Models for Understanding and Controlling Global Infectious Diseases HUMBIO 154D / HRP 204

Session 6

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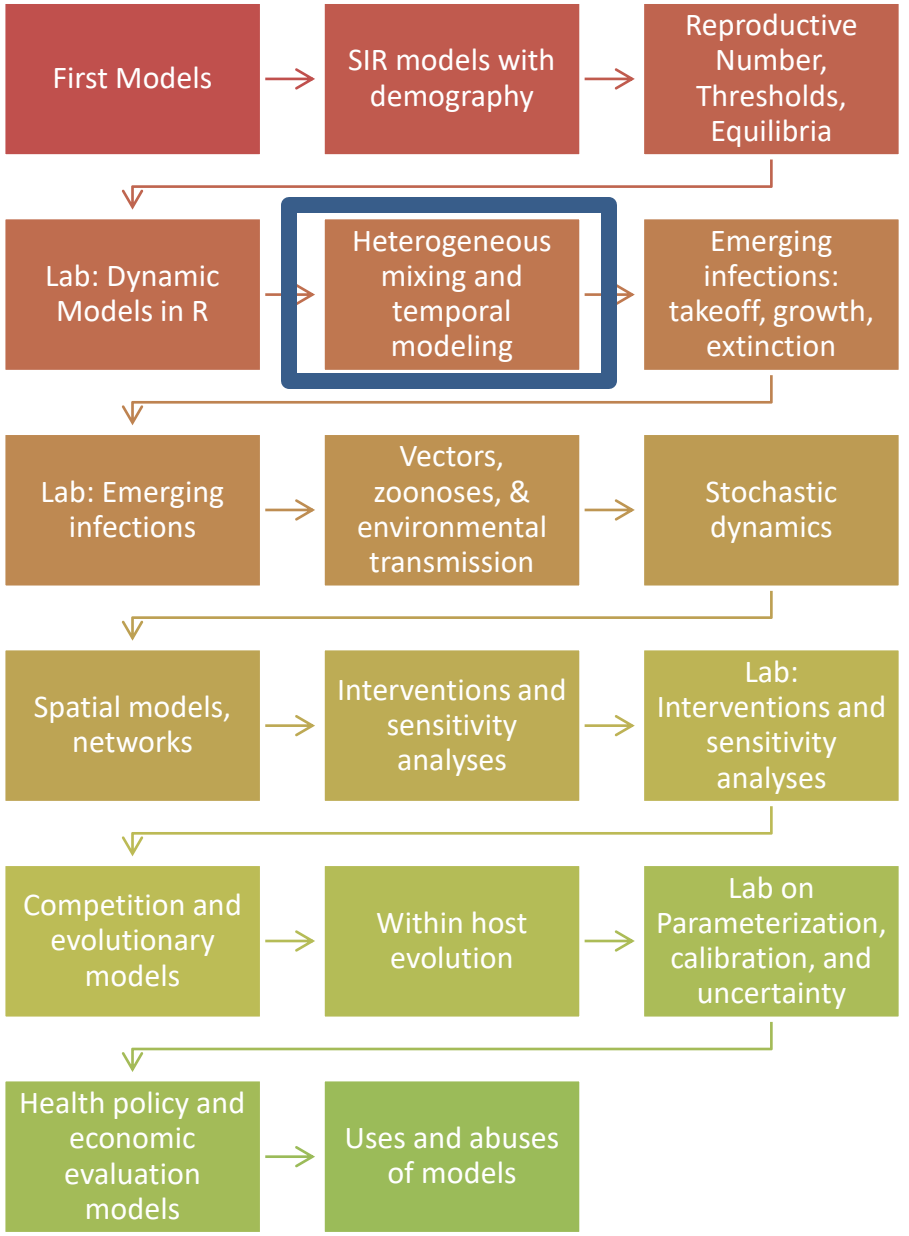
2020

Course Roadmap



Practical Questions

How does heterogeneity (stratifying our model by subgroups) affect its prediction about spread of disease and equilibria? About effects of interventions?

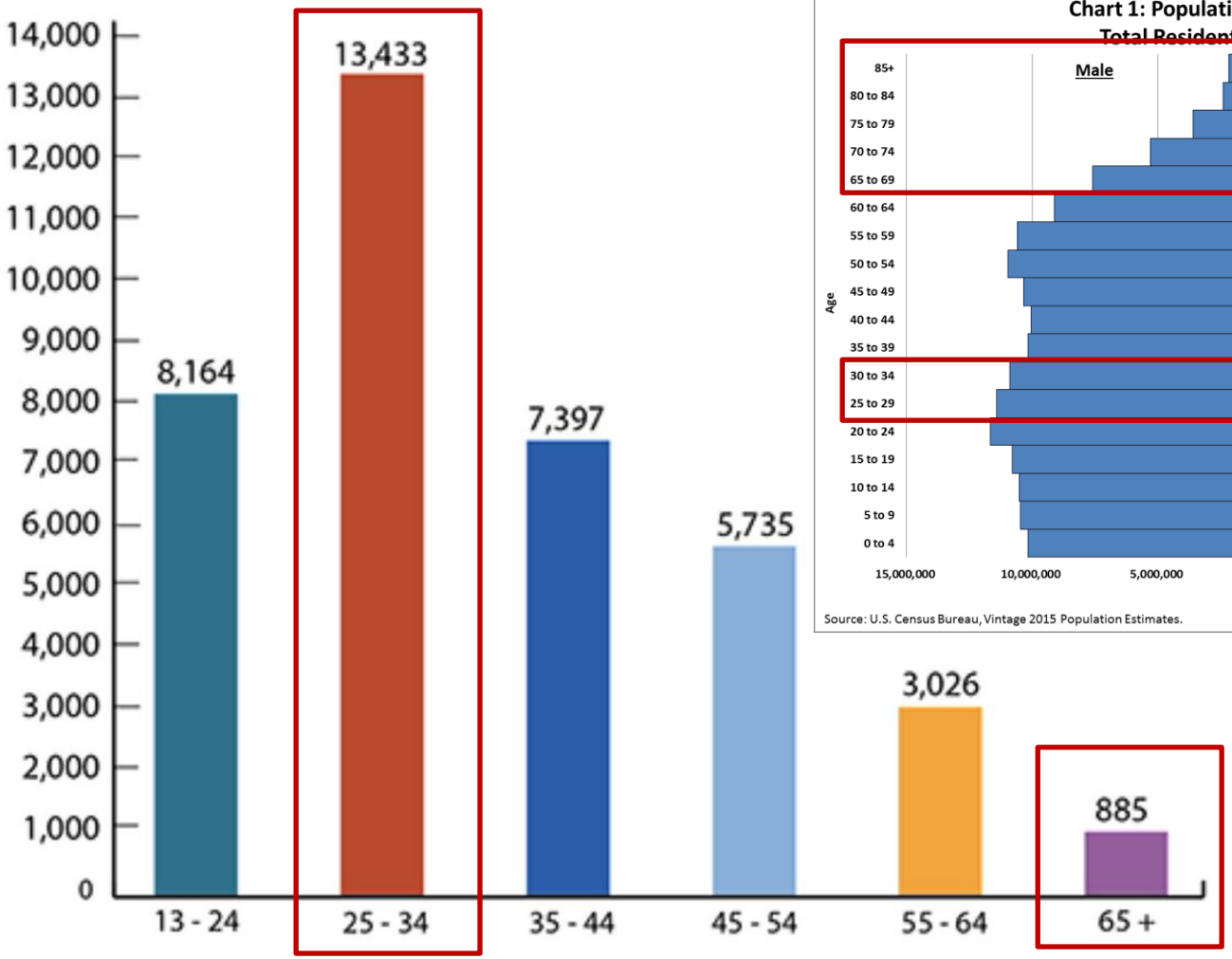
In addition to the reasons we discussed last time for oscillations in endemic equilibria to occur for SIR models with demographics, are there other reasons for oscillations? How do these interact? Can they help us explain observed patterns?

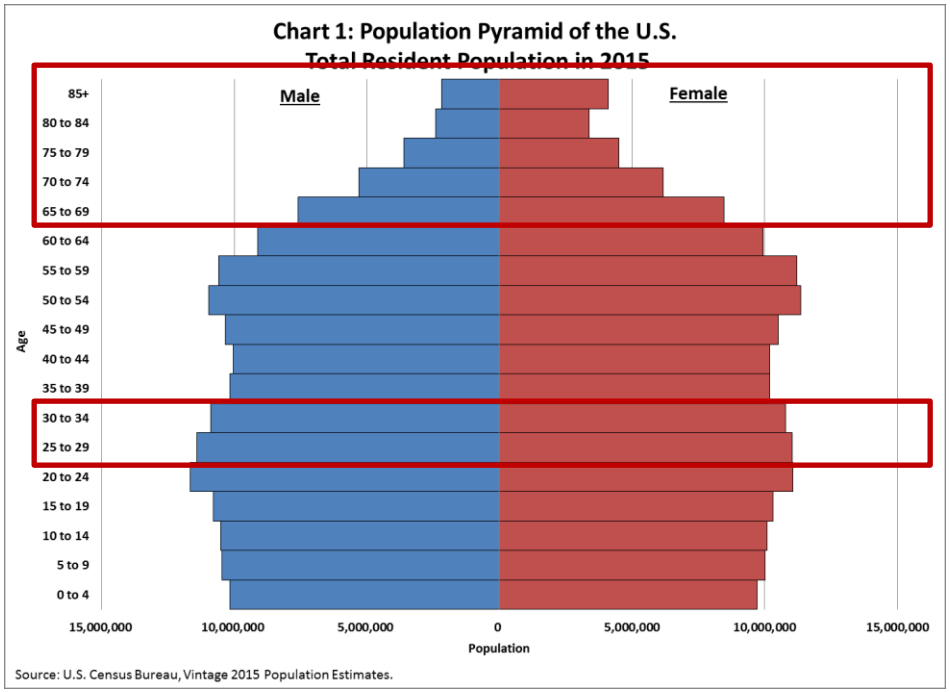
Learning Objectives

- Describe how and why structured models have different equilibria from otherwise similar unstructured models
- Differentiate between structured and age-stratified models
- Define what a contact matrix is and describe several ways (and their pros and cons) for estimating them from data and/or theory
- Explain how seasonal forcing may arise
- Understand why seasons forcing can amplify or damp oscillations in an SIR model with demography
- Enumerate other types of patterns that might emerge in such situations
- Interpret bifurcation diagrams

RISK GROUPS

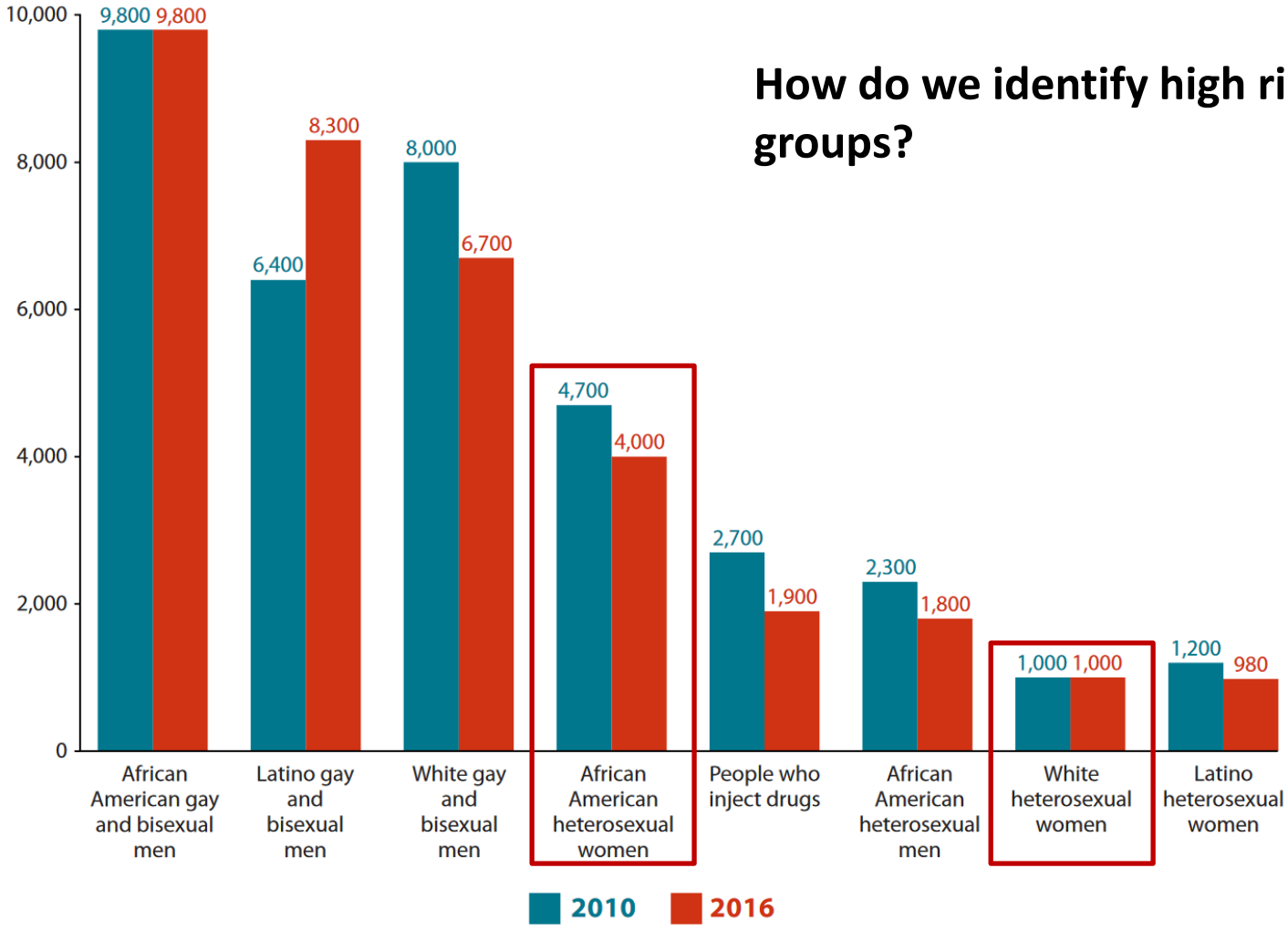
New HIV Diagnoses in the US and Dependent Areas by Age, 2018





https://www.cdc.gov/hiv/statistics/overview/ataglance.html; https://www.census.gov/newsroom/blogs/random-samplings/2016/06/americas-age-profile-told-through-population-pyramids.html

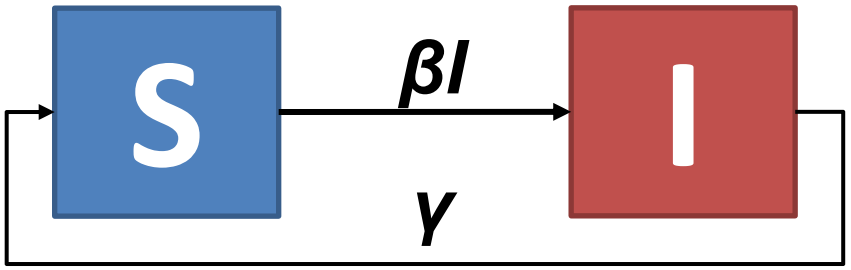
New HIV Infections by Race and Transmission Group, U.S. 2010 vs. 2016



How do we identify high risk groups?

https://www.hiv.gov/hiv-basics/overview/data-and-trends/statistics

Remember: Unstratified SIS Models



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

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

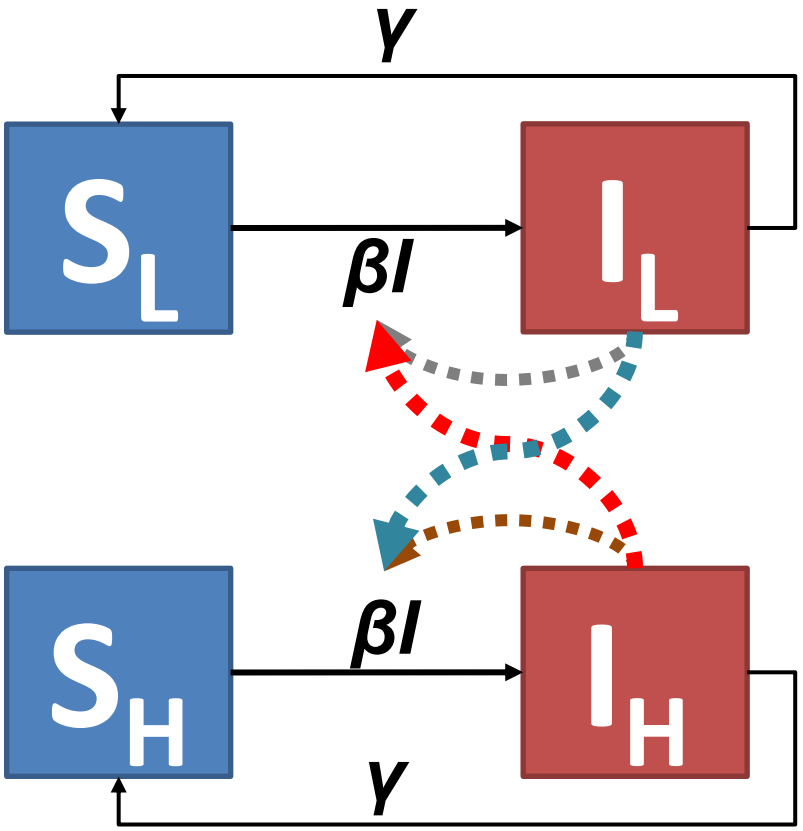
What is the endemic equilibrium?

$$\left(\frac{\gamma}{\beta}, 1 - \frac{\gamma}{\beta}\right)$$

When $R_0 > \frac{\beta}{\gamma}$ and endemic equilibrium reached w/o oscillations

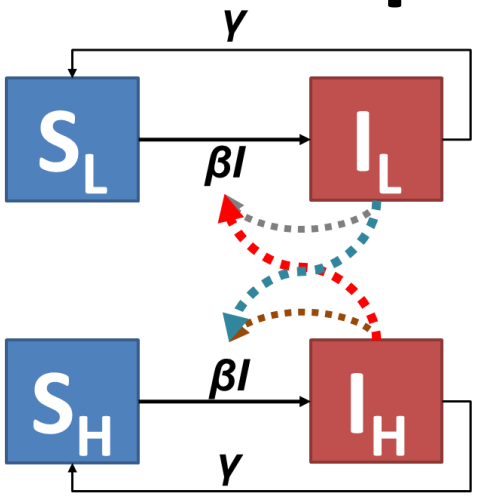
If gamma=0, then this can be a simple model of HIV (ignoring mortality)

Simplest Stratified SIS Models



Note that in this model risk group membership does not change (Hs remain Hs and Ls remain Ls)

Simplest Stratified SIS Models



$$\frac{dS_L}{dt} = \gamma I_L - \beta_{LL} S_L I_L - \beta_{LH} S_L I_H$$

$$\frac{dI_L}{dt} = \beta_{LL} S_L I_L + \beta_{LH} S_L I_H - \gamma I_L$$

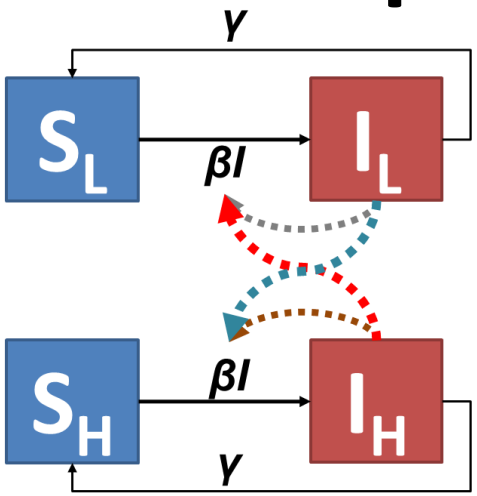
$$\frac{dS_H}{dt} = \gamma I_H - \beta_{HH} S_H I_H - \beta_{HL} S_H I_L$$

$$\frac{dI_H}{dt} = \beta_{HH} S_H I_H + \beta_{HL} S_H I_L - \gamma I_H$$

WHO-ACQUIRES-INFECTION-FROM-WHOM MATRIX (WAIFW) or

CONTACT MATRIX $\boldsymbol{\beta} = \begin{pmatrix} \beta_{HH} & \beta_{HL} \\ \beta_{LH} & \beta_{LL} \end{pmatrix}$

Simplest Stratified SIS Models



WAIFW or CONTACT MATRIX

$$\boldsymbol{\beta} = \begin{pmatrix} \beta_{HH} & \beta_{HL} \\ \beta_{LH} & \beta_{LL} \end{pmatrix}$$

In general a risk group is "higher" risk because:

$$\beta_{HH} + \beta_{HL} > \beta_{LL} + \beta_{LH}$$

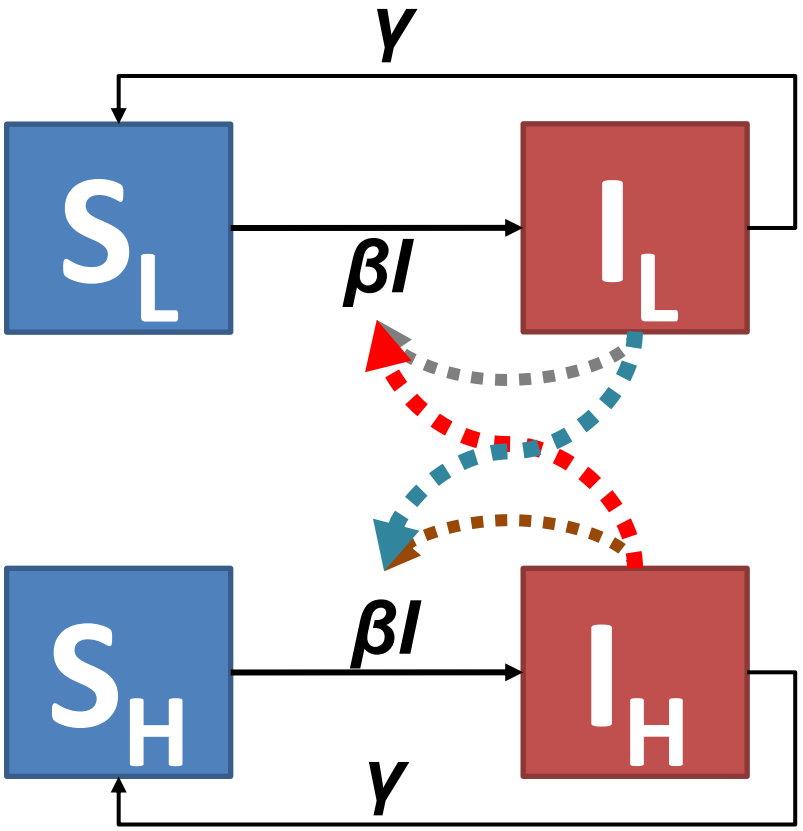
Assortative (non-homogenous mixing)

$$\beta_{HH} > \beta_{HL} \; and \; \beta_{LL} > \beta_{LH}$$

If likelihood of infection|contact same

$\beta_{HL} = \beta_{LH}$ **=> symmetry**

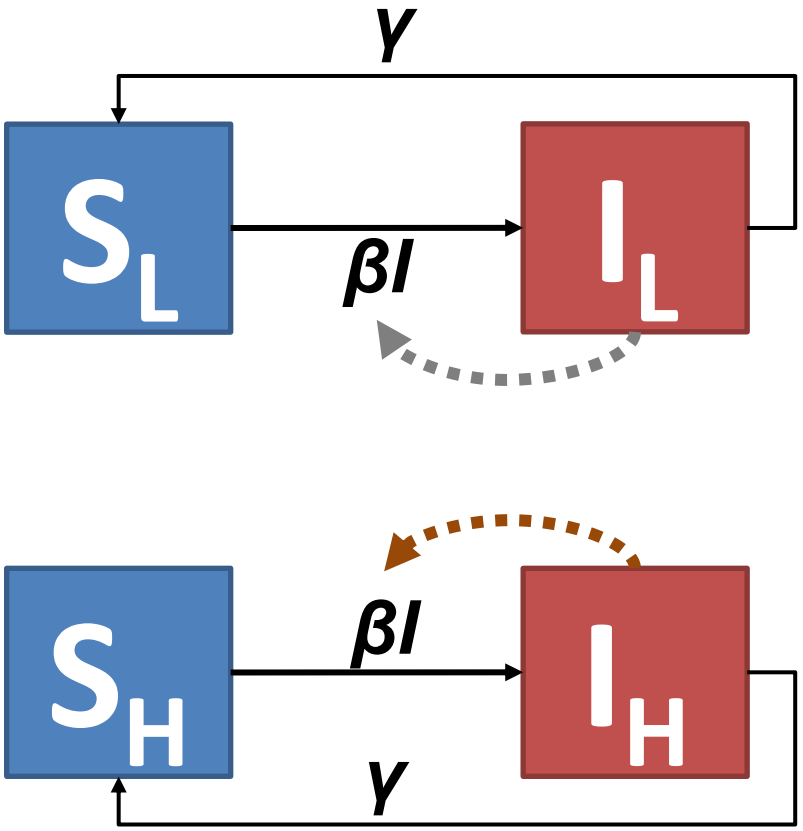
Implications of Risk Stratification



Imagine we have our model but without the interactions across the groups

$$\boldsymbol{\beta} = \begin{pmatrix} \beta_{HH} & 0 \\ 0 & \beta_{LL} \end{pmatrix}$$

Implications of Risk Stratification



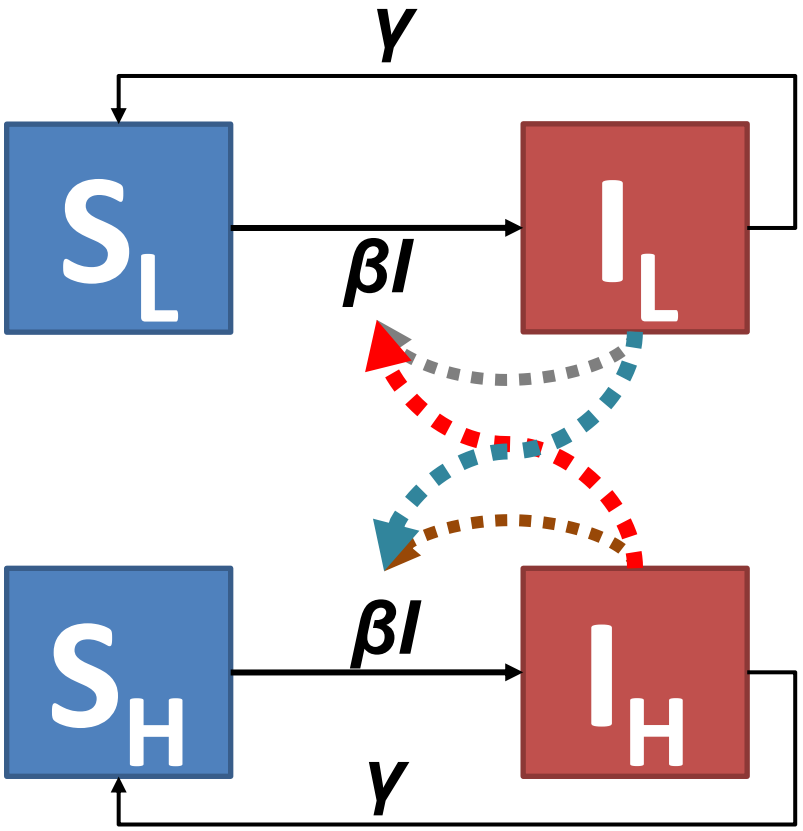
What if β_{LL} is low enough so that R0 for L < 1?
What if β_{HH}=> R0 for H >1?
What happens?

$$\boldsymbol{\beta} = \begin{pmatrix} \beta_{HH} & 0 \\ 0 & \beta_{LL} \end{pmatrix}$$

Implications of Risk Stratification

- No endemic equilibrium in the L subgroup
  - So if a few I's were imported into the L subgroup their prevalence would decline over time to 0
- An endemic equilibrium in the H subgroup

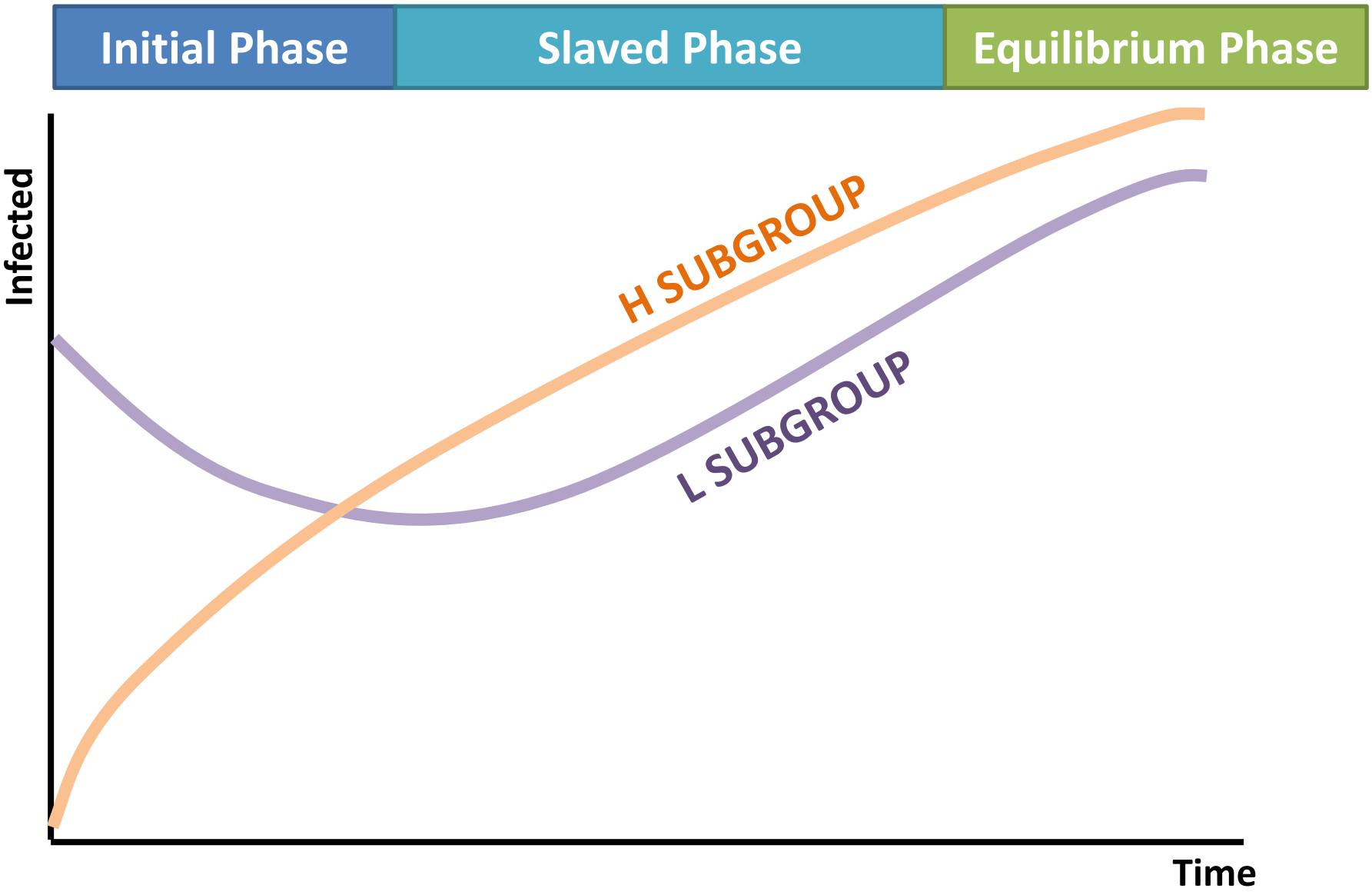
Implications of Risk Stratification



However, if β_{LH} is large enough to sustain an endemic equilibrium in the L subgroup, then….

$$\boldsymbol{\beta} = \begin{pmatrix} \beta_{HH} & \beta_{HL} \\ \beta_{LH} & \beta_{LL} \end{pmatrix}$$

Implications of Risk Stratification



Implications of Risk Stratification

- Initial Phase: L subgroups dynamics behave similarly to if there were not interactions between subgroups (b/c not so many infected H people yet); H grows in size.
- Slaved Phase: Growth in both groups is drive primarily by the "dominant" group's dynamics, other subgroups become synchronized or slaved (see Eigenvalue approach in Box 3.10)
- Equilibrium Phase: Reached because the dominant group's prevalence stops growing

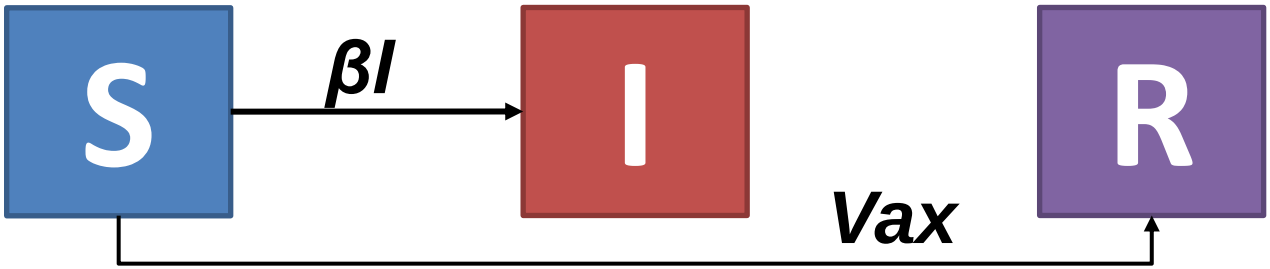
Implications of Risk Stratification

For stratified models like these, the Initial Phase (whether there is rise or fall) and ultimately where the system goes depends both on R0s and on initial conditions (amount of infectious individuals in each subgroup at time 0)

Stratified models can sustain an endemic equilibrium with relatively low levels of overall prevalence (higher fraction of H subgroup infected though) as they have higher R0s than otherwise similar unstructured models (harder to achieve complete eradication)

Control Measures in Stratified Models

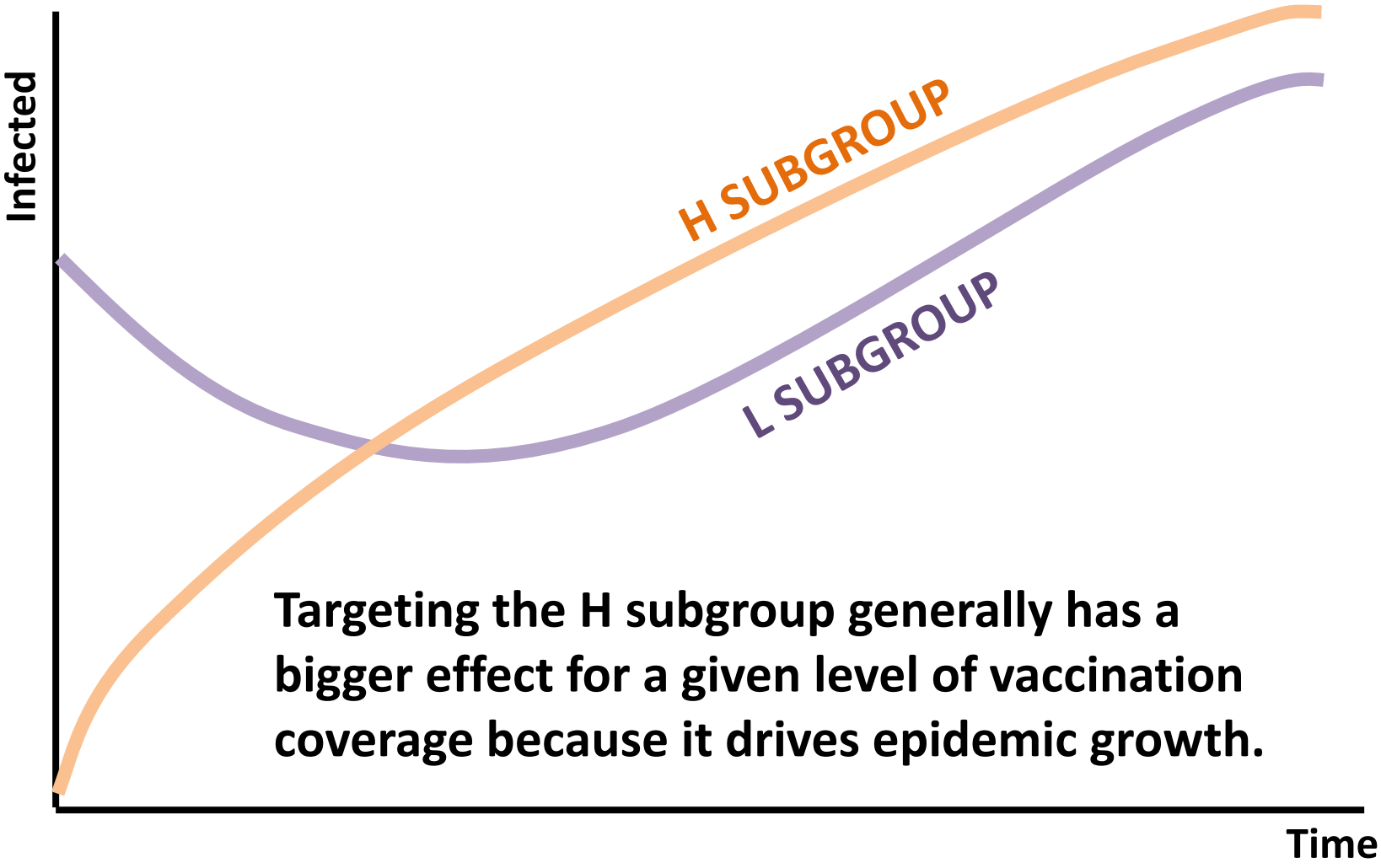
- In an unstructured SI model, an intervention like vaccination transforms it into an SIR model (vaccinated people are immune like recovered people but without having been sick)
  - The one decision to make is what fraction of the population to vaccinate for optimal control



Control Measures in Stratified Models

- In a structured SI model, interventions like vaccination have two important, related decision
  - What fraction of the population to vaccinate for optimal control (like the unstructured model)
  - How targeted should the intervention be (what proportion of those vaccinated should be recruited from the L subgroup and what fraction from the H subgroup)

Which group should be target and why?



Targeting the H subgroup generally has a bigger effect for a given level of vaccination coverage because it drives epidemic growth.

REVISITING CONTACT MATRICES

How do we estimate contact matrices?

- As we have more input parameters (2 risk groups => 4 Betas) than in a non-stratified model, we need to think about where this data comes from and strategies for dealing with incomplete (but needed) data
  - For n risk groups, we require n^2 Betas

One Strategy: Random Partnership Model

- If we assume that contacts occur at random between people of types i and j (where a person of type k has k partners), then the fraction of partnerships is given by

$$\frac{ij}{\sum_k kn_k}$$

- And transmission matrix is given by

$$\beta_{ij} = \beta \frac{ij}{\sum_k kn_k}$$

- Advantage: Only need to figure out one parameter (β) and the entire mixing matrix (β_{ij}) is determined

One Strategy: Random Partnership Model

- Random partnership model's R_0

$$R_0 = \frac{\beta}{\gamma}\frac{M^2 + V}{M}$$

- Where M and V are the mean and variance of the number of partners
- Notice: in an unstructured model $R_0 = \frac{\beta}{\gamma} M$
- R_0 is larger in the structured model (V>0)
- Heterogeneity matters and infections concentrate in people with large number of partners who continue to transmit to others

One Strategy: Random Partnership Model

- Disadvantage: The random partnership model is not assortative (people who have lots of partners do not tend to mix more frequently with others who have lots of partners at all)
- Extension:

$$\beta_{ij} = \beta(1-\alpha)\frac{ij}{\sum_k kn_k}, \beta_{ii} = \beta\left[\alpha\frac{i}{n_i} + (1-\alpha)\frac{i^2}{\sum_k kn_k}\right]$$

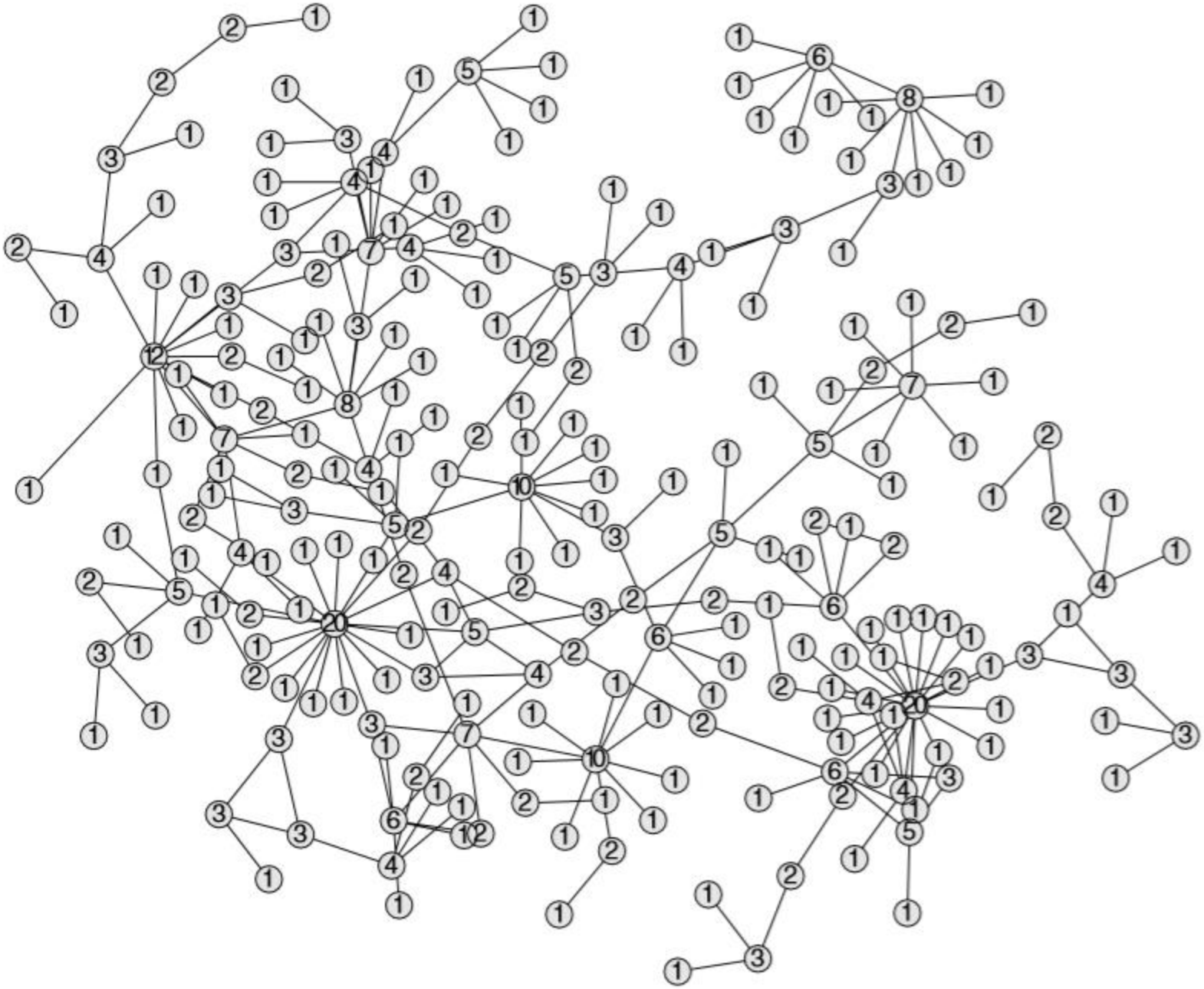
- The α controls how much additional mixing happens within a given group (α=1 => we have a diagonal matrix, separate non-mixing models by group; α=0 => random partnership); **What does this mean for optimal vaccination?**

Another Strategy: Survey Methods

- If we want to establish mixing patterns empirically, one approach is to survey people about their behaviors/contacts
- Advantage: do not have to make assumptions about how mixing occurs (or at least we can make assumptions consistent with what we observe)
- Two main types of surveys:
  - Surveys that attempt to establish contact networks (more appropriate for sexual mixing or shared injection drug use but much more intensive and sampling harder)
  - Surveys that measure #s of contacts (not networks) (more appropriate for respiratory contacts for example)

Another Strategy: Survey Methods: Sampling the Network

- Consider the case of a sexual mixing network
- We ask people for a list of partners
- We then go to their partners and get a list of their partners, etc….
- We can eventually reconstruct a connected graph (network) and characterize things like:
  - What is the distribution of the number of partners people have
  - Do the partners of people with more partners tend to have more partners themselves



$$\beta \approx \beta \begin{pmatrix} 0 & 0.8 & 1.6 & 2.5 & 3.2 & 4.8 & 4.4 & 8.1 & 12.1 & 9.7 & 17.7 \\ 0.8 & 3.1 & 1.9 & 4.8 & 4.3 & 6.9 & 8.7 & 3.5 & 3.5 & 13.9 & 13.9 \\ 1.6 & 1.9 & 5.7 & 6.1 & 7.1 & 6.8 & 5.7 & 11.4 & 5.7 & 22.7 & 28.4 \\ 2.5 & 4.8 & 6.1 & 5.9 & 9.6 & 0 & 19.2 & 0 & 0 & 19.2 & 28.8 \\ 3.2 & 4.3 & 7.1 & 9.6 & 7.8 & 12.5 & 7.8 & 0 & 15.6 & 0 & 62.5 \\ 4.8 & 6.9 & 6.8 & 0 & 12.5 & 0 & 12.5 & 25 & 250 & 0 & 50 \\ 4.4 & 8.7 & 5.7 & 19.2 & 7.8 & 12.5 & 0 & 62.5 & 31.3 & 62.5 & 0 \\ 8.1 & 3.5 & 11.4 & 0 & 0 & 25 & 62.5 & 0 & 0 & 0 & 0 \\ 12.1 & 3.5 & 5.7 & 0 & 15.6 & 25 & 31.3 & 0 & 0 & 0 & 0 \\ 9.7 & 13.9 & 22.7 & 19.2 & 0 & 0 & 62.5 & 0 & 0 & 0 & 0 \\ 17.7 & 13.9 & 28.4 & 28.8 & 62.5 & 50 & 0 & 0 & 0 & 0 & 0 \end{pmatrix}$$

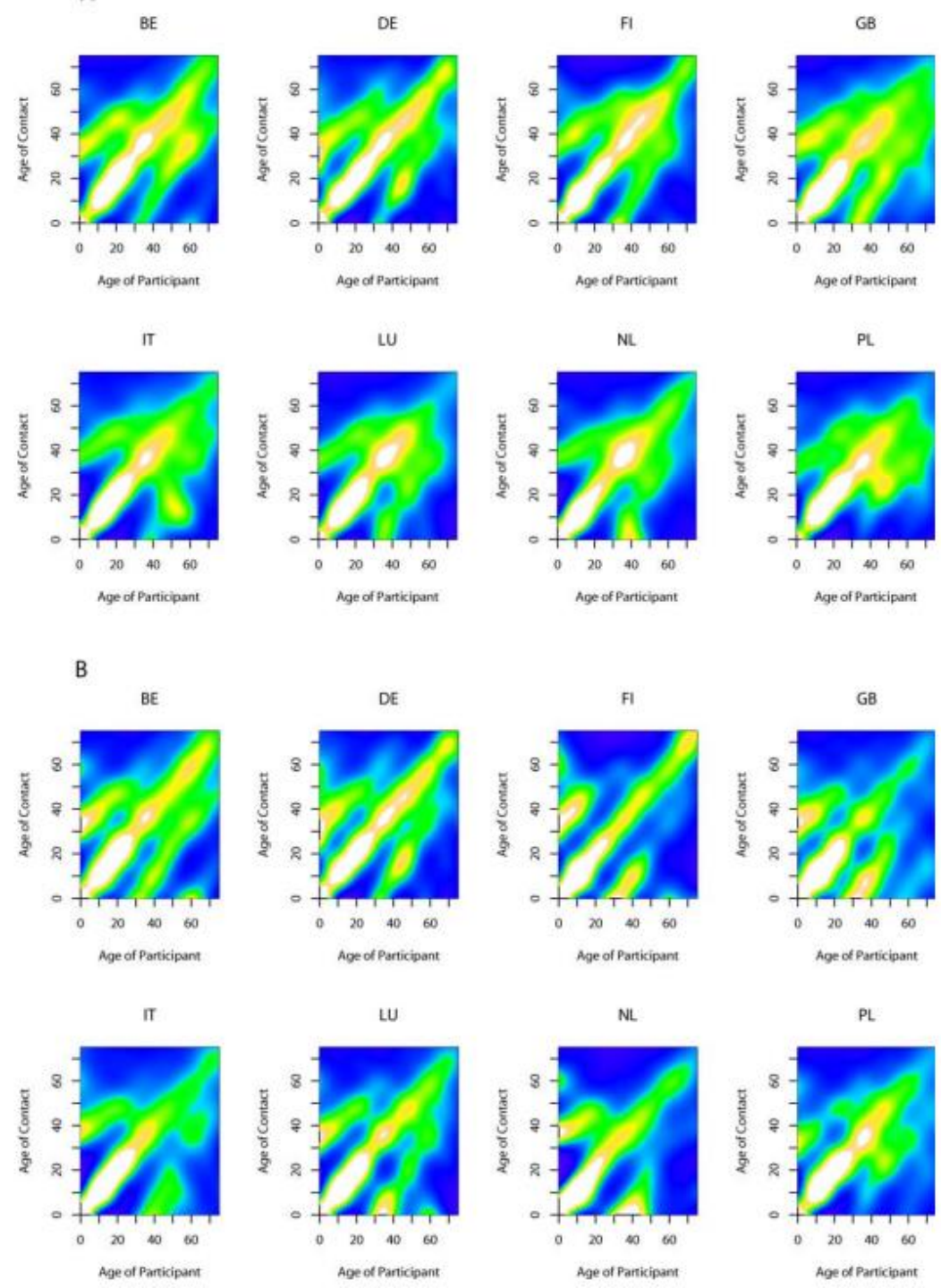
Rows (i) represent people with 1, 2, 3, …, 9, 10, 12, and 20 partner
Columns (j) represent whether the partners are people with 1, 2,…,10,12, or 20 partners themselves
Entries are proportionate to number of i-j partnerships divided by the product of the number of people of type i and number of people of type j (when will this be large?)

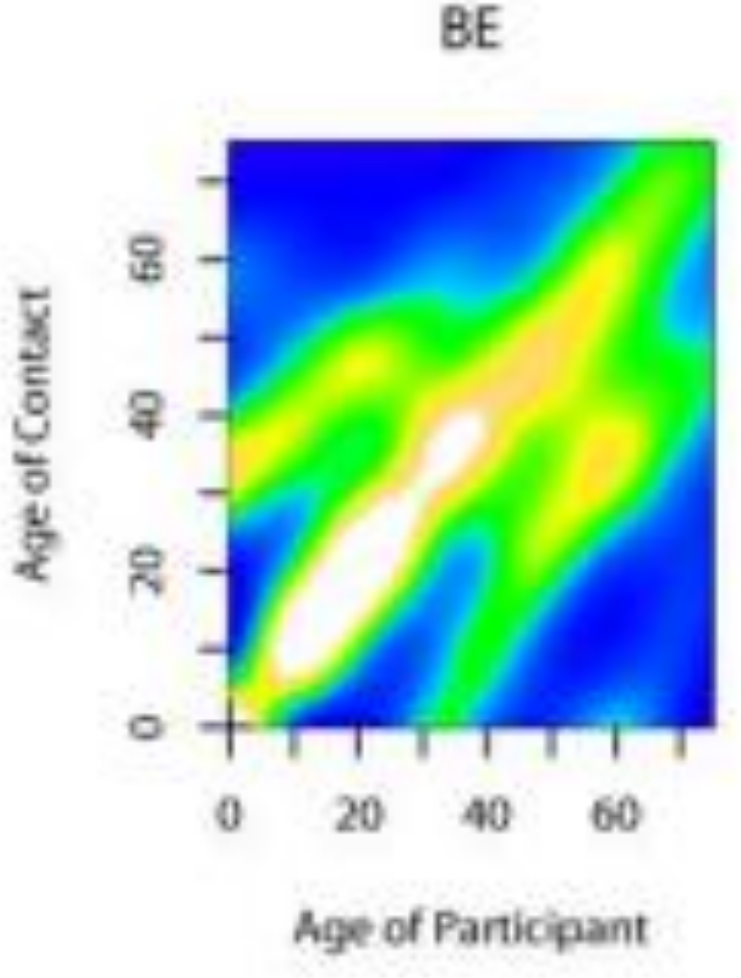
Another Strategy: Survey Methods: Large-Scale Frequency/Intensity Surveys

- Mossong et al. Social contacts and mixing patterns relevant to the spread of infectious diseases. *PLoS Medicine*, 2008.
- Information on social contacts from cross-sectional surveys in 8 European countries
- Participants were recruited to be representative of the population in terms of geographical spread, age, and sex

Another Strategy: Survey Methods: Large-Scale Frequency/Intensity Surveys

- Diaries recorded basic sociodemographic and household information. Participants were assigned a random day of the week to record every person they had contact with for 24 hours starting at 5 A.M.
- Participants recorded contacted individuals only once in the diary (defined as either skin-to-skin contact or a two-way conversation of at least minimal duration).
- Participants provided age and sex of each contact

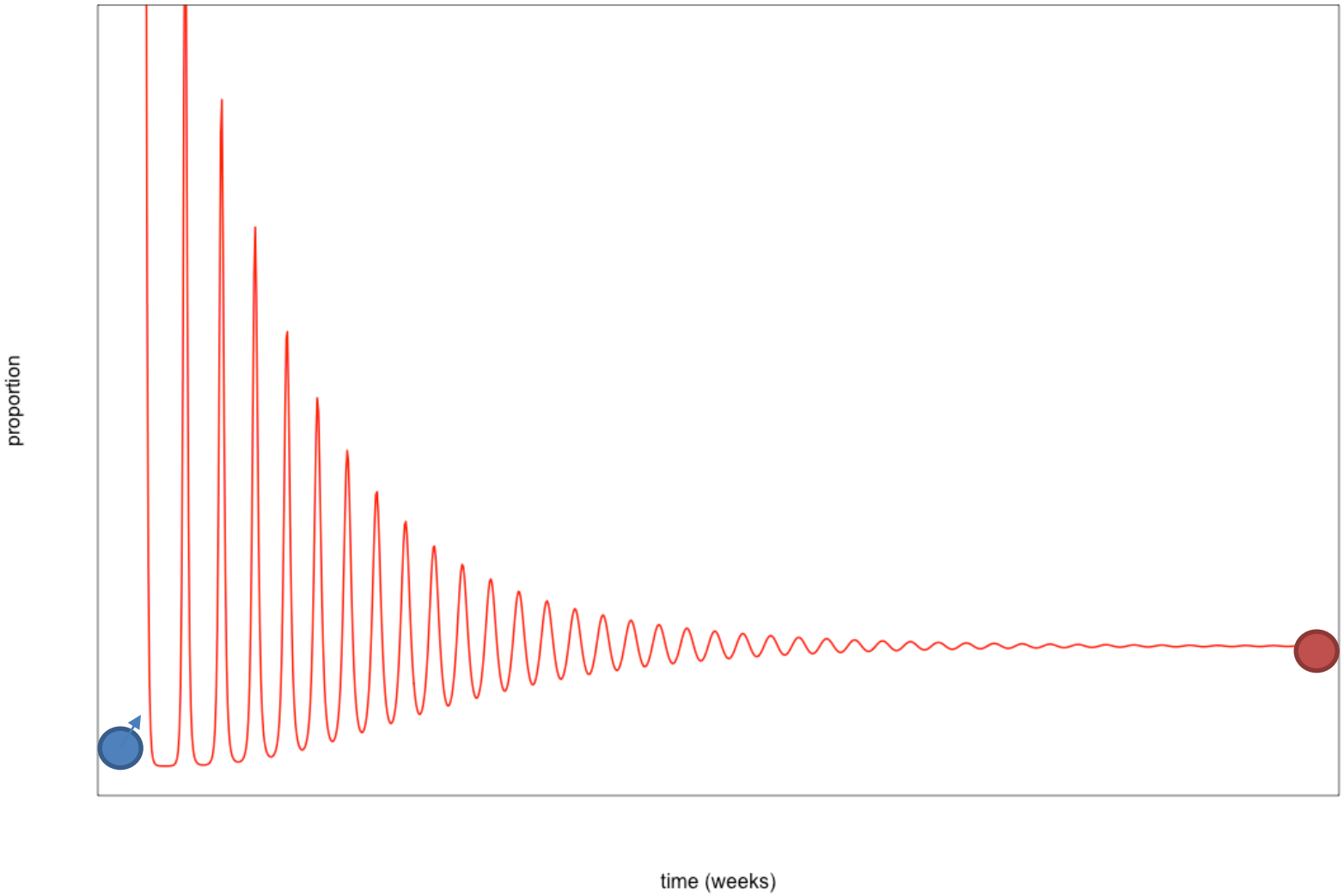




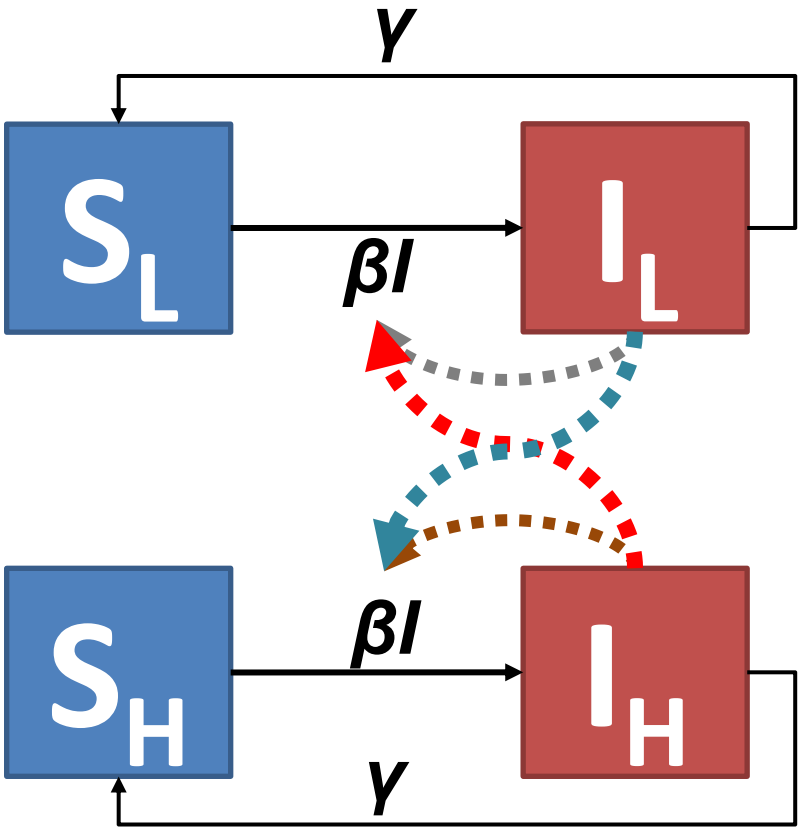
How do we expect infections to spread throughout age groups if the first is in a 10 year-old? Which group will dominate the dynamics of growth during the slaved phase and why?

AGE-STRUCTURED MODELS SIMILAR TO BUT DIFFERENT TO RISK STRUCTURED MODELS

SIR model with demography: Damped Oscillatory Dynamics



Remember: In the Stratified Models, People Stay in Their Original Risk Group



Note that in this model risk group membership does not change (Hs remain Hs and Ls remain Ls)

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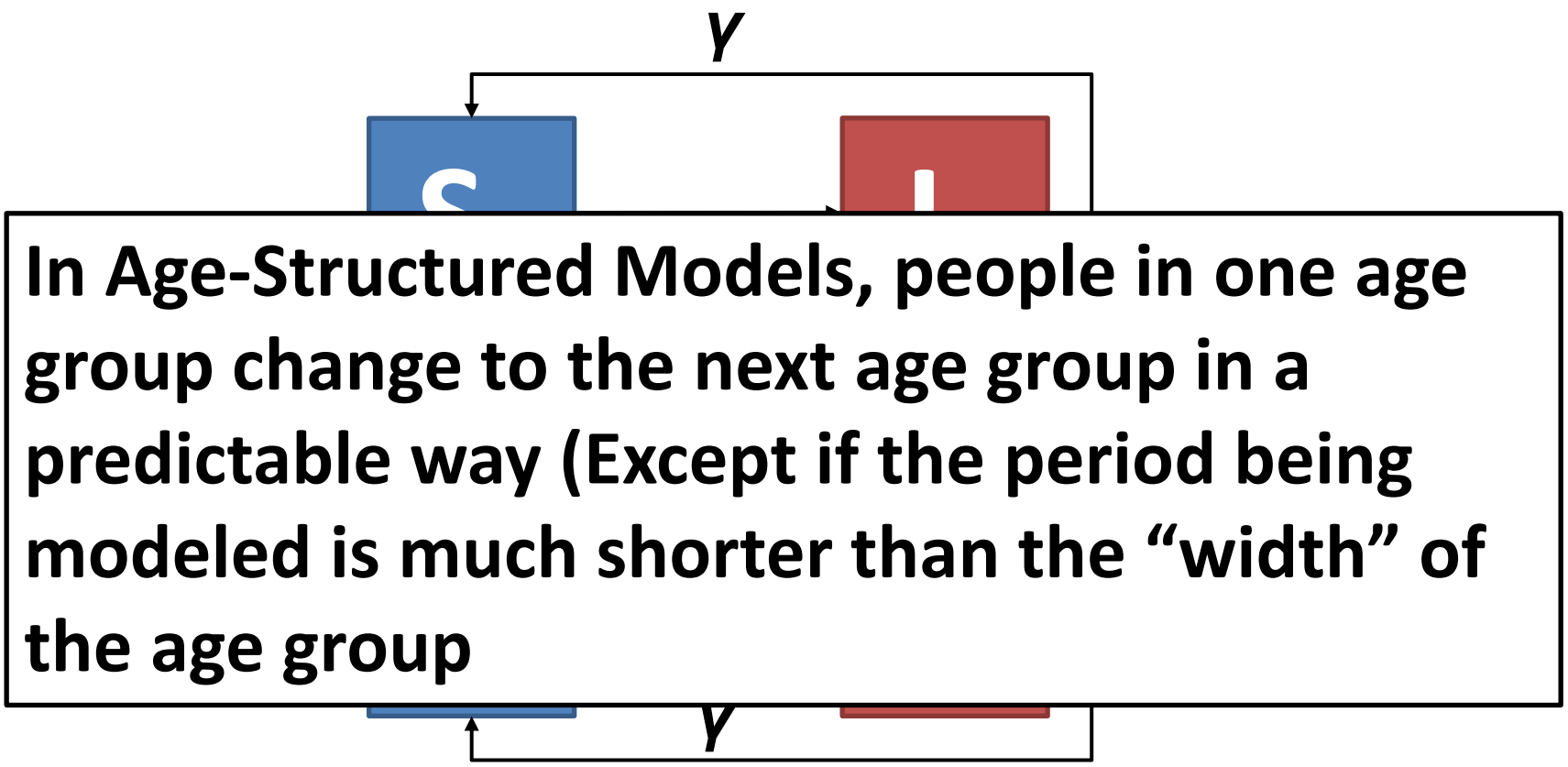

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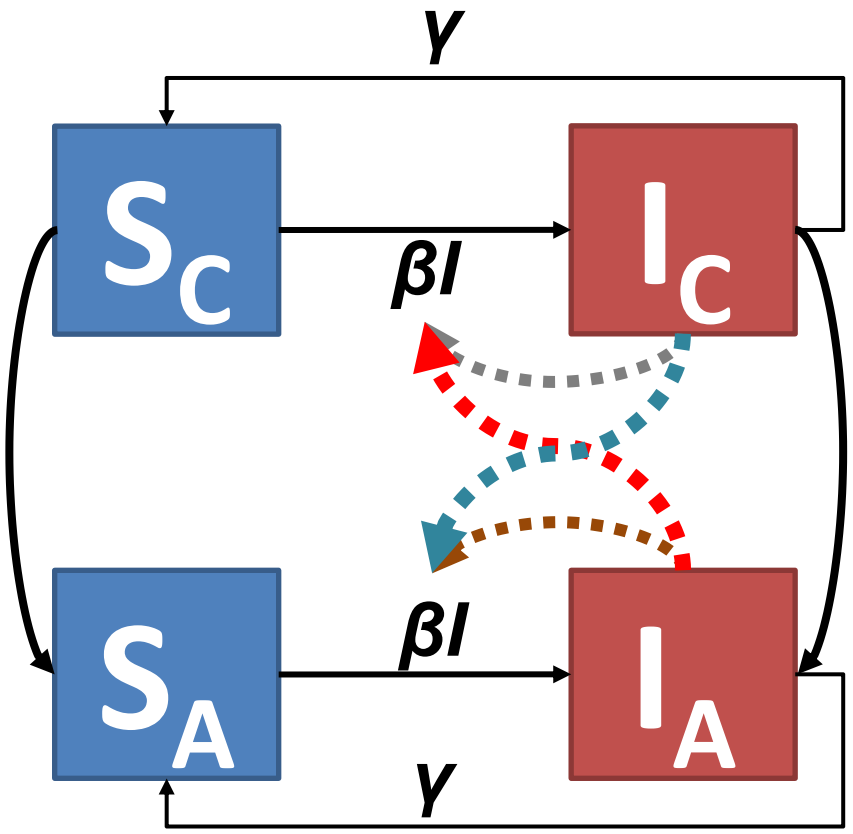
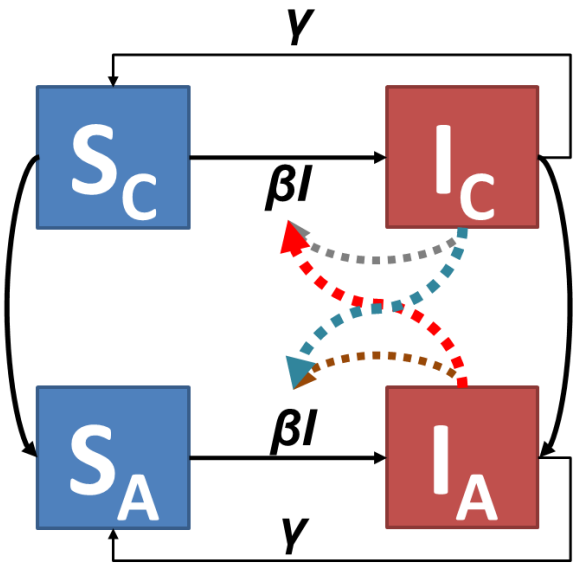
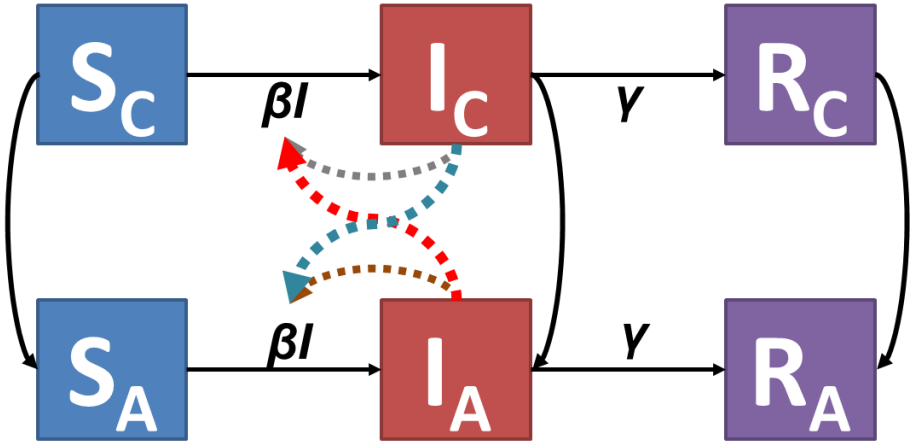
Age-Structured Model of Children (C) and Adults (A): Like Stratified Models but with Aging



How will the age patterns of a serosurvey differ for an Age-Structured SIS vs. an Age-Structured SIR Model? Why? What if there is waning immuninty?





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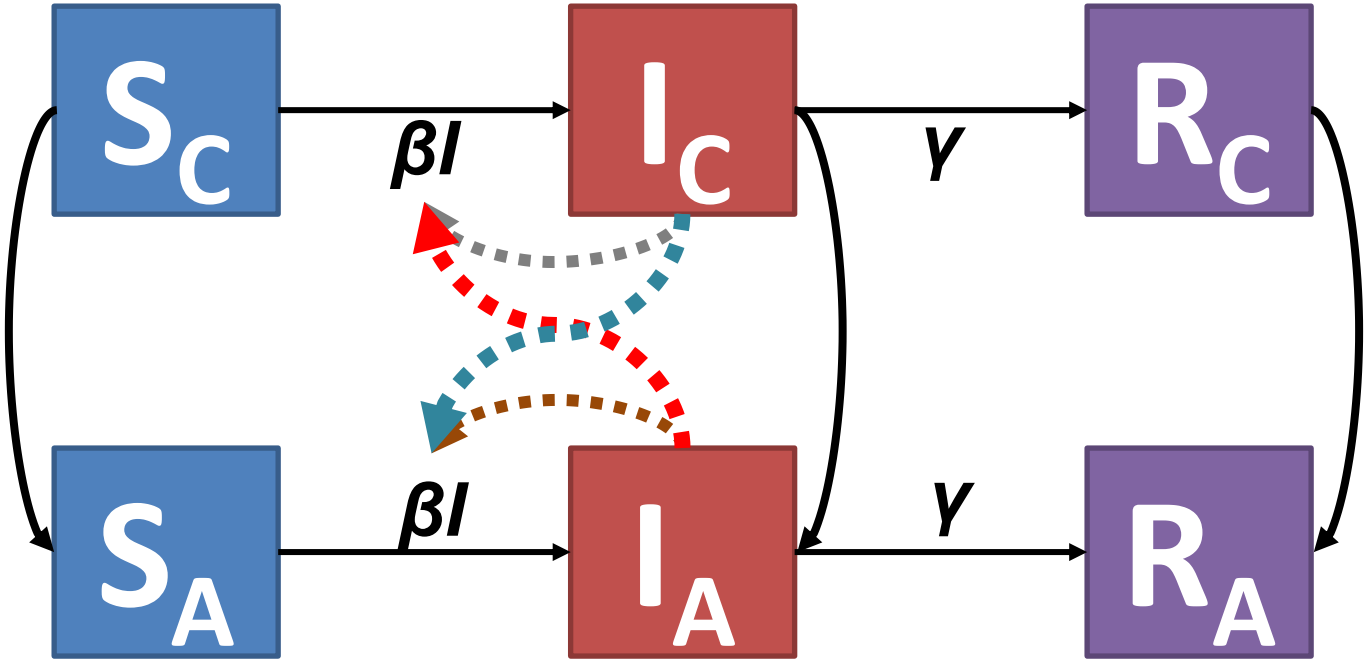
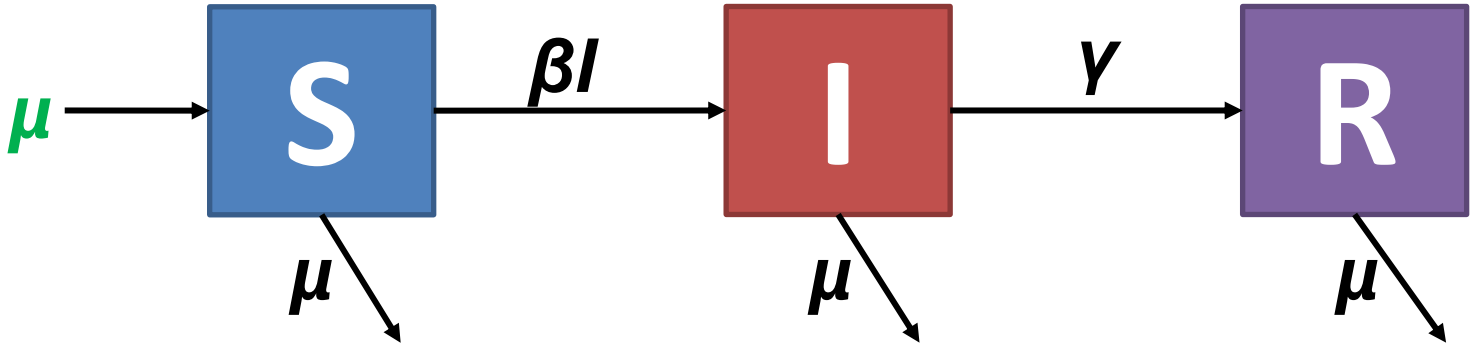
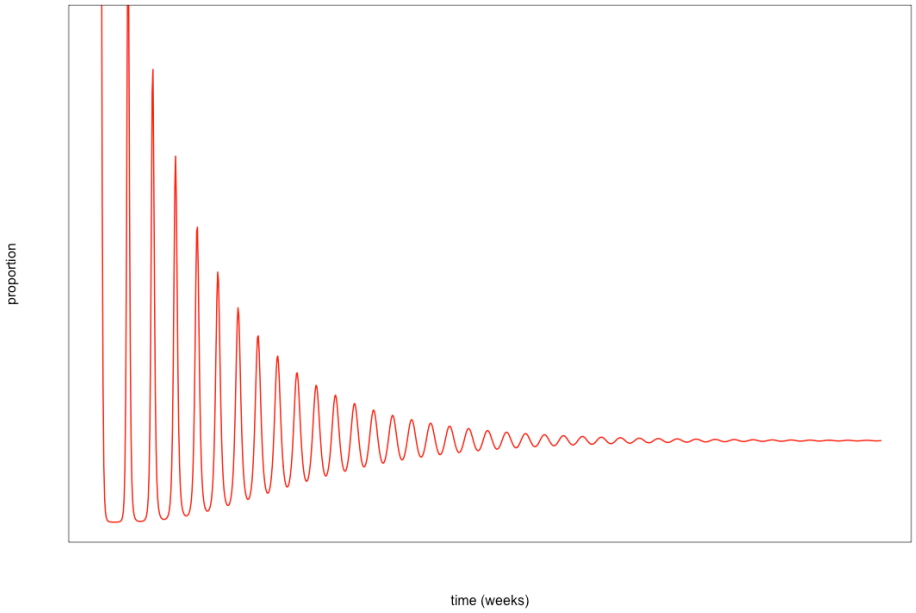


FIXED AND TIME-VARYING MODEL PARAMETERS

Remember: SIR model with demography have Damped Oscillatory Dynamics if their endemic equilibria are feasible





Seasonal variation in contacts

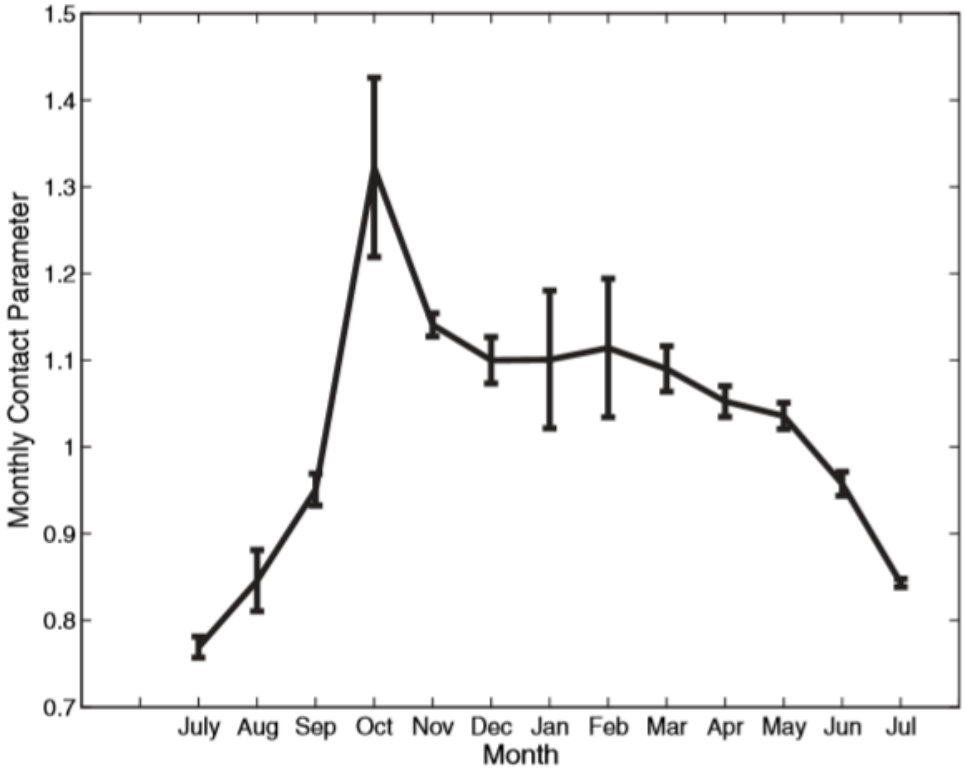


Figure 5.2. Average monthly contact coefficient for measles in Glasgow 1905–1916, as estimated by Soper (1929). The graph clearly highlights the non-constant nature of transmission, with the highest intensity observed during the fall/winter months. Error bars represent standard errors.

Define contacts as oscillating over time

$$\beta = \beta_0\left(1 + \beta_1 cos(\omega t)\right), where\ 0 \leq \beta_1 \leq 1$$

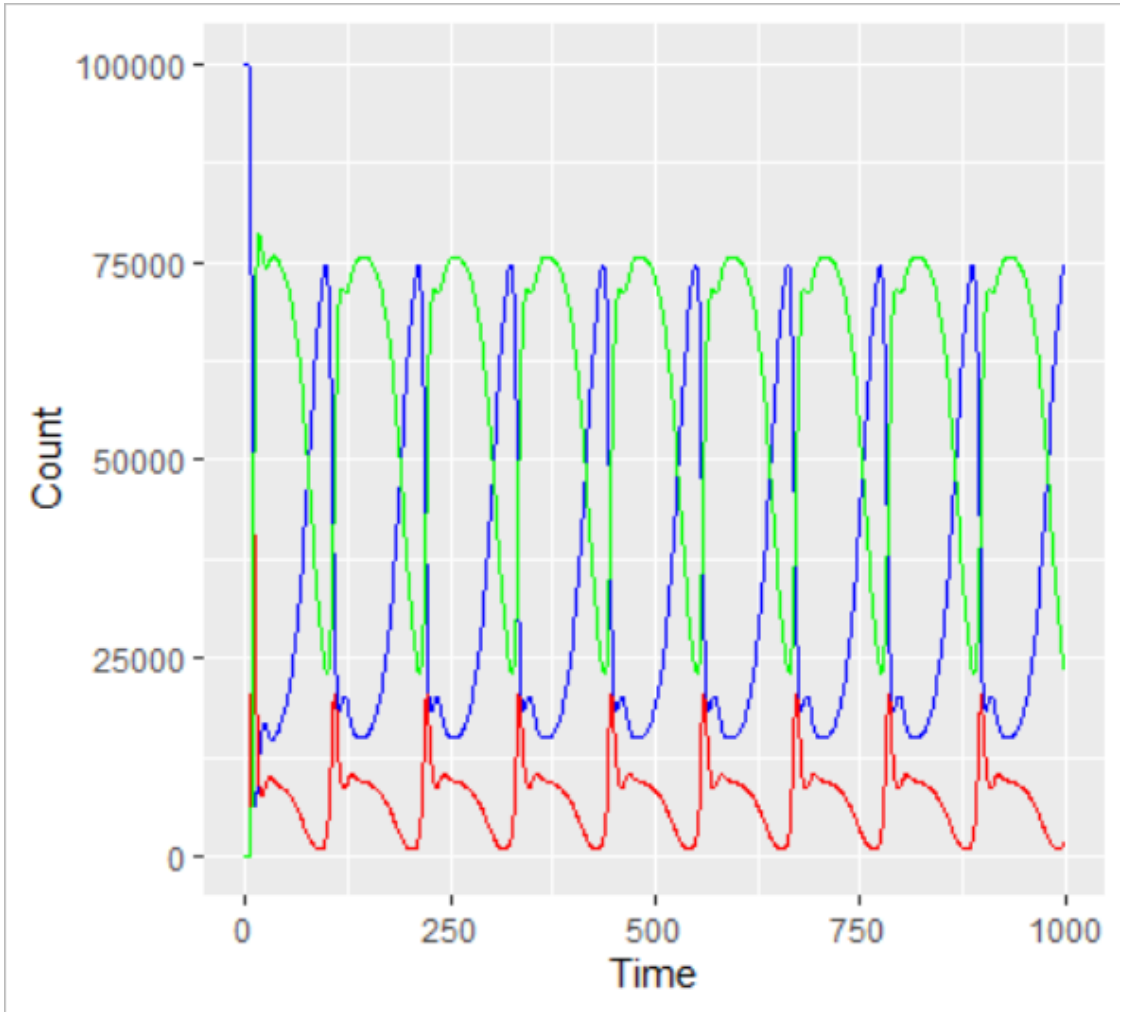
$$\frac{dS}{dt} = \mu - \beta IS - \mu S$$

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

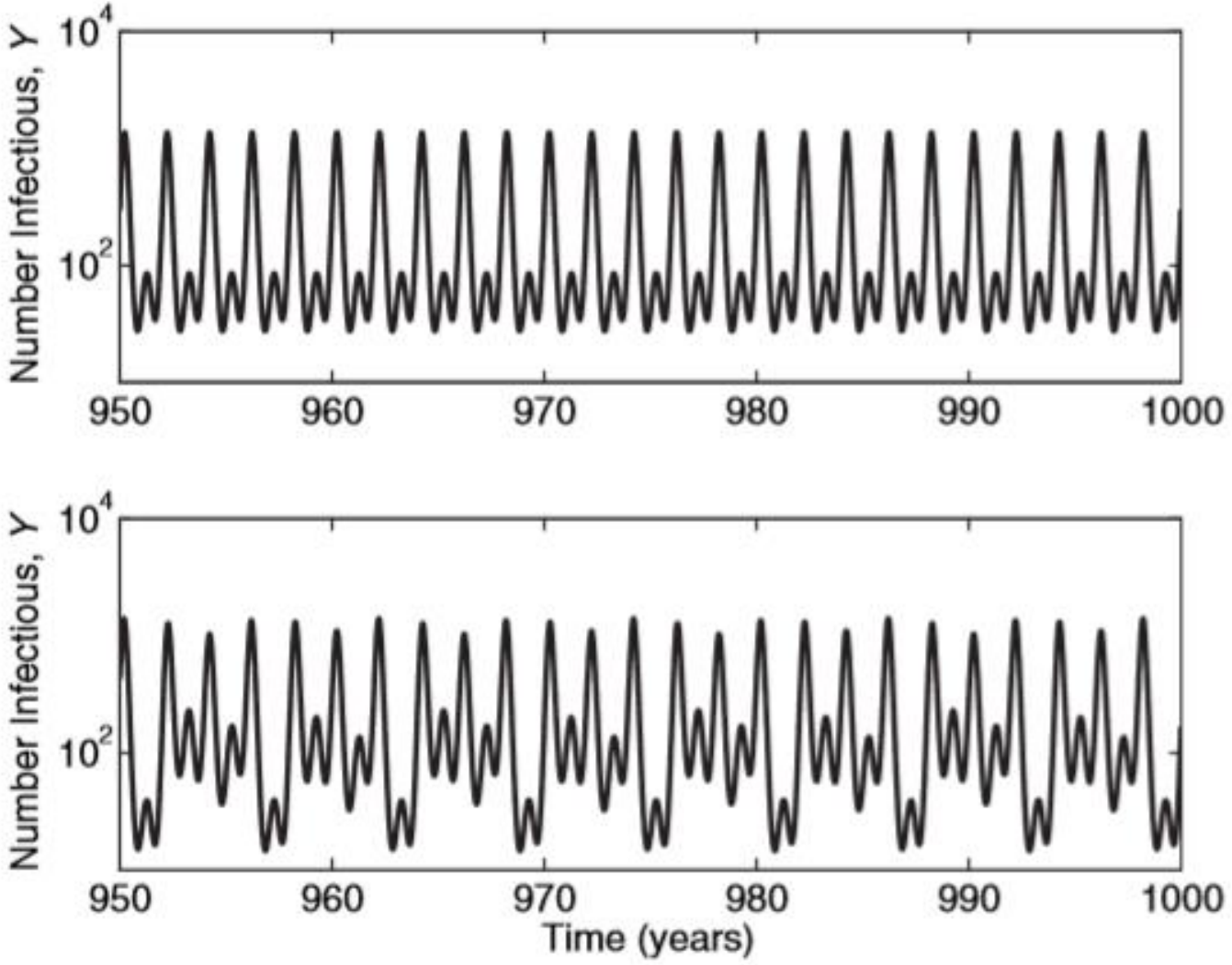
$$\frac{dR}{dt} = \gamma I - \mu R$$

Overall oscillations bigger when forcing (the push) happens in (near) synchrony with the frequency of the underlying oscillation

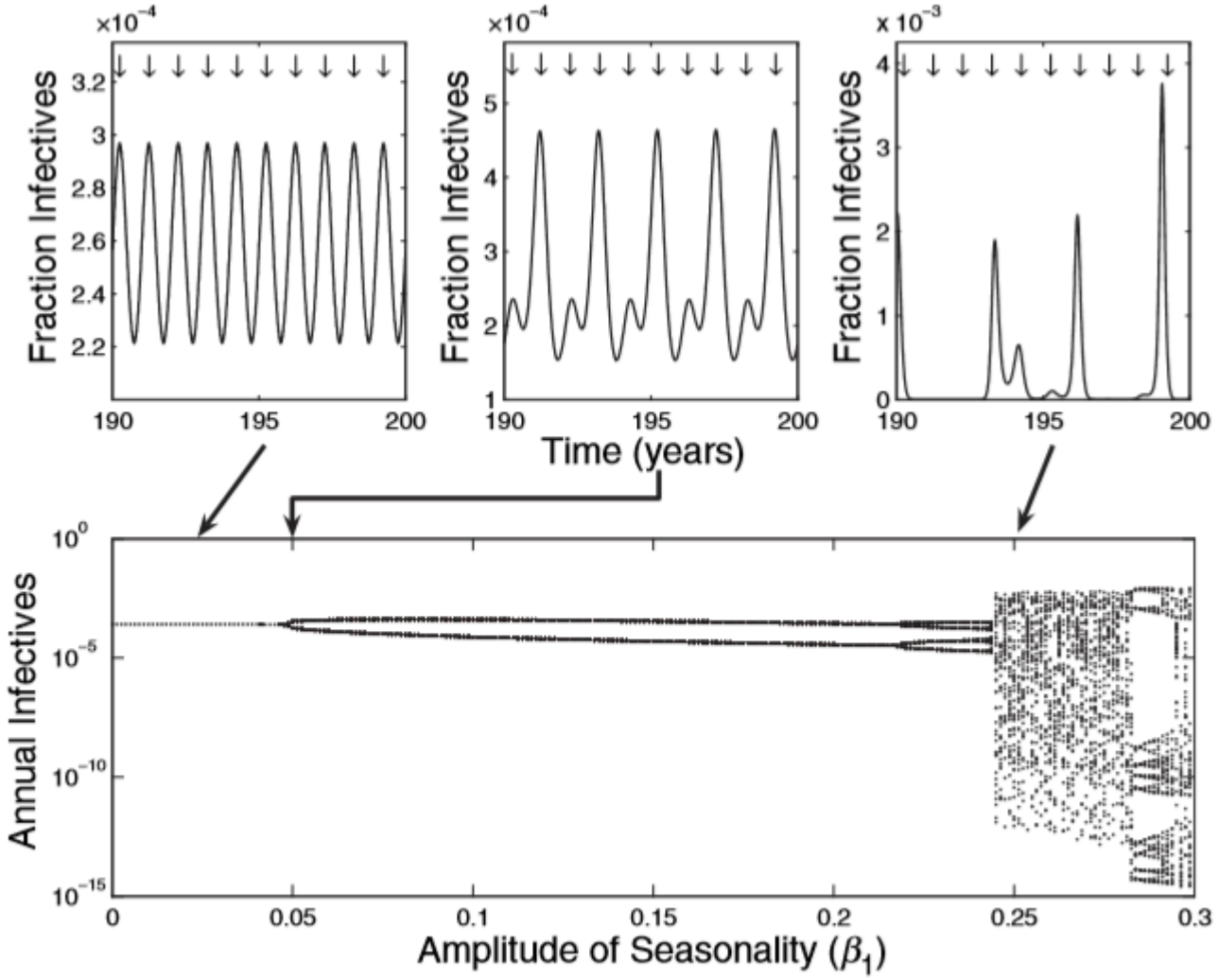
Complicated dynamics can emerge: The combination of damped oscillation and the seasonal forcing oscillation



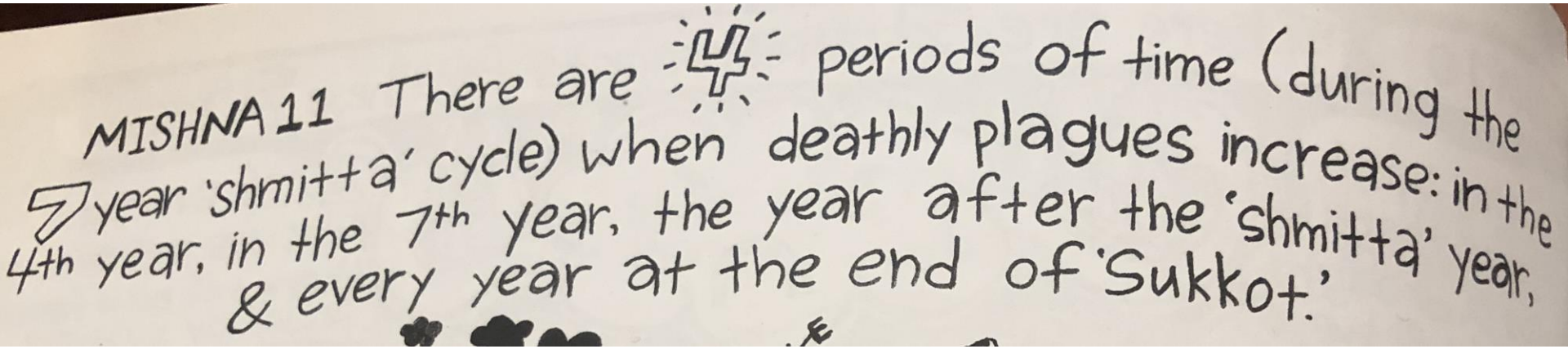
Complicated dynamics can emerge: They also depend on initial conditions



Bifurcation Diagrams Can Show How the Periodicity (or Chaotic Nature) of the System Depends on Parameters (Beta1)



People were aware of these phenomena a long time ago



Misha ~450 BCE

3 deathly plague years during the 8-year (shmitta) cycle:

What is the periodicity?

Annual plagues that occur at a specific time of year (Sukkot) right after people would congregate as a pilgrims, coming from many places and live in little outdoor booths for a week in Jerusalem

Can we expect certain years to be particularly bad plagues? Why?

Important Announcements