

On the applicability of Darwinian principles to chemical evolution that led to life

Randall S. Perry^{1*} and Vera M. Kolb^{2*}

¹Department of Earth and Space Sciences, Astrobiology Center for Early Evolution, Box 351310, University of Washington, Seattle, WA 98195-1310, USA
e-mail: rsp@u.washington.edu

²Department of Chemistry, University of Wisconsin – Parkside, Kenosha, WI 53141-2000, USA
e-mail: kolb@uwp.edu

Abstract: Chemical evolution at the primitive prebiotic level may have proceeded toward increased diversity and complexity by the adjacent possible process (originally proposed by Kauffman). Once primitive self-replicating systems evolved, they could continue evolution via Eigen's hypercycles, and by Prigogine's emergence of order at the far-from-the-equilibrium, non-linear systems. We envisage a gradual transition from a complex pre-life system, which we call the transition zone. In this zone we find a mixture of complex chemical cycles that reproduce and secure energy. Small incremental changes in the structure and organization of the transition zone eventually lead to life. However, the chemical systems in this zone may or may not lead to life. It is possible that the transition to life might be the result of an algorithm. But, it is uncertain whether an algorithm could be applied to the systems in which chance plays a role.

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Introduction

One of NASA's astrobiology goals is to look for life on Mars (and other habitable planetary bodies) and search for organic materials that are believed to be necessary for the development of life. NASA plans to search for extant life, by looking for various biosignatures and for past-fossilized life. A central question is if chemical evolution elsewhere has or has not led to life. While many prebiotic and biotic chemical processes on Earth are known, less attention has been paid to chemical processes that lead to complex pre-life organic mixtures. We attempt to remedy this problem, and introduce the concept of a transition zone, which is a complex pre-life organic system that may or may not further evolve to life.

Here we examine some aspects of primitive prebiotic chemistry, and then those of a proposed transition zone. Next we look at some relatively recent advances in prebiotic chemistry, and the theory of complex systems, which we feel could be applied to early chemical systems. Also, we attempt to extrapolate features of Darwinian biotic evolution to non-biotic systems and answer the question, did life emerge suddenly, or was it a gradual process?

This study, hopefully, sheds light on the emergence of complexity, diversity, and organization in the organic world. Chance plays an important role in evolution and at every step only some paths became developed systems. A final path,

which leads to life, may have occurred on other planetary bodies such as Mars, and may have proceeded to life or stopped just short of life. Complex chemical systems in the transition zone that have been built over time, might have led to life or deteriorated to a chaotic mixture of chemicals, which could still be disintegrating. In this case, there should be some remaining evidence, perhaps with some polymers remaining. They would have some regularity in their structures, some self-templating fragments, or some remnants of the failed chemistry of reproduction. These polymers or fragments would be the chemical signatures of the transition zone.

Chemical properties before life

About chemical properties of the primordial chemical systems

The primordial chemical systems include organic and inorganic compounds in a physical environment such as a tidal pool, a hydrothermal vent, the surface of a mineral, or a primordial pond (in Darwin's terms), a primordial soup (as often pictured by Miller 1953; Miller & Orgel 1974; Miller 1998). A primordial chemical systems contained many reactive chemicals that were brought to Earth by comets (Chyba *et al.* 1990) or meteorites (e.g. Cronin 1998). Chemical analyses of meteorites (carbonaceous chondrites) show that virtually every class of organic compounds is found in them: amino acids, aromatic compounds, aliphatic compounds,

* Corresponding author. Randall S. Perry; or Vera M. Kolb, Phone: 262-595-2133. Fax: 262-595-2056.

amines, amides, carboxylic acids, ketones, alcohols, sugar polyols, heterocyclic compounds, and others (Cronin & Chang 1993; Cronin 1998; Cooper *et al.* 2001; Pizzarello *et al.* 2001). Many compounds in this primordial organic world have been formed by Miller-Urey type experiments (Miller 1953; Miller & Orgel 1974; Miller 1998), by an electrical or other energy discharge in the gases in prebiotic Earth's atmosphere.

Syntheses of organic compounds and their further transformations under prebiotic conditions, that simulate diverse environments such as ponds, atmospheres (Miller & Orgel 1974; Mason 1991; Sutherland & Whitfield 1997; Miller 1998), volcanic environments (Basiuk & Navarro-González 1996), hydrothermal vents (Siskin & Katritzky 1991; Kuhlmann *et al.* 1994; Simoneit 1995; Katritzky *et al.* 1996; Imai *et al.* 1999; McCollom *et al.* 1999; Ogassawara *et al.* 2000), and mineral surfaces (Wächtershäuser 1988, 1992; Ertem & Ferris 1996; Schwartz 1996; Hill *et al.* 1998; Liu & Orgel 1998; Orgel 1998; Ferris 2002) bring us closer to an understanding of a primordial organic world. Many products resulted from these syntheses, including those that are now present in biological systems and considered essential, such as amino acids, sugars, nucleic acid bases, and lipids.

We assume that a mixture of compounds that were found on meteorites and were synthesized in the laboratory under the simulated prebiotic conditions are representative of those that existed in the primordial organic world. The number of compounds and diversity of their structures may depict a complexity level of the primordial organic world.

About chemical properties of the transition zone

The transition zone bridges the primordial organic world and the biotic world. We offer here our view of chemical properties of the transition zone. First, we believe that there is a functional difference between the original primordial organic world and the transition zone. The primordial organic world contained many reactive chemicals that were brought to Earth by comets, meteorites, or formed by Miller-Urey type experiments. As time went by, the impacts on Earth were fewer, the supply of new chemicals dwindled, and the reactive compounds that were originally present in the primordial organic world were transformed into more stable, and thus less reactive compounds. How would the latter compounds react further? Generally, in today's living systems, we do not find chemicals that are very reactive, as they might indiscriminately attack and damage numerous vital molecules. Instead less reactive molecules are present, and their reactions are enzymatically driven. Enzymes compensate for the lack of intrinsic reactivity of molecules by catalysis, which lowers the energy of the transition state for a reaction. The same concept would apply to the prebiotic systems that contained less reactive compounds. These compounds also could have reacted with the help of catalysts. The original catalysts may have been based on clays, various metals, inorganic and organic species that happened to be present and possess some catalytic activity. In the transition zone, as compared to the primordial organic world, evolution of the catalysts

would have gone further, the catalyst supply was more diverse, and would probably involve various peptides.

Another feature of the transition zone was that the energy supply for its reactions was steadier, more reliable and somewhat secured, as compared to the primordial organic world. In the latter, we could envision chemical reactions that were flourishing during daylight, when UV light and heat were abundant. During the night, however, such reactions would subside. Molecules that could capture and store energy, and processes by which this energy could be delivered to another set of molecules, would make reactions possible in the absence of the original energy source. At least some of the chemical systems present in the transition zone had the capability of storing energy and transferring it as chemical energy.

A central problem of any chemical process involves the supply of chemicals, as the supply becomes depleted with time, and may not be replenished in the same amounts with identical chemicals. This would be most likely if the major suppliers of chemicals were comets and meteorites. A chemical system that survives better would be able to make its own starting materials. This would be possible in a chemical cycle. A chemical cycle would have a better chance of reproducing itself if it were coupled with an energy cycle, which would ensure a reliable source of energy. Various chemical cycles were present in the transition zone, involving also molecules that had the capacity to first reproduce (Dyson 1985) and later self-replicate. Initially they were primitive and had poor fidelity of replication. An abundance of errors in replication caused the 'information content' to dissipate.

This was not life yet. Replicating systems were prone to errors and were not coupled efficiently to other cycles, those of enzyme production and energy storage/transfer. Chemical 'evolution' in the transition zone continued by diverse means, including merging, dissolving, and re-assembling.

The self-replicating molecules/cycles may have co-evolved with other molecules/cycles that are necessary for their synthesis and maintenance (i.e. enzymes and energy molecules). This view avoids a possible pitfall of the naked replicator of Dawkins, one of which was pointed out by Deutsch (1997): 'Not everything that can be copied is a replicator. A replicator *causes* its environment to copy it: that is, it contributes casually to its own copying'. In our view, a replicator and the environment that makes its copies co-evolve.

The concept of the transition zone may be helpful in the search for life on Mars or elsewhere, since development may have occurred in the transition zone but not lead to fully functioning life. We might find polymers, with some regularity in their structures, self-templating fragments, or remnants of the failed chemistry of reproduction. These would be the chemical signatures of the transition zone on Mars.

The transition zone concept allows us to utilize various models that have been proposed to explain the development of pre-life in general. Examples include, among others, the following models:

(a) Coacervates, which are small colloidal systems (Menger & Sykes 1998). They act as chemical reactors, as they

accumulate small organic compounds and also inorganic catalysts, and hence grow. They eventually divide by surface tension effects (Oparin 1953, 1964, 1966). According to Oparin, competition exists between individual coacervate systems for the available chemicals. Perhaps a primitive type of 'natural selection' operates. The coacervates that grow faster will reproduce faster. Eventually, chemical cycles will begin to emerge inside the coacervates. Related to coacervates are other self-assembling systems, such as micelles and vesicles (Menger 1991). Oparin's ideas were furthered and advanced by application to these systems (Bachmann *et al.* 1991; Chakrabarti *et al.* 1994; Walde *et al.* 1994a, 1994b; Szostak *et al.* 2001).

- (b) Protected environment for chemical reactions that are going on inside them. These would include protocells, which are protenoid, lipid, or lipid-protenoid envelopes; (e.g. Yanagawa *et al.* 1988; Fox 1991; Zhang *et al.* 1993).
- (c) RNA World, in which RNA was the sole genetic material, but also acted as a catalyst (e.g. Orgel 1986; Joyce & Orgel 1999).
- (d) Autocatalytic cycles of Kauffman, which are the result of the order that arises spontaneously in a complex system when it is at 'the edge of the chaos'. These autocatalytic cycles would spontaneously form out of the complex mixture of polypeptides (Kauffman 1993).
- (e) Eigen's hypercycles, in which replication and primitive translation are interlocked (Eigen 1981, 1992).
- (f) Wächtershäuser's model of iron-sulfur world, in which surface metabolism occurs with a favorable energy sources (Wächtershäuser 1988, 1992).

Each of these proposed models might have had an important role in the emergence and co-evolution of three major cycles: those of energy, self-replication, and enzyme development.

Mergers

It has been proposed that a genetic takeover happened in which the early prebiotic genetic systems were replaced by more sophisticated systems that were later made enzymatically. This idea of takeover is very useful, not only for the primitive genetic systems, but also for the primitive energy storage/transfer systems. While the term 'takeover' is usually used to depict final separation between life and pre-life, we introduce the term 'merger', which is helpful in depicting the chemical evolution occurring in the transition zone. We suggest that in the transition zone, a merger occurred between the cycles that produced energy, genetic replicators, and primitive enzymes. The merging systems 'evolved' and instead of a vertical leap from the transition zone to life, where the system 'clicked' and became alive, we think that a series of horizontal mergers occurred which ironed out problems such as non-reliability of the replicators. This would have linked the systems even tighter, such that the 'knowledge' of making molecules was better preserved and implemented and that this was gradual.

An example of chemistry in the transition zone: alternative genetic systems

Orgel (1987) summarized the difficulties in prebiotic syntheses of the nucleoside components of RNA (nucleo-base + sugar). The condensation of nucleo-bases adenine or guanine with sugar ribose gives only minute amounts of nucleosides with correct stereochemistry, and synthesis of pyrimidine nucleosides is even more difficult. Shapiro (1995, 1999) addressed difficulties in prebiotic syntheses of nucleo-bases adenine and cytosine. Orgel (1987) suggested that some of the original nucleo-bases may not have been purines and pyrimidines. Orgel (1987) concluded: 'RNA is an evolutionary advanced molecule that was preceded by one or more simpler genetic polymers'. Shapiro (1995) holds the same view: 'An alternative and attractive possibility is that some other replicator preceded RNA (or RNA-like substances) in the origins of life'.

Some examples of alternative nucleo-bases, nucleosides, and nucleic acid with alternative backbones or sugars, prepared in the laboratory are: urazole as uracil mimic and urazole nucleosides (Kolb *et al.* 1994), nucleo-bases that extend the genetic alphabet (Piccirilli *et al.* 1990), nucleic acids with sulfone and peptide backbones, rather than phosphate (Benner & Hutter 2002), and nucleic acids with sugars with different structures and configurations (Beier *et al.* 1999). While some syntheses were prebiotic and some were not, the compounds synthesized were at least models of the alternative genetic systems.

The transition zone leads to life

What is life?

In order to design effective experiments to look for life on other planetary bodies we need a practical definition of life. However, there are no broadly accepted definitions (Cleland & Chyba 2002). NASA has adopted a definition of 'life', which states that life is 'a system which is self-sustained by utilizing external energy/nutrients owing to its internal process of component production and coupled to the medium via adaptive changes that persist during the time history of the system' (Luisi 1998). The idea that life can exist on other planets with suitable environments is the subject of several investigations in astrobiology (Chela-Flores 2001; Morrison 2001; Hornek & Baumstark-Khan 2002). Nealson & Conrad (2002) say that they are not interested in a life definition, if it is not measurable in the context of finding life in our solar system. We too share this concern. There exists then a need for a useful definition that can be extended to experiments, but one that does not constrain our thinking. We hope that this investigation and those of others will lead to a better understanding of the nature of living systems and eventually a definition that will allow us to recognize extinct or extant life as well as life based on a different chemistry than our own. For this study we accept both NASA's definition and the eventuality of a universal life (Raulin-Cerceau *et al.* 1998).

On the transition from non-living to living systems

Let us address the transition from non-living to living systems. How did this transition happen? We may envisage three scenarios, borrowed from the evolutionary theory of living systems: gradual transition, quantum evolution, and punctuated equilibria.

Gradual transition is a transition that occurs as a result of a small accumulation of changes over a period of time. Quantum evolution, by extrapolation of the ideas of Simpson (1949) and McFadden (2000), would imply a sudden change. The punctuated equilibrium idea of Gould and Eldredge (for instance Eldredge 1995) would imply long periods of stasis, followed by burst of changes.

Gradual evolution in a primordial organic world might produce a rather complex and diverse mixture of organic compounds and their inorganic partners. The complexity of these systems might increase or decrease over time but the greatest complexity tends to grow larger with time (Gell-Mann 1994). These complex chemical systems lead us to the transition zone out of which life emerged.

Schrödinger (1944) described biological replication by the quantum-mechanical stability of molecular structure and metabolism. A quantum leap in evolution may be considered either a figure of speech inspired by some features of quantum physics (Simpson 1949), or an event related more closely to quantum physics laws (McFadden 2000). Let us examine these concepts more closely.

In his 'Tempo and Mode in Evolution', Simpson (1949) states: 'Perhaps the most important outcome of this investigation, but also the most controversial and hypothetical, is the attempted establishment of the existence and characteristics of quantum evolution. A "quantum", in a sense more general than but including the definition of physics, is a prescribed or sufficient quantity. The term is applicable to situations in which sub-threshold actions produce no reactions but super-threshold actions produce reactions of definite (not necessarily) equal magnitude (this magnitude being strictly the quantum involved). For the sake of brevity, the term "quantum evolution" is here applied to the relatively rapid shift of a biotic population in disequilibrium to an equilibrium distinctly unlike an ancestral condition ... In quantum evolution equilibrium is lost, and a new equilibrium is reached. There is an interval between the two equilibria, the biological analogue of a quantum, in which the system is unstable and cannot long persist without either falling back to its previous state (rarely or never accomplished in fact), becoming extinct (the usual outcome), or shifting the whole distance to the new equilibrium (quantum evolution, strictly speaking) ... the most disputable point is whether the transition is instantaneous, in close analogy with the quantum of physics, or whether quantum evolution occurs at rapid, but finite rates. Strong reasons have been adduced for believing that the latter is the case'. Although the quantum evolution of Simpson has been criticized (for the summary see Eldredge 1995), at least some parts of the concept may be usable.

McFadden (2000) attempts to apply quantum principles to live systems and also to the emergence of life. He suggests that prebiotic syntheses were performed in natural nanostructures, such as pores of a rock, which would have protected the coherence of the quantum states inside. The synthesis of e.g. peptides would have taken place inside the pores as a quantum superposition of all peptides, and not by a classical synthesis by addition of single amino acids. No experimental proof exists for this or for other proposed roles of quantum phenomena in the emergence of life.

On the complexity of the transition zone

We believe that a major pathway for building complexity in the transition zone was by the way of the merger of various chemical cycles. Should such a merger be considered a sudden leap rather than a gradual transition? We still consider it a gradual transition, as it sometimes takes some time leaping stone by stone to get over the gray river.

An anticipated question on the complexity of the transition zone concerns its magnitude. Gould (1996) and Sterelny (2001) present a graph that depicts the evolution of the complexity of life. The horizontal axis represents complexity and the vertical axis the number of species. Parallel to the vertical axis, there is a line that depicts the 'wall', signifying the minimum complexity required for life (in Gould's consideration it was a basic cell). On the right side of the wall the complexity of life increases. This graph shows Gould's view by which more complex life evolves over time, but still the most predominant species are those having basic, minimal complexity, namely bacteria.

If the wall of complexity exists, then a clear-cut line between life and pre-life, in terms of complexity is still interesting as long as it can be linked metaphorically to quantum physics, as one would need a quantum leap or some sort of quantum tunneling to get to the other side of the wall (Beiser 1987; McMahan 2003).

While quantum leap metaphor is now 'quite common' in everyday speech, most readers are less familiar with quantum tunneling. The latter mechanism allows a particle without sufficient energy to go over a barrier to tunnel through it. The de Broglie waves that represent the particle are partly reflected but also partly transmitted through the barrier. Thus the particle has a finite chance of penetrating the barrier, (Beiser 1987). Quantum tunneling has been demonstrated also in various chemical reactions that involve tunneling by hydrogen, carbon, or oxygen. Such reactions are important for chemical catalysis, in enzyme reactions, and interstellar chemistry (McMahan 2003).

Let us consider the complexity just on the left side of the wall, which would be our transition zone. One could easily imagine a sort of primitive replication, which would not be able to survive more than a limited number of replicating cycles, due to poor fidelity and error build-up in each replicating cycle. Whenever such a primitive self-replicating cycle would fall apart, its pieces could be assimilated by another self-replicating system. This might be analogous to the horizontal transfer of genes observed in the living systems

(Gogarten 1995; Miller 1998; Raymond *et al.* 2003). Thus, some of the ‘knowledge’ of the self-replication would be preserved. In addition, some sort of primitive self-repair system would be ‘evolving’. A gradual co-evolution of the primitive merged cycles would bring us to life. Thus, we do not see the need for a wall separating transition zone from life.

Chemical feasibility of autocatalytic and merging cycles

We mention first two significant developments in prebiotic chemistry that would result in the increasing complexity of the chemical mixtures and thus would bring us a step closer to understanding the formation and function of more advanced autocatalytic and merging cycles.

The first development is the organic chemistry in superheated water (Siskin & Katritzky 1991; Kuhlman *et al.* 1994; Katritzky *et al.* 1996), which provides additional ways for building chemical complexity under primordial conditions.

It is noteworthy that the solvent properties of water at high temperatures and pressures, such as those in hydrothermal vents, are similar to those of polar organic solvents. For example, solvent properties of water at 300 °C resemble those of acetone at room temperature. Dissociation constant of superheated water is substantially increased, e.g. by 3 orders of magnitude at 200 °C over the room temperature. This imparts acid/base properties to superheated water, which thus acts as a catalyst. Chemical reactions occur in superheated water between organic molecules that were previously considered to be unreactive. Especially important are condensation reactions. For example, alkenes and alcohols react in superheated water in the presence of clays to give ethers (Siskin & Katritzky 1991). Such ethers could be the primordial precursors of ether lipids that are used as cell membranes of Archaea (Koga *et al.* 1993).

The second advancement is in the chemistry of self-replication. We cite here work by Ghadiri’s research group on the chemical systems that are capable of self-replication (Lee *et al.* 1996), symbiosis through a hypercyclic network (Lee *et al.* 1997), chiral selection (Saghatelian *et al.* 2001), and error correction (Severin *et al.* 1998). Although the systems studied are peptides and they are not synthesized in a prebiotic manner, they illustrate that complicated networks, in which catalytic and autocatalytic processes are cooperatively coupled and have error-correction properties and chiral selectivity, can now be prepared in the laboratory.

Darwinian evolution

Biotic Darwinian evolution as an algorithmic process

Dawkins (1996) says, ‘The one thing that makes evolution such a neat theory is that it explains how organized complexity can arise out of primeval simplicity.’ Dennett introduced the idea that Darwinian evolution of biotic systems takes place in an algorithmic process, that of natural selection (Dennett 1995, 1996). The latter was presented by Bell as a set of 175 selection rules (Bell 1997). An algorithm is a formal

process consisting of a limited number of steps, which are mechanical and often repetitious (Dennett 1995, 1996). We adopt Dennett’s definition of three key features of the algorithm for natural selection.

The first feature is ‘substrate neutrality’. The power of an algorithmic process results from its logical structure, and not the materials involved.

The second feature is ‘underlying mindlessness’. Despite the fact that the evolutionary process appears sophisticated, and yields complex results, each step of the process is simple. Complicated ‘design’ may be a result of a series of elementary steps.

The third feature is ‘guaranteed results’. An algorithm is a foolproof recipe that always yields its characteristic results, if executed without errors. This algorithm has been applied also to the evolution of secondary metabolites, in search of a methodology for drug design by biomimicry (Kolb 1998). Storrie-Lombardi *et al.* (2002) have applied advanced techniques in complexity analysis for the detection of biosignatures in ancient and modern stromatolites.

Mars *et al.* (1996) examines the process of Darwinian evolution as a mechanism of optimization by which the organisms adapt to the ever-changing environment. This optimization mechanism is presented as an algorithm which lays a foundation for a new field of research, that of simulated evolution (Mars *et al.* 1996). The latter provides a powerful general optimization tool that has been used successfully for solving numerous practical problems in biotic, as well as abiotic systems. Examples include: the discovery of protein signal sequences (Levin 1995), adaptation to non-stationary environments by considering gene activation and chromosome redundancy (Dasgupta 1995), optimization of routing in telecommunication, automatic control of nonlinear systems, aircraft and jet turbine designs, robot motion planning and seismic applications, among many others (Mars *et al.* 1996; Michalewicz 1996). Research in simulated evolution encompasses three conceptually similar methods: those of genetic algorithms, evolutionary strategies, and evolutionary programming (Mars *et al.* 1996).

As order evolves in complex systems that are far-from-the-equilibrium under non-linear conditions in a system, only one out of many possible paths for evolution is chosen (Prigogine *et al.* 1972a,b; Prigogine & Stengers 1984; Prigogine 1997). This suggests that an absolute algorithm for evolution of life might be too deterministic.

On the applicability of Darwinian evolution to prebiotic chemical evolution

We use the term ‘prebiotic chemical evolution’ as synonymous to ‘chemical evolution’ in its common usage that refers to the evolution of chemical systems (e.g. Mason 1991). The word ‘prebiotic’ is introduced to avoid any identification with the ‘biotic’ chemical evolution, such as the evolution of secondary metabolites. The word ‘prebiotic’, which implies that the system will eventually lead to a biotic system, is a subcategory of ‘abiotic’. Not all abiotic evolution will lead to life.

Let us now consider prebiotic chemical evolution from three current points of view. The first is Eigen's, about the evolution of primordial genetic systems (e.g. Eigen 1981; Eigen *et al.* 1981; Eigen & Schuster 1982; Eigen 1992). The second is Kauffman's about the emergence of self-replicating non-genetic systems (e.g. Kauffman 1993, 1995, 2000). The third is that of Prigogine and his co-workers (Prigogine *et al.* 1972a, b; Prigogine & Stengers 1984; Prigogine 1997) about nonequilibrium order and the search for stability as an extension of Darwinian concepts to prebiotic stage.

In the first approach (Eigen's) the Darwinian principle of selection is found to be insufficient to account for the emergence of life. If one assumes that life emerges from RNA/DNA with the present bases (A, U, G, C, T) and with no enzymes present, one finds that such self-replicating systems are limited by an inherent inaccuracy of base pairing. Because of this limitation, the primitive genes cannot be accurately self-reproduced to the extent necessary to contain enough information for a translation process. Maximum gene lengths available to such prebiotic non-enzymatic system are 50–100 nucleotides. Imposition of Darwinian selection to these systems results in 'quasispecies', composed of the master sequence and a swarm of mutants. The latter are formed because non-enzymatic self-replication is error-prone. Only when 'hypercycles' are introduced, in which replication and primitive translation are interlocked, does fidelity of replication improve, as it becomes enzyme-assisted. However, the hypercycles are cooperating systems, rather than competing (Eigen 1981, 1992).

In the second approach (Kauffman's), living organisms are considered as thermodynamically orderly systems, which are nonequilibrium, dissipative structures that maintain order by importing and exporting matter and energy. The order in the first live systems is proposed to be the result of the spontaneous order of self-organized systems, rather than of a selection process. Life is proposed to emerge as a natural property of complex chemical systems. It is further proposed that when a number of different types of chemicals in the primordial chemical systems pass a certain threshold, a self-sustained network of reactions suddenly appears. The latter constitutes an autocatalytic metabolism. A new paradigm, that life emerges complex rather than simple, is postulated. Autocatalytic sets without a genome, and their evolutionary capacities are elaborated on, and a non-Darwinian hypothesis of the origins of life emerges (Kauffman 1993, 1995, 2000).

In the third approach, Prigogine and co-workers looked at evolution, including the prebiotic one, from a point of view of non-equilibrium thermodynamics (Prigogine *et al.* 1972a, b; Prigogine & Stengers 1984; Prigogine 1997). They proposed that a prebiological system might evolve via successive transitions that lead to more complex and more organized states of the system. Such transitions would arise in non-linear systems that are maintained far from equilibrium (Prigogine *et al.* 1972b). One characteristic of non-linear systems is that small inputs can trigger massive consequence. The orderly structures that arise in the system, so-called dissipative structures, require more energy to be sustained than

their simpler precursors. Under non-equilibrium conditions entropy may produce order and organization, and thus life. The fluctuations in a far-from-equilibrium condition leads to a bifurcation point, at which it is not possible to predict the system's path, since there are many (including a disintegration into chaos and a leap into order). But once a path is chosen (out of many), the system continues to evolve (to the next bifurcation point). Prigogine & Stengers (1984) propose that the appearance of chirality was the result of selection at an appropriate bifurcation point. Various aspects of prebiotic evolution were examined via mathematical models, e.g. prebiotic polymer formation, self-reproductive hypercycles of Eigen, appearance of new substances, etc. (Prigogine *et al.* 1972b). For the prebiotic evolution, Prigogine and co-workers kept the Darwinian principle of evolution via selection, but they modified the 'survival of the fittest' criterion. It no longer was equivalent to the maximum number of offspring, but, instead, factors such as the increase in dissipation. It is of interest that the bifurcation points may be conceptually similar to punctuated equilibria leaps. The bifurcation points are irreversible leaps towards different systems.

Chemical selectivity in the primordial environment

Can we apply Darwinian selection principle to the prebiotic organic world? One approach would be to look at the adaptation in prebiotic chemical systems, since adaptation goes hand-in-hand with selection. This approach is not fruitful, however, as it is not clear how the adaptation process can be applied. This point is illustrated by examining several fundamental questions about adaptation, which we quote from the work of Holland (1993), 'To what parts of its environment is the organism (system, organization) adapting? How does the environment act upon the adapting organism (system, organization)? What structures are undergoing adaptation? What are the mechanisms of adaptation? What part of the history of its interaction with the environment does the organism (system, organization) retain? What limits are there to the adaptive process? How are different (hypotheses about) adaptive processes to be compared?' The answers to these questions might be applicable to many complex adaptive systems (Holland 1993, 1995), but might not be obviously applicable to simple chemical systems.

However, the principle of chemical selectivity in the primordial environment can be related to Darwinian selection in at least a metaphorical sense. Out of many theoretically possible chemical options, only certain ones prevail, and some are definitely favored. Support for this assertion is provided by the analyses of the organic material from meteorites (e.g. Cronin 1998; Cooper *et al.* 2001; Pizzarello *et al.* 2001), and by the outcomes of many types of chemical reactions, which were run under simulated prebiotic conditions (e.g. Miller & Orgel 1974; Mason 1991; Miller 1998). In order to develop a theory for these processes, a starting point might be the consideration of chemical species as primitive autonomous agents, but ones less developed than

the Kauffman's autonomous agents (Kauffman 2000a). The chemical autonomous agents, like Kauffman's, would 'act in their own behalf' in the primordial environment, but, unlike Kauffman's, would not yet be autocatalytic, self-reproducing systems that are able to perform one or more thermodynamic work cycles. We propose that the chemical autonomous agents follow their intrinsic reactivity pattern, related to their molecular structure, such as when they combine with nucleophiles, electrophiles, free radicals, carbenes, or get involved in other applicable reactions (Carroll 1998; Carey & Sundberg 2000). The capacity for the chemical autonomous agents 'to act in their own behalf' is intrinsic. However, the actual realization of this capacity is determined by the primordial environment, which contains chemical partners, the energy sources and the catalysts needed to promote the reactions. If one accepts this idea of the chemical autonomous agents, then one can also adopt another valuable concept developed by Kauffman- that of 'the adjacent possible' (Kauffman 2000b). The latter concept explains how Kauffman's autonomous agents 'forever push their way into novelty – molecular, morphological, behavioral, and organizational ...' (Kauffman 2000b, p. 22). According to Kauffman, the molecular species that exist are in 'the actual'. The molecules that are one reaction step away from the actual, but have not been made yet are 'the adjacent possible'. The adjacent possible is infinitely expandable. This concept can be adapted to the chemical autonomous agents, and can explain how molecular complexity builds. The adjacent possible is clearly influenced by the environment, which contains chemical partners, energy and the catalysts. The environment thus can select and shape the structures of the molecules that result from the realization of the adjacent possible, namely the new actual molecules. This continual interplay between actual molecules and the environment of their adjacent possible, results in chemical evolution.

The environment of the adjacent possible in the interstellar medium, on the asteroids, meteorites, comets, and bodies such as Mars, Europa, Titan, and the primordial Earth, may be similar in many respects, but is also expected to have differences, perhaps critical. We believe that such differences are important not only for sorting out the extraterrestrial chemical evolution, but also for NASA's planetary protection program. Different environments may give the chemical autonomous agents an opportunity to fulfill the aspects of their reactivity that are not promoted on Earth. This could result in novel actual molecules, and, after many actual-adjacent possible turnovers, perhaps unusual complex molecules that could interfere with life, as we know it.

Chemical selectivity in the transition zone

Could we apply Darwinian selection principle to the transition zone? Based on the examples above, we can conclude that Darwinian selection may have algorithmic power in biotic and some complex abiotic systems. The 'hypercycle' hypothesis by Eigen and 'life by self-organization of complex chemical systems' by Kauffman, start at a very complex level of the primordial chemical systems, either that of the

RNA/DNA, or of an even greater chemical diversity, and thus could be representative of the transition zone. Simply by virtue of some cycles surviving and some falling apart, we could assume that some cycles have been 'selected' over others. However, other principles may be operating. There was an element of chance involved, at various bifurcation points. The laws of non-equilibrium thermodynamics and chance need to be considered, and 'the survival of the fittest' or the 'selection of the fittest' only metaphorically can fit the transition zone swarm of chemical cycles that are still not linked to function as life.

Conclusions

The search for life on Mars (or other habitable planetary body) will be greatly facilitated if some insights are provided into the following question: would prebiotic chemical evolution elsewhere produce the same or reasonably similar types of life as we have on Earth, and if not, can we anticipate what non-Earth biosignatures would look like? To help answer this question we introduce the concept of the transition zone, which would involve the inorganic and complex organic world of prebiotic chemicals. We attempt to extend Darwinian evolution to prebiotic systems in the transition zone. It is uncertain, however, whether 'quantum evolution', and punctuated equilibrium in the transition zone are important. Chemical evolution at the primitive prebiotic level could be explained by application of Kauffman's adjacent possible process and we envisage the buildup of the initial chemical diversity and complexity via this process. Once the primitive self-replicating systems evolved, their further evolution can be explained by Eigen's hypercycles, and by Prigogine's emergence of order in the far-from-the equilibrium, non-linear systems. The transition of primitive self-replicating cycles to life could perhaps be the result of some algorithm. We envisage a gradual transition from pre-life to life with some elements of 'punctuation', where the small incremental changes in the structure and organization of the system which eventually lead to life. The changes would occur in some of the chemical and energy cycles, which may be cooperative to some extent, rather than being only competitive. In the transition zone, we find a complex mixture of chemical compounds that reproduce and secure energy. These systems may not be alive, and may never become alive. However, if they were found on another planet, they might show us how our life evolved on Earth.

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