Proton gradients at the origin of life

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Chemiosmotic coupling – the harnessing of electrochemical ion gradients across membranes to drive metabolism – is as universally conserved as the genetic code. As argued previously in these pages, such deep conservation suggests that ion gradients arose early in evolution, and might have played a role in the origin of life. Alkaline hydrothermal vents harbour pH gradients of similar polarity and magnitude to those employed by modern cells, one of many properties that make them attractive models for life's origin. Their congruence with the physiology of anaerobic autotrophs that use the acetyl CoA pathway to fix CO_2 gives the alkaline vent model broad appeal to biologists. Recently, however, a paper by Baz Jackson criticized the hypothesis, concluding that natural pH gradients were unlikely to have played any role in the origin of life. Unfortunately, Jackson mainly criticized his own interpretations of the theory, not what the literature says. This counterpoint is intended to set the record straight.

Keywords:
acetyl CoA pathway; alkaline hydrothermal vent; ATP; chemiosmotic coupling; origin of life; pH gradient

Introduction

Few researchers have a problem with the idea that LUCA, the last universal common ancestor of life, possessed DNA, RNA and ribosomes, despite the intimidating complexity of the molecular machines involved in transcription and translation. Yet the idea that chemiosmotic coupling might be equally ancient [1] is treated with reservation, for the superficially good reason that it requires not only a rotor-stator ATP synthase, but also (apparently) ion-tight lipid membranes and complex proton pumps to generate electrochemical ion gradients [2]. All that might seem too complex to be primitive, and so it is understandable that most researchers have put the vexed question of its origins aside until more is known. Nonetheless, the fact remains that the ATP synthase is as universally conserved across life as the ribosome itself, and shares the same deep split between the bacteria and archaea [3–8]. Some form of chemiosmotic coupling probably evolved very early in the history of life, arguably before LUCA [1]; the question is how, and why?

In dismissing the possibility that natural proton gradients could have played any role in the origin of life [9], Jackson ignores this comparative structural and phylogenetic evidence, instead positing that chemiosmotic coupling arose later, for trivial reasons; he suggests "to drive weak acids and weak bases across the membrane" [9]. Not only is this inconsistent with phylogenetics [8, 10–12] and microbial physiology [13–17], but it also begs a secondary question, on which Jackson is silent – why would such inconsequential selective forces go on to fix chemiosmotic coupling across all life?

The idea that LUCA was chemiosmotic is not actually particularly challenging, as LUCA certainly had genes and proteins, and the ATP synthase is no more complex than the ribosome. It is a product of natural selection, and presumably the recruitment of subunits with pre-existing functions [6]. The more interesting question is, in what context did the ATP synthase evolve? Again, phylogenetics gives a clue. LUCA was the common ancestor of bacteria and archaea [8, 18–20]. Eukaryotes are not relevant as they arose some 2 billion years later from an archaeal host cell [20–22] and a bacterial endosymbiont [23–25]. Traits shared by bacteria and archaea might therefore have arisen in LUCA, while those that differ between the two domains arguably arose later. These issues are discussed in detail elsewhere [8, 13, 17, 18, 26–28]. Suffice to say that these studies imply that LUCA was an autotroph [12, 13], and used some form of the acetyl CoA pathway to reduce CO_2 using H_2 [14, 15, 28–32] this being the only one of six known pathways of carbon fixation found in both bacteria and archaea [16]. The antiquity of the acetyl CoA pathway is supported by several other features: it is short, linear, exergonic overall, and replete in proteins whose active sites contain Fe(Ni)S clusters, similar in structure to hydrothermal Fe(Ni)S minerals [16, 27, 32–34]. Equally importantly, phylogenetics shows that LUCA was chemiosmotic and had an ATP synthase [1, 3–8], but does not seem to have had a modern

DOI 10.1002/bies.201600217

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phospholipid membrane [26, 27, 35–37], or even the proton-pumps used to generate ion gradients [13]. While that might seem paradoxical, it is not so if LUCA lived in an environment that harbored natural proton gradients [1].

There is plainly a long evolutionary distance between the genetically encoded biochemistry of LUCA and the prebiotic chemistry that gave rise to the first organic molecules. It is therefore possible that there is no direct link between the biochemistry of LUCA and those remote abiotic pathways. Some researchers accordingly ignore the biological perspective, instead proposing alternative mechanisms such as a cyanosulphidic protometabolism [38], driven by UV radiation [38, 39], or ZnS photosynthesis [40], neither of which bears any resemblance to extant biochemistry. While this work is impressive as systems chemistry, it does not narrow the gap between prebiotic chemistry (in any geochemical environment) and the origins of biochemistry as we know it [17]; on the contrary, it widens the gap. If life did start with cyanoacetylene activated by UV radiation, then protometabolism must have been overwritten by modern biochemistry for unknown reasons. Equally problematic, there is no indication from geochemistry that the Earth ever contained the significant amounts of cyanide required for this chemistry to work [41–45].

Biochemistry emerged from geochemistry

The alternative hypothesis posits that there is continuity between prebiotic chemistry and the origins of biochemistry: that the emergence of genetically encoded catalysts (either ribozymes or enzymes) amplified processes that occurred naturally and spontaneously in some geochemical setting [46, 47]. This argument would have force even if no geochemical environment were known that could narrow the gap between the biochemistry of LUCA and geochemistry. It gains a lot more force from the fact that there is an environment that closely matches the reconstructed chemistry of LUCA – alkaline hydrothermal vents. The properties of these vents have been discussed in detail in many papers [1, 8, 17, 26–28, 32, 48–55]. Suffice to say here that in the Hadean, 4 billion years ago, such vents should have provided high concentrations of H_2 in alkaline hydrothermal fluids [26–28, 32, 50–55] and CO_2 in ocean waters [42–44], which would have percolated through a catalytic labyrinth of interconnected pores, with Fe(Ni)S minerals in the thin walls separating them [26–28]. The difference in pH between the ocean waters (probably mildly acidic, conservatively around pH 6, in the Hadean [43, 44]) and alkaline hydrothermal fluids (probably around pH 11, as today [26–28, 32, 48–55]) means that vent pores could have transected pH gradients of up to 5 pH units [1, 26–28, 32, 48–55]. While little is known about how steep the pH gradients can be, even in modern alkaline vents, microfluidic studies show that laminar flow can support gradients of up to 6 pH units across micrometer-scale distances, even in the absence of barriers [56].

This is the context that Jackson ignores. The top-down view from biology suggests that LUCA was an autotroph that used the acetyl CoA pathway to grow from H_2 and CO_2 alone, and to do so depended on Fe(Ni)S cofactors and chemiosmotic coupling [1, 8, 13, 16, 17, 27, 31, 34]. The bottom-up view from geochemistry indicates that alkaline hydrothermal systems provided high concentrations of H_2 and CO_2, and natural proton gradients across thin inorganic barriers containing Fe(Ni)S minerals with structures similar to the Fe(Ni)S clusters common in the acetyl CoA pathway [1, 8, 17, 26–28, 32, 48–55]. This congruence between geochemistry and biochemistry is at the level of broad-brush stroke. How exactly the geochemistry of vents gave rise to the biochemistry of cells is as yet unresolved; this is the subject of several distinct, but testable, hypotheses [13, 27, 57–63]. Unfortunately, Jackson [9] conflates these different hypotheses (which he labels as "RML") – by trying to shoehorn disparate hypotheses into the same box, he misrepresents them all, fails to recognize that views have evolved over decades, and makes some basic errors in his calculations.

Lipid membranes and inorganic barriers

The biggest problem is that Jackson conflates thin inorganic barriers with organic membranes (lipid bilayers) throughout his article. There is an issue with language here. Geologists frequently use the term membrane to refer to thin, pliable sheets, or inorganic layers [48, 49, 58, 59]. On reading the term membrane, however, most biologists tend to think of a lipid bilayer, about 5 nm thick, compared with perhaps a few micrometers for the inorganic barriers in vents [51, 64, 65]. Jackson is careful to distinguish between these two types of barrier, but does not seem to appreciate that many papers on life's origins in alkaline vents actually call on both, for different reasons.

Jackson argues that proton gradients could not have driven the origin of life because he envisages some kind of proton-driven machine – analogous to the proteins found today in lipid membranes – embedded in these inorganic barriers. But that is not what is claimed. Proton-powered machines such as the ATP synthase or the energy-converting hydrogenase (Ech) are posited to operate within some form of lipid bilayer, and this is very clearly depicted and articulated in numerous papers [1, 17, 27, 60–63]. In BioEssays in 2010, for example, we wrote: "We do not envisage the ancestral ATPase as embedded in the inorganic walls, but rather in organic lipids lining the walls ... An ancestral ATPase embedded in such organic membranes could tap proton gradients across the side walls and hydrothermal effluent flow would maintain the gradient through replenishing alkalinity inside" [1].

Mike Russell and colleagues have recently introduced a more mechanical perspective on the origin of life, discussing mineral chemistry in terms of "disequilibrium-converting engines" [58, 59]. They discuss the mechanical properties of minerals such as green rust (ferrous hydroxide) in relation to enzymes such as the pyrophosphatase. Russell et al. are perfectly capable of defending themselves, and I will not do so here. But the key point is that this is a distinct and quite recent hypothesis. The question is not whether Russell's recent

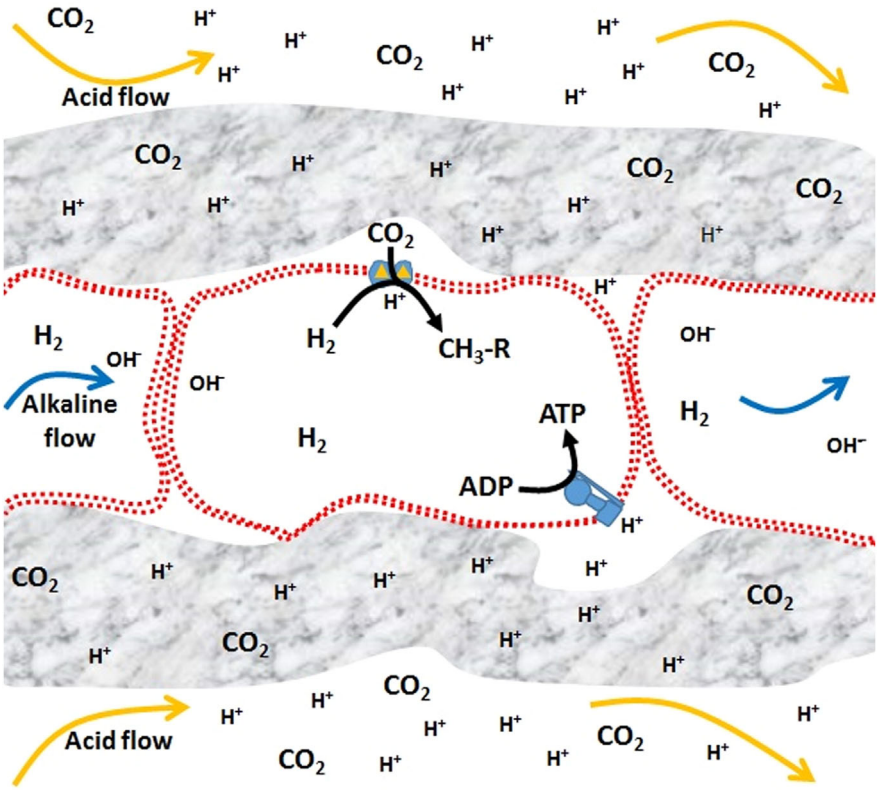

Figure 1. How natural proton gradients could promote CO_2 reduction in organically lined vent pores. A simple leaky protocell within a vent pore, with an Ech and ATP synthase in the lipid membrane, driving both carbon and energy flux, hence, growth and ultimately replication within the vent pores. CH_3-R depicts a methyl group attached to a cofactor and is shorthand for one of the key products of the acetyl CoA pathway, en route to intermediary metabolism.

approach is correct; that is a matter of experimental testing. The problem is that Jackson has projected his own meanings into Russell's words, and then generalized them onto other approaches that do not call for minerals to change conformational state in any way.

Almost all work discussing molecular machines (i.e. proteins) in vents envisages them embedded in organic membranes: some form of bilayer, perhaps composed of fatty acids and other amphiphiles. The problem with specifying the lipid composition of early membranes is that the phospholipids of bacteria and archaea are distinct, so it is far from clear what kind of membrane LUCA might have possessed [1, 26, 27, 35–37, 60–63]. But LUCA certainly had membrane proteins, adapted (as today) to 5 nm lipid bilayers, or we would not be able to recognize their transmembrane sequences in proteins dating back to LUCA [66]. That can only mean that LUCA did indeed possess a lipid bilayer, even if it was not genetically encoded. If the membrane was not genetically specified, where might those lipids have come from? Possibilities discussed in previous papers include Fischer-Tropsch synthesis, which forms long-chain hydrocarbons and amphiphiles under mild hydrothermal conditions [67, 68]. Fatty acid synthesis is thermodynamically favored under anoxic alkaline hydrothermal conditions [69, 70] so any organics formed in vents would likely include fatty acids, which in turn spontaneously form bilayers when concentrated.

Jackson eschews the point that even in a vent-bound LUCA, membrane proteins were embedded in lipid bilayers. This might have little directly to do with the first steps of prebiotic chemistry, but still begs the question, how did LUCA come to be that way? This takes us back toward the origin of life. If LUCA was chemiosmotic, yet lacked the membrane pumps needed to generate its own gradients, then early cells in vents could have depended on geochemically sustained proton gradients. So the question becomes – could natural proton gradients power the metabolism of early cells in vents via proteins such as the ATP synthase or the Ech? If so, there was no requirement for active pumping in early cells, a very significant energy saving. The fact that pH differences alone could drive the chemiosmotic machinery in classical experiments by Jagendorf in chloroplasts [71] and Oesterhelt in *Halobacterium* [72] implies that this is indeed possible. However, those experiments worked in part because the membrane systems studied were permeable to counter-ions such as Cl^- via specific channels [73]. For LUCA to evolve in vents, the steady-state flux of ions across membranes must balance in such a way that the continuous flux of protons is sufficient to drive metabolism, unopposed by any build-up of electrical charge on the membranes.

Proton flux across *lipid* membranes and through *protein* machines

Our computational modeling shows that natural proton gradients could indeed have driven carbon and energy metabolism in LUCA, but only if the lipid membranes were highly permeable to protons, with a permeability equivalent to fatty acid vesicles [62]. The model assumes steep pH gradients across vent pores, which is plainly a best-case scenario. But there are two separate questions here, which Jackson characteristically conflates: (i) if such steep gradients existed, could they in principle drive molecular machines in lipid membranes? The answer to this is yes, with a free energy equivalent to that available in modern cells [62]. That leads us to: (ii) are such steep gradients in fact realistic, or even necessary? For example, could fluctuating flow, where pH changes over timescales of seconds to minutes, produce a similar effect [62]? This question is important, but only becomes relevant after it has been shown that, under a best-case scenario, natural proton gradients can indeed drive molecular machines in lipid membranes.

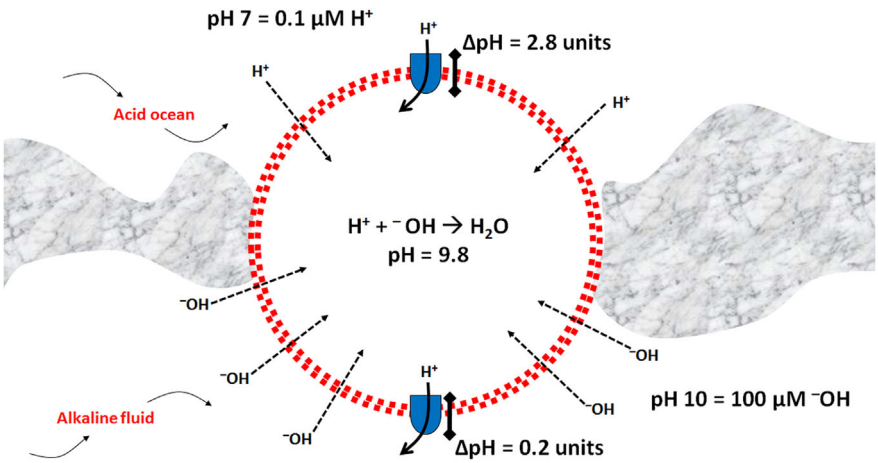

Figure 2. How natural proton gradients can drive net work. Even if equivalent proteins (blue half-ovals) are inserted in opposite sides of a leaky protocell (red dashed circle) in a natural H^+ gradient, the H^+ flux will drive net work (such as ATP synthesis). That is because the influx of H^+ depends on both membrane permeability (which is taken to be equal for H^+ and ^-OH) and concentration. Because the concentration of ^-OH at pH 10 is 1,000-fold greater than the concentration of H^+ at pH 7, the influx of ^-OH through the leaky membrane is much faster than the influx of H^+. The inside of the protocell accordingly becomes relatively alkaline. The driving force for work through proteins on the "acid ocean" side is therefore substantially greater than the driving force over the "alkaline side." This enables net ATP synthesis. Only if the pH of the ocean were 4 and alkaline fluid 10 (symmetrical around pH 7) would the driving forces exactly balance, and net ATP synthesis would then fall to zero.

In his preoccupation with the structure of Lost City (which is only partially relevant), Jackson misses two critical points. First, flow in hydrothermal systems is often laminar rather than turbulent [56, 74], which in experimental microfluidic systems can generate very steep pH gradients (6 pH units over micrometre distances) even in the absence of physical barriers – flow alone can maintain the gradient [56]. Physical barriers allow steep gradients to be maintained at lower flow rates [56]. Second, if lipid membranes or simple protocells line the thin inorganic barriers (which have hydrophobic surfaces [75–77]), then the steepness of the proton gradient would depend on several factors: (i) the proton permeability of the wall itself; (ii) the flow rates through neighboring pores (potentially some distance away); and (iii) the proton permeability of the lipid membrane lining the pore. It is feasible that the main barrier to proton flux – responsible for steepening natural pH gradients – is not the inorganic walls themselves but the lipid membranes lining and insulating them (Fig. 1). As noted above, many papers depict lipid bilayers lining thicker inorganic barriers [1, 17, 27, 60–63]. Jackson fails to acknowledge that in any of his figures or text, which imply the contrary.

This misrepresentation is compounded by a conceptual error in Jackson's own Fig. 2 [9], which shows molecular machines operating in a matrix of inorganic barriers (which was never proposed, as noted above). Jackson then asserts that the proton fluxes are equal and opposite, so that the inward flux of protons through the molecular machines on one side is completely offset by the outward flux on the opposite side. That is not the case, because pH units are not equal and opposite, as Jackson depicts them, but a log scale representing the concentration of protons and hydroxide ions. Sojo et al. [62] calculated the proton flux through a protocell with lipid membranes, from ocean waters at pH 7 to alkaline hydrothermal fluids at pH 10. The flux depends on two main factors: (i) the permeability of the membrane to H^+ and OH^- ions (which we took to be equivalent) and (ii) the actual concentration of the ions. That is far from equivalent. The concentration of protons at pH 7 is 10^{-7} M (0.1 μM). The concentration of OH^- ions at pH 10 is 10^{-4} M (100 μM), a 1,000-fold difference. Thus the rate of influx of OH^- ions into the organic protocell is much faster than the rate of influx of protons.

As a result the inside of the cell is relatively alkaline, not exactly intermediate between the two pHs (which is only the case if pH is offset symmetrically around pH 7, e.g., pH 4 vs. 10). Therefore the pH gradient across the ocean side is much steeper (nearly 3 pH units) than the pH gradient across the vent side (about 0.2 U). This difference means that molecular machines set in opposite sides of a lipid protocell in a natural proton gradient could power ATP synthesis or CO_2 reduction via Ech even when the pH dependent machines are present in equal abundance on opposite sides of the cell [62] (Fig. 2). In principle, once cells with genes, proteins, and membranes existed, natural proton gradients could have powered their growth without the need for membrane pumps, so long as the membrane was leaky to protons – potentially explaining why LUCA did not have a modern proton-tight phospholipid membrane equivalent to either bacteria or archaea, and greatly simplifying the problem of how chemiosmotic coupling might have first evolved.

Electron transfer across *inorganic* barriers – no "prebiotic machines" needed

Jackson's major preoccupation is with the proton permeability of the inorganic barriers at an earlier stage of prebiotic chemistry, and his assumption that some kind of prebiotic machine is needed to take advantage of proton flux. Again, he misses the point. Putting aside the ATPase as a genetically encoded protein, the question is: how could natural proton gradients have been harnessed before the evolution of genetically encoded machines? One possibility is that prebiotic carbon and energy metabolism entailed the synthesis of reactive thioesters analogous to acetyl CoA, such as methyl thioacetate, coupled to substrate-level phosphorylation, generating acetyl phosphate and ultimately ATP [1, 17, 27, 60–63] as still happens in bacteria [14, 31].

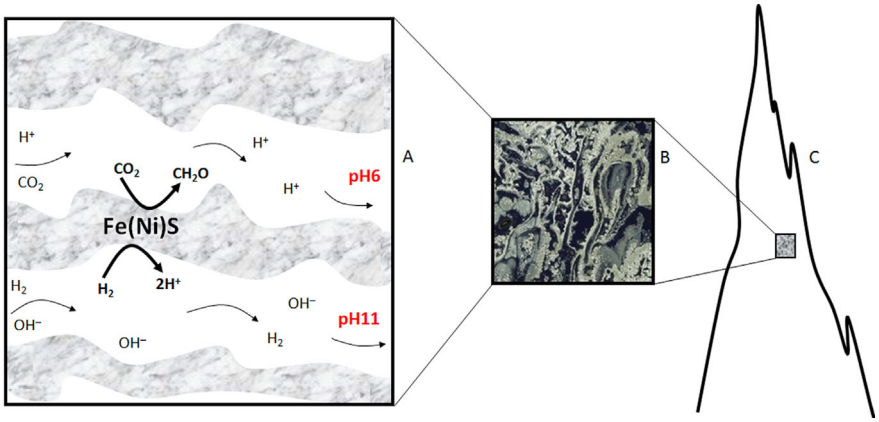

Figure 3. Reduction of CO_2 by H_2 across Fe(Ni)S barriers deep within an alkaline hydrothermal vent. **A:** Electrons can theoretically be transferred across even quite thick (μm–cm) semiconducting barriers containing Fe(Ni)S minerals from H_2 in alkaline hydrothermal solutions to CO_2 in relatively acidic ocean waters to form organics (see text for more details). **B:** Any organics formed are not lost to the ocean as the pores are part of a microporous labyrinth deep within the vent; this is a section of Lost City, courtesy of Deborah Kelley, University of Washington. **C:** Alkaline vents can be up to 60 m tall; thermal gradients and convection currents within the vent can concentrate organics by thermophoresis.

There is no requirement for proton gradients to play a role in the synthesis of reactive thioesters [78]. On the basis of differences between methanogenic archaea and acetogenic bacteria in the methyl synthesis branch of the acetyl CoA pathway, Bill Martin and Filippa Sousa have argued that reactive methyl groups could have been plentiful in Hadean vents, perhaps in the form of CH_3SH produced by the serpentinization process [34, 57]. While CH_3SH is uncommon in modern alkaline vents, and in at least one case seems to be derived from thermogenic decomposition [79], it could be consumed by cells living deeper in the crust [13, 34, 60] given that modern systems are carbon limited [80], may be swiftly oxidized in modern aerobic systems [60] or indeed reduced further by H_2 to form CH_4 and H_2S [79]. An alternative hypothesis from Russell and Nitschke [81–83] is that protometabolism proceeded via form of anaerobic methanotrophy, in which methane (derived from serpentinization) was oxidized by nitrate (derived from the oceans) to form methyl groups that could then react with CO (derived from partial reduction of CO_2) to form acetate. The difficulty here is that if the oceans really were as oxidizing as this chemistry suggests, then the net synthesis of organic matter would not be favored [69, 70]. That problem could be solved by the redox compartmentalization of alkaline vents (in which some pores are highly reducing [13, 60]). But again the point is not whether these hypotheses are correct or not; that is a matter of experimental testing. Neither of them specifically require proton gradients in vents to drive primordial chemistry. This might be exactly what Jackson contends [9], but he omits to mention that these are explicit hypotheses laid out in earlier papers [34, 27, 57, 81–83].

An alternative hypothesis more germane to the Jackson paper is that the reduction of CO_2 to methyl groups could be driven by natural pH gradients within vents [60, 84]. Critically, this process does not depend on proton transfer across barriers, and the thickness of the barriers is practically irrelevant, dispelling much of Jackson's argument. The barriers need to be semi-conducting for electrons, not protons. The reason relates to the pH modulation of reduction potential. At pH 7, H_2 cannot reduce CO_2 to CH_2O (formaldehyde, not some generic carbohydrate as Jackson mistakenly claims) because its reduction potential is not low enough [60, 61, 84–86]. But reduction potential depends on pH whenever protons are involved in a reaction [73]. In alkaline conditions, H_2 becomes more reducing (by about −59 mV per pH unit), and is likely to reduce any Fe^{3+} to Fe^{2+} within the barrier. Across the barrier, in acidic conditions, CO_2 is more easily reduced, and so is more likely to be reduced by Fe^{2+} in the barrier. The semiconducting barrier should transfer electrons from Fe^{2+} on the alkaline side to Fe^{3+} on the acidic side. The thickness of the barrier does not matter, so long as it is semiconducting. The two phases do not come into direct contact – H_2 and CO_2 do not react directly (Fig. 3). These are hardly stringent properties and have been demonstrated for equivalent FeS minerals in black smoker vents, which conduct electrical currents across entire chimneys up to 10 cm thick [87]. In principle, pH differences across Fe(Ni)S barriers could drive the entire incomplete reductive Krebs cycle, as in methanogens [86].

So this is a pH dependent mechanism that involves an inorganic barrier separating two phases with different pH – alkaline hydrothermal fluids (pH 10–12) and relatively acidic ocean waters (pH 5–7). Both fluids percolate through the microporous labyrinth inside vents. The reduction of CO_2 on the "ocean side" does not mean that any organics formed necessarily disappear into the ocean – they are formed inside the vent, where they could be concentrated by thermophoresis [84, 88, 89] (Fig. 3).

Contrary to Jackson's claims, there is no requirement for ΔpH-utilizing molecular machines, just an inorganic barrier containing spontaneously precipitated FeS minerals. Electrons, not protons, are transferred across this barrier from H_2 to CO_2. This specific hypothesis was touched on in 2012 [61], laid out in detail in 2014 by Herschy et al. [84] and is being explicitly tested in a simple bench-top reactor designed to simulate the pH gradients across thin inorganic barriers of alkaline hydrothermal vents. Jackson claims that "A simple, crystalline array ... would not have sufficed ... the chance assembly of such a machine ... is astronomically unlikely" [9]. But there is no need for a machine: we propose only that a pH gradient across a simple crystalline array should drive the reduction of CO_2 to form organics such as formaldehyde (CH_2O), and this is what we have reported [84]. The proton gradient should modulate

reduction potential giving an overall effect not dissimilar to applying a voltage, and experiments by other groups have shown that a voltage of about 1V can indeed reduce CO_2 to formate, acetate, and even pyruvate [90, 91].

Jackson is correct that the transfer of electrons across a barrier would generate a charge on the barrier, but this charge is dissipated by mixing of the hydrothermal fluids and ocean waters within the vent. That mixing is not equivalent to the retention of charge across a cell membrane, because in this case (unlike a cell, which is what Jackson discusses, incorrectly) the charged fluids physically mix. The slower passage of other ions, including protons, across inorganic barriers also forms salt bridges that help dissipate charge.

This pH-dependent mechanism could promote the reduction of CO_2 and the formation of organics within the vent pores, where they should concentrate by processes such as thermophoresis, and potentially form structures such as lipid membranes lining hydrophobic walls [1, 17, 27, 60–63]. Herschy et al. [84] showed that even small organics can be concentrated at least 5,000-fold within an open microporous matrix by thermophoresis, so organics formed within vent pores as described can easily be concentrated to form lipid membranes. Jackson's Fig. 4 [9], which shows a variety of pH gradients across thick inorganic walls of various structure, purportedly driving molecular machines embedded within the walls, utterly misrepresents this hypothesis, and the mechanisms he ascribes to us are nowhere to be found in our papers.

Conclusions

In condemning the hypothesis that natural proton gradients in alkaline hydrothermal vents played a role in the origin of life, Jackson ignores the biological and geochemical context for the hypothesis. Recent work in microbiology [15, 16], comparative genomics [8, 10–12] and geochemistry [52–55] all points to a congruence between conditions in alkaline hydrothermal vents and the physiology of anaerobic bacteria and archaea, which finally begins to close the gap between geochemistry and biochemistry [17]. Jackson instead favors a cyanosulfidic protometabolism [38, 39] or Zn sulfide photosynthesis [40], neither of which resembles the biochemistry of known cells [1, 17, 34, 60].

Cells such as methanogens and acetogens use the short, linear, exergonic acetyl CoA pathway to reduce CO_2 with H_2 [16, 27, 32–34]. The reaction is catalyzed by Fe(Ni)S proteins and the free energy is harnessed to generate electrochemical ion gradients across membranes – exactly what alkaline vents provide for free [1, 8, 13, 26, 27, 48–55]. Methanogens use the proton-motive force to drive the reduction of ferredoxin via the Ech, as well as energy metabolism via ATP synthase [15–17, 26, 27, 29–34], which we have postulated could have been the primordial metabolism in vents (Fig. 1) [60]. This is just one of several different hypotheses for how natural proton gradients might have powered metabolism at the origin of life [13, 27, 57–63]. Not only does Jackson ignore the entire biological context for life originating in alkaline vents, but he conflates these different hypotheses, misrepresents them all, and makes basic errors in his calculations. His paper says little about the origins of life in alkaline hydrothermal vents, and rather too much about his own reading of the literature. Unfortunately, it is already being cited as evidence that life could not have started in alkaline hydrothermal vents [92, 93]. That is not sustained in his paper. Whatever the detailed mechanisms of harnessing may turn out to be, there is little doubt that natural proton gradients in alkaline hydrothermal vents could in principle have helped power the origins of life.

Acknowledgments

Bill Martin was co-author on a previous version of this paper, but asked not to appear as an author on the current version. I thank the Leverhulme Trust and bgc3 for financial support, and Victor Sojo for his comments on the MS.

The author has declared no conflict of interest.

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