LIFE DATA EPIDEMIOLOGY

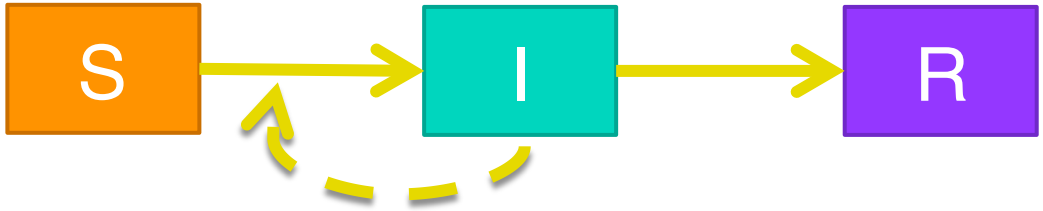
Lecture 4: Extended SIR models

Leonardo Badia

leonardo.badia@unipd.it

SIR model

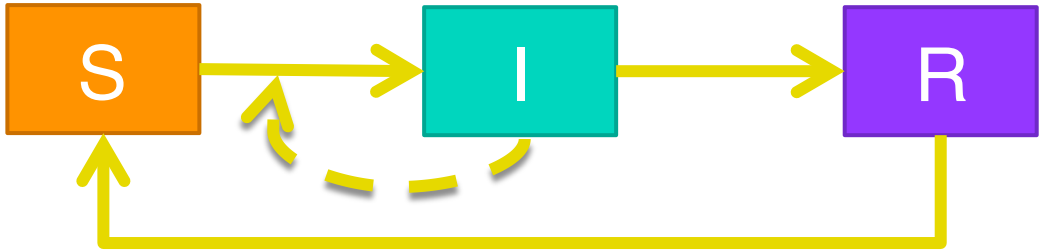
- Susceptible-Infected-Recovered model



- Actually, this can be generalized to any other similar compartmental model
  - for example, including incubation of a disease or vanishing immunity

SIRS model (waning immunity)

- In the SIRS model, immunity acquired by recovered individuals is not permanent



- Rate of exit transitions from R: *w*
  - i.e., one spends an exponentially distributed time with average 1/*w* in class R

SIRS model

- SIR equations (with demography) can be modified as:

$$\frac{\mathrm{d}s}{\mathrm{d}t} = \lambda + wr - \beta sx - \lambda s$$

$$\frac{\mathrm{d}x}{\mathrm{d}t} = \beta sx - \mu x - \lambda x$$

(analogous solution)

$$\frac{\mathrm{d}r}{\mathrm{d}t} = \mu x - wr - \lambda r$$

- If $w = 0$, the model is just a plain SIR; if $w \gg \mu$ then this becomes an SIS model

SIRS model

- Still, basic reproductive ratio $R_0 = \beta / (\lambda+\mu)$
  - and stable endemic solution if $R_0 > 1$
- The average age at 1st infection can be found to be

$$A = \frac{w + \mu + \lambda}{(w + \lambda)(\beta - \mu - \lambda)}$$

SIRS model

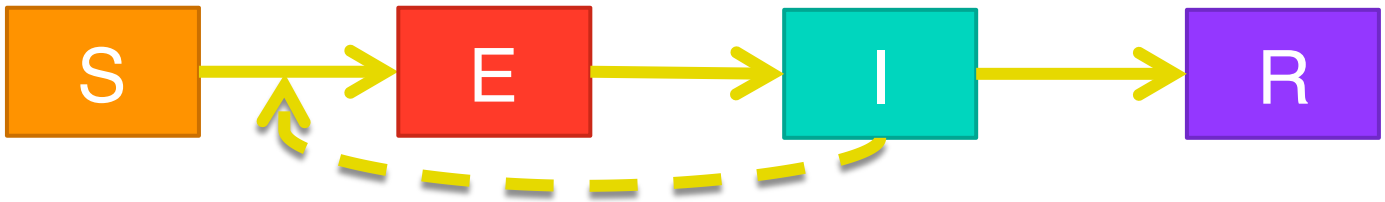
- Once again the endemic equilibrium is reached through damped oscillations of period

$$T = \frac{4\pi}{\sqrt{4(R_0 - 1)\frac{1}{G_I G_R} - \left(\frac{1}{G_R} - \frac{1}{A}\right)^2}}$$

  - where $G_I = 1/(\lambda+\mu)$ and $G_R = 1/(w+\mu)$ are the avg time spent in I and R classes, resp.

Latent period: SEIR

- Many diseases have an “incubation” for individuals before becoming infective
  - the individual already has contracted the disease and will eventually become infected



- Thus, we can add an “exposed” (E) state

SEIR model

- SEIR equations (with demography) can be written as:

σ

where E = #{class E}
and $y = E / N$

and σ = transition rate class S → class E

$$\frac{ds}{dt} = \lambda - (\beta x + \lambda)s$$

$$\frac{dy}{dt} = \beta s x - (\lambda + \sigma)y$$

$$\frac{dx}{dt} = \sigma y - (\lambda + \mu)x$$

$$\frac{dr}{dt} = \mu x - \lambda r$$

Endemic equilibrium of SEIR

- We can derive $R_0 = \beta\sigma / [(\lambda+\mu) (\lambda+\sigma)]$
  - this can be found by directly interpreting the physical meaning of R_0 with "merged" states E and I; but we account for that only during the I phase the individual is infective
  - yet, typically $\sigma \gg \lambda$ → as before $R_0 = \beta / (\lambda+\mu)$ and stable endemic solution if $R_0 > 1$
  - actually, to prove stability is slightly more complicated but doable (3rd deg equations)

Endemic equilibrium of SEIR

- Endemic equilibrium also analogous to SIR as still (albeit R_0 is slightly different: it is $R_0 = \beta\sigma / [(\lambda+\mu) (\lambda+\sigma)])$
  we have $s_\infty = 1/R_0 \quad x_\infty = (R_0 - 1)\, \lambda / \beta$
- We also derive $y_\infty = (R_0 - 1)\, \lambda\, (\lambda+\mu) / (\sigma\, \beta)$
  and naturally $r_\infty = 1 - s_\infty - x_\infty - y_\infty$

- For $\sigma \longrightarrow \infty$ we re-obtain the results of SIR (duration of incubation is infinitesimal)

SEIR at invasion

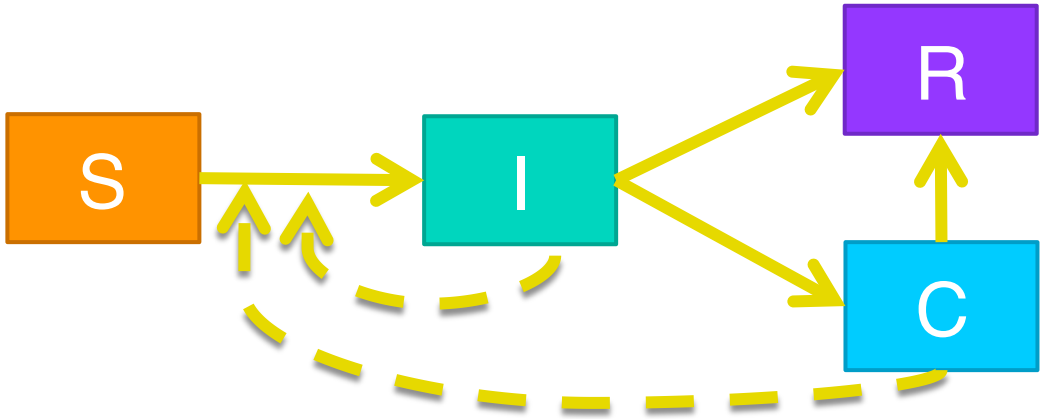
- SEIR may seem a useless complication
  - indeed, for small $\lambda \ll \mu, \sigma$ R_0 is same as SIR, only longer disease recovery $(1/\mu)+(1/\sigma)$
  - however, models are very different at the initial phase of the disease (invasion) where state E slows down the spreading

$$x_{SEIR}(t) \approx x_0 e^{\left(\sqrt{4(R_0-1)\sigma\mu+(\sigma+\mu)^2}-(\sigma+\mu)\right)t/2} \approx x_0 e^{\left(\sqrt{R_0}-1\right)\mu t}$$

  - whereas $x_{SIR}(t) \approx x_0 e^{(R_0-1)\mu t}$

Permanent carriers: SICR

- Some infecteds may enter a “chronic” state from which they slowly (or never) recover



  - Good model for some permanent infections such as herpes simplex or hepatitis B

SICR model

- C = #carriers, $c = C / N$
  - C→R has rate Γ
  - I→C or I→R with split probabilities, q or 1-q, resp.
  - C and I cause undistinguishable infection, but C's is weaker by $\varepsilon<1$

$$\frac{ds}{dt} = \lambda - (\beta x + \varepsilon\beta c + \lambda)s$$

$$\frac{dx}{dt} = [\beta(x + \varepsilon c)]s - (\lambda + \mu)y$$

$$\frac{dc}{dt} = \mu q x - (\Gamma + \lambda)c$$

$$\frac{dr}{dt} = \mu(1-q)x + \Gamma c - \lambda r$$

SICR model

- To compute R_0 and apply threshold criterion $R_0 > 1$ we observe that

contagions by I + contagions by C

$$R_0 = \frac{\beta}{\lambda + \mu} + \frac{q\,\mu}{\lambda + \mu}\,\frac{\varepsilon\beta}{\lambda + \Gamma}$$

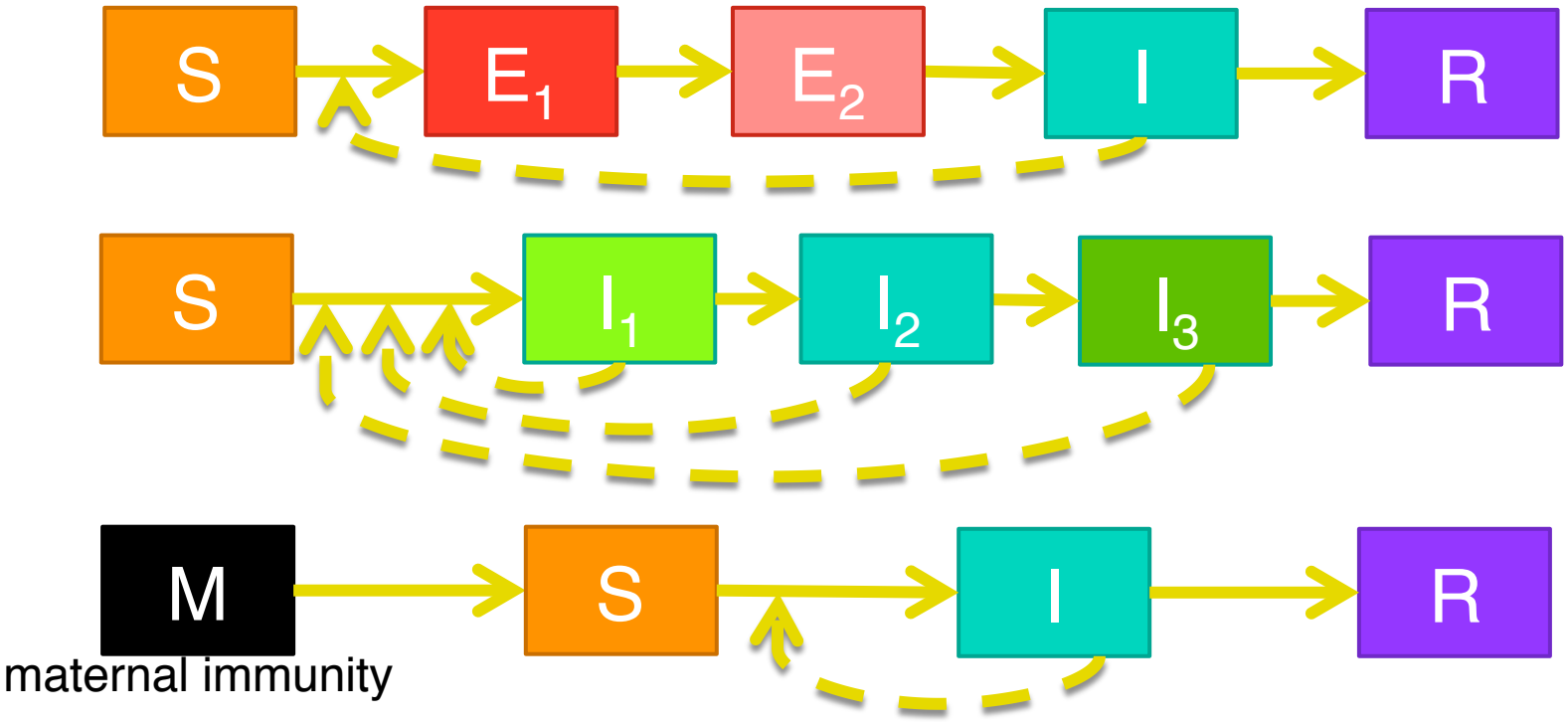
fraction of I that become C (neither dying while I, nor becoming immediately R)

force of infection of class C divided by time spent in C

SICR model

- After some tedious math, one can find the endemic equilibrium where $s_\infty = 1/R_0$
  - and similar results for the other classes
- Generally, in these models the number of acute infected individual is much smaller than the number of carriers
  - because the time spent as acute infected (I) is much smaller than that spent as carrier C – think of AIDS or similar diseases

Generalizations with more states



- if exponential sojourn time = exponential, their sum is Erlang-distributed

Parameter estimation

- Even though a more detailed model may seem a good idea, also the number of parameters greatly increases
  - it is usually difficult to estimate all parameters with good accuracy
  - more experimental data are required
  - and good insight on the process is needed (modeling assumptions)

Change of population size

- Given the origin of the SIR model (closed system) we often impose the condition that birth rate = (natural) death rate = λ
  - sensible for short-time periods

- But sometimes the population size matters
  - longer time windows
  - or demography is influenced by disease

Mass action

- What if the population size changes?
- In our formulation, we just consider fractions of a population of size N
  - for SIR: $s = S/N$, $x = X/N$, $r = R/N$
- If we want to change N over time:
  - we rescale the variables (no big deal)
  - but also we need to check whether the parameters are constant for different N

Mass action

- The SIR model with "force of infection" φ assumes it is linear in X : $\varphi = \beta x = \beta X / N$

$$\frac{dS}{dt} = -\varphi S$$

$$\frac{dX}{dt} = \varphi S - \mu X$$

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

- Underlying assumption: contact rate independent of N (true if contagions spread just around you)
- → β is constant in N

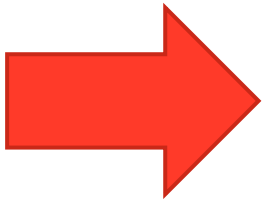
Mass action

- If we put $B = \beta / N$, it is just a rescaling

$$\frac{dS}{dt} = -\frac{\beta}{N} XS$$

$$\frac{dX}{dt} = \frac{\beta}{N} XS - \mu X$$

$$\frac{dR}{dt} = \mu X$$



$$\frac{dS}{dt} = -BSX$$

$$\frac{dX}{dt} = BSX - \mu X$$

$$\frac{dR}{dt} = \mu X$$

  - also called frequency-dependent model

Pseudo-mass (density-based)

- The assumption that #contacts is constant in *N* reflects intuition for many diseases
- However, other diseases have the **parameter** β being itself linear in *N*
  - the rationale is that #contacts depends on #individuals crammed in the ecosystem
  - called density-dependent compartmental model or pseudo-mass action

Discussion

- Frequency dependent is the common assumption for **human**-carried diseases
  - idea: humans are social beings, interacting despite distance, looking for each other (even more true in tech or social contexts)
- Density dependent is better for **animals** (or plants) crammed in a given space
  - when individuals die, fewer interactions
- Actually, also intermediate situations

Disease-induced mortality

- What happens if the disease is deadly and removes individuals from the population?
- To answer, we need some parameters:
  - now birth rate = $\lambda \neq$ natural death rate = ν
  - the individual probability of succumbing to the disease (between 0 and 1) = ρ
- We have a dynamically variable *N*
  In the absence of the disease, $N \longrightarrow \lambda / \nu$

Disease-induced mortality

- Exit from state I can happen because:
  - the infected recovers, rate = μ
  - the infected dies of natural death, rate = ν
  - the infected dies because of the disease
- The impact of the latter is that the infectious period is cut short by a factor of (1-ρ) as on average only those survive
  - the exit rate is thus (ν+μ)/(1-ρ)

Disease-induced mortality

- Infected equations is now:

$$\frac{dX}{dt} = \frac{\beta}{N} SX - \frac{\nu + \mu}{1 - \rho} X$$

(analogous for *S* and *R*)

  - density-dependent: $B = \beta / N$ = constant
  - but for frequency-dependent model, *N* is not a constant anymore and must be included

- + population equation:

$$\frac{dN}{dt} = \lambda - \nu N - \rho \mu X$$

Disease-induced mortality

- Both choices can be the right one
  - frequency-dependent (mass action): describes situations where #contact per infected is same (even with decimated *N*)
  - density-dependent: if *N* shrinks→ we have less frequent contacts among individuals
- It really depends on the phenomenon
  - besides, there are also intermediate choices

Disease-induced mortality

- In both models, 2 equilibria: disease-free or endemic, the latter if $R_0>1$ (also stable)
  - e.g., for frequency-dep:

$$x_\infty = \frac{\nu}{\beta(1-\rho)}(R_0-1) \qquad s_\infty = \frac{\nu+\mu}{\beta(1-\rho)} = 1/R_0$$

and we also need $N_\infty = \frac{\lambda}{\nu}\left(\frac{R_0(1-\rho)}{(R_0-\rho)}\right)$

  - for density-dep: $R_0 = (\lambda/\nu)\,\boxed{(1-\rho)\beta / (\nu+\mu)}$

$=1/s_\infty$

Vertical transmission

- Certain diseases exhibit transmission from an infected parent to the offspring
  - we can incorporate this in the model by assuming that newborns are susceptible, except for a fraction proportional to x

$$\frac{ds}{dt} = \lambda - h\lambda x - \beta sx - \nu s$$

$$\frac{dx}{dt} = h\lambda x + \beta sx - \mu x - \nu x$$

just rescales parameters

(and does not affect the analysis, as we will see)

General model

- Even if all parameters are different, we get

$$\frac{\mathrm{d}s}{\mathrm{d}t} = \lambda - h\lambda x - \beta s x - \nu s + w r$$

$$\frac{\mathrm{d}x}{\mathrm{d}t} = h\lambda x + \beta s x - \mu x - \nu x$$

$$\frac{\mathrm{d}r}{\mathrm{d}t} = \mu x - w r - \nu r$$

- which can be solved in x and r ($s = 1\text{-}x\text{-}r$)

General model

$$\frac{dx}{dt} = \left(h\lambda + \beta(1 - x - r) - (\mu + \nu)\right)x$$

$$\frac{dr}{dt} = \mu x - (w + \nu)r$$

- set $\omega = w + \nu$ and $\psi = h\lambda + \beta - \mu - \lambda$

endemic equilibrium

$$\frac{dx}{dt} = \left(\psi + \beta x - \beta r\right)x$$

$$\frac{dr}{dt} = \mu x - \omega r$$

$$s_\infty = \frac{\beta - \psi}{\beta} = \frac{\mu + \lambda(1 - h)}{\beta},\ x_\infty = \frac{\omega\psi}{\beta(\mu + \omega)},\ r_\infty = \frac{\mu\psi}{\beta(\mu + \omega)}$$