Notes for Math 310

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Contents

Chapter 1

Modeling infectious diseases

There are many different types of diseases that affect humans and animals. As indicated by the chapter title we will focus on ***infectious diseases***, which are pathogens that are passed between individuals. A ***pathogen*** is broad term and is used to describe any disease-causing agent such as bacteria, viruses, etc. In contrast, ***non-infectious*** diseases are not caused by pathogens and cannot be transmitted between individuals. For example, diabetes and arthritis are non-infectious diseases.

We can further divide infectious diseases into two categories: macroparasites (e.g. helminths) and microparasites (e.g. bacteria). Each of these categories can once again be broken down into two categories: direct and indirect transmission. Direct transmission occurs when a pathogen is transmitted between individuals through close contact (saliva, etc). Indirect transmission occurs when a pathogen survives outside of its host before causing infection. This can occur through vector-borne diseases in which a secondary vector (or host), such as mosquitoes and ticks, transmits the pathogen to a new human or animal host. Dengue virus and malaria are both examples of vector-borne diseases.

This chapter will primarily focus on microparasitic directly transmitted infectious diseases. This is summarized in Figure 1.1.

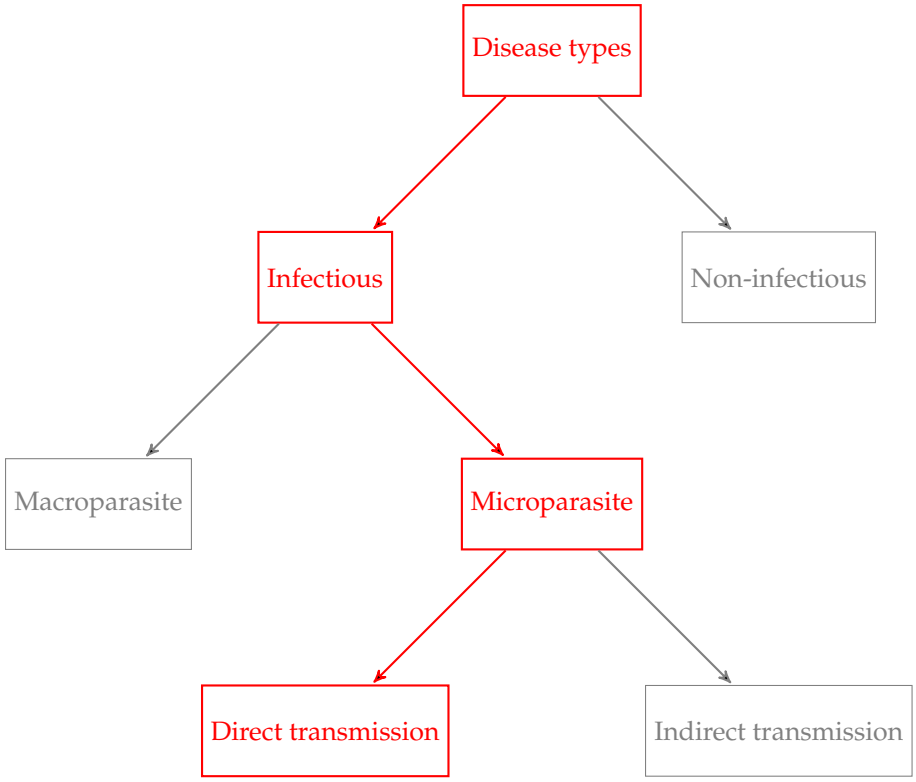

Figure 1.1. Characterization of diseases. The categories highlighted in red will be the primary focus in this course.

1.1 Creating compartmental models

Epidemic models are generally constructed as "compartmental models." In other words, we take a given population and divide it into compartments based on an individual's infection status (e.g. susceptible, infected, etc.). In the most simple model, we make a number of assumptions:

1. The population is "closed" (no deaths – natural or disease-induced, no births, population size N is fixed)
2. Only two processes occur: infection and recovery
3. and so on.

Such a model is shown in the schematic diagram in Figure 1.2.

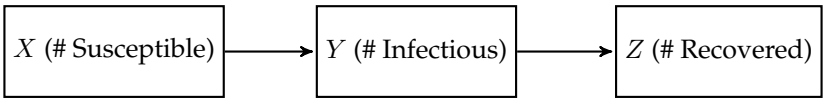

Figure 1.2. Schematic representation disease model

To model the infection process, we let λX be the rate of new infections occurring in a population. λ has important meaning and it is called the ***force of infection***, or the *per capita* rate at which susceptible individuals

acquire infection. Intuitively, new infections must somehow be related to Y – the number of infectives – and there are two ways to do this. Let N be the population size (again, we are assuming this is fixed). The two formulations are:

1. ***Density dependent transmission***: $\lambda = \beta Y$. Here, β is the transmission rate and inherently contains two components: contact rate multiplied by transmission probability. In density dependent transmission, λ increases with Y.
2. ***Frequency dependent transmission***: $\lambda = \beta \frac{Y}{N}$. Here, λ is independent of population size and instead depends on the fraction of individuals who are infective in a population. This is usually the formulation used in directly transmitted infectious diseases in human populations, and what we will consider in this course.

The only other process we need to consider in this model is recovery from infection. Here, we let γ be the recovery rate. Note that $1/\gamma$ is the average duration of time spent in the infectious class. Now, our model is given by:

$$\begin{aligned} \frac{dX}{dt} &= -\beta \frac{Y}{N} X \\ \frac{dY}{dt} &= \beta \frac{Y}{N} X - \gamma Y \\ \frac{dZ}{dt} &= \gamma Y \end{aligned}$$

Notice that the population size is given by

$$N = X + Y + Z$$

and that the population size is not changing, i.e.

$$N' = X' + Y' + Z' = 0$$

When modeling infectious diseases using frequency-dependent transmission, it is often useful to nondimensionalize the state variables X, Y, and Z. Assuming that N (population size) is constant, we define new variables:

$$S = X/N, I = Y/N, R = Z/N$$

so that S, I, and R are the fractions of the population that are susceptible, infectious, and recovered, respectively, to disease. This leaves us with the simpler model:

$$\begin{aligned} \frac{dS}{dt} &= -\beta SI \\ \frac{dI}{dt} &= \beta SI - \gamma I \\ \frac{dR}{dt} &= \gamma I \end{aligned}$$

There are a couple of important properties to point out. Namely,

$$S + I + R = 1$$

and

$$S' + I' + R' = 0$$

Because S, I, and R sum to one, we can find R implicitly:

$$R = 1 - S - I$$

and from this,

$$R' = -S' - I'$$

We can see that the final equation holds by looking at the original differential equations.

There are a couple of questions that we can ask about this model. First, under what conditions will a disease die out? In other words, when will it fail to invade? Suppose we want to consider the dynamics at $t = 0$. Then the disease will fail to invade if:

$$I'|_{t=0} < 0$$

We can first rewrite the differential equation for I as

$$I' = \beta SI - \gamma I = I\left(\beta S - \gamma\right)$$

Now, we want to consider

$$I'|_{t=0} = I(0)\left(\beta S(0) - \gamma\right) < 0$$

We know that $I(0) \geq 0$ so we only consider

$$I'|_{t=0} = \beta S(0) - \gamma < 0 \Rightarrow \frac{\beta}{\gamma} S(0) < 1$$

In other words, the initial fraction of susceptibles multiplied by the transmission rate and the duration of time spent in the infectious class must be small enough so that the epidemic cannot take off. At the onset of an epidemic, I is close to zero and in the limit of a fully susceptible population $S(0) = 1$. Therefore, we simplify this so that

$$\frac{\beta}{\gamma} < 1$$

implies the disease will die out and, in contrast, if

$$\frac{\beta}{\gamma} > 1$$

the disease will successfully invade. This is a ***threshold phenomenon*** and the quantity $\frac{\beta}{\gamma}$ is called R_0, or the ***basic reproductive number***. R_0 is defined as the "average number of secondary cases arising from an average primary case in an entirely susceptible population." We note that each model will have an R_0 dependent on model parameters. This quantity is arguably the most important quantity in disease modeling.

Before adding complexity to these models, we ask the question: do any susceptible individuals "escape" infection? In other words, what is:

$$\lim_{t \to \infty} S(t) = ?$$

We will use a couple of convenient steps to answer this question. First, by the chain rule we know that:

$$\frac{dS}{dt} = \frac{dS}{dR}\frac{dR}{dt}$$

Let's take a closer look at $\frac{dS}{dR}$:

$$\begin{aligned}\frac{dS}{dR} &= \frac{dS}{dt}/\frac{dR}{dt} \\ &= \frac{-\beta SI}{\gamma I} \\ &= -\frac{\beta}{\gamma}S \\ &= -R_0 S\end{aligned}$$

We can solve this new differential equation and arrive at:

$$S(t) = Ce^{-R_0 R(t)}$$

If we assume that $R(0) = 0$ (given that we are considering the beginning of an epidemic, this is reasonable), then we see that

$$S(t) = S(0)e^{-R_0 R(t)}$$

Recalling our original question, we want to find:

$$\lim_{t\to\infty} S(0)e^{-R_0 R(t)}$$

However, by definition $R_0 > 0$ and $0 \leq S(0), R(t) \leq 1$ so this limit is a positive number. This is counterintuitive! Our model assumes that the only processes affecting the dynamics are infection and recovery from infection. However, as time approaches ∞ there is still a positive fraction of susceptible individuals remaining! This is called ***epidemic burnout*** because transmission eventually dies out because there are not enough *infected* individuals to sustain transmission. Super cool.

Note that we coded this model in MATLAB and used the program to explore the effects of varying R_0 as well as varying γ while fixing R_0,

SIR model with demography

Now that we have a handle on the SIR model, we can begin relaxing assumptions and explore the implications of more biologically realistic models. The first assumption that we'll relax is that there are no births and deaths. To include demography in the SIR model, we need to keep in mind that we nondimensionalized the state variables under the assumption that population size is constant. This requires that:

$$N' = X' + Y' + Z' = 0$$

or, equivalently,

$$\frac{X'}{N} + \frac{Y'}{N} + \frac{Z'}{N} = S' + I' + R' = 0$$

Therefore, any "inputs" (births) must equal the "outputs" (deaths) from the population. We now assume that birth and death rates are equal and denote this rate by μ, noting that $1/\mu$ is interpreted as the average lifespan of an individual in our population. We assume that death rates are the same within each class, each class has the same birth rate, and births result in new susceptible individuals. Now, our model is given by:

$$\begin{aligned}\frac{dS}{dt} &= \mu(S+I+R) - \beta SI - \mu S \\ \frac{dI}{dt} &= \beta SI - \gamma I - \mu I \\ \frac{dR}{dt} &= \gamma I - \mu R\end{aligned}$$

Because $S + I + R = 1$ we can rewrite this model as:

$$\begin{aligned}\frac{dS}{dt} &= \mu - \beta SI - \mu S \\ \frac{dI}{dt} &= \beta SI - (\gamma+\mu) I \\ \frac{dR}{dt} &= \gamma I - \mu R\end{aligned}$$

We can now find R_0 as we did in the previous section:

$$I'|_{t=0} = (\beta S(0) - \gamma - \mu)\, I(0) < 0$$

Again, since $I(0) \geq 0$, we only want to look at

$$\beta S(0) - \gamma - \mu < 0 \Longrightarrow \frac{\beta S(0)}{\gamma + \mu} < 1$$

and in the limit of an entirely susceptible population, this leaves us with the basic reproductive number:

$$R_0 = \frac{\beta}{\gamma + \mu}$$

Thus far, we have not explored equilibria in these compartmental models. In epidemiology, models generally have two important equilibria:

a.) ***Disease-free equilibrium*** **(DFE)**: This equilibrium requires there to be no infected individuals in the population, or $I^* = 0$. In the SIR model presented in this section, the DFE is given by $(S^*, I^*, R^*) = (1, 0, 0)$.

b.) ***Endemic equilibrium***: Here, infected individuals are able to persist in the population long-term. In other words, $I^* \neq 0$. Solving for this equilibrium we see that

$$(S^*, I^*, R^*) = \left(\frac{1}{R_0}, \frac{\mu}{\beta}(R_0 - 1), 1 - \frac{1}{R_0} - \frac{\mu}{\beta}(R_0 - 1)\right)$$

Notice how the quantity R_0 keeps appearing – it is very important and ubiquitous in disease modeling.

Now that we have introduced the two types of equilibria, we can use a linear stability analysis to show that the endemic equilibrium is:

$$\begin{cases} \text{stable} & \text{if } R_0 > 1 \\ \text{unstable} & \text{if } R_0 < 1 \end{cases}$$

In contrast, the DFE is:

$$\begin{cases} \text{unstable} & \text{if } R_0 > 1 \\ \text{stable} & \text{if } R_0 < 1 \end{cases}$$

Note: this model was also programmed in MATLAB and we explored the effects of demography by varying μ.

1.2 Modifying the SIR model

The standard SIR model is an extremely powerful model and creates a framework in which to develop models of other infectious disease. The SIR inherently makes many assumptions: lifelong immunity, immediate transfer of individuals between classes, no disease-induced mortality, etc. While this may be appropriate to model things like the common cold, it is not applicable to more complex pathogens. In the following sections, we will introduce a few modifications of the SIR model under various assumptions.

The purpose of this section is to introduce the reader to constructing a compartmental model based on a set of assumptions, and become comfortable with the types of corresponding analyses.

Fatal infections

Consider a disease such as Ebola virus. Transmission occurs from animals to humans and then humans are able to transmit the virus to other humans, allowing Ebola to spread. Ebola has an extremely high *case fatality rate* – proportion of infections that are fatal – of up to 0.9, or 90% of infections result in death. For viruses such as Ebola, it may be reasonable to assume that *all* infections result in death. Of course, this is a simplification, but may be appropriate. Let's also relax the assumptions that births equal deaths, and assume that μ is the *per capita* death rate and ν is the *per capita* birth rate.

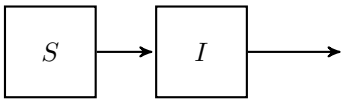

Figure 1.3. SI model

The resulting model includes only two classes – susceptible and infectious – and is called the SI model (schematic in Figure 1.3). Under these assumptions, we can write down the equations:

$$S' = \nu - \beta SI - \mu S$$

$$I' = \beta SI - (\gamma + \mu)I$$

Again, we are assuming that $S+I = 1$. Here, $1/\gamma$ is again the average number of days spent in the infectious class, but now it is equivalent to the average number of days being infected prior to death.

In this model, we need to be careful! We are assuming that N is changing, both because $\mu \neq \nu$ and through disease-induced mortality. It's ok to write the model as we did above, but we need to *clearly state this is the case*. Also, it is critical to keep track of N when programming the model. We can put this back in terms of X and Y to see exactly how N is changing:

$$\begin{aligned} X' &= \nu N - \beta \frac{XY}{N} - \mu X \\ Y' &= \beta \frac{XY}{N} - (\gamma + \mu)Y \end{aligned}$$

Since $N = X + Y$, we know that

$$N' = X' + Y' = \nu N - (X + Y)N - \gamma Y = (\nu - \mu)N - \gamma Y$$

Finally, we can find R_0 in the same way as we did in the previous section, and see see that

$$R_0 = \frac{\beta}{\gamma + \mu}.$$

Why is R_0 the same as it was for the SIR model?

No immunity, multiple infections

In this section, let's consider a pathogen such as rotavirus. Prior to the introduction of vaccination in 2006, almost all children in the U.S. were infected by the age of 5. Following infection, there is no immunity and individuals can be infected multiple times. Also, let's ignore any demographic behavior. This can be described by an SIS model, where individuals become infected and upon recovery re-enter the susceptible class (schematic in Figure 1.4).

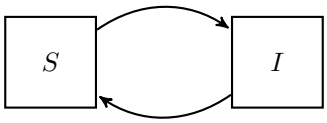

Figure 1.4. SIS model

This model can simply be described by

$$\begin{aligned} S' &= -\beta SI + \gamma I \\ I' &= \beta SI - \gamma I \end{aligned}$$

We are assuming $S + I = 1$, or $S = 1 - I$. We can use this relationship to implicitly find the S dynamics and rewrite the equation for I as:

$$I' = \beta(1 - I)I - \gamma I$$

$$\begin{aligned} &= I(\beta - \gamma - \beta I) \\ &= (\beta - \gamma) I \left(1 - \frac{\beta}{\beta - \gamma} I\right). \end{aligned}$$

This is exactly the logistic equation! Here,

$$I^* = 1 - \frac{1}{R_0}.$$

Here, if $R_0 > 1$, the endemic equilibrium is positive (and therefore exists). In this case, we know that the endemic equilibrium is stable. In contrast, if $R_0 < 1$ the endemic equilibrium does not exist and the DFE is the only stable equilibrium. This echoes our results from previous sections.

1.3 $SEIR$ model and the next generation matrix

Let's return to models that assume that following infection, individuals confer lifelong immunity. For example, consider measles. Following successful transmission to an individual, they first enter an *incubation* period in which they are not transmitting measles. This period usually lasts 10-12 days before the individual progresses to the infectious period. They then remain infectious for 5-6 days and recovery. Individuals acquire lifelong immunity following natural infection. Therefore, we modify the SIR model to include an exposed (E) class. This is known as the $SEIR$ model and essentially introduces a time delay before exposed individuals progress to the infectious class (Figure 1.5. We will include demography in this model and assume that birth and death rates are equal.

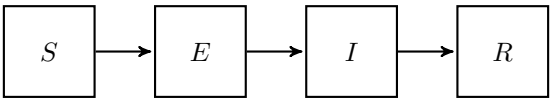

Figure 1.5. $SEIR$ model

If we let $1/\sigma$ be the average time spent in the E class, we can write the model as:

$$\begin{aligned} \frac{dS}{dt} &= \mu - \beta SI - \mu S \\ \frac{dE}{dt} &= \beta SI - (\sigma + \mu) E \\ \frac{dI}{dt} &= \sigma E - (\gamma + \mu) I \\ \frac{dR}{dt} &= \gamma I - \mu R \end{aligned}$$

Since $S + E + I + R = 1$, we can verify that the population size is constant. An interesting observation about this model is that the DFE is given by $(S^*, E^*, I^*, R^*) = (1, 0, 0, 0)$, and the endemic equilibrium is given by:

$$\begin{aligned} S^* &= 1/R_0 \\ E^* &= \frac{\mu(\mu + \gamma)}{\beta\sigma}(R_0 - 1) \\ I^* &= \frac{\mu}{\beta}(R_0 - 1) \end{aligned}$$

Notice that in terms of R_0, these two models have the same equilibrium! However, this equilibrium depends on R_0 and we have not yet determined what R_0 is given by. Suppose we want to find R_0 using the same methods as before. We run into trouble because we want to examine the behavior of I at $t = 0$, and in contrast to previous sections we cannot factor out an I. Instead, we have exposed individuals affecting the dynamics. To address this issue, we can use a method that generalizes the computation of R_0. Keep in mind that our previous method determined when $I' < 0$ to see when the change in I is negative. Equivalently, we can set $I' = 0$ and find this critical value.

Here, we will outline the *next generation matrix* method for finding R_0 and use the $SEIR$ model as an example to demonstrate how it works. First, we want to create a "new" model that only considers the "disease" compartments. The disease compartments are those that include any individuals that are in a stage of infection. In the $SEIR$ model, this includes the exposed and infectious individuals. We want to write this model in the form:

$$\frac{dx_i}{dt} = F_i(x) - V_i(x)$$

where x_i is a vector of each of the i disease compartments (E and I, respectively) and $F_i(x)$ is a vector of the rates of *new* infections entering compartment i. Lastly, $V_i(x)$ is a vector containing all other inputs and outputs from each compartment i, and more specifically it is defined as

$$V_i(x) = V_i^-(x) - V_i^+(x)$$

Here, $V_i^-(x)$ is a vector of the rate of transfer out of each disease class i and $V_i^+(x)$ is the rate of transfer into i. For the $SEIR$ model, we can find each of these vectors:

$$\begin{aligned}
\frac{dx_i}{dt} = \begin{bmatrix} E' \\ I' \end{bmatrix} &= F_i(x) - V_i(x) \\
&= \begin{bmatrix} \beta SI \\ 0 \end{bmatrix} - \left(\begin{bmatrix} (\mu+\sigma)E \\ (\mu+\gamma)I \end{bmatrix} - \begin{bmatrix} 0 \\ \sigma E \end{bmatrix} \right) \\
&= \begin{bmatrix} \beta SI \\ 0 \end{bmatrix} - \begin{bmatrix} (\mu+\sigma)E \\ (\mu+\gamma)I - \sigma E \end{bmatrix}
\end{aligned}$$

We can now rewrite this in matrix form so that:

$$\begin{aligned}
\begin{bmatrix} E' \\ I' \end{bmatrix} &= \left(\begin{bmatrix} 0 & \beta S \\ 0 & 0 \end{bmatrix} - \begin{bmatrix} \mu+\sigma & 0 \\ -\sigma & \mu+\gamma \end{bmatrix} \right) \begin{bmatrix} E \\ I \end{bmatrix} \\
&= (\mathbf{F} - \mathbf{V}) x_i
\end{aligned}$$

noting that we defined these matrices as $\mathbf{F}$ and $\mathbf{V}$. This is essentially the 2-dimensional version of the initial methods we used to find R_0 in the SIR model. Again, we want to determine if the change is positive or negative near the DFE. Therefore, we set:

$$\mathbf{F} - \mathbf{V} = 0 \tag{1.1}$$

Since we are looking at this near the DFE, in the limit we can simply evaluate each matrix at the DFE. This only affects $\mathbf{F}$, which is now given by

$$\mathbf{F}|_{(1,0,0,0)} = \begin{bmatrix} 0 & \beta \\ 0 & 0 \end{bmatrix}$$

Now, to solve Equation 1.1 we bring $\mathbf{V}$ to the right hand side. In one dimension, we can divide both sides by a constant but here we have to do the 2-dimensional equivalent which requires taking a matrix *inverse*.

For the purposes of this course, we will ignore the details on finding matrix inverses, but given a matrix

$$\mathbf{A} = \begin{bmatrix} a & b \\ c & d \end{bmatrix}$$

the inverse is given by

$$\begin{aligned} \mathbf{A}^{-1} &= \frac{1}{\text{Det}A} \begin{bmatrix} d & -b \\ -c & a \end{bmatrix} && (1.2) \\ &= \frac{1}{(ad-bc)} \begin{bmatrix} d & -b \\ -c & a \end{bmatrix} && (1.3) \\ &= \begin{bmatrix} \frac{d}{ad-bc} & \frac{-b}{ad-bc} \\ \frac{-c}{ad-bc} & \frac{a}{ad-bc} \end{bmatrix} && (1.4) \end{aligned}$$

Also, evaluating

$$\mathbf{A}\mathbf{A}^{-1} = \mathbf{I}$$

In other words, the identity matrix is returned. We can use this definition to find the solution to Equation 1.1, which is given by

$$\mathbf{F}\mathbf{V}^{-1} = \mathbf{I}$$

The proof is omitted here, but it turns out that R_0 is given by the eigenvalue with the largest absolute value of $\mathbf{F}\mathbf{V}^{-1}$. This is also called the ***spectral radius*** and is denoted by

$$\rho(\mathbf{F}\mathbf{V}^{-1}).$$

Evaluating $\mathbf{F}\mathbf{V}^{-1}$ for the $SEIR$ model leaves us with the matrix:

$$\mathbf{F}\mathbf{V}^{-1} = \begin{bmatrix} \frac{\beta\sigma}{(\sigma+\mu)(\mu+\gamma)} & \frac{\beta}{\mu+\gamma} \\ 0 & 0 \end{bmatrix}$$

R_0, or the spectral radius, is given by

$$\frac{\beta\sigma}{(\sigma+\mu)(\mu+\gamma)}$$

Here, notice that

$$\frac{\sigma}{\sigma+\mu}$$

essentially discounts R_0 according to the fraction of individuals who suffer natural mortality in the E class.

1.4 Risky behavior

The epidemiological models that we have considered thus far are all unstructured. This means that they do not distinguish between age, sex, or other types of structure. In this section, we will develop and analyze a model of a particular type of structure: risk structure. Risk structure is most easy applied to sexually transmitted infections (STIs), and we will determine how this structure changes the model predictions as compared to an unstructured model. We will consider to classes of risky behavior:

a.) ***Low risk***: low risk of acquiring STIs. This type of behavior is usually characterized by no or few sexual partners, safe sex practices, etc.

b.) ***High risk***: high risk of acquiring STIs. This type of behavior is usually characterized by multiple sexual partners, unprotected sex, needle sharing by intravenous drug users (e.g. transmission of HIV or hepatitis), etc.

We need to make a number of assumptions. First, we will ignore demographic behavior. Second, we will assume that the model falls within the SIS paradigm. In other words, individuals recover from infection and immediately following recovery they become susceptible again. This is the case for treatable STIs; for example, chlamydia and gonorrhea. To divide the classes according to risk, there will be four classes in total: high risk susceptible and infectious and low risk susceptible and infectious. Classes containing the low risk group will always have a subscript L and classes containing the high risk group will always have a subscript H.

To define the model, we begin by talking about numbers of individuals rather than fractions. We define each let N be the total population such that:

$$N = N_L + N_H$$

where $N_L = X_L + Y_L$ and $N_H = X_H + Y_H$. Now, we can define each class by fractions of individuals in the population:

$$\begin{aligned} S_L &= X_L/N \\ I_L &= Y_L/N \\ S_H &= X_H/N \\ I_H &= Y_H/N \end{aligned}$$

From this, notice that $S_L + I_L + S_H + I_H = 1$. Further, we define:

$$\begin{aligned} n_L &= S_L + I_L \leq 1 \\ n_H &= S_H + I_H \leq 1 \end{aligned}$$

Now that we have constructed each of our compartments, we create a schematic diagram (Figure 1.6). This model is similar to the standard SIS model, but I_H individuals may infect S_L individuals and I_L individuals may infect S_H individuals.

We assume that γ_H is the recovery rate for high risk infections individuals and γ_L is the recovery rate for low risk infectious individuals (note that these may be equal, but here we will assume that they are distinct). Further, we let β_{ij} be the transmission rate from individuals in class j to class i. Now, we can write down the model:

$$\begin{aligned} S_L' &= -\beta_{LL} S_L I_L - \beta_{LH} S_L I_H + \gamma_L I_L \\ I_L' &= \beta_{LL} S_L I_L + \beta_{LH} S_L I_H - \gamma_L I_L \\ S_H' &= -\beta_{HH} S_H I_H - \beta_{HL} S_H I_L + \gamma_H I_H \\ I_H' &= \beta_{HH} S_H I_H + \beta_{HL} S_H I_L - \gamma_H I_H \end{aligned}$$

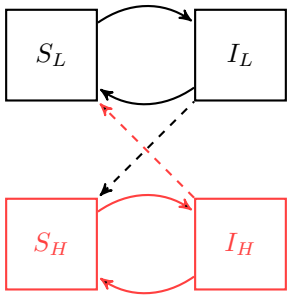

Figure 1.6. Risk-structured SIS model. Black boxes indicate low-risk groups and red boxes indicate high-risk groups. The red dashed line indicates that individuals from I_H can infect individuals in S_L and the black dashed line indicates that individuals from I_L can infect individuals in S_H.

Recall that the force of infection (FOI), λ, is equal to the *per capita* rate at which susceptibles acquire infection. In this model, we have two distinct FOIs: one for high risk and the other for low risk individuals. These are given by:

$$\begin{aligned} \lambda_L &= \beta_{LL} I_L + \beta_{LH} I_H \\ \lambda_H &= \beta_{HH} I_H + \beta_{HL} I_L \end{aligned}$$

We can also write this in matrix form as:

$$\begin{bmatrix} \lambda_L \\ \lambda_H \end{bmatrix} = \begin{bmatrix} \beta_{LL} & \beta_{LH} \\ \beta_{HL} & \beta_{HH} \end{bmatrix} \begin{bmatrix} I_L \\ I_H \end{bmatrix}$$

The matrix containing the transmission rates has a special name, and it is known as the ***Who Acquires Infection From Whom*** (WAIFW) (they clearly thought long and hard about making a clever acronym that is easy to remember). It is often useful to make some assumptions about this matrix to determine what the appropriate β_{ij} values should be. For example:

a.) ***Assortative mixing***: this means that high risk individuals are more likely to partner with other high risk individuals, and low risk individuals are more likely to partner with other low risk individuals. Under these assumptions, $\beta_{LL}, \beta_{HH} > \beta_{HL}, \beta_{LH}$. Further, transmission is most likely to be highest between high risk individuals, so $\beta_{HH} = \max(\beta_{ij})$

b.) ***Symmetric mixing***: under this assumption, the number of interactions between high and low risk individuals is the same as the number of interactions between low and high risk individuals. In other words, $\beta_{HL} = \beta_{LH}$.

Now, we want to find R_0 using the next generation matrix. To do this, we need to know what the DFE is. Here, it is slightly different compared to other models that we have studied because the total population is divided into the low and high risk categories. Therefore, the DFE is given by:

$$(S_L^*, I_L^*, S_H^*, I_H^*) = (n_L, 0, n_H, 0)$$

Now, we want to find $\mathbf{F}$ and $\mathbf{V}$. These are given by:

$$\mathbf{F} = \begin{bmatrix} \beta_{LL} S_L & \beta_{LH} S_L \\ \beta_{HL} S_H & \beta_{HH} S_H \end{bmatrix}$$

and

$$\mathbf{V} = \begin{bmatrix} \gamma_L & 0 \\ 0 & \gamma_H \end{bmatrix}$$

After evaluating at the DFE, we can show that

$$\mathbf{FV}^{-1} = \begin{bmatrix} \frac{\beta_{LL} n_L}{\gamma_L} & \frac{\beta_{LH} n_L}{\gamma_H} \\ \frac{\beta_{HL} n_H}{\gamma_L} & \frac{\beta_{HH} n_H}{\gamma_H} \end{bmatrix}$$

If we try to find the eigenvalues of this (the largest magnitude of which is R_0), we end up with a big messy equation. However, in the special case that β_{ij} is separable (i.e. for β_{ij} there exists α_i, σ_j such that $\beta_{ij} = \alpha_i \beta_j$), we can show that the dominant eigenvalue is given by:

$$\begin{aligned} R_0 &= \frac{\beta_{HH} n_H + \beta_{LH} n_L}{\gamma_H} + \frac{\beta_{LL} n_L + \beta_{HL} n_H}{\gamma_L} \\ &= R_0^H + R_0^L \end{aligned}$$

This is just a weighted sum of the R_0 values for each risk class! This is significantly different from an unstructured model, in which transmission would be weighted equally between classes. For example, notice how R_0 would change as the relative values of n_L and n_H change. We will explore this further using MATLAB.

1.5 Temporally forced models

An important consideration in SIR-type models is changes in parameter values through time. Here, we briefly introduce one type of "forcing": seasonal transmission. Because contact rates may change over time (especially in the case of childhood infectious diseases), transmission rates can change as a consequence. We can now write the standard SIR model with seasonal transmission as

$$\begin{aligned} S' &= \mu - \beta(t) SI - \mu S \\ I' &= \beta(t) SI - (\gamma + \mu) I \end{aligned}$$

where $\beta(t)$ is now the time-dependent seasonal transmission rate. The most common way to define this is:

$$\beta(t) = \beta_0 \left(1 + \beta_1 \cos\left(\omega t\right)\right).$$

Here, β_0 is the average (or "baseline") transmission rate, β_1 is the amplitude of seasonal forcing ($0 \leq \beta_1 \leq 1$), and ω is the period of seasonal transmission. Assuming it is annually periodic and time is measured in days,

$$\omega = \frac{2\pi}{365}$$

As shown in class, we can determine when I is increasing based on the number of susceptibles at time t. In particular, I is increasing when

$$S(t) > 1 - \frac{1}{R_0}$$

An alternative way to introduce seasonal transmission is through "term-time" forcing, where transmission only occurs during school terms. Here,

$$\beta(t) = \beta_0 \left(1 + \beta_1 \text{TERM}(t)\right)$$

where $\text{TERM}(t) = 1$ during school terms and -1 otherwise.