Epidemic models 1

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motivation

- P & I data from Philadelphia 1918 flu:

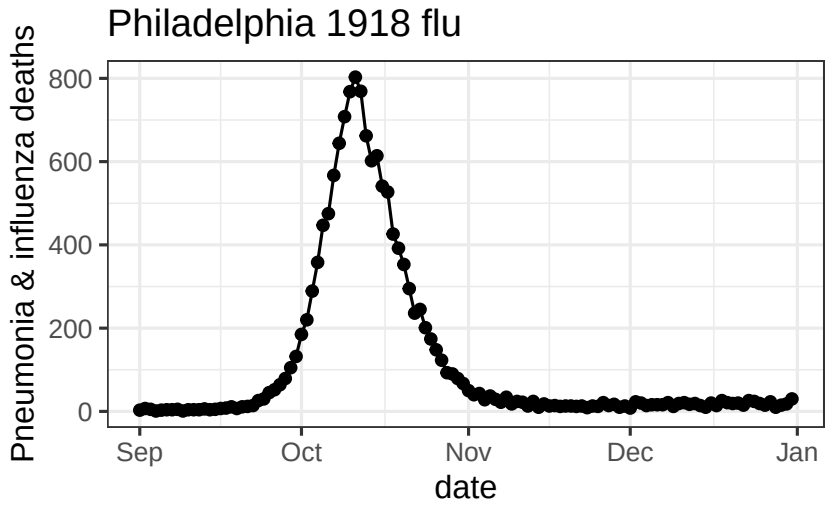

Figure 1: Phila. 1918 flu data

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
- $S \to I$ 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? $\rightarrow$ equation

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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!

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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**

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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 $\lim \Delta t \to 0$ (and solve):

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

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

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

$$\text{proportion uninfected} = \exp(-\gamma t)$$

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

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

$$\text{substitute } x = \gamma t \quad \to \quad dx = \gamma \, dt$$

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

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) $\to I/N$

compare with data???

Original scale:

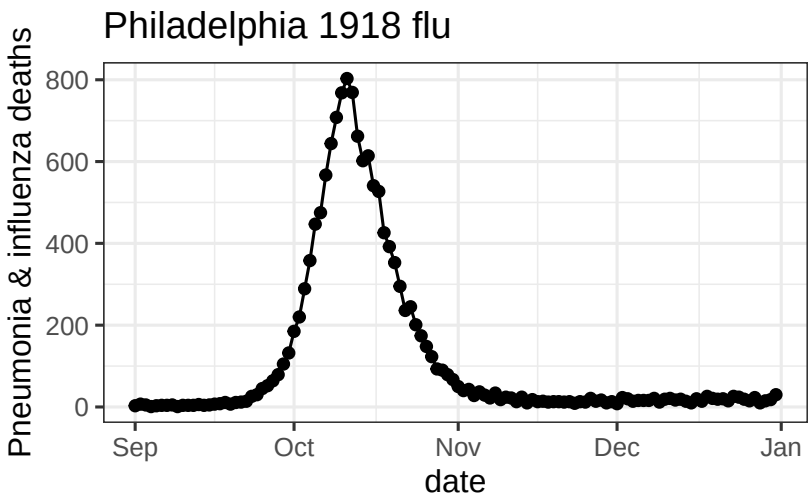


Figure 2: Philadelphia P&I

Log scale:

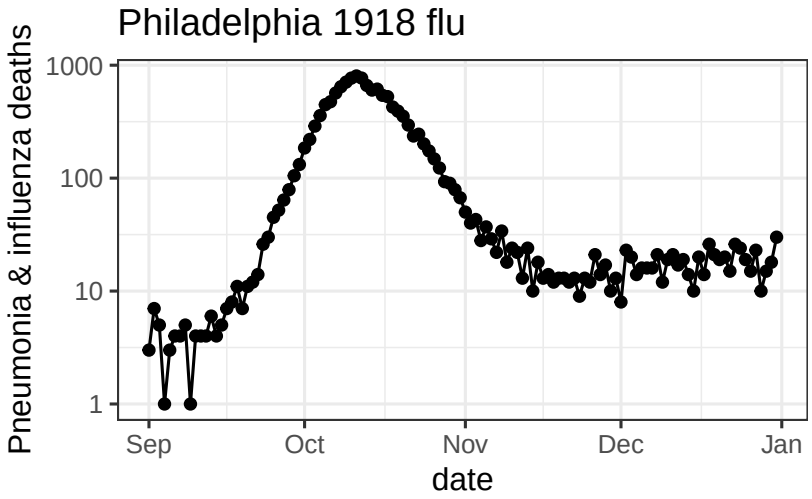


Figure 3: Philadelphia P&I, log scale

- 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)

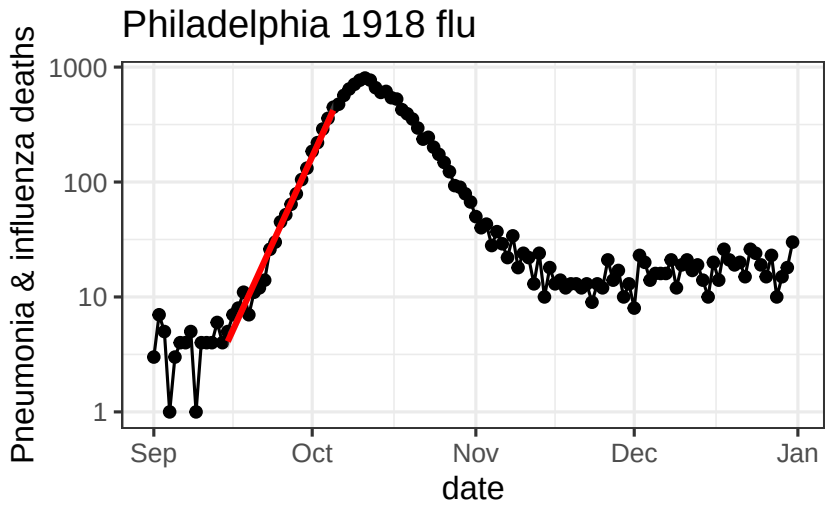


Figure 4: log-scale flu with regression

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**

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

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

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

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

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

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

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

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

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

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

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

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

?? $\equiv I(0)\exp(\beta N t)/(1 + (I0/N)(\exp(\beta N t) - 1))$??

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)
```

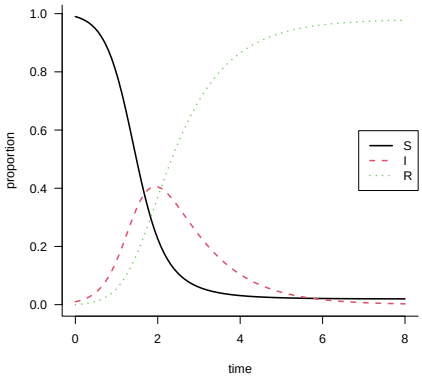


Figure 5: SIR model (R)

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))
```

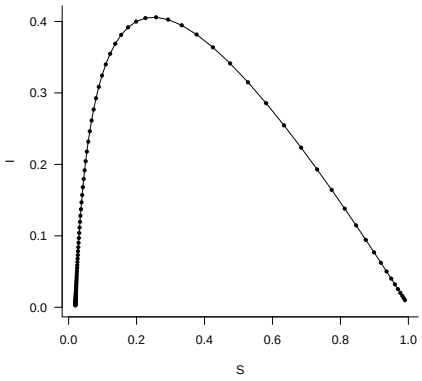


Figure 6: SIR phase plane (R)

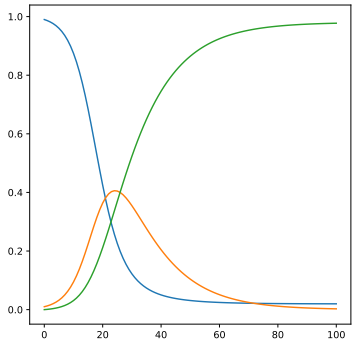
Solve using Python

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

Biological well-posedness

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

- $t \to \infty$:

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

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

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

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

Epidemic threshold

Comparing Epidemic threshold vs. final size

references

Levins, R. 1966. "The Strategy of Model Building in Population Biology." *American Scientist* 54: 421–31. https://www.jstor.org/stable/27836590.

Levins, Richard. 1993. "A Response to Orzack and Sober: Formal Analysis and the Fluidity of Science." *Quarterly Review of Biology* 68 (4): 547–55.

Orzack, Steven Hecht, and Elliott Sober. 1993. "A Critical Assessment of Levins's the Strategy of Model Building in Population Biology (1966)." *Quarterly Review of Biology* 68 (4): 533–46.

Weisberg, Michael. 2007. "Forty Years of 'the Strategy': Levins on Model Building and Idealization." *Biology & Philosophy* 21 (5): 623–45. https://doi.org/10.1007/s10539-006-9051-9.