SCHRÖDINGER'S *WHAT IS LIFE?*: THE BIOPHYSICAL LEGACY 50 YEARS LATER

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Erwin Schrödinger's *What is Life?* (Cambridge University Press, 1944) is one of the most talked-about books in twentieth-century science. Most discussion in recent years has focused on its legacy in the area of molecular genetics. Notwithstanding, from my own reading of *What is Life?*, I am struck by three broad areas of enduring biophysical import outside the realm of genetics.

THERMODYNAMICS AND BIOLOGICAL ORDER

First, there is Schrödinger's discussion of thermodynamics and biological order. He reasoned that living systems maintain their internal organization by feeding on negative entropy (or " negentropy") from the environment. Most likely, this idea came from some late 19th-century writings of Boltzmann, in whose scientific shadow Schrödinger studied at the University of Vienna [1]. Perhaps unbeknownst to Schrödinger, Boltzmann's biological thinking had been recognized long before by Lotka, Rashevsky, and Bertalanffy (reviewed in [2]). While his biothermodynamical view may not have been original, Schrödinger's attention here was very perceptive. He was writing at a point in time when the union of nonequilibrium thermodynamics and biology was not yet consummated. In today's parlance, his point is that, for an open system (*e.g.*, a living cell), the total entropy change per unit time is split into the internal part (which is positive-definite) and an external (or transport) part, which must have a negative value to balance the internal part in the steady state. We have now come to realize that the dissipation of Gibbs energy (or the entropy production), measured intensively, is intimately related to the living state (reviewed in [2]). In recent decades, both the near-equilibrium [3] and the far-from-equilibrium [4] branches of thermodynamics have allowed us to rationalize the existence of life as an epiphenomenon of cosmic evolution. Schrödinger's *What is Life?* constitutes an early, perspicacious, and powerful recognition of this connection.

THE APERIODIC CRYSTAL

Second, there is Schrödinger's famous "aperiodic crystal" metaphor for depiction of genetic structure [5]. I read more into his usage of this metaphor than its application just to the molecular interpretation of the genome. Symmetry/asymmetry has come to be the most central *dynamical* element in 20th-century theoretical physics [6], and no doubt this conceptual background carried over into Schrödinger's generative view of the genome in biological organization. During the course of the 20th century, symmetry/asymmetry principles analogous to those in physics have found their way into the formulation of the hierarchical and dynamical properties of living systems (reviewed in [2]). The "aperiodic crystal" metaphor in biology can be traced to the 19th-century works of Pasteur and Curie [7]. While we cannot thank Schrödinger solely for the appearance of this paradigm in biology, his analogical thinking is noteworthy.

BIOLOGY AND NEW PHYSICAL LAWS

Third, there is Schrödinger's aspiration for a unification of physics and biology, with the emergence of new physical laws or principles as a by-product. In my opinion, this is the most profound and far-reaching message in *What is Life?*. There has been much development along this frontier over the last 50 years. One has only to open the pages, for example, of Paul Davies' book *The New Physics* (Cambridge University Press, 1989), to sense the exciting holism in present-day physics and the urgency in its merger with biology. Hopefully, such physicalist philosophy can counter the analytic reductionism which is running rampant in the "molecular biology" era of today. There is a prevailing tendency to reduce biology to chemistry and physics and to reduce life itself to mere "objects" (*e.g.*, DNA). We are on the wrong epistemological path. Rather, we should be following the issue of scientific unity from the standpoint of a *theory reduction* [8], whereby theoretical biology and theoretical physics are viewed as each subsumable to a larger, qualitative, all-encompassing theoretical edifice which can be unfolded in various empirical domains [9]. Indeed, pursuit of such theory unification is an occupation of present-day thinkers in both biology and physics (reviewed in [2]). I think Schrödinger would be happy at the direction in which this marriage is going [10].

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