NOT YOUR GRANDFATHER'S Origin OF Life THEORY

BY KRISTA ZALA

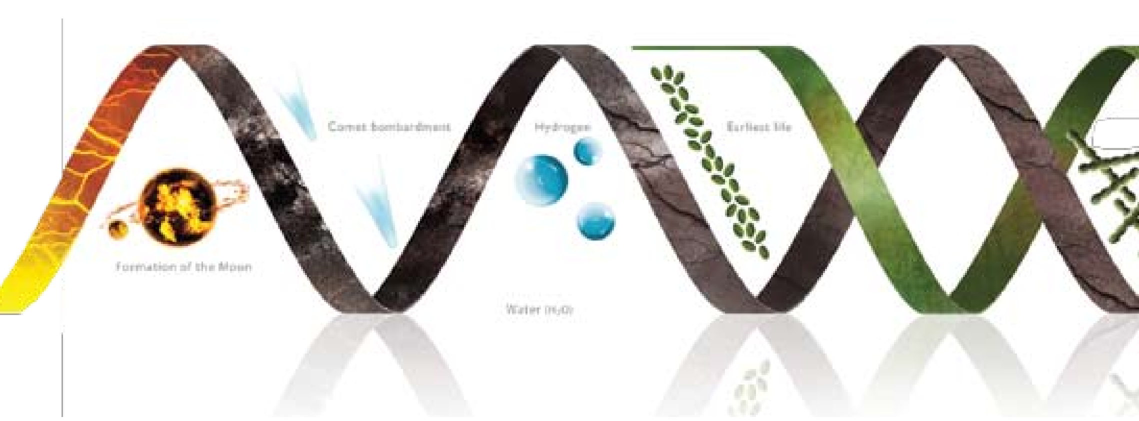
With just a glimpse, early Earth could almost be mistaken for a contemporary—but lifeless—landscape. A vast ocean swept shores in cycles, wind and rain chipped at cliffs, while vents and volcanoes leaked fresh compounds. Yet Earth's features and rhythms both above and below its surface did differ, often operating much more chaotically than those they've settled into over the eons.

The planet spun faster; days went by in half the time. The young moon was closer, drawing a much greater tidal swell—possibly rising as high as a kilometer instead of the few meters of today—and its proximity meant it simply looked bigger, too, though no creature was around to notice. The Earth's crust was more cracked, and the tidal bustle drove seawater through it like a hose blasting a sponge rather than at today's trickle. Somehow, these conditions created life.

"From the solar system, through the formation of Earth, to the chemistry of rocks and water, the phylogenetic tree is clearly tied to the chemistry of Earth," says SFI External Professor Eric Smith. The question is, how did we get from thermodynamics to thoroughbred horses?

Sketching Life

Origin of life theory has itself faced a rocky path. Amid the rise of chemistry as a science, the "vital force theory" drew a thick line between organic and inorganic chemicals, splitting Earth into biotic and abiotic worlds where living begat living all the way back to God's kitchen. The line remained impenetrable until the 19th century, when



the German chemist Friedrich Wöhler accidentally synthesized urea out of decidedly inorganic ammonium cyanate and opened scientific thinking to the wondrous possibility of chemical crossovers between life and the rest of Earth.

In the 1920s, Alexander Oparin and J.B.S. Haldane proposed the now-famous "primordial soup" theory: an early ocean rife with nutrients that provided the balanced breakfast for life to get its eventual start. Three decades later, Stanley Miller and Harold Urey demonstrated how organic molecules could arise from simple inorganic compounds under the right, vaguely prehistoric conditions.

Like all good science, those early revolutionary findings gave rise to many more directions for research: how the chemistry of rocks and water relates to Earth's position in the solar system, how the chemistry of Earth is tied to the tree of life, and which parts of biochemistry are absolutely fundamental to life.

Studies since then concerning the origin of life have branched across many disciplines including statistical physics, interstellar chemistry, geochemistry, microbiology, and computational biology. Quiet incremental advances in the shadows of research have been balanced by astounding discoveries and insights. At SFI, research indicates that any plausible origin of life theory is going to be broad and sophisticated, as well as a messy confluence of dynamic systems. In short, it's not going to be your grandfather's origin of life theory.

Finding Life's Essence

SFI Science Board Chair Emeritus Harold Morowitz, a biochemist at George Mason University, has made the thermodynamics of living systems his life's work. When the discipline was just starting in the 1960s, the first approach was to study Mycoplasma; the bacterium with the smallest known genome and no cell wall seemed a natural starting point in cracking the great mystery of life. (Geneticist and co-founder of Synthetic Genomics Craig Venter is currently using it in his project to synthesize cells from a genome.) But as a clue to life's beginning it turned out to be a false lead. Rather than it being an ancient organism, Mycoplasma is a modern minimalist, having trimmed its superfluous functions and genes over time as it specialized its niche.

Later, while working with an origin of life group at NASA-Ames, Morowitz discovered how to make the amino acid glutamic acid—a main player in the citric acid cycle—from its precursor compounds without using enzymes. Reasoning that the process predated more sophisticated biomolecules that boost reaction speed, Morowitz decided to look at a potentially sturdy bridge between

Below: This Origin of Life timeline, part of the "Emergence" exhibit at the New Mexico Museum of Natural History, depicts 4.6 billion years of change, from early Earth's chaotic, lifeless era to the Blue Green Earth as we know it, with a relatively warm and stable climate that allows plants and animals to flourish.

BOTTOM: GABRIEL GARCIA; LEFT & RIGHT: iSTOCKPHOTO.COM

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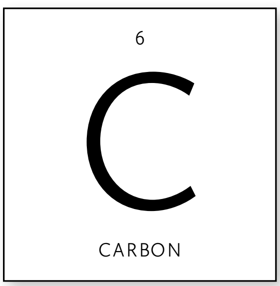
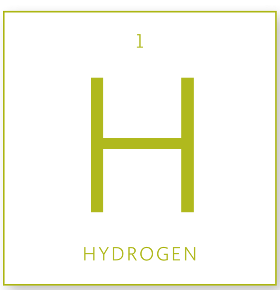




geochemistry and life: the citric acid cycle.

The citric acid cycle stands as the metabolic heart of cellular respiration in all organisms that use oxygen. A true biofuel engine, it breaks down fats, sugars, and proteins, tapping the energy in the compounds' chemical bonds as it turns complex molecules into carbon dioxide.

"The core metabolism hasn't changed in the last four billion years," Morowitz points out, "but it's been kept alive in bacteria that turn over every 20 minutes." Such a tightly conserved mechanism indicates the pathway arose one of three ways. It could be simply an accident that happened and worked well (which Morowitz rejects as it doesn't lead to other useful questions about the emergence of life—i.e., it's a scientific dead end). It could be the best way to synthesize biologically useful compounds from inorganic surroundings, which the biosphere on Earth eventually or fortuitously happened upon. Or it could be the only way—which means it would be found everywhere in the universe where there is life.

"We could go to Mars and find the same intermediary metabolism," he says. "It could even mean that life will form on any planet with the right chemistry, temperature, and gravitational pull."

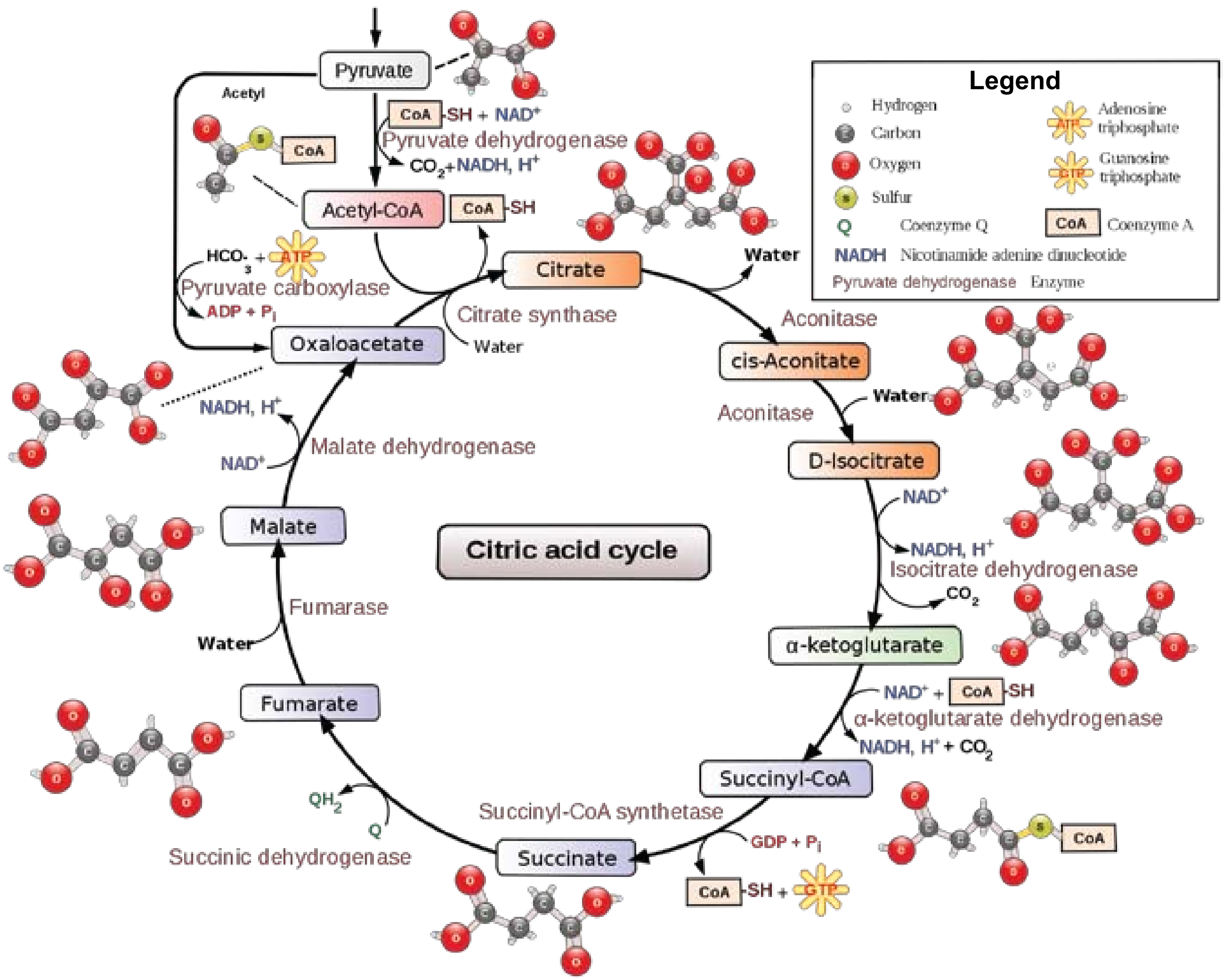
A Fracture that Opens Everything to Sense

A major conundrum in origin of life theory was that the citric acid cycle relies on a steady source of complex organic molecules, which makes a fairly profound assumption that they run in rampant supply. (Plants, in contrast, rely on the even more complex Calvin cycle to harness light energy and use it to build organic compounds from inorganic matter.) Where could these complex biomolecules have arisen?

It took a voyage to the deep to boost origin of life theory. In 1977, Jack Corliss, Richard von Herzen, and Robert Ballard led the deep-water submersible Alvin to the oceanic trenches off the Galapagos, where they discovered life at the seemingly hostile hydrothermal vents. On examining the organisms thriving amid the scalding temperatures, immense pressures, and sulfur-spewing chimneys, they found some of the deepest-branching organisms on the tree of life. These included bacteria that ran the citric acid cycle—but in reverse.

The revelation that the cycle could run the other way "was like watching a fracture form that opens everything to sense," says Smith. After decades of struggling with the chicken-or-egg paradox of complex and simple molecules that each required the other for its existence, the solution came from the lightless biosphere: The mechanism originally arose to build small molecules into bigger ones. What we call the reverse cycle was the original direction, and the only way it ran for the first billion years, he says.

Morowitz's recent work has shown that some small molecules can, in fact, speed metabolic reactions. He has also discovered how metals ranging through the transition elements of the Periodic Table from titanium to zinc, especially iron, cobalt, and nickel, can grab on to small organic molecules and nudge the cluster into an arrangement that catalyzes other biochemical reactions. Armed with such intriguing insights into the citric acid cycle development, Morowitz is now focusing on the stage where the compound citrate splits, adding a side path to form fatty acids, to determine why the cycle is



structured that way. "If it is the only solution, or the best one, to metabolism, we have to learn why it is so," he says.

Miraculous or Inevitable?

Whereas Morowitz looks at the biochemical reactions from the top down, Smith is approaching the problem from the bottom up. A statistical physicist, Smith came to SFI in 2001 to pursue his interest in the processes by which order stems from dynamic systems. As he grew to know the SFI community, members recommended he meet Harold. "They remarked that when the two of you talk, you sound a lot alike, even though you talk about different things," he recalls.

Smith turns conventional origin of life theory upside down. From a dynamic systems perspective, life may have been forced into existence as an outlet for the mounting free energy from the sun and geosphere. Rather than being miraculous, life could be inevitable. It could even be construed as a natural consequence of Earth's thermodynamic order, where the myriad and diverse high-energy systems on early, lifeless Earth "may have forced life into existence as a means to alleviate the buildup of free energy stresses," as he and Morowitz explained in a 2006 paper.

Recently, Morowitz and GMU colleague Vijay Srinivasan's search for a minimal metabolic pathway has whittled the field to about 125 molecular contenders, which Smith is drawing from in charting the drivers in the rise of metabolism.

Above: The citric acid cycle is a series of chemical reactions used by all aerobic living organisms to generate energy. In addition, the cycle provides precursors for the biosyntheses of compounds.

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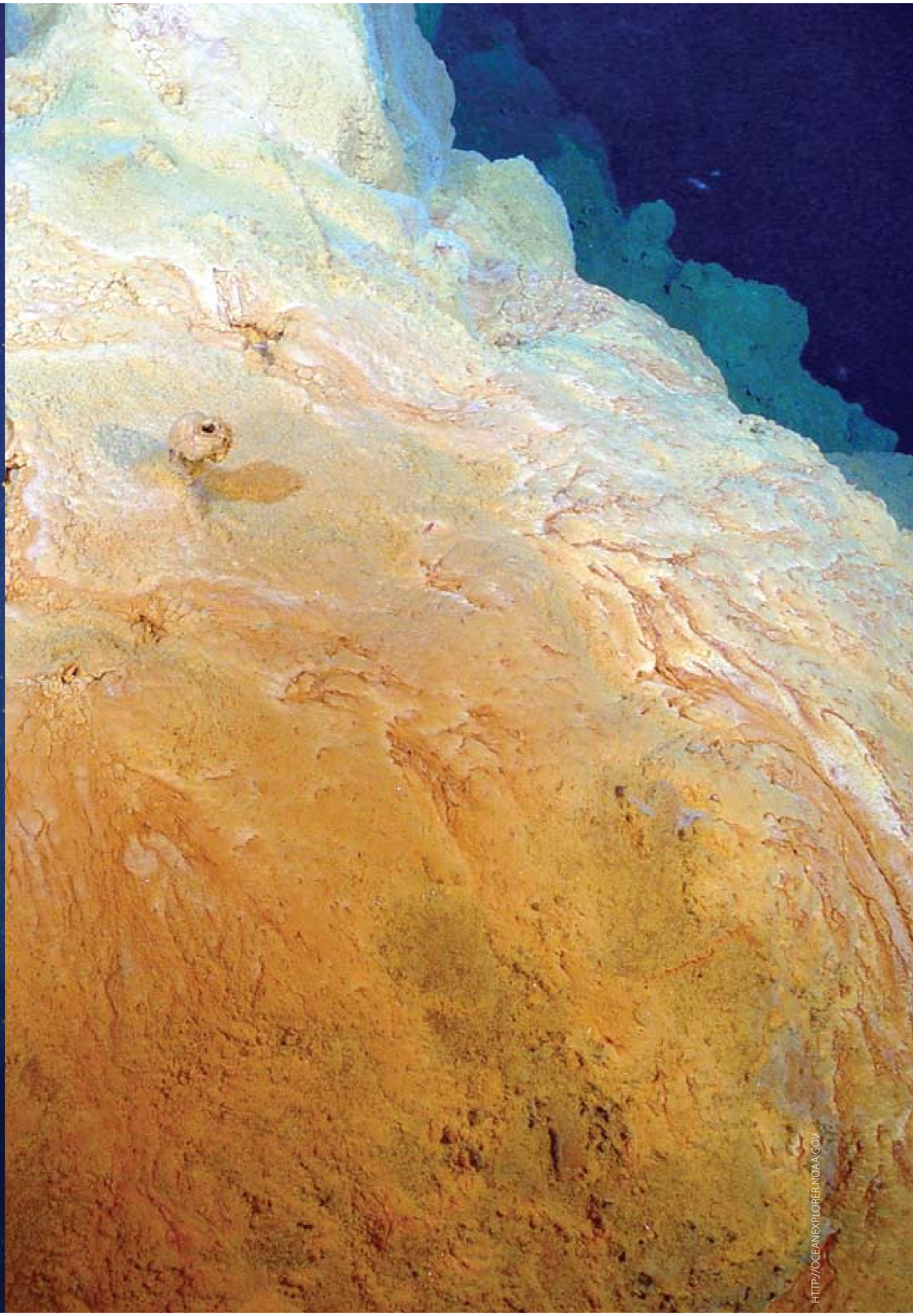
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Exploring Metabolic Pathways

SFI Omidyar Fellow Rogier Braakman brings a systems-level approach to reconstructing the deep evolutionary history of life. Braakman's interest in how chemical organization evolves prompted his graduate research in interstellar chemistry and led him to join SFI's 2006 Complex Systems Summer School in Beijing. Due to his interest in the bridging of the abiotic-biotic gap, he was drawn to Morowitz's and Smith's work. On a colleague's encouragement, Braakman contacted the two, who invited him to SFI in 2008. They've been working together on this puzzle ever since.

In contrast to traditional approaches to evolutionary history, which largely involve poring over the countless branches of the phylogenetic tree, Braakman took another approach. In his effort to map innovation of core metabolism through the biosphere, he focuses on the handful of core metabolic pathways that diversified around the split of the bacteria and archaea, traditionally the two main branches of the tree of life.

Braakman's recent work with Smith and Morowitz combines the constraints of physics and chemistry in developing an empirical framework that ties phylogenetics to metabolism. They hope to use it to determine what metabolic strategies organisms used at divergent points in the evolution of capturing carbon and turning it into biologically useful molecules. "If you can show how these pathways are related, and what guided their evolution, you can say a lot about the nature of life and evolution," says Braakman.

Like the bewildering, chaotic array of components and energy from which life emerged, the journey to an origin of life theory has leapt and stumbled through wild advancements and missteps amid overwhelmingly diverse efforts.

We couldn't be at our current stage of understanding without dozens of breakthroughs that have accumulated in all the areas that bear on the origin of life, Smith points out.

"Only in the last 30 years have fast computing and massive storage come together to bring deeper understanding," he adds.

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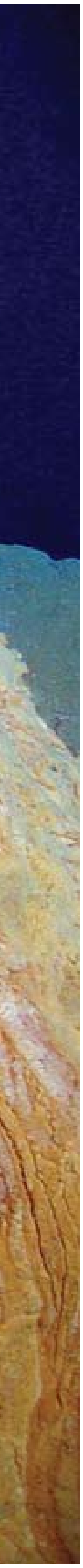
"Advances in statistical physics, genetic sequencing, and much richer understanding of interstellar chemistry, geochemistry, and biochemistry have brought us to the point where scientists can see from all sides how natural systems might have pushed, or pulled, life into existence."

Throughout the journey, "a lot of this work has been accomplished by researchers patiently trying to thoroughly understand particular systems, not expecting that a few 'big ideas' should command all the focus," he says. In other words, the next generation of SFI thinkers are well positioned to discover just how Earth's systems converged to squeeze life out of rock. ◀

Krista Zala is a freelance science writer in Victoria, BC Canada, who balances computer-screen time with guiding kayak trips on the British Columbia coast.



Left: Hydrothermal vents and chimneys reside on the ocean floor. Upon examining the organisms thriving amid the scalding temperatures released from them, researchers found some of the deepest-branching organisms on the tree of life. These included bacteria that ran the citric acid cycle—but in reverse. Image courtesy of the New Zealand American Submarine Ring of Fire 2007 Exploration.

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