

Open Questions on the Origin of Life at Anoxic Geothermal Fields

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Abstract We have recently reconstructed the ‘hatcheries’ of the first cells by combining geochemical analysis with phylogenomic scrutiny of the inorganic ion requirements of universal components of modern cells (Mulkidjanian et al. Proc Natl Acad Sci U S A 109: E821–830, 2012). These ubiquitous, and by inference primordial, proteins and functional systems show affinity to and functional requirement for K^+ , Zn^{2+} , Mn^{2+} , and phosphate. Thus, protocells must have evolved in habitats with a high K^+/Na^+ ratio and relatively high concentrations of Zn, Mn and phosphorous compounds. Geochemical reconstruction shows that the ionic composition conducive to the origin of cells could not have existed in marine settings but is compatible with emissions of vapor-dominated zones of inland geothermal systems. Under an anoxic, CO_2 -dominated atmosphere, the ionic composition of pools of cool, condensed vapor at anoxic geothermal fields would resemble the internal milieu of modern cells. Such pools would be lined with porous silicate minerals mixed with metal sulfides and enriched in K^+ ions and phosphorous compounds. Here we address some questions that have appeared in print after the publication of our anoxic geothermal field scenario. We argue that anoxic geothermal fields, which were identified as likely cradles of life by using a top-down approach and phylogenomics analysis, could provide geochemical

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conditions similar to those which were suggested as most conducive for the emergence of life by the chemists who pursue the complementary bottom-up strategy.

Keywords Geothermal separation · Hydrothermal alteration · Formamide · Borate · Zinc sulfide · K^+/Na^+ ratio

Introduction

Recently we have put forward a detailed evolutionary scenario on the origin of the first cells at anoxic geothermal fields of the primordial Earth (Mulkidjanian et al. 2012). This study has drawn some attention including several critical comments and substantial questions. Below, after a brief outline of our model, we address these open questions. We are grateful to all the colleagues for scrutinizing our evolutionary reconstruction.

Anoxic Geothermal Fields as Cradles of Life

Our reconstruction is based on the fact that the inorganic chemistry of the cytoplasm is highly similar in bacteria, archaea and eukaryotes. The internal pH in almost all cells is close to neutral, the phosphate level is about 10 mM, the concentrations of Zn and Fe are in the range of hundreds of micromoles, and the K^+/Na^+ ratio is typically >10 (see Williams and Frausto da Silva 1991; Nies 2007; Mulkidjanian and Galperin 2009 and references therein). According to the principle of chemistry conservation (Mulkidjanian and Galperin 2007), this ionic composition most likely is inherited from the very first cells as originally suggested by Macallum as early as 1926 (Macallum 1926). However, the membranes of the first cells, according to available reconstructions (Deamer 1997; Szostak et al. 2001; Szathmáry 2007; Mansy et al. 2008; Mulkidjanian et al. 2009; Mulkidjanian and Galperin 2010), while occluding biological polymers, could not prevent (almost) free exchange of small molecules and ions with the environment. Furthermore, before the emergence of diverse membrane translocators, the exchange of small molecules via leaky membranes should have been of vital importance for the first cells, which also implies that their interior was equilibrated with the surroundings, at least with respect to small molecules and ions. Thus, the first cellular organisms could have dwelt in specific habitats that were enriched for the inorganic ions that are most prevalent in cells (Macallum 1926; Mulkidjanian and Galperin 2007; Natochin 2007; Mulkidjanian 2009; Mulkidjanian et al. 2012). A potential alternative to this explanation is that the chemical differences between the intracellular milieu and the environment are unrelated to the conditions under which the first cells evolved (Dupont et al. 2010). Then, the dramatic enrichment of modern cells for K^+ , Fe^{2+} , Zn^{2+} , and phosphate could be viewed as a relatively late shift that came after the emergence of powerful ion-translocating membrane pumps and was driven by the growing demand of the newly evolving enzymes for particular inorganic ions as catalysts or substrates.

To distinguish between these two explanations, we performed a comparative genomics analysis and turned to the set of protein-coding genes that are ubiquitous to all cellular organisms with sequenced genomes (Koonin 2003; Charlebois and Doolittle 2004) and accordingly almost certainly were present in the Last Universal Cellular Ancestor (LUCA) (Gogarten et al. 1989; Woese 1998; Lazcano and Forterre 1999; Koonin 2003) and even earlier life forms. These ubiquitous proteins and functional systems showed affinity to and functional requirement for K^+ , Zn^{2+} , Mn^{2+} , and phosphorous compounds; by contrast, none of the surveyed ancestral

proteins specifically requires Na^+ (Mulکیدjianian et al. 2012). Thus, we proposed that protocells evolved in habitats with a high K^+/Na^+ ratio and relatively high concentrations of Zn, Mn and phosphorous compounds (Mulکیدjianian 2009; Mulکیدjianian et al. 2012).

We examined a variety of environments in search of natural habitats with high levels of transition metals and phosphorous compounds, as well as a K^+/Na^+ ratio >1 . We focused on the high K^+/Na^+ ratio rather than the absolute levels of K^+ and Na^+ which could vary widely in endorheic basins, depending on the ratio between the surface area of a basin and its depth. The ionic composition conducive to the origin of cells was found to be compatible only with the emissions of vapor-dominated zones of inland geothermal systems. A major distinctive feature of such systems is the separation of the vapor phase from the liquid phase due to the boiling of the ascending hot hydrothermal fluids. The ascending vapor, after reaching the surface of the rock, discharges via numerous fumaroles and mud pots, which make a geothermal field. The chemical composition of the two phases differs dramatically: the liquid phase contains large amounts of Na and Cl whereas the vapor phase is specifically enriched in H_2S , CO_2 , and NH_3 (Aver'ev 1961; White et al. 1971; Fournier 2004; Bortnikova et al. 2009; Bychkov 2009; Mulکیدjianian et al. 2012). We found that the higher volatility of K^+ ions within the vapor phase leads to the enrichment of the emissions from the vapor-dominated zones in K^+ ions, yielding $\text{K}^+/\text{Na}^+ >1$ (Mulکیدjianian et al. 2012).

Although terrestrial geothermal systems have been occasionally suggested as potential habitats of the early life (Deamer et al. 2006; Ricardo and Szostak 2009), the unique role of their vapor-dominated zones as natural chemical separators, to our knowledge, has not been specifically addressed. The principal reason why the vapor-dominated fields were not considered as suitable hatcheries for the protocells is that the fluids at such fields are highly acidic with pH values reaching -0.5 (Fournier 2004; Mulکیدjianian et al. 2012) and hence inhospitable to life. This acidity is due to the fact that the ascending vapor carries large amounts of hydrogen sulfide which, on reaching the surface, is oxidized by atmospheric oxygen to the strong sulfuric acid.

In the absence of oxygen on the primordial Earth, the geochemistry of vapor-dominated geothermal fields should have been substantially different: (1) The pH of the discharges from the vapor-dominated zones should have been closer to neutral because both H_2S and CO_2 , which ascend with the vapor, are weak acids, and their acidity would be compensated by the interaction with basic rocks; (2) at neutral pH, silica would precipitate at the outlets of hot springs and around them not as mud, as it does now, but as porous, ordered silicate minerals. Thus, the formation of clays such as smectite/montmorillonite and illite, as well as zeolites such as laumontite and natrolite, should be expected; (3) in the absence of oxygen, sulfide ions would cause precipitation of metal sulfides, yielding metal-sulfide-contaminated clays and zeolites. The precipitation of silica at anoxic geothermal fields should have been to some extent analogous to its precipitation within the steam-delivering pipes of modern geothermal stations. Within such pipes, where the interaction with oxygen is prevented by the pipe walls, formation of unusual saponite-like smectites with montmorillonite-type structures, enriched in Mg and transition metals, has been independently reported for power stations in Philippines (Reyes and Cardile 1989) and El Salvador (Raymond et al. 2005).

Two types of environments relevant for the early stages of evolution can be expected at anoxic geothermal fields, namely (i) periodically wetted, illuminated mineral surfaces that could serve as templates and (photo)catalysts for diverse abiotic syntheses and (ii) puddles and pools of cooled, condensed vapor that would function as concentrators of prebiotic organic molecules. Each such pool would “harvest” substrates from its catchment area and should have contained a mixture of water, simple amides, silica, metal sulfides and amphiphilic molecules (which could be present as micelles). We proposed that the porous

sediments of such pools, enriched in sulfides of Zn and Mn, could serve as reactors where the first replicating polymers would form (Mulkidjanian et al. 2012). Hence, a stratified system could be established within geothermal ponds where the illuminated upper layers would be involved in harvesting and production of reduced organic compounds, whereas the deeper, less productive but better protected layers would provide shelter for the replicators. Both the light gradient and the interlayer metabolite exchange are typical of modern stratified phototrophic microbial communities (Nold and Ward 1996).

Answers to the Open Questions

The model described has prompted the following questions:

1. “The ‘principle of chemistry conservation’ is a postulate rather than a proven principle; it may be true on short time scales, but who can say what has happened since the origin of life?” (Jim Cleaves cited in ref. (Biello 2012)).

The idea of chemistry conservation was introduced by Archibald Macallum to explain the similarity between the chemistry of animal body fluids and sea water; Macallum explained this similarity by the emergence of the first animals in the sea (Macallum 1926). This explanation remains valid up to now. The same approach was used by George Wald in 1964 to explain why the cellular metabolism is anoxic (Wald 1964); he argued that the cellular biochemistry was established on an anoxic Earth and could hardly be modified after the oxygenation of the atmosphere (2.5 Gyr ago, according to most recent data (Hazen et al. 2011)). Since this explanation has not been challenged, the principle of chemistry conservation appears solid on the time scale of ~2.5 Gyr. This is anything but a “short time scale”. Critically, all modern cells (those of archaea, bacteria and eukaryotes) share highly similar intracellular ionic conditions. Because it is hardly debatable that these cells are separated from the LUCA by at least 3 billion years of evolution, application of the chemistry conservation principle to the emergence of the first cells some 3.5–4.2 Gyr ago is not too much of a stretch and helps to explain some key biochemical traits that remained enigmatic, e.g. $K^+/Na^+ \gg 1$ within the cells. Like any statement in historical study, the chemistry conservation principle cannot be mathematically proven, but it is an assumption that is extremely well compatible with all the available data.

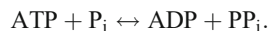
2. “The basic question is whether the observed high K–Na ratio reflects the historical environment in which life originated or underwent early evolution, or instead reflects some underlying chemical necessity, such as better functioning of certain cellular components.” (Jack Szostak cited in refs. (Biello 2012; Brouwers 2012)).

We argue that the high demand for K^+ , most likely, reflects the emergence of the translation machinery in an environment with a high K^+/Na^+ ratio during pre-LUCA times. A conceivable alternative would be that the primordial cells could synthesize proteins under conditions of low K^+/Na^+ and that this ability, which was extremely useful for survival (except in geothermal fields, $K^+/Na^+ < 1$ in natural environments), was then lost, requiring the evolution of ion-tight membranes and energy-driven ion-pumping machinery. This scenario appears to be rather unrealistic, particularly when one goes into the details on the K^+ -dependent stages of translation. Specifically, phylogenetic analysis of GTPases clearly shows that extensive diversification of GTPase domains antedated the LUCA (Leipe et al. 2002). The K^+ -binding sites are highly conserved in diverse GTPases, indicating that they were already present in the primordial GTPase domains, long before LUCA (Mulkidjanian

et al. 2012). The peptidyl transferase center, which apparently is K^+ dependent (Miskin et al. 1970), is the core, ancestral part of the ribosome (Bokov and Steinberg 2009; Davidovich et al. 2009). Thus, the K^+ -dependent components of the translation system appear to stem from the pre-LUCA stages of evolution.

In addition, the following observations are best compatible with the origin and early evolution of life in potassium-enriched environments:

- 1) The reactions of formation and cleavage of phospho(di)ester bonds should have been involved from the very beginning of life because these reactions comprise the core of cell biochemistry. These reactions can be modeled by a non-enzymatic transphosphorylation reaction:



where P_i is inorganic phosphate and PP_i is inorganic pyrophosphate. This reaction, which strictly requires divalent cations (e.g. Mg^{2+}), is accelerated approximately three-fold by K^+ and NH_4^+ but not by Na^+ (Lowenstein 1960). This feature is likely to be related to the functional dependence of many GTPases and ATPases on K^+ but not on Na^+ (see ref (Mulkidjanian et al. 2012) for details).

- 2) K^+ ions are needed for the folding of RNA (Shiman and Draper 2000; Sigel and Pyle 2007); specifically, they stabilize tetraloop receptors, widespread elements of RNA tertiary structure (Butcher and Pyle 2011).
- 3) A high K^+/Na^+ ratio appears to be crucial for stabilization of membrane vesicles that consist of either phospholipids or fatty acids. In the absence of divalent cations, phospholipid liposomes start to aggregate already at 400 mM Na^+ but stay in solution at >1 M of K^+ (Ohki et al. 1982). In the presence of divalent cations, the concentrations of Na^+ ions that cause aggregation are respectively lower (Ohki et al. 1982). Fatty acid vesicles are also more stable in K^+ -containing solutions: it is common knowledge that potassium soaps remain liquid whereas sodium soaps solidify. (Common soaps are none other than fatty acids). Therefore, at notable concentration of Mg^{2+} or Ca^{2+} , primitive lipid vesicles could better subsist in K^+ -containing primeval basins.

The catalytic capacities of K^+ and Na^+ are roughly similar (Williams and Frausto da Silva 1991), so the selective acceleration of such key cellular reactions as protein synthesis and hydrolysis of ATP and GTP by K^+ , but not by Na^+ ions is unlikely to be incidental. In our view, this fact strongly suggests that K^+ -rich environments indeed have shaped life as we know it.

3. “Overall, I think it is questionable that organisms would have kept their original composition, given the variability observed in present cells. Is it not at least equally likely that they have modified their cytosolic composition once they had control over this process? Any modern environment which matches this composition would then be purely coincidental” (Jim Cleaves cited in refs. (Biello 2012; Brouwers 2012)).

In fact, there is not much variability in the inorganic chemistry of modern cells, the cytoplasm of which is usually characterized by neutral pH, $K^+/Na^+ > 1$, and high levels of phosphate and some transition metals (Williams and Frausto da Silva 1991; Nies 2007; Mulkidjanian and Galperin 2009). This similarity cannot be explained simply by adaptation to similar environments; the natural environments differ dramatically with respect to ionic compositions. Strikingly, no known inhabited environment matches the internal inorganic composition of the cells; as we discussed in our paper, the basins at extant geothermal fields,

which show inorganic patterns similar to cytoplasm (high K^+/Na^+ ratio and high levels of phosphate and transition metals), are too acidic ($pH < 0$) to be inhabited by life forms. No modern organisms, which in principle can control their intracellular ion content, equilibrate their inorganic composition with the composition of their habitats. Apparently, modern organisms cannot control the requirements of their enzymes and RNA complexes for particular inorganic ions. Therefore, instead of matching the environment, organisms invest energy into ion pumping to satisfy the demands of their enzymatic systems for high levels of particular ions, just as they have to maintain highly reducing environment in the cytoplasm that is required for activity of those enzymes.

4. “To suggest that the ionic composition of primordial cells should reflect the composition of the oceans is to suggest that cells are in equilibrium with their medium, which is close to saying that they are not alive. Cells require dynamic disequilibrium—that is what being alive is all about.” (Nick Lane cited in ref. (Switek 2012)).

In fact, ionic disequilibria are energetically counterproductive because cells spend a lot of energy to maintain them given that even modern sophisticated membranes are intrinsically leaky for small ions. The ionic disequilibria exist precisely because the cells have to survive in the environments that are far from being optimal for their functional systems: not enough K^+ , too much Na^+ , and so on. Microbiologists know that a cell culture grows best in an iso-osmotic medium that contains plenty of amino acids, vitamins, proper mixture of mineral salts and more potassium than sodium. In an appropriate, K^+ -based medium, *Escherichia coli* cells grow well enough even in the presence of uncouplers of oxidative phosphorylation, in the absence of the proton-motive force (Kinoshita et al. 1984).

Notably, the proposed equilibria, as concerns small molecules and ions in primordial cells, do not imply equilibria with respect to large, polymeric molecules. The concentration of polymers, such as RNA and DNA, should have been far greater within the protocells than outside.

5. “...life started on an Earth that may not have had continent-size landmasses but rather a series of archipelagos formed by volcanoes, much like the islands of Japan today. As a result, the water cycling through these areas may have been very different” (Jeffrey Bada cited in ref. (Biello 2012)).

The only information on geology of the Hadean comes from the analysis of the data on zircon grains. These data indicate that there were continents 4.3–4.4 Gy ago (Wilde et al. 2001) and subduction zones 4.0–4.2 Gyr ago (Hopkins et al. 2008). The existence of subduction zones implies stability of continent(s) on a time scale of millions of years, at least, and the existence of inland geothermal fields.

6. “It may be impossible to tell what early life—or even the first universal common ancestor of life—was like, given all the intervening evolution. It’s akin to trying to infer an abacus from a modern PC. You might be able to infer a TRS-80, but then it all gets a bit hazy and there might be no vestigial remains of the intervening stages of biological evolution.” (Jim Cleaves cited in refs. (Biello 2012; Brouwers 2012)).

The abacus is built on different principles than a PC and TRS-80. (The coding is binary in PCs and TRS-80 but decimal in a classical abacus). Therefore the analogy used by Cleaves implies a discontinuity between modern life and some early life that would be based on different principles. We agree with Cleaves that in such a case any attempts to infer the properties of early life forms from the properties of modern organisms are likely to fail, leaving the entire origin of life field in dire straits. However, to our knowledge, there is not a

single piece of experimental or theoretical evidence of a discontinuity between early life and modern life, at least starting with the first cells which are the main focus of our study. Therefore, we base our research on Rudolf Virchow's "*omnis cellula e cellula*" principle. In this case, the reconstruction of the early life from the properties of modern organisms is a legitimate and potentially attainable scientific goal.

The requirement of uninterrupted replication of life forms in the course of evolution implies the existence of a primordial RNA World, where RNA-like molecules could serve both as information and catalytic molecules (Belozersky 1959; Gilbert 1986). Then, however, the bottom-up approach to the problem of the origin of life, which is complementary to the top-down approach that we have used, could be reduced to the search for (geo)chemical conditions conducive to abiogenic formation of ribonucleotides and their polymerization into RNA-like oligomers (Benner et al. 2006).

The chemists pursuing this line of research argue that specific formation of activated (cyclic) natural ribonucleotides with a potential for polymerization could take place in formamide-rich solutions, particularly under the action of UV light and in the presence of borate and phosphorous compounds (Schoffstall 1976; Costanzo et al. 2007; Powner et al. 2009; Barks et al. 2010; Saladino et al. 2012). It has remained unclear, however, whether geochemical settings enriched in formamide, phosphorous compounds, and borate could exist on the primordial Earth. Enrichment in simple amides, apparently, is incompatible with marine environments. Benner and colleagues have suggested—as cradles of life—desert environments where formamide, after forming in the atmosphere, could accumulate during the dry periods owing to its high boiling temperature (200 °C) and serve as a building block for primordial syntheses (Benner et al. 2006).

Anoxic geothermal fields should have been even better suited for abiogenic synthesis of ribonucleotides and their polymerization than primordial deserts. Formamide could form not only in the atmosphere, but also via hydrolysis of hydrogen cyanide which is found both in volcanic gases and in the exhalations of geothermal fields (Mukhin 1976). In addition, elimination of a water molecule from ammonia salts of carboxylic acids could also yield amides; specifically, dehydration of ammonia formate yields formamide. The exhalations of geothermal fields contain high amounts of ammonia (up to 130 mg/L in the mud pot solutions of Kamchatka (Bortnikova et al. 2009)) part of which is of non-sedimentary origin (Holloway and Dahlgren 2002). The high CO₂ content of the primordial atmosphere (Sleep et al. 2011) would boost the production of formate and other carboxylic acids at geothermal fields in diverse types of abiotic syntheses within the rock bodies of geothermal systems (see ref. (Sleep et al. 2004; Mulkidjanian et al. 2012) for details). In addition, diverse organic molecules could be produced by abiotic photosynthesis catalyzed by particles of metal sulfides, such as ZnS and MnS (Zhang et al. 2004, 2007; Guzman and Martin 2009; Mulkidjanian 2009). Although the geothermal fields should have been covered by moisture, water could be present only in limited amounts; its continuous evaporation, similarly to the desert model, would result in selective accumulation of the least volatile compounds, which in this case should have been simple amides.

Unlike deserts, geothermal systems could continuously deliver further key elements for primeval syntheses, such as phosphorous and boron compounds. The exhalations of geothermal fields are enriched in phosphorus (up to ~1 mM in the acidic mud pots of Kamchatka (Bortnikova et al. 2009; Mulkidjanian et al. 2012)). This high level might be related to the discovery of highly soluble phosphite in a Californian pristine geothermal pool, which is fed by bicarbonate-rich geothermal waters (Pech et al. 2009). Furthermore, the vapor condensates at geothermal fields can contain up to 10 mM borate (Nikolaeva and Bychkov 2007; Mulkidjanian et al. 2012) which, on the one hand, specifically partitions into

vapor upon geothermal separation (Schatz et al. 2004) and, on the other hand, has exceptional ability to stabilize pentoses (Benner et al. 2006). Not to mention that simple carbonaceous compounds, ammonia, and sulfide, which redistribute into the vapor phase upon geothermal separation, are the major building blocks of life.

Outlook

It seems highly encouraging that the anoxic geothermal fields, which we identified as tentative cradles of life by using the top-down approach and phylogenomic analysis, could provide exactly those geochemical conditions that were suggested as most conducive for the emergence of life by the chemists who pursued the complementary bottom-up strategy. It is our hope that our reconstruction informs and stimulates further chemical experiments aimed at approximation of the conditions for the origin of life in the laboratory.

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References

- Aver'ev VV (1961) Conditions for the discharge of the Pauzhetka high-temperature waters in Southern Kamchatka. In: Proceedings of the Volcanology Laboratory of the Russian Academy of Sciences, Issue 19. Moscow, pp 90–98
- Barks HL, Buckley R, Grieves GA, Di Mauro E, Hud NV, Orlando TM (2010) Guanine, adenine, and hypoxanthine production in UV-irradiated formamide solutions: relaxation of the requirements for prebiotic purine nucleobase formation. *ChemBioChem* 11(9):1240–1243
- Belozersky AN (1959) On the species specificity of the nucleic acids of bacteria. In: Oparin AI, Pasynskii AG, Braunshtein AE, Pavlovskaya TE, Clark F, Synge RLM (eds) *The origin of life on the earth*. Pergamon Publishers, London, pp 322–331
- Benner SA, Carrigan MA, Ricardo A, Frye F (2006) Setting the stage: the history, chemistry and geobiology behind RNA. In: Gesteland RF, Cech TR, Atkins J (eds) *The RNA world*, 3rd edn. Cold Spring Harbor Laboratory Press, Cold Springs Harbor
- Biello D (2012) Did life's first cells evolve in geothermal pools? *Scientific American* (on-line edition, <http://www.scientificamerican.com/article.cfm?id=did-life-first-evolve-in-geothermal-pools>)
- Bokov K, Steinberg SV (2009) A hierarchical model for evolution of 23S ribosomal RNA. *Nature* 457(7232):977–980
- Bortnikova SB, Gavrilenko GM, Bessonova EP, Lapukhov AS (2009) The hydrogeochemistry of thermal springs on Mutnovskii Volcano, southern Kamchatka. *J Volcanol Seismol* 3(6):388–404
- Brouwers L (2012) Did life evolved in a “warm little pond”. *Scientific American* (Blogs, <http://blogs.scientificamerican.com/thoughtomics/2012/2002/2016/did-life-evolve-in-a-warm-little-pond/>)
- Butcher SE, Pyle AM (2011) The molecular interactions that stabilize RNA tertiary structure: RNA motifs, patterns, and networks. *Acc Chem Res* 44(12):1302–1311
- Bychkov AY (2009) Geochemical model of present-day ore formation in the Uzon Caldera. *GEOS*, Moscow
- Charlebois RL, Doolittle WF (2004) Computing prokaryotic gene ubiquity: rescuing the core from extinction. *Genome Res* 14(12):2469–2477
- Costanzo G, Saladino R, Crestini C, Ciciriello F, Di Mauro E (2007) Nucleoside phosphorylation by phosphate minerals. *J Biol Chem* 282(23):16729–16735
- Davidovich C, Belousoff M, Bashan A, Yonath A (2009) The evolving ribosome: from non-coded peptide bond formation to sophisticated translation machinery. *Res Microbiol* 160(7):487–492

- Deamer D, Singaram S, Rajamani S, Kompanichenko V, Guggenheim S (2006) Self-assembly processes in the prebiotic environment. *Philos Trans R Soc Lond B Biol Sci* 361(1474):1809–1818
- Deamer DW (1997) The first living systems: a bioenergetic perspective. *Microbiol Mol Biol Rev* 61(2):239–261
- Dupont CL, Butcher A, Valas RE, Bourne PE, Caetano-Anolles G (2010) History of biological metal utilization inferred through phylogenomic analysis of protein structures. *Proc Natl Acad Sci U S A* 107(23):10567–10572
- Fournier RO (2004) Geochemistry and dynamics of the Yellowstone National Park Hydrothermal System. US Geological Survey, Menlo Park
- Gilbert W (1986) The RNA world. *Nature* 319:618
- Gogarten JP et al (1989) Evolution of the vacuolar H⁺-ATPase: implications for the origin of eukaryotes. *Proc Natl Acad Sci U S A* 86(17):6661–6665
- Guzman MI, Martin ST (2009) Prebiotic metabolism: production by mineral photoelectrochemistry of alpha-ketocarboxylic acids in the reductive tricarboxylic acid cycle. *Astrobiology* 9(9):833–842
- Hazen RM et al (2011) Needs and opportunities in mineral evolution research. *Am Mineral* 96(7):953–963
- Holloway JM, Dahlgren RA (2002) Nitrogen in rock: occurrences and biogeochemical implications. *Glob Biogeochem Cycles* 16(4)
- Hopkins M, Harrison TM, Manning CE (2008) Low heat flow inferred from >4 Gyr zircons suggests Hadean plate boundary interactions. *Nature* 456(7221):493–496
- Kinoshita N, Unemoto T, Kobayashi H (1984) Proton motive force is not obligatory for growth of *Escherichia coli*. *J Bacteriol* 160(3):1074–1077
- Koonin EV (2003) Comparative genomics, minimal gene-sets and the last universal common ancestor. *Nat Rev Microbiol* 1(2):127–136
- Lazcano A, Forterre P (1999) The molecular search for the last common ancestor. *J Mol Evol* 49(4):411–412
- Leipe DD, Wolf YI, Koonin EV, Aravind L (2002) Classification and evolution of P-loop GTPases and related ATPases. *J Mol Biol* 317(1):41–72
- Lowenstein JM (1960) The stimulation of transphosphorylation by alkali-metal ions. *Biochem J* 75:269–274
- McCallum AB (1926) The paleochemistry of the body fluids and tissues. *Physiol Rev* 6(2):316–357
- Mansy SS, Schrum JP, Krishnamurthy M, Tobe S, Treco DA, Szostak JW (2008) Template-directed synthesis of a genetic polymer in a model protocell. *Nature* 454(7200):122–125
- Miskin R, Zamir A, Elson D (1970) Inactivation and reactivation of ribosomal subunits: the peptidyl transferase activity of the 50 s subunit of *Escherichia coli*. *J Mol Biol* 54(2):355–378
- Mukhin LM (1976) Volcanic processes and synthesis of simple organic compounds on primitive earth. *Orig Life* 7(4):355–368
- Mulkidjanian AY (2009) On the origin of life in the zinc world: 1. Photosynthesizing, porous edifices built of hydrothermally precipitated zinc sulfide as cradles of life on Earth. *Biol Direct* 4:26
- Mulkidjanian AY, Bychkov AY, Dibrova DV, Galperin MY, Koonin EV (2012) Origin of first cells at terrestrial, anoxic geothermal fields. *Proc Natl Acad Sci U S A* 109(14):E821–E830
- Mulkidjanian AY, Galperin MY (2007) Physico-chemical and evolutionary constraints for the formation and selection of first biopolymers: towards the consensus paradigm of the abiogenic origin of life. *Chem Biodivers* 4(9):2003–2015
- Mulkidjanian AY, Galperin MY (2009) On the origin of life in the zinc world. 2. Validation of the hypothesis on the photosynthesizing zinc sulfide edifices as cradles of life on Earth. *Biol Direct* 4:27
- Mulkidjanian AY, Galperin MY (2010) Evolutionary origins of membrane proteins. In: Frishman D (ed) *Structural bioinformatics of membrane proteins*. Springer, Vienna, pp 1–28
- Mulkidjanian AY, Galperin MY, Koonin EV (2009) Co-evolution of primordial membranes and membrane proteins. *Trends Biochem Sci* 34(4):206–215
- Natochin YV (2007) The physiological evolution of animals: sodium is the clue to resolving contradictions. *Her Russ Acad Sci* 77(6):581–591
- Nies DH (2007) Bacterial transition metal homeostasis. In: Nies DH, Silver S (eds) *Molecular microbiology of heavy metals*. Springer, Berlin, pp 117–142
- Nikolaeva IY, Bychkov AY (2007) Gas-liquid distribution of boron in hydrothermal springs of Mutnovski volcano. *Her Kamchatka Res Cent (Vestnik KRAUNZ)* 10(2):34–43
- Nold SC, Ward DM (1996) Photosynthate partitioning and fermentation in hot spring microbial mat communities. *Appl Environ Microbiol* 62(12):4598–4607
- Ohki S, Duzgunes N, Leonards K (1982) Phospholipid vesicle aggregation: effect of monovalent and divalent ions. *Biochemistry* 21(9):2127–2133
- Pech H, Henry A, Khachikian CS, Salmassi TM, Hanrahan G, Foster KL (2009) Detection of geothermal phosphite using high-performance liquid chromatography. *Environ Sci Technol* 43(20):7671–7675
- Powner MW, Gerland B, Sutherland JD (2009) Synthesis of activated pyrimidine ribonucleotides in prebiotically plausible conditions. *Nature* 459(7244):239–242

- Raymond J, Williams-Jones AE, Clark JR (2005) Mineralization associated with scale and altered rock and pipe fragments from the Berlin geothermal field, El Salvador; implications for metal transport in natural systems. *J Volcanol Geotherm Res* 145(1–2):81–96
- Reyes AG, Cardile CM (1989) Characterization of clay scales forming in Philippine geothermal wells. *Geothermics* 18:429–446
- Ricardo A, Szostak JW (2009) Origin of life on earth. *Sci Am* 301(3):54–61
- Saladino R, Crestini C, Pino S, Costanzo G, Di Mauro E (2012) Formamide and the origin of life. *Phys Life Rev* 9(1):84–104
- Schatz OJ, Dolejs D, Stix J, Williams-Jones AE, Layne GD (2004) Partitioning of boron among melt, brine and vapor in the system haplogranite-H₂O-NaCl at 800 °C and 100 MPa. *Chem Geol* 210(1–4):135–147
- Schoffstall AM (1976) Prebiotic phosphorylation of nucleosides in formamide. *Orig Life* 7(4):399–412
- Shiman R, Draper DE (2000) Stabilization of RNA tertiary structure by monovalent cations. *J Mol Biol* 302(1):79–91
- Sigel RKO, Pyle AM (2007) Alternative roles for metal ions in enzyme catalysis and the implications for ribozyme chemistry. *Chem Rev* 107(1):97–113
- Sleep NH, Bird DK, Pope EC (2011) Serpentinite and the dawn of life. *Philos Trans R Soc Lond B Biol Sci* 366(1580):2857–2869
- Sleep NH, Meibom A, Fridriksson T, Coleman RG, Bird DK (2004) H₂-rich fluids from serpentinization: geochemical and biotic implications. *Proc Natl Acad Sci U S A* 101(35):12818–12823
- Switek B (2012) Debate bubbles over the origin of life. *Nature* (online issue, <http://www.nature.com/news/debate-bubbles-over-the-origin-of-life-1.10024>)
- Szathmáry E (2007) Coevolution of metabolic networks and membranes: the scenario of progressive sequestration. *Philos Trans R Soc Lond B Biol Sci* 362(1486):1781–1787
- Szostak JW, Bartel DP, Luisi PL (2001) Synthesizing life. *Nature* 409(6818):387–390
- Wald G (1964) The origins of life. *Proc Natl Acad Sci U S A* 52(2):595–611
- White DE, Muffler LJP, Truesdell AN (1971) Vapor-dominated hydrothermal systems compared with hot-water systems. *Econ Geol* 66:75–97
- Wilde SA, Valley JW, Peck WH, Graham CM (2001) Evidence from detrital zircons for the existence of continental crust and oceans on the Earth 4.4 Gyr ago. *Nature* 409(6817):175–178
- Williams RJP, Frausto da Silva JJR (1991) *The biological chemistry of the elements*. Clarendon, Oxford
- Woese C (1998) The universal ancestor. *Proc Natl Acad Sci U S A* 95(12):6854–6859
- Zhang XV, Ellery SP, Friend CM, Holland HD, Michel FM, Schoonen MAA, Martin ST (2007) Photodriven reduction and oxidation reactions on colloidal semiconductor particles: implications for prebiotic synthesis. *J Photochem Photobiol A Chem* 185(2–3):301–311
- Zhang XV, Martin ST, Friend CM, Schoonen MAA, Holland HD (2004) Mineral-assisted pathways in prebiotic synthesis: photoelectrochemical reduction of carbon(+IV) by manganese sulfide. *J Am Chem Soc* 126(36):11247–11253