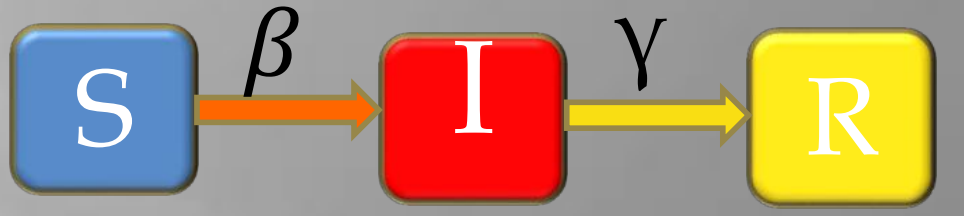
Thursday

Threshold and Sensitivity Analysis

Threshold Analysis

SIR Model without Demography



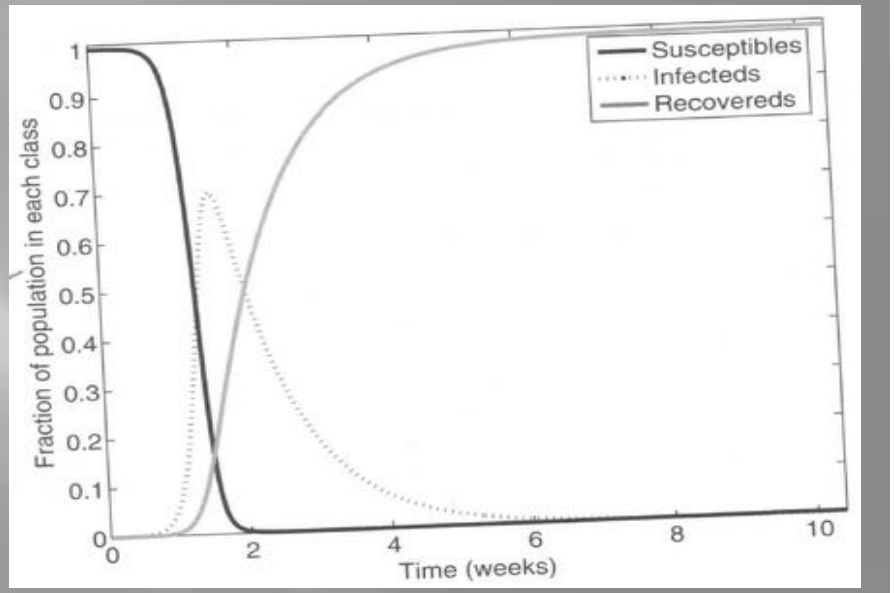
$$\frac{dS}{dt} = -\beta SI \qquad (2.1)$$

$$\frac{dI}{dt} = \beta SI - \gamma I \qquad (2.2)$$

$$\frac{dR}{dt} = \gamma I \qquad (2.3)$$

With initial conditions $S(0) > 0, I(0) > 0$, and $R(0) = 0$.

This model can be solved numerically and not explicitly despite its simplicity; this is due to its nonlinearity.



Threshold Phenomenon

What factors will determine whether an epidemic will occur or if the infection will fail to invade?

Threshold Phenomenon

First, consider the initial stages after $I(0)$ infectives are introduced into a population consisting of $S(0)$ susceptibles. Rewrite equation (2.2) in the form

$$\frac{dI}{dt} = (\beta S - \gamma)I \quad (2.4)$$

If $S(0) < \gamma/\beta$ then $\frac{dI}{dt} < 0$ and the infection **"dies out".**

This result is referred to as the **"threshold phenomenon"** because initially the proportion of susceptibles in the population must exceed this critical threshold for an infection to invade or persist in the population.

Alternatively, we can interpret this result as requiring γ/β, the relative removal rate, to be small enough to permit the disease to spread.

The inverse of the relative removal rate is called the **basic reproductive ratio** ($R_0 = \frac{\beta}{\gamma}$) and is one of the most important quantities in epidemiology.

It is defined as:
the average number of secondary cases arising from an average number of primary case in an entirely susceptible population
and essentially measures the maximum reproductive potential for an infectious disease.

We can use R_0 to re-express the threshold phenomenon; assuming everyone in the population is initially susceptible ($S(0) = 1$), a pathogen can only invade if $R_0 > 1$.

This makes very good sense because any infection that, on average, cannot successfully transmit to more than one new host is not going to spread.

Some example diseases with their estimated R_0s are presented in Table 2.1; due to differences in demographic rates, rural-urban gradients, and contact structure, different human populations may be associated with different values of R_0 for the same disease.

The value of R_0 depends on both the disease and the host population.

Mathematically, we can calculate R_0 as the rate at which new cases are produced by an infectious individual (when the entire population is susceptible) multiplied by the average infectious period.

Note that the above observations are informative about the initial stages, after an infectious agent has been introduced.

Some Estimated Basic Reproductive Ratios.

Infectious Disease	*Host*	*Estimated R_0*	*Reference*
FIV	Domestic Cats	1.1–1.5	Smith (2001)
Rabies	Dogs (Kenya)	2.44	Kitala et al. (2002)
Phocine Distemper	Seals	2–3	Swinton et al. (1998)
Tuberculosis	Cattle	2.6	Goodchild and Clifton-Hadley (2001)
Influenza	Humans	3–4	Murray (1989)
Foot-and-Mouth Disease	Livestock farms (UK)	3.5–4.5	Ferguson et al. (2001b)
Smallpox	Humans	3.5–6	Gani and Leach (2001)
Rubella	Humans (UK)	6–7	Anderson and May (1991)
Chickenpox	Humans (UK)	10–12	Anderson and May (1991)
Measles	Humans (UK)	16–18	Anderson and May (1982)
Whooping Cough	Humans (UK)	16–18	Anderson and May (1982)

Table 2.1

Population thresholds in epidemic dynamics

R_0 has been the central concept in epidemic dynamics since ~1980,

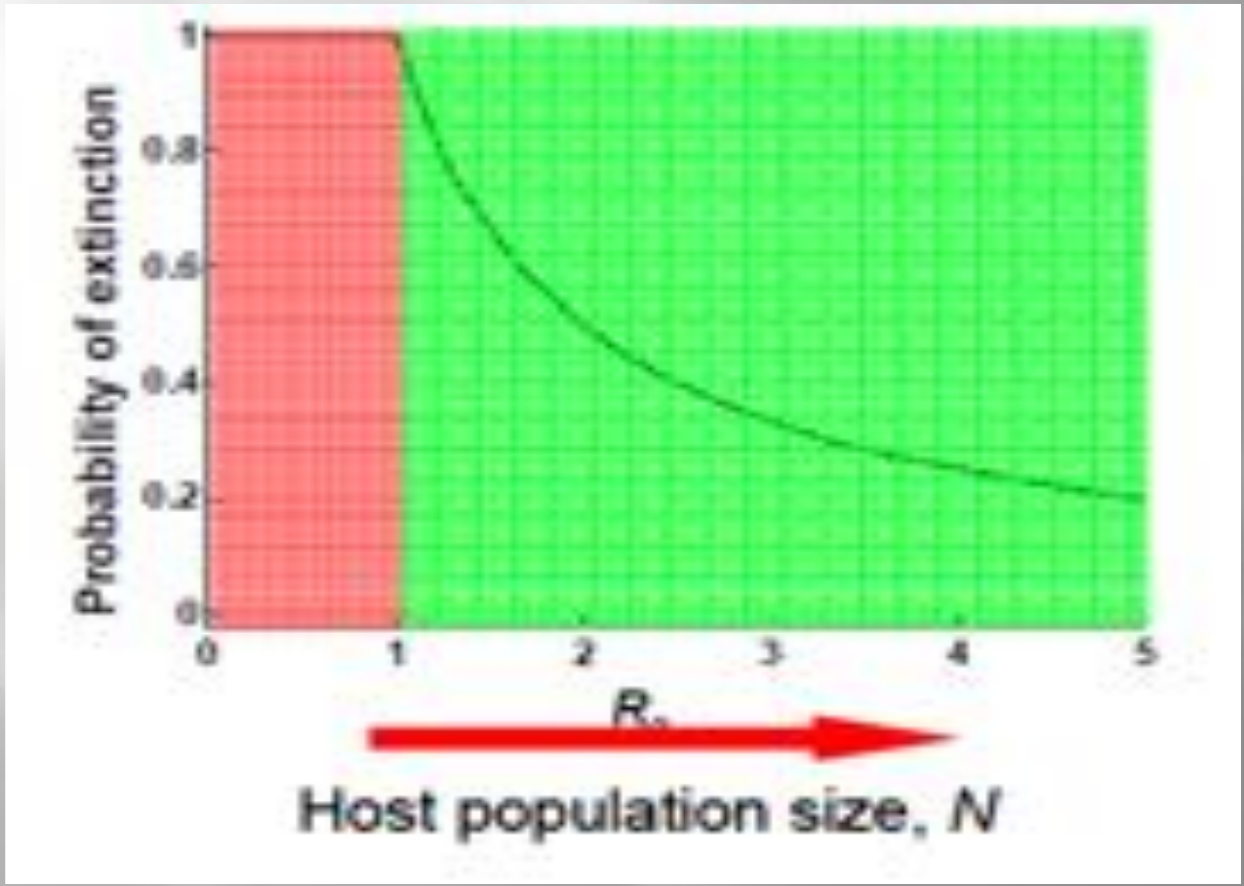
Long before this, people studying epidemic dynamics have focused on population thresholds.

• Population threshold for :
host population size below which disease cannot invade.

• Population threshold for persistence, or the critical community size:
host population size below which disease cannot persist long-term.

Population threshold for disease invasion

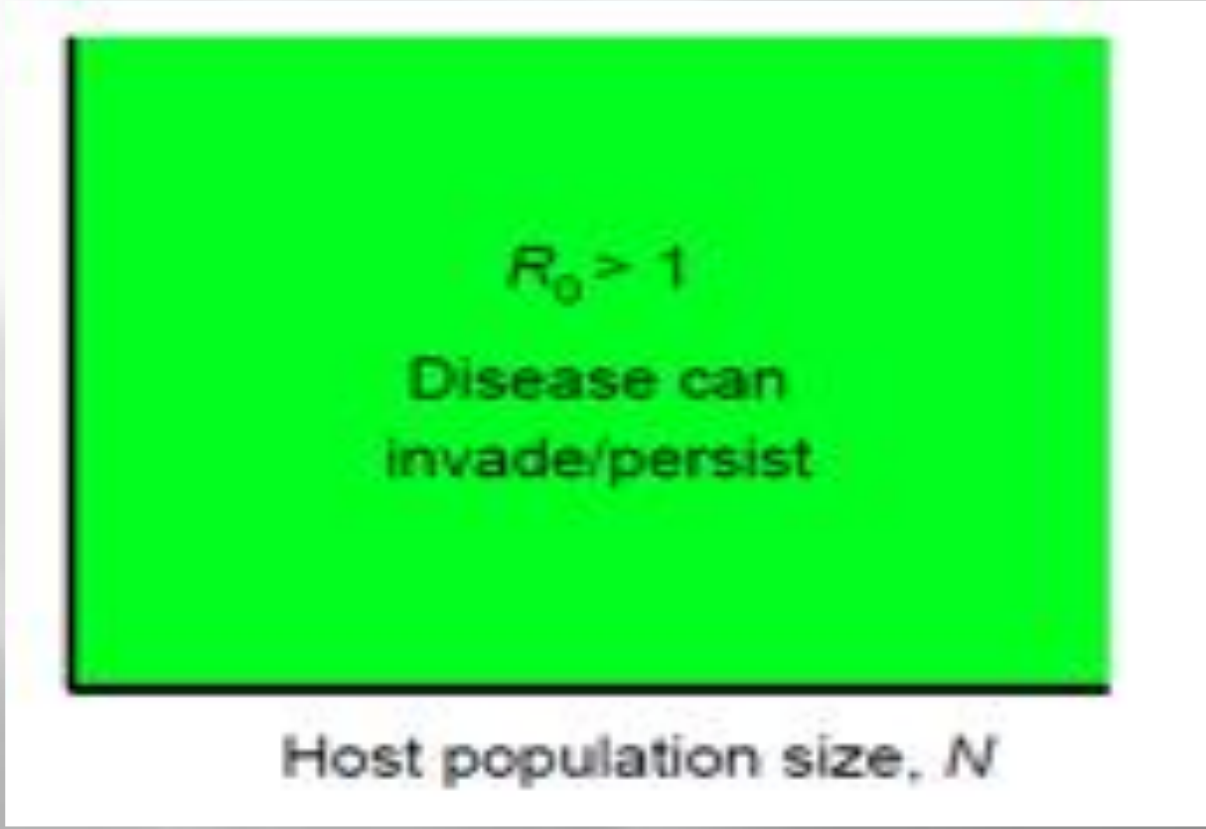
Under density-dependent transmission, $R_0 = \beta N D$
or in fact R_0 is any increasing function of *N*.
$\rightarrow R_0 > 1$ corresponds to a population threshold $N > N_T$.



Population threshold for disease invasion

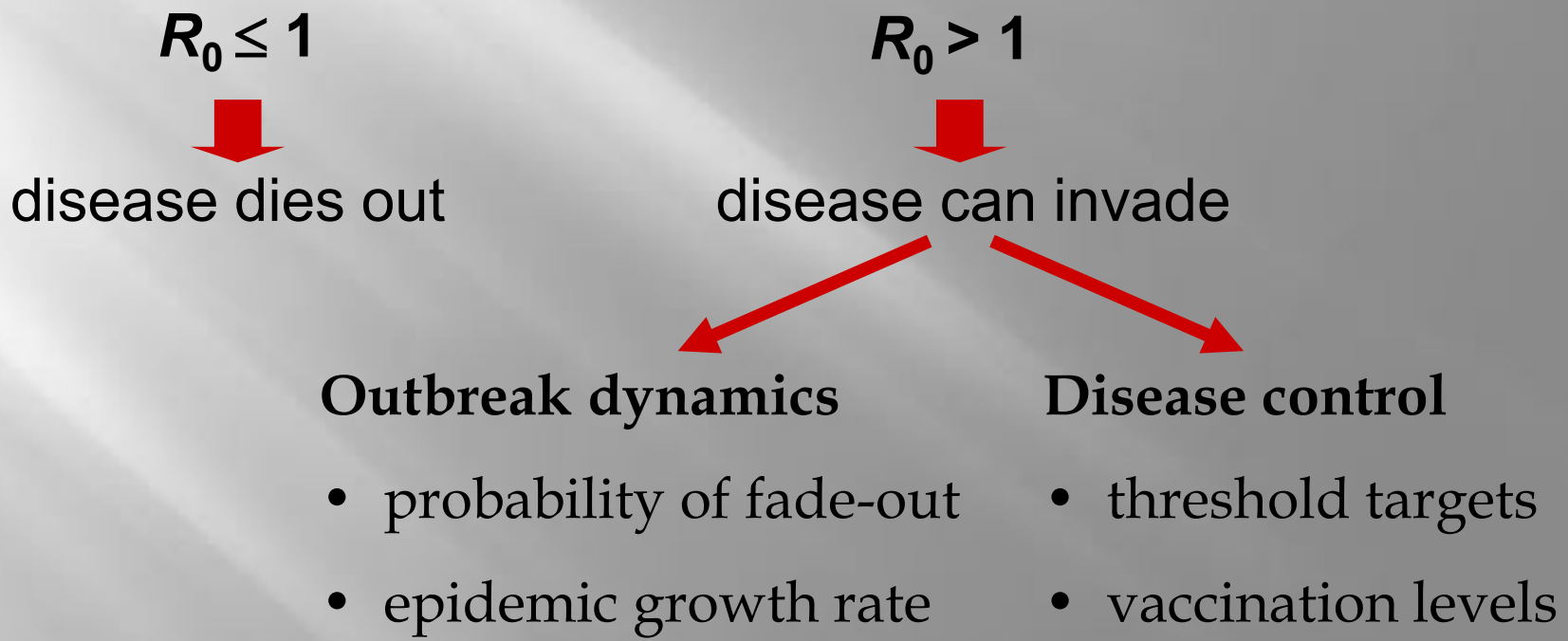
Under frequency-dependent transmission, $R_0 = \beta D$.

→ No threshold *N* for $R_0 > 1$.



Basic reproductive number, R_0

Expected number of cases caused by a typical infectious individual in a susceptible population.



Calculating R_0 – Intuitive approach

R_0 = Per capita rate of infecting others × Duration of infectiousness

… in a completely susceptible population.

Under frequency-dependent transmission:

Rate of infecting others $= \beta S/N$
$= \beta$ in wholly susceptible population

Duration of infectiousness = 1/recovery rate
$= 1/\gamma$

→ $R_0 = \beta / \gamma$

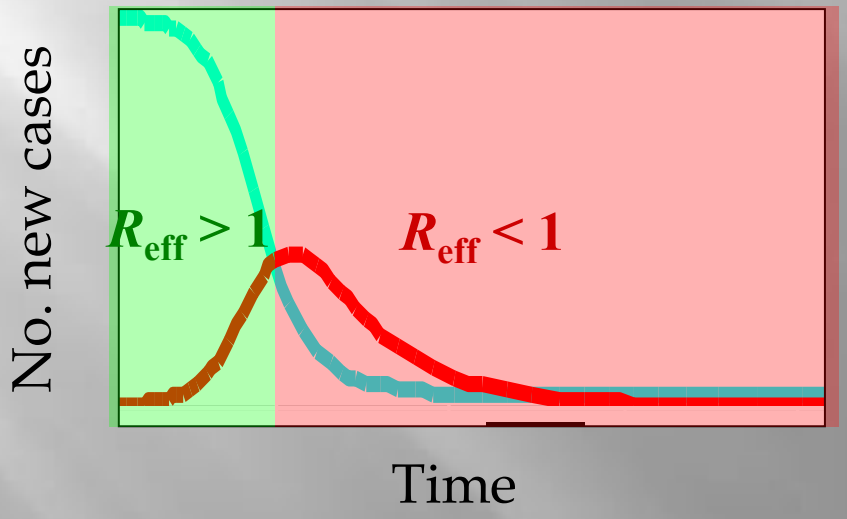
Effective reproductive number

Expected number of cases caused by a typical infectious individual in a population that is not wholly susceptible.

$$R_{\text{effective}} = R_0 \times S/N$$

Endemic disease: At equilibrium $R_{\text{eff}} = 1$, so that $S^*/N = 1/R_0$

Epidemic disease: R_{eff} changes as epidemic progresses, as susceptible pool is depleted.



Note: Sometimes "effective reproductive number" is used to describe transmission in the presence of disease control measures.

This is also called R_{control}.

$R_{effective}$ and herd immunity

$$R_{effective} = R_0 \times S/N$$

If a sufficiently high proportion of the population is immune, then $R_{effective}$ will be below 1 and the disease cannot circulate.

The remaining susceptible are protected by **herd immunity**.

The critical proportion of the population that needs to be immune is determined by a simple calculation:

- For $R_{eff} < 1$, we need $S/N < 1/R_0$
- Therefore we need a proportion $1-1/R_0$ to be immune.

What does R_0 tell you?

- Epidemic threshold

  NOTE: not every epidemic threshold parameter is R_0!
- Probability of successful invasion
- Initial rate of epidemic growth
- Prevalence at peak of epidemic
- Final size of epidemic (or the proportion of susceptibles remaining after a simple epidemic)
- Mean age of infection for endemic infection
- Critical vaccination threshold for eradication
- Threshold values for other control measures

Epidemic Burnout

Next, we consider the long-term (or "asymptotic") state. First divide equation (2.1) by equation (2.3):

$$\frac{dS}{dR} = -\beta\frac{S}{\gamma} = -R_0 S \qquad (2.5)$$

Upon integrating with respect to t, we obtain

$$S(t) = S(0)\mathrm{e}^{-R(t)R_0}. \qquad (2.6)$$

assuming $R(0) \neq 0$. So, as the epidemic develops, the number of susceptible decline and therefore, with a delay to take the infectious period into account, the number of recovered increases.

Note that S always remains above zero because $e^{-R\,R_0}$ is always positive; in fact given that $R \leq 1$, S must remain above e^{-R_0}.

Therefore, there will always be some susceptible in the population who escape the infection.

This leads to an important **and rather counter-intuitive conclusion :**

The chain of transmission eventually breaks due to the decline in infective, not due to a complete lack of susceptible.

This approach can be used to understand the fraction of the population who eventually contract an infection.

Following equation (2.6), and noting by definition that $S + I + R = 1$, and that the epidemic ends when $I = 0$, we can rewrite the long-term behavior of equation (2.6):

$$S(\infty) = 1 - R(\infty) = S(0)\mathrm{e}^{-R(\infty)R_0}.$$

$$\Longrightarrow 1 - R(\infty) - S(0)\mathrm{e}^{-R(\infty)R_0} = 0. \qquad (2.7)$$

where $R(\infty)$ is the final proportion of recovered individuals, which is equal to the total proportion of the population that gets infected.

This equation is transcendental and hence an exact solution is not possible.

However, by noting that when $R(\infty) = 0$ equation (2.7) is positive, whereas if $R(\infty) = 1$ then the equation is negative,

we know that at some point in between the value must be zero and a solution exists.

Using standard methods, such as the Newton-Raphson, it is possible to obtain an approximate numerical solution for equation (2.7); this is shown for the standard assumption of $S(0) = 1$ in Figure 2.2.

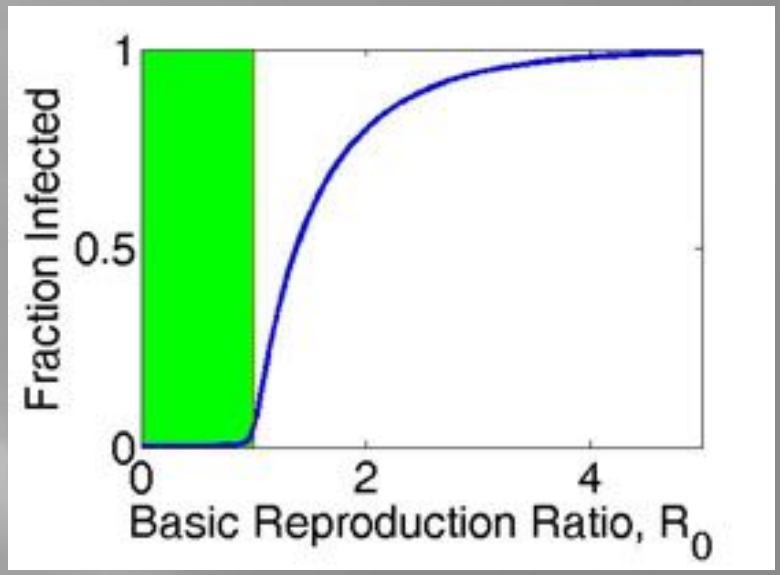


Figure 2.2.

This figure reinforces the message that if $R_0 < 1$ then no epidemic occurs. It also demonstrates the principle that whenever an infectious disease has a sufficiently large basic reproductive Ratio R_0, essentially everyone in a well mixed population is likely to get infected.

An exact solution of the SIR model ((2.1) - (2.3)) is not feasible due to the nonlinear transmission term, βSI.

We can, however, obtain an approximate solution for the **"epidemic curve“,** which is defined as the number of new cases per time interval.

A classic example of the epidemic curve is provided in Figure 2.3 which shows the number of deaths per week from the plague in Bombay during 1905-1906.

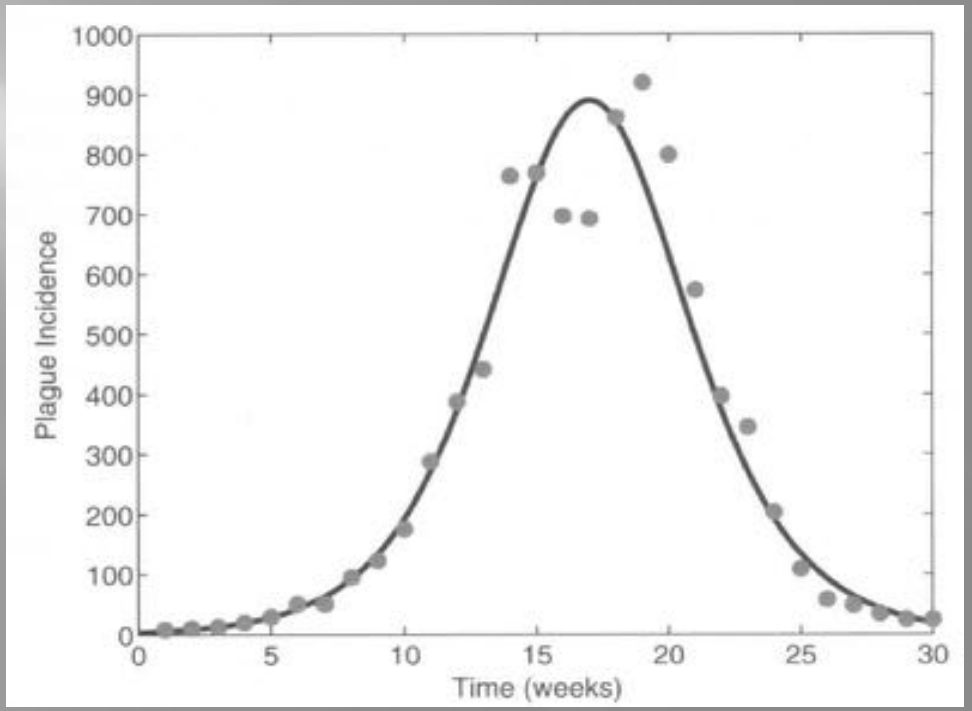


Figure 2.3. The epidemic curve. The tilled circles represent weekly deaths from plague in Bombay from December 17. 1905 to July 21, 1906. The solid line is Kermack and McKendrick's approximate solution given by $dR/dt = 890\ \mathrm{sech}^2\ (0.2t/-3.4)$.

SIR Model with Demography

In the last section, we presented the basic framework for the compartmental model with the assumption that the time scale of disease spread is sufficiently fast so as not to be affected by population births and deaths.

Some important epidemiological lessons were learned from this model, but ultimately, the formalism ensured the eventual extinction of the pathogen.

If we are interested in exploring the longer-term persistence and endemic dynamics of an infectious disease, then clearly demographic processes will be important

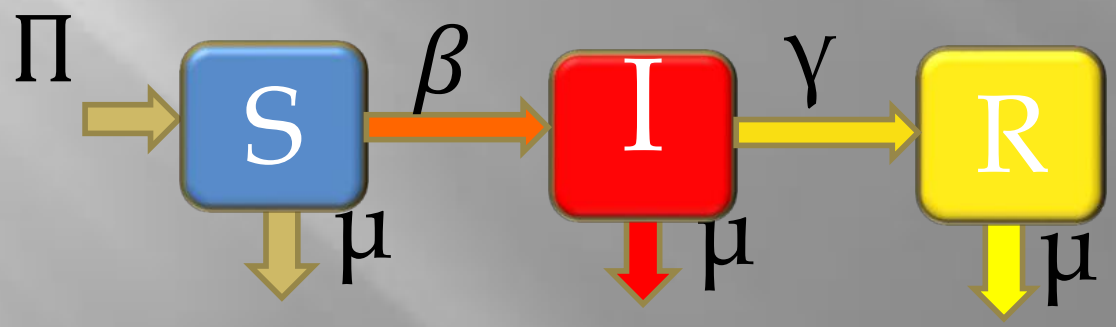
SIR Model with Demography

$$\frac{dS}{dt} = \mu - \beta SI - \mu S \qquad (2.13)$$

$$\frac{dI}{dt} = \beta SI - \gamma I - \mu I \qquad (2.14)$$

$$\frac{dR}{dt} = \gamma I - \mu R \qquad (2.15)$$

With initial conditions
$S(0) > 0, I(0) > 0,$ and $R(0) = 0.$



The Threshold (R_0)

Starting with the basic definition of R_0 (number of secondary infective per index case in a naive population of susceptible), we can look closely at equation (2.14) to work out R_0.

The parameter β represents the transmission *rate* per infective, and the negative terms in the equation tells us that each infectious individual spends an average $\frac{1}{\gamma+\mu}$ time units in this class—the infectious period is effectively reduced due to some individuals dying while infectious.

Therefore, if we assume the entire population is susceptible ($S = 1$), *then the average number of new infections per infectious individual is determined by the transmission rate multiplied by the infectious period:*

$$R_0 = \frac{\beta}{\gamma+\mu} \qquad (2.16)$$

This value is generally similar to, but always smaller than, R_0 for a closed population because the natural mortality rate reduces the average time an individual is infectious.

The Reproduction number (R_0)

The basic reproduction number, denoted R_0, is "***the expected number of secondary cases produced, in a completely susceptible population, by a typical infective individual***"

If $R_0 < 1$, then on average an infected individual produces less than one new infected individual over the course of its infectious period, and the infection cannot grow.

Conversely, if $R_0 > 1$, then each infected individual produces, on average, more than one new infection, and the disease can invade the population.

Thus, R_0 is clearly a threshold parameter that can be used as an indicator for disease control.

Mathematical implication of R_0

If the reproduction is less than unity (i.e. $R_0 < 1$), then the disease free equilibrium (DFE), the equilibrium at which the population remains in the absence of disease, is ***locally asymptotically stable***; whereas if $R_0 > 1$, then the equilibrium is ***unstable.***

Implication for public health

If $R_0 < 1$, then the disease cannot invade the population, will die out in the community. This means it can be controlled and can be eliminated.

However, if $R_0 > 1$, invasion is always possible and the disease will persist in the community. With this scenario, the goal will be to manage the transmission of the disease in the community.

Note:

For the case of a single infected compartment, R_0 is simply the product of the infection rate and the mean duration of the infection.

However, for more complicated models with several infected compartments this simple heuristic definition of R_0 is insufficient.

A more general basic reproduction number can be defined as the ***number of new infections produced by a typical infective individual in a population at a DFE.***

Calculating The Reproduction Number R0

To estimate R_0, we shall use the ***next generation matrix method.***

The basic reproduction number cannot be determined from the structure of the mathematical model alone, but depends on the definition of infected and uninfected compartments.

The distinction between infected and uninfected compartments must be determined from the epidemiological interpretation of the model and cannot be deduced from the structure of the equations alone.

It is plausible that more than one interpretation is possible for some models.

In order to compute R_0, it is important to distinguish new infections from all other changes in the population.

First sort the compartments so that the first m compartments correspond to infected individuals.

We define X_s to be the set of all disease free states. That is

$$X_s = \{x \geq 0 \,|\, x_i = 0, i = 1, \ldots, m\}.$$

Let $\mathcal{F}_i(x)$ be the rate of appearance of new infections in compartment i,

$\mathcal{V}_i^+(x)$ be the rate of transfer of individuals into compartment i by all other means, and

$\mathcal{V}_i^-(x)$ be the rate of transfer of individuals out of compartment i.

Then, the disease transmission model consists of nonnegative initial conditions together with the following system of equations:

$$\dot{x}_i = f_i(x) = \mathcal{F}_i(x) - \mathcal{V}_i(x), \qquad i = 1, \ldots, n, \qquad (1)$$

where $V_i = \mathcal{V}_i^- - \mathcal{V}_i^+$

The reproduction number is given by

$$R_0 = \rho(FV^{-1}), \qquad (4)$$

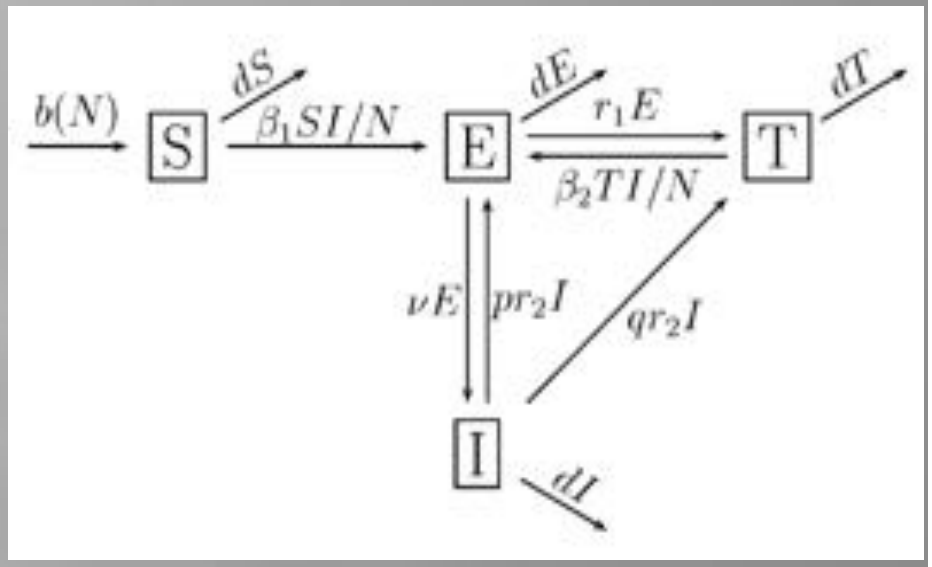
where $\rho(A)$ denotes the spectral radius of a matrix A and F and V are the $m \times m$ matrices defined by

$$F = \left[\frac{\partial \mathcal{F}_\mathrm{i}}{\partial \mathrm{x_j}}(\mathrm{x_o})\right] \quad \text{and} \quad \mathrm{V} = \left[\frac{\partial \mathcal{V}i}{\partial xj}(x_o)\right] \quad with\ 1 \leq i, j \leq m.$$

Further, F is nonnegative, V is a nonsingular M-matrix.

Example

The decomposition of $f(x)$ into the components $\mathcal{F}$ and $\mathcal{V}$ is illustrated using a simple tuberculosis treatment model based on the model of Castillo-Chavez and Feng.



Progression of infection from susceptible (S) individuals through the exposed (E), infected (I), and treated (T) compartments for the treatment model

First sort the compartments

$$\dot{E} = \beta_1 SI/N + \beta_2 TI/N - (d+\nu+r_1)E + pr_2 I,$$
$$\dot{I} = \nu E - (d+r_2)I,$$
$$\dot{S} = b(N) - dS - \beta_1 SI/N,$$
$$\dot{T} = -dT + r_1 E + qr_2 I - \beta_2 TI/N.$$

Progression from E to I and failure of treatment are not considered to be new infections, but rather the progression of an infected individual through the various compartments.

The infected compartments are E and I, giving m = 2.

$$\mathcal{F} = \begin{pmatrix} \beta_1 SI/N + \beta_2 TI/N \\ 0 \\ 0 \\ 0 \end{pmatrix}, \quad \text{and } \mathcal{V} = \begin{pmatrix} (d+\nu+r_1)E - pr_2 I \\ -\nu E + (d+r_2)I \\ -b(N) + dS + \beta_1 SI/N \\ dT - r_1 E - qr_2 I + \beta_2 TI/N \end{pmatrix}.$$

The disease free equilibrium (DFE) with $E = I = 0$ has the form

$$x_0 = (0, 0, S_0, 0)^t,$$

Then,

$$F = \begin{pmatrix} 0 & \beta_1 \\ 0 & 0 \end{pmatrix}, \qquad V = \begin{pmatrix} d+\nu+r_1 & -pr_2 \\ -\nu & d+r_2 \end{pmatrix},$$

$$V^{-1} = \frac{1}{(d+\nu+r_1)(d+r_2) - \nu p r_2} \begin{pmatrix} d+r_2 & pr_2 \\ \nu & d+\nu+r_1 \end{pmatrix},$$

$$\mathcal{R}_o = \frac{\beta_1 \nu}{(d+\nu+r_1)(d+r_2) - \nu p r_2}.$$

A heuristic derivation of the (2,1) entry of V^{-1} and R_0 are as follows: a fraction $h_1 = \nu/(d + \nu + r_1)$ of exposed individuals progress to compartment I, a fraction $h_2 = pr_2/(d + r_2)$ of infectious individuals re-enter compartment E.

Hence, a fraction h_1 of exposed individuals pass through compartment I at least once, a fraction $h_1^2 h_2$ pass through at least twice, and a fraction $h_1^k h_2^{k-1}$ pass through at least k times, spending an average of $\tau = 1/(d + r_2)$ time units in compartment I on each pass.

Thus, an individual introduced into compartment E spends, on average,

$$\tau(h_1 + h_1^2 h_2 + \ldots) = \tau h_1/(1 - h_1 h_2) = \nu/((d + \nu + r_1)(d + r_2) - pr_2)$$

time units in compartment I over its expected lifetime. Multiplying this by β_1 gives R_0.

The decomposition of $f_i(x)$ is not restrict to a single choice for $\mathcal{F}_i$, only one such choice is epidemiologically correct. Different choices for the function $\mathcal{F}$ lead to different values for the spectral radius of FV^{-1}.

	(a)	(b)
$\mathcal{F}$	$\begin{pmatrix} \beta_1 SI/N + \beta_2 TI/N + pr_2 I \\ 0 \\ 0 \\ 0 \end{pmatrix}$	$\begin{pmatrix} \beta_1 SI/N + \beta_2 TI/N + pr_2 I \\ \nu E \\ 0 \\ 0 \end{pmatrix}$
$\mathcal{V}$	$\begin{pmatrix} (d+\nu+r_1)E \\ -\nu E + (d+r_2)I \\ -b(N) + dS + \beta_1 SI/N \\ dT - r_1 E - qr_2 I + \beta_2 TI/N \end{pmatrix}$	$\begin{pmatrix} (d+\nu+r_1)E \\ (d+r_2)I \\ -b(N) + dS + \beta_1 SI/N \\ dT - r_1 E - qr_2 I + \beta_2 TI/N \end{pmatrix}$
F	$\begin{pmatrix} 0 & \beta_1 + pr_2 \\ 0 & 0 \end{pmatrix}$	$\begin{pmatrix} 0 & \beta_1 + pr_2 \\ \nu & 0 \end{pmatrix}$
V	$\begin{pmatrix} d+\nu+r_1 & 0 \\ -\nu & d+r_2 \end{pmatrix}$	$\begin{pmatrix} d+\nu+r_1 & 0 \\ 0 & d+r_2 \end{pmatrix}$
$\rho(FV^{-1})$	$\dfrac{\beta_1\nu + pr_2\nu}{(d+\nu+r_1)(d+r_2)}.$	$\sqrt{\dfrac{\beta_1\nu + pr_2\nu}{(d+\nu+r_1)(d+r_2)}}$

Table 1
Decompositions of f leading to alternative thresholds

In column (a), treatment failure is considered to be a new infection and in column (b), both treatment failure and progression to infectiousness are considered new infections.

In each case the condition $(FV^{-1}) < 1$ yields the same portion of parameter space.

Thus, (FV^{-1}) is a threshold parameter in both cases. The difference between the numbers lies in the epidemiological interpretation rather than the mathematical analysis.

For example, in column (a), the infection rate is $\beta_1 + pr_2$ and an exposed individual is expected to spend $\nu/((d+\nu+r_1)(d+r_2))$ time units in compartment I.

However, this reasoning is biologically flawed since treatment failure does not give rise to a newly infected individual.

Home Work

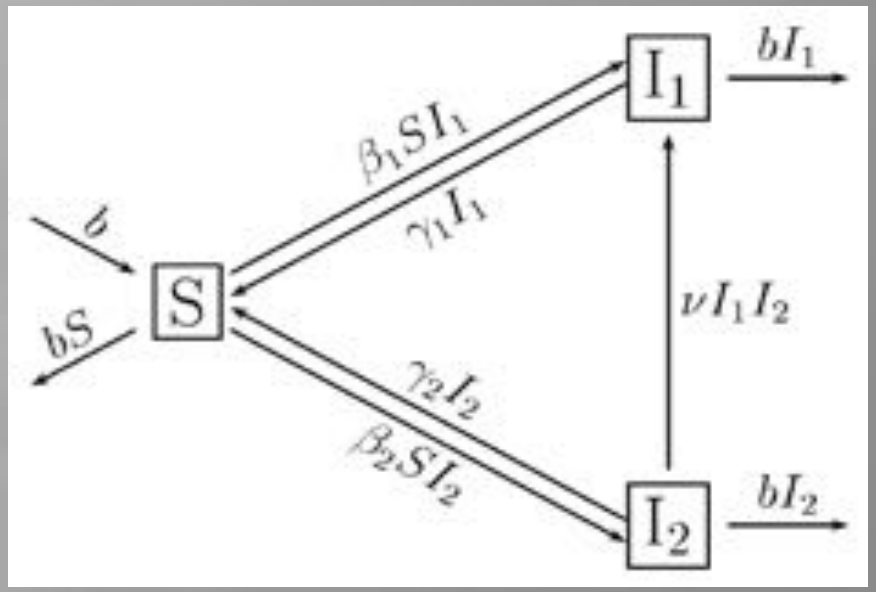
Using the models from the last homework rearrange the equations and state

1. the $\mathcal{F}$ matrix of new infections and

2. The $\mathcal{V}$ matrix of transfers either to or fro each compartments

Multistrain model

$$\dot{I}_1 = \beta_1 I_1 S - (b+\gamma_1) I_1 + \nu I_1 I_2,$$
$$\dot{I}_2 = \beta_2 I_2 S - (b+\gamma_2) I_2 - \nu I_1 I_2,$$
$$\dot{S} = b - bS + \gamma_1 I_1 + \gamma_2 I_2 - (\beta_1 I_1 + \beta_2 I_2) S.$$



For simplicity we have scaled the birth and death rates to $b > 0$. Hence, the disease free equilibrium is $x_0 = (0,0,1)^t$, and

$$F = \begin{pmatrix} \beta_1 & 0 \\ 0 & \beta_2 \end{pmatrix}, \qquad V = \begin{pmatrix} b+\gamma_1 & 0 \\ 0 & b+\gamma_2 \end{pmatrix}$$

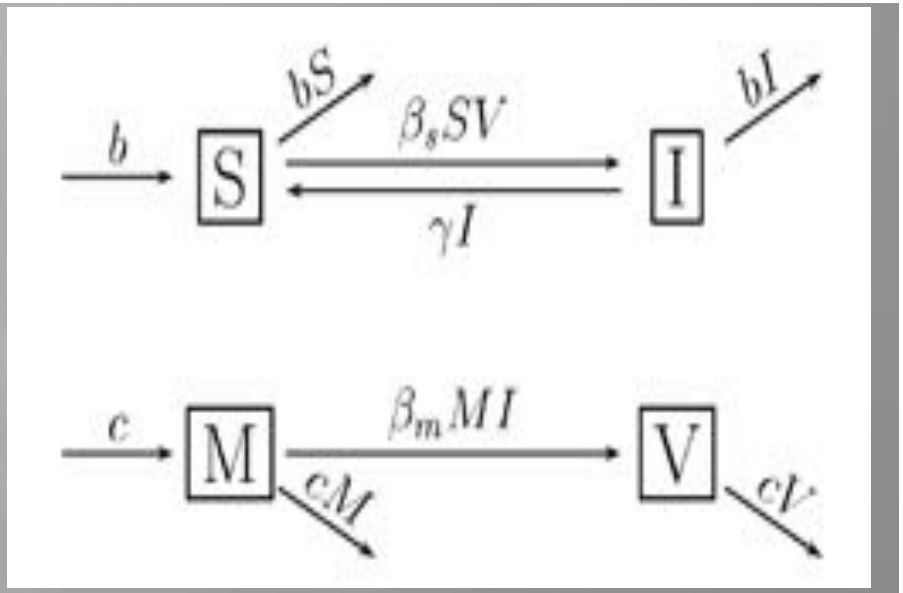
$$\mathcal{R}_i = \frac{\beta_i}{b+\gamma_i}, \qquad i = 1,2.$$

The basic reproduction number for the system is the maximum of the two. That is,

$$\mathcal{R}_o = \max_{i \in \{1,2\}} \mathcal{R}_i.$$

Vector-Host Model

$$\dot{I} = \beta_s SV - (b+\gamma)I,$$
$$\dot{V} = \beta_m MI - cV,$$
$$\dot{S} = b - bS + \gamma I - \beta_s SV,$$
$$\dot{M} = c - cM - \beta_m MI.$$



The birth and death rates have been scaled to $b > 0$ for the host and $c > 0$ for the vector. Thus, the DFE is $x_0 = (0,0,1,1)^t$,

$$F = \begin{pmatrix} 0 & \beta_s \\ \beta_m & 0 \end{pmatrix}, \qquad V = \begin{pmatrix} b+\gamma & 0 \\ 0 & c \end{pmatrix},$$

with V nonsingular, and the basic reproduction number is

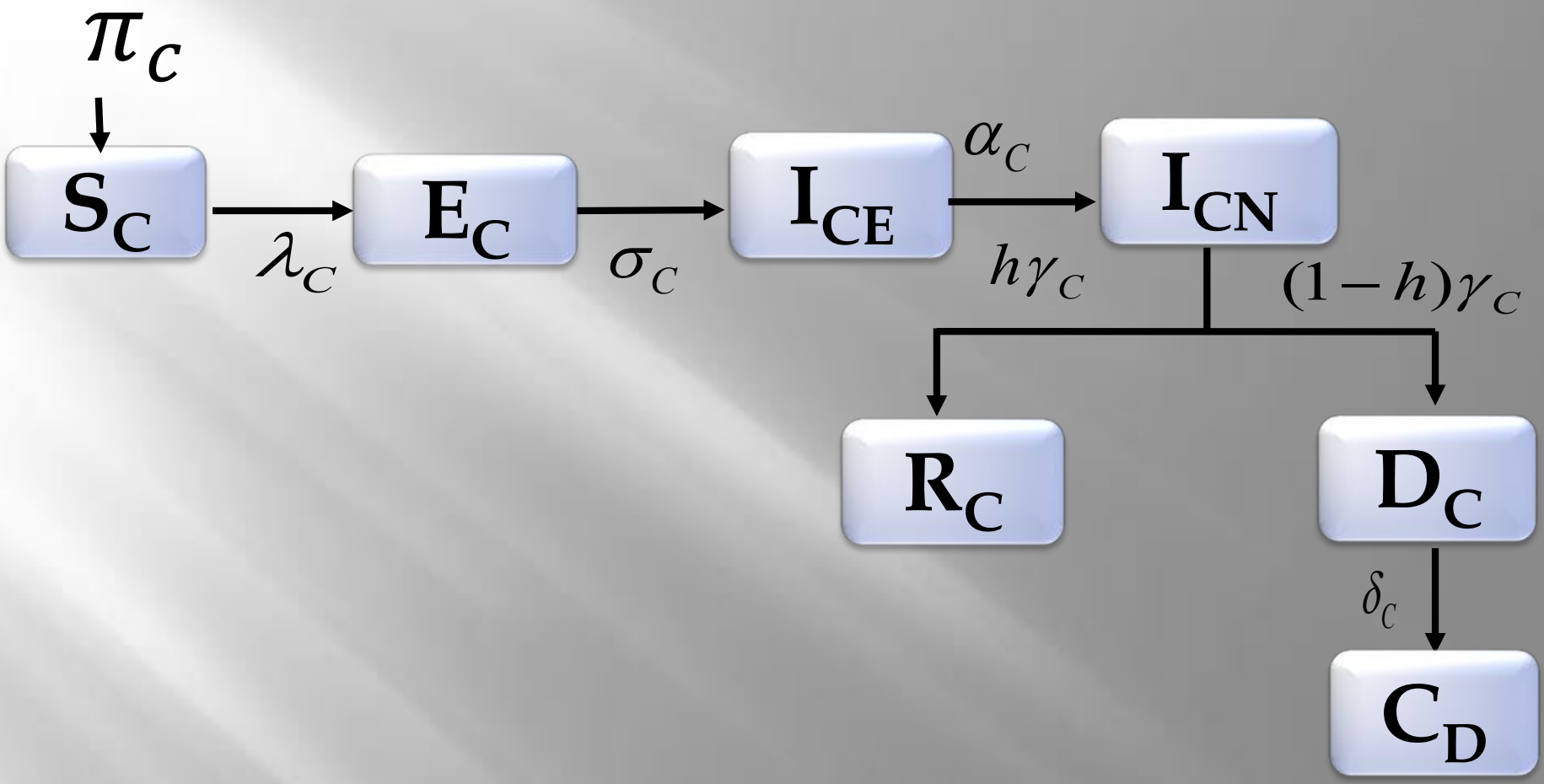
$$\mathcal{R}_o = \sqrt{\frac{\beta_s \beta_m}{c(b+\gamma)}}.$$

Near the DFE, each infected host produces β_m/c new infected vectors over its expected infectious period, and each infected vector produces $\beta_s/(b+\gamma)$ new infected hosts over its expected infectious period. The square root arises from the two `generations' required for an infected vector or host to `reproduce' itself.

Home Work

Determine the reproduction number for the following systems involving the Ebola pre-intervention model

Ebola Pre-Intervention Model



$$\lambda_C(I_{CE}, I_{CN}, D_C) = \frac{\beta_C \phi_C (I_{CE} + I_{CN} + \tau_C D_C)}{S_C + E_C + I_{CE} + I_{CN} + R_C + D_C}$$

Sensitivity analysis

Sensitivity analysis is commonly used to determine the robustness of model predictions to parameter values (since data collection and presumed parameter values are flawed with errors).

In determining how best to reduce disease induced mortality and morbidity, it is necessary to know the relative importance of the different factors responsible for its transmission and prevalence. We do this by determining parameters that have a high impact on the reproduction number R_0. These parameters are then targeted by control intervention strategies.

Sensitivity and uncertainty analysis

Uncertainty arises from two main sources in epidemic models:

- parameter values: often unknown or imprecise
- model structure: does it capture the right mechanisms?

Uncertainty analysis aims to assess the variability in model outputs that arises from uncertainty in model inputs.

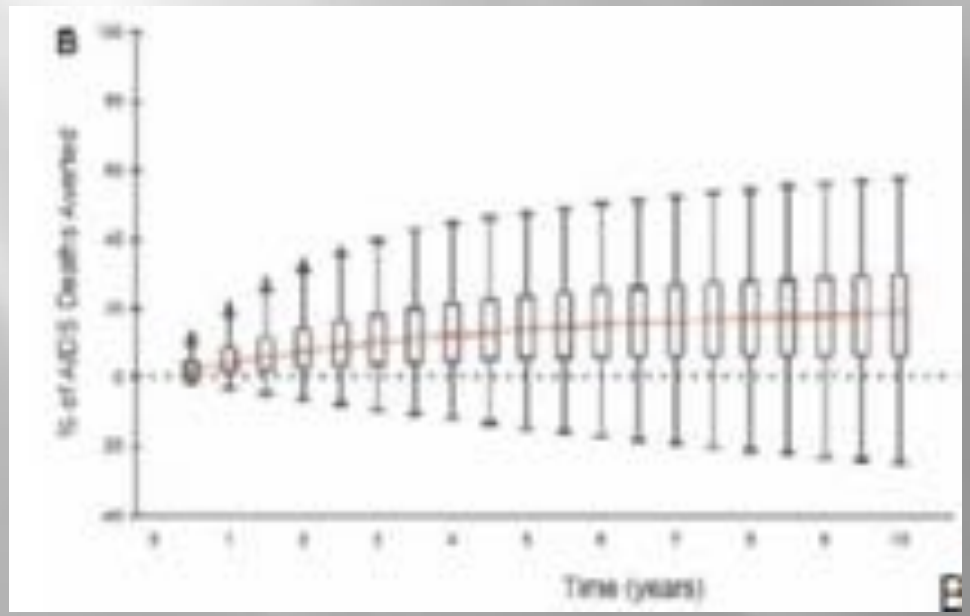
Sensitivity analysis extends this to determine which parameters (or changes in model structure) are most important in determining the model output, and to quantify the influence of each parameter on particular outputs.

Why do uncertainty analysis?

• Determine how much confidence should be placed in quantitative projections generated by models.

What “error bars” should be placed on output quantities?

• Understand whether differences between model outputs (or between model outputs and data) are significant.

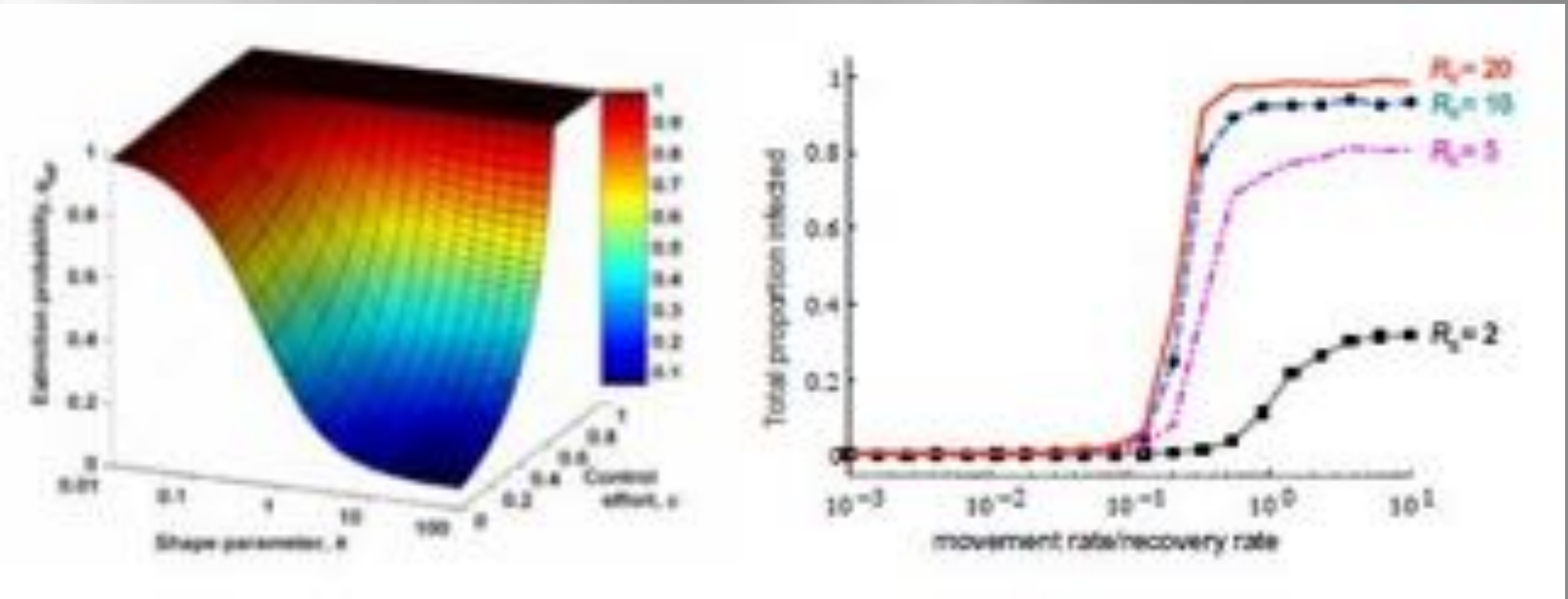


Why do sensitivity analysis?

• Understand the relative importance of different mechanisms in generating observed patterns.

• Determine which points in the system are good targets for intervention efforts.

• Guide collection of further data – gather more information on those parameters that are most influential



To implement the sensitivity analysis, we calculate the sensitivity indices of the reproductive number, R_0, to the parameters in the model. These indices tell us how crucial each parameter is to disease transmission and prevalence.

Sensitivity indices

Sensitivity indices allow us to measure the relative change in a state variable when a parameter changes. The ***normalized forward sensitivity index of a variable to a parameter is the ratio of the relative change in the variable to the relative change in the parameter.***

When the variable is a differentiable function of the parameter, the sensitivity index may be alternatively defined using partial derivatives.

Definition. The normalized forward sensitivity index of a variable, u, that depends differentiably on a parameter, p, is defined as:

$$\Upsilon_p^u := \frac{\partial u}{\partial p} \times \frac{p}{u}.$$

Sensitivity indices of R_0

Given the reproduction number R_0 in (2.16),

$$R_0 = \frac{\beta}{\gamma + \mu}$$

we derive an analytical expression for the sensitivity of R_0,

$$\Upsilon_p^{R_0} = \frac{\partial R_0}{\partial p} \times \frac{p}{R_0},$$

to each of the different parameters.

For example, the sensitivity index of R_0 with respect to β,

$$\Upsilon_{\beta}^{R_0} = \frac{\partial R_0}{\partial \beta} \times \frac{\beta}{R_0} = 1,$$

does not depend on any parameter values. Indices of the two other parameters (γ and μ) are:

$$\Upsilon_{\gamma}^{R_0} = \frac{\partial R_0}{\partial \gamma} \times \frac{\gamma}{R_0} = -\frac{\mu}{\gamma + \mu}$$

$$\Upsilon_{\mu}^{R_0} = \frac{\partial R_0}{\partial \mu} \times \frac{\mu}{R_0} = -\frac{\gamma}{\gamma + \mu},$$

Estimating the Sensitivity indices

Suppose $\mu = 0.008,\ \gamma = 0.5$, then

Parameters	Sensitivity Indices
β	1
μ	-0.016
γ	-0.984

Implication for control

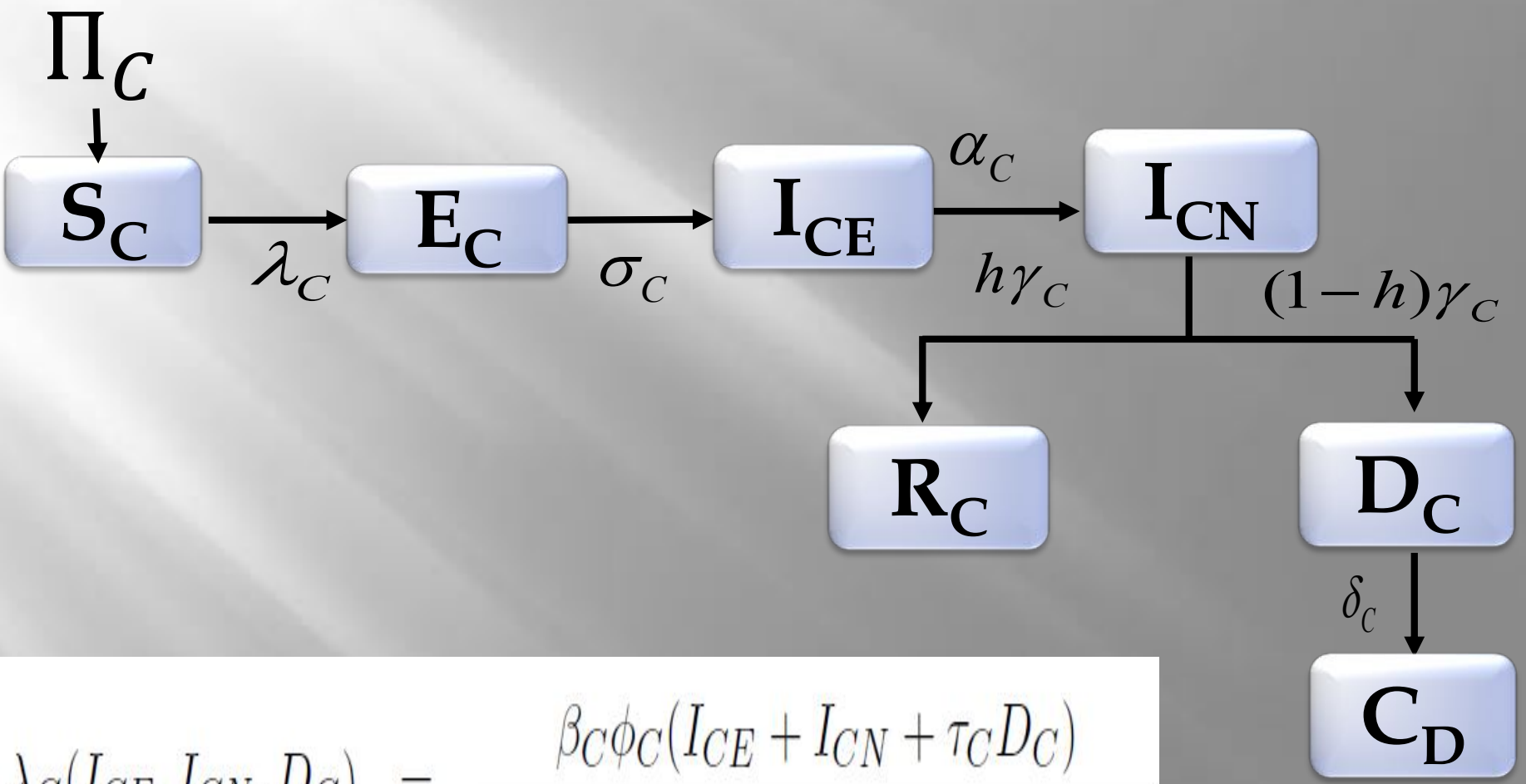
The most sensitive parameter is the disease transmission probability β, followed by the recovery rate, γ, and then the death rate μ.

Since $\Upsilon_{\beta}^{R_0}$ =1, decreasing (or increasing) β by 10% decreases (or increases) R_0 by $1 * 10\% = 10\%$. Similarly, as $\Upsilon_{\gamma}^{R_0}$ = - 0.984, increasing (or decreasing) γ by 10% increases (or decreases) R_0 by about $0.984 * 10\% = 9.84\% \approx 10\%$.

A 10% change in μ is negligible and we therefore ignore it.

Home Work

Estimate the sensitivity indices of the reproduction number for the Ebola pre-intervention model



$$\lambda_C(I_{CE}, I_{CN}, D_C) = \frac{\beta_C \phi_C (I_{CE} + I_{CN} + \tau_C D_C)}{S_C + E_C + I_{CE} + I_{CN} + R_C + D_C}$$

Using the following parameter values, determine the values of the sensitivity indices of the reproduction number for the Ebola pre-intervention model.

From the values of the sensitivity indices determine which parameter has the most impact on the reproduction number of the Ebola model

β_C	0.3045/day
μ_H	1/58 per year
τ_C	2 0.21/day
ϕ_C	1.2532
σ_C	0.5239/day
α_C	0.5472/day
h	0.42, 0.48/day
γ_C	0.5366/day
δ_C	0.5/day
π_C	555/day