Epidemic models 1

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motivation

- P & I data from Philadelphia 1918 flu:

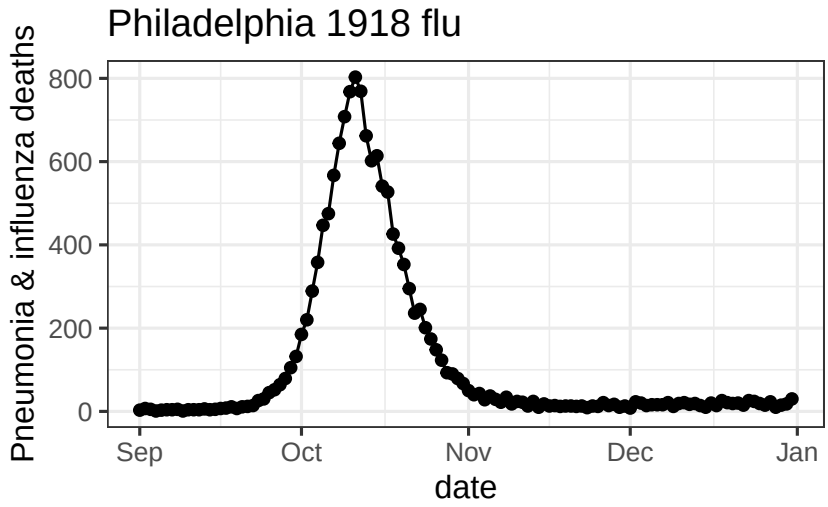

Figure 1: Phila. 1918 flu data

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:

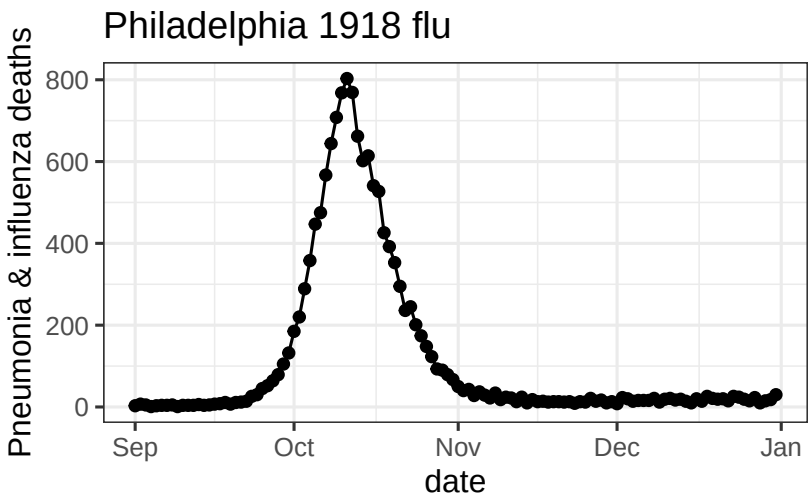


Figure 2: Philadelphia P&I

Log scale:

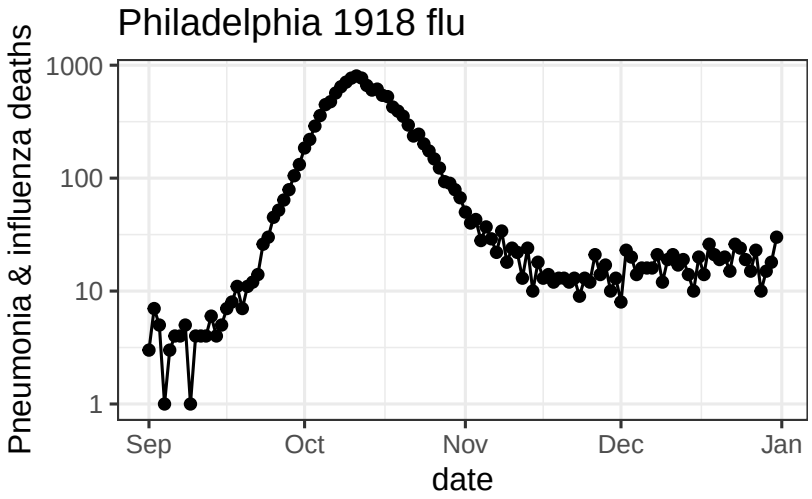


Figure 3: Philadelphia P&I, log scale

- 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)

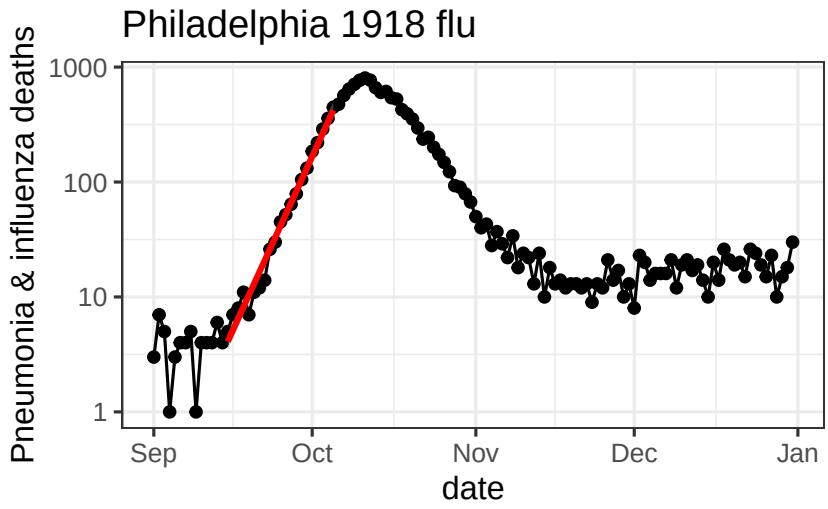


Figure 4: log-scale flu with regression

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)
```

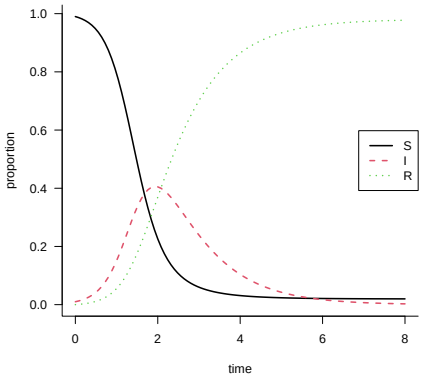


Figure 5: SIR model (R)

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))
```

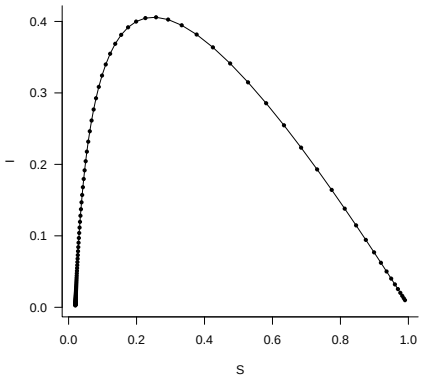


Figure 6: SIR phase plane (R)

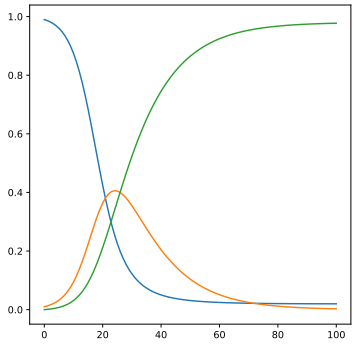
Solve using Python

```
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)

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))
```

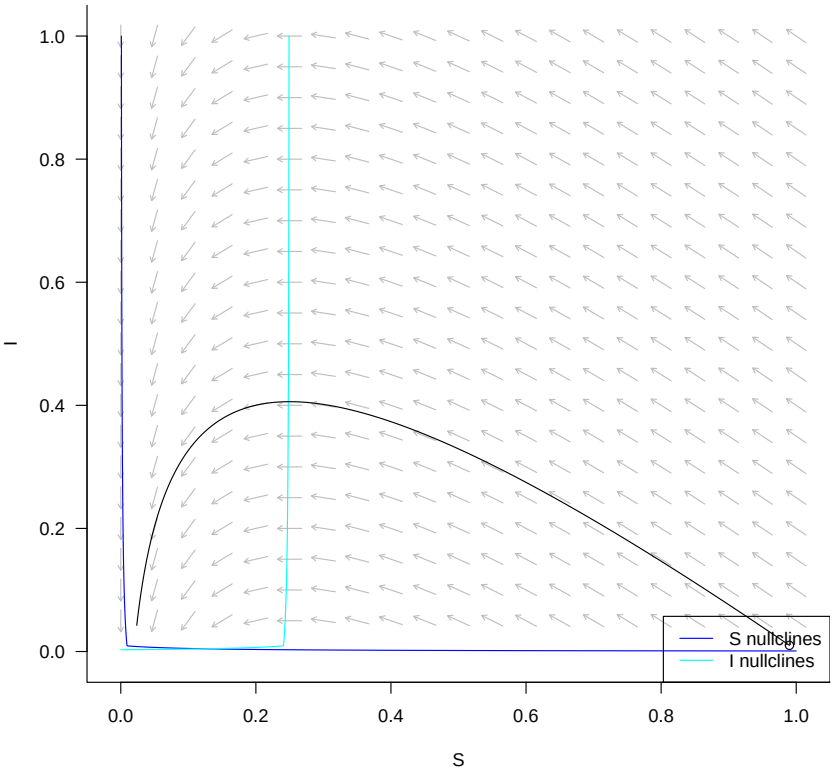


Figure 7: phase plane analysis in R

```
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

- $t \to \infty$:

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

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

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:

$$\begin{aligned} \beta SI - (\gamma + \phi)I &< 0 \\ I(\beta - \gamma - \phi) &< 0 \\ \phi &> (\beta - \gamma) = r \end{aligned}$$

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)
```

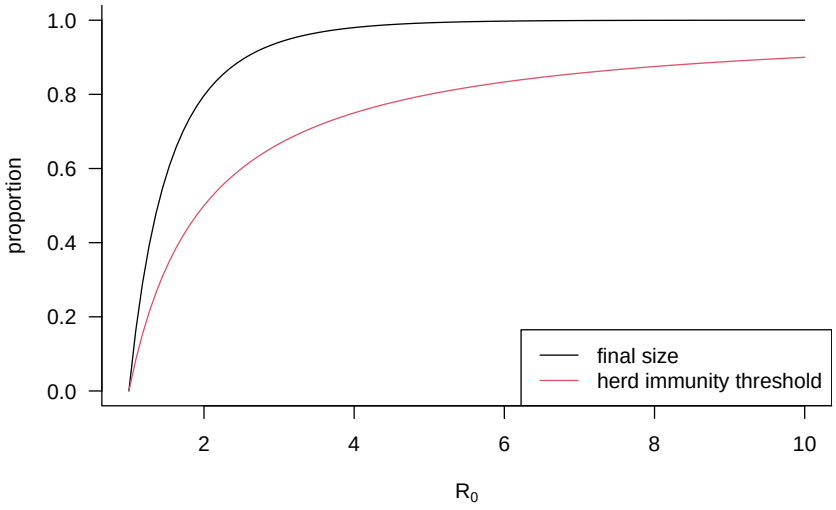


Figure 8: final size vs herd immunity

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.