EMERGENT PHENOMENA—A MISSING PHYSICAL PRINCIPLE

TO THE EDITOR: Peter Macklem (1) makes important points relating to life most cogently. What we observe on the surface of the earth is most decidedly not what we might immediately predict from the Second Law of Thermodynamics, and this arises only through the constant supply of energy. In a sense, however, this is a permissive explanation—it says that we may observe ordered systems, but not necessarily that we should. Why should we observe ordered systems? At the heart of this lies an asymmetry. On the one hand, disordered configurations have the potential through their very nature (disordered) to self-replicate. It is this asymmetry that allows imposition of order onto disorder and that generates the phenomena that we observe on earth. Within his article, Peter Macklem (1) describes autocatalytic sets in peptide chemistry as examples of such systems that have been generated in the laboratory. We lack, however, a more abstract understanding of the process. Questions include what sorts of objects and interactions have to be present for self-replicating systems to develop; how big do such sets have to be; how long do interactions have to run; and, so important to life, how do hierarchical layers of self-replicating systems develop? In this sense, life should be seen as the remarkable result of some physical law concerning a fundamental asymmetry between order and disorder.

REFERENCES

Peter A. Robbins
Academic
Department of Physiology, Anatomy and Genetics
University of Oxford

EMERGENT THOUGHTS ON THE SECRETS OF LIFE

TO THE EDITOR: Man has always speculated on the secrets of life. For millennia, explanations invariably touched on the supernatural. But in 1944, Nobel Prize-winning physicist Erwin Schrödinger (3) attempted an answer based on chemistry and physics. He proposed two essential ingredients: order from disorder and that maintains life. Whether these thoughts are meaningful, they constitute emergent phenomena in the author’s brain arising in response to the non-equilibrium constraints Dr. Macklem’s provoking essay has generated.

REFERENCES
EMERGENT PHENOMENA

TO THE EDITOR: Macklem’s definition of “emergent phenomena” lists features we biologists intuit, but it is not a settled issue in physics where many come close to denying the importance of emergence because everything ultimately rests on quantum field theory. Philip Anderson and Steven Weinberg, both Nobelists in physics, have taken strongly contrasting positions on reductionism and emergence. I think discussion of the issue should begin with them.

Macklem invokes some almost ritual citations to make his points, viz., to Schrödinger, Prigogine, Kauffman, slime molds, and the Second Law. Like emergence, the Second Law is not warmly welcomed by physicists; many regard it as merely a statistical feature of non-equilibrium macroscopic fields not evident microscopically. (The great theories of physics deal mainly with conservative fields where the Second Law plays little or no role.)

In biology, time has a direction from past to present to future. In powerful physical theories, time is isotropic, reversible in the laws.

These three disjunctions between biology and physics may seem to justify the phrase “secret of life” in Macklem’s title, but there are many versions of the “secret,” from autopoiesis to Boolean networks on the edge of chaos. They address varying but there are many versions of the “secret,” from autopoiesis to cellular fields theory. Philip Anderson and Steven Weinberg, both Nobelists in physics, have taken strongly contrasting positions on reductionism and emergence. I think discussion of the issue should begin with them.

Macklem invokes some almost ritual citations to make his points, viz., to Schrödinger, Prigogine, Kauffman, slime molds, and the Second Law. Like emergence, the Second Law is not warmly welcomed by physicists; many regard it as merely a statistical feature of non-equilibrium macroscopic fields not evident microscopically. (The great theories of physics deal mainly with conservative fields where the Second Law plays little or no role.)

In biology, time has a direction from past to present to future. In powerful physical theories, time is isotropic, reversible in the laws.

These three disjunctions between biology and physics may seem to justify the phrase “secret of life” in Macklem’s title, but there are many versions of the “secret,” from autopoiesis to Boolean networks on the edge of chaos. They address varying aspects of the mystery of life, but not the core. Meanwhile, “The Secret sits in the middle and knows” (Robert Frost).

The best part of the article is the figure. However, I would position LIFE closer to equilibrium. Biological processes mostly run smoothly with low duty cycles—they don’t “knock.”

REFERENCE


F. Eugene Yates
Department of Medicine
University of California, Los Angeles

EMERGENCY MEDICINE

TO THE EDITOR: Macklem (1) hits the nail on the head when he identifies emergence as the key mechanism underlying life and disease. Indeed, emergent phenomena are manifest at every level of scale in both space and time (2), which is what gives richness to our existence. Without complex, nonlinear and dynamic interactions between multiple entities, the universe would be a pretty boring place, and we would be too boring to notice. Fortunately, nature has seen to it that complex emergent phenomena abound, ensuring that we shall be trying to understand them for a very long time. In fact, the challenge of understanding the grand emergent phenomena of life is so daunting that it takes considerable moral fortitude to even look it in the eye; it is much safer to focus on circumscribed issues amenable to conventional investigative techniques. Nevertheless, at the end of the day, we still want to know how the body works, and how to fix it when it goes wrong. This is why Macklem’s essay is so important; medical science needs a broader perspective on disease than the conventional viewpoint that things ought to be fixable if we can just find the right magic bullet. In fact, an understanding of emergence may eventually teach us that some diseases are not fixable at all once they are underway. This would then fuel the growing trend toward preventative medicine, which is effectively the manipulation of biological emergence. In fact, this is really what we should be calling “emergency” medicine.

REFERENCES


Jason H. T. Bates
Professor of Medicine
University of Vermont
Letters To The Editor

1850

Peter comes and we begin to think in terms of complexity, we shall have to master vocabulary (4), tools and concepts, under penalty of generating confusion.

REFERENCES

RESPONSE TO MACKLEM’S VIEWPOINT “EMERGENT PHENOMENA”

TO THE EDITOR: Peter Macklem’s essay (3) raises questions related to the analysis of nonliving and living systems. Classic methods of statistical mechanics compute phase transitions in closed physical systems based on the minimization of free energy. Although Prigogine (4) extended these concepts to nonequilibrium systems “near equilibrium,” it has not been easy to predict organization in dynamic systems based on Prigogine’s principle of minimum entropy production.

Rather, changes of stability and dynamics in complex systems are analyzed using nonlinear dynamics. As parameters in nonlinear equations change, there may be a qualitative change of dynamics—a bifurcation (1).

Michael Mackey and I (2) used the term “dynamical disease” to capture the concept that qualitative changes in dynamics as a consequence of changes in the structure or parameters of physiological systems can lead to abnormal dynamics associated with disease. This approach continues to find rich applications: for example, it forms a foundation for theoretical and experimental studies of mechanisms of cardiac arrhythmias and sudden cardiac death (6).

Nonlinear dynamic concepts lend a definiteness to discussion of dynamic phenomena in living systems. To me the phrases “edge of chaos” and “living in a phase transition” are vague. A program for studying cellular and physiological dynamics is to formulate equations based on chemical kinetics and nonlinear control and to analyze the bifurcations in the dynamics using nonlinear dynamics. Of course, the multiple time and space scales combined with inevitable stochastic effects due to small numbers make this a challenge (5).

REFERENCES

Leon Glass
Isodore Rosenfeld Chair in Cardiology and Professor of Physiology
Department of Physiology
McGill University

LIFE, EMERGENCE AND ENTROPY PRODUCTION

TO THE EDITOR: Peter Macklem (2) challenges physiologists to grapple with “a deep understanding of life, not merely a description,” and invokes nonequilibrium thermodynamics as fundamental to this understanding. While the second law of thermodynamics explains why there is degradation of quality of energy available to do work, why nature seeks to break down gradients and why order tends to disorder, it also informs us that the process of emergence of internal order (negative entropy) within complex systems must be accompanied by export of even greater quantities of entropy to the environment, as net change in entropy must be greater than zero. Understanding life as entropy producing systems, we return to Peter Macklem’s provocative figure and the contention that “we the living exist in the phase-transition between order and chaos,” that is between near- and far-from equilibrium open-thermodynamic systems. While “phase transition” requires further clarification in this context, Macklem’s distinction between near and far-from-equilibrium systems is further supported with evidence regarding entropy production (3, 4). For systems near equilibrium with fixed boundary conditions, steady states are characterized by minimal entropy production (3), whereas non-linear systems far-from-equilibrium with no fixed boundary conditions select steady states characterized by maximal entropy production (1). Although not yet well characterized, living organisms appear to display optimal entropy production, further supported with evidence of optimal entropy production (3, 4). For systems near equilibrium with fixed boundary conditions, steady states are characterized by minimal entropy production (3), whereas non-linear systems far-from-equilibrium with no fixed boundary conditions select steady states characterized by maximal entropy production (1). Although not yet well characterized, living organisms appear to display optimal entropy production, tuned to changing environmental conditions, and variable metabolic needs for growth, reproduction, and repair. Understanding how and why entropy production is optimized, and indeed how it is altered by illness, represent critical components to addressing Peter Macklem’s insightful challenge.

REFERENCES

Andrew J. E. Seely
Clinician Scientist
Ottawa Health Research Institute

Thomas Similowski
Head of Respiratory Medicine and Intensive Care
Christian Straus
Marie-Noelle Fiamma
Université Paris 6, EA2397, Paris, France

