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PERSPECTIVE

Temporal variation of planetary iron as a driver of evolution

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Edited by Donald E. Canfield, Syddansk Universitet, Odense M, Denmark, and approved October 22, 2021 (received for review July 10, 2021)

Iron is an irreplaceable component of proteins and enzyme systems required for life. This need for iron is a well-characterized evolutionary mechanism for genetic selection. However, there is limited consideration of how iron bioavailability, initially determined by planetary accretion but fluctuating considerably at global scale over geological time frames, has shaped the biosphere. We describe influences of iron on planetary habitability from formation events >4 Gya and initiation of biochemistry from geochemistry through oxygenation of the atmosphere to current host–pathogen dynamics. By determining the iron and transition element distribution within the terrestrial planets, planetary core formation is a constraint on both the crustal composition and the longevity of surface water, hence a planet's habitability. As such, stellar compositions, combined with metallic core-mass fraction, may be an observable characteristic of exoplanets that relates to their ability to support life. On Earth, the stepwise rise of atmospheric oxygen effectively removed gigatons of soluble ferrous iron from habitats, generating evolutionary pressures. Phagocytic, infectious, and symbiotic behaviors, dating from around the Great Oxygenation Event, refocused iron acquisition onto biotic sources, while eukaryotic multicellularity allows iron recycling within an organism. These developments allow life to more efficiently utilize a scarce but vital nutrient. Initiation of terrestrial life benefitted from the biochemical properties of abundant mantle/crustal iron, but the subsequent loss of iron bioavailability may have been an equally important driver of compensatory diversity. This latter concept may have relevance for the predicted future increase in iron deficiency across the food chain caused by elevated atmospheric CO_2.

iron | oxygenation | evolution | complex life | planetary habitability

A planet's suitability to sustain life is the combination of a number of chemical and physical characteristics, including planetary size and stellar metallicity. Among these is the requirement for the presence of liquid water and hence, the planet's position in the circumstellar habitable zone. The initial development of life on Earth is also linked to iron. Cells utilize iron in numerous and highly conserved processes, including DNA replication, intermediate metabolism, and gene expression, exploiting the chemical properties of iron that facilitate redox reactions and bond formation in multiple orientations (1–3). That iron plays such a fundamental role across the gamut of biology suggests that its utilization is ancestral and hence, may reflect environmental conditions at the initiation of life (4).

Planetary Formation and Initial Mantle Compositions Conducive to Life

The composition of the terrestrial planets reflects that of their undifferentiated meteorite building blocks, with their rocky mantles all exhibiting broadly similar ratios of the refractory rock-forming elements. Of these, it is iron that exhibits the greatest range in mantle abundance across the terrestrial bodies, ranging from below 3 wt % FeO in the mantle of Mercury to greater than 18 wt % in that of

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Mars (5). Furthermore, of the major rock-forming elements (Mg, Al, Ti, Ca, Si, and Fe), it is only iron that exhibits multiple valence states on the terrestrial surface.

The diverse mantle iron contents of the terrestrial planets arise from the processes accompanying planetary accretion and are set by the prevailing physical and chemical conditions of planetary core formation. Core–mantle differentiation initiates after the asteroidal bodies grow to around 10 km in diameter and attain enough mass to retain a significant proportion of the heat derived from short-lived radionuclides, primarily ^{26}Al (with a half-life ~700,000 y) and to a lesser extent, ^{60}Fe (6). As accretion progresses, liquid metal segregates from the initially intermixed silicate, aided by the conversion of gravitational energy to heat as the metal percolates to the center of the body. The iron content of the silicate is then determined by the chemical equilibria:

$$\mathrm{Fe(core)} + \tfrac{1}{2}\mathrm{O_2} = \mathrm{FeO(mantle)}.$$

With core segregation occurring at upper mantle pressures, the majority of the terrestrial mantle's iron content is present in the reduced form (Fe^{2+}) (7); the concentration of the more oxidized Fe^{3+} in silicates is negligible. A planet's silicate iron content is, therefore, determined by the prevailing redox conditions of core–mantle segregation, which in turn, is primarily inherited from the planet's precursor "building blocks." As a rule, material that forms in the outer solar system and beyond the distance from the sun at which water ice will sublime (the "snow line" or "frost line") is more oxidized in nature. Addition of water to planetesimal bodies undergoing internal heating and differentiation will inevitably result in the oxidation of iron by both reaction of metallic iron with water and hydrothermal silicate weathering. Indeed, the primitive phyllosilicate-bearing carbonaceous-Ivuna (CI) class of carbonaceous chondrite meteorites contains very little metallic iron, with the majority in the more oxidized Fe^{3+} form, representing formation in oxidizing, water-rich conditions (8). Recent isotopic evidence from Ru and Mo stable isotopes (9, 10) together with solar system dynamical simulations (11) suggests that the solar system initially possessed solids composed of two distinct compositional and isotopic reservoirs. These comprised a reduced and volatile depleted inner reservoir from which the terrestrial bodies initially formed and a volatile, water-rich outer reservoir formed beyond the snow line and likely physically separated by the early formation of Jupiter. Although the terrestrial bodies initially accreted from locally sourced volatile depleted material, bodies nearer the solar system's snow line, the heliocentric distance at which water vapor condenses to ice, would have received an increased contribution of oxidized material as accretion progressed. For example, the elevated FeO content of the Martian mantle (18 wt % FeO) indicates the planet formed under conditions ~10× more oxidizing than those of the Earth (8 wt % FeO) (12), reflecting its proximity to the solar system's paleosnow line. In contrast, Mercury, the closest planet to the sun, possesses mantle iron contents of less than 3 wt % FeO and hence, formed under conditions over 100× more reducing than that of the Earth, reflecting the minimal contribution made by outer solar system material. From the perspective of extrasolar planets, however, these observations imply that beyond a broad observation of planetary bodies becoming increasingly oxidized and volatile rich with distance from their home star, the final iron content of rocky mantles is dependent on the stochastic addition of material at the tail end of a planet's accretionary history.

Iron Composition Contributes to Water Availability

The conditions of core–mantle differentiation determine not only the mantle iron abundance but also, the abundance of other redox-sensitive transition elements frequently utilized by life (e.g., V, Cr, Ni, Mo) (13). These alloy-forming elements generally mirror the behavior of iron, such that when compared with Earth, the rocky portions of reduced planets, like Mercury (14), exhibit significant depletions in transition elements (Fig. 1). The surface availability of elements that express redox-sensitive changes in speciation is, therefore, greatly diminished, with S being the only likely abundant candidate. This reduction in transition element abundance potentially contributes to unfavorable conditions for the development of life, as incorporation of such elements in metalloproteins is critical for cellular biochemistry.

The development and/or sustained presence of life on more oxidized planets, such as Mars, may also be problematic despite possessing an abundance of Fe and transition elements. The higher mantle iron content lowers the temperature at which it undergoes melting, leading to both higher melt productivities and magmas that become increasingly iron and aluminum rich. These evolved, iron-bearing magmas, erupted (15) or emplaced (16) onto a wet planetary surface may be assumed to efficiently hydrate, consuming water in the process (17). Assuming efficient loss of hydrogen to space, this process will lead to oxidation of the planetary surface. On Mars, this process very likely led to the rapid sequestration of surface water, away from a potential biosphere, within the first billion years (18). Indeed, observations of xenon isotope fractionation in the Earth's Archaean atmosphere suggest that significant hydrogen escape occurred up until the Great Oxygenation Event (GOE) ~2.3 Gya (19), which may account for up to an ocean's worth of hydrogen being lost to space (20). Importantly, given the young sun's lower solar flux (21), the liberation of hydrogen by such

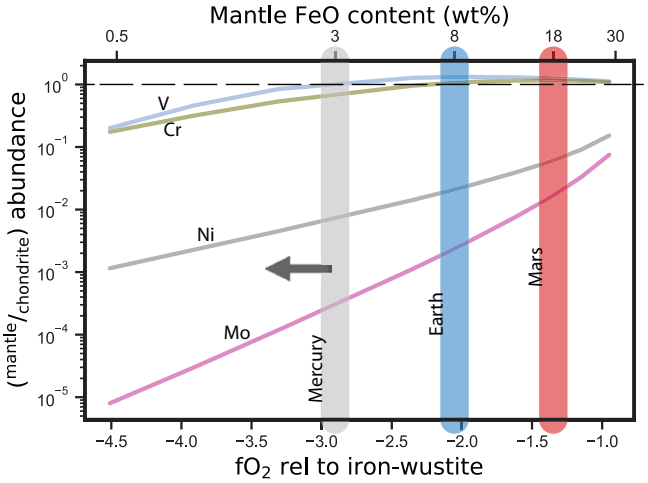

Fig. 1. The iron content of terrestrial bodies of approximate Mars size reflects the mean redox conditions of core formation (oxygen fugacity, fO_2, shown relative to the iron-wüstite [FeO] buffer). A Mars-like planet forming under conditions around 10× more oxidizing than the Earth possesses a mantle in excess of double the FeO content. In contrast, a Mercury-like planet forming under conditions ~100× more reducing leaves its mantle denuded in FeO (<0.5 Earth) and also, a host of other transition elements (Cr < 0.5 Earth, Ni ~ 0.1 Earth, Mo ~ 0.01 Earth). The arrow represents the upper limit of Mercury's mantle FeO content (14). The model follows ref. 75 and assumes all planets are of Mars mass, with metallic cores fully equilibrating with the mantle at depths of ~1/3 of the growing mantle; further details are given in *SI Appendix*.

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hydration reactions appears to be key to generating terrestrial and Martian surface temperatures high enough to sustain liquid water (22). On Earth, metamorphic reactions also play a crucial role in the lubrication of present-day plate tectonics, and it is tempting to speculate that, prior to plate tectonics, the lower iron content of terrestrial rocks may have assisted the retention of water on the Earth's surface. Unlike their iron-rich Martian cousins, primitive terrestrial rocks are buoyant once hydrated, with the result that any water contained within is retained close to the Earth's surface. When hydrated, Martian basalts are denser than their anhydrous counterparts, such that water may be transferred and sequestered into the Martian interior and irretrievably lost from the surface (18).

Geology Generates Iron Species Relevant for Biochemistry

The high availability of iron on the very early Earth was likely a key component in the synthesis of biological precursor molecules (23). It has been recently demonstrated that the close proximity of all three (ferric, ferrous, and native) iron species may be key in the abiologic synthesis of a number of biological precursor molecules (24). However, the terrestrial environments where all Fe species coexist are extremely uncommon since at least one end member species must be, at best, metastable at the prevailing redox conditions. One possibility is the oxidation of iron via aqueous alteration at hydrothermal vents. Serpentinization of olivine results in the oxidation of ferrous iron (Fe^{2+}) to ferric (Fe^{3+}) such that, simplistically,

$$2\left(Fe^{2+}O\right)_{(olivine)} + H_2O \rightarrow \left(Fe^{3+}{}_2O_3\right)_{(magnetite)} + H_2.$$

Given a sufficient production of hydrogen, reduction of (Fe, Ni)$^{2+}$ to native metals occurs:

$$\left(Fe^{2+}O\right) + 3\left(Ni^{2+}O\right) + 4H_2 \rightarrow Ni_3Fe_{(awaruite)} + 4H_2O.$$

Although hydrothermal vents provide potential localities where all three valence states of iron were colocated, the hydrothermal origin for life has been criticized on the grounds of the elevated temperatures and the adverse kinetics of peptide bond formation in dilute aqueous environments (25). Alternatively, the antiquity of the last universal common ancestor) suggests life's appearance may have coincided with the cessation of the last terrestrial sterilizing event (26), the result of the final significant addition of mass to the Earth around 4 Ga (27). These events potentially "seeded" the terrestrial surface with meteoritic Fe and phosphides (24) and would have colocated these with atmospheric CO_2. By concentrating biological precursors in temperate, ephemeral surface pools (28), a subaerial origin (29) for life potentially overcomes many of the limitations presented by a hydrothermal origin. Such an origin scenario is not, however, without its detractors, not least because the presence of significant subaerial land masses at this point in Earth history is contested. The elevated mantle potential temperature of the Archean Earth and the resultant low lithospheric strength point to subaerial land being rare, or perhaps even absent, prior to ~2.5 Ga (30); however, such assumptions are dependent upon the timing and origin of surface water and its volumetric quantity. Unfortunately, evidence is scant—the geological rock record is, unsurprisingly, increasingly patchy with age and contains no Early Archean subaerial rocks. However, it is possible that the chemistry of life and the ubiquity of iron utilization record conditions that have been eroded from the rock record.

The Temporal Evolution of Iron Bioavailability

Given the abundance of both water-rich planetary bodies and life's elemental building blocks, it is likely that simple life is common in the universe. However, the Earth's transition to complex, multicellular life required it to clear multiple environmental hurdles, not least those presented by temporal changes in elemental abundance. One difficult challenge life faced arose from its initial success exploiting the utilization of abundant soluble Fe and the consequential eventual rise in atmospheric oxygen that caused loss of soluble iron. The GOE marked the initial notable rise of atmospheric oxygen within the rock record, resulting in a marked decrease in surface water iron content. However, the Proterozoic oceans were also likely redox stratified, with deeper waters retaining the broadly ferruginous conditions of the Archaean (31) and the appearance of transient euxinic and sulfur-rich but relatively soluble iron–poor waters (32). The redox stratification and the transient euxinic conditions of deeper waters suggest that the dramatic fall in bioavailable iron in the photic zone, which arose from the GOE (see below), gave impetus to the emergence of biological and metabolic coping strategies that facilitated evolution of complex life.

Fe is a primary cofactor in many of the oxidoreductase enzymes associated with Earth's most ancient metabolisms (nitrogenases, hydrogenases, sulfate reduction, methanogenesis, anoxygenic photosynthesis) (33, 34). This is potentially a consequence of the evolution of these metabolisms in an Archaean ocean in which iron was both abundant and soluble, and so, it was relatively bioavailable. Indeed, the Archaean gene expansion was relatively enriched in encoded proteins that bound Fe or Fe-S, which were likely involved in electron transport and energy-generating pathways (35). The more primitive domains of Bacteria and Archaea have a higher incidence of Fe usage in their proteomes when compared with the younger Eukarya (36), which likely reflects the evolution of the latter in a more recent environment in which Fe is poorly bioavailable due to lower solubility in the presence of oxygen (37).

Although the GOE occurred over the interval 2.43 to 2.22 Ga (38) and led to a drop in the solubility of iron in surface ocean water, the more recent Neoproterozoic Oxygenation Event (NOE) exacerbated the decrease in soluble iron (Fig. 2). Moreover, the oxidizing conditions of the GOE may have caused a mass extinction event (39), in part because oxygen is harmful to life unless biochemical processes are available to safely detoxify and utilize it. The abundance of many other bioessential elements was also altered by the GOE (40): for example, levels of oxidized arsenic increased, likely selecting specific defensive genetic innovations (41). Despite the depletion of bioavailable iron, throughout the rebound of life post-GOE and its subsequent diversification (and passage through other successive mass extinction events), iron has retained its preeminence in biological systems. In fact, there may have been a small increase over time in the number of genes that utilize iron (35). Presumably, this is because iron has unique electrochemical properties that make possible, or make efficient, a range of biochemical processes such that other elements cannot be broadly substituted for iron within proteins without causing a significant disadvantage. Lifeforms that do not require iron are exceedingly rare; indeed, only two are known (*Borrelia burgdorferi* and *Lactobacilli*) (42).

Siderophores and Behavioral Diversity

Cells need to assimilate iron and post-GOE, increasingly would need to do so in oxidative conditions where iron is insoluble.

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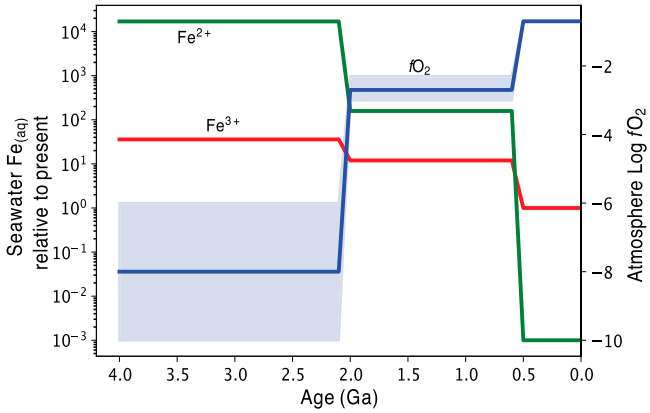

Fig. 2. Concentration and speciation of iron in surface seawater through time. Putative Fe concentrations were taken from the literature (*SI Appendix* has details). The redox state of the oceans in the Early Archean is not precisely constrained but was certainly many orders of magnitude more reducing than the present day (uncertainty of prevailing oxygen fugacity, fO_2, represented by light blue bands). Assuming the Archean oceans were broadly in equilibrium with an atmosphere derived primarily from gases emanating from the mantle implies that the oceanic near-surface waters were significantly more reducing and lower in pH than present (76) and importantly, Fe(II) enriched (77). Local oxidation of Fe by either biological or abiogenic actions would have led to significant temporal iron limitation. Additionally, significantly higher Fe concentration also implies a possible Fe(III) component in the reduced oceans of similar magnitude to present. The evolution of Fe(III) selecting siderophores may then be a response to both temporal Fe limitations and also, a mechanism to both select and control cellular Fe acquisition.

Siderophores are small organic molecules synthesized and secreted by almost all known bacterial species (and by plants and fungi) that chelate Fe^{3+} with very high affinity (43). After locked onto iron in the extracellular milieu, siderophores are (re-)captured by specific transporter systems at the surface of bacteria and internalized, and the iron is assimilated (44, 45). Mathematical modeling suggests that siderophores are most effective when extracellular iron is in the form of solid-phase mineral (increasingly prevalent after the GOE), as solubilized chelated iron leads to a local increase in concentration of bioavailable iron (46). Gathering of bacterial cells in spatial structures near to the iron source assists in iron capture and inevitably leads to increasingly complex cell–cell interactions (47).

The origin of siderophores may have predated the GOE, as siderophore-synthesizing systems are present across cyanobacteria (48). This raises the obvious question of why, in an ancient anoxic environment awash with soluble Fe^{2+}, life would develop the capability to acquire Fe^{3+}. Arising from the oxidation of ferrous iron in shallow environments by anoxygenic photoferrotrophic precipitation or abiogenic photooxidation, banded iron formations (BIFs) are not restricted to the GOE interval but occur intermittently during the Archaean and Neoproterozoic. BIFs also occurred during the Mesoproterozoic (49) and Paleozoic, where they may have derived from ferruginous bottom waters (50). Within the surface photic zone, early life may have been exposed to regular periods of highly fluctuating iron solubilities, including in localities where iron was concentrated in solid phase. The early evolution of siderophores may have been an adaptation to these spatial and temporal resource restrictions. It is also noteworthy that cyanobacteria are among the most ancient producers of siderophores (51) (e.g., anachelin) and may have been particularly immersed in local increases of Fe^{3+} after they had developed the oxygenic photosynthesis capability that contributed to the GOE.

Post-GOE and post-NOE, the relative abundance of Fe^{2+} and Fe^{3+} in surface water flipped markedly by many orders of magnitude (Fig. 2). There would be considerable variability in the solubility of iron as a function of depth, and particulate iron can be a nutritional source of iron. Nevertheless and despite this variation, overall the relative decrease in easily bioavailable soluble Fe^{2+} in surface waters in the photic zone would have been enormous, as is evident in the geological record of BIFs. Indeed, low iron in surface waters results in iron currently being a limiting nutrient for primary marine biological productivity. We propose that in toto and at planetary scale over millions of years, the loss of ferrous iron as a consequence of oxygenation events would act as a major selection pressure favoring survival and development of organisms possessing siderophore-based (or other) mechanisms to efficiently acquire ferric iron.

The use of siderophores to acquire iron shapes behavior. Variants of a bacterial species that lose the capacity to synthesize siderophores but retain transporter systems to capture and internalize them may have a relative advantage—although the benefits of such cheating can be short lived. Cooperating bacteria that produce and acquire the same siderophores as "public goods" survive the influence of cheaters by adopting spatial structures to maximize mutual benefit and by fine regulation of siderophore production and recycling. Bacterial species may also acquire the ability to capture siderophores produced by a different species, and different species produce different types of siderophores that confer advantages in the context of particular forms of iron sources. Thus, "social" interactions of competition, cheating, and cooperativity, focused on iron acquisition, have evolved among and between bacterial species and are in a permanent state of flux (52) (Fig. 3*A*). Iron-oriented behavioral complexity and evolutionary development are even more evident when the source of iron is able to defend itself against capture: in host–pathogen relationships.

Competition for Iron Drives Genetic Diversity and Complexity

One view of infection is that it is the theft of one organism's nutritional resources by another. Clinical trials finding that iron supplementation in human populations exacerbates malaria (53), experimental studies of many different infectious pathogens in animals (54), and several independent lines of genetic evidence together show that iron assimilation is a critical player influencing the outcome of infection, exerting selection pressure on both the host and the pathogen. In many bacteria, virulence is determined by clusters of genes colocated in the genome in high pathogenicity islands—genes in these islands work together to enable high-affinity iron capture from hosts (55), and in their absence, normally lethal bacteria are rendered relatively harmless—unless the host harbors a particularly rich source of iron (56). Mammalian hosts utilize a protein lipocalin-2 that captures siderophores in order to prevent iron scavenging by invading bacteria (57); however, virulent bacteria encode genes that synthesize variant siderophores, which evade this host defense mechanism (58). Some bacteria (*Neisseria* and *Haemophilus*) capture transferrin, the mammalian protein that carries iron in the circulation, in order to assimilate iron. Selection of DNA sequences encoding transferrin variants is driven by evading capture by bacteria. However, counterselection of

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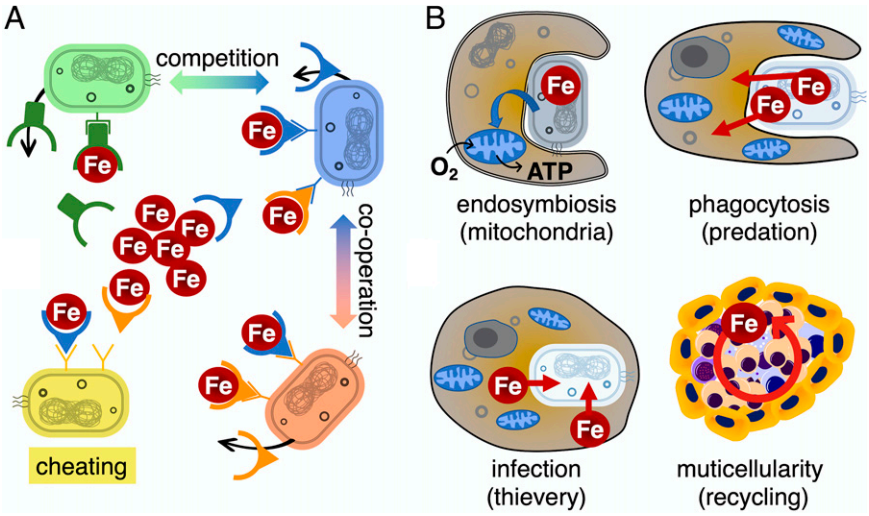

Fig. 3. Adaptation to low iron availability. (*A*) Competitive, cheating, and cooperative behaviors among single-cell organisms. Siderophore secretion allows iron acquisition from mineralized sources but also leads to complex interactions between bacterial cells and species, which may drive genetic variation. (*B*) Trafficking of iron in development of eukaryotes (mitochondria), phagocytosis (predation), intracellular infection, and multicellularity. In these processes, biotic sources of iron are utilized in behaviors that can be mutually beneficial, piratical, or more efficiently self-sufficient.

Neisseria and *Haemophilus* strains occurs, with variant bacterial transferrin binding proteins able to reacquire the new hominid transferrin variant (59). These iterations of evasion, adaptation, and recapture over relatively short evolutionary timescales indicate that the battle for iron is important enough to alter and fix hominid genomes, as well as driving variation in bacteria. Over much longer timescales and against a background of widely fluctuating environmental availability of iron (in particular, during the GOE and the NOE), we propose that more extreme adaptations in genomes and cellular behavior may be expected.

The first eukaryotes and eukaryotic multicellular organisms arose after the GOE, and eukaryotic diversity substantially increased around the time of the NOE (60). The GOE and NOE time frames are characterized by multiple redox changes and alterations in geochemical balance. Iron speciation measurements are among the proxies used to estimate timing of oxygenation events (60, 61); however, given the fundamental requirement of iron for life, we propose that declining iron availability should be considered as a specific actor influencing diversification of life. The endosymbiotic event that led to mitochondria is believed to have occurred ~1.85 Gya (62). The entrance of mitochondria into biology eventually facilitated the generation of energy via oxidative phosphorylation, detoxifying potentially dangerous oxygen in the process. The respiratory chain protein complexes I to IV are particularly rich in iron, using heme and Fe-S clusters to shuttle electrons and generate intermediates upstream of adenosine triphosphate (ATP) synthesis. The energy produced by the iron-dependent mitochondrial processes is used by the host cell for its benefit, while mitochondrial nutritional needs are partially handed over to the host cell, which routes iron to mitochondria. Thus, at a single-cell level, mitochondria allow a division of labor with respect to iron accumulation from the external environment and its use to generate energy. Eukaryotic cells also evolved phagocytosis, a form of predation (ingestion of whole bacteria) that allows for nutrient capture on a macroscale in comparison with siderophores (63). Infection, predation, and endosymbiosis are all behaviors that switch the focus of iron acquisition from mineral sources to other life-forms (Fig. 3*B*), and each of the three behaviors may evolve into the others over time—for example, initially exploitative infections may become mutually symbiotic (64).

Development of multicellularity, which in eukaryotes occurred between the GOE and the NOE (60), allows for a degree of recycling of nutrients over the lifetime of the organism, which is particularly important for nutrients such as iron that are poorly bioavailable. In humans, around 25 times as much iron is recycled per day as is acquired from the diet (1). Multicellular organisms derive benefit from increased oxygen pressures as a source of energy, and although multicellular animals likely arose during the NOE, it appears that oxygen itself does not drive the development of multicellularity (65). However, it is noteworthy that iron is required for key conserved mechanisms of oxygen sensing that may have allowed complex tissues to evolve in the presence of fluctuating oxygen concentrations (66). Efficient use of more limited nutritional resources such as iron, via its recycling from dying cells in order to provide for new cells, may serve as one important selective advantage favoring multicellular organisms (Fig. 3*B*). Interestingly, sulfur limitation, impairing key iron-and sulfur-dependent processes, can drive *Dictyostelium discoideum* toward adoption of multicellular development (67).

The requirement for iron is well characterized as a selection pressure acting on specific genes, gene clusters, and behavior in bacteria and also, on genes in higher organisms in relatively short time frames in specific circumstances such as infection and nutritional stress. High-magnitude alterations in global iron availability over geological eras (the GOE, the "boring billion," and the NOE) would have more profound evolutionary effects. We propose that developments in complexity of life, such as phagocytosis, predation, endosymbiosis and evolution of mitochondria, and multicellularity, were substantially influenced by the necessity for acquisition and efficient utilization of iron against the background of temporal variation in its bioavailability. Future genomic, biogeochemical and evolutionary investigations should, in our view, incorporate fluctuating nutrient availability into their thinking.

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Summary and Application of the Concept to Exoplanets and Future Earth

The role of core formation in the subsequent habitability of the Earth is well known with regard to the subsequent generation of the Earth's magnetic field. However, the consequences of these events and their influence on the composition of the Earth's mantle are perhaps less obvious. We contend that it is the iron content of the silicate mantle—a result of the conditions and mechanisms of core formation—that has a significant, perhaps predominant, role in the Earth's habitability and subsequent evolution of life. From the perspective of habitable worlds, two competing factors are at play; first, mantles must contain transition element inventories capable of initiating and supporting simple life, and second, mantles must also be capable of conserving surface water for periods of time relevant to the evolution of complex life. The former would preclude planets that underwent core formation under very reducing, Mercury-like conditions. The latter suggest that planets with Fe-rich Mars-like mantles may sequester surface water on geologically rapid timescales (18). Although the Earth appears to occupy a compositional and positional "sweet spot," the sensitivity of planet habitability to mantle Fe content and how this may change with planet mass remain unclear. We propose that the combination of both an Fe-abundant early Earth and the subsequent removal of Fe during surface oxidation provides a unique set of environmental pressures that influenced the evolution of life over Earth history. Simple, unicellular life may, possibly, be relatively common in the universe, but the combined set of conditions and temporal events that have led the Earth to develop more complex life-forms could be significantly rarer. A time line of the different roles that iron has played influencing the habitability of Earth, in the development of the biosphere, and as an irreplaceable but limiting nutrient during evolution is shown in Fig. 4. The implications of this view for the search for exoplanets are that the relative proportion of metallic core to mantle (that is, the core mass fraction) may provide an observable constraint on the iron content of an exoplanet's mantle and hence, its suitability for the emergence and evolution of complex life (68).

Lastly, back on Earth, continued anthropogenic escalations in atmospheric CO_2 are anticipated to increase the prevalence of iron deficiency via relatively poor iron uptake into plants that are iron sources for humans and livestock (69, 70). Iron deficiency is the most common micronutrient deficiency in humans, affecting well over a billion people (71). Iron deficiency can protect against some bacterial infections and malaria (72); however, it causes anemia and impairs immunity (73), and it can inhibit growth (74). Therefore, looking to the future, modulation of iron availability on a planetary scale brought about, potentially rapidly, by climate change would be expected to generate

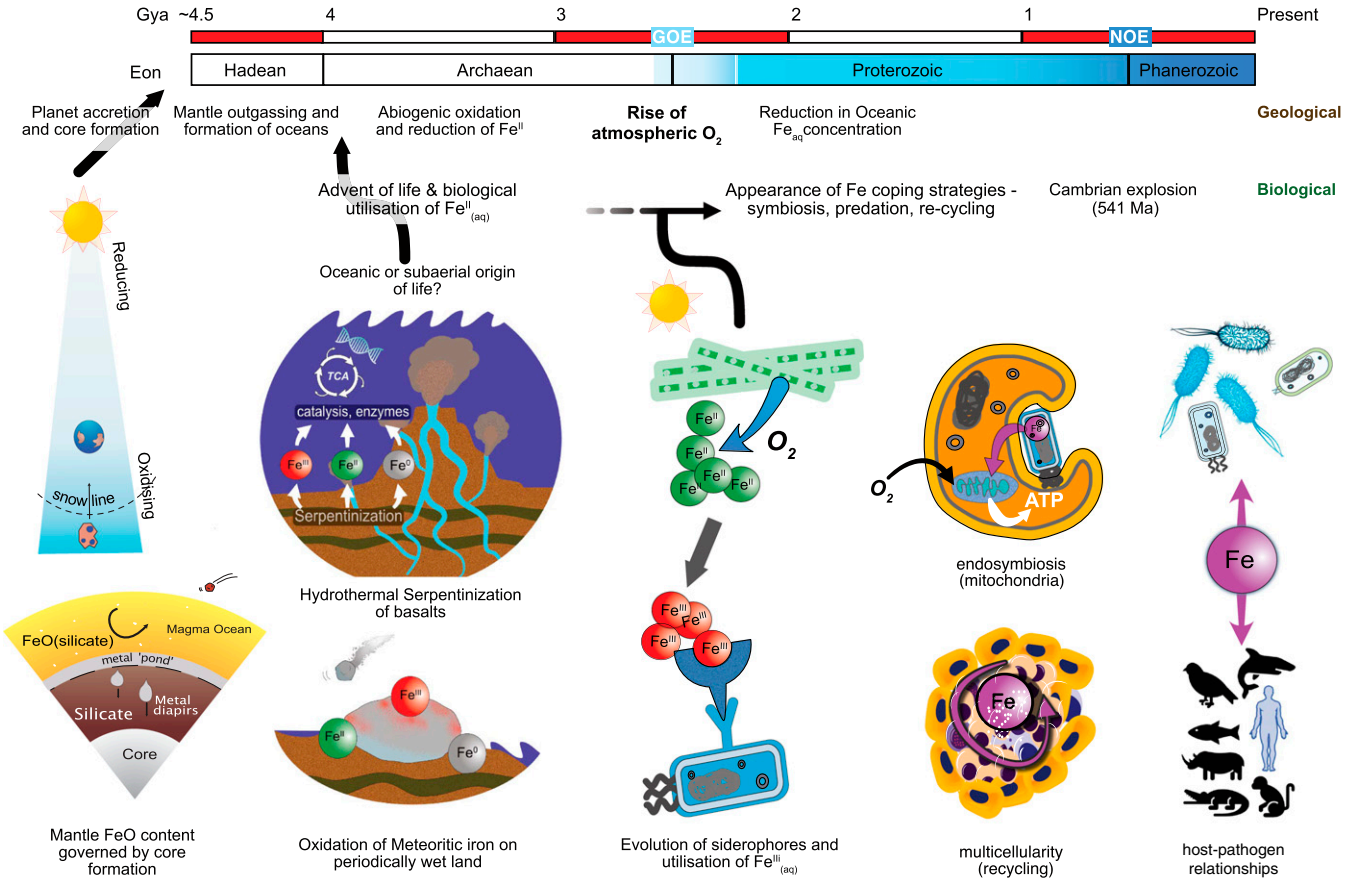

Fig. 4. Time line of an iron-centric view of development and evolution of life on Earth. Mantle iron content and surface water retention are governed by early planetary accretion events, including distance from the sun and prevailing redox conditions. Initiation of foundational biochemical processes may have been facilitated by co-occurrence of native, ferrous, and ferric iron at hydrothermal vents or subaerial wet land. Oxygenic photosynthesis depleted oceanic iron, favoring deployment of Fe^{3+}-capturing siderophores from bacteria. Complex social, endosymbiotic, predatory, infectious, and multicellular behaviors allow more efficient utilization, or appropriation, of relatively scarce iron. Host–pathogen relationships are strongly influenced by iron availability, selecting genetic variants. TCA, tricarboxylic acid cycle.

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selection pressures on hosts and pathogens throughout the biosphere, inevitably impacting human health.

Data Availability. All study data are included in the article and/or *SI Appendix*.

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