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Physicist Erwin Schrödinger also probed questions of molecular biology.

IN RETROSPECT

What Is Life?

Philip Ball revisits Erwin Schrödinger's influential book, which crystallized key concepts in modern biology.

In *What Is Life?* (1944), Austrian physicist and Nobel laureate Erwin Schrödinger used that (still-unresolved) question to frame a more specific but equally provocative one. What is it about living systems, he asked, that seems to put them at odds with the known laws of physics? The answer he offered looks prescient now: life is distinguished by a "code-script" that directs cellular organization and heredity, while apparently enabling organisms to suspend the second law of thermodynamics.

These ideas inspired the public and a number of scientific luminaries, but exasperated others. Although their elements were not original, the formulation brilliantly anticipated Francis Crick and James Watson's discovery in 1953 of how DNA's double helix encodes genes. As Crick wrote to Schrödinger that year, he and Watson had "both been influenced by your little book".

What Is Life? The Physical Aspect of the Living Cell
ERWIN SCHRÖDINGER
Cambridge University Press (1944)

Elegant and accessible, *What Is Life?* grew from a series of enormously popular public lectures that Schrödinger gave at Trinity College Dublin in 1943, in the depths of the Second World War. Exiled from Austria when it was annexed by Nazi Germany, Schrödinger had been invited to Ireland to help establish the Dublin Institute for Advanced Studies. (This September, Trinity will mark the lectures' anniversary with a conference called Schrödinger at 75 — The Future of Biology.)

Since the 1930s, biology had been turning from a largely descriptive science into one concerned with mechanism. Thanks to studies such as those by geneticist Thomas Hunt Morgan on fruit flies, researchers were starting to understand heredity in terms of the transmission of genes, envisaged as large molecules arranged on chromosomes. Many expected genes to be proteins. However, even as Schrödinger was preparing his lectures, the microbiologist Oswald Avery was finding evidence that they were nucleic acids. Thus, *What Is Life?* dropped into a tumultuous time for science as well as for sociopolitics.

Schrödinger steps into these cross-disciplinary waters cautiously. He declares himself a "naive physicist", pondering how life sustains itself and transmits genetic mutations stably across generations. His work on quantum mechanics had earned him a Nobel prize in 1933, but that was hardly qualification for commenting on biology, in which Schrödinger had previously shown little interest beyond forays into the physiology of vision. Arguably, that naivety is the source of the book's strengths as well as its weaknesses.

The puzzle in the title stemmed from how physicists and chemists then thought of the molecular world, as wholly governed by statistical behaviour. In the classical molecular physics of James Clerk Maxwell and Ludwig Boltzmann, atomic motions are random (see E. Schrödinger *Nature* **153**, 704–705; 1944). Precise, robust physical laws, such as those linking the temperature, pressure and volume of a gas, emerge from the average behaviour of countless atoms.

How, in that case, can a specific macroscopic outcome — a phenotype, an organism's observable inherited traits — arise from an individual genetic mutation at the molecular level? Here, perhaps, is a ghost of Schrödinger's cat, formulated in 1935, whose macroscopic life or death hinges on a single quantum event. (Mathematician Roger Penrose has said of the thought experiment that "it would not surprise me if Schrödinger had something of this issue partly in mind" when he wrote *What Is Life?*.) Looking at an inherited characteristic (such as the protruding lower jaw common among members of Europe's Habsburg dynasty), Schrödinger asks how the allele responsible remained "unperturbed by the disordering tendency of the heat motion for centuries?".

Here, he cites experiments by another former quantum physicist, Max Delbrück, whose use of high-energy radiation to induce genetic mutations allowed him to estimate a gene's size at around 1,000 atoms. Schrödinger claims that this seems too small for "lawful activity" — durable inheritance — to persist in the face of statistical fluctuations. But he asserts that quantum mechanics can explain the matter. Atoms in molecules can typically be arranged in many stable ways, and each configuration has an associated energy; this is how Schrödinger envisages different gene alleles. But "quantum jumps" between them are generally inhibited by high energy barriers.

He goes on to propose that such gene-encoding molecules (he was among those who suspected that they were large proteins) have enough potential variety in their configurations to encode huge amounts of information, and that this variety can furnish a cell's "code-script". The position of each atom matters, but the pattern does not repeat — hence his description of the molecules as being like an aperiodic (irregular) solid. It wasn't an entirely new idea; Delbrück had suggested something of the kind in 1935. And biologists Hermann Muller and J. B. S. Haldane had independently proposed that chromosomes might act as templates for their own replication, in the same way that new crystal layers build up on pre-existing ones.

"What Is Life? dropped into a tumultuous time for science as well as for sociopolitics."

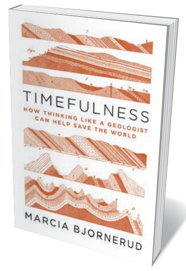
None of this, Schrödinger admits, answers the deeper question of "how the hereditary substance works" — that is, how it is used in development and metabolism, enabling an organism to build and sustain itself from moment to moment in what Schrödinger calls its "four-dimensional pattern" in space and time. But he makes a start on that issue by posing the question in thermodynamic terms.

This isn't a matter of energy (organisms' energy intake and output must be balanced, or they'd burn up), but of entropy, the measure of atomic disorder. The second law of thermodynamics states that entropy must increase in all processes of change. But organisms somehow stave off entropic dissolution. As Schrödinger put it, they feed on "negative entropy", using it to sustain the organization apparent in the structures and functions of cells, while paying their thermodynamic dues by heating the environment.

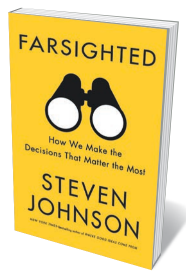
How they mine negative entropy, he could not say. He was forced to suggest that, in living systems, "we must be prepared to find a new type of physical law". Today, no such drastic solution seems to be needed.

The concept missing from his analysis is information. The information theory of Claude Shannon and the cybernetics of Norbert Wiener in the 1940s and 1950s began to fill that lacuna, although only more recently have researchers begun to understand how information truly features in biology. As Schrödinger's talk of negative entropy hinted, life is a pocket of out-of-equilibrium order in an open system, and the DNA code is just part of what sustains it. It's a shame that Schrödinger didn't touch on ▶

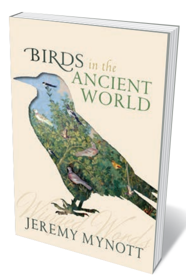
Books in brief



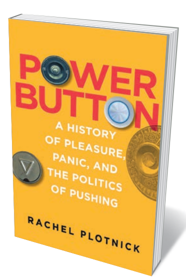
Timefulness
Marcia Bjornerud Princeton University Press *(2018)*
As a geologist, Marcia Bjornerud works in many time frames: the 4.5-billion-year history of Earth, the academic year, the daily grind. That layered perspective has made her aware of the short-term thinking common in a society wedded to political terms of office and the news cycle — all of which has, she argues, contributed to our inadequate, sometimes wrongheaded response to climate change. In this trenchant study, Bjornerud calls for a new geological literacy to instil deeper knowledge of planetary rhythms and processes — "thinking like a mountain", as ecologist Aldo Leopold put it.



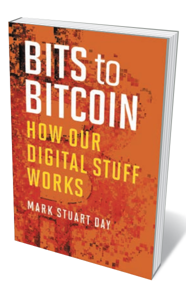
Farsighted
Steven Johnson Riverhead *(2018)*
Many researchers (notably psychologist Daniel Kahneman) have wrestled with the subtle mechanics of decision-making. Now, science writer Steven Johnson has his decisive moment, looking at the deep deliberations — mapping of variables, predictions of outcomes and balancing of aims and possibilities — that underpin life-changing choices. He draws on research and compelling examples, from George Eliot's 1871 novel *Middlemarch* (which examines the "threadlike pressure" on the deciding mind) to the supercomputer-based climate models now influencing climate-relevant decisions across the globe.



Birds in the Ancient World
Jeremy Mynott Oxford University Press *(2018)*
From nightingales trilling in ancient Rome's suburbs to the migrating cranes minutely observed by Aristotle in his fourth-century-BC *History of Animals*, birds pervaded early Mediterranean civilizations. Jeremy Mynott's masterful cultural and scientific history tours their roles as timepieces, soundscapes, pets, messaging services — even intermediaries with the supernatural. The vivid artworks and literary passages give this wings: here is the Greek poet Aratus on finches "chirruping shrilly at dawn" before a storm; there, a surreal Roman recipe for flamingo stewed with coriander.



Power Button
Rachel Plotnick MIT Press *(2018)*
Push buttons pop up on everything from blenders to aeroplanes. Yet, as Rachel Plotnick reveals in this unusual technological history, the mechanism had an explosive impact on culture from its debut in the 1880s to the 1920s and beyond. The idea that huge machines or even bombs could be activated by a finger became a metaphor for human hegemony, and a source of fear and wonder. And, as Plotnick notes, some 'buttonized' inventions (such as the electrified tie pin) may be defunct, but in an era of nuclear weaponry and disruptive leadership, one-touch technology still has the power to shock.



Bits to Bitcoin
Mark Stuart Day MIT Press *(2018)*
In this methodical primer, technologist Mark Day examines the computational infrastructure — the elements that underlie the workings of digital devices and networks. He unpicks operating systems, examines processes, explains esoteric defensive techniques such as cryptography and reveals Bitcoin to be an "intriguing combination of self-interest and mathematics". If you want to know why data streams turn lumpy when compressed, or yearn to get inside the cloud, a handy reference awaits. **Barbara Kiser**

fellow physicist Leo Szilard's work on Maxwell's demon, a thought experiment that revealed how entropic disorder could be undone by making use of molecular-level information that looks like mere statistical noise at the macroscopic level.

What's more, Schrödinger gave his code-script too much agency by imagining that its readout was mapped directly onto the phenotype. This isn't how it works: you can't read the arrangement of the body's organs in the genome. The information functions as a resource, not a step-by-step guide. To acquire meaning, it must have context: a cell's history and environment. Tracing how the phenotype emerges from interactions of genes with each other and with their environment is the key puzzle of modern genomics.

What is Life? helped to make influential biologists out of several physicists: Crick, Seymour Benzer and Maurice Wilkins, among others. But there's no indication from contemporary reviews that many biologists grasped the real significance of Schrödinger's code-script as a kind of active program for the organism. Some in the emerging science of molecular biology were critical. Linus Pauling and Max Perutz were both damning about the book in 1987, on the centenary of Schrödinger's birth. Pauling considered negative entropy a "negative contribution" to biology, and castigated Schrödinger for a "vague and superficial" treatment of life's thermodynamics. Perutz grumbled that "what was true in his book was not original, and most of what was original was known not to be true even when the book was written".

Although these judgements are uncharitable, they are not without substance. Why, then, was the book so influential? Rhetorical theorist Leah Ceccarelli argues that it was down to Schrödinger's writing style: he managed to bridge physics and biology without privileging either. But today, we can find more than that. Schrödinger's thoughts on the entropic balance of life can be regarded as precursors to studies of how biological prerogatives such as replication, memory, ageing, epigenetic modification and self-regulation must be understood as processes of non-equilibrium complexity that cannot ignore the environment. It is intriguing that similar considerations of environment and contingency are now seen to be central in quantum mechanics, with its ideas of entanglement, decoherence and contextuality. Whether this is more than coincidence, we can't yet say. ■

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SECURITY

How smart connectivity is stupider by design

Steven Aftergood assesses a warning about the future of the Internet.

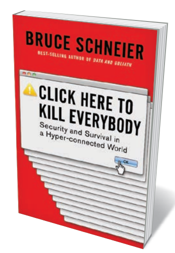
Hardly a day now passes without reports of a massive breach of computer security and the theft or compromise of confidential data. That digital nightmare is about to get much worse, asserts security technologist Bruce Schneier in *Click Here to Kill Everybody*, his critique of government inertia on Internet security.

The burgeoning threat, writes Schneier, arises from the rapid expansion of online connectivity to billions of unsecured nodes. The Internet of Things, in which physical objects and devices are networked together, is well on its way to becoming an Internet of Everything. Over the past decade or so, a growing number of products have been sold with embedded software and communications capacity: household appliances, cars, medical instruments and even clothing can now be monitored and controlled from afar. More of the same is on the way, as smart homes yield to smart cities and automated systems assume a larger role in the management of critical infrastructure. The Stuxnet computer worm used to attack Iran's uranium-enrichment programme remotely in 2010 was an early, audacious indicator of the threat.

Enhanced global connectivity has many advantages for knowledge sharing, commerce and convenience. Securing it, however, is a daunting prospect. The all-too-familiar vulnerability of computer networks — their susceptibility to failure, disruption and interference by malware, viruses and other factors — is amplified as practically everything becomes computerized. That relentless expansion of cyberspace into the physical domain brings with it new threats to power systems, mass transportation, public health and safety, and even political institutions, as effectively demonstrated by the Russian information operations that targeted the 2016 US presidential election.

"When the Internet starts killing people it will be regulated."

Despite its lurid title, Schneier's book is sober, lucid and often wise in diagnosing how the security challenges posed by the expanding Internet came about, and



Click Here to Kill Everybody: Security and Survival in a Hyper-connected World
BRUCE SCHNEIER
W. W. Norton (2018)

in proposing what should (but probably won't) be done about them.

As he notes, security was not a primary concern in the early design of the Internet in the mid to late twentieth century. Developers of early efforts, from the US Department of Defense's ARPANET onwards, did not anticipate the Internet's explosive growth or coming role in global commerce and communication. Even today, there is little incentive to prioritize security above other concerns — so, for example, e-mails may or may not be from the sender named.

SURVEILLANCE CAPITALISM

Surprisingly to some, much of the business of the Internet is predicated on insecurity. 'Surveillance capitalism' — the collection of user data and its sale to advertisers and others — depends on vulnerable Internet practices, as does intelligence collection for national security and law enforcement. Governments act as if their need to monitor the Internet can be satisfied without any larger compromise of security. That, writes Schneier, is not so.

In principle, he explains, securing the Internet is straightforward, but it would demand concerted government action at each step. Financial incentives should be realigned to promote security and penalize failure by mandating that manufacturers disclose defects in commercial software, making them legally liable for defects. Security should be required in new devices, and rewarded through subsidies and tax breaks. Data should be encrypted to secure them against unwanted collection. Critical infrastructure — power grids, communications and transportation — should be protected by bolstering network security or disconnecting them from the network altogether.

Government agencies are fully aware that the expanding Internet "will create