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Mind over matter

From Strange Simplicity to Complex Familiarity: A Treatise on Matter, Information, Life and Thought by Manfred Eigen. Oxford University Press, 2013. US$225/£125/€148, hbk (715 pp.), ISBN 978-0-19-857021 9

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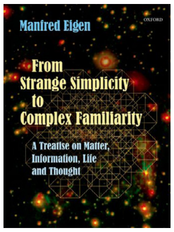

As an invited speaker at the Institute for Advanced Study in Princeton, Manfred Eigen once stood by as his host ran through an impressive list of accolades: his work as a young researcher measuring the rates of ultrafast chemical reactions, for which he shared the Nobel Prize in Chemistry in 1967; his directorship of the Max Planck Institute for Biological Chemistry in Göttingen; his contributions to understanding of the self-organization of prebiotic systems and the 'RNA world'; and his formulation of the quasi-species and hypercycle theories (together with Peter Schuster). 'Yes,' he added when the introduction was done, 'but you forgot to mention that I am also extremely modest!'

There is no need for modesty in Eigen's most recent publication *From Strange Simplicity to Complex Familiarity: A Treatise on Matter, Information, Life and Thought*. In this volume, as in his life's work, Eigen addresses the most fundamental yet challenging questions in science. This time, he asks (as some others, including Schrödinger [1], have before him): 'What is life?' Through incredible detail of both the history of scientific thought on the topic and of the specific theories and experiments that drove progress, Eigen details what we know about this mysterious entity called 'life', and how we know it.

As Eigen explains, the fundamental physical structures that comprise the matter of the universe exist as a consequence of particular physical laws. There is no particular physical structure that corresponds to life, neither is there any *a priori* division between living and nonliving matter. Instead, life is a type of behavior of matter. Life is governed by its function, not by its structure. This function is simply to continue to exist, in a constantly changing environment. This existence requires the ability to organize a particular piece of information, and then to be able to conserve, proliferate, vary, and select this information. Error-prone replication is a particular system that is capable of these tasks. As a result of the organization and replication of this information, particular logical structures may emerge, although the principles that govern these structures are only apparent *a posteriori*. There is a variety of possible structures that could satisfy the functions necessary of life. In understanding this interpretation, the reader is guided through chapters on matter, energy, entropy, information, and complexity.

Eigen frequently returns to the intersection of physics and biology, a boundary that he has straddled throughout his impressive career. He clarifies that there are two fundamentally different ways in which these disciplines can inform one another. In what is traditionally called 'biophysics', one tries to understand the physics behind the molecular structures that operate within living organisms. The double-helix architecture of DNA or the force generated by a myosin molecule [2] are examples. He coins 'the physics of biology' as having a different purpose, which is to understand the principles of information and complexity as they pertain to the existence of life. It is the latter issue that the book focuses on. With either approach, Eigen frequently reaffirms his belief in experimental inspiration and validation.

Eigen gives particular attention to his work with Peter Schuster during the 1970s that led to the development of one of the fundamental theories of evolutionary dynamics [3,4]. Now commonly known as 'quasi-species theory' [5], this work brought together the concepts of sequence space (the set of all possible genetic sequences of a particular length, arranged by their Hamming distance) and fitness landscapes to describe the outcomes of molecular evolution. It demonstrated that, depending on the mutation rate, the genome representing the global maximum in the fitness landscape might not be selected. Instead, the ensemble of mutants with the highest average fitness is selected, replacing the idea of 'survival of the fittest genome' with 'survival of the fittest quasi-species'. A key result was the discovery of the error threshold: if the mutation rate per base is higher than one over the sequence length, evolutionary adaptation is not possible. Eigen and Schuster delved further into the chemical complexity and mathematical formalization of evolution with their 'hypercycle' theories [4], describing a series of intricate and cooperative reactions undertaken by molecular replicators. The hypercycle can be seen as one of the first explorations of evolutionary game dynamics, and in fact generates a particular form of the now ubiquitous replicator equation [6]. Eigen addresses the open question of how such replication machinery itself came to be, and more recent work has suggested how the transition from chemical kinetics to evolutionary dynamics unfolded [7,8].

In looking to the future of the field, Eigen suggests that the grand challenge for the theory of life is to understand how evolution solves search problems in sequence space, which are of exponential complexity, in polynomial time. The information-based view of self-organizing biology that he promotes throughout his book certainly finds a use here.

Much more than being a collection of scientific facts, this book is a comprehensive history of scientific thought related to matter, life, and complexity. Eigen presents a lively

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chronology of the important thinkers and the big questions they asked, and the few that they managed to answer. It is fascinating to learn how these ideas have evolved over time, driven by new theories and new evidence. Given that many of these noteworthy figures are his contemporaries, Eigen can sprinkle his narrative with personal anecdotes and insights. He shares a memorable exchange prompted by Werner Heisenberg's reading of his early paper on biological self-organization. A few minutes after complementing Eigen's ideas on the origin of life, Heisenberg queried: 'Are you really sure that it was not the Lord?' Eigen quickly returned: 'Well, if it was the Lord, it must have been the same Lord who created your theory.'

Despite all appearances, this book is not meant to be the capstone to Eigen's brilliant career, but merely the first volume of a larger, forthcoming collection. Eigen's complete *magnum opus* is yet to be published.

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0169-5347/$ – see front matter
http://dx.doi.org/10.1016/j.tree.2013.10.004 Trends in Ecology & Evolution, February 2014, Vol. 29, No. 2

A primer of Darwinian medicine

Evolution and Medicine by Robert L. Perlman, Oxford University Press, 2013. US$49.50/£27.50/€31.35 pbk (xiii + 162 pp.), ISBN 978-0-19-966171-5

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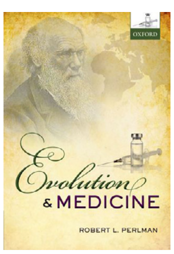

I have always been interested in how different disciplinary fields are merged and, since Williams and Nesse's landmark article that introduced us to evolutionary medicine [1], I have followed the field with rapt attention. Recently, I teamed up with a physician, Barbara Natterson-Horowitz, and co-founded UCLA's evolutionary medicine program. I spend a lot more time than I ever had before with physicians, and believe I am getting a boots-on-ground education in how one cultivates interdisciplinary discourse, as well as how one develops a pipeline to generate genuinely interdisciplinary advances. Evolutionary medicine is one of those fields where discourse and advances are sorely needed. In addition, this need is perplexing, if, for no other reason than, as Robert Perlman elegantly reminds us, Darwin studied medicine. However, since Darwin, the field of medicine has focused on individuals, not populations, and teaching new medical advances has edged out the strong comparative training that physicians used to have.

Perlman outlines his view of evolutionary medicine in a crisply written, 11-chapter primer. It is exceptionally accessible (a glossary defines some key terms) and I genuinely enjoyed reading it and believe that it will help students (of biology or medicine) understand why evolution matters for medicine, public health, and biomedical research.

The first few chapters provide background knowledge. Chapter 1 introduces readers to evolution and explains the different foci of most evolutionary biological research versus biomedical research (populations versus individuals). I think Perlman misses an opportunity to outline Niko Tinbergen's framework [2–4] and show how this can guide the integration of proximate and ultimate research, as Nesse and Stearns have done [5]. The chapter does highlight an insight that I had not realized: by explaining to patients the evolutionary explanations of disease, the patients might be less likely to explain them with unhelpful folk beliefs. Chapter 2 introduces readers to the importance of demography, which underlies human and pathogen population biology, and Chapter 3 is a succinct introduction to evolutionary genetics.

The remainder of the book focuses on specific maladies and highlights lessons that emerge from an explicitly evolutionary approach. Chapter 4 focuses on cystic fibrosis and tells us how a proper genetic identification is essential for the correct treatment and that even 'easy' genetic issues may be complex. Chapter 5 is a wonderful treatment of the evolutionary biology of aging and highlights the importance of understanding life-history tradeoffs. Chapter 6 focuses on cancer. Lessons include how understanding the ecology of the disease, as well as its precise genetic identification, may help. It also reminds us that tradeoffs (e.g., an adaptive immune system) may predispose us for certain cancers (e.g., leukemia). Chapter 7 is an outstanding guide to host–parasite coevolution and explains how virulence may often evolve and the conditions under which it may not. Chapter 8 focuses specifically on sexually transmitted diseases. The thought-provoking comment that a given human heterosexual encounter is more likely to lead to a sexually transmitted

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