Examples of single location, single population models using ordinary differential equations

Durban – Lecture 02

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September 2023

Outline

The SLIRS models

Extensions of the KMK model

A few other models

Something different – Discrete-time

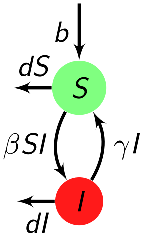
Note on demography

- We have already discussed some different possible forms for demography

- In the models with demography here, unless otherwise required, we use demography such that for the total population

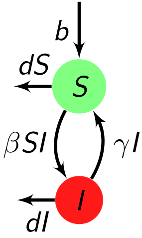
$$N' = b - dN$$

Simplifying the SIRS model



- We have already seen the epidemic KMK SIR model and the endemic SIRS model
- By making some simplifications of the endemic SIRS model, we obtain the SIS model: assume the time spent in the R compartment goes to zero, i.e., $\nu \to \infty$

The main characteristics of the model are the same as the SIRS



$$S' = b + \gamma I - dS - \beta SI \tag{1a}$$
$$I' = \beta SI - (d+\gamma)I \tag{1b}$$

with initial conditions $S(0) = S_0 \geq 0$ and $I(0) = I_0 \geq 0$

Clearly, the DFE is similar as for the SIRS

$$\boldsymbol{E}_0 := (S^\star, I^\star) = (N^\star, 0)$$

with $N^\star = b/d$. Also easy to check (exercise!) that

$$\mathcal{R}_0 = \frac{\beta}{d+\gamma}$$

Incubation periods

- SIS and SIR: progression from S to I is instantaneous

- Several incubation periods:

Disease	Incubation period
Yersinia Pestis	2-6 days
Ebola haemorrhagic fever (HF)	2-21 days
Marburg HF	5-10 days
Lassa fever	1-3 weeks
Tse-tse	weeks–months
HIV/AIDS	months–years

Hypotheses

- There is demography
- New individuals are born at a constant rate b
- There is no vertical transmssion: all “newborns” are susceptible
- The disease is non lethal, it causes no additional mortality
- New infections occur at the rate $f(S, I, N)$
- There is a period of incubation for the disease
- There is a period of time after recovery during which the disease confers immunity to reinfection (immune period)

SLIRS

The model is as follows:

$$S' = b + \nu R - dS - f(S, I, N) \tag{2a}$$
$$L' = f(S, I, N) - (d + \varepsilon)L \tag{2b}$$
$$I' = \varepsilon L - (d + \gamma)I \tag{2c}$$
$$R' = \gamma I - (d + \nu)R \tag{2d}$$

Meaning of the parameters:

- $1/\varepsilon$ average duration of the incubation period
- $1/\gamma$ average duration of infectious period
- $1/\nu$ average duration of immune period

The SLIRS models

- SIS models
- SLIRS model with constant population
- Computing $\mathcal{R}_0$ more efficiently
- Global properties of the SLIRS model
- SLIRS in variable population

The basic reproduction number $\mathcal{R}_0$

Used frequently in epidemiology (not only math epi)

Definition 1 (R_0)

The basic reproduction number $\mathcal{R}_0$ is the average number of secondary cases generated by the introduction of an infectious individual in a wholly susceptible population

- If $\mathcal{R}_0 < 1$, then on average, each infectious individual infects less than one other person, so the epidemic has chances of dying out
- If $\mathcal{R}_0 > 1$, then on average, each infectious individual infects more than one other person and the disease can become established in the population (or there will be a major epidemic)

Computation of $\mathcal{R}_0$

Mathematically, $\mathcal{R}_0$ is a bifurcation parameter aggregating some of the model parameters and such that the disease free equilibrium (DFE) loses its local asymptotic stability when $\mathcal{R}_0 = 1$ is crossed from left to right

- As a consequence, $\mathcal{R}_0$ is found by considering the spectrum of the Jacobian matrix of the system evaluated at the DFE
- The matrix quickly becomes hard to deal with (size and absence of "pattern") and the form obtained is not unique, which is annoying when trying to interpret $\mathcal{R}_0$

The next generation operator

Diekmann and Heesterbeek, characterized in the ODE context by van den Driessche and Watmough

Consider only individuals harbouring the pathogen, in a vector $\mathcal{I}$, and form the vectors

- $\mathcal{F}$ of infection fluxes
- $\mathcal{V}$ of other fluxes (with $-$ sign)

so that

$$\mathcal{I}' = \mathcal{F} - \mathcal{V}$$

Then compute the Fréchet derivatives $D\mathcal{F}$ and $D\mathcal{V}$ with respect to the infected variables $\mathcal{I}$ and evaluate $F = D\mathcal{F}(DFE)$ and $V = D\mathcal{V}(DFE)$. Then

$$\mathcal{R}_0 = \rho(FV^{-1})$$

where ρ is the spectral radius

Short summary of van den Driessche and Watmough

Theorem 2 (van den Driessche and Watmough)

Suppose that the DFE exists. Let then $\mathcal{R}_0$ be defined by

$$\mathcal{R}_0 = \rho(FV^{-1})$$

with matrices F and V as indicated before. Then,

- *if $\mathcal{R}_0 < 1$, the DFE is LAS,*
- *if $\mathcal{R}_0 > 1$, the DFE is unstable.*

Example of the SLIRS model (2)

Variation of the infected variables in (2) are described by

$$
\begin{aligned}
L' &= f(S, I, N) - (\varepsilon + d)L \\
I' &= \varepsilon L - (d + \gamma)I
\end{aligned}
$$

Write

$$
\mathcal{I}' = \begin{pmatrix} L \\ I \end{pmatrix}' = \begin{pmatrix} f(S, I, N) \\ 0 \end{pmatrix} - \begin{pmatrix} (\varepsilon + d)L \\ (d + \gamma)I - \varepsilon L \end{pmatrix} =: \mathcal{F} - \mathcal{V} \qquad (3)
$$

Denote

$$f_L^\star := \frac{\partial}{\partial L} f\bigg|_{(S,I,R)=\boldsymbol{E}_0} \qquad f_I^\star := \frac{\partial}{\partial I} f\bigg|_{(S,I,R)=\boldsymbol{E}_0}$$

the values of the partials of the incidence function at the DFE $\boldsymbol{E}_0$

Compute the Jacobian matrices of vectors $\mathcal{F}$ and $\mathcal{V}$ at the DFE $\boldsymbol{E}_0$

$$F = \begin{pmatrix} f_L^\star & f_I^\star \\ 0 & 0 \end{pmatrix} \quad \text{and} \quad V = \begin{pmatrix} \varepsilon + d & 0 \\ -\varepsilon & d + \gamma \end{pmatrix} \tag{4}$$

Thus

$$V^{-1} = \frac{1}{(d+\varepsilon)(d+\gamma)} \begin{pmatrix} d+\gamma & 0 \\ \varepsilon & d+\varepsilon \end{pmatrix}$$

Also, in the case N is constant, $\partial f/\partial L = 0$ and thus

$$FV^{-1} = \frac{\frac{\partial \bar{f}}{\partial I}}{(d+\varepsilon)(d+\gamma)} \begin{pmatrix} \varepsilon & d+\varepsilon \\ 0 & 0 \end{pmatrix}$$

As a consequence,

$$\mathcal{R}_0 = \varepsilon \frac{\frac{\partial \bar{f}}{\partial I}}{(d+\varepsilon)(d+\gamma)}$$

Theorem 3

Let

$$\mathcal{R}_0 = \frac{\varepsilon \frac{\partial \bar{f}}{\partial I}}{(d+\varepsilon)(d+\gamma)} \tag{5}$$

Then

- *if* $\mathcal{R}_0 < 1$, *the DFE is LAS*
- *if* $\mathcal{R}_0 > 1$, *the DFE is unstable*

It is important here to stress that the result we obtain concerns the **local** asymptotic stability. We see later that even when $\mathcal{R}_0 < 1$, there can be several locally asymptotically stable equilibria

Application

The DFE is

$$(\bar{S}, \bar{L}, \bar{I}, \bar{R}) = (N, 0, 0, 0)$$

- Mass action incidence (frequency-dependent contacts):

$$\frac{\partial \bar{f}}{\partial I} = \beta \bar{S} \Rightarrow \mathcal{R}_0 = \frac{\epsilon \beta N}{(\epsilon + d)(\gamma + d)}$$

- Standard incidence (proportion-dependent contacts):

$$\frac{\partial \bar{f}}{\partial I} = \frac{\beta \bar{S}}{N} \Rightarrow \mathcal{R}_0 = \frac{\epsilon \beta}{(\epsilon + d)(\gamma + d)}$$

Links between SLIRS-type models

$$
\begin{aligned}
S' &= b + \nu R - dS - f(S, I, N) \\
L' &= f(S, I, N) - (d + \varepsilon)L \\
I' &= \varepsilon L - (d + \gamma)I \\
R' &= \gamma I - (d + \nu)R
\end{aligned}
$$

SLIR	SLIRS where $\nu = 0$
SLIS	Limit of SLIRS when $\nu \to \infty$
SLI	SLIR where $\gamma = 0$
SIRS	Limit of SLIRS when $\varepsilon \to \infty$
SIR	SIRS where $\nu = 0$
SIS	Limit of SIRS when $\nu \to \infty$
	Limit SLIS when $\varepsilon \to \infty$
SI	SIS where $\nu = 0$

Values of $\mathcal{R}_0$

$(\bar{S}, \bar{I}, \bar{N})$ values of S, I and N at DFE. Denote $\bar{f}_I = \partial f / \partial I(\bar{S}, \bar{I}, \bar{N})$.

SLIRS	$\frac{\varepsilon \bar{f}_I}{(d+\varepsilon)(d+\gamma)}$
SLIR	$\frac{\varepsilon \bar{f}_I}{(d+\varepsilon)(d+\gamma)}$
SLIS	$\frac{\varepsilon \bar{f}_I}{(d+\varepsilon)(d+\gamma)}$
SLI	$\frac{\varepsilon \bar{f}_I}{(d+\varepsilon)(d+\gamma)}$
SIRS	$\frac{\varepsilon \bar{f}_I}{d+\gamma}$
SIR	$\frac{\bar{f}_I}{d+\gamma}$
SIS	$\frac{\bar{f}_I}{d+\gamma}$
SI	$\frac{\bar{f}_I}{d+\gamma}$

Lyapunov function for SLIR and SLIS

(A. Korobeinikov) Consider an SLIR in constant population (normed to 1), with vertical transmission.

$$S' = d - \beta SI - pdI - qdL - dS \tag{6a}$$
$$L' = \beta SI + pdI - (\varepsilon + d - qd)L \tag{6b}$$
$$I' = \varepsilon L - (\gamma + d)I \tag{6c}$$

p proportion of progeny of I that are I at birth, q proportion of progeny of L that are L at birth.

R does not play a role in the dynamics of (6), it is not shown.

Equilibria

- DFE: $\boldsymbol{E}_0 = (1, 0, 0)$.
- EEP: $\boldsymbol{E}_\star = (S^\star, L^\star, I^\star)$ with

$$S^\star = \frac{1}{\mathcal{R}_0^v} \quad L^\star = \frac{d}{\varepsilon + d}\left(1 - \frac{1}{\mathcal{R}_0^v}\right) \quad I^* = \frac{d\varepsilon}{(\varepsilon + d)(\gamma + d)}\left(1 - \frac{1}{\mathcal{R}_0^v}\right)$$

where

$$\mathcal{R}_0^v = \frac{\beta\varepsilon}{(\gamma + d)(\varepsilon + d) - qd(\varepsilon + d) - pd\varepsilon}$$

is the basic reproduction number with vertical transmission

We have $\mathcal{R}_0 = \mathcal{R}_0^v \iff p = q = 0$ or $\mathcal{R}_0^v = \mathcal{R}_0 = 1$

$\boldsymbol{E}_\star$ exists (in a biologically plausible way) only when $\mathcal{R}_0^v > 1$

Consider the Goh Lyapunov function

$$V = \sum a_i (x_i - x_i^\star \ln x_i)$$

Theorem 4

- *If* $\mathcal{R}_0 > 1$*, then* (6) *has the globally asymptotically stable equilibrium* $\boldsymbol{E}_\star$
- *If* $\mathcal{R}_0 \leq 1$*, then* (6) *has the globally asymptotically stable equilibrium* $\boldsymbol{E}_0$*,* $\boldsymbol{E}_\star$ *is not biologically plausible*

Li, Muldowney and van den Driessche

Study an SLIRS model with incidence of the form

$$f(S, I, N) = \beta g(I) S \tag{7}$$

where g is such that $g(0) = 0$, $g(I) > 0$ for $I \in (0, 1]$ and $g \in C^1(0, 1]$

They normalise the total population, so that $S + L + I + R = 1$

They make the following asumption about g:

(H) $c = \lim_{I \to 0^+} \frac{g(I)}{I} \leq +\infty$; when $0 < c < +\infty$, $g(I) \leq cI$ for all sufficiently small I

We have

$$\frac{\partial \bar{f}}{\partial I} = \beta \frac{\partial \bar{g}}{\partial I}$$

Since $\dfrac{\partial \bar{g}}{\partial I} = \lim_{I \to 0^+} \dfrac{g(I)}{I} = c$,

$$\mathcal{R}_0 = \frac{c\beta\varepsilon}{(d+\varepsilon)(d+\gamma)}$$

The LAS results already established hold here, since (7) is a special case of the function f with which the results were obtained

The system is **uniformly persistent** if there exists $0 < \varepsilon_0 < 1$ s.t. any solution $(S(t), L(t), I(t), R(t))$ of (2) with initial condition $(S(0), L(0), I(0), R(0)) \in \overset{\circ}{\Gamma}$ satisfies

$$\begin{array}{cc} \liminf_{t\to\infty} S(t) \geq \varepsilon_0, & \liminf_{t\to\infty} E(t) \geq \varepsilon_0 \\ \liminf_{t\to\infty} I(t) \geq \varepsilon_0, & \liminf_{t\to\infty} R(t) \geq \varepsilon_0 \end{array} \tag{8}$$

Theorem 5

*If $g(I)$ satisfies hypothesis (**H**), then* (2) *with incidence* (7) *is uniformly persistent iff* $\mathcal{R}_0 > 1$

Theorem 6

Suppose that incidence (7) *satisfies* (***H***) *and that*

$$|g'(I)|I \leq g(I) \ \mathit{for} \ I \in (0,1] \tag{9}$$

Suppose additionally that $\mathcal{R}_0 > 1$ *and that one of the following conditions holds*

$$\gamma\nu < \epsilon_0(\beta\eta_0 + \gamma + d)(\beta\eta_0 + \nu + d)$$
$$\varepsilon - \gamma - d < \nu$$

where

$$\eta_0 = \min_{I \in [\varepsilon_0, 1]} g(I) > 0$$

and ε_0 *is defined by* (8)
Then there are no closed rectifiable curve that is invariant under (2). *Furthermore, every semi-trajectory of* (2) *in* Γ *converges to an EP*

The SLIRS models

- SIS models
- SLIRS model with constant population
- Computing $\mathcal{R}_0$ more efficiently
- Global properties of the SLIRS model
- SLIRS in variable population

Liu, Levin et Iwasa

SIRS of the form

$$
\begin{aligned}
S' &= B(N) - dS - f(S,I)I + \nu R && (10a)\\
I' &= f(S,I)I - (d+\gamma)I && (10b)\\
R' &= \gamma I - (d+\nu)R && (10c)
\end{aligned}
$$

Authors discuss the general case of f differentiable and s.t. $f(0,I) = 0$ for all I and $\partial f/\partial S > 0$

They assume that the demographic component of the model, ruled by

$$N' = B(N) - dN$$

admits a stable EP

Using the fact that N has a stable EP, they reduce the system

After establishing generic conditions leading to the existence of a Hopf bifurcation, they study the system in more detail when incidence takes the form

$$f(S, I) = \beta I^{p-1} S^q$$

Liu & van den Driessche

Liu and van den Driessche consider an SLIS model and an SLIRS model in which the population is not constant and where the latent period depends on the number of infected individuals in the population

In the case of the SLIS model, the behaviour is not modified by this function

In the case where immunity is temporary (SLIRS), they find (numerically) a Hopf bifurcation

The SLIRS models

Extensions of the KMK model

A few other models

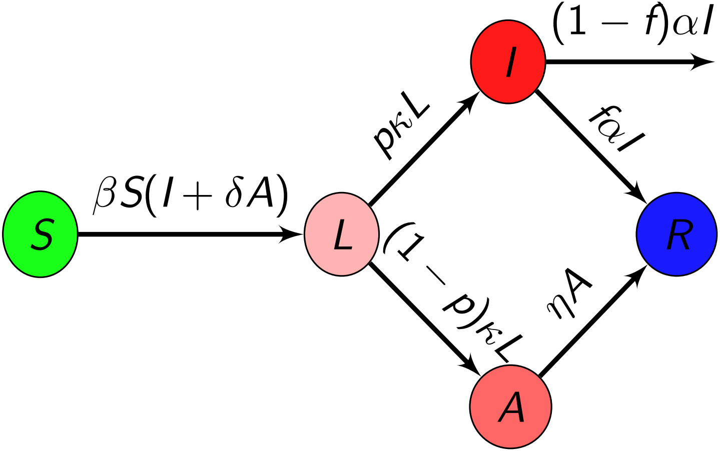
Something different – Discrete-time

SIR is a little too simple for many diseases:

- No incubation period
- A lot of infectious diseases (in particular respiratory) have mild and less mild forms depending on the patient

$\implies$ model with SIR but also L(atent) and (A)symptomatic individuals, in which I are now symptomatic individuals

Arino, Brauer, PvdD, Watmough & Wu. Simple models for containment of a pandemic (2006)


S
$\beta S(I + \delta A)$
L
$p\kappa L$
$(1-p)\kappa L$
I
$(1-f)\alpha I$
$f\alpha I$
A
ηA
R

Basic reproduction number

We find the basic reproduction number

$$\mathcal{R}_0 = S_0\beta\left(\frac{p}{\alpha} + \frac{\delta(1-p)}{\eta}\right) = \frac{S_0\beta\rho}{\alpha} \tag{11}$$

where

$$\rho = \alpha\left(\frac{p}{\alpha} + \frac{\delta(1-p)}{\eta}\right)$$

Final size relation

$$S_0(\ln S_0 - \ln S_\infty) = \mathcal{R}_0(S_0 - S_\infty) + \frac{\mathcal{R}_0 I_0}{\rho} \tag{12}$$

A method for computing $\mathcal{R}_0$ in epidemic models

- This method is not universal! It works in a relatively large class of models, but not everywhere

- If it doesn't work, the next generation matrix method does work, **but** should be considered only for obtaining the reproduction number, not to deduce LAS

- Here, I change the notation in the paper, for convenience

Standard form of the system

Suppose system can be written in the form

$$\boldsymbol{S}' = \mathbf{b}(\boldsymbol{S}, \boldsymbol{I}, \boldsymbol{R}) - \boldsymbol{D}\boldsymbol{S}\beta(\boldsymbol{S}, \boldsymbol{I}, \boldsymbol{R})\boldsymbol{h}\boldsymbol{I} \tag{13a}$$

$$\boldsymbol{I}' = \Pi\boldsymbol{D}\boldsymbol{S}\beta(\boldsymbol{S}, \boldsymbol{I}, \boldsymbol{R})\boldsymbol{h}\boldsymbol{I} - \mathbf{V}\boldsymbol{I} \tag{13b}$$

$$\boldsymbol{R}' = \mathbf{f}(\boldsymbol{S}, \boldsymbol{I}, \boldsymbol{R}) + \mathbf{W}\boldsymbol{I} \tag{13c}$$

where $\boldsymbol{S} \in \mathbb{R}^m$, $\boldsymbol{I} \in \mathbb{R}^n$ and $\boldsymbol{R} \in \mathbb{R}^k$ are susceptible, infected and removed compartments, respectively

IC are ≥ 0 with at least one of the components of $\boldsymbol{I}(0)$ positive

$$\boldsymbol{S}' = \mathbf{b}(\boldsymbol{S}, \boldsymbol{I}, \boldsymbol{R}) - \boldsymbol{D}\boldsymbol{S}\beta(\boldsymbol{S}, \boldsymbol{I}, \boldsymbol{R})\boldsymbol{h}\boldsymbol{I} \tag{13a}$$

- $\mathbf{b} : \mathbb{R}_+^m \times \mathbb{R}_+^n \times \mathbb{R}_+^k \to \mathbb{R}^m$ continuous function encoding recruitment and death of uninfected individuals
- $\boldsymbol{D} \in \mathbb{R}^{m \times m}$ diagonal with diagonal entries $\sigma_i > 0$ the relative susceptibilities of susceptible compartments, with convention that $\sigma_1 = 1$
- Scalar valued function $\beta : \mathbb{R}_+^m \times \mathbb{R}_+^n \times \mathbb{R}_+^k \to \mathbb{R}_+$ represents infectivity, with, e.g., $\beta(\boldsymbol{S}, \boldsymbol{I}, \boldsymbol{R}) = \beta$ for mass action
- $\boldsymbol{h} \in \mathbb{R}^n$ row vector of relative horizontal transmissions

$$\boldsymbol{I}' = \Pi \boldsymbol{D}\boldsymbol{S}\beta(\boldsymbol{S},\boldsymbol{I},\boldsymbol{R})\boldsymbol{h}\boldsymbol{I} - \mathbf{V}\boldsymbol{I} \tag{13b}$$

- $\Pi \in \mathbb{R}^{n\times m}$ has (i,j) entry the fraction of individuals in j^{th} susceptible compartment that enter i^{th} infected compartment upon infection
- $\boldsymbol{D} \in \mathbb{R}^{m\times m}$ diagonal with diagonal entries $\sigma_i > 0$ the relative susceptibilities of susceptible compartments, with convention that $\sigma_1 = 1$
- Scalar valued function $\beta : \mathbb{R}_+^m \times \mathbb{R}_+^n \times \mathbb{R}_+^k \to \mathbb{R}_+$ represents infectivity, with, e.g., $\beta(\boldsymbol{S},\boldsymbol{I},\boldsymbol{R}) = \beta$ for mass action
- $\boldsymbol{h} \in \mathbb{R}^n$ row vector of relative horizontal transmissions
- $\mathbf{V} \in \mathbb{R}^{n\times n}$ describes transitions between infected states and removals from these states due to recovery or death

$$\boldsymbol{R}' = \mathbf{f}(\boldsymbol{S}, \boldsymbol{I}, \boldsymbol{R}) + \mathbf{W}\boldsymbol{I} \tag{13c}$$

- $\mathbf{f} : \mathbb{R}_+^m \times \mathbb{R}_+^n \times \mathbb{R}_+^k \to \mathbb{R}^k$ continuous function encoding flows into and out of removed compartments because of immunisation or similar processes
- $\mathbf{W} \in \mathbb{R}^{k \times n}$ has (i, j) entry the rate at which individuals in the j^{th} infected compartment move into the i^{th} removed compartment

Suppose $\boldsymbol{E}_0$ is a locally stable disease-free equilibrium (DFE) of the system without disease, i.e., an EP of

$$\boldsymbol{S}' = \mathbf{b}(\boldsymbol{S}, \mathbf{0}, \boldsymbol{R})$$
$$\boldsymbol{R}' = \mathbf{f}(\boldsymbol{S}, \mathbf{0}, \boldsymbol{R})$$

Theorem 7

Let

$$\mathcal{R}_0 = \beta(\boldsymbol{S}_0, \mathbf{0}, \boldsymbol{R}_0)\boldsymbol{h}\mathbf{V}^{-1}\Pi\boldsymbol{D}\boldsymbol{S}_0 \tag{14}$$

- *If $\mathcal{R}_0 < 1$, the DFE $\boldsymbol{E}_0$ is a locally asymptotically stable EP of* (13)
- *If $\mathcal{R}_0 > 1$, the DFE $\boldsymbol{E}_0$ of* (13) *is unstable*

If no demography (epidemic model), then just $\mathcal{R}_0$, of course

Final size relations

Assume no demography, then system should be writeable as

$$\boldsymbol{S}' = -\boldsymbol{D}\boldsymbol{S}\beta(\boldsymbol{S},\boldsymbol{I},\boldsymbol{R})\boldsymbol{h}\boldsymbol{I} \tag{15a}$$

$$\boldsymbol{I}' = \Pi\boldsymbol{D}\boldsymbol{S}\beta(\boldsymbol{S},\boldsymbol{I},\boldsymbol{R})\boldsymbol{h}\boldsymbol{I} - \mathbf{V}\boldsymbol{I} \tag{15b}$$

$$\boldsymbol{R}' = \mathbf{W}\boldsymbol{I} \tag{15c}$$

For $w(t) \in \mathbb{R}_+^n$ continuous, define

$$w_\infty = \lim_{t\to\infty} w(t) \quad \text{and} \quad \hat{w} = \int_0^\infty w(t)\; dt$$

Define the row vector

$$\mathbb{R}^m \ni \mathbf{\Gamma} = (\Gamma_1, \ldots, \Gamma_m) = \beta(\boldsymbol{S}_0, \mathbf{0}, \boldsymbol{R}_0)\boldsymbol{h}\mathbf{V}^{-1}\mathbf{\Pi}\boldsymbol{D}$$

then

$$\mathcal{R}_0 = \mathbf{\Gamma}\boldsymbol{S}(0)$$

Suppose incidence is mass action, i.e., $\beta(\boldsymbol{S}, \boldsymbol{I}, \boldsymbol{R}) = \beta$ and $m > 1$

Then for $i = 1, \ldots, m$, express $\boldsymbol{S}_i(\infty)$ as a function of $\boldsymbol{S}_1(\infty)$ using

$$\boldsymbol{S}_i(\infty) = \boldsymbol{S}_i(0) \left(\frac{\boldsymbol{S}_1(\infty)}{\boldsymbol{S}_1(0)} \right)^{\sigma_i/\sigma_1}$$

then substitute into

$$\begin{aligned} \frac{1}{\sigma_i} \ln \left(\frac{\boldsymbol{S}_i(0)}{\boldsymbol{S}_i(\infty)} \right) &= \Gamma \boldsymbol{D}^{-1} \left(\boldsymbol{S}(0) - \boldsymbol{S}(\infty) \right) + \beta \boldsymbol{h} \mathbf{V}^{-1} \boldsymbol{I}(0) \\ &= \frac{1}{\sigma_1} \ln \left(\frac{\boldsymbol{S}_1(0)}{\boldsymbol{S}_1(\infty)} \right) \end{aligned}$$

which is a final size relation for the general system when $\boldsymbol{S}_i(0) > 0$

If incidence is mass action and $m = 1$ (only one susceptible compartment), reduces to the KMK form

$$\ln\left(\frac{S_0}{S_\infty}\right) = \frac{\mathcal{R}_0}{S_0}(S_0 - S_\infty) + \beta \boldsymbol{h}\mathbf{V}^{-1}\boldsymbol{I}_0 \tag{16}$$

In the case of more general incidence functions, the final size relations are inequalities of the form, for $i = 1, \ldots, m$,

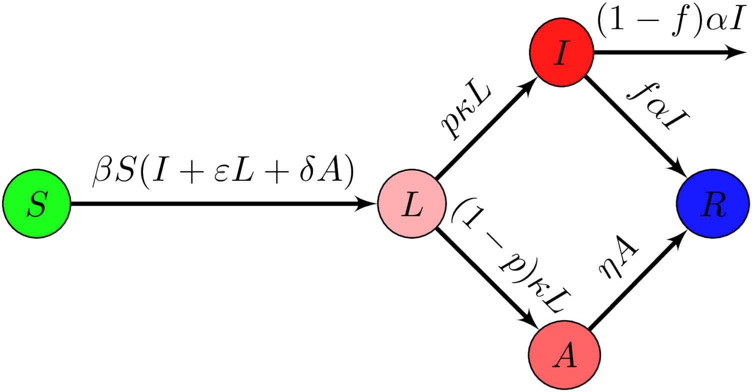
$$\ln\left(\frac{\boldsymbol{S}_i(0)}{\boldsymbol{S}_i(\infty)}\right) \geq \sigma_i \Gamma \boldsymbol{D}^{-1}\left(\boldsymbol{S}(0) - \boldsymbol{S}(\infty)\right) + \sigma_i \beta(K) \boldsymbol{h} \mathbf{V}^{-1} \boldsymbol{I}(0)$$

where K is the initial total population

The SLIAR model

- Paper we have already seen: Arino, Brauer, PvdD, Watmough & Wu. Simple models for containment of a pandemic (2006)

- However, suppose additionally that L are also infectious


S
$\beta S(I + \varepsilon L + \delta A)$
L
$p\kappa L$
$(1-p)\kappa L$
I
$(1-f)\alpha I$
$f\alpha I$
A
ηA
R

Here, $\boldsymbol{S} = S$, $\boldsymbol{I} = (L, I, A)^T$ and $\boldsymbol{R} = R$, so $m = 1$, $n = 3$ and

$$\boldsymbol{h} = [\varepsilon\ 1\ \delta], \quad \boldsymbol{D} = 1, \quad \boldsymbol{\Pi} = \begin{pmatrix} 1 \\ 0 \\ 0 \end{pmatrix} \quad \text{and} \quad \mathbf{V} = \begin{pmatrix} \kappa & 0 & 0 \\ -p\kappa & \alpha & 0 \\ -(1-p)\kappa & 0 & \eta \end{pmatrix}$$

Incidence is mass action so $\beta(\boldsymbol{E}_0) = \beta$ and thus

$$\begin{aligned} \mathcal{R}_0 &= \beta \boldsymbol{h} \mathbf{V}^{-1} \boldsymbol{\Pi} \boldsymbol{D} \boldsymbol{S}_0 \\ &= \beta\ [\varepsilon\ 1\ \delta] \begin{pmatrix} 1/\kappa & 0 & 0 \\ p/\alpha & 1/\alpha & 0 \\ (1-p)/\eta & 0 & 1/\eta \end{pmatrix} \begin{pmatrix} 1 \\ 0 \\ 0 \end{pmatrix} S_0 \\ &= \beta S_0 \left(\frac{\varepsilon}{\kappa} + \frac{p}{\alpha} + \frac{\delta(1-p)}{\eta} \right) \end{aligned}$$

For final size, since $m = 1$, we can use (16):

$$\ln\left(\frac{S_0}{S_\infty}\right) = \frac{\mathcal{R}_0}{S_0}(S_0 - S_\infty) + \beta \boldsymbol{h}\mathbf{V}^{-1}\boldsymbol{I}_0$$

Suppose $\boldsymbol{I}_0 = (0, I_0, 0)$, then

$$\ln\left(\frac{S_0}{S_\infty}\right) = \mathcal{R}_0 \frac{S_0 - S_\infty}{S_0} + \frac{\beta}{\alpha} I_0$$

If $\boldsymbol{I}_0 = (L_0, I_0, A_0)$, then

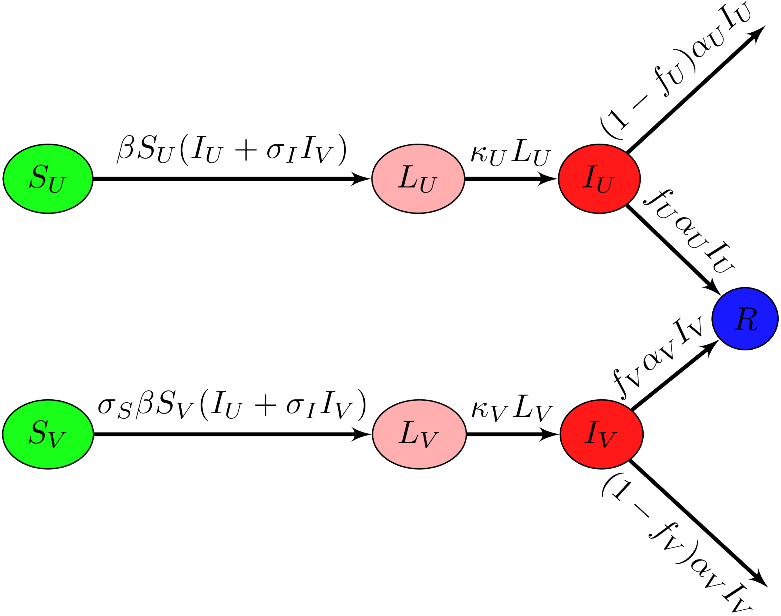
$$\ln\left(\frac{S_0}{S_\infty}\right) = \mathcal{R}_0 \frac{S_0 - S_\infty}{S_0} + \beta\left(\frac{\varepsilon}{\kappa} + \frac{p}{\alpha} + \frac{\delta(1-p)}{\eta}\right) L_0 + \frac{\beta\delta}{\eta} A_0 + \frac{\beta}{\alpha} I_0$$

A model with vaccination

Fraction γ of S_0 are vaccinated before the epidemic; vaccination reduces probability and duration of infection, infectiousness and reduces mortality

$$S_U' = -\beta S_U[I_U + \sigma_I I_V] \tag{17a}$$
$$S_V' = -\sigma_S \beta S_V[I_U + \sigma_I I_V] \tag{17b}$$
$$L_U' = \beta S_U[I_U + \sigma_I I_V] - \kappa_U L_U \tag{17c}$$
$$L_V' = \sigma_S \beta S_V[I_U + \sigma_I I_V] - \kappa_V L_V \tag{17d}$$
$$I_U' = \kappa_U L_U - \alpha_U I_U \tag{17e}$$
$$I_V' = \kappa_V L_V - \alpha_V I_V \tag{17f}$$
$$R' = f_U \alpha_U I_I + f_V \alpha_V I_V \tag{17g}$$

with $S_U(0) = (1-\gamma)S_0$ and $S_V(0) = \gamma S_0$


S_U
$\beta S_U(I_U + \sigma_I I_V)$
L_U
$\kappa_U L_U$
I_U
$(1 - f_U)\alpha_U I_U$
$f_U \alpha_U I_U$
R
$f_V \alpha_V I_V$
S_V
$\sigma_S \beta S_V(I_U + \sigma_I I_V)$
L_V
$\kappa_V L_V$
I_V
$(1 - f_V)\alpha_V I_V$

Here, $m = 2$, $n = 4$,

$$\boldsymbol{h} = [0\ 0\ 1\ \sigma_I], \quad \boldsymbol{D} = \begin{pmatrix} 1 & 0 \\ 0 & \sigma_S \end{pmatrix}, \quad \boldsymbol{\Pi} = \begin{pmatrix} 1 & 0 \\ 0 & 1 \\ 0 & 0 \\ 0 & 0 \end{pmatrix}$$

and

$$\mathbf{V} = \begin{pmatrix} \kappa_U & 0 & 0 & 0 \\ 0 & \kappa_V & 0 & 0 \\ -\kappa_U & 0 & \alpha_U & 0 \\ 0 & -\kappa_V & 0 & \alpha_V \end{pmatrix}$$

So

$$\mathbf{\Gamma} = \left[\frac{\beta}{\alpha_U} \; \frac{\sigma_I \sigma_S \beta}{\alpha_V}\right], \quad \mathcal{R}_c = S_0 \beta \left(\frac{1-\gamma}{\alpha_U} + \frac{\sigma_I \sigma_S \gamma}{\alpha_V}\right)$$

and the final size relation is

$$\ln\left(\frac{(1-\gamma)S_U(0)}{S_U(\infty)}\right) = \frac{\beta}{\alpha_U}[(1-\gamma)S_U(0) - S_U(\infty)] + \frac{\sigma_I \beta}{\alpha_V}[\gamma S_V(0) - S_V(\infty)] + \frac{\beta}{\alpha_U} I_0$$

$$S_V(\infty) = \gamma S_U(0) \left(\frac{S_U(\infty)}{(1-\gamma)S_0}\right)^{\sigma_S}$$

The SLIRS models

Extensions of the KMK model

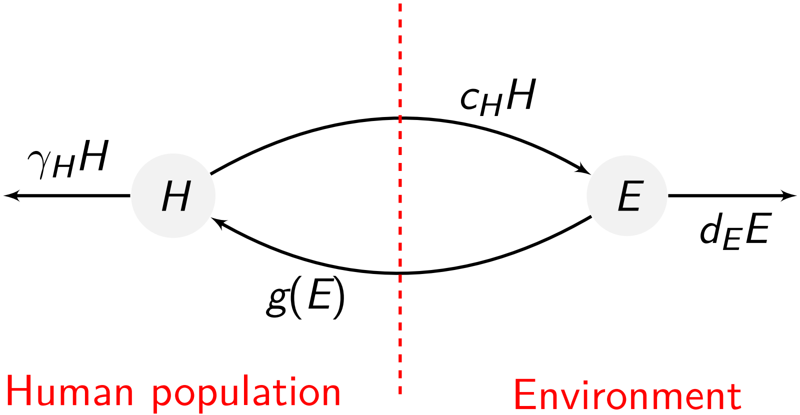
A few other models

Something different – Discrete-time

A few other models

- A model of Capasso for ETP
- A model for zoonotic transmission of waterborne disease
- A few models of schistosomiasis

A minimal model of V. Capasso



$1/\gamma_H$ mean infectious period, $1/d_E$ mean lifetime of the agent in the environment, c_H growth rate of the agent due to the human population, $g(E)$ "force of infection" (I would say "incidence") of the agent on human population

Incidence function

$$g(E) = N\beta p h(E) \qquad (18)$$

where

- N total human population
- β fraction of susceptible individuals in N
- p fraction exposed to contaminated environment per unit time ("probability per unit time to have a "snack" of contaminated food")
- $h(E)$ probability for an exposed susceptible to get the infection

Typically, we would assume p and β independent of E and H and h to be saturating

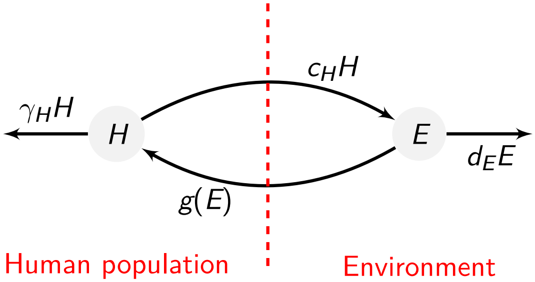
To ensure (18) satisfies these conditions, we can assume

- $0 < g(e_1) < g(e_2)$ for $0 < e_1 < e_2$
- $g(0) = 0$
- $g''(z) < 0$ for all $z > 0$
- $0 < g'_+(0) < \infty$ (right derivative)
- $\lim_{z\to\infty} \frac{g(z)}{z} < \frac{d_E \gamma_H}{c_H}$

Of course, we also assume $d_E, c_H, \gamma_H > 0$

The model

$$E' = c_H H - d_E E \tag{19a}$$
$$H' = g(E) - \gamma_H H \tag{19b}$$



Pay attention to the flows..! E' does not have a $-g(E)$ and H' does not have $-c_H H$. Why?

Let

$$\mathcal{R}_0 = \frac{g'_+(0)c_H}{d_E\gamma_H} \tag{20}$$

Theorem 8

- *If* $0 < \mathcal{R}_0 < 1$, *then* (19) *admits only the trivial equilibrium in the positive orthant, which is GAS*
- *If* $\mathcal{R}_0 > 1$, *then two EP exist:* $(0,0)$, *which is unstable, and* $z^\star = (E^\star, H^\star)$ *with* $E^\star, H^\star > 0$, *GAS in* $\mathbb{R}^2_+ \setminus \{0,0\}$

Adding a periodic component

Assume p in (18) takes the form

$$p(t) = p(t+\omega) > 0, \quad t \in \mathbb{R} \tag{21}$$

i.e., p has period ω. So we now consider the incidence

$$g(t,E) = p(t)h(E) \tag{22}$$

with h having the properties prescribed earlier. Letting

$$p_{min} := \min_{0\leq t\leq\omega} p(t), \quad p_{max} := \max_{0\leq t\leq\omega} p(t) \tag{23}$$

then we require that

$$\lim_{z\to\infty} \frac{g(z)}{z} < \frac{d_E\gamma_H}{c_H p_{max}} \tag{24}$$

Let

$$\mathcal{R}_0^{min} = \frac{c_H p_{min} h'_+(0)}{d_E \gamma_H}, \quad \mathcal{R}_0^{max} = \frac{c_H p_{max} h'_+(0)}{d_E \gamma_H} \tag{25}$$

Theorem 9

- *If* $0 < \mathcal{R}_0^{max} < 1$, *then* (19) *with incidence* (29) *always goes to extinction*
- *If* $\mathcal{R}_0^{min} > 1$, *then a unique nontrivial periodic endemic state exists for* (19) *with incidence* (29)

Simulating (in R) – Incidence function

```
h = function(E, params) {
  # Use Michaelis Menten (Holling type II) growth
  OUT = params$g_max * E / (params$g_half+E)
  return(OUT)
}
g = function(E, params) {
  OUT = params$N * params$beta * params$p * h(E,params)
  return(OUT)
}
```

The right hand side

```
rhs_Capasso_ODE = function(t, x, params) {
  with(as.list(c(x, params)), {
    dE = c_H*H-d_E*E
    dH = g(E, params)-gamma_H*H
    list(c(dE, dH))
  })
}
```

Setting parameters

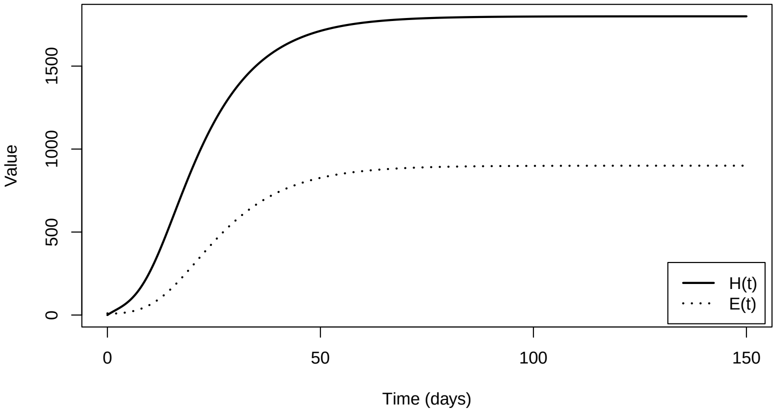
```r
# Put parameters in a list
params = list()
params$N = 1000       # Total population
params$gamma_H = 1/10 # Infectious period
params$d_E = 1/5      # Lifetime agent
params$c_H = 0.1      # Flow from humans
# Human characteristics and behaviour
params$beta = 0.2 # Fraction susceptible
params$p = 0.1    # Probability of having "snack"
# Growth function
params$g_max = 10
params$g_half = 100
# Final time
params$t_f = 150
```

Running and plotting (base)

```
IC <- c(E = 10, H = 0)
tspan = seq(from = 0, to = params$t_f, by = 0.1)

sol_ODE = ode(y = IC,
              func = rhs_Capasso_ODE,
              times = tspan,
              parms = params)

plot(sol_ODE[,"time"], sol_ODE[,"H"],
      type = "l", lwd = 2,
      xlab = "Time (days)", ylab = "Value")
lines(sol_ODE[,"time"], sol_ODE[,"E"],
      lwd = 2, lty = 3)
legend("bottomright", legend = c("H(t)", "E(t)"),
        lwd = c(2,2), lty = c(1,3), inset = 0.01)
```



Value
0
500
1000
1500
0
50
100
150
Time (days)
H(t)
E(t)

Let

$$\mathcal{R}_0 = \frac{g'_+(0)c_H}{d_E\gamma_H} \tag{26}$$

Theorem 10

- *If* $0 < \mathcal{R}_0 < 1$*, then* (19) *admits only the trivial equilibrium in the positive orthant, which is GAS*
- *If* $\mathcal{R}_0 > 1$*, then two EP exist:* $(0,0)$*, which is unstable, and* $z^\star = (E^\star, H^\star)$ *with* $E^\star, H^\star > 0$*, GAS in* $\mathbb{R}^2_+ \setminus \{0,0\}$

Computing $\mathcal{R}_0$

With the chosen g, we have

$$g'(E) = \frac{N\beta p g_{half} g_{max}}{(g_{half} + E)^2}$$

whence

$$g'_+(0) = \frac{N\beta p g_{max}}{g_{half}}$$

and thus

$$\mathcal{R}_0 = \frac{N\beta p g_{max}}{g_{half}} \frac{c_H}{d_E \gamma_H} \tag{27}$$

```
R0 = function(params) {
  with(as.list(params), {
    R0 = N*beta*p*g_max*c_H / (g_half*d_E*gamma_H)
    return(R0)
  })
}
```

Showing things dynamically using Shiny

Shiny is an `R` library (made by RStudio) to easily make interactive displays

See some documentation here

Some examples here and here

Create a subdirectory with the name of your app and a file called `app.R` in there

Structure of a Shiny app

Need to use library `shiny`

Define two elements

- `ui`, which sets up the user interface
- `server`, which handles the computations, generation of figures, etc.

I explain different elements as we progress. See the code in the `CODE` folder and `Capasso_simpleETP_shiny` subdirectory

The `ui` part

Here, we use `fluidPage` to create the UI. There are other functions: `fillPage`, `fixedPage`, `flowLayout`, `navbarPage`, `sidebarLayout`, `splitLayout` and `verticalLayout`

```
# Define UI
ui <- fluidPage(
)
```

We now fill this function

A title and some sliders

```
# Application title
titlePanel("Simple ETP model of Capasso"),
# Sidebar with slider inputs for some parameters
sidebarLayout(
    sidebarPanel(
      sliderInput("inv_gamma_H",
                  "Average infectious period (days):",
                  min = 0,
                  max = 30,
                  value = 10),
      sliderInput("c_H",
                  "Flow from humans:",
                  min = 0,
                  max = 2,
                  value = 0.1),
```

Plus other sliders for all other parameters

Note the little trick...

```
sliderInput("inv_gamma_H",
"Average infectious period (days):",
min = 0,
max = 30,
value = 10),
```

I want to give a user friendly version of the parameter value, using the number of days rather than the inverse, whereas the model uses the latter. So I prefix the variable name by `inv_` and then process as follows in the `server` part

```
params <- list()
for (param_name in names(input)) {
  if (grepl("inv_", param_name)) {
    new_param_name = gsubs("inv_", "", param_name)
    params[[new_param_name]] = 1/input[[param_name]]
  } else {
    params[[param_name]] = input[[param_name]]
  }
}
```

The simulation functions can be outside of `ui` or `server`, this makes the code neater

These functions are the same as before (right hand side, g, h, R0), so they are not shown here

The server part

```r
# Define server logic required to draw the result
server <- function(input, output) {
  ##
  ## Expression that generates the plot
  ##
  output$a_odePlot <- renderPlot({
    params <- list()
    params$N = 1000 # We could let this vary, we don't here..
    for (param_name in names(input)) {
      if (grepl("inv_", param_name)) {
        new_param_name = gsub("inv_", "", param_name)
        params[[new_param_name]] = 1/input[[param_name]]
      } else {
        params[[param_name]] = input[[param_name]]
      }
    }
    # Initial conditions and time span
    IC <- c(E = 10, H = 0)
    tspan <- seq(from = 0, to = params$tf, by = 0.1)
```

The server part (continued)

```
    # Compute solution
    sol_ODE = ode(y = IC,
                  func = rhs_Capasso_ODE,
                  times = tspan,
                  parms = params)
    # Make the plot
    y_max = max(max(sol_ODE[,"H"]),sol_ODE[,"E"])
    plot(sol_ODE[,"time"], sol_ODE[,"H"],
          type = "l", lwd = 2,
          xlab = "Time (days)", ylab = "Value",
          ylim = c(0, y_max),
          main = sprintf("R_0=%1.2f", round(R0(params),2)))
    lines(sol_ODE[,"time"], sol_ODE[,"E"],
          lwd = 2, lty = 3)
    legend("topleft", legend = c("H(t)", "E(t)"),
            lwd = c(2,2), lty = c(1,3), inset = 0.01)
  })
}
```

Finally, run the code

```
# Run the application
shinyApp(ui = ui, server = server)
```

Adding a periodic component

Assume p in (18) takes the form

$$p(t) = p(t+\omega) > 0, \quad t \in \mathbb{R} \tag{28}$$

i.e., p has period ω. So we now consider the incidence

$$g(t, E) = p(t)h(E) \tag{29}$$

with h having the properties prescribed earlier. Letting

$$p_{min} := \min_{0 \le t \le \omega} p(t), \quad p_{max} := \max_{0 \le t \le \omega} p(t) \tag{30}$$

then we require that

$$\lim_{z \to \infty} \frac{g(z)}{z} < \frac{d_E \gamma_H}{c_H p_{max}} \tag{31}$$

Let

$$\mathcal{R}_0^{min} = \frac{c_H p_{min} h'_+(0)}{d_E \gamma_H}, \quad \mathcal{R}_0^{max} = \frac{c_H p_{max} h'_+(0)}{d_E \gamma_H} \qquad (32)$$

Theorem 11

- *If* $0 < \mathcal{R}_0^{max} < 1$, *then* (19) *with incidence* (29) *always goes to extinction*
- *If* $\mathcal{R}_0^{min} > 1$, *then a unique nontrivial periodic endemic state exists for* (19) *with incidence* (29)

How to add periodicity in numerics?

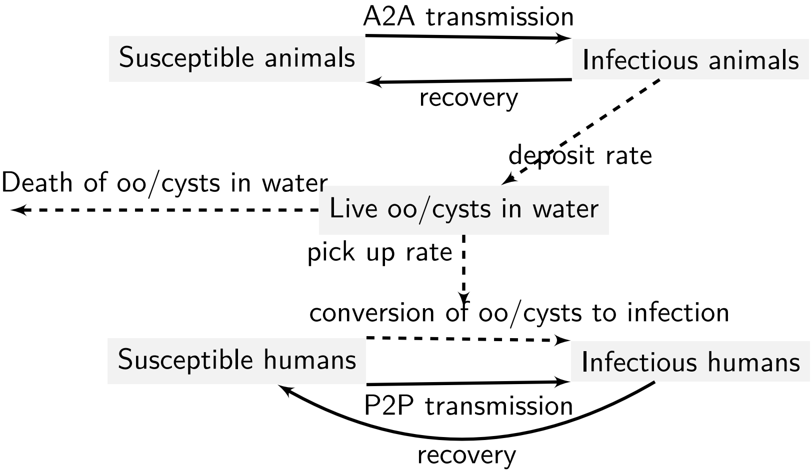
```
p_t = function(t, params) {
  angle = 2*pi/params$p_period
  OUT = cos(angle*t) # Make the base cos wave
  OUT = OUT/2*(params$p_max-params$p_min) # Scale
  OUT = OUT-min(OUT)+params$p_min # Shift up
  return(OUT)
}
g = function(E, params, t) {
  OUT = params$N * params$beta * p_t(t, params) * h(E,params)
  return(OUT)
}
R0 = function(params) {
  with(as.list(params), {
    R0 = list()
    R0$min = N*beta*p_min*g_max*c_H / (g_half*d_E*gamma_H)
    R0$max = N*beta*p_max*g_max*c_H / (g_half*d_E*gamma_H)
    return(R0)
  })
}
```

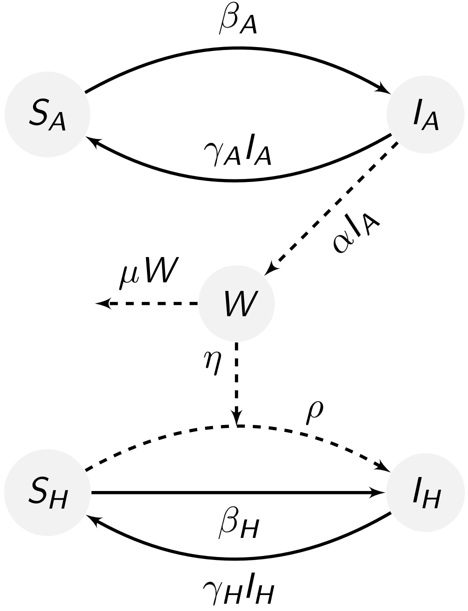
A few other models

- A model of Capasso for ETP
- A model for zoonotic transmission of waterborne disease
- A few models of schistosomiasis

Zoonotic transmission of waterborne disease

Waters, Hamilton, Sidhu, Sidhu, Dunbar. Zoonotic transmission of waterborne disease: a mathematical model. *Bull Math Biol* (2016)
Used for instance to model Giardia transmission from possums to humans


A2A transmission
Susceptible animals
Infectious animals
recovery
deposit rate
Death of oo/cysts in water
Live oo/cysts in water
pick up rate
conversion of oo/cysts to infection
Susceptible humans
Infectious humans
P2P transmission
recovery


β_A
S_A
I_A
$\gamma_A I_A$
αI_A
μW
W
η
ρ
S_H
I_H
β_H
$\gamma_H I_H$

The full model

$$
\begin{aligned}
S_A' &= -\beta_A S_A I_A + \gamma_A I_A && \text{(33a)}\\
I_A' &= \beta_A S_A I_A - \gamma_A I_A && \text{(33b)}\\
W' &= \alpha I_A - \eta W(S_H + I_H) - \mu W && \text{(33c)}\\
S_H' &= -\rho\eta W S_H - \beta_H S_H I_H + \gamma_H I_H && \text{(33d)}\\
I_H' &= \rho\eta W S_H + \beta_H S_H I_H - \gamma_H I_H && \text{(33e)}
\end{aligned}
$$

Considered with $N_A = S_A + I_A$ and $N_H = S_H + I_H$ constant

Simplified model

Because N_A and N_H are constant, (33) can be simplified:

$$I_A' = \beta_A N_A I_A - \gamma_A I_A - \beta_A I_A^2 \tag{34a}$$

$$W' = \alpha I_A - \eta W N_H - \mu W \tag{34b}$$

$$I_H' = \rho\eta W(N_H - I_H) + \beta_H N_H I_H - \gamma_H I_H - \beta_H I_H^2 \tag{34c}$$

Three EP: DFE $(0,0,0)$; endemic disease in humans because of H2H transmission; endemic in both H and A because of W

Three EP: DFE $(0,0,0)$; endemic disease in humans because of H2H transmission; endemic in both H and A because of W

Let

$$\mathcal{R}_{0A} = \frac{\beta_A}{\gamma_A} N_A \quad \text{and} \quad \mathcal{R}_{0H} = \frac{\beta_H}{\gamma_H} N_H \tag{35}$$

- DFE LAS if $\mathcal{R}_{0A} < 1$ and $\mathcal{R}_{0H} < 1$, unstable if $\mathcal{R}_{0A} > 1$ or $\mathcal{R}_{0H} > 1$
- If $\mathcal{R}_{0H} > 1$ and $\mathcal{R}_{0A} < 1$, (34) goes to EP with endemicity only in humans
- Endemic EP with both A and H requires $\mathcal{R}_{0A} > 1$ and $\mathcal{R}_{0H} < 1$

Note that proof is **not** global

A few other models

- A model of Capasso for ETP
- A model for zoonotic transmission of waterborne disease
- A few models of schistosomiasis

A few other models

A model of Capasso for ETP

A model for zoonotic transmission of waterborne disease

A few models of schistosomiasis

A first model of Woolhouse

A second model of Woolhouse – Latency

A model of Woolhouse

Woolhouse. On the application of mathematical models of schistosome transmission dynamics. I. Natural transmission. *Acta Tropica* **49**:241-270 (1991)

The model

Population of H individuals using a body of water containing N snails

i_H mean number of schistosomes per person and i_S the proportion of patent infections in snails (prevalence)

$$i_H' = \alpha N i_S - \gamma i_H \tag{36a}$$

$$i_S' = \beta H i_H (1 - i_S) - \mu_2 i_S \tag{36b}$$

- α number of schistosomes produced per person per infected snail per unit time
- $1/\gamma$ average life expectancy of a schistosome
- $1/\mu_2$ average life expectancy of an infected snail
- β transmission parameter

Let the basic reproductive rate for schistosomes be

$$\mathcal{R}_0 = \frac{\alpha N \beta H}{\gamma \mu_2} \tag{37}$$

(36) has two EP

- $(i_H^\star, i_S^\star) = (0,0)$, LAS when $\mathcal{R}_0 < 1$ and unstable when $\mathcal{R}_0 > 1$
- $(i_H^\star, i_S^\star) = \left(\frac{\alpha N}{\gamma} - \frac{\mu_2}{\beta H}, 1 - \frac{1}{\mathcal{R}_0}\right)$, which only "exists" when $\mathcal{R}_0 > 1$ (and is LAS then)

Extending the model

Interval between infection of a snail and onset of patency (release of cercariae) is *prepatent* or *latent* period

$$i_H' = \alpha N i_S - \gamma i_H \tag{38a}$$
$$\ell_S' = \beta H i_H (1 - \ell_S - i_S) - \sigma \ell_S - \mu_1 \ell_S \tag{38b}$$
$$i_S' = \sigma \ell_S - \mu_2 i_S \tag{38c}$$

- $1/\sigma$ average duration of prepatent period
- $f = \sigma/(\sigma + \mu_1)$ fraction of infected snails surviving prepatent period

The basic reproductive rate for schistosomes is now

$$\mathcal{R}_0 = f\frac{\alpha N \beta H}{\gamma \mu_2} \tag{39}$$

(38) has endemic EP

$$(i_H^\star, i_S^\star) = \left(\frac{\alpha N \sigma}{\gamma(\sigma+\mu_2)} - \frac{\mu_2(\sigma+\mu_1)}{\beta H(\sigma+\mu_2)}, \frac{\sigma}{\sigma+\mu_2}\left(1-\frac{1}{\mathcal{R}_0}\right)\right)$$

Also has models

- where snails lose infectiousness (assumed to happen sometimes)
- with larval population dynamics
- single variable models
- human immigration and emigration
- reservoir hosts

Really worth a read

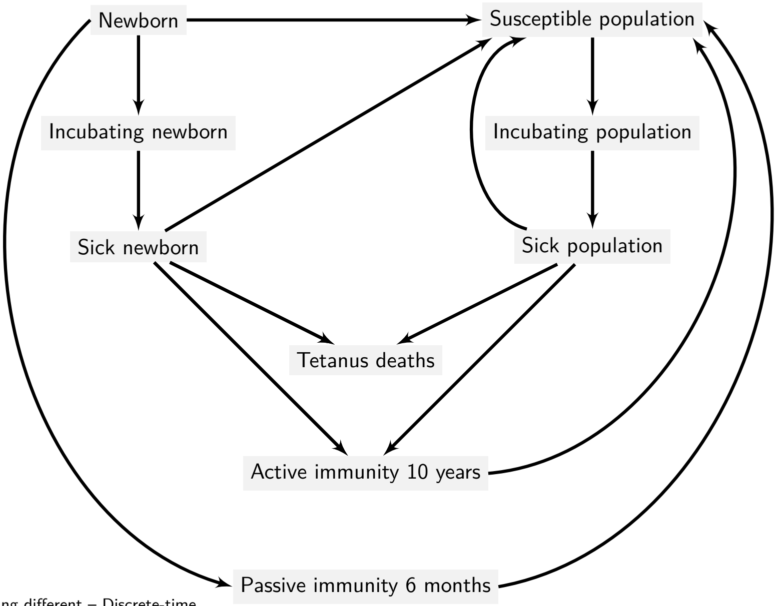
The SLIRS models

Extensions of the KMK model

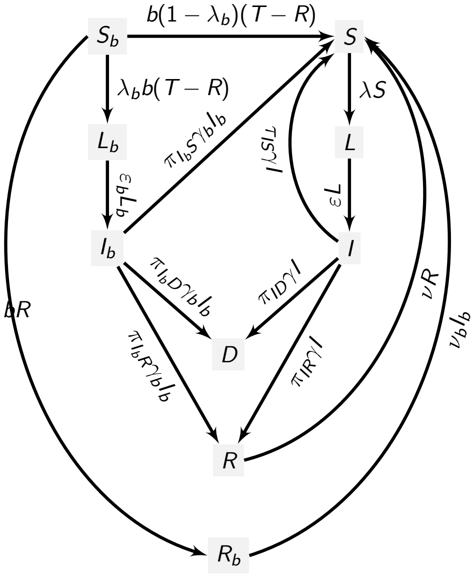
A few other models

Something different – Discrete-time

A tetanus model of Cvjetanović



Flow diagram (demography not shown)



The discrete-time tetanus model (notation mine)

$$\Delta S_b = bT \tag{40a}$$

$$\Delta S = b(1-\lambda_b)(T-R) + \nu R + \nu_b I_b + \nu I + \pi_{I_bS}\gamma_b I_b + \pi_{IS}\gamma I \tag{40b}$$

$$- (\lambda + d - \delta_T)S$$

$$\Delta L_b = \lambda_b b(T-R) - (\varepsilon_b + d - \delta_T)L_b \tag{40c}$$

$$\Delta L = \lambda S - (\varepsilon + d - \delta_T)L \tag{40d}$$

$$\Delta I_b = \varepsilon_b L_b - (\gamma_b + d - \delta_T)I \tag{40e}$$

$$\Delta I = \varepsilon L - (\gamma + d - \delta_T)I \tag{40f}$$

$$\Delta R = \pi_{I_bR}\gamma_b I_b + \pi_{IR}\gamma I - (\nu + d - \delta_T)R \tag{40g}$$

$$\Delta R_b = bR - (\nu_b + d - \delta_T)R_b \tag{40h}$$

$$\Delta D = \pi_{I_bD}\gamma_b I_b + \pi_{ID}\gamma I \tag{40i}$$

where

$$T = S + L_b + L + I_b + I + R + R_b \quad \text{and} \quad \delta_T = \frac{\Delta D}{T} \tag{40j}$$

Parameter assumptions – Tetanus

- **Incubation period** – Mean duration 6 days for newborn and 8 days for general population $\Rightarrow$ daily rate of exit (d.r.e.) $\varepsilon_b = 0.1667$ and $\varepsilon = 0.125$
- **Period of sickness** – Mean duration 3 days for newborn and 14 days for general population $\Rightarrow$ d.r.e. $\gamma_b = 0.3333$ per sick newborn and $\gamma = 0.0714$ for sick general in general population
- **Mortality from tetanus** – Untreated tetanus cases, fatality rate 90% for newborn S_b and 40% for general population. Treated: 80% for newborn and 30% general population
- **Immunity** – Tetanus cases do not lead to immunity to reinfection. But as a general rule, recovered people are vaccinated. Convalescents and general population effectively immunised by complete course of vaccination go to R for average 10 years, d.r.e. $\nu = 0.000274$ per person.
- **Immunity of newborns** – Newborn to women vaccinated during pregnancy are temporarily protected by maternal antibodies and pass through R_b for a mean duration of 6 months. D.r.e $\nu_b = 0.005479$ per immunised newborn

Deciding on infection outcome – π

Parameters π are proportion of individuals who follow a certain route post-infection

- $\pi_{I_b\bullet}$ proportion of infected newborn who
  - π_{I_bS} recover without immunity
  - π_{I_bR} recover with immunity
  - π_{I_bD} die (0.9)

  $\pi_{I_bS} + \pi_{I_bR} + \pi_{I_bD} = 1$

- $\pi_{I\bullet}$ proportion of infected who
  - π_{IS} recover without immunity
  - π_{IR} recover with immunity
  - π_{ID} die (0.4)

  $\pi_{IS} + \pi_{IR} + \pi_{ID} = 1$

Parameter assumptions – Demography

Live birth rate 35 per 1,000 population and annual crude death rate 15 per 1,000 population (annual rate of growth 2%) $\Rightarrow$ daily birth and death rates $b = 0.00009889$ and $d = 0.0000411$ per person, respectively

Parameter assumptions – Force of infection

No H2H transmission $\Rightarrow$ incidence proportional to number of susceptible individuals and force of infection, which quantifies combined effect of all variables involved in infection process:

- degree of soil contamination with *Clostridium tetani*
- climate
- frequency of lesions
- proportion of rural population
- socioeconomic conditions
- level of medical care for the wounded and during deliveries

Force of infection acting on newborn (λ_b) and susceptible population (λ) fixed at 3 different levels adequate for reproducing the following stable annual incidence rates of tetanus cases in the community

- For newborn, 200 cases, 400 cases and 600 cases per 100,000 newborn
- For general population (without newborn), 9, 18 and 27 cases

A crash course on discrete-time systems

We have seen systems of ordinary differential equations (ODE) of the form

$$\frac{d}{dt}x(t) = f(x(t))$$

often written omitting dependence on t, i.e.,

$$x' = f(x) \tag{41}$$

where $x \in \mathbb{R}^n$ and $f: \mathbb{R}^n \to \mathbb{R}^n$. The system is considered together with an initial condition $x(t_0) = x_0 \in \mathbb{R}^n$.

The **independent** variable $t \in \mathbb{R}$

A discrete-time system takes the form

$$x(t + \Delta t) = f(x(t)) \tag{42}$$

where $x(t) \in \mathbb{R}^n$ and $f : \mathbb{R}^n \to \mathbb{R}^n$

In a discrete-time system, t is discrete and can be assumed to be in $\mathbb{Z}$ or $\mathbb{N}$ (in practice, before "recasting", it is in $\mathbb{Q}$), we often write $x(t + 1) = f(x(t))$, assuming $\Delta t = 1$..

Together with an initial condition $x(t_0) = x_0 \in \mathbb{R}^n$, this constitutes a sequence that describes the evolution of the state x

Similarities/differences

$$x' = f(x), x(t_0) = x_0, x \in \mathbb{R}^n$$

$$x(t + \Delta t) = f(x(t)), x(t_0) = x_0, x \in$$

Equilibria (EP) $x^\star$ s.t. $f(x^\star) = 0_{\mathbb{R}^n}$

Fixed points (FP) $x^\star$ s.t. $f(x^\star) =$

LAS EP $\Leftrightarrow s(Df(x^\star)) < 0$

LAS FP $\Leftrightarrow \rho(Df(x^\star)) < 1$

Notation – if $A \in \mathcal{M}_n$ is a matrix,
$\mathrm{Sp}(A) = \{\lambda \in \mathbb{C} : A\boldsymbol{v} = \lambda \boldsymbol{v}, \boldsymbol{v} \neq \boldsymbol{0}\}$ is its **spectrum**, i.e., the set of all its eigenvalues and

- $s(A) = \max\{\mathrm{Re}\,(\lambda),\ \lambda \in \mathrm{Sp}(A)\}$ is its **spectral abscissa**
- $\rho(A) = \max\{|\lambda|, \lambda \in \mathrm{Sp}(A)\}$ is its **spectral radius**

Simulating the system

The R package we use for ODE (deSolve) can also do discrete-time systems, with very little adaptation..

The function call is then of the form

```
sol <- ode(func = tetanus_Cvjetanovic, y = IC, times = 0:30,
           parms = params, method = "iteration")
```

From the help for ode

> *Method "iteration" is special in that here the function* func *should return the new value of the state variables rather than the rate of change*

The right hand side

```
tetanus_Cvjetanovic = function(t, y, params) {
  with(as.list(c(y, params)), {
    T = S+L_b+L+I_b+I+R+R_b
    dD = pi_IbD*gamma_b*I_b+pi_ID*gamma*I
    delta_T = dD/T
    dS_b = b*T
    dS = b*(1-lambda_b)*(T-R)+nu*R+nu_b*I+pi_IbS*gamma_b*I_b +
      pi_IS*gamma*I-(lambda+d-delta_T)*S
    dL_b = lambda_b*b*(T-R)-(epsilon_b+d-delta_T)*L_b
    dL = lambda*S-(epsilon+d-delta_T)*L
    dI_b = epsilon_b*L_b-(gamma_b+d-delta_T)*I
    dI = epsilon*L-(gamma+d-delta_T)*I
    dR = pi_IbR*gamma_b*I_b+pi_IR*gamma*I-(nu+d-delta_T)*R
    dR_b = b*R-(nu_b+d-delta_T)*R_b
    list(c(S_b+dS_b,S+dS,L_b+dL_b,L+dL,I_b+dI_b,I+dI,R+dR,R_b+dR_
     b,D+dD))
  })
}
```

Set parameters

```
params = list()
params$epsilon_b = 0.1667
params$epsilon = 0.125
params$gamma_b = 1/3
params$gamma = 0.0714
params$nu = 0.000274
params$nu_b = 0.005479
params$b = 0.00009889
params$d = 0.0000411

params$pi_IbS = 0.05
params$pi_IS = 0.3
params$pi_IbR = 0.05
params$pi_IR = 0.3
params$pi_IbD = 0.9
params$pi_ID = 0.4

params$lambda_b = 0.1
params$lambda = 0.1
```

A last few things then run

```r
IC = c(S_b = 0,
  S = 100000,
  L_b = 0,
  L = 0,
  I_b = 0,
  I = 0,
  R = 0,
  R_b = 0,
  D = 0)
tspan = 0:30
sol <- ode(func = tetanus_Cvjetanovic, y = IC, times = tspan,
      parms = params, method = "iteration")
```

A few remarks about this model

To set λ_b and λ, we need to explore numerically model response

Discrete-time models can be analysed in pretty much the same way as continuous time ones, but this one will be hard: there is no DFFP!

This means the usual methods for computing $\mathcal{R}_0$ will not work, as there is no DFFP to perturb away from...