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BOOK REVIEW

From butterflies to bits: A sweeping vision for the code of life

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What is life?: Five great ideas in biology
Paul Nurse
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Do you know any scientist-walks-into-a-bar jokes? As a computational biophysicist working with many types of scientists, I am only too familiar with such stereotypes of biologists, physicists, chemists, mathematicians, computer scientists, and engineers. Although some of these portrayals are reductionist and silly, others ring a little true because they reflect tools of the trade.

Biologists collect, catalog, describe, and annotate, necessarily focusing on small details. Physicists like grand theories, such as scaling laws, wave versus particle, or small versus large, and shy away from units and minutiae. Chemists occupy a middle ground between these two, practical about details but also relying on many natural laws to explain chemical reactions or environmental pollution. Mathematicians love to dream big and connect ideas and disciplines but are also content to spend a lifetime on one equation or theorem in their specialty. Computer scientists see beauty and value in algorithms and simulations to address both real and hypothetical problems. Finally, engineers are a practical bunch; they solve real-life problems as efficiently as possible.

In Paul Nurse's book *What is Life?*, the renowned biologist and 2001 Nobel Prize Winner in Physiology or Medicine successfully depicts life as an information message-processing pipeline by unveiling how the basic units of biology, the cell and the gene, are merged through the chemistry and physics concepts of evolution by natural selection and life as chemical reactions. On his wide canvas, Nurse brings to life the stories and breakthroughs of a cast of multidisciplinary scientists to argue how the elementary code imprinted in the DNA of every species on our planet is transformed by a feat of chemistry, physics, mathematics, computer science, and engineering into a complex entity. The bedrock on which this miracle of science occurs, our planet, thus produces self-sustaining life forms of bewildering variety through a linear flow of information from our genes shaped by our environment.

Nurse goes beyond this intriguing scientific assembly of life's passage. He argues that, because humans are unique in our ability to think and analyze, we have a strong responsibility to preserve our biosphere for generations to come. Thus, a beautiful yellow butterfly with elaborate veins and patterns that Nurse observed as a teenager and that propelled him on a quest to understand what it means to be alive, is connected to our vast network of living forms through the gene-based and environmentally shaped information pipeline. Our biosphere, which offers us life and sustenance, also requires us to take action to care for it and to preserve it to allow for future life.

In less skilled hands and voice, this visionary science journey could have been dry and inaccessible. Nurse, however, adroitly takes us on his wings to glimpse the small and large by weaving well-known stories about the scientists who made these discoveries and their key experiments that yielded breakthroughs.

We read about the 17th century Dutch tradesman Antonie van Leeuwenhoek's high-quality yeast drawings and the father of chemistry Antoine Lavoisier's studies of basic chemical reactions, such as those that transform sugarcane to alcohol. Following on their footsteps, circa 1857, French biochemist Louis Pasteur

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came to the rescue of an industrial alcohol producer concerned that some fermented sugar beet in his distillery soured instead of producing ethanol; Pasteur showed that the single-cell microbe yeast was essential for alcohol-making chemical reactions and, hence, the solution to a good Chardonnay or Pinot Noir. Instead, vats that soured lacked yeast but contained other microbes that produced lactic acid, an impediment to a good glass of vino.

We visit Gregor Mendel's abbey garden in the Czech town of Brno, where pea-breeding experiments accented by statistical analysis around 1860 led him to define genes as discrete hereditary physical units. Nurse takes us along Charles Darwin's 1830s Beagle voyage, where systematic observations were gathered to support evolution by natural selection. We read about the pneumonia bacterial infection experiments by American microbiologist Oswald Avery in 1944 (with collaborators Colin MacLeod and Maclyn McCarty), proving that the transformative agent is DNA and not proteins. After the DNA double-helix structure elucidation in the 1950s and early 1960s (which suggested mechanisms by which genetic information is passed) and the subsequent genetic code (which established the chemistry of life as an information flow), we arrive at Nurse's own yeast cell-cycle experiments in the 1970s that cracked the cell-signaling code. He showed how numerous chemical reactions, which control an information flow and signaling pathway within a complex living machine, define checkpoints and maintain orderly transformations to regulate cell division and development.

Although these and many other scientific discoveries and principles may be well appreciated, Nurse's integrative viewpoint and unique perspective of a brew shaped by a variety of pathways makes for a very satisfying and delightful read. The book, which grew out of the 2020 James Martin Memorial Lecture that Nurse delivered at Oxford University, is slim enough that it can be read over a lazy rainy afternoon. Nurse moves gradually from basic elements to ideas that progress to reveal ``principles that define life on Earth.''

The sweeping vision that Nurse builds to a crescendo can be encapsulated by the following concepts: 1) living organisms are self-organized, reproducing using basic hereditary units called genes; 2) life evolves by natural selection, through reproduction and variability shaped by our environment; 3) the cell is the basic structural and functional unit, responsive to its environment; 4) life is based on carbon chemistry, in which nucleic acids, proteins, and other biomolecules are connected by chemical reactions; 5) life relies on information management in which instructions encoded in these polymers are transcribed and translated to create three-dimensional living forms; and 6) all living forms are related by an interconnected network.

A key to Nurse's thesis is the message passing of biological information through cellular connections and signaling. The regulation of gene networks or human organs within one entity is analogous to a vast electronic circuit in which digital processing operates. Effective instructions, communication, and adaptive response to changes within these living machines are cues to achieving specificity and variety, including walking or thinking and avoiding disease.

A deeper understanding of such biological signaling through epigenetics is part of our related quest to diagnose and treat human disease. Epigenetics refers to events that do not change our DNA sequence but, rather, how it is processed in individual cells at specific times. This formidable discipline, which we are just beginning to explore using the treasure trove of genetic information from the Human Genome Project concerns gene regulation by silencing or editing. Such instructions can alter how the information encoded in our genes is processed, thereby allowing for very different expressions of traits or disease manifestation in individuals with identical genes.

Like a mathematical model, slight changes in input variables or instructions to process the given information can generate vastly different outcomes for this intricately wired network. In living systems, this difference can mean life or death. Nurse quotes Sydney Brenner, the father of molecular biology, shrewdly noting that ``Mathematics is the art of the perfect. Physics is the art of the optimal. Biology, because of evolution, is the art of the satisfactory.''

The notion that life on Earth is exquisitely connected via evolution and controlled by a complex interdependent network of information flow is not only a scientific thread; it serves as a political call for action. Nurse ends the book, completed during the early part of the coronavirus disease 2019 (COVID-19) pandemic, with a reflection on how all this knowledge and understanding of evolution by natural selection and biological information as a digital processor can be used to change our world. With scientific and medical research advances, including the genetic basis to diseases like some cancers and the complex life cycle of the COVID-19 RNA viral genome, we can induce tailored scientific and behavioral changes to alter outcomes. With gene editing or engineering tools like clustered regularly interspaced short palindromic repeats (CRISPR), novel antiviral therapy, and vigilant monitoring of symptoms associated with genetic diseases, we can fight genetic and degenerative diseases or new viral threats, as well as improve our environment and the quality of our lives. ``Make no mistake,'' Nurse cautions us. ``The value of science itself is not up for debate. The world needs science and the advances it can offer."

Likely because of the COVID-19 pandemic, artists and scientists have been particularly focused on our own existence as of late. Carl Zimmer's book, *Life's Edge: The Search For What It Means to Alive*, ponders similar questions to Nurse's and provides us stories of scientists who defined key signposts in metabolism, evolution, origin of life, viruses, and other breakthroughs that defined life's components. The recent novel *Real Life*, by Brandon Taylor, relates the story of a biochemistry minority student from Alabama who is trying to find emotional and physical connections with his fellow students at a university in the Midwest as he dissects and conducts gene-engineering worm experiments in the lab. The touching new autobiography *How to Be Human: An Autistic Man's Guide to Life*, by Jory Fleming with Lyric Winik, describes the painful story of what it is like to live inside a gifted but different mind, the mind of the first young adult with autism to attend Oxford University as a Rhodes Scholar. However unrelated by subject or intention, these recent books remind us how complex it is to be human and how fundamental this quest for life's secrets is. Both Nurse and Zimmer acknowledge the physicist Erwin Schrödinger, who searched for the meaning of life in his 1944 groundbreaking book *What is Life?* and whose ideas on order-from-disorder and chaos on a small scale combined with physical laws on a large scale have so far stood the test of time.

Nurse concludes that, because as far as we know, humans are the only species who can analyze our own lives and the world around us, we owe to it not only preservation but improvement. This responsibility bestowed upon us ends a beautiful and reflective gem of a book with a heavy but important missive. Whether you think like a biologist, physicist, chemist, mathematician, computer scientist, engineer, artist, writer, or other, the privilege to be here and the duty to make our planet a better place is shared by all in our complex interconnected world.

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