Between a rock and a living place:
Natural selection of elements and the search for life in the universe

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Abstract: The suite of life’s essential chemical elements on Earth constitutes only one possible evolutionary outcome. A greater understanding of factors governing the natural selection of elements in Earth’s past will create a predictive capacity for detecting and assessing life’s existence on worlds where alternate evolutionary paths may have been taken.

1 Atoms before molecules; molecules before life

What are the essential attributes of life, and how should they shape our notions of habitability and the search for life on other worlds? To guide this search, one key is to understand the rules governing the natural selection of the elements that compose life’s molecular architecture. Life as we know it requires ~30 chemical elements, including carbon (C), hydrogen (H), oxygen (O), nitrogen (N), phosphorous (P), and sulfur (S), as well as a variety of others critically important for catalysis, structural elements, electron transport and cellular signaling. Whereas scientists have learned a tremendous amount in the past 50 years about how these elements are used in biochemistry, there remains deep uncertainty about why evolution selected for these elements.

This knowledge gap must be narrowed. Within the next decade, the search for life on other worlds will require difficult decisions about Mars sample selection, Solar System mission destinations, and exoplanet observational priorities. We may also face the challenge of interpreting potential signs of life. These decisions and interpretations will be guided by ideas about how the physico-chemical characteristics of various planetary environments determine their habitability, how they shape the emergence and evolution of life, and how they affect the detection of life. These ideas are inevitably rooted in predictions about the chemical needs of possible alien biochemistries. The quality of these predictions depends on the knowledge of the evolutionary rules that determine the natural selection of chemical elements.

Studies should be undertaken to (1) investigate the interplay between element function and availability on Earth; (2) envision and, wherever possible, test alternate evolutionary scenarios and elemental incorporation mechanisms that could play out in other planetary circumstances. The natural selection of elements operates at the intersection between the geochemical abundances of elements through time and across planetary bodies, and the biological processes that use these elements. In order to better understand the meaning of these gross chemical signals it is imperative that we develop a better understanding of the physico-chemical roles of the major elements and their interactions in such a way that the identity of each element is in context for its function. Astrobiology investigators should follow an innovative scientific approach rooted in the experimental reconstruction of ancient life and biosignatures from the genomic record, constrained by the data-driven reconstruction of ancient environments from the geologic record. Additionally, the function of the major elements in biological cycling must be understood within the framework of a planetary geochemistry. This knowledge would help to potentially predict biological chemistries that account for the bulk chemistry of other planets. Additionally, the interaction of these elements will also help us understand the geochemistry of our own planet and better our understanding of oceans of the past. This need requires expanded investment in research that explores these topics. This work requires biochemists, evolutionary biologists, microbiologists, computational biologists, geobiologists, and planetary scientists. This investment would not only give a scaffold for understanding the complexity of the biological/geological system but also the roles of elements and the evolutionary events that drive their biogeochemical cycles.

2 Ancient Earth as a natural laboratory to study “life as we don’t know it”

We need to approach this challenge by using ancient Earth as a “natural laboratory” in which to discover the rules governing the elemental requirements of life. The environmental abundances
of several elements have changed over Earth history in ways that allow us to probe the interplay between function and availability in their natural selection. Are some elements so essential for biological functions that evolution will select for them despite low availability? Or does the coevolutionary history of life and the Earth environment reveal other possibilities? And how would this play out on other worlds, with different relative element abundances?

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<td>● What were the abundances and sources of biologically important elements on early Earth?</td>
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<td>● What were the elemental requirements of prebiotic synthesis? Of key biological processes, including transcription, translation, and biogeochemical cycling on early Earth?</td>
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<td>● Are there alternatives to the elements used in modern biological processes?</td>
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<td>● What different trajectories might planetary coevolution take given different biological elemental requirements and environmental availabilities?</td>
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<td>● How large a deviation from Earth’s elemental abundances and distributions is needed to push evolution in novel and unpredictable directions?</td>
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Studying ancient Earth is not new in astrobiology, but elucidating general principles – “selection rules” – has not been a focus. This needs to change in the coming decade because NASA is broadening its search strategy beyond an exclusive framework of “life as we know it” on “Earth 2.0”. Geochemical records of ancient Earth, and our increased understanding of factors that drove the chemical origins of life, permit us to explore alternate possibilities. Would the coevolution of life and the Earth environment have worked out differently if we “replayed the tape” of evolution under slightly different conditions — as seems inevitable on other worlds? Notably, we do not know how large a deviation from Earth’s elemental abundances and distributions is needed to push evolution in novel and unpredictable directions. We should expect that surprisingly small deviations will lead to biospheres that are radically different from Earth, in ways that will complicate our abilities to detect or interpret. If space exploration has taught us anything, it is that we should not be surprised to be surprised! But in what ways will these biospheres differ, and hence, how should our knowledge of extrasolar planetary environments shape our search strategies?

To answer these questions, we ultimately will need a predictive capacity — a theory of planet-life coevolution — that incorporates the rules governing the natural selection of the elements. Such a theory will constitute a radical leap. Its construction begins by taking the key incremental step of deducing the path of element selection during the evolution of life on Earth, understanding why it took that path, and considering alternative possibilities.
3 A focus on metals

Astrobiologists are confident about some of the rules of selection as they relate to C, H, O, N, P, and S. However, there is vast uncertainty for other elements, namely, several redox-sensitive metals that have changed in their environmental abundances over billions of years as a consequence of Earth’s progressive surface oxygenation\(^5,6\). Understanding how the changing availabilities of these metals modulated the evolution of the biosphere is critical because they catalyze key, pervasive and/or primordial biosynthetic and energy transduction processes\(^1,7-10\). A focus on metals thus provides a tractable target to explore the natural selection of elements more broadly.

The utility of this approach is highlighted with two example cornerstone studies that complement prior NASA Astrobiology investment in exploring the origins of life and the evolution of key biogeochemical innovations:

*Prebiotic synthesis.* NASA has long invested in studying the circumstances in which life can originate in conjunction with assessing how to determine whether signals from a planet indicate habitability or the presence of life. This is because if NASA knew where life was more likely to originate, it could focus its resources to those places and increase its chances of detecting life. It is therefore important to determine if there are unique (and perhaps indispensable) metal needs for driving prebiotic chemical synthesis, and if the metal needs of prebiotic processes correlate with obligatory biological metal utilization. If so, it is important to determine if the presence or absence of these metals on an exoplanetary surface may also be regarded as diagnostic and fundamental to the presence of life. As just one example, it was recently shown that Na and Cl ions play an unexpected role in facilitating chemosynthetic shortcuts to nucleotide synthesis\(^11\); it is unclear whether nucleotides can be generated under prebiotic circumstances without these specific elements or similar inorganic photosensitive metals functioning as catalytic intermediates. As another example, the divalent Mg\(^{2+}\) and Zn\(^{2+}\) ions appear to be biologically critical for coordinating with and stabilizing ribonucleotide sequences\(^12,13\), but researchers have suggested that Pb\(^{2+}\), Mg\(^{2+}\) or Fe\(^{2+}\) may be needed to assist prebiotic, non-enzymatic replication of RNA strands\(^14-16\) and/or early translation machinery\(^17\). It is important to reconcile the elemental needs for prebiotic chemistry, and to determine which (if any) of these needs carry over into facilitating habitable conditions on exoplanets.

*Evolution of nitrogen fixation.* The most common biochemical mechanism that obtains biologically essential N from the environment (N-fixation) uses molybdenum (Mo) as a cofactor\(^18\). The biosphere as we know it would not exist without this metal. Yet, Mo is exceedingly rare on Earth’s surface and most especially in Earth’s ancient oceans when this biochemical mechanism likely first evolved\(^5,6,9\). Thus, it has been widely thought that early variants of this metabolic process were Mo-independent, and perhaps more reliant on iron (Fe), which was substantially more abundant than Mo in oceans for the first half of Earth history\(^9,19,20\). This story is so simple and
elegant that it is almost a dogma, making Mo the type-example of an element for which it is often thought that biochemical use and evolutionary adaptation were tightly coupled to changes in environmental availability. However, this story is at odds with recent biogeochemical and genomic discoveries that imply that the Mo-dependent mode of N-fixation was ancestral\(^\text{21,22}\) and potentially operating despite early Mo scarcity\(^\text{23}\). If so, then the evolution of Mo in N-fixation might not have been so tightly governed by environmental availability after all; rather, evolution may have discovered the utility of Mo to become ecologically important despite its scarcity in Earth’s early oceans. This presents an intriguing possibility that there is something fundamentally unknown about Mo’s elemental properties that may have predisposed its incorporation into emergent N-fixation enzymes, despite the widespread availability of alternative cofactors. If true, then the potentially universal preference for Mo in early N-fixation may then need to be considered in assessments of planetary habitability\(^\text{24}\).

**Implications for where we search for life**

Metal availability is determined by planetary geophysical and geochemical processes, especially differentiation and subsequent geodynamic and tectonic evolution, and by planetary formation processes that determine bulk planetary chemical inventories. Hence, research such as that outlined above intersects with research into exoplanet geophysics and geochemistry, as well as exoplanetary solar system science, in non-trivial ways that will shape our understanding of which planets are and are not likely to be habitable. It also has relevance for exploration of our Solar System as we begin to ask more sophisticated questions about the habitability of subsurface oceans on icy worlds, and meso- and micro-environments on Mars, informed by future data from these settings.

4 Future directions

**Recommendation:** Investment into the development of novel experimental techniques that can probe the contingency or indispensability of the physico-chemical roles of major elements, in both the pre-biological and biological modes of chemoautotrophy, is viewed as essential to constraining the pervasiveness and architectural variability of life in our universe. **We therefore advocate a robust, interdisciplinary program of exploring beyond biology’s extant atomic and molecular limitations.**

Life is a highly specialized arrangement of atoms and molecules that, when acting in concert, avoid a collapse to equilibrium. Perturbing this arrangement (i.e., substituting for alternative catalytic or biophotonic cofactors, alternative phosphorylation compounds, etc.) is often limited by life’s tight tolerances that arise from within these networks of constraints. It is possible, however, that Earth life’s specific chemical arrangement represents only one particular solution among many possible such solutions with similar behavioral properties. By generating novel interfaces between self-organizing biotic and self-organizing abiotic chemical systems, entirely novel chemosynthetic capabilities can be uncovered that are not limited by life’s extant genetic, enzymatic and metal co-factor-catalyzed molecular architecture. Specific techniques that have demonstrated promise in generating and probing such novel interfaces include:

- genetic and enzymatic molecular resurrection through phylogeny;
- synthetic biology and directed evolution experiments with alternative substrates and cofactors;
- generating genetic libraries that are subjected to laboratory selection experiments for identification and generation of novel alien chemistries and metabolisms.
• continuously driven systems of (likely self-organizing) prebiotic compound synthesis as proto-metabolic proxies; and
• targeted genetic perturbation of highly conserved cellular modules, with accompanied multi-level (genetic, enzymatic and metabolite concentration) monitoring of cellular adaptive responses

Taken together, these novel methods are likely to generate entirely new experimental means of perturbing, analyzing, de-coupling, and constraining the fundamental elemental constituents that enable living systems to persist and flourish. By extension, the data generated can directly inform the targeted and strategic use of observational resources and infrastructure to guide the search for forms of life in our universe that may be quite dissimilar from our own.

5 References


