Group Name: The Rolling Stones

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

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

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

$$\tau = (\gamma + \mu)t, \tag{2a}$$

and the dimensionless parameters

$$\mathcal{R}_0 = \frac{\beta}{\gamma + \mu}\,, \tag{2b}$$

$$\varepsilon = \frac{\mu}{\gamma + \mu}\,. \tag{2c}$$

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. ...beautifully clear and concise text to be inserted here... $\qquad\square$

(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. ...beautifully clear and concise text to be inserted here... $\qquad\square$

(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. ...beautifully clear and concise text to be inserted here... $\qquad\square$

(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. ...beautifully clear and concise text to be inserted here... $\qquad\square$

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

$$L(S, I) = S - \hat{S}\log S + I - \hat{I}\log I\,, \tag{3}$$

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

$$L(X) > L(X_*) \quad \text{for all} \quad X \in \mathcal{O} \setminus \{X_*\}\,. \tag{4}$$

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

(h) Prove that the approach to the EE occurs via damped oscillations if and only if $\varepsilon < \varepsilon^*$, where
$$\varepsilon^* = \frac{4(\mathcal{R}_0 - 1)}{\mathcal{R}_0^2}. \tag{5}$$
For which diseases that you are familiar with would you expect damped oscillations versus monotonic convergence to the equilibrium?

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

(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 ® 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
$$\begin{bmatrix} -\epsilon\mathcal{R}_0 & -1 \\ \epsilon(\mathcal{R}_0 - 1) & 0 \end{bmatrix}$$
where its characteristic equation is given by
$$\lambda^2 + \epsilon\mathcal{R}_0\lambda + \epsilon(\mathcal{R}_0 - 1) = 0$$
Then, its eigenvalues are given by
$$\lambda = \frac{-\epsilon\mathcal{R}_0 \pm \sqrt{\epsilon^2\mathcal{R}_0^2 - 4\epsilon(\mathcal{R}_0 - 1)}}{2}.$$
When
$$\epsilon < \frac{4(\mathcal{R}_0 - 1)}{\mathcal{R}_0^2},$$
the eigenvalues of the Jacobian matrix are given by
$$\lambda = -\frac{\epsilon\mathcal{R}_0}{2} \pm i\frac{\sqrt{4\epsilon(\mathcal{R}_0 - 1) - \epsilon^2\mathcal{R}_0^2}}{2}$$
For convenience, denote
$$\eta = \frac{\sqrt{4\epsilon(\mathcal{R}_0 - 1) - \epsilon^2\mathcal{R}_0^2}}{2}$$
$$\alpha = -\frac{\epsilon\mathcal{R}_0}{2}.$$
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:
$$\frac{d}{dt}\vec{x} = \begin{bmatrix} -\epsilon\mathcal{R}_0 & -1 \\ \epsilon(\mathcal{R}_0 - 1) & 0 \end{bmatrix}\vec{x},$$

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 sine and cosine term "proves" the oscillatory dynamics). Furthermore, period of damped osccilation is given by $2\pi/\eta$ which is equal to

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

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

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

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 $\epsilon = 1/20$ with initial conditions $S(0) = 0.99, I(0) = 0.01$. First, we want to confirm the rate of exponential decay first. To illustrate that the rate of exponential decay matches, we plot

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

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

```r
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")
)
```
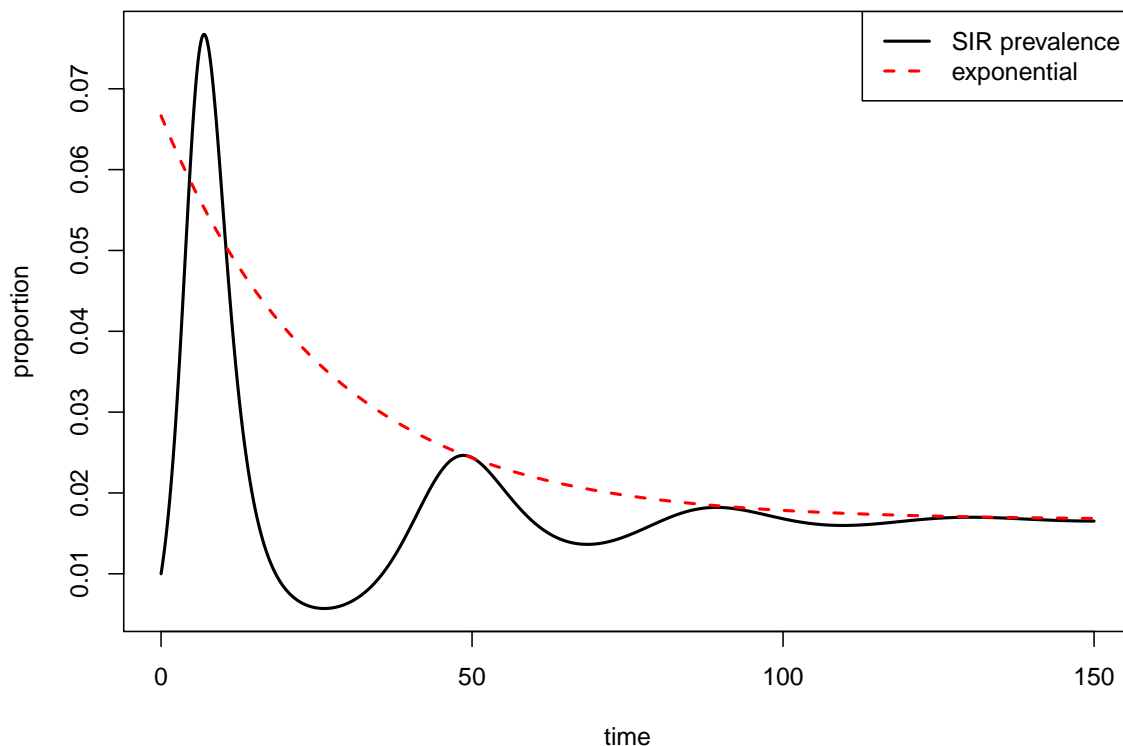

We find that the exponential curve matches subsequent peaks (after the second peak) of the prevalence curve. It does not match the first peak but we do not expect the SIR model to behave like its linearized model immediately. Hence, the discrepancy between

the exponential curve and the first peak prevalence does not necessarily imply that the rate of exponential is different from what we expected.

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

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

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 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]))
```

```r
        }, 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")
```
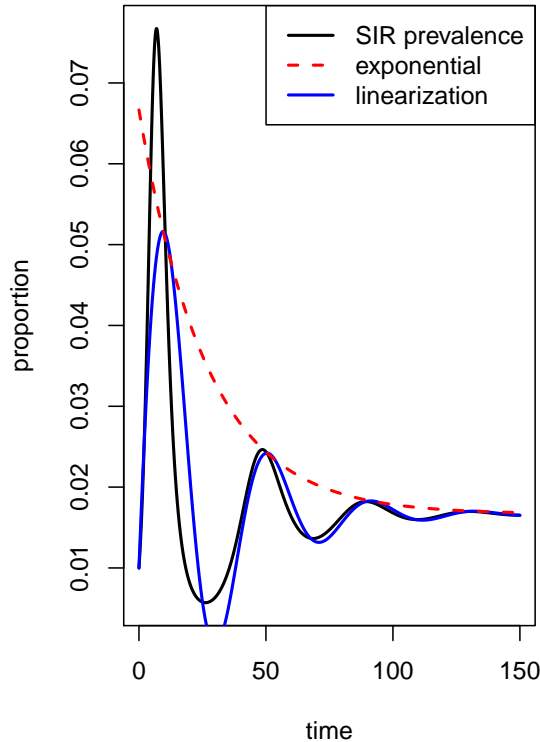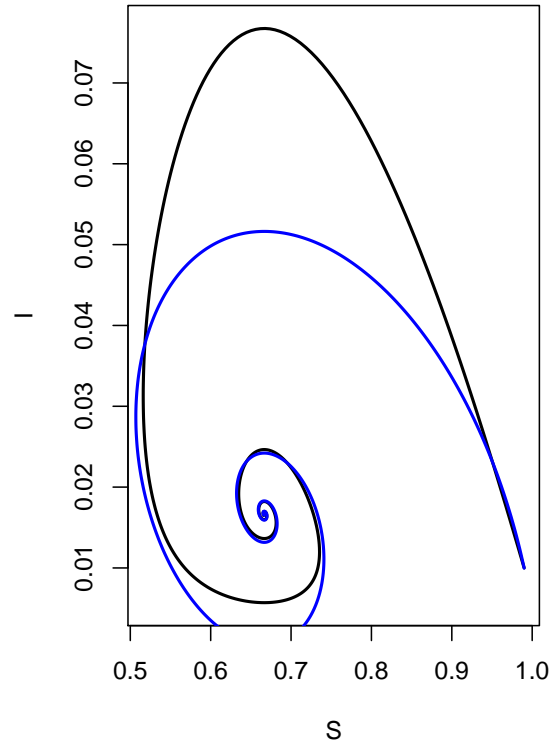
Comparison of prevalence curves   **Comparison of phase portraits**

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

Rearranging, we have

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

Hence, we find that

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

are two bifurcation points provided that

$$\frac{4 - \sqrt{16 - 16\epsilon}}{2\epsilon} > 1. \tag{6}$$

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

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

Its eigenvalues are given by

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

So when

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

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

To show four bifurcations, we fix $\epsilon^* = 0.4$. This is a good choice for epsilon because this value stisfies (6):

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

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))
```

```r
    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")
```
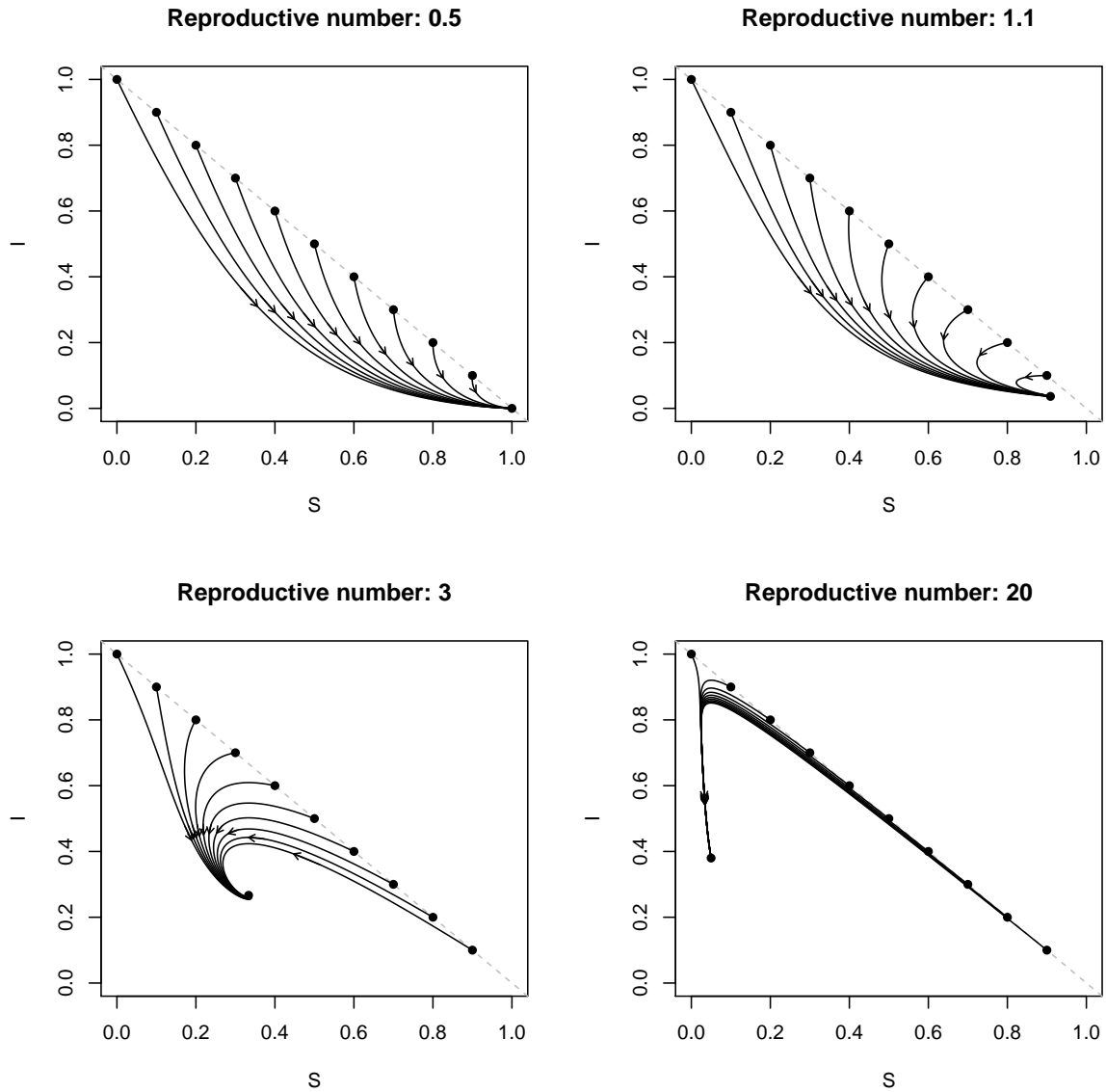
Reproductive number: 0.5

Reproductive number: 1.1

Reproductive number: 3

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 26, 2018 @ 1:42