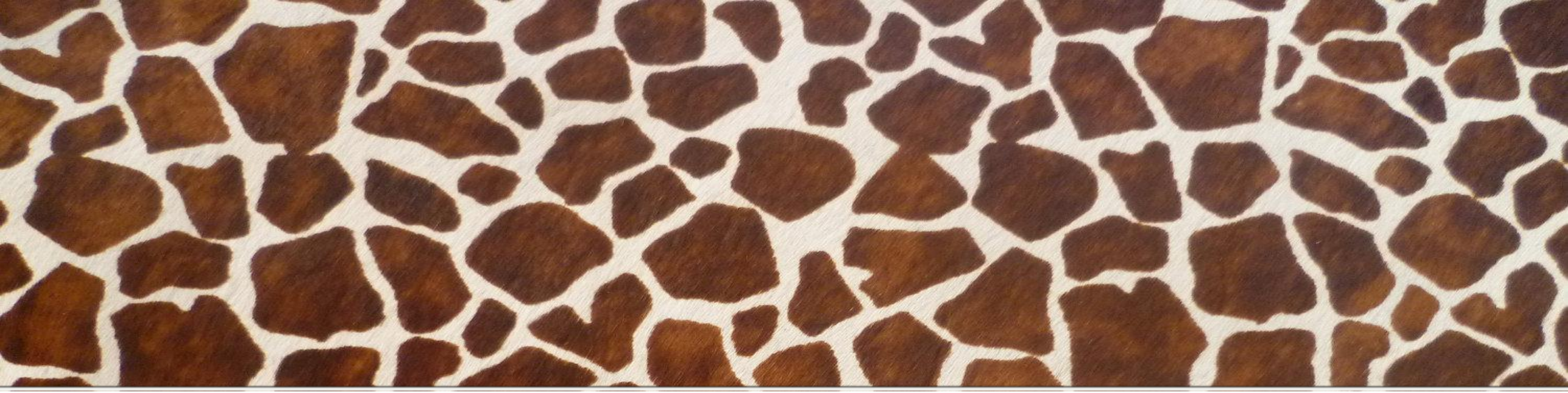
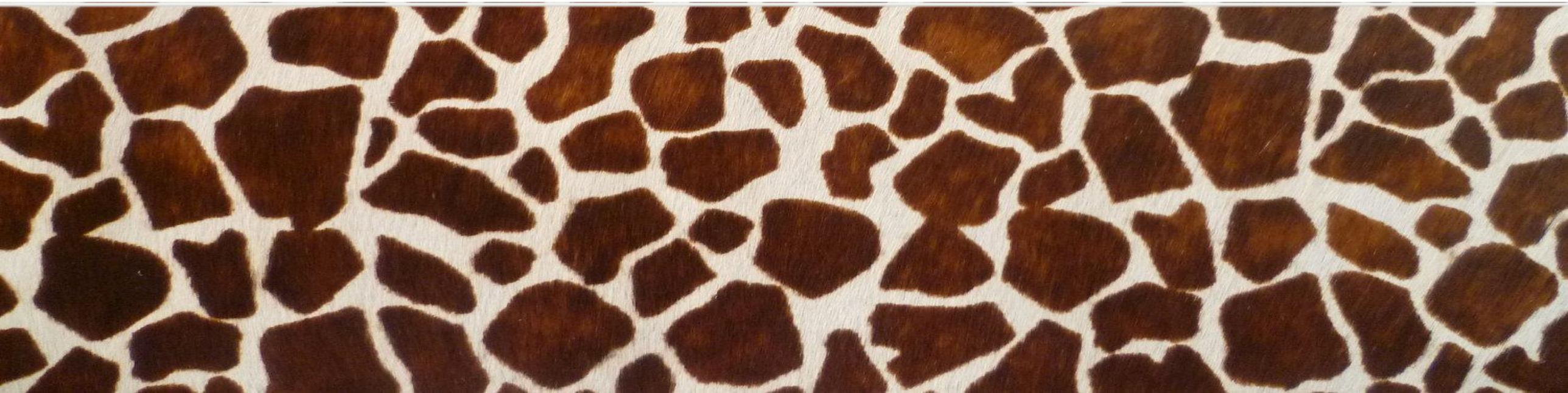
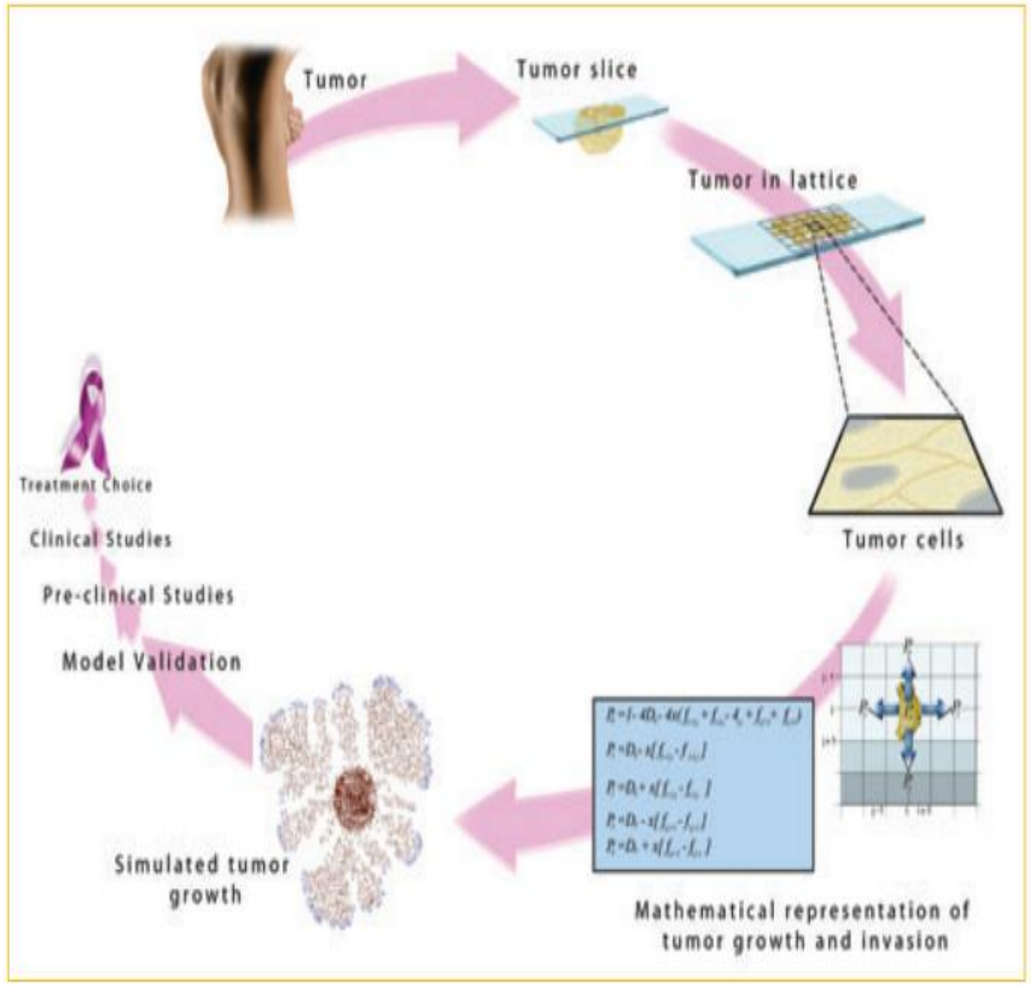


Mathematical Biology - Lecture 2 – diseases and epidemics



diseases and epidemics

- infectious and non-infectious diseases
- in non-infectious diseases, the objective is to model the spread of the disease and see when it becomes dangerous
- in infectious diseases, the objective is to look at how the disease spreads in a population
- we will look at modeling of infectious disease spread – contagion, epidemics etc



Forecasting Invasion. This graphic depiction of a mathematical model developed by Vito Quaranta and Alexander Anderson predicts whether a tumor will become invasive. The tumor is represented on a two-dimensional grid. Each virtual cell is accounted for on the grid and its behavior (e.g., growth, movement, death) is tracked based on mathematical functions and partial differential equations. Solving these equations in sequential time-steps generates a computer simulation of tumor growth and invasion. This approach has the potential to predict disease outcome based on precise quantities measured in the tumor of a specific patient. The model was described in: Anderson et al. Cell. 2006 Dec 1;127(5):905-15. Courtesy of the journal Cell. Graphic by Dominic Doyle.

disease models – first models

Simplest possible epidemic model: population has susceptibles and Infectives and the disease spreads through contact with the infectives.

SI model: S(t) + I(t) = N,

Mean-field model: $\frac{dS}{dt} = -f(S,I), \frac{dI}{dt} = f(S,I)$

f(S,I) – incidence of disease – increasing function of S and I

simplest model: $f(S,I) = \lambda(I)S = \beta \mathrm{IS}$ – law of mass action

$\lambda(I)$- force of infection – probability density a given susceptible will contract disease

β – pairwise infectious contact rate

disease models – first models

SIS model – model with recovery – bacterial infections give no immunity

S(t) + I(t) = N, $\frac{dS}{dt} = -f(S,I) + g(I)$, $\frac{dI}{dt} = f(S,I) - g(I)$

g(I) – recovery function = γI, γ - rate of recovery – probability each infective will recover in $\delta\tau$ is $\gamma\delta\tau + O(\delta\tau^2)$ – equivalent to saying amount of time spent in the I class is exponentially distributed with mean $1/\gamma$

$\frac{du}{d\tau} = -(R_0 u - 1)v$; $\frac{dv}{d\tau} = (R_0 u - 1)v$; $R_0 = \frac{\beta N}{\gamma}$ - basic reproductive ratio

R_0 - expected number of infectious contacts made by an infective in a population of susceptibles

disease models – first models

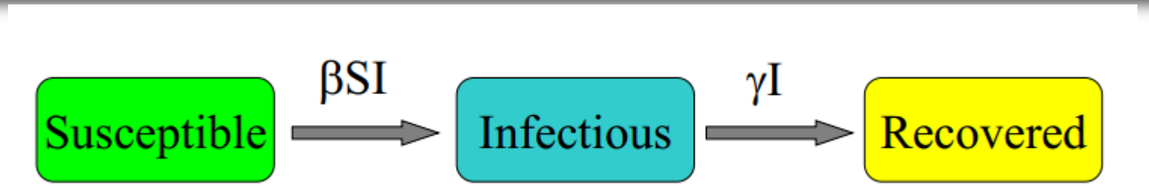
$$\frac{du}{d\tau} = -(R_0 u - 1)v;\ \frac{dv}{d\tau} = (R_0 u\ - 1)v$$

stability analysis: fixed points for v = 0, any u

start with disease-free initial state and see if it is stable
If R_0 < 1, stable – disease dies out if a new infective is introduced
If R_0 > 1, unstable – endemic – the disease remains in the population
with steady-state value of v = $1 - \frac{1}{R_0}$
the infective population follows a logistic equation with carrying capacity

$$1 - \frac{1}{R_0}$$

disease models - SIR



classic paper by Kermack and McKendrick in 1927

simple `compartmental´ model that describes certain kinds of diseases such as mumps, rubella, measles etc. where the epidemic duration is much smaller than the life expectancy of the host

total population remains constant: N
number susceptible: S
number infectious: I
number recovered: R
S + I + R = N

disease models - SIR

ODE mean-field model for SIR:

$$\frac{dS}{dt} = -\beta SI;\ \frac{dI}{dt} = \beta \mathrm{SI}\ -\gamma I;\ \frac{dR}{dt} = \gamma I$$

Non-dimensionalizing the equations we get

$$\frac{du}{d\tau} = -R_0 uv;\ \frac{dv}{d\tau} = (R_0 u\ - 1)v;\ \frac{dw}{dt} = v$$

disease models – SIR - analysis

The values of u, v and w are such that

$$0 \leq u \leq 1, 0 \leq v \leq 1, 0 \leq w \leq 1, u + v + w = 1$$

v = 0 is a fixed point for any value of u – no infection, no disease

u = 1, v = 0 is the disease-free initial state
Everyone is susceptible but no one is infectious

let us look at the dynamics, the stability of these fixed points etc.

disease models – SIR - analysis

consider the disease-free initial state (1,0) (which is also a steady-state for the system)

the Jacobian matrix for this system is given by

$$\begin{bmatrix} -R_0 v & -R_0 u \\ R_0 v & R_0 u - 1 \end{bmatrix}$$

so the state (1,0) is stable (but not asymptotically stable) for small perturbations if $R_0 < 1$; else it is unstable – epidemic!

disease models – SIR - analysis

$$\frac{du}{d\tau} = -R_0 uv; \frac{dv}{d\tau} = (R_0 u - 1)v$$

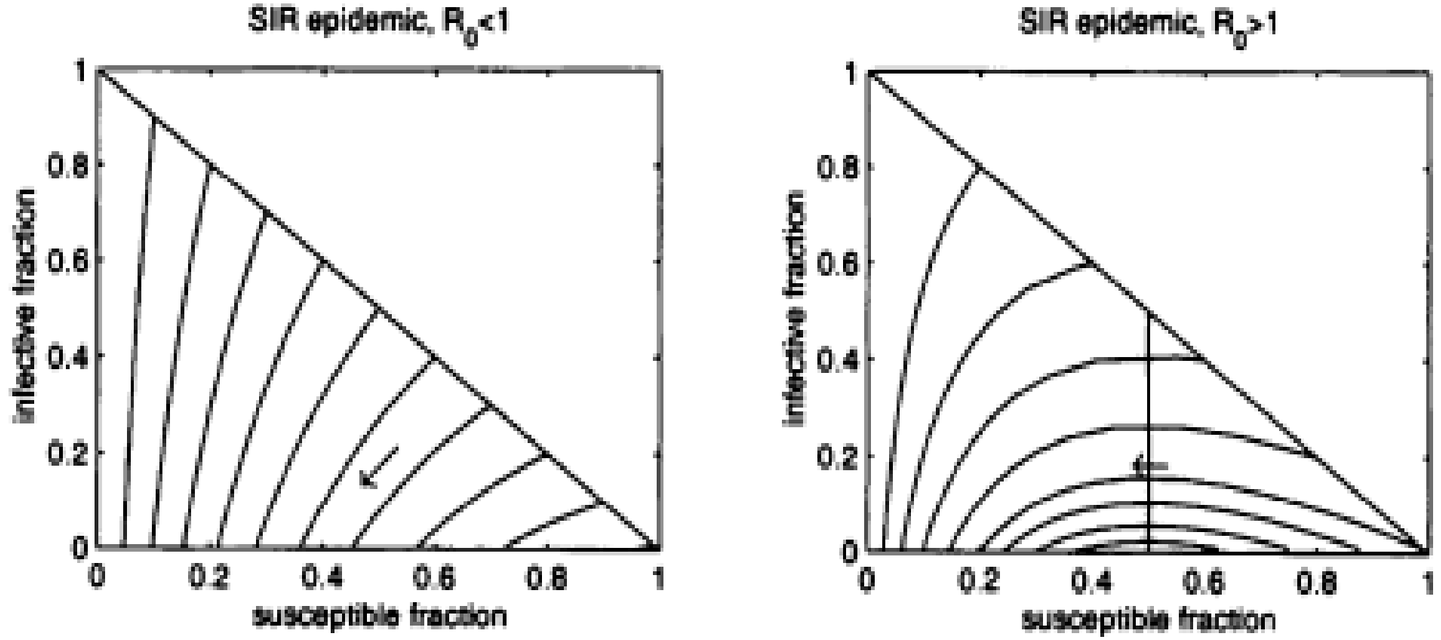


Figure 3.2 Phase plane for the SIR epidemic, in the cases $R_0 < 1$ and $R_0 > 1$.

disease models – SIR - analysis

the size of the epidemic is the number of people in R
Rewriting the equations as

$$\frac{dw}{du} = -\frac{1}{R_0 u}, \frac{dv}{du} = -1 + \frac{1}{R_0 u}$$

$u = \exp(-R_0 w)$ starting from (1,0,0)

since u, w are monotonic, bounded functions of t, they tend to limits

$(1 - w_1, 0, w_1)$ is a final steady state if $1 - w_1 = \exp(-R_0 w_1)$

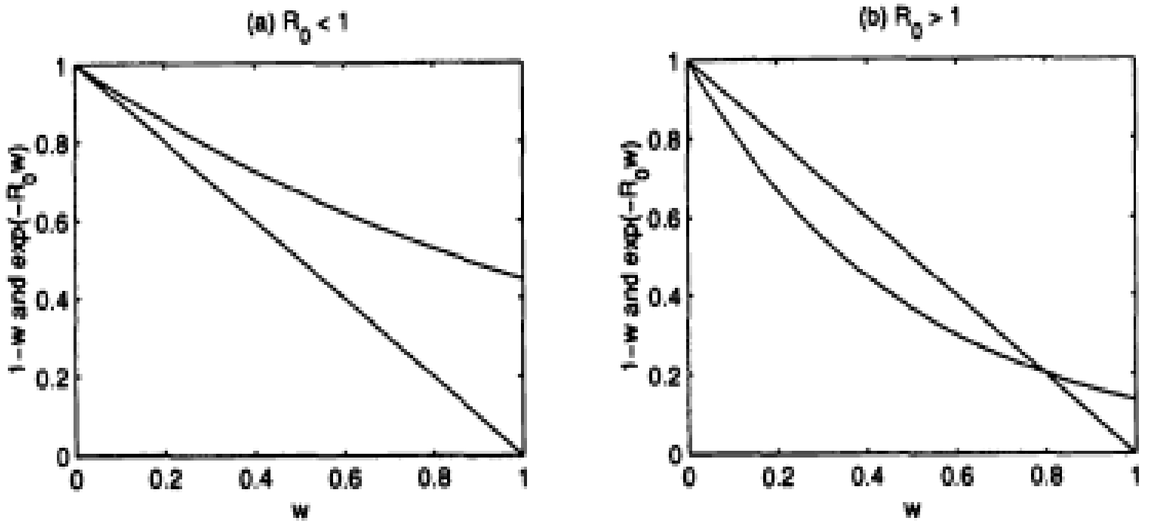


Figure 3.3 The functions $1 - w_1$ and $\exp(-R_0 w_1)$, for $R_0 < 1$ and $R_0 > 1$. The intersection point determines the final size of the epidemic, if any.

disease models - SIR

R_0 gives a quick idea of how fast an epidemic can spread
it can be estimated from the initial per capita growth rate

$$r = (R_0 - 1)\gamma$$

Disease	Transmission	R_0
Measles	Airborne	12–18
Pertussis	Airborne droplet	12–17
Diphtheria	Saliva	6–7
Smallpox	Social contact	5–7
Polio	Fecal-oral route	5–7
Rubella	Airborne droplet	5–7
Mumps	Airborne droplet	4–7
HIV/AIDS	Sexual contact	2–5
SARS	Airborne droplet	2–5[2]
Influenza (1918 pandemic strain)	Airborne droplet	2–3[3]

disease models - extensions

SIRS model – diseases which give only limited immunity

$$\frac{dS}{dt} = -\beta SI + \delta R;\ \frac{dI}{dt} = \beta \mathrm{SI}\ \ - \gamma I;\ \frac{dR}{dt} = \gamma I - \delta R$$

SEIR model – diseases where there are latent infectives

$$\frac{dS}{dt} = -\beta SI;\ \frac{dE}{dt} = \beta \mathrm{SI}\ \ - \delta E;\ \frac{dI}{dt} = \delta E - \gamma I; \frac{dR}{dt} = \gamma I$$

Similarly, MSIR - measles, SIR with carriers – `Typhoid Mary´ etc

disease models – with vital dynamics

SIR model with births and deaths
assume no vertical transmission – not true for AIDS etc
birth rate B, death rates c (due to disease), d (unrelated to disease)

birth rate etc depends on population model
assume B = bN, we get

$$\frac{dS}{dt} = bN - \beta IS - dS; \frac{dI}{dt} = \beta IS - cI - dI - \gamma I; \frac{dR}{dt} = \gamma I - dR$$

$$R_0 = \frac{\beta}{d + c + \gamma}$$

Normally, γ dominates the denominator – mean infectious period much smaller than life expectancy of host

disease models – with vital dynamics

suppose d = b, c = 0: steady-state for population, non-fatal disease

$$\frac{du}{dt} = \frac{b}{\gamma + b}(1 - u) - R_0 uv; \frac{dv}{dt} = (R_0 u - 1)v; \frac{dw}{dt} = \frac{\gamma}{\gamma + b}v - \frac{b}{\gamma + b}w$$

endemic steady state exists if $R_0 > 1$ – disease does not die out

steady-state given by $u^* = \frac{1}{R_0}, v^* = \frac{b}{\gamma + b}(1 - \frac{1}{R_0})$

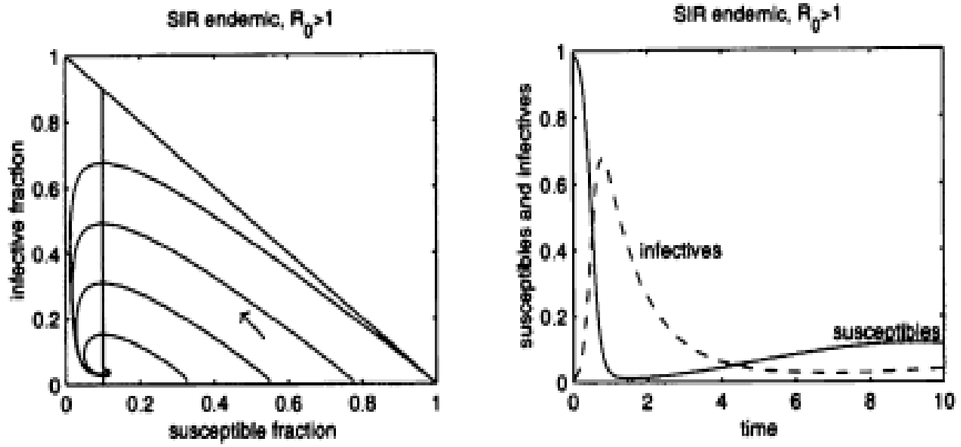


Figure 3.5 Numerical solution of Equations (3.4.12), for $R_0 > 1$ (in fact $R_0 = 10$). We have taken $\gamma/b = 0.1$, much larger than is realistic for most diseases, so that the final infective fraction is large enough to be easily seen. For $R_0 < 1$ the disease dies out.

disease models – vaccination

suppose there is a perfect vaccine, what proportion p of the population needs to be vaccinated to remove threat of an epidemic?

in the case of the simple SIR model, it is equivalent to moving a fraction p to R, and keeping only q = 1-p in S initially. There will be no epidemic if (q,0) is stable, which implies $qR_0 < 1 \; or \; p \geq p^* = 1 - R_0^{-1}$

in the endemic case with vital dynamics we have the following model:

$$\frac{dS}{dt} = bqN \; - \beta IS \; - dS; \frac{dI}{dt} = \beta IS - \mathrm{cI} - dI - \gamma I; \frac{dR}{dt} = bpN + \gamma I - dR$$

in this model, like in the SIR case, there is no steady state with disease p and it can be shown that it is sufficient to vaccinate p^* of the population

disease models – vaccination

Disease	Transmission	R_0
Measles	Airborne	12–18
Pertussis	Airborne droplet	12–17
Diphtheria	Saliva	6–7
Smallpox	Social contact	5–7
Polio	Fecal-oral route	5–7
Rubella	Airborne droplet	5–7
Mumps	Airborne droplet	4–7
HIV/AIDS	Sexual contact	2–5
SARS	Airborne droplet	2–5[2]
Influenza (1918 pandemic strain)	Airborne droplet	2–3[3]

Infection	R_0	$\hat{p}$, %
Smallpox	3–5	67–80
Measles	12–13	92
Pertussis (whooping cough)	13–17	92–94
Rubella (German measles)	6–7	83–86
Chickenpox	9–10	89–90
Diphtheria	4–6	75–83
Scarlet fever	5–7	80–86
Mumps	4–7	75–86
Poliomyelitis	6	83