Mathematics 4MB3/6MB3 Mathematical Biology

http://www.math.mcmaster.ca/earn/4MB3

2019 ASSIGNMENT 3

Group Name: The Plague Doctors

Group Members: Sid Reed, Daniel Segura, Jessa Mallare, Aref Jadda

This assignment is **due in class** on **Monday 25 February 2019 at 9:30am**.

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) Since equations (1) represent all changes in the size of each population compartment, the net change in the total population should be the sum of the change in each compartment, i.e. the sum of all equations (1). If the sum of all equations (1) is zero, $\frac{dS}{dt} + \frac{dI}{dt} + \frac{dR}{dt} = 0$, the the change in total population size must be zero and the total population size N must be constant.

$$\frac{dS}{dt} + \frac{dI}{dt} + \frac{dR}{dt} = \mu N - \frac{\beta}{N} SI - \mu S + \frac{\beta}{N} SI - \gamma I - \mu I + \gamma I - \mu R \tag{2}$$

$$= \mu N - \mu S - \mu I - \mu R(-\frac{\beta}{N} SI + \frac{\beta}{N} SI)(-\gamma I + \gamma I) \tag{3}$$

$$= \mu(N - (S + I + R)) \tag{4}$$

Since $N = S + I + R$, i.e. the sum of all population compartments is equal tot the total population size, 4 evaluates to 0. Thus the sum of population changes in all population compartments is 0 and the total population size remains constant.

Definition 1. *Forward Invariant Set*
Given a dynamical system $\dot{x} = f(x)$*, a solution* $x(t, x_0)$ *with initial condition* x_0*, a set* $\Delta = \{x \in \mathbb{R} \mid \phi(x) = 0\}$ *for some positive definite function* $\phi(x)$ *is forward invariant if* $x_0 \in \Delta \implies x(t, x_0) \in \Delta \ \forall\ t \geq 0$.

Since the population size has been shown to be constant and equal to N, the function $\phi(S, I, R) = N - (S + I + R)$ is always equal to zero, given any initial condition.

Definition 2. *Biologically Meaningful States*
Define the set $\Delta = \{(S, I, R) \mid 0 \leq S, I, R \text{ and } \phi(S, I, R) = 0\}$ *where* $\phi(S, I, R) = N - (S + I + R)$*, to be the set of biologically meaningful states for this model.*

Once the total population is equal to N, it will remain equal to N in all subsequent time steps due to the population size constancy. If all initial conditions are defined such that they satisfy $\phi(S, I, R) = 0$, then they can only evolve towards other states that satisfy $\phi(S, I, R) = 0$ due to the constant population size. Thus if the set Δ is defined to include all initial conditions x_0 that have a total population equal to N (i.e. all 3-tuples of positive integers $x_0 = (S, I, R)$ such that $\phi(S, I, R) = 0$), then they must necessarily include all possible time steps for solutions to the dynamical system with initial condition x_0, since the total population must remain constant over all time.

(b) Set the following variables:

$$S_p = \frac{S}{N} \tag{5a}$$

$$I_p = \frac{I}{N} \tag{5b}$$

$$R_p = \frac{R}{N} \tag{5c}$$

$$N_p = \frac{N}{N} = 1 \tag{5d}$$

Then substituting equations 5 into equations (1)

$$\begin{aligned}
\frac{dS_p}{dt} &= \mu N_p - \frac{\beta}{N_p} S_p I_p - \mu S_p \\
&= \mu 1 - \frac{\beta}{1} S_p I_p - \mu S_p \\
&= \frac{1}{N}(\mu N - \beta S I - \mu S) \\
&= \frac{1}{N}\frac{dS}{dt} && (6) \\
\frac{dI_p}{dt} &= \frac{\beta}{N_p} S_p I_p - \gamma I_p - \mu I_p \\
&= \frac{\beta}{1} S_p I_p - \gamma I_p - \mu I_p \\
&= \frac{1}{N}(\beta S I - \gamma I - \mu I) \\
&= \frac{1}{N}\frac{dI}{dt} && (7) \\
\frac{dR_p}{dt} &= \gamma I_p - \mu R_p \\
&= \frac{1}{N}(\gamma I - \mu R) \\
&= \frac{1}{N}\frac{dR}{dt} && (8)
\end{aligned}$$

From equations 6,7 and 8 it is clear that the proportional equations are equivalent to the original equations (1) scaled by a constant factor of $\frac{1}{N}$, and thus will retain the same dynamical behaviour.

(c) Using the equations

$$\tau = (\gamma + \mu)t \tag{9a}$$

$$\mathcal{R}_0 = \frac{\beta}{\gamma + \mu} \tag{9b}$$

$$\varepsilon = \frac{\mu}{\gamma + \mu} \tag{9c}$$

First we express dt in terms of τ

$$\begin{aligned}
\tau &= t(\gamma+\mu) \\
d\tau &= dt(\gamma+\mu) \\
\frac{d\tau}{dt} &= (\gamma+\mu) \\
\frac{d\tau}{dt}\frac{d}{d\tau} &= \frac{d}{dt} \\
(\gamma+\mu)\frac{d}{d\tau} &= \frac{d}{dt} \\
\frac{d}{d\tau} &= \frac{1}{(\gamma+\mu)}\frac{d}{dt} \qquad (10)
\end{aligned}$$

Next we isolate γ, β, μ,

$$\begin{aligned}
\varepsilon &= \frac{\mu}{\gamma+\mu} \\
\varepsilon(\gamma+\mu) &= \mu \qquad\qquad \gamma+\mu = \frac{\mu}{\varepsilon} \\
\varepsilon\gamma+\varepsilon\mu &= \mu \\
\varepsilon\gamma &= \mu(1-\varepsilon) \\
\gamma &= \frac{\mu}{\varepsilon}(1-\varepsilon) \\
\gamma &= (\gamma+\mu)(1-\varepsilon) \qquad (11)
\end{aligned}$$

From 9 it follows that $\beta = (\gamma+\mu)\mathcal{R}_0$ (12)

From 9 it follows that $\mu = (\gamma+\mu)\varepsilon$ (13)

Next, expressing $\frac{dS}{dt}$ in terms of τ using 10 and substituting equations 11,12 and 13 gives

$$\begin{aligned}
\frac{dS}{d\tau} &= \frac{1}{\gamma+\mu}\frac{dS}{dt} \\
&= \frac{1}{\gamma+\mu}[\mu-\beta SI-\mu S] \\
&= \frac{1}{\gamma+\mu}[\mu(1-S)-\beta SI] \qquad (14) \\
&= \frac{1}{\gamma+\mu}[\varepsilon(\gamma+\mu)(1-S)-(\gamma+\mu)\mathcal{R}_0 SI] \\
&= \frac{1}{\gamma+\mu}(\gamma+\mu)[\varepsilon(1-S)-\mathcal{R}_0 SI] \\
&= \varepsilon(1-S)-\mathcal{R}_0 SI \qquad (15)
\end{aligned}$$

Solving for $\frac{dI}{d\tau}$ using 10, 11, 12 and 13 gives

$$\begin{aligned}
\frac{dI}{d\tau} &= \frac{1}{\gamma+\mu}\frac{dI}{dt} \\
&= \frac{1}{\gamma+\mu}[\beta SI - \gamma I - \mu I] \\
&= \frac{1}{\gamma+\mu}[(\gamma+\mu)\mathcal{R}_0 SI - (\gamma+\mu)(1-\varepsilon)I - (\gamma+\mu)\varepsilon I] \\
&= \frac{1}{\gamma+\mu}(\gamma+\mu)[\mathcal{R}_0 SI - (1-\varepsilon)I - \varepsilon I] \\
&= \mathcal{R}_0 SI - (1-\varepsilon)I - \varepsilon I \\
&= \mathcal{R}_0 SI - (1-2\varepsilon)I \qquad (16)
\end{aligned}$$

Finally, solving for $\frac{dR}{d\tau}$ using 10, 11, 12 and 13 gives

$$\begin{aligned}
\frac{dR}{d\tau} &= \frac{1}{\gamma+\mu}\frac{dR}{dt} \\
&= \frac{1}{\gamma+\mu}[\gamma I - \mu R] \\
&= \frac{1}{\gamma+\mu}[(\gamma+\mu)(1-\varepsilon)I - (\gamma+\mu)\varepsilon R] \\
&= \frac{1}{\gamma+\mu}(\gamma+\mu)[(1-\varepsilon)I - \varepsilon R] \\
&= (1-\varepsilon)I - \varepsilon R
\end{aligned}$$

The biological meanings of $\tau, \mathcal{R}_0$ and ε are

- τ is the average proportion of the population infected
- $\mathcal{R}_0$ is the number of secondary infections per infection
- ε is the mortality rate for the infected.

One reason these are good choices for non-dimensionalizing equations because they do not create more complex equations than the originals. These choices also reduce the total number of parameters from 3 (β, μ, γ) to 3 $(\varepsilon, \mathcal{R}_\prime)$. They all also have clear biological interpretations, making it easier to understand the biological relationships represeted by any mathematical reasoning done with them. In the UK the morality rate from penumonia between 2001-2010 was estimated to be 0.0214% of people[1]. Ebola Virus Diesase is estimated by the WHO to have an average case fatality rate of 50%[2]. The CDC estimates measles to have a mortality rate between 0.1% to 0.2% [3].

(d) tmp

(e) tmp

(f) tmp

(g) tmp

(h) Since the EE is GAS, any oscillations will be damped and approaching the EE. Oscillations will occur if the imaginary parts of the eigenvalues of the Jacobian, evaluated at the EE $(\hat{S},\hat{I}) = (\frac{1}{\mathcal{R}_0}, \varepsilon(1-\frac{1}{\mathcal{R}_0})$, are non-zero. Since the Jacobian is a 2×2 matrix, the eigenvalues are the roots of the equation $\lambda^2 - T\lambda + D = 0$ where T and D are the trace and determinant of the Jacobian respectively. The roots can be found using the quadratic formula $\frac{-b\pm\sqrt{b^2-4ac}}{2a}$. The imaginary part of the roots will only be non-zero if $\sqrt{b^2-4ac} < 0$, thus proving $\sqrt{b^2-4ac} < 0$ implies damped oscillations approaching the EE.

The Jacobian at the EE is

$$J = \begin{bmatrix} \frac{\partial S}{\partial S} & \frac{\partial S}{\partial I} \\ \frac{\partial I}{\partial S} & \frac{\partial I}{\partial I} \end{bmatrix} \tag{17}$$

$$= \begin{bmatrix} -\beta I - \mu & -\beta S \\ \beta I & \beta S - (\gamma+\mu) \end{bmatrix} \tag{18}$$

$$J(\hat{S},\hat{I}) = J(\frac{1}{\mathcal{R}_0}, \varepsilon(1-\frac{1}{\mathcal{R}_0}) \tag{19}$$

$$= \begin{bmatrix} -\beta\varepsilon(1-\frac{1}{\mathcal{R}_0}) - \mu & -\beta\frac{1}{\mathcal{R}_0} \\ \beta\varepsilon(1-\frac{1}{\mathcal{R}_0}) & \beta\frac{1}{\mathcal{R}_0} - (\gamma+\mu) \end{bmatrix} \tag{20}$$

Next substitute β, γ, μ using equations 11,12,13

$$= \begin{bmatrix} -(\gamma+\mu)\mathcal{R}_0\varepsilon(1-\frac{1}{\mathcal{R}_0}) - \varepsilon(\gamma+\mu) & -(\gamma+\mu)\mathcal{R}_0\frac{1}{\mathcal{R}_0} \\ (\gamma+\mu)\mathcal{R}_0\varepsilon(1-\frac{1}{\mathcal{R}_0}) & (\gamma+\mu)\mathcal{R}_0\frac{1}{\mathcal{R}_0} - (\gamma+\mu) \end{bmatrix} \tag{21}$$

$$= (\gamma+\mu)\begin{bmatrix} -\varepsilon\mathcal{R}_0 & -1 \\ \varepsilon(\mathcal{R}_0 - 1) & 0 \end{bmatrix} \tag{22}$$

Next the trace T, determinant D, and the terms of the quadratic formula a, b, c are

$$T = -\varepsilon\mathcal{R}_0 + 0 \tag{23}$$

$$D = (-\varepsilon\mathcal{R}_0)(0) - (-1)(\varepsilon(\mathcal{R}_0 - 1) \tag{24}$$

$$= \varepsilon(\mathcal{R}_0 - 1) \tag{25}$$

$$0 = \lambda^2 - T\lambda + D \implies a = 1 \quad b = -T \quad c = D \tag{26}$$

$$b = \varepsilon\mathcal{R}_0 \tag{27}$$

$$c = \varepsilon(\mathcal{R}_0 - 1) \tag{28}$$

$$\sqrt{b^2-4ac} = \sqrt{\varepsilon^2{\mathcal{R}_0}^2 - 4(1)(\varepsilon(\mathcal{R}_0 - 1))} \tag{29}$$

$$= \sqrt{\varepsilon^2{\mathcal{R}_0}^2 - 4(\varepsilon(\mathcal{R}_0 + 4\varepsilon} \tag{30}$$

$$= \sqrt{\varepsilon(\varepsilon{\mathcal{R}_0}^2 - 4\mathcal{R}_0 + 4)} \tag{31}$$

Now if we show that the when the inequality

$$\sqrt{\varepsilon(\varepsilon{\mathcal{R}_0}^2 - 4\mathcal{R}_0 + 4)} < 0 \tag{32}$$

holds it implies $\varepsilon < \varepsilon^* = \frac{4\mathcal{R}_0 - 1}{{\mathcal{R}_0}^2}$, then this proves that the approach to EE via damped oscillations occurs iff $\varepsilon < \varepsilon^*$

$$\sqrt{\varepsilon(\varepsilon{\mathcal{R}_0}^2 - 4\mathcal{R}_0 + 4)} < 0 \tag{33}$$

$$\sqrt{\frac{4\mathcal{R}_0 - 1}{{\mathcal{R}_0}^2}(\frac{4(\mathcal{R}_0 - 1)}{{\mathcal{R}_0}^2}{\mathcal{R}_0}^2 - 4\mathcal{R}_0 + 4)} < 0 \tag{34}$$

$$\sqrt{\frac{4\mathcal{R}_0 - 1}{{\mathcal{R}_0}^2}(4(\mathcal{R}_0 - 1) - 4\mathcal{R}_0 + 4)} < 0 \tag{35}$$

$$\sqrt{\frac{4\mathcal{R}_0 - 1}{{\mathcal{R}_0}^2}(4\mathcal{R}_0 - 4 - 4\mathcal{R}_0 + 4)} < 0 \tag{36}$$

$$\sqrt{\frac{4\mathcal{R}_0 - 1}{{\mathcal{R}_0}^2}(0)} < 0 \tag{37}$$

$$0 < 0 \text{which is false} \tag{38}$$

Since **??** is 0 when $\varepsilon = \varepsilon^*$, increasing ε will cause $\sqrt{\varepsilon(\varepsilon{\mathcal{R}_0}^2 - 4\mathcal{R}_0 + 4)}$ to become positive and decreasing ε will cause $\sqrt{\varepsilon(\varepsilon{\mathcal{R}_0}^2 - 4\mathcal{R}_0 + 4)}$ to become negative. Since $\sqrt{\varepsilon(\varepsilon{\mathcal{R}_0}^2 - 4\mathcal{R}_0 + 4)}$ is only negative when $\varepsilon < \varepsilon^*$ and $\sqrt{\varepsilon(\varepsilon{\mathcal{R}_0}^2 - 4\mathcal{R}_0 + 4)} < 0$ implies non-negative imaginary components of the eigenvalue of $J(\hat{S}, \hat{I})$, which in turn implies dampened oscillations when the model is approaching the EE. Thus $\varepsilon < \varepsilon^*$ is a necessary condition for dampened oscillations in the model while approaching the EE.

(i)

(j)

(k) There are no diseases that display recurrent epidemics for which the SIR model with vital dynamics is adequate to explain the observed epidemic dynamics. From results in parts (g) and (h), given that $\mathcal{R}_0 > 1$ (such that an epidemic occurs) the EE is GAS and that for all initial conditions, $I(0) > 0, S(0) > 0$, the system approaches the EE with damped oscillations. Additionally, by observing the Jacobian evaluated at the EE, the complex eigenvalues have negative real part and non-zero imaginary part, implying that the dynamics are always oscilatory. Thus recurrent epidemics with no evidence of damping out (like measles) cannot be explained by the SIR model with vital dynamics.

References

1. Foundation, B. L. *Pneumonia Statistics* https://statistics.blf.org.uk/pneumonia.
2. Organization, W. H. *Ebola Virus Disease* https://statistics.blf.org.uk/pneumonia.
3. Control, C. F. D. & Prevention. *Measles (Rubeola)* https://www.cdc.gov/measles/about/complications.html.

— END OF ASSIGNMENT —

Compile time for this document: February 27, 2019 @ 1:31