Mathematics 4MB3/6MB3 Mathematical Biology 2019 ASSIGNMENT 1

Group Name: The Plague Doctors

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

1 Analysis of the SI model

The SI model can be written

$$\frac{dI}{dt} = \beta I(N - I), \qquad (1)$$

where I denotes prevalence and N = S + I is the total population size.

(a) Prove that the endemic equilibrium (EE) is a globally asymptotically stable (GAS) equilibrium by finding an appropriate Lyapunov function. Note that "global" here refers to all biologically relevant initial conditions except the (unstable) disease free equilibrium (DFE).

Hint: Lyapunov functions often look paraboloidal.

Note: Notions of stability and Lyapunov functions were discussed in Math 3F03 Lecture 27 in 2013 (http://www.math.mcmaster.ca/earn/3F03).

Proof.

Consider the open set $D: \{I \in \mathbb{R} | 0 < I < N + \epsilon\}$ containing the the endemic equilibrium (EE) $I_* = N$ of equation (1), where $\epsilon > 0$ is constant. Suppose a continuous differentiable function $L: D \to \mathbb{R}$ is in the form

$$L(I) = a(N - I)^b (2)$$

where a and b are constants and a, b > 0.

Then by Lyapunov's Direct Method,

(a)
$$L(I_*) = a(N-N)^b = 0$$
 and $L(I) > 0 \quad \forall I \in D \backslash \{I_*\}$

(b)
$$\begin{split} \dot{L}(I) &= \frac{dL}{dI} \frac{dI}{dt} \\ &= -ab(N-I)^{b-1} \beta I(N-I) \\ &= -ab\beta I(N-I)^b \\ \text{Let } a = 1 \text{ and } b = 2. \text{ Assuming } \beta > 0, \text{ then } \\ \dot{L}(I) &= -2\beta I(N-I)^2 \leq 0 \quad \forall I \in D \backslash \{I_*\} \end{split}$$

(c) $\dot{L}(I) < 0 \quad \forall I \in D \setminus \{I\}$

Since the above (a), (b), and (c) hold true for $L(I) = (N - I)^2$, then by Lyapunov's Stability Theorem, $I_* = N$ is globally asymptotically stable.

(b) In class we proved only stability of the EE, not asymptotic stability. Prove GAS "directly" in two distinct ways:

(i) find the exact solution of the model and take the limit as $t \to \infty$, and conclude that every solution that starts in the interval (0, N) converges to the EE (this approach works only in situations where you can find the exact solution);

$$\begin{aligned} & Proof. \\ & \frac{dI}{dt} = \beta I(N-I) \\ & \int \frac{1}{I(N-I)} = \int \beta dt \\ & \frac{1}{N} \int (\frac{1}{I} + \frac{1}{N-1}) dI = \beta t + C \\ & \frac{1}{N} (ln|I| - ln|N-I|) = \beta t + C \\ & ln \left| \frac{I}{N-I} \right| = N\beta t + NC \\ & \frac{N-I}{I} = \pm e^{-NC} e^{-N\beta t} \end{aligned}$$

Let
$$k = \pm e^{-NC}$$

 $\frac{N-I}{I} = ke^{-N\beta t}$
 $\frac{N}{I} - 1 = ke^{-N\beta t}$
 $\frac{N}{I} = 1 + ke^{-N\beta t}$
 $I(t) = \frac{N}{1 + ke^{-N\beta t}}$

To solve for
$$k$$
, let $I(0) = I_0$.
$$I(0) = I_0 = \frac{N}{1+k}$$
$$k = \frac{N-I_0}{I_0}$$

So the exact solution of the model is

$$I(t) = \frac{N}{1 + \frac{N - I_0}{I_0} (e^{-\beta Nt})}$$
 (3)

Since

$$\lim_{t \to \infty} e^{-\beta Nt} = 0$$

$$N$$

$$\lim_{t \to \infty} I(t) = \frac{N}{1 + \frac{N - I_0}{I_0}(0)} = N$$

then every solution that starts in the interval (0, N) converges to the EE.

(ii) given $\epsilon > 0$, prove that for any $I(0) \in (0, N) \exists t < \infty$ such that $I(t) \in [N - \epsilon, N)$ and use this to establish GAS. (Do not use your exact solution in this part; the point is to use an approach that also works for models that cannot be solved exactly.)

Proof. ... beautifully clear and concise text to be inserted here... \Box

2 Analysis of the basic SIR model

The basic SIR model is specified by the following system of differential equations.

$$\frac{dS}{dt} = -\mathcal{R}_0 SI \tag{4a}$$

$$\frac{dI}{dt} = \mathcal{R}_0 SI - I \tag{4b}$$

$$\frac{dR}{dt} = I \tag{4c}$$

The state variables S, I and R are the proportions of the population that are susceptible, infectious and removed, respectively. The parameter \mathcal{R}_0 is the basic reproduction number. The time unit has been chosen to be the mean infectious period for convenience.

(a) A quantity of some practical importance is the **peak prevalence** of disease in the population, *i.e.*, the maximum proportion of the population that is simultaneously infected. Find an exact expression for the peak prevalence, given initial conditions (S_0, I_0) . Why might a public health official want to know this quantity?

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

- (b) It would be helpful to have an analytical expression for the solution of the model. Most valuable would be a formula for I(t), which is most closely related to time series data. You probably will not find a formula for I(t) (extra credit if you do!!) but it is definitely possible to find an exact expression that relates R (proportion removed) and t (time).
 - (i) Find such an expression. *Hint:* Combine the equations for dS/dt and dR/dt into one equation that can be solved for S as a function of R. Then recall that S+I+R=1 and use the dR/dt equation again. *Note:* You will end up with an expression for t as a function of R, not R as a function t.

Solution. ... beautifully clear and concise text to be inserted here... \Box

(ii) Use your expression for t(R) to find an expression for the time at which peak prevalence will occur. Why might this be useful?

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

- (iii) How could your expressions be used to compare with the time series for pneumonia and influenza in Philadelphia in 1918? (Don't actually do it; just clearly explain your thinking including any assumptions you are making.) Would you advise your assistant who just graduated with a degree in math and biology to do this (to help you prepare your report for the public health agency)? Why or why not?
- (iv) Is it possible to find an exact analytical expression for t as a function S?

(c) Prove that all solutions of the basic SIR model approach I=0 asymptotically, and explain why this makes biological sense. *Hint:* Is the function L(S,I)=I a Lyapunov function? Read the Notes on Lyapunov functions below.

Answers....beautifully clear and concise text to be inserted here... Since no numerical analysis or graphics were requested, there is no need to use R to answer these questions. Note, incidentally, that the \Rlogo command that produces R simply includes the image file images/Rlogo.pdf and scales it appropriately for text within a paragraph. If we really loved that logo and wanted to display as we would a figure, we easily could...



(d) Find and classify the stability of all <u>equilibria</u> of the basic SIR model.

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

Notes on Lyapunov functions

Consider Lyapunov's Stability Theorem as stated in Math 3F03 Lecture 28 in 2013:

Theorem 1 (Lyapunov's Direct Method). Consider an equilibrium X_* of X' = F(X) and an open set \mathcal{O} containing X_* . If \exists a differentiable function $L: \mathcal{O} \to \mathbb{R}$ such that

(a)
$$L(X_*) = 0$$
 and $L(X) > 0$ $\forall X \in \mathcal{O} \setminus \{X_*\}$ (L positive definite on \mathcal{O})

(b)
$$\dot{L}(X) \leq 0 \quad \forall X \in \mathcal{O} \setminus \{X_*\}$$
 (L negative semi-definite on \mathcal{O})

then X_* is stable and L is called a **Lyapunov function**. If, in addition,

(c)
$$\dot{L}(X) < 0 \quad \forall X \in \mathcal{O} \setminus \{X_*\}$$
 (L negative definite on \mathcal{O})

then X_* is asymptotically stable and L is called a **strict Lyapunov function**.

Theorem 1 can be generalized for analysis of stability of sets more complicated than isolated equilibria, such as periodic orbits or line segments. If you think through the proof of the theorem above (e.g., [?, §9.2, theorem stated on p. 193 and proved on p. 196]), you should be able to convince yourself that the proof still works if the equilibrium X_* is replaced by any closed forward-invariant set (often simply called a closed invariant set). This observation allows us to state the following more general theorem.

Theorem 2 (Lyapunov's Direct Method for Closed Invariant Sets). Consider a closed invariant set C of X' = F(X) and an open set C containing C. If \exists a differentiable function $L: \mathcal{O} \to \mathbb{R}$ such that

(a)
$$L(X) = 0 \ \forall X \in \mathcal{C}$$
 and $L(X) > 0 \ \forall X \in \mathcal{O} \setminus \mathcal{C}$ (L positive definite on \mathcal{O})

(b)
$$\dot{L}(X) \leq 0 \quad \forall X \in \mathcal{O} \setminus \mathcal{C}$$
 (\dot{L} negative semi-definite on \mathcal{O})

then C is stable and L is called a **Lyapunov function**. If, in addition,

(c)
$$\dot{L}(X) < 0 \quad \forall X \in \mathcal{O} \setminus \mathcal{C}$$
 (\dot{L} negative definite on \mathcal{O})

then C is asymptotically stable and L is called a **strict Lyapunov function**.

Note in the above theorems that open sets are defined relative to the subset of interest; in our case this subset is $\Delta = \{(S, I) : S \geq 0, I \geq 0, S + I \leq 1\}$, not all of \mathbb{R}^2 . An open set of Δ is a set of the form $U \cap \Delta$ where U is an open set of \mathbb{R}^2 . (These sets are said to be open in the **relative topology** on Δ .) In particular, note that Δ is open as a subset of itself, in spite of the fact that it is not open as a subset of \mathbb{R}^2 , whereas Δ is closed in both the relative topology on Δ and the usual topology on \mathbb{R}^2 .

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