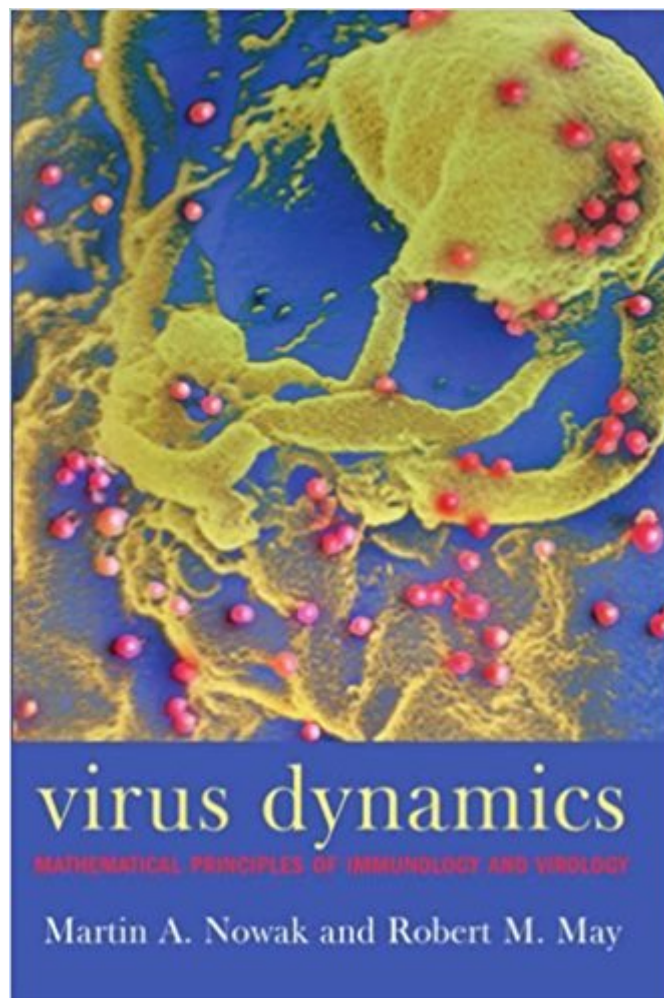




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Virus Dynamics: Mathematical Principles Of Immunology And Virology



Synopsis

We know, down to the tiniest details, the molecular structure of the human immunodeficiency virus (HIV). Yet despite this tremendous accomplishment, and despite other remarkable advances in our understanding of individual viruses and cells of the immune system, we still have no agreed understanding of the ultimate course and variability of the pathogenesis of AIDS. Gaps in our understanding like these impeded our efforts towards developing effective therapies and preventive vaccines. The authors describe the emerging field of theoretical immunology in this accessible and well-written text. Using mathematical modelling techniques, the authors set out their ideas about how populations of viruses and populations of immune system cells may interact in various circumstances, and how infectious diseases spread within patients. They explain how this approach to understanding infectious diseases can reveal insights into the dynamics of viral and other infections, and the interactions between infectious agents and immune responses. The book is structured around the examples of HIV/AIDS and Hepatitis B virus, although the approaches described will be more widely applicable. The authors use mathematical tools to uncover the detailed dynamics of the infection and the dynamics of immune responses, viral evolution, and mutation. The practical implications of this work for optimization of the design of therapy and vaccines are discussed. The book concludes with a glance towards the future of this fascinating, and potentially highly useful, field of study.

Book Information

Paperback: 256 pages

Publisher: Oxford University Press; 1 edition (January 25, 2001)

Language: English

ISBN-10: 0198504179

ISBN-13: 978-0198504177

Product Dimensions: 8.9 x 0.6 x 5.9 inches

Shipping Weight: 1 pounds (View shipping rates and policies)

Average Customer Review: 4.0 out of 5 stars 1 customer review

Best Sellers Rank: #559,878 in Books (See Top 100 in Books) #35 in [Books > Medical Books](#) > [Basic Sciences > Virology](#) #109 in [Books > Textbooks > Medicine & Health Sciences > Medicine > Basic Sciences > Immunology](#) #175 in [Books > Textbooks > Medicine & Health Sciences > Medicine > Basic Sciences > Microbiology](#)

Customer Reviews

... an excellent introduction to a field that has the potential to advance substantially our understanding of the complex interplay between virus and host * Nature *

Martin Nowak is at Institute for Advanced Study, Princeton. Robert M. May is at University of Oxford.

This book is best described as the application of nonlinear ordinary differential equations to immunology and virology. Its primary emphasis is on understanding the time development of viral infections, drug treatments, and viral resistance of the HIV and hepatitis-B viruses. The authors do a good job of describing the relevant equations needed to model virus dynamics. The book would be a good beginning for mathematicians interested in going into the field of mathematical immunology. And, even though it should be classified as a monograph, rather than a textbook, since there are no problem sets, students of mathematical immunology should find this book a useful introduction to the subject. In addition, the authors give a large list of references at the end of each chapter for further reading. Mathematicians who need a background in the biology of the HIV virus will find a good discussion in Chapter 2 of the book. The authors give an historical summary of the origins and treatment of the virus in this chapter. This sets the stage for the mathematical modeling of virus dynamics in Chapter 3, where the authors define the basic reproductive ratio and write down a system of three coupled nonlinear ordinary differential equations as the basic equations of virus dynamics. They remark, though without justification, that an analytical solution of the time development is not possible, and so they use approximation schemes to solve the equations. The equations are a phenomenological representation of virus dynamics, and no attempt is made to relate the rate constants to the underlying microscopic properties/structures/processes of viruses. They do however discuss the empirical data associated with studies of SIV infections, and show convincingly there is a correlation between the initial growth of the virus and its value at equilibrium. They caution the reader that the basic model does not give the true reproductive ratio, and show how to correct for this by introducing time delays. The efficacy of drug therapy is treated from both a mathematical and experimental viewpoint in the next chapter. This is a very enlightening discussion from the standpoint of the validation of the virus models. The authors switch gears in the next chapter and talk about the dynamics of the Hepatitis B virus. Again, they do a good job of introducing the reader to the experimental evidence for the models of this virus. In chapter 6, they bring in the contribution of the immune system to the basic equations. They assume that the reader is familiar with the concept of CTL responsiveness. The resulting equations are somewhat more

complicated, and the authors show how the ubiquitous Lotka-Volterra equations arise with the virus being the prey, and the immune system the predator. No detailed phase space analysis is done however to study any of the equations in this chapter, which would have been useful to the reader. The chapter on quasispecies is the most interesting one in the book, as the authors not only give a rudimentary definition of quasispecies, but they also give an indication of their complexity. Disappointingly, they mention the idea of mutation rates and their connection with chaos and self-organized criticality, but do not elaborate on this at all. The Bonhoeffer's laws of anti-viral treatment are discussed in the next chapter and the authors show how to derive them using the basic model. The emergence of resistance during drug treatment is modeled by parameters which reflect the replication rates of the virus, but these parameters are again not connected with any underlying microscopic properties of the virus. Some interesting dynamical behavior occurs for the case of multiple epitopes where the existence of quasiperiodic oscillations is shown to occur. They authors refer to this as "unpredictable" but they do not define this term in the book. The existence of quasiperiodic orbits in a dynamical system does not by itself make the system "unpredictable" or random of some sort. This book is a very addition to the literature, and most importantly, it emphasizes the role of validating mathematical models experimentally, which takes on even greater importance given the medical ramifications of the topics in this book.

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