

**AMS/CIMPA
School KENYA
2023**

**Mathematical Models of Chemical Reaction
Networks; Basic tools, applications
and open challenges.**

University of Nairobi, Kenya

Introduction to Epidemiological Models

Josephine Kagunda

Department of Mathematics, FST
University of Nairobi, Kenya

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SI Model

SIS Model

The Basic Reproductive Number (R_0)

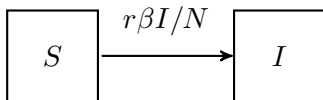
SIR Model

SEIR Model

- 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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 - ▶ Can be **deterministic** or stochastic
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 - Ordinary differential equations
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Susceptible-Infectious Model: applicable to HIV.



$$\frac{dS}{dt} = -r\beta S \frac{I}{N}$$

$$\frac{dI}{dt} = r\beta S \frac{I}{N}$$

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,

$$\frac{dI}{dt} = r\beta(N - I)\frac{I}{N},$$

with solution,

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

for $I(0) = I_0$.

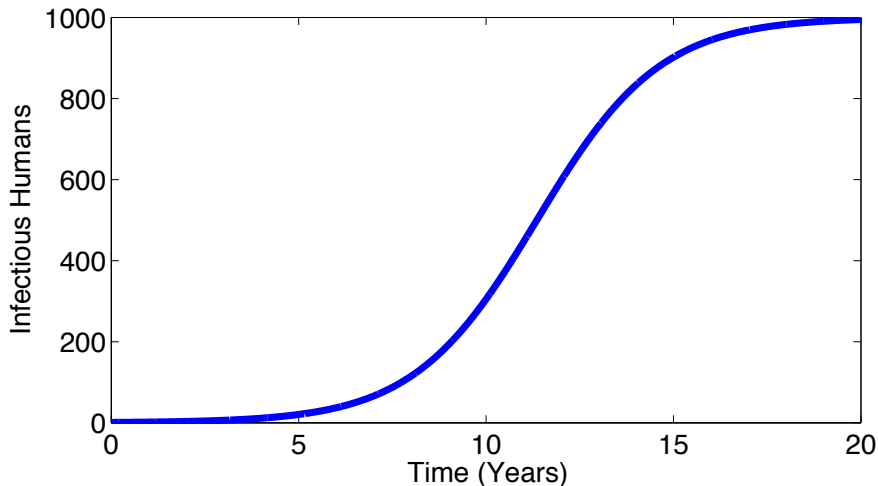
Equilibrium Points:

$$I_{dfe} = 0$$

$$I_{ee} = N$$

$$\frac{dI}{(N-I)I} = r\beta dt$$

$$\left(\frac{A}{N-I} + \frac{B}{I} \right) \frac{1}{I} = r\beta dt$$



With $r = 365/3 \text{ years}^{-1}$, $\beta = 0.005$, $N = 1000$, 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.

SI Model

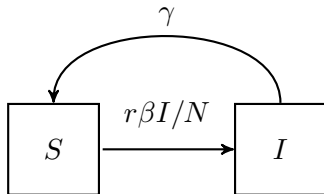
SIS Model

The Basic Reproductive Number (R_0)

SIR Model

SEIR Model

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



$$\frac{dS}{dt} = -r\beta S \frac{I}{N} + \gamma I$$
$$\frac{dI}{dt} = r\beta S \frac{I}{N} - \gamma I$$

γ : Per-capita recovery rate

The system can be reduced to one dimension,

$$\frac{dI}{dt} = r\beta(N - I)\frac{I}{N} - \gamma I,$$

with solution,

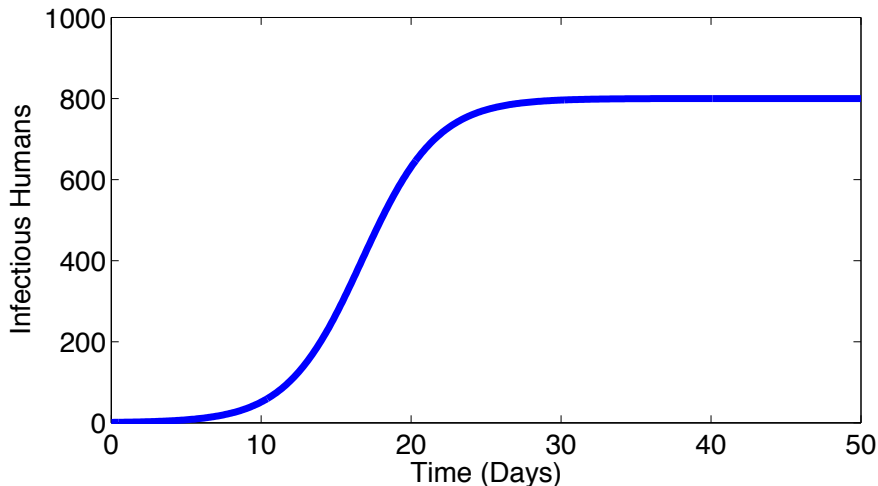
$$I(t) = \frac{\frac{N}{r\beta} \cdot (r\beta - \gamma)}{1 + \left(\frac{N}{r\beta} \frac{(r\beta - \gamma)}{I_0} - 1\right) e^{-(r\beta - \gamma)t}},$$

for $I(0) = I_0$.

Equilibrium Points:

$$I_{dfe} = 0$$

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



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

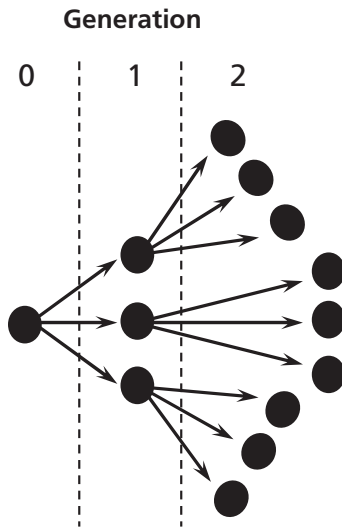
SI Model

SIS Model

The Basic Reproductive Number (R_0)

SIR Model

SEIR Model



Initial phase of epidemic ($R_0 = 3$)

- 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.

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.

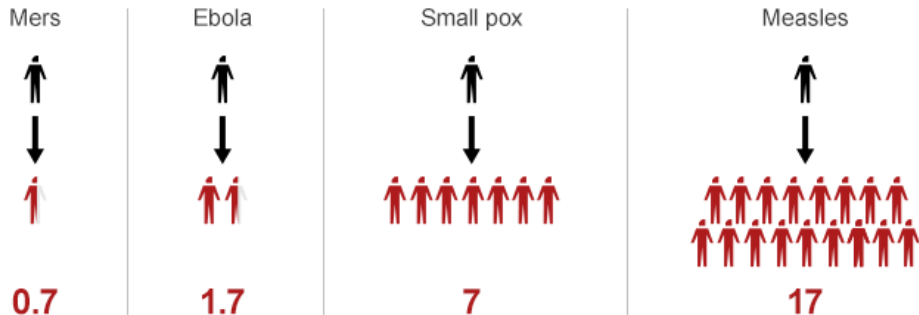
$$R_e(t) = \left(\begin{array}{c} \text{Number of} \\ \text{contacts} \\ \text{per unit time} \end{array} \right) \left(\begin{array}{c} \text{Probability of} \\ \text{transmission} \\ \text{per contact} \end{array} \right) \left(\begin{array}{c} \text{Duration of} \\ \text{infection} \end{array} \right)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

For SIS model:

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

How quickly does it spread?

Basic reproduction value



Source: ECDC, UMICH, Lancet

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

SI Model

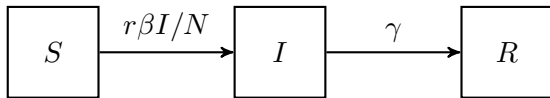
SIS Model

The Basic Reproductive Number (R_0)

SIR Model

SEIR Model

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



$$\begin{aligned}\frac{dS}{dt} &= -r\beta S \frac{I}{N} \\ \frac{dI}{dt} &= r\beta S \frac{I}{N} - \gamma I \\ \frac{dR}{dt} &= \gamma I\end{aligned}$$

R : Recovered humans
with $N = S + I + R$.

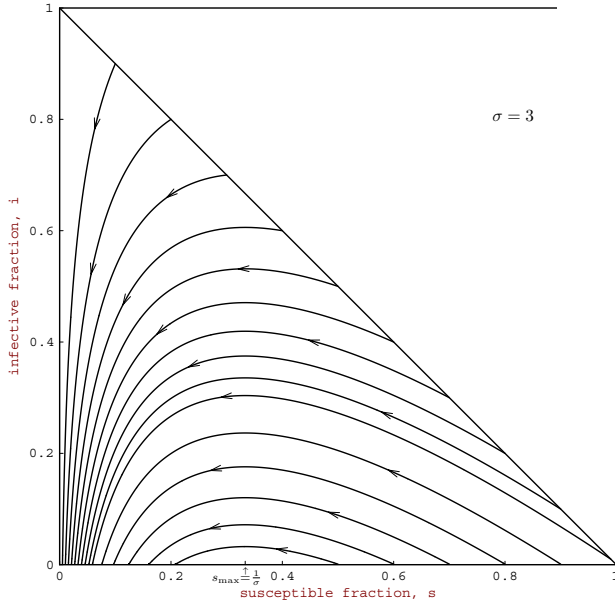
- Can reduce to two dimensions by ignoring the equation for R and using $R = N - S - I$.
- Can no longer analytically solve these equations.
- Infinite number of equilibrium points with $I^* = 0$.
- Perform phase portrait analysis.
- Estimate final epidemic size.

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

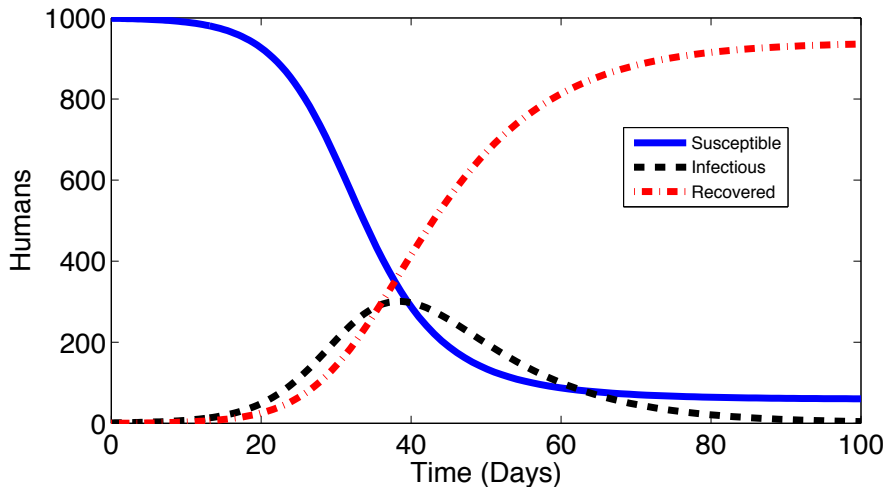
$$\begin{aligned} R_0 &= r \times \beta \times \frac{1}{\gamma} \\ &= \frac{r\beta}{\gamma} \end{aligned}$$

- 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).

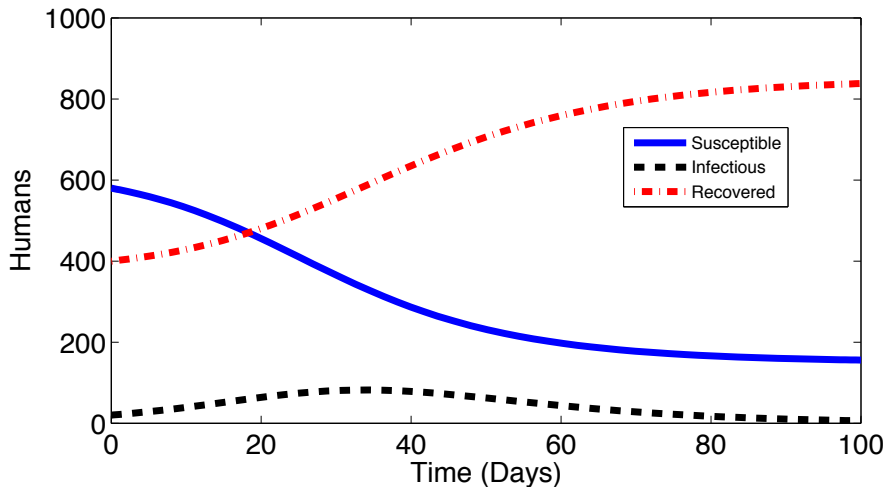
$$R_e(t) = \frac{r\beta}{\gamma} \frac{S(t)}{N}$$



Hethcote (2000)

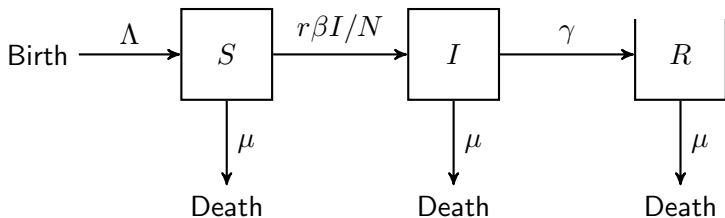


With $r\beta = 0.3 \text{ days}^{-1}$, $\gamma = 0.1 \text{ days}^{-1}$, $N = 1000$, and
 $S(0) = 999$, $I(0) = 1$ and $R(0) = 0$.



With $r\beta = 0.3 \text{ days}^{-1}$, $\gamma = 0.1 \text{ days}^{-1}$, $N = 1000$, 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.



$$\frac{dS}{dt} = \Lambda - r\beta S \frac{I}{N} - \mu S$$

$$\frac{dI}{dt} = r\beta S \frac{I}{N} - \gamma I - \mu I$$

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

$$N = S + I + R$$

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

$$S_{\text{dfe}} = \frac{\Lambda}{\mu}$$

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

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

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

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

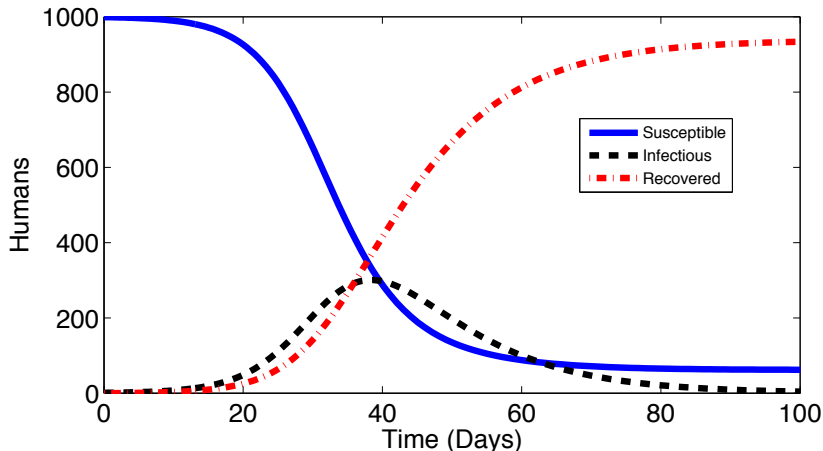
$$R_{\text{ee}} = \frac{\gamma\Lambda(r\beta - (\gamma + \mu))}{r\beta\mu(\gamma + \mu)}$$

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

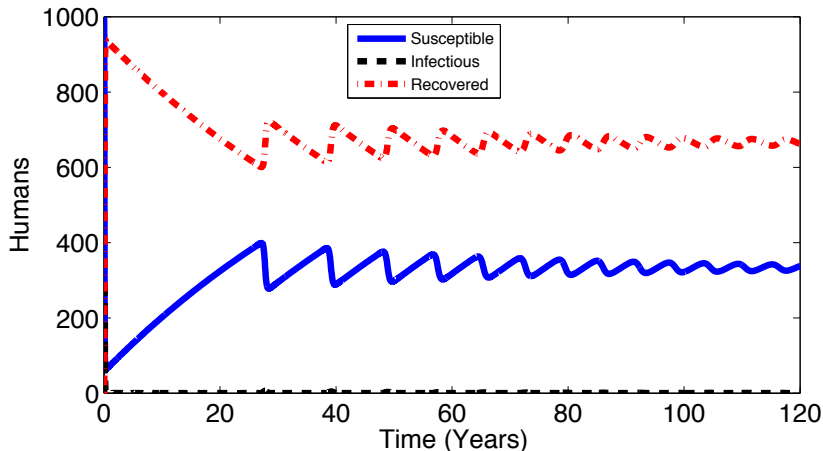
$$R_0 = \left(\begin{array}{c} \text{Number of} \\ \text{contacts} \\ \text{per unit time} \end{array} \right) \left(\begin{array}{c} \text{Probability of} \\ \text{transmission} \\ \text{per contact} \end{array} \right) \left(\begin{array}{c} \text{Duration of} \\ \text{infection} \end{array} \right)$$

$$\begin{aligned} R_0 &= r \times \beta \times \frac{1}{\gamma + \mu} \\ &= \frac{r\beta}{\gamma + \mu} \end{aligned}$$

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



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

SI Model

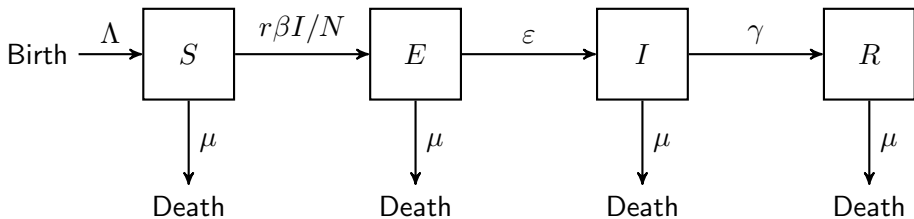
SIS Model

The Basic Reproductive Number (R_0)

SIR Model

SEIR Model

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



E : Exposed (latent) humans

ε : Per-capita rate of progression to infectious state

$$\frac{dS}{dt} = \Lambda - r\beta S \frac{I}{N} - \mu S$$

$$\frac{dE}{dt} = r\beta S \frac{I}{N} - \varepsilon E$$

$$\frac{dI}{dt} = \varepsilon E - \gamma I - \mu I$$

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

with

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

$$R_0 = \begin{pmatrix} \text{Number of} \\ \text{contacts} \\ \text{per unit time} \end{pmatrix} \begin{pmatrix} \text{Probability of} \\ \text{transmission} \\ \text{per contact} \end{pmatrix} \begin{pmatrix} \text{Duration of} \\ \text{infection} \end{pmatrix} \\ \times \begin{pmatrix} \text{Probabililty of} \\ \text{surviving} \\ \text{exposed stage} \end{pmatrix}$$

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

- 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*.

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