

# Einführung in die Mathematische Epidemiologie: Introduction to Mathematical Epidemiology: Deterministic Compartmental Models

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## 1 Introduction

Deterministic compartmental models form the simplest models in the mathematical study of infectious disease dynamics. They assume that a population is homogenous (all people are the same) and the only distinction is in their disease state. Unlike stochastic models, deterministic compartmental models consider the population level mean behavior of the system. In deriving and analyzing these models, we usually perform the following five steps.

1. Derive model and compartments.
2. Write equations corresponding to these compartments.
3. Derive parameter values from data/literature.
4. Numerically simulate equations.
5. Mathematically analyze equations.
  - Analytically solve equations.
  - Evaluate equilibrium points.
  - Determine stability of equilibrium points.
  - Derive threshold conditions.
  - Draw phase portraits.
  - Perform bifurcation analysis.
  - Perform sensitivity analysis.

## 2 Susceptible-Infectious (SI) Model

The susceptible-infectious (SI) model of an infectious pathogen divides the host population into two groups: susceptible hosts (who are not infected with the pathogen but can get infected),  $S$ , and infectious hosts (who are infected with the pathogen,  $I$ ). Assuming a per capita mass-action model, the rate at which susceptible hosts become infected is a product of the number of contacts each host has per unit time,  $r$ , the probability of transmission of infection per contact,  $\beta$ , and the proportion of the host population that is infectious,  $I/N$ , where  $N = S + I$  is the total population size. Infectious hosts remain infectious for life. This represents pathogens such as the human immunodeficiency virus (HIV) where there is no recovery. A schematic of the model is shown in Figure 1; a summary of model variables is in Table 1 and parameters in Table 2.

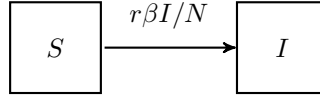


Figure 1: Susceptible-Infectious model.

$$\frac{dS}{dt} = -r\beta S \frac{I}{N} \quad (1a)$$

$$\frac{dI}{dt} = r\beta S \frac{I}{N} \quad (1b)$$

Table 1: Description of state variables of compartmental models of infectious disease dynamics.

$S$ : Susceptible humans  
 $I$ : Infectious humans  
 $R$ : Recovered humans

Table 2: Description of parameter values in compartmental models of infectious disease dynamics.

$r$ : Number of contacts per unit time  
 $\beta$ : Probability of disease transmission per contact  
 $\gamma$ : Per-capita recovery rate  
 $\Lambda$ : Constant recruitment rate  
 $\mu$ : Per-capita removal rate

Since the population size is fixed, we can reduce the system to one dimension with the substitution,  $S = N - I$ , to provide the logistic equation,

$$\frac{dI}{dt} = r\beta(N - I) \frac{I}{N}. \quad (2)$$

We can analytically solve (2) with  $I(0) = I_0$  to provide,

$$I(t) = \frac{I_0 N}{(N - I_0)e^{-r\beta t} + I_0}. \quad (3)$$

We show a numerical simulation of (1) in Figure 2.

This differential equation (2) has two equilibrium points. The disease-free equilibrium point,

$$I_{dfe} = 0, \quad (4)$$

and the endemic equilibrium point,

$$I_{ee} = N. \quad (5)$$

Linear stability analysis shows that  $I_{dfe}$  is unstable, while  $I_{ee}$  is locally asymptotically stable. As long as there is at least one infectious host, the population will tend towards becoming fully infectious.

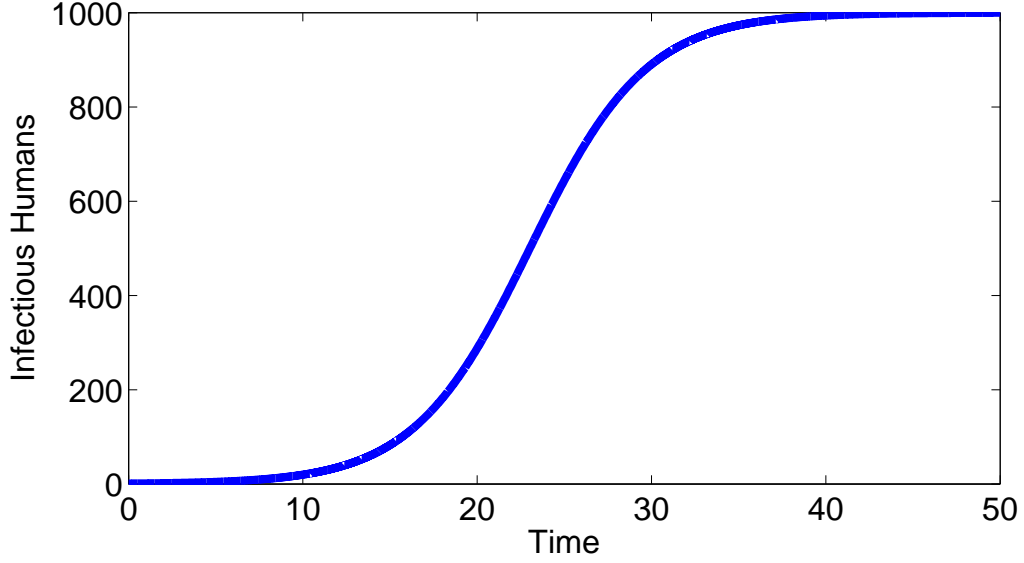


Figure 2: A numerical simulation of the SI model with  $r = 6$  and  $\beta = 0.05$ ; and initial conditions,  $S(0) = 999$ , and  $I(0) = 1$ .

### 3 Susceptible-Infectious-Susceptible (SIS) Model

The susceptible-infectious-susceptible model (SIS) is similar to the SI model but it allows the infectious humans to recover from the infection and return to the susceptible class (where they can get infected again). Infectious hosts recover at a constant per capita rate,  $\gamma$ , so  $1/\gamma$  is the duration of the infectious period with an exponential waiting time. This is a simple model for bacterial infections, or fast evolving viral infections like the common cold, where infection does not provide immunity. A schematic of the model is shown in Figure 3; a summary of model variables is in Table 1 and parameters in Table 2.

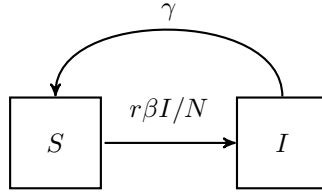


Figure 3: Susceptible-Infectious-Susceptible model

$$\frac{dS}{dt} = -r\beta S \frac{I}{N} + \gamma I \quad (6a)$$

$$\frac{dI}{dt} = r\beta S \frac{I}{N} - \gamma I \quad (6b)$$

Since the population size is fixed, similar to the SI model, we can reduce the system to one equation with the substitution,  $S = N - I$ , to provide,

$$\frac{dI}{dt} = r\beta(N - I) \frac{I}{N} - \gamma I. \quad (7)$$

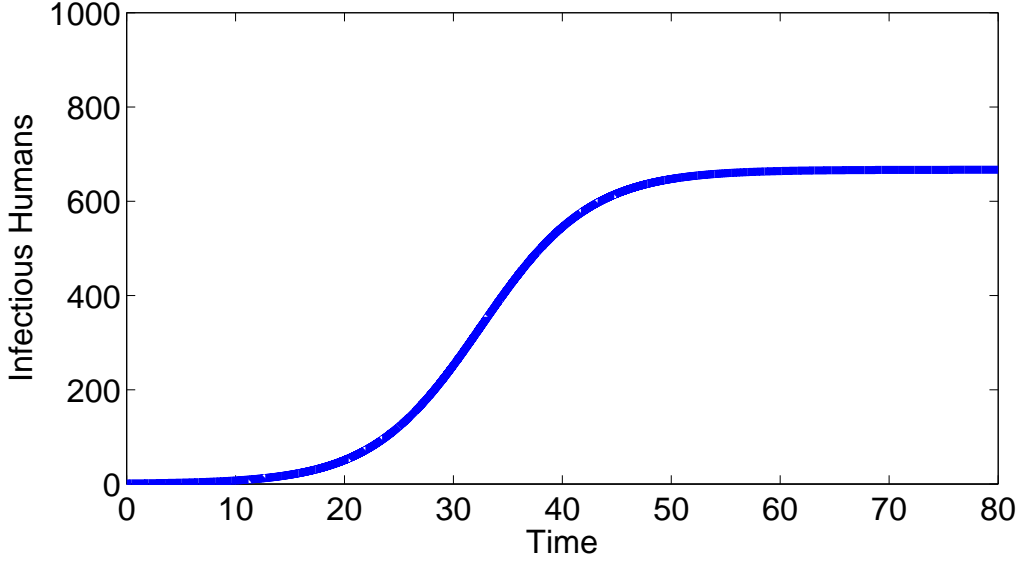


Figure 4: A numerical simulation of the SIS model with  $r = 6$ ,  $\beta = 0.05$ , and  $\gamma = 0.1$ ; and initial conditions,  $S(0) = 999$ , and  $I(0) = 1$ .

We can analytically solve (7) with  $I(0) = I_0$  to provide,

$$I(t) = \frac{\frac{N}{r\beta} \cdot (r\beta - \gamma)}{1 + \left( \frac{N}{r\beta} \frac{(r\beta - \gamma)}{I_0} - 1 \right) e^{-(r\beta - \gamma)t}}. \quad (8)$$

We show a numerical simulation of (6) in Figure 4.

This differential equation (7) has two equilibrium points. The disease-free equilibrium point,

$$I_{dfe} = 0, \quad (9)$$

and the endemic equilibrium point,

$$I_{ee} = \frac{(r\beta - \gamma)N}{r\beta}. \quad (10)$$

Note that the endemic equilibrium point is only positive (and in the domain of interest) if  $r\beta > \gamma$ . Linear stability analysis shows that  $I_{dfe}$  is locally asymptotically stable if  $r\beta < \gamma$  and unstable if  $r\beta > \gamma$ , while  $I_{ee}$  is locally asymptotically stable if  $r\beta > \gamma$  and unstable if  $r\beta < \gamma$ . Furthermore, at  $r\beta = \gamma$ ,  $I_{ee} = I_{dfe}$ , so there is a transcritical bifurcation at  $r\beta = \gamma$ , where the two equilibria collide and exchange stability.

Since  $(1/\gamma)$  is the average duration of the infectious period, the product,  $(r)(\beta)(1/\gamma)$ , is the expected number of new infections from one infected individual in a fully susceptible population through the entire duration of the infectious period. We denote this quantity as the basic reproductive number,  $R_0$ ,

$$R_0 = \left( \begin{array}{c} \text{Number of} \\ \text{contacts} \\ \text{per unit time} \end{array} \right) \left( \begin{array}{c} \text{Probability of} \\ \text{transmission} \\ \text{per contact} \end{array} \right) \left( \begin{array}{c} \text{Duration of} \\ \text{infection} \end{array} \right), \quad (11a)$$

$$= \frac{r\beta}{\gamma}. \quad (11b)$$

If  $R_0 > 1$ , an introduced infectious individual leads to more than one infection so the number of infectious individuals increases and the pathogen spreads in the population. If  $R_0 < 1$ , the infection in one individual

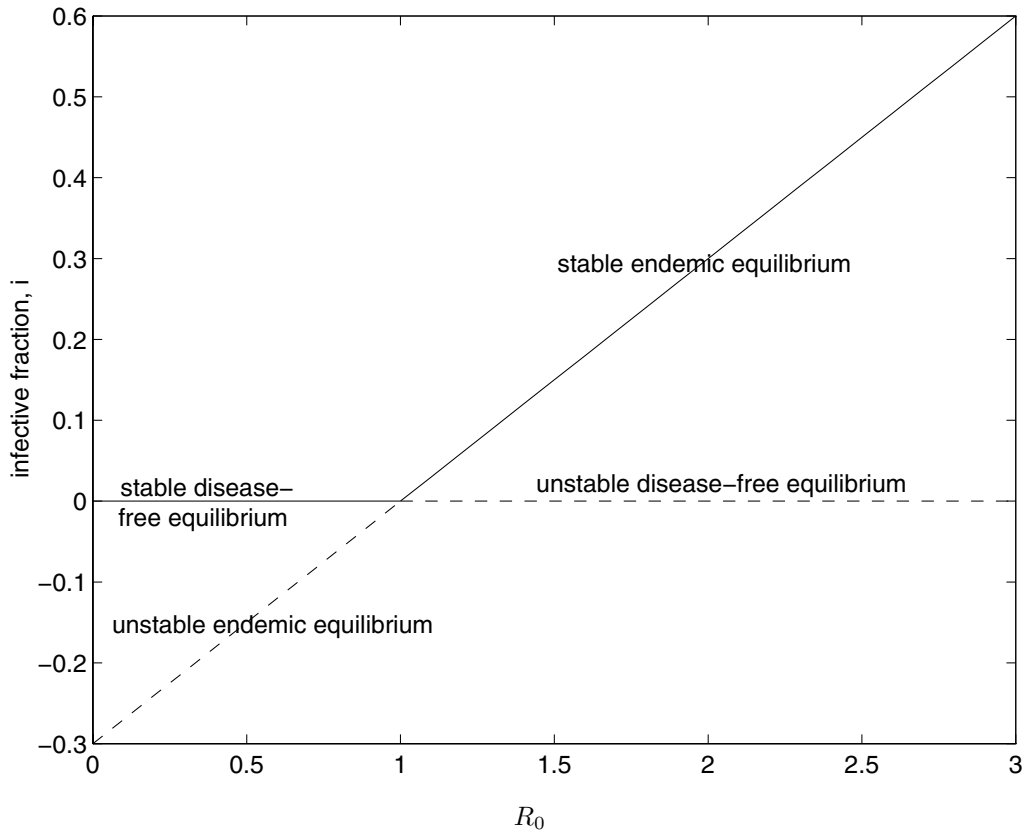


Figure 5: A schematic of a bifurcation diagram for SIS model. At  $R_0 = 1$ , there is a transcritical bifurcation where the disease-free and endemic equilibrium point collide and exchange stability. This figure is reproduced from Hethcote (2000) [2].

cannot replace itself so the pathogen dies out. The threshold condition,  $R_0 = 1$  is equivalent to the threshold condition described earlier,  $r\beta = \gamma$ , so  $R_0 = 1$  describes a transcritical bifurcation, as shown in Figure 5.

## 4 Epidemic Susceptible-Infectious-Recovered (SIR) Model

The epidemic susceptible-infectious-recovered (SIR) is similar to the SIS model, except that infection with the pathogen leads to lifelong immunity. Therefore, we introduce a new class of recovered individuals,  $R$ , that have recovered from infection and are immune to reinfection, with the total population size,  $N = S + I + R$ . This model is appropriate to viral diseases such as measles, mumps and rubella. A schematic of the model is shown in Figure 6; a summary of model variables is in Table 1 and parameters in Table 2.

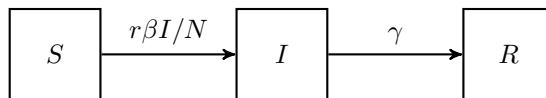


Figure 6: Epidemic Susceptible-Infectious-Susceptible model.

$$\frac{dS}{dt} = -r\beta S \frac{I}{N} \quad (12a)$$

$$\frac{dI}{dt} = r\beta S \frac{I}{N} - \gamma I \quad (12b)$$

$$\frac{dR}{dt} = \gamma I \quad (12c)$$

Since the population size is fixed, we can reduce (12) to a system of two equations, with  $R = N - S - I$ . To focus on the proportion of individuals who are infectious,  $i$ , and susceptible,  $s$ , we can also normalize the variables by the population size,

$$\begin{aligned} s &= S/N, \\ i &= I/N, \end{aligned}$$

with  $r = (1 - s - i)$ . Some calculations show that,

$$\begin{aligned} \frac{ds}{dt} &= \frac{1}{N} \frac{dS}{dt}, \\ &= -r\beta si, \end{aligned} \quad (13a)$$

$$\begin{aligned} \frac{di}{dt} &= \frac{1}{N} \frac{dI}{dt}, \\ &= r\beta si - \gamma i. \end{aligned} \quad (13b)$$

Unlike the previous models, the SIR model has no analytical solution, but we can still conduct numerical simulations and perform equilibrium analysis. We show two simulations of (12) in Figure 7.

The system of equations (13) has infinitely many equilibrium points,

$$i^* = 0, \quad (14a)$$

$$s^* = \xi, \quad (14b)$$

for any  $\xi \in [0, 1]$ . The Jacobian of (13) is,

$$J = \begin{pmatrix} -r\beta i & -r\beta s \\ r\beta i & r\beta s - \gamma \end{pmatrix}. \quad (15)$$

Evaluating the Jacobian (15) at any equilibrium point (14),

$$J^* = \begin{pmatrix} 0 & -r\beta\xi \\ 0 & r\beta\xi - \gamma \end{pmatrix}. \quad (16)$$

This matrix,  $J^*$ , has two eigenvalues,

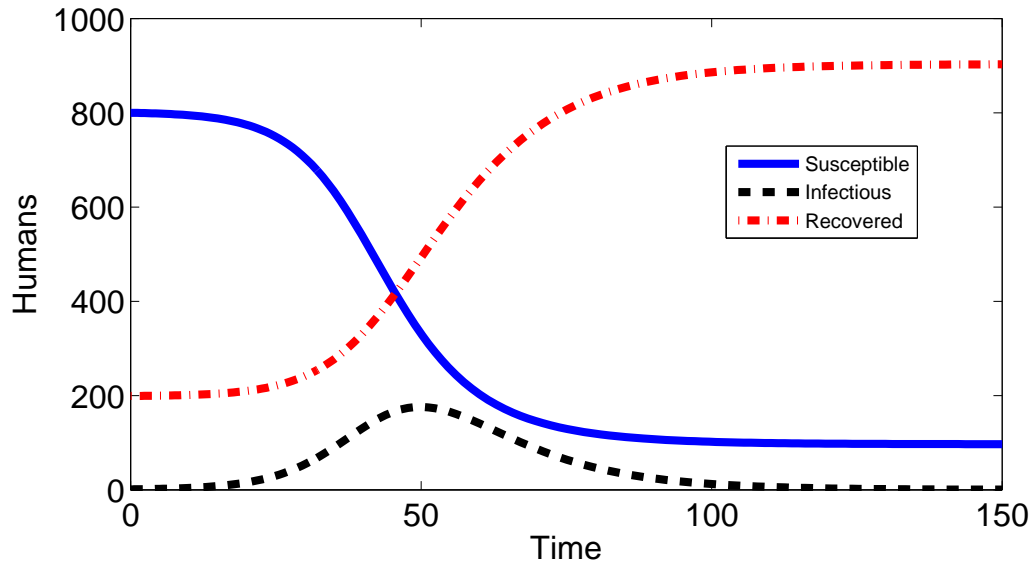
$$\lambda_1 = 0, \quad (17a)$$

$$\lambda_2 = r\beta\xi - \gamma. \quad (17b)$$

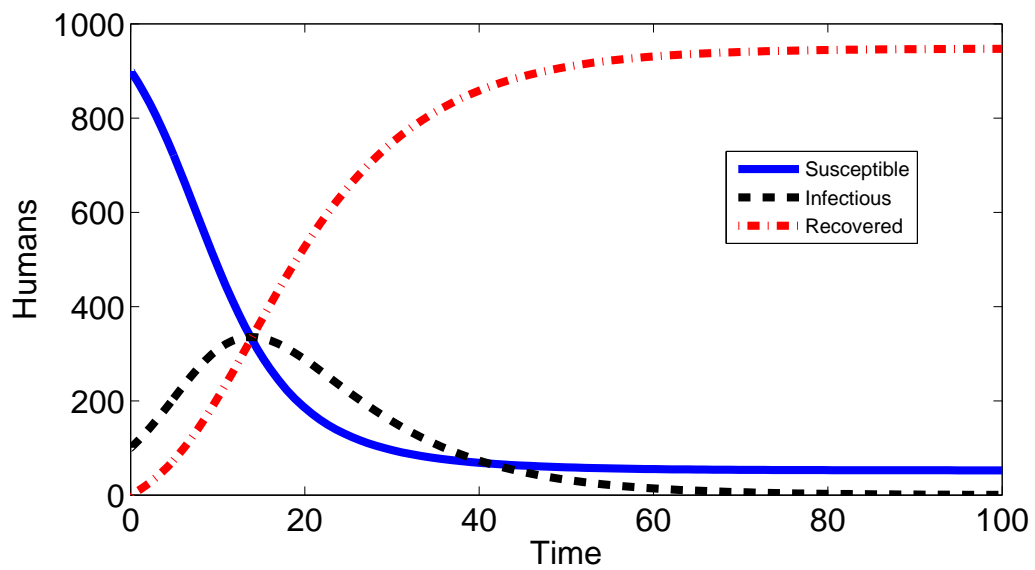
Thus, the equilibrium point (14) is unstable if  $\xi > \gamma/(r\beta)$  ( $\xi > 1/R_0$ ), and neutrally stable if  $\xi < \gamma/(r\beta)$  ( $\xi < 1/R_0$ )<sup>1</sup>, as seen in the phase portrait diagram in Figure 8.

Remember that the basic reproductive number,  $R_0$ , is defined as the expected number of secondary infections that one infected person would produce in a *fully susceptible* population through the entire duration of the infectious period. When the population is not fully susceptible, the replacement number,  $R_e(t)$  defines

<sup>1</sup>Since one eigenvalue is equal to zero, we need additional methods to linear analysis to show neutral stability for  $s^* < (1/R_0)$ .



(a) Initial conditions:  $S(0) = 800$ ,  $I(0) = 1$ ,  $R(0) = 199$ .



(b) Initial conditions:  $S(0) = 900$ ,  $I(0) = 100$ ,  $R(0) = 0$ .

Figure 7: A numerical simulation of the SIR model with  $r = 6$ ,  $\beta = 0.05$ , and  $\gamma = 0.1$  so that  $R_0 = 3$  for two different initial conditions.

the expected number of secondary infections that one infected person would produce through the entire duration of the infectious period,

$$R_e = \left( \begin{array}{c} \text{Number of} \\ \text{contacts} \\ \text{per unit time} \end{array} \right) \left( \begin{array}{c} \text{Probability of} \\ \text{transmission} \\ \text{per contact} \end{array} \right) \left( \begin{array}{c} \text{Duration of} \\ \text{infection} \end{array} \right) \left( \begin{array}{c} \text{Proportion of} \\ \text{susceptible} \\ \text{population} \end{array} \right), \quad (18a)$$

$$= \frac{r\beta s(t)}{\gamma} \quad (18b)$$

$$= R_0 s(t). \quad (18c)$$

When  $R_e(t) > 1$ , the number of infectious individuals increases, while when  $R_e(t) < 1$ , the number of infectious individuals decreases.

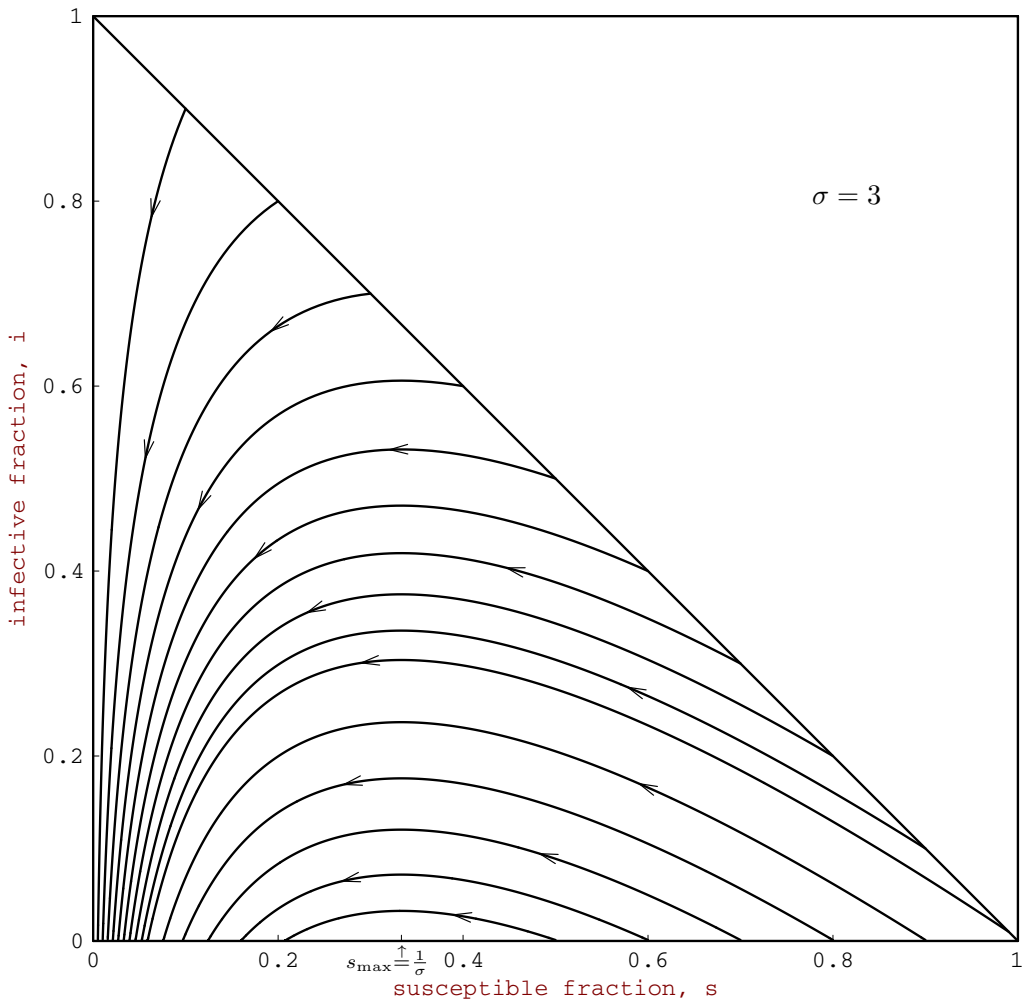


Figure 8: A phase portrait of the normalized epidemic SIR model (13). Here,  $\sigma = R_0 = 3$ . There are infinitely many equilibrium points in the continuum,  $i = 0$  from  $s = 0$  to  $s = 1$ . All equilibrium points where  $s > 1/R_0$  are unstable while those where  $s < 1/R_0$  are neutrally stable. The maximum proportion of infectious individuals occurs when  $s = 1/R_0$ . This figure is reproduced from Hethcote (2000) [2].



## 5 Endemic Susceptible-Infectious-Recovered (SIR) Model

The endemic SIR model is an extension of the epidemic SIR model that allows for birth and death. In this case, we consider a model with a constant birth rate (that's independent of the population size),  $\Lambda$ , and a constant per-capita death rate,  $\mu$ . A schematic of the model is shown in Figure 9; a summary of model variables is in Table 1 and parameters in Table 2.

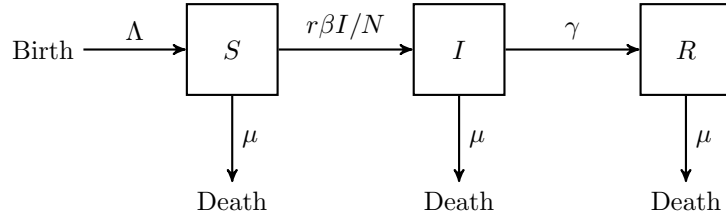


Figure 9: Endemic Susceptible-Infectious-Susceptible model with birth and death.

$$\frac{dS}{dt} = \Lambda - r\beta S \frac{I}{N} - \mu S \quad (19a)$$

$$\frac{dI}{dt} = r\beta S \frac{I}{N} - \gamma I - \mu I \quad (19b)$$

$$\frac{dR}{dt} = \gamma I - \mu R \quad (19c)$$

Again, we cannot analytically solve this system of equations and since the population size,  $N = S + I + R$ , is not constant, we cannot reduce the dimension of the system of equations. We show a numerical simulation of (19) in Figure 10. We can still, however, conduct equilibrium stability analysis. Summing the equations of the SIR model (19), leads to the linear equation,

$$\frac{dN}{dt} = \Lambda - \mu N, \quad (20)$$

for the dynamics of the total population size,  $N$ . This equation has one equilibrium point,

$$N^* = \frac{\Lambda}{\mu}, \quad (21)$$

which is globally asymptotically stable.

Since in the endemic SIR model, infectious individuals can either leave through recover or death, the duration of the infectious period is  $1/(\gamma + \mu)$ , and the basic reproductive number is defined as,

$$R_0 = \frac{r\beta}{\gamma + \mu}. \quad (22)$$

The model (19) has two equilibrium points. The disease-free equilibrium point is,

$$S_{dfe} = \Lambda/\mu, \quad (23a)$$

$$I_{dfe} = 0, \quad (23b)$$

$$R_{dfe} = 0, \quad (23c)$$

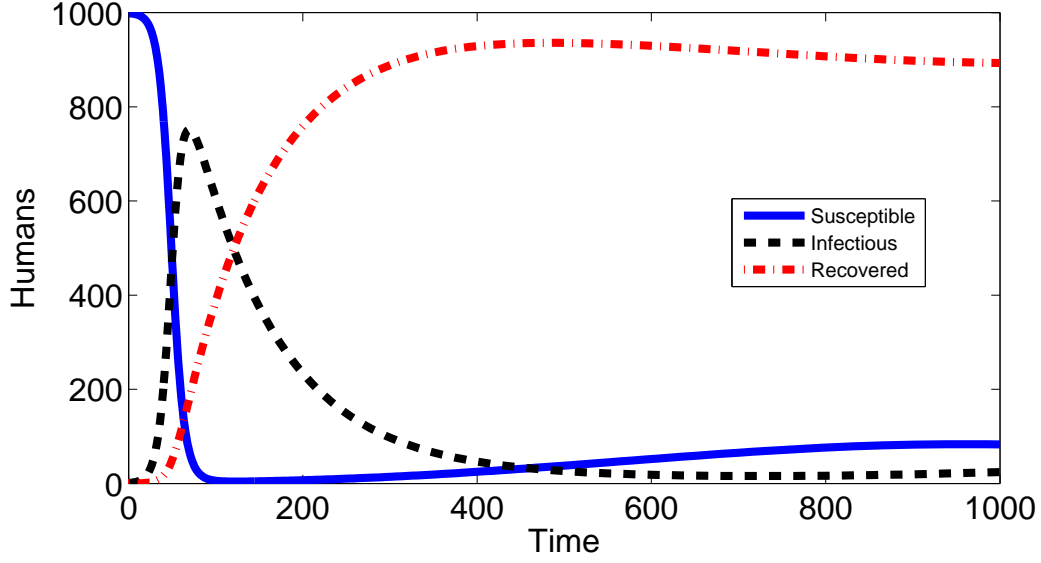


Figure 10: A numerical simulation of the endemic SIR model with  $r = 3$ ,  $\beta = 0.05$ ,  $\gamma = 0.01$ ,  $\mu = 0.0003$ , and  $\Lambda = 0.3$ ; and initial conditions,  $S(0) = 999$ , and  $I(0) = 1$ .

or equivalently,

$$S_{dfe} = N^*, \quad (24a)$$

$$I_{dfe} = 0, \quad (24b)$$

$$R_{dfe} = 0. \quad (24c)$$

The endemic equilibrium point is,

$$S_{ee} = \frac{\Lambda(\gamma + \mu)}{\mu r \beta}, \quad (25a)$$

$$I_{ee} = \frac{\Lambda(r\beta - (\gamma + \mu))}{r\beta(\gamma + \mu)}, \quad (25b)$$

$$R_{ee} = \frac{\Lambda\gamma(r\beta - (\gamma + \mu))}{\mu r \beta(\gamma + \mu)}, \quad (25c)$$

or equivalently,

$$S_{ee} = \frac{N^*}{R_0}, \quad (26a)$$

$$I_{ee} = \frac{\mu N^*}{r\beta} (R_0 - 1), \quad (26b)$$

$$R_{ee} = \frac{\gamma N^*}{r\beta} (R_0 - 1). \quad (26c)$$

Thus, at  $R_0 = 1$ , the endemic equilibrium is equal to the disease-free equilibrium; and the endemic equilibrium is only positive when  $R_0 > 1$ . Note that at the endemic equilibrium point, the replacement number,  $R_e(t) = R_0 S_{ee} / N = 1$ , so the number of infectious individuals exactly replace themselves over time.

The eigenvalues of the Jacobian of (19) at the disease-free equilibrium point are,

$$\lambda_1 = -\mu, \tag{27a}$$

$$\lambda_2 = -\mu, \tag{27b}$$

$$\lambda_3 = r\beta - (\gamma + \mu), \tag{27c}$$

so when  $R_0 < 1$ , the disease-free equilibrium point is locally asymptotically stable, and when  $R_0 > 1$ , the disease-free equilibrium point is unstable. Correspondingly, we can show that the endemic equilibrium is locally asymptotically stable when  $R_0 > 1$ . The bifurcation diagram of the endemic SIR model is similar to that of the SIS model shown in Figure 5.

## 6 Extensions to Basic Compartmental Models

We have described the simplest compartmental models here. There are many possible extensions to these models, depending on the pathogen under investigation and the questions being asked. Some of these extensions are listed here.

### 6.1 Population Dynamics

The endemic SIR model considered linear population dynamics with a constant recruitment rate. The population dynamics can be extended to include,

- Constant per-capita birth rate.
- Density-dependent death rate leading to a logistic model for population dynamics.
- Disease-induced death rate leading to disease-dependent population dynamics.

### 6.2 Additional Disease Stages

We only considered three disease stages. There are many other possible stages including,

- Maternal immunity: infants with maternal antibodies that prevent infection.
- Exposed: individuals with latent infections that have yet to become infectious.
- Vaccination: vaccinated individuals that are protected from infection.
- Asymptomatic: infected individuals that show no symptoms but can be infectious.
- Treatment: infected individuals undergoing treatment that may have lower infectivity and faster recovery times.
- Additional infectious stages for multiple strains of the pathogen.

We can also add movement from the recovered stage to the susceptible stage for diseases with temporary immunity.

### 6.3 Heterogeneity

The models considered here have assumed that the host population is homogeneous (everyone is the same). We can relax this assumption by allowing the population to be differentiated according to various characteristics, including,

- Age.
- Location.
- Sociability (number of contacts).
- Socioeconomic status.

We can model heterogeneity either through replicating the equations for multiple groups with discrete characteristics, leading to higher dimensional ordinary differential equations; or by allowing these characteristics to vary continuously leading to partial differential equations.

## 6.4 Seasonality

We have assumed that all parameters are constant in time, but in many diseases, parameters may vary periodically. This may occur due to climatic variations for diseases such as malaria. Alternatively, there could be periodic changes in human behavior, such as the opening and closing of schools through the year, which may be important for childhood diseases. Including seasonality usually leads to periodically-forced differential equations.

## 6.5 Vector-Borne Diseases

Many diseases such as malaria and schistosomiasis are not transmitted directly from one human host to another. They require an intermediate vector. These diseases require the modeling of two or more interacting populations of hosts.

## 6.6 Macroparasites

Macroparasites such as helminths cannot reproduce within the human body and humans need to be continually reinfected to sustain the infection. Models of such parasites cannot simply treat infected individuals as infected, but need to explicitly include the intensity of infection.

## 6.7 Basic Reproductive Number

For more complicated models, especially those incorporating heterogeneity and seasonality, it is possible to define threshold quantities like  $R_0$  that determine when the disease-free equilibrium point loses stability; and methods for calculating these quantities exist [1, 3]. However the interpretation of such a threshold quantity may not be straightforward and it may not represent the expected number of new infections that one infected individual would produce through the entire duration of the infectious period, as is the case for the simple homogeneous models.

## References

- [1] J. A. P. HEESTERBEEK AND M. G. ROBERTS, *Threshold quantities for infectious diseases in periodic environments*, Journal of Biological Systems, 3 (1995), pp. 779–787.
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- [3] P. VAN DEN DRIESSCHE AND J. WATMOUGH, *Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission*, Mathematical Biosciences, 180 (2002), pp. 29–48.