

Cambridge
Astrobiology

Fitness of the Cosmos for Life

BIOCHEMISTRY AND FINE-TUNING



Edited by

**John D. Barrow, Simon Conway Morris,
Stephen J. Freeland and Charles L. Harper, Jr.**

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FITNESS OF THE COSMOS FOR LIFE

Biochemistry and Fine-Tuning

This highly interdisciplinary book highlights many of the ways in which chemistry plays a crucial role in making life an evolutionary possibility in the universe. Cosmologists and particle physicists have often explored how the observed laws and constants of nature lie within a narrow range that allows complexity and life to evolve and adapt. Here, these anthropic considerations are diversified in a host of new ways to identify the most sensitive features of biochemistry and astrobiology. Celebrating the classic 1913 work of Lawrence J. Henderson, *The Fitness of the Environment*, this book looks at the delicate balance between chemistry and the ambient conditions in the universe that permit complex chemical networks and structures to exist. It will appeal to scientists, academics, and others working in a range of disciplines.

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Cambridge Astrobiology

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Foreword: The improbability of life

George M. Whitesides

How did life begin?

I (and most scientists) would answer, “By accident.” But what an absolutely unlikely accident it must have been! The earth on which life first appeared – prebiotic earth – was most inhospitable: a violent place, wracked by storms and volcanoes, wrenched by the pull of a moon that was much closer than the one we know now, still battered by cosmic impacts. On its surface and in its oceans were myriads of organic compounds, some formed in processes occurring on earth, some imported by infalls from space. Out of this universe of tumult and molecules, somehow a small subset of chemical processes emerged and accidentally replicated, thus stumbling toward what became the first cells. How could such a chaotic mixture of molecules have generated cells? Order usually decays toward disorder: *Why do the tracks that led to life point in the opposite direction?*

The origin of life is one of the biggest of the big questions about the nature of existence. *Origin* tends to occur frequently in these big questions: the *origin* of the universe, the *origin* of matter, the *origin* of life, the *origin* of sentience. We, scientists and non-scientists alike, have troubles with such “origins” – we were not there watching when the first events happened, we can never replicate them, and, when those first events happened, there was, in fact, no “we.” I believe that one day we will be able to describe life in physical terms – that is, we will rationalize life satisfactorily in molecular detail based on accepted scientific law and scientific theory using the scientific method. But we certainly do not know yet how to do it.

Understanding how organized living cells emerged from disorganized mixtures of molecules is an entrancingly, seductively difficult problem – so difficult, as we now understand it, that science does not even have well-formulated, testable hypotheses about how it might have happened, only guesses and intuitions. This

problem deserves our most careful thought. Its solution will tell us about our origins and describe how disorder can spontaneously become order. It will also test the capability of current science to understand systems comprising many interacting parts.

Before trying to answer the question *How did life begin?*, we must first think about what the question really is that we are trying to answer: What is the “life” whose origins we are trying to understand? What are the characteristics of a cell, the simplest embodiment of life, that might allow us to trace back to its origins? How do we recognize an “origin”? When does a set of molecules, and of processes that convert these molecules into one another, cross a line separating “not-alive” from “alive”? And what is the tool – the “scientific method” – that science will use to try to address this problem?

Let us begin with the scientific method, a very useful and quite reliable strategy for doing science. Although it sometimes seems plodding, the scientific method can tease apart astonishingly difficult and complicated problems by careful attention to detail. It starts with rigorously reproducible empirical observations: “Things fall down, not up.” “Two objects at different temperatures, when placed in contact, reach the same temperature.” “Hydrogen atoms absorb only light that has specific frequencies.” The scientific method codifies and quantifies these observations as “physical laws,” builds theories (Newtonian mechanics, thermodynamics, quantum mechanics) based on those laws, and then tests new observations or hypotheses for their compatibility with these theories. Based on these theories, science rationalizes the physical world and predicts aspects of it not previously observed. The tools of the scientific method are the millstones and the oven that science uses to grind observations into theory and bake theory into prediction.

The scientific method works most rigorously when it identifies observations that are incompatible with current hypotheses. Faced with a new observation, scientists list all hypotheses that might explain it and then discard those that are incompatible with accepted physical law. Hypotheses that are not discarded as incompatible remain possibilities. If only one remains, it is promoted to theory. If disproving all hypotheses but one is not possible, we may retreat to demonstrating compatibility with theory, recognizing that compatibility is weaker than proof. In science, we use the phrases “I think . . .” and “I believe . . .” as synonyms, both implying “. . . based on known physical law.” In other words, “This theory accommodates all the observations that we currently know.”

So, what is life? We can describe what it looks like and what it does, but not how it works (most of us are in the same situation even with much simpler systems: computers, electric toothbrushes, refrigerator magnets). I suggest that life has five major physical attributes (other scientists may suggest other lists, but the general principles will usually be the same):

1. *Life is compartmentalized.* All life that we know is embodied in cells, and all cells have a continuous, closed membrane that separates “inside” from “outside.”
2. *Life is dissipative, or out-of-equilibrium.* Life requires a flow of energy. If the chemical and physical processes in living cells reach equilibrium, and there is no flux of energy through the cell, it is, so far as we know, dead (or, at least, “not-alive”).
3. *Life is self-replicating.* The most evident characteristic of the cell is that it was produced by the division of a parent cell, and, in many cases, it too will divide and produce daughter cells.
4. *Life is adaptive.* The cell can adapt its internal environment so that it functions even when the outside environment changes; in some circumstances, it can even modify the outside environment to make its inside more comfortable.
5. *Life occurs in water.* All life, so far as we know, involves molecules and salts dissolved or organized in a medium that is mostly water. We do not know whether water is essential to all life or just to life as we know it. But, at this time, we know no exceptions: life occurs in water.

So, according to this view, life is a spatially distinct, highly organized network of chemical reactions that occur in water and is characterized by a set of remarkable properties that enable it to replicate itself and to adapt to changes in its environment. We can, thus, describe what we are still ignorant about, but not much more.

How remarkable is life? The answer is: *very*. Those of us who deal in networks of chemical reactions know of nothing like it. We understand some – but only some – of the characteristics of the network that make it so remarkable. One key to its behavior is catalysis. The rates of essentially all cellular reactions – the processes that convert one molecule into another – are controlled by other molecules (usually by a class of protein catalysts called enzymes). The catalysts are (in some sense) like valves in a chemical plant (which, in some sense, is what a cell is): they control the rate at which one kind of molecule becomes another in a way loosely analogous to that in which a valve controls the rate at which fluid flows through a pipe. The complexity of the network becomes clear when one realizes that the catalysts – the valves – are themselves controlled by the molecules they produce: the products of one reaction can control the rate at which another reaction takes place.

The catalysts provide plausible connections among the elements of the network. The conversations among catalysts – conversations controlled by the very molecules the catalysts are controlling – allow the components of the network to form a single, coherent, interconnected, albeit very complicated, entity rather than an inchoate collection of independent processes. And how intricate these “conversations” are! The molecules whose production is required for the cell to live and to replicate itself modify the activities of the catalysts that make them. These already very complex interactions are further modulated by additional signals that come from outside the cell and by signals generated by an internal “clock.” (This clock – the

“cell cycle” – is itself a set of chemical reactions that oscillates spontaneously in time and defines the sequence of stages through which the cell progresses as it replicates.) Many molecules in the cell also have multiple roles: intermediates in one or many synthetic pathways, controllers of the activity of catalysts, signals for generating the catalysts and other molecules, sources of energy, and components of the physical structure of the cell.

Today, we understand many aspects of the behavior of the cell and many fragments of the network, but not how it all fits together. We particularly do not understand the stability of life and of the networks that compose it. Our experience with other very complicated networks (e.g. the global climate, air-traffic-control systems, the stock market) is that they are puzzlingly unstable and idiosyncratic. But unlike these and other such networks, life is stable – it is able to withstand, or adapt to, remarkably severe external jolts and shocks; and its stability is even more puzzling than the instability of the climate. We have a hard enough time understanding even simple sets of coupled chemical reactions. And we have, at this time, no idea how to understand (and certainly not how to construct) the network of reactions that make up the simplest cell.

So, at least for now, the cell is beyond our ability to understand it. The community of people working on the nature of life has, nonetheless, great (and probably warranted) confidence that understanding life in purely physical terms is a tractable, if difficult, problem. This confidence is enormously bolstered by two facts.

First, we are surrounded by uncountable varieties of life, especially by multitudes of different types of living cells; we thus have many examples of different forms of life. We ourselves are communities of cells with the added complexities of hierarchical organization of these cells into tissues, of tissues into organs, and of organs into the organisms that are “we.”

Second, the tools of modern molecular biology have given us an astonishing capability to examine, modify, deconstruct, and reconstruct the molecular components of cells to see how they respond to our tinkering. The simplest cells (such as those of the primitive intracellular parasite *Mycoplasma genitalium*) appear to have fewer than a thousand proteins. That number of catalysts is still very complicated, and we have as yet no conceptual tools for understanding a network of reactions of such complexity. But this level of complexity does not, in principle, seem unreachably beyond our understanding. A cellular network of a thousand proteins (catalysts and molecules that sense, signal, and control passage across membranes; act as the structural skeleton; and perform many other functions) talking to one another in groups through the compounds they produce seems to be something that we will be able to disentangle. Certainly, those who call themselves “systems biologists” believe we will. Still, the path that scientists are now following in trying to understand the molecular basis of life will test their creativity and strain their endurance:

first, understanding the pieces of the networks as thoroughly as possible; then, perhaps, devising a computer model of a cell; and ultimately, in some distant future, validating the correctness of the principles suggested by this model by designing a set of reactions entirely different from those in the cells we now know.

It is one thing to analyze a Bach fugue; it is quite a different thing to play one, or to write one, or to create the kind of communication between humans that we call “music.” We shall, I confidently believe, eventually analyze the fugue of life – the interplay of metabolic processes in the cell – as a network of compartmentalized, adaptive chemical reactions that can, astonishingly, replicate repeatedly into identical, distinct, separate networks. This is a very difficult job, but one that we humans can accomplish. But where did the cell come from? How did this wonderfully, astonishingly complex system come into existence? We do not know. If it is very difficult to understand the operation of cellular life as we observe it today, it is even more difficult to understand how it might have originated in the past.

Thoughtful, deeply creative people from a wide range of backgrounds have been captivated by the question of the origin of life. There is no shortage of ideas about pieces of this puzzle. We know how the surfaces of minerals might have provided elementary, non-biological catalysts to start the process and how heat or sunlight might have contributed other reactions. We can guess why certain types of molecules and reactions tend to occur in metabolism. We understand how any number of plausible natural events occurring in a conceivable prebiotic earth – events that formed complex mixtures of chemicals in geothermal vents, in lightning, on impacts, and under intense solar irradiation – might have contributed relevant bits of chemistry. But we do *not* understand how something as subtle and complicated as the network of reactions that we recognize the cell to be – a network both responsive and robust – might have emerged from these rudimentary processes. How could a chemical sludge spontaneously become a rose, even with billions of years to try?

We can take two approaches in our research directed toward the origin of life: reasoning *backward* and reasoning *forward*. “Backward” starts with life as we know and characterize it now – cells, DNA, RNA, enzymes, membranes, metabolites, membrane receptors, channels, and import/export proteins – and extrapolates back to simpler and simpler systems to try to infer an origin. This approach has been spectacularly successful in “reverse engineering” evolution, at least part of the way; but it has always been guided by examples provided by the types of cells that are now alive. Still, there seems little doubt that evolution could proceed once there was a primitive cell, with RNA or an RNA-like molecule, and reactions that used RNA as a catalyst and also translated RNA into protein or protein-like catalysts that were part of the network of reactions. Several hundreds of millions of tidal pools, together with enormous volumes of lakes and oceans, over several hundreds of millions of years provided many opportunities to produce cellular and organismic

complexity. This part of the development of the complexity of life no longer seems to be a serious issue, at least conceptually. And the anatomical and physiological structures that now so enthrall us – the eye, the ear, the kidney, tentacles, muscles – these all seem to me transfixingly interesting products of evolution, but not ones whose origins are incomprehensibly improbable. If we and the squid have the same camera eye, why not? With enough tries, “best” solutions are bound to emerge many times. If some creatures walk on two legs, some on four, some on six or eight – again, why not? Many solutions may work well enough to survive the rigors of evolutionary selection.

Reasoning “forward” is much more problematic. Although we can imagine many possible manglers for the birth of life – deep smokers in the abyssal depths, tidal pools, hot springs, and many others – and although each could plausibly produce primitive precursors to many of the reactions that now constitute cellular metabolism, we have (in my opinion) no idea how these simple reactions might have blundered together to make the first protocell. Monkeys sitting at typewriters pecking out Shakespeare seems child’s play by comparison. For example, we still do not know:

- *What were the first catalysts?* Were they protein-analogs or RNA-analogs or minerals or some other species of which there is now no trace?
- *How did the first networks form, and why did they persist?* One can imagine countless catalytic reactions that might have occurred, but how some of these reactions became self-sustaining networks is entirely obscure.
- *How could the process that stores the information that specifies the catalysts – the RNA or precursor of the primitive cells – have evolved?* The connection between RNA (or its younger, more evolved cousin, DNA) and the proteins that are catalysts, the enzymes, is not at all obvious; how the two co-evolved is even less clear.
- *How did the energetic cycles that power every cell emerge?* Why is there potassium ion on the inside of the cell and sodium ion on the outside? What was the origin of chemiosmosis? Given the extraordinary complexity of the ATPases – the complicated aggregates of proteins that generate ATP using the free energy that derives from differences in the concentration of ions across membranes – how could they have evolved? We simply do not know.

Nothing in the cell violates the fundamental laws of physical science. The second law of thermodynamics, the law that describes everything that occurs in the range of sizes relevant to life, can sleep untroubled. The flux of energy – now (although not necessarily originally) produced in nuclear reactions in our sun, transferred to the surface of earth as sunlight, absorbed by plants in photosynthesis, captured as glucose and other compounds, used in the cell to generate the intermediates that make metabolism possible, and ultimately dissipated to space by radiation as heat – can evidently support life. But how life originated is simply not apparent. It seems

so improbable! The complexity of the simplest cell eludes our understanding – how could it be that any cell, even one simpler than the simplest that we know, emerged from the tangle of accidental reactions occurring in the molecular sludge that covered the prebiotic earth? We (or, at least, I) do not understand. It is not impossible, but it seems very, very improbable.

This improbability is the crux of the matter. The scientific method can be paralyzed by problems that require understanding the very improbable occurrences that result from very, very large numbers of throws of the dice. Sometimes we can understand the statistics of the problem; sometimes we cannot. How likely is it that a comet will hit the earth? We now have good geological records. How likely is it that a star will explode into a nova? There are many, many observable stars, and we now understand the statistics of nova formation quite well.

But how likely is it that a newly formed planet, with surface conditions that support liquid water, will give rise to life? We have, at this time, no clue, and no convincing way of estimating. From what we do now know, the answer falls somewhere between “impossibly unlikely” and “absolutely inevitable.” We cannot calculate the odds of the spontaneous emergence of cellular life on a plausible prebiotic earth in any satisfying and convincing way.

What to do? For all its apparent improbability, life does seem to have happened here (or perhaps on some similar planet that transferred life to here). Rationalizing the origin of life is a problem that chemists are probably best able to solve. Life is a molecular phenomenon. The possibilities of alternative universes and different distributions of the elements are irrelevant from the vantage point of the particular universe and planet – our earth – that we share with so many other forms of life. We understand the chemical elements (we do not need to know about exotic forms of matter or energy in this enterprise), the molecules they form, and their reactivities. We know the players in the game, and we understand the game they play. We can guess (albeit only roughly) the distribution of the elements on the surface of the earth in the epoch in which we believe that life emerged, and we can infer the abundances of the molecules that were probably present. We understand how catalysts function. But we do not see how it all fits together.

Is this a problem in which science can make progress? Yes, and perhaps no. Those researchers who have taken the approach of reasoning “backward” to infer how life might have been born have made rapid progress. They have used the tools of molecular biology to trace the early stages of evolution back to the point where DNA gave way to RNA, which in turn probably gave way to some more primitive molecule whose composition we don’t know, but which was probably related to RNA. The paths are fainter and fainter as the trail becomes older and colder and as we move from fact into speculation beyond RNA. We still do not understand the connections between RNA, or its forgotten ancestor, and enzymes, or their

also forgotten ancestors, and the metabolic web that supports and constitutes life. Moving “forward” – spinning and weaving the threads that connect “molecules” to “life” – has been technically and conceptually more difficult.

Still, compelling connections are apparent between what might have existed on the prebiotic earth and the molecules of surprising complexity that are now vital to life. We understand, for example, how molecules of astonishing sophistication, such as the porphyrins – the precursors to the “green” of the pigments that serve plants in photosynthesis and the “red” of the hemoglobin that transports oxygen in our blood – could have arisen from aqueous solutions of hydrogen cyanide, one of the simplest of molecules and a possible component of the atmosphere of prebiotic earth. But these demonstrations, marvelous as they are, do not bridge the gap between “forward” pathways from prebiotic molecules to life and “backward” pathways from modern cells to possible progenitors, those emerging from the gray area between “alive” and “not-alive.” As yet, no step goes from solutions of molecules to the networks of interconverting molecules that make up living cells. I believe that no one yet knows how to bridge that gap.

How to progress? The best lead to the hardest part of the problem – the “forward” problem – is the hypothesis that life evolved, somehow, from autocatalytic reactions (that is, reactions whose products are themselves catalysts for the reactions that produce them). We know something about autocatalytic reactions: flames are autocatalytic, and so are explosions (and one speaks, sometimes, of the “explosion” of life). We also know other reactions that are autocatalytic, although the subject of “autocatalysis” has not been a particular preoccupation of chemistry or biochemistry. Autocatalysis offers, I believe, a plausible trail into the wilderness.

Here, I suggest, is a *process* that science can use to examine this question. Let us build and understand autocatalytic reactions; extend that understanding to other networks of catalytic reactions; and develop simple, and then more complex, networks of autocatalytic and catalytic reactions. If, in time, we can trace a pathway from “chemical sludge” to “life,” we shall have provided an argument based on plausibility, if not on proof, for the origin of life.

If, in time, we cannot trace such a path, what then? In science, until it has been proven that something cannot be done, it is always possible that it can be done. Proving that life did not originate by accident in tidal pools or black smokers will be more difficult than proving that it might have done so. Also, patience may be in order. What is impossible for science today may be trivial for science in the future.

There is still much that we do not understand about nature. As we learn more, I believe that we will ultimately see a path – based on principles of chemistry and physics and geology – that could plausibly have led from disorganized mixtures of inanimate chemicals to the astonishingly ordered, self-replicating networks of reactions that provide the basis for life. The fact that I cannot yet understand how an

inconceivably large number of tries at an extraordinarily improbable event might lead to “life” is more a reflection of my limited ability to understand than evidence of a requirement for some new principle. But, having said all of that, I do not know, and in some sense do not care, whether physical science as I now know it ultimately explains the origin of life or whether the explanation will require principles entirely new to me. I do care that science makes every effort to develop the explanation.

Although I believe that science will ultimately be successful in rationalizing the origin of life in terms of physical principles, it should be cautious and claim credit only for the puzzles it has already solved, not those whose solutions still lie in the future. The central conundrum about the origin of life – that, as an accidental event, it seems so very improbable – is not one that science has yet resolved. Claiming credit prematurely – claiming, in effect, that current science holds all the answers – may stunt the growth of the new ideas that a resolution may require.

What, then, do I know? I know that I do not, yet, understand how life originated (and that I may not live long enough to do so). Order from disorder! How could it have happened?

I also know that my father never imagined cloning, and his father would not have believed television. Go far enough back, and the wheel was beyond comprehension. Difficult problems may take time – lots of time – to solve.

And so now, after I wake in the morning – at least on a good morning after I’ve had my coffee and am not distracted by the countless midges that constitute most of reality-as-we-know-it – my overwhelming response to existence, and to life, remains one of delight in its wonderfully wild improbability.

For now, call it what you will. *L’Chaim!*

Preface

This book is part of a two-part program focused on the broad theme of “biochemistry and fine-tuning.” *Fitness of the Cosmos for Life* began with a symposium held at Harvard University in October 2003¹ in honor of the 90th anniversary of the publication of Lawrence J. Henderson’s *The Fitness of the Environment*.² The symposium was an interdisciplinary, exploratory research meeting of scientists and other scholars that served as a stimulus for the creative thinking process used in developing the content of this book. The chapters in this volume were developed following the symposium and take advantage of the rich technical and interdisciplinary exchange of ideas that occurred during the in-person discussions.

The *Fitness of the Cosmos* program has provided a high-level forum in which innovative research leaders could present their ideas. In the spirit of multidisciplinary, the fields represented by the meeting participants and book contributors are diverse. From the sciences, the fields of physics, astronomy, astrophysics, cosmology, organic and inorganic chemistry, biology, biochemistry, earth science, medicine, and biomedical engineering are represented; the humanistic disciplines represented include the history of science, philosophy, and theology.

This volume explores in greater depth issues around which the 2003 meeting was convened. It addresses the broad inquiry *Is the cosmos “biocentric” and “fitted” for life?* Keeping this question in mind, the authors presented their thoughts in the context of their own research and knowledge of others’ writings on topics of “fitness” and “fine-tuning.” This work pays tribute to the groundbreaking inquiry of L. J. Henderson.

¹ *Fitness of the Cosmos for Life: Biochemistry and Fine-Tuning – An Interdisciplinary, Exploratory Research Project Commemorating the 90th Anniversary of the Publication of Lawrence J. Henderson’s THE FITNESS OF THE ENVIRONMENT*,² held at the Harvard–Smithsonian Center for Astrophysics, October 11–12, 2003. See <http://www.templeton.org/archive/biochem-finetuning>.

² Henderson, L. J. (1913). *The Fitness of the Environment: An Inquiry into the Biological Significance of the Properties of Matter*. New York: MacMillan. Repr. (1958) Boston, MA: Beacon Press; (1970) Gloucester, MA: Peter Smith.

The editors sought to develop in this collection of essays a variety of approaches to illuminating ways in which the sciences address questions of purpose with respect to the nature of the universe and our place within it. The chapters offer a range of insights reflecting themes and questions around which the meeting was organized and cover key areas of debate and uncertainty. In addition to George Whitesides' thought-provoking Foreword, twenty-four distinguished authors contributed twenty-one chapters, grouped according to four broad thematic areas:

Part I *The fitness of "fitness": Henderson in context*

Part II *The fitness of the cosmic environment*

Part III *The fitness of the terrestrial environment*

Part IV *The fitness of the chemical environment*

The various research agendas engaging questions of "fitness" and "fine-tuning" applied to the cosmos stress that important future opportunities exist for continued and expanded inquiry into areas where the sciences touch on wider, deeper issues of human interest. It is important to note that the preliminary discussion recorded here represents relatively early-stage exploration into what may in time become a much larger and more coherent area of research.

We hope that we have produced a book that will serve to stimulate thinking and new investigations among many scientists and scholars concerned with "really big questions," such as *Why can and does life exist in our universe?* If we have succeeded in any way, *Fitness of the Cosmos for Life* will serve as a stimulus to the creative thinking of people who can take the inquiry much farther.³

³ A follow-up symposium, *Water of Life: Counterfactual Chemistry and Fine-Tuning in Biochemistry*, took place in Varenna, Italy, in April 2005; a research volume based on that symposium is currently in development. See <http://www.templeton.org/archive/wateroflife>.

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¹ See <http://www.templeton.org/>.

Part I

The fitness of “fitness”: Henderson in context

1

Locating “fitness” and L. J. Henderson

Everett Mendelsohn

Crane Brinton, Harvard historian, friend of Lawrence J. Henderson, and fellow member of The Saturday Club, wrote the obituary for Henderson in the Club’s third commemorative volume (Brinton, 1958, p. 207). Noting that Henderson was somewhat out of the ordinary – crossing the Charles River on several occasions to keep appointments at the Medical School (Boston) and the College (Cambridge) and then recrossing it to get to the Business School (Boston) – Brinton went on to note Henderson’s other non-traditional characteristics: “Ticketed as a biological chemist, he later took the title *physiologist* and, although he would not have liked the name, at the end of his career he was a *sociologist* [emphasis added].”

Brinton went on: “A cross section of his publications may indeed be so drawn up as to seem an academic scandal.” Brinton ran through the publications, from the well-known *The Fitness of the Environment* (1913) and *The Order of Nature* (1917); the more esoteric *On the Excretion of Acid from the Animal Organism* (1910, 1911); the simple volume *Blood: A Study in General Physiology* (1928); the unexpected transcript of an interview on the experiments in the Liberty Bread Shop (Brinton, 1958, p. 208); in his later life, *The Study of Man* (1941); to *Pareto’s General Sociology: A Physiologist’s Interpretation* (1935). Brinton jocularly added that a piece by Henderson – a biographical memoir on the life of the poet Edwin Arlington Robinson (a close friend from his student days) written as a memoir for the American Academy of Arts and Sciences – is to be found in the Woodberry Poetry Room of Harvard’s Lamont Library.

To Brinton, “the conclusion is inescapable: Henderson, who was so much else, was also a philosopher.” But Brinton also modified his praises: Henderson did not have the gifts of a popularizer. He was not a polymath, despite his interests in many areas. Nor was he a Renaissance figure; he had no interest in music or in the fine

arts. And – almost mockingly – Brinton noted Henderson’s very high regard for “the art of eating and drinking.”

So who was this man whose *The Fitness of the Environment*, published some ninety years before, was chosen as the emblem of the project, *Fitness of the Cosmos for Life*?¹

Who was L. J. Henderson?

Lawrence Joseph Henderson was born in Lynn, Massachusetts, an industrial city just north of Boston, on June 3, 1878. The son of a businessman, he received his early education in Salem, Massachusetts, the more upscale town of his father’s family, before going to Harvard as a sixteen-year-old – actually not that unusual in the late nineteenth century. His father’s business connections in the St. Pierre and Miquelon Islands of the Gulf of St. Lawrence, where the young Henderson spent his vacations, stimulated his interest in learning French.

After graduating in 1898, he went on to Harvard Medical School, receiving his M.D. degree in 1902 (although he never intended to be a physician). He followed the path of those Americans interested in advanced scientific training by spending two years in the Strasbourg (then in Germany) laboratory of the biochemist Franz Hofmeister. After returning to Harvard, he spent a year in the chemistry laboratory of Theodore W. Richards (his former teacher and later brother-in-law). In 1905, he was appointed Lecturer in Biochemistry at the Harvard Medical School. He then moved to the college and, rising through the ranks, became a professor in 1919. In 1934, he was appointed the Abbott and James Lawrence Professor of Chemistry, a post he held until his death on February 10, 1942.

Henderson was a key figure in establishing the Department of Physical Chemistry in the Medical School (1920), and seven years later he helped establish the Fatigue Laboratory at the Graduate School of Business Administration. Together with Alfred North Whitehead (whom he helped bring to Harvard) and President Abbott Lawrence Lowell, he founded the Society of Fellows at Harvard. As early as 1911, Henderson started teaching a general course in the history of science (one of the earliest in any university) and played an instrumental role in bringing the Belgian George Sarton, the pre-eminent historian of science, to Harvard in 1916. He received the obvious forms of scientific recognition, including election to the National Academy of Sciences (becoming its Foreign Secretary) and the American Academy of Arts and Sciences, and was also decorated with the French *Légion d’honneur*.

But Henderson was not a good experimenter, did not like manipulating the complex apparatus of his field (he later confessed to this in his unpublished series

¹ See www.templeton.org/biochem-finetuning/participants.html.

of “Memories” [1936–39]), was judged by colleagues to be incapable of writing or speaking simply, was known for making “passionate and intolerant assertions and suffered fools not at all.” He consciously took the role of gadfly, (often rudely) wanting to shake people out of their comfort zone and stimulate them to respond. Brinton noted that despite his warmth, which he hid from the world, he appeared to many as “a cold scientist, pompous, even pedantic” (Brinton, 1958, pp. 211–12).

Many of those who recounted episodes from Henderson’s life or who had encounters with him noted special characteristics. His very fair-minded former student and colleague John T. Edsall, the Harvard biochemist, noted in his entry on Henderson in the *Dictionary of American Biography* that

his mind and temperament were complex. Especially in his later years, he spoke often with intense distrust of “intellectuals,” liberals, and uplifters, who he felt failed to understand the deep non-rational sentiments that are an essential foundation for a satisfactory and stable society . . . he could infuriate some of his hearers . . . (Edsall, 1973, p. 352)

George Homans, Harvard professor of sociology and young disciple of Henderson’s later work on the social theorist Vilfredo Pareto, put it more bluntly in his own autobiographical volume: “Henderson was always an extreme and outspoken conservative . . . his manner in conversation was feebly imitated by a pile driver” (Homans, 1984, p. 90). Or, as he put it in another context: “Henderson never lost his tastelessness” (p. 117). This, from a deep admirer of his work, a close younger colleague, and the co-author with Charles P. Curtis of a volume on Pareto’s sociology.

Where did *The Fitness of the Environment* come from and where did L. J. Henderson go with it? In spite of the several fields in which Henderson worked, a number of commentators, his contemporaries, and later analysts noted a markedly similar approach in many of his endeavors. Looking back at his work later in life, Henderson himself noted more unity than he had been aware of at the time. His focus was on organization and system: the organism, the universe, and society. John Parascandola, the author of a doctoral dissertation and several important articles on Henderson, put it succinctly: “The emphasis in his work was always on the need to examine whole systems and to avoid the error of assuming that the whole was merely the sum of its parts” (1971, p. 63).

But if that is the general outlook – and there is no real contest about this among the commentators on Henderson’s work – what were the proximate causes and immediate contexts of Henderson’s first full statements of the system of organism and environment? What were its visible and tacit sources? A connected sub-question examines how Henderson’s ideas compared with those of other contemporary biologists who were similarly examining the ideas of life and matter: Walter Bradford

Cannon, a Harvard colleague and author of *The Wisdom of the Body* (1932) and of a very full biographical memoir published by the National Academy of Sciences (Cannon, 1945), and Jacques Loeb, a Rockefeller Institute protagonist whose classic essay “The Mechanistic Concept of Life” (1912) stood in sharp contrast to the organicism of the two Harvard scientists.

The obvious first sources for Henderson’s fitness argument were the studies he began in 1905 on the equilibrium between acids and bases achieved in the organism. These studies represented some of his most sustained scientific work. The buffer systems he noted served to maintain neutrality in physiological fluids. What he saw in this was “a remarkable and unsuspected degree of efficiency [and] a high factor of safety” (Parascandola, 1968, p. 70). In his 1908 paper “The theory of neutrality regulation in the animal organism,” Henderson noted that, in part, this efficiency depended on the properties of some of the substances involved in physiological reactions: that is, the dissociation constants of carbonic acid and monosodium phosphate and the gaseous nature of carbon dioxide, which allows easy excretion. This buffer action is a key to the stability of all living organisms – but, even more, it served to stabilize hydrogen ion concentrations in oceans and other waters. Henderson realized that water, with its extraordinary properties, together with carbon dioxide seemed uniquely fit to serve as the basis for all living systems (Edsall, 1973, p. 350).

Reflecting on this early work in “Memories,” Henderson cited this as the point at which he became interested in the “fitness” of those substances for physiological processes (1936–9, p. 134). According to Cannon (1945), the discovery of the “extraordinary capacity” of carbonic acid to preserve neutrality had “far-reaching influences in Henderson’s thinking.” Henderson extended research into neutrality-maintenance capacity, which became a key element in his later work on physico-chemical systems (Cannon, 1945, p. 35).

In his report on Henderson’s early work, younger colleague John Edsall noted that these “basic facts pointed clearly to a ‘teleological order’ in the universe.” But Edsall immediately went on to indicate that Henderson “explicitly disavowed any attempt to associate this order with notions of design or purpose in nature, and considered his views fully compatible with a mechanistic outlook on the problems of biology” (Edsall, 1973, p. 350).

Henderson also credited John Theodore Merz’ *History of European Thought in the Nineteenth Century* for its influence on the philosophical sections of the *Fitness* volume. Merz’ four-volume study, with a whole volume devoted to the sciences, is fundamentally organismic in its outlook, and Merz was quite adept at identifying scientific and philosophical interactions (Henderson, 1936–9, p. 173).

Retrospectively, Henderson also identified a “eureka moment” that occurred on or about Washington’s Birthday, 1912, while he was walking down the slopes of

Monadnock (a southern New Hampshire mountain) and thinking about the history of science course he was teaching. He recounted: “. . . it occurred to me suddenly, unexpectedly, and without any preliminary symptoms that I was aware of what I had been looking for in thinking about the fitness of the environment; [it remained] vivid and unforgettable” (1936–9, p. 175). It seemed to come together for him when he saw phosphate systems as very efficient buffers; he pondered the “usefulness of substances” and wondered whether “usefulness was an accident” (p. 177).

But to make sure that he would not be misunderstood, Henderson hurriedly assured his readers (and himself?) “that at this stage, I knew nothing of the literature of natural theology.” Although he vaguely recollected William Paley and the watchmaker, he confessed that there was nothing in the history of thought “of which I was more ignorant and to which I was more indifferent.” Having grown up in a period dominated by Darwin, he had known nothing of the *Bridgewater Treatises* (in which natural theology was explored at length by nineteenth-century scientists), and he had not been worried by the introduction of final causes into science. He was aware of, but not thoroughly knowledgeable about, the teleological literature and arguments (pp. 170–9).

By February 1912, however, having become fully convinced of the primacy of carbonic acid and water in the environment and the importance of the buffer concept, he set about writing *The Fitness of the Environment*. He claimed that he made no outline of the book (or of later ones, for that matter, including the treatise on *Blood*) and spent less than sixty days (and probably closer to fifty) writing the volume (p. 186).

In structuring his argument in *Fitness*, Henderson pointed to the Darwinian view of fitness as involving a mutual relationship between the organism and the environment and stressed the essential role of the environment as being of equal importance to the evolution of the organism. He opened his argument with the following paragraph:

Darwinian fitness is compounded of a mutual relationship between the organism and the environment. Of this, fitness of [the] environment is quite as essential a component as the fitness which arises in the process of organic evolution; and in fundamental characteristics the actual environment is the fittest possible abode of life. Such is the thesis which the present volume seeks to establish. This is not a novel hypothesis. In rudimentary form it has already a long history behind it, and it was a familiar doctrine in the early nineteenth century. It presents itself anew as a result of the recent growth of the science of physical chemistry. (p. v)

His strong claim was that the actual environment is the fittest one possible for living organisms. Let me now locate Henderson’s claims.

Locating Henderson's claims

Even as a sophomore at Harvard, Henderson confided in his “Memories” that he had “a vague feeling that there are not only many undiscovered simple uniformities behind the complexities of things, but also undiscovered unifying principles and explanations” (1936–9, p. 16). But there was more. Alongside this explanation, he recounted that he came upon William Prout’s hypothesis (1815–16) concerning the periodic classification of chemical elements (all are multiples of the atomic mass of hydrogen) and felt the order involved must have an explanation. Was he retrospectively claiming that *he had himself become “fit”* to search for an understanding of the “fitness principle”? He was certainly willing to stray beyond the boundaries of the laboratory and the conceptual borders of the sciences.

By 1908, just as he was embarking on the construction of the fitness theory, Henderson began attending the philosophy and logic seminars of Josiah Royce in Harvard’s Department of Philosophy. Through this channel, he came to know the works of Alfred North Whitehead, Bertrand Russell, and other contemporary philosophers. He continued to sit in on philosophy seminars in subsequent years. In the preface to *Fitness*, he generously acknowledged Royce: “His learning and generosity have in the past aided me to reach an understanding of the philosophical problems of science, and in the preparation of this book have repeatedly guided me aright” (p. xi). Royce himself had expressed belief in a form of universal teleology in his 1901 book *The World and the Individual*, and he enthusiastically called Henderson’s work to the attention of other philosophers. In a long footnote at the conclusion of *Fitness*, Henderson cited Royce’s teleological vision from the 1896 volume *The Spirit of Modern Philosophy* (Henderson, 1913, p. 311). The two joined with other Harvard faculty to discuss issues in the history and philosophy of science. These meetings went on for a full decade (1936–9, pp. 209–12; Parascandola, 1968, p. 71).

In his work, Henderson’s ideas of fitness developed along with a growing interest in regulation of the physiological processes of the organism. Although he only later referred to this work, it was very much in accord with the concept of maintaining the *milieu intérieur* developed in the later decades of the nineteenth century by Claude Bernard and other contemporaries. (Henderson wrote a preface to an English translation of *Experimental Medicine* [Henderson, 1927] and made significant use of Bernard in setting out the problem he explored in *Blood: A Study of General Physiology* [1928]). But in his paper on the excretion of acids (1911), Henderson zeroed in on the seeming fitness of certain substances for physiological processes, pointing to the excretion of phosphoric acid as an indicator of renal action needed to maintain an acid–base balance: “There seems to be nothing in evolutionary theory to explain it and for the present it must be considered a happy chance . . .” (1911, p. 21; Parascandola, 1968, p. 73).

In “Memories,” Henderson looked back and noted that he had questioned whether the role of carbon dioxide and phosphates was somehow linked in retrospect to special properties that made them more appropriate for physiological processes. As noted earlier, he located the moment at which the idea of the reciprocal nature of biological fitness came to him on Washington’s Birthday, 1912:

I saw that fitness must be a reciprocal relation, that adaptations in the Darwinian sense must be adaptations to something, and that complexity, stability, and intensity and diversity of metabolism in organisms could not have resulted through adaptation unless there were some sort of pattern in the properties of the environment that, as I now partly knew, is both intricate and singular. (1936–9, pp. 177–80)

His research focus became water, carbon dioxide, and other carbon compounds (see the bibliography in Cannon, 1945, pp. 52–3. At the level of theory, he looked for a single order that linked biological and cosmic evolution. (He addressed this latter theme at length in his second fitness book, *The Order of Nature*, 1917.) Was the explanation he sought mechanical or teleological? But teleology, as he used the term, was limited. There were *no final causes*, *no entelechy* (emphasis added). The “teleological principle” in his understanding was inherent in matter and energy. These natural phenomena have original principles “essentially not by chance.” But Henderson was consciously agnostic and refused to seek or find religious links for teleology. (His aversion to religious thought went back to his boyhood and was described vividly in “Memories” [1936–9, pp. 31–3].) For Henderson, teleology stood in parallel to mechanism, not as a replacement for it. As he put it in the preface to *The Order of Nature*: “Beneath all the organic structures and functions are the molecules and their activities . . . [they] . . . have been moulded by the process of evolution . . . and have also formed the environment” (1917, p. iv).

Henderson was struggling not to be misunderstood, and he concluded his preface with a plea:²

I beg the reader to bear this in mind and constantly to remember one simple question: What are the physical and chemical origins of diversity among inorganic and organic things, and how shall the adaptability of matter and energy be described? He may then see his way through all the difficulties which philosophical and biological thought have accumulated around a problem that in the final analysis belongs only to physical science, and at the end he will find a provisional answer to the question.

But misunderstood he was. At least he thought he was. His correspondence was filled with letters attempting to clarify and define teleology. I include a long excerpt from a letter to Paul Lawson (Henderson, 1918b) so that the reader can better understand what Henderson was attempting to achieve:

² He returned directly to this issue in his review of J. S. Haldane’s *Mechanism, Life and Personality*, 1913, discussed later in this chapter.

It is a little difficult for me to reply to your remarks concerning my two books and the idea of teleology. My own opinion is that what I have said is considerably less philosophical than your interpretation of it. If you will look at a living organism, or at a watch, you will find that it possesses, like many other things in the world, a pattern. There is a certain peculiarity, however, about the pattern of the watch which resembles the peculiarity of the pattern of the living organism, and differs from the peculiarity of the pattern of certain other things possessing other well-marked patterns, such as, for instance, the orbit of a planet, or a geometrical figure. This seems to me to be an objective characteristic of the watch which we know to have been an excellent proof of the fact that the watch was designed. It seems to me also to be an objective characteristic of the organism, and, in the case of the organism, the current interpretation of explanations of it is that it is natural selection.

What I maintain is that there is a pattern in the ultimate properties of the chemical elements and in the ultimate physico-chemical properties of all phenomena considered in relation to each other. I do not mean to say that this pattern is exactly of the same nature as the pattern of the watch or an organism. Still less do I mean to say or to imply anything about design or mind. The only minds that I know are the minds of the individual organisms that I encounter upon the earth. But I feel perfectly justified, in spite of a certain unavoidable vagueness and ambiguity, in using the word "teleology" for the pattern in which I am interested.

The important thing to my mind is, nevertheless, not any doubtful talking about the proper name to discuss such a thing, but the fact itself. That is to say, the objective fact that the properties of the elements bear a certain very curious relationship to the process of evolution.

In *The Order of Nature*, Henderson's philosophical explorations came farther forward as he recounted the ideas of natural organization and teleology in a wide array of earlier authors from Aristotle through Descartes, Leibniz, Kant, Goethe, Bernard, Dreisch, J. S. Haldane, and Bosanquet. But the problem of reconciling mechanism in nature with indications of purpose was the way Cannon had set out the problem in his biographical memoir: There was indeed "a teleological appearance of the world . . . It is something that is real . . ." The solar system, meteorological cycle, and organic cycle seem to imply "a harmony which corresponds to an order in nature." As for Henderson's question "What is the mechanistic origin of the present order of nature?" the answer, Cannon suggested, "may be approximately solved by discovering, step by step, how the general laws of physical science work together upon the properties of matter and energy so as to produce that order" (1945, p. 38).

Henderson had already indicated in the closing pages of *Fitness* what he thought he had achieved and what limits he had set on teleology:

At length we have reached the conclusion which I was concerned to establish. Science has finally put the old teleology to death. Its disembodied spirit, freed from vitalism and all material ties, immortal, alone lives on, and from such a ghost science has nothing to fear. The man of science is not even obliged to have an opinion concerning its reality, for it dwells in another world where he as a scientist can never enter. (1913, p. 311)

But Henderson had struggled to reach this point in his argument. As he summed up his thinking, he again asked the question “What then becomes of fitness?” He had already banished all metaphysical teleology from science and was left to explore two possibilities: “An unknown mechanistic explanation” of both cosmic and organic evolution exists – or it does not. While Henderson found it hard to credit such an “unknown” explanation, he added, with the historian’s eye, that before Darwin’s enunciation of natural selection it was hard to imagine a mechanical explanation of biological fitness. Therefore, at the end of *Fitness* he warned: “We shall do well not to decide against such a possibility” (1913, pp. 305–6). But let me be clear. When Henderson was composing *Fitness*, he had rejected the then current theories of vitalism and that of a designer for nature; but he had insisted on maintaining the term “teleology,” albeit adjusted as he saw “fit.” Was there ambiguity in his text? Let us turn to Henderson’s contemporaries for a response.

What did Henderson’s contemporaries say about his work?

Henderson’s two early books, *Fitness* (1913) and *The Order of Nature* (1917), were reviewed by contemporary scientists and philosophers. Their reception, not dramatic by any standard, gives a good indication of the role of his ideas. It is interesting to note that Henderson’s “reflective” and philosophically structured presentations antedated his fuller theoretical-scientific volume on *Blood: A Study in General Physiology* (1928), which itself developed from a sequence of papers in the *Journal of Biological Chemistry*, entitled “Blood as a physico-chemical system,” beginning in 1921 and concluding in 1931.

One of the earliest, but also the fullest, reviews of *Fitness* appeared in *Science* (the journal of the American Association for the Advancement of Science) in September 1913 by the physiologist Ralph S. Lillie, who was at the time teaching at Clark University and later taught at the University of Chicago. His opening lines set out his view: “This book is essentially a discussion of the nature and implications of organic adaptation, that is, of the relation between the living organism and the environment, but is written from an unusual point of view.” Lillie took the time and space to follow Henderson through his argument chapter by chapter with the full identification of carbon, hydrogen, and oxygen and their unique characteristics “which make possible the production of living protoplasm.” They demonstrate “the greatest possible fitness for life” Lillie (1913), p. 337.

But Lillie was not completely satisfied with the adaptive teleology that Henderson had developed. He noted the transfer of the conception of fitness from the organic to the inorganic environment, which thereby achieves the reciprocal nature of biological adaptation. However, Lillie countered that Henderson had not dealt in detail with the organism itself and the interrelation between organisms and the environment:

. . . in other words, what adaptation is, as a general condition or process . . . Of course, the universe is a fit environment for life because it continues to exist in it. Granted, systems having the properties of living beings could not have arisen had the properties of carbon, hydrogen, and oxygen, and of their combinations, been other than they are, but what does this prove?

Most biologists, Lillie asserted, would see the central thesis Henderson advanced “as either self-evident or inherently unprovable.” He seemed to mock Henderson in a footnote by saying, sure, this world is the best possible environment for the organisms that came to live in it – almost a truism, he implies – but what of other organisms in a different cosmos? Biologists may well see the book as an essay on the elements and compounds that form protoplasm, thus calling attention to often overlooked “facts and principles” (p. 340).

But Lillie was not satisfied with this reading; instead, he wanted to probe the questions “of the final significance of biological adaptations and the novel and interesting manner in which they are raised.” He was amazed at Henderson’s surprise that the environment and the organism possess similar characteristics. The surviving organic forms are those that have been able to maintain equilibrium with their environment. If conditions change and organisms can’t compensate, they will fail. That, after all, is what natural selection is all about. “The task of biological science is thus left where we found it: to account for the characteristics of organisms on the basis of the physico-chemical characteristics of their component elements and compounds . . .” and to demonstrate how these living characteristics are formed by the environment (p. 341). Does that mean that life was somehow potential or implicit in matter, in the universe? “To the scientific investigator,” Lillie announced, “such a statement can have little meaning, since it is remote from the possibility of verification” (p. 341).

J. D. Bernal, the materialist, in his book *The Origin of Life* (1967) summed it up succinctly: all of Henderson’s evidence shows that “life had to make do with what it had, for if it failed to do so it would not have been there at all” (p. 169). Is there a way out by postulating a universe biocentric from its inception? Lillie joined Henderson in a cautious welcome to this view, in that the complexity, peculiarities, and stability of organisms would be unintelligible except for something of this sort.

For the final question posed by his reading of *Fitness*, Lillie asked: “How then is it possible to reconcile teleology and the existence of will and purpose in nature with the existence of a physico-chemical determinism which appears the more rigid the further scientific analysis proceeds?” This question, which he did not answer in the review, Lillie admitted (and which is often pushed to the side by scientists), would require biological knowledge for a solution – if one is ever achieved. Lillie concluded that Henderson’s book points biologists to the “importance and urgency of these questions (p. 342).” A polite, friendly, but hardly full endorsement.

Writing in *The Dial*, *A Fortnightly Journal of Literary Criticism, Discussion and Information*, Raymond Pearl, the population biologist, opened his 1913 review with reference to a metaphysical diversion “of my academic and intellectually irresponsible youth,” in which orthodox Darwinism was turned on its head. “Is there not quite as much justification, so far as the objective facts of nature are concerned, for one to say that the environment is adapted to the organism as there is for him to make the converse propositions?” (Pearl 1913, p. 111). Could natural selection, “or any other mechanistic hypothesis,” stand up to the task? It would utterly fail, Pearl argued. Before Henderson’s *Fitness*, no systematic efforts had been made to examine the fitness of the elements of the environment for sustaining life.

Henderson’s own examination, Pearl opined, was in many ways a remarkable one. He showed “conclusively” that the known environment of the earth is better adapted to the needs of organisms than any other that could be constructed. He praised the collection and critical digestion of a great mass of data, describing it as a “masterly contribution to scientific synthesis that establishes the now well-known conclusions.” But having recited those findings, Pearl announced: “At this point the book as a contribution to natural *Science* [in original] comes to an end.” Turning to the final chapter, “Life and the Cosmos,” which Pearl called “a consideration of the philosophical consequences” of the earlier scientific material, he was much less kind. While this part of the book was well done, “[I]t seems to this reviewer, at least, to fall short in compelling logical force of the purely scientific part of the work” (p. 112). Henderson showed, Pearl noted, that “existing science” was unable to give any “satisfactory mechanical explanation” to the reciprocal fitness of organism and environment while not ruling out its possibility. Pearl was clearly not enthralled by Henderson’s proposal of a “devitalized teleology in the form of a purposive ‘tendency’ working steadily through the whole process of evolution.” The objection was direct: “This ‘tendency’ is not something which can be weighed or measured” but is rather an original property of matter “assumedly not by chance, which organized the universe in space and time.” In other words, it falls beyond the bounds of science. But Pearl’s overall commentary on *Fitness* was adulatory. Notwithstanding his assessment of the concluding philosophical chapter, he conferred on the book the highest of honors, calling it a “logical sequel to the *Origin of Species*” (p. 112).

An array of additional reviews appeared both in scientific journals, such as *Nature*, and in philosophical ones, such as *Mind*, with the *Hibbert Journal* generally praising the scientific data brought forward but scattering various interpretations of the philosophical conclusion throughout. The mechanism, vitalism, and teleology debates current in the opening decades of the twentieth century had already been rehearsed in the responses to Henderson’s own attempts to reconcile the mechanical and the vital in a single system.

One interaction in the review literature, however, adds an additional element to Henderson's ideas among other philosophically oriented biologists: the exchange between Henderson and J. S. Haldane, the physiological vitalist. Haldane's own entry into the discussion came in his earliest book on the debate, *Mechanism, Life and Personality: An Examination of the Mechanistic Theory of Life and Mind*, published in 1913, the same year as Henderson's own contribution to the philosophical discourse. In *Science*, September 17, 1915, Henderson produced an extensive review, opening in what almost might be considered an "airy" fashion: "Dr. J. S. Haldane has long been known as a philosophic physiologist. Indeed it is now for more than three decades that he has occasionally relieved the labors of an orthodox and eminent scientific investigator with the pleasures of idealistic metaphysics" (Henderson 1915, p. 378). Henderson recounted at length Haldane's understanding of the claims of mechanism and the failings inherent in them, as well as the fundamental claim that Haldane finally reached: "The phenomena of life are of such a nature that no physical or chemical explanation of them is remotely conceivable" (p. 379). If the concept of "organism" had been the first major stumbling block for mechanism in Haldane's view, psychology, or mind, raised the bar for mechanism even higher.

Henderson would have none – or very little – of it: "It is no light task for a man of science to form a critical judgment of this book, for I believe that its weakness is on the philosophical side" (p. 381). Henderson had, of course, recently been put through some criticisms of his own philosophical endeavors. While he was quite willing to quickly accept the critique of childish or crude mechanistic explanations, he by no means gave way to Haldane's broad rejection: "When we turn to Haldane's philosophical objections to the mechanistic standpoint we encounter, I believe, grave inconsistencies in his argument" (p. 381). Henderson was unwilling to accept Haldane's claim of the prior impossibility of providing a mechanistic explanation. He referred to T. H. Morgan's work in developing a mechanistic theory of heredity, called "inconceivable" by Haldane. Henderson also referred to Darwin's feat of making a mechanistic explanation of evolution conceivable.

The structure of Henderson's arguments was cast very much in the mode of Claude Bernard's earlier use of levels of explanation and referred to Cannon's work on fear and rage, which adopted this Bernardian outlook. Henderson vigorously rejected Haldane's claim that "all attempts to trace the ultimate mechanism of life must be given up as meaningless." Instead, he countered with his own stand: "And for my own part I am obliged to say regarding [Haldane's] statement, 'The phenomena of life are of such a nature that no physical or chemical explanation of them is remotely conceivable,' that is true only in a sense quite different from its apparent meaning and is of no *scientific* interest." In having to confront the antimechanism of Haldane, Henderson further identified his own location as he attempted to reconcile the worlds of life and matter.

In 1917, Haldane undertook a review in *Nature* of Henderson’s second book, *The Order of Nature* (1917), which he saw as a follow-up to *Fitness*. He noted that with the wide adoption of natural selection the nineteenth-century conception of teleology had largely dropped from scientific discourse. He further noted that Henderson accepted natural selection, yet wanted to maintain a version of teleology based on the physical properties of matter in the universe and the organisms existing in a functional relationship – the teleological arrangement: “[Henderson] avoids all theological inference, and leaves us with teleological arrangement as an ultimate and mysterious empirical fact” (Haldane 1917, p. 263).

But Haldane was not satisfied. Must we assume, he asked, that the universe is composed at the outset of matter – eternal, unchangeable, and independent? He was unhappy with the concept of system that Henderson proffered: “Biology deals, not merely with the ‘efficient’ causes of ordinary physics and chemistry, but also with what Aristotle called ‘final’ causes.” It is in the biological facts that “teleology is revealed as immanent in nature – as of its essence and no mere accident” appearing in the physical environment – and not only in organisms. Biological concepts, Haldane believed, must be extended to the inorganic world. While knowledge of how this would work is not now present, it requires only a further extension of knowledge. Haldane’s hope for the future was that physics and chemistry would be penetrated by conceptions akin to those of biology. If this occurs, “teleological reasoning will take a natural place in the physical sciences” (p. 263). As I understand it, this is not where Henderson was going; and in a later criticism of Henderson’s book *Blood: A Study in General Physiology* (1928), Haldane stressed how his and Henderson’s divergent views and also the extent to which Henderson’s commitment to the understanding that living things (for example, protoplasm) are physico-chemical systems further separated them (Haldane, 1929).

In the years following publication of *Fitness of the Environment* and *The Order of Nature*, Henderson reported in “Memories” that he stepped back even farther from teleological guides. He also stated that after his work on the sociologist Pareto, he became significantly more skeptical of metaphysics – to the extent that he regretted some of his earlier writings, seeing the discussion of “teleology, vitalism, and so forth, more or less irrelevant and immature.” He noted that he had been less skeptical than he should have been and claimed that much of what he wrote in attempting to explain fitness in metaphysical and teleological terms was meaningless (Parascandola, 1968, p. 107; Henderson, 1936–9: pp. 173ff.). But he did not reject fitness as a concept and continued to see it as a valuable, and perhaps even the most interesting, part of his scientific work.

As he moved to the close of *Blood* (1928), Henderson restated the claims he originally made in *The Order of Nature* (1917) for the critical role of carbon, hydrogen, and oxygen, which “make up a unique ensemble of properties . . . [which are] of the highest importance in the evolutionary process,” making diversity possible.

These elements, he emphasized, provide the “fittest ensemble of characteristics for durable mechanism.” In 1928, he still claimed: “For these facts I have no explanation to offer. All that I can say is that they exist, that they are antecedent to organic adaptations, that they resemble them, and that they can hardly be due to chance” (1928, pp. 355–6; 1917, pp. 184–5).

Did *Fitness* challenge and provoke his contemporaries to take up the concept and use it as a guide to further scientific work? Reviews do not suggest this. By comparison, his later work on *Blood* as a physiological system much more clearly evoked the laboratory labors of his contemporaries. Its detailed analysis of what he referred to as “an immensely complex system in equilibrium” served as a vigorous stimulant to further experiment and explanation. *Fitness* remains to this day a symbol of attempts to provide broader explanation of the complexity of the worlds of the living and the non-living. When George Wald, the Harvard biochemist, was asked to write the introduction to the 1970 reprint of *Fitness*, he tried to set Henderson’s book in time: pre-World War I, a time when the atom was gaining its redefinition at the hands of Rutherford, Rydberg, Mosley, and Bohr. This was before important new forms of chemical bonding had been established, and biochemistry was still in its infancy. What Wald did not suggest was that Henderson’s book stimulated new scientific endeavors. Instead, he alluded to the significant advances that had been made in the sciences, often obviating some of Henderson’s questions. He pointed to one conjecture: “A possible abode of life not unlike the earth apparently must be a frequent occurrence in space” and that perhaps even “‘thousands’ of such planets” exist. He further noted the current expectation of there being “many thousand million millions” of such possible abodes for life.” This conjecture should arise, in Wald’s view, wherever it can (1970, p. xxii). It is in this sense that Henderson’s “fitness” takes on an expansive meaning. It has fueled renewed interest in the origin of life and the obvious extension: the synthesis of life in the laboratory.

Concluding remarks

As other chapters in this volume indicate, “Fitness” and “Order” have taken on other meanings, perhaps meanings that are more expansive than Henderson himself intended. But it has always been clear that a book once published no longer belongs to the author, and its interpretation is no longer controlled by him. As indicated in the pages above, Henderson tried in his response to reviewers to limit what he saw as some of the metaphysical turns given to their readings. In some ways, these views were unavoidable given Henderson’s own often imprecise ideas and his choice to use a term like “teleology” and attempt to give it his own meaning.

From early on in the years after *Fitness*, Henderson kept making clear his lack of sympathy with ideas of vitalism; and although he resisted announcing himself a committed mechanist, he clearly indicated his receptiveness to its explanatory outlook. In his paper “Mechanism, from the standpoint of physical science” (1918a) he once again revisited the debate begun as early as 1915 in his review of J. S. Haldane’s *Mechanism, Life and Personality* (see above) and rejected the vitalism proposed by Hans Driesch and Haldane: “. . . for my part, I can only come back to the conviction that Driesch is talking too confidently about things that none of us understand, and that . . . the weight of the evidence is greatly against him” (1918a, p. 574). As for “. . . Haldane’s conviction that it is impossible to conceive organization in physical and chemical terms, this seems by no means impossible to most physiologists. . . . I accept the mechanistic hypothesis as, upon the whole, most consistent with the evidence” (1918a, pp. 575–6).

Even when Henderson turned to the organismic views of Alfred North Whitehead he was cautious. Henderson liked Whitehead, was influential in bringing him to Harvard, and together with Harvard’s President A. Lawrence Lowell involved him as one of the three founders of Harvard’s Society of Fellows. Yet in his review of Whitehead’s *Science and the Modern World*, the Lowell Lectures for 1925, while clearly appreciative of the development of the concept of organization, the “. . . doctrine Whitehead calls the theory of organic mechanism,” Henderson is not fully enthusiastic. He notes a “lack of unity in the exposition,” with the author “still engaged in working out his theories.” Although he can “dimly . . . perceive” the possibility of overcoming the difficulties “. . . that have produced the conflicts between mechanism and vitalism, and between freedom and determinism . . . hope has been so long deferred . . . it is natural to be a skeptic” (1926, pp. 292–3).

By the end of his life, Henderson had turned his interest from biological systems to social systems. Complexity, interpretation, and organization were still very present, but the early challenges of “fitness” seemed largely absent.

Bibliography

- Bernal, J. D. (1967). *The Origin of Life*. London: Weidenfeld & Nicolson.
- Brinton, C. (1958). Lawrence Joseph Henderson, 1878–1942. In *The Saturday Club, A Century Completed, 1920–1956*, ed. E. W. Forbes and J. H. Finley, Jr. Boston, MA: Houghton Mifflin, pp. 207–14.
- Cannon, W. B. (1932). *The Wisdom of the Body*. New York, NY: W. W. Norton.
- Cannon, W. B. (1945). Biographical memoir of Lawrence Joseph Henderson, 1878–1942 presented to the National Academy of Sciences in the fall of 1943. In *Biographical Memoirs*. Washington, DC: National Academy of Sciences, vol. 23, 1945, pp. 31–58. [Contains the fullest bibliography of Henderson’s publications, but is not complete.]

- Cross, S. J. and Albury, W. R. (1987). Walter B. Cannon, L. J. Henderson and the organic analogy. *Osiris*, 2nd series, **3**, 165–92.
- Edsall, J. T. (1973). Henderson, Lawrence Joseph. *Dictionary of American Biography*. Suppl. III. New York, NY: Charles Scribner's Sons, pp. 349–52.
- Fry, I. (1996). On the biological significance of the properties of matter: L. J. Henderson's theory of the fitness of the environment. *Journal of the History of Biology*, **29**, 155–96.
- Fry, I. (2000). *The Emergence of Life on Earth: A Historical and Scientific Overview*. New Brunswick, NJ: Rutgers University Press.
- Haldane, J. S. (1913). *Mechanism, Life and Personality: An Examination of the Mechanistic Theory of Life and Mind*. London: J. Murray.
- Haldane, J. S. (1917). *The Order of Nature* [book review]. *Nature*, **100** (December 6), pp. 262–3.
- Haldane, J. S. (1929). Claude Bernard's conception of the internal environment. *Science*, **69**, 453–4.
- Henderson, L. J. (1908). The theory of neutrality regulation in the animal organism. *American Journal of Physiology*, **21**, 427–48.
- Henderson, L. J. (1910). On the excretion of acid from the animal organism. *VIII. Internationaler Physiologen-Kongress*, Wien.
- Henderson, L. J. (1911). A critical study of the process of acid excretion. *Journal of Biological Chemistry*, **9**, 403–24.
- Henderson, L. J. (1913). *The Fitness of the Environment: An Inquiry into the Biological Significance of the Properties of Matter*. New York, NY: Macmillan. Repr. (1958) Boston, MA: Beacon Press.
- Henderson, L. J. (1915). *Mechanism, Life and Personality: An Examination of the Mechanistic Theory of Life and Mind*. *Science*, September 17, **42**, 378–82.
- Henderson, L. J. (1917) *The Order of Nature: An Essay*. Cambridge, MA: Harvard University Press.
- Henderson, L. J. (1918a). Mechanism, from the standpoint of physical science. *Philosophical Review*, **27** (6), 571–6.
- Henderson, L. J. (1918b). Letter to Paul Lawson. Henderson Papers, Harvard University Archives.
- Henderson, L. J. (1926). A philosophical interpretation of nature, review of A. N. Whitehead, *Science and the Modern World* (1925). *Quarterly Review of Biology*, **1** (2), 289–94.
- Henderson, L. J. (1927). Introduction. In *Introduction to the Study of Experimental Medicine*, Claude Bernard, transl. H. C. Greene. New York, NY: Macmillan Company.
- Henderson, L. J. (1928). *Blood: A Study in General Physiology*. New Haven, CT: Yale University Press.
- Henderson, L. J. (1935). *Pareto's General Sociology, A Physiologist's Interpretation*. Cambridge, MA: Harvard University Press.
- Henderson, L. J. (1936–9). Memories (typescript of unpublished manuscript). Copies are found in the Harvard Archives, HUG 4450.7, and the Baker Library, Harvard Business School, Cambridge, MA.
- Henderson, L. J. (1941). *The Study of Man*. Philadelphia, PA: University of Pennsylvania Press.
- Heyl, B. S. (1968). The Harvard Pareto circle. *Journal of the History of Behavioral Science*, **4**, 316–34.

- Homans, G. C. (1984). *Coming to My Senses, The Autobiography of a Sociologist*. New Brunswick, NJ: Transaction Books.
- Lillie, R. S. (1913). *Fitness of the Environment* [book review]. *Science*, **38**, 337–42.
- Loeb, J. (1912). *The Mechanistic Concept of Life: Biological Essays*. Chicago, IL: University of Chicago Press.
- Parascandola, J. L. (1968). *Lawrence J. Henderson and the Concept of Organized Systems*. Ph.D. dissertation, University of Wisconsin.
- Parascandola, J. L. (1971). Organismic and holistic concepts in the thought of L. J. Henderson. *Journal of the History of Biology*, **4** (1), 63–113.
- Parascandola, J. L. (1973). Henderson, Lawrence Joseph. *Dictionary of Scientific Biography*, vol. 6, pp. 260–2.
- Parascandola, J. L. (1992). L. J. Henderson and the mutual dependence of variables, from physical chemistry to Pareto. In *Science at Harvard University, Historical Perspectives*, ed. C. A. Elliott and M. W. Rossiter. Bethlehem, PA: Lehigh University Press.
- Pearl, R. (1913). Natural theology without theistic implications. *The Dial*, **55** (Aug. 16), 111–12.
- Prout, W. (1815, 1816). On the relation between the specific gravities of bodies in their gaseous state and the weight of their atoms. *Annals of Philosophy*, **6**, 321–30; **7**, 111–13.
- Wald, G. (1970). Introduction to L. J. Henderson, *The Fitness of the Environment: An Inquiry into the Biological Significance of the Properties of Matter*. Gloucester, MA: P. Smith.

Revisiting *The Fitness of the Environment*

Owen Gingerich

In 1913, long after Charles Darwin had argued for the fitness of organisms for their environment, the Harvard chemist Lawrence J. Henderson pointed out that the organisms would not exist at all except for the fitness of the environment itself. “Fitness there must be, in environment as well as in organism,” he declared near the outset of his classic work, *The Fitness of the Environment* (1913, p. 6). While most of Henderson’s contemporaries ignored the philosophical implications of this work, as John Barrow and Frank Tipler have noted, it “still comprises the foundation of the Anthropic Principle as applied to biochemical systems” (1986, p. 143).

Henderson pointed out the uniqueness of hydrogen, carbon, and oxygen in the chemistry of living organisms. Another two decades would pass before astronomers would establish that these were three of the four most abundant elements in the cosmos; but Henderson was at least aware that these atoms were commonly found in the stars and planets. In his treatise, he began with the properties of water, just as William Whewell had done eight decades earlier in his far more teleologically oriented *Bridgewater Treatise* (1833).

Henderson grouped the notable qualities of water under two headings: (1) thermal properties and (2) interaction with other substances. As far as he was concerned, these were empirical, observed properties with minimal theoretical explanation. (Remember that Rutherford’s nuclear atom was still a future concept, while quantum mechanics and the nature of the hydrogen bond lay many more years ahead.)

Let me list water’s notable properties in a somewhat different order and present a variety of specific examples. Water comes closer to being a universal solvent than any other known substance, a basic property familiar to anyone putting sugar into a cup of coffee. In the human body, the digestive process takes place after nourishment has been dissolved into a liquid – water – solution. Even rocks can be subject to water’s dissolving powers: witness the ocean’s salinity. The solubility of

carbon dioxide in water is particularly remarkable and so important in its consequences that Henderson devoted an entire chapter specifically to carbonic acid (formed when CO_2 joins with H_2O to form H_2CO_3), a topic akin to his own research interests.

The significance of this particular solubility is spectacularly demonstrated by comparing the earth with its sister planet, Venus. The atmospheric pressure at the surface of Venus is nearly a hundred times greater than at the surface of the earth, and the Cytherean atmosphere itself is more than 96 percent carbon dioxide. The earth's atmosphere would be similar if the oceans had not dissolved the carbon dioxide and precipitated the excess in the form of limestone. One can scarcely begin to imagine the tons of Indiana limestone resting on our shoulders if the earth, like Venus, had no oceans.

Carbon dioxide is highly soluble not only in water, but also in air, capable of dissolving essentially to the same extent in equal volumes of either substance. This closely balanced solubility is vividly demonstrated to anyone opening a carbonated beverage after vigorously shaking the can. In human metabolism, a complex series of enzymes enables carbohydrates to be “burned” to produce the energy for life. In this process, the oxygen combines with the carbon and hydrogen to form carbon dioxide and water, waste products that must be eliminated. Fortunately, carbon dioxide can be dissolved in the blood, and equally fortunately it can be released into the air by the lungs, a process Henderson described clearly:

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 blood, the acid can circulate partly free . . . and in the lungs [carbon dioxide] can escape into the 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 existing physiological processes would be impossible. (1913, pp. 139–40)

Michael Denton, who quoted this passage in *Nature's Destiny*, went on to say:

As every medical student learns, it can be shown, from estimates of the total amount of carbon dioxide dissolved in the blood and from estimates of the difference in the amount of dissolved carbon dioxide in arterial and venous blood, that most of the 200 milliliters of carbon dioxide produced per minute in an average adult human cannot be transported in simple physical solution to the lungs. (1998, p. 132)

In fact, the carbonic acid formed when carbon dioxide dissolves in the water gradually ionizes to form an acidic H^+ ion and a bicarbonate base, HCO_3^- :



In the lungs, the process is reversed, releasing the carbon dioxide. If an excess of H^+ ions accrues through metabolism, this excess also drives the process toward H_2O and CO_2 , and the acidity is removed essentially by exhaling the carbon dioxide. Thus, this process not only eliminates the waste product of metabolism, but also preserves the neutrality of the blood. Henderson lauded the accuracy of this system, and Denton remarked that “It is a solution of breathtaking elegance and parsimony” (1998, p. 133). The same buffering that plays such a remarkable role for large air-breathing organisms also preserves the neutrality of the oceans.

Henderson pointed out another property of water: its high surface tension, which is substantially higher than that of any other common liquid except mercury. This curious property allows water striders to walk across the surface of ponds or, as a parlor trick, partyers to float a double-edged razor blade in a bowl of water. More important, this property helps water to flow upward, against the force of gravity, in the tiny veins of even tall plants.

Because of the very high specific heat of water, a comparatively large amount of heat energy is required to raise its temperature. This property accounts for the general constancy of ocean temperatures and keeps the earth’s oceans in a liquid state. Coupled with this high specific heat is the remarkably high latent heat of vaporization – the amount of energy required to turn water into steam – “by far the highest known,” as Henderson described it. More than five times more energy is required to vaporize a given quantity of water than to raise the temperature of the water from its freezing point to its boiling point.

At the other side of the temperature scale, water has a most peculiar property: it expands as it freezes, contrary to most known substances. Anyone who has suffered the misfortune of frozen water pipes in the winter will be all too familiar with this property. Were it not for this anomalous expansion, ice would sink when it freezes and form a frozen reservoir at the bottom of the oceans. Because of the low thermal conductivity of water, the oceans would not thaw out in the summer. “Year after year the ice would increase in winter and persist through the summer, until eventually all or much of the body of water, according to the locality, would be turned to ice” (Henderson, 1913, p. 109). Henderson further stated that “[t]his unique property of water [the anomalous expansion on freezing] is the most familiar instance of striking natural fitness of the environment, although its importance has perhaps been overestimated”; but he added that “on the basis of its thermal properties alone . . . water is the one fit substance for its place in the process of universal evolution, when we regard that process biocentrically” (1913, p. 107).

The crucial role of carbon in the formation of life, so obvious to any organic chemist, comes later in Henderson’s treatment. He was obviously fascinated by the environment, writ large – the oceans and the atmosphere – more than with the circumstances of life itself. Perhaps this was because the latter topic was and

is shrouded in so much mystery, all the more so in 1913, compared with the present. Nevertheless, he extolled the virtues of the complexity afforded by carbon chemistry. Fundamental to carbon's versatility is its central location in the first long row of the periodic table:

3	4	5	6	7	8	9	10
Li	Be	B	C	N	O	Fl	Ne
1	1	7	c. 2300	7	2	1	0

Below the elements, I have listed the number of hydrides formed by each of them. (Because this table is taken from my chemistry notes of a half-century ago, the numbers for carbon probably need updating. A Google search gives “thousands,” “vast,” and “near infinite” as the number of hydrocarbons.) Whatever the current number – which of course does not count the numerous compounds of carbon with oxygen or nitrogen – it is clear that carbon greatly exceeds any atom, other than hydrogen, in the number of different molecules it can make.

In the years following the publication of Henderson's book, insights into atomic structure made the role of carbon much clearer and the unusual properties of water more understandable, without in any way diminishing Henderson's arguments or the awe that accompanies appreciation of this fine-tuning of our environment.

From the astrophysical perspective concerning carbon, oxygen, and hydrogen, the massive nucleus is the chief consideration. For chemistry, the much lighter surrounding swarm of electrons is the key to a deeper understanding of these fitness properties. With the discovery of the nuclear structure of the atom and the subsequent development of quantum mechanics, a number of ways to envision atomic structure developed. Here I shall adopt one of the chemist's favorite models, using a tetrahedron to model the carbon atom. Two of carbon's six electrons fill the inner shell, and four are distributed at the corners of the tetrahedron. It is only these outer electrons in the second shell that are modeled by the tetrahedron, but this is the only part of the atom normally of interest to chemistry. (I disregard here, for example, the use of radioactive isotopes as tracers in determining chemical structures.)

Eventually, to make sense of the data accumulating in the 1920s, physicists proposed another degree of freedom (called “electron spin”) in arranging the electrons, suggesting that two electrons (with opposite spin) could occupy the same position. Thus, in the carbon tetrahedral representation, each vertex could accommodate an additional electron, which could be an electron shared with a partner – for example, a hydrogen atom with its single electron – provided the electrons were paired with opposite spins. Such a sharing is known as a covalent bond. Four hydrogen atoms, one at each corner, would give the carbon tetrahedron its full complement of eight electrons, and, by sharing, each hydrogen atom would have

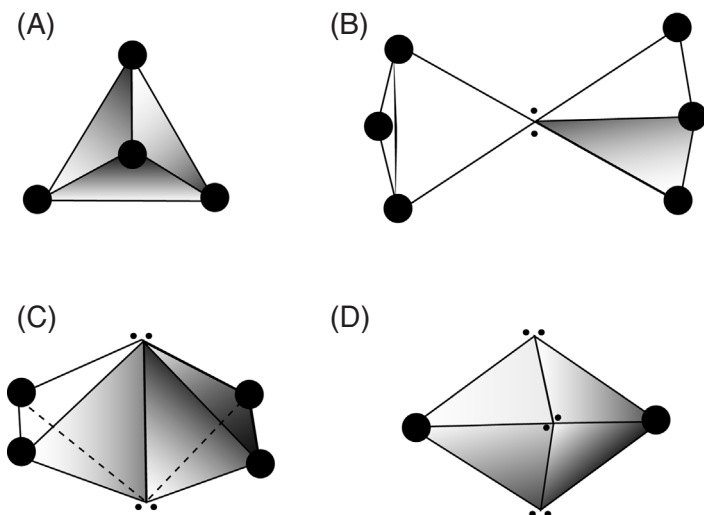


Figure 2.1. (A) The tetrahedral model for methane. The small black spheres represent the positions of the hydrogen atoms surrounding the tetrahedron of carbon. (B) Ethane, C_2H_6 , with a pair of singly bonded carbon atoms. (C) Ethylene, C_2H_4 , with a pair of doubly bonded carbon atoms. (D) Acetylene, C_2H_2 , with a pair of triply bonded carbon atoms.

its full complement of two electrons in its inner shell. This stable configuration, shown in Figure 2.1A, is the molecule methane. Carbon, with its half-full quota of electrons, is as willing to lend as to receive; therefore, one carbon can bond with another, again provided that the shared electrons in each pair have opposite spins. The tetrahedral geometry allows a single, double, or triple covalent bond between two carbon atoms, as shown in Figure 2.1B–D. When the remaining vertices are filled with hydrogen atoms, the resulting gases are ethane, ethylene, and acetylene. This self-bonding property of carbon is the key to its prodigious fecundity.

Oxygen can also be approximated with a tetrahedral structure. This example, because of the light it sheds on the structure of water, is actually more informative than that of carbon. With six electrons for the outer shell, the oxygen atom will have two full vertices (with two electrons each) and two partly filled vertices (with a single electron each). Oxygen, like carbon, can form covalent bonds with itself, with either a single or a double bond. With a double bond (Figure 2.2C), no partly filled vertex remains, and the stable binary molecule that results is the normal form of oxygen gas found in the atmosphere. With a single bond, the two partly filled vertices can each join a hydrogen atom to form hydrogen peroxide (HO_2H) (Figure 2.2B) or join an additional oxygen atom to form a tight ring, ozone (O_3) (Figure 2.2D).

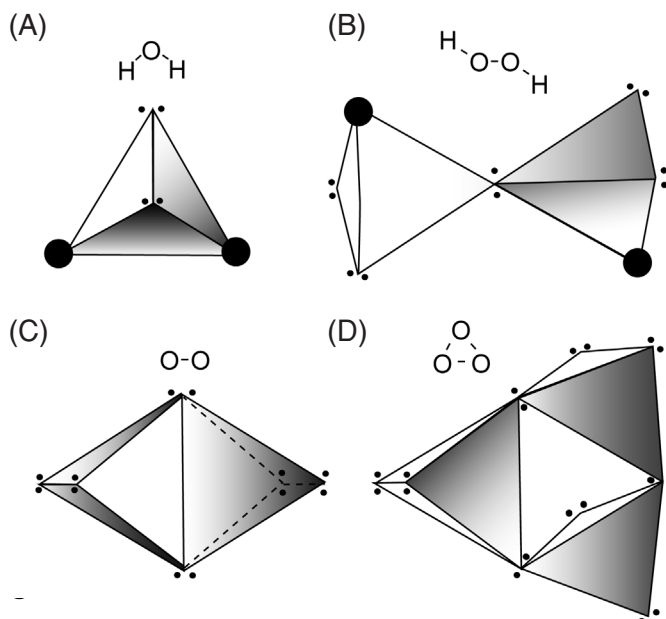


Figure 2.2. (A) Water, with the oxygen atom represented by the central tetrahedron. The small dots represent electron pairs that fill the open vertices. The model clearly shows the bent nature of the water molecule. (B) Hydrogen peroxide, with a pair of oxygen atoms forming a single covalent bond between them. (The atoms can rotate around the covalent bond.) (C) An oxygen molecule, O_2 , with two double-bonded oxygen atoms. (D) An ozone molecule, O_3 , with three double-bonded oxygen atoms.

The two partly open vertices of a single oxygen atom can be filled by the electrons shared with two hydrogen atoms to make a water molecule. The model shows that the hydrogen atoms will not lie on a straight line with the oxygen atom, a crucial fact if one is to understand the special properties of water. The tetrahedral angle is a reasonable approximation to the measured $104^{\circ}30'$ angle in the water molecule.

In what was undoubtedly the most significant chemical treatise of the twentieth century, *The Nature of the Chemical Bond* (1939), Linus Pauling highlighted another extraordinarily important type of chemical bond, the so-called hydrogen bond. Although the double-bonding property of hydrogen was hinted at as early as 1912, Pauling used the principles of quantum mechanics and atomic modeling to show that hydrogen could participate in only a single covalent bond (that is, using shared electron pairs), so that a secondary bonding had to arise from something else, such as a weak electrostatic coupling. The “bent” model of the water molecule (Figure 2.2A) gives a qualitative idea of how this might work. The electron shared from each hydrogen atom is pulled toward the oxygen, leaving the flank of the positive hydrogen nucleus somewhat exposed. Meanwhile, the positive nucleus of

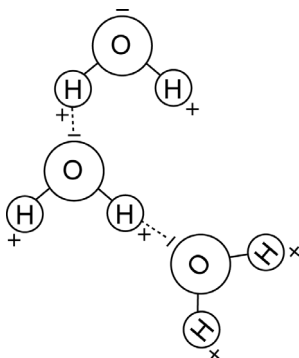


Figure 2.3. The negative shoulder of the oxygen atom in the water molecule couples briefly with the positive flank of a hydrogen atom in an adjoining molecule to produce a transitory hydrogen bond, giving liquid water its remarkably stable physical properties.

the oxygen atom is more than balanced by the extra shared electrons, leaving the broad shoulder of the water molecule with a residual negative charge. Therefore, an outlying positive hydrogen wing of one water molecule can be weakly and momentarily coupled with the negative oxygen shoulder of another water molecule, as shown in Figure 2.3. The duration of coupling is a second that is split very finely indeed, typically around 10^{-11} second.

Nevertheless, this continual coupling and recoupling give water its remarkable thermal properties. Although liquid at average terrestrial temperatures and pressures, the water molecules are subtly linked by the hydrogen bonds, and so an unusual amount of energy is required to raise the temperature of water, or to vaporize it. Similarly, the electrostatic (or ionic) properties of the water molecule act to make it a powerful solvent. Furthermore, as Pauling noticed, liquid water's statistical structure is akin to that of ice, and not just a single form of close packing. The temperature change in the equilibrium of two types of packing causes the anomalous expansion of water as it falls below 4 °C; the lower density of ice itself results from the more open crystal structure of the solid water (Pauling, 1939, p. 284).

Thus, we have been given a far deeper understanding of many of the extraordinary properties of water and its constituent atoms since *The Fitness of the Environment* was written. Also, totally unknown to Henderson in 1913 were the complex chemical shapes and coding in the structures of life: the DNA and protein molecules. These architectures depend critically not only on the presence of the key atoms, but also on the action of the hydrogen bond. The strands of the DNA double helix are joined by hydrogen bonds, strong enough to hold the long chromosomes together yet weak enough to permit the strands to unzip when replication begins. Similarly, the crucial folding of the proteins, where shape plays a vital role in their efficacy, is guided by the sites of hydrogen bonding.

Of course, these unique properties would have been of little avail had it not been for the substantial abundance of oxygen and carbon. But since hydrogen and oxygen rank numbers one and three, respectively, in cosmic abundance, water is guaranteed ubiquitous throughout the universe, while carbon is number four in the cosmic population. However, neither oxygen nor carbon emerged in the first three minutes of the Big Bang. At first glance, this might be labeled “God’s Goof.” That’s how the physicist George Gamow felt when he discovered the presumed flaw in the nature of the light elements that prevented the heavier elements from forming. In the first minute of the Big Bang, energetic photons transformed into protons, and through collisions these protons fused into deuterium (nuclear particles of mass 2), tritium (nuclear particles of mass 3), and alpha particles (which would serve as mass 4 nuclei of helium atoms). But because there was no stable mass 5, at mass 4 the fusion process stopped – well short of the 12 mass units needed for carbon or the 16 for oxygen.

Gamow, with his impish wit, wrote his own version of Genesis 1, in which God, in His excitement at creating the universe, failed to call for a stable mass 5. Disappointed by the error, God “wanted to contract the universe again and start everything from the beginning. But, that would be much too simple. Instead, being Almighty, God decided to make heavy elements in the most impossible way”:

And so God said: “Let there be Hoyle.” And there was [Fred] Hoyle. And God saw Hoyle and told him to make heavy elements in any way he pleased.

And so Hoyle decided to make heavy elements in stars, and to spread them around by means of supernova explosions. But in doing so, Hoyle had to follow the blueprint of abundances which God prepared earlier when He had planned to make the elements from Ylem [the primordial soup of high-energy photons].

Thus, with the help of God, Hoyle made all heavy elements in stars, but it was so complicated that neither Hoyle, nor God, nor anybody else can now figure out exactly how it was done.
(Gamow, 1970, p. 127)¹

Far from being a design flaw in our universe, however, the missing mass 5 seems essential to our existence. Suppose that mass 5 were stable. Then, with the overwhelming abundance of protons in the opening minutes of the universe, atom building could have taken place in mass steps of one, right up the nuclear ladder toward iron. This would have left no special abundance of carbon and oxygen, two essential building blocks of life. Because no stable mass 5 exists, element-building in the stars actually takes place in a two-step process. First, the hydrogen is converted into helium. Then, in a second process, the abundant helium is built up into atoms whose nuclei consist of integer numbers of helium nuclei of mass 4. This includes oxygen

¹ Gamow speculated that this parody might account for his not having received an invitation to the 1958 Solvay Congress on cosmology.