



University  
of Manitoba

## Models using age of .. something MATH 8xyz – Lecture 20

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Winter 20XX

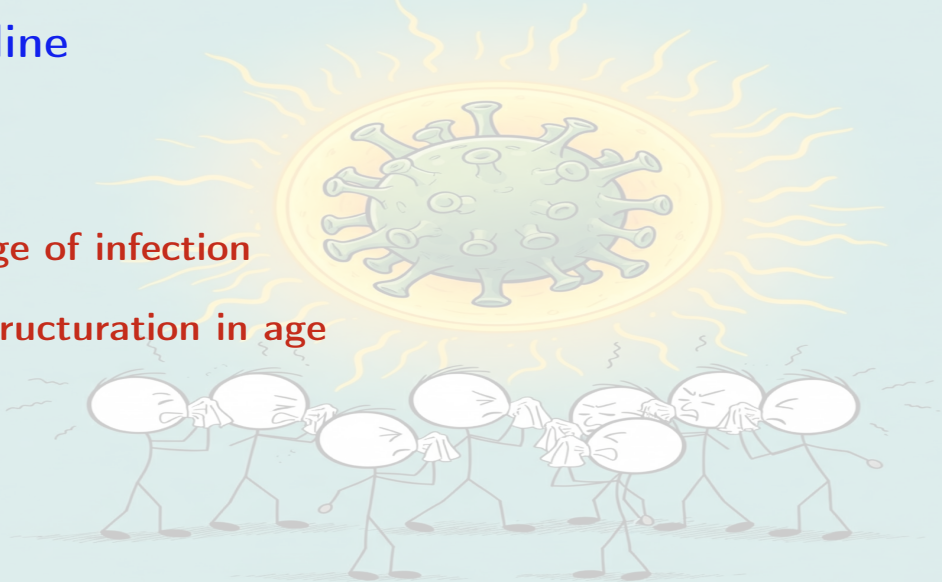
The University of Manitoba campuses are located on original lands of Anishinaabeg, Ininew, Anisininew, Dakota and Dene peoples, and on the National Homeland of the Red River Métis.

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

Age of infection

Structuration in age



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 (??)

Here we take a closer look at this type of model

FIGS/BowmanArinoMoghadas-2011-cover.png

## How to model time between vaccine doses

$$S' = -fS - V_1(t, 0) \quad (1a)$$

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

$$I' = (pS + p_1\delta_1 \tilde{V}_1 + p_2\delta_2 V_2)f - \mu I \quad (1c)$$

$$V_2' = V_1(t, a^*) - \delta_2 f V_2(t) \quad (1d)$$

$$\left( \frac{\partial}{\partial t} + \frac{\partial}{\partial a} \right) V_1(t, a) = -\delta_1 f V_1(t, a), \quad 0 \leq a \leq a^* \quad (1e)$$

and boundary condition

$$V_1(t, 0) = \begin{cases} \gamma S_0 \left( \frac{S(t)}{S(t)+A(t)} \right) & \text{if } T \leq t \leq T_e \text{ and } S > 0 \\ 0 & \text{otherwise} \end{cases} \quad (1f)$$

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



## Simplifying a bit

Integrate (1e) using characteristics along lines  $a = s$  and  $t = T + s$ , with  $s$  as a new variable

$$V_1(t, a) = V_1(t - a, 0) \exp \left( \int_{t-a}^t -\delta_1 f(\xi) d\xi \right) \quad (2)$$

Define

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

and substitute into (2), giving

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

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

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

$$S' = -fS - V_1(t, 0) \tag{3a}$$

$$A' = \left( (1 - p)S + (1 - p_1)\delta_1 \tilde{V}_1 + (1 - p_2)\delta_2 V_2 \right) f - \mu_A A \tag{3b}$$

$$I' = (pS + p_1\delta_1 \tilde{V}_1 + p_2\delta_2 V_2)f - \mu I \tag{3c}$$

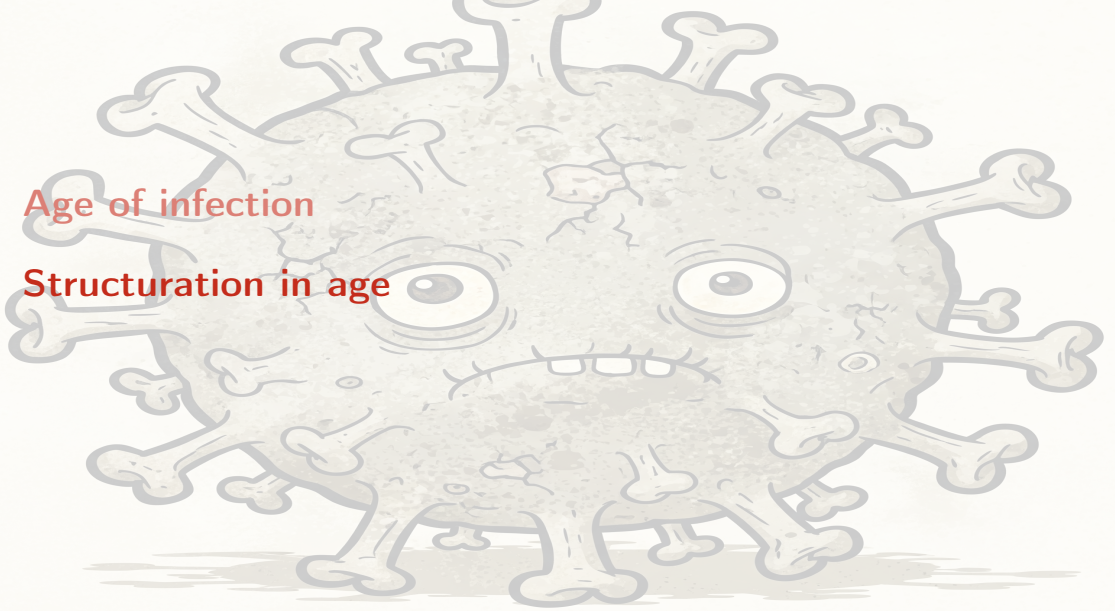
$$V_2' = V_1(t - a^*, 0) e^{\zeta(t - a^*)} - \delta_2 f V_2(t) \tag{3d}$$

$$\zeta' = \delta_1 f \tag{3e}$$

$$\nu' = V_1(t, 0) e^{\zeta(t)} \tag{3f}$$

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

FIGS/BrauerPvdDWu-book.png

## 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  $\mu$  and  $\gamma$ , 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

$$(\partial_t + \partial_a)S(t, a) = \Lambda(a) - (\mu(a) + \lambda(t, a))S(t, a) \quad (4a)$$

$$(\partial_t + \partial_a)I(t, a) = -(\mu(a) + \gamma(a) + \delta(a))I(t, a) + \lambda(t, a)S(t, a) \quad (4b)$$

$$(\partial_t + \partial_a)R(t, a) = \gamma(a)I(t, a) \quad (4c)$$

Boundary conditions are

$$S(t, a_0) = B \quad (4d)$$

$$I(t, a_0) = 0 \quad (4e)$$

$$R(t, a_0) = 0 \quad (4f)$$

while initial conditions take the form

$$S(0, a) = \Phi(a) \quad (4g)$$

$$I(0, a) = \Psi(a) \quad (4h)$$

$$R(0, a) = 0 \quad (4i)$$



## 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

$$\lambda(t, a) = r(a)f(a) \int_{a_0}^{\infty} g(s)\rho(a, s) \frac{I(t, s)}{N(t, s)} ds \quad (5)$$

## 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  $\rho$  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

$$(\partial_t + \partial_a)u = -\mu(a)u - \tilde{\lambda}(t, a)S^0(a)$$

$$(\partial_t + \partial_a)I = -(\mu(a) + \gamma(a) + \delta(a))I + \tilde{\lambda}(t, a)S^0(a)$$

$$(\partial_t + \partial_a)R = \gamma(a)I$$

Let

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

and denote

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

Then

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

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

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

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

Therefore

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

Let then

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

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

We have

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

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

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

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

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

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 (4), with a few differences

The  $I$  compartment contains individuals 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

$$(\partial_t + \partial_a)S(t, a) = \Lambda(a) - (d(a) + \lambda(t, a))S(t, a) \quad (6a)$$

$$(\partial_t + \partial_a)I(t, a) = -(d(a) + \gamma(a))I(t, a) + \lambda(t, a)S(t, a) \quad (6b)$$

$$(\partial_t + \partial_a)A(t, a) = \gamma(a)A(t, a) - (d(a) + \delta(a))A(t, a) \quad (6c)$$

Assume

$$\lambda(t, a) = h(a) \int_{a_0}^{\infty} \rho(a, a') \frac{I(t, a')}{T(t, a')} da' \quad (6d)$$

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  $\omega$  be the maximum age. The system in proportions takes the form

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

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

$$(\partial_t + \partial_a)y(t, a) = (1 - y)(-\gamma(a)y + \lambda(t, a)) \tag{7a}$$

$$\lambda(t, a) = h(a) \int_0^\omega p(a, a')y(t, a')da' \tag{7b}$$

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  $X \rightarrow X$

Let  $\Omega = \{f \in X, 0 \leq f \leq 1 \text{ a.e.}\}$ . Then (7) takes the form

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

Let

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

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 resolvent 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