

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

Durban – Lecture 02

Julien Arino

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The SLIRS models

Extensions of the KMK model

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The SLIRS models

- SIS models

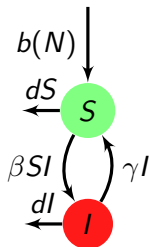
- SLIRS model with constant population

- Computing \mathcal{R}_0 more efficiently

- Global properties of the SLIRS model

- SLIRS in variable population

Simplifying the SIRS model



► We have already seen the epidemic KMK SIR model and the endemic SIRS model

► By making some simplifications, we can obtain the SIS model: assume the time spent in the R compartment goes to zero, i.e., $\nu \rightarrow \infty$

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

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

and determines whether we go to the DFE $(N^*, 0)$ or to the endemic equilibrium

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Incubation periods

- ▶ SIS and SIR: progression from S to I 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 transmission: 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)

The model is as follows:

$$S' = b + \nu R - dS - f(S, I, N) \quad (1a)$$

$$L' = f(S, I, N) - (d + \varepsilon)L \quad (1b)$$

$$I' = \varepsilon L - (d + \gamma)I \quad (1c)$$

$$R' = \gamma I - (d + \nu)R \quad (1d)$$

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

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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 (1)

Variation of the infected variables in (1) are described by

$$L' = f(S, I, N) - (\varepsilon + d)L$$

$$I' = \varepsilon L - (d + \gamma)I$$

Write

$$\mathcal{I}' = \begin{pmatrix} L \\ I \end{pmatrix}' = \begin{pmatrix} f(S, I, N) \\ 0 \end{pmatrix} - \begin{pmatrix} (\varepsilon + d)L \\ (d + \gamma)I - \varepsilon L \end{pmatrix} =: \mathcal{F} - \mathcal{V} \quad (2)$$

Compute the Jacobian matrices of vectors \mathcal{F} and \mathcal{V} , giving

$$F = \begin{pmatrix} \frac{\partial \bar{f}}{\partial L} & \frac{\partial \bar{f}}{\partial I} \\ 0 & 0 \end{pmatrix}, \quad V = \begin{pmatrix} \varepsilon + d & 0 \\ -\varepsilon & d + \gamma \end{pmatrix} \quad (3)$$

where we denote

$$\frac{\partial \bar{f}}{\partial L} := \frac{\partial f}{\partial L}(\bar{S}, \bar{I}, \bar{N}) \quad \frac{\partial \bar{f}}{\partial I} := \frac{\partial f}{\partial I}(\bar{S}, \bar{I}, \bar{N})$$

and $(\bar{S}, \bar{I}, \bar{N})$ are the values of S, I and N at the DFE.

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

$$\mathcal{R}_0 = \frac{\varepsilon \frac{\partial \bar{f}}{\partial I}}{(d + \varepsilon)(d + \gamma)} \quad (4)$$

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

$$S' = b + \nu R - dS - f(S, I, N)$$

$$L' = f(S, I, N) - (d + \varepsilon)L$$

$$I' = \varepsilon L - (d + \gamma)I$$

$$R' = \gamma I - (d + \nu)R$$

SLIR	SLIRS where $\nu = 0$
SLIS	Limit of SLIRS when $\nu \rightarrow \infty$
SLI	SLIR where $\gamma = 0$
SIRS	Limit of SLIRS when $\varepsilon \rightarrow \infty$
SIR	SIRS where $\nu = 0$
SIS	Limit of SIRS when $\nu \rightarrow \infty$ Limit SLIS when $\varepsilon \rightarrow \infty$
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	$\frac{\bar{f}_I}{d+\gamma}$

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Lyapunov function for SLIR and SLIS

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

$$S' = d - \beta SI - pdI - qdL - dS \quad (5a)$$

$$L' = \beta SI + pdI - (\varepsilon + d - qd)L \quad (5b)$$

$$I' = \varepsilon L - (\gamma + d)I \quad (5c)$$

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 (5), it is not shown.

Equilibria

- ▶ DFE: $E_0 = (1, 0, 0)$.
- ▶ EEP: $E^* = (S^*, L^*, I^*)$ with

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

where

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

is the basic reproduction number with vertical transmission.

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

E^* exists (in a biologically plausible way) only when $\mathcal{R}_0^\vee > 1$.

Consider the Goh Lyapunov function

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

Theorem 4

- ▶ *If $\mathcal{R}_0 > 1$, then (5) has the globally asymptotically stable equilibrium E^* .*
- ▶ *If $\mathcal{R}_0 \leq 1$, then (5) has the globally asymptotically stable equilibrium E_0 , E^* is not biologically plausible.*

Mukherjee, Chattopadhyay et Tapaswi tentent une approche par les fonctions de Lyapounov. Ils considèrent le système (1) dans le cas d'une incidence sous la forme $f(S, I, N) = \beta S^q I^p$. Après avoir établi l'uniforme bornitude du système, ils définissent la fonction suivante:

$$V(S, E, I) = \frac{1}{2} ((S - S^*)^2 + (E - E^*)^2 + (I - I^*)^2)$$

ce qui leur permet, en définissant la matrice

$$A = \begin{pmatrix} \beta I^{*p}g(S) + d + \nu & \frac{1}{2}(\nu - \beta I^{*p}g(S)) & \frac{1}{2}(\beta S^q h(I) + \nu) \\ \frac{1}{2}(\nu - \beta I^{*p}g(S)) & \varepsilon + d & -\frac{1}{2}(\beta S^q h(I) + \varepsilon) \\ \frac{1}{2}(\beta S^q h(I) + \nu) & -\frac{1}{2}(\beta S^q h(I) + \varepsilon) & \gamma + d \end{pmatrix}$$

avec les fonctions g et h telles que

$$S^q - S^{*q} = (S - S^*)g(S), \quad I^p - I^{*p} = (I - I^*)h(I)$$

d'obtenir le résultat qui suit.

Theorem 5

La fonction V est telle que $V' < 0$ si

1. $4(\beta I^{*p}g(S) + d + \nu)(\varepsilon + d) > (\nu - \beta I^{*p}g(S))^2,$
2. $\det A > 0.$

Il est bien entendu qu'un résultat comme le Théorème 5 est difficile à utiliser en pratique, et ce système a donc fait l'objet d'autres études.

Li, Muldowney and van den Driessche study an SLIRS model with incidence of the form

$$f(S, I, N) = \beta g(I)S \quad (6)$$

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 assumption about g :

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

We have

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

$$\text{Since } \frac{\partial \bar{g}}{\partial I} = \lim_{I \rightarrow 0^+} \frac{g(I)}{I} = c,$$

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

The LAS results already established hold here, since (6) is a special case of the function f with which the results were obtained.

Theorem 6

Si $g(I)$ satisfait l'hypothèse **H**, le système (1) avec incidence (6) est uniformément persistant si, et seulement si, $\mathcal{R}_0 > 1$.

Le système est *uniformément persistant* si il existe $0 < \epsilon_0 < 1$ telle que toute solution $(S(t), E(t), I(t), R(t))$ de (1) de condition initiale $(S(0), E(0), I(0), R(0)) \in \overset{\circ}{\Gamma}$ vérifie

$$\begin{aligned} \liminf_{t \rightarrow \infty} S(t) &\geq \epsilon_0, & \liminf_{t \rightarrow \infty} E(t) &\geq \epsilon_0 \\ \liminf_{t \rightarrow \infty} I(t) &\geq \epsilon_0, & \liminf_{t \rightarrow \infty} R(t) &\geq \epsilon_0 \end{aligned} \quad (7)$$

Theorem 7

Supposons que l'incidence (6) satisfait H , et que

$$|g'(I)|I \leq g(I) \text{ pour } I \in (0, 1] \quad (8)$$

Supposons en outre que $\mathcal{R}_0 > 1$, et que l'une des conditions

$$\begin{aligned} \gamma\nu &< \epsilon_0(\beta\eta_0 + \gamma + d)(\beta\eta_0 + \nu + d) \\ \varepsilon - \gamma - d &< \nu \end{aligned}$$

est vérifiée, where

$$\eta_0 = \min_{I \in [\epsilon_0, 1]} g(I) > 0$$

et ϵ_0 défini par (7). Alors il n'y a pas de courbe fermée rectifiable qui soit invariante par rapport à (1). De plus, chaque semi-trajectoire de (1) dans Γ converge vers un équilibre.

Remarques

- ▶ Le modèle SEIRS, et plus encore ses sous-systèmes, ont fait l'objet de beaucoup de travail. Les premiers travaux remontent à Kermack et McKendrick, et concernent le modèle SIR sans démographie (mais avec infection des individus remis).
- ▶ Je ne connais pas de SEIRS à population constante qui ait un comportement exotique.

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SIRS of the form

$$S' = B(N) - dS - f(S, I)I + \nu R \quad (9a)$$

$$I' = f(S, I)I - (d + \gamma)I \quad (9b)$$

$$R' = \gamma I - (d + \nu)R \quad (9c)$$

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 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

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- The SLIAR model

- Computing the final size more efficiently

- Final size relations

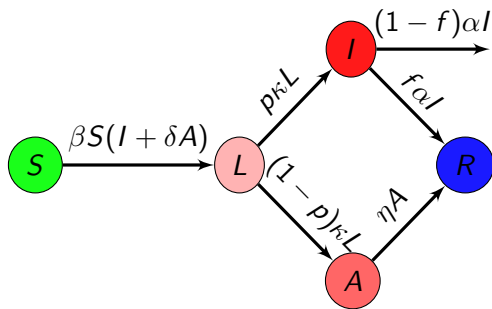
- Examples

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

⇒ 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)



Basic reproduction number

We find the basic reproduction number

$$\mathcal{R}_0 = S_0 \beta \left(\frac{\rho}{\alpha} + \frac{\delta(1-\rho)}{\eta} \right) = \frac{S_0 \beta \rho}{\alpha} \quad (10)$$

where

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

Final size relation

$$S_0(\ln S_0 - \ln S_\infty) = \mathcal{R}_0(S_0 - S_\infty) + \frac{\mathcal{R}_0 I_0}{\rho} \quad (11)$$

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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

$$S' = b(S, I, R) - DS\beta(S, I, R)hI \quad (12a)$$

$$I' = \Pi DS\beta(S, I, R)hI - VI \quad (12b)$$

$$R' = f(S, I, R) + WI \quad (12c)$$

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

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

$$S' = b(S, I, R) - DS\beta(S, I, R)h \quad (12a)$$

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

$$I' = \Pi D S \beta(S, I, R) h I - V I \quad (12b)$$

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

$$R' = f(S, I, R) + WI \quad (12c)$$

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

Suppose E_0 is a locally stable disease-free equilibrium (DFE) of the system without disease, i.e., an EP of

$$S' = b(S, 0, R)$$

$$R' = f(S, 0, R)$$

Theorem 8

Let

$$\mathcal{R}_0 = \beta(S_0, 0, R_0) h V^{-1} \Pi D S_0 \quad (13)$$

- ▶ If $\mathcal{R}_0 < 1$, the DFE E_0 is a locally asymptotically stable EP of (12)
- ▶ If $\mathcal{R}_0 > 1$, the DFE E_0 of (12) is unstable

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

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Final size relations

Assume no demography, then system should be writeable as

$$S' = -DS\beta(S, I, R)hI \quad (14a)$$

$$I' = \mathbf{I}DS\beta(S, I, R)hI - VI \quad (14b)$$

$$R' = WI \quad (14c)$$

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

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

Define the row vector

$$\mathbb{R}^m \ni \mathbf{\Gamma} = (\Gamma_1, \dots, \Gamma_m) = \beta(S_0, 0, R_0) h V^{-1} \mathbf{\Pi} D$$

then

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

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

Then for $i = 1, \dots, m$, express $S_i(\infty)$ as a function of $S_1(\infty)$ using

$$S_i(\infty) = S_i(0) \left(\frac{S_1(\infty)}{S_1(0)} \right)^{\sigma_i/\sigma_1}$$

then substitute into

$$\begin{aligned} \frac{1}{\sigma_i} \ln \left(\frac{S_i(0)}{S_i(\infty)} \right) &= \Gamma D^{-1} (S(0) - S(\infty)) + \beta h V^{-1} I(0) \\ &= \frac{1}{\sigma_1} \ln \left(\frac{S_1(0)}{S_1(\infty)} \right) \end{aligned}$$

which is a final size relation for the general system when $S_i(0) > 0$

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

$$\ln \left(\frac{S_0}{S_\infty} \right) = \frac{\mathcal{R}_0}{S_0} (S_0 - S_\infty) + \beta h V^{-1} I_0 \quad (15)$$

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

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

where K is the initial total population

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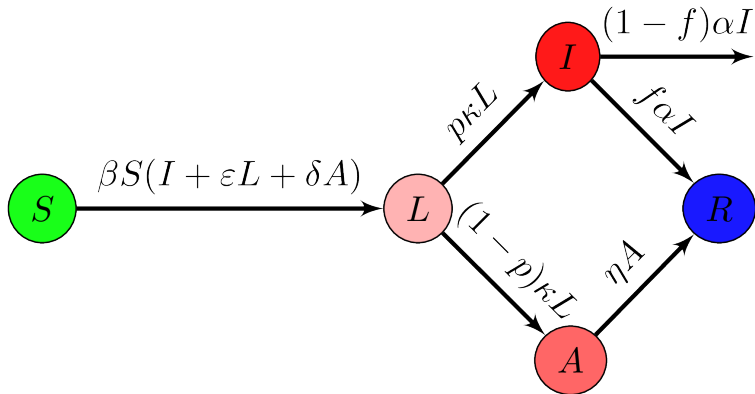
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The SLIAR model

- ▶ 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



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

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

Incidence is mass action so $\beta(E_0) = \beta$ and thus

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

For final size, since $m = 1$, we can use (15):

$$\ln \left(\frac{S_0}{S_\infty} \right) = \frac{\mathcal{R}_0}{S_0} (S_0 - S_\infty) + \beta h V^{-1} l_0$$

Suppose $l_0 = (0, l_0, 0)$, then

$$\ln \left(\frac{S_0}{S_\infty} \right) = \mathcal{R}_0 \frac{S_0 - S_\infty}{S_0} + \frac{\beta}{\alpha} l_0$$

If $l_0 = (L_0, l_0, A_0)$, then

$$\ln \left(\frac{S_0}{S_\infty} \right) = \mathcal{R}_0 \frac{S_0 - S_\infty}{S_0} + \beta \left(\frac{\varepsilon}{\kappa} + \frac{p}{\alpha} + \frac{\delta(1-p)}{\eta} \right) L_0 + \frac{\beta\delta}{\eta} A_0 + \frac{\beta}{\alpha} l_0$$

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

$$S'_U = -\beta S_U [I_U + \sigma_I I_V] \quad (16a)$$

$$S'_V = -\sigma_S \beta S_V [I_U + \sigma_I I_V] \quad (16b)$$

$$L'_U = \beta S_U [I_U + \sigma_I I_V] - \kappa_U L_U \quad (16c)$$

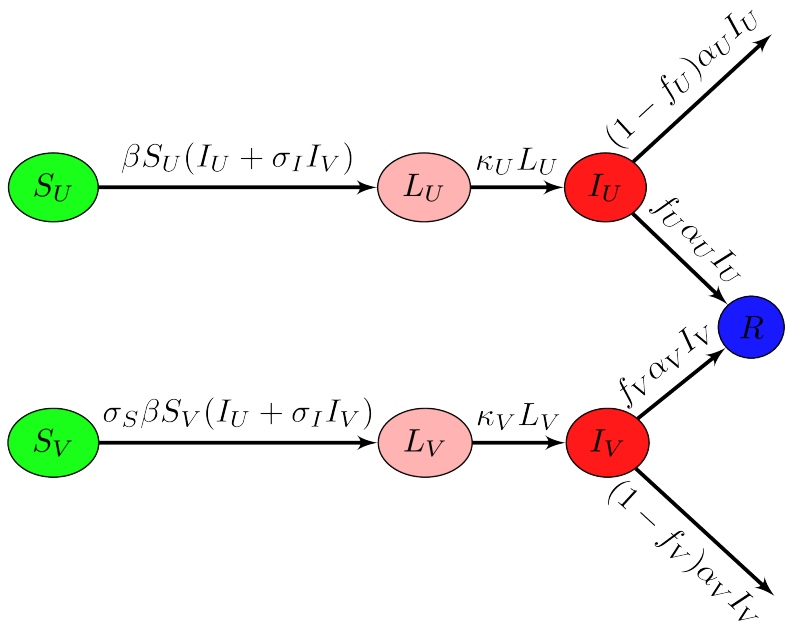
$$L'_V = \sigma_S \beta S_V [I_U + \sigma_I I_V] - \kappa_V L_V \quad (16d)$$

$$I'_U = \kappa_U L_U - \alpha_U I_U \quad (16e)$$

$$I'_V = \kappa_V L_V - \alpha_V I_V \quad (16f)$$

$$R' = f_U \alpha_U I_U + f_V \alpha_V I_V \quad (16g)$$

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



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

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

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

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

and the final size relation is

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

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