Mathematics 4MB3/6MB3 Mathematical Biology
2018 ASSIGNMENT 3

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This assignment is **due in class** on **Wednesday 28 February 2018 at 11:30am**.

Analysis of the standard SIR model with vital dynamics

Consider the standard SIR model with vital dynamics,

$$\frac{dS}{dt} = \mu N - \frac{\beta}{N} SI - \mu S \tag{1a}$$

$$\frac{dI}{dt} = \frac{\beta}{N} SI - \gamma I - \mu I \tag{1b}$$

$$\frac{dR}{dt} = \gamma I - \mu R \tag{1c}$$

where S, I and R denote the numbers of susceptible, infectious and removed individuals, respectively, and $N = S + I + R$ is the total population size. The *per capita* rates of birth and death are the same (both are equal to μ). As usual, β is the transmission rate and γ is the recovery rate.

(a) Prove that the population size N is constant and that equations (1) are biologically well-defined, *i.e.,* the set Δ of biologically meaningful states is forward-invariant. (Note that you will need to begin by defining precisely the set Δ and the term "forward-invariant".)

Proof. First, we need to show that the population size ($N = S + I + R$) is constant. We note that the population size is constant if $dN/dt = dS/dt + dI/dt + dR/dt = 0$, as this implies that the change in each compartment of the population results in overall no change.

$$\begin{aligned} &\frac{dS}{dt} + \frac{dI}{dt} + \frac{dR}{dt} \\ &= (\mu N - \frac{\beta}{N} SI - \mu S) + (\frac{\beta}{N} SI - \gamma I - \mu I) + (\gamma I - \mu R) \\ &= \mu(N - S - I - R) \\ &= \mu(N - N) \\ &= 0 \end{aligned} \tag{2}$$

The biologically relevant region Δ is given by

$$\Delta = \{(S, I, R) : 0 \leq S, I, R \leq N, S + I + R = N\},$$

since none of the compartments can have negative population nor exceed the total population. In order to show that Δ is a forward invariant set, we wish to show that if $(S_0, I_0, R_0) = (S(t_0), I(t_0), R(t_0)) \in \Delta$ at some time t_0, then $(S(t'), I(t'), R(t'))$ at $t' = t_0 + \varepsilon$. To show this we will prove that if any of the compartments are 0, then its derivative is non-negative, and if any of the compartments holds the entire population N, then its derivative is non-positive. This ensures that all compartments remain in Δ.

- Suppose that $S = 0$. Then $dS/dt = \mu N > 0$.
- Suppose that $S = N$. Then this forces $I = 0$ since $S + I + R = N$ and $S, I, R \geq 0$. Then $dS/dt = \mu N - \mu N = 0$.
- Suppose that $I = 0$. Then $dI/dt = 0 - 0 - 0 = 0$.
- Suppose that $I = N$. Then this forces $S = 0$ since $S + I + R = N$ and $S, I, R \geq 0$. Then $dI/dt = -N(\gamma + \mu) < 0$.
- Suppose that $R = 0$. Then, $dR/dt = \gamma I$. As $I \in \Delta$, we have that $I \geq 0$. Thus, $dR/dt \geq 0$.
- Suppose that $R = N$. Then this forces that $I = 0$ since $S + I + R = N$ and $S, I, R \geq 0$. Thus, $dR/dt = -\mu N < 0$.

This then shows that none of the compartments can escape the biologically relevant region Δ provided that the initial condition is in Δ. □

(b) Show that equations (1) are equivalent dynamically to equations for the proportions (rather than numbers) of individuals in each disease state. For the remainder of this problem, use the equations in proportional form.

Proof. To put the equations in the proportional form, we can consider the proportional quantities defined by $\tilde{S} = S/N$, $\tilde{I} = I/N$, and $\tilde{R} = R/N$. We then define a new set of differential equations based on these proportional quantities:

$$\begin{aligned}
\frac{d\tilde{S}}{dt} &= \mu - \frac{\beta}{N^2} SI - \frac{\mu S}{N} \\
&= \mu - \beta \tilde{S}\tilde{I} \\
\frac{d\tilde{I}}{dt} &= \frac{\beta}{N^2} SI - \frac{\gamma I}{N} - \frac{\mu I}{N} \\
&= \beta \tilde{S}\tilde{I} - \gamma \tilde{I} - \mu \tilde{I} \\
\frac{d\tilde{R}}{dt} &= \frac{\gamma I}{N} - \frac{\mu R}{N} \\
&= \gamma \tilde{I} - \mu \tilde{R}
\end{aligned} \tag{3}$$

However this is equivalent to a scaled version of the original system:

$$\begin{aligned} \frac{d\tilde{S}}{dt} &= \frac{1}{N}\frac{dS}{dt} \\ \frac{d\tilde{I}}{dt} &= \frac{1}{N}\frac{dI}{dt} \\ \frac{d\tilde{R}}{dt} &= \frac{1}{N}\frac{dR}{dt} \end{aligned} \tag{4}$$

and so this system of population proportions is dynamically equivalent to the original system. □

(c) Re-express the equations for proportions in *dimensionless* form using the dimensionless time coordinate

$$\tau = (\gamma + \mu)t\,, \tag{5a}$$

and the dimensionless parameters

$$\mathcal{R}_0 = \frac{\beta}{\gamma + \mu}\,, \tag{5b}$$

$$\varepsilon = \frac{\mu}{\gamma + \mu}\,. \tag{5c}$$

What are the biological meanings of τ, $\mathcal{R}_0$ and ε? Why are they good choices for non-dimensionalizing the equations? For a few diseases that you are familiar with, what is the order of magnitude of ε?

Proof. In order to rewrite the equations using the dimensionless time coordinate $\tau = (\gamma + \mu)t$, we wish to write out the equations for $dS/d\tau$, $dI/d\tau$, and $dR/d\tau$. To do this, we note that $dS/d\tau = dS/dt * dt/d\tau$, $dI/d\tau = dI/dt * dt/d\tau$, and $dR/d\tau = dR/dt * dt/d\tau$. This yields the following equations:

$$\begin{aligned} \frac{dS}{d\tau} &= \frac{dS}{dt}\frac{dt}{d\tau} = \frac{dS}{dt}\frac{1}{\gamma+\mu} = \frac{\mu}{\gamma+\mu} - \frac{\beta}{\gamma+\mu}SI - \frac{\mu}{\gamma+\mu}S = \varepsilon - \mathcal{R}_0 SI - \varepsilon S \\ \frac{dI}{d\tau} &= \frac{dI}{dt}\frac{dt}{d\tau} = \frac{dI}{dt}\frac{1}{\gamma+\mu} = \frac{\beta}{\gamma+\mu}SI - \frac{\gamma}{\gamma+\mu}I - \frac{\mu}{\gamma+\mu}I = \mathcal{R}_0 SI - I \\ \frac{dR}{dt} &= \frac{dR}{d\tau}\frac{dt}{d\tau} = \frac{dR}{dt}\frac{1}{\gamma+\mu} = \frac{\gamma}{\gamma+\mu}I - \frac{\mu}{\gamma+\mu}R = (1-\varepsilon)I - \varepsilon R \end{aligned} \tag{6}$$

These equations demonstrate that ε is the dimensionless birth rate and $\mathcal{R}_0$ is the dimensionless transmission rate. Biologically, we note that $\gamma + \mu$ is the rate at which an individual leaves the infected class. Therefore, $\tau = t(\gamma + \mu)$ is a unitless scaling of time such that one unit is the mean infectious period (which is equal to $1/(\gamma + \mu)$). This implies that $\varepsilon = \mu/(\gamma + \mu)$ is the natural death rate per capita expressed as deaths per individual per mean infectious period. Finally, $\mathcal{R}_0$ is the mean number of secondary cases caused by a primary case in a fully susceptible population. We can see this because β is

the mean transmission rate and $1/(\gamma+\mu)$ is the mean infectious period. These parameters are good choices for non-dimensionalizing the equations because they have intuitive biological interpretations. This allows us to obtain external estimates for these parameters so that we do not have to estimate them from the data. For ε for instance, if we can experimentally obtain the mean recovery period $(1/\gamma)$ and obtain a population-wise death rate from census data, we can estimate ε independently of the data.

Here we will estimate ε for chicken pox. For simplicity, we can assume that mean life expectancy is 70 years. Then, $\mu = 1/70\,\text{year}^{-1}$. Chicken-pox is known for full recovery to take about a week. Then, $\gamma = 1/7\,\text{days}^{-1} = 365/7\,\text{years}^{-1} \approx 52\,\text{years}^{-1}$. Our estimate of ε for chicken pox is

$$\varepsilon = \frac{1/70}{1/70+52} \approx 0.00027$$

For rubella, recovery period is approximately 1.5 weeks. Then, $\gamma = 1/1.5\,\text{weeks}^{-1} = 52/1.5\,\text{weeks}^{-1} \approx 34.7\,\text{years}^{-1}$. Our estimate of ε for rubella is

$$\varepsilon = \frac{1/70}{1/70+34.7} \approx 0.00041$$

□

(d) Show that there are exactly two equilibria: the disease free equilibrium (DFE) at $(S,I) = (1,0)$ and an endemic equilibrium (EE) at $(S,I) = (\hat{S},\hat{I})$, where $\hat{S}$ and $\hat{I}$ can be expressed compactly in terms of $\mathcal{R}_0$ and ε. Are both equilibria always biologically relevant?

Proof. In this question we take R, S, I to be the proportional quantities; in other words, we take them to be what was previously referred to as $\tilde{R}$, $\tilde{S}$, and $\tilde{I}$. The system is at equilibrium iff

$$\frac{dS}{dt} = \frac{dI}{dt} = \frac{dR}{dt} = 0.$$

Note that $dI/dt = 0$ if and only if $I(\mathcal{R}_0 S - 1) = 0$ if and only if either $I = 0$ or $\mathcal{R}_0 S - 1 = 0$, (i.e. $S = 1/\mathcal{R}_0$). Note that if $I = 0$ and $dS/dt = \varepsilon - \mathcal{R}_0 SI - \varepsilon S = 0$, then we must have $S = 1$, which gives the the $(\hat{S},\hat{I}) = (0,0)$ disease-free equilibrium (DFE).

Using the $dS/dt = 0$ expression, we can solve for the corresponding I value when $S = 1/\mathcal{R}_0$. This yields $\varepsilon - \mathcal{R}_0 I(1/\mathcal{R}_0) - \varepsilon S = 0$. After rearranging this expression, we have that $I = \varepsilon(1-(1/\mathcal{R}_0))$. Thus, we note that we only have two equilibria, as $dI/dt = 0$ is only satisfied when either $I = 0$ or $\mathcal{R}_0 S - 1 = 0$, and we have just shown that each of these two conditions only happen at one distinct (S,I) point.
The equilibrium expression $(\hat{S},\hat{I}) = (1/\mathcal{R}_0, \varepsilon(1-1/\mathcal{R}_0))$ is biologically relevant when $\mathcal{R}_0 \geq 1$. However, note that this equilibrium expression does not yield a second distinct equilibrium when $\mathcal{R}_0 = 1$; in that case, the expression gives the disease free equilibrium. Thus, if $\mathcal{R}_0 = 1$, we have only the disease free equilibrium, while if $R_0 > 1$, we have a distinct endemic equilibrium. If $R_0 < 1$, then we have that $\hat{S} > 1$ and $\hat{I} < 0$, which is not biologically relevant. In summary, for all R_0, we have the existence of the disease free equilibrium. However, when $\mathcal{R}_0 > 1$, we have the additional existence of an endemic equilibrium. □

(e) Show that the DFE is locally asymptotically stable (LAS) if $\mathcal{R}_0 < 1$ and the EE is LAS if $\mathcal{R}_0 > 1$.

Proof. To prove asymptotic stability for the endemic equilibrium, we examine the Jacobian given by the system $dS/dt = \varepsilon - \mathcal{R}_0 SI - \varepsilon S$ and $dI/dt = \mathcal{R}_0 SI - I$. We find that the Jacobian of this system is:

$$\begin{bmatrix} -\mathcal{R}_0 I - \varepsilon & -\mathcal{R}_0 S \\ \mathcal{R}_0 I & \mathcal{R}_0 S - 1 \end{bmatrix} \tag{7}$$

At the disease free equilibrium $(1, 0)$, this matrix is

$$\begin{bmatrix} -\varepsilon & -\mathcal{R}_0 \\ 0 & \mathcal{R}_0 - 1 \end{bmatrix} \tag{8}$$

which has eigenvalues $\lambda_1 = -\varepsilon < 0$ and $\lambda_2 = \mathcal{R}_0 - 1 < 0$ when $\mathcal{R}_0 < 1$. Therefore, when $\mathcal{R}_0 < 1$, the disease-free equilibrium is locally asymptotically stable, since both eigenvalues are negative.

After plugging in the point for endemic equilibrium given by $(\hat{S}, \hat{I}) = (1/\mathcal{R}_0, \varepsilon(1 - (1/\mathcal{R}_0))$, this matrix becomes:

$$\begin{bmatrix} -\mathcal{R}_0 \varepsilon & -1 \\ \varepsilon(\mathcal{R}_0 - 1) & 0 \end{bmatrix} \tag{9}$$

The eigenvalues of this of this matrix are:

$$\lambda_1 = \frac{1}{2}\left(-\sqrt{\varepsilon}\sqrt{\varepsilon\mathcal{R}_0^2 - 4\mathcal{R}_0 + 4} - \varepsilon\mathcal{R}_0\right) < 0$$

and

$$\lambda_2 = \frac{1}{2}\left(\sqrt{\varepsilon}\sqrt{\varepsilon\mathcal{R}_0^2 - 4\mathcal{R}_0 + 4} - \varepsilon\mathcal{R}_0\right).$$

Note that $\lambda_2 < 0$ if and only if

$$\begin{aligned} \varepsilon\mathcal{R}_0 &> \sqrt{\varepsilon}\sqrt{\varepsilon\mathcal{R}_0^2 - 4\mathcal{R}_0 + 4} \\ \varepsilon^2\mathcal{R}_0^2 &> \varepsilon(\varepsilon\mathcal{R}_0^2 - 4\mathcal{R}_0 + 4) \\ 0 &> -4\mathcal{R}_0 + 4 \\ -4 &> -4\mathcal{R}_0 \\ 1 &< \mathcal{R}_0. \end{aligned} \tag{10}$$

which is when the endemic equilibrium is biologically relevant.
Thus, we have demonstrated that the endemic equilibrium is locally asymptotically stable when $R_0 > 1$ which is the biologically relevant region for the endemic equilibrium.

We note that we could have done an alternative proof for the disease free equilibrium stability using Lyapunov's Direct Method. We now show that second approach to the proof. Define $L(S, I, R) = I + R$, and let $(S_0, I_0, R_0) = (1 - \delta_1, \delta_2, \delta_1 - \delta_2) \in \Delta$. We

wish to show that $(S_*, I_*, R_*) = (1, 0, 0)$ is asymptotically stable using Lyapunov's Direct Method (Theorem 1 on Assignment 1).

We begin by checking the first condition in the theorem. We claim that the region $\mathcal{O}\{(S, I, R) \in \Delta \mid I < \varepsilon(1-S)/(\mathcal{R}_0 S)\} \subset \Delta$. Thus, we wish to verify that $L(S, I, R) = 0$ when $(S, I, R) = (1, 0, 0)$, and that $L(S, I, R) > 0$ when $(S, I, R) \neq (1, 0, 0)$ and $(S, I, R) \in \mathcal{O}$. The first part of this condition is clearly true given that $L(S, I, R) = I + R$ and $I = 0,\ R = 0$ at (S_*, I_*, R_*). We verify the second part of the first condition, as for $(S, I, R) \in \mathcal{O}$ we know that $I = 0$ and $R = 0$ only occur simultaneously if $S = 1$. This is because for $(S, I, R) \in \mathcal{O} \subset \Delta$, we have that $S + I + R = 1$. Therefore, one of S or I is non-zero. As $S, I \in \mathcal{O}$ have that $S, I \in [0, 1]$, it must be that for $(S, I, R) \neq (S_*, I_*, R_*)$, $L(S, I, R) > 0$.

Next, we check the second condition in the theorem. Namely, we verify that $\dot{L}(S, I, R) < 0$ for $\{(S, I, R) \in \mathcal{O} \mid (S, I, R) \neq (1, 0, 0)\}$. We note that $\dot{L}(S, I, R) = dI/dt + dR/dt$. Thus, we wish to verify that $\mathcal{R}_0 SI - I + (1 - \varepsilon)I - \varepsilon R < 0$. Cancelling terms and using that $R = 1 - S - I$, we need to verify that $\mathcal{R}_0 SI - \varepsilon + \varepsilon S < 0$. Now, if $(S, I, R) \in \mathcal{O}$, then $I < \varepsilon(1 - S)/\mathcal{R}_0 S$, and

$$\dot{L} = \mathcal{R}_0 SI - \varepsilon + \varepsilon S < \mathcal{R}_0 S \frac{\varepsilon(1 - S)}{\mathcal{R}_0 S} - \varepsilon + \varepsilon S = \varepsilon(1 - S) - \varepsilon(1 - S) = 0$$

Thus, as the Lyapunov function $L(S, I, R) = I + R$ in the region $\mathcal{O} = \{(S, I, R) \in \Delta \mid I < \varepsilon(1 - S)/\mathcal{R}_0 S\}$ satisfies the conditions for asymptotic stability in Lyapunov's direct method, we have that the disease free equilibrium is locally asymptotically stable when $\mathcal{R}_0 < 1$. □

(f) Prove that the DFE is, in fact, globally asymptotically stable (GAS) if $\mathcal{R}_0 \leq 1$. *Hint:* This requires some careful analysis. Begin by using the function $L(S, I) = I$, and Theorem 2 stated in Assignment 1 under "Notes on Lyapunov Functions", to prove that all initial states in Δ are attracted to the S axis.

Proof. Define $L(S, I, R) = I$ and let $(S_0, I_0, R_0) = (1 - \delta_1, \delta_2, \delta_1 - \delta_2) \in \Delta$. We wish to show that $\mathcal{C} := \{(S, 0, R) | S + R = 1, S, R \geq 0\} \subset \mathcal{O} = \Delta$ is globally asymptotically stable using Lyapunov's Direct Method for Closed Invariant Sets (Theorem 2 on Assignment 1). First, $L(X) = I = 0$ for all $X = (S, 0, R) \in \mathcal{C}$, and if $X \in \Delta \setminus \mathcal{C}$, then $X = (S, \delta, R)$ for some $\delta > 0$. We then have that $L(X) = I = \delta > 0$ in $\Delta \setminus \mathcal{C}$. Then, consider $\dot{L}(X)$ where $X \in \Delta \setminus \mathcal{C}$.

$$\dot{L}(X) = \frac{dL}{dt} = \frac{dI}{dt} = \mathcal{R}_0 SI - I. \tag{11}$$

We can expand this to obtain

$$\begin{aligned} \dot{L}(X) &= \mathcal{R}_0 SI - I \\ &= I\left(\mathcal{R}_0 S - 1\right). \end{aligned} \tag{12}$$

However, if we assume that $\mathcal{R}_0 \leq 1$ and $X \notin \mathcal{C}$, then $S < 1$ and therefore $\mathcal{R}_0 S < 1$, i.e. $\mathcal{R}_0 S - 1 < 0$. It follows then that

$$\dot{L}(X) = I\,(\mathcal{R}_0 S - 1) < 0 \tag{13}$$

as required. Since we have shown this for all $X \in \Delta \setminus \mathcal{C}$, by Lyapunov's Direct Method for Closed Invariant Sets, $\mathcal{C}$ is globally asymptotically stable. □

(g) Prove that the EE is GAS if $\mathcal{R}_0 > 1$. *Hint:* Consider

$$L(S, I) = S - \hat{S} \log S + I - \hat{I} \log I\,, \tag{14}$$

and convince yourself that condition (a) in Theorem 1 stated in Assignment 1 under "Notes on Lyapunov Functions" can be replaced with

$$L(X) > L(X_*) \quad \text{for all} \quad X \in \mathcal{O} \setminus \{X_*\}\,. \tag{15}$$

Note: By GAS we mean here that *almost all* initial states are attracted to the EE. One way of making this precise is to say that the *basin of attraction* of the EE is an open, dense subset of Δ. You should completely describe the basins of attraction of both the EE and the DFE. Do your results make biological sense?

Proof. □

(h) Prove that the approach to the EE occurs via damped oscillations if and only if $\varepsilon < \varepsilon^*$, where

$$\varepsilon^* = \frac{4(\mathcal{R}_0 - 1)}{\mathcal{R}_0^2}\,. \tag{16}$$

For which diseases that you are familiar with would you expect damped oscillations versus monotonic convergence to the equilibrium?

Proof. □

(i) For $\varepsilon < \varepsilon^*$, derive expressions for the period of damped oscillations onto the EE and the e-folding time for decay of the amplitude of oscillation. Use R to make a plot that displays your results graphically for some biologically relevant and illustrative parameter values.

Proof. Recall that the Jacobian of the system (ignoring R) at the endemic equilibrium is given by

$$\begin{bmatrix} -\varepsilon\mathcal{R}_0 & -1 \\ \varepsilon(\mathcal{R}_0 - 1) & 0 \end{bmatrix}$$

where its characteristic equation is given by

$$\lambda^2 + \varepsilon\mathcal{R}_0\lambda + \varepsilon(\mathcal{R}_0 - 1) = 0$$

Then, its eigenvalues are given by

$$\lambda = \frac{-\varepsilon\mathcal{R}_0 \pm \sqrt{\varepsilon^2\mathcal{R}_0^2 - 4\varepsilon(\mathcal{R}_0 - 1)}}{2}.$$

When

$$\varepsilon < \frac{4(\mathcal{R}_0 - 1)}{\mathcal{R}_0^2},$$

the eigenvalues of the Jacobian matrix are given by

$$\lambda = -\frac{\varepsilon\mathcal{R}_0}{2} \pm i\frac{\sqrt{4\varepsilon(\mathcal{R}_0 - 1) - \varepsilon^2\mathcal{R}_0^2}}{2}$$

For convenience, denote

$$\eta = \frac{\sqrt{4\varepsilon(\mathcal{R}_0 - 1) - \varepsilon^2\mathcal{R}_0^2}}{2}$$
$$\alpha = -\frac{\varepsilon\mathcal{R}_0}{2}.$$

Furthermore, denote corresponding eigenvectors by $\vec{v}_1 = \vec{a} + \vec{b}i$ and $\vec{v}_2 = \vec{a} - \vec{b}i$. Consider the following linear system:

$$\frac{d}{dt}\vec{x} = \begin{bmatrix} -\varepsilon\mathcal{R}_0 & -1 \\ \varepsilon(\mathcal{R}_0 - 1) & 0 \end{bmatrix}\vec{x},$$

where

$$\vec{x}(t) = \begin{bmatrix} S(t) \\ I(t) \end{bmatrix}$$

Then, by the result derived from 3MB3 course, we find that the solution to this linear system is given by

$$\vec{x}(t) = \left[c_1\left(\cos(\eta t)\vec{a} - \sin(\eta t)\vec{b}\right) + c_2\left(\sin(\eta t)\vec{a} + \cos(\eta t)\vec{b}\right)\right]\exp(\alpha t),$$

where c_1, c_2 are determined by the initial conditions. Indeed, this shows that the oscillation is damped because $\alpha < 0$ (and the oscillatory dynamics are determined by the sine and cosine terms, and the exponential term determines the magnitude of the oscillations). Furthermore, period of damped oscillation is given by $2\pi/\eta$ which is equal to

$$\frac{4\pi}{\sqrt{4\varepsilon(\mathcal{R}_0 - 1) - \varepsilon^2\mathcal{R}_0^2}}.$$

Furthermore, e-folding time for decay of the amplitude of oscillation is given by

$$-\frac{1}{\alpha} = \frac{2}{\varepsilon\mathcal{R}_0}$$

We expect our original SIR model to have similar e-folding time as well as period as this system. We want to confirm these facts numerically.

First, we need to load some packages:

```
library(deSolve)
library(dplyr)
```

Following the previous assignment, we start by writing the gradient function:

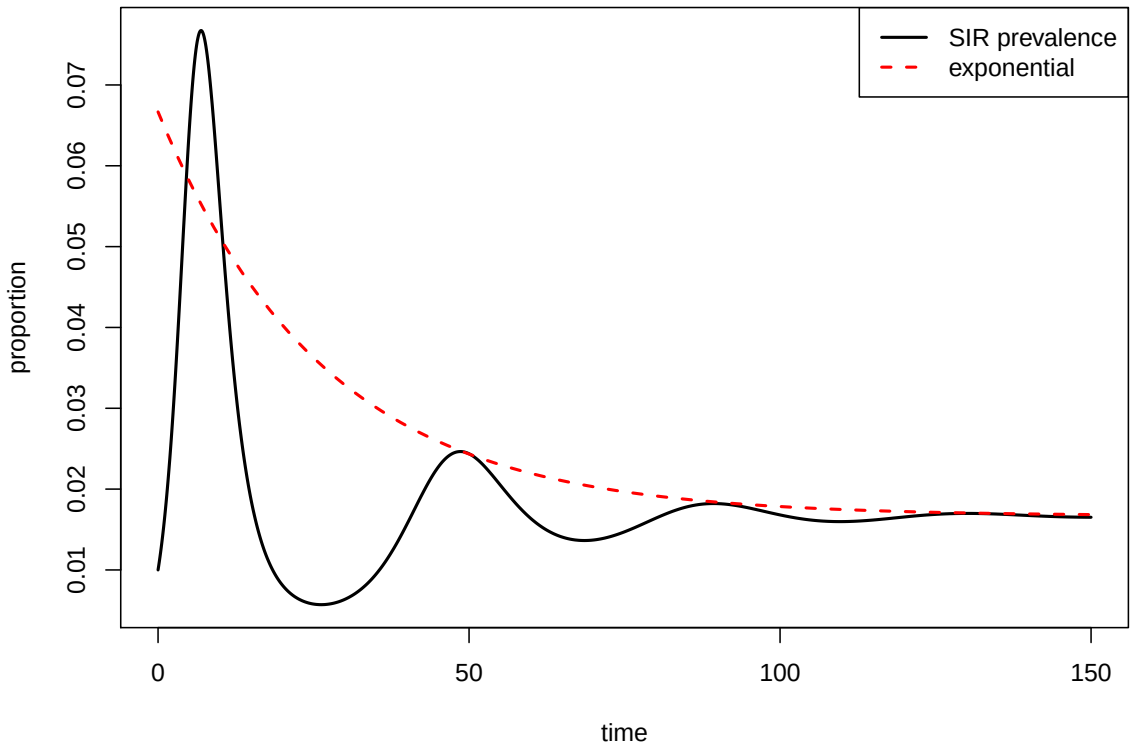
```
SIR.grad <- function(t, y, param) {
    with(as.list(c(param, y)), {
        dS <- epsilon - R0 * S * I - epsilon * S
        dI <- R0 * S * I - I
        dR <- (1-epsilon) * I - epsilon * R

        list(c(dS, dI, dR))
    })
}
```

Here, we will use $\mathcal{R}_0 = 1.5$ and $\varepsilon = 1/20$ with initial conditions $S(0) = 0.99, I(0) = 0.01$. First, we want to confirm the rate of exponential decay. To illustrate that the rate of exponential decay matches our expected value, we plot

$$c_3 \exp(-\varepsilon \mathcal{R}_0 t/2) + \varepsilon(1 - 1/\mathcal{R}_0)$$

along with the prevalence curve where c_3 is found by trial and error to match the second peak in the figure below.

```
par <- c(R0=1.5, epsilon=1/20)
y <- c(S=1-1e-2, I=1e-2, R=0)
tvec <- seq(0, 150, by=0.1)

df <- as.data.frame(ode(y, tvec, SIR.grad, par))

plot(tvec, df$I, type="l", ylab="proportion", xlab="time", lwd=2)
with(as.list(par),{
    curve(0.05 * exp(-epsilon * R0*x/2)+ epsilon * (1-1/R0), add=T, col=2, lty=2, lwd
})
legend(
    "topright",
    col=c(1, 2),
    lty=c(1, 2),
    lwd=c(2,2),
    legend=c("SIR prevalence", "exponential")
)
```



We find that the exponential curve matches subsequent peaks (after the second peak) of the prevalence curve. It does not match the first peak but we do not expect the SIR model to behave like its linearized model immediately. Hence, the discrepancy between the exponential curve and the first peak prevalence does not necessarily imply that the rate of exponential decay is different from what we expected. We expect the exponential curve to match the linear model much better.

To provide stronger evidence, we plot the linearized system along with the numerical solution to the ODE. Note that the approximate solution converges to the $(0, 0$ equilibrium instead of the endemic equilibrum. Instead of plotting the approximate solution directly, we compute

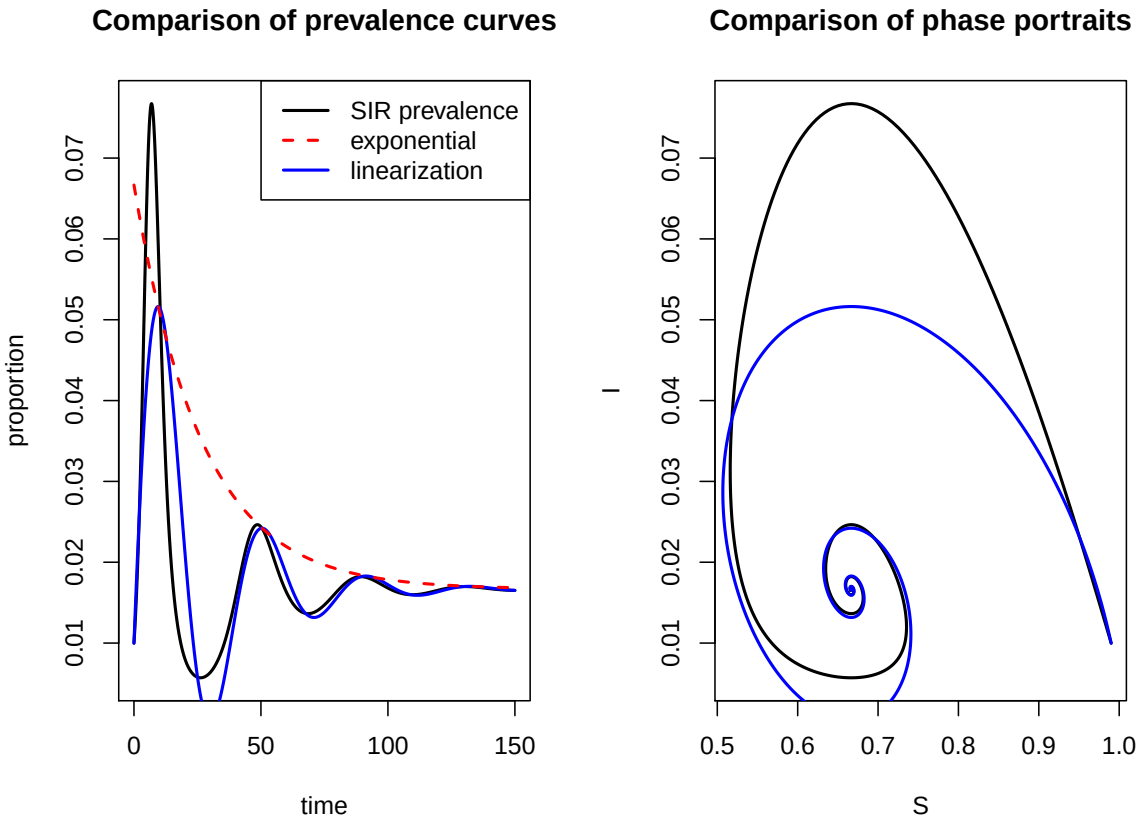
$$\vec{x} + \begin{bmatrix} \frac{1}{\mathcal{R}_0} \\ \varepsilon(1 - 1/\mathcal{R}_0) \end{bmatrix}$$

so that the approximate solution converges to the endemic equilibrium. We find c_1, c_2 numerically by minimizing the sum of squared difference between the initial condition of the ODE with the initial condition of the approximate solution (so that both curves start at the same place). We compare prevalence as well as the phase portrait. Once again, we plot the same exponential curve on top of prevalence curves.

```
approxSIR <- function(t, y, param) {
    with(as.list(param), {
```

```
        eq <- c(1/R0, epsilon * (1-1/R0))

        approxfun <- function(t, c1, c2) {
            (c1 * (cos(eta * t) * avec
                   - sin(eta * t) * bvec) +
                c2 * (sin(eta * t) * avec
                      + cos(eta * t) * bvec)) * exp(alpha * t) + eq
        }

        jac <- matrix(c(-epsilon*R0, epsilon*(R0-1), -1, 0), 2, 2)
        ee <- eigen(jac)

        alpha <- Re(ee$values[1])
        eta <- Im(ee$values[1])

        avec <- Re(ee$vectors[,1])
        bvec <- Im(ee$vectors[,1])

        res <- optim(par=c(0, 0), fn=function(x) {
            sum((y[c("S", "I")]-approxfun(min(t), c1=x[1], c2=x[2]))^2)
        })

        pp <- res$par

        ss <- sapply(t, function(t) {
            c(t, approxfun(t, c1=pp[1], c2=pp[2]))
        }, simplify=FALSE)

        solution <- as.data.frame(do.call('rbind', ss))

        names(solution) <- c("time", "S", "I")

        solution
    })
}

approxdf <- approxSIR(tvec, y, par)

par(mfrow=c(1,2))

plot(tvec, df$I, type="l", lwd=2, ylab="proportion", xlab="time")
lines(tvec, approxdf$I, col=4, lwd=2)
with(as.list(par),{
    curve(0.05 * exp(-epsilon * R0*x/2)+epsilon * (1-1/R0),
```

```
        add=TRUE, col=2, lty=2, lwd=2)
})
legend(
    "topright",
    col=c(1, 2, 4),
    lty=c(1, 2, 1),
    lwd=2,
    legend=c("SIR prevalence", "exponential", "linearization")
)
title("Comparison of prevalence curves")

plot(df$S, df$I, type="l", lwd=2, xlab="S", ylab="I")
lines(approxdf$S , approxdf$I, col=4, lwd=2)
title("Comparison of phase portraits")
```



We note that as time increases, the prevalence curve generated by the SIR model behaves like the linear model in both figures, confirming our prediction. Furthermore, the exponential curve we estimated previously agrees with the peaks of the linear model prevalence curve, again confirming our prediction.

□

(j) Prove that as $\mathcal{R}_0$ is increased from 0 to ∞, three "bifurcations" occur. In addition, use R to make a four-panel plot that illustrates the different dynamics (phase portraits) in each of the four $\mathcal{R}_0$ intervals that have distinct dynamics. (*Hint:* I suggest you choose $\varepsilon = 8/9$ for this figure, but you should explain why this is a good choice.)

Theoretical note: The word "bifurcation" is in quotes above because many dynamicists would consider only one of the three transitions to be a genuine bifurcation (it happens to be a *transcritical bifurcation*). The other two dynamical transitions yield biologically relevant qualitative changes, but the phase portraits on either side of the "bifurcation point" are actually topologically conjugate.

R *note:* Computing phase portraits should be easy based on code you've written for solving ODEs in R "from scratch". However, if you wish, you can use the `phaseR` package (or another R package of your choice) to make the phase portraits.

Proof. When $\mathcal{R}_0 < 1$, the disease free equilibrium is globally asympotically stable and when $\mathcal{R}_0 > 1$, the endemic equilibrium is globally asymptotically stalbe. Hence, $\mathcal{R}_0 = 1$ is one bifurcation point. Now, consider when $\mathcal{R}_0 > 1$. Recall that damped oscillation occurs when

$$\varepsilon < \frac{4(\mathcal{R}_0 - 1)}{\mathcal{R}_0^2}.$$

Rearranging, we have

$$\varepsilon\mathcal{R}_0^2 - 4\mathcal{R}_0 + 4 < 0 \implies \frac{4 - \sqrt{16 - 16\varepsilon}}{2\varepsilon} < \mathcal{R}_0 < \frac{4 + \sqrt{16 - 16\varepsilon}}{2\varepsilon}.$$

Hence, we find that

$$\mathcal{R}_0 = \frac{4 - \sqrt{16 - 16\varepsilon}}{2\varepsilon}, \frac{4 - \sqrt{16 + 16\varepsilon}}{2\varepsilon}$$

are two bifurcation points provided that

$$\frac{4 - \sqrt{16 - 16\varepsilon}}{2\varepsilon} > 1. \tag{17}$$

Recall again that the Jacobian of the system (ignoring R) at the endemic equilibrium is given by

$$\begin{bmatrix} -\varepsilon\mathcal{R}_0 & -1 \\ \varepsilon(\mathcal{R}_0 - 1) & 0 \end{bmatrix}$$

Its eigenvalues are given by

$$\lambda = \frac{-\varepsilon\mathcal{R}_0 \pm \sqrt{\varepsilon^2\mathcal{R}_0^2 - 4\varepsilon(\mathcal{R}_0 - 1)}}{2}.$$

So when

$$\mathcal{R}_0 < \frac{4 - \sqrt{16 - 16\varepsilon}}{2\varepsilon} \text{ or } \mathcal{R}_0 > \frac{4 + \sqrt{16 - 16\varepsilon}}{2\varepsilon},$$

we no longer have complex eigenvalues and hence the oscillation disappears.

To show four bifurcations, we fix $\varepsilon^* = 0.4$. This is a good choice for epsilon because this value stisfies (17):

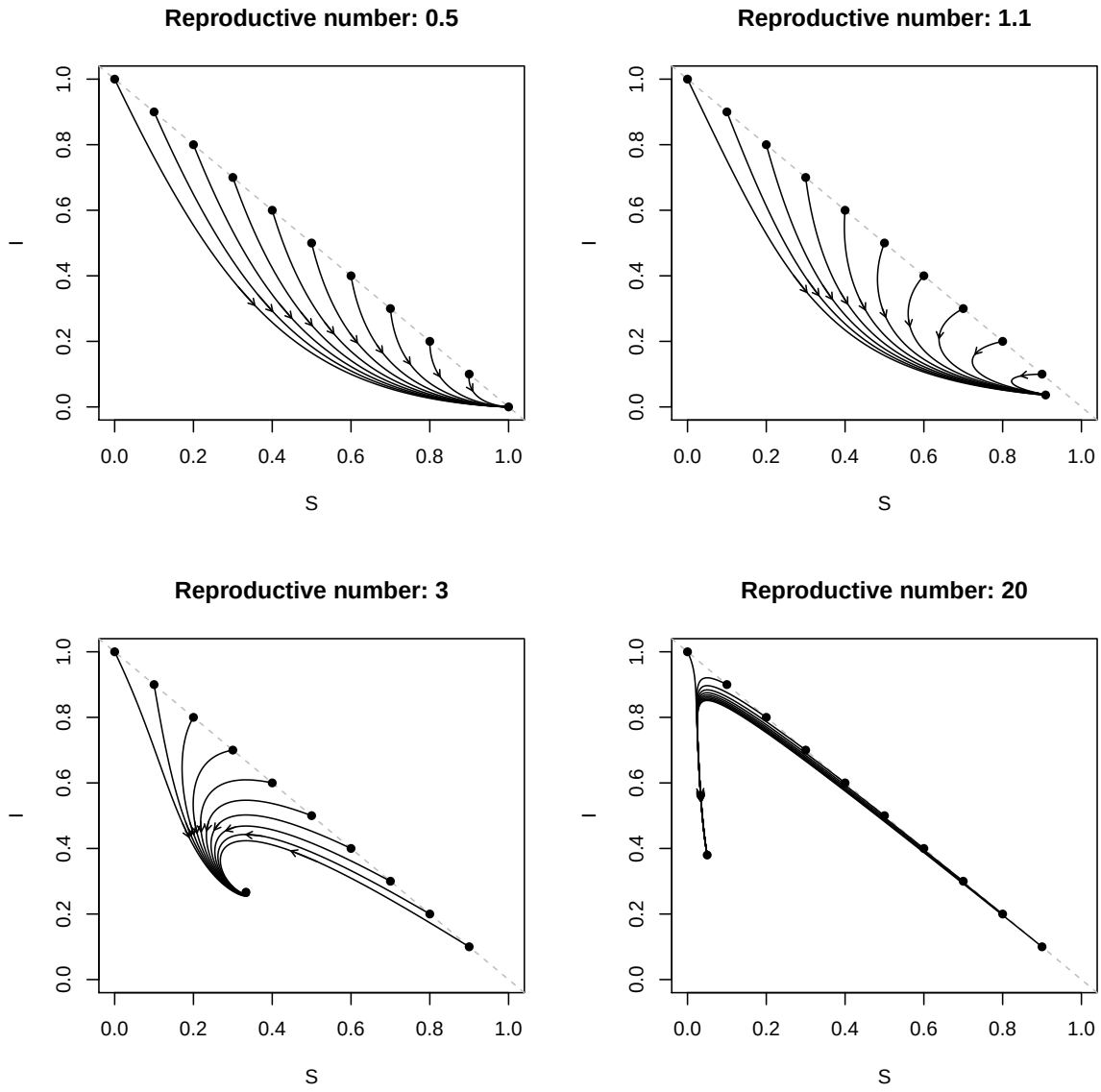
$$\frac{4 - \sqrt{16 - 16\varepsilon^*}}{2\varepsilon^*} = 1.127 > 1.$$

Hence, four intervals that we are interested in are

$$(0, 1), (1, 1.127), (1.127, 8.873), (8.873, \infty)$$

```
par1 <- par2 <- par3 <- par4 <- c(R0 = 0.5, epsilon=0.4)
par2[["R0"]] <- 1.1
par3[["R0"]] <- 3
par4[["R0"]] <- 20

tvec3 <- seq(1, 20, by=0.01)
arrowt1 <- 2.1
arrowt2 <- 2.3

phasefun <- function(t, y, param, ...) {
    df <- as.data.frame(ode(y, t, SIR.grad, param))
    lines(df$S, df$I, ...)
    a1 <- df[df$time==arrowt1,]
    a2 <- df[df$time==arrowt2,]
    arrows(x0=a1$S, y0=a1$I, x1=a2$S, y1=a2$I, length=0.05)
    invisible()
}

ylist <- lapply(seq(0.1, 1, by=0.1), function(i){
    c(S=1-i, I=i, R=0)
})

par(mfrow=c(2,2))
plot(NA, xlim=c(0, 1), ylim=c(0, 1), xlab="S", ylab="I")
abline(a=1, b=-1, lty=2, col="gray")
L <- lapply(ylist, phasefun, t=tvec3, param=par1)
L <- lapply(ylist, function(x) points(x=x[1], y=x[2], pch=16))
points(1, 0, pch=16)
title("Reproductive number: 0.5")

plot(NA, xlim=c(0, 1), ylim=c(0, 1), xlab="S", ylab="I")
abline(a=1, b=-1, lty=2, col="gray")
L <- lapply(ylist, phasefun, t=tvec3, param=par2)
L <- lapply(ylist, function(x) points(x=x[1], y=x[2], pch=16))
points(1/1.1, 0.4 * (1-1/1.1), pch=16)
title("Reproductive number: 1.1")
```

```
plot(NA, xlim=c(0, 1), ylim=c(0, 1), xlab="S", ylab="I")
abline(a=1, b=-1, lty=2, col="gray")
L <- lapply(ylist, phasefun, t=tvec3, param=par3)
L <- lapply(ylist, function(x) points(x=x[1], y=x[2], pch=16))
points(1/3, 0.4 * (1-1/3), pch=16)
title("Reproductive number: 3")

plot(NA, xlim=c(0, 1), ylim=c(0, 1), xlab="S", ylab="I")
abline(a=1, b=-1, lty=2, col="gray")
L <- lapply(ylist, phasefun, t=tvec3, param=par4)
L <- lapply(ylist, function(x) points(x=x[1], y=x[2], pch=16))
points(1/20, 0.4 * (1-1/20), pch=16)
title("Reproductive number: 20")
```



□

(k) Are there real diseases that display recurrent epidemics for which the standard SIR model that you have studied in this problem might be adequate to explain the observed epidemic dynamics? If so, which diseases? If not, why not?

Proof. . . . beautifully clear and concise text to be inserted here. . . □

— END OF ASSIGNMENT —

Compile time for this document: February 27, 2018 @ 19:45