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The Evolution and Emergence of RNA Viruses.—Edward C. Holmes, author. Oxford University Press, 2009. xii+254 pp. ISBN 978-0-19-921112-8. $130, £65 (hardback). ISBN 978-0-19-921113-5. $60, £29.95 (paperback).

Viruses traditionally have been marginalized from evolutionary biology, as noted in one of the first sentences of *The Evolution and Emergence of RNA Viruses*. Consequently, a central goal of Edward Holmes' (Center for Infectious Disease Dynamics, Pennsylvania State University) book is to show that they are as valuable a system to study evolutionary processes as are other model systems.

Although it is obvious that the specific questions addressed by evolutionary virologists often differ from those working in other fields, the basic evolutionary processes at play are very much the same, as well as the phylogenetic methods available. However, the study of RNA viruses, in particular, has two added bonuses. First, hypotheses can be tested far more directly and with more precision because virus evolution is so fast that it can be observed within months or even days. Second, the study of RNA viruses has immediate practical implications, as they constitute an important global health concern; some very well-known cases are the viruses causing AIDS, hepatitis C, influenza, measles, and dengue fever. In this sense, this new book is particularly timely.

The Evolution and Emergence of RNA Viruses may be viewed as a concise guide and also a good starting point for people with some background in evolutionary biology and who are interested in viruses. In general, the book deals with the "cause and consequence of evolutionary change in RNA viruses" and links the mechanisms of viral evolution within their hosts to the

epidemiological outcomes. Holmes warns us that his book focuses on evolutionary aspects, not on general, basic, or molecular virology. However, many different topics are covered in the form of snapshots. In 200 pages, there are nearly 100 subheadings, organized in seven chapters. At this scale, it is essential that a sufficiently large and carefully selected list of references be provided, as is clearly the case here.

Probably the central point made by Holmes is that comparative analyses and experimental data provide extensive evidence that RNA virus evolution is profoundly conditioned by their extremely high rates of spontaneous mutation, which are orders of magnitude higher than those of cellular DNA-based organisms (Drake et al. 1998). Such high rates impose a limit on genome sizes because otherwise the genetic load would become intolerably high. In turn, this implies that genetic information is densely stored and that most mutations are deleterious and pleiotropic. Therefore, despite being very rapid, RNA virus evolution is more constrained than is often thought. They may be considered, metaphorically speaking, as "restless beasts pacing a small cage" (Belshaw et al. 2008). The author discusses the many implications of this idea from the phylogenetic, population genetics, and epidemiological perspectives.

This driving argument is presented right from the start and is implicitly present throughout the book. Chapter 1 contains a brief but useful revision of the principles of viral biology. There are also some clear and well-explained figures of virus life cycles and the replication process. From then on, the focus moves to more specifically evolutionary topics, starting with discussion in Chapter 2 of the origins of viruses. This includes the pre-cellular theory, which considers viruses as remnants of an ancient RNA world, and two other theories that are less favored by the author: the regressive evolution theory and the escaped gene theory. However, extreme sequence divergence resulting from high mutation rates poses a big challenge to studies that try to resolve the deepest phylogenetic relationships among viruses and requires new methods in order to identify homologies, for instance at the level of protein structure. This constitutes a good example showing that the study of RNA viruses can motivate the development of new research tools of general interest.

Holmes convincingly argues that the processes of microevolution in RNA viruses are the key to understanding their macroevolution. The thorough Chapter 3 focuses on this microevolution, providing a well-structured and informative discussion of the usefulness of various measures of selective pressure and the factors that influence these pressures in RNA viruses. One section in this chapter reviews a selection of recent literature on the "arms race" between the genes involved in host immunity and RNA viruses. There is also a discussion of the role of complementation and defective interfering particles. The author then moves on to the roles of epistasis and RNA secondary structure, indicating that recent research suggests very important roles for the two phenomena in RNA viruses. The end of Chapter 3 deals with intrahost viral diversity, including a variety of useful examples.

Although some of the topics covered in this book converge with classical discussions in evolutionary biology, as for instance the roles played by natural selection and random genetic drift, others are more virus specific, yet also interesting for the wider audience. For instance, if the selection/drift debate has been called the "great obsession of population genetics" (Gillespie 1998), the quasispecies theory could be similarly termed the great obsession of evolutionary virologists. This theory, which describes the mutation/selection dynamics of highly mutable replicons, is very popular among virologists (Domingo 2006), but it also has prominent detractors, including Holmes. Chapter 4 discusses whether quasispecies are relevant to evolution of RNA viruses in nature. For those who are not familiar with this topic, the author first takes a few pages to provide a succinct definition and to describe the truly defining features of the theory. The widespread misuse of the term quasispecies in the scientific literature is clearly pointed out. The concept of lethal mutagenesis (Bull et al. 2007) is also introduced, together with experiments suggesting its usefulness as a therapeutic strategy against RNA viruses.

Chapter 5 moves from micro- to macroevolution, tackling some fundamental questions in viral evolution, starting with sections on the evolution of genome size, genome segmentation, genome orientation, and overlapping reading frames in RNA viruses. It then goes on to discuss allopatric and sympatric speciation in relation to viruses. The last two subsections of the chapter are on a birth–death model of viral evolution, discussing how phylogenetic tree topographies would vary by taking into account extant and extinct virus species. It ends with some interesting examples of how viruses have integrated into human genomes and the phylogeny and divergence times that can be inferred.

Extremely high mutation rates, a defining property of RNA viruses, imply that genetic changes at the population level occur so fast that the evolution and epidemiology of RNA viruses overlap in time. This has motivated the development of phylodynamics, a new area of research that attempts to achieve a synthesis between epidemiology and phylogenetics (Grenfell et al. 2004). These important notions are introduced in the first section of Chapter 6, which then considers the historical and geographic patterns of viral emergence. The following sections discuss cross-species transmission and illustrate how human history has shaped the population dynamics of various diseases. This smoothly leads us to Chapter 7, which provides case studies of the recent evolution of four high-profile RNA viruses: influenza A virus, HIV-1, rabies virus, and dengue virus. These examples also help illustrate the major points covered in the book. Lastly, Chapter 8 proposes future research priorities that would be useful for making better phylogenetic inferences.

In general, the text is accompanied by a good mix of graphs, maps, phylogenetic trees, and a variety of other

figures. On occasions, these are taken from the literature and updated to correct any known errors, making them valuable reference tools. Within each chapter, there is a balanced view of the arguments for and against various theories, combining a range of recent literature on each topic. Mechanisms of viral evolution are skilfully linked with disease dynamics, inciting the reader's interest with the aid of examples and bringing up some of what are perhaps the most interesting and topical issues and theories. This clearly was not an easy task, considering the quantity of unanswered questions in the field of viral evolution. Even though Holmes frequently is unable to come to definitive conclusions due to this lack of good evidence, he very often states a personal view on the subject and provides useful hypotheses for future testing.

If we are to find one drawback of this book, which the author himself acknowledges, it is that there is a clear focus on RNA viruses that infect humans. The bias comes not only from the fact that there are more data available for these viruses, but also from the author's own interests. This may slightly limit the book's flexibility by not targeting readers who are interested in other types of RNA viruses. On the other hand, this problem reflects the current state of affairs, where data availability is probably the main factor limiting our progress. Surely, the advent of higher-throughput sequencing technologies will rapidly remove this barrier. Another thing that is perhaps missing is a glossary of the main terms, to allow for quick reference or as a means of rephrasing, and giving more examples of concepts for those who seek more clarification after reading the text, especially for some of the more complicated terms of population genetics.

Omissions aside, *The Evolution and Emergence of RNA Viruses* would be a useful addition to the bookshelves of academicians and researchers. The combination of topical examples, appropriate and useful diagrams, and manageable scope are also sure to attract young researchers and graduate-level students. It can also be viewed as an aid to help students understand the interconnections between different areas of biology. Holmes manages to bring together evolutionary biology, epidemiology, virology, disease ecology, and population genetics in a clear and concise way. The book highlights the results of new computational phylogenetic approaches that have been applied to viruses and the potential they have for elucidating the mechanisms of viral evolution, which will hopefully encourage more research in the future.

This book represents an important step along the way to one of the author's self-proclaimed ambitions, an ambition that has surely been shared by other evolutionary virologists: to place RNA viruses firmly within the mainstream of modern evolutionary biology.

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