Swiss TPH

Swiss Tropical and Public Health Institute
Schweizerisches Tropen- und Public Health-Institut
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Department of Epidemiology and Public Health
Health Systems Research and
Dynamical Modelling Unit

Introduction to SEIR Models

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Workshop on Mathematical Models of Climate Variability,
Environmental Change and Infectious Diseases
Trieste, Italy
8 May 2017

- Population-based models
  - Can be deterministic or stochastic
  - Continuous time
    - Ordinary differential equations
    - Partial differential equations
    - Delay differential equations
    - Integro-differential equations
  - Discrete time
    - Difference equations
- Agent-based/individual-based models
  - Usually stochastic
  - Usually discrete time

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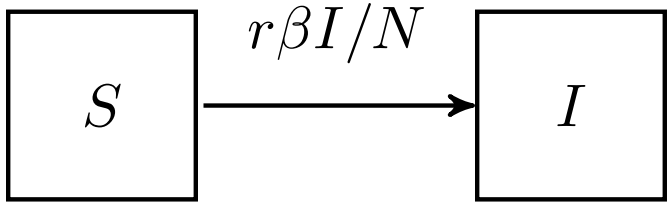
Susceptible-Infectious Model: applicable to HIV.



$$\frac{\mathrm{d}S}{\mathrm{d}t} = -r\beta S\frac{I}{N}$$
$$\frac{\mathrm{d}I}{\mathrm{d}t} = r\beta S\frac{I}{N}$$

S: Susceptible humans
I: Infectious humans
r: Number of contacts per unit time
β: Probability of disease transmission per contact
N: Total population size: $N = S + I$.

The system can be reduced to one dimension,

$$\frac{\mathrm{d}I}{\mathrm{d}t} = r\beta(N - I)\frac{I}{N},$$

with solution,

$$I(t) = \frac{I_0 N}{(N - I_0)e^{-r\beta t} + I_0},$$

for $I(0) = I_0$.

Equilibrium Points:

$$I_{\text{dfe}} = 0$$

$$I_{\text{ee}} = N$$

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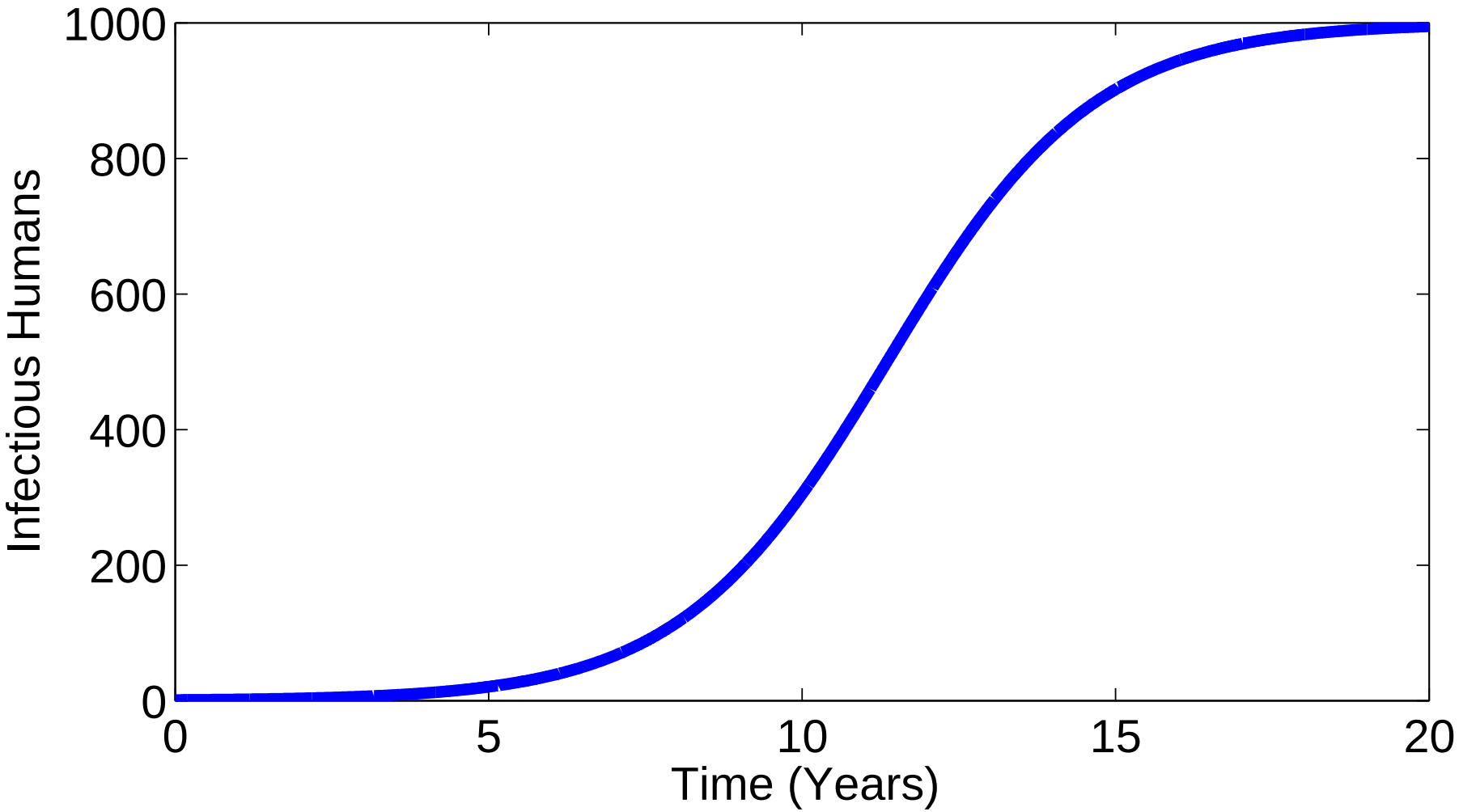
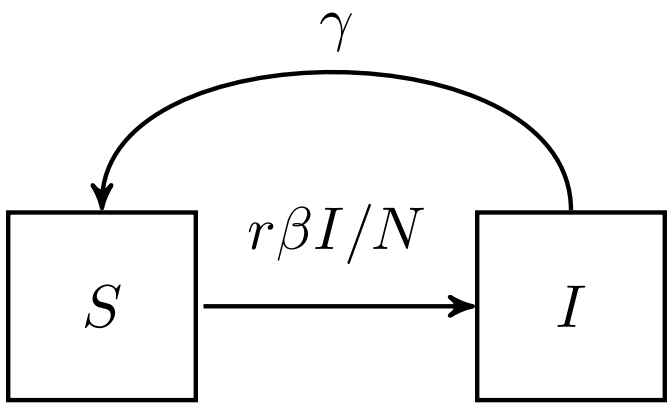


With $r = 365/3$ years^{-1}, $\beta = 0.005$, $N = 1000$, and $I(0) = 1$.

- Note that in some models, usually of diseases where contacts are not well defined, $r\beta$ (the number of contacts per unit time multiplied by the probability of disease transmission per contact) are combined into one parameter (often also called β — the number of adequate contacts per unit time).
- For diseases where a contact is well defined (such as sexually transmitted diseases like HIV or vector-borne diseases like malaria), it is usually more appropriate to separate the contact rate, r, and the probability of transmission per contact, β.
- For diseases where contacts are not well defined (such as air-borne diseases like influenza) it is usually more appropriate to combine the two into one parameter.

Susceptible-Infectious-Susceptible Model: applicable to the common cold.



$$\frac{\mathrm{d}S}{\mathrm{d}t} = -r\beta S\frac{I}{N} + \gamma I$$
$$\frac{\mathrm{d}I}{\mathrm{d}t} = r\beta S\frac{I}{N} - \gamma I$$

γ: Per-capita recovery rate

The system can be reduced to one dimension,

$$\frac{\mathrm{d}I}{\mathrm{d}t} = r\beta(N - I)\frac{I}{N} - \gamma I,$$

with solution,

$$I(t) = \frac{\frac{N}{r\beta} \cdot (r\beta - \gamma)}{1 + \left(\frac{N}{r\beta}\frac{(r\beta-\gamma)}{I_0} - 1\right) e^{-(r\beta-\gamma)t}},$$

for $I(0) = I_0$.

Equilibrium Points:

$$I_{\text{dfe}} = 0$$

$$I_{\text{ee}} = \frac{(r\beta - \gamma)N}{r\beta}$$

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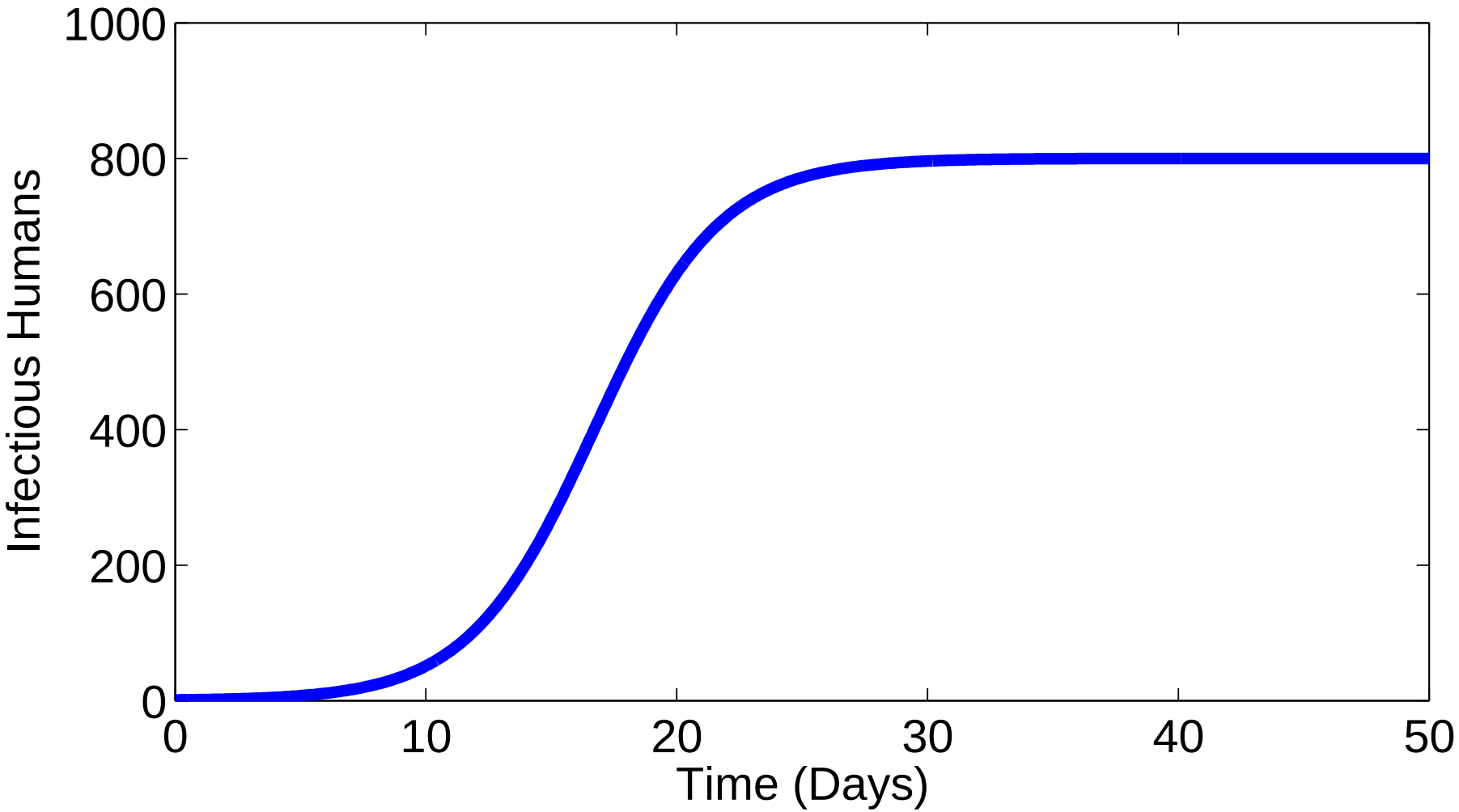
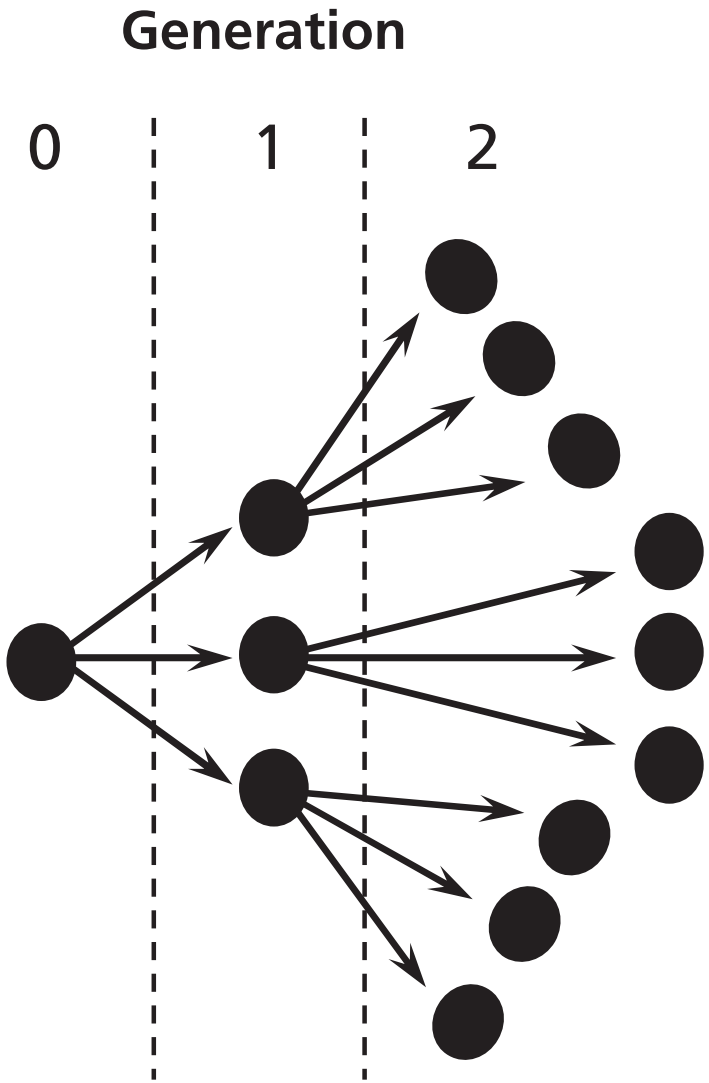


With $r\beta = 0.5$ days^{-1}, $\gamma = 0.1$ days^{-1}, $N = 1000$, and $I(0) = 1$.



Initial phase of epidemic ($R_0 = 3$)

Pan-InfORM (2009)

- The basic reproductive number, R_0, is the number of secondary infections that one infected person would produce in a fully susceptible population through the entire duration of the infectious period.
- R_0 provides a threshold condition for the stability of the disease-free equilibrium point (for most models):
  - The disease-free equilibrium point is locally asymptotically stable when $R_0 < 1$: the disease dies out.
  - The disease-free equilibrium point is unstable when $R_0 > 1$: the disease establishes itself in the population or an epidemic occurs.
  - For a given model, R_0 is fixed over all time.
- This definition is only valid for simple homogeneous autonomous models.
- Can define similar threshold conditions for more complicated models that include heterogeneity and/or seasonality but the basic definition no longer holds.

Definition of R_0

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R_0 can be expressed as a product of three quantities:

$$R_0 = \left(\begin{array}{c} \text{Number of} \\ \text{contacts} \\ \text{per unit time} \end{array} \right) \left(\begin{array}{c} \text{Probability of} \\ \text{transmission} \\ \text{per contact} \end{array} \right) \left(\begin{array}{c} \text{Duration of} \\ \text{infection} \end{array} \right)$$

For SIS model:

$$R_0 = r \times \beta \times \frac{1}{\gamma}$$

- The (*effective*) reproductive number, R_e, is the number of secondary infections that one infected person would produce through the entire duration of the infectious period.
- Typically, *but not always*, R_e is the product of R_0 and the proportion of the population that is susceptible.
- R_e describes whether the infectious population increases or not. It increases when $R_e > 1$; decreases when $R_e < 1$ and is constant when $R_e = 1$. When $R_e = 1$, the disease is at equilibrium.
- R_e can change over time.
- The control reproductive number, R_c, is the number of secondary infections that one infected person would produce through the entire duration of the infectious period, in the presence of control interventions.

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$$R_e(t) = \left(\begin{array}{c} \text{Number of} \\ \text{contacts} \\ \text{per unit time} \end{array} \right) \left(\begin{array}{c} \text{Probability of} \\ \text{transmission} \\ \text{per contact} \end{array} \right) \left(\begin{array}{c} \text{Duration of} \\ \text{infection} \end{array} \right) \times \left(\begin{array}{c} \text{Proportion of} \\ \text{susceptible} \\ \text{population} \end{array} \right)$$

For SIS model:

$$\begin{aligned} R_e(t) &= R_0 \times \frac{S(t)}{N(t)} \\ &= \frac{r\beta S(t)}{\gamma N(t)}. \end{aligned}$$

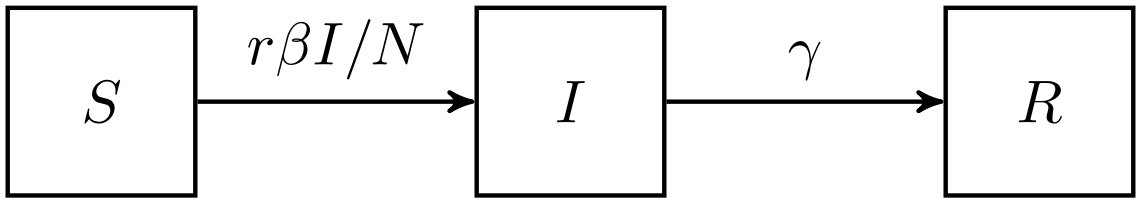
How quickly does it spread?

Basic reproduction value

Source: ECDC, UMICH, Lancet

http://www.cameroonweb.com/CameroonHomePage/NewsArchive/Ebola-How-does-it-compare-316932

Susceptible-Infectious-Recovered Model: applicable to measles, mumps, rubella.



$$\frac{\mathrm{d}S}{\mathrm{d}t} = -r\beta S\frac{I}{N}$$
$$\frac{\mathrm{d}I}{\mathrm{d}t} = r\beta S\frac{I}{N} - \gamma I$$
$$\frac{\mathrm{d}R}{\mathrm{d}t} = \gamma I$$

R: Recovered humans

with $N = S + I + R$.

- Can reduce to two dimensions by ignoring the equation for R and using $R = N - S - I$.
- Can no longer analytically solve these equations.
- Infinite number of equilibrium points with $I^* = 0$.
- Perform phase portrait analysis.
- Estimate final epidemic size.

$$R_0 = \left(\begin{array}{c}\text{Number of}\\ \text{contacts}\\ \text{per unit time}\end{array}\right)\left(\begin{array}{c}\text{Probability of}\\ \text{transmission}\\ \text{per contact}\end{array}\right)\left(\begin{array}{c}\text{Duration of}\\ \text{infection}\end{array}\right)$$

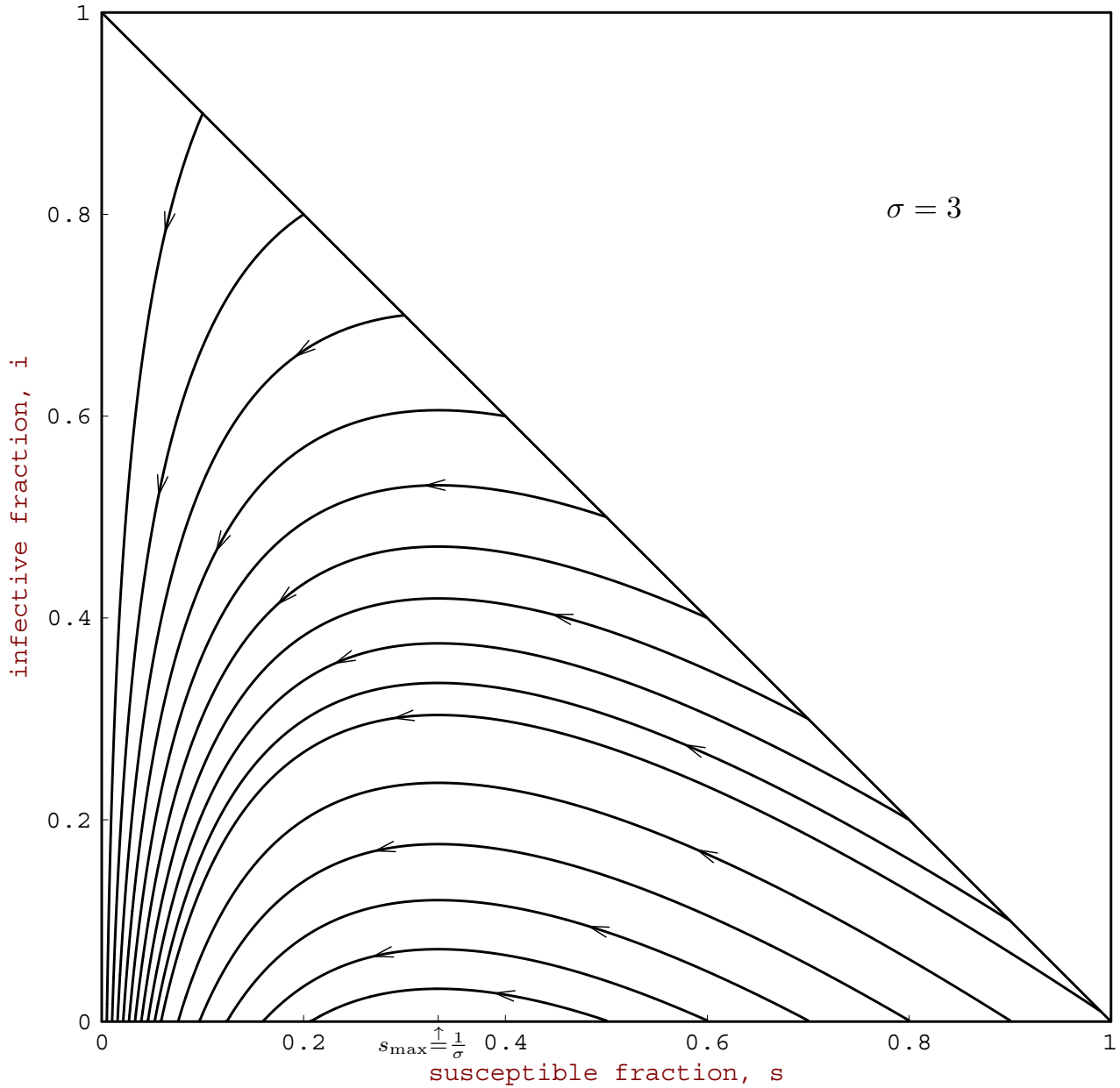
$$R_0 = r \times \beta \times \frac{1}{\gamma}$$

$$= \frac{r\beta}{\gamma}$$

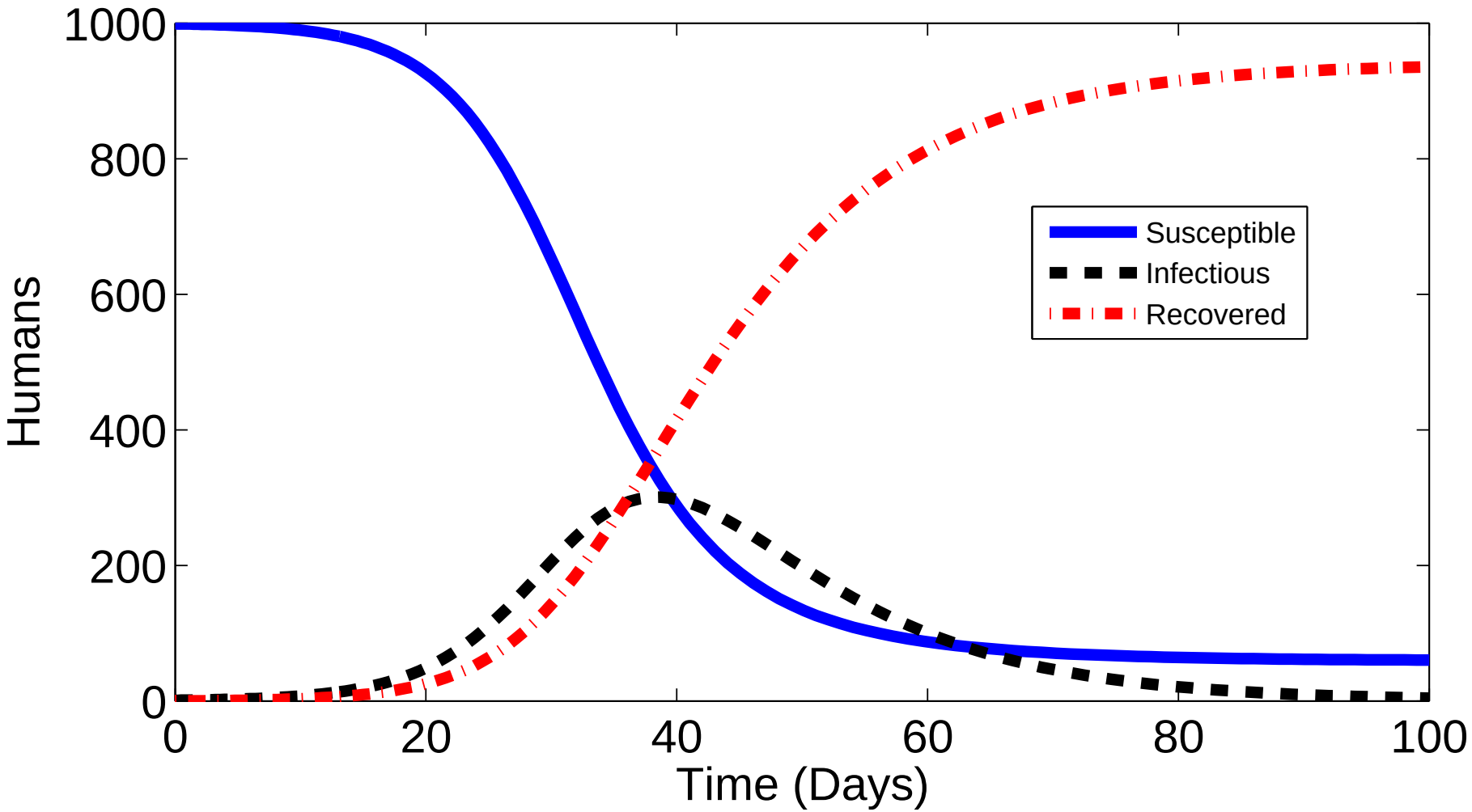
- If $R_0 < 1$, introduced cases do not lead to an epidemic (the number of infectious individuals decreases towards 0).
- If $R_0 > 1$, introduced cases can lead to an epidemic (temporary increase in the number of infectious individuals).

$$R_e(t) = \frac{r\beta}{\gamma}\frac{S(t)}{N}$$

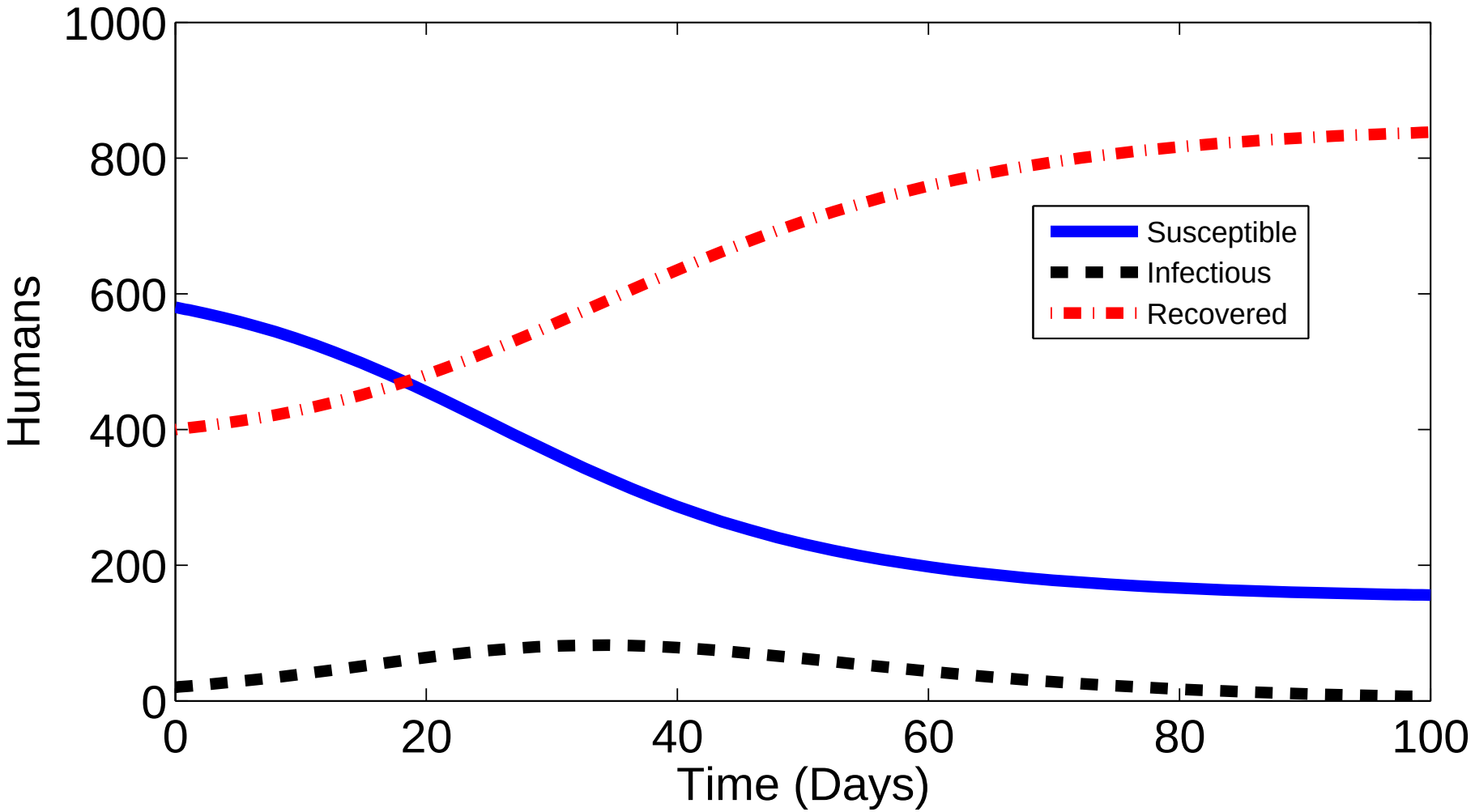
Phase Portrait of SIR Model



Hethcote (2000)

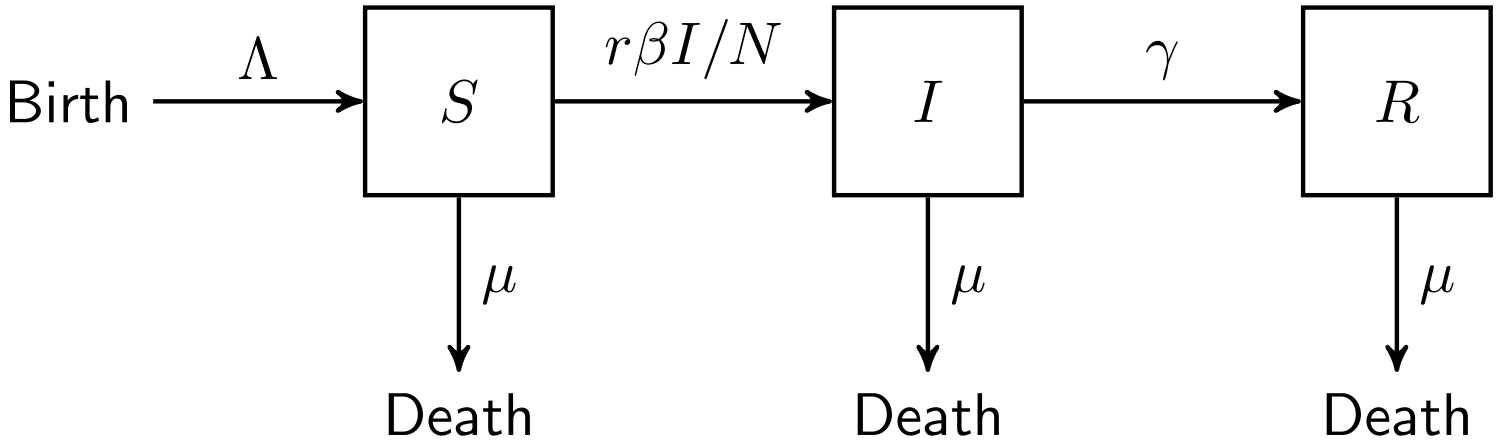


With $r\beta = 0.3$ days^{-1}, $\gamma = 0.1$ days^{-1}, $N = 1000$, and $S(0) = 999$, $I(0) = 1$ and $R(0) = 0$.



With $r\beta = 0.3$ days^{-1}, $\gamma = 0.1$ days^{-1}, $N = 1000$, and $S(0) = 580$, $I(0) = 20$ and $R(0) = 400$.

- Need to include human demographics for diseases where the time frame of the disease dynamics is comparable to that of human demographics.
- There are many different ways of modeling human demographics
  - Constant immigration rate
  - Constant per-capita birth and death rates
  - Density-dependent death rate
  - Disease-induced death rate.



$$\frac{\mathrm{d}S}{\mathrm{d}t} = \Lambda - r\beta S\frac{I}{N} - \mu S$$
$$\frac{\mathrm{d}I}{\mathrm{d}t} = r\beta S\frac{I}{N} - \gamma I - \mu I$$
$$\frac{\mathrm{d}R}{\mathrm{d}t} = \gamma I - \mu R$$
$$N = S + I + R$$

Λ: Constant recruitment rate

μ: Per-capita removal rate

- Can no longer reduce the dimension or solve analytically.
- There are two equilibrium points: disease-free and endemic

$$S_{\text{dfe}} = \frac{\Lambda}{\mu} \qquad S_{\text{ee}} = \frac{\Lambda(\gamma+\mu)}{r\beta\mu}$$

$$I_{\text{dfe}} = 0 \qquad I_{\text{ee}} = \frac{\Lambda(r\beta-(\gamma+\mu))}{r\beta(\gamma+\mu)}$$

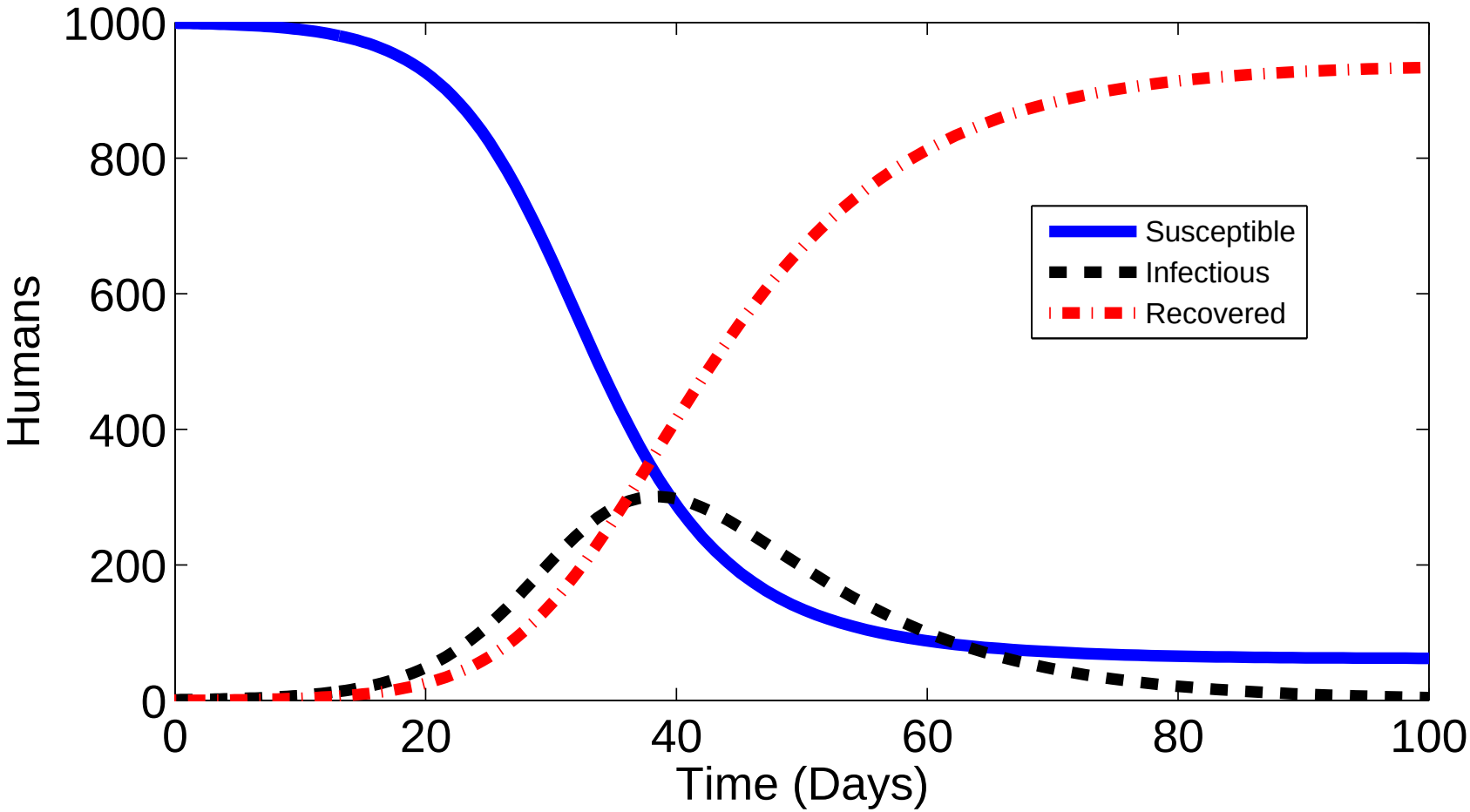
$$R_{\text{dfe}} = 0 \qquad R_{\text{ee}} = \frac{\gamma\Lambda(r\beta-(\gamma+\mu))}{r\beta\mu(\gamma+\mu)}$$

- Can perform stability analysis of these equilibrium points and draw phase portraits.

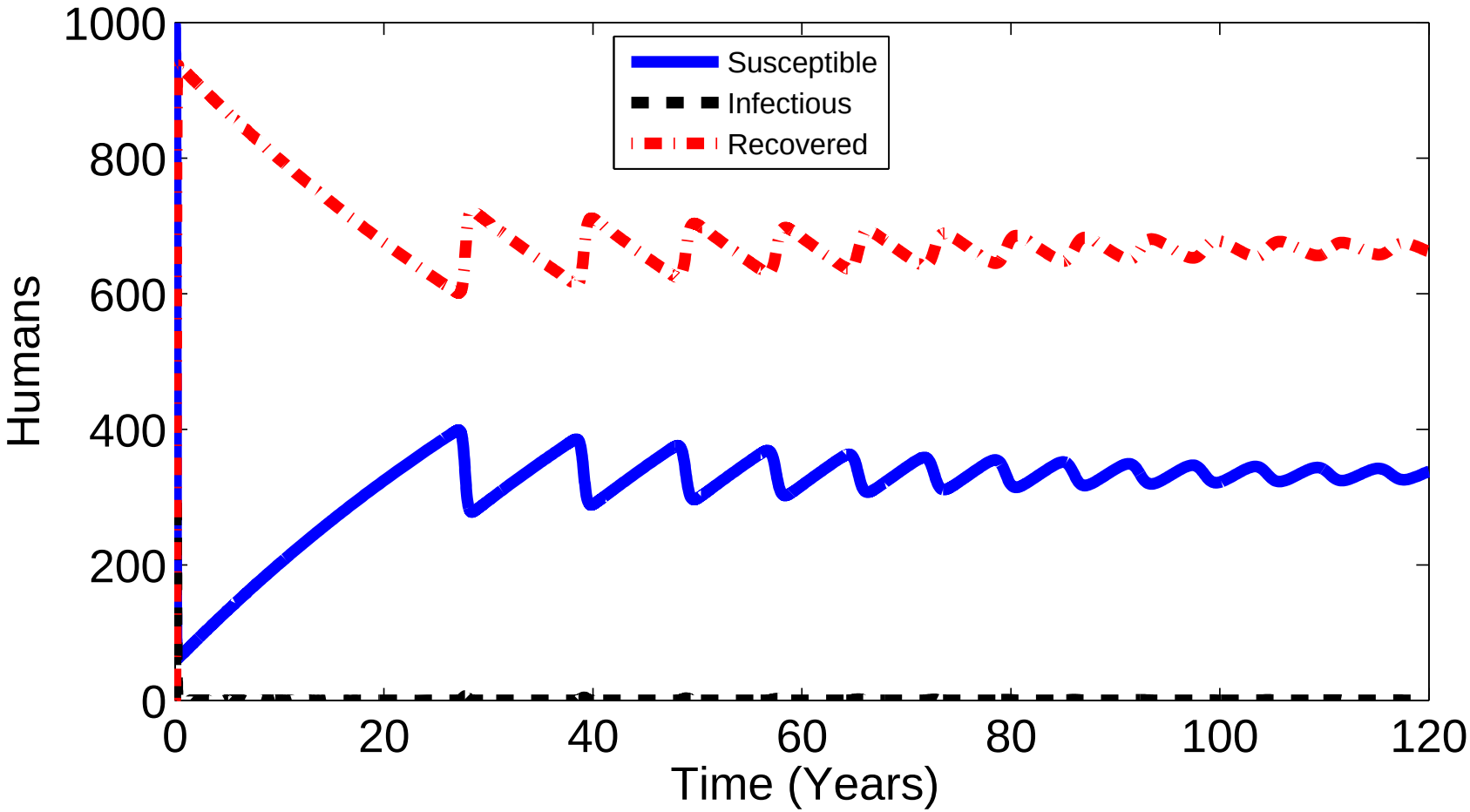
$$R_0 = \left(\begin{array}{c}\text{Number of}\\ \text{contacts}\\ \text{per unit time}\end{array}\right)\left(\begin{array}{c}\text{Probability of}\\ \text{transmission}\\ \text{per contact}\end{array}\right)\left(\begin{array}{c}\text{Duration of}\\ \text{infection}\end{array}\right)$$

$$R_0 = r \times \beta \times \frac{1}{\gamma + \mu}$$
$$= \frac{r\beta}{\gamma + \mu}$$

- If $R_0 < 1$, the disease-free equilibrium point is globally asymptotically stable and there is no endemic equilibrium point (the disease dies out).
- If $R_0 > 1$, the disease-free equilibrium point is unstable and a globally asymptotically stable endemic equilibrium point exists.



With $r\beta = 0.3$ days^{-1}, $\gamma = 0.1$ days^{-1}, $\mu = 1/60$ years^{-1}, $\Lambda = 1000/60$ years^{-1}, and $S(0) = 999$, $I(0) = 1$ and $R(0) = 0$.



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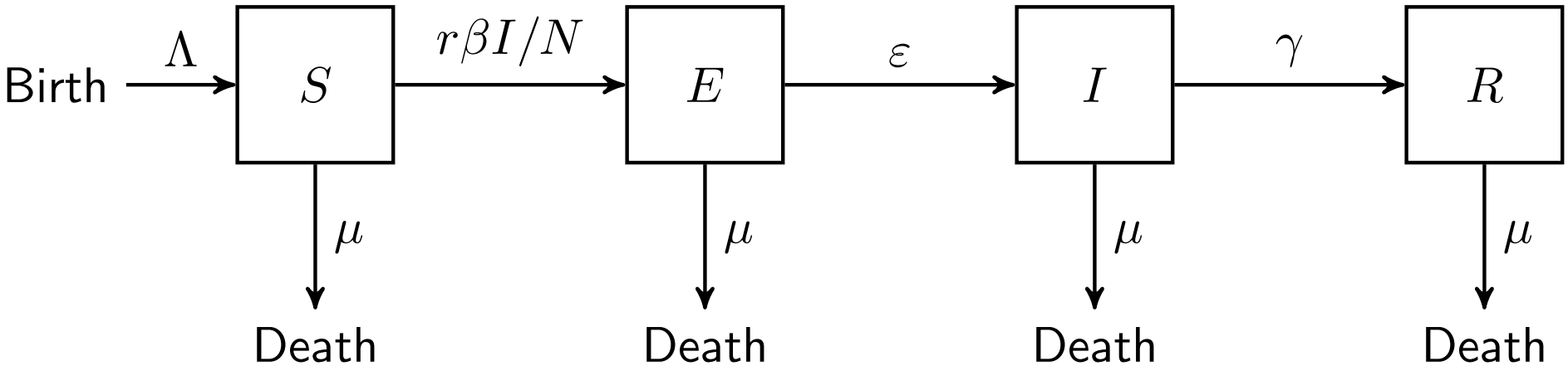
Susceptible-Exposed-Infectious-Recovered Model: applicable to measles, mumps, rubella.



E: Exposed (latent) humans

ε: Per-capita rate of progression to infectious state

$$\frac{\mathrm{d}S}{\mathrm{d}t} = \Lambda - r\beta S\frac{I}{N} - \mu S$$
$$\frac{\mathrm{d}E}{\mathrm{d}t} = r\beta S\frac{I}{N} - \varepsilon E$$
$$\frac{\mathrm{d}I}{\mathrm{d}t} = \varepsilon E - \gamma I - \mu I$$
$$\frac{\mathrm{d}R}{\mathrm{d}t} = \gamma I - \mu R$$

with

$$N = S + E + I + R.$$

$$R_0 = \left(\begin{array}{c}\text{Number of}\\ \text{contacts}\\ \text{per unit time}\end{array}\right)\left(\begin{array}{c}\text{Probability of}\\ \text{transmission}\\ \text{per contact}\end{array}\right)\left(\begin{array}{c}\text{Duration of}\\ \text{infection}\end{array}\right)$$
$$\times \left(\begin{array}{c}\text{Probabililty of}\\ \text{surviving}\\ \text{exposed stage}\end{array}\right)$$

$$R_0 = r \times \beta \times \frac{1}{\gamma + \mu} \times \frac{\varepsilon}{\varepsilon + \mu}$$
$$= \frac{r\beta\varepsilon}{(\gamma + \mu)(\varepsilon + \mu)}$$

- If $R_0 < 1$, the disease-free equilibrium point is globally asymptotically stable and there is no endemic equilibrium point (the disease dies out).
- If $R_0 > 1$, the disease-free equilibrium point is unstable and a globally asymptotically stable endemic equilibrium point exists.

- Basic compartmental models assume a homogeneous population.
- Divide the population into different groups based on infection status:
  - M: Humans with maternal immunity
  - S: Susceptible humans
  - E: Exposed (infected but not yet infectious) humans
  - I: Infectious humans
  - R: Recovered humans.
- Can include time-dependent parameters to include the effects of seasonality.
- Can include additional compartments to model vaccinated and asymptomatic individuals, and different stages of disease progression.
- Can include multiple groups to model heterogeneity, age, spatial structure or host species.


O. Diekmann, H. Heesterbeek, and T. Britton, *Mathematical Tools for Understanding Infectious Disease Dynamics*.
Princeton Series in Theoretical and Computational Biology. Princeton University Press, Princeton, (2013).


H. W. Hethcote, "The mathematics of infectious diseases", *SIAM Review* **42**, 599–653 (2000).


M. J. Keeling and P. Rohani, *Modeling Infectious Diseases in Humans and Animals*.
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