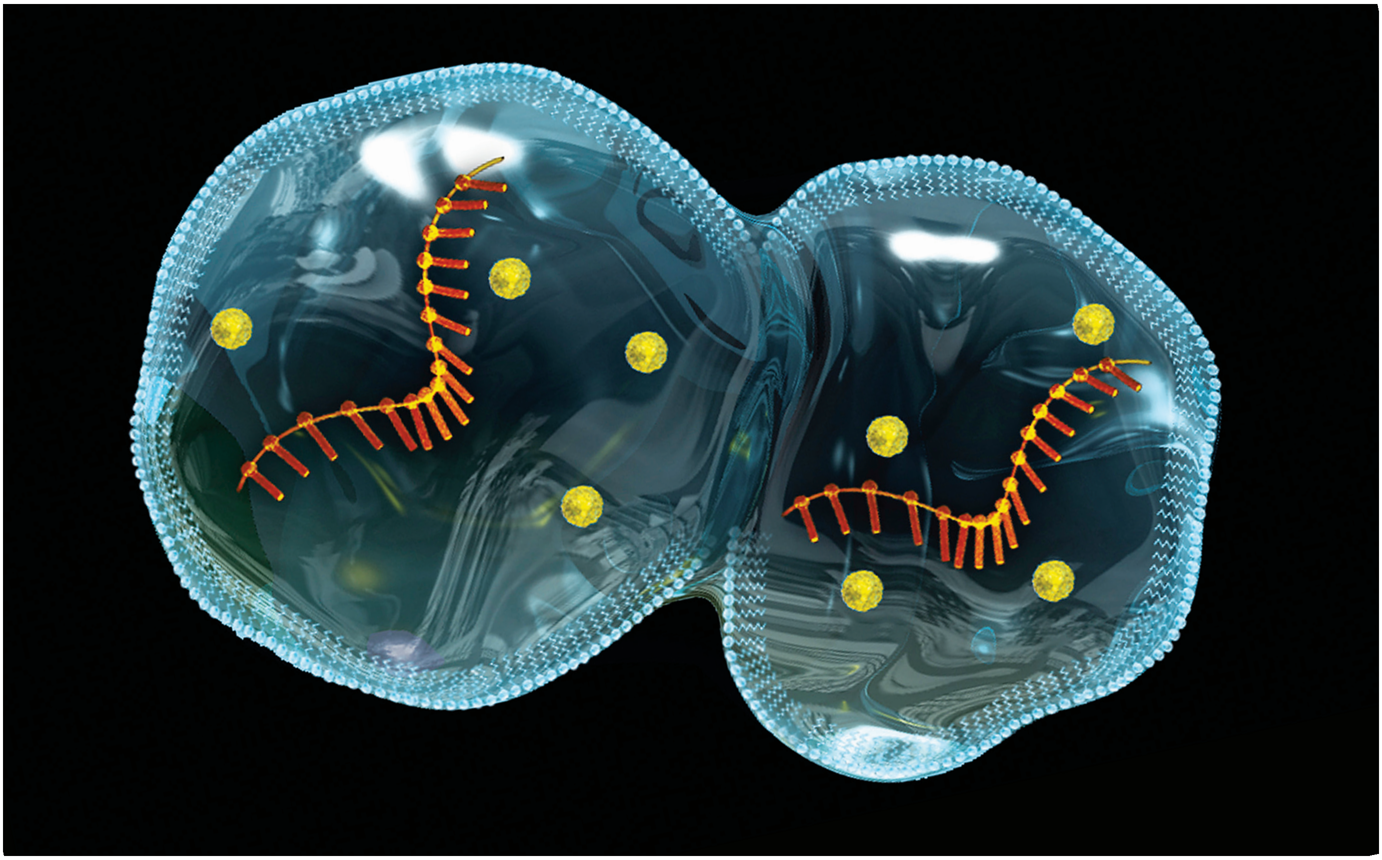


HENNING DALHOFF/SPL

An artist's impression of early 'protocells' proliferating.

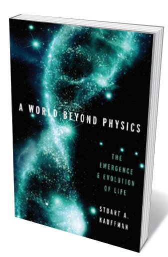
ABIOGENESIS

A new lens on life's origins

Stuart Kauffman's provocative book energizes **Sara Imari Walker**.

Among the great scientific puzzles of our time is how life emerged from inorganic matter. Scientists have probed it since the 1920s, when biochemists Alexsandr Oparin and J. B. S. Haldane (separately) investigated the properties of droplets rich in organic molecules that existed in a 'prebiotic soup' on the primitive Earth (see T. Hyman and C. Brangwynne *Nature* **491**, 524–525; 2012). Each hypothesized that organic compounds underwent reactions leading to more complex molecules, and eventually to the first life forms.

What was missing then, as now, is a concrete theory for the physics of what life is, testable against experiment — which is likely to be more universal than the chemistry of life on Earth. Decades after Oparin and Haldane, Erwin Schrödinger's 1944 book *What Is Life?* (see P. Ball *Nature* **560**, 548–550; 2018) attempted to lay conceptual foundations for such a theory. Yet, more than 70 years and two generations of physicists later, researchers still ponder whether the answers lie in unknown physics. No one has led the charge on these questions quite like Stuart Kauffman.



A World Beyond Physics: The Emergence and Evolution of Life
STUART A. KAUFFMAN
Oxford University Press (2019)

In the 1980s and 1990s, Kauffman — a complex-systems researcher — developed a highly influential theory for life's origins, based on molecules that reproduce only collectively, called autocatalytic sets. He posited that if a chemical soup of polymers was sufficiently diverse, these sets would emerge spontaneously as a phase transition — that is, a significant change in state or function, akin to the shift from solid to liquid. The sets function holistically, mutually catalysing the formation of all their molecular members. (His inspiration was advances in the mathematics of networks by Paul Erdős and Alfréd Rényi, who had demonstrated how phase transitions occur in random networks as connectivity is increased.) Now, in *A World Beyond Physics*, Kauffman elaborates.

His key insight is motivated by what he calls "the nonergodic world" — that of objects more complex than atoms. Most atoms are simple, so all their possible states can exist over a reasonable period of time. Once they start interacting to form molecules, the number of possible states becomes mind-bogglingly massive. Only a tiny number of proteins that are modestly complex — say, 200 amino acids long — have emerged over the entire history of the Universe. Generating all 20^{200} of the possibilities would take aeons. Given such limitations, how does what does exist ever come into being?

This is where Kauffman expands on his autocatalytic-sets theory, introducing concepts such as closure, in which processes are linked so that each drives the next in a closed cycle. He posits that autocatalysing sets (of RNA, peptides or both) encapsulated in a sphere of lipid molecules could form self-reproducing protocells. And he speculates that these protocells could evolve. Thus, each new biological innovation begets a new functional niche fostering yet more innovation. You cannot predict what will exist, he argues, because the function of everything biology generates will depend on what came before, and what other things exist now, with an ever-expanding set of what is possible next.

Because of this, Kauffman provocatively concludes, there is no mathematical law that could describe the evolving diversity and abundance of life in the biosphere. He writes: "we do not know the relevant variables prior to their emergence in evolution." At best, he argues, any 'laws of life' that do exist will describe statistical distributions of aspects of that evolution. For instance, they might predict the distribution of extinctions. Life's emergence might rest on the foundations of physics, "but it is not derivable from them", Kauffman argues.

> *"The function of everything biology generates will depend on what came before."*

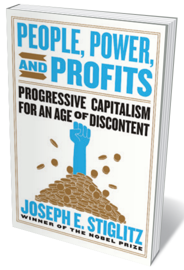
If biology cannot be reduced to physics, however, is it "beyond physics", as Kauffman claims? This is an interesting time to work on life's origins: there is intensive debate in the field about whether current physics is adequate, or whether new principles are necessary. Will a deep understanding of life ultimately come from comprehending how form and function arise from flows of information? Will life be understood only as a planetary-scale process, fundamentally linked to exoplanet sciences? Or will merging theory and experiment lead to new approaches to creating artificial life? Those approaches are being developed as an international effort, which coalesced in the 2015 conference Re-Conceptualizing the Origins of Life, drawing researchers from institutions including the Santa Fe Institute in New Mexico, the Earth-Life Science Institute at the Tokyo Institute of Technology and Arizona State University in Tempe.

WITHIN, NOT BEYOND

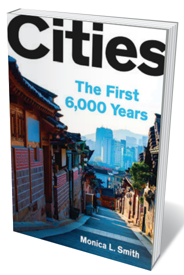
I agree with Kauffman that life cannot be explained by our current laws of physics, but dispute his argument that the explanation is 'beyond' physics. The distinction might be semantic, but it is important.

Physics has already grown far beyond simply describing aspects of reality, such as the very big (astronomy, cosmology), the very small (quantum systems, particle physics) or the human-sized (mechanics, as studied by Galileo Galilei and Isaac Newton). Interesting work is emerging from the study of complexity in areas such as economics, electronics, climate physics, the science of societies and non-equilibrium thermodynamics. ▶

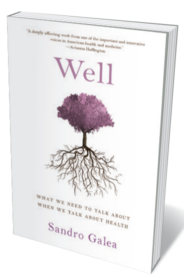
Books in brief



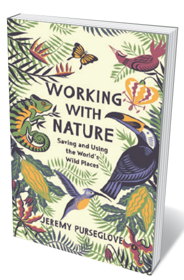
People, Power, and Profits
Joseph E. Stiglitz W. W. NORTON *(2019)*
The US economy is in thrall to corporate monopoly, inequality and slow growth — so argues Nobel-prizewinning economist Joseph Stiglitz in this powerful, grounded analysis. Excoriating supply-side "voodoo economics", Stiglitz proposes a progressive agenda echoing those of presidents Theodore and Franklin Delano Roosevelt. This aims to build shared prosperity by managing globalization, supporting basic research and reforming taxation and the judiciary. A country's might, he reminds us, lies in scientific advance, education, the rule of law — and the "countervailing power" of the voting booth.



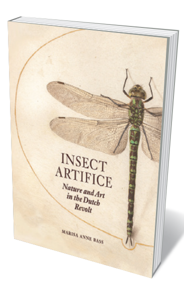
Cities: The First 6,000 Years
Monica L. Smith VIKING *(2019)*
Seedbeds of civilization and economic nodes, cities have thrummed with enterprise and wallowed in waste from the start, some 6,000 years ago. Archaeologist Monica Smith examines the evolution of urbanization through the lens of her field, showing the remarkable persistence of material and social norms — takeaway shops, upward mobility, crime and more. From digs such as Tell Brak in Syria and India's Sisupalgarh, Smith's journey explores methodologies and advances including magnetic gradiometry, but is at heart a revelation of the drive and creative flux of the metropolis over time.



Well
Sandro Galea OXFORD UNIVERSITY PRESS *(2019)*
US citizens top world spending on health, yet have shorter 'healthspans' than people in other rich countries. Why? Cogently and often movingly, epidemiologist Sandro Galea argues that an obsession with drugs, doctors and insurance obscures the fact that the roots of sickness and health are life circumstances: money, status, education, environment and a range of other socio-economic issues. With the richest 1% living for up to 15 years longer than the poorest 1%, investment in public goods such as education, universal health coverage and environmental regulation is ever more urgent.



Working With Nature
Jeremy Purseglove PROFILE *(2019)*
As a 'broker for nature conservation', Jeremy Purseglove has worked with developers in China, Ghana, Papua New Guinea, Tajikistan and beyond to ensure that engineering projects do not encroach on biodiversity. His compelling account, glinting with highlights from a nomadic life, is packed with case studies — whether successes such as integrated rice and fish cultivation in Bangladesh, or more sobering stories such as the agricultural enclosure sweeping Africa and the ongoing struggle to rejuvenate Central Asia's Aral Sea. A trove of experiential insight into on-the-ground sustainability.



Insect Artifice
Marisa Anne Bass PRINCETON UNIVERSITY PRESS *(2019)*
One of the most arresting natural-history works of the sixteenth century is a compendium of known animals depicted in exquisite miniature paintings. *Four Elements*, by Dutch merchant and artist Joris Hoefnagel, is a "stunning and eccentric assemblage" of knowledge, notes art historian Marisa Anne Bass. Her study beds the manuscripts in early-modern empiricism, and beautifully complements the plates — a jewel box of exquisitely rendered sunfish, chameleons, bees, an Indian elephant and more. **Barbara Kiser**

Such cross-disciplinary advances suggest that physics itself should not be defined merely by systems it has described in the past. It is a way to view the world, one that values the most abstract, fundamental and unifying descriptions of reality, from atoms to the Universe.

Within that span is biological and technological complexity in phenomena from humans to cities. So far, this has been the hardest area in which to gain traction from first-principles approaches, because of the density of interactions across components and scales. The question of whether there is a physics of life demands that we consider that all examples of life might at their core be part of the same fundamental phenomenon; otherwise, 'life' is not an objective property, but a collection of special cases. This unified view seems to be in line with what Kauffman is after. But it suggests that an explanation might demand new physics.

STATISTICAL POWER

The unifying thread that explains life could be something statistical, as Kauffman proposes, and still have 'law-like' properties. After all, some physical laws are statistical by nature, such as the second law of thermodynamics.

But conventional approaches to life's origins — such as the 'RNA world' and other genetics-first models — cannot yet be formulated in this way. That is because they make many assumptions on the basis of properties that might be unique to the chemistry of life on Earth, such as that RNA is necessary to life's origins.

The emerging areas of 'messy chemistry' and artificial-life approaches to origins research start from bottom-up chemical mixtures with minimal assumptions about what emerging life might look like. (The chemist Lee Cronin, for example, experiments on self-assembly and self-organization in large molecules such as metal oxides.) In this sense, the field is attempting to take an ensemble approach, and could provide new paths for developing theories on the universal principles bridging non-organic matter and life. It might inspire the next conceptual leap.

In a way that only he can, Kauffman has asked the questions we need to solve the mystery of life and its origins. But there is much work for the next generation to do to answer them. ■ SEE NEWS & VIEWS P.47 AND LETTER P.104

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The Eagle Nebula's 'Pillars of Creation', by the NASA/ESA/Hubble Heritage Team (2015).

PHOTOGRAPHY

Curating the cosmos

Amelia Hennighausen extols a tome on how ever-evolving photography has captured the glory of scientific phenomena.

CORRECTION

The Books & Arts article ‘A new lens on life’s origins’ (*Nature* **569**, 36–38; 2019) should have said that there are 20^{200} possible proteins 200 amino acids long.