1 Analysis of the SI model

The SI model can be written

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

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

(a) Prove that the endemic equiliibrium (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. The EE is $I_* = N$. Let $L(I) = (N - I)^2$. Then $L(N) = 0$ and $L(I) > 0 \ \forall I \neq N$ so L is positive definite on $\mathbb{R}$. Now,

$$\dot{L}(I) = \frac{\partial L}{\partial I} \cdot \frac{dI}{dt} = -2(N - I) \cdot \beta I(N - I) = -2\beta I(N - I)^2,$$

from which we infer that $\dot{L}(0) = \dot{L}(N) = 0$ and $\dot{L} < 0 \ \forall I \in (0, N)$. Hence $\dot{L}$ is negative definite on the interval $(0, N)$. L is therefore a strict Lyapunov function for the EE on the entire biologically relevant space (excluding the DFE), which implies the EE is GAS. $\square$

(b) In class we proved only stabiliity 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);

Solution. Equation (1) is easily separated,

$$\int_{I_0}^{I_1} \frac{dI}{I(N - I)} = \int_{t_0}^{t_1} \beta \, dt.$$

Noting that

$$\int \frac{dx}{x(N - x)} = \frac{1}{N} \log \frac{x}{N - x},$$

we obtain

$$\frac{1}{N} \log \left(\frac{I_1}{N - I_1} \cdot \frac{N - I_0}{I_0} \right) = \beta(t_1 - t_0),$$

i.e.,

$$\frac{I_1}{N - I_1} \cdot \frac{N - I_0}{I_0} = \exp \left(\beta N (t_1 - t_0) \right),$$

i.e.,

$$\frac{I_1}{N - I_1} = \frac{I_0}{N - I_0} \exp \left(\beta N (t_1 - t_0) \right).$$

Setting the RHS above to A for convenience, we have

$$I_1 = A(N - I_1),$$

i.e.,

$$I_1 = \frac{AN}{1 + A}.$$

Setting $t_0 = 0$, $t_1 = t$ and writing $I(t)$ for I_1 we have

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

If $I_0 = 0$ we obtain $I(t) = 0$ for all t, and if $I_0 = N$ we obtain $I(t) = N$ for all t, as expected. For any $I_0 \in (0, N)$, $\lim_{t \to \infty} I(t) = N$, implying that $I = N$ is a GAS equilibrium. $\qquad \square$

(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.)

Note: The diagram below, which shows dI/dt as a function of I, may help you visualize the argument given in the proof. The diagram is drawn assuming $\epsilon < N/2$, and the argument implicitly assumes this, which is fine because we care only about small ϵ. The key idea is that if we can find a positive lower bound (say K) for the rate of change of I on some time interval, then $dI/dt \geq K$ on that time interval, so $I(t) \geq I(0) + Kt$.

Proof. Let

$$f(I) = \beta I (N - I).$$

$f(I)$ is non-negative throughout the biologically relevant region, $0 \leq I \leq N$. Moreover, $f(I)$ is a parabola with maximum at $I = N/2$ and zeros only at the endpoints of the biologically relevant region.

Given $\epsilon > 0$, we want to show that all solutions with initial condition $I_0 \in (0, N)$ reach the interval $[N - \epsilon, N)$ in finite time. If $I_0 \geq N - \epsilon$ then there is nothing to prove, so consider an initial condition $I_0 \in (0, N - \epsilon)$. Let

$$K_\epsilon = f(N - \epsilon) = \beta \epsilon (N - \epsilon).$$

Thus, K_ϵ is the rate of change of I (*i.e.*, dI/dt) when I has the least possible value in the interval $\{I : N - \epsilon \leq I < N\}$. Also let
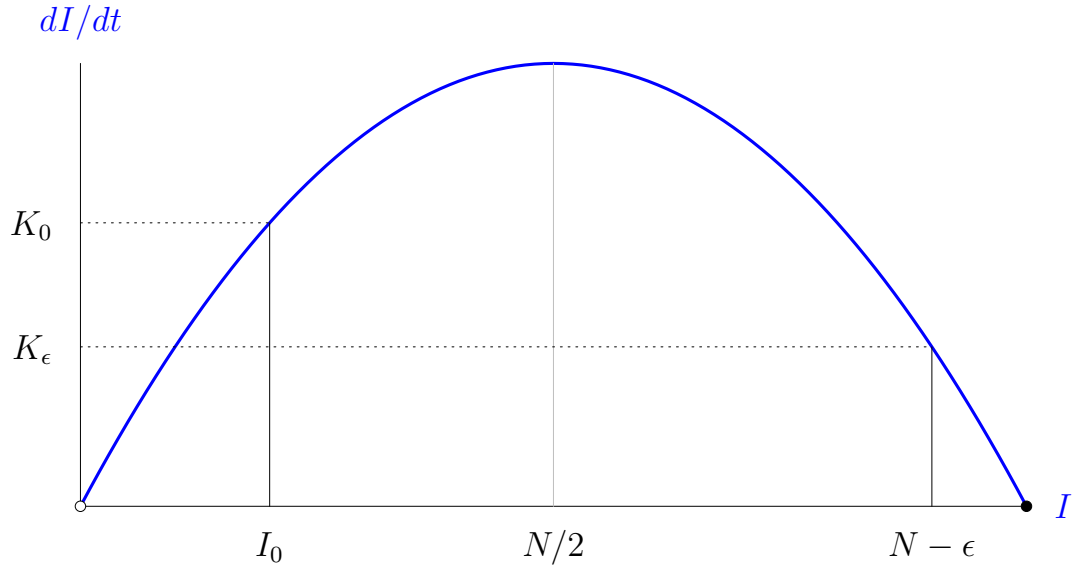
$$K_0 = f(I_0),$$

i.e., K_0 is the initial rate of range of I.

If $K_0 \geq K_\epsilon$ then $I(t) \geq K_\epsilon t$ (as long as $I(t)$ remains in the interval $[I_0, N - \epsilon]$; see the diagram below) so if

$$t_\epsilon = (N - \epsilon)/K_\epsilon$$

then $I(t_\epsilon) \geq N - \epsilon$ and we can infer that $I(t) = N - \epsilon$ at some time $t \leq t_\epsilon$.

If $K_0 < K_\epsilon$ then $I_0 < N/2$, so $dI/dt > K_0$ for all $I \in (I_0, N/2]$, hence I will reach $N/2$ in a time less than $N/(2K_0)$ and we can then apply the first part of the argument again.

□

2 Analysis of the basic SIR model

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

$$\frac{dS}{dt} = -\mathcal{R}_0 SI \tag{2a}$$

$$\frac{dI}{dt} = \mathcal{R}_0 SI - I \tag{2b}$$

$$\frac{dR}{dt} = I \tag{2c}$$

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. In class (Lecture 4, Slide 52) we found the exact solution for the phase portrait of this system,

$$I(S) = I_0 - (S - S_0) + \frac{1}{\mathcal{R}_0} \log\left(S/S_0\right). \tag{3}$$

We can find the maximum value of I using elementary calculus. We have

$$I'(S) = -1 + \frac{1}{\mathcal{R}_0 S}, \tag{4}$$

$$I''(S) = -\frac{1}{\mathcal{R}_0 S^2}. \tag{5}$$

Hence, the unique critical point of $I(S)$ is at $S = 1/\mathcal{R}_0$. Moreover, $I''(1/\mathcal{R}_0) < 0$ so this is a maximum point. Therefore, the maximum value of I, *i.e.,* the peak prevalence, is

$$I_{\text{peak}}(S_0, I_0) = I(1/\mathcal{R}_0) = I_0 - \left(\frac{1}{\mathcal{R}_0} - S_0\right) + \frac{1}{\mathcal{R}_0} \log\left(\frac{1}{\mathcal{R}_0 S_0}\right). \tag{6}$$

A public health official might be interested in this quantity because it is likely to be strongly correlated with peak pressure on hospital beds and other resources during an epidemic.

It's always a good idea to check analytical calculations numerically. So let's check we got it right for some particular initial state. The ®️ code below plots a big yellow dot at the peak prevalence as determined by the full solution curve evaluated at the maximum point and puts a big black dot inside that using the formula for the peak prevalence. If the two agree, we'll see a bulls-eye at the point of peak prevalence on the plot.

```
IofS <- function(Si,Ii,R0=2,S) {
  ## Si,Ii are initial conditions
  ## R0 is reproduction number, not initial removed!
  return(Ii - (S-Si) + (1/R0)*log(S/Si))
}
Ipeak <- function(Si,Ii,R0=2) {
  ## Si,Ii are initial conditions
  ## R0 is reproduction number, not initial removed!
  return(Ii - ((1/R0)-Si) + (1/R0)*log(1/(R0*Si)))
}
Ii <- 0.0001
```

```
Si <- 1-Ii
R0 <- 4
Svals <- seq(0,Si,length=100)
plot(Svals,IofS(Si,Ii,R0,Svals), typ="l", lwd=2, col="red",
     xlab="S", ylab="I", bty="L", xaxs="i", yaxs="i",
     xlim=c(0,1),ylim=c(0,1))
## mark the maximum point with a big yellow dot:
points(1/R0, IofS(Si,Ii,R0,1/R0), pch=21, bg="yellow", cex=2)
## and put a black dot on top using our peak prevalence formula:
points(1/R0, Ipeak(Si,Ii,R0), pch=19)
```
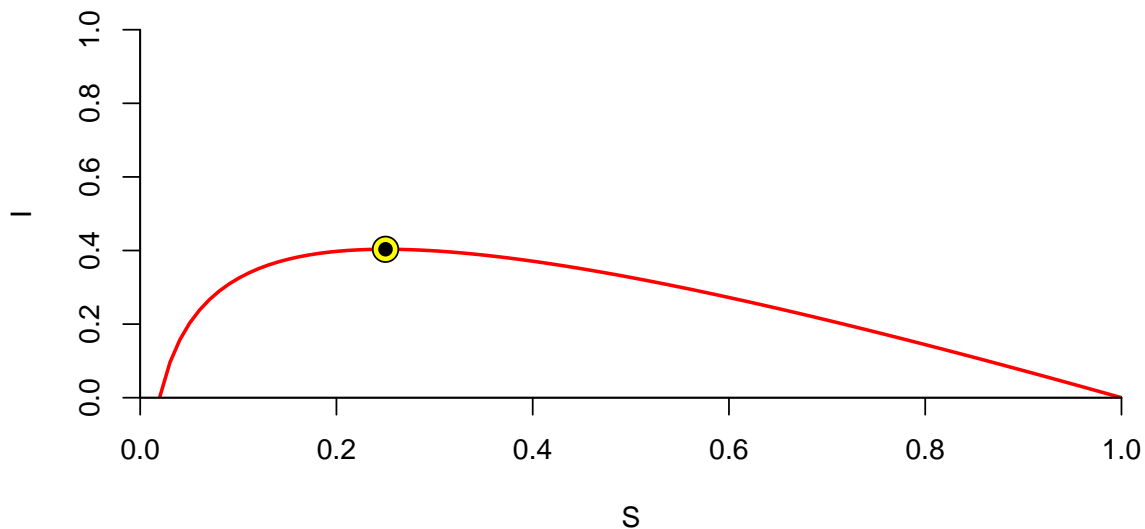

(b) It would be helpful to have an analytical expression for the solution of the model. Most valuable would be a formula for $I(t)$, which is most closely related to time series data. You probably will not find a formula for $I(t)$ (extra credit if you do!!) but it is definitely possible to find an exact 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. <u>*Note:*</u> You will end up with an expression for t as a function of R, not R as a function t.

   Solution 1. Putting together the $\dot{S}$ and $\dot{R}$ equations we have

   $$\frac{1}{S}\frac{dS}{dt} = -\mathcal{R}_0 \frac{dR}{dt}.$$

Integrating from 0 to t we have

$$\int_{S_0}^{S(t)} \frac{dS}{S} = -\mathcal{R}_0 \int_{R_0}^{R(t)} dR \, ,$$

i.e.,

$$\log S/S_0 = -\mathcal{R}_0(R - R_0) \, , \qquad\qquad (\heartsuit)$$

and hence

$$S = S_0 e^{-\mathcal{R}_0(R - R_0)} \, .$$

Now noting from Equation (2c) that $dR/dt = I = 1 - (S + R)$ we have

$$\frac{dR}{dt} = 1 - S - R = 1 - R - S_0 e^{-\mathcal{R}_0(R - R_0)} \, ,$$

and hence

$$\frac{dt}{dR} = \frac{1}{1 - R - S_0 e^{-\mathcal{R}_0(R - R_0)}} \, .$$

We can now integrate to find

$$t(R) = \int_{R_0}^{R} \frac{dR}{1 - R - S_0 e^{-\mathcal{R}_0(R - R_0)}} \, . \qquad\qquad (*)$$

$\square$

Solution 2. A slight variation on the start of the above solution is to first find the phase portrait in the (R, S) plane via

$$\frac{dR}{dS} = \frac{dR/dt}{dS/dt} = -\frac{1}{\mathcal{R}_0 S} \, , \qquad\qquad (7)$$

and then use Equation (2c) as above. $\square$

(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. Since $S + I + R = 1$ at all times, we have

$$R_{\text{peak}} = 1 - [S_{\text{peak}} + I_{\text{peak}}]$$

$$= 1 - \left[\frac{1}{\mathcal{R}_0} + I_0 - \left(\frac{1}{\mathcal{R}_0} - S_0 \right) + \frac{1}{\mathcal{R}_0} \log \left(\frac{1}{\mathcal{R}_0 S_0} \right) \right] \, ,$$

where we have inserted $S_{\text{peak}} = 1/\mathcal{R}_0$, and I_{peak} from equation (6). The time at which peak prevalence occurs can then be written

$$t_{\text{peak}} = \int_{R_0}^{R_{\text{peak}}} \frac{dR}{1 - R - S_0 e^{-\mathcal{R}_0(R - R_0)}} \, . \qquad\qquad (**)$$

Note that since we chose the time unit to be the mean infectious period for convenience, this expression gives the time of peak prevalence in units of the mean infectious period. $\square$

This could be useful because public health planners are likely to want to predict when pressure on hospital beds and other resources will be most severe.

(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?

Answers. If the infectious period T_{inf} were the same for every individual (rather than exponentially distributed) then the current value of dR/dt would be equal to incidence a time T_{inf} in the past. In general, dR/dt is a reasonable approximation of incidence a time T_{inf} in the past, where T_{inf} is the *mean* infectious period. Similarly, dR/dt (scaled by the case fatality proportion) is a reasonable approximation of the mortality curve (our observed quantity) time-translated by the mean time from loss of infectiousness to death. Although we cannot do the integral in equation (*) analytically, for any given initial conditions and $\mathcal{R}_0$ we can certainly do it numerically with ℝ. We can therefore obtain $R(t)$ numerically, and we can then plug this into our expression for dR/dt as a function of R to obtain dR/dt as a function of t. However, I would not advise my assistant to do this. Instead, I would suggest using a standard, well-tested numerical ODE solver applied to the original equations. It is certainly possible that the integral expression (*) for $t(R)$ could be used for some useful analytical work, but it is not obvious what that would be. One approach would be to approximate the exponential in the denominator of (*) in some way in order to obtain an integral that can be computed in terms of elementary functions; this was done by Kermack and McKendrick (1927). □

(iv) Is it possible to find an exact analytical expression for t as a function S?

Solution. Yes! Exploiting the exact solution for $I(S)$ given in (3) we have

$$\frac{dS}{dt} = -\mathcal{R}_0 S\, I(S) = -\mathcal{R}_0 S\Big(I_0 - (S - S_0) + \frac{1}{\mathcal{R}_0}\log\left(S/S_0\right)\Big),\qquad(8)$$

and we can now use the same approach that yielded $t(R)$ to obtain $t(S)$. The result looks a little nicer if we let $u = -\log\left(S/S_0\right)$ and solve for $t(u)$ rather than $t(S)$ directly. This yields

$$-\frac{du}{dt} = \mathcal{R}_0\Big(I_0 - S_0(e^{-u} - 1)\Big) + u\,,\qquad(9)$$

i.e.,

$$t(u) = \int_0^u \frac{du}{\mathcal{R}_0\big[I_0 + S_0(1 - e^{-u})\big] + u}\,.\qquad(10)$$

□

(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.

Note: It would probably have been better to reverse the order of parts (c) and (d).

Proof. The set of biologically meaningful states is the triangle

$$\Delta = \{(S, I) : S \geq 0,\ I \geq 0 \text{ and } S + I \leq 1\}. \tag{11}$$

Our goal is to show that any initial state in Δ lies on a solution that converges to the S axis. Any state on the S axis itself must remain there (since all such states are equilibria), so our problem is to prove that any biologically meaningful initial state with $I > 0$ converges to one of the stable equilibria on the subset of Δ that consists of the interval $[0, 1/\mathcal{R}_0]$ on the S axis, *i.e.,* the set

$$\mathcal{C} = \{(S, 0) : 0 \leq S \leq 1/\mathcal{R}_0\}. \tag{12}$$

So, consider initial conditions in $\tilde{\Delta} = \{(S, I) \in \Delta : S < 1/\mathcal{R}_0,\ I > 0\}$. On this set, Equation (2b) yields

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

suggesting asymptotic stability according to Lyapunov's theorem, but we need to be careful.

The standard result is stated as Theorem 1 below. We are in trouble if we want to apply this theorem because we do not have an isolated equilibrium. Nevertheless, as explained after Theorem 1 below and stated precisely in Theorem 2 below, it is enough to have L vanish on the closed segment $\mathcal{C}$ to which we are hoping to establish solutions are attracted. $L(S, I) = I$ does vanish on $\mathcal{C}$. To apply Theorem 2, let

$$\mathcal{O} = \{(S, I) \in \Delta : S < 1/\mathcal{R}_0\}, \tag{14}$$

i.e., $\mathcal{O}$ is the open subset of Δ to the left of the nullcline at $S = 1/\mathcal{R}_0$. Then with $\mathcal{C}$ defined by (12), all the hypotheses of Theorem 2 are easy to verify and we have attraction from all points in $\mathcal{O}$ to $\mathcal{C}$.

What remains to show is that initial states in $\tilde{\Delta} \setminus \mathcal{O}$ necessarily enter $\mathcal{O}$ in finite time. To that end, suppose $(S_0, I_0) \in \tilde{\Delta} \setminus \mathcal{O}$. For as long as $S \geq 1/\mathcal{R}_0$, we have $dI/dt = (\mathcal{R}_0 S - 1)I \geq (\mathcal{R}_0/\mathcal{R}_0 - 1)I = 0$, so $I(t) \geq I_0$ and consequently $dS/dt = -\mathcal{R}_0 SI < -I_0$. Since dS/dt is bounded above by a negative number, $S(t)$ must decrease to $1/\mathcal{R}_0$ in finite time (*cf.* problem (1)bii above). Once $S = 1/\mathcal{R}_0$, we have $dS/dt = -\mathcal{R}_0 SI = -I < 0$ for any $I > 0$, so the solution must enter $\tilde{\Delta} \setminus \mathcal{O}$, as required. $\qquad \square$

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

Solution. The three derivatives in Equation (2) are zero if $I = 0$, and $dR/dt = 0$ if and only if $I = 0$. So all points in the set $\{(S_0, 0) : 0 \leq S_0 \leq 1\}$ are equilibria and there are no others.

If $S_0 > 1/\mathcal{R}_0$, then $dI/dt > 0$ for any $I > 0$ so all equilibria with $S_0 > 1/\mathcal{R}_0$ are unstable.

If $S_0 = 0$ then $dS/dt = 0$ and $dI/dt < 0$ for any $I > 0$, so any point on the I axis moves along the I axis closer to $(0,0)$, so $(0,0)$ is a stable equilibrium.

If $0 < S_0 \leq 1/\mathcal{R}_0$, then for any $I > 0$ we have $dS/dt < 0$ and $dI/dt \leq 0$. Consequently, the trajectory remains in the closed rectangle formed by the origin $(S,I) = (0,0)$ and the initial state $(S,I) = (S_0, I_0)$. More generally, if $S \leq 1/\mathcal{R}_0$ then the trajectory beginning at (S,I) remains in the closed rectangle $F_{(S,I)}$ with corners at the origin and the point (S,I). Furthermore, it follows that trajectories that start at points (S',I') in the interior of $F_{(S,I)}$ remain in the interior of $F_{(S,I)}$ (since they remain in $F_{(S',I')}$, which is a subset of $F_{(S,I)}^{\circ}$). This observation will help us complete the stability proof:

> Let $U \subseteq \Delta$ be an open rectangle containing the equilibrium $(S,I) = (S_0, 0)$, where
> $$0 < S_0 < \frac{1}{\mathcal{R}_0}.$$
> We must show that there is an open set $V \subseteq U$ such that (i) V also contains the focal equilibrium point and (ii) V has the property that if $(S',I') \in V$ then the trajectory beginning at (S',I') never leaves U. To that end, choose S_1 and S_2 such that
> $$0 < S_1 < S_0 < S_2 < \frac{1}{\mathcal{R}_0}$$
> and such that $(S_1, 0) \in U$ and $(S_2, 0) \in U$. Let W be the interior of the set bounded by the solution curves that pass through $(S_1, 0)$, $(S_2, 0)$ and the boundary of Δ. By the existence and uniqueness theorem, solutions that start in W remain in W. In addition, from the observation above, solutions that start in the interior of $F_{(S_2, 1-S_2)}$ remain in it. Therefore, the open set
> $$V = U \cap W \cap F_{(S_2, 1-S_2)}^{\circ}$$
> satifies our requirements and establishes that $(S_0, 0)$ is stable if $0 < S_0 < 1/\mathcal{R}_0$. The one equilibrium that remains is $(S,I) = (1/\mathcal{R}_0, 0)$. In this case, we can show that if U is an open rectangle containing this point then there is a complete solution that lies in U, so we can define W to be the open set bounded by that solution and the lower boundary of Δ (the S axis). Solutions that start in W stay in U because $W \subseteq U$.

None of the equilibria is asymptotically stable, since any open set containing one equilibrium also contains other equilibria.

Note: Together with the stability established in this part, the analysis in part (c) proves that the line segment $\mathcal{C}$ defined in Equation (12) is GAS.

$\square$

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

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

(c) $\dot{L}(X) < 0$ $\forall X \in \mathcal{O} \setminus \{X_*\}$ *($\dot{L}$ 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.,* [1, §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 $\mathcal{C}$ of $X' = F(X)$ and an open set $\mathcal{O}$ containing $\mathcal{C}$. 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) $\dot{L}(X) \leq 0$ $\forall X \in \mathcal{O} \setminus \mathcal{C}$ *($\dot{L}$ negative semi-definite on $\mathcal{O}$)*

*then $\mathcal{C}$ is stable and L is called a **Lyapunov function**. If, in addition,*

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

*then $\mathcal{C}$ 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 $\mathbb{R}^2$.

<div align="center">— END OF ASSIGNMENT —</div>

References

[1] Hirsch MW, Smale S, Devaney RL. Differential equations, dynamical systems, and an introduction to chaos. 3rd ed. Waltham, MA: Academic Press; 2013.

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