Chapter 1

Chemical Evolution: An Introduction

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Evolution, the process by which systems under non-random selective pressure become more complex, has been a pervasive force over 4.5 billion years of Earth history. Evolutionary episodes, including the prebiotic synthesis of biomolecules, the selection and organization of those molecules into self-replicating systems, the subsequent co-evolution of the geo- and biospheres, and the modern-day acceleration of chemical evolution through human invention, serve to illustrate this recurrent theme.

Introduction

Complex evolving systems are a hallmark of the natural world and are observed in a variety of natural and human contexts, including nucleosynthesis in stars, diversification of minerals on terrestrial planets, prebiotic organic synthesis, development of languages, progress in material culture, and the biological evolution of life (*1-4*). In each of these complex systems the distribution of "species" evolves through non-random selective mechanisms, and each system displays such qualitatively similar characteristics as diversification into niches (radiation), episodic periods of innovation (punctuation), and the loss and replacement of previous species (extinction). However, these systems differ from each other in fundamental respects, notably in the degree to which their species demonstrate mutability, heritability and lateral transfer of traits. Comparisons among these disparate evolving systems thus point to general principles of emergent complexity.

Of all the chemical transformations that have shaped the Cosmos since its origin 14 billion years ago, none is more remarkable than the chemical origins of life. How did the raw materials of primitive Earth – oceans, atmosphere, rocks and minerals, and a diverse inventory of organic molecules – become alive? Details of that chemical history continue to foster intense debate, but the overarching narrative, as represented in the collected essays of these proceedings, is becoming clear.

This volume is the second of two that explore epic chemical changes in the Cosmos. The first volume (*1*) considered the emergence of chemical complexity from the earliest era of stellar evolution and the consequent emergence of elemental diversity, through planetary evolution and the emergence of mineralogical diversity, and ultimately to prebiotic chemical complexification and the emergence of life. Here the focus shifts to chemical and biological evolution on Earth. The story begins with the prebiotic origin of biomolecules, progresses to processes by which those molecules were selected and organized into self-replicating systems, examines the co-evolution of the geo- and biospheres, and culminates in human manipulation of the chemical realm.

The Building Blocks of Life

The first crucial step in life's emergence on Earth was the synthesis and gradual accumulation of abundant carbon-based biomolecules. In the beginning, life's raw materials consisted of oceans, an atmosphere of simple volcanic gases, varied rocks and minerals, and an expanding inventory of organic molecules that inexorably emerged from cosmochemical and geochemical environments. To understand life's origins we must decipher the chemical processes by which these basic ingredients reacted and complexified.

By the first decades of the 20th century experts agreed that life's chemical origins, wherever and however the processes occurred, depended on three key resources. First, water is the medium of all known life forms. All living cells,

even those that survive in the most extreme desert ecosystems, are formed largely of water. Consequently, the first cells are assumed to have arisen in an aqueous environment. The second requirement for life is a reliable energy source. The Sun's radiation provides the most obvious supply for life today, but bolts of lightning, impacts of asteroids, Earth's inner heat, and the chemical energy of minerals have also been invoked as life-triggering energy sources. Life's third requirement is an inventory of carbon, oxygen, hydrogen, and nitrogen, with lesser amounts of sulfur, phosphorus, and other elements as well.

The first step in life's chemical origins must have been the synthesis and accumulation of abundant biomolecules (*5-7*). Cleaves and Lazcano (*this volume*) review the rich variety of geochemical and astrochemical environments that promote synthesis of amino acids, carbohydrates, purines, pyrimidines, and a wide variety of other organic compounds. The experimental pursuit of geochemical organic synthesis, arguably the best understood aspect of life's origin, began in the early 1950s with the pioneering studies of University of Chicago graduate student Stanley Miller and his distinguished mentor Harold Urey (*8,9*). Together they demonstrated rapid organic synthesis triggered by the ionizing effects of simulated lightning. Other experiments using ultraviolet radiation or alpha particles revealed similar chemical synthetic pathways (*10,11*). So facile were these reactions that some researchers assumed that the problem of prebiotic chemical evolution had been solved.

The discovery of abundant organic molecules in some carbonaceous meteorites points to additional important extraterrestrial sources of organic molecules (*12-14*). Reactions of UV-irradiated small molecules in the cold vacuum of interstellar space produce complex suites of organics (*15,16*) – processes that have been replicated in laboratory experiments (*17,18*). Comets and asteroids continuously delivered supplies of these molecules to the early Earth.

Lightning, alpha particles, and ultraviolet radiation promote chemical reactions through ionization and the formation of energetic free radicals. Living cells, on the other hand, build organic molecules through sequences of less-energetic metabolic redox reactions. Many origins-of-life researchers therefore point to natural geochemical environments, including deep-ocean hydrothermal vents and reactive surfaces of transition-metal minerals, as equally plausible energy sources for prebiotic synthesis (*19-22*). Astrobiologists have strong incentives for examining the possibility of such mineral-mediated deep origins. If life is constrained to form in a warm little pond or ocean surface then Earth, and perhaps ancient Mars or Venus, are the only possible places where life could have begun in our Solar System. However, if cells can emerge from deeply buried wet zones, then Europa, Callisto, Titan, and other bodies become promising targets for astrobiological exploration.

Russell and Hall (*this volume*) adopt this premise and suggest that life first emerged where dissolved H_2 from submarine hot springs reduced dissolved CO_2 in the ancient ocean. They propose that iron-nickel sulfide minerals served as catalysts in the generation of essential biomolecules. Other important thermodynamic energy sources, Russell and Hall note, resulted from the strong pH and thermal gradients between the acidic ocean and alkaline hydrothermal fluids.

Amend and McCollom (*this volume*) echo and amplify this view by calculating thermochemical parameters of redox reactions that must have constituted the earliest metabolisms at geochemically relevant temperatures, pressures, and chemical compositions. They thus demonstrate that the molecular components that make up a prokaryotic cell can be produced through aqueous synthesis from inorganic precursors.

The conclusion of more than half a century of research is that prebiotic synthesis of biomolecules took place in numerous astrochemical and geochemical environments. Consequently, Earth's primitive oceans must have been a complex, if dilute, broth of organic chemicals. Regardless of their synthetic sources, these simple organic compounds, so widely dispersed in the primitive oceans, had to be concentrated and organized by simple physicochemical mechanisms.

Molecular Selection and Organization

The abundant synthesis of varied prebiotic organic molecules was a prerequisite for life, and it is satisfying that so many plausible mechanisms for their formation have been demonstrated experimentally. However, this profligate production raises another question: how were the essential molecules of life selected, concentrated and organized from the messy prebiotic soup. The authors of this volume demonstrate a range of possibilities.

The oceans are of little help because they are so vast – a volume greater than a billion cubic kilometers. Even given the most optimistic estimates of prebiotic organic synthesis (*5*), the oceans were never more than a hopelessly dilute solution. Making biological macromolecules is further complicated by the fact that for every potentially useful small molecule in the prebiotic milieu, dozens of other molecular species had no obvious role in biology. Life is remarkably selective in its building blocks; the vast majority of carbon-based molecules synthesized in prebiotic processes have no biological use whatsoever. In such a random, weak solution it would have been difficult for just the right combination of molecules to bump into one another to make anything useful in the chemical path to life.

Consider sugar molecules, for example (*23*). All living cells rely on two species of 5-carbon sugar molecules, ribose and deoxyribose (the "R" and "D" in RNA and DNA, respectively). Several plausible prebiotic synthesis pathways yield a small amount of these essential sugars, but for every ribose molecule produced many other kinds of 5-carbon sugar also appear – xylose, arabinose, and lyxose, for example. Adding to this chemical complexity are the numerous 3-, 4-, 6- and 7-carbon sugars, in chain, branch and ring structures. Furthermore, many sugar molecules, including ribose and deoxyribose, come in mirror-related pairs – left- and right-handed varieties that possess the same chemical formula and many of the same physical properties, but differ in shape like left and right hands. Prebiotic synthesis pathways generally yield equal amounts of left- and right-handed sugars, but cells employ only the right-handed sugar varieties. Consequently, many origins researchers focus on the processes by which

molecules might have been selected, concentrated and organized into the essential structures of life.

Molecular self-organization represents one solution to the problem, as illustrated by the behavior of phospholipid molecules. These long, slender building blocks of cell membranes feature one hydrophilic (water loving) end, while the rest of the molecule is hydrophobic (water hating). Consequently, when placed in water, life's lipids spontaneously self-organize into tiny cell-like spheres – a self-organizing process that is rapid and spontaneous (*24-26*).

Zimmerman *et al*. (*this volume*) demonstrate an example of this self-selection process in the base-pairing of adenine and thymine (the A and T of the genetic alphabet), which together display unexpected stability. Zimmerman and colleagues employed both experiments and computations to compare the free energy of formation of numerous base pairs. The exceptional results for the A-T combination suggest that this pairing may represent a deterministic aspect of life's chemical origins.

Continuing on this theme, Seidel and Zaikowski (*this volume*) review examples of coordination-driven self-assembly of macromolecular structures, including a variety of polyhedral forms, as well as large rings and cages. The observed processes of supramolecular assembly have direct parallels to self-assembly of structures in biological systems. Similar self-assembly phenomena must also have played a significant role in the origin of the first RNA-like polymers, according to Bean, Lynn, and Hud (*this volume*). They hypothesize that life's first informational polymers incorporated chemical modules similar to those of RNA, but were distinct in that they self-organized in prebiotic environments. Furthermore, they suggest, small catalytic peptides formed through drying-heating reactions and assembled into surfaces and vesicles. This postulated co-evolution of peptide enzymes and genetic polymers represents one viable compromise solution in the chicken-and-egg dilemma of whether a metabolic cycle or genetic polymers came first in life's origins.

In spite of these advances, most molecules don't self organize. Consequently, many scientists have focused on surfaces as an alternative solution to the problem of selection and organization. Chemical complexity often arises at surfaces, where different molecules can congregate and interact. The surface of the ocean where air meets water is one promising interface, where a primordial oil slick might have concentrated organic molecules (*27*). Evaporating tidal pools where rock and water meet and cycles of evaporation concentrate stranded chemicals provide another appealing scenario for origin-of-life chemistry (*28*). Deep within the crust and in hydrothermal volcanic zones mineral surfaces may have embraced a similar role, selecting, concentrating and organizing molecules on their periodic crystalline surfaces (*29-32*).

Solid rocks provide especially attractive surfaces for concentration and assembly of molecules. Experiments reveal that amino acids concentrate and polymerize on clay particles to form small, protein-like molecules, while layered minerals also have the ability to adsorb and assemble the building blocks of RNA or accumulate small organic molecules in the relatively large spaces between layers (*33-35*). Once confined and concentrated, these small molecules tend to react to form larger molecular species that aren't otherwise likely to emerge from the soup.

One of the most intriguing and confounding examples of prebiotic molecular selection is the ancient incorporation of handedness. Many of the most important biomolecules, amino acids and sugars included, come in mirror image "chiral" pairs. These left- and right-handed molecules have virtually the same energies and physical properties, and all known prebiotic synthesis pathways produce chiral molecules in essentially 50:50 mixtures. Thus, no obvious inherent reason exists why left or right should be preferred, yet living cells display the most exquisite selectivity, choosing right-handed sugars over left, and left-handed amino acids over right (*7,32,36,37*).

Some analyses of chiral amino acids in carbonaceous meteorites point to the possibility that Earth was seeded by amino acids that already possessed a left-handed bias (*38-40*), though recent analyses of amino-acid-rich meteorites may cast doubt on these findings (*14*). According to one scenario, left-handed molecules could have been concentrated if circularly polarized synchrotron light from a rapidly rotating neutron star selectively photolyzed right-handed amino acids in the solar nebula (*41-43*). However, it is also difficult to eliminate entirely the possibility of a left-handed overprint imposed in the laboratory during the difficult extraction and analysis of trace quantities of meteorite organics.

Alternatively, many origin-of-life researchers argue that the chirality of life occurred as a chance event – the result of an asymmetric local physical environment on Earth. Such local chiral environments abounded on the prebiotic Earth, both as chiral molecules, themselves, and in the form of asymmetric mineral surfaces (*44,45*). Minerals often display chiral crystal faces, which might have provided templates for the assembly of life's molecules. Experiments show that left- and right-handed mineral surfaces provide one possible solution for separating a 50:50 mixture of L and D molecules (*46,47*).

Whatever the origin, either global or local, of chiral molecular excesses, the subsequent amplification of chirality has been successfully tackled by Klussmann and Blackmond (*this volume*). They provide an experimental demonstration of physical mechanisms based on the phase behavior of chiral amino acids in aqueous systems and in equilibrium, making it a robust and likely model for the prebiotic soup.

The emergence of highly selected and organized macromolecular structures is an essential step, but not the final one, in the progression from geochemistry to biochemistry. Life requires that macromolecules be incorporated into a self-replicating system. Two contrasting models of the first self-replicating system are debated. On the one hand, metabolism, by which chemicals react to release energy and manufacture molecules that reinforce the metabolic cycle, requires a sequence of chemical reactions that work in concert (*3,7,29,48*). On the other hand, the genetics-first scenario assumes a self-replicating and catalytic molecule like RNA that promotes its own replication while passing information from one generation to the next (*49-51*). Whichever scenario proves correct, a self-replicating molecular system, with its intrinsic potential for small chemical mutations and thus competition from competing cycles, would have experienced rapid evolution by the process of natural selection (*52,53*). This chemical origin of life forever transformed Earth's surface and led to the co-evolution of the geo- and biospheres.

Co-Evolution of the Geo- and Biospheres

Four billion years ago the seeds of life had been firmly planted. The Archean Earth boasted substantial repositories of serviceable organic molecules, which became locally concentrated and assembled into vesicles and polymers of biological interest. Once the first molecular replicator emerged, molecular natural selection took off. In such a world, nascent biology and ancient geochemistry became inextricably entwined. For example, Earth's surface mineralogy diversified as a result of varied microbial influences, which altered ocean and atmospheric chemistries at scales from local to global (*2*).

Authors in this volume then explore how the chemical environment at Earth's surface has evolved since life began. The greatest single change in Earth's 4.5 billion year history was the transition from an anoxic world to the oxygenated world of today – the byproduct of oxygenic photosynthesis, which greatly increased the energy available to the biosphere. We now recognize two major increments in atmospheric oxygen – the Great Oxygenation Event of 2.2 to 2.0 Ga (*54-56*) and the post-glacial Neoproterozoic events of 0.75 to 0.54 Ga (*57,58*). These transitions created profound biochemical challenges, because life had to develop new strategies to harvest redox-sensitive, bioessential elements such as Fe, Cu and Mo, while combating oxidative cellular damage. Burrows (*this volume*) explores how eukaryotes, which emerged about 2 billion years ago, initiated DNA repair to survive in the presence of reactive oxygen species. She reviews the remarkable evolution of DNA polymerase and repair enzymes that deal with the estimated thousands of daily oxidative damage events.

Continuing in this vein, Hemming (*this volume*) considers more recent feedbacks between life and atmospheric changes that affect climate. He uses boron isotopes, which serve as a proxy for ancient ocean pH. Because of interactions between the atmosphere and surface ocean, these isotopic data reveal natural variations in atmospheric CO_2 concentrations. Understanding such natural co-variability in atmospheric composition and climate is essential if we are to document and predict the role of anthropogenic influences on present and future climates.

In this volume's concluding contribution, Palumbi considers a troubling aspect of the intimate connection between the geo- and biospheres – that is, the rapid biological evolution that may result from human-induced environmental changes. Significant changes in the biosphere, including landscape fragmentation, overuse of antibiotics, application of pesticides, overfishing and climate change, exert strong bio-selection pressures. Palumbi explains that for species with large populations and rapid generation times, including many pathogens and insects, rapid evolution is often the result. However, species with relatively small populations and long reproductive cycles (polar bears and the great apes come to mind) often exhibit rapid population declines under such environmental changes. These evolutionary consequences of human-induced environmental changes are not abstract findings. The emergence of new highly-virulent anti-biotic-resistant pathogens and aggressive herbicide-resistant weeds has resulted in increased costs for medical care and agricultural products. However, such unintended consequences of human activities are only part of the modern story of chemical evolution.

Directed Chemical Evolution

The past two centuries have seen the arrival of a new era of chemical evolution, one fostered by human invention and creativity. Hoye (*this volume*) reviews this rapid evolution of chemistry through developments in synthesis, especially organic synthesis. He emphasizes how progress has been accelerated through the use of theoretical models, analytical developments, and a host of novel catalysts.

A number of challenging chemical problems serve to illustrate advances in the modern era of directed chemical evolution. Muckerman and Fujita (*this volume*) consider efforts to develop artificial photosynthesis, by which sunlight, water and carbon dioxide are converted into carbohydrates and oxygen. They summarize two distinct approaches to realizing the goal of artificial photosynthesis: structural models vs. functional models of the natural systems. Shen and Rajski (*this volume*) describe a similar natural systems strategy to developing drugs that mimic biological products, which are the basis for most new drug discovery and development. He observes that advances in genetics and in documenting biosynthetic pathways are making it possible to identify valuable natural products and to craft new synthetic chemicals.

Marti and Turro (*this volume*) discuss the flourishing field of fluorescent responsive molecular probes for use in the detection of oligonucleotides. Varied strategies, including molecular beacons and binary probes, are now used to track mRNA *in vivo*, quantify the polymerase chain reaction *in vitro*, and many other applications. The implementation of dye combinations, excimer-forming molecules, and metal complexes is further expanding the range of applications for these fluorescent markers.

Given the vast number of possible useful chemicals, combinatorial approaches to chemical synthesis and testing are proving to be a valuable way to identify highly functional molecules. A step beyond this synthesis of individual chemical species is the nano-world of molecular machines, such as artificial molecular motors, which require the collective interactions of numerous specialized molecules. Bell (*this volume*) considers major types of natural and artificial molecular motors, with an emphasis on recent research to design energy-efficient molecular subunits.

Conclusions: Complex Evolving Systems

This volume outlines how three distinct stages of chemical evolution – prebiotic, biological, and human-directed – have framed Earth's 4.5-billion year history. Each stage saw significant chemical complexification driven by varied selection processes. In the prebiotic era equilibrium physico-chemical mechanisms prevailed, as atmosphere, oceans, and rocks interacted under a wide range of environments on and beneath Earth's solid surface. Synthesis was promoted by solar and geothermal energy sources, amplified by such geochemical complexities as thermal and compositional gradients, fluid fluxes, solid-fluid and fluid-fluid interfaces, and cycles of light, heat, and tides. These environmental variables promoted the synthesis, selection, concentration and

organization of organic molecules into the first self-replicating, mutable chemical entities – the first form of life.

Life, with its paired abilities to mutate and to pass those mutations on to subsequent generations, promoted our planet's second stage of chemical evolution and inexorably increased the variety and modified the distribution of chemical substances in Earth's near-surface environment. The innovation of catalytic proteins and polynucleotides, in particular, altered the chemical landscape of our planet. Consequently, for at least three billion years microbial activities have altered the chemistries of Earth's atmosphere and oceans, thus driving the co-evolution of the geo- and biospheres. Atmospheric oxygenation, the innovation of biomineralized skeletons, and the colonization of terrestrial habitats all expanded the influence of life on Earth's surface chemistry.

The past two centuries have seen a third, far more rapid stage of human-directed chemical evolution, with global-scale exploitation of minerals and fossil fuels, and the synthesis of countless new chemical products. These dramatic developments have resulted in remarkable improvements in human health and productivity, but changes in our chemical environment have also led to unintended consequences, both known and as yet unresolved. Let us hope that with our new ability to guide chemical evolution will also come the insight and desire to use that power wisely.

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