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## Introduction

Infectious diseases have been a part of the human condition since time immemorial. Some, such as herpes or chicken pox, usually have mild symptoms and vanish of their own accord. Others, such as HIV, tuberculosis or malaria, are responsible for millions of deaths each year. Diseases have been the source of fear and superstition throughout the ages; sociological upheavals following the black plague led to the demise of the church as an all-powerful institution, the destruction of the serf system and subsequent creation of labour movements, and the creating of colonialism. Malaria is likely the greatest killer of human beings of all time, being thought to have killed one in two humans who ever lived (see Page 201). The 1918 Spanish influenza pandemic killed 50–100 million people in the space of six months (about 5.5% of the entire world; this would be equivalent to 350 million deaths today).

Mathematical epidemiology has its roots in 1760, when Daniel Bernoulli formulated and solved a model for smallpox. In 1906, Hamer used a discrete-time model of measles to understand recurrent epidemics. In 1911, Sir Ronald Ross used mathematical models to help demonstrate that malaria was spread by mosquitos (later winning a Nobel prize for his work). This work was later followed up by public-health physician William Kermack and biologist Anderson McKendrick in 1927, who showed that mortality rates were much more dependent on the year of birth than the year of death, as previously thought. This was particularly impressive, since Kermack had been blinded three years earlier and did all the mathematics in his head.

Since the middle of the twentieth century, mathematical epidemiology has grown exponentially. The appearance of HIV/AIDS saw a further explosion in the growth of models, as ways of predicting the spread of the disease became crucial. Mathematical models were used to design the triple-drug cocktail, responsible for saving the lives of millions of people. In recent years, mathematics has been used to determine intervention strategies for the foot and mouth outbreak in Britain, the SARS epidemic, human papillomavirus vaccination and West Nile virus. Mathematics can determine the critical proportion of

individuals who must be vaccinated against a disease, the minimum amount of drug required to treat an infection, the frequency of use of an insecticide to control mosquitos or the number of doses of a drug regimen that may be missed before drug resistance emerges.

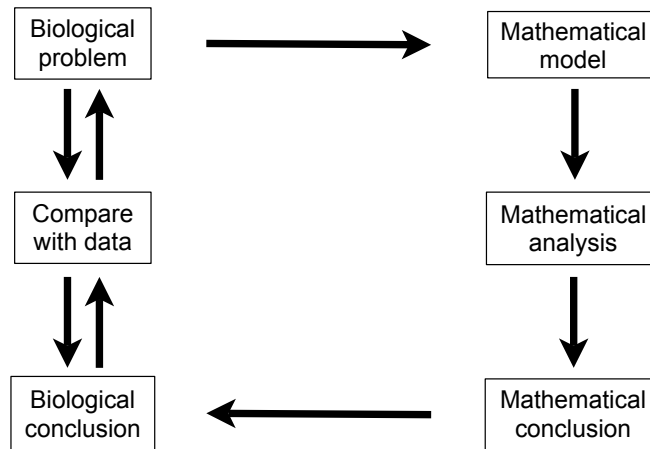
Mathematical modelling has become a tool that is now widely used to study problems and questions in public health. Such models have focussed on the spread of an infectious agent in a population, the pathogenesis of an infectious agent in a host and its effect on the immune system, the growth and spread of tumour cells in a body, and even the economics of vaccine and drug delivery at the population or individual level. However, public-health workers rarely have the mathematical skills to develop informative models for public-health policy.

In recent years, the rise of detailed electronic surveillance of infectious disease and improvements in computing power, electronic data management, rapid diagnostic tests, genetic sequence analysis and the ability to share and deposit data over the internet has given rise to a vastly improved ability to monitor the spread of diseases. Statistical methods have been integrated into the modelling process, allowing estimation of key parameters and the testing of hypotheses using available data.

Mathematical modelling is analogous to map-making. Without a decent map, even finding our way home is difficult, let alone exploring new avenues. Like any good map, we aren't trying to create a perfect replica of reality; rather, we hope to elucidate key features and ignore what isn't relevant. Often, what we leave out is as important as what we include. To solve biological problems, first we translate the biology into a mathematical model. (Despite appearances, usually borne out of math phobia, this is often the most challenging part of the process.) Once we are satisfied with the model, we perform mathematical analysis. Assuming we do this correctly, we can be confident that what happens here is a series of entirely logical steps. Our mathematical conclusion then needs to be translated back to a biological conclusion. Since the process of mathematical analysis is rigorous, it follows that the strength of our conclusions are wholly dependent upon the formulation of the mathematical model. See Figure 2.1. Thus it is vital to understand the mechanisms, as well as the limitations, of this modelling cycle.

More formally, mathematical modelling of infectious disease is a framework designed to convey ideas about the components of host-pathogen interactions. It requires a clear understanding of the interaction between the infectious agent and the host within an individual, the mode and rate of transmission between individuals and host-population characteristics, such as demography and behaviour. Models can be used to determine the dominant factors that generate observed patterns and phenomena. They can aid data collection, interpretation and parameter estimation. They can identify possible approaches for disease control and for assessing the potential impact of different intervention measures. Importantly, they can do all this without costly and time-consuming experiments.





**Fig. 2.1.** The mathematical modelling cycle.

This monograph facilitates the learning of mathematical biology for public-health researchers and mathematical modellers, who may have a range of skills and knowledge drawn from mathematics, clinical medicine, sociology, economics, decision-making, risk analysis, psychology, industrial production capacity and politics. There needs to be a symbiosis between these areas; people working in these disciplines need to communicate to each other effectively so that key questions in health can be addressed.

This monograph specifically introduces mathematical modelling to those in the public-health sector who have had no formal training in mathematics. It allows people working in a range of disciplines to understand the strengths and weaknesses of models. Mathematical models are formulated that represent current diseases; the tools needed to analyse these models are introduced as necessary. Through Matlab exercises, numerical simulations are developed that provide the reader with the ability to formulate control strategies, test hypothetical interventions and explore disease-management options. The exposition of the material is mainly addressed to researchers and graduate students interested in the application of mathematics to biological problems.

One of the objectives is to familiarise public-health workers with questions and outcomes that can be produced by simple mathematical models. Ultimately, policy-makers need to understand the importance and limitations of models, in order to be confident in basing decisions on them. Mathematicians need to be able to connect the equations to the biology. And, crucially, both groups need to be able to talk to each other. Only then will we make real progress in solving some of the world's most difficult problems.