamental and causative than physicodynamics?

1. Is physicality chaotic, or organized?

This question may pose a false dichotomy, but naturalistic science tends to just metaphysically presuppose initial disorganization in its various cosmologies and cosmogonies. Mass/Energy is allowed, but not formal organization. Sometimes initial order is considered in the notion of a cosmic egg. But not bona fide organization as the primal force. How was it determined that reality was initially chaotic and only physical? Certainly not scientifically. The preassumption of ultimate chaos is not only purely metaphysical; it is antithetical to repeated observations of current reality, and to abundant formal prediction fulfillments of an underlying organization. It is contrary to the logic theory upon which math and science are based. Overwhelming empirical evidence exists that reality is *not* fundamentally chaotic. Not only repeated observation, but innumerable fulfilled predictions of physical interactions based solely on mathematical models is far more suggestive that physicality unfolds according to formalism's ultimate integration, organization and control of physicality.

The effectiveness of mathematics in science is only "*un*reasonable" if we are foolish enough to begin our thinking with purely physicalistic metaphysical pre-assumptions. The Formalism > Physicality (F > P) Principle explains away this supposedly "unreasonable" effectiveness of mathematics in the natural sciences. What is unreasonable is a materialistic belief system that ignores or tries to deny the supremacy of formalism. Materialism has never been empirically or logically established to be absolute Truth. This physicalistic faith system is inherently self-contradictory. No "ism" is physical. Naturalism is illegitimately incorporated into the very definition of science. The term, "Naturalistic science" is an oxymoron. Science is a formal enterprise from beginning to end. "Naturalistic science" exists only in name. Science itself is an abstract, cognitive, epistemological quest of mind. There is nothing "natural" about it, at least as philosophic naturalism would define "natural." All of the formalisms inherent in scientific method cannot be reduced to cause-and-effect physicodynamic determinism. Mathematics and science cannot be practiced within a consistently held materialistic and naturalistic metaphysical worldview. Neither can cybernetic pursuits—activities involving any form of control.

Science is an epistemological system. Science from the beginning was the pursuit of an ever-increasing collective knowledge of the way things actually are. The abandonment of realism led only to the decline of quality science.

The acquisition of information "about" reality is a purely formal enterprise. Whatever qualitative aspects of science that cannot be quantified are still dealt with logically. Linguistic logic theory, like mathematics, is also formal. Science also depends upon categorization. Categorization in turn depends upon drawing conceptual conclusions about distinctions between classes of objects and events. Categorization is formal, not physical.

The collection, categorization and organization of data, the reporting of results using representational symbols (e.g. in tables), and the drawing of conclusions are formal enterprises, not physicodynamic interactions. Physicality doesn't govern science. Nonphysical formalism governs science. In short, *formalism predominates,* not physicodynamics.

As Pattee has pointed out many times [14-18], even initial physical conditions must be formally represented with numbers within the laws of physics. Physical conditions themselves cannot be plugged into the nonphysical mathematical equalities and inequalities that we call "the laws of physics." We insert numerical *representations* of initial conditions. Initial conditions cannot measure or symbolically represent themselves. Without formal representations of initial conditions and formal manipulations using equations, no physicist could predict any physical outcome. The physics practiced by physicalists is not physical. It is nonphysical and formal. In order to practice physics, the materialist must violate his own metaphysical imperative; he must violate his or her own contention that physicality is all there is. Thus a dichotomy exists that categorizes physicodynamic reality from its formal representation and prediction. Physics and chemistry as sciences are dead without formalism. The scientific method cannot be practiced without abiding by the formal rules (not laws) of logic, mathematics and scientific ethics. In view of the historical existence of mathematical orderliness in nature (presumed by naturalism itself) prior to Homo sapiens, how should the scientific community respond to such a ridiculous, totally metaphysical pontification as, "The physical cosmos is all there is, ever was, or ever will be!"? [19] Professional philosophers of science typically respond to such dogma with, "SEZ WHO?" or at least, "How was this statement of absolute Truth established?"

2. Formalism is more than mathematics

We usually think of scientific formalism in terms of numerical axioms, quantifications, and manipulations of mathematical equations. But the essence of formalism is not just the use of number systems. Formal systems also involve choosing with intent characters from a finite alphabet of symbols, syntax, grammar, and assigned meanings to those symbols and symbol combinations. Additional formal linguistic rules also apply. In the broadest sense, formal enterprises include language itself, the rules of syllogistic deduction, abduction, induction, semantics, derived theorems and corollaries, and cybernetic steering of events and calculations towards pragmatic benefit. The pursuit of utility is a rational and formal pursuit that cannot be reduced to mass and energy.

3. The two subsets of contingency revisited

As covered in Chapter 2, *contingent* in a past tense context means that an event could have occurred other than how it happened. In a present and future context, contingency means that events can unfold in multiple ways despite both local and seemingly universal law-like constraints. Contingency is not forced by physicodynamic necessity. Contingency embodies an aspect of *freedom* from physicochemical determinism. Refusal to acknowledge the reality of contingency tends to make the practice of even weighted statistics rather difficult. No law of motion renders absolutely reliable predictions. Even the most dogmatic adherents to "hard determinism" can easily be cornered into admitting the reality of some degree of contingency.

But there are two kinds of contingency. The first is *chance contingency.* Chance contingency gives rise to random variation—"noise." The Brownian movement caused by the heat agitation of molecules is a seeming example of chance contingency. "Just how random is randomness?" remains an open question. Many have argued that seemingly random events are actually the result of unknown causes and complex interactions between multiple known physicodynamic causes [20-22]. But the bottom line of chance contingency is a non-willful, non-steered independence from straightforward cause-and-effect determinism. Possibilities and options are not purposefully chosen, but result from "the roll of dice."

The second type of contingency is *choice contingency.* Choice contingency is a purposeful selection from among real options. Choice contingency is exercised with directionality for a reason and purpose. The goal of choice contingency is almost always some form of utility that is valued by the chooser.

4. The essence of any formalism is purposeful choice contingency

Contingency—freedom from determinism—alone is not adequate to generate nontrivial function. No computationally successful program was ever written by a random number generator. Nontrivial programs can only be written by purposeful, wise choices at bona fide decision nodes. What is the garbage in the programmer's phrase, "Garbage in, garbage out!"? Usually it's bad data, but garbage can be bad programming choices too—something less than wise choice contingency—something moving either in the direction of chance contingency or physicodynamic self-ordering, neither of which can program formal function.

Randomness is contingent, but not formally determinative. To contingency must be added "choice with intent." Randomly occurring events have never been shown to generate optimized algorithms, nontrivial conceptual instructions, or sophisticated programming [8, 23, 24]. All formal systems, including mathematics, require *purposeful choice contingency*. Equation manipulations are a form of choice-contingent behavior.

Neither the rules of computation nor the computation itself are physical. What is computation? More than any other factor, the bottom line of *any* formalism is the exercise of *expedient choice with intent at bona fide decision nodes*. "Natural process" experiments that purport to have generated spontaneously occurring new programming, computational success, or non- trivial formal function can be shown invariably to be guilty of "investigator involvement" in experimental design and methodology [9]. Artificial rather than natural selection has been introduced.

Choice contingency has been thoroughly distinguished from chance contingency and law-like necessity in prior publications [2, 8, 9, 24]. Choice contingency cannot be derived from a combination of the chance contingency and necessity of physicodynamics. Any attempt to extirpate purposeful choice contingency from the explanation of sophisticated function invariably results in the rapid deterioration of that function. Noise replaces meaningful communication with gibberish. "Bugs" and "blue screens" replace programming. Failure to halt replaces successful computation. Nonsense replaces sound reason. No escape exists from choice contingency in any rational explanation of sophisticated function. Sophisticated utility is realized only at the behest of wise purposeful choices—the essence of formalism.

5. Formalism not only describes reality, it prescribes and controls reality.

The ability of mathematics to *predict* future physical interactions is a far more daunting problem for the physicalist than explaining how mathematics is able to *describe* so well those same interactions. Thus Wigner, Hamming, Steiner and Einstein, if anything, understated the problem. To the degree that mathematical formulae and their logical manipulations predict future physical interactions, it could be argued that they not only describe, but prescribe and control physical world unfoldings.

Statistical predictions are a special case in science. Assuming a theoretical total independence from any law-like orderliness, descriptions of future quantum outcomes are purely probabilistic. We would not consider statistical predictions to be determinative or controlling in any sense. Chance doesn't cause or even influence any physical event to happen. Chance is only a descriptive mental construct, not a physical cause of effects.

Most macroscopic "chance" events, however, do not conform to this theoretical total independence from law-like orderliness. Coin flips, for example, are not absolutely random because they are not absolutely "fair." The heads side may weigh ever so slightly more than the tails side. Thus a "fair coin flip" is theoretical rather than real unless a coin can be manufactured that has absolutely no variance of one side from the other. To whatever degree the coin is not "fair," law-like influence must be incorporated into "weighted means." In the quantum mechanical world, decoherence from expected events becomes an issue. But in the macroscopic world, mathematical formulae and rules govern physicodynamic unfoldings with amazing accuracy.

6. The derivation of formalism

How could purely formal mathematics and biological Prescriptive Information (PI) [6] utilizing linear digital programming choices be derived naturalistically from physicality alone? Much has been accomplished in science through reductionism. Let us therefore attempt to reduce the problem at hand to a maximally reduced and simplified query: Could inanimate physicodynamics have generated cybernetics, the mathematics of physics, the highly fine-tuned numerical force constants, and the linear digital programming upon which all life depends [25-27]?

Physical explosions (e.g., the Big Bang) do not create mathematical constructs and computational algorithms. The physical laws may have become *apparent* at 10^{-43} seconds. But that does not establish that they didn't exist prior to becoming physically instantiated and actualized. In addition, it does not establish that physicality produced those nonphysical formalisms. Indeed, as one of the reviewers of this paper pointed out, circular logic is involved in arguing that Physicality produced formalism which then produced physicality. It is much more likely that the nonphysical formal laws pre-existed the cosmic egg "explosion," and only became apparent at 10^{-43} seconds within the time-space physical medium. If true, the Big Bang was not a chaotic explosion, but a controlled unfolding of prescribed physical organization and reality.

7. The valuation and pursuit of utility in "applied science" is formal

The pursuit of functionality arises first out of a desire for and valuation of "usefulness." Inanimate nature (e.g., a prebiotic environment) possesses none of these formal attributes or motives. The environment does not value and does not pursue organization over disorganization. Physicodynamics *can* self-order spontaneously (e.g., Prigogine's dissipative structures: hurricanes, tornadoes, candle flames, falling drops of water forming spheres, etc.). But inanimate nature cannot self-organize itself into formal step-wise processes/procedures (e.g., algorithms) in pursuit of utility. A prebiotic environment had no sense of pragmatism. It exerted no pressure towards function over non-function. Only our minds imagine an environmental preference for function over nonfunction in order to make our molecular evolution models "work for us." Rationalization prevails rather than progressive communal discovery of what the objective world is actually like.

The postmodern concept of something "working for us" boils down to providing psychological, sociological and seemingly rational and empirical support for our already presupposed beliefs. Naturalism is already committed to the metaphysical presupposition that "physicality is sufficient to explain everything." Most of us bring with us this axiomatic pre-assumption *to* science. We were told from an early age on that science requires it. So most of us have cooperated fully with the incorporation of philosophic materialism and naturalism into our very definition of science.

If anyone dares to raise an eyebrow of healthy scientific skepticism about the all-sufficiency of mass and energy at any stage of our education, we are immediately pounced upon, ridiculed, shouted down by peers, and flunked out by professors. If we wait to raise any questions about the all-sufficiency of materialism until after we hold a degree, we are silenced by the peer review of true believers in physicalism. If we are fortunate enough to get a few open-minded peer reviewers, we are still stifled by a concerted effort of physicalists not to cite any paper that dares to challenge the all-sufficiency of physicodynamics to explain the whole of observational reality.

The subject of this paper is nothing more than a statement of what should have been obvious to every scientist all along. Mass and energy cannot represent meaning or programming choices using arbitrary symbol assignments. Mass and energy cannot state or manipulate mathematical equations. Physicality cannot organize data or draw abstracted conclusions. It cannot predict outcomes or practice any aspect of the scientific method.

Applied science values and pursues useful applications of academic scientific principles, data, results and conclusions in each specific field of study. To ascribe value to something is a formal function. To pursue utility is a formal undertaking. Cause-and-effect determinism knows nothing of value or function. It cannot identify or pursue "usefulness." In a materialistic world, whatever effects are caused are just "the way it is." Benefit is irrelevant.

Grant money is a lot easier to come by when academic interests are applied to solving everyday practical problems. The value of science is often judged by its practical usefulness to humans. NASA received a lot more funding when the general public and their political representatives started seeing the practical every day devices and benefits that arose directly out of the space program. Seeking knowledge for knowledge sake is noble, but rarely generates much grant money or pays anyone's salary. Thus a forensic scientist who is able to generate reliable methods of identifying serial rapists and murderers tends to get more attention and grant money than the scientist who first figured out how to sequence DNA for purely academic reasons. The forensic science wouldn't have been possible without the academics. Both the scientific academics and the pragmatic application of those academics are abstract, conceptual and formal, not merely mass/energy cause-and-effect determined interactions.

8. Controls and rules, not constraints and laws, achieve pragmatism

Science must follow certain rules. Rules are not laws [7]. Rules are agreed-upon conventions that govern voluntary behavior. Rules exist to guide choices. Rules can be broken at will. Rules govern procedures, competing interests, and ethical behavior. Rules are formal. The rules of the scientific method require honesty in the reporting of results, for example. There is nothing physical about the expectation of and demand for honesty. Science would collapse without adherence to certain ethical standards. We castigate scientists who falsify results or who plagiarize the work of others. Yet it is widely acknowledged that such moral "shoulds" and "oughts" are not derivable from a purely material world. Yet without these metaphysical and ethical demands, science could not be trusted as a source of reliable knowledge. Thus, science depends upon formal values, rules and honest behavior. It cannot be reduced to the chance and necessity of physicality.

Obedience to rules is not constrained. It is voluntary. But for any formalism to proceed, choices must be voluntarily made according to arbitrary rules with the intent of achieving formal function. This includes any mathematical or logical pursuit in science. It includes language. And it includes cybernetic programming. Loss of formal utility usually accompanies the disobedience of those rules unless a pragmatically superior rule system is being explored.

Most of what is really interesting in life was produced by choice contingency, not chance contingency or law. Our most fundamental problem in naturalistic science lies in explaining how physicodynamic determinism could have produced the bona fide choice contingency that we all observe and practice on a daily basis. The most fundamental question of biology is, "How did law-constrained physicochemical interactions along with "random" heat agitation generate a formally prescriptive linear digital genetic system?"

Language and any other form of sign/symbol/token system require deliberately choosing alphanumeric symbols from an alphabet of multiple options. Linguistic *rules* of language convention also must be arbitrarily chosen and adhered to. By arbitrary, we mean choice contingent, not chance contingent. Arbitrary does not mean that the chooser flips a coin to decide, or that the chooser does not care what is chosen. In addition to being choice contingent, "arbitrary" also means "unconstrained by natural law." Arbitrariness excludes determinism by law-like self-ordering. Self-ordering phenomena are extremely low in information [9]. High uncertainty and freedom are needed as a pretext to programming. No linguistic or cybernetic system has ever been organized by chance contingency or physicochemical determinism.

All forms of cybernetic programming in computer science are formal. Computational success can only be prescribed through formal choices with intent. The same is true of algorithmic optimization, the engineering of sophisticated function, and organization of any kind. Such formal utility cannot be achieved through after-the-fact selection of the best algorithms. A pool of "potential solutions" first has to exist before optimization is pursued. These stepwise discrete procedures ("potential solutions" are algorithms) must be programmed *at the decision node level*. A mere stochastic ensemble of symbols is not a potential solution. When Scrabble tokens are dumped out of the box onto the board and lined up upside down in strings, they sometimes contain happenstantial "words" when turned over. But this is only because our minds pick out those random sequences of letters by prior association. They are in reality just as random as any other letters in the string. Similarly, a random pool of supposed "potential solutions" are not the problem solutions they are claimed to be. Only our minds select them in pursuit of the solution and optimization we are pursuing. Consciousness is always smuggled in subconsciously in successful Markov processes. Strings of symbols have to be processed to function as programmed computational solutions. This requires either the selection of logic gate settings according to arbitrary conventions prior to the existence of any function [5], or the reading and processing of these instructions according to previously agreed upon rules, or both. Optimization requires motivation, the declaration of value, and the pursuit of a desired ever-improving utility. All of these factors are formal, not physicodynamic.

What empirical evidence and prediction fulfillment support do we have for the metaphysical belief that physicality generated formalism (e.g., that physical brain generated mind)? Has anyone ever observed a single instance of chance and necessity generating nontrivial computational function? Has anyone ever observed constraints generating bona fide controls that specifically steer events toward formal nontrivial utility? Do the laws of physics and chemistry ever generate creative new Prescriptive Information (PI)?

Says Howard Pattee:

> "The concept of control does not enter physical theory because it is the fundamental condition for physical laws that they describe only those relations between events which are invariant with respect to different observers, and consequently those relations between events over which the observer has no control. At the least, control requires, in addition to the laws, some form of local, structural constraint on the lawful dynamics. Pragmatic control also requires some measure of utility. To say that the river bed controls the flow of the river is a gratuitous use of

> control since there is no utility, and the simpler term 'constraint' serves just as well." [21, pg. 69]

Without exception every sophisticated pragmatic tool, machine or mechanistic procedure known to humanity required decision-node programming or integrative configurable switch setting to achieve. No bona fide nontrivial organization has ever arisen without purposeful steering, controlling and regulating the process. Constraints and invariant laws cannot perceive or pursue utility. Constraints and laws could not have generated a single complex machine, let alone life.

9. The Law of Organizational and Cybernetic Decline (The OCD Law)

The OCD Law states that, absent the intervention of formal agency, any nontrivial organization or cybernetic/computational function instantiated into physicality (e.g., integrated circuits) will invariably deteriorate and fail through time. This deterioration may not be continual. But it will be continuous (off and on, but overall consistently downhill). Computers, robots, all forms of Artificial Intelligence and Artificial Life, messages instantiated into material symbol systems or electronic impulses, will invariably progress toward dysfunction and fail.

The OCD Law is not to be confused with the Second Law of Thermodynamics. The OCD Law is not concerned with the entropy of statistical mechanics or the "entropy" or "mutual entropy" of Shannon's probabilistic combinatorial uncertainty. Heat exchange, heat dissipation, phase changes, order and disorder are not at issue. The OCD Law addresses only the formal organization and utility already instantiated into physical media and environments. Only purposeful choice contingency at bona fide decision nodes can rescue from deterioration the organization and function previously programmed into physicodynamics.

Thermodynamicists differ widely in opinion as to whether entropy is physical. Most materialists find themselves seriously trying to argue that the negatives of log functions of probabilities are physical! Even if they were, entropy tells us nothing about organization or achieving nontrivial formal function.

The OCD Law, of course, raises the question of how organization arose in the first place. *The Organization (O) Principle* states that nontrivial formal organization can only be produced by Choice Contingency Causation and Control (CCCC). The O Principle, like the OCD Law, can still be treated as a mere null hypothesis if desired by skeptics and critics. The firm prediction is made that neither the OCD Law nor the O Principle will ever be falsified by empirical evidence or prediction fulfillment data. It will never be overturned by sound Aristotelian logic, either. A single legitimate exception to either generalization would serve as falsification. It is incumbent upon those who religiously believe in spontaneous self-organization of mass/energy into non-trivial formal utility to provide empirical evidence or prediction fulfillment support for their blind belief. Thus far, any logical defense of belief in self-organization has also been sorely lacking [9]. In the absence of scientific support, informationless self-organization hypotheses and models such as Ganti's [28] remain little more than superstition.

10. Is entropy physical?

Many thermodynamicists are uncertain as to whether "entropy" is physical. "Energy unavailable for work" is one of several common definitions of entropy. "Energy" would certainly have to be considered physical. But "unavailable for work" is a formal characterization, not a physical entity. "Work" as used in this context obviously does not refer to mere heat exchange between bodies. It refers to formal utilitarian potential. Can the energy be used to achieve function? When taken as a whole, "energy unavailable for work" is a formal construct that cannot be reduced to physicality. In addition, nonphysical formal mathematics is required to define entropy and measure it in scientific terms. Nevertheless, as mentioned above, most metaphysical naturalists find themselves seriously trying to argue that the negative of a log function is physical. This is especially true of those who insist that statistical mechanical entropy is one-in-the-same with Shannon entropy. Shannon uncertainty is a probabilistic measure. Reduced uncertainty (R) is still a mathematical subtraction based on "before" minus "after" uncertainty. Reduced uncertainty is equated with gained knowledge. But even reduced uncertainty is formal.

Neurophysiology has never had much success trying to reduce epistemology to physicodynamics. But even if entropy were physical, entropy tells us nothing about organization or achieving nontrivial formal function.

Many try to define 'entropy" in terms of "increasing disorder." But clearly many forms of crystallization simultaneously increase order while moving towards greater entropy within the system. This confusion was caused by the initial confusion of order with organization, and the confusion of constraints with controls. Self-ordering phenomena and constraints are physicodynamic properties. Organization and controls are formal properties. Physicality cannot generate nonphysical formalisms. They lie in different categories. Self-ordering phenomena and constraints arise from the near side of The Cybernetic Cut (Chap 3). Organization and controls arise only from the far side of The Cybernetic Cut. The one-way Configurable Switch (CS) Bridge allows controls to travel into the physicodynamic world from the formal non-physical world. Under no circumstances do physicodynamic phenomena ever traverse the CS Bridge from the near physicodynamic side to the far formal side. What makes reality especially interesting is not order, but organization. What generates utilitarian work is choice contingency and controls, not constraints and laws. We must learn to get order and disorder out of the discussion of organization.

11. Formalism's instantiation can alone temporarily and locally circumvent The 2^nd Law

James Clerk Maxwell first stated his well known "demon paradox" in a letter to Peter Tait in 1867. A controllable trap door separating two compartments allows an imaginary demon to separate warmer and cooler ideal gas molecules on opposite sides of the door separating the two compartments. The temperature differential between compartments was to provide an energy potential needed to drive a potential heat engine.

There are good reasons why naturalism is forced to view Maxwell's demon as only a "thought experiment" [29]. Abstract concept and volition are required for the demon to *selectively* open and close the trap door. He must choose with intent to concentrate the fastest-moving particles on one side of the partition. No energy is required in this thought experiment for Maxwell's demon's *mind* to choose whether and when to open the trap door. No accounting is provided for the demon's brain or muscle energy requirements, either, to operate the trap door. The demon has no brain or physical reality. He and his purposeful choices are transcendent to physicality. The hotter faster-moving particles cannot be concentrated on one side of the partition without his purposeful choices. It is true that the actual opening of the trap door would require a physical force and energy. But the *vectors of door pull up or push down are not physically determined. They are formally chosen.* And the all-important choice of *when* to open or close the trap door is also purely formal.

The demon has always been prominent in physics and thermodynamics precisely because *he provides the energy-free formal agency that alone can explain temporary and local circumvention of the Second Law.* Take away the demon's formal purposeful choices—his agency—and equilibration of heat in both compartments is inevitable according to the 2^nd Law of Thermodynamics. What is the natural-process equivalent of such a mystical demon? None exists in the naturalist's materialistic metaphysical world. The demon's persistence in physics texts is nothing less than a classic demonstration of naturalistic rational inconsistency. The physical cosmos clearly cannot be "all there is, ever was, or ever will be" [19]. Seemingly local and temporary circumvention of the Second Law is too evident and common; but only because the demon lives and purposefully chooses. All energy transduction mechanisms making non-trivial function possible can be traced back to the same formal controls. Mere constraints, laws and phase changes do not produce functional "work" and sophisticated utility.

But why couldn't some yet-to-be discovered natural-process law operate the trap door? The answer is that laws always preclude freedom of programming choice and control. The trap door would always be held open, or always locked closed, *by law*!

It could be argued that not even life violates the 2nd Law, at least the physical manifestation of life. But life's formal controls and regulation are nonphysical. Formalisms are not subject to the 2nd law because they are non-physical. The instantiation of formalisms into physicality is alone what makes possible the seeming temporary and local circumvention of the 2nd law.

In the microscopic world, circumvention of the 2nd Law is considered a given by many. But the quantum world is highly laced with human epistemological factors. Some might argue that the microscopic world may be more of a subjective human mental construction than ontologic reality. Others might point to the role of mathematics, probabilism and imagination in quantum theory as further evidence of formalism being the most fundamental level and ultimate cause of overall reality, including physicality.

We might be quick to deny "vitalism;" but we will not succeed in denying the reality of life's formal programming, regulation and control. We will not be able to sweep under the rug the prokaryotes' representational symbol systems, cybernetic programming, tens of thousands of nanocomputers, firmware, operating systems, various application softwares, semiosis (messaging), coding and decoding, translation, and its orientation around the pragmatic goal of staying alive. All of these are formalisms, not mere physicochemical interactions. This leaves us with the uncomfortable question, "What exactly is the difference between the undeniable transcendence of all these formalisms that program and regulate life, and the vitalism we so vociferously decry?

In Rolf Landauer's review [30] of *Maxwell's Demon: Why Warmth Disperses and Time Passes* by Hans Christian von Baeyer [31], Landauer points out, "It is impossible to sort molecules without expending more energy than the work that can be extracted from the sorted molecules. The second law of thermodynamics does indeed hold true."

Szilard rightly argued that Maxwell's Demon must be "informed" in order to know when to open and close the trap door [32]. Uninformed and undirected constraints cannot operate the trap door so as to deliberately separate hot and cold particles. Only choice-based control can.

Gilbert Lewis wrote: "Gain in entropy always means loss of information, and nothing more." [4, 33, pg. 573). Conversely, to reduce entropy requires increased information—not only increased Shannon information, but increased prescriptive information {Abel, 2007 #6367]. It takes prescriptive information for the demon to know how to achieve heat engine potential. But the problem is far greater than one of knowledge. It is one of deliberate steering, control, management and goal. The Demon must *decide* when to open and close the door *for some useful reason.* The Demon must have desire and motive. With every approaching particle he must make a purposeful binary choice of whether to open or to close the door so as to create a future energy potential. By what naturalistic physical mechanism is this choice accomplished? The Cybernetic Cut {Abel, 2008 #6969;Abel, 2008 #8037} and The F > P Principle declares that no natural mechanism exists that can choose with intent to deliberately design, engineer and maintain a *Sustained Functional System (SFS)* [34] such as a thermal engine for pragmatic reasons. Prigogine's dissipative structures in chaos theory have little in common with SFSs. Falsification of the assertion that nontrivial SFSs do not spontaneously form in nature is simple: cite a single exception. Such falsification is invited to promote further discovery and to test axiomatic principles such as The F > P Principle "in the real world."

12. The source of Prescriptive Information (PI) is formal

Prescriptive information (PI) either instructs or directly produces nontrivial function [2, 8]. PI usually accomplishes this through programmed algorithmic processing. "Prescriptive Information either tells us what choices to make, or it is a recordation of wise choices already made" [6]. Prescription requires formal selective steering at successive decision nodes. The purpose of PI is to generate pragmatic results. Such utility is valued and pursued by agents. Inanimate nature cannot value or pursue a formal goal. Not even evolution has a goal. Expedient choice commitments must be made prior to the realization of function at each successive decision node in any program. Bifurcation points can be traversed randomly; but no significant computational halting success can be expected at the end of a random path. Decision nodes require true decisions, not "coin flips" or "dice rolls," to generate PI and sophisticated function.

The definition of PI centers on selection *for potential (not yet existent) function*. What exactly do we mean by function? "A function is a goal-oriented property of an entity" [35]. Says Voie, "Functional parts are only meaningful under a whole, in other words it is the whole that gives meaning to its parts" [35].

The road to utility is paved with algorithmic intent [36]. A goal-based algorithm is a step-wise, usually discrete process or procedure leading to *future* utility. Natural selection cannot generate such procedures. Evolution is blind to potential function and the future. It can only eliminate inferior formal programs (highly integrated computational haltings manifested as already-computed phenotypic organisms [The GS Principle] [5]). Goal-based algorithms control events and behavior, steering them toward organized, predictable usefulness. But such steering requires free and purposeful choices at bona fide decision nodes. Neither chance nor necessity can generate or optimize algorithms. These programming decisions must be made wisely with the intent to achieve computational halting. The only known source of conceptually integrated function is formally-generated PI.

Given the right processing algorithms, PI not only instructs, but can actually produce sophisticated function. But, to accomplish this pragmatism, at the very least constraints must be purposefully chosen through the selection of particular initial conditions in order to influence physical interactions to move towards Aristotelian "final function." Constraints are blind to function. Constraints and laws have no pragmatic goal. Constraints cannot generate the symbol systems used by semiosis. It is only the purposeful choice of certain constraints (e.g., the choice of initial conditions in designing an experiment) that creates bona fide controls. The F > P Principle states that the fundamental ingredients of any semiotic system are *representationalism* and *choice contingency*, not chance contingency or necessity. Meaning is always formal, never physicodynamic.

13. Naturalistic "efficient causation" (Aristotle) is grossly inadequate

Physicodynamic cause-and-effect was classified by Aristotle as "efficient causation." Naturalistic science attempts to explain seemingly teleological (teleonomic) phenomena solely in terms of efficient causation. Naturalistic biologists universally just presuppose functionality in scientific literature without any explanation of its derivation: "The purpose of the kidneys is to excrete waste products from the blood stream." "Mitochondria function as the powerhouse of the cell." "Each amino acyl tRNA synthetase is present *in order to* bind the appropriate amino acid to its own tRNA." Naturalistic science has to be able to explain all of these purely formal "in order to's" with nothing but mass/energy interactions. It fails miserably.

How can we refine evolutionary explanations to incorporate "in order to" into efficient causation? We point to selection pressure as the cause. But environmental selection favors only the best already-living phenotypic "effects." It does not explain the cause—the programming, algorithmic processing, preservation schemes and optimization that produced those effects (The GS Principle) [5].

In evolutionary theory, the chaperone proteins cannot come into existence "in order to" fill the need of helping other proteins fold correctly. They, too, have to be folded. For the consistent naturalist, "Folding correctly" must ultimately be purely accidental prior to secondary selection for after-the-fact fitness. Virtually every player in homeostatic metabolism participates actively in pursuing and eventually achieving cooperative holistic integration. Evolution theory provides no mechanism for anticipation or pursuit of goals. In addition, the probability of thousands of needed players all coming together at the same place and time, all to contribute their role in achieving the final function of homeostatic metabolism, is statistically prohibitive for any purely materialistic conglomerate. The notion that physicodynamics alone can accomplish even a protometabolism can be definitively falsified by the Universal Plausibility Metric and Principle [37].

14. The genomic symbol system's prescription, control and regulation are formal

Küppers [38, pg 166] makes the same point as Jacques Monod [39], Ernst Mayr [40, 41], and Hubert Yockey [42, 43], that physics and chemistry do not explain life. Niels Bohr argued that "Life is consistent with, but undecidable from physics and chemistry."[44] "Undecidable" means that life cannot be explained by mere physical interactions alone. What exactly is the missing ingredient that renders life unique from inanimate physics and chemistry? The answer lies in the fact that life, unlike inanimacy, traverses the Cybernetic Cut (See Chapter 3) [4] . The Cybernetic Cut dichotomizes reality into two fundamental categories. The dynamics of physicality ("chance and necessity") lie on one side of the great divide. On the other side lies the ability to choose with intent what aspects of ontological being will be preferred, pursued, selected, rearranged, integrated, organized, preserved, and used (formalism). Algorithmic programs and their optimization require traversing the Cybernetic Cut. Life is further differentiated from non-life by its linear digital Prescriptive Information that uses a material symbol system (MSS) [45, 46]. Says Hubert Yockey, "The existence of a genome and the genetic code divides living organisms from non-living matter. . . . There is nothing in the physico-chemical world that remotely resembles reactions being determined by a sequence and codes between sequences." [26, pg. 54]

Linear digital programming occurs prior to any folding. The source of this programming lies in the selection and sequencing of rigidly bound nucleotide (token) "choices." Primary structure (sequencing) is the main determinant of tertiary structure (the globular molecular machine). Chaperones and other factors contribute to folding. But rigidly-bound monomeric sequencing largely determines what folding thermodynamic tendencies will be. And chaperones are themselves prescribed by the same linear digital symbol system. The far weaker H bonding of average folding is primarily mediated by primary structure. Thus true selection must take place at the point of polymerization of each additional monomer onto the forming positive strand. Since polymerization of the primary single strand is nearly dynamically inert in coding regions, physicodynamics plays no role in sequencing. Nothing is left but randomness with which to program in a naturalistic context. Yet coin flips have never been observed to program computational halting in any cybernetic system. There is no escaping the reality that all known organisms are prescribed and largely controlled by this linear digital programming. A representational MSS is clearly employed in the triplet codon table of amino acid prescription. Even most epigenetic factors are produced only through linear digital instruction and control (e.g. regulatory peptides, proteins and small RNAs) [47-49]. Even DNA methylation and protein binding to histone tails are at least indirectly prescribed by nucleotide sequencing. Non-coding regulatory RNA prescribed by DNA controls much of the genome [48-51].

Even more confounding is that all of these processes require sophisticated nanocomputers, firmware, "high tech" operating systems and software. Formal algorithms are required. Sequencing has no meaning or function independent of an overarching formal system of arbitrary assignment of specific amino acid correspondences. No physical force or law explains these arbitrary correspondence assignments. Their formal functions are not physicodynamically mandated. They are formally prescribed.

DNA genetic sequencing *seems* 99% "random" when considered only from a Shannon probabilistic and combinatorial perspective. But of course this perspective is blind to the meaning or function of any message or program. A string of 1s and 0s, as the result of compiled computer source code, can look random even though every logic gate position represented in that string was purposefully chosen for maximized utility. From a Shannon point of view, any truly random mutation in a genetic sequence would seem to have minimal effect on the already *seemingly* random frequency of the four nucleotides. Since 99% of genes already appear to be random, random mutations would tend to randomize only the 1% of *apparent* order within that gene's bit content. Random mutations would have a much more dramatic effect on the Shannon uncertainty found in redundant sequences (e.g., in introns rather than exons).

But genes are in reality programming strings. They are not analogous to programming strings. They ARE programming strings. It could be seriously argued that computer programs are analogous to genetic and genomic programming. Each nucleotide added to the string is an additional configurable switch setting added to the programming syntax. If genetic prescription is random, why are we spending billions of dollars on ascertaining reference sequences? Further, a mutation of a random sequence is more than bordering on a non-sequitur.

Mutations, whether random or ordered by varying degrees of physicodynamic determinism, corrupt existing programming "choices." Random mutations of PI strings will consistently result in noise pollution and degradation of the meaning and function of that PI. Mutations resulting from extremely low-informational cause-and-effect determinism will also reduce any programming efficiency of an existing gene. The fixed orderliness of nature described by laws cannot program formal function because it freezes up logic gates. Switches must be freely configurable to program formal function.

The GS Principle (See Chapter 7) [5, 52] states that genetic determinism's strong contribution to life requires selection at its *formal* configurable-switch level, not just at the post-computational phenotypic level. Nucleotides must be selected and covalently bound into primary structures (sequence strings) prior to the realization of selectable function. Environmental selection cannot occur until final function and the fittest already-living organisms exist.

Replicative function is often confused with information prescription in the literature. These two functions have nothing to do with each other. Templating and complementary base-pairing are purely physicodynamic. They are both highly ordered with high probability and very low uncertainty. There is no formal component to templating or base pairing. It is largely "forced" via physicochemical constraints ("laws" and local initial conditions). Templating and base-pairing, therefore, are unrelated to Prescriptive Information (PI) generation. The only exception to this is the prescriptive sequencing of the template itself. Naturalistic templates are all low informational (e.g., clay adsorption produces homopolymers, not informational strands). Yet templating and self-replication are often erroneously appealed to as an explanation for the source of biological information. Point mutations and wobbles are noise producers, not programmers. Pointing to a template does not explain the origin of PI in the initial linear digital sequence of the template itself. No explanation is ever provided by naturalism for the *source* of PI in any template or biopolymer. The *sequencing* of nucleotides in a single, positive, prescriptively informational strand is formal, not physical. Untemplated, merely physicochemical polymerizations of over 100 mers at higher temperatures produce homopolymers, not PI polymers [53].

Once the functional sequencing is established in a positive informational strand, base-pairing is purely physicochemical. In our naïveté, we would expect that replication would merely copy the existing PI in reverse direction. The discovery that the complementary negative strand of DNA is simultaneously prescriptive of entirely different regulatory function only bespeaks the added dimensions of formal causality instantiated into molecular biology that totally defy all physicodynamic explanation. Mere physicodynamic base-pairing will never answer how each complementary strand is able to prescribe a different formal function.

Technically, duplication yields no new information even in the Shannon sense of "information." Duplication plus variation does yield new Shannon uncertainty. But duplication plus variation has never been demonstrated to produce new nontrivial Prescriptive Information (PI) [6].

How can nonphysical formal mathematics and formal biological cybernetics be derived naturalistically from physicality alone? Admits Weinberger, " . . . a theory such as ours must explicitly acknowledge purposeful action, or 'agency', in such diverse fields as evolutionary theory . . ." [54, pg. 105] Yet the whole point of evolutionary theory was to obviate the need for purposeful action and "agency."

15. Formal biocybernetics predates *Homo sapiens* and our cognition

All known life is cybernetic. If one assumes that humans evolved from previous lesser life forms in only the last one thousandth of life's history on earth, it follows that cybernetics predates humans. The simplest known life forms all display undeniable evidence of linear digital prescription using a representational Material Symbol System (MSS) [45, 46] and cybernetic regulation [4]. The biosemiosis that produced life, humans and their minds included, is formal. Even at a primordial life level, each ribonucleotide selection in a polymer is a configurable switch-setting [2, 8]. It is a memory token in a material symbol system [55]. In a theoretical RNA World, each linear digital symbol sequence (syntax) prescribes a certain three-dimensional configuration space of potential ribozyme function [5, 9, 56].

Pre-metazoan life utilizes the same representational symbol systems, linear digital programming, coding/decoding/translation between language/operating systems, and redundancy block-coding for noise reduction. They cannot be attributed to human mentation or heuristics. Neither chance nor necessity can explain these phenomena. Linear, digital, genetic algorithmic programming requires ontologically real selection contingency. Life could have arisen only through selection operating at the covalently-bound level of primary structure formation. Environmental selection of the fittest already-computed phenotypes is irrelevant to the question of how initial genes were programmed. Formally functional configurable switch settings could not possibly have been programmed by physicodynamics.

The destination of any message must have knowledge of the cipher and possess the ability to use it. Deciphering is a formal function—as formal as mathematics and the rules of inference. Deciphering of the source's code and prescriptive intent at the destination cannot be done by the chance and necessity of physicodynamics. An abstract and conceptual handshake must occur between source and destination. Shared lexicographical meaning must exist between source and destination. Source and destination must be in sync regarding pragmatic significance of the arbitrarily chosen language system in order to create a protocol in a communication sense.

Natural selection is always *post-computational.* Natural selection is *after-the-fact* of relatively bug-free program halting. Environmental selection does not explain how the program got "written." Genetic digital selections must be distinguished from analog dynamic folding and from environmental phenotypic selection. Molecular evolution models of the spontaneous generation of life must be able to demonstrate selection at the covalently-bound decision-node level. No such theory or model currently exists in naturalistic scientific literature. No empirical evidence or rational support exists for attributing genetic programming to stochastic ensembles. This would be like attributing a Ph.D. thesis to nothing but a secretary's typographical errors. Although a stochastic ensemble could happen to match a reference sequence, no operational context would exist for that particular sequence to mean anything metabolically. An entire formal operating system (or several), power plant, and manufacturing factory would have to simultaneously arise from sequence space at the same time and place. Cybernetics is required to generate homeostatic metabolic utility in the face of thermodynamic decline. Since cybernetics is a formalism, and since life at all levels is cybernetic, formalism predates not only *Homo sapiens*, but even invertebrates. Cybernetics cannot be reduced to human mentation. Cybernetics is not just a heuristic tool or metaphorical epistemology generated by our minds [55]. Molecular biological cybernetics produced our consciousness, not the other way around.

16. The F > P Principle

The Formalism > Physicality (F > P) Principle states that Formalism not only describes, but preceded, prescribed, organized, and continues to control, regulate, govern and predict physicodynamic reality and its interactions. The F > P Principle is an axiom that defines the ontological primacy of formalism. Formalism is the source of all aspects of reality, both nonphysical and physical. Formalism organized physicality before the fact of physicality's existence. Formalism gave rise to the equations, structure and orderliness of physicality rather than to chaos. This alone explains why the scientific method must be conducted in a rational manner, why the applicability of mathematics to physical interactions is reasonable rather than unreasonable, and why such formalism can predict physical interactions.

The quest for a mathematical unified field of knowledge presupposes the F > P Principle. The F > P Principle further states that reality is fundamentally arbitrary—rule and choice-contingency-based, not indiscriminately forced by an infinite regress of cause-and-effect determinism. Physicality cannot even spawn a study of itself—physics—because physics is a formal enterprise. Nothing within the "chance and necessity" of physicality itself is capable of generating formal logic, computation, mathematical relationships, or cybernetic control. Only formalisms can measure, steer, manage, and predict physicality. Physicodynamics constrains; formalism controls.

In this paper, we have defined critical terms, presented fundamental concepts related to emergence, and reviewed repeated and predictable observations that collectively demand acknowledgement of the F > P Principle as the most fundamental axiom of science. Reality is first and foremost formal; physicality is realized only secondarily. Formalism can be instantiated into physicality through the use of configurable switches, material symbol systems, and through the integration of components into a holistic functional system.

Physicality cannot merge with formalism. Physicality can *be used by* logical formalism, but physicality cannot merge with or control formalism. Only formalism can measure, steer, organize, manage, and predict physicality. The F > P Principle explains why and how design and engineering principles can be incorporated into physicality to render it uniquely functional and/or computational. Physicality cannot do this on its own.

A corollary of the F > P Principle is acknowledgement that humans did not create the formal physical laws; our minds just discovered them. Before our minds existed, physicality obeyed these mathematical rules of physical interaction. Their prescription and control are in no way dependent upon human consciousness. $F = ma$ governed physicality long before human mentation arrived on the scene to recognize such formal relationships.

While the initial formal rules were arbitrary (choice-contingent), once instantiated into physicality they became physical fixed "laws." Their formal prescription and control became translated into fixed invariant directives of physicodynamic determinism. Cause-and-effect chains became "ordered" or forced into regularities. The fundamentally formal rules became physical laws. From the physicality side of The Cybernetic Cut [4], the choice contingency of the initial rule-writing and instantiation can seem imperceptible. We see only the forced regularities described by the laws of nature. But the prescription of these regularities prior to instantiation into physicality was free, choice-contingent, and purely formal.

This formal rationality extends even to the roles of heat agitation, undetermined degrees of freedom in nature, and stochastic quantum events. Even randomness, chaos and dissipative structures can be formally and mathematically described, defined and predicted. The only thing that Einstein got wrong in his statement "How is it possible that mathematics, a product of human thought that is independent of experience, fits so excellently the objects of physical reality?" [13] was that mathematics is “a product of human thought.” Human thought did not create mathematics. Human thought is just progressively discovering it and its role in cosmic organization. As we have learned throughout this anthology, it is a logical impossibility for order to have produced PI or organization. The orderliness of nature could not have produced mathematics, cybernetics, language capacity, the scientific method, scientific ethics, and all the other non-material formalisms; rather, it’s the other way around.

The F > P Principle states that the flow of control and organization is unidirectional from formalism to physicality. No reversibility exists between the law-based necessity of physicality and the rule-based choice contingency of formalism. Physicality cannot generate formalism. Phase changes at the edge of chaos, fitness landscapes, so-called evolutionary algorithms, neural networks, cellular automata, and the infodynamics perspective cannot circumvent the F > P Principle. In every case, nontrivial function requires formal, choice-based, behind-the-scenes, artificial selection in experimental design in order to produce nontrivial utility. The fundamental modus operandi of all uphill climbs to optimize the “fitness functions” of evolutionary algorithms is subtle choice contingency. Markov processes (“Drunken walks”) are not devoid of experimenter steering. Optimization of fitness functions is formal, not physicodynamic. Genetic algorithms start with a pool of potential *formal solutions* to a problem. The preferred choices can be instantiated secondarily into material tokens and into Material Symbol Systems (MSS) [57]. Once instantiated into physicality, MSS’s then can cause physicodynamic effects. But their utility was formally, not physico-dynamically, programmed.

The F > P Principle is a far more contemporary and less metaphysical axiom than Plato’s original notion of Form [58, 59]. The F > P Principle adds to Plato’s and Aristotle’s early metaphysical explorations many benefits of the Enlightenment, modern and postmodern scientific thought and empirical experience. This axiom should be considered the most foundational principle of science. Without it, no basis exists for demanding science's subjection to logic theory. It explains science's demand for quantification (formal representation with numbers followed by numerical manipulations). The axiom provides a basis for trust in repeated observations and demand for prediction fulfillment. It explains why falsifiability is a valid test of scientific objectivity. Apart from the F > P Principle, the requirement of mathematical quantification in science makes little sense. The sciences of physics, chemistry, and biology, along with applied mathematics, computer science, and engineering, all *demand* formalism's dominion and control over physicality.

Belief in "self-organization" and "emergence" in the absence of choice contingency is blind belief bordering on superstition. It completely lacks empirical confirmation, prediction fulfillment, and rational justification. The hypotheses of "self-organization" and "emergence" are not even falsifiable. What is potentially falsifiable is the null hypothesis that nontrivial *"self-organization does not happen absent choice contingency."* This null hypothesis was first published quite succinctly in peer-reviewed literature around the turn of the millennium [23, 60] and many times thereafter [1-9, 34, 52, 61-64]. The scientific community has been rigorously invited to provide such falsification. After a decade, no falsification has been provided. The firm scientific prediction is hereby made that no falsification of this null hypothesis will ever be provided without behind-the-scenes investigator involvement in experimental design (artificial selection rather than natural selection). After another decade or two with no worldwide success at falsification, the above formal scientific prediction should become a mature generalized theory or theorem, if not a tentative law of science. This proposed tentative law states that inanimate physicodynamics is completely inadequate to generate, or even explain, formal processes and procedures leading to sophisticated function (The Law of Physicodynamic Incompleteness). Chance and necessity alone cannot steer, program or optimize algorithmic/computational success to provide desired nontrivial utility.

The time has come to extend this null hypothesis into a formal scientific prediction"No nontrivial algorithmic/computational utility will *ever* arise from chance and/or necessity alone."

How can such a bold, dogmatic prediction possibly be made by any reputable scientist? The answer lies first in the fact that it is just a null hypothesis designed for open-minded testing. The author of the hypothesis himself actively pursues falsification. Its deliberately absolutist tone begs falsification all the more in the challenging spirit of quality science. Second, the hypothesis itself arises from logical inference in addition to seemingly universal empirical observation. The statement is not just a product of inductive reasoning. The latter would be subject to overturning with minimal new data that could arise around the next blind empirical corner. The prediction is rather a logically valid inference enjoying deductive absoluteness within its own axiomatic system. Baring fallacious inference, the only possibility of falsehood would be that the logic flows from a faulty axiom. If a presupposition (pre-assumption about the nature of reality) is "out of touch with reality (ontologic, objective being)" then the prediction might not be "helpful." Unhelpfulness would be realized in the form of a prediction failure. Since no axiom is ever proven, science tends to proceed by assuming an axiomatic system to be tentatively valid, and testing it from many different directions through time. In this sense, all laws of science are considered best-thus-far generalizations subject to continuing experiment falsification.

After another decade or two with no worldwide success at falsification, the above formal scientific prediction should become a mature generalized theory, if not a tentative law of science, which Abel has named in advance ***"The Law of Physicodynamic Incompleteness."*** This proposed tentative law states that inanimate physicodynamics is completely inadequate to generate, or even explain, the mathematical nature of physical interactions (the laws of physics and chemistry). The Law further states that physicodynamic factors cannot institute formal processes and procedures leading to sophisticated function. Chance and necessity alone cannot steer, program or optimize algorithmic/computational success to provide desired nontrivial utility.

When we see sophisticated function of any kind, we have strong evidence suggesting that the Cybernetic Cut has been traversed across the one-way-only CS Bridge [4]. Nonphysical formalisms are the product of purposeful choice contingency [4, 7]. Choice contingency is instantiated into physicality via logic gates, configurable switch-settings, the purposeful selection of tokens from an alphabet of tokens, or cooperative integration of physical components into formal systems or conceptually complex machines [1-9, 23, 34, 55, 61, 62]. Mere physicodynamic constraints can accomplish none of the above examples of formal organization. Organization and sophisticated function in the physical world are all the products of formalisms instantiated into physicality. Physicality cannot generate nonphysical formalisms.

Physicality can self-order. But it cannot organize itself into or optimize formal algorithmic systems [9]. Physicodynamics cannot integrate parts into holistic, cooperative, functional metasystems. Inanimate physicality is incapable of producing organization because it cannot generate choice from among options or pursue the goal of function. The environment has no pragmatic preferences or values. It cannot generate nonphysical Prescriptive Information (PI) [6]. It cannot program logic gates or configurable switches [1]. Physicodynamics *does* include spontaneous non-linear phenomena; but it cannot practice the formal applied-science/math known as "non-linear dynamics." The latter is produced only by agents, not by inanimate nature.

But what is the utility of the F > P Principle? What does it *do* for us? The principle tells us to stop wasting time and hundreds of millions of research dollars trying to explain algorithmic optimization from physicodynamics alone. The Principle states that formal computational function cannot be generated by chance and necessity. Organization cannot be produced by physicodynamic self-ordering phenomena. Organization can only be generated through educated, expedient "choice with intent" at successive decision nodes. Organization arises out of the formal pursuit of desired utility.

Philosophical and metaphysical considerations are minimized in accord with Einstein's tenet of exercising a "minimum metaphysic" in scientific thought. Science, however, simply cannot be practiced competently without presupposing The F > P Principle. We already do this without realizing it. We just need to name and acknowledge the axiom we already subconsciously presuppose, and scrap the one we consciously incorporate erroneously into the very definition of science.

17. The axiomatic nature of all laws and principles

The axiom of ontological primacy of Formalism and its governance of Physicality flows from a combination of repeated observation and rational plausibility. It is still axiomatic, of course, as are all laws and principles of science and mathematics. But human experience and reason are far more consistent with the axiom of formalism's primacy than the pre-assumption of chaos and/or physicality's primacy.

It is easy to demand proof of The F > P Principle, and in the absence of proof immediately discount it. This is true of all axiomatic principles. It is not so easy to falsify it, or to find the slightest bit of evidence inconsistent with the Principle. Metaphysical naturalism's rejection of the Principle is purely philosophic, not scientific. The dogmatic pontification that physicality is everything is easily falsified. The bottom line of reality repeatedly traces back to formalism's choice contingency and organization (e.g., the periodic table; the Anthropic Principle, the reliability of mathematical laws to predict future physical interactions).

Like all axioms and "universal" laws, absolute proof of such principles is unattainable. Whether hypothetico-deductive or empirico-inductive, universal principles and laws must be viewed tentatively. At best, they represent "best-thus-far" knowledge. We accept them primarily because they are internally consistent and because they seem to work for us across a broad array of disciplines. Note that both of these criteria are formal requirements.

Principles should support a metanarrative (an over-arching story) of our experience of the whole of reality. We typically have a large sample space of observational data which conform to the principle. Fulfilled predictions made by the principle are especially convincing when they occur in unrelated and unexpected areas of science. But the principle nonetheless must be potentially falsifiable to be considered scientific [65, 66]. The F > P Principle is indeed potentially falsifiable. Only one example of physicodynamic causation of a single formalism is required.

Theorems are deduced from unproven axiomatic commitments. We choose to tentatively believe these axioms, and we choose to abide by the rules of logic theory within the deductive systems that flow from those axioms. We presuppose that self-contradiction cannot lead to progressive discovery of an objectivity outside our minds. We obey the rules of inference believing it will lead to pragmatic benefit or some computational utility. Obeying the rules seems to "work for us."

The reason Einstein advocated a "minimum metaphysic" in science rather than banning metaphysics from science was his realization of the inseparability of science from philosophy. He appreciated the axiomatic nature of mathematics and the presuppositional starting point of all scientific logic. The nature of the human condition is such that even scientific knowledge is inescapably finite, perspectival, and tentative. Some ideas must be pre-assumed to be true without absolute certainty. It is a non-sequitur to fallaciously conclude from our epistemological problem that objective reality is relative. Objective reality is exactly what it IS. We can only validly conclude that *our knowledge of* objectivity is subjective and relative, not reality itself.

Short-term usefulness can be provided even by ill-founded axiomatic systems. But long-term usefulness in many unrelated areas strongly suggests that an axiomatic system *corresponds to* objective reality—to the way things actually are. This is the realist's interpretation, at least. For the anti-realist, the centrality of choice with intent is all the more true. The solipsist's dreams of reality are not forced by external constraints and laws. The dream is a formal one, free and unconstrained by physicality or any inescapable objectivity outside of the solipsist's mind. Thus reality for the realist and anti-realist, for the modernist and the post-modernist, is ultimately formal, not physical. The F > P Principle holds either way.

The F > P Principle is nothing new. But it does need parsimonious expression using a formal term, and it needs to take its place as the most fundamental principle of science. It should not be surprising or controversial to presuppose that formalism preceded and controlled the very birth of physicality and physicodynamic relationships (Figure 3). Only dogmatic metaphysical imperatives and a long-standing Kuhnian paradigm rut preclude our admission of the obvious. Physics flows from formalism, not from physicality (its object of study). Physicality cannot explain physicality.

The F > P Principle is fully falsifiable through documentation of a single observed incident of nontrivial spontaneous physicodynamic enlightenment of any formalism. The firm scientific prediction is made that no exceptions to the F > P Principle will ever be observed.

References

1. Abel, D.L. 2009, The capabilities of chaos and complexity, Int. J. Mol. Sci., 10, (Special Issue on Life Origin) 247-291 Open access at http://mdpi.com/1422-0067/10/1/247
2. Abel, D.L.; Trevors, J.T. 2006, More than metaphor: Genomes are objective sign systems, Journal of BioSemiotics, 1, (2) 253-267.
3. Abel, D.L. 2007, Complexity, self-organization, and emergence at the edge of chaos in life-origin models, Journal of the Washington Academy of Sciences, 93, (4) 1-20.
4. Abel, D.L. 2008, 'The Cybernetic Cut': Progressing from description to prescription in systems theory, The Open Cybernetics and Systemics Journal, 2, 234-244 Open access at www.bentham.org/open/tocsj/articles/V002/252TOCSJ.pdf
5. Abel, D.L. 2009, The GS (Genetic Selection) Principle, Frontiers in Bioscience, 14, (January 1) 2959-2969 Open access at http://www.bioscience.org/2009/v14/af/3426/fulltext.htm.
6. Abel, D.L. 2009, The biosemiosis of prescriptive information, Semiotica, 2009, (174) 1-19.
7. Abel, D.L. 2010, Constraints vs. Controls, Open Cybernetics and Systemics Journal, 4, 14-27 Open Access at http://www.bentham.org/open/tocsj/articles/V004/14TOCSJ.pdf.
8. Abel, D.L.; Trevors, J.T. 2005, Three subsets of sequence complexity and their relevance to biopolymeric information., Theoretical Biology and Medical Modeling, 2, 29 Open access at http://www.tbiomed.com/content/2/1/29.
9. Abel, D.L.; Trevors, J.T. 2006, Self-Organization vs. Self-Ordering events in life-origin models, Physics of Life Reviews, 3, 211-228.
10. Wigner, E.P. 1960, The unreasonable effectiveness of mathematics in the natural sciences, Comm. Pure Appl., 13 (Feb).
11. Hamming, R.W. 1980, The unreasonable effectiveness of mathematics, The American Mathematical Monthly, 87, (2 February) 81-90.
12. Steiner, M. 1998, The Applicability of Mathematics as a Philosophical Problem. Harvard University Press: Cambridge, MA.
13. Einstein, A. 1920, Sidelights on Relativity. Dover: Mineola, N.Y.
14. Pattee, H.H. 1972, Laws and constraints, symbols and languages. In Towards a Theoretical Biology, Waddington, C. H., Ed. University of Edinburgh Press: Edinburgh, Vol. 4, pp 248-258.
15. Pattee, H.H. 1973, Physical problems of the origin of natural controls. In Biogenesis, Evolution, and Homeostasis, Locker, A., Ed. Springer-Verlag: Heidelberg, pp 41-49.
16. Pattee, H.H. 1995, Evolving Self-Reference: Matter, Symbols, and Semantic Closure, Communication and Cognition-Artificial Intelligence, 12, 9-28.
17. Pattee, H.H. 1995, Artificial Life Needs a Real Epistemology. In Advances in Artificial Life Moran, F., Ed. Springer: Berlin, pp 23-38.
18. Pattee, H.H. 2001, The physics of symbols: bridging the epistemic cut, Biosystems, 60, (1-3) 5-21.
19. Sagan, C. 2000, Cosmos, PBS TV series.
20. Koons, R.C. 2000, Realism Regained: An Exact Theory of Causation, Teleology, and the Mind. Oxford University Press: Oxford.
21. Pattee, H.H. 2000, Causation, Control, and the Evolution of Complexity. In Downward Causation: Minds, Bodies, and Matter, Andersen, P. B.; Emmeche, C.; Finnemann, N. O.Christiansen, P. V., Eds. Aarhus University Press: Aarhus, DK, pp 63-77.
22. Pearle, J. 2000, Causation. Cambridge University Press: Cambridge.
23. Abel, D.L. 2002, Is Life Reducible to Complexity? In Fundamentals of Life, Palyi, G.; Zucchi, C.Caglioti, L., Eds. Elsevier: Paris, pp 57-72.
24. Trevors, J.T.; Abel, D.L. 2004, Chance and necessity do not explain the origin of life, Cell Biology International, 28, 729-739.
25. Yockey, H.P. 2000, Origin of life on earth and Shannon's theory of communication, Comput Chem, 24, (1) 105-123.

26. Yockey, H.P. 2002, Information theory, evolution, and the origin of life. In Fundamentals of Life, Palyi, G.; Zucchi, C.Caglioti, L., Eds. Elsevier: Paris, pp 335-348.
27. Yockey, H.P. 2002, Information theory, evolution and the origin of life, Information Sciences, 141, 219-225.
28. Gánti, T. 2003, The Principles of Life. Oxford University Press: Oxford, UK.
29. Leff, H.S.; Rex, A.F. 1990, Maxwell's Demon, Entropy, Information, Computing. Princeton Univer. Press: Princeton, N.J.
30. Landauer, R. 1991, How molecules defy the demon. Book Review of Maxwell's Demon: Why Warmth Disperses and Time Passes by Hans Christian von Baeyer, reprinted 1998 by Random House, New York, last accessed in Oct of 2006 at http://physicsweb.org/articles/review/12/1/1. In Physics World
31. von Baeyer, H.C. 1998, Maxwell's Demon: Why Warmth Disperses and Time Passes. Random House New York.
32. Szilard, L. 1964, On the decrease of entropy in a thermodynamic system by the intervention of intelligent beings, Behav Sci, 9, (4) 301-10.
33. Lewis, G.N. 1930, The symmetry of time in physics, Science, 71, 569-576.
34. Abel, D.L. 2011, Moving 'far from equilibrium' in a prebitoic environment: The role of Maxwell's Demon in life origin. In Genesis - In the Beginning: Precursors of Life, Chemical Models and Early Biological Evolution Seckbach, J.Gordon, R., Eds. Springer: Dordrecht.
35. Voie, A. 2006, Biological function and the genetic code are interdependent, Chaos, Solitons & Fractals, 28, (4) 1000-1004.
36. Berlinski, D. 2000, The Advent of the Algorithm: The Idea that Rules the World. Harcourt, Inc.: New York.
37. Abel, D.L. 2009, The Universal Plausibility Metric (UPM) & Principle (UPP), Theor Biol Med Model, 6, (1) 27 Open access at http://www.tbiomed.com/content/6/1/27.
38. Küppers, B.-O. 1990, Information and the Origin of Life. MIT Press: Cambridge, MA.
39. Monod, J. 1972, Chance and Necessity. Knopf: New York.
40. Mayr, E. 1988, Introduction, pp 1-7; Is biology an autonomous science? pp 8-23. In Toward a New Philosophy of Biology, Part 1, Mayr, E., Ed. Harvard University Press: Cambridge, MA.
41. Mayr, E. 1982, The place of biology in the sciences and its conceptional structure. In The Growth of Biological Thought: Diversity, Evolution, and Inheritance Mayr, E., Ed. Harvard University Press: Cambridge, MA, pp 21-82.
42. Yockey, H.P. 1992, Information Theory and Molecular Biology. Cambridge University Press: Cambridge.
43. Yockey, H.P. 2005, Information Theory, Evolution, and the Origin of Life. Second ed., Cambridge University Press: Cambridge.
44. Bohr, N. 1933, Light and life, Nature, 131, 421.
45. Rocha, L.M. 1997, Evidence Sets and Contextual Genetic Algorithms: Exploring uncertainty, context, and embodiment in cognitive and biological systems. . State University of New York, Binghamton.
46. Rocha, L.M. 2000, Syntactic autonomy: or why there is no autonomy without symbols and how self-organizing systems might evolve them, Annals of the New York Academy of Sciences, 207-223.
47. Ledford, H. 2010, Mystery RNA spawns gene-activating peptides: Short peptides that regulate fruitfly development are produced from 'junk' RNA. In NATURE, Vol. Published online 15 July.
48. Craig, J.M.; Wong, N.C. 2011, Epigenetics: A Reference Manual | Book Caister Academic Press: p 450.
49. Robertson, M. 2010, The evolution of gene regulation, the RNA universe, and the vexed questions of artefact and noise, BMC Biology, 8, (1) 97.

50. Beiter, T.; Reich, E.; Williams, R.; Simon, P. 2009, Antisense transcription: A critical look in both directions, Cellular and Molecular Life Sciences (CMLS).
51. Royo, H.; Cavaille, J. 2008, Non-coding RNAs in imprinted gene clusters, Biol Cell, 100, (3) 149-66.
52. Abel, D.L. The GS (Genetic Selection) Principle [Scirus Topic Page]. http://www.scitopics.com/The_GS_Principle_The_Genetic_Selection_Principle.html (Last accessed September, 2011).
53. Costanzo, G.; Pino, S.; Ciciriello, F.; Di Mauro, E. 2009, RNA: Processing and Catalysis: Generation of Long RNA Chains in Water, J. Biol. Chem., 284, 33206-33216.
54. Weinberger, E.D. 2002, A theory of pragmatic information and its application to the quasi-species model of biological evolution, Biosystems, 66, (3) 105-19.
55. Abel, D.L.; Trevors, J.T. 2007, More than Metaphor: Genomes are Objective Sign Systems. In BioSemiotic Research Trends, Barbieri, M., Ed. Nova Science Publishers: New York, pp 1-15
56. Durston, K.K.; Chiu, D.K.; Abel, D.L.; Trevors, J.T. 2007, Measuring the functional sequence complexity of proteins, Theor Biol Med Model, 4, 47 Free on-line access at http://www.tbiomed.com/content/4/1/47.
57. Rocha, L.M. 2001, Evolution with material symbol systems, Biosystems, 60, 95-121.
58. Plato 1996, Parmenides In Parmenides' Lesson, Sayre, K. M., Ed. University of Notre Dame Press: Notre Dame.
59. Plato 1999, Allegory of the Cave, Book 7 of the Republic (514A–520A) 360BC. In Great Dialogues of Plato: Complete Texts of the Republic, Apology, Crito Phaido, Ion, and Meno, WarmingtonRouse, Eds. Signet Classics: New York, Vol. 1, p 316.
60. Abel, D.L. 2000 Is Life Reducible to Complexity?, Workshop on Life: a satellite meeting before the Millennial World Meeting of University Professors, Modena, Italy,
61. Abel, D.L. 2006 Life origin: The role of complexity at the edge of chaos, Washington Science 2006, Headquarters of the National Science Foundation, Arlington, VA
62. Abel, D.L. 2008 The capabilities of chaos and complexity, Society for Chaos Theory: Society for Complexity in Psychology and the Life Sciences, International Conference at Virginia Commonwealth University, Richmond, VA., Aug 8-10.
63. Abel, D.L. The Cybernetic Cut [Scirus Topic Page]. http://www.scitopics.com/The_Cybernetic_Cut.html (Last accessed Sept, 2011).
64. Abel, D.L. Prescriptive Information (PI) [Scirus Topic Page]. http://www.scitopics.com/Prescriptive_Information_PI.html (Last accessed September, 2011).
65. Popper, K. 1963, Conjectures and Refutations. Harper: New York.
66. Popper, K.R. 1972, The logic of scientific discovery. 6th impression revised. ed., Hutchinson: London.

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Glossary

Abiogenesis—the belief that life emerged spontaneously from non-life through natural process.

“Adjacent other”—the wonderfully inviting, mystical, poetic notion of Stuart Kauffman describing his belief in a spontaneously arising formal capability of physicodynamics (the inanimate mass/energy interactions, forces and laws of motion that are the subject of physics). Unfortunately, such imagination is purely metaphysical, never once observed, unfalsifiable, and has never logged a single prediction fulfillment. It can best be described as superstition or fairy tale—certainly not science.

Agency—the ability to choose from among real options and to voluntarily pursue goals such as formal utility. Agents are able to program logic gates, steer courses of action through long strings of decision nodes, and assemble and organize objects and events to create potential function—function not yet existent at the time choices must be made. Agency is invariably associated with life. Life itself is utterly dependent upon cybernetic programming—a phenomenon never observed independent of agency.

Algorithm—a step-wise, discrete process or procedure—often computational—leading to future utility. Algorithms require wise choices at decision nodes, logic gates and configurable switches prior to the realization of any function. Algorithms cannot be generated by after-the-fact natural selection of the fittest computational result or already-programmed species.

Animate—living.

Arbitrary—unconstrained by initial conditions or cause-and-effect determinism. As used in the context of cybernetics, arbitrary means more specifically choice-contingent, not chance-contingent. Arbitrary does not mean that the chooser flips a coin to decide, or that the chooser does not care what is chosen. Symbol systems, for example, require purposeful, choice-contingent assignment of certain symbolic “strokes of pen” to represent specific meaning. By convention, arbitrary rules of interpretation are followed that allow sender and receiver to communicate the same meaning and function from those symbols and symbol syntax.

Artificial Selection—change brought about by the purposeful choice contingency of agents selecting from among real options at bona fide decision nodes.

Change induced by choice-contingent causation and control (CCCC). Selection FOR POTENTIAL fitness—something that natural selection cannot do.

Axiom—A deductively underivable, and empirically and logically unprovable, propositional statement that is tentatively assumed to be true, or self-evident, and which serves as the basis for a whole deductive system of thought and inference.

Bijection—a mapping, correspondence, or translation, usually one to one, of one symbol system to another. When Hamming redundancy block-coding is used to reduce noise pollution in the Shannon channel, mapping can be many to one (e.g. triplet codons prescribing each amino acid).

Blueprint—a two-dimensional picture, or composite of signs, representing the plans of a building or other physical structure. The term blueprint is often misapplied to genetic and genomic instruction. Genomics does not employ signs or blueprints. Codons serve only as block codes of symbols in a formal linear digital material symbol system (MSS). No direct physicochemical interaction is involved in the polycodonic prescription of polyamino acid sequencing that determines which protein is produced in ribosomes.

Chance contingency—non-willful, non-steered independence from apparent "necessity" (cause-and-effect determinism). Possibilities and options are not purposefully chosen, but result from "the roll of the dice." Chance contingency gives rise to random variation—"noise." The Brownian motion caused by the heat agitation of molecules is an example of seeming chance contingency. "Just how random is randomness?" remains an open question. Many have argued that seemingly random events are actually the result of thus-far unknown causes, and highly complex interactions between multiple known physicodynamic causes.

Chaos—disorganization, not disorder! Abundant highly-ordered dissipative structures of Prigogine's chaos theory form momentarily out of chaos in nature. No spontaneous dissipative structure shows any evidence of formal organization. In fact, most self-ordered dissipative structures such as hurricanes and tornadoes only destroy organization.

Chemoton—Tibor Ganti's abstract model of the simplest all-or-none unit of life. It consists of three non-living, autocatalytic chemical components: a motor, boundary, and prescriptive information system. The stable motor is capable of self-reproduction and synthesis of everything needed for the other two subsystems. The chemical boundary is envisioned to be semipermeable and to allow transport in of needed nutrients and the excretion of wastes. The prescriptive information must be capable of self-replication and must control, not just constrain, metabolism, growth, and reproduction. The chemoton model lacks enzymes and genetic code. The problems with Ganti's model are many, starting with the fact that no one has ever observed such a minimal unit of life short of the cell itself. The mechanisms provided in the model are entirely inadequate to explain the derivation of most of this unit's attributes and capabilities.

Choice contingency—freedom from determinism involving a purposeful selection from among real options. Choice contingency is exercised by agents with intent for a reason and purpose. The goal of choice contingency is almost always some form of utility that is valued by the chooser.

Choice-Contingent Causation and Control (CCCC)—the steering of physical events and the organizing of physical entities into potential usefulness. CCCC can generate extraordinary degrees of unique functionality that have never been observed to arise from randomness or law-described necessity. Neither physicodynamics nor evolution can pursue potential utility (e.g., the programming of computational success prior to its realization). CCCC does. CCCC is the only known cause and governor of formalisms.

Code—a representational symbol system used to assign associations (e.g. via a codon table) or to convey meaningful messages (e.g., messenger molecules). In an everyday connotation, coding signs and symbols are usually substituted for letters or words. Most codes (e.g., ASCII, Zip code) are "open," (non-encrypted) with arbitrary meaning to communicate between two independent worlds. The codon/amino acid code is the most widely known code in life, but more than 20 other biosemiotic codes have been discovered in the past decade, each with no known physicochemical "cause." In molecular biology, genetic code is specifically used for:

1. instantiation of formal, immaterial programming choices into physicality
2. efficiency in translation between two different material symbol systems where molecules serve as "physical symbol vehicles" (tokens) in two different material symbol systems (MSS) rather than being mere physicochemical interactants/reactants
3. ease-of-transmission
4. noise pollution prevention in the Shannon channel (e.g., redundancy block coding)

5. proof reading and error correction (e.g. the processing of parity bit coding to detect noise pollution)

Complexity—the opposite of regularity, order, redundancy, and pattern. Complexity does not lend itself to algorithmic compressibility. Maximum complexity corresponds to randomness which contains no order, pattern or compressibility. Complexity is at opposite extremes with order on a bidirectional vector. Combinatorial complexity itself has nothing to do with functionality or the choice-contingent causation and control (CCCC) that generates nontrivial utility. The only relation of complexity to positive formalism is the mathematical probabilism used to measure complexity's negative uncertainty.

Composome—a hypothesized "metabolism-first" model referred to as an "ensemble replicator" or "compositional genome." The model imagines a self-reproducing assembly of different molecular species that manifests protometabolic "networks." The model was advanced because of serious problems with 1) template replication, 2) non-enzymatic biopolymer synthesis, and 3) a lack of Prescriptive Information (PI) source to program functional sequencing in RNA-World related models. No explanation has ever been provided for how protometabolic cybernetic networks could have spontaneously organized from physicodynamics alone, or how an ensemble of molecular species could have reliably reproduced themselves. Recent work by well-known and respected investigators has shown that the replication of compositional "information" is so inaccurate that fitter composomes could not possibly have evolved into metabolism-first life forms.

Configurable Switch—a purely physical device designed specifically to record (instantiate) nonphysical, formal choices into physical reality without any influence of physicodynamic forces, laws and constraints. Configurable switch settings are physicodynamically indeterminate (inert, decoupled, incoherent).

Configurable Switch (CS) Bridge—the one-way bridge that spans The Cybernetic Cut. Choice contingency causation and control (CCCC) traverses the vast ravine known as The Cybernetic Cut allowing traffic only from the formal far side to the physicodynamic near side. All formal meaning, function and bona fide organization enters the physical realm via this one-way bridge. Through "configurable" switch settings, formal choice contingency can become a source of physical causation. The setting of these configurable switches and logic gates constitutes the building of the CS Bridge. Nonphysical formalism itself can never be physical. In addition, the chance and necessity of physicality cannot steer objects and events towards formal utility. Chance and necessity cannot compute or make programming choices. Mere constraints cannot control or regulate. The inanimate environment does not desire or pursue function over nonfunction. So how does physicality ever get organized into usefulness of any kind? How does stone and mortar ever become a building? The answer lies in our ability to build a CS Bridge from the far side of The Cybernetic Cut—the formal side of reality—to the near side—the physicodynamic (physical) side of the ravine. The scaffolding needed to build this bridge consists of devices that allow instantiation of formal choices into physical recordations of those choices. This is accomplished through the construction of physical logic gates—the equivalent of Maxwell's demon's trap door. The gate can be opened or closed by agent choice at different times and in difference contextual circumstances. The open or shut gate corresponds to "yes" vs. "no," "1" vs. "0." Because the gate can be opened or closed by the operator at will, we call it a "configurable" switch. Another means of crossing the one-way CS Bridge across The Cybernetic Cut is to select physical symbol vehicles (tokens) from an alphabet of tokens available in a material symbol system. Assembling components into a holistic Sustained Functional System (SFS) or machine is another example of the one-way traffic flow across the CS Bridge from formalism to physicality.

Computational halting—a program finishes running rather than going on forever. Computational "success" is usually implied with the term halting, meaning that the program does what it is supposed to do within a finite period of time.

Constraints—a restriction or limitation of possibilities caused by initial (starting) conditions or by the regularities of nature described by physical law. Constraints themselves play no role in steering, controlling or regulating events to achieve formal function. Constraints are blind to formalisms. However, constraints can constitute barricades and bottlenecks for agent-pursued goals.

Contingency—in a past-tense context, contingency means that an event could have occurred other than how it happened. In a present and future context, contingency means that events can unfold in multiple ways despite both local and seemingly universal law-like constraints. Contingent behavior is not forced by physicodynamic necessity. Contingency embodies an aspect of freedom from physicochemical determinism.

Control—to purposefully steer toward the goal of formal function and pragmatic success. To regulate. To select for potential usefulness.

Cybernetic Cut—the most fundamental dichotomy of reality. The dynamics of physicality ("chance and necessity") lie on one side of a great divide. On the other side lies the ability to choose with intent what aspects of ontological being will be preferred, pursued, selected, rearranged, integrated, organized, preserved, and used (formalism). Life is unique from inanimate physics and chemistry in that life's control and regulation arise from the far side of The Cybernetic Cut.

Cybernetics—the study of control and of various means of programming, organizing, steering, and regulating physicality. Mere physicodynamic constraints are blind and indifferent to formal success. Only controls, not constraints, steer events toward pragmatic goals such as being alive and staying alive.

Decision nodes—bifurcation points which cannot be traversed by a mere "flip of the coin," at least not if one expects pragmatic results or reliable escape from danger. Decision nodes, as the name implies, require wise purposeful choices to achieve goals. A classic example is the purposeful setting of a "logic gate" in computing in order to integrate circuits or achieve computational success.

Decision theory—the study of various outcomes resulting from purposeful decisions at bona fide decision nodes. Decision nodes are more than mere "bifurcation points," which could be traversed using a fair coin flip to determine which way to go at each "fork in the road." When decision nodes are replaced with mere bifurcation points, universal experience shows a rapid deterioration of formal function potential.

Decode—to decipher the meaning of a message through mapping representational symbols to meaningful language or computation. The interpretation of symbols and symbol syntax in a symbol system.

Decrypt—to decode, but with the connotation that the original encoding was not "open," but written with the intent to make decoding very difficult by an enemy at war, for example.

Descriptive Information (DI)—positive background semantic information coming from an external source that serves to reduce uncertainty and to educate one's knowledge. DI provides valued common-sense knowledge to human beings about the way things already are. Thus, being can be described to provide one form of Functional Information (FI: intuitive and semantic information). However, the DI subset of FI is very limited and grossly inadequate to address many forms of instruction (Prescriptive Information (PI) and "how to" information for design, creativity, engineering, control and regulation.

Dissipative Structures of Chaos Theory—spontaneously self-ordered, momentary phenomena usually occurring in rapid succession so as to give the impression of a sustained structure (e.g., a candle flame; a tornado). Dissipative structures occur naturally out of mass/energy interactions alone. They require no choice-contingent causation and control (CCCC). Dissipative structures are often mistakenly viewed as evidence of self-organization in nature when in fact they example nothing more than spontaneous self-ordering with no formal components and no attention to the goal of functionality of any kind.

Edge of Chaos— the wonderfully inviting and mystical notion of complexity pursued by Christopher Langton, Doyne Farmer, J.P. Crutchfield, Melanie Mitchell, Stuart Kauffman and others that loosely describes a state of spontaneously realizable formal capability and self-organization arising out of physicodynamics alone. Melanie Mitchell has since questioned the validity of this notion. Such imagination is purely metaphysical, unobserved in inanimate nature, unfalsifiable, and no record exists of a single prediction fulfillment. It can best be described only as superstition or fairy tale, except where formalism is smuggled in through the back door to illegitimately redefine such terms as "phase transitions" and "constraints" (e.g., using the word "constraints" to mean formal "controls," where the constraints of inanimate cause-and-effect determinism are illegitimately granted the ability to purposefully steer events toward formal functionality or pragmatic success).

Emergence—the spontaneous occurrence in nature of more complex patterns arising from multiple simpler interactions. The spontaneous formation of symmetrical patterns in snowflakes during atmospheric precipitation is an example of emergence arising from purely physicodynamic self-ordering. Candle flame shapes, vortices of swirling water at bathtub drains, tornadoes and hurricanes all self-order spontaneously into rapid successions of momentary dissipative structures (the subject of chaos theory). Poorly understood is that no known cases of emergent self-ordering have anything to do with organization, and especially not "self-organization." Organization is formal and always arises through choice contingent causation and control (CCCC) from the far side of The Cybernetic Cut. No instance of bona fide "self-organization" has ever been observed; only unimaginative, redundant, lo-informational, self-ordering occurs spontaneously in inanimate nature out of chaos (which means disorganization, not disorder!).

Encode—To use a symbol system to represent, record and communicate meaningful messages. Molecular biology stores and passes along into progeny Prescriptive Information (PI, of which linear digital cybernetic programming is a major component) needed for organization and metabolic function. Encoding involves conversionary algorithms that biject or translate one symbol system into another.

Encrypt—to encode using a symbol system not easily deciphered and purposefully inaccessible to unwanted decoders.

Entropy—energy not available for formally useful work; the progressing formal disorganization observed in nature that is so often erroneously confused with increasing "disorder." Evidence of the 2nd Law is regularly observed with simultaneous increases in order, as with crystallization. Clearly, increasing entropy is not synonymous with increasing disorder. Physicodynamic entropy is not the same as informational entropy, which is a measure of epistemological uncertainty associated with a random variable. Informational entropy is a purely formal concept which, being nonphysical, has nothing to do with mass or energy, and everything to do with mathematical probabilism.

Epigenetic—the study of variation in heritable gene expression that is not caused by variation in nucleotide sequence of the genes. Histone deacetylation and DNA methylation are classic examples of gene suppression that does not affect nucleotide sequencing. Such alterations continue to alter gene expression throughout multiple future generations. Differentiation of the zygote (fertilized egg) into different cell types during development involves still other aspects of epigenetic control.

Epigenomics—the study of factors such as epigenetic DNA methylation, histone protein modifications, and chromatin structure on overall genomics and upper-level DNA structural (three-dimensional) Prescriptive Information (PI).

Falsifiability—the possibility that a claim, particularly a universal assertion, can be evaluated and potentially refuted by empirical testing showing results incongruous with that claim. The capability of disproving a proposition, hypothesis or theory by showing logical contradiction, or by finding, through experimentation, repeatable contradictory exceptions.

Fits—functional bits. The measurement of Functional Sequence Complexity, denoted as ζ, is defined as the change in functional uncertainty from the ground state $H(X_g(t_i))$ to the functional state $H(X_f(t_i))$, or $\zeta = \Delta H (X_g(t_i), X_f(t_j))$. The resulting unit of measure is defined on the joint data and functionality variable. The unit Fit thus defined is related to the intuitive concept of functional information, including genetic instruction and, thus, provides an important distinction between functional information and Shannon information.

Formal—relating to Plato's forms and Aristotle's appreciation of general classes of form and function that transcend particular physical structure and shape. Formal behavior is abstract, mental, arbitrary, nonphysical, and choice-contingent. The cognitive behavior of agents is typically goal- and function-oriented.

Formalism—a system of rules of thought or action typically involving symbol systems and requiring choices to be made at decision nodes, logic gates or configurable switch settings. Formalisms employ conceptual representationalism, mathematics, language, and/or categorical groupings of related ideas. Formalisms arise out of uncoerced choices in the pursuit of function and utility. Formalisms are typically computationally successful, integrated-circuit producing, and/or algorithmically optimizing. Formalisms require bona fide decision nodes, not just "bifurcation points. Language, mathematics, programming, and logic theory are all formalisms. Formalisms are governed by arbitrary rules, not laws. Listed below are aspects of reality that are all formalisms. None of these formalisms can be encompassed by a consistently held naturalistic worldview that seeks to reduce all things to physicodynamics:

1. Mathematics
2. Language
3. Inferential and deductive logic theory
4. The sign/symbol/token systems of semiosis
5. Decision theory
6. Cybernetics (including computer science)
7. Computation
8. Integrated circuits
9. Bona fide organization (as opposed to mere self-ordering in chaos theory)
10. Semantics (meaning)
11. Pursuits of goals
12. Pragmatic procedures and processes
13. Art, literature, theatre, ethics, aesthetics
14. The personhood of scientists themselves

All of the above formalisms depend upon choice contingency rather than chance contingency or necessity. Formalism also entails choices made in pursuit of potential function. Natural selection (NS) cannot select for potential function. NS can only favor the fittest already-programmed, already-existing, already living phenotypic organisms.

Formalism > Physicality (F > P) Principle—the most fundamental axiom of science states that Formalism not only describes, but preceded, prescribed, organized, and continues to control, regulate, govern and predict physicodynamic reality and its inter-actions. The F > P Principle is an axiom that defines the ontological primacy of formalism. Formalism is the source of all aspects of reality, both nonphysical and physical. Formalism organized physicality before the fact of physicality's existence. Formalism gave rise to the equations, structure and orderliness of physicality rather than to chaos (disorganization, not disorder!). This alone explains why the scientific method must be conducted in a rational manner, why the applicability of mathematics to physical interactions is reasonable rather than unreasonable, and why formalism can reliably predict physical interactions. The quest for a mathematical unified field of knowledge presupposes the F > P Principle. The F > P Principle further states that reality is fundamentally arbitrary—rule and choice-contingency based, not indiscriminately forced by an infinite regress of cause-and-effect determinism. Physicality cannot even spawn a study of itself—physics—because physics is a formal enterprise. Nothing within the "chance and necessity" of physicality itself is capable of generating formal logic, computation, mathematical relationships, or cybernetic control. Only formalisms can measure, steer, manage, and predict physicality. Physicodynamics constrains; formalism controls.

Function—usefulness; utility; contributing to productivity and efficiency. "A function is a goal-oriented property of an entity," Says Voie. "Functional parts are only meaningful under a whole, in other words it is the whole that gives meaning to its parts" [35].

Functional Sequence Complexity (FSC)—a sequence of subunits that produces utility in some larger context, as a string of amino acids performing a protein function of importance and value in a larger metabolic scheme. Also, a linear, digital, cybernetic string of symbols representing syntactic, semantic and pragmatic prescription; each successive symbol in the string is a representation of a decision-node configurable switch setting---a specific selection for potential function. FSC prescribes or produces usefulness, usually via algorithmic processing.

Functional Information (FI)—Intuitive semantic information that serves some purpose such as educating prior uncertainty, or instructing how to accomplish some goal. FI technically has two subsets: Descriptive (DI) and Prescriptive (PI), each discussed in this glossary.

Genetic Code—the arbitrary representational symbol system used by life to assign associations (e.g. via a codon table) or to convey meaningful messages (e.g., messenger molecules). In an everyday connotation, coding signs and symbols are usually substituted for letters or words. The codon/amino acid code is the most widely known code in life, but more than 20 other biological semiotic codes have been discovered in the past decade, each with no known physicochemical "cause." In molecular biology, genetic code is specifically used for:

1. instantiation of formal, immaterial programming choices into physicality
2. efficiency in translation between two different material symbol systems where molecules serve as "physical symbol vehicles" (tokens) in two different material symbol system (MSS) rather than being mere physicochemical interactants/reactants
3. ease-of-transmission
4. noise pollution prevention in the Shannon channel (e.g., redundancy block coding)
5. proof reading and error correction (e.g. the processing of parity bit coding to detect noise pollution)

Genetic Selection (GS) Principle—states that biological selection must occur at the point when the sequencing of monomers is established. Nucleotides must be selected at the molecular-genetic level of 3'5' phosphodiester bond formation. After-the-fact differential survival and reproduction of already-programmed, already-living phenotypic organisms (natural selection) does not explain polynucleotide sequence prescription and coding.

Genetics—the study of the prescription of form, function and metabolic contribution by the arbitrarily programmed material symbol system of polynucleotide sequencing in DNA. Triplet codon sequence in coding regions is translated into amino acid sequence in ribosomes which in turn determines minimum Gibbs-free-energy folding into three-dimensional protein globular structure. Genetics includes not only the study of coded genetic control through the inheritance of discrete units called genes, but variation through mutations, environmental factors, and the effects of many non-coding regulatory RNAs and epigenetic elements that affect biomolecular structure, function, metabolism and phenotypic expression.

Genomics—a more holistic study than genetics that investigates the interactions of all of the various networks of the entire genome, mRNA transcriptome, and proteome. Genetics tends to focus more on the effects of individual gene knock-outs. Genomics includes a study of pleiotropy (where one gene affects multiple phenotypic traits), epistasis (where additional modifier genes affect a single main gene), and heterosis (where outbreeding leads to hybrid vigor).

Hamming Block Code—an error-correcting redundancy code using a fixed or constant number of multiple loci comprising each "block" of a linear string of symbols to represent each prescribed unit of instruction. Triplet codons in coding regions of DNA, for example, always consist of a block of three nucleotides in a row to prescribe each amino acid. Discounting the stop codons, 61 ways exist to prescribe formally 20 amino acid options in the ribosomes. Catastrophic "frame shift" errors can result if decoding is not begun at the correct starting locus in the string, or if the number of loci in each block does not remain constant, or if additional amino acids are added to the code through time (each of which needing a new triplet codon block of representational symbols). The latter realities make the notion of gradual evolution of the genetic code from purely physicodynamic factors fraught with seemingly insurmountable problems.

Hypercycle—an autocatalytic cycle induced by circular constraints that lead to redundant self-replication. Hypercycles are envisioned to generate formal self-organization and progressively higher levels of formal organization. The model suffers from the confusion of formal programming and organizational controls with mere circular physicodynamic constraints. In the real world, these self-reinforcing loops lead only to the consumption of all resources in the production of the same few redundant products. The result is the depletion of the tremendous phase space that would be needed for any other theoretically contributing players to "evolve" into a legitimate protometabolism. Like all molecular evolution models of life origin, it suffers from a lack of organizational directionality and pursuit of formally useful interactive products. Empirical support for Eigen and Schuster's original notion of spontaneous hypercycles and their ever-increasing protometabolic competence has never accumulated.

Inanimate—non-living.

Instantiate—to insert or infuse aspects of one category into another normally separate and distinct category. In the context of cybernetics, the term is used to denote incorporating programming choices into physical computational devices. Nonphysical formalisms can only be instantiated into physical reality through the setting of configurable switches, the selection of "physical symbol vehicles" (tokens) from an alphabet of tokens, or though the design and engineering of physical devices (e.g., sophisticated machines, robots). In object-oriented analysis, design and programming, creating an object from a class is called instantiating the class. A class has certain aspects that are "infused", or become aspects of the object. Therefore, the word "instantiate" in this context involves not a "separate and distinct" category, but an "instance" of the category (class).

Law of Organizational and Cybernetic Deterioration/Decline (OCD Law)—The OCD Law states that, absent the intervention of formal agency, any nontrivial organization or cybernetic/computational function instantiated into physicality (e.g., integrated circuits; programmed computational success) will invariably deteriorate and fail through time. This deterioration may not be continual. However, it will be continuous (off and on, but overall consistently downhill). Computers, robots, all forms of Artificial Intelligence and Artificial Life, messages instantiated into material symbol systems or electronic impulses, will invariably progress toward dysfunction and fail. The OCD Law is not to be confused with the Second Law of Thermodynamics. The OCD Law is not concerned with the entropy of statistical mechanics or the "entropy" or "mutual entropy" of Shannon's probabilistic combinatorial uncertainty. Heat exchange, heat dissipation, phase changes, order and disorder are not at issue. The OCD Law addresses only the formal organization and utility already instantiated into physical media and environments. Only purposeful choice contingency at bona fide decision nodes can rescue from deterioration the organization and function previously programmed into physicality.

Law of Physicodynamic Incompleteness—an axiomatic proposition stating that physicochemical interactions are inadequate to explain the mathematical and formal nature of physical law relationships. Physicodynamics cannot generate formal processes and procedures leading to nontrivial function. Chance, necessity and mere constraints cannot steer, program or optimize algorithmic/computational success to provide desired nontrivial utility. nanimate physicodynamics is completely inadequate to generate, or even explain, the mathematical nature of physical interactions (the laws of physics and chemistry). The Law further states that physicodynamic factors cannot institute formal processes and procedures leading to sophisticated function. Chance and necessity alone cannot steer, program or optimize algorithmic/computational success to provide desired nontrivial utility. As a major corollary, physicodynamics cannot explain or generate life. Life is invariably cybernetic. Inanimate physics and chemistry are inadequate to explain the spontaneous self-organization of even a protometabolism, let alone the generation of life from non-life (abiogenesis.)**Laws**—generalized reduction algorithms, extracted and derived from observed regularities in reams of data, describing and predicting different aspects of regular physical interactions in nature despite varying initial conditions.

Linear digital symbol system—A system of recordation, transmission, and communication of messages between sender and receiver made possible by both following the same set of arbitrarily assigned rules of formal symbolization. Messages consist of a succession of discrete symbols and symbol syntax having arbitrarily assigned meaning and communicative function. Language, computer programs consisting of a succession of 0's and 1's, and polycodonic prescription of amino acid sequence in proteins by coding DNA are examples of linear digital symbol systems.**Liposomes**—artificially produced vesicles designed to deliver drugs and other agents to various locations within living cells, and used to mimic hypothesized protocells in life-origin studies.

Logic gates—a type of cybernetic configurable switch that can be set to either open or closed in a binary programming mode. Logic gates allow formal purposeful choices to be instantiated into physical computational systems and integrated circuits.

Machine— a physical device, often a relatively independent functioning contrivance, that utilizes mass and energy to accomplish a nonphysical formal function. The classical definition of machine involved the forces of motion and power to accomplish some desired task referred to as "work." Such "work" is far more than the mere transfer of energy. Even the "simple machines" are used by agents to transform the direction or magnitude of a force in order to accomplish a desired goal. Physicodynamics do not pursue goals. The advent of electronics and computers broadened our definition of "machine" no longer to require moving parts. Molecular biology has opened our eyes further to a vast array and coordinated interplay of the most sophisticated machines of all—molecular machines.

Macroevolution—the belief that evolution can spontaneously give rise to ever more sophisticated genetic and genomic PI programming, and to increasing conceptual complexity in organisms, giving rise to "higher" families, orders, classes, and phyla. No observations or prediction fulfillments exist in support of macroevolution. Falsification is not possible, raising the question of whether the notion of macroevolution is a scientifically respectable theory.

Material Symbol System (MSS)—A symbol system that formally assigns representational meaning to physical objects (tokens, physical symbol vehicles). The Game of Scrabble employs physical symbol vehicles, wood block tokens with inscribed symbols, that can be resorted to spell meaningful words and messages.

Meaning—Aboutness; function; the sense, importance, significance, implication, value, consequence, import or purpose of a message; the reason for sending a communication. In molecular biology, "meaning" is usually defined in terms of contribution to biofunction and holistic metabolism.

Mechanism—a means, directed process, programmed procedure, technique, system, or component of a machine that achieves some pragmatic goal. "Mechanism" is a formal term, not a physicodynamic term. "Mechanism," like the term "useful work," has no place in a consistently held naturalistic physics and chemistry context. The etiology of "mechanism" from both Latin and Greek derives from the word "machine." Metaphysical naturalism has never demonstrated the ability of physicodynamics and so-called "natural process" to produce nontrivial machines or sophisticated pragmatic mechanisms.

Message—a signal that contains interpretable meaning, and that manifests or fosters functionality at its destination. A signal that conveys Descriptive (DI) and/or Prescriptive Information (PI), both of which are subsets of Functional Information (FI).

Metabolism-First World—A model of life-origin that proposes that a protometabolism spontaneously self-organized, probably in a vesicle, without the aid of any Prescriptive Information contained in a material symbol system (such as DNA nucleotide or codon sequence) or RNA memory or catalysis. Variations include the Garbage-First model, Clay Life and other Mineral First models, Chemoton World, Peptide World, Lipid World, and Protein world.

Micelle— A spherical aggregate of surfactant molecules containing often containing a liquid colloid. In water, the surfactant molecules spontaneously self-order (NOT formally organize) with the hydrophilic (water-loving) "heads" aimed outward towards the aqueous solvent, and the hydrophobic (waterhating) tails aimed into the center of the sphere. A micelle is a crudely self-ordered structure similar to an oil-in-water droplet.

Microevolution—the universally acknowledged, spontaneously acquired, change in heritable phenotypic traits within a species, possibly within a family, but never extending to evolutionary transition to a more conceptually complex ("higher") order, class or phyla.

Molecular evolution—as used in this volume, molecular evolution pertains mostly to prebiotic evolution from inanimate molecules into a living state—abiogenesis. Of prime interest is how ordinary molecules could have self-organized, in a formal sense, under the influence only of physicochemical forces and attractions, to produce so many integrated biochemical pathways, cycles, highly tailored "parts" or components, and such goal-oriented holistic metabolism. All of these are needed to organize and sustain even the simplest conceivable life form.

Multiverse—the purely metaphysical rather than scientific notion that this Universe is only one of countless universes.

Mutations—alterations in genomic nucleotide sequencing, including the ribonucleotide sequencing of RNA viruses. A special case of mutation is when protein structure "mutates" (misfields) in prions in a way that affects the folding of other protein molecules in that family. Prion misfoldings are contagious and are subject to natural selection. Replication errors, mutagenic chemicals, radiation, transposons and deliberate hypermutation in immune cells are common causes of mutations. Mutations can be neutral (having no selective advantage, and no immediate apparent deleterious phenotypic effect), deleterious (most mutations), or in extremely rare instances, beneficial, at least in some very indirect way (e.g., sickle cell anemia rendering erythrocytes more resistant to the malaria parasite). The very recent discovery of vast new areas of functionality performed by non-coding DNA and non-mRNAs raises the question of whether most supposedly neutral mutations are really neutral. Far more likely is the progressive accumulation of noise pollution of what were highly refined regulatory instructions, the effects of which will only become apparent through time as our knowledge of molecular biology and microRNA regulation grows.

Natural selection—differential survivability and reproduction of the best already-programmed, already-living phenotypic organisms. Natural selection (NS) has no creative programming ability at the genetic or genomic level (See The GS Principle). NS is purely eliminative of less fit phenotypes. It cannot program genomes or other material symbol systems at the molecular level. Natural selection results only in the differential preservation and reproduction of the fittest already-existing organisms.

Necessity—a term often used almost synonymously with Law, as in Monod's Chance and Necessity, referring to the physicodynamic cause-and-effect determinism of inanimate nature. Necessity refers to regular physical interactions in nature that are so dependable, despite varying initial conditions, that the outcomes seem unavoidable, completely predictable, or "necessary."

Neural net—originally, the central nervous system consisting of circuits of neurons and their interconnections. Artificial neural networks are mathematical and computational models of the central nervous system and are used to model information processing and artificial intelligence. Neural networks are formal cybernetic constructs, not just physicodynamic "buttons and strings."

Noise—chance-contingent, meaningless, non-functional, unwanted disturbances or perturbations that corrupt meaningful, functional, desired, choice-contingent messages and Prescriptive Information (PI) commands.

Order—regularity, recurring pattern, redundancy, algorithmic compressibility. Order is antithetical to complexity and at opposite extremes with complexity on a bidirectional vector. Maximum complexity corresponds to randomness, which contains no order or compressibility. Order contains very little information, whereas organization typically contains high Prescriptive Information (PI) content from instantiated choice contingent causation and control (CCCC).

Ordered Sequence Complexity (OSC)—a linear string oflinked units, the sequencing of which is patterned either by the naturalregularities described by physical laws (necessity) or by statistically weightedmeans (e.g., unequal availability of units), but which is not patterned bydeliberate choice contingency (agency). OSC is marked by repetition or redundancy, or recurring pattern in its sequence. Reuse of programing modules or structures needed for construction can create the illusion of OSC when in fact the recurring pattern is generated by choice contingency (FSC). . The more highly ordered (patterned) a sequence, the more highly compressible that sequence becomes, the less Shannon uncertainty, and the less potential prescriptive information that can be instantiated into that sequence.

Organization—the choice-contingent association, categorization, configuring, steering, controlling, arranging or integrating of ideas or physical parts into a productive scheme, system or device that accomplishes formally useful work. Organization should never be confused with low-informational "order" or "pattern." Organization typically arises only out of high Prescriptive Information (PI) and sophisticated choice-contingent causation and control (CCCC).

Organization (O) Principle—Nontrivial formal Organization can be produced only by Choice-Contingent Causation and Control (CCCC). See Chap 12, Sec 9.

Panspermia— the belief that life originated elsewhere in the Universe and was spread to earth, probably by meteoroids or asteroids. This same definition applies to exogenesis. Panspermia suggests that life is more generalized throughout the Cosmos, whereas exogenesis does not necessarily make this claim. The notion of panspermia does nothing to help explain how life could have spontaneously self-organized out of nothing but physicodynamics. It does little to extend the time available for molecular evolution since the Big Bang, since the age of the cosmos is believed to be only three times that of the earth.

Pattern—predictable, regular or repetitive form. A recurring, compressible order that reduces Shannon uncertainty and the ability to instantiate functional choices (semantic information) into that medium. Patterns can arise, however, in meaningful messages and programs from deliberate reuse of linguistic elements and programming modules.

Peptide World hypothesis—the belief that life arose as a metabolism-first self-organization from interactions between short peptides and polypeptides. Adherents to this model point to the near impossibility of spontaneous ribonucleotide formation in a prebiotic environment, activation problems of ribonucleotides, difficulties of polymerization bond formation in water, short half-lives, etc.

Phenotype—the already-programmed, already-organized, already-living, holistic physical organism.

Physical symbol vehicle—a token; a physical object employed as a formal representational symbol. Meaning is consciously assigned arbitrarily to each physical object, thereby making possible the instantiation of choice contingency into the physical world. The physical token then functions as a formal meaningful and functional symbol in a material symbol system rather than as a physical interactant. The blocks of wood with inscribed letters in a Scrabble game, or the nucleotides in genes serve as physical symbol vehicles.

Physicodynamic determinism—cause-and-effect physicochemical interactions that lead back in an infinite regress of determinism to some physical first cause. Physicodynamic determinism, often referred to as "necessity," does not explain the reality of choice contingency—the freedom to choose from among real options to achieve choice-contingent causation and control (CCCC). It also does not explain the rational, mathematical and formal nature of reality.

Physicodynamically indeterminate—Contingent; undetermined by cause-and-effect determinism; could have happened other than it did; having multiple possible options despite initial constraints and the laws of physics and chemistry.

Physicodynamically inert—physicodynamically indeterminate; contingent; undetermined by cause-and-effect determinism; could have happened other than it did; having multiple possibilities or options of occurrence despite initial constraints under the laws of physics and chemistry.

Physicodynamically incoherent— physicodynamically indeterminate; contingent; undetermined by cause-and-effect determinism; could have happened other than it did; having multiple possibilities or options of occurrence despite initial constraints under the laws of physics and chemistry.

Physicodynamic discontinuity— physicodynamically indeterminate; contingent; undetermined by cause-and-effect determinism; could have happened other than it did; having multiple possibilities or options of occurrence despite initial constraints under the laws of physics and chemistry.

Potential function—Formal function not yet existent, which, when nontrivial, only comes into existence through advanced planning, assembling of component parts or processes, programming and engineering choices. Physicodynamics alone is incapable of producing sophisticated formal function. Natural selection (NS) cannot select for potential function at the genetic programming level (The GS Principle). NS can only prefer existing fittest phenotypic organisms.

Pragmatic—functional, useful, helpful, utilitarian, productive, contributory to a larger or higher organization or goal.

Prebiotic—referring to the inanimate physical environment (nature) that existed prior to the origin of life.

Prescriptive Information (PI)—a subset of Functional Information (FI) that either instructs or indirectly produces nontrivial formal function. PI is semantic "how to" information. PI provides the instructions required to organize and program sophisticated utility. Potential formal function and computational success must be prescribed in advance by PI programming prior to halting, not just described after the fact. PI requires anticipation and "choice with intent" at bona fide decision nodes. PI either tells us what choices to make, or it is a recordation of wise choices already made. PI is positive, as opposed to negative uncertainty. Prescriptive information (PI) does far more than merely describe (Descriptive Information [DI])). We can thoroughly describe a new Mercedes automobile, providing a great deal of DI in the process. However, this functional DI might tell us almost nothing about how to design, engineer and build that Mercedes. PI provides the instructions required to organize and program sophisticated utility. PI designs, creates, engineers, controls and regulates. The inanimate physical environment is incapable of participating in such formal pursuits. So-called "natural" physicodynamics cannot generate nonphysical PI. PI can perform nonphysical "formal work." PI can then be instantiated into physicality to marshal physical work out of nonphysical formal work. Cybernetic programming is only one of many forms of PI. Ordinary language itself, various communicative symbol systems, logic theory, mathematics, rules of any kind, and all types of controlling and computational algorithms are forms of PI. Neither chance nor necessity has been shown to generate PI. Choice contingency, not chance contingency, prescribes nontrivial function. PI typically is recorded into a linear digital symbol system format. Symbols represent purposeful choices from an alphabet of symbol options. Symbol selection is made at bona fide decision nodes.

ProtoBioCybernetics—the study of the derivation of control and regulation in the first life forms. Cybernetics incorporates Prescriptive Information (PI) into various means of steering, programming, communication, instruction, integration, organization, optimization, computation and regulation to achieve formal function. "Bio" refers to life. "Proto" refers to "first." Thus, the scientific discipline of ProtoBioCybernetics specifically explores the often-neglected derivation through "natural process" of initial control mechanisms in the very first theoretical protocell.

Protobiont—a hypothesized initial precursor of living organisms, usually thought to have been a protocell with some semblance of a vesicular-like phospholipid or bilayer "membrane." Contained within this vesicle is believed to have been the minimal unit of protolife or life. Tibor Ganti's minimal unit of life, the chemoton, includes the vesicular or membrane-like barrier.

ProtoBioSemiotics—the study of meaningful or functional messaging and how it arose within and between the first protobionts.

Protocell—a hypothesized initial "cell" with a vesicular-like phospholipid or bilipid "membrane" in which life is imagined to have spontaneously self-organized.

Protometabolism—the hypothesized first semblance of integration of bio-chemical pathways and cycles into a holistic, organized, functional metabolic system.

Random Sequence Complexity (RSC)—a linear string of stochastically linked units, the sequencing of which is dynamically inert, statistically un-weighted, and is unchosen by agents; a random sequence of independent and equiprobable unit occurrence. RSC is the most complex of the three kinds of sequence complexity, the reason being that a random sequence contains no al-gorithmically compressible order. Its sequence cannot be enumerated using any representational string shorter than itself. RSC manifests the absence of any order or pattern. RSC represents maximum uncertainty, and therefore con-tains the maximum number of Shannon bits. Although maximally complex, RSC does nothing functional, emphasizing that complexity is not an explana-tion for utility or pragmatic worth.

Regulation—the choice-contingent steering, controlling, adjusting and fine-tuning of some formal process, procedure, or reaction sequence. To regulate presupposes freedom from law sufficient to manage events by formal choice-contingent causation and control (CCCC).

RNA analogues— Molecules similar in structure to RNA, but having the phosphate, ribose or nucleobase replaced with some alternative. Alternate nu-cleobase Molecules similar in structure to RNA, but having the phosphate, ri-bose or nucleobase replaced with some alternative. Altering nucleobases (e.g. fluorophores) typically result in altered base pairing and stacking properties. Peptide nucleic acid (PNA) is a phosphate-sugar backbone analogue. Other backbone analogues include threose nucleic acid (TNA), glycol nucleic acid (GNA), Morpholino or locked nucleic acid (LNA). Originally, it was hoped that RNA analogues might solve the many problems of prebiotic RNA chemis-try that threatened the RNA World hypothesis. However, the Pre-RNA World hypothesis has encountered many roadblocks of its own.

RNA World hypothesis—the belief that initial life consisted primarily of RNA rather than the DNA and protein necessary for current life. RNA can potentially retain nonphysical information in its physical matrix and self-replicate. RNA can act as a crude catalyst compared to proteins. Numerous biochemical hurdles in a prebiotic environment have rendered the RNA World hypothesis highly suspect. The PreRNA, RNA analog, and RNA World models probably remain the most favored models in life origin theory today. Ribonucleoprotein enzymes such as ribosomes are thought to have arisen from molecular evolution prior to DNA-protein life.

Rules—Choice-contingent guidelines intended to guide procedures, competing interests, and ethical behavior. Rules are nonphysical, formal, mental constructions. Rules are not laws. Laws describe and predict deterministic physicodynamic interactions. Loss of formal utility usually accompanies the disobedience of rules unless a pragmatically superior rule system is being explored. Rules can also be arbitrarily agreed-upon conventions that govern language and voluntary behavior. Rules exist to guide choices. Rules can be broken at will, often at the expense of efficiency or efficaciousness in accomplishing some pragmatic goal.

Semantic—meaningful or functional.

Semiotics—the study of symbolization using sign and symbol systems, meaningful message generation, language, programming, and the communication methods employed. The three main branches of semiotics are 1) semantics—the meaning generated by how symbols are arbitrarily assigned to represent objects and ideas, 2) Syntactics—the sequencing and relation of symbols to one another to create higher meaning, and 3) Pragmatics—the usefulness of symbol system applications and their communication.

Sign—a two-dimensional picture or drawing conveying representational meaning to one's senses. The picture or drawing is self-explanatory because we recognize by sight physical objects that are being depicted from our every-day empirical world. A visual image of real world objects is delivered by the sign. Our consciousness links the two-dimensional picture with our experience of and with that object. A picture of an automobile with two wavy lines emanating from behind its rear tires is a street sign conveying the message of slippery road conditions.

Signal—a transmission of mass/energy from one location to another, as a pulsating emission of light from a distant star. A signal need not have any meaning or function, and should be carefully distinguished from "message." Messages always contain formal meaning, and can only be instantiated into physicality through choice contingent causation and control (CCCC) from the far side of The Cybernetic Cut. Signals, on the other hand, can be entirely physicodynamic.

Stoichiometry—the branch of chemistry dealing with the relative quantities of reactants and products. Whole numbers usually represent the ratio of reactants to products.

Structure—a recognizable framework of categorization, pattern or order in an entity or relationship between entities. The manner in which the parts of a whole are assembled. Primary structure refers to the sequencing of monomers in a linear polymer. Secondary structure refers to the two-dimensional representation, at least, of alpha helices and beta strands (in proteins) and helices and stem-loops (in nucleic acids) due to base pairing and base stacking. Tertiary structure refers to the three-dimensional globular shape of folded proteins, ribozymes, and chromatin.

Sustained Functional Systems (SFS)—Any device, machine, network or system that both 1) continues on in time (is a non-dissipative structure in the sense of Prigogine's chaos theory) and that 2) generates sustained non trivial functionality. Prescriptive Information (PI) and Organization alone make Sustained Functional Systems (SFS) far from equilibrium possible. Maxwell's Demon's choice contingency of when to open and close the trap door so as to accomplish the goal of a sustained energy potential represents the very first true decision-node instantiation into physicality. The Demon's first choice is the birth of engineering and the artificial intelligence movement. Deciding when to open and close the trap door is the very first logic gate—the very first configurable switch-setting. The Demon's voluntary (arbitrary) trap-door operation represents the birth of integrated circuits, computational cybernetics, and life's regulatory mechanisms. No natural mechanism exists that can choose with intent to deliberately design, engineer and maintain a SFS. Yet without SFS's, life is impossible. SFS's predate and produced Homo sapiens. They therefore cannot be attributed solely to human mentation and creativity.

Symbol—an arbitrarily-shaped/generated character representing some assigned meaning by definition. The meaning of these "strokes of pen" is just arbitrary assigned by the sender and agreed to by the recipient. Otherwise, the message will not have meaning or function at its destination. A symbol, unlike a sign, conjures no meaning from one's sight memory of physical objects. The letters of most language alphabets are not signs, but symbols. Strings of such symbol characters spell words leading to lexicons of words. Hierarchies of phrases, clauses, sentences, and paragraphs can be constructed from the lexicon of words according to syntactical rules. Sometimes only one letter symbol, such as "H" or "C" on a faucet handle, conveys meaning. Mathematical symbols such as π, Ω, ξ, Δ, $=$, and $\neq$ are symbols, not signs. We cannot ascertain the meaning of these symbols from the symbol itself, except that we sometimes become so familiar with a certain symbol's assigned meaning that it begins to take on a function similar to a picture or drawing, thereby having a sign-effect from our sight memory (e.g., the symbol " = " begins to be recognized visually as the a physical sign of equality). Codons function as symbols in molecular biology, not as direct physicochemical reactants or pictorial signs. Genes are not blueprints (two-dimensional pictures).

Symbol Systems—a means of recordation or communication that employs symbols to represent and encode meaning. Symbol systems allow recordation of deliberate choices and the transmission of linear digital prescriptive information. Formal symbol selection can be instantiated into physicality using physical symbol vehicles (tokens). Material symbol systems (MSS) formally assign representational meaning to physical objects. Even the analog perturbations of verbal semiosis can be symbolized with numerical representations in voice recognition software.

Token—a physical symbol vehicle. A physical object on which a symbol has been inscribed or to which symbolic meaning has been ascribed.

Transcribe—in molecular biology, to synthesize meaningful/functional RNA sequences containing Prescriptive Information (PI) using RNA polymerase enzymes from a DNA template.

Translate—to map one symbol system onto another in an effort to decode the initial system.

Turing machine and tape—a thought experiment imagining a device that can algorithmically process a string of successive symbols on a linear tape according to a table of rules. An infinite memory is afforded by an infinite tape. Each symbol represents not only meaning, but also arbitrary choice contingency rather than chance and/or necessity. The rules are also choice- contingent. The thought experiment can simulate the function of modern computers and their computational limits.

Undecidable— a decision problem that is impossible to always answer with a "Yes" or "No" using a single algorithm. The term is most applicable to computational complexity theory. Alan Turing, for example, proved that the halting problem is undecidable for Turing machines. A verbal statement can also be considered "undecidable" with relation to Gödel's incompleteness theorems when that statement is neither provable nor refutable within a certain deductive axiomatic system.

Universal Probability Bound (UPB)—A quantifiable limit to an extremely low probability resulting from the limitation of probabilistic resources in that context. Statistical prohibitiveness cannot be established by an exceedingly low probability alone. Rejection regions and probability bounds need to be established independent of (preferably prior to) experimentation in any experimental design.

Universal Plausibility Metric—a numerical value measuring the plausibility (not probability) of extremely low probability events in view of the probabilistic resources in each context. The UPM employs the symbol ξ (Xi, pronounced zai in American English, sai in UK English, ksi in modern Greek) to represent the computed UPM according to the following equation:

$$\xi = \frac{f\,{}^{L}\Omega_{A}}{\omega}$$

where f represents the number of functional objects/events/scenarios that are known to occur out of all possible combinations (lower case omega, ω) (e.g., the number [f] of functional protein family members of varying sequence known to occur out of sequence space [ω]), and ${}^{L}\Omega_{A}$ (upper case Omega, Ω) represents the total probabilistic resources for any particular probabilistic context. The "L" superscript context of Ω describes which perspective of analysis, whether quantum (q) or a classical (c), and the "A" subscript context of Ω enumerates which subset of astronomical phase space is being evaluated: "u" for universe, "g" for our galaxy, "s" for our solar system, and "e" for earth. Note that the basic generic UPM (ξ) equation's form remains constant despite changes in the variables of levels of perspective (L: whether q or c) and astronomic subsets (A: whether u, g, s, or e).

Universal Plausibility Principle—states that definitive operational falsification of any chance hypothesis is provided by the inequality of:

$$\xi < 1$$

where ξ is the measured UPM for that context. This definitive operational falsification holds for hypotheses, theories, models, or scenarios at any level of perspective (quantum or classical) and for any astronomical subset (Universe, galaxy, solar system, and earth). The UPP inequality's falsification is valid whether the hypothesized event is singular or compound, independent or conditional. Both UPM and UPP pre-exist and are independent of any experimental design and data set. No low-probability hypothetical plausibility assertion should survive peer-review without subjection to the UPP inequality standard of formal falsification ($\xi < 1$).

Utility—formal usefulness or functionality, usually as decided or evaluated by agents with reference to their desires and goals. A more objective concept of "utility" might be found in the biofunctionality of molecular machines, for example, with reference to the holistic metabolic goals of cells and organisms.

Vesicles—a complex version of the micelle containing one or more phospholipid bilayers that can enclose, transport and digest other substances. Cellular vacuoles, lysosomes, transport and secretory vesicles in living organisms have attracted much attention as models of possible protobionts (protocells) with crude "membranes." Phospholipids can form bilipid layer walls of artificially prepared liposomes.

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