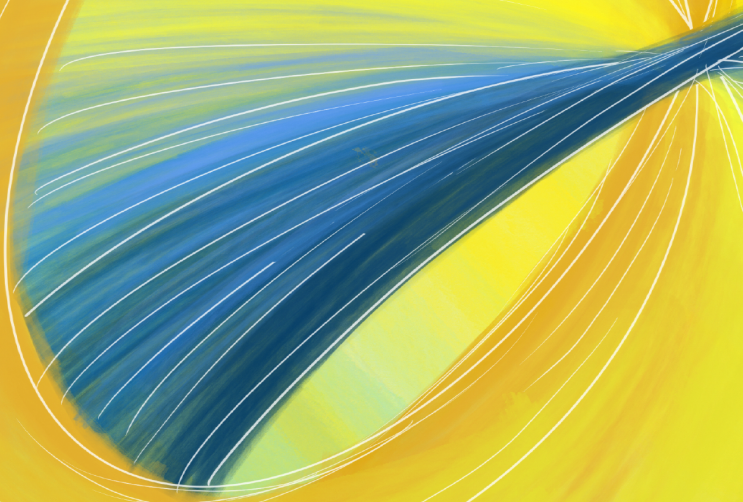
Differential Equation Models in Epidemiology



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Preface

The purpose of this short course is to introduce some models of infectious diseases that are expressed as systems of ordinary differential equations (ODEs). The background expected of the reader is the introductory knowledge of ODEs that students usually acquire in calculus courses, together with matrix theory through eigenvalues and eigenvectors. Three good texts for furthering your knowldge of differential equations are Perko (2001), Schaeffer and Cain (2016), and Sotomayor (1979). However, we will introduce ideas about ODEs that may be new to you as they are needed.

The motivation for the course is the Covid-19 pandemic. During the pandemic the general public has become aware of the importance of mathematical models, both to anticipate the course of the pandemic and to evaluate possible interventions.

Researchers in mathematical epidemiology attempt to model a wide variety of infectious diseases using a variety of mathematical tools. To give some context for the course, we will describe some of this variety of both diseases and tools, and then describe our focus in this course.

Infectious diseases

Infectious diseases are disorders caused by organisms such as bacteria, viruses, fungi, or parasites. They have been responsible for enormous suffering and death throughout recorded history.

New infectious diseases have emerged continually during recorded history and

will continue to emerge in the future. The source is often some sort of transmission of diseases of other species.

Infectious diseases and their spread can be viewed as byproducts of human progress. Domestication of animals and human penetration into all global biomes have helped diseases to migrate from other species to humans. Global trade, which has existed since ancient times, has helped diseases to spread.

Progress in scientific understanding, sanitation, prevention measures, and treatments has led to improved control of many infectious diseases in most parts of the world. Our increased knowledge and experience have given us remarkable tools to bring to bear on the Covid-19 pandemic and on the infectious diseases that will emerge in the future.

Modes of transmission

We will give a few examples of especially deadly infectious diseases and their modes of transmission.

Plague is caused by a bacterium that is typically transmitted by the bite of a flea that previously bit an infected animal. It can also be transmitted from person to person by coughing. Plague pandemics have been among the most devastating episodes in human history (Frith 2012). The Justinian Plague originated in Ethiopia and reached Constantinople (now Istanbul) in 541 AD. It killed some 5,000 to 10,000 people per day in the city, and ultimately killed perhaps 100 million people in Africa, Asia and Europe over the next few years. There were repeated outbreaks over the next 200 years. In Europe, according to Frith (ibid.), "the social and economic disruption caused by the pandemic marked the end of Roman rule and led to the birth of culturally distinctive societal groups that later formed the nations of medieval Europe."

Plague reappeared in Europe in 1347 (the Black Death), brought from Asia Minor to Crimea by a Tartar army. It killed a quarter of the population of Europe, 25 million people, by 1350. Outbreaks continued in Africa, Asia and Europe for over 300 years. The Black Death led to the breakdown of medieval society and the growth of a middle class.

Plague reemerged in China in 1855 and was not fully controlled for a hundred years, by which time it had killed 15 million people, mostly in India.

Smallpox is caused by a virus that is spread by contact with patients' sores, by contact with contaminated objects such as bedding or clothing, and by coughing and sneezing. It was already present in 3rd century BC Egypt. It was brought to

the Americas, where it was unknown and there was no immunity, by Europeans starting in the 1520s. It is estimated that Old World diseases, principally smallpox, killed 90 to 95% of the indigenous population of the Americas. Although vaccination campaigns began in the 19th century, smallpox still killed 300 million to 500 million people during the 20th century. Smallpox was declared eradicated in 1979 (Wikipedia 2021e).

Malaria is caused by a parasite that is transmitted by mosquito bites. There were 229 million cases of malaria in 2019, leading to 409,000 deaths. 94% of cases and deaths were in Africa (CDC 2021).

Cholera is a bacterial disease usually spread through contaminated water. There have been seven cholera pandemics since the 19th century. Cholera currently kills at least 21,000 people per year (WHO 2021). A cholera epidemic in Haiti that began in 2010, following an earthquake, sickened almost 800,000 people (Wikipedia 2021b).

Acquired immunodeficiency syndrome (AIDS) is caused by the human immunodeficiency virus (HIV). It is transmitted sexually, by contact with infected blood or contaminated needles, and from mother to child. AIDS has killed around 33 million people since it was first identified in the 1980s (Wikipedia 2021f). It probably jumped from chimpanzees or gorillas to humans in Central Africa in the 1920s (Wikipedia 2021d).

While mathematical epidemiologists attempt to model all these diseases, in this course we shall be concerned with infectious diseases that are principally transmitted directly from one person to another.

Influenza is the prime example. It is caused by a family of viruses that are spread by coughing or sneezing. The first documented flu pandemic began in Asia in 1510 and spread along trade routes (Wikipedia 2021a).

The so-called Spanish flu pandemic of 1918–1920 killed as many as 100 million people worldwide. It was first observed in the state of Kansas in the United States in January 1918 (Wikipedia 2021h). It rapidly spread to other parts of the United States and Europe, and then around the world, reaching Brazil by August 1918. In Rio de Janeiro, the Spanish flu killed about 15,000 people and sickened another 600,000—about 66% of the city's population. "The city soon saw itself poised on the verge of collapse. There was not enough food, not enough medicine, not enough doctors, and not enough hospitals to take in the sickest. …The city streets gradually were transformed into a sea of unburied bodies, as there were not enough gravediggers to inter the bodies or caskets in which to place them." (Goulart 2005)

Mutations of the 1918 virus are responsible for most influenza cases since then

(Taubenberger and Morens 2006). Flu pandemics in 1957–58 and 1967–68 killed 1 to 4 million people worldwide (Wikipedia 2021g).

Coronaviruses are spread like influenza viruses. SARS-CoV was first reported in China in February 2003 and probably originated from bats. It spread to the Americas, Europe, and Asia and killed almost 800 people. MERS-CoV was first reported in Saudi Arabia in 2012. It emerged from bats via camels as an intermediate host, and has killed over 800 people. SARS-CoV-2, first reported in Wuhan, China, in December 2019, causes the syndrome known as Covid-19, which is presently a global pandemic. It is also generally believed to have emerged from bats. It has caused almost three million deaths as of mid-April 2021 (Wikipedia 2021c).

Models used in mathematical epidemiology

Our course will describe the use of ODEs to model the spread of diseases like influenza and the coronavirus diseases. ODE models are the ones most commonly used to anticipate the spread of these diseases and to explore the likely effect of countermeasures. ODE models divide a population into categories, called compartments, and describe the evolution of the populations fractions in the compartments over time. There may be just two compartments, infected and not infected, or a large number of compartments that divide the population in whatever ways seem important.

Here are some other types of models used in mathematical epidemiology, which we will not discuss.

Stochastic models

Especially at the start of an epidemic, when only a few people are infected, the element of chance is important in whether the epidemic spreads or dies out. ODE models are deterministic. Stochastic models take the probabilistic aspect of epidemics into account. An introductory reference is Allen (2008).

Network models

Both ODE models and stochastic models divide a population into compartments, and assume that members of compartments encounter each other at certain rates. Network models by contrast represent individuals as nodes in a network, and represent their contacts with each other by edges that connect the nodes. Similar to

stochastic models, disease is transmitted across edges probabilistically. Such models achieve added realism but are hard to analyze unless strong assumptions are made. A good reference is Kiss, Miller, and Simon (2017).

Another type of network model uses two types of nodes, one for individuals and one for mixing locations such as workplaces, stores, and schools. Edges connect individuals to mixing locations. These models have become important during the Covid-19 pandemic due to the availability of aggregate cellphone data that records the movement of people from homes to mixing locations (Chang et al. 2021).

Agent-based models

Agent-based models are computer programs that simulate the interactions of individuals (agents) in a given society over a period of time. They can be remarkably realistic.

In 2006 a group at Imperial College (London) created agent-based models to simulate flu epidemics in the United Kingdom and United States, based on data about population density, household size and age structure, schools, workplaces, and commuting; see Ferguson, Cummings, et al. (2006). The models were repurposed in a report of Ferguson, Laydon, et al. (2020) to predict the possible course of the Covid-19 pandemic in the UK and US. This report greatly influenced the response of the UK and US governments to the pandemic (Booth 2020).

COMORBUSS, an agent-based model developed in Brazil, is intended to carefully model a single city in order to advise which disease mitigation efforts would be most effective there (`https://comorbuss.org`, `http://www.cemeai.icmc.usp.br/ModCovid19/comorbuss`).

Problems with agent-based models include the effort required to build them, the time required to run them, and the fact that their interactions are probabilistic, so many runs may be required to get good predictions.

PDE models

In ODE models the variables are functions of time only. In partial differential equation (PDE) models the variables are functions of time and space. Thus PDE models can be used to study the spread of an epidemic in space. For example, Berestycki, Roquejoffre, and Rossi (2021) used a PDE model to study the early spread of Covid-19 by road networks in Italy.

ODE models in mathematical epidemiology

The fundamental ODE model of mathematical epidemiology is the SIR model, whose name represents its compartments, susceptible, infective, and recovered. It was introduced in a 1927 paper by A. G. McKendrick, a Scottish physician with experience fighting malaria in Sierra Leone and dysentery and rabies in India, and W. O. Kermack, a blind Scottish chemist (Kermack and McKendrick 1927). We shall discuss their model in Chapter 2. The SIS model (susceptible, infective, susceptible) is even simpler; we discuss it in Chapter 1.

A basic result underpinning a large part of applied mathematics is the Perron–Frobenius Theorem, which says, roughly speaking, that the principal eigenvalue of a positive matrix is positive and corresponds to a positive eigenvector. It is behind two important results of mathematical epidemiology. One explains why in many epidemiological models, if the susceptible population is renewed by a mechanism such as loss of immunity or births, a disease can become endemic; see Hethcote (1978). Another, the next generation matrix method, shows how to calculate the basic reproduction number in a complicated model.

The Perron–Frobenius Theorem is beyond the scope of this course. However, in Chapter 3, we use simpler arguments to show how renewal of the susceptible population in a simple SIR model can lead to a disease becoming endemic. And in Chapter 4 we explain the next generation matrix and how to use it, without going into proofs. Our main example in that chapter is an extension of the SIR model that represents the main features of Covid-19.

Chapter 5 introduces spontaneous human behavioral change. You know from experience that when infection levels rise, many people who can stay home will do so, and many will practice stricter hygiene and social distancing. When infection levels fall, people relax. This evident fact greatly affects the spread of an infectious disease, but is rarely accounted for in epidemiological models. How to deal with human behavioral change is at the research frontier in mathematical epidemiology. We explain an approach that uses imitation dynamics, an idea from game theory.

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