

Mathematical Immunology of Virus Infections

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The immune system is primarily about host survival of infections and for this we also need to understand the biology of the system.

Rolf M. Zinkernagel
(from “On Immunity Against Infections and Vaccines: Credo 2004”. *Scandinavian Journal of Immunology*, 2004, 60:9–13)

Preface

Understanding the cellular and molecular mechanisms that control the ability of the immune system to mount a protective response against pathogen-derived foreign antigens, but avoid a pathological response to self-antigens, is a central problem in immunology. From the new high-throughput technologies, i.e. various omics measurements, 3D visualization and immunophenotyping, we have now a static view of the numerous components of the immune system and the links between them with unprecedented resolution. However, similar to the Classical Physics of the seventeenth century before the invention of the differential calculus by Sir Isaac Newton, a dynamical systems paradigm has to be developed and enter everyday immunological research. This requires the integration of mathematical methods to complement experimentation with the aim to represent, interpret and predict the observable characteristics of infections.

Mathematics is the universal language for expressing causal and functional relationships between observations. Its mainstream developments have been inspired by the needs of Physics, Chemistry and Engineering. For the twenty-first century, it is widely expected that Biology becomes a frontier for Mathematics. The challenge is to establish an interdisciplinary dialogue between mathematicians and experimentalists so that experimentation and mathematical modelling becomes an iterative process that boosts the different disciplines. The generated models that inevitably present simplifications of the underlying biological complexity must not lose touch with reality and generate testable predictions that drive, for example, perceptions of pathogen–host interactions. The problem of how to develop, in a systematic manner, such consistent models that provide a basis for quantitative analysis and predictions raises challenges for applied mathematicians related to the formulation of genuine approaches for representing the phenotypic complexity, spatial heterogeneity, hierarchical organization and control principles inherent to the infectious disease courses and outcomes.

This book is based on several lecture courses and seminars given by us at the Lomonosov Moscow State University, University of Chester, Saarland University, University of Zurich, University Lyon 1, and University Pompeu Fabra (Barcelona). It consists of eight chapters covering basic facts on viral infections and

biological systems analysis, model formulation and parameter estimation, mathematical models of experimental and human infections and multi-scale and integrative modelling approaches. We follow the route expressed in Andrew and colleagues (2007) that there is no better way to proceed with application of Mathematics to Immunology than to formulate mathematical models that correspond qualitatively to the existing theories and to form a range of models ordered according to their qualitative and quantitative consistency with the experimental and clinical observations.

Moscow, Villeurbanne, St. Gallen, Barcelona
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Acronyms

Ag	Antigen
Ab	Antibody
CFSE	Carboxyfluorescein succinimidyl ester
CI	Confidence interval
CTL	Cytotoxic T lymphocyte
DDE	Delay differential equation
HBV	Hepatitis B Virus
HCV	Hepatitis C Virus
HIV	Human immunodeficiency virus
hPDE	Hyperbolic partial differential equation
LCMV	Lymphocytic choriomeningitis virus
MHV	Murine hepatitis virus
MLE	Maximum likelihood estimation
ODE	Ordinary differential equation
pDC	Plasmacytoid dendritic cell
PDE	Partial differential equation
RDE	Reaction-diffusion equation