Epidemic models 1

Ben Bolker

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motivation

• P & I data from Philadelphia 1918 flu:

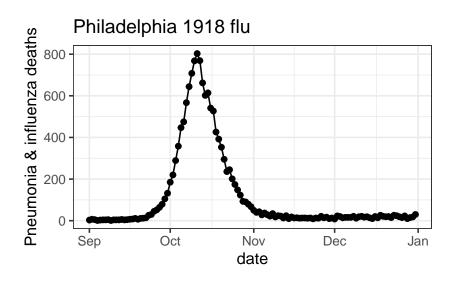


Figure 1: Phila. 1918 flu data

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 = o)
- 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 $\lim \Delta t \to 0$ (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

$$I(t) = I(0) \exp(-\gamma t)$$
 proportion uninfected = $\exp(-\gamma t)$ proportion infected = $1 - \exp(-\gamma t) (= \text{CDF} := C(t))$
$$\text{PDF} := C'(t) = \gamma \exp(-\gamma t)$$
 substitute $x = \gamma t \quad \rightarrow \quad dx = \gamma \, dt$
$$\text{mean} = E[t] = \int t \exp(-\gamma t) \, dt = \int x \exp(-x) \, dx/\gamma = 1/\gamma$$

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) $\rightarrow I/N$

compare with data???

Original scale:

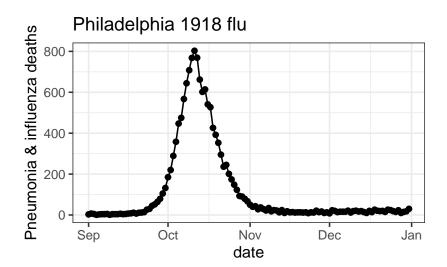


Figure 2: Philadelphia P&I

Log scale:

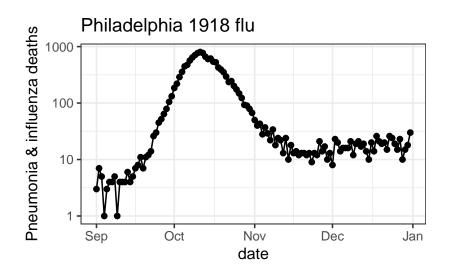


Figure 3: Philadelphia P&I, log scale

- 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)

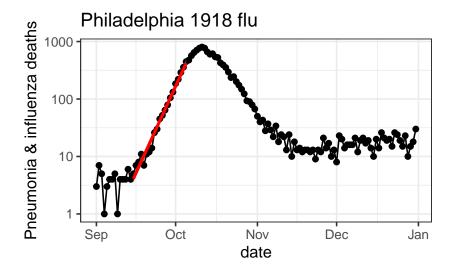


Figure 4: log-scale flu with regression

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

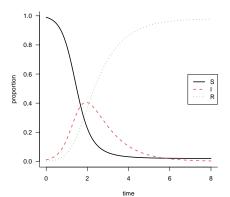


Figure 5: SIR model (R)

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))
```

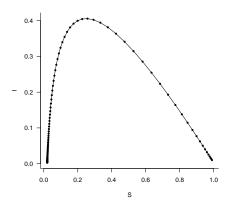
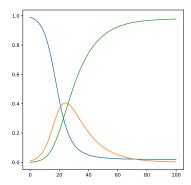


Figure 6: SIR phase plane (R)

Solve using Python

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

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

$$= (\beta S - \gamma)I$$

$$\approx (\beta - \gamma)I \quad \text{near } DFE$$

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

$$\left(\begin{array}{ccc}
-\beta I & -\beta S & 0 \\
\beta I & \beta S - \gamma & 0 \\
0 & \gamma & 0
\end{array}\right)$$

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

$$\left(\begin{array}{ccc}
0 & -\beta & 0 \\
0 & \beta - \gamma & 0 \\
0 & \gamma & 0
\end{array}\right)$$

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):

$$\frac{dX}{dt} = Xf(X, Y, Z, \dots)$$

$$\frac{\frac{dX}{dt}}{X} = f(X, Y, Z, \dots)$$

$$\frac{d\log(X)}{dt} = f(X, Y, Z, \dots)$$

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 $S \leq 1$, $\mathcal{R}_0 < 1 \rightarrow \text{deriv of log } I$ 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) {</pre>
   g <- with(as.list(c(y,parms)), {</pre>
       c(-beta*S*I, beta*S*I-gamma*I)
   })
   return(list(q))
```

```
}
## plot(0:1,0:1,type="n",xlab="S",ylab="I")
f1 <- flowField(SIRgrad_2d,</pre>
          xlim=c(0,1),
          ylim=c(0,1),
          parameters=p0,
          state.names=c("S","I"),
          add=FALSE)
n1 <- nullclines(SIRgrad,</pre>
                 xlim=c(0,1),
                 ylim=c(0,1),
                 parameters=p0,
                  state.names=c("S","I"))
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
                                               S nullclines
      0.4
                                                Lnullclines
                       0.2
                                0.4
              0.0
                                         0.6
                                                  8.0
                                                            1.0
```

S

```
## $add
## [1] TRUE
##
## $col
## [1] "black"
##
## $deriv
   function(t, y, parms) {
       g <- with(as.list(c(y,parms)), {</pre>
##
##
            c(-beta*S*I, beta*S*I-gamma*I)
##
       })
##
       return(list(g))
## }
```

```
## <bytecode: 0x560fda701fb0>
##
## $n
## NULL
##
## $parameters
    beta gamma
##
             1
##
## $system
## [1] "two.dim"
##
## $t
     [1] 0.00 0.01 0.02 0.03 0.04 0.05 0.06 0.07 0.08 0.09 0.10 0.11 0.12 0.13 0.14
##
   [16] 0.15 0.16 0.17 0.18 0.19 0.20 0.21 0.22 0.23 0.24 0.25 0.26 0.27 0.28 0.29
  [31] 0.30 0.31 0.32 0.33 0.34 0.35 0.36 0.37 0.38 0.39 0.40 0.41 0.42 0.43 0.44
## [46] 0.45 0.46 0.47 0.48 0.49 0.50 0.51 0.52 0.53 0.54 0.55 0.56 0.57 0.58 0.59
  [61] 0.60 0.61 0.62 0.63 0.64 0.65 0.66 0.67 0.68 0.69 0.70 0.71 0.72 0.73 0.74
## [76] 0.75 0.76 0.77 0.78 0.79 0.80 0.81 0.82 0.83 0.84 0.85 0.86 0.87 0.88 0.89
## [91] 0.90 0.91 0.92 0.93 0.94 0.95 0.96 0.97 0.98 0.99 1.00 1.01 1.02 1.03 1.04
## [106] 1.05 1.06 1.07 1.08 1.09 1.10 1.11 1.12 1.13 1.14 1.15 1.16 1.17 1.18 1.19
## [121] 1.20 1.21 1.22 1.23 1.24 1.25 1.26 1.27 1.28 1.29 1.30 1.31 1.32 1.33 1.34
## [136] 1.35 1.36 1.37 1.38 1.39 1.40 1.41 1.42 1.43 1.44 1.45 1.46 1.47 1.48 1.49
## [151] 1.50 1.51 1.52 1.53 1.54 1.55 1.56 1.57 1.58 1.59 1.60 1.61 1.62 1.63 1.64
## [166] 1.65 1.66 1.67 1.68 1.69 1.70 1.71 1.72 1.73 1.74 1.75 1.76 1.77 1.78 1.79
## [181] 1.80 1.81 1.82 1.83 1.84 1.85 1.86 1.87 1.88 1.89 1.90 1.91 1.92 1.93 1.94
## [196] 1.95 1.96 1.97 1.98 1.99 2.00 2.01 2.02 2.03 2.04 2.05 2.06 2.07 2.08 2.09
## [211] 2.10 2.11 2.12 2.13 2.14 2.15 2.16 2.17 2.18 2.19 2.20 2.21 2.22 2.23 2.24
## [226] 2.25 2.26 2.27 2.28 2.29 2.30 2.31 2.32 2.33 2.34 2.35 2.36 2.37 2.38 2.39
## [241] 2.40 2.41 2.42 2.43 2.44 2.45 2.46 2.47 2.48 2.49 2.50 2.51 2.52 2.53 2.54
## [256] 2.55 2.56 2.57 2.58 2.59 2.60 2.61 2.62 2.63 2.64 2.65 2.66 2.67 2.68 2.69
## [271] 2.70 2.71 2.72 2.73 2.74 2.75 2.76 2.77 2.78 2.79 2.80 2.81 2.82 2.83 2.84
## [286] 2.85 2.86 2.87 2.88 2.89 2.90 2.91 2.92 2.93 2.94 2.95 2.96 2.97 2.98 2.99
## [301] 3.00 3.01 3.02 3.03 3.04 3.05 3.06 3.07 3.08 3.09 3.10 3.11 3.12 3.13 3.14
## [316] 3.15 3.16 3.17 3.18 3.19 3.20 3.21 3.22 3.23 3.24 3.25 3.26 3.27 3.28 3.29
## [331] 3.30 3.31 3.32 3.33 3.34 3.35 3.36 3.37 3.38 3.39 3.40 3.41 3.42 3.43 3.44
## [346] 3.45 3.46 3.47 3.48 3.49 3.50 3.51 3.52 3.53 3.54 3.55 3.56 3.57 3.58 3.59
## [361] 3.60 3.61 3.62 3.63 3.64 3.65 3.66 3.67 3.68 3.69 3.70 3.71 3.72 3.73 3.74
## [376] 3.75 3.76 3.77 3.78 3.79 3.80 3.81 3.82 3.83 3.84 3.85 3.86 3.87 3.88 3.89
## [391] 3.90 3.91 3.92 3.93 3.94 3.95 3.96 3.97 3.98 3.99 4.00 4.01 4.02 4.03 4.04
## [406] 4.05 4.06 4.07 4.08 4.09 4.10 4.11 4.12 4.13 4.14 4.15 4.16 4.17 4.18 4.19
## [421] 4.20 4.21 4.22 4.23 4.24 4.25 4.26 4.27 4.28 4.29 4.30 4.31 4.32 4.33 4.34
## [436] 4.35 4.36 4.37 4.38 4.39 4.40 4.41 4.42 4.43 4.44 4.45 4.46 4.47 4.48 4.49
## [451] 4.50 4.51 4.52 4.53 4.54 4.55 4.56 4.57 4.58 4.59 4.60 4.61 4.62 4.63 4.64
```

```
## [466] 4.65 4.66 4.67 4.68 4.69 4.70 4.71 4.72 4.73 4.74 4.75 4.76 4.77 4.78 4.79
## [481] 4.80 4.81 4.82 4.83 4.84 4.85 4.86 4.87 4.88 4.89 4.90 4.91 4.92 4.93 4.94
## [496] 4.95 4.96 4.97 4.98 4.99 5.00
## $tlim
## [1] 0 5
## $tstep
## [1] 0.01
##
## $x
##
                [,1]
##
     [1,] 0.99000000
     [2,] 0.98959816
##
     [3,] 0.98918443
##
##
     [4,] 0.98875847
     [5,] 0.98831992
##
     [6,] 0.98786843
##
##
     [7,] 0.98740363
##
     [8,] 0.98692514
     [9,] 0.98643258
##
   [10,] 0.98592556
##
   [11,] 0.98540366
   [12,] 0.98486647
##
   [13,] 0.98431356
## [14,] 0.98374449
##
   [15,] 0.98315882
   [16,] 0.98255608
## [17,] 0.98193581
## [18,] 0.98129752
## [19,] 0.98064071
## [20,] 0.97996488
  [21,] 0.97926952
## [22,] 0.97855409
## [23,] 0.97781805
  [24,] 0.97706084
## [25,] 0.97628190
## [26,] 0.97548065
## [27,] 0.97465650
## [28,] 0.97380883
## [29,] 0.97293704
## [30,] 0.97204048
## [31,] 0.97111851
## [32,] 0.97017047
```

- ## [33,] 0.96919570
- ## [34,] 0.96819349
- ## [35,] 0.96716316
- ## [36,] 0.96610399
- ## [37,] 0.96501526
- ## [38,] 0.96389622
- ## [39,] 0.96274611
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- ## [44,] 0.95650235
- ## [45,] 0.95514930
- ## [46,] 0.95375954
- ## [47,] 0.95233221
- "" [17] 013323322
- ## [48,] 0.95086644
- ## [49,] 0.94936135
- ## [50,] 0.94781604
- ## [51,] 0.94622962
- ## [52,] 0.94460117
- ## [53,] 0.94292976
- ## [54,] 0.94121446
- ## [55,] 0.93945433
- ## [56,] 0.93764841
- ## [57,] 0.93579575
- ## [58,] 0.93389537
- ## [59,] 0.93194631
- ## [60,] 0.92994760
- ## [61,] 0.92789824
- ## [62,] 0.92579726
- ## [63,] 0.92364367
- ## [64,] 0.92143647
- **##** [65,] 0.91917468
- ## [66,] 0.91685732
- ## [67,] 0.91448339
- ## [68,] 0.91205192
- ## [69,] 0.90956192
- ## [70,] 0.90701243
- ## [71,] 0.90440249
- ## [72,] 0.90173113
- ## [73,] 0.89899743
- ## [74,] 0.89620046
- ## [75,] 0.89333929
- ## [76,] 0.89041303

- ## [77,] 0.88742081
- ## [78,] 0.88436176
- ## [79,] 0.88123505
- ## [80,] 0.87803988
- ## [81,] 0.87477545
- ## [82,] 0.87144102
- ## [83,] 0.86803586
- ## [84,] 0.86455927
- ## [85,] 0.86101062
- ## [86,] 0.85738928
- ## [87,] 0.85369468
- ## [88,] 0.84992628
- ## [89,] 0.84608361
- ## [90,] 0.84216622
- ## [91,] 0.83817374
- "" [31)] 0.0301/3/
- ## [92,] 0.83410581
- ## [93,] 0.82996218
- ## [94,] 0.82574261
- ## [95,] 0.82144695
- ## [96,] 0.81707510
- ## [97,] 0.81262702
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- ## [99,] 0.80350241
- ## [100,] 0.79882614
- ## [101,] 0.79407421
- ## [102,] 0.78924695
- ## [103,] 0.78434474
- ## [104,] 0.77936807
- ## [105,] 0.77431749
- ## [106,] 0.76919365
- ## [107,] 0.76399727
- ## [108,] 0.75872915
- ## [109,] 0.75339019
- ## [110,] 0.74798137
- ## [111,] 0.74250373
- ## [112,] 0.73695843
- ## [113,] 0.73134671
- ## [114,] 0.72566988
- ## [115,] 0.71992935
- ## [116,] 0.71412660
- ## [117,] 0.70826321
- ## [118,] 0.70234084
- ## [119,] 0.69636123
- ## [120,] 0.69032619

- ## [121,] 0.68423761
- ## [122,] 0.67809748
- ## [123,] 0.67190783
- ## [124,] 0.66567079
- ## [125,] 0.65938854
- ## [126,] 0.65306333
- ## [127,] 0.64669748
- ## [128,] 0.64029336
- ## [129,] 0.63385340
- ## [130,] 0.62738008
- ## [131,] 0.62087593
- ## [132,] 0.61434351
- ## [133,] 0.60778545
- ## [134,] 0.60120438
- ## [135,] 0.59460298
- ## [136,] 0.58798396
- ## [137,] 0.58135004
- ## [138,] 0.57470396
- /-
- ## [139,] 0.56804847
- ## [140,] 0.56138633
- ## [141,] 0.55472029
- ## [142,] 0.54805312
- ## [143,] 0.54138757
- ## [144,] 0.53472637
- ## [145,] 0.52807224
- ## [146,] 0.52142788
- ## [147,] 0.51479596
- ## [148,] 0.50817912
- ## [149,] 0.50157997
- ## [150,] 0.49500108
- ## [151,] 0.48844496
- ## [152,] 0.48191409
- ## [153,] 0.47541090
- ## [154,] 0.46893776
- ## [155,] 0.46249698
- ## [156,] 0.45609082
- ## [157,] 0.44972147
- ## [158,] 0.44339105
- ## [159,] 0.43710161
- ## [160,] 0.43085515
- ## [161,] 0.42465357
- ## [162,] 0.41849872
- ## [163,] 0.41239235
- ## [164,] 0.40633616

- ## [165,] 0.40033175
- ## [166,] 0.39438065
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## [497,] 0.04414504
## [498,] 0.04374737
## [499,] 0.04335321
## [500,] 0.04296253
## [501,] 0.04257531
##
## $y0
##
                Ι
## [1,] 0.99 0.01
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):

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

$$\int_{I(0)}^{I} (t) dI = \int_{S(0)}^{S(t)} \left(-1 + \frac{1}{\mathcal{R}_0 S} \right) dS$$

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

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

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 $I(0) \rightarrow 0$:

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

- "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 $W \exp(W) = Z$

$$Z = 1 + \frac{1}{\mathcal{R}_0} W(-\mathcal{R}_0 \exp(-\mathcal{R}_0))$$

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) {</pre>
    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)
```

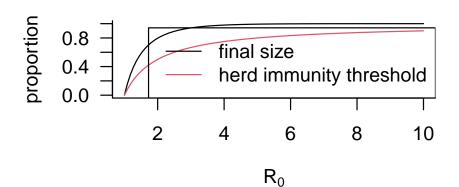


Figure 8: final size vs herd immunity

SIR with vital dynamics

references

- Corless, Robert M., G. H. Gonnet, D. E. G. Hare, D. J. Jeffrey, and D. E. Knuth. 1996. "On the Lambert \$W\$ Function." Advances in Computational Mathematics 5 (4): 329-59.
- 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.