



Mathematics
and Statistics

$$\int_M d\omega = \int_{\partial M} \omega$$

Mathematics 4MB3/6MB3 Mathematical Biology

Instructor: David Earn

Lecture 1
Epidemic Modelling Intro
Monday 8 January 2018

Where to find course information

- The course web page:
<http://www.math.mcmaster.ca/earn/4MB3>
- Click on “Course information”.
- Download pdf or read online.
- Let's [have a look now...](#)

Who is NOT available at these times?

- Monday 10:30-11:30
- Monday 12:30-1:30
- Wednesday 10:30-11:30
- Wednesday 12:30-1:30
- Friday 12:30-1:30
- Friday 2:30-3:20

Group formation

Most work in this course will be done in groups.

- Attempt to form a group of 4 students (you and 3 others) **no later than Thursday night this week.**
- After you have done your best to form a group of four, **exactly one** member of your group must **e-mail the instructor no later than Thursday night this week:**
 - Include “Math 4MB3” and your proposed group name in the subject line.
 - **Copy your message to all members of your proposed group so I have everyone’s e-mail in the thread.**
- If you were unable to form a group, then e-mail the instructor explaining what you did to try to form a group, and describe your skills/preferences. (*This is a last resort – please try your best to form a group.*)
- *Instructor may change groups based on survey results.*

Online Surveys

You will be required to fill in online surveys during this course. Doing so in a timely manner contributes to your participation mark.

The first online survey has been posted:

- Go to the [Surveys page](#) on the [course web site](#).
- Follow the link for [Background and Group formation Survey](#).
- Complete the survey **no later than 11:59pm this Thursday (11 Jan 2018)**.
- It should take only ~ 5 minutes.
- Note that *surveys sometimes fail to save*.
 - Type long answers into a file first and paste them into the survey. Then you won't get as frustrated if it fails to save.

Software

- **ASAP**, install the software discussed on the [Software page](#) on the [course web site](#):

- L^AT_EX



- R



- RStudio



- XPPAUT

- Emacs

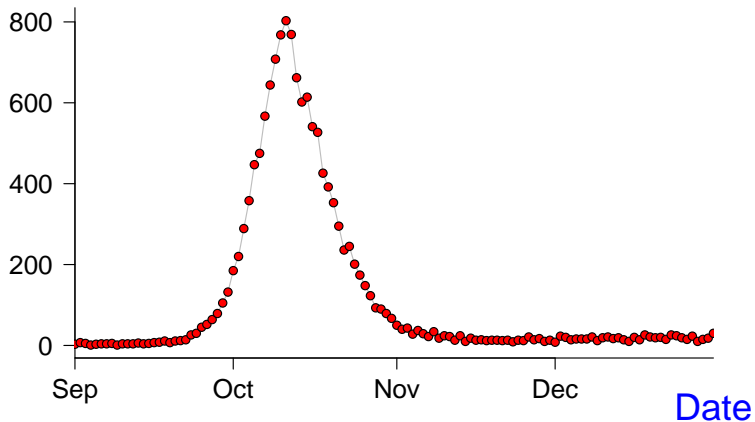


- If you have installation problems, please contact [Ken Moyle](#) <moylek@mcmaster.ca>, who created the [Software page](#).
- **Note:** the [Software page](#) also contains some info about spell-checking and counting words in L^AT_EX documents.

Epidemic Modelling

Pneumonia & Influenza Mortality, Philadelphia, 1918

P&I Deaths



Modelling challenge

Develop a model that helps us understand the [graph on the previous slide](#), based on mechanisms of disease spread.

- Only one variable is observed (P&I deaths per day) so construct a model containing only one variable.
- Think about how disease spreads and express your thoughts with mathematical notation.
- Derive a differential equation that models the process of disease transmission.
- Analyze the model and determine its strengths and weaknesses/limitations.

Make (Biological) Assumptions Clear

- 1 *Assume* the disease is transmitted by contact between an infected individual and a susceptible individual.
- 2 *Assume* the latent period (delay between being infected and becoming infectious) is so short that it can be ignored (technically assume it is zero).
- 3 *Assume* all members of the population are identical and respond identically to the disease. In particular, all susceptible individuals are equally susceptible and all infected individuals are equally infectious.
- 4 *Assume* the population size is fixed during the epidemic, *i.e.*, ignore births, migration, and deaths from causes other than the disease, and count individuals who have died from the disease as part of the population.

About Assumptions. . .

- Note that the first assumption on the [previous slide](#) is actually correct.
- The other assumptions are wrong, but are reasonable approximations.
- It is best to *start as simple as possible and add complexity later*, in order to:
 - obtain a model that actually succeeds in explaining [the data](#) with as few assumptions as possible;
 - check that inferences we draw from our model(s) are robust to the inclusion of more biological details/realism.

What variables should we include in our model?

- Independent variable: time (t)
- Dependent variable: Many options, e.g.,
 - Incidence (number of new infections per unit time)
 - Prevalence (total current number of infected individuals)
 - Death rate (number of deaths per unit time)
 - Death toll (number of deaths so far)
- So, what would be best?
- Not deaths, because whether or not you die may be unrelated to how much you transmit.
- But deaths are what **we observe!** What to do?!?
- Make another assumption. . .

Additional assumption(s)

- We actually want to know incidence or prevalence, but we **observe deaths**.
- Under what circumstances would daily deaths be a good estimate of incidence? (*i.e.*, What must we assume in addition to the **assumptions we have already made**.)
 - 5 **Assume** that the time from infection to death is exactly the same (a certain number of days) for every individual who dies.
 - 6 **Assume** that the probability of dying from the disease is the same for every individual who is infected.
- Then daily death counts are proportional to daily incidence a certain number of days in the past, *i.e.*, the “mortality curve” that **we observe** is a translated and scaled version of the “epidemic curve” (new cases per day).

So... what variables should we include in our model?

- Independent variable: time (t)
- Dependent variable: one of:
 - Incidence (number of new infections per unit time)
 - Prevalence (total current number of infected individuals)
- Which one?
- Choose prevalence (I) because anybody who is currently infectious can infect others, so it will probably be easier to formulate a transmission model based on prevalence. (Try not to lose sight of underlying biological mechanisms.)
- But our **mortality curve** is related to incidence, not prevalence!?! Argh. What to do?!?
- Let's work with prevalence and see how it works out. Maybe we'll be able to derive the incidence curve from a model based on prevalence.



Mathematics
and Statistics

$$\int_M d\omega = \int_{\partial M} \omega$$

Mathematics 4MB3/6MB3 Mathematical Biology

Instructor: David Earn

Lecture 2
SI Model

Wednesday 10 January 2018

Announcements

- Group names and members are listed on the [Groups page](#) on the course web site.
- [Assignment 1](#) is due when class starts on Monday 22 Jan 2018.
- Links to GitHub and Dropbox are posted on the [Software page](#). There are many other tools for online collaboration, some specific to \LaTeX .
- Have you successfully installed the required software?

Notational note

- We use I for prevalence because prevalence is the number of infected individuals.

- So, let's try to write down a model...

A first (naïve) attempt at an epidemic model

- Variables: time t , prevalence $I(t)$
- How does I increase?
- Start with I_0 infected individuals at time $t = 0$. What happens for $t > 0$.
- Let $B =$ average number of contacts with susceptible individuals that lead to a new infective per unit time per infective in the population (and suppose B is constant). Then

$$I(t + \Delta t) \simeq I(t) + B I(t)\Delta t$$

- In the limit $\Delta t \rightarrow 0$, we have

$$\frac{dI}{dt} = BI \quad \Longrightarrow \quad I(t) = I_0 e^{Bt}$$

Beware: implicit assumptions that should be explicit

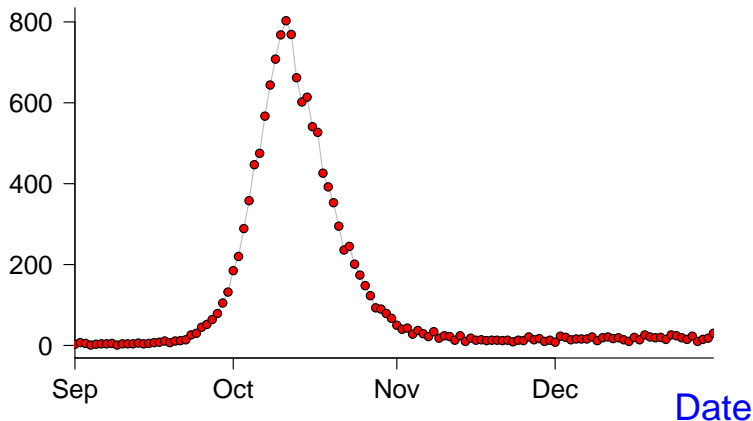
- Ignored discrete nature of individuals when taking limit.
- *Ignored finite infectious periods!*
 - Sometimes it isn't obvious that we've made some assumptions until after we see what the model predicts.

How can we tell if our model is good?

- Compare model predictions with **data**.
- What is the best way to do that?
- Depends on what predictions we're trying to test.
- Model predicts exponential growth.
How should we test that prediction?
- Transforming **the data** might help.

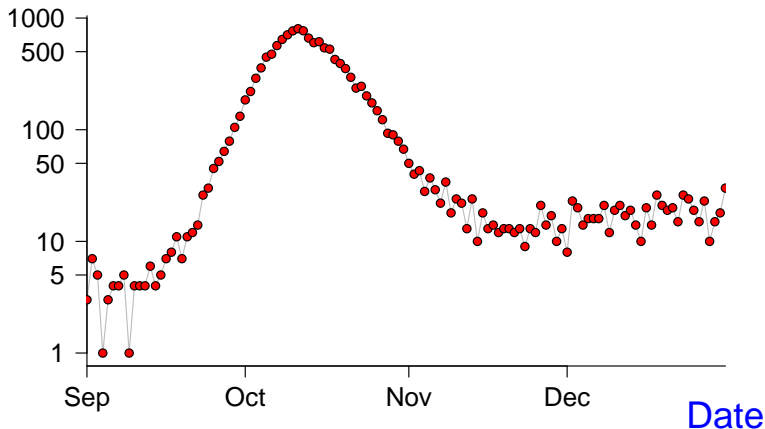
Original data: P&I Mortality, Philadelphia, 1918

P&I Deaths



Logarithmic scale: P&I Mortality, Philadelphia, 1918

P&I Deaths



Parameter estimation

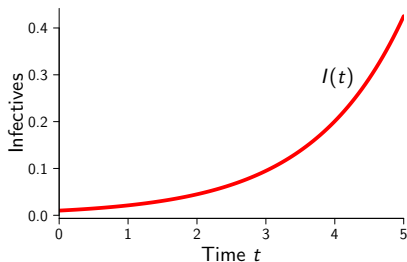
How can we estimate the model parameters, I_0 and B , from the P&I data?

- Fit a straight line through the part of the **logarithmic mortality curve** that looks straight.
- The slope of the line is B .
- The “intercept” is $\log I_0$.
 - “Intercept” in quotes because we need to define $t = 0$ as the time when exponential growth begins.
- **Note:** Parameter estimation is, in general, a very tricky business and deserves a great deal of attention (beyond the scope of this course).

Naïve epidemic model

- Variables: time t , prevalence $I(t)$
- Parameter B = average number of contacts with susceptible individuals that lead to a new infective per unit time per infective in the population

$$\frac{dI}{dt} = BI \quad \Longrightarrow \quad I(t) = I_0 e^{Bt}$$



Naïve model: the good and the bad

- Good:
 - Makes clear predictions
 - Predictions can be tested
 - Estimation of parameter (B) is easy
 - B is the slope of the straight portion of the epidemic curve on the log scale. (Why?)
 - Remember we are imagining that the mortality curve is equivalent to the epidemic curve after translation and scaling.
 - Why do translation and scaling not affect the estimate of B ? Assignment 2. . .
- Bad:
 - Model is consistent only with exponential growth phase.
 - Absurd long-term prediction: unbounded growth in $I(t)$
 - Implicitly assumed that population size $N = \infty$.

How can we improve our model?

- Insist that population size is finite ($N < \infty$).
- Keep track of both **infectives** $I(t)$ and **susceptibles** $S(t)$.
- Assume individuals who are *not infected* are **susceptible**:

$$I(t) + S(t) = N = \text{constant.}$$

New model parameter(s)?

- B = average number of contacts with **susceptible** individuals that lead to a new **infective** *per unit time per infective*
- In the naïve model, we assumed $B = \text{constant}$.
Is B really constant?
- B depends on how many **susceptibles** there are.
- $B = \beta S(t)$
- β = average number of contacts between **susceptibles** and **infectives** that lead to a new **infective**
per unit time
per infective
per susceptible
- β is called the **transmission rate**.

Revised epidemic model: "SI model"

$$\frac{dI}{dt} = \beta S(t)I(t)$$

- Two state variables. One equation. Problem? No:

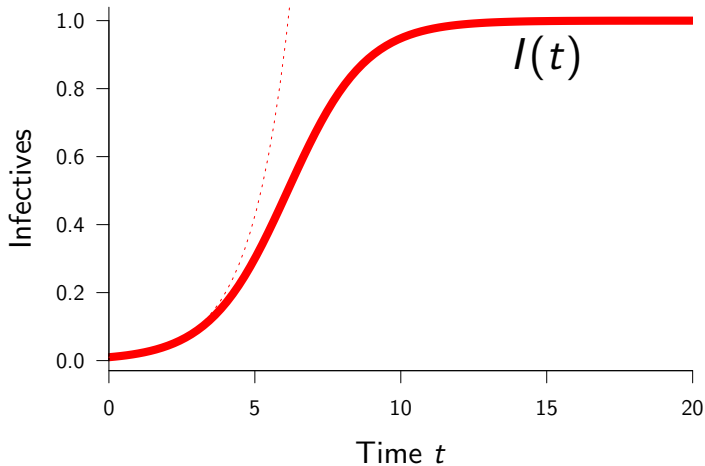
$$\frac{dS}{dt} = -\beta S(t)I(t)$$

- But $S(t) = N - I(t) \implies I(t)$ is still the only variable:

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

- Is this a better model?
- What does it predict?

SI model: Example solution



SI model: Analysis

- We can find the exact solution. How?

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

- But exact solution is not particularly enlightening.
- Qualitative analysis:
 - Initially $I \ll N$. What does the model predict then?
Exponential growth. Great!
 - As I grows, growth rate slows. Why?
Fewer and fewer **susceptibles** to infect.
 - Asymptotic behaviour? Equilibria? Periodic orbits?
(periodic orbit = recurrent epidemics)
 - (Non-trivial) periodic orbits impossible in one dimension
(existence-uniqueness theorem).
 - Consider equilibria. . .

SI model: Equilibrium Analysis

$$\frac{dI}{dt} = \beta I(N - I), \quad I \in [0, N]$$

- Two equilibria:
 - $I = 0$ Disease Free Equilibrium (**DFE**)
 - $I = N$ Endemic Equilibrium (**EE**)
- Stability:
 - DFE is unstable ($0 < I < N \implies dI/dt > 0$)
 - EE is locally asymptotically stable (**LAS**)
 - EE is globally asymptotically stable (**GAS**)
 (stability of EE follows from $0 < I < N \implies dI/dt > 0$)
 (GAS requires a little more analysis... Assignment 1)
 - *Note:* In one dimension, global analysis always easy.
 In higher dimensions, often try to find Lyapunov function.
 (Lyapunov function for EE of SI model?... Assignment 1)
- Conclusions identical for any $\beta > 0$.

SI model: Biological Inferences

- For *any* transmission rate β :
 - Initially, exponential growth of cases.
 - Eventually, convergence to equilibrium (EE) at which *everyone* in the population is **infective**. hmmm...
- Is this model better than our first naïve model?
YES.
 - Still correctly predict initial exponential growth.
 - Can match epidemic curve for longer (up to the peak).
 - Does not predict absurd unbounded growth in **infective** population.
 - But this model cannot explain the decline of the epidemic.
- What should we do? Two obvious options:
 - 1 Get depressed, drop the course.
 - 2 Try to improve the model.



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Mathematics 4MB3/6MB3 Mathematical Biology

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Lecture 3

SIR Model

Friday 12 January 2018

Motivating data: 1918 flu in Philadelphia

- Mortality curve (linear scale)
- Mortality curve (log scale)

How can we improve on the SI model?

- Include a key biological fact:
Individuals do not stay infectious with flu forever
- Either they *recover* and are immune thereafter, or they *die* (doesn't matter which) (well, maybe to them it does)
- Why don't we care if someone recovers or dies?
(*i.e.*, Why doesn't it affect our dynamical inferences?)
- Because in either case the individual is *removed* from the transmission process, hence cannot affect the future pattern of the epidemic.

The SIR model

Introduce new class of **removed** individuals:

- $R(t)$ = number of individuals who have either recovered and are now immune or have died
- Let γ = rate of removal from the **infective** class (via recovery or death)

$$\frac{dS}{dt} = -\beta SI$$

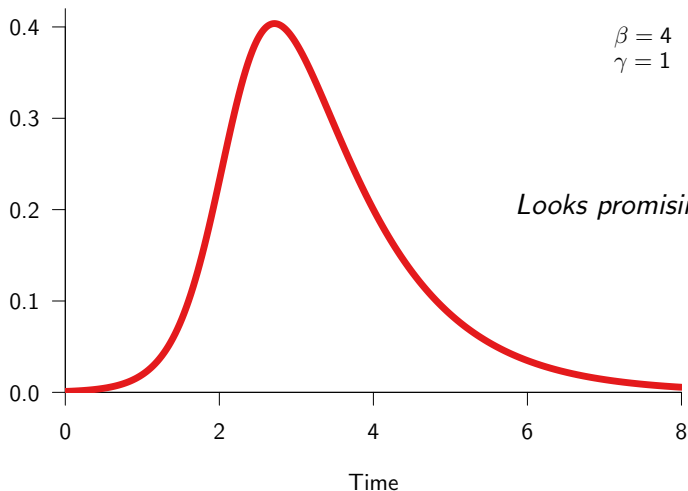
$$\frac{dI}{dt} = \beta SI - \gamma I$$

$$\frac{dR}{dt} = \gamma I$$

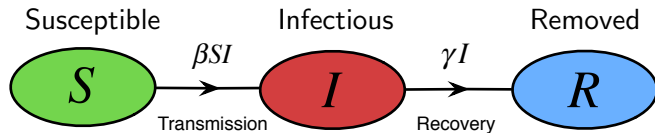
- Note: $\frac{dS}{dt} + \frac{dI}{dt} + \frac{dR}{dt} = 0 \implies S + I + R = N = \text{constant}$
- Convenient to rescale variables by N and interpret S, I, R as *proportions* of the population in each disease state.

The SIR model: Example numerical solution

Proportion infected $I(t)$



The SIR model: Flow Chart and Parameters



$$\frac{dS}{dt} = -\beta SI$$

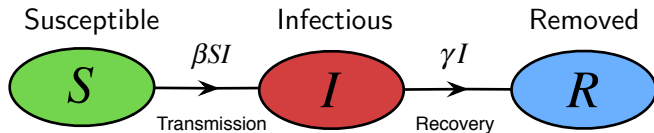
$$\frac{dI}{dt} = \beta SI - \gamma I$$

$$\frac{dR}{dt} = \gamma I$$

■ Parameters:

- Transmission rate β
- Recovery rate γ
(or Removal rate)

The SIR model: Derived Parameters



$$\frac{dS}{dt} = -\beta SI$$

$$\frac{dI}{dt} = \beta SI - \gamma I$$

$$\frac{dR}{dt} = \gamma I$$

■ Derived Parameters:

- Initial growth rate $\beta - \gamma$
- Mean infectious period $\frac{1}{\gamma}$
- Basic Reproduction Number

$$\mathcal{R}_0 = \frac{\beta}{\gamma}$$

The SIR model: Derived parameters

The initial growth rate

- How do we calculate the initial growth rate from our model?
- Consider change in prevalence initially (when $I \ll 1$):

$$\begin{aligned}\frac{dI}{dt} &= \beta SI - \gamma I \\ &= (\beta S - \gamma)I \\ &\approx (\beta - \gamma)I \quad \text{if } S \sim 1 \text{ initially.}\end{aligned}$$

- \therefore Initially $I(t) \approx I_0 e^{(\beta - \gamma)t}$.
- \therefore Initial slope of logged prevalence curve is $\beta - \gamma$.

The SIR model: Derived parameters

The mean infectious period

- How do we calculate the mean infectious period from our model?
- Suppose at time 0 there are I_0 infectious individuals, and suppose we can *prevent contact with susceptibles*.
- The [equation for \$I\$](#) then simplifies to

$$\frac{dI}{dt} = -\gamma I, \quad I(0) = I_0$$

- We can solve this immediately to find

$$I(t) = I_0 e^{-\gamma t}$$

The SIR model: Derived parameters

The mean infectious period, continued...

- Thus, after time t , the number of people still infectious is reduced by a factor $e^{-\gamma t}$
- *i.e.*, the proportion of individuals who have an infectious period shorter than t is $1 - e^{-\gamma t}$
- *i.e.*, the cumulative distribution of the infectious period is $C(t) = 1 - e^{-\gamma t}$.
- Therefore, the probability density of the infectious period is $p(t) = C'(t) = \frac{d}{dt}(1 - e^{-\gamma t}) = \gamma e^{-\gamma t}$
- The mean of this exponential probability distribution is $\int_0^{\infty} t p(t) dt = \int_0^{\infty} t \gamma e^{-\gamma t} dt = \frac{1}{\gamma}$

The SIR model: Derived parameters

The basic reproduction number \mathcal{R}_0

$$\begin{aligned}\mathcal{R}_0 &= \beta \cdot \frac{1}{\gamma} \\ &= (\text{transmission rate}) \\ &\quad \times (\text{mean infectious period})\end{aligned}$$

- \mathcal{R}_0 is dimensionless
- \mathcal{R}_0 is the average number of secondary cases caused by a primary case (in a wholly susceptible population).
- We must have $\mathcal{R}_0 > 1$ to have an epidemic. Why?
 - $\frac{dI}{dt} = \beta SI - \gamma I = (\mathcal{R}_0 S - 1)\gamma I$
 - $\therefore \mathcal{R}_0 \leq 1 \implies \frac{dI}{dt} \leq 0$ for all $(S, I) \in [0, 1]^2 \implies$ no growth

The SIR model: Analysis (biological well-posedness)

$$\frac{dS}{dt} = -\beta SI$$

$$\frac{dI}{dt} = \beta SI - \gamma I$$

- We need S , I and R all non-negative at all times.
- Does $0 \leq S(0) + I(0) \leq 1$ imply $0 \leq S(t) + I(t) \leq 1$ for all $t > 0$?
 - $S = 0 \implies S' = 0$, so
 $S(0) \geq 0 \implies S(t) \geq 0 \forall t > 0$.
 - $I = 0 \implies I' = 0$, so
 $I(0) \geq 0 \implies I(t) \geq 0 \forall t > 0$.
 - $(S + I)' = S' + I' = -\gamma I \leq 0$
 $\implies S + I$ is always non-increasing
 $\implies S(t) + I(t) \leq S(0) + I(0) \leq 1$.

**Be careful:
Is this a sensible
biological
model?**

The SIR model: Analysis (equilibria *etc.*)

$$\frac{dS}{dt} = -\beta SI$$

$$\frac{dI}{dt} = \beta SI - \gamma I$$

■ Equilibria:

$(S, I) = (S_0, 0)$ for any $S_0 \in [0, 1]$

- Continuum of equilibria.
- Does this make sense?
- Biological meaning of equilibria?

■ Linearization:

- $DF_{(S,I)} = \begin{pmatrix} -\beta I & -\beta S \\ \beta I & \beta S - \gamma \end{pmatrix}$

- $DF_{(S_0,0)} = \begin{pmatrix} 0 & -\beta S_0 \\ 0 & \beta S_0 - \gamma \end{pmatrix}$

- All equilibria are *non-hyperbolic*.

■ Periodic orbits:

- $(S + I)' = -\gamma I$
 \implies no periodic orbits. Why?
 - If $I(0) = 0$ then equilibrium.
 - If $I(0) > 0$ then $(S + I)' < 0$, so cannot increase back to initial state.
- Also follows from [Index Theorem](#) (cannot enclose any equilibria).



Mathematics
and Statistics

$$\int_M d\omega = \int_{\partial M} \omega$$

Mathematics 4MB3/6MB3 Mathematical Biology

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Lecture 4
SIR Model II
Monday 15 January 2018

Announcements

- **Groups** are formed.
- **Assignment 1** is due when class starts on Monday 22 Jan 2018.

The SIR model: Analysis

$$\frac{dS}{dt} = -\beta SI$$

$$\frac{dI}{dt} = \beta SI - \gamma I$$

Nullclines:

- $S' = 0 \implies S = 0$ or $I = 0$
 - S nullclines: both coordinate axes

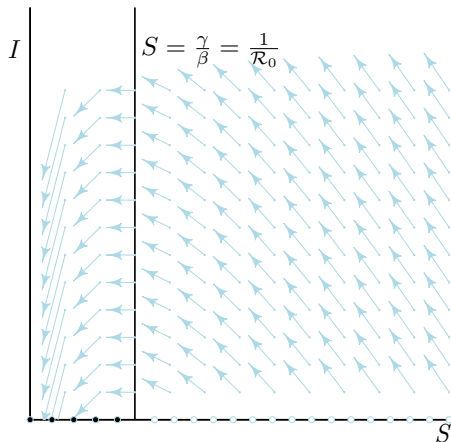
- $I' = 0 \implies I = 0$ or $S = \gamma/\beta$
 - I nullclines: S axis and vertical line at $S = 1/\mathcal{R}_0$
 - Is the I nullcline at $S = 1/\mathcal{R}_0$ always relevant?
 - If, and only if, $\mathcal{R}_0 > 1$.
 - If $\mathcal{R}_0 < 1$ then $S = 1/\mathcal{R}_0$ is outside the biologically relevant region of the (S, I) phase plane.

The SIR model: Analysis

Nullclines and Direction Field ($\mathcal{R}_0 = 4$):

$$\frac{dS}{dt} = -\beta SI$$

$$\frac{dI}{dt} = \beta SI - \gamma I$$



The SIR model: Analysis

$$\frac{dS}{dt} = -\beta SI$$

$$\frac{dI}{dt} = \beta SI - \gamma I$$

- *i.e.*, we can find an expression $I(S)$ for solution curves in the (S, I) phase plane.
- Slope of $I(S)$ depends only on S :

$$\frac{dI}{dS} = \frac{dI/dt}{dS/dt} = -1 + \frac{1}{\mathcal{R}_0 S} \quad (*)$$

Phase Portrait:

- We cannot find solutions $S(t)$ and $I(t)$ for this system.
- We *can* find exact analytical solution for the phase portrait!

- *Note:* Slope is flat for $S = 1/\mathcal{R}_0$, so max or min of $I(S)$ occurs on I nullcline if $\mathcal{R}_0 > 1$
- Easy to integrate (*):

$$\int_{I_0}^I dI = \int_{S_0}^S \left(-1 + \frac{1}{\mathcal{R}_0 S}\right) dS$$
- $I - I_0 = -(S - S_0) + \frac{1}{\mathcal{R}_0} \log(S/S_0)$

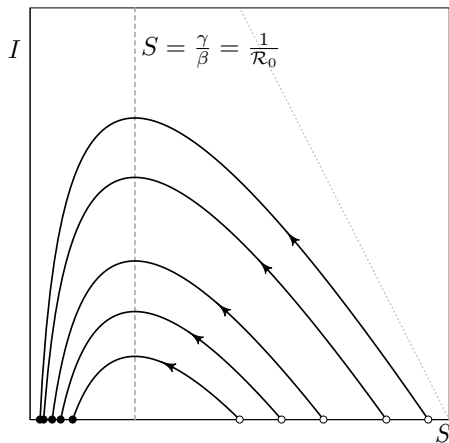
The SIR model: Analysis

Model Equations:

$$\frac{dS}{dt} = -\beta SI$$

$$\frac{dI}{dt} = \beta SI - \gamma I$$

Phase Portrait ($\mathcal{R}_0 = 4$):



**Solution Curves in
Phase Plane:**

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

The SIR model: Analysis

Model Equations:

$$\frac{dS}{dt} = -\beta SI$$

$$\frac{dI}{dt} = \beta SI - \gamma I$$

Solution Curves in Phase Plane:

$$\begin{aligned} I + S - (I_0 + S_0) \\ = \frac{1}{\mathcal{R}_0} \log(S/S_0) \end{aligned}$$

Final Size of Epidemic:

- As $t \rightarrow \infty$ we have
 $(I_\infty + S_\infty) - (I_0 + S_0) = \frac{1}{\mathcal{R}_0} \log S_\infty/S_0$
- But for a newly invading pathogen:
 $S_0 \simeq 1, I_0 \simeq 0, I_\infty = 0$
- In the limit $I_0 \rightarrow 0$, we have
 $(S_\infty - 1) = \frac{1}{\mathcal{R}_0} \log S_\infty$
- Define “Final Size” $Z = 1 - S_\infty$
- $\therefore -Z = \frac{1}{\mathcal{R}_0} \log(1 - Z)$, *i.e.*,

$$Z = 1 - e^{-\mathcal{R}_0 Z}$$

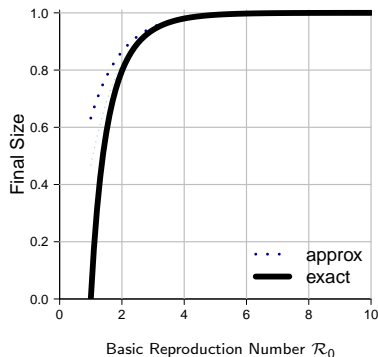
- This is a famous formula, derived by Kermack and McKendrick in 1927.

The SIR model: Analysis

Final Size Formula:

$$Z = 1 - e^{-\mathcal{R}_0 Z}$$

- Final size is determined entirely by \mathcal{R}_0
- Final size is never the whole population ($Z < 1$)
- Formula is valid for much more realistic models (Ma & Earn, 2006)



- For 1918 flu: $1.5 \lesssim \mathcal{R}_0 \lesssim 2$
- Proportion of world population infected?
- $\sim 60\text{--}80\%$

From Final Size to Reproduction Number

- The **final size relation** allows us to estimate the proportion of the population that will be infected *given* an estimate of \mathcal{R}_0 .
- But we can turn it around: if we know the **final size** Z then we can easily estimate \mathcal{R}_0 :

$$Z = 1 - e^{-\mathcal{R}_0 Z} \quad \implies \quad \mathcal{R}_0 = -\frac{1}{Z} \log(1 - Z)$$

- This is useful *post-hoc* only (*after* an epidemic).

The SIR model: Non-dimensionalization

- Often helpful to use dimensionless parameters.
- How do we identify “the right” dimensionless parameters?
- $\frac{\beta}{\gamma}$? $\frac{\gamma}{\beta}$? $\frac{\beta}{\beta+\gamma}$? $\frac{\beta^2}{\beta^2+\gamma^2}$?
- We choose β/γ because it has a natural interpretation.
- But we are still left with γ as a second parameter.
- Can we simplify the model somehow?
- γ defines a time scale ($1/\gamma$ is the mean infectious period).
- If time unit is mean infectious period, then $\gamma = 1$.
- So in these “natural” time units, the SIR model is

$$\frac{dS}{dt} = -\mathcal{R}_0 SI, \quad \frac{dI}{dt} = \mathcal{R}_0 SI - I$$

- There is really only one parameter in the model. The other is just a time scale and does not affect the *qualitative* dynamics.

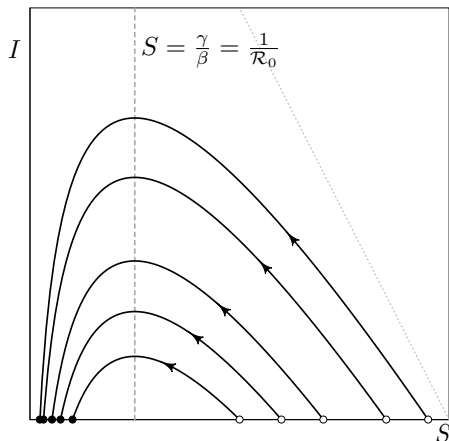
The SIR model: Results so far

Mathematical Results:

- Model is biologically well-posed
 - $0 \leq S(0) + I(0) \leq 1 \implies 0 \leq S(t) + I(t) \leq 1 \quad \forall t > 0$
- No periodic orbits.
- Continuum of equilibria.
- Stability of equilibria:
 - Linearization useless (all equilibria non-hyperbolic).
 - Further analysis necessary.
- Exact solution for phase portrait:
$$I(S) = I_0 + (S_0 - S) + \frac{1}{\mathcal{R}_0} \log(S/S_0)$$
- Final size formula: $Z = 1 - e^{-\mathcal{R}_0 Z}$

The SIR model: Stability of equilibria

Phase Portrait ($\mathcal{R}_0 = 4$):



Model Equations:

$$\frac{dS}{dt} = -\beta SI, \quad \frac{dI}{dt} = \beta SI - \gamma I$$

Which equilibria are:

- Unstable?
 - $S_0 > 1/\mathcal{R}_0$
- Stable?
 - $S_0 \leq 1/\mathcal{R}_0$
- Asymptotically stable?
 - None!
- How do we prove these facts? (**Assignment 1**)

The SIR model: Effects of Control Measures

- How could the final size of the 1918 pandemic have been reduced?
- Any intervention that reduces \mathcal{R}_0 reduces the final size.
- What could have been done to reduce \mathcal{R}_0 ?
- Masks? Quarantine? Isolation?
- Ideally a vaccine, but no such luck in 1918.
- Even in 2009, it took months to mass-produce vaccine.
- But suppose there had been a vaccine immediately. . .
- What proportion (p) of the population do we need to vaccinate to eradicate an infectious disease?

The SIR model: Effects of Control Measures

Suppose a proportion (p) of the population is vaccinated before an epidemic starts. Then:

- At the start of the epidemic, the proportion of the population that is susceptible is $S_0 = 1 - p$.
- \therefore Initially (at time $t = 0$) the rate of change of prevalence is

$$\begin{aligned}\left. \frac{dI}{dt} \right|_{t=0} &= \left((\mathcal{R}_0 S - 1) I \right) \Big|_{t=0} = (\mathcal{R}_0 S_0 - 1) I_0 \\ &= (\mathcal{R}_0(1 - p) - 1) I_0 < 0 \iff \mathcal{R}_0(1 - p) < 1\end{aligned}$$

- \therefore An epidemic will be prevented if

$$p > p_{\text{crit}} = 1 - \frac{1}{\mathcal{R}_0}$$

- \therefore Public Health Agency will ask you to estimate \mathcal{R}_0 .

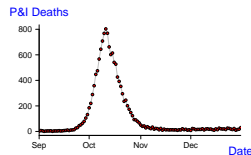
The SIR model: Results so far

Biological inferences:

- \mathcal{R}_0 is extremely important to estimate in practice!
- Epidemic occurs if and only if $\mathcal{R}_0 > 1$.
- Single epidemic, then disease disappears.
 - Proof?
Hint: Every non-equilibrium solution is a heteroclinic orbit.
- Can prevent epidemic by vaccinating (or otherwise removing) a proportion $1 - \frac{1}{\mathcal{R}_0}$ from the transmission process.

The SIR model: Does it explain our data?

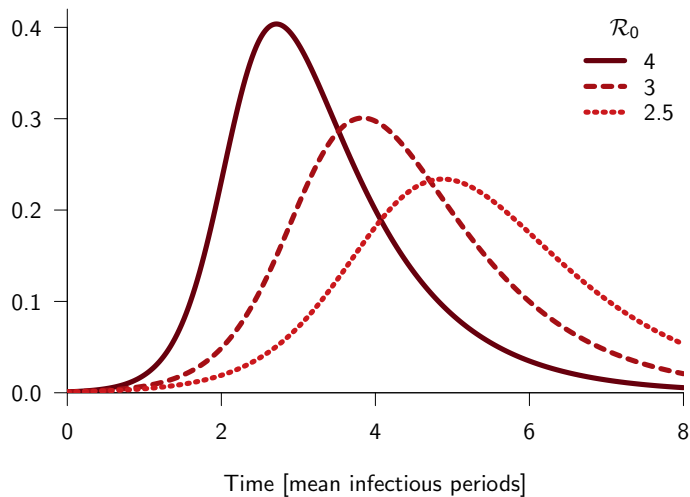
What about 1918 flu in Philadelphia?



- Does the SIR model explain these data?
- Can we fit the SIR model to the P&I time series?
- If so, are our estimated parameter values (for \mathcal{R}_0 and $1/\gamma$) biologically reasonable?
- Answers: **Assignment 2...**

The SIR model: How solutions depend on \mathcal{R}_0

Proportion infected $I(t)$





Mathematics
and Statistics

$$\int_M d\omega = \int_{\partial M} \omega$$

Mathematics 4MB3/6MB3 Mathematical Biology

Instructor: David Earn

Lecture 5

LaTeX Intro

Wednesday 17 January 2018



Announcements

- **Groups** are formed.
- **Assignment 1** is due when class starts on Monday 22 Jan 2018.

L^AT_EX



T_EX and L^AT_EX

- T_EX is a computer-based typesetting system designed and implemented by [Donald Knuth](#) in the 1970s.
- L^AT_EX is a particular T_EX format written by [Leslie Lamport](#). It has become the *de facto* standard for mathematical typesetting (e.g., books, journal articles, ...).
- T_EX has played an important role in the evolution of principles of software development.
 - [Literate programming](#)
 - [Reproducible research](#)
- Immediate goal: learn enough L^AT_EX to do Assignment 1.
- Goal for the term: become sufficiently competent with L^AT_EX and  so that the final project can be submitted as a fully reproducible document that “knits” L^AT_EX and  together.



Mathematics
and Statistics

$$\int_M d\omega = \int_{\partial M} \omega$$

Mathematics 4MB3/6MB3 Mathematical Biology

Instructor: David Earn

Lecture 6

R Intro

Friday 19 January 2018

Announcements

- [Assignment 1](#) is due when class starts on Monday 22 Jan 2018.



Getting started



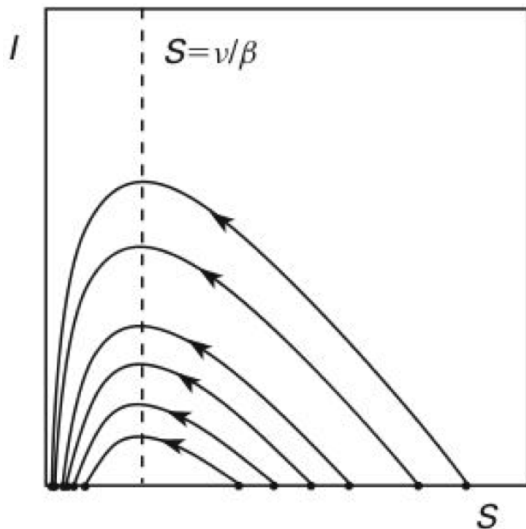
- Start RStudio
- Work by constructing an  script (see [Rexamples.R](#), accessible from [Lecture Schedule](#)).
- Try some arithmetic and basic plotting.
- Then try to make publication-quality graphs.
- Other resources:
 - [Jonathan Dushoff's !\[\]\(5d2b0686f24c91a69ec6f054f466d184_img.jpg\) intro](#)
 - [Ben Bolker's !\[\]\(ef97c4cf774c94401d40a852a635219b_img.jpg\) intro](#)
 - [R Project home page](#)
 - The official “Introduction to ” by Venables and Smith ([html](#), [pdf](#))

Figure 11.2 from HSD* (original from book)



*Hirsch, Smale and Devaney (2013), "Differential equations, dynamical systems, and an introduction to chaos".

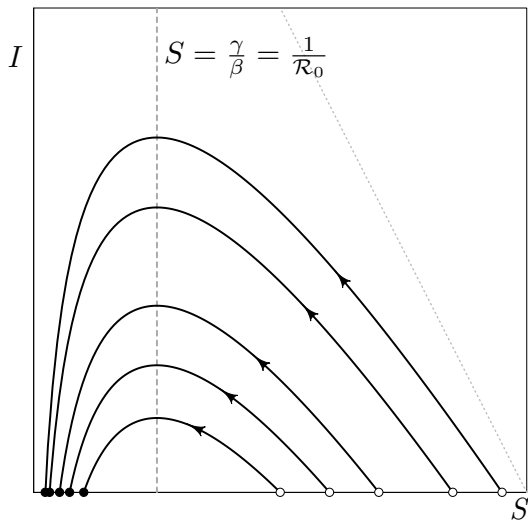
Figure 11.2 from HSD (made from scratch in )

Figure 11.1 from HSD (original from book)

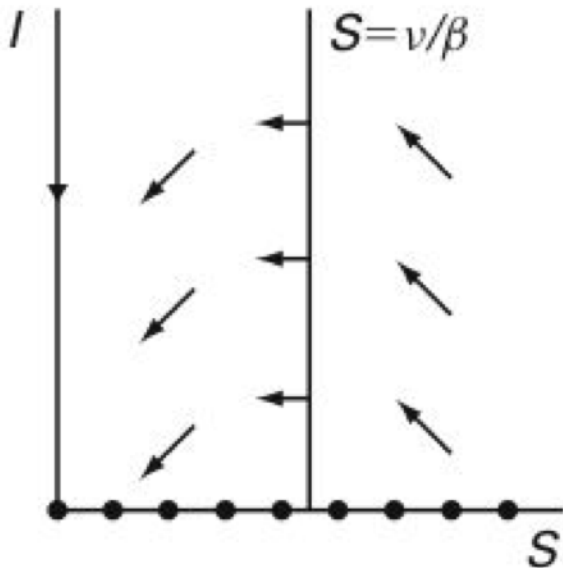
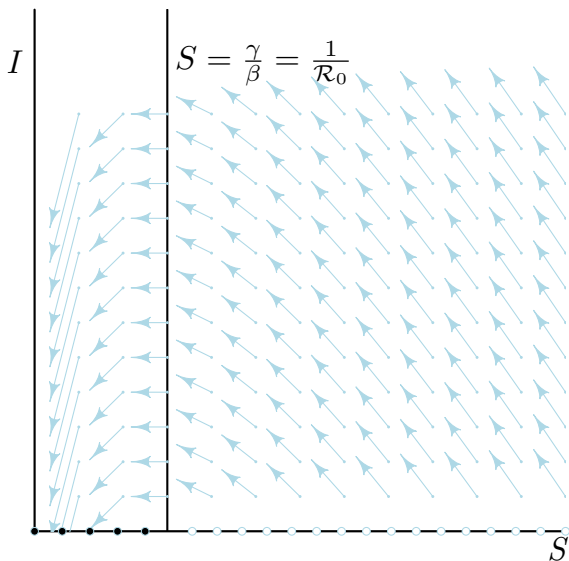


Figure 11.1 from HSD (made from scratch in )



Mathematics
and Statistics

$$\int_M d\omega = \int_{\partial M} \omega$$

Mathematics 4MB3/6MB3 Mathematical Biology


Instructor: David Earn

Lecture 7

R Intro II

Monday 22 January 2018

Announcements

- [Assignment 1](#) was due at the start of class today.
- Please complete the [Group Contribution Survey](#) TODAY.
- [Assignment 2](#) is due on Monday 5 Feb 2018 before class. It was posted over the weekend. It is designed to teach you the basics of solving ODEs and fitting them to data using . Make sure each group member really understands how to do this.
- Today: finish working through [Rexamples.R](#).