Critical Review

The Place of Life and Man in Nature: Defending the Anthropocentric Thesis

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Abstract

Here I review the claim that the order of nature is uniquely suitable for life as it exists on earth (Terran life), and specifically for living beings similar to modern humans. I reassess Henderson's claim from *The Fitness of the Environment* that the *ensemble* of core biochemicals that make up Terran life possess a unique synergistic fitness for the assembly of the complex chemical systems characteristic of life. I show that Henderson's analysis is still remarkably consistent with the facts one century after it was written. It is still widely accepted even among researchers in astrobiology. I also review the evidence for believing that many of the properties of the same core set of biochemicals are specifically fit for the physiology of complex terrestrial beings resembling modern humans. I show that none of the recent advances in the field of extremophile biology, alternative biochemistries, or recent allusions to apparent defects in the fitness of nature for Terran life significantly undermine the core argument, that nature is peculiarly fit for carbon-based Terran life, and especially for the physiology of complex terrestrial beings resembling modern humans.

INTRODUCTION

> The question of questions for mankind—the problem which underlies all others, and is more deeply interesting than any other—is the ascertainment of the place which mankind occupies in nature and of his relations to the universe of things."
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> – Thomas Huxley, *Man's Place in Nature* [1: p. 59]

For centuries the traditional teleological anthropocentric framework provided the answer to Thomas Huxley's "question of questions." But following the Copernican revolution and particularly after the publication of Darwin's *On the Origin of Species*, the traditional framework was seen to be increasingly untenable; mankind, so it seemed, had *no special place in nature*. However, as I show, discoveries in chemistry and biochemistry in the 19th and early 20th centuries, and in cosmology and fundamental physics and comparative physiology during the course of the 20th century, have reopened the 'grand debate' by providing intriguing new support for the old and seemingly obsolete anthropocentric paradigm.

One of the first authors to allude to the new evidence was, ironically, Alfred Russell Wallace, cofounder with Darwin of the theory of evolution by natural selection, in his *World of Life*, published a little over a century ago in 1910 [2: ch. 7]. Just three years later, in 1913, Lawrence Henderson presented the first detailed defence of the notion in his great classic *The Fitness of the Environment* (called *The Fitness* hereafter) [3]. Henderson made the claim that the *ensemble* of core biochemicals that make up Terran life possesses a unique synergistic fitness for life as it has developed here on earth. It is this classic work that will be the focus of much of my discussion here.

As Henderson stressed, the conception of the "fitness of the environment" is something quite different from the Darwinian conception of the "fitness of the organism" [3: pp. v–ix, ch. 8]. Darwin claimed that the fitness of organisms was the outcome of a purely naturalistic, non-teleological process, which gradually fits or fashions living organisms *for* particular environments via incremental steps. But no such mechanism can account for the fitness of the environment for life. As

Henderson comments, "Natural selection does but mold the organism; the environment it changes only secondarily, without truly altering the primary quality of environmental fitness. This latter component of fitness, antecedent to adaptations … is as yet nowise accounted for [by natural selection]" [3: pp. 274–275]. In other words, Henderson applied the notion of fitness to the environment rather than to organisms. He argued that the environment *itself* was "fit" for biological life, meaning that its properties were uniquely well suited for living things. Throughout this article, we retain the use of "fitness" as Henderson employed it, meaning suitability of the environment for life as we know it. It is important to distinguish this meaning from the more limited meaning of fitness used by evolutionary biologists, and not to confuse the two.

At the outset it is also important to note that logically the cosmos *must be* fit for life on earth (Terran life) and human existence. Otherwise we would not be here to observe it and ask Huxley's question. To claim that the cosmos is fit for human existence on the basis of our presence alone is essentially trivial, as Carl Sagan points out:

> There is something stunningly narrow about how the Anthropic Principle is phrased. Yes, only certain laws and constants of nature are consistent with our kind of life. But essentially the same laws and constants are required to make a rock. So why not talk about a Universe designed so rocks could one day come to be, and strong and weak Lithic Principles? [4: p. 34].

To make the radical claim that the universe is *designed for our existence*, an idea implicit in the traditional anthropocentric framework, therefore requires a cosmos where the laws of nature are uniquely fit for Terran life and uniquely fit for biological beings similar to modern humans, and one that *excludes* all other alternatives, from exotic biochemistries to *Star Trek*-like aliens.

Here I review some of the arguments presented by Henderson and show that after a century of enormous advances in biological knowledge, his views have been entirely vindicated. The current evidence suggests very strongly, as I argued in *Nature's Destiny* [5], that the cosmos is indeed uniquely fit for Terran life and for beings similar to modern humans.

This is a complex topic. In a journal article of this sort, space constraints necessarily mean that much of the evidence, including some of the most intriguing, has been omitted or touched on only briefly. Examples include the fitness of the hydrosphere and atmosphere, the fitness of the geophysics of the earth (including the tectonic and hydrolytic cycles), and the fitness of the physical design of the human body. A more thorough discussion may be found in *Nature's Destiny* [5].

FITNESS OF NATURE FOR TERRAN LIFE

In *The Fitness,* Henderson argued that the core chemical constituents of all living organisms on earth—water, carbon dioxide, oxygen and organic compounds—make up a *vital ensemble* that together possess a unique mutual or synergistic fitness for the assembly of living systems:[1]

> The fitness of the environment results from characteristics which constitute a series of maxima—unique or nearly unique properties of water, carbonic acid, the compounds of carbon, hydrogen and oxygen … so numerous, so varied, so nearly complete among all things which are concerned in the problem that together they form certainly the greatest possible fitness. No other environment consisting of … other known elements … could possess … such great fitness to promote complexity, durability and active metabolism in the organic mechanism which we call life [3: p. 272].

Simply put, Henderson believed that if we wish to assemble any type of chemical system capable of exhibiting those properties we associate with life, we must utilize this *vital ensemble*: water as a matrix, and organic carbon compounds for the construction of molecular components. Consequently, according to Henderson, only Terran life—the form of life existing on earth—is ordained in the natural order.

Carbon

To defend his thesis, Henderson systematically reviewed most of the known properties of his *ensemble* at the time. One of his key points was that carbon is unique in its ability to combine with other atoms, forming a vast and unparalleled number of compounds in combination with hydrogen, oxygen and nitrogen [3: ch. 6]. This universe of organic chemistry—with its huge diversity of chemical and physical properties—is precisely what is needed for the assembling of complex chemical systems. Furthermore, the general 'metastability' of carbon bonds and the consequent relative ease with which they can be assembled and rearranged by living systems [3: pp. 220–222, 232–237] contributes greatly to the fitness of carbon chemistry for biochemical life. Thus Henderson argued that no other atom is nearly as fit as carbon for the formation of complex biochemistry.

Today, one century later, no one doubts these claims. Indeed the peerless fitness of the carbon atom to build chemical complexity and to partake in biochemistry has been affirmed by a host of researchers since Henderson [5: ch. 5; 11: Ch. 2; 12: pp. 6–14; 13: ch. 3]. In particular, the characteristic metastability of carbon compounds was noted by Needham [13: ch. 3] and more recently by Plaxco and Gross [12: pp. 7–12]. They conclude:

> In the end there may very well be only a single element—carbon … the basis of all life on earth—that is able to support the complex chemistry presumably required to create any self-replicating chemical system [12: p. 6].

[1] Henderson defined living systems [3: pp. 32–35] as durable physiochemical mechanisms exhibiting a high degree of complexity, and capable of self-regulation and homeostasis via metabolic processes that involve an exchange of energy and matter with their surroundings. Since Henderson's day, many other authors have formulated definitions of life and organisms [6], most of which include the same basic elements alluded to by Henderson [7; 8: p. 155; 9; 10: ch. 1; 11: p. 42; 12: ch. 1].

Water

Henderson also argued that water, one of the other core constituents of his *vital ensemble*, is uniquely fit to function as the matrix in which the complex chemistry of life can be carried out. He referred to its power as a solvent, far greater than that of almost any other common fluid. Water is able to hold in solution an enormous, unequalled range of diverse chemical compounds. Its particularly high dielectric constant [3: pp. 118–125], is responsible for its ability to dissolve virtually all charged molecules [3: p. 118–126]. Its power as a solvent, along with its relative chemical inactivity, confers on water ideal properties to serve as the matrix of living systems [3: pp. 111–118; 14: p. 20]. Alluding to other elements of fitness, Henderson pointed out that water is involved in two of the key and ubiquitous biochemical processes in the cell—hydrolysis (addition of a hydroxyl group), and its reverse reaction, condensation—that occur in the metabolism of virtually all organic compounds [3: pp. 232–237]. He also discussed the role its unique thermal properties play in buffering organisms against sudden temperature changes as well as stabilizing and ameliorating the global climate [3: pp. 82–110].

Advances since Henderson have revealed additional reasons for water's special fitness for carbon-based life. One important discovery only became apparent after the molecular biological revolution in the mid 20th century, with the elucidation of the 3-D structure of the key macromolecules in the cell. By vital coincidence, the temperature range in which water is a fluid, 0–100°C, overlaps with the temperature range in which chemical bonds can be readily manipulated by biochemical systems [5: pp. 112–116]. This is true for both covalent carbon bonds (the strong bonds between atoms involved in sharing of electrons) and weak bonds (hydrogen bonds and electrostatic bonds that hold together the 3-D structures of bio-macromolecules). Another new discovery, the so-called hydrophobic effect, arises mainly from the high dielectric constant of water. The hydrophobic effect plays an essential role in protein folding and in the formation of the cell membrane, by forcing uncharged molecules like lipids into water-excluding complexes [15]. Since Henderson's day it has also become apparent that water is uniquely fit for proton conductance [16: pp. 152–154], a process crucial to all life that is now known to play a key role in biological energy transfers.[2]

There is hardly an author today who is conversant with the facts who would contest Henderson's verdict: no substance can rival the fitness of water as the *milieu intérieur* of carbon-based life. Plaxco and Gross echo Henderson's claim: "Water's ability to form the basis of biochemistry may well be unique ... no other liquid has a fraction of the favorable attributes of water ... Life not only has an absolute requirement for a liquid solvent but water is by far the most qualified solvent to fulfil that role" [12: pp. 14–17].

Carbon Dioxide

Another member of the *vital ensemble* is carbon dioxide (CO_2). Henderson points out that CO_2 is an innocuous gas soluble in water, and present therefore wherever there is water throughout the biosphere [3: pp. 136–139]. He argues that if water is the *matrix of life*, CO_2 is the *mercury of life*, carrying the crucial carbon atom throughout the earth's hydrosphere. In Henderson's words, "Its occurrence is universal and its mobility a maximum" [3: p. 139]. No other carbon compound is known which could serve to distribute carbon in this way throughout the biosphere. Needham comments, "The good fortune of its being gaseous should be emphasized since it is one of the very few gaseous oxides at ordinary temperatures" [13: p. 35]. Henderson also alludes to the fact that when CO_2 dissolves in water it is converted to bicarbonate, which has excellent buffering capacities critical for maintaining acid-base neutrality in the body and in the hydrosphere [3: ch. 4]. Indeed its buffering ability in water is such that Henderson could claim that "except in celestial mechanics [there is] no other case of such accuracy in a natural regulation of the environment" [3: p. 153]. So CO_2 not only distributes carbon to all corners of the hydrosphere, it also maintains the acid-base balance of the hydrosphere, generating a controlled aqueous environment in which the carbon it distributes can be assembled into living systems. No less than water, then, CO_2 is uniquely fit for carbon-based life.

Oxygen

Finally there is the fitness of oxygen, a component in two of the most important members of Henderson's *ensemble,* water (H_2O) and CO_2, and one of the key atomic building blocks of organic compounds. The fact that oxidations, particularly of carbon and hydrogen, provide more energy than nearly all other types of chemical reactions is of particular importance [3: pp. 243–248].[3] Henderson saw this as one of the most "potent evidences" of the unique fitness of carbon chemistry for life, pointing out, "The very chemical changes, which for so many other reasons seem to be best fitted to become the processes of physiology, turn out to be the very ones which can divert the greatest flood of energy into the stream of life" [3: p. 247]. Today no one doubts the unique energy-generating powers of oxidations. In fact, astrobiologists currently look for oxygen in the atmospheres of extrasolar planets as a signature indicating the potential for advanced life forms, because it is widely conceded that only oxidations provide energy in sufficient quantities for the high metabolic rates assumed to be necessary for advanced carbon-based life [18].

Henderson sums up his case by saying, "The fitness of water, carbonic acid, and the three elements [hydrogen, carbon and oxygen] make up a unique ensemble of fitness for the organic mechanism ... There is nothing about these substances which is ... inferior to the same thing in any other substance ... not a single disability of the primary constituents ... has come to

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[2] Many other elements of water's fitness have been discovered during the 20th century [5; 14]. For example, water's unique thermal properties promote atmospheric and oceanic circulation, as well as climatic amelioration, as is now described in detail in standard texts of oceanography [17].

[3] This is a fact that, as I will show, has a critical relevance to advanced metabolically active organisms, whose existence is to a very great extent reliant on the energy of oxidation.

light" [3: pp. 266–267]. And he concludes *The Fitness* with the challenging claim: "The biologist may now rightly regard the universe in its very essence as biocentric."

New evidence: Cosmic fine-tuning

Since Henderson's day, a number of advances in various fields have provided additional support for the claim that nature is biocentric. Perhaps the most celebrated has been the discovery of the so-called 'cosmic coincidences,' the notion that the fundamental physical constants that determine the overall structure of the universe and the laws of nature must be very close to the values observed to generate a universe capable of harboring life [19; 20; 21]. Another supportive revelation has been the discovery that interstellar space is replete with vast quantities of simple organic compounds, including many of the basic building blocks of Terran biochemistry [5: ch, 4; 7; 9: p. 18; 22].

One widely publicized coincidence is the 'lucky' fact that the nuclear resonances of the isotopes ^{12}C and ^{16}O are exactly what they need to be if carbon is to be synthesized and accumulate in any quantity in the interior of stars [20: pp. 250–255]. The energy levels of these resonances ensure that ^{12}C is first synthesized in stellar interiors from collisions between ^{8}Be (beryllium) and He (helium) nuclei, and that the carbon synthesized is not depleted later. Hoyle made this discovery in 1953 while working at Caltech with William Fowler [23]. An intriguing aspect of the discovery is that Hoyle made it based on a prediction from the anthropic principle [24: p. 256]. Hoyle himself famously commented:

> If you wanted to produce carbon and oxygen in roughly equal quantities by stellar nucleosynthesis, these are the two levels you would have to fix, and your fixing would have to be just about where these levels are found to be … A common sense interpretation of the facts suggests that a super intellect has monkeyed with physics, as well as chemistry and biology, and that there are no blind forces worth speaking about in nature [19: p. 118].

This discovery was acclaimed not only as a major scientific discovery but also as further evidence of the biocentricity of nature. Hoyle may have been one of the first to notice that the conditions necessary to permit carbon-based life require a very narrow range of basic physical constants, but the idea is now widely accepted [19; 20; 21]. If those constants had been very slightly different, the universe would not have been conducive to the development of matter, astronomical structures, or elemental diversity, and thus the emergence of complex chemical systems [21].

New evidence: Extremophiles

Another development since Henderson's day has been the discovery that many carbon-based life forms—extremophiles—can survive in conditions very far removed from those on the earth's surface. Some survive at temperatures above 100°C,

others in strong acids and alkalis, others at very high pressure [25; 9: p. 32]. Many extremophiles obtain energy from exotic chemical reactions, including nitrate reduction, the reduction of sulphur to hydrogen sulphide, the oxidation of hydrogen sulphide to sulphate, the oxidation of ferrous to ferric iron, and the reduction of CO_2 to methane (by methanogenic bacteria) [25]. The bacterium *Shewanella putrefaciens* uses metal atoms (in this case, manganese) in its metabolism in the same fashion as we use oxygen atoms. In effect, it "breathes" metal.[4] Thomas Gold has claimed (controversially) that the crustal rocks contain a vast mass of extremophiles making up what he terms the 'deep hot biosphere,' composing a total biomass equal to the total of all familiar life on the earth's surface [26].

Despite their remarkable diversity, all extremophiles conform to the basic biological design shared by all extant life on earth; that is, their polymers are composed of the canonical six atoms—carbon, nitrogen, hydrogen, oxygen, sulphur and phosphorus—and all require liquid water and use DNA, RNA, and proteins.

In December 2010, the exciting possibility was raised that some extremophiles might build their polymers using an alternative to phosphorus. At a press conference hastily organized by NASA, a research group led by NASA researcher Felisa Wolfe-Simon [27] reported that certain extremophiles inhabiting Lake Mono (a shallow saline soda lake in California) could substitute arsenic for phosphorus in their DNA if grown in cultures lacking phosphate but rich in arsenic. The result was described as having "profound evolutionary and geochemical importance" [27]. Certainly, if verified, this would have been the first instance of the use of an atom other than the canonical six (carbon, oxygen, hydrogen, nitrogen, sulphur and phosphorus) to construct the key polymers of life. As it turned out, the result was not confirmed and the interpretation of the experimental evidence proved faulty [28]. If it had been confirmed, this would have been an important result extending further the boundaries of earth-like life. But given that arsenic is very similar to phosphorus, and given that the basic design of life would remain the same, it would still not threaten 'carbon chauvinism,' the view that only carbon-based life in a water matrix is feasible.

There is nothing in the currently known extremophile universe that threatens Henderson's core argument that the *vital ensemble* is uniquely fit for the construction of the complex chemical systems associated with life. However, the discovery of so many extremophile species over the past few decades, many deriving energy from exotic chemical reactions, does raises the possibility that even more weird and exotic extremophiles remain to be discovered on earth. Some may depart radically from the canonical carbon-based design of all known extant life [29]. Candidates might be RNA organisms (carbon-based life, but not utilizing DNA or proteins), the remnants of an RNA world [30]. Perhaps even non-carbon life forms resembling Cairns Smith's clay-based replicants (a type of silicon-based life) might be found [31].

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[4] http://www.spaceref.com/news/viewnews.html?id=463

New evidence: Astrobiology

Several researchers have speculated on the feasibility of life based on non-carbon chemistries beyond the earth [9; 32; 33; 34]. Some of the possible scenarios were discussed in a major NASA study entitled "The Limits of Organic Life in Planetary Systems" [9], bringing together most of the leading researchers in the area. A scenario that has been considered in some detail is silicon life in liquid methane or liquid nitrogen [34]. The 'hydrocarbon seas' of Titan [34: p. 679] or the hypothesized sub-surface liquid nitrogen ocean on Triton [33: p. 146] have been cited as possible habitats for silicon life in our solar system [11: p. 264; 33: p. 160]. Interestingly, the possibility of silicon life was also mentioned briefly by Henderson [3: p. 66].

Judging the plausibility of alien life is obviously problematical. Perhaps the laws of nature might permit 'Floaters'—immense gaseous beings that Carl Sagan hypothesized might thrive in the Jovian atmosphere [35: pp. 30–31]—or electronic life forms in stellar interiors, such as the 'plasmobes' of Feinberg and Shapiro in *Life Beyond the Earth* [32: p. 382]. However, until relatively detailed descriptions of such alien life forms are provided, with descriptions of how they originated, how they grow and reproduce, the nature of their 'sense organs,' how they 'think' and so forth, it's very hard to see them as a serious challenge to 'carbon chauvinism.'

Even in the case of perhaps the most plausible alien scenario—silicon life at low temperatures [9; 33; 34]—only some of the basic chemical building blocks (the monomers of the alien life forms), some possible energy sources to drive syntheses, and how the monomers might be built into more complex molecules, have been suggested. The higher organization of the hypothetical silicon life forms, including possible analogs of cell membranes, enzymes, coding systems, etc., are never discussed. Regarding silicon macromolecules, the NASA authors point out, "Few thoughts suggest how they might have emerged spontaneously to support a biosphere" [9: p. 2, 6]. Rothschild, a leading researcher in the extremophile field, confessed, "While silicon is also common (though not nearly as common as carbon in the Universe as a whole) and can form interesting polymers … its flexibility pales in comparison with organic chemistry, particularly in the ability of carbon to form polymers" [36: p. 2792]. These views were echoed by Pace, who also emphasized the unique fitness of carbon compared with silicon [7].

Moreover, Irwin and Schultze-Makuch comment:

> A world in which silicon would provide a better back-bone for life than carbon would be either extremely cold with no oxygen, and a stable liquid other than water (for silanes), or a world so warm that the only liquid would likely be molten mineral (silicates). In either case, the choice for complicated chemical reactions comparable to carbon-based metabolism would appear to be much less likely because of the temperature extremes … Finally the empirical evidence argues against silicon-based life … [although silicon]

is much more abundant than carbon on most rocky planets including our own, no forms of life based exclusively on silicon have been found, while many complicated organic compounds including amino acids (protein building blocks) have been found in meteorites brought to earth from outer space [11: p. 29].

Plaxco and Gross [12: p. 13] are also silicon sceptics:

> Silicon is less well suited to support complex chemistry and it seems much less likely that silicon-based life could form than carbon-based life. Thus if aliens ever do visit us, the smart money says we should welcome them with carbon-based cakes and not with silicon-based rocks. So carbon wins over silicon … and the other naturally occurring elements … fare even worse!

In sum, if silicon is discounted, then this may well mean that only the carbon atom can form the basis of living systems.

The problem of emergence

A major problem in judging these scenarios is the phenomenon of emergence. Nearly all molecular species, even the simplest such as water, have properties that cannot be predicted from even the most exhaustive examination of the properties of their constituents [37; 38].[5] Emergence is a particularly challenging problem in the mesoscopic domain of matter [38; 42], where judgments of the feasibility of exotic biochemistries and exotic supra-molecular structures must be made. In effect, the plausibility of alien life forms can only be secured empirically in the lab, by attempts at synthesis of at least some of their basic components and some more complex supra–molecular structures. But even these preliminary steps have not been taken. We are nowhere near creating self-replicating silicon life forms in the lab or carbon-based life forms capable of thriving in liquid ammonia. We just can't say whether life based on other chemistries is feasible.

Indeed we don't yet know whether the best candidate for an alternative life—RNA life—is actually possible [see footnote 5]. Even if we allow the possibility of an RNA world on the early earth, or perhaps surviving today in some yet-unexplored niche, RNA organisms would still be aqueous carbon-based life forms that use most of the constituents of Henderson's *ensemble*. As

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[5] A good example of the challenge of emergence in this area is the pointed fact that despite a huge increase in knowledge regarding the chemical and physical properties of RNA molecules, and vast effort devoted to searching RNA sequence space for functional ribozymes, no one knows if a self-replicating ribozyme exists. Certainly no one is able to design one from first principles. A first step towards finding it was taken in 2001 with the identification of a ribozyme that could copy a short RNA sequence (18 nucleotides), but not itself (189 nucleotides) [39]. A second step was taken in 2009 when Joyce's group reported a cross-replicating pair of ribozymes (RNA enzymes), each about 70 nucleotides long, that could catalyse each other's synthesis [40]. Last year Hollinger's group identified a ribozyme capable of copying a sequence 95 nucleotides long, nearly half its length [41]. This is still a long way from the self-replicating ribozyme necessary for the RNA-world hypothesis, i.e., a molecule that can copy itself and any other ribozyme. This endeavour, still ongoing, serves as a classic reminder that complex macromolecules have emergent properties. Precisely the same phenomenon of emergence is bound to be met in any attempt to actualize any type of alien life, including even those with relatively detailed scenarios.

the literature stands, none of the more 'far out' astrobiological scenarios poses a serious challenge to Henderson. Chris McKay, one of the founding fathers of astrobiology, concedes that much of the writing and discussion of astrobiology is highly speculative. In a recent interview he concedes: "A lot of people lately—because astrobiology has become so fashionable—like to write what you could call Sunday afternoon theories. Well, maybe life could be based on boron, for example, and they write about it—all just speculation" [43: p. 210].

Summary

Nothing in the field of exobiology or extremophile biology threatens Henderson's claim about the unique and exclusive fitness of the *vital ensemble* for assembling complex chemical systems. Neither does anything threaten his claim that the universe is "in its essence biocentric." This claim does not imply, however, that the fitness of the *vital ensemble* is so constraining that only the very specific type of carbon-based life currently extant on earth (D-sugars, the canonical L-amino acids, DNA, RNA, and protein) is compatible with the laws of nature. Life could include, for example, organisms built out of proteins using different amino acids or using different genetic polymers [9: ch. 4; 44], perhaps including the recently reported xeno-DNA [45], or even hypothetical RNA organisms.

It is, however, remarkable that despite the diversity of extremophile life, all are examples of carbon-based life in a water matrix. Even more remarkable, none depart in any way (especially now that the arsenic-eaters have proven illusory) from the canonical familiar biochemical design made up of the six canonical atoms, with proteins made up of the familiar twenty amino acids, DNA and RNA made up of the canonical nucleotides, having the same genetic code, sharing many of the same metabolic pathways, and surrounded by the same bilayer lipid membrane!

Until life forms are discovered that depart markedly from the standard Terran design, or until new life forms markedly different from extant life are created in the lab, the claim that the laws of nature are fit for radically different 'non-Terran' types of life will remain without empirical foundation. Although there are still some detractors [33; 34; 46], most researchers acknowledge that Henderson's basic argument has stood the test of one hundred years of advances in scientific knowledge. Henderson's claim that the core biochemicals of life on earth make up a unique, synergistic *ensemble* of chemical fitness for life [3] has never been invalidated, either by the discovery of any alternative biochemistry or any well-worked-out hypothetical alternative scenario. Moreover, many researchers, probably a majority, still defend the unique fitness of carbon and water. Even Carl Sagan conceded he was at heart a carbon-and-water chauvinist [35: p. 105]. Ironically, although NASA researchers speculate about the possibility of alternative biologies, these speculations remain so ill-defined that when designing *actual* programs to detect life in space, they invariably seek signatures of carbon-based life, such as evidence of an oxygenic atmosphere [18]. This is a further tacit admission of the unique suitability of nature for Terran life.

FITNESS OF NATURE FOR HUMAN PHYSIOLOGY

In *The Fitness*, Henderson extols the biocentricity of nature, but steers clear of any explicit claim that the properties of the core biochemicals—*the vital ensemble*—possess a unique fitness for advanced carbon-based beings like us, with our physiological design. *This would be a far stronger and more specific anthropocentric claim*. However, throughout *The Fitness*, in discussing the properties of a particular chemical, Henderson often emphasizes its special fitness *for human biology* [3: pp. 89, 102, 139]. When he talks of "the marvellous beneficence of the ocean for the community of living beings," [3: p. 190] or when he claims that the planetary environment is "an extremely favourable abode for the living organism" [3: p. 53] he is clearly thinking of fitness not merely for simple carbon-based life forms, i.e., generic carbon-based life, but more specifically for higher organisms, including beings like ourselves.

Indeed, the fitness of the properties of the *vital ensemble* for "an animal like man" [3: p. 102] becomes obvious, when one considers the properties of some of the key biochemicals of the *ensemble*. Some properties of the *ensemble* are beneficial for human physiology, but are irrelevant or even maladaptive to other carbon-based life forms. While much of the evidence of fitness for generic carbon-based life was in place in 1913, much of the evidence concerning mammalian physiology, reviewed below, has been elucidated since Henderson's day. This evidence provides support for the notion that nature is specifically fit for organisms resembling ourselves.

Water

The fitness of the thermal properties of water for life were first discussed by Whewell in his Bridgewater Treatise [47], and later touched on by Wallace [2: ch. 7]. In *The Fitness*, Henderson pointed out that water's high thermal capacity assists in the maintenance of a constant body temperature in warm-blooded organisms [3: p. 89], while its high evaporative cooling greatly assists terrestrial warm-blooded organisms in losing heat when the ambient temperature approaches 38°C. As he put it:

> In *an animal like man,* whose metabolism is very intense, heat is a most prominent excretory product, which has constantly to be eliminated in great amounts, and to this end only three important means are available: conduction, radiation and the evaporation of water ... At a low temperature there is little evaporation of water, but at body temperature or above there can be no loss of heat at all by conduction and radiation, and the whole burden is therefore thrown on evaporation. [3: p. 102; emphasis added]

Curiously, the irrelevance of these two properties to the vast majority of carbon-based life forms on earth was not alluded to. A very obvious case is the complete irrelevance of the high thermal capacity or high evaporative cooling of water to extremophiles close to black smokers in the ocean depths, or the denizens of the deep hot biosphere proposed by Gold [26].

Another case might be low temperature extremophiles that can grow at -15°C, perhaps in the Martian sands [9: p. 32], a possibility currently being examined by the Martian Rover *Curiosity*. Finally, the majority of all aquatic organisms, derive little if any direct adaptive utility from water's high latent heat of evaporation.[6]

The high thermal capacity of water also poses a challenge for exotherms seeking to warm themselves on cold mornings. Small terrestrial organisms like bumble bees and dragonflies must shiver to raise the temperature of their muscles before flying. Even large cold-blooded organisms such as lizards and snakes may be torpid on cold mornings, and must warm themselves by basking. Some have specific adaptations, such as the blood-filled scales of crocodiles, which act as solar panels to warm them [48]. The Permian mammal-like reptile *Dimetrodon* used a large sail on its back as a heat absorber to raise its body temperature. The sail could be pointed towards the sun for rapid warming, which may have allowed *Dimetrodon* to hunt before its prey became active. Bramwell and Fellgett [49] calculate that without the sail it would take a 250 kg (440 lb) Dimetrodon approximately three and a half hours to raise its body temperature from 26° to 32°C (79° to 90°F).

A particularly fascinating aspect of the high latent heat of evaporation of water is that it may be the only element of environmental fitness that is perhaps of greater utility for modern humans than for any other warm blooded terrestrial animal. Being hairless, humans lose heat via evaporative cooling more efficiently than any other mammal. Consequently, in the heat of the midday African sun, humans can run continuously for longer periods of time than any other animal, a capacity which may have greatly assisted early man in hunting prey on the Pleistocene savannah [50].

Another property of water that was not discussed in *The Fitness*, but which is particularly fit for large, metabolically active organisms, is its low viscosity. This makes possible the passage of the blood through the capillary bed, and it also facilitates rapid diffusion of the essential nutrients and waste products of metabolism to and from the tissues to the blood stream.[7] Because water's low viscosity permits the passage of the blood through very narrow conduits only three or four microns in diameter, the volume of the capillary bed takes up only a relatively small fraction of the mass of the tissues. If the viscosity of water had been any greater, the circulation system as it exists in higher organisms, or indeed any circulatory system, would not have been possible.

A complex cardiovascular system for the circulation of nutrients, the elimination of waste, and the exchange of gases is an essential aspect of the design of all advanced metabolically active organisms. In contrast, simple, single-celled, carbon-based life forms can obtain the nutrients to supply their metabolic needs by diffusion directly from the environment, thus dispensing with the need for physiological support systems. Moreover, it is doubtful that many unicellular organisms would be negatively affected even if the viscosity of water were twice or three times what it is. As the temperature increases from 20°C to 100°C, the viscosity of water decreases nearly four times [52], so high-temperature extremophiles, for example, would still experience very rapid diffusion of metabolites, even if the viscosity of water were twice what it is. Some organisms, such as molds, can actually thrive at ambient temperatures in very viscous concentrated sugar solutions [9: p. 32]. It seems many types of unicellular life could thrive even if the viscosity of water were several times higher, but not complex metazoan organisms like ourselves.

Oxygen

Another constituent of Henderson's *vital ensemble* that possesses properties that are specifically fit for large, air-breathing, homeothermic (warm-blooded) organisms like humans is oxygen [3: p. 272]. Many aspects of its fitness for our biology have only been clearly elucidated since Henderson's time.

Energy generation in humans and all complex multicellular animals occurs as follows:

$$\text{reduced carbon compounds} + \text{oxygen} = \text{Water} + CO_2 + \text{heat} + \text{chemical energy} \quad (1)$$
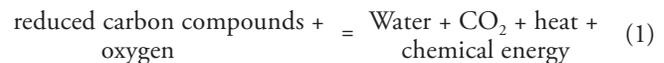
This formula might seem to be too familiar to need any comment; but this is an instance where familiarity with a phenomenon dulls appreciation of just how remarkable it is. This key life-giving reaction is only possible in beings like ourselves because the physical and chemical properties of the reactants and end products—oxygen, water, CO_2 — are almost exactly as they are!

Oxidation provides far more energy than the vast majority of chemical reactions, and it is universally acknowledged that only oxidations provide sufficient energy to support metabolically active organisms [53]. This will hold wherever there is complex carbon-based life. Hence, as mentioned above, the identification of oxygen in the atmospheres of extra-solar planets is taken as a possible signature of advanced carbon-based life [18].

It is hard to envisage how else the energy of oxidations could be used by terrestrial beings, except by breathing oxygen as a gas from an atmosphere. (Scenarios where terrestrial organisms use liquid or solid oxygen have never been seriously proposed.) The fact that oxygen is a gas at ambient temperatures is therefore of obvious utility as it permits air-breathing in organisms such as ourselves.

Highly active organisms like ourselves need oxygen in copious quantities. Surprisingly, an adult human consumes about 250 ml of oxygen each minute at rest and 5000 ml per minute during vigorous exercise [54: p. 26]. Such high consumption rates of oxygen can only be satisfied by directly absorbing oxygen from an oxygen-rich atmosphere, at concentrations high enough to allow its rapid and efficient uptake within our lungs. (For reasons why absorption of oxygen dissolved in water, i.e., through gills, cannot substitute, see below.)

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[6] The high evaporative cooling of water does play an important role in maintaining the temperature stability of the hydrosphere, which is of benefit indirectly for all life on earth. Henderson discusses the importance of this property of water in *The Fitness* (3: 92-102). An updated consideration of its contribution to global temperature stability is given in Tom Garrison's *Oceanography* (17: chapter 6).

[7] The rate of diffusion is sufficiently high that small molecules can traverse the average distance across a body cell in a fraction of a second [51: p. 18; 5: pp. 32–34].

Our current atmosphere contains about 21% oxygen, generating a partial pressure of about 150 mm Hg. Oxygen is needed at this level in order to sustain active metabolism, as is shown by the fatigue associated when climbing at high altitudes, where the partial pressure falls significantly below 150 mm Hg. On the other hand, if atmospheric levels of oxygen rise much above 21%, spontaneous combustion of carbon compounds becomes an increasing danger [22: p. 34]. The fact that oxygen levels sufficient to support high levels of metabolism by air-breathing organisms do not at the same time support spontaneous conflagrations is clearly a coincidence of great relevance for terrestrial life.

In fact, oxygen levels can only reach 21% because it is relatively inert at temperatures below 50°C, the result of its peculiar atomic structure, which attenuates its reactivity at ambient temperatures [55]. The high metabolic rates of mammals could never be sustained without this attenuation. As Boulatov comments, "The biosphere benefits greatly from this inertness of O_2 as it allows the existence of highly reduced organic matter in an atmosphere rich in a powerful oxidant" [56: p. 304]. Ironically the chemical inertness is so marked that it poses a physiological problem. Boulatov continues, "Such inertness also means that rapid aerobic oxidation will only occur if energy is put into the system to overcome the intrinsic kinetic barriers, or the reaction is catalyzed" [56: p. 304]. Prokofieva *et al.*, discussing the inertness of oxygen, also note the need for catalysis to activate the oxygen atom at ambient temperatures:

> Dioxygen is the most environmentally friendly and cheapest reactant for oxidising organic substrates. However, because of its kinetic inertness, dioxygen needs to be activated before it can be used in oxidation chemistry. To perform this task under mild conditions, nature has evolved clever enzymes that contain either iron or copper ions within their active sites [57: p. 1005].

Fortuitously the transitional metals such as iron and copper have just the right atomic characteristics to activate the oxygen atom for chemical reaction [5: ch. 9]. So the inertness of oxygen at ambient temperatures is rescued by the unique properties of the transitional metals, restoring its utility for energy generation for air-breathing active organisms, whose high metabolic rates and 'active life styles' depend critically on the energy of oxidations.

Fitness of oxygen for air-breathing organisms

The inertness of oxygen at relatively high concentrations and ambient temperatures is, like the evaporative cooling of water, especially suited to air-breathing organisms that obtain their oxygen in gaseous form. This suitability does not translate to water-breathing organisms. The solubility of oxygen in water is relatively low and this fact, in conjunction with the much greater viscosity of water compared with air, greatly limits the rate at which oxygen can be extracted from water. As Maina comments:

> As a respiratory medium, air is a more cost-effective respiratory fluid: water is 50 times more viscous than air; the concentration of dissolved oxygen in water is about one-thirtieth that in air; the rate of diffusion of oxygen in water is lower by a factor of 8×10^3 compared with that in air; and the capacitance coefficient, i.e., increment of concentration per increment in partial pressure of oxygen in water, is 30 times lower than in air. In saturated water, at 20°C, 1 mL of oxygen is contained in 200 g of water while 1 mL of oxygen is present in 5 mL of air (mass, 7g). All other conditions being equal, owing to the greater viscosity of water, compared with air breathing, water breathing requires more energy to procure an equivalent amount of oxygen [58: p. 284].

The greater effort required to extract oxygen from water is the major reason why the basal metabolic and maximal metabolic rates of fish are 6 to 10 times lower than those of mammals and birds [59: p. 448]. Moreover, a further constraint arises from the fact that the solubility of oxygen rapidly decreases as the temperature rises (the solubility at 30°C is only half that at 0°C [5: p 124]), and this imposes a limitation on the thermal tolerance of water breathing organisms [60]. Clearly, a number of factors rule out the attainment of high metabolic rates in water-breathing life forms. No active, warm-blooded organism extracts oxygen using 'gills' from water, and except in science fiction scenarios, no intelligent life form in our cosmos ever will breathe through gills!

While the low solubility of oxygen is a major factor constraining water-breathing life, it could hardly be increased significantly without risk to the environment within cells. Despite the attenuated reactivity of dioxygen at ambient temperatures, Davies points out, "The reductive environment of the cellular milieu provides ample opportunities for oxygen to undergo unscheduled univalent reduction" [61], resulting in the production of highly damaging reactive oxygen species (ROS) [62; 58: p. 283]. ROS are also produced photochemically in cells by UVA radiation [25]. These cause diverse oxidative damage, including lipid peroxidation and DNA mutagenesis, and are implicated in aging and disease [63]. At current oxygen levels (21%), if oxygen's solubility were higher the increased concentrations of ROS in biological systems would likely be prohibitive.

Clearly many of the characteristics of oxygen are finely tuned for air-breathing organisms but not for organisms extracting their supply of oxygen from water. And of course they are completely irrelevant to anaerobic bacteria and extremophiles in the crustal rocks far removed from the concerns of 'life with oxygen.'

Fitness of metabolic end products for air-breathing organisms

Despite the great utility of oxidation, the chemical energy of oxidative metabolism would not be available to complex organisms unless the end products of oxidative metabolism were innocuous and easy to dispose of. Three of the final end products of the oxidative breakdown of organic compounds (see Equation 1) are *water, CO_2 and heat*.

Water and CO_2. Water is not only entirely innocuous, it is the very matrix of life. The other chemical end product of oxidative breakdown of organic compounds is the compound CO_2. If this had been a toxic substance, if it had been a liquid insoluble in water, if it had been an insoluble solid, or if it had dissolved in water forming a strong acid, the complete oxidation of carbon to CO_2 would have been impossible.

However, CO_2 is none of these things. It is a relatively unreactive compound and a gas at ambient temperatures. That it is a gas is fortuitous, since it is one of the very few gaseous oxides at ordinary temperatures [13: p. 35]. Moreover, it is fully oxidized and stable in the presence of oxygen, a crucial element of fitness in an atmosphere containing 21% oxygen! In addition, CO_2 is *soluble* and can be readily excreted in the lungs of terrestrial organisms via respiration—the same route through which oxygen is absorbed. These properties are of critical utility for air-breathing organisms. As Henderson points out:

> In the course of a day a man of average size produces, as a result of his active metabolism, nearly two pounds of carbon dioxide. All this must be rapidly removed from the body. It is difficult to imagine by what elaborate chemical and physical devices the body could rid itself of such enormous quantities of material were it not for the fact that in the lungs … [carbon dioxide] can escape into air which is charged with but little of the gas. Were carbon dioxide not gaseous, its excretion would be the greatest of physiological tasks; were it not freely soluble, a host of the most universal physiological processes would be impossible [3: pp. 139–140].

Just as the evaporative cooling effect of water is of little utility for aquatic organisms or extremophiles in the deep hot biosphere, just as many of the characteristics of oxygen are of no direct relevance to anaerobic bacteria, so the gaseous nature of CO_2 is of less direct relevance to many unicellular organisms or even complex aquatic vertebrates like fish, as we shall see below.

Heat. A third product of oxidative metabolism, heat, is an inevitable product of many chemical reactions, including oxidation. In moderate amounts, heat is not only harmless but essential for warm-blooded organisms such as ourselves. But excess heat must be eliminated from the body. It is only through the properties of water (one of the other two end products of oxidative metabolism) that complex multi-cellular organisms are able to eliminate excess heat from the body. And it is not just *one* property of water that comes to the rescue. Water's high thermal capacity provides a first defence against an increase in body temperature. Its low viscosity makes possible the circulatory system, which carries the heat to the skin, where its high evaporative cooling 'draws the excess heat out of the body.'

Fitness of the bicarbonate buffer system

Most of the CO_2 produced as the end product of oxidative metabolism reacts with water to generate a weak acid, carbonic acid (H_2CO_3), which hydrolyses spontaneously, generating hydrogen ions (H^+) and bicarbonate anions (HCO_3^-).

$$\text{water} + CO_2 = \text{carbonic acid} = \begin{array}{l}\text{hydrogen ions} + \\ \text{bicarbonate anions}\end{array} \quad (2)$$
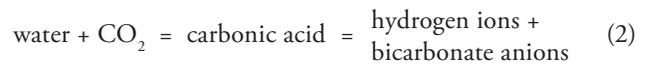
The bicarbonate anions (HCO_3^-) produced as a result of this reaction, together with carbonic acid (H_2CO_3), form a remarkable buffer system having exactly the right characteristics to defend organisms like ourselves against increases in acidity in the blood or interstitial fluids. The bicarbonate buffer is important for all carbon-based life on earth, since it plays a role in defending the oceans and hydrosphere against departures from neutrality. But it also has unique features specifically fit for complex air-breathing organisms like ourselves.[8] Henderson waxed lyrical about the fitness of the bicarbonate buffer [3: p. 153], and he was not exaggerating. Subsequent work during the 20th century has confirmed its remarkable fitness, especially for acid-base homeostasis in air-breathing organisms.

A word about buffer systems. Typical buffer systems are systems in which there is a significant amount of a weak acid HA, and its so-called conjugate base A^-, present in a solution. In the case of the bicarbonate buffer the weak acid is carbonic acid (H_2CO_3), and the conjugate base is the bicarbonate anion (HCO_3^-). This coupling provides a resistance to change in the solution's pH. When acid is added to the solution, increasing the hydrogen ion concentration in the solution, the hydrogen ions H^+ react with the conjugate base A^-, forming the weak acid HA, thereby soaking up the excess hydrogen ions and tending to neutralize the solution. When alkali is added to the solution, decreasing the hydrogen ion concentration, the weak acid HA, gives up hydrogen ions, i.e., $HA = H^+ + A^-$, again tending to neutralise the solution. Too much acid or alkali will exceed the buffer's *capacity*, however, resulting in significant pH changes.

As mentioned above, in the case of the bicarbonate buffer system the weak acid form is H_2CO_3 and the conjugate base is HCO_3^-. The hydrogen concentration (or pH)[9] at which these two forms are in equilibrium, i.e., their concentrations are equal, is termed 'the acid dissociation constant' or pKa.

$$\text{pKa} = \text{pH when } [HCO_3^-] = [H_2CO_3] \quad (3)$$

The pKa of carbonic acid is close to 6.1 in blood and other body fluids [64: pp. 50–51], much lower than the actual pH of blood, which is 7.3. This, on the face of it, appears anomalous. To function efficiently as a buffer, the concentration of the acid and basic forms of the buffer should be in equilibrium (be present in equal concentrations) at the level of acidity in the extracellular fluids, which is about pH 7.4. However, the bicarbonate buffer functions optimally at a pH level of 6.1, which is considerably lower than pH 7.4. From this it would appear that the bicarbonate system is not ideally adapted to buffer body fluids. The anomaly is only apparent, though. Remarkably, because of this anomaly the buffer is particularly fit for maintaining acid-base homeostasis in air-breathing organisms, and provides further evidence of the fitness of nature for beings like ourselves.

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[8] Note: bicarbonate plays only a minor role in intracellular buffering, both in higher organisms and unicellular forms.

[9] pH is defined as the log of the hydrogen ion concentration.

Because the pKa of carbonic acid is considerably less than the pH of blood, the concentration of bicarbonate in the blood is far greater than it would be if the pKa were close to 7.4. Rose points out in his *Clinical Physiology of Acid Base and Electrolyte Disorder* that the anomaly "raises the amount of bicarbonate available to soak up acid" [65: p. 176]. The body thus has a reserve of base to soak up any sudden excess of acid (such as during vigorous exercise when lactic acid is generated in the muscles). However, this reserve can only be utilized because of the ease with which the acid form H_2CO_3 can dissociate into water and CO_2, and the ease with which CO_2 can be breathed out of the body in the lungs, drawing the reaction (shown below in equation 4) to the right:

$$H^+ + HCO_3^- = H_2CO_3 = CO_2 + H_2O \qquad (4)$$
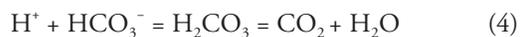
When hydrogen ion concentration rises in the case of an 'ordinary buffer,' the hydrogen ions combine with the base, forming the acid, i.e., $H^+ + A^- = HA$. But because the acid cannot be eliminated and exit the body as a volatile gas (as in the case of carbonic acid), soon the acid concentration rises to an equilibrium point when the reaction reverses, and the hydrogen ions are drawn by the law of mass action from the acid (HA) back into the solution. In fact, as Rose comments, "calculation shows that because of the ease with which the carbon dioxide (and with it in effect the hydrogen ions) can be breathed away the buffering capacity of the bicarbonate system is in effect increased by between 10 to 20 times (compared with an ordinary buffer) and is far more efficient than 'an ordinary buffer' working even at its pH optimum" [65: p. 176].

Many authors have commented on the fitness of the bicarbonate buffering system for the maintenance of acid-base homeostasis in air-breathing organisms. Like Henderson [3: p. 153], Edsall and Wyman were also struck by the remarkable nature of the system: "The combination of the acidity and buffering power of H_2CO_3 with the volatility of CO_2 provides a mechanism of unrivalled efficiency for maintaining constancy of pH in systems which are constantly being supplied as living organisms are with acidic products of metabolism" [66: p. 550].[10]

Moreover, because of the volatility of CO_2 and the ease with which its levels in the body can be regulated by alterations in ventilation—the ease with which Equation 4 can be pushed to the left or right—the bicarbonate buffer system provides

air-breathing organisms with a ventilatory means to regulate the hydrogen ion concentration in their body fluids. If acid accumulates, ventilation may be increased to breathe the acid out of the body in the lungs. If acid levels decrease, then by slowing ventilation rates CO_2, and hence acid, may be retained in the body!

This means that two absolutely fundamental but very different physiological processes, (1) the maintenance of acid-base balance in the body, and (2) the excretion of one of the end products of oxidative metabolism, CO_2, depend crucially on the chemical and physical properties of CO_2 itself, and its hydration product HCO_3^-. As I summed up the situation in *Nature's Destiny*:

> Thus, both the problem of excretion of the end product of carbon metabolism and the problem of acid-base balance are both elegantly solved in the properties of the same remarkable compound—carbon dioxide. It is a solution of breathtaking elegance and parsimony based on another set of mutual adaptations in life's constituents [5: p. 133].

The bicarbonate buffer in fish

A further indicator that the fitness of nature is specific for air-breathing organisms rather than water-breathing ones is the fact that the bicarbonate buffer is nothing like as efficient in a fish as in a mammal. To begin with, fish blood contains less bicarbonate than mammalian blood [68: p. 181]. Why? As James Claiborne explains, fish must maintain high rates of water flow across the gills to obtain sufficient oxygen for their metabolic needs, and as the level of CO_2 in natural bodies of water is low, the blood CO_2 levels in fish are much lower than in a mammal (where the blood is exposed in the lungs to relatively high pCO_2 levels). Consequently bicarbonate levels are also lower [68: p. 181]. Claiborne comments: "A 2 mm Hg increase in fish pCO_2 will ... change the pH by 0.18 units ... a fifty% increase in $[H^+]$. This same absolute pCO_2 change in humans results in only a negligible 0.01 units; approximately 2% pH alteration" [68: p. 181]. This is a clear indication of the fitness of the bicarbonate buffer for air breathers rather than water breathers.

We have already seen that the effort of breathing is far greater for a fish than for an air-breathing vertebrate. In man at rest, the cost of breathing requires 2% of overall oxygen consumption, whereas in a fish it varies between 10 and 12% in an eel and between 19 and 25% in a trout [69: p. 304]. Consequently, as Perry and Gilmour comment [70: p. 199], "Ventilation in fish is keyed primarily to the demands of extracting oxygen from a medium of low oxygen content. [Consequently] the capacity to utilize respiratory compensation of acid-base disturbances is limited" [see also 71: p. 117]. While an air breather can readily draw acid out of the body (as shown in Equation 4 above), for a fish the cost of increased ventilation is prohibitive because of the viscosity of water. Again, a fish does not have the luxury of decreasing ventilation to correct a metabolic alkalosis, as the low oxygen content of water would induce a serious hypoxia. Fish such as the Gar [72], which have lungs as well as gills, can and

[10] Every detail of this buffer system reveals further aspects to its fitness. For example take the actual process of hydration itself, described by Edsall and Wyman in Biophysical Chemistry [66: p. 554]: "The hydration of CO_2 to H_2CO_3 is a process requiring a rearrangement of the valence bonds, the two C—O bonds of CO_2, 180° apart and 1.15 Å long, being transformed to the three C—O bonds of H_2CO_3, approximately 120° apart and not far from 1.3 Å long. We shall not attempt to comment here on the details of the electronic rearrangements that must be involved in the process, and indeed little is known of them. It is not surprising, however, that a process such as this should require an appreciable time, in contrast for example to a process such as the hydration of NH_3 to NH_4OH in which the hydration process simply involves the formation of a hydrogen bond between the unshared electron pair in the ammonia molecule." This apparently esoteric point, the slowness of the hydration of CO_2, may be of considerable physiological importance. Hydration is much slower in the blood than in the red cell, which possesses the enzyme carbonic anhydrase [67]. If hydration were instantaneous, this would mean that whenever CO_2 levels in the blood or body tissues increased suddenly following some respiratory distress, this might well provoke a lethal acidosis.

do use ventilation as a means of acid-base control in the same way as a mammal, and fare much better in hypoxic water than gill breathers. While there is some evidence that some fishes do use ventilation to a minor degree to compensate for departures from acid-base homeostasis [70: p. 199], it cannot be exploited to the degree it is in air-breathing vertebrates because of the constraints of oxygen extraction from water [73].

Simply put, all the factors that make the bicarbonate buffer so fit for air-breathing organisms cannot be exploited by even advanced water-breathing creatures. Together, the fitness of the anomalous pKa value of the bicarbonate buffer system, the large build-up of HCO_3^- in the blood, and the efficiency resulting from the fact that the acid form H_2CO_3 can be readily converted to an innocuous gas and breathed out of the body in the lungs, is a synergy of fitness of little relevance for aquatic life forms.

Summary

Many of the properties of the key members of Henderson's *vital ensemble*—water, oxygen, CO_2, HCO_3^-—are in several instances fit specifically for warm-blooded, air-breathing organisms such as ourselves. These include the thermal properties of water, its low viscosity, the gaseous nature of oxygen and CO_2 at ambient temperatures, the inertness of oxygen at ambient temperatures, and the bicarbonate buffer, with its anomalous pKa value and the elegant means of acid-base regulation it provides for air-breathing organisms. Some of their properties are irrelevant to other classes of organisms or even maladaptive.

It is very hard to believe there could be a similar suite of fitness for advanced carbon-based life forms. If carbon-based life is all there is, as seems likely, then the design of any active complex terrestrial being would have to closely resemble our own. Indeed the suite of properties of water, oxygen, and CO_2 together impose such severe constraints on the design and functioning of the respiratory and cardiovascular systems that their design, even down to the details of capillary and alveolar structure *can be inferred from first principles*. For complex beings of high metabolic rate, the designs actualized in complex Terran forms *are all that can be*. There are no alternative physiological designs in the domain of carbon-based life that can achieve the high metabolic activity manifest in man and other higher organisms.

APPARENT DEFECTS AND DESIGN

Problems with water

Critics of the fitness argument point to various supposed defects in some of the core constituents of the *vital ensemble*. For example, it is claimed that water is *too reactive* to be considered ideally fit because it tends to hydrolyse organic compounds. As the authors of the NASA study comment [9: p. 16], "The reactivity of water creates problems ... in particular many molecules are unstable in water ... requiring another round of metabolism for their replacement." Again they comment [9: p. 27], "Water reacts with many biomolecules in a way that damages them ... The disadvantageous reactivity of water is especially obvious

when considering RNA and DNA, as the bases deaminate in water with the subsequent loss of genetic information." In yet another section entitled "The Reactivity of Water Constrains Routes to Origins," they comment [9: p. 60], "The assembly of biopolymers and the assembly of nucleosides from component sugars and nucleobases, the assembly of nucleotides from nucleosides and phosphates, [and] the assembly of oligonucleotides from nucleotides, are all thermodynamically uphill in water." The same is also true in the case of the assembly of proteins from amino acids.

This tendency of water to degrade complex organic molecules they term an "obstacle" on the route to life in the same NASA study. Other researchers concur. Benner *et al.* comment, "The toxicity of water creates special problems for the prebiotic chemistry, as repair mechanisms presumably require a living system" [34: p. 681]. In other words, the properties of water are *not fit for the origin of life* as they conceive of it in an aqueous medium. The authors of the NASA study also point out that the carbon-nitrogen double bond is unstable in water and cannot be utilized readily by life forms based in a water matrix [9: p. 70]. They also cite as a defect the tendency of water to disrupt hydrogen bonding, pointing out, "The ability of water to form strong hydrogen bonds disrupts the hydrogen bonding useful for supramolecular structures" [9: p. 70]. Consequently, chemists working on self-organizing systems tend to avoid water because it "disrupts non-covalent directional bonding such as hydrogen bonding" [9: p. 70].

They also argue [9: p. 69] that although the familiar ice on earth (ice 1) is less dense than water and floats, other forms of ice formed under very high pressures, perhaps on bodies more massive than the earth (ice 2 and other forms of ice), are actually heavier than water. They do concede that the familiar ice that forms on earth (ice 1) is beneficial to life, since it does keep water liquid beneath the floating ice, but they consider the increased albedo (reflectivity) of ice compared with water as a *defect* that may have contributed to repeated ice ages suffered by the earth many times over its geological history.

The 'problem' with most of these defects, except for the increased albedo of ice compared to water (a defect difficult to judge because of the great complexity of climatic modelling), is that nearly all of them are '*obstacles on the route to life*' [9: p. 60]. The reactivity of water and its hydrolytic activity poses a serious challenge to envisaging how a water-based life form could have originated in water without the synthetic machinery of modern cells. But as the route to life is *not understood*, and given that the hydrolytic activity of water is probably playing an important role in the turnover of matter in all extant cells, something the NASA panel does concede [9: p. 27], it is hard to see these defects as seriously threatening the fitness of water for life as it is on earth at present.

Problems with oxygen

Many authors have alluded to the potential danger of oxygen to carbon-based life because of its reactivity, the generation of ROS, and the consequent necessity for anti-oxidant defensives [36; 54; 60; 61]. Critics of fitness might well allude to the

reactivity of oxygen as a major defect in nature. Maina comments [58: p. 283]:

> The assault by the ROSs on the DNA, proteins and other macromolecules is profound. It is estimated, for example, that about 2–3% of oxygen taken up by aerobic cells results in production of O_2^- [superoxide anion] radical and H_2O_2 [hydrogen peroxide] [74]; about 10^{12} oxygen molecules are handled by a rat cell daily, generating about 2×10^{10} (i.e. 2%) O_2^- and H_2O_2; about 9×10^4 attacks on the DNA per day per cell occur in a rat [75]; and RORs are responsible for 10,000 or so DNA base modifications per cell per day [76].

Modern cells defend themselves effectively against these reactive products by means of antioxidant metalloenzymes, including the superoxide dismutases, catalases, and peroxidases. These enzymes are a prerequisite for the adaptation of all living cells to the utilization of oxygen [63]. These enzymes are in some instances extraordinarily efficient [62], so that *extant* organisms are able to survive and indeed thrive in the presence of oxygen. Some trees may live for several thousand years [77: p. 2], clams [78] for several hundred years, and tortoises more than one hundred years [79]. Thus the transitional metals are able to tame the reactivity of oxygen effectively, and complex organisms can derive their energies from oxidations and thrive. Indeed, certain forms of life such as flatworms [80] and the jellyfish *Turritopsis* [81, ch. 2] may even be in effect immortal, revealing that, at least in certain cases, the damage inflicted by free radicals on *extant* life, now protected by a battery of antioxidant enzymes, has *no long-term deleterious effect*.

Of course, just as the reactivity of water poses an obstacle on the route to life, so the reactivity of oxygen poses a problem in envisaging how cyanobacteria without the modern zoo of oxygen-taming enzymes could contemplate attempting to utilise or manufacture such a dangerous element. The problem faced by any *primeval* organism attempting oxygenic photosynthesis without the protection of enzymes capable of degrading ROS is obvious, but this cannot be claimed to be evidence that nature is unfit for humans or that oxygen is unfit for *extant* life on earth.

Another possible 'defect' might be the very slow hydration of CO_2 [see footnote 10]. While this may be a crucial adaptation which prevents sudden changes in acidity when CO_2 levels increase in the blood, it is sufficiently slow that the time needed for full equilibration is, as Albers points out [82], "200 times longer than the time spent in the gills or the lungs." Given that CO_2 is transported mainly as bicarbonate, this would seem to be a hurdle hindering the excretion of CO_2 in the lungs. Organisms are able to overcome this challenge because their red cells [and gills of fish] contain the enzyme carbonic anhydrase, which catalyzes the reaction and converts CO_2 to bicarbonate in the tissues and bicarbonate to CO_2 in the lungs.

Sagan famously claimed, in criticizing the anthropocentric model [4: p. 31]: "Our universe is *almost* incompatible with life ... Even if every star in a hundred billion galaxies had an earth-like planet ... life could prosper in only about 10^{-37} the volume of the Universe." But the claim that the laws of nature are specially fit for mankind is not negated by the fact that we cannot live in every part of the surface of the planet or in every quarter of space. The existence of volcanoes, arctic ice caps, or ocean depths, habitats that are inimical to human life, has no bearing on the argument. The only way to show that the cosmos is not uniquely (or exclusively) fit for life as it exists on earth and for advanced forms like ourselves is to show that the cosmos is fit for *Star Trek* aliens or alternative biochemistries.

The design inference

Can we infer that anthropocentric fine-tuning is the result of intelligent design? Although nowhere in *The Fitness* does Henderson follow Wallace and advocate intelligent design, some of Henderson's claims, for example, that the unique *ensemble* exhibits "unrivalled fitness" or "not a single disability" or the "greatest possible fitness" lend themselves to the design inference [3: pp. 266, 267, 272]. However, these claims are not entirely convincing. As we have seen, not all of the properties of Henderson's *ensemble* are maximally fit for all types of life. One example discussed above is the low solubility of oxygen in water, a decided disadvantage for large aquatic water-breathing organisms deriving energy from oxidative metabolism. Also, the hydration of CO_2 is so slow it necessitates the enzyme carbonic anhydrase to ensure that CO_2 excretion and uptake is adequate (see above). Two more examples, not mentioned previously, are that the maximum absorbance of chlorophyll is not coincident with the maximum radiant energy output of the sun [83], and another that some harmful UV light reaches the surface of the earth. Lastly, as discussed above, free radicals cause disease.

Nonetheless, despite these apparent defects, it is very hard not to be struck by the fact that the properties of the members of the *vital ensemble* are peculiarly fit for life as it is on earth, in a profoundly synergistic and parsimonious way. For example, all members are fit in not just one way but in multiple ways. The compound water is not only fit to serve as the matrix of the cell, but also fit because of its low viscosity for the circulatory system in higher organisms. Its thermal properties are fit for homeostasis in warm-blooded organisms, and also to ameliorate the climate of the planet. Similarly, CO_2 is fit to distribute the carbon atom throughout the biosphere, and at the same time fit to assist in the maintenance of the acid-base balance of the hydrosphere in a range suitable for life.

Henderson also was struck by the same wonderful synergy and parsimony by which each compound satisfies several different ends. His prose grows practically rhapsodic as he considers the fact that water and CO_2 are not only physically fit in so many ways for carbon-based life, but are made up of the three atoms that together form the universe of organic chemicals, the material basis of all living things [3: p. 220]. The same few atoms which are uniquely fit to make up the complex molecular fabric of living things (proteins, DNA, etc.) are also uniquely fit to form an ideal matrix and ideal buffer for the thriving of those same 'life forms.' As we saw above, with regard to oxidation he comments, "The very chemical changes which for so many

other reasons seem to be best fitted to become the processes of physiology, turn out to be the very ones which can divert the greatest flood of energy into the stream of life" [3: p. 247–248].

Some of the most striking examples of synergy and parsimony among the properties of *ensemble* members, those that make nature fit for "an animal like man," come from the properties that underlie our ability to utilize the energy of oxidations. First, oxygen and CO_2 are both gases at temperatures where water is liquid. Second, the two chemical end products of oxidative metabolism, water and CO_2, react together chemically to generate the *bicarbonate* buffer, which has ideal characteristics for buffering body fluids of air-breathing organisms. Third, the chemical compound that makes up this buffer (HCO_3^-) is used to transport CO_2 to the lungs. Fourth, liquid water not only chemically reacts with CO_2 to generate HCO_3^-, but water *physically transports* it to the lungs, a task dependent on the *low viscosity of water*. (As discussed above, the design of the circulatory system depends critically on this property of water). Fifth, by virtue of its high heat capacity, water soaks up excess heat (the third end product of oxidative metabolism) and transports it to the periphery also, where its high latent heat of evaporation facilitates greatly the body's cooling. That respiration in higher organisms should depend upon such a profoundly beautiful synergy and parsimony in the physical and chemical properties of the key compounds involved is entirely consistent with the intelligent design inference. One might aptly paraphrase Hoyle, "A common sense interpretation of the facts suggests that a super intellect has monkeyed with the laws of chemistry and biology towards the specific end of organisms like us."

CONCLUSION

There can be few books that have stood the test of time as well as Henderson's *The Fitness*. Subsequent work in biochemistry,

molecular biology, physiology, and other fields of fundamental science throughout the 20th century, right up to the present, have largely confirmed Henderson's claim that the cosmos is exclusively fit for life as it exists on earth and for "an animal like man." Nearly everything discovered in the 20th century from biochemistry to cosmology supports the notion he first clearly defended. In looking for life in space, NASA looks for water and carbon-based life forms. When they search for signals of intelligent life they look for oxygen. While the supposed 'defects' of some of the key biochemicals may challenge the notion that *all* the laws of nature are *perfectly* fit for *all* types of carbon-based life, they undermine neither the claim that the cosmos is uniquely fit for carbon-based life nor the anthropocentric claim that nature is uniquely fit for beings of our biology and physiological design.

Finally, it is surely one of the most intriguing ironies of scientific history that the five decades from the publication of *The Origin of Species* in 1859 to the onset of World War I, when the old teleological anthropocentric paradigm was unravelling in mainstream culture because of the Darwinian revolution, was also when the new biochemical evidence for our uniqueness was first emerging. At the very same time that Nietzsche famously proclaimed, "Nihilism stands at the door" [84], new discoveries in organic chemistry and biochemistry, unrecognized at the time, were providing the first hint that life on earth might after all be the result of design and not the accident of deep time and chance that was increasingly assumed.

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