

Epidemic models 1

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motivation

- P & I data from Philadelphia 1918 flu:

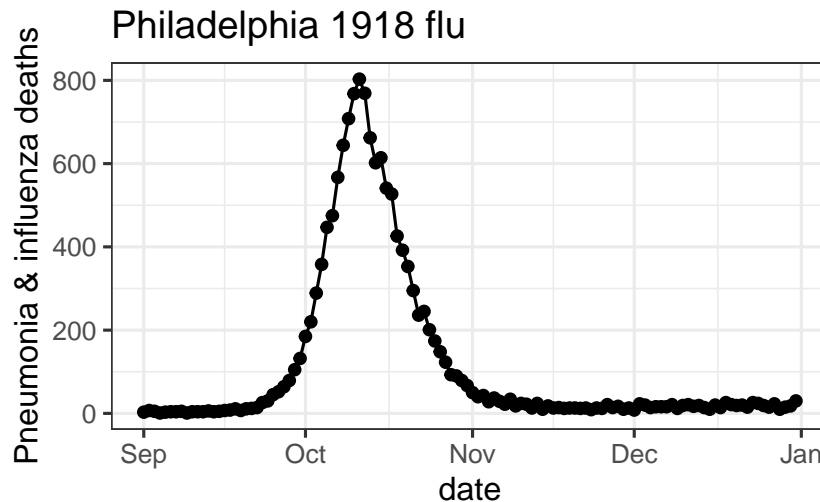


Figure 1: Phila. 1918 flu data

what do we want to figure out?

what shall we assume?

- classify individuals as S , I (**compartmental** model; **microparasite** or **intensity-independent**)
- disease is transmitted from S to I
- $S \rightarrow I$ instantaneously (zero latent period, no E)
- population is **homogeneous** (no heterogeneity in susceptibility, infectiousness, contact)
- fixed population size (birth = migration = 'natural' death = 0)
- transmission rate is time-invariant

-
- assumption 2 is OK (Pasteur, Koch's postulates ...)
 - all the rest are approximations

start simple!

- parsimony

- robustness?
- applicability/estimation?

Levins (1966) (also Orzack and Sober (1993), Levins (1993), Weisberg (2007))

exponential growth

- one variable (=1D model)
 - how does disease spread? → equation
-

what variables should we use?

- time (t)
- state variable: incidence, prevalence, death rate, death toll (= cumulative death?)
- deaths loosely connected to transmission

but deaths are observed!

when are deaths a good **proxy** for incidence?

- infection → death time is fixed
- homogeneity? (might not matters?)
- mortality curve is shifted epidemic

(COVID context ... we observe case reports, number of tests, hospitalizations, and deaths)

- **incidence**: number of infections per unit time (rate or flow)
- **prevalence**: number of currently infected people (quantity or stock)

prevalence is closer to the **mechanism**

model components:

- $I(t)$ (state variable: prevalence)
- $I(0)$ (initial conditions)
- β (parameter) = avg contacts **per susceptible per infective per unit time**

$$I(t + \Delta t) \approx I(t) + \beta I(t) \Delta t$$

Take $\lim \Delta t \rightarrow 0$ (and solve):

$$\frac{dI}{dt} = \beta I \rightarrow I(t) = I(0) \exp(\beta t)$$

model criticism

- Ignored discrete nature of individuals
- Ignored time-varying β (e.g. **diurnal** fluctuations)
- Ignored finite infectious periods (recovery/death)

Next: What if we make infectious periods finite? (i.e., including recovery (**clearance**) or death

$$dI/dt = \beta I - \gamma I$$

mean infectious period

$$I(t) = I(0) \exp(-\gamma t)$$

proportion uninfected = $\exp(-\gamma t)$

proportion infected = $1 - \exp(-\gamma t)$ (= CDF := $C(t)$)

$$\text{PDF} := C'(t) = \gamma \exp(-\gamma t)$$

$$\text{substitute } x = \gamma t \rightarrow dx = \gamma dt$$

$$\text{mean} = E[t] = \int t \exp(-\gamma t) dt = \int x \exp(-x) dx / \gamma = 1/\gamma$$

dimensional analysis

rates and characteristic times/scales

- is I a proportion or a density or a number ... ?
- what are the units of β, γ ?

nondimensionalization

- standardize any values that can be eliminated **without loss of (mathematical) generality**
- what can we do here?
- $\gamma = 1$
- I ? (depends on how we have defined it initially) $\rightarrow I/N$

compare with data???

Original scale:

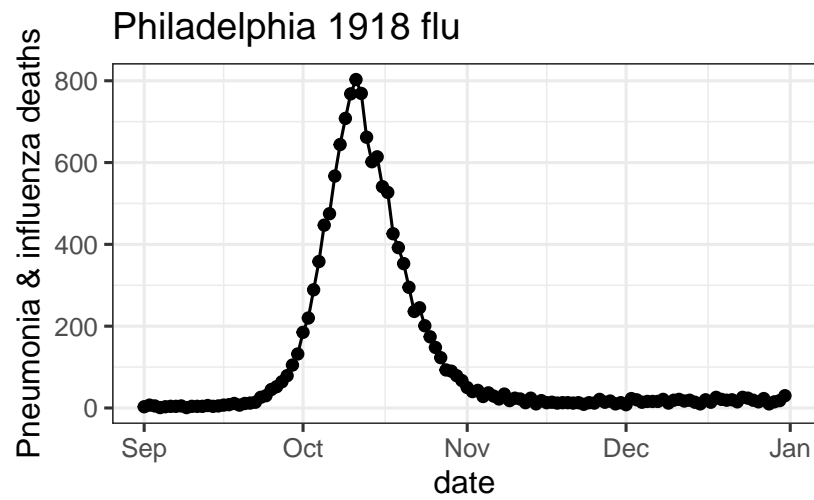


Figure 2: Philadelphia P&I

Log scale:

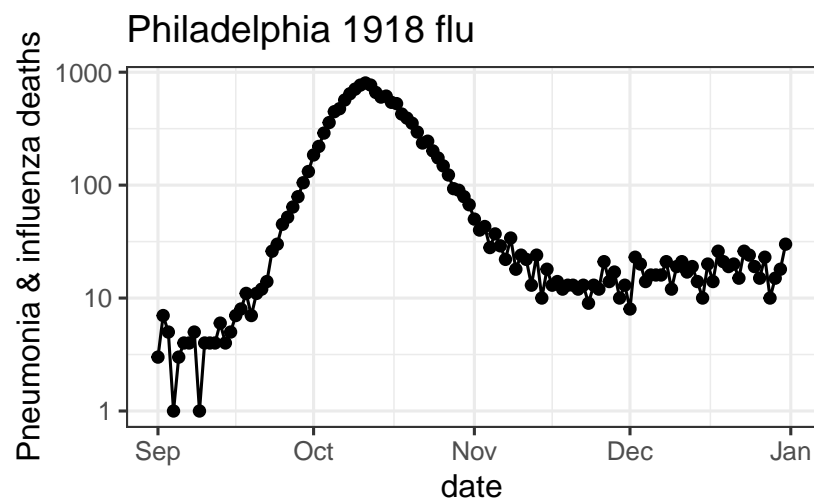


Figure 3: Philadelphia P&I, log scale

-
- Fit a straight line through the straight part of the curve
 - slope is βN
 - “intercept” is $\log(I(0))$ (zero is defined in a tricky way)

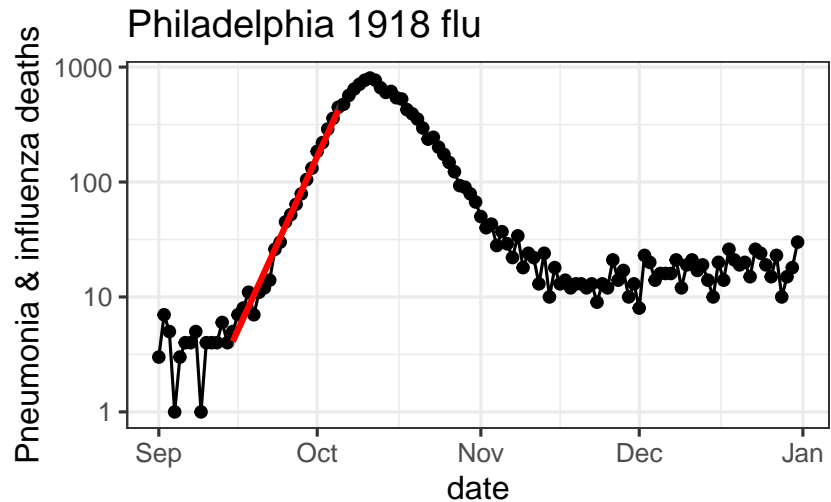
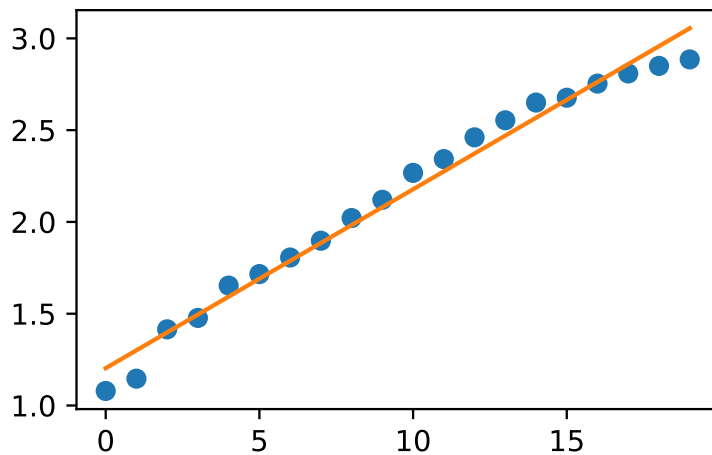


Figure 4: log-scale flu with regression

```
import pandas as pd
import numpy as np
import matplotlib.pyplot as plt
from sklearn.linear_model import LinearRegression
dd = pd.read_csv("data/pim_us_phila_city_1918_dy.csv")
## plt.plot(dd.pim)
## plt.plot(np.log10(dd.pim))
t = np.arange(20)
lw = np.log10(dd.pim)[20:40]
plt.plot(t, lw, 'o')
## https://docs.scipy.org/doc/scipy/reference/generated/scipy.linalg.lstsq.html
## https://scikit-learn.org/stable/modules/generated/sklearn.linear\_model.LinearRegression.html
ta = t.reshape(-1,1) ## make this into a column vector
reg = LinearRegression().fit(ta, lw)
plt.plot(t, reg.intercept_+reg.coef_[0]*t)
```



model assessment

- math is super-easy!
- clear, testable predictions
- parameter estimation is easy
- only consistent over a short time window
 - small t : arbitrarily close to zero
 - large t : ridiculous

Simple (SI) epidemic

- what are we missing?
- **depletion of susceptibles**
- let's take a step back and ignore death & recovery for now

$$dS/dt = -\beta SI$$

$$dI/dt = \beta SI$$

This looks 2D **but** what if we assume $S + I = N$ is constant? Then
 $S = N - I$

$$dI/dt = \beta(N - I)I$$

How do we solve this? **Partial fractions**

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

$$dI \left(\frac{A}{N-I} + \frac{B}{I} \right) = dI \cdot \frac{A + B(N-I)}{I(N-I)}$$

$$A = B; \quad B = 1/N$$

$$\frac{1}{\beta N} (-\log(N-I) + \log(I)) \Big|_{I(0)}^I = t - t_0$$

$$(-\log(N-I) + \log(I)) \Big|_{I(0)}^I = (\beta N)(t - t_0) \quad (\text{set } t_0 = 0)$$

$$\log \left(\frac{I}{N-I} \right) - \log \left(\frac{I(0)}{N-I(0)} \right) = \beta N t$$

$$\log \left(\frac{I}{N-I} \right) = \beta N t + -\log \left(\frac{I(0)}{N-I(0)} \right)$$

$$\frac{I}{N-I} = \exp(\beta N t) \frac{I(0)}{N-I(0)} \equiv Q$$

$$I = Q(N-I)$$

$$I(t)(1+Q) = QN$$

$$I(t) = \frac{QN}{1+Q} = \frac{N}{1+\frac{1}{Q}}$$

$$= \frac{N}{1 + \left(\frac{N-I(0)}{I(0)} \right) \exp(-\beta N t)}$$

$$?? \equiv I(0) \exp(\beta N t) / (1 + (I(0)/N)(\exp(\beta N t) - 1)) ??$$

Qualitative analysis

- $I \ll N$? exponential growth
- **per capita growth rate** $((dI/dt)/I = d(\log(I))/dt)$ decreases monotonically with increasing I
- asymptotic behaviour? equilibria? periodic orbits?
- periodic orbits impossible in 1D (uniqueness of flows)

equilibrium analysis

- $I = 0$, **disease free equilibrium** (DFE)
- $I = N$, **endemic equilibrium** (EE)

Stability? (Assume $\beta > 0$)

- **local asymptotic stability**
- **global asymptotic stability** (Lyapunov functions)

model criticism/conclusions

(Comparison to metapop, logistic growth model)

SIR model

Basic SIR model

- put the pieces together

$$\begin{aligned}\frac{dS}{dt} &= -\beta SI \\ \frac{dI}{dt} &= \beta SI - \gamma I \\ \frac{dR}{dt} &= \gamma I\end{aligned}$$

- really 2D (because $S + I + R = N$)
- rescale to $N = 1$ (S, I, R as proportions)

Numerical solution (R version):

```
## define gradient function
SIRgrad <- function(t, y, parms) {
  g <- with(as.list(c(y,parms)), {
    c(-beta*S*I, beta*S*I-gamma*I, gamma*I)
  })
  return(list(g))
}
library(deSolve)
## initial conditions and parameters
y0 <- c(S=0.99, I=0.01, R=0)
p0 <- c(beta=4, gamma=1)
tvec <- seq(0,8,length=101)
## solve (LSODA by default)
sir_R <- ode(y=y0, times=tvec, parms=p0, func=SIRgrad)

## plot
par(las=1,bty="l") ## cosmetic
matplot(tvec, sir_R[,-1],
        type="l", lwd=2, ## solid lines, thicker
        xlab="time", ylab="proportion")
legend("right", names(y0), col=1:3, lty=1:3, lwd=2)
```

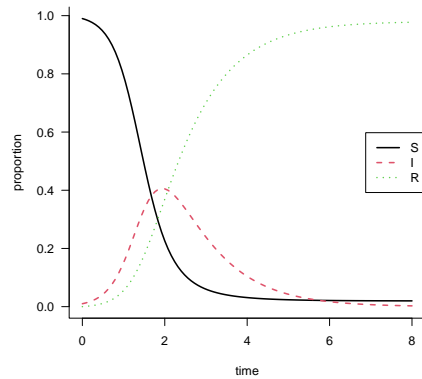



Figure 5: SIR model (R)

Phase plane plot

```
par(las=1,bty="l") ## cosmetic
plot(I~S,type="l",data=as.data.frame(sir_R))
with(as.data.frame(sir_R), points(S,I, cex=0.75,pch=16))
```

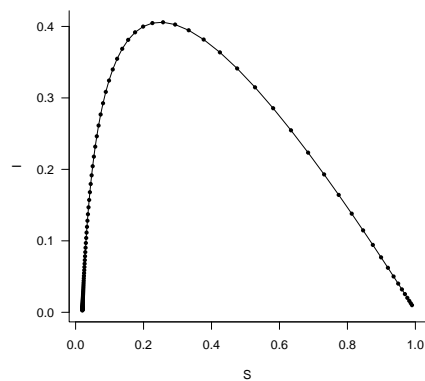


Figure 6: SIR phase plane (R)

Solve using Python

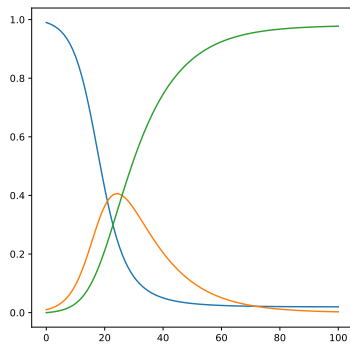
```
import numpy as np
import scipy.integrate
def SIR_grad(x,t,params):
    """basic gradient definitions for SIR model"""
    beta,gamma = params    ## unpack parameters
    S,I,R = x              ## unpack state variables
    return(np.array([-beta*S*I, beta*S*I-gamma*I, gamma*I]))

t_vec = np.linspace(0,8,101)
params = (4,1) ## extra parameters (beta, gamma)
y0 = (0.99, 0.01, 0)
SIR_sol1 = scipy.integrate.odeint(SIR_grad,
                                   y0=y0,
```

```
t=t_vec,
args=(params,))
```

<https://community.rstudio.com/t/how-to-display-the-plot-in-the-python-chunk/22039/3>

```
import matplotlib.pyplot as plt
fig, ax = plt.subplots()
ax.plot(SIR_sol1);
plt.show()
```



dimensional analysis

- initial growth rate (time⁻¹) $\beta - \gamma$
- mean infectious period $1/\gamma$ (time)
- basic reproduction number $\mathcal{R}_0 = \beta/\gamma$

initial growth rate

$$\begin{aligned}\frac{dI}{dt} &= \beta S - \gamma I \\ &= (\beta S - \gamma)I \\ &\approx (\beta - \gamma)I \quad \text{near DFE}\end{aligned}$$

or calculate **Jacobian** ($\partial X_i / \partial X_j$):

$$\begin{pmatrix} -\beta I & -\beta S & 0 \\ \beta I & \beta S - \gamma & 0 \\ 0 & \gamma & 0 \end{pmatrix}$$

Evaluate at DFE ($\{1, 0, 0\}$):

$$\begin{pmatrix} 0 & -\beta & 0 \\ 0 & \beta - \gamma & 0 \\ 0 & \gamma & 0 \end{pmatrix}$$

Eigenvalues of this are pretty boring! But useful approach.

Per capita rates

In general we can express *per capita* gradients in X as gradients of $\log(X)$:

$$\begin{aligned}\frac{dX}{dt} &= Xf(X, Y, Z, \dots) \\ \frac{\frac{dX}{dt}}{X} &= f(X, Y, Z, \dots) \\ \frac{d \log(X)}{dt} &= f(X, Y, Z, \dots)\end{aligned}$$

Another way to see that $\beta - \gamma$ is the slope on the log scale.

Stability of DFE

- $\beta > \gamma$ ($r > 0$)
- $\beta/\gamma > 1$ ($\mathcal{R}_0 > 1$)

Local asymptotic stability **or**

- $\frac{dI}{dt} = \beta SI - \gamma I$
- non-dimensionalize: $\gamma = 1, \beta = \mathcal{R}_0$
- $\frac{dI}{dt} = (\mathcal{R}_0 S - 1)I$
- $\frac{d \log I}{dt} = \mathcal{R}_0 S - 1$

Since $S \leq 1, \mathcal{R}_0 < 1 \rightarrow$ deriv of $\log I$ is always negative (don't really need the last step)

Automated analysis

library(phaseR)

```
## -----
## phaseR: Phase plane analysis of one- and two-dimensional autonomous ODE systems
## -----
##
## v.2.1: For an overview of the package's functionality enter: ?phaseR
##
## For news on the latest updates enter: news(package = "phaseR")

par(las=1,bty="l",xaxs="i",yaxs="i") ## cosmetic
SIRgrad_2d <- function(t, y, parms) {
  g <- with(as.list(c(y,parms)), {
    c(-beta*S*I, beta*S*I-gamma*I)
  })
  return(list(g))
}
```

```

}
## plot(0:1,0:1,type="n",xlab="S",ylab="I")
f1 <- flowField(SIRgrad_2d,
  xlim=c(0,1),
  ylim=c(0,1),
  parameters=p0,
  state.names=c("S","I"),
  add=FALSE)
n1 <- nullclines(SIRgrad,
  xlim=c(0,1),
  ylim=c(0,1),
  parameters=p0,
  state.names=c("S","I"))
t1 <- trajectory(SIRgrad_2d,parameters=p0,
  state.names=c("S","I"),
  ## n=10,
  y0=y0[1:2],
  tlim=c(0,5))

```

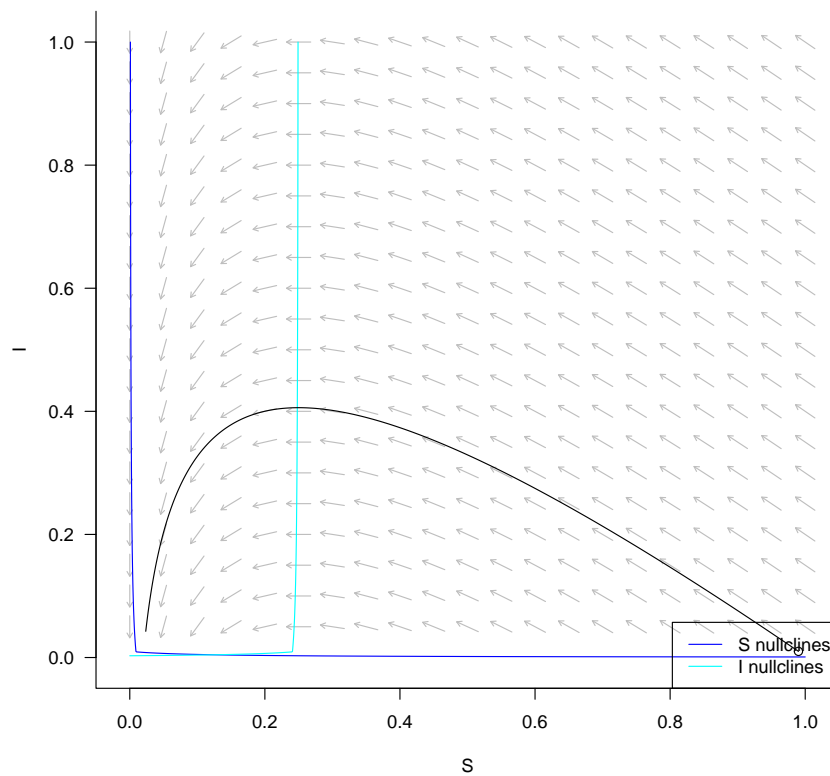


Figure 7: phase plane analysis in R

```

phasePlaneAnalysis(SIRgrad_2d,xlim=c(0,1),
  parameters=p0,

```

```
state.names=c("S", "I"),
ylim=c(0,1))
```

Solution

- can't get analytical solution for $S(t)$, $I(t)$
- **but:** we can solve for $I(S)$:

$$\begin{aligned}\frac{dI}{dS} &= \frac{dI/dt}{dS/dt} = -1 + \frac{1}{\mathcal{R}_0 S} \\ \int_{I(0)}^I (t) dI &= \int_{S(0)}^{S(t)} \left(-1 + \frac{1}{\mathcal{R}_0 S} \right) dS \\ I - I(0) &= -(S - S(0)) + \frac{1}{\mathcal{R}_0} \log(S/S(0)) \\ I + S - (I(0) + S(0)) &= \frac{1}{\mathcal{R}_0} \log(S/S(0))\end{aligned}$$

Final size calculations

- $t \rightarrow \infty$:

$$(I_\infty + S_\infty) - (I(0) + S(0)) = \frac{1}{\mathcal{R}_0} \log S_\infty/S(0)$$

- newly invading pathogen: $S \approx 1$, $I(0) \ll 1$ (≈ 0), $I_\infty \rightarrow 0$
- in the limit $I(0) \rightarrow 0$:

$$S_\infty - 1 = \frac{1}{\mathcal{R}_0} \log S_\infty$$

- “final size” $Z = 1 - S_\infty$
- $-Z = \frac{1}{\mathcal{R}_0} \log(1 - Z)$

Lambert W functions

- How do we solve this?
- Newton's method (or whatever)
- *Lambert W* (Corless et al. 1996): solves $W \exp(W) = Z$

```
import sympy as sym
z, R = sym.symbols('z R')
sym.solve(sym.Eq(z, -1/R*sym.log(1-z)), z)

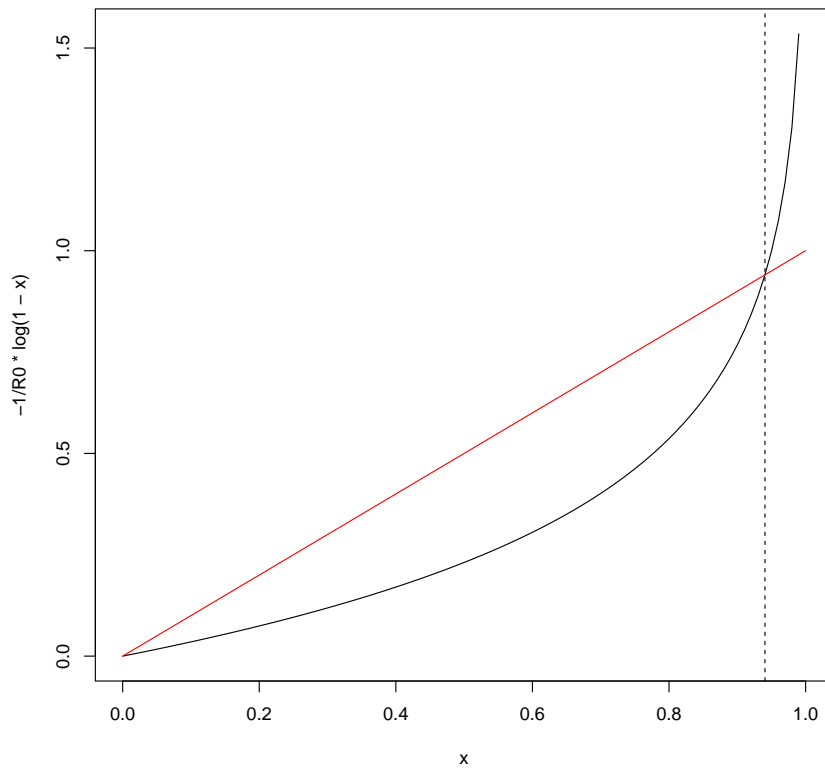
## [(R + LambertW(-R*exp(-R)))/R]

finalsize <- function(R0) {
  1+1/R0*LambertW(-R0*exp(-R0))
}
```

```

R0 <- 3
curve(-1/R0*log(1-x), from=0,to=1)
curve(1*x, add=TRUE,col="red")
library(emdbook)
abline(v=finalsize(R0),lty=2)

```



Epidemic threshold

Assuming vaccination (or other perfect *prophylaxis* [protection]) at rate p

$$R_0 = 1 - 1/p$$

speed-based intervention:

$$\beta SI - (\gamma + \phi)I < 0$$

$$I(\beta - \gamma - \phi) < 0$$

$$\phi > (\beta - \gamma) = r$$

Comparing Epidemic threshold vs. final size

```

library(emdbook)
finalsize <- function(R0) {

```

```

1+1/R0*lambertW(-R0*exp(-R0))
}
par(las=1,bty="l")
curve(finalsize(x), from=1, to=10, xlab=expression(R[0]),
      ylab="proportion")
curve(1-1/x, add=TRUE, col=2)
legend("bottomright",
      c("final size", "herd immunity threshold"),
      col=1:2, lty=1)

```

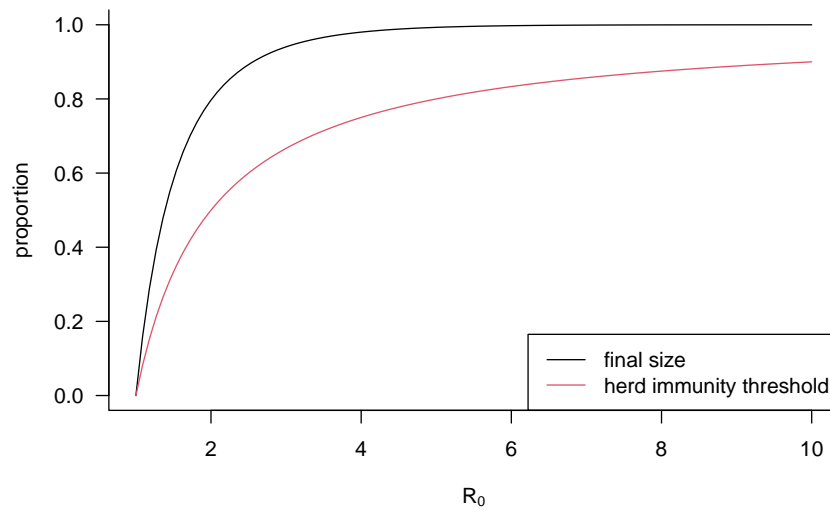


Figure 8: final size vs herd immunity

Estimating R from data

- Euler-Lotka equation

$$\begin{aligned}
 I(t) &= \int_0^t I(t-\tau)K(\tau) d\tau \\
 I(0)\exp(rt) &= \int_0^t I(0)\exp(r(t-\tau))K(\tau) d\tau \\
 1 &= \int_0^t \exp(-r\tau)K(\tau) d\tau \\
 1 &= \int_0^t \exp(-r\tau)\mathcal{R}_0 g(\tau) d\tau \\
 \frac{1}{\mathcal{R}_0} &= \int_0^t \exp(-r\tau)g(\tau) d\tau
 \end{aligned}$$

SIRS/SIR with vital dynamics

- models of **endemic** disease

- e.g. “childhood diseases” (measles, mumps, rubella, pertussis, polio, chickenpox, ...)
 - directly transmitted, acute, immunizing
- SIRS model
- SIR model *with vital dynamics*

$$\begin{aligned}\frac{dS}{dt} &= \mu N - \beta/NSI - \mu S \\ \frac{dI}{dt} &= \beta/NSI - \gamma I - \mu I \\ \frac{dR}{dt} &= \gamma I - \mu R\end{aligned}$$

- Balanced population (birth rate = μN). Can consider more complex demography but often don’t need to
 - disease-induced death rates low relative to natural mortality
 - demographic time scales much longer than epidemic time scales
- Scaling β/N is much easier for dealing with applications/real data, scaling $N = 1$ is easier for doing math
- \mathcal{R}_0 is $\beta/(\mu + \gamma)$ ($\approx \beta/\gamma$ for most human diseases)

Most of the following is taken from Brauer, Castillo-Chavez, and Feng (2019)

$$\begin{aligned}S^* &= \frac{\mu + \gamma}{\beta} = 1/\mathcal{R}_0 \quad (\text{this is **very general**}) \\ I^* &= \frac{\mu}{\mu + \gamma} - \frac{\mu}{\beta} = \frac{\mu}{\beta}(\mathcal{R}_0 - 1)\end{aligned}$$

- at equilibrium the **force of infection** is βI^* , so the **average age at infection** is $A = 1/(\beta I^*)$
- average lifespan is $L = 1/\mu$
- $L/A = \beta I^*/\mu = \mathcal{R}_0 - 1$
 - another way to estimate \mathcal{R}_0 ! (also, $S^* = 1/\mathcal{R}_0$)
 - tells us something about risk by age, effects of vaccination

Jacobian at EE:

$$\begin{pmatrix} -\mu\mathcal{R}_0 & -(\mu + \gamma) \\ \mu(\mathcal{R}_0 - 1) & 0 \end{pmatrix}$$

$$\text{Trace} = -\mu\mathcal{R}_0, \text{Det} = \mu(\mu + \gamma)(\mathcal{R}_0 - 1)$$

$$\begin{aligned}
\lambda &= (1/2) \left(-\mu\mathcal{R}_0 \pm \sqrt{\mu^2\mathcal{R}_0^2 - 4\mu(\mathcal{R}_0 - 1)(\mu + \gamma)} \right) \\
&\approx (1/2) \left(-\mu\mathcal{R}_0 \pm \sqrt{-4\mu(\mathcal{R}_0 - 1)\gamma} \right) \\
&= (1/2) - \mu\mathcal{R}_0 \pm i\sqrt{(1/L)(L/A)(1\gamma)}
\end{aligned}$$

- So the imaginary part is $\sqrt{A\tau}$ where τ is the length of the infective period.
- e.g. for measles $A \approx 70\text{yr}$, $\tau \approx 1/26$, epidemic interval is about 2.76 years.

`2*pi*sqrt(5/26)`

`## [1] 2.755359`

- **Damping factor:** amplitude decreases by a factor $\exp(-\mu\mathcal{R}_0T/2)$ per cycle

Stochasticity

- Reed-Frost model
 - household infection model: fixed (small) population, discrete infection generations
 - start with **index cases**
 - then ...
- Gillespie algorithm
- stochastic ODEs

References

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