Continuous spatial spread models

MATH 8xyz – Lecture 19

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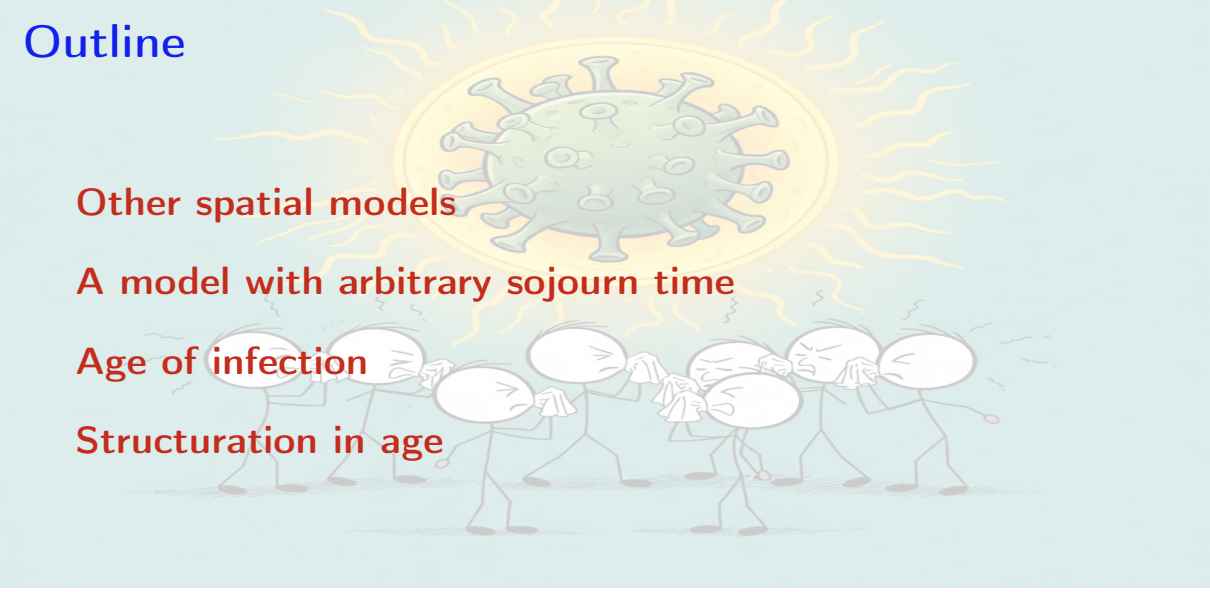
The University of Manitoba campuses are located on original lands of Anishinaabeg, Ininew, Anisininew, Dakota and Dene peoples, and on the National Homeland of the Red River Métis.
We respect the Treaties that were made on these territories, we acknowledge the harms and mistakes of the past, and we dedicate ourselves to move forward in partnership with Indigenous communities in a spirit of Reconciliation and collaboration.

Outline

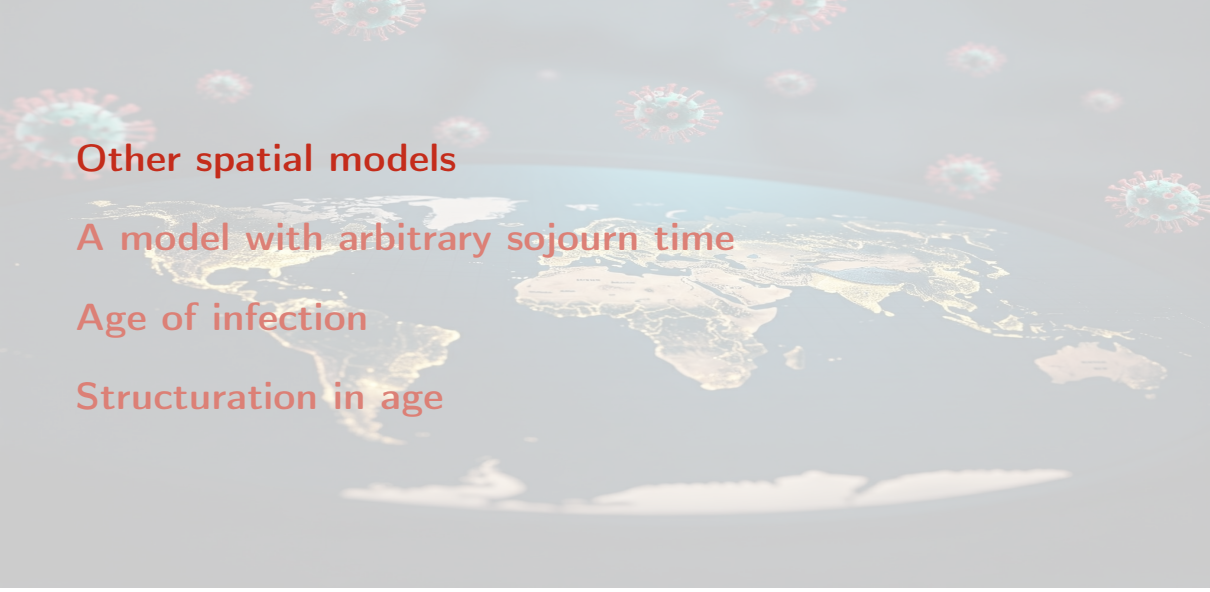


Other spatial models

A model with arbitrary sojourn time

Age of infection

Structuration in age



Other spatial models

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Other spatial models

- Spatial propagation on a “road”
- A diffusion spatial spread model

PERGAMON Mathematical and Computer Modelling 29 (1999) 55–69

MATHEMATICAL AND COMPUTER MODELLING

Modelling the Spread of Infections When the Contact Rate Among Individuals is Short Ranged: Propagation of Epidemic Waves

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Spatial spread of an epidemic on a "road"

- SIS and SIR models
- Consider a road of length L
- $S(x,t)$, $I(x,t)$ and (when relevant) $R(x,t)$ are the densities of individuals in the different compartments at location $x \in [0, L]$ at time t
- For simplicity, denote

$$\frac{\partial}{\partial t} X(x,t) = X_t(x,t)$$

The SIR model on the road

$$S_t(x,t) = -\beta(x,t)S(x,t) - dS(x,t) + dN(x) + \lambda_1 I(x,t) \tag{1a}$$
$$I_t(x,t) = \lambda(x,t)S(x,t) - dI(x,t) - (\gamma_1 + \gamma_2)I(x,t) \tag{1b}$$
$$R_t(x,t) = \gamma_2 I(x,t) - dR(x,t) \tag{1c}$$

where the force of infection is

$$\lambda(x,t) = \frac{1}{N}\int_0^L \beta(x,x')I(x,x')dx' \tag{1d}$$

and the total population along the road is

$$N = \int_0^L N(x')dx' \tag{1e}$$

Take the SIS model as an example ($\gamma_2 = 0, \gamma_1 = \gamma$). Solve (1b) in terms of λ:

$$
\begin{aligned}
I(x,t) = & \exp\left(-\int_0^t \lambda(x,s) - (d+\gamma)tds\right) \\
& \times \int_0^t \lambda(x,t')N(x)e^{\int_0^{t'} \lambda(x,s)+(d+\gamma)t'ds} dt' \\
& + I(x,0)\exp\left(-\int_0^t \lambda(x,s) - (d+\gamma)tds\right)
\end{aligned} \tag{2}
$$

Substitute (2) into (1d)

$$\lambda(x,t) = \int_0^L \beta(x,x')n(x') \int_0^t \lambda(x',t')e^{-\int_{t'}^t \lambda(x',s)-(d+\gamma)(t-t')ds} dt'dx'$$
$$+ \int_0^L \beta(x,x')i(x',0)e^{-\int_0^t \lambda(x',s)-(d+\gamma)tds} dx'$$

where $n(x) = N(x)/N$ and $i(x,t) = I(x,t)/N$. Without demography ($d = 0$):

$$\lambda(x,t) = \int_0^L \beta(x,x')n(x') \int_0^t \lambda(x',t')e^{-\int_{t'}^t \lambda(x',s)-\gamma(t-t')ds} dt'dx'$$
$$+ \int_0^L \beta(x,x')i(x',0)e^{-\int_0^t \lambda(x',s)-\gamma tds} dx'$$

Thus the problem is in the form

$$\boldsymbol{B}\lambda(x,t) = \lambda(x,t)$$

In both cases, $\boldsymbol{B}$ is a Hammerstein-type operator in x

- SIR case: $\boldsymbol{B}$ is a nonlinear Volterra operator in t $\Rightarrow$existence and uniqueness of solutions
- SIS case: $\boldsymbol{B}$ is not a nonlinear Volterra operator in t. However, it resembles one and the authors establish existence and uniqueness of solutions

In both cases, there is a travelling wave front then convergence to a steady state

In the SIS case

$$\lambda(x) = \lim_{t\to\infty} \boldsymbol{B}\lambda(x,t) = \boldsymbol{B}_\infty\lambda(x) = \int_0^L \beta(x,x')n(x')\frac{\lambda(x',\infty)}{\lambda(x',\infty)+\gamma}$$

which does not depend on t

They then discuss conditions s.t. this limit $\neq 0$, by looking for values of z s.t. $\boldsymbol{B}_\infty\lambda(x) = z\lambda(x)$ has a positive solution

Show there exists a threshold $z_{\text{threshold}} = \mathcal{R}_0$ s.t. $\lambda(x) \equiv 0$ if $\mathcal{R}_0 < 1$ and a positive solution if $\mathcal{R}_0 > 1$

Other spatial models

- Spatial propagation on a “road”
- A diffusion spatial spread model

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On the Spatial Spread of Rabies Among Foxes with Immunity

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(*Received on* 10 *December* 1990, *Accepted in revised form on* 10 *December* 1991)

Spatial spread of rabies with immunity

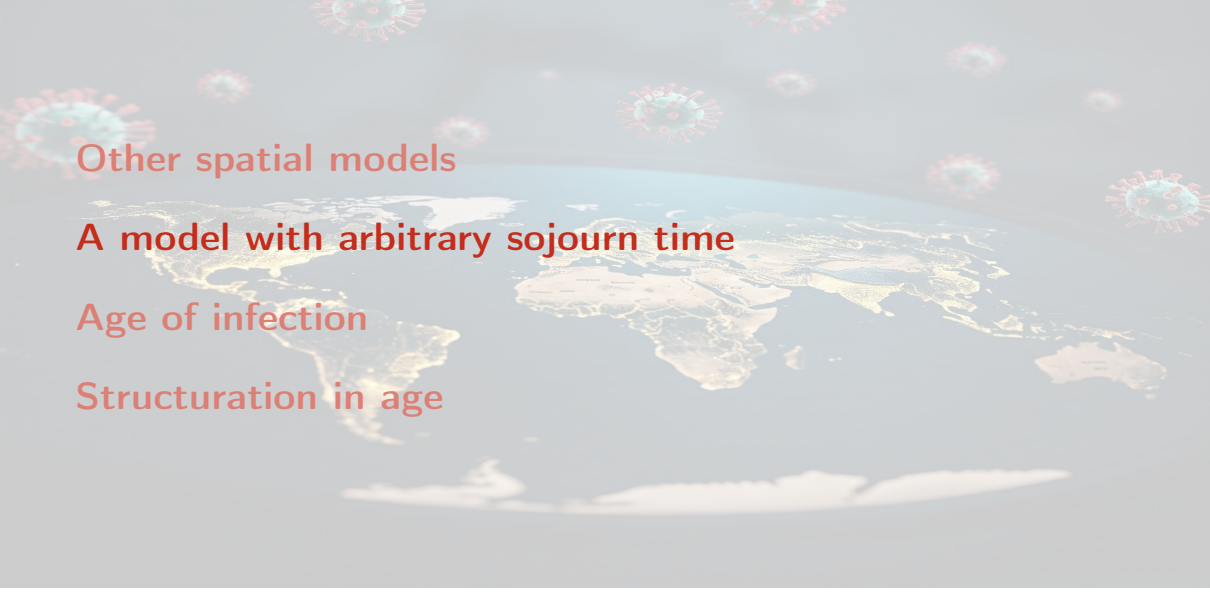
$$\frac{\partial S}{\partial t} = (a-b)\left(1-\frac{N}{K}\right)S + a^{\star}R - \beta SI \tag{3a}$$

$$\frac{\partial L}{\partial t} = \beta SI - \sigma L - \left(b + (a-b)\frac{N}{K}\right)L \tag{3b}$$

$$\frac{\partial I}{\partial t} = \sigma L - \alpha I - \gamma I - \left(b + (a-b)\frac{N}{K}\right)I + D_I\frac{\partial^2 I}{\partial x^2} \tag{3c}$$

$$\frac{\partial R}{\partial t} = \gamma I + (a-a^{\star})R + \left(b + (a-b)\frac{N}{K}\right)R \tag{3d}$$

where $N = S + L + I + R$



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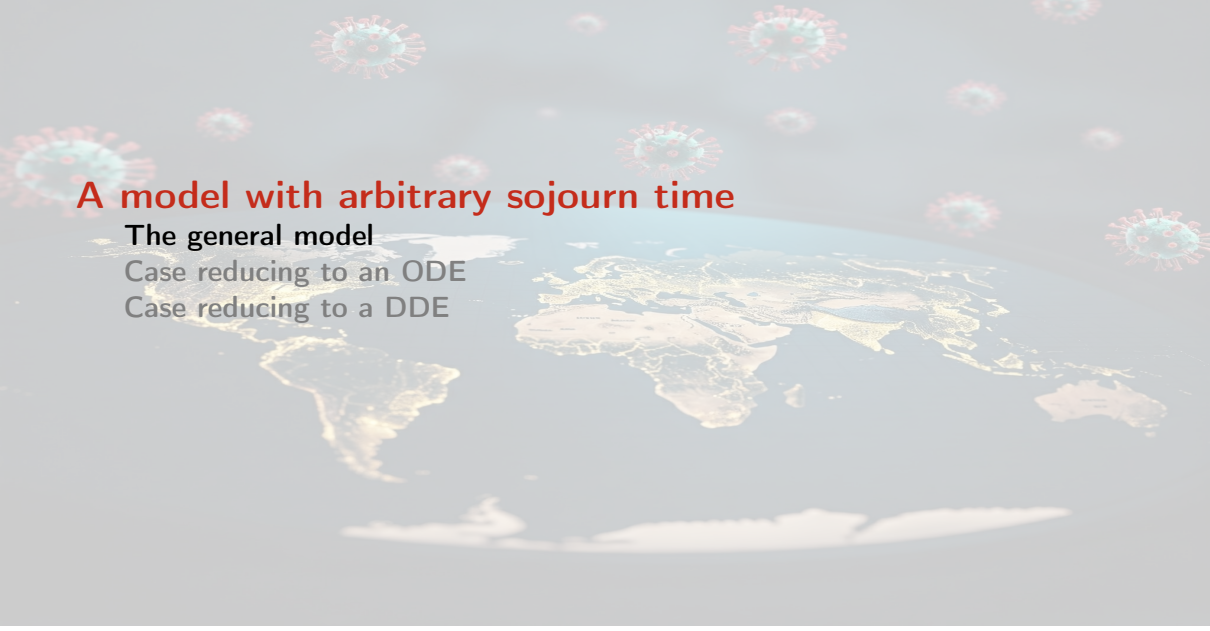

A model with arbitrary sojourn time

- The general model
- Case reducing to an ODE
- Case reducing to a DDE

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AN EPIDEMIOLOGY MODEL THAT INCLUDES A LEAKY VACCINE WITH A GENERAL WANING FUNCTION

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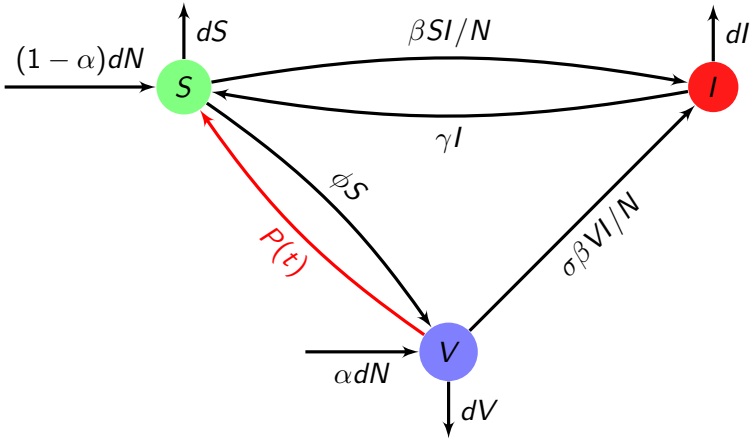
(Communicated by Linda Allen)

A model with vaccine efficacy and waning

- Exponential distribution of recovery times (rate γ)
- Susceptible individuals are vaccinated (number of vaccinated at time t is denoted $V(t)$)
- Vaccination wanes, a fraction $P(t)$ of the vaccinated at time $t = 0$ remain protected by the vaccine
- Vaccination is imperfect, $0 \leq 1 - \sigma \leq 1$ is the vaccine **efficacy**

Model structure



Parametres

- $d > 0$: mortality rate
- $\gamma \geq 0$: recovery rate
- $\beta > 0$: infectiousness of the disease
- $\phi \geq 0$: vaccination rate of susceptible individuals
- $\alpha \in [0, 1)$: fraction of newborns vaccinates
- $0 \leq 1 - \sigma \leq 1$: efficacy of the vaccine. From now on, assume $0 \leq \sigma < 1$

- Disease transmission: standard incidence

- Vaccination of newborns

- Birth and death rate equal ($\Rightarrow$constant total population)

Assumptions on P: $P(t)$ is a nonnegative and nonincreasing function with $P(0^+) = 1$, and such that $\int_0^\infty P(u)du$ is positive and finite

Constant total population $\Rightarrow S(t) = N - I(t) - V(t)$; further, we switch to **proportions**: S, I and V represent the proportions in the population, and $N = 1$ (S used in equations for conciseness)

The SIS model with vaccination

$$\frac{dI(t)}{dt} = \beta(S(t) + \sigma V(t))I(t) - (d + \gamma)I(t) \tag{4a}$$

$$V(t) = V_0(t) + \int_0^t (\phi S(u) + \alpha d)P(t-u)e^{-d(t-u)}e^{-\sigma\beta\int_u^t I(x)dx}du \tag{4b}$$

- αd proportion of vaccinated newborns,
- $\phi S(u)$ proportion of vaccinated susceptibles,
- $P(t-u)$ fraction of the proportion vaccinated still in the V class $t-u$ time units after going in,
- $e^{-d(t-u)}$ fraction of the proportion vaccinated not dead due to natural causes,
- $e^{-\sigma\beta\int_u^t I(x)dx}$ fraction of the proportion vaccinated not gone to the infective class.

Obtaining the initial condition

Let $v(t,\tau)$ be the (density) proportion of individuals in vaccination class-age τ still vaccinated at time t, then

$$\left(\frac{\partial}{\partial t}+\frac{\partial}{\partial \tau}\right) v(t,\tau) = -(\sigma\beta I(t) + d + \eta(\tau))v(t,\tau) \tag{5}$$

where $V(t) = \int_0^\infty v(t,\tau)d\tau$. $\eta(\tau)$ is the vaccine waning rate coefficient, with proportion still in the vaccination class-age τ being $P(\tau) = \exp\left(-\int_0^\tau \eta(q)dq\right)$. It is assumed that P is a survival function

Inflow in class-age zero is

$$v(t,0) = \phi S(t) + \alpha d$$

and $v(0,\tau) \geq 0$ is assumed

Integrating (5) along characteristics, dividing the integral for $V(t)$ at t, substituting in the solutions, and changing integration variables, we get

$$V_0(t) = e^{-\int_0^t (\sigma\beta I(x)+d)dx} \int_0^\infty v(0,u)\frac{P(t+u)}{P(u)}du \tag{6}$$

The ratio $P(t+u)/P(u) = \exp\left(\int_u^{t+u} \eta(q)dq\right)$ is well defined for $t+u \geq u \geq 0$ and bounded above by 1.

Since $V(0)$ is finite, the integral in $V_0(t)$ converges, and thus $V_0(t)$ is nonnegative, nonincreasing and $\lim_{t\to\infty} V_0(t) = 0$

Let

$$\mathcal{D} = \{(S, I, V); S \geq 0, I \geq 0, V \geq 0, S + I + V = 1\}$$

Theorem 1

The set $\mathcal{D}$ is positively invariant under the flow of (4) with $I(0) > 0, S(0) > 0$

With the assumed initial conditions in $\mathcal{D}$, it can be shown that the system defined by (4a) and (4b) is equivalent to the system defined by (4a) and

$$\frac{d}{dt}V(t) = \frac{d}{dt}V_0(t) + \phi S(t) + \alpha d - (d + \sigma\beta I(t))(V(t) - V_0(t)) + Q(t) \qquad (7)$$

where to simplify notation, we denote

$$Q(t) = \int_0^t (\phi S(u) + \alpha d) d_t(P(t-u)) e^{-d(t-u)} e^{-\sigma\beta \int_u^t I(x)dx} du$$

The system defined by (4a) and (7) is of standard form, therefore results of Hale [?] ensure the local existence, uniqueness and continuation of solutions of model (4)

$\mathcal{R}_0$

Define $\mathcal{R}_0$ with vaccination as

$$\mathcal{R}_v = \mathcal{R}_0 \left[\frac{1 + \sigma\phi\tilde{P} - (1-\sigma)\alpha d\tilde{P}}{1 + \phi\tilde{P}} \right] \tag{8}$$

where $\mathcal{R}_0 = \frac{\beta}{d+\gamma}$ is the reproduction number in the absence of vaccination and

$$\tilde{P} = \lim_{t\to\infty} \int_0^t P(v) e^{-dv} dv$$

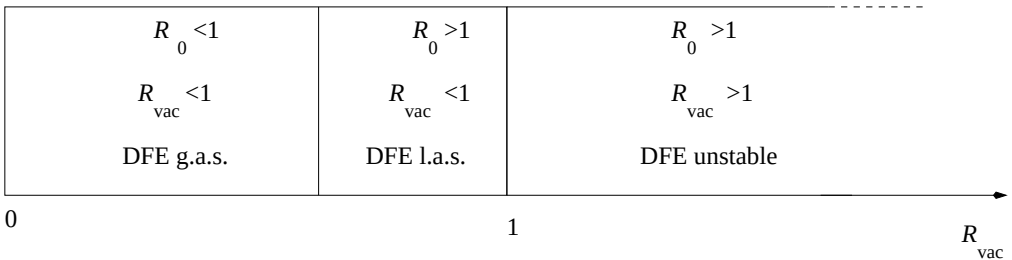
in such a way that $\tilde{P} < 1/d$

- $\mathcal{R}_v \leq \mathcal{R}_0$ and, in absence of vaccination, $\mathcal{R}_v = \mathcal{R}_0$

Theorem 2

System (4) *with an arbitrary loss of vaccination function* $P(t)$ *always admits the disease-free equilibrium*

- *If* $\mathcal{R}_0 < 1$*, then the DFE is the only equilibrium of the system and the disease goes extinct*
- *If* $\mathcal{R}_v < 1$*, the DFE is LAS; if* $\mathcal{R}_v > 1$*, the DFE is unstable*



A model with arbitrary sojourn time

- The general model
- **Case reducing to an ODE**
- Case reducing to a DDE

Reduction of the system using specific $P(t)$ functions

As before, two examples

- The distribution of waning times is exponential, which leads to an ODE system. Treated briefly here, just so as to emphasize the presence of a so-called *backward bifurcation*, a rather uncommon phenomenon in epidemiological models

- The waning time is a constant, which leads to a DDE model. We show that the backward bifurcation is also present

Case reducing to an ODE system

Assume $P(v) = e^{-\theta v}$, $\theta > 0$. $V_0(t) = V_0(0)e^{-(d+\theta)t}e^{-\int_0^t \sigma\beta I(x)dx}$ from (6). Then (4a) and (7) give the ODE system

$$\frac{dI}{dt} = \beta(1 - I - (1-\sigma)V)I - (d+\gamma)I \tag{9a}$$

$$\frac{dV}{dt} = \phi(1 - I - V) - \sigma\beta IV - (d+\theta)V + \alpha d \tag{9b}$$

which with no newborn vaccination ($\alpha = 0$) is the model studied in Kribs-Zaletta & Velasco-Hernandez, 2000 (extended to SIR with vaccination: Arino, McCluskey and van den Driessche).

From Theorem 2 the DFE always exists, with

$$I_{DFE} = 0, S_{DFE} = \frac{\theta + d(1-\alpha)}{d+\theta+\phi}, V_{DFE} = \frac{\phi + \alpha d}{d+\theta+\phi}$$

Backward bifurcation

Assume that $\mathcal{R}_0 > 1$, then endemic equilibria (positive I equilibria, denoted by $I^\star$) can be obtained analytically from the quadratic equation

$$\mathcal{P}(I) = AI^2 + BI + C = 0$$

where

$$\begin{aligned} A &= -\sigma\beta \\ B &= \sigma(\beta - (d+\gamma)) - (d+\theta+\sigma\phi) \\ C &= (d+\gamma)(d+\theta+\phi)(\mathcal{R}_v - 1)/\beta \end{aligned}$$

with

$$\mathcal{R}_v = \mathcal{R}_0 \frac{d+\theta+\sigma\phi-\alpha(1-\sigma)d}{d+\theta+\phi}$$

from (8).

Backward bifurcation leading to two endemic equilibria occurs for $\sigma > 0$ if $\mathcal{P}'(0) = B > 0$, $\mathcal{P}(0) = C < 0$ and $B^2 > 4AC$ (we always have $\mathcal{P}(1) < 0$)

▶ On an $(\mathcal{R}_v, I)$ bifurcation diagram, this occurs for $\mathcal{R}_c < \mathcal{R}_v < 1$, where $\mathcal{R}_c$ is the value of $\mathcal{R}_v$ at the saddle node bifurcation point where the two values of I coincide, *i.e.*, $I = I_c = B/(-2A)$

▶ For $\mathcal{R}_v < \mathcal{R}_c$, there is no endemic equilibrium (EEP). For $\mathcal{R}_v > 1$, the constant term $C > 0$, and there is a unique EEP

▶ In the case of forward bifurcation, $\mathcal{R}_c = 1$; this is the case in particular if the vaccine is totally effective ($\sigma = 0$)

By standard planar ODE arguments the following can be shown

Theorem 3

For the ODE system (9) with $V(0) \geq 0$, $I(0) > 0$, and $\mathcal{R}_0 > 1$

(i) if $\mathcal{R}_v < \mathcal{R}_c$, then the disease dies out,

(ii) if $\mathcal{R}_c < \mathcal{R}_v < 1$, then the EEP with larger I is l.a.s., and the EEP with smaller I is unstable

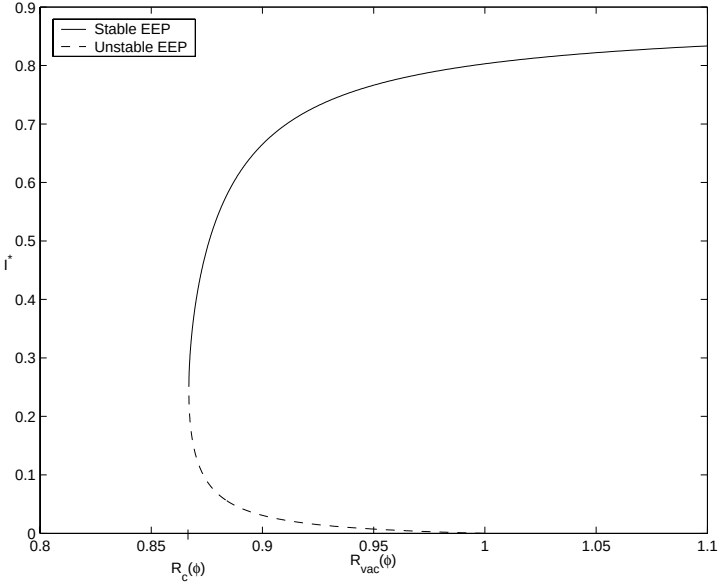
(iii) if $\mathcal{R}_v > 1$, then the unique EEP is globally asymptotically stable in $\mathcal{D} - \{I = 0\}$

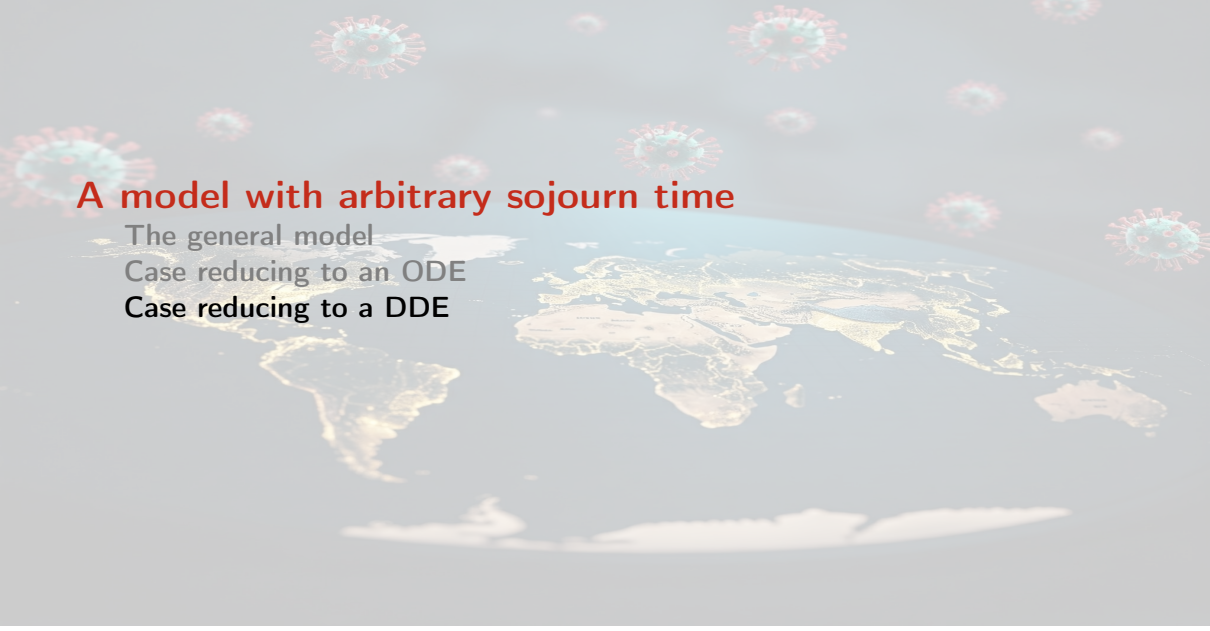
Pertussis:

- 3 week average disease duration ($\gamma = 0.04762$)
- Average lifetime 75 years ($d = 3.6530E - 05$)
- Average number of adequate contacts per infective per day is estimated at 0.4 ($\beta = 0.4$)
- Most newborns are vaccinated in the first few months of life ($\alpha = 0.9$)
- Vaccine is effective, $\sigma = 0.1$ (90% effective vaccine).
- Pertussis vaccine begins to wane after about 3 years and the average waning time of the vaccine $1/\theta$ is assumed to be 5 years, giving $\theta = 5.4794E - 04$

With these parameter values, there is backward bifurcation for a range of ϕ values given by $0.0254 \leq \phi \leq 0.1506$

With the above parameter values, $\mathcal{R}_0 = 8.3936$ and $\mathcal{R}_v(\phi) = 0.8807$ for $\phi = 0.1$, which is in the range of backward bifurcation since the critical value $\mathcal{R}_c(\phi) = 0.8669 < \mathcal{R}_v(\phi) < 1$





A model with arbitrary sojourn time

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Step function case: a delay integral model

Suppose that

$$P(v) = \begin{cases} 1 \text{ if } v \in [0, \omega] \\ 0 \text{ otherwise} \end{cases}$$

Since $V_0(t) = 0$ for $t > \omega$, with $S = 1 - I - V$ the integral equation (4b) becomes, for $t > \omega$

$$V(t) = \int_{t-\omega}^{t} (\phi(1 - I(u) - V(u)) + \alpha d) e^{-d(t-u)} e^{-\sigma\beta \int_u^t I(x)dx} du \qquad (10)$$

Differentiating (10) (see equation (7)) gives the model as the two dimensional system, for $t > \omega$

$$\frac{d}{dt}I(t) = \beta(1 - I(t) - (1-\sigma)V(t))I(t) - (d+\gamma)I(t) \tag{11a}$$

$$\begin{aligned}\frac{d}{dt}V(t) = {} & \phi(1 - I(t) - V(t)) \\ & - \phi(1 - I(t-\omega) - V(t-\omega))e^{-d\omega}e^{-\sigma\beta\int_{t-\omega}^{t} I(x)dx} \\ & - \sigma\beta IV - dV + \alpha d\left(1 - e^{-d\omega}e^{-\sigma\beta\int_{t-\omega}^{t} I(x)dx}\right)\end{aligned} \tag{11b}$$

Hereafter, shift time by ω so that these equations hold for $t > 0$

The well posedness of the problem follows from Theorem 1 and from the fact that solutions of (4) exist and are unique. For a constant waning period, the basic reproduction number from (8) is

$$\mathcal{R}_v = \mathcal{R}_0 \frac{d + (\sigma\phi - \alpha(1-\sigma)d)(1 - e^{-d\omega})}{d + \phi(1 - e^{-d\omega})} \tag{12}$$

With $I_{DF} = 0$, from Theorem 2

$$V_{DF} = \frac{(\phi + \alpha d)(1 - e^{-d\omega})}{d + \phi(1 - e^{-d\omega})}, \; S_{DF} = \frac{d - \alpha d(1 - e^{-d\omega})}{d + \phi(1 - e^{-d\omega})} \tag{13}$$

Finding the EEP's

From nullclines, there exists one (or more) endemic equilbria (EEP) iff there exists $0 < I^\star \leq 1$ such that

$$V^\star = f(I^\star) = g(I^\star) \tag{14}$$

where

$$f(I) = \frac{1 - 1/\mathcal{R}_0 - I}{1 - \sigma} \tag{15}$$

for $\sigma < 1$, and

$$g(I) = \frac{(\phi(1 - I) + \alpha d)(1 - e^{-d\omega - \sigma\beta\omega I})}{\phi(1 - e^{-d\omega - \sigma\beta\omega I}) + d + \sigma\beta I} \tag{16}$$

Visualising and locating the bifurcation

From the nullcline equations, an EEP exists iff there exists an $I^\star \in (0, 1]$ such that equations (14)-(16) hold. So we study the zeros of

$$H(I) = \frac{1 - 1/\mathcal{R}_0 - I}{1 - \sigma} - \frac{(\phi(1 - I) + \alpha d)(1 - e^{-d\omega - \sigma\beta\omega I})}{\phi(1 - e^{-d\omega - \sigma\beta\omega I}) + d + \sigma\beta I}$$

To state the problem in a formal way, let $\mathcal{A} = \{\alpha, \beta, \gamma, \omega, \phi, \sigma\}$ be the set of parameters of interest, and denote

$$H(I, \mathcal{A}) = f(I) - g(I) \tag{17}$$

to show the dependence on these parameters.

We proceed as follows.

1. Choose a parameter $a_i \in \mathcal{A}$.
2. Fix all other a_j's ($j \neq i$).
3. Choose $a_{i,min}$, $a_{i,max}$ and Δa_i for a_i.
4. For all $a_{i,k} = a_{i,min} + k\Delta a_i$ (k such that $a_{i,k} \leq a_{i,max}$), compute $I^\star$ such that $H(I^\star, a_{i,k}) = 0$.

Step 4 is carried out using the MatLab `fzero` function.
Further precision can be gained by showing that

$$H(0) = \frac{\mathcal{R}_v - 1}{(1-\sigma)\mathcal{R}_0}$$

and that, for $\sigma < 1$

$$H(1) = -\frac{1}{(1-\sigma)\mathcal{R}_0} - \frac{\alpha d(1 - e^{-d\omega - \sigma\beta\omega})}{\phi(1 - e^{-d\omega-\sigma\beta\omega}) + d + \sigma\beta} < 0$$

Define $\mathcal{R}_c$ as previously. For $\mathcal{R}_0 > 1$ and $\mathcal{R}_v < 1$, there are several possibilities.

- If $\mathcal{R}_v < \mathcal{R}_c$, then there is no EEP. $H(0)$ and $H(1)$ are strictly negative, and numerical simulations seem to indicate that H has no roots in $(0, 1]$ (*i.e.*, that $H < 0$ on this interval).
- If $\mathcal{R}_c < \mathcal{R}_v < 1$, then there are endemic equilibria. Here, since $H(0)$ and $H(1)$ are strictly negative, the only possibility is thus to have an even number of zeros of H. Numerical simulations appear to indicate that the number of endemic equilibria is 2.

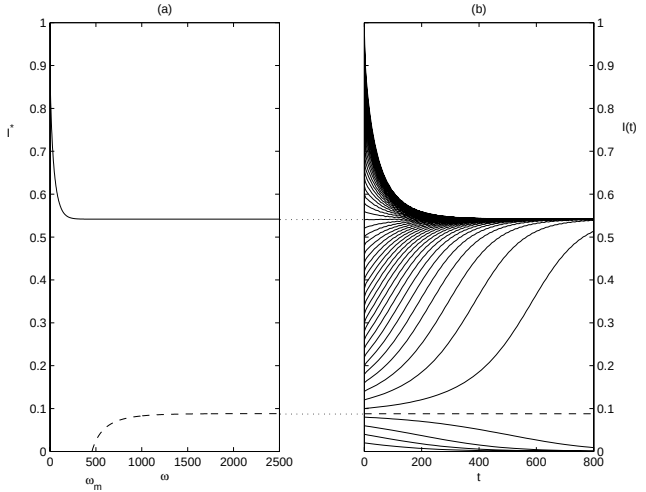
In between these two situations $\mathcal{R}_v = \mathcal{R}_c$ and there is one endemic equilibrium $I^\star$. Using the same procedure as for the visualisation of the bifurcation, it is possible to compute $\mathcal{R}_c$ by finding the value $I^\star$ such that $H(I^\star, \mathcal{A}) = 0$ and $H'(I^\star, \mathcal{A}) = 0$, for a given parameter $a_i \in \mathcal{A}$.
If $\mathcal{R}_v > 1$ then $H(0) > 0$ and so there is an odd number of endemic equilibria. Numerical simulations indicate that there is a unique EEP.

Numerical bifurcation analysis

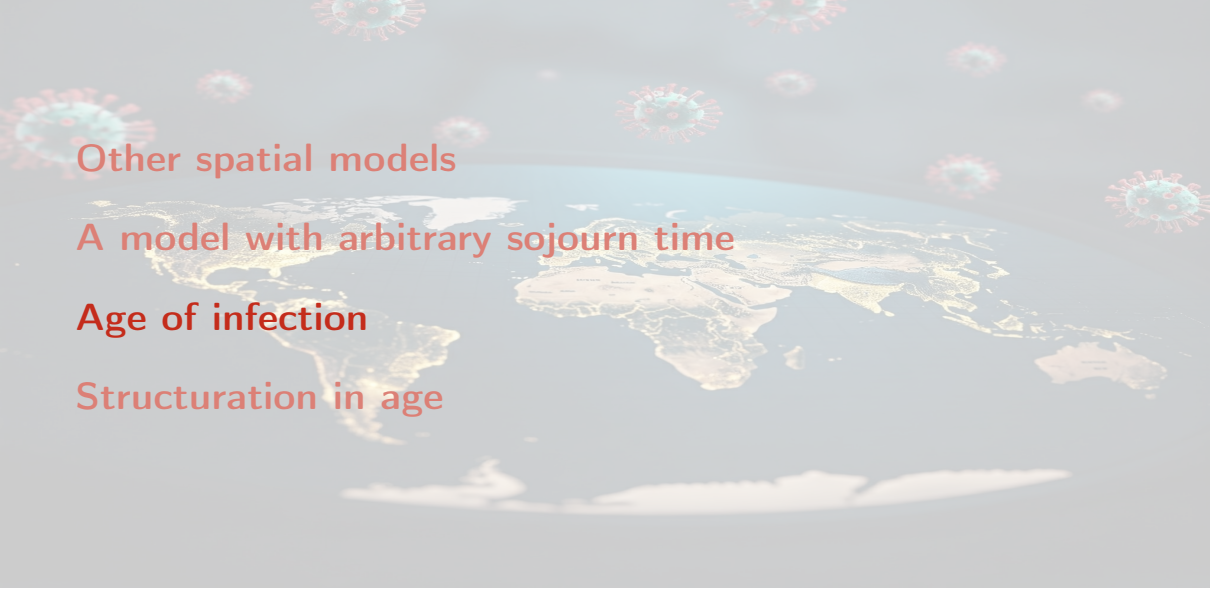
Same parameter values as in ODE case, except that the constant waning time (the delay) ω has to be substituted for θ. We take $\omega = 1825$, *i.e.*, corresponding to a 5 years waning time

These parameters give $\mathcal{R}_0 = 8.3936$ and $\mathcal{R}_v(\phi) = 0.8819$, which is in the range of the backward bifurcation since (using the above method) $\mathcal{R}_c(\phi) = 0.8675$

The bifurcation diagram is very like that depicted in earlier for the ODE. Numerical simulations of the DDE model (using `dde23`) indicate that there are no additional bifurcations; solutions either go to the DFE or to the (larger) EEP



(a) Values of $I^\star$ as a function of ω by solving $H(I, \mathcal{A}) = 0$ with $a_i = \omega$. (b) Value of $I(t)$ versus time, obtained by numerical integration of system (11) with initial data $I(t) = c$, for $t \in [-\omega, 0]$, $\omega = 1825$, c varying from 0 to 1 by steps of 0.02



Other spatial models

A model with arbitrary sojourn time

Age of infection

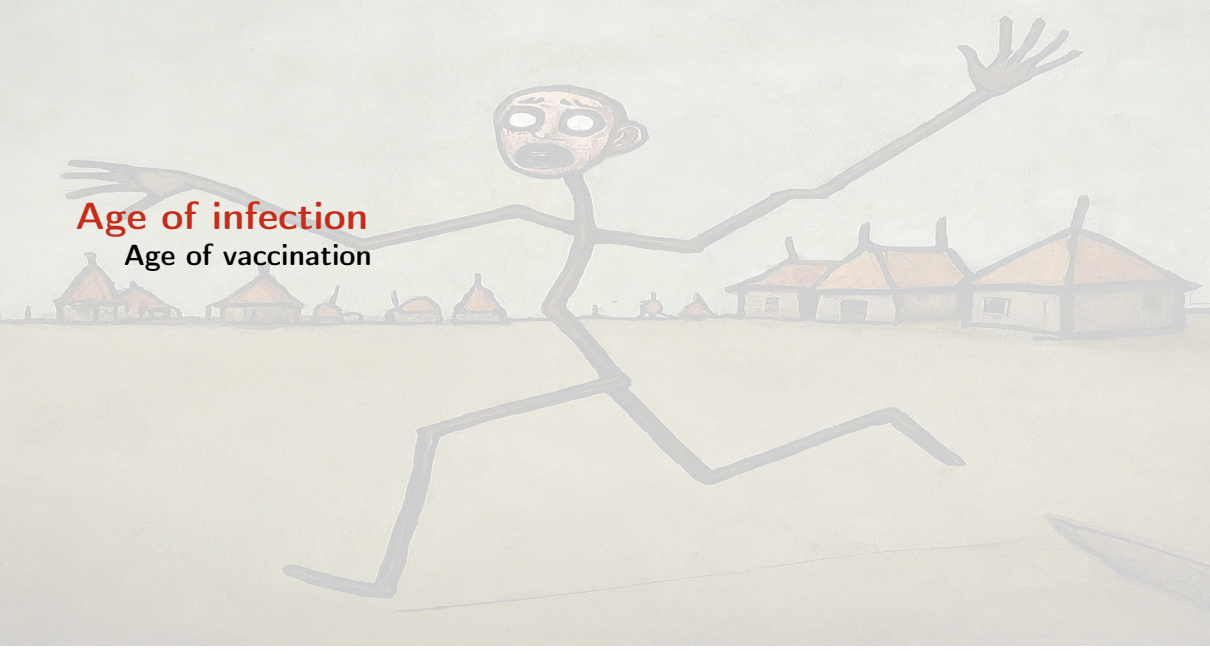
Structuration in age

Age of infection

We have seen that infinite dimensionality could result from a detailed description (or an unspecified one) of the sojourn time in compartments

Originally, age of infection was introduced to account for differences in infectivity depending on the time since an individual became infected

For instance, it is known that infectiousness of HIV positive patients vary as a function of time since infection


Age of infection
Age of vaccination

Age of vaccination

We used age of vaccination to find the initial condition of (4)

Here we take a closer look at this type of model

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EVALUATION OF VACCINATION STRATEGIES DURING PANDEMIC OUTBREAKS

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How to model time between vaccine doses

$$S' = -fS - V_1(t,0) \tag{18a}$$

$$A' = \Big((1-p)S + (1-p_1)\delta_1\tilde{V}_1 + (1-p_2)\delta_2 V_2\Big) f - \mu_A A \tag{18b}$$

$$I' = (pS + p_1\delta_1\tilde{V}_1 + p_2\delta_2 V_2)f - \mu I \tag{18c}$$

$$V_2{}' = V_1(t,a^\star) - \delta_2 f V_2(t) \tag{18d}$$

$$\left(\frac{\partial}{\partial t} + \frac{\partial}{\partial a}\right) V_1(t,a) = -\delta_1 f V_1(t,a), \quad 0 \le a \le a^\star \tag{18e}$$

and boundary condition

$$V_1(t,0) = \begin{cases} \gamma S_0 \left(\frac{S(t)}{S(t)+A(t)}\right) & \text{if } T \le t \le T_e \text{ and } S > 0 \\ 0 & \text{otherwise} \end{cases} \tag{18f}$$

where $f = \beta(\delta_A A + I)$ and $\tilde{V}_1(t) = \int_0^{a^\star} V_1(t,a)da$

Simplifying a bit

Integrate (18e) using characteristics along lines $a = s$ and $t = T + s$, with s as a new variable

$$V_1(t, a) = V_1(t - a, 0) \exp\left(\int_{t-a}^{t} -\delta_1 f(\xi)\ d\xi\right) \tag{19}$$

Define

$$\zeta(t) = \int_0^t \delta_1 f(\xi) d\xi$$

and substitute into (19), giving

$$V_1(t, a) = V_1(t - a, 0) \exp\left(\zeta(t - a)\zeta(t)\right)$$

So the distributed delay is now discrete

Simplifying a bit more

Let

$$\nu(t) = \int_0^t V_1(s,0)e^{\zeta(s)}ds$$

Then the total number of individuals having been vaccinated with a single dose is

$$\tilde{V}_1(t) = e^{-\zeta(t)}\left(\nu(t) - \nu(t-a^\star)\right)$$

$$S' = -fS - V_1(t,0) \tag{20a}$$

$$A' = \Big((1-p)S + (1-p_1)\delta_1\tilde{V}_1 + (1-p_2)\delta_2 V_2\Big)f - \mu_A A \tag{20b}$$

$$I' = (pS + p_1\delta_1\tilde{V}_1 + p_2\delta_2 V_2)f - \mu I \tag{20c}$$

$$V_2{}' = V_1(t-a^\star,0)e^{\zeta(t-a^\star)} - \delta_2 f V_2(t) \tag{20d}$$

$$\zeta' = \delta_1 f \tag{20e}$$

$$\nu' = V_1(t,0)e^{\zeta(t)} \tag{20f}$$

Other spatial models

A model with arbitrary sojourn time

Age of infection

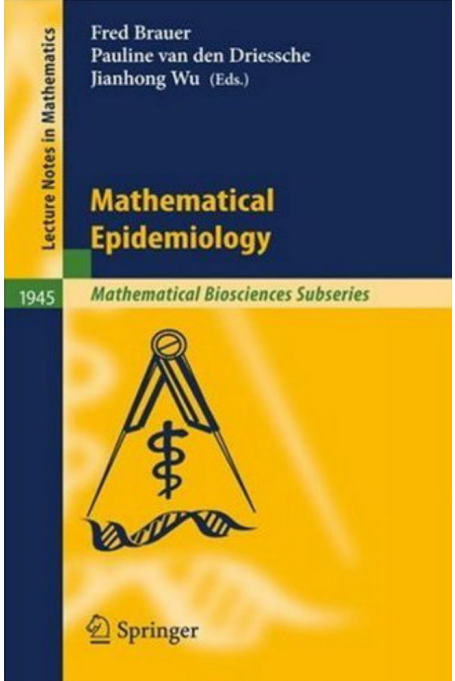
Structuration in age

Age structure

Taking into account age can be important in some cases

- Demographic characteristics vary with age
- Interactions are in general more frequent between people of a similar age. They are also more frequent in younger individuals
- Some diseases attack preferentially younger individuals
- The immunity of individuals changes with age, so for instance, older people may be more susceptible to some diseases than younger people

This is based on courses given by Jia Li during a Banff summer school in 2004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1945
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Springer

Note on age

Chronological age, as a structuring variable, is "easier" than other structuring variables

Indeed, if a is (chronological) age, then

$$\frac{d}{dt}a = 1$$

Formulation of an SIR model

Let a be the age. Assume that natural death and recovery occur at the rates μ and γ, respectively, both dependent on a

When an individual is sick, they are subject to disease-induced death at the rate $\delta(a)$

Governing equations are

$$(\partial_t + \partial_a)S(t,a) = \Lambda(a) - (\mu(a) + \lambda(t,a))S(t,a) \tag{21a}$$
$$(\partial_t + \partial_a)I(t,a) = -(\mu(a) + \gamma(a) + \delta(a))I(t,a) + \lambda(t,a)S(t,a) \tag{21b}$$
$$(\partial_t + \partial_a)R(t,a) = \gamma(a)I(t,a) \tag{21c}$$

Boundary conditions are

$$S(t, a_0) = B \tag{21d}$$
$$I(t, a_0) = 0 \tag{21e}$$
$$R(t, a_0) = 0 \tag{21f}$$

while initial conditions take the form

$$S(0, a) = \Phi(a) \tag{21g}$$
$$I(0, a) = \Psi(a) \tag{21h}$$
$$R(0, a) = 0 \tag{21i}$$

Force of infection

Transmission $\lambda(t, a)$ of the disease takes the form

$$\lambda(t, a) = r(a) \int_{a_0}^{\infty} \beta(a, s)\rho(a, s)\frac{I(t, s)}{N(t, s)} ds$$

where

- $r(a)$ is the number of contacts by individuals of age a per unit time
- $\beta(a, s)$ is the probability of disease transmission to a susceptible of age a by an infectious of age s
- $\rho(a, s)$ is the meeting rate between people of age a and people of age s
- $N(t, a) = S(t, a) + I(t, a) + R(t, a)$ is the distribution of total population

To simplify, assume that $\beta(a, s)$ is separable

$$\beta(a, s) = f(a)g(s)$$

where $f(a)$ is the susceptibility of individuals aged a and $g(s)$ is the force of infection of individuals aged s

Then

$$\lambda(t, a) = r(a)f(a) \int_{a_0}^{\infty} g(s)\rho(a, s)\frac{I(t, s)}{N(t, s)} ds \tag{22}$$

Analysis of the SIR model

We seek the DFE by setting $I = 0$

We find $(S, I, R) = (S^0(a), 0, 0)$ with

$$S^0(a) = Be^{-M(a)} + e^{-M(a)} \int_{a_0}^{a} e^{M(x)} \Lambda(x) dx$$

where

$$M(a) = \int_{a_0}^{a} \mu(s) ds$$

Consider the perturbed solution $u(t,a) = S(t,a) - S^0(a)$. Assume that the meeting rate ρ is also separable,

$$\rho(a,s) = p_1(a)p_2(s)$$

Then

$$\tilde{\lambda}(t,a) := r(a)f(a)p_1(a)\int_{a_0}^{\infty} \frac{g(s)p_2(s)}{S^0(s)} I(t,s)ds \simeq \lambda(t,a)$$

and we obtain the linearisation

$$\begin{aligned}
(\partial_t + \partial_a)u &= -\mu(a)u - \tilde{\lambda}(t,a)S^0(a) \\
(\partial_t + \partial_a)I &= -(\mu(a) + \gamma(a) + \delta(a))I + \tilde{\lambda}(t,a)S^0(a) \\
(\partial_t + \partial_a)R &= \gamma(a)I
\end{aligned}$$

Let

$$u(t,a) = \tilde{u}(a)e^{c(t-a)} \qquad I(t,a) = \tilde{I}(a)e^{c(t-a)}$$

and denote

$$b(a) = S^0(a)r(a)f(a)p_1(a) \qquad W = \int_{a_0}^{\infty} \frac{g(s)p_2(s)}{S^0(s)} e^{-cs}\tilde{I}(s)ds$$

Then

$$\frac{d\tilde{u}(a)}{da} = -\mu(a)\tilde{u}(a) - b(a)e^{ca}W$$
$$\frac{d\tilde{I}(a)}{da} = -(\mu(a) + \gamma(a))\tilde{I}(a) + b(a)e^{ca}W$$

$$\tilde{I}(a) = We^{-M(a)-\Gamma(a)} \int_{a_0}^{\infty} e^{M(s)+\Gamma(s)} b(s)e^{cs} ds$$

where $\Gamma(a) = \int_{a_0}^{a} \gamma(s)ds$

Therefore

$$W = W \int_{a_0}^{\infty} \frac{g(s)p_2(s)}{S^0(s)} e^{-M(s)-\Gamma(s)} \int_{a_0}^{s} e^{M(v)+\Gamma(v)} b(v)e^{-c(s-v)} dvds$$

Let then

$$H(c) := \int_{a_0}^{\infty} \frac{g(s)p_2(s)}{S^0(s)} e^{-M(s)-\Gamma(s)} \int_{a_0}^{s} e^{M(v)+\Gamma(v)} b(v) e^{-c(s-v)} dvds$$

We seek roots of the characteristic equation $H(c) = 1$

We have

$$\frac{dH(c)}{dc} = -\int_{a_0}^{\infty} \frac{g(s)p_2(s)}{S^0(s)} e^{-M(s)-\Gamma(s)} \int_{a_0}^{s} (s-v) e^{M(v)+\Gamma(v)} b(v) e^{-c(s-v)} dvds < 0$$

implying that $H(c)$ is a decreasing function

- Let $c^\star$ be a real solution to $H(c) = 1$. If $H(0) > 1$, then $c > 0$, whereas if $H(0) < 1$, $c < 0$

- Suppose that $c^\star = \alpha + i\beta$ is a complex root of $H(c) = 1$. Then

$$\mathrm{Re}\, H(c) = \int_{a_0}^{\infty} \frac{g(s)p_2(s)}{S^0(s)} e^{-M(s)-\Gamma(s)} \int_{a_0}^{s} e^{M(v)+\Gamma(v)} b(v) e^{-\alpha(s-v)} \cos\beta(s-v) dv ds$$

As a consequence, $H(0) < 1 \implies \alpha < 0$

So $H(0) = 1$ is a threshold and we take $\mathcal{R}_0 = H(0)$

Analysis using semigroups: SIA model

To illustrate the use of the semigroup method in this context, we consider an SIA model describing the evolution of HIV/AIDS

The model is almost equivalent to (21), with a few differences

The I compartment contains inviduals bearing HIV, but not yet in the AIDS stage

The rate $\gamma(a)$ represents the progression towards the AIDS stage

The AIDS stage is represented by compartment A, where individuals are subject to a specific mortality rate

$$(\partial_t + \partial_a)S(t,a) = \Lambda(a) - (d(a) + \lambda(t,a))S(t,a) \tag{23a}$$
$$(\partial_t + \partial_a)I(t,a) = -(d(a) + \gamma(a))I(t,a) + \lambda(t,a)S(t,a) \tag{23b}$$
$$(\partial_t + \partial_a)A(t,a) = \gamma(a)A(t,a) - (d(a) + \delta(a))A(t,a) \tag{23c}$$

Assume

$$\lambda(t,a) = h(a)\int_{a_0}^{\infty} \rho(a,a')\frac{I(t,a')}{T(t,a')}da' \tag{23d}$$

where $T(t,a') = S(t,a') + I(t,a')$

An individual in AIDS stage no longer has contacts. Therefore the dynamics of S and I do not depend on the dynamics of A, and we consider the system consisting of the first two variables

Let ω be the maximum age. The system in proportions takes the form

$$x := \frac{S}{T} \qquad y := \frac{I}{T}$$

As we are only considering S and I, we have $x + y = 1$ and the system reads

$$(\partial_t + \partial_a) y(t,a) = (1-y)(-\gamma(a) y + \lambda(t,a)) \tag{24a}$$

$$\lambda(t,a) = h(a) \int_0^\omega p(a,a') y(t,a') da' \tag{24b}$$

Let $X = \{f \in L^1(0,\omega)\}$. Define

$$(Af)(a) := -\frac{d}{da}f(a), \quad f \in D(A)$$

with $D(a) = \{f \in X,\ f \text{ is absolutely continuous, } f(0) = 0\}$, and

$$F(f)(a) \equiv (1 - f(a)) \left(-\gamma(a)f(a) + h(a) \int_0^\omega p(a,a')f(a')da' \right)$$

an operator from $X \to X$

Let $\Omega = \{f \in X,\ 0 \leq f \leq 1 \text{ a.e.}\}$. Then (24) takes the form

$$\frac{dy}{dt} = Ay + F(y)$$
$$y(0) = y_0 \in \Omega$$

Let

$$(\mathcal{B}f)(a) = -\frac{df(a)}{da} - \gamma(a)f(a) \qquad (\mathcal{P}f)(a) = h(a)\int_0^\omega p(a,a')f(a')da'$$

We have

$$(\partial_t + \partial_a)y = -\gamma(a)y + h(a)\int_0^\omega \rho(a,a')y(t,a')da' \Leftrightarrow \frac{dy}{dt} = (\mathcal{B}+\mathcal{P})y$$

$\mathcal{B}+\mathcal{P}$ generates a C_0-semigroup $T(t)$, $t \geq 0$, which is eventually uniformly continuous

The resolvant of $\mathcal{B}+\mathcal{P}$ is

$$R(\lambda;\mathcal{B}+\mathcal{P}) = (S_\lambda - I)^{-1} G$$

with

$$(Gf)(a) = \int_0^a e^{-\lambda(a-\sigma)} \frac{\Gamma(a)}{\Gamma(\sigma)} f(\sigma) d\sigma$$

$$(S_\lambda f)(a) = \int_0^\omega \int_0^a e^{-\lambda(a-\sigma)} \frac{\Gamma(a)}{\Gamma(\sigma)} \rho(\sigma,\xi) d\sigma f(\xi) d\xi$$

where we denoted

$$\Gamma(a) = \exp\left(-\int_0^a \gamma(a')da'\right)$$

$\mathcal{R}_0$

$\mathcal{R}_0$ is the spectral radius of the operator

$$(Sf)(a) = \int_0^\omega \int_0^a \frac{\Gamma(a)}{\Gamma(\sigma)} h(\sigma) p(\sigma, \xi) d\sigma f(\xi) d\xi$$

Pair formation

$\rho(t, a, a')$ proportion of partners of an individual aged a who are aged a'

$r(t, a)$ mean number of partners of an individual aged a

$T(t, a)$ total number of individuals aged a

The following conditions must hold

- $0 \leq \rho \leq 1$
- $\int_0^\infty \rho(t, a, a')da' = 1$
- $\rho(t, a, a')r(t, a)T(t, a) = \rho(t, a', a)r(t, a')T(t, a')$
- $r(t, a)T(t, a)r(t, a')T(t, a') = 0 \Rightarrow \rho(t, a, a') = 0$

Bibliography I