

Preface

It has been almost a century since the inquiry into life's origin has been reinvigorated following several decades of quiescence influenced by Louis Pasteur's elegant experimental demonstration that microbes were not spontaneously generated in flasks of nutrient broth appropriately aerated to prevent the entry of airborne particles. It has been a century in which biochemistry and biophysics have completely altered our core understanding of the living world and consequently opened up a series of powerful experimental, theoretical, and computational approaches. In this new light, two of us independently thinking of first life were some fifteen years ago introduced by colleagues at the Santa Fe Institute who had detected some common points of interest in what we were investigating, one from the top down and the other from the bottom up – from the phenomenology of the living world with an emphasis on biochemistry and biophysics and from the underlying physics and chemistry and statistical theory that impose a necessary order.

A common theme was that life on Earth was not the outcome of an isolated event as suggested by the *Chance and Necessity* school but a planetary property that appeared early in the history of the planet and spread in a spontaneous way. What we designate life or proto-life has existed over most of the lifetime of planet Earth. The universality of the phenomenon and the massive flux of matter and energy due to the huge interaction of organisms and their products with the rest of planetary matter led us to return to the perceptive book *Geochemistry* by Kalervo Rankama and Th. G. Sahama [664], a work highly praised to one of us by the polymath G. Evelyn Hutchinson, dean of American ecologists. The two Finnish geochemists, acting as geological generalists, divided the planet into four *geospheres*: the lithosphere, the hydrosphere, the atmosphere, and the biosphere. The term "biosphere" had been introduced in 1875 by Eduard Suess and used in its modern sense some years later by the perceptive geochemist Vladimir Vernadsky.

What we wish to understand from a scientific point of view is how the newly formed planet, condensing approximately 4.6 billion years ago, was transformed over time into the present verdant world, home to millions of species and the abode of *Homo sapiens*, a nation including individuals like ourselves, who are somehow impelled to ask the foundational questions that this work tries to answer. What was clear from the outset was that such a study must be embedded in the domains of physicists, chemists, geologists, and biologists

aided by the analytical tools of mathematics and reified by database mining and computation. Using the baseball phraseology of the double play (Tinker to Evers to Chance), we are in the world of Pauli to Pauling to Woese. Wolfgang Pauli provided a formalism to generate the periodic table of elements within the domain of quantum mechanics and particle physics. Linus Pauling has provided the context to see in a systematic way how these atomic elements give rise to a huge number of structures, large and small, that, comprehensibly, are able to perform exquisitely complex chemical functions. Carl Woese showed why in the whole world of biota, phylogeny in its most general sense must be understood from its biochemical foundations as well as seen from its more classical perspectives. He worked at incorporating biochemistry and molecular biology into a more global biological perspective. The whole and its parts must be studied jointly. Several names of scientists have been and will be mentioned in this preface and throughout the book. We tend to think of the discipline in terms of those predecessors upon whose shoulders we stand. Science at its best is a community of scholars, and we have been privileged to have some of these as colleagues and friends.

The universe of entities we deal with has something on the order of twenty million species, yet the metabolic charts of all of these species map in major parts onto a single chart of intermediary metabolism, whose representation was developed and refined by the lifetime labors of scientist Donald Eliot Nicholson and his colleagues. This continuity of metabolism over four billion years and countless present and extinct species argues against the view of life as the outcome of an improbable event. We reject the idea developed in *Chance and Necessity* by Jacques Monod [561] that life is a result of chance whose origin is unfathomable. This view is inconsistent with the world that we know and with the way the living geosphere functions as part of it. We have thus rejected all reliance on "frozen accidents" as a dead end to our investigation of the earliest biosphere. We have also minimized appeals to panspermia, because there is often too much of a "biogenesis-of-the-gaps" character to arguments: we reason at the level of components where we have been unable to form a systems understanding of chemistry on Earth. When some components seem difficult to account for on this planet, we appeal to planets whose chemistry is less well understood than our own as a source for them, generating a host of new system-assembly and causation problems seemingly more intransigent than those with which we began.

We have tried to be guided by an "Earth Scientists Oath" or paraphrasing the prophet Micah we have tried "To achieve a scientist's love of honesty, to seek our limits of understanding, and to walk humbly in our universe." Where we have tried to say things that are genuinely new, we have kept our approach embedded in well-understood science.

The wide range of opinions expressed in the scientific community makes it clear that we do not yet have a paradigm, even in its broadest outlines, to explain in any detail the origin of life. The number of fundamental transitions it entailed has been large and some have probably been overwritten by subsequent innovations. The problem will be with us for a long time to come. Within these limitations we hope that this book will aid the community in framing the best and most productive questions within reach of

current understanding. With this goal we include a more eclectic body of material than that usually found in writings on this subject. For example in Chapter 4 and Chapter 6 we review both experimental results on mineral organosynthesis and extensive analysis of variations within the post-LUCA diversification of metabolism, despite the fact the former are too simple and the latter too complex to serve as close models for the transition from geochemistry to the first biochemistry that is our main interest. We have attempted to make our choices so as not to bury the reader in details¹ but to illustrate the extent of repetition or convergence of key motifs, with citations to the primary literature that the interested reader might pursue. From each body of evidence we call out the patterns or mechanisms that we believe impose significant constraints on theories of origins at the difficult and obscure era when the metabolic substrate and its control systems were emerging.

From a somewhat different perspective, in Chapter 7 we provide a basic but wide-ranging review of the theory of stability from statistical mechanics and related disciplines. In part this is necessary because the key mathematical ideas underlying the theory of robust order, which have been one of the main achievements of mathematical physics within the last century, are poorly communicated outside the specific fields where they were derived. The application of formal principles of stability from non-equilibrium statistical mechanics to systems chemistry is a field currently in its infancy, bringing together complex suites of concepts from two already sophisticated fields. Yet it is an inevitable merger, because the emergence of the biosphere was not a compounding of misadventures but a restructuring of systems.

We believe that one of the greater services we can offer may be to lower the costs of entry for readers into each other's literature and main ideas. For human minds in society, professional disciplines have been the portals to expertise, but the emergence of the biosphere was not a respecter of human silos. Few readers who have spent a lifetime becoming experts in geochemistry, biochemistry, or microbiology will have happened across the fact that the theory of robustness in non-equilibrium systems continues seamlessly to the mathematics of asymptotically optimal error correction. Yet this continuity must have been fundamental to the emergence of hierarchical architecture capable of memory and control over metabolism on the route from minerals to cells. Conversely, for readers to whom the "thermodynamics" of error correction is every day's bread and butter (its carbohydrate and triglyceride), there are no easy paths into the enormous literatures of geochemistry and biochemistry that review, at affordable cost, the basic principles of organization in those disciplines. Yet it can only be in context of these principles that any theory of error correction might contribute to an understanding of biogenesis. Our choice of materials and approach is aimed at providing such bridges, so that as a community we might be less outsiders to each other's sensibilities to order in the world.

¹ Christian de Duve, in the fine book *Blueprint for a Cell* [183] deliberately avoided such byways in order to maintain focus on a central narrative and increase reader accessibility. His book, which rewards re-reading even after many years, deserves if anything more than the considerable influence it has already had.

Starting with the belief that conceptual frameworks as well as acquired empirical knowledge, technical methods, and examples from physics, chemistry, biology, and geology are necessary components of the study of biogenesis, we have tried to present material at levels satisfying to domain specialists as well as penetrable from a more general perspective. This sometimes involves saying things more than once at varying levels of detail. A series of boxes set off sub-topics or derivations that will be of interest to readers who want more detail, or glossaries of domain-specific terms to which the text refers repeatedly. Terms of art that might be mistaken for common-language expressions (a frequent problem in the shorthand of technical fields) are typeset in *italic* where they are first used in a chapter. A small subset of terms are highlighted with **boldface** where they are first discussed: these are topics that play a special role in the structure of arguments or signal key ideas. We have tried to strike a balance between inclusiveness and economy to engage the broad range of colleagues whose insights are essential to this story. Of course, our own limitations must be acknowledged.

In a more philosophical mode, we envision the goal of this branch of science as showing how the core of intermediary metabolism is a necessary consequence of galactic processes giving rise to some distribution of the elements of the periodic table, which under the right geochemical boundary conditions generate an autocatalytic network of chemicals capable of emerging subsequently through a series of transitions into more complex molecules and structures: the biosphere. This series of transitions follows matter and its internal states of organization from simplicity to complexity. At the lowest level, non-equilibrium thermal physics appears to be the analytical method of choice. At each transition, new paradigms become necessary as complexification leads to a broader range of possibilities and structures, and opportunities for path dependence. This we have envisioned as biology standing between physics and history, deterministic at the simplicity roots and rife with possibilities at its complexity shoots.

With the above in mind we turn to the organization of this monograph. The first five chapters deal with the phenomenological and its generalizations. What is life on the planet Earth like and how did it get that way? In choosing which aspects to review, we draw on what the core scientific disciplines have made it possible to understand, and within this we select the patterns that we believe best assemble into a system that is coherent within the more inclusive body of scientific laws. Chapter 6 sketches the synthesis that we believe the foregoing facts support.

Facts, however, are not self-interpreting, and proposed scenarios are not theories. Everything we review in the first five chapters is known within the scientific community, but the system we propose in Chapter 6 has not seemed an inevitable or even compelling interpretation to all readers, for reasons we understand. Chapters 7 and 8 introduce other parts of the reasoning that we believe are needed for inference from facts to theories. Chapter 7, like the first five chapters, does not speculate and sticks to what we know, but in this case we consider what is known about stability and its relation to information. To gently contradict Wittgenstein, the world is a totality of facts, *and* of things, and we believe the introductions to both work best when made in each other's company. Chapter 8 brings these two streams

together in what we hope will provide a foundation for a proper theory. It explains some of the priorities we have expressed in the first five chapters, from the perspective in Chapter 7 that a formal theory of stability and robustness exists and that it has implications. We note there, too, that one measure of the plausibility of a theory of biogenesis that begins in geochemistry is how naturally it connects to the concepts and not only the metaphor of evolution as biology understands them today.

The opening chapter attempts to explain and justify treating the planet's biota as a geosphere. This perspective, which makes life a planetary property or perhaps a galactic property, opens the way to a more general treatment of biology at its core as a system science rather than a strictly historical discipline as the *Chance and Necessity* adherents or some evolutionary theorists would urge us to believe. It makes the case that the biological generalist must take geochemistry and geophysics seriously. From the other side, recent studies in geochemistry show why mineralogy must recognize major influences from the biosphere.

Chapter 2 is an overview of life as we know it, and our first attempt to come to grips with its extraordinary unity-in-diversity. The biosphere is a hierarchical complex system that has created novel order at scales ranging from electrons to ecosystems. Patterns at many levels can inform us about earlier ages, and more informative than any one pattern is the way they fit together as a system. Life on the planet Earth probably began 3.8 to 4.0 billion years ago. At first it seems extraordinary that present-day organisms and ecosystems could tell us much about the earliest ancestors, but when we consider that all are linked by laws as well as by descent, the diversity of modern life offers windows on the laws that created pasts older than the deepest we can reach with historical reconstruction. This prospect first came into focus in 1955 when it was noted that there was a single metabolic chart onto which all species mapped fully or in part. Thus metabolism is a living fossil possibly older than any extant rock. This amazing persistence becomes more compelling and more comprehensible as a feature of metabolism in physiological and ecological context, where metabolic order is recapitulated and given its functional semantics. We might note parenthetically that a 1999 paper of ours on the reductive citric acid cycle brought a letter of interest from the then 90 year old still hard working map maker of metabolism, Dr. Nicholson.

Our ability to comprehend life as a meaningful system, not only recording the past in extant diversity but also expressing elements of timeless order, has been aided by Carl Woese's revolutionary phylogeny and the growth of vast databases such as KEGG, MetaCyc, and Reaxys to mention just a few. At many points in Chapter 2 we are compelled to recognize ecosystems as forms of organization in their own right, not merely as communities of taxa but as the carriers of patterns that remain necessary even if all the taxa are changed. From the chemical propensities of metabolism to the invariants of ecology we are encouraged to look for empirical generalizations and theoretical principles applicable to non-equilibrium systems.

Chapter 3 considers energy sources for the kinetic processes of the maturing planet and energy exchanges among the geospheres. Sources include fusion energy coming as radiation from the Sun, fission energy from radioactive elements, and above all the

disequilibrium between our planet's formative condition, still trapped in its interior, and an outer shell driven relentlessly away from that condition. The hero in this story is the active mantle, whether through volcanism, melt-separation of elemental states, or long-range subduction and upwelling in tectonics. These are the processes by which heat – alone too diffuse an energy source to drive chemistry far from equilibrium – is nonetheless the cause for a gateway through which the Earth's chemical disequilibrium is focused at narrow points in covalent bond dynamics. One of our most central messages will be that the biosphere, first and foremost, is a chemical conduit for the flow of electrons from higher to lower potentials. The thermodynamic "problem" of a lifeless Earth, which on our planet was "solved" by the emergence of a biosphere, was to facilitate the descent of electrons. In Earth's first life, and in some life today, part of this electron flux is not only coupled to, but occurs by means of, carbon fixation, the reduction of CO_2 by the formation of multi-carbon molecules. That conduit with accompanying chemistry self organized, we argue, a chemical phenomenon for which we find precedent in physical processes such as weather or lightning, the far from equilibrium yet inevitable ordered states of the atmosphere. This chapter focuses on the planetary restlessness that may have made it impossible to remain lifeless, and the ways the same processes sustain parts of the biosphere directly today.

Chapter 4 offers a detailed view of metabolism where the top down and bottom up approaches must make contact. There is now an enormous amount of data on genome sequence, chemical mechanism, macromolecular structure, and enzymology. By combining these, we may understand what functions molecules perform, what variations have been open to them, and how their present diversity came into existence historically. To understand metabolism we must recognize at least four levels of organization: the small-molecule synthetic networks, crucial intermediate cofactors (vitamins) that transfer components and complete networks, macromolecule synthesis and catalysis, and in some cases the organizational functions of cellular compartments. We argue that the historical sequence followed the molecular sequence from simple to complex, from small molecules to large, and that the layers of order we find in metabolism today likely reflect historical accretions that were watersheds, but not history-erasing floods. The elaboration of metabolism was not only hierarchical but also modular, indicating parallel streams of innovation, which could have occurred in somewhat independent places and times. The multilevel patterns of life suggest that constraints on what would ever be possible originated in metabolism and then propagated to higher levels.

On any account it is impressive that a small, network-autocatalytic cycle (the rTCA cycle) should be found running through the termini of the synthesis pathways of all essential monomers. Also remarkable is the almost mineral-like simplicity of direct reduction of one-carbon units used ubiquitously in extant life, sometimes furnishing alternative starting points to synthesize a few amino acids. The significance of these patterns compounds as we find that the same networks have anchored the very little innovation that ever occurred in carbon fixation, and that their catalysts are among the most distinctive and conserved in the biosphere. The bottom up focus on reaction mechanisms and considerations of control and stability privileges the same pathways that historically have been unchanging points of

reference to which all innovations were anchored. Metabolism is not only a list of components but a logic of relations, and it is in that logic that we find non-arbitrary constraints strong enough to have entrained later accretions of complexity.

Metabolism by itself does not a geosphere make, so Chapter 5 turns to the hierarchy of biology, the series of transitions that moves to macromolecules, coding and memory molecules, control, containment, and the integration of bioenergetics. These higher-level systems define the context for the chemistry of life as we know it, and the question central to biogenesis is whether they inherited or dictated that chemistry's logic. Whether we can infer the path from geochemistry to the first cells by extrapolating modern biochemistry backward in time turns on the answer to this question.

The chapter considers three distinct higher forms of organization: the emergence of ribosomal translation of peptides and with it a genetic code, the integration of redox and phosphate energy systems, and the diverse forms and functions of compartmentalization realized in modern cells. We find, in all three cases, either common modes of constraint expressed in biochemistry and in its higher-level supports, or more remarkably, the imprint of metabolic logic in systems that have evolved to distance and insulate their internal functions from the substructure of metabolism. The modular unfolding of metabolism seen in Chapter 4 must have been interwoven with innovations at higher levels that increased the interdependence of prebiotic systems on each other and led to their progressive separation from lithosphere/hydrosphere chemistry to become a distinct geosphere. The layers in this interweaving have led to the dense interdependence of forms of order at many levels in modern life, which appears as a chicken-egg problem if viewed as a whole. The remarkable observation is that enough independent identity or partial autonomy has been preserved in different subsystems to suggest at coarse scale the alternation of moves through which the unification of cellular life and its distinct planetary role were attained. Cellular life is both unified and diverse because it is a confederacy, a gathering together of diverse opportunities for order from the abiotic geospheres to create a new identity that remembers its roots but is distinct from them all.

The first five chapters describe the world as it functions today, or as we can reconstruct its past from directly available evidence. We interpret some strong and invariant patterns as necessary features or as remnants of stages through which life must have passed, when the historical reconstruction and mechanism jointly support such interpretations. In Chapter 6 we weave these interpretations into a proposed web of stages in biogenesis. Our proposed sequence is not a detailed scenario – many important transitions occurred about which we can offer little or no detail. Our sequence is meant as a kind of skeleton provided by the strong constraints – those stages that seem to us sufficiently necessary that they should both constrain scenarios and guide the questions we ask about how to bridge the gaps between them.

Chapter 7 introduces the idea that gives precision to an intuition of many investigators that the emergence of life may have been stochastic, but it was not accidental. We introduce the ideas of both equilibrium and non-equilibrium thermodynamic states, and the robust transitions between them known as phase transitions. Our most important problem

issuing from the first six chapters is how to describe and account for strong regularities in dynamical systems that also exhibit constant variation. Thermal phases provide the needed concept and a developed mathematics to study its ramifications. These phases are the carriers of physical laws even as the entities and events that make them up undergo constant change. This chapter provides a means to state, in language that is not metaphor or analogy, what we believe must be the foundation for a theory of the origin of life: via whatever chemical mechanisms are experimentally plausible, the emergence of the biosphere, particularly in its early stages, can only make sense as a cascade of non-equilibrium phase transitions.

Non-equilibrium states and their transitions have in recent years been extensively studied in certain areas of physics and chemistry. A gulf exists, however, between the relatively simple phenomena for which their potential is routinely explored, and the structurally rich phenomena that are the normal interests of most geochemists, organic chemists, biochemists, microbiologists, and specialists in other domains where they are almost unknown. We believe that any effort to separate what is chance in life from what is necessity, and to distinguish the patterns that reflect each, must eventually face questions of robustness and the relation between material and information, which will bring non-equilibrium statistical mechanics and structurally rich systems together to create a new frontier.

We provide systematic introductions to the most central concepts, which may be followed using elementary methods with some time and work. The reader who is unfamiliar with, or does not wish to push through, the various formalisms need not be put off. Our concern is with concepts, and although we will not traffic in metaphor, we describe these so that their applications to emergence can often be understood without heavy formalism.

One of the most important insights from the theory of phase transitions (equilibrium or otherwise) is that reductionist science is an enterprise of floors and ceilings. Each phase transition creates the robust forms of order that will participate in dynamics at or below its immediate scale. These ordered states, in chemistry, have been the building blocks from which life and evolution design. They remain in effect until the next phase transition constrains some of them, creating new levels of organization and typically greater complexity. Reductionist science, in its best sense, works because we can make falsifiable predictions at a given level without knowing what is above the ceiling or below the floor. In other words, the strength of reductionism is due to the simplifying effects of emergence. For the same mathematical reason, the emergence of a biosphere could only have been possible through a cascade of phases that buffered innovations at different levels from each other. If we can identify the transitions, we recognize the stages as lawful rather than accidental.

The earliest ordered phases in geochemistry were organizationally simple, though the search for them in the wide parameter range of the lithosphere/hydrosphere interface may be very difficult. As metabolic order developed, forms of individuality emerged, and evolutionary dynamics entered, they became increasingly complex.

An important consequence of the phase transition paradigm is that the origin of life and the organization of the biosphere cannot be understood as two separate topics. The

emergence of the biosphere was the Earth's departure from a metastable lifeless state and its subsequent collapse into the more stable condition that includes life. Chapter 8 develops the ramifications of these conclusions, and argues that from them we must reconceptualize the nature of the living state.

This chapter introduces three new topics, which have been present in the context of all the earlier chapters, and which must now be addressed in their own right. The first is the modular and hierarchical architecture of life. Fully understanding hierarchy invokes all dimensions of the phase transition paradigm: material stability and layers, information requirements and buffering, the needs for control in hierarchical systems, and the way life meets these by following paths of least resistance. The second is the emergence of individuality and with it the Darwinian world. We invert the conventional view of life as a property inherent in individuals, and recognize individuality as one mode of organization – albeit an important one – among many that enable life. From this perspective for the first time, we find it most natural to expect what we observed empirically in Chapter 2: that metabolism and the ecosystem define two of life's most fundamental universals, to which individuals may form many different relations.

Finally we offer systematic arguments for a view of what is essential to the living state that could not have stood on its own from intuition and scenarios, but from the full development of the phase transition paradigm seems to us inevitable. The biosphere is, most fundamentally, the geosphere on Earth that opens otherwise unreachable domains of organic chemical states and processes. It is maintained for the same reason as it emerged: the chemistry of life and all the hierarchy of structures that maintain it constitute a channel for relaxation of redox and other energetic stresses. This view reaches much further than is at first evident. Chemistry unifies the extraordinary diversity of living order – its complexity, its stability, the particularity of its conserved features, and its tight integration with the other geospheres – to a degree that no other starting point can.

With these eight chapters, then, we will hope to have left the reader with the following main contributions.

1. The major transitions that constituted the emergence of the biosphere were not defined by single and rare microscopic events, but by regime shifts in the behavior that was typical in dynamical, stochastic ensembles. Some of these are the familiar phase transitions of equilibrium condensed matter, but the distinctively biotic ones are inherently dynamical.
2. One of us wrote in 1968 that "The energy that flows through a system acts to organize that system." Forty five years later two of us reiterate that point, but today a much more detailed picture can be drawn for the descent of electrons. A few channels for flow, used repeatedly, have given rise to the particular structures of biochemistry and life. Both from history and from mechanism, they are remarkably well positioned for the task. With a more advanced empirical and computational chemistry, it may not be beyond the ability of near generations to prove they are unique, at least in this planetary context.

3. A vision of the lawful nature of life might be expressed as "deriving intermediary metabolism from the periodic table of elements." The larger question of whether biogenesis was a chance event or a necessary event is closely related. If it was necessary, to what extent are major features predictable from first principles? We argue for a large role for predictability in the earliest stages, with contingency and complexity entering through later transitions. The periodic table is not all the law needed to derive metabolism, but significant structure in biochemistry does derive all the way from properties of the elements. In some other cases we argue that it follows from higher-level but still essentially physical and energetic regularities such as orbital structure, network topology, and kinetics.
4. The phase transition paradigm, which accepts heavy dependence on complex and diverse boundary conditions (such as the Earth has likely always provided), but rejects a large early role for miracles even in catalysis, supports a view that the progression in molecular size and complexity defined the progression of emergence as well. Early geo-organic chemistry cast the die for metabolism, and metabolism then cast it for the rest of biochemistry. The earliest important regime change in catalysis was not through macromolecules but through cofactors; the progression to macromolecules was a complicated transition, made possible by a biosynthetic foundation that was stable and already partly selective.
5. Historical reconstruction can sometimes help us see beyond the history we can directly reconstruct. With appropriate functional context, it can identify the relative ages and directions of change even of very ancient features. In some cases we can argue not only that universal features are primordial, but that they reflect causes that were at work before genetic history originated and perhaps before cells. These are windows on some of the earliest steps from prebiotic to nascent biotic chemistry.
6. Our understanding of the biosphere must be chemical. Organic chemistry is not an accidental stage on which abstract principles of life perform a play that could be performed elsewhere. Chemistry matters in detail because it matters in principle. Some of the most important sources of stability and complexity in life would not be expressible in any other system. The ecosystem is the bridge from geochemistry to life, and carries much of what is deterministic and necessary in metabolic order. Species emerge further into the domain of chance and are secondary. Thus we never need to call the ecosystem a "super-organism" to acknowledge its integrity, because we recognize this as in some ways prior to organisms.
7. Higher levels of living organization seem to require not single transitions, but many transitions for each form. Among these the most enigmatic is the emergence of an oligomer world in which mRNA, tRNA, rRNA, and proteins are unified by ribosomal translation. Yet, as complex as this sequence of transitions must have been, and with large gaps remaining in our understanding of its intermediate stages, it emerged carrying striking signatures of metabolic order that are not parts of its modern function. The long exploration that led to cells, at the end of its wandering, arrived still at the order of metabolism, and enables us to know some things about it for the first time.