The SIR Model in Historical Context

This project revolves around mathematical epidemiology. This document is a starting point for our project; it is a guided exploration of SIR models for disease spreading. It mostly consists of reading assignments, trying a few mathematical challenges on your own, and keeping track of what you're learning by answering the questions listed to form a written report.

The Indian Plague Epidemic of Early 1900s

In the early 1900s, an outbreak of plague erupted in India which back then was <u>part of the British Empire</u>. For general information about the events, see the <u>Wikipedia article on the Third Plague Pandemic</u> and pay particular attention to the section titled *Political Impact in Colonial India*.

The *Indian Plague Commission* was instituted by the British government to study the situation, understand the causes of the diseases, and help stop the epidemic. The written report produced by the Commission was very thorough (see Additional Notes and Resources for a link to the full document).

★ Please read this excerpt from The Etiology and Epidemiology of Plague - A Summary of the Work of the Plague Commission (1908). Note that the "General Conclusions" (on page 12 of the linked PDF) are taken from the very end of the report.

When reading, focus your attention on answering the following questions:

- 1. According to the report, how is the plague transferred to humans?
- 2. What is definitely not true about the way the plague is transferred to humans?
- 3. Does any of this surprise you?
- 4. Do you think there is a parallel between the spreading of the disease among rats and humans?

Now that you've had a first introduction to the report, choose one Part from it and read it carefully (the table of content of the full report is on page 7 of the PDF linked above). At our next meeting, be ready to present a summary of what you learned to the group. Note that this report was written in 1908 for a technical audience, it is understandable if you don't understand everything right away.

This short <u>Plague fact sheet</u> from the CDC (U.S. Centers for Disease Control and Prevention) answers a lot of questions regarding the disease itself. If you want more information about it, <u>this is the full CDC Plague webpage</u>.

Kermack and McKendrick, 1927

Now that you have some historical context of the plague epidemic, we're going straight to the (mathematical) source.

★ Please read the paper that first defined the SIR model as we know it today by following the instructions below. The manuscript titled <u>A Contribution to the Mathematical Theory of Epidemics</u> was written by W.O. Kermack and A.G. McKendrick in 1927.

This is a technical mathematical paper with notation from 1927, you are not supposed to be comfortable with all of its content. Once again, it is expected for all students to struggle through the first reading of this manuscript.

Skim the entire paper, but pay particular attention to:

- The *Introduction* (from the middle of page 1 to the middle of page 3 of the PDF).
- The *General Theory* (through the middle of page 10 of the PDF). This part is long and gets tedious after a while; it's important to understand through the end of page 4. We will discuss this together.

As you're reading, try to take notes of what you're understanding and any questions that come up for you. The ideal way of reading a Mathematics paper is to follow the authors' argument by deriving their equations along with them. This may only be possible for parts of this paper, but give it a try!

Please answer the following questions:

- 5. Summarize, in your own words and in a bullet point format, the process of an epidemic from beginning to end, as described in the *Introduction*.
- 6. Look for any assumptions the authors make in the *Introduction*. Do you think each of them is reasonable? Why or why not?
- 7. How do these assumptions relate to the assumptions or conclusions drawn in the Report? Does anything jump out at you?

We expect students to come to our meetings with questions and comments about what they read. Don't be discouraged if this is tough, it's hard for everyone, including the instructors! Be kind to yourself: It's your first time reading a technical Mathematics paper and this is a manuscript from 1927!

While the early part of the paper should go by more quickly, you may need some help in deriving some of the equations, so here are some tips.

The process to derive equation (17) requires using series, the method of integrating factor to solve first order linear ODEs, and patience. In particular, the first few lines of the calculation require some leaps of faith on your part, but once the paper shows you the expression for x:

$$x = f_0(t) + \lambda f_1(t) + \lambda^2 f_2(t) + \dots$$

at the top of page 706, you should be able to follow along all the way through to successfully deriving equation (17). This is a link to the <u>Volterra integral equations</u>; the authors mention that they haven't found a way to solve equation (16) explicitly, but they are going to base their solution process on the observation that (16) is a Volterra-like equation (of the second kind). Do not focus on this too much, i.e. believe that this is possible and accept their solution form reported above. If you want to read more about why they can use the given expression for x, this <u>1909 paper by G.C. Evans</u> (<u>famous mathematician</u>) should be useful. Please be aware that this part is beyond the scope of our reading of the Kermack & McKendrick paper, so please only read Evans' work if you're interested.

After agonizing over some of the details of the *General Theory*, we are now jumping ahead to the *Special Cases* section: Part B. *Constant Rates* (from the bottom of page 712).

The constant rates referenced in the title of the section are the *rate of infectivity* $(t) = \kappa$ (read *kappa*) and the *rate of removal* $\psi(t) = l$, where both κ and l are constants. In particular, note:

- a) The nonlinear system of three first order ODEs on page 713 of the PDF (equation (29) on the paper) is essentially the first so-called SIR model. The variables x, y, and z represent the number of *Susceptibles*, *Infected*, and *Removed/Recovered* people in the population, respectively; note that x + y + z = N, the total population density (see also *General Theory*).
- b) Pay particular attention to the plot on page 714 and its caption which continues to page 715 of the PDF (slightly smaller font than the main text). In the plot, the small black dots correspond to the measured data for rat deaths during the Indian plague epidemic, and the line with the open circles represents the predicted rat deaths per week by this model. Answer the following questions:
 - 8. Look for any additional assumptions the authors make in the figure on page 714 of the PDF. Do you think these are reasonable? As mentioned, the figure represents rat deaths over time, not human. Does this make sense in the context of the report of the Indian Plague Commission?
 - 9. Overall, is there anything that stood out to you in the parts you read?

Now let's focus on the equations. We have worked on deriving some of them but a lot of things may have gotten lost in the mathematical details. So now we want you to take a step back and really try to understand their meaning. Here are the equations of the SIR (Susceptible, Infected, Removed) model from the 1927 paper by Kermack and McKendrick, written using modern notation for the variables:

$$\frac{dS}{dt} = -\kappa S(t) I(t), \qquad \frac{dI}{dt} = +\kappa S(t) I(t) - l I(t), \qquad \frac{dR}{dt} = +l I(t).$$
Susceptible Infected Removed

Diagram thanks to Dr. Manuchehr Aminian.

Let's look at them in more detail. Read below and answer the following questions:

• The dependent variables are S(t), I(t), and R(t) representing the number of people (or rats, as in the paper) in each of the groups (respectively *Susceptible*, *Infected*, and *Removed*). The variable t represents time since the beginning of the infection (the time units change depending on the situation at hand, i.e. years, days, months, weeks, minutes, etc.).

The parameters κ and l affect how quickly people move from one group to the other. Please answer:

- 10. What happens if κ is large? Do people get infected more or less quickly than if κ was small? Explain why.
- 11. What happens if l is large? Explain your answer.
- The derivatives $\frac{dS}{dt}$, $\frac{dI}{dt}$, and $\frac{dR}{dt}$ represent the net rate of change of the population of each of the three groups due to all the factors taken into account in the model.
- The $\kappa S(t) I(t)$ term is based on the **Law of Mass Action**. This law states that the rate at which people get infected in a population is dependent on the product of the number of healthy and infected people. Please answer:
 - 12. If there is a very small number of infected people, *I* , and a large number of healthy people, *S* , how will the rate of new infections be?
 - 13. If there is a large number of infected people, *I* , and a very small number of susceptible people, *S* , how will the rate of new infections be? Does this make sense to you?
- The lI(t) term is more familiar than you think. This assumes that people get *removed* from the infectious group, I, continuously at a rate l.
 - 14. What type of mathematical function would describe this decay accurately?
 - 15. If l = 0.5, what is the continuous rate at which people are removed from the infected group at each time unit?
 - 16. What do the positive and negative signs of each term indicate? (See the diagram above for a hint.)

Now that you have a better understanding of all the terms in the equations, please answer the questions below:

- 17. Summarize with your own words what the second equation is expressing. Use the diagram of the compartment model above to understand this better.
- 18. What does it mean physically if dR/dt = 0?
- 19. What happens if l = 0 and $\kappa \neq 0$?
- 20. What do you expect would happen if $l \neq 0$ and $\kappa = 0$?

Now let's *modernize* the parameters in the equations as well, not just the variables. In today's version of the SIR model:

- $\kappa = \frac{\beta}{N}$, where β is called the **contact rate** and takes into account the probability of contracting the disease in a contact between a susceptible and an infected subject. It is more realistic to consider a force of infection that does not depend on the absolute number of infectious subjects, but on their fraction with respect to the total constant population N.
- $l = \gamma$, where γ is the **rate of recovery or death**. If the duration of the infection is denoted with D, then $\gamma = 1/D$, since an individual experiences one recovery in D units of time.

Hence, the modern SIR model is defined as:

$$\frac{dS}{dt} = -\frac{\beta}{N} S(t) I(t),$$

$$\frac{dI}{dt} = +\frac{\beta}{N} S(t) I(t) - \gamma I(t),$$

$$\frac{dR}{dt} = +\gamma I(t).$$

As mentioned earlier, this is a nonlinear system of three first order ODEs. In general, it cannot be solved exactly. However, given some assumptions, solutions for special cases can be derived. Before we attempt to visualize solutions to the problem, let's analyze some key aspects of this system.

- 21. If we wanted to solve this system exactly, how many initial conditions would we need to fix the undetermined constants of integration?
- 22. Add the equations to one another to find: $\frac{dS}{dt} + \frac{dI}{dt} + \frac{dR}{dt} = 0$. What does this imply about the sum of S(t), I(t), and R(t)?
- 23. How many equations need to be solved to find an expression for S(t), I(t), and R(t)?

The dynamics of the infectious group depends on the **basic reproduction number** R_0 defined as $R_0 = \frac{\beta}{\gamma}$. This ratio can be interpreted as the number of cases one case generates on average over the course of its infectious period in an otherwise uninfected population. This is a useful metric because it is understood that for $R_0 < 1$ the infection will die out (in this case the disease is named dud), while for $R_0 > 1$ the infection will spread in a population (and the disease is named an *epidemic*). That is because for $R_0 > 1$, the infection rate β is large relative to the recovery rate γ , and the total number of people to be infected is expected to be large. On the other hand, if $R_0 < 1$ the recovery rate is fast enough that, while a few more people may get infected, the spreading is very slow and not considered to be a full-blown epidemic. See table below to get an idea of typical R_0 -values for well-known infectious diseases.

Now it's time to solve the problem. There are a variety of ways to approach the solution to this system. You should have realized by now (see question 23.) that we only need to solve two equations out of the three. That is because the sum of the three populations is always equal to N (the total population density), so once we have the first two we can take advantage of this fact to write the third solution.

Values of R_0 for well-known infectious diseases.

Disease	Transmission	R ₀
Measles	Airborne	12-18
Diphtheria	Saliva	6–7
Smallpox	Airborne droplet	5–7
Polio	Fecal-oral route	5–7
Rubella	Airborne droplet	5–7
Mumps	Airborne droplet	4-7
HIV/AIDS	Sexual contact	2-5
Pertussis	Airborne droplet	5.5[2]
SARS	Airborne droplet	2-5[3]
Influenza (1918 pandemic strain)	Airborne droplet	2–3 ^[4]
Ebola (2014 Ebola outbreak)	Bodily fluids	1.5-2.5[5]

Table from History and Epidemiology of Global Smallpox Eradication.

Pair together two equations of your choice and try to solve them. Note that while you have a few options here (three equations can be paired in six ways if the order matters), there are some pairings that make solving easier and others that make it very hard or impossible.

- 24. Explore the possibilities and report all of your tries, even those that didn't quite work out. Try combining equations by adding, subtracting, multiplying, and dividing them. Remember that our goal is to find a solution in the simplest possible way. These are first order equations, so let's strive for combining two equations to obtain a simple separable equation to be solved. Use $R_0 = \frac{\beta}{\gamma}$ wherever you can.
- 25. Can you combine them to solve for S(t)? Write a solution for S(t) in terms of R(t).
- 26. Can you do the opposite (that is, write out a solution for R(t) in terms of S(t))?
- 27. Note that each of these solutions should be depending on only one undetermined constant. Take the expression you found for S(t) (question 25.) and set the constant by applying the following initial conditions: $S(0) = s_0$, $R(0) = r_0$. Why do we need two conditions for one constant?
- 28. Now substitute the solution for S(t) found above in the second equation (for $\frac{dI}{dt}$) and solve, with $R(0) = r_0$, and $I(0) = i_0$. You should find an expression for I(t) that depends on R(t) only (i.e. not on S(t)).
- 29. Finally, derive the solution for R(t) based on the relationship between S, I, R, and N (as discussed earlier). Note that you do not need to write this solution explicitly.

If you followed all the steps above, you should now have solutions to all three ODEs (where the susceptibles model S(t) depends on R(t) only, the infectious model I(t) depends on R(t) only, and the recovered model R(t) is not written explicitly).

- 30. Compute the limit as $t \to \infty$ for R(t).
- 31. What does this limit represent from an epidemiological point of view? Assuming that $t \to \infty$ represents the *end* of the epidemic and that $S(0) \ne 0$: What does this limit imply with regard to the susceptible population?
- 32. Based on the conclusion above, how is the end of an epidemic defined? What is it caused by?
- 33. As we discussed earlier, the basic reproduction number R_0 is very important in this model. Rewrite the second equation as: $\frac{dI}{dt} = (\frac{R_0 S}{N} 1)\gamma I$ and study the sign of the derivative (i.e. the sign of $\frac{dI}{dt}$) in terms of R_0 . Can you relate your conclusions to what was stated right below question 23.?

Now that you've read and understood the original SIR paper, you should be ready to read and thoroughly understand a recent SIAM (Society of Industrial and Applied Mathematics) article discussing the Ebola epidemic of 2014-2016 in West Africa.

★ Please read <u>Emerging Disease Dynamics - The Case of Ebola</u>, written by Sherry Towers, Oscar Patterson-Lomba, and Carlos Castillo-Chavez (SIAM News, November 2014). In the article there are a few technical terms. Take a look at the last page of this document for some definitions.

Please answer the following questions:

- 34. What are the variables the article uses in the graphs? Which of the variables in the SIR model you are familiar with do these represent?
- 35. What is the chosen unit for time?
- 36. What type of model do they use to fit their data?
- 37. What do they do to try to validate their model?
- 38. Was there anything confusing for you in the article? Anything that you think is explained poorly?
- 39. Can you spot any weaknesses of the SIR model after reading this? What does the basic SIR model not take into account that is discussed in the article?

Optimal Control Strategies

A general term indicating the fact that having a limited amount of resources means not all possible measures to prevent an outbreak can be implemented. The issue is then: which approaches should be taken to have the greatest impact in slowing the spread of the disease? Full quarantine? Medical treatment? Isolation? Something else? And how much money should be put towards each?

Dimensionless Quantity

Refers to quantities like R_0 which determine the qualitative behavior of a model. Unsurprisingly, the word *dimensionless* specifically refers to the fact that R_0 has no physical units.

Ansatz

A hypothesis, an educated guess, a particular form of a mathematical model. Their model is piecewise exponential. The word <u>ansatz</u> comes from German.

Time series

Basically, a plot with time on the horizontal axis.

95% Confidence Interval

A statistical term representing the uncertainty in a prediction. It practically means that the authors were 95% confident that the number of new Ebola cases would be somewhere in their predicted interval.

Additional Notes and Resources:

- The link https://tinyurl.com/UROP-SIR takes to this document in viewing mode.
- The full Report of the Indian Plague Commission is available <u>online through the FSU</u> <u>Library system</u>.
- Wikipedia article on the basic reproduction number R_0 . <u>View</u>.
- Article about interpreting an SIR model graph. View.
- <u>Computational and Mathematical Epidemiology</u>, written by Dr. Fred S. Roberts (Science Magazine | Careers, 2004).