THE STAIRWAY TO LIFE

THE STAIRWAY TO LIFE:

An Origin-of-Life Reality Check

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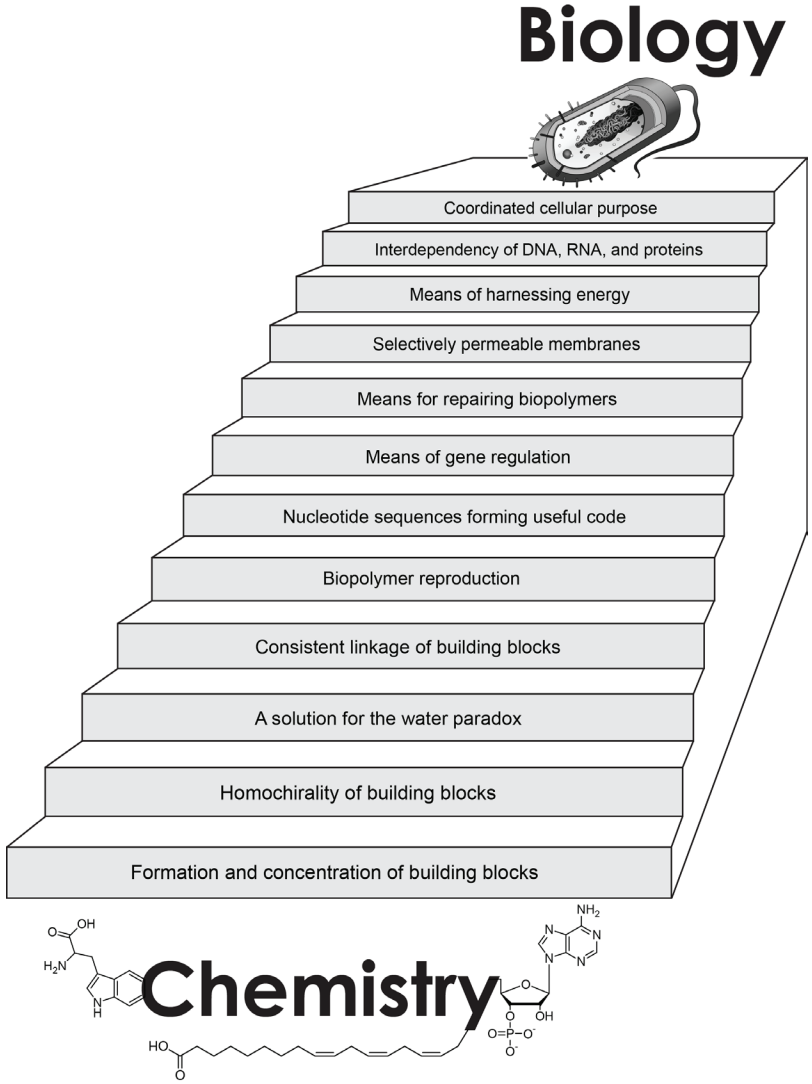

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Introduction

Among the myriad of dubious theories from the distant past, the theory of spontaneous generation has enjoyed exceptional endurance. Belief in the spontaneous formation of living organisms, without the need for seeds or eggs or parents of any kind, was already prevalent at the time of Aristotle, but he is largely credited with formalizing the concept. From his book *The History of Animals*, from the fourth century BC:

> With animals, some spring from parent animals according to their kind, whilst others grow spontaneously and not from kindred stock; and of these instances of spontaneous generation some come from putrefying Earth or vegetable matter, as is the case with a number of insects, while others are spontaneously generated in the inside of animals out of the secretions of their several organs [1].

Due to his work, the theory of spontaneous generation is also known as "Aristotelian abiogenesis," where the more general term "abiogenesis" refers to life arising naturally from nonliving matter.

Over the next two millennia, support for the spontaneous generation of larger organisms like lions, rats, and mice eroded very slowly, retreating over centuries to bastions of support for spontaneous generation of smaller forms of life. Support remained strong for spontaneous generation of insects. Rotting flesh was believed to be a source of spontaneous generation of maggots, and this belief survived without formidable opposition until the time of Francesco Redi, an Italian physician, biologist, and poet. In 1668, he published his magnum opus, *Experiments on the Generation of Insects*, in which he demonstrated experimentally that maggots did not arise from decaying flesh when placed in a jar covered by gauze. He concluded:

> Although content to be corrected by anyone wiser than myself, if I should make erroneous statements, I shall express my belief that the Earth, after having brought forth the first plants and animals at the beginning by order of the Supreme and Omnipotent Creator, has never since produced any kinds of plants or animals, either perfect or imperfect; and everything which we know in past or present times that she has produced, came solely from the true seeds of the plants and animals themselves, which thus, through means of their own, preserve their species ([2], 160).

Despite the powerful insight that Redi's simple experiment provided, proponents of spontaneous generation merely retreated to smaller scales, continuing to support spontaneous generation of microscopic life. Redi's 1668 publication was contemporaneous with Robert Hooke's *Micrographia*, wherein a coarse compound microscope led to the first descriptions of a cell. Hooke also observed

mold growing on leather but was unable to observe any form of "seed" and therefore concluded that the mold had generated spontaneously, either from natural or artificial heat. Spontaneous generation of microscopic life continued to enjoy strong support over the next two centuries; indeed, simply soaking hay in pure water generated a veritable zoo of microscopic life with no trace of seed, egg, or progenitor of any form. A noteworthy late proponent of spontaneous generation was Erasmus Darwin, the grandfather of Charles Darwin. His book *The Temple of Nature* (an unconventional mixture of poetry and science, published posthumously in 1803) summarized his beliefs ([3], Canto I. 1. 227):

> Hence without parent by spontaneous birth
> Rise the first specks of animated earth.

For which he provided the following explanation in an appendix:

> From the misconception of the ignorant or superstitious, it has been thought somewhat profane to speak in favour of spontaneous vital production… There is therefore no absurdity in believing that the most simple animals and vegetables may be produced by the congress of the parts of decomposing organic matter, without what can properly be termed generation, as the genus did not previously exist; which accounts for the endless varieties, as well as for the immense numbers of microscopic animals.

In the mid-nineteenth century, the French Academy of Sciences offered a prize to anyone who could experimentally

support or refute spontaneous generation of microscopic life. In 1859, Louis Pasteur conducted an elegant experiment with meat broth in swan-necked bottles, showing that nothing would grow in a bottle of boiled broth unless particles entered from the air. This provided cogent evidence that even microscopic life could not arise spontaneously. Pasteur concluded:

> Never will the doctrine of spontaneous generation recover from the mortal blow of this simple experiment. There is no known circumstance in which it can be confirmed that microscopic beings came into the world without germs, without parents similar to themselves [4].

Yet Pasteur's confident assertion was flatly denied. Like a phoenix, abiogenesis immediately began a new life, although retreating yet again to a smaller scale. You may recognize that the year of Pasteur's experiment (1859) was the same year of another renowned scientific accomplishment: the publication of Darwin's *On the Origin of Species*. Undoubtedly greatly influenced by his grandfather Erasmus, Charles Darwin maintained a belief, or at least a hope, that life could arise spontaneously. The former Aristotelian abiogenesis implied a rapid arrival of an intact organism without seed, egg, or parents. Darwin's abiogenesis retreated further to the molecular level, applied only to the first life to arrive on the planet, and required an expanse of time. Darwin expressed this view in an 1871 letter to his friend Joseph Hooker:

> It is often said that all the conditions for the first production of a living organism are now present, which could ever have been present—But if (and Oh! what a big if!) we could conceive in some warm little pond with all sorts of ammonia and phosphoric salts,—light, heat, electricity etc., present, that a protein compound was chemically formed, ready to undergo still more complex changes, at the present day such matter would be instantly devoured, or absorbed, which would not have been the case before living creatures were formed [5].

Darwin's espousal of this new form of spontaneous generation, and its role in his overall theory of evolution, has drawn new battle lines in a conflict that remains very active today. Darwin is joined by every atheist because the absence of god necessitates a naturalistic explanation for the start of life, even if it happened on some other planet. Francis Crick, the codiscoverer of the structure of DNA, eventually warmed to abiogenesis, although his initial pessimism on the likelihood of abiogenesis led him to propose the theory of panspermia (the possibility that life on Earth came from elsewhere in the universe) [6]. NASA strongly supports abiogenesis, recently forming the Prebiotic[1] Chemistry and Early Earth Environments Consortium to unite experts across the world to study the origin of life [7, 8]. Bill Nye affirmed his alliance in a book chapter called "The Sparks That Started It All," where he states, "The origin of life just requires some raw material that could allow the spark of life to emerge" ([9], 285). Those who control public school curricula in the United States tend to support abiogenesis, perhaps somewhat out of fear of legal action, because special interest groups argue that even questioning abiogenesis is tantamount to promoting religion, in violation of the Establishment Clause of

1. The term "prebiotic" refers to the period before life existed.

the U.S. Constitution.[2] Many modern biology textbooks are clearly written to encourage millions of students to accept abiogenesis. The following are a few examples from well-known textbooks:

> Because Pasteur's data were so conclusive—meaning that there was no other reasonable explanation for them—the results persuaded most biologists that the all-cells-from-cells hypothesis was correct. However, you will see that biologists now have evidence that life did arise from nonlife early in Earth's history, through a process called chemical evolution ([10], 4).

> Life began when organic molecules assembled in a coordinated manner within a cell membrane and began reproducing. Whether the organic molecules formed on Earth or elsewhere and were transported to Earth within meteors is an open question ([11], 507).

> Although life as we would identify it has not been created in the lab from scratch, these results support the hypothesis that life could have been formed spontaneously on Earth ([12], 248).

> Life arose from nonlife via chemical evolution ([13], 3).

2. The First Amendment to the Constitution of the United States of America states: "Congress shall make no law respecting an establishment of religion." This is the "Establishment Clause," intended to prohibit the government from establishing a national religion. Publicly funded schools therefore cannot encourage belief in a particular religion.

On the other side of the conflict are people who do not believe that life originated from purely natural processes, thus requiring at least a minimum of supernatural intervention. They remain unconvinced by claims that science supports abiogenesis. For the time being, those who doubt abiogenesis have the simple but powerful element of scientific observation on their side because indeed no one has ever observed life arise from nonlife. As biochemist Michael Denton said, "Considering the way the prebiotic soup is referred to in so many discussions of the origin of life as an already established reality, it comes as something of a shock to realize that there is absolutely no positive evidence for its existence" ([14], 261).

The only known way to create a new cell (the basic unit of life) is from an existing cell.

Perhaps with one exception…

This book examines new insights into abiogenesis, as prompted by a substantial milestone in molecular biology: the creation of "the first self-replicating species that we've had on the planet whose parent is a computer" [15]. This milestone was announced in May 2010 by Craig Venter and his colleagues—the culmination of over fifteen years of work, more than forty researchers, and an estimated forty million dollars [15, 16].

Believing that "what I cannot build, I cannot understand" [16], the Venter team set out to understand life by synthesizing life, and Venter's claim of a "self-replicating species whose parent is a computer" provides a strong suggestion that he synthesized de novo life. For some supporters of abiogenesis, Venter's work implied that spontaneous initiation of life is a real possibility.

Publication of the first self-replicating synthetic life (a single-celled organism named *Mycoplasma mycoides* JCVI-syn1.0, but better known as *Synthia*) sent ripples throughout the scientific community [17–24]. The prestigious journal *Nature* asked eight

biology experts about the implications for science and society [17].[3] President Obama asked the White House Bioethics Commission to study the issues raised by synthetic biology and report back to him within six months [20]. The environmental protection nonprofit group Friends of the Earth asked the Environmental Protection Agency and the Food and Drug Administration to fully regulate all synthetic biology experiments and products [21]. In the words of Georgios Zenonos (a neurosurgeon at the University of Pittsburgh) and Jeong Eun Kim (a neurosurgeon at Seoul National University), "Not only did Venter's audacious statements and claims of 'synthetic' life mark a triumph of biotechnological ingenuity, but they also undermined the foundations of religions, cosmotheories, cultures, ethics, and law, questioning the essence of life itself" [18]. Arthur Caplan, a professor of bioethics at the University of Pennsylvania and one of the eight synthetic biology experts, said that Venter's achievement "undermines a fundamental belief about the nature of life that is likely to prove as momentous to our view of ourselves and our place in the Universe as the discoveries of Galileo, Copernicus, Darwin and Einstein" [17]. Such an impactful milestone deserves careful attention.

In Part I of this book, we briefly review Venter's approach to synthetic life, with an emphasis on applications to abiogenesis. Although Venter's work does not directly address abiogenesis, it does provide powerful insights into the required constituents, complexity, and information content of the simplest forms of life. Part I may be too technical for some readers. If so, we recommend

3. These are eight people with eight opinions, as glimpsed from the titles of their essays: "The Power and the Pitfalls" by Mark Bedau, "Now Let's Lower Costs" by George Church, "'Bottom-up' Will Be More Telling" by Steen Rasmussen, "The End of Vitalism" by Arthur Caplan, "Synthesis Drives Innovation" by Steven Benner, "Nature's Limits Still Apply" by Martin Fussenegger, "Got Parts, Need Manual" by Jim Collins, and "Origin of Life Just Got Closer" by David Deamer [17].

reading the chapter summaries and advancing to Part II. In Part II, we combine the learnings from Venter with other recent discoveries in biology to arrive at a fundamental set of requirements for life, organized into a structure called "the Stairway to Life." The Stairway to Life provides a new perspective on abiogenesis because each of the twelve required steps is profoundly unlikely to occur in a prebiotic world, and the improbabilities of each step must be multiplied to arrive at the infinitesimal overall likelihood of abiogenesis. Part III then discusses the implications of the Stairway to Life in an effort to resolve the conflict over abiogenesis.

ABOUT THE AUTHORS

Change Laura Tan received a BS in chemistry from Hunan Normal University, an MS in organic chemistry from Nan Kai University, and a PhD in biochemistry from University of Pennsylvania, and also completed postdoctoral training in genetics at Harvard Medical School. She is currently an associate professor of biological sciences at the University of Missouri. Her research interests include genetics, developmental biology, molecular biology, origin of life, and origin of biodiversity. She teaches molecular biology, signal transduction, and general biology to graduate and undergraduate students.

Photo Credit:
Michael Dodd

Rob Stadler is the author of *The Scientific Approach to Evolution: What They Didn't Teach You in Biology*. He received a BS in biomedical engineering from Case Western Reserve University, an MS in electrical engineering from MIT, and a PhD in medical engineering from the Harvard/MIT Division of Health Sciences and Technology. As a scientist in the medical device industry for over twenty years, he has obtained more than 140 US patents, has been elected fellow of the American Institute of Medical and Biomedical Engineers, and has contributed to medical devices that are implanted in millions of patients worldwide.

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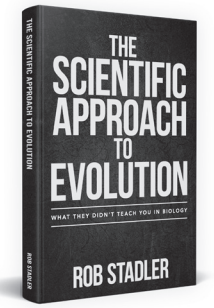
Also from Rob Stadler:



For more than 150 years, continuous debate has swirled around the topic of evolution. From Darwin to Dawkins, extensive scientific evidence has been presented for evolution, yet almost half of contemporary society still isn't convinced. *The Scientific Approach to Evolution: What They Didn't Teach You in Biology* provides a rational new perspective on this debate. Scientific evidence is not all created equally. Some forms of evidence only provide low confidence, while other forms of evidence provide high confidence. Rob Stadler describes a compelling approach to determine the level of confidence and applies it to the commonly cited evidence for evolution. When high-confidence evidence is appropriately prioritized over low-confidence evidence, the result is a profound new view of evolution—one that they did not teach you in biology.