Mathematical Modeling and Analysis of Infectious Disease Dynamics

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MTH 323: Mathematical Modeling
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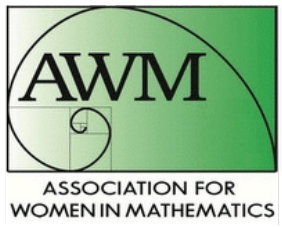

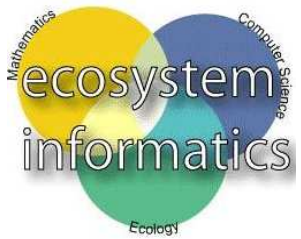

What is Infectious Disease Epidemiology?

Epidemiology: Study of diseases and their determinants in populations

- Epidemiology identifies groups of individuals in populations that have similar characteristics (sex, age, size etc.), ignoring the uniquess of individual members.
- It tries to determine whether this division of individuals into groups tells us something more than we could have learned by merely observing each individual separately.
- The goal is to describe, analyze or understand patterns of disease in such groups.

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Dynamics of infections occur at multiple scales: (micro) within-host, (meso) between hosts, (macro) between populations. We will focus on the meso scale of microparasitic infections (viruses, bacteria, protozoa!)

Why do Mathematical Modeling?

We would like to:

- Understand the competing risks of death from diseases.
- Attempt to limit the extent of infection through some form of control (vaccination, quarantining, social distancing measures, culling in animals and contact tracing)
- Data/resources are limited. Unethical to experiment (humans). We must decide what is the optimal combination and use of our resources.

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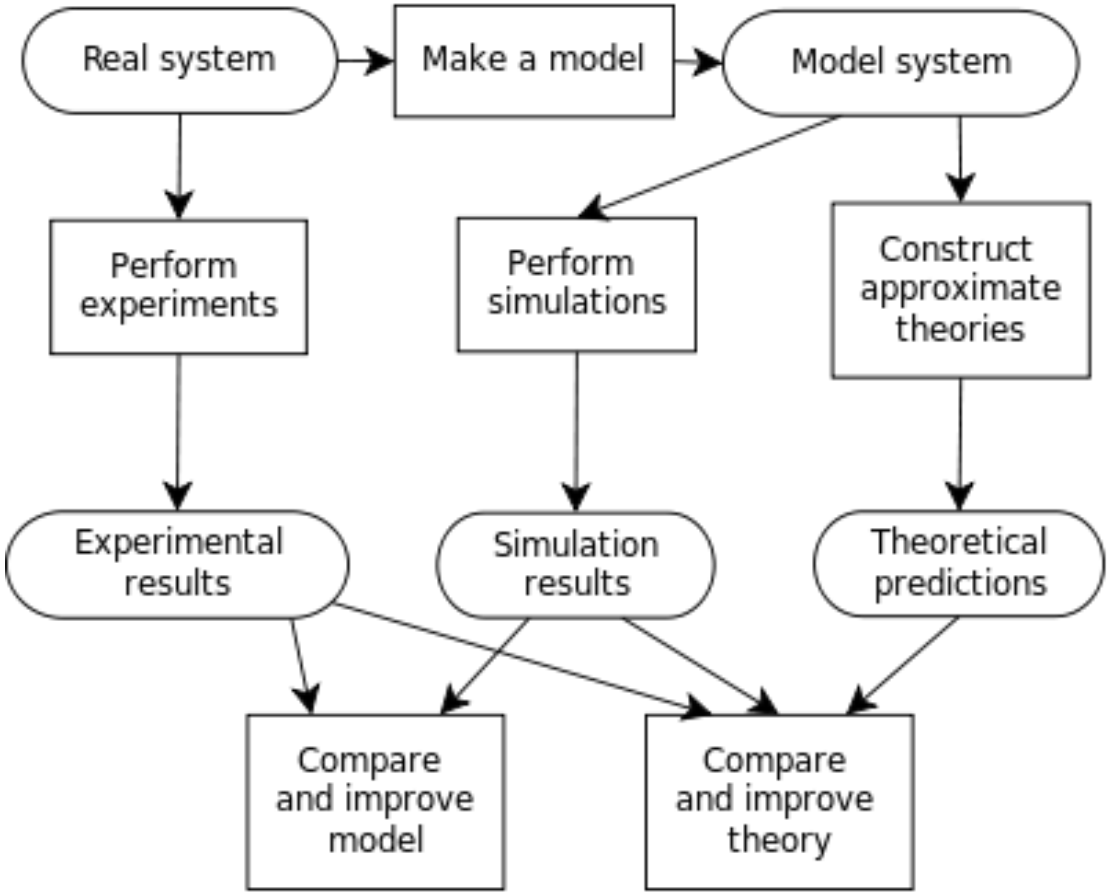
Motivation for Mathematical Modeling: Understand the salient features of infection dynamics; forecast or predict outcomes of diseases in communities and from changes in demographics, community structure, disease characteristics and control.

Scientific Computation: Mathematical Modeling, Analysis, Numerics



Courtesy: Wikipedia

The Beginnings of Mathematical Epidemiology

1. Bernoulli: 1760
   - Daniel Bernoulli formulated and solved a model for smallpox in 1760
   - Using his model, he evaluated the effectiveness of (vaccination) inoculating of healthy people against the smallpox virus.
2. Hamer: 1906
   - Hamer formulated and analyzed a discrete time model in 1906 to understand the recurrence of measles epidemics.
3. Ross: 1911
   - Ross developed differential equation models for malaria as a host-vector disease in 1911.
   - He won the second nobel prize in medicine
4. Kermack and McKendrick: 1926
   - Extended Ross's models.
   - Obtained the epidemic threshold results.

Deterministic Compartmental Models

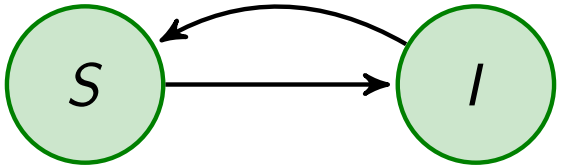
Basic Ideas and Assumptions

- Populations under study are divided into compartments.
- (constant) Rates of transfer between compartments are expressed mathematically as derivatives with respect to time of the sizes of the compartments: systems of ordinary differential equations
- The community size is constant over the duration of the epidemic and is a large number, N.
- The infection is transmitted primarily by person-to person contacts (e.g., measles)
- Individuals are homogeneous and mix uniformly.
- Ignore demography, i.e., births and deaths

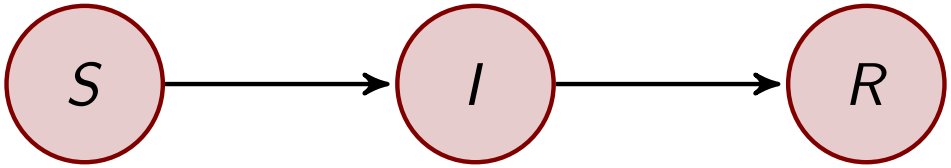
Basic Compartmental Deterministic Models

SIS, SIR, SEIR

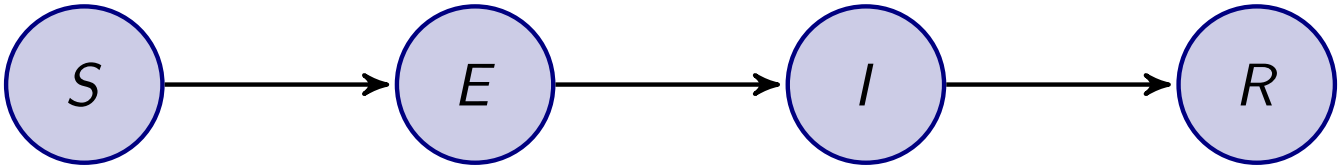
SIS Model



SIR Model



SEIR Model



Basic Compartmental Deterministic Models

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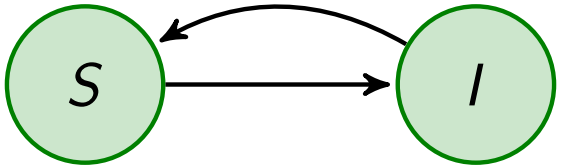
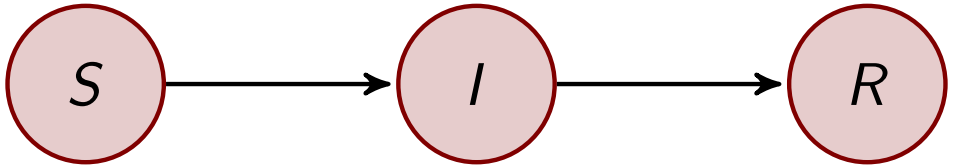
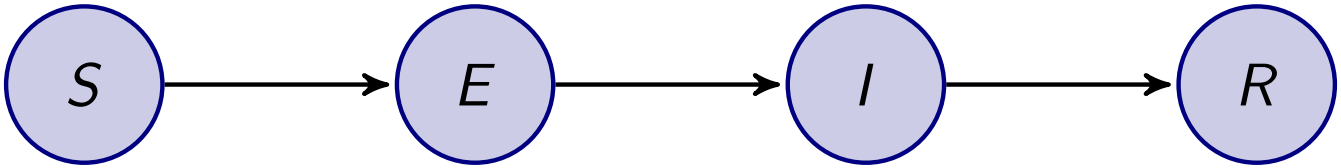


SIR Model



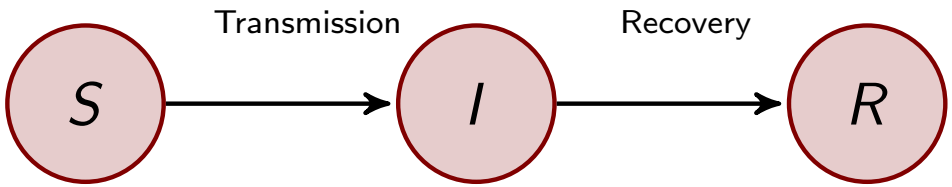
SEIR Model



The choice of which compartments to include depends on the characteristics of the particular disease being modeled and the purpose of the model.

The SIR Epidemic Model

The SIR Epidemic Model



Compartments

- Susceptibles (S): Individuals susceptible to the disease
- Infectious (I): Infected Individuals able to transmit the parasite to others
- Recovered (R): Individuals that have recovered, are immune or have died from the disease and do not contribute to the transmission of the disease

$S = S(t), I = I(t), R = R(t)$ and $N = S(t) + I(t) + R(t)$

SIR Epidemic Model: Compartmental Transfer Rates

Transmission Assumptions

- $\beta =$ Average number of adequate contacts (i.e., contacts sufficient for transmission) of a person per unit time.
- $\frac{\beta I}{N}$ Average number of contacts with infectives per unit time of one susceptible.
- $\left(\frac{\beta I}{N}\right) S$ Number of new cases per unit time due to the S susceptibles. (*Horizontal Incidence*)

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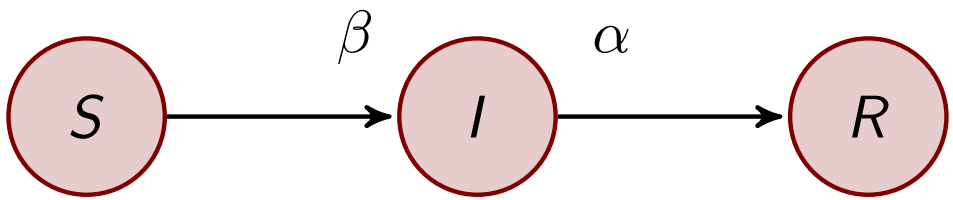
Recovery Assumptions

- A fraction α of infectives leave the infective class in unit time.
- There is no entry or departure from the population except possibly through death from the disease.

The Basic SIR Epidemic Model

The SIR Epidemic Model



The deterministic SIR epidemic model for this process is

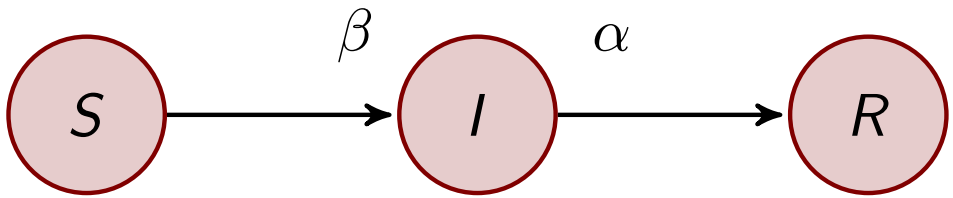
$$\frac{dS}{dt} = -\beta I \frac{S}{N}$$
$$\frac{dI}{dt} = \beta I \frac{S}{N} - \alpha I$$
$$\frac{dR}{dt} = \alpha I$$

The parameters of the model are

- $\beta =$ the transmission rate (effective contact rate)
- $\alpha =$ the recovery or removal rate

The Basic SIR Deterministic Epidemic Model

The SIR Epidemic Model



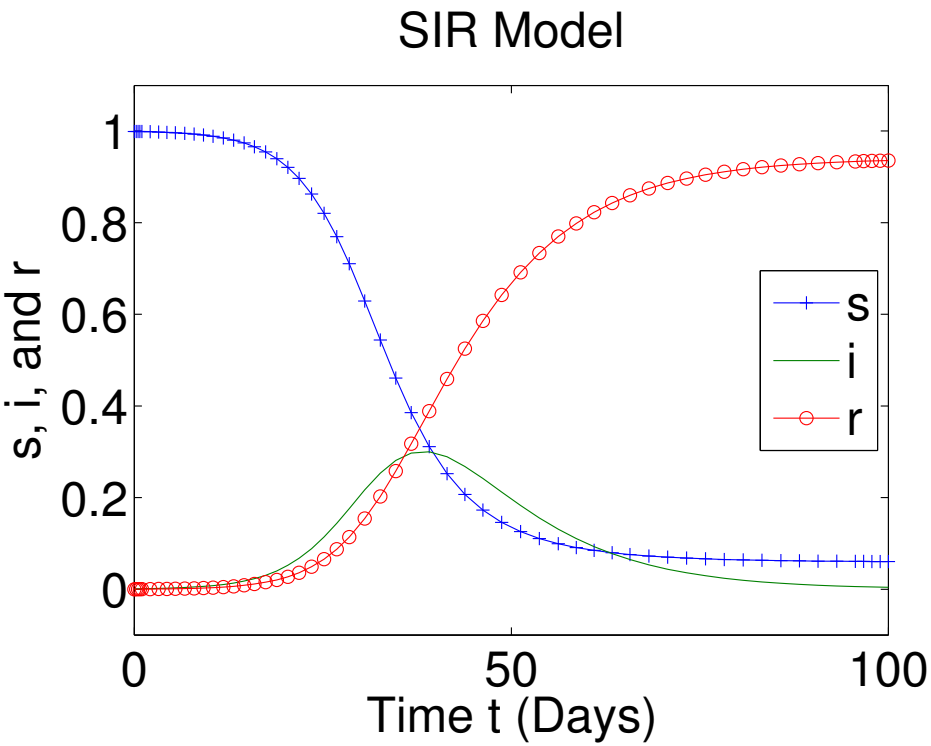
Let $s = S/N$, $i = I/N$ and $r = R/N$. Dividing the equations for S, I and R by N we get the deterministic SIR epidemic model for this process in the form

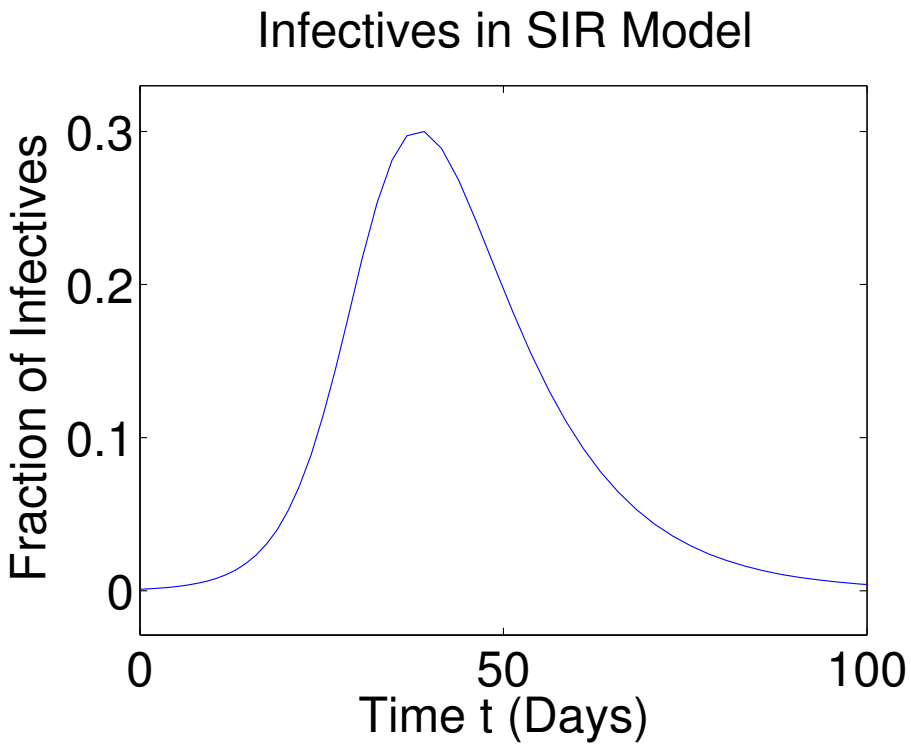
$$\frac{ds}{dt} = -\beta si$$
$$\frac{di}{dt} = \beta si - \alpha i$$
$$\frac{dr}{dt} = \alpha i$$

The Basic SIR Deterministic Epidemic Model: A Numerical Simulation

Example 1

- Initial values are: $i(0) = 0.001$, $s(0) = 0.999$, $r(t) = 0$,
- Parameter values are: $\beta = 0.3$, $\alpha = 0.1$.

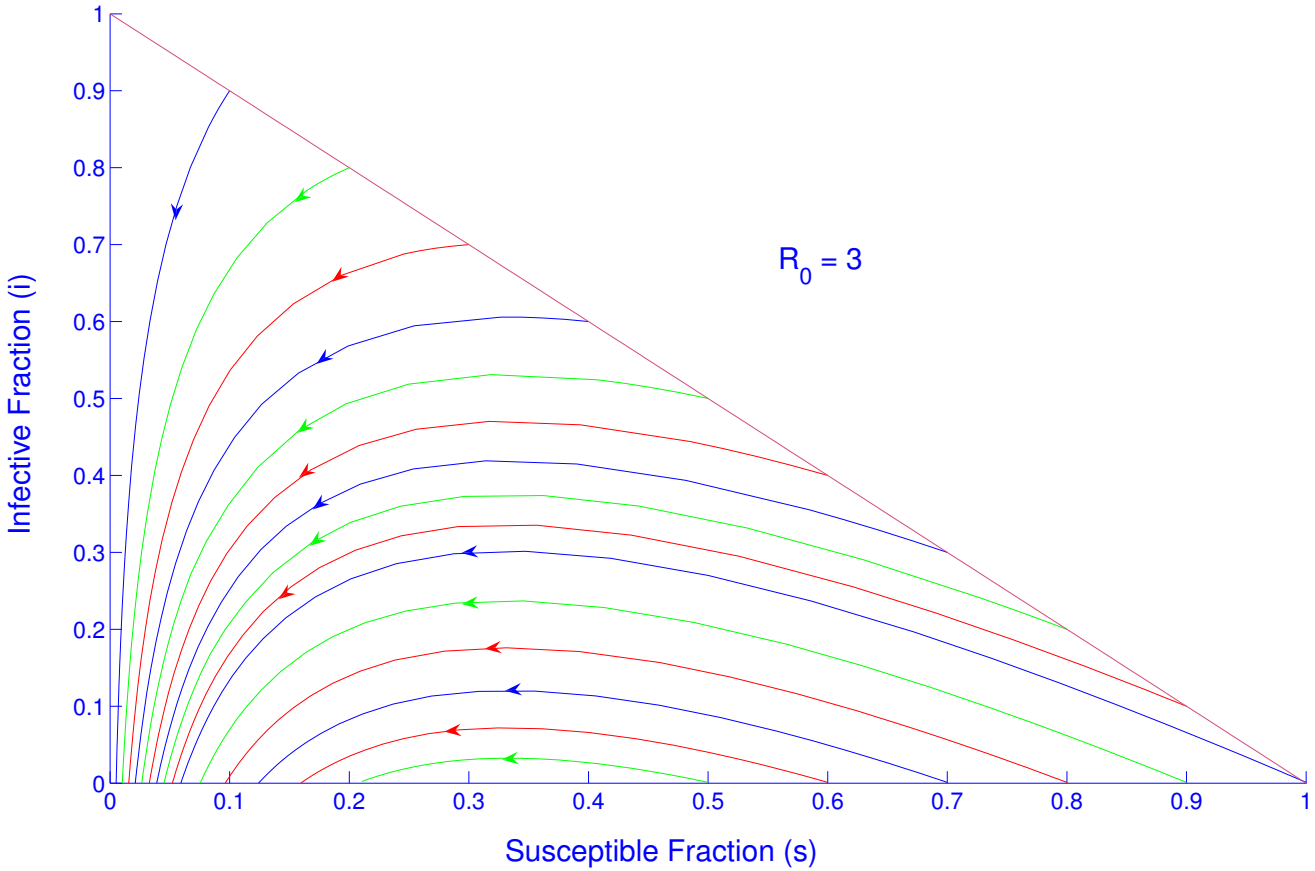




Model predicts that there is an epidemic.

The Basic SIR Epidemic Model: Phase Plane Portrait for Example 1

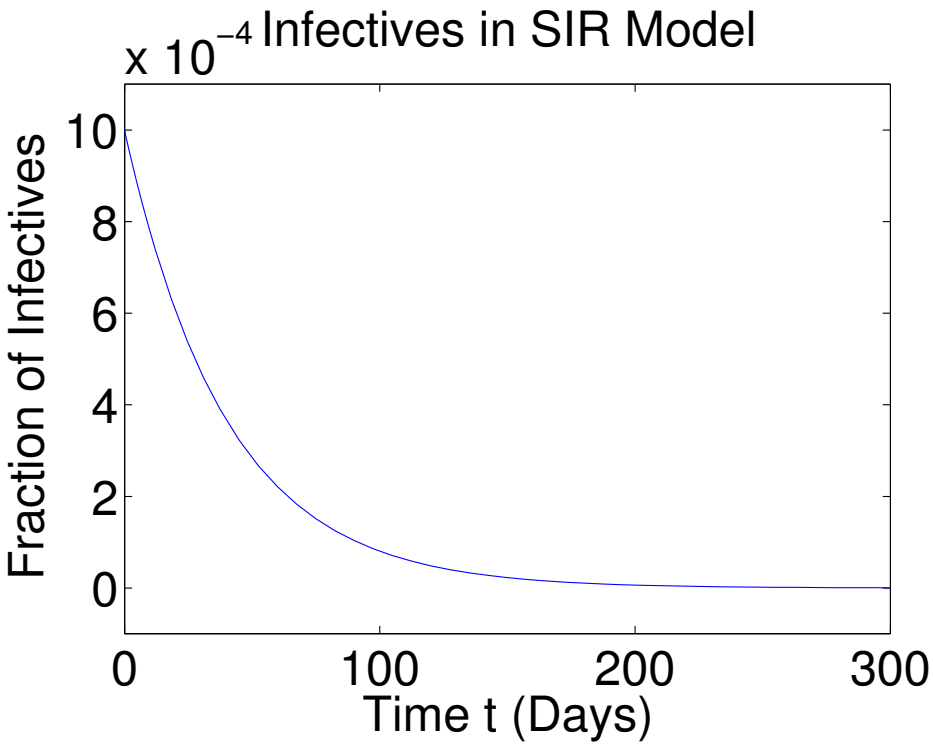
- Parameter values are: $\beta = 0.3$, $\alpha = 0.1$.
- The Basic Reproduction Number (BRN) $R_0 = \dfrac{\beta}{\alpha} = 3$

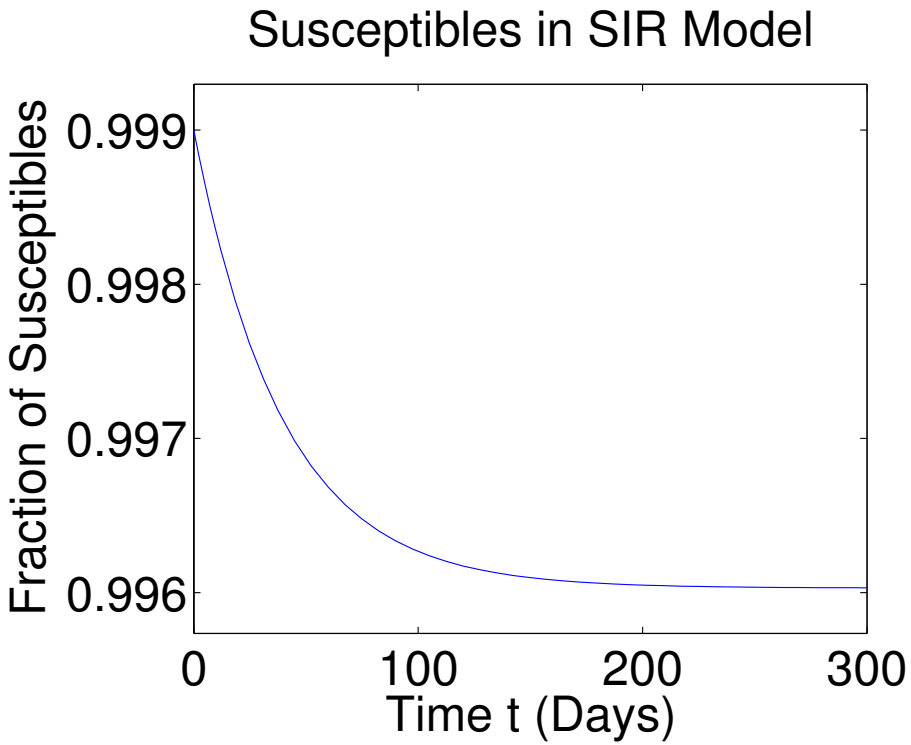


The Basic SIR Deterministic Epidemic Model: A Numerical Simulation

Example 2

- Initial values are: $i(0) = 0.001$, $s(0) = 0.999$, $r(t) = 0$,
- Parameter values are: $\beta = 0.3/4$, $\alpha = 0.1$.

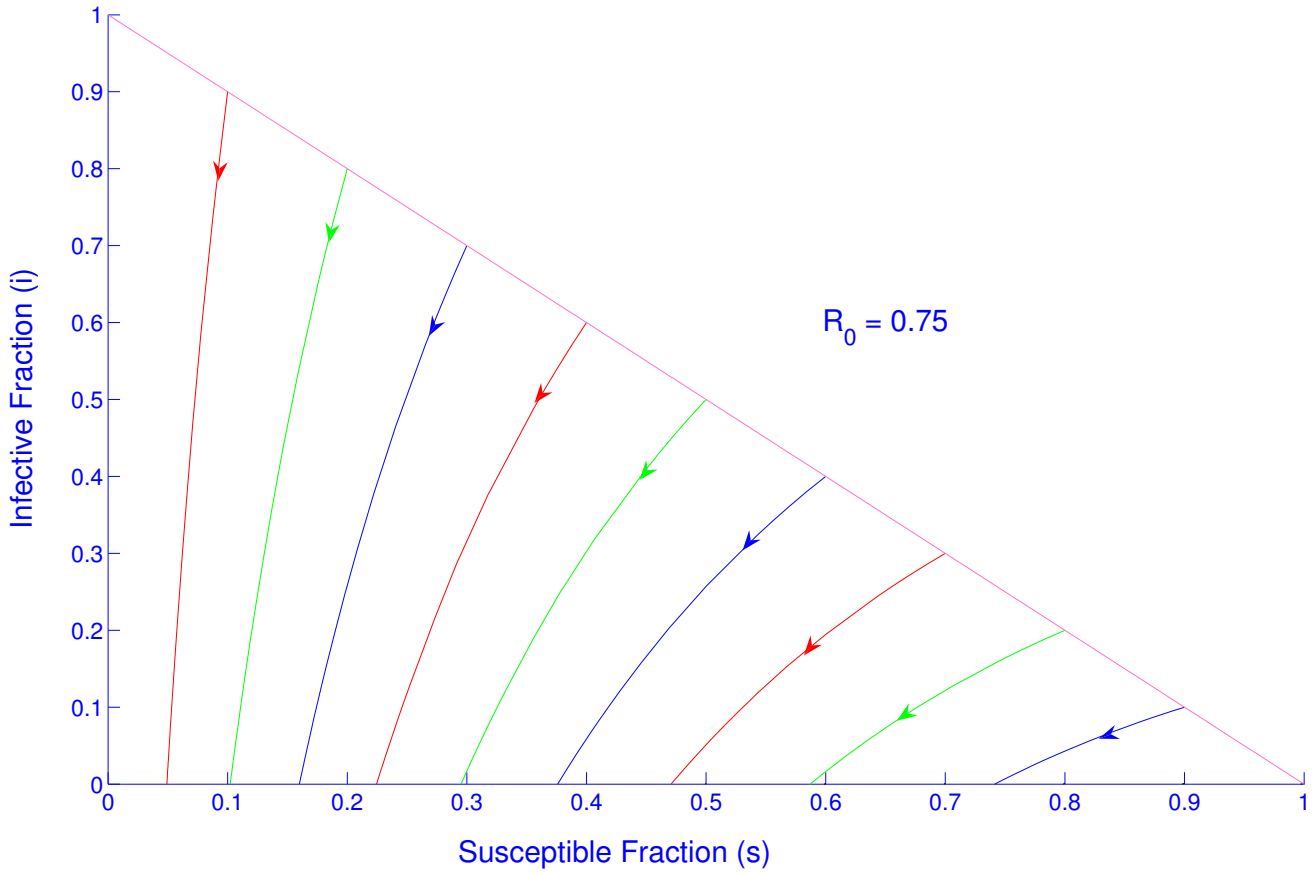




Model predicts that the disease dies out

The Basic SIR Epidemic Model: Phase Plane Portrait for Example 2

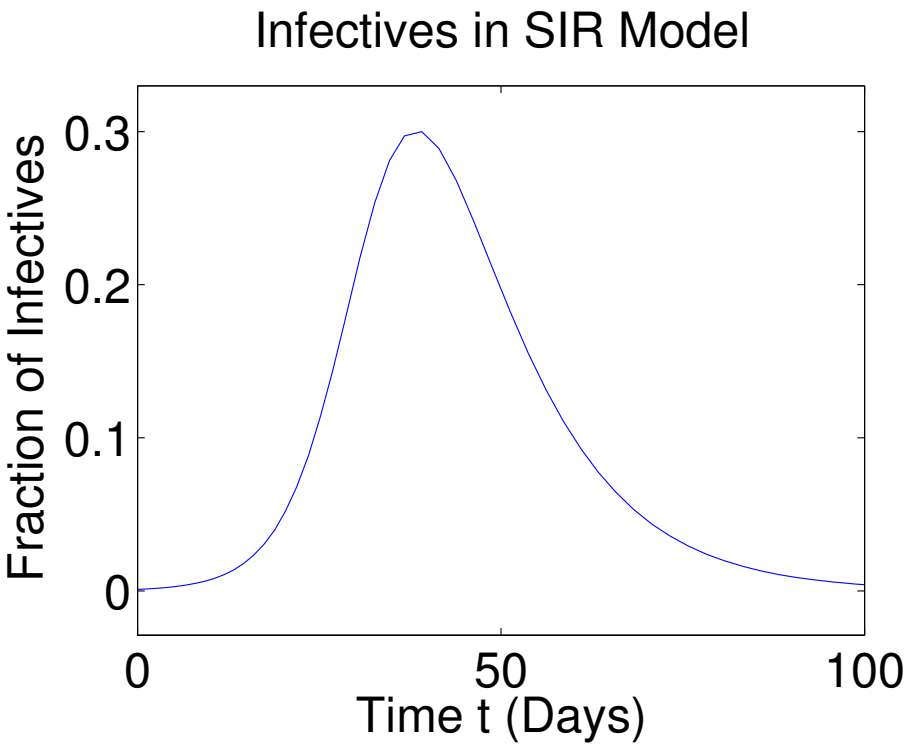
- Parameter values are: $\beta = 0.3/4$, $\alpha = 0.1$.
- The BRN $R_0 = \dfrac{\beta}{\alpha} = 0.75$



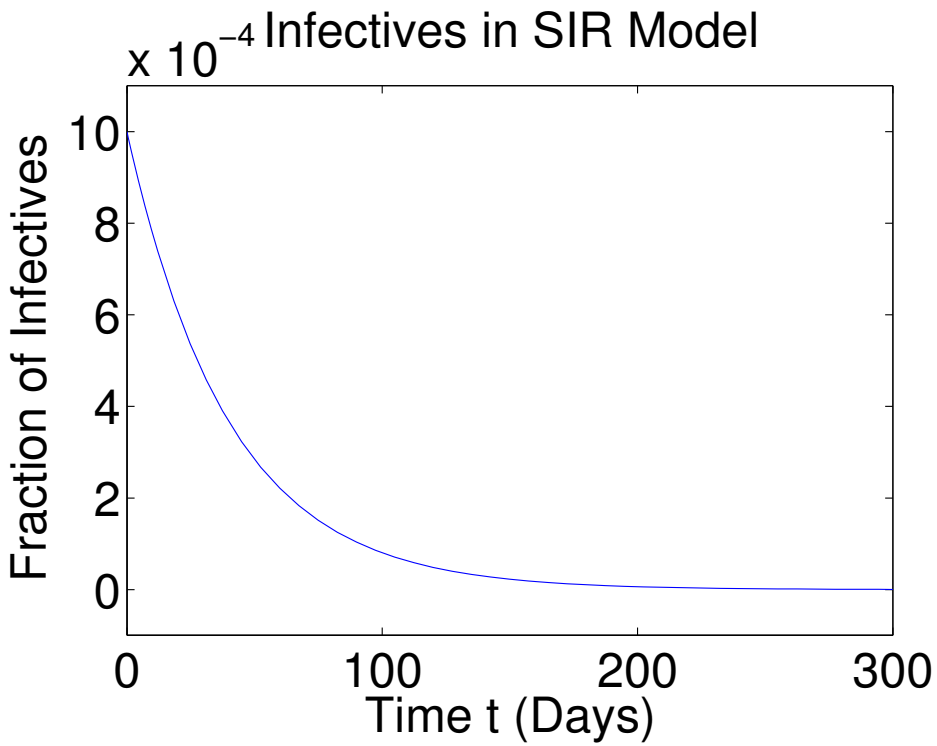
SIR Epidemic Model:
Two Types of Outcomes

We have seen two types of outcomes

$R_0 = 3$

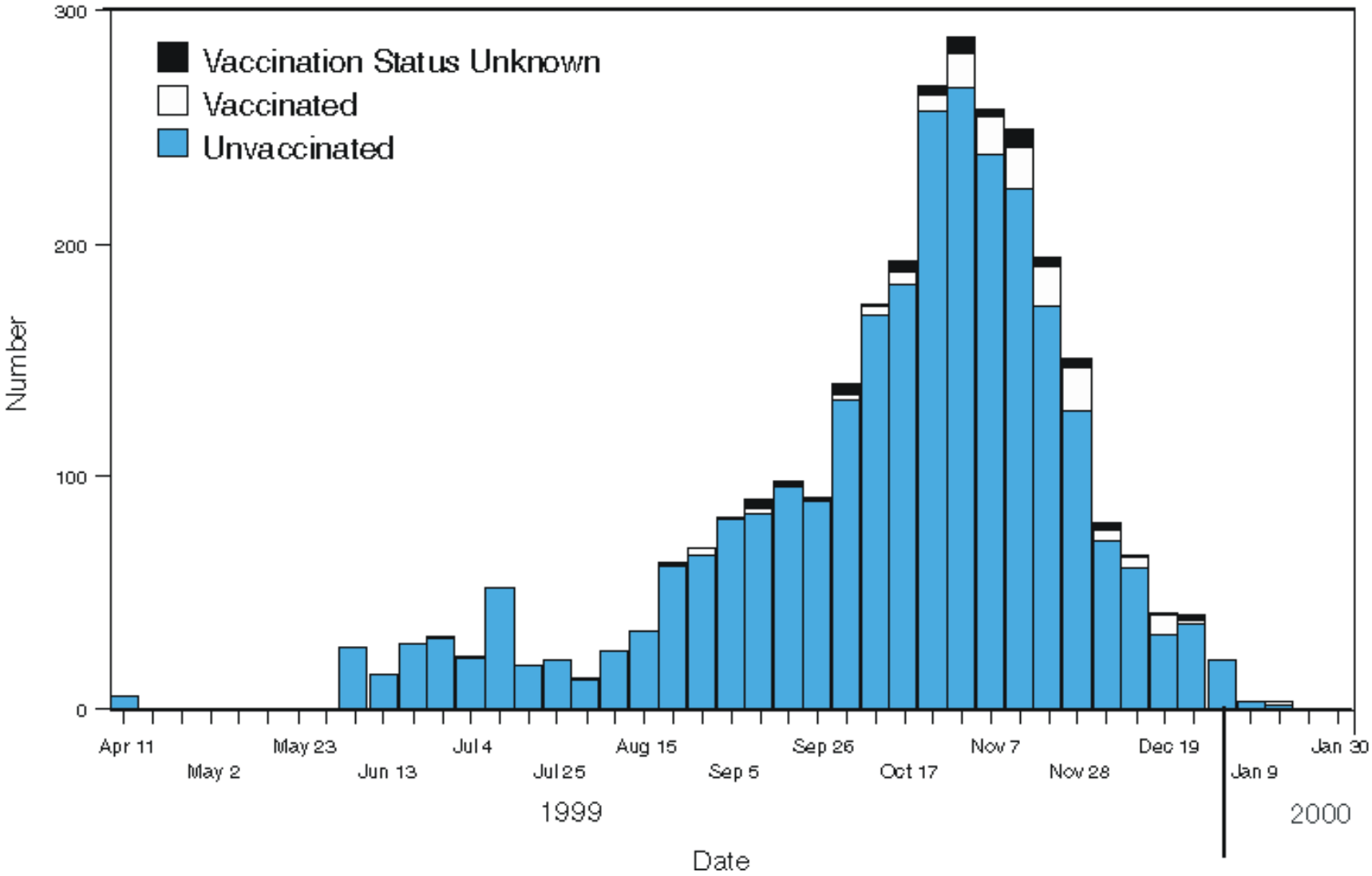


$R_0 = 0.75$



What values of parameters determine the behavior of the model?

What do Real Curves Look Like?



Conditions for an Epidemic

Equation for Infecteds

$$\frac{di}{dt} = \beta si - \alpha i = (\frac{\beta s}{\alpha} - 1)\alpha i$$

- Initially $s(0) \approx 1$
- An epidemic occurs if the number of infecteds increases initially

$$\frac{di}{dt} > 0 \implies \frac{\beta}{\alpha} > 1$$

- The disease dies out if the number of infecteds decreases initially

$$\frac{di}{dt} < 0 \implies \frac{\beta}{\alpha} < 1$$

- Example 1: $\frac{\beta}{\alpha} = 3 > 1$ Example 2: $\frac{\beta}{\alpha} = 0.75 < 1$
- The number $\frac{\beta}{\alpha} = R_0$, is called The Basic Reproduction Number

The Basic Reproduction Number

R_0 for the Basic SIR Model

$$R_0 = \frac{\beta}{\alpha} = \beta \times \frac{1}{\alpha}$$
$$= (\text{average } \# \text{ of adequate contacts of a person/unit time})$$
$$\times (\text{mean waiting time in the infectious compartment})$$

Definition of R_0

The mean number of secondary infections generated by a single infected in a completely susceptible population

Conditions for an Epidemic

- If $R_0 > 1$ an epidemic occurs in the absence of intervention.
- If $R_0 < 1$ the disease dies out.

Qualitative Analysis of SIR Model

Let $T = \{(s, i) \,|s \geq 0, i \geq 0, s + i \leq 1\}$. Then T is *positively invariant* and unique solutions to the SIR model exist in T for all positive times, so that the SIR model is mathematically and epidemiologically well-posed.

THEOREM: Let $((s(t), i(t))$ be a solution of the SIR model in T.

1. If $R_0 s(0) > 1$, then $i(t)$ first increases up to a maximum value $i_{\max} = i(0) + s(0) - 1/R_0 - [\ln(R_0 s(0))]/R_0$ and then decreases to zero as $t \to \infty$. The susceptible fraction $s(t)$ is a decreasing function and the limiting value s_∞ is the unique root in $(0, 1/R_0)$ of the equation
$$i(0) + s(0) - s_\infty + \ln(s_\infty/s(0))/R_0 = 0$$
2. If $R_0 s(0) < 1$, then $i(t)$ decreases to zero at $t \to \infty$.

What Else Does the Model Tell Us?

Preventing Epidemics

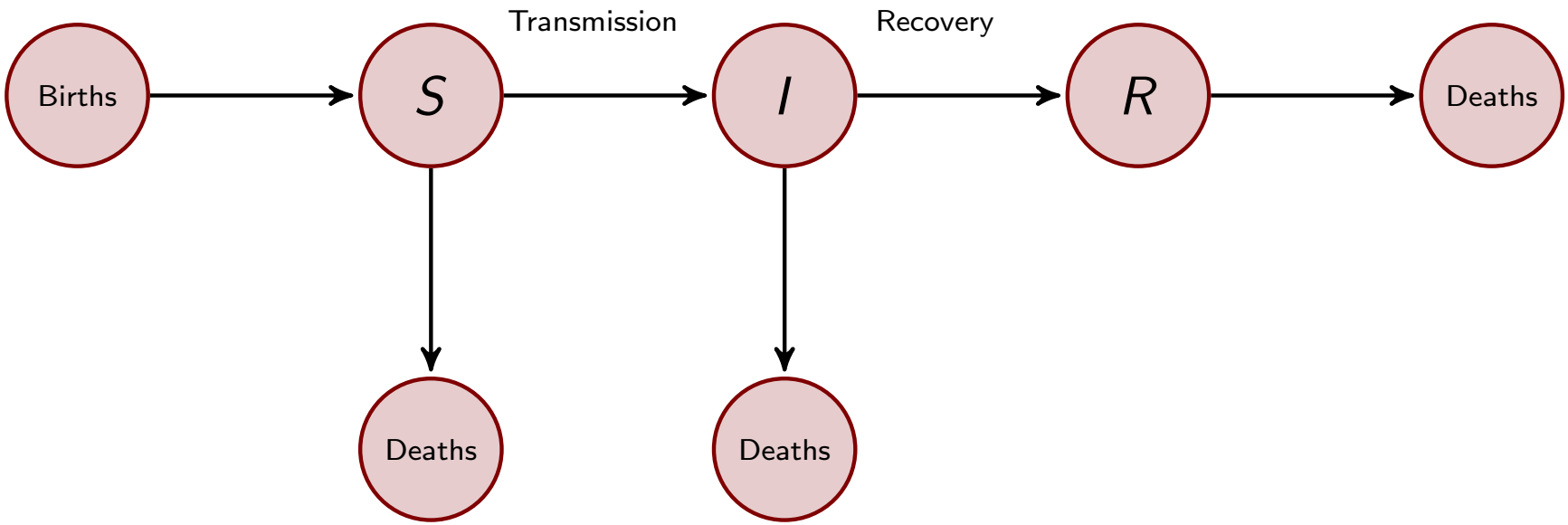
If $R_0 > 1$ an epidemic is prevented when $R_0 s(0) < 1$. Thus, if the initial susceptible fraction has been reduced to less than $1/R_0$, for example by immunization, then an epidemic can be prevented.

The SIR Endemic Model

Additional Assumptions

Include demography, i.e., births and deaths

The SIR Endemic Model



The Basic SIR Deterministic Endemic Model

Assumptions

- An infection is endemic in a community when transmission persists.
- This requires replenishment of susceptibles.
- This happens by including births and deaths.
- We are now working on longer time scales.

The Basic SIR Deterministic Endemic Model

Let $s = S/N$, $i = I/N$ and $r = R/N$.

SIR endemic model

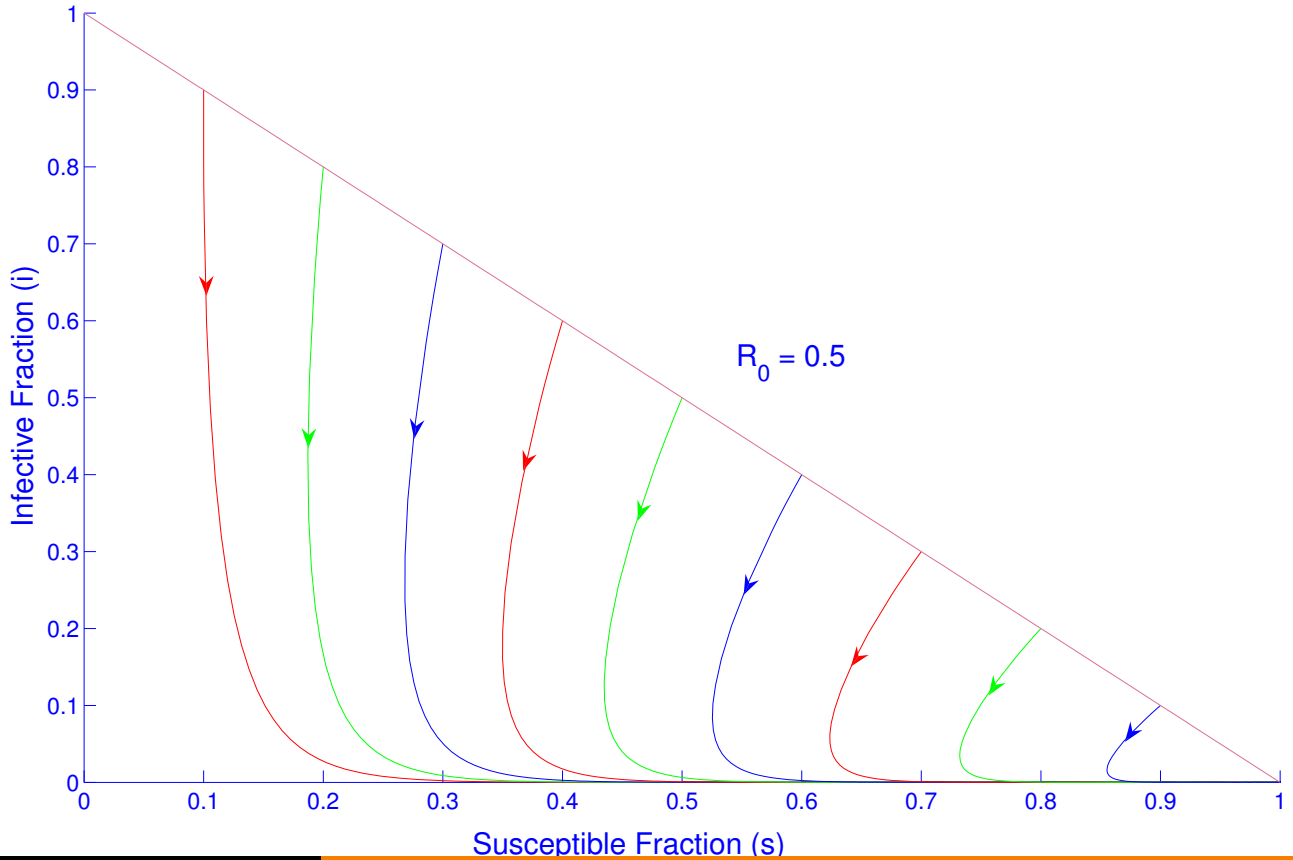
$$\frac{ds}{dt} = \lambda - \lambda s - \beta si$$
$$\frac{di}{dt} = \beta si - \alpha i - \lambda i$$
$$\frac{dr}{dt} = \alpha i - \lambda r$$

Parameters

- $\beta =$ the transmission rate (effective contact rate)
- $\alpha =$ the recovery or removal rate
- $\lambda =$ birth, death rate

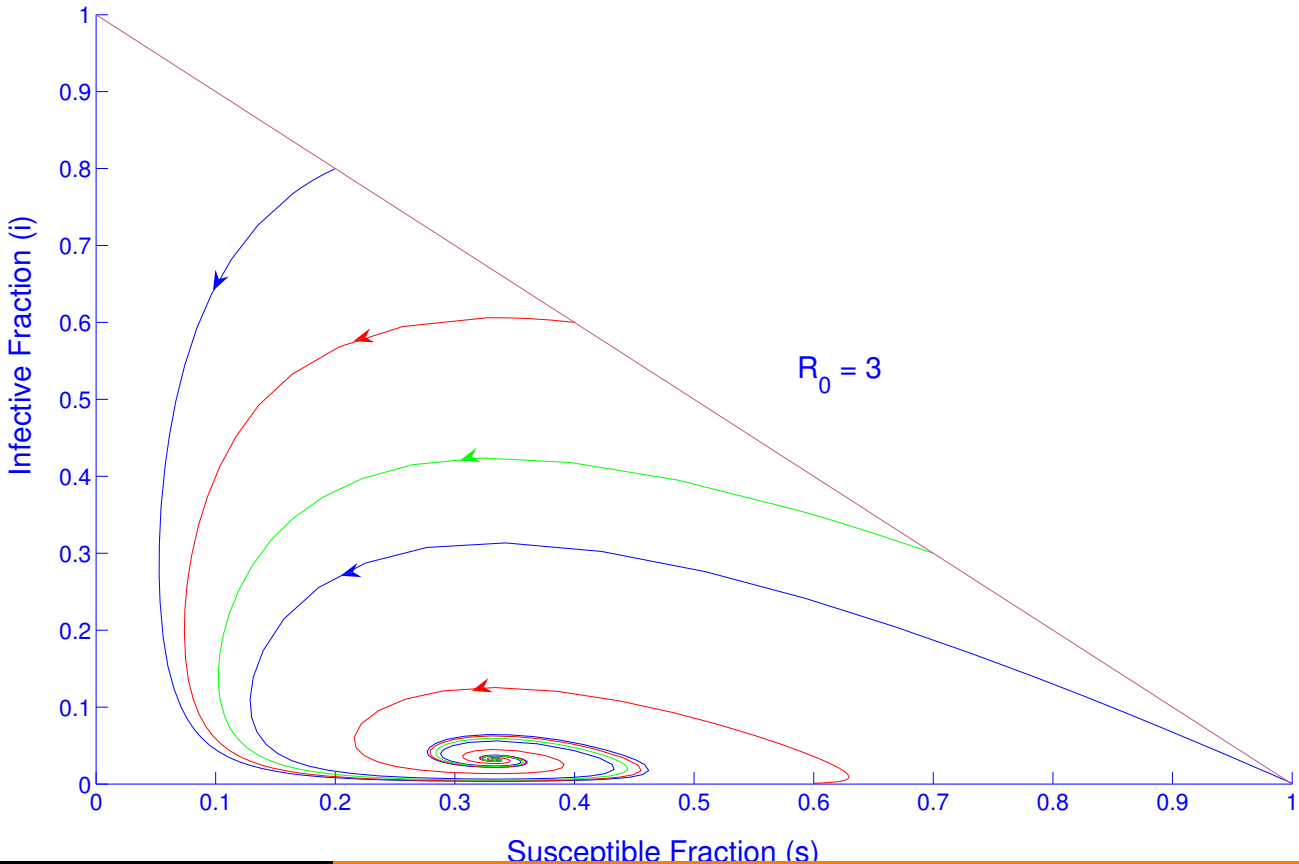
SIR Endemic Model: Phase Portrait, Disease-Free Equilibrium

- Parameter values are: $\lambda = 1/60$, $\beta = 1.05$, $\alpha = 1/3$.
- The BRN $R_0 = \dfrac{\beta}{\alpha + \lambda} = 0.5$
- The endemic SIR model eventually settles down to a Disease Free Equilibrium (DFE).



SIR Endemic Model: Phase Plane Portrait, Endemic Equilibrium

- Parameter values are: $\lambda = 1/60$, $\beta = 1.05$, $\alpha = 1/3$.
- The BRN $R_0 = \dfrac{\beta}{\alpha + \lambda} = 3$
- The endemic SIR model eventually settles down to an *Endemic Equailibrium*.



The SIR Endemic Model: Disease Free OR Endemic Equilibrium

THEOREM: Let $(s(t), i(t))$ be a solution of the endemic SIR model in T. The solution to the endemic SIR model eventually settles down to a steady state. We determine this steady state by solving the equations

$$\frac{ds}{dt} = 0, \quad \text{and} \quad \frac{di}{dt} = 0$$

1. If $R_0 < 1$ or $i(0) = 0$ then all solution paths approach the *Disease Free Equilibrium (DFE)* $s_e = 1,\ i_e = 0$.
2. If $R_0 > 1$ then all solution paths with $i(0) > 0$ approach the *endemic equilibrium* $s_e = \dfrac{\alpha + \lambda}{\beta} = \dfrac{1}{R_0}$ and $i_e = \dfrac{\lambda(R_0 - 1)}{\beta}$.

Limitations of Models

- The two classic models presented assume that the total population size remains constant
- They assume that the population is uniform and homogeneously mixing. Mixing depends on many factors including age.
- Different geographic and social-economic groups have different contact rates.
- These models ignore random effects, which can be very important when s or i are small, e.g., during early stages.

Two Species Disease and Population Dynamics

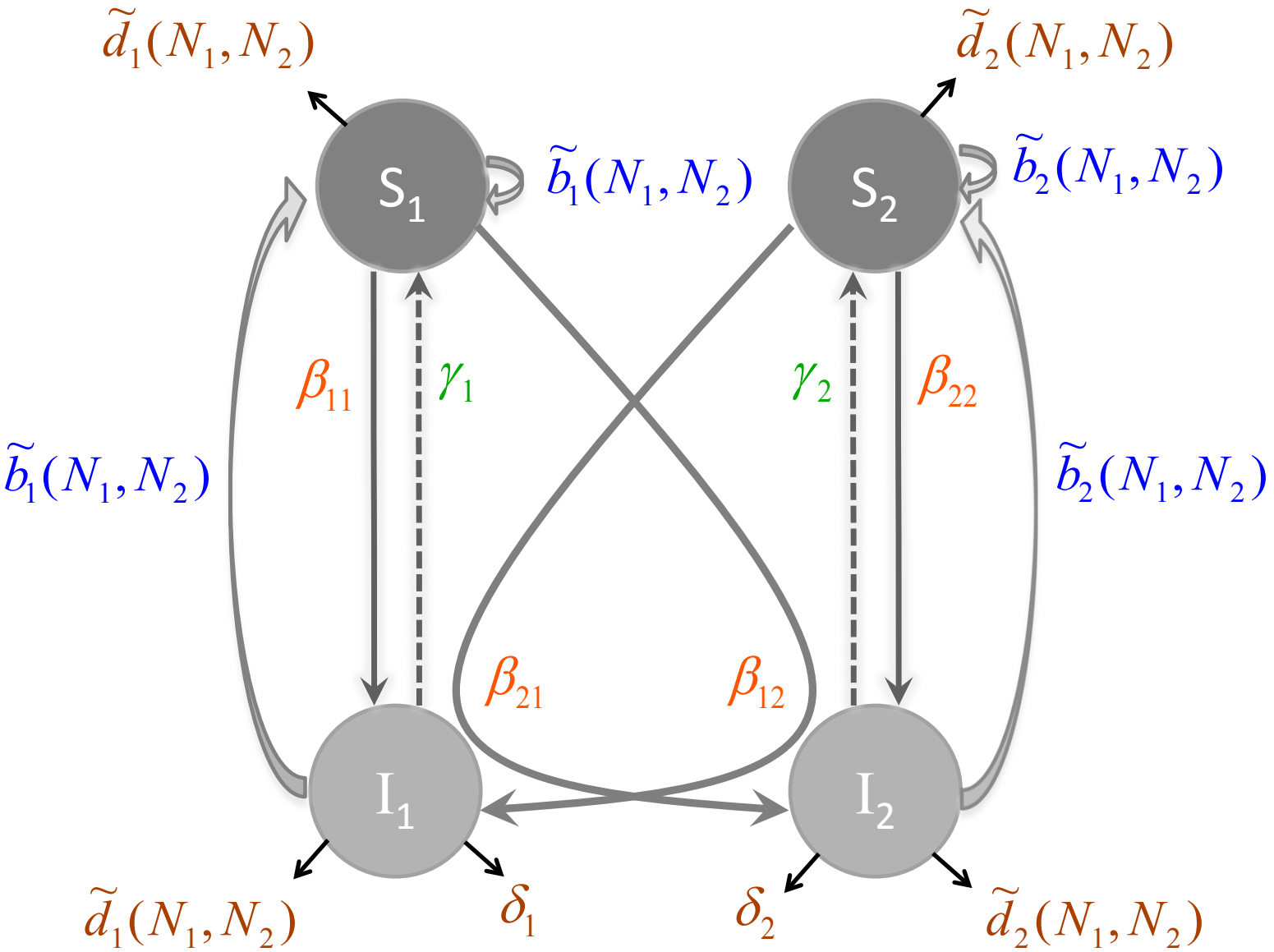
Disease models with birth and growth included are designed to determine long-term dynamics of a population of hosts with a common disease

General Disease and Population Model

$$\frac{dS_1}{dt} = g_1(N_1, N_2) - B_1(S_1, S_2, I_1, I_2)$$
$$\frac{dI_1}{dt} = B_1(S_1, S_2, I_1, I_2) - d_1 I_1$$
$$\frac{dS_2}{dt} = g_2(N_1, N_2) - B_2(S_1, S_2, I_1, I_2)$$
$$\frac{dI_2}{dt} = B_2(S_1, S_2, I_1, I_2) - d_2 I_2$$

- g_i are growth functions, B_i are disease incidence functions for ith species,
- $d_i = \delta_i + \gamma_i$:rates at which members of the infectious class are lost due to disease (δ_i), or recovery (γ_i).

SIS Model: Two Species Transfer Diagram



Competing Species with a Pathogen

We consider n competing species that are affected by one pathogen.

$$\frac{dS_i}{dt} = \overbrace{b_i N_i \left(1 - \sum_{j=1}^{n} a_{ij} \frac{N_j}{\theta_{ij}}\right)}^{\text{birth}} - \overbrace{d_i S_i \left(1 + \sum_{j=1}^{n} (1 - a_{ij}) \frac{N_j}{\psi_{ij}}\right)}^{\text{death}}$$

$$- \underbrace{S_i \sum_{j=1}^{n} \alpha_{ij}(N_j) \frac{I_j}{N_j}}_{\text{infection}} + \underbrace{\gamma_i I_i}_{\text{recovery}},$$

$$\frac{dI_i}{dt} = S_i \sum_{j=1}^{n} \alpha_{ij}(N_j) \frac{I_j}{N_j} - \gamma_i I_i - d_i I_i \left(1 + \sum_{j=1}^{n} (1 - a_{ij}) \frac{N_j}{\psi_{ij}}\right) - \overbrace{\delta_i I_i}^{\text{virulence}},$$

$$\frac{dN_i}{dt} = r_i N_i \left(1 - \sum_{j=1}^{n} \frac{N_j}{K_{ij}}\right) - \delta_i I_i,$$

Disease and Population Model

Why do we care?

A key issue at the interface of community ecology and infectious disease epidemiology is how the interdependence of hosts and parasites affects species coexistence (Collinge and Ray, 2006)

Red and Grey Squirrels

- Native red squirrels are being replaced by non-native grey squirrels in the U.K.
- Simulations indicate competition alone cannot account for the rate of red squirrel decline
- Experiments show that parapoxvirus, carried by grey squirrels, has almost no effect on grey squirrels but causes death in red squirrels (Tompkins, White, and Boots (2003)
- Tompkins, et. al., use a competition and disease model for red and grey squirrels to show that the virus can help ecologists fully understand the process leading to the extinction of red squirrels.

Non Spatial Models of Competition and Disease: Other Examples

Several examples in the literature

- Red and Grey squirrels affected by the *Parapox* virus [Tompkins et. al.] in the United Kingdom.

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- Native and introduced grass species affected by the *Barley and Cereal Yellow dwarf* viruses in Western California and Oregon [Moore et. al.].

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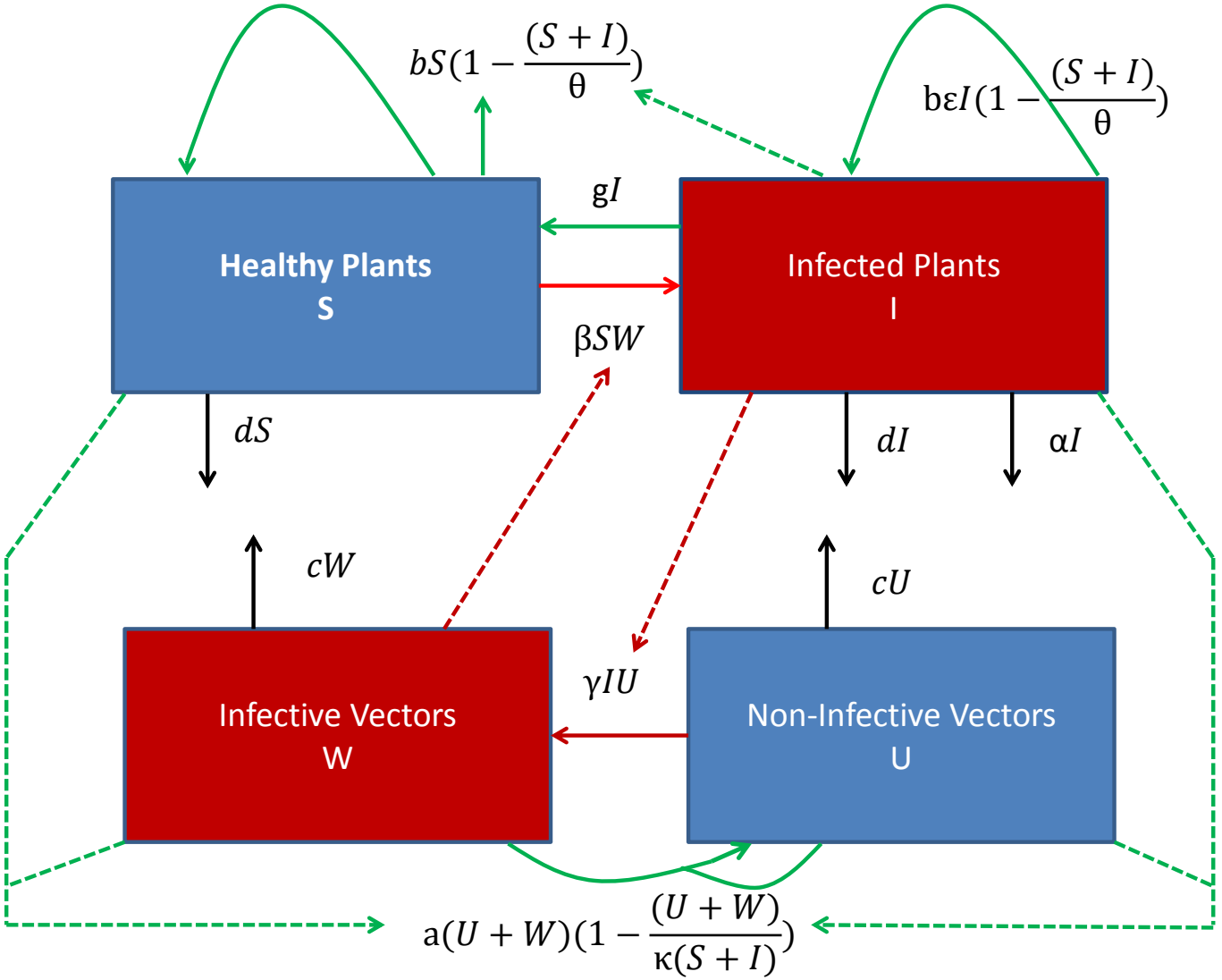
- Native and introduced grass species affected by the *Barley and Cereal Yellow dwarf* viruses in Western California and Oregon [Moore et. al.].
- Multiple species of larval amphibians and a pathogenic water mold *Saprolegnia ferax* [Kiesecker et. al.]




Current Work: Plant Vector Pathogen Model & Infected Planting

Case Study: African Cassava Mosaic Virus



Conclusions

- Different deterministic models can be constructed by choosing different number and types of compartments.
- Analysis based on theory of dynamical systems.
- Modeling clarifies what the underlying assumptions are
- Model analysis and simulation predictions suggest crucial data that should be gathered
- Model analysis and simulation suggest control strategies that could be implemented.
- Estimates of R_0 for various diseases, although crude ballpark estimates for the vaccination-acquired immunity level in a community required for herd immunity, are useful for comparing diseases.

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