An introduction to evolutionary epidemiology of infectious diseases

Part 1

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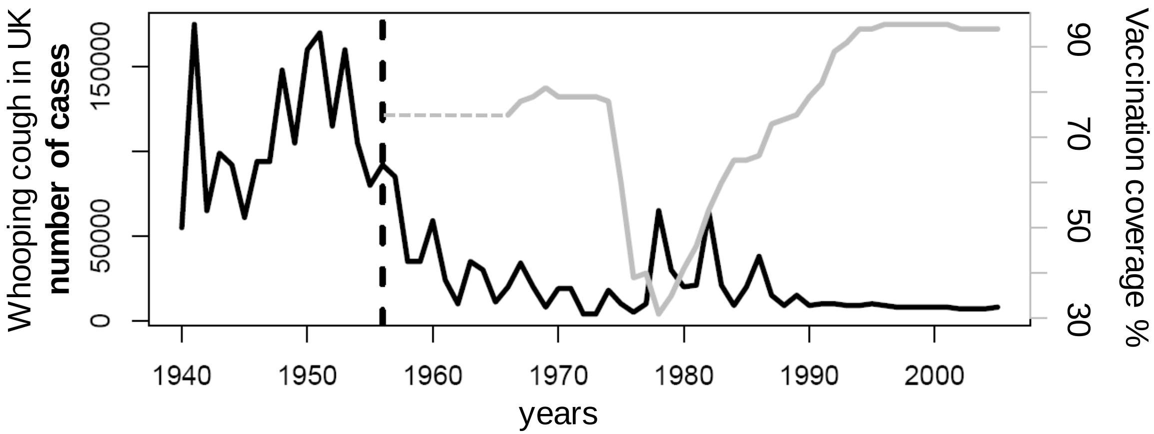
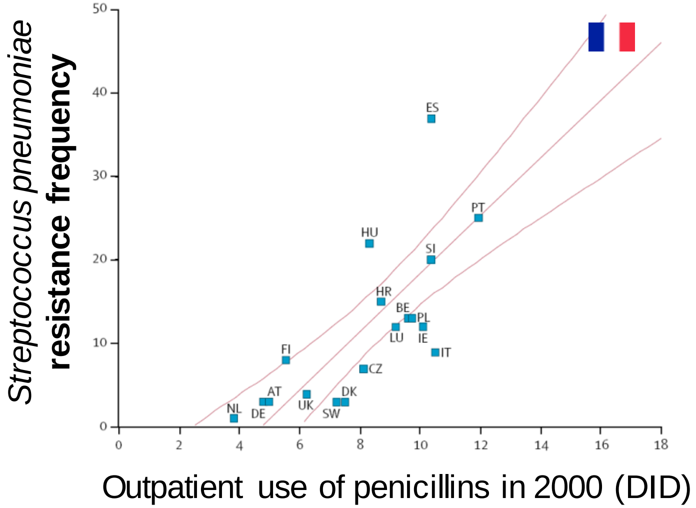
Evolutionary epidemiology of infectious diseases

Epidemiology:

Rohani et al. 1999, *Science*.



Evolution:

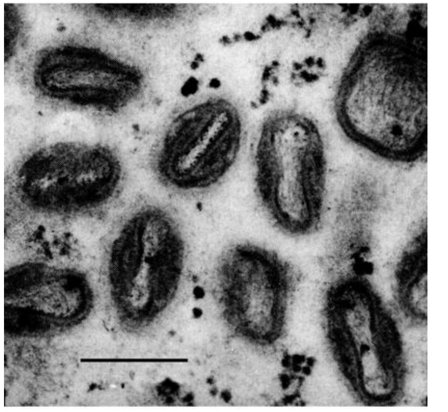


Goossens et al. 2005, *The Lancet*.

Outline

1. **Two examples :**
   - Myxomatosis
   - Smallpox
2. **Epidemiological dynamics**
3. **Adaptive dynamics**
4. **Evolutionary epidemiology**

Myxomatosis



Poxviridae virus (DNA virus, ~161kb)

Indirect life cycle (rabbit-insect vector)

Pathology :

Variable, depends on both the virus type and its host

History :

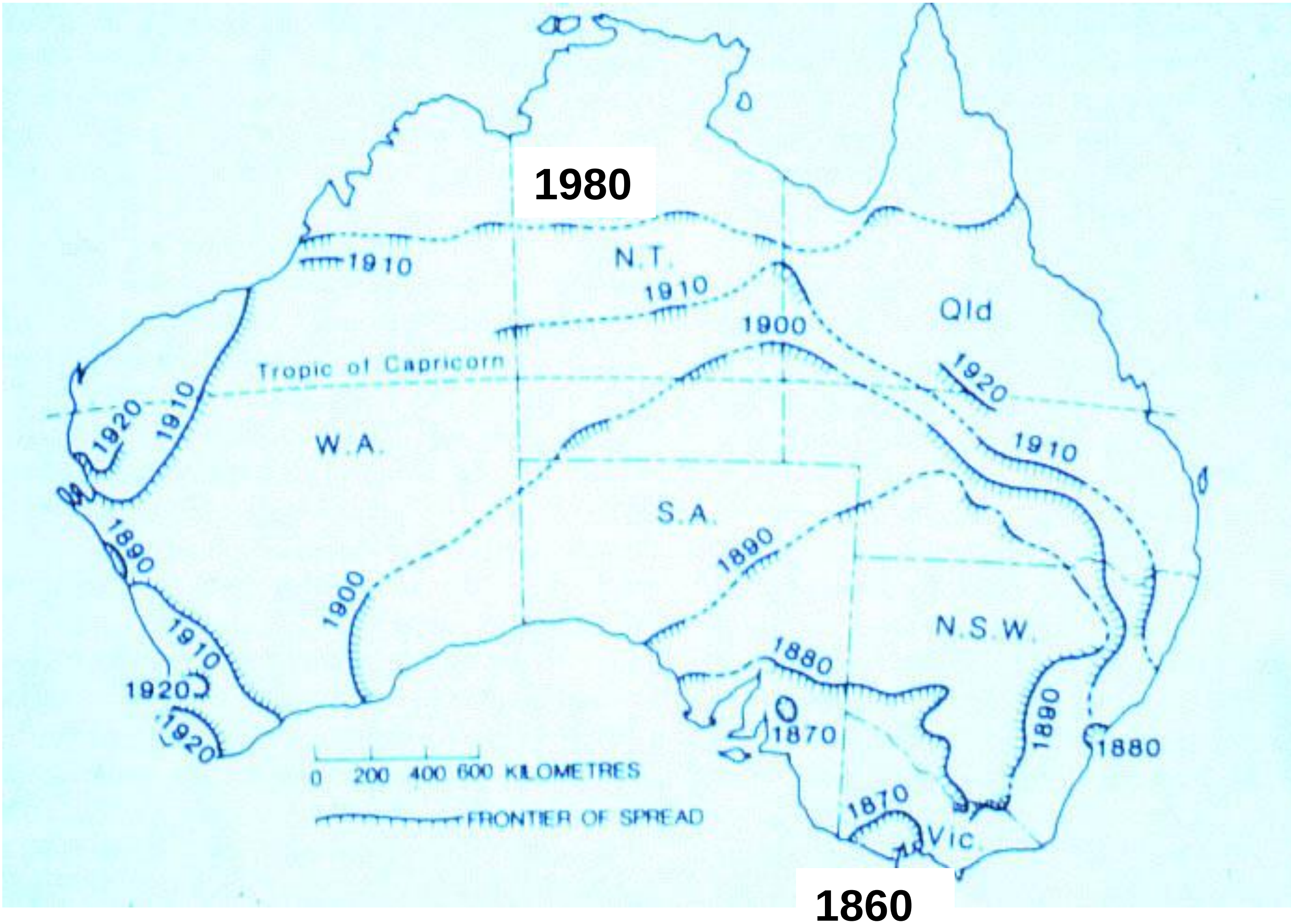
Old rabbit disease in south america

1859 introduction of rabbits in Australia

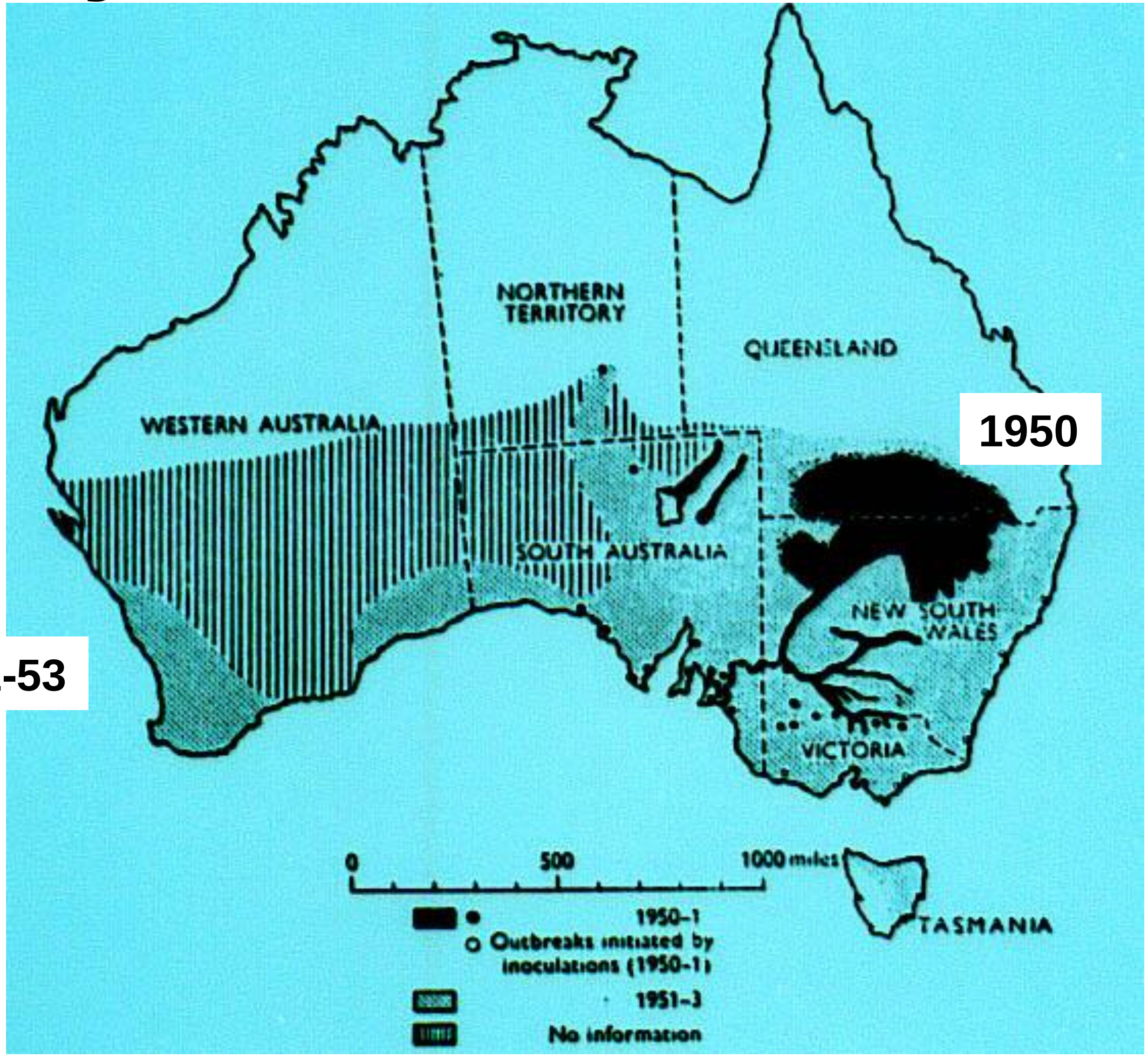
1950 introduction of myxomatosis in Australia

1952 introduction in France and Europe

Rabbit invasion



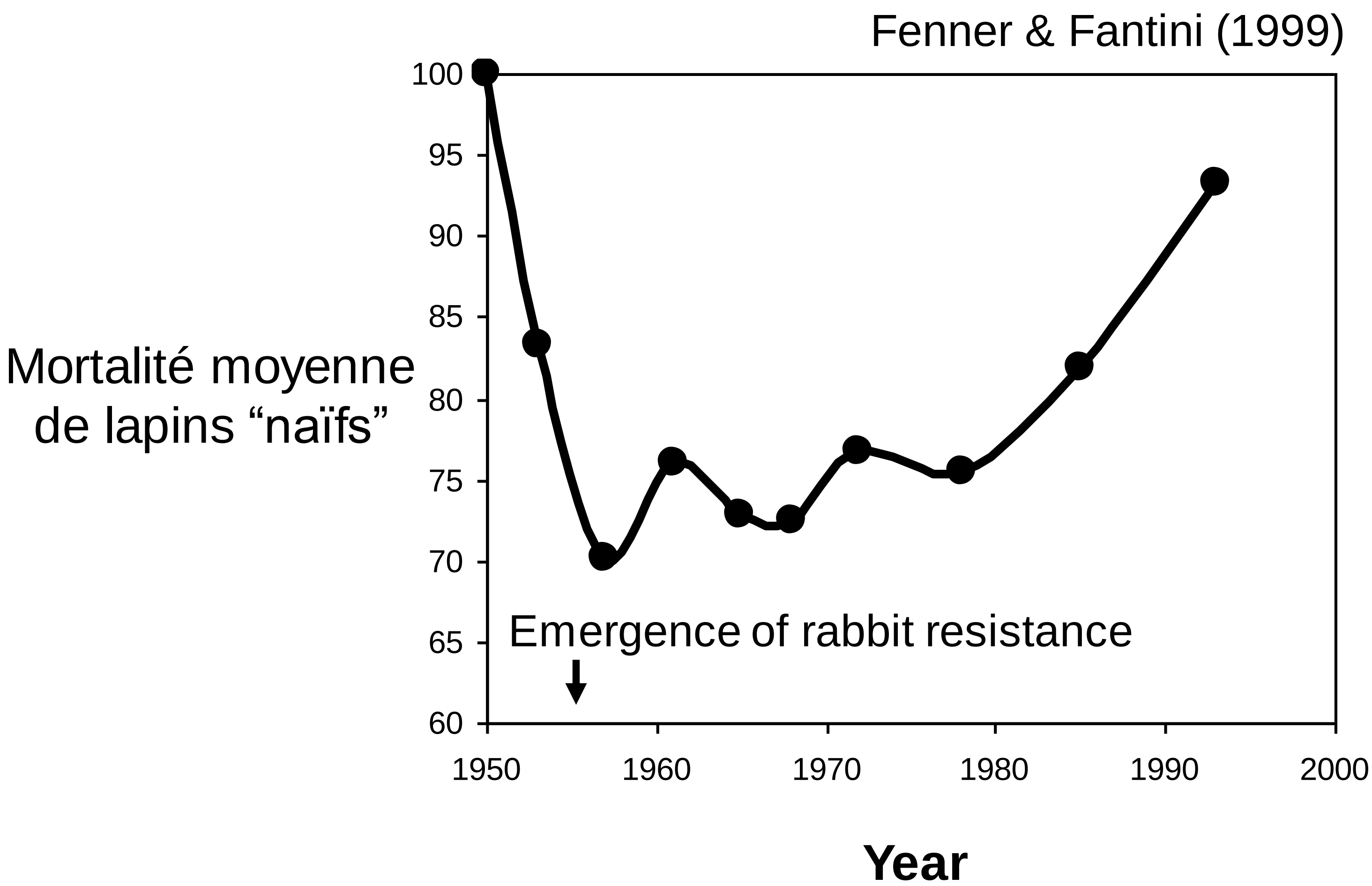
Myxomatosis invasion



1950

1951-53

Myxoma evolution



Smallpox (variole)

Poxviridae virus (DNA virus, ~200kb)

Direct life cycle (only human-human transmission)

Pathology :

Variable (~30% mortality case for *Variola major*)
Depends on both the virus type and its host

History :

Old human disease (at least 3000 years old)

Major role in human history (new world colonization)

1796: Vaccination

1980: Eradication

Vaccination:
an empirical science

1700: reports reach the Royal Society (England) about a Chinese procedure (variolation) in which dried matter from smallpox lesions is soaked into a moistened cotton swab and inserted into the nostrils of persons who had not had the disease and that this creates resistance to the disease

1798: Edward Jenner demonstrates vaccination with cowpox

1860: Louis Pasteur's germ theory

1880: Virulence attenuation (Pasteur)

1880-85: Attenuated vaccines against anthrax, rabies… (Pasteur)

1967: WHO eradication campain of smallpox

1980: smallpox is officially eradicated…(stocks in US and Russian labs)

Now: Development of new vaccines (HIV, Malaria, Flu…)

Ethical constraints limit progress but increase safety

Perfect Vaccines

Edward Jenner, 1796

conclusion

- **Epidemiology:**

  - both host and parasite density can change

  - human interventions can affect epidemiology (vaccination and eradication)

- **Pathology:**

  - depends on both the parasite and the host

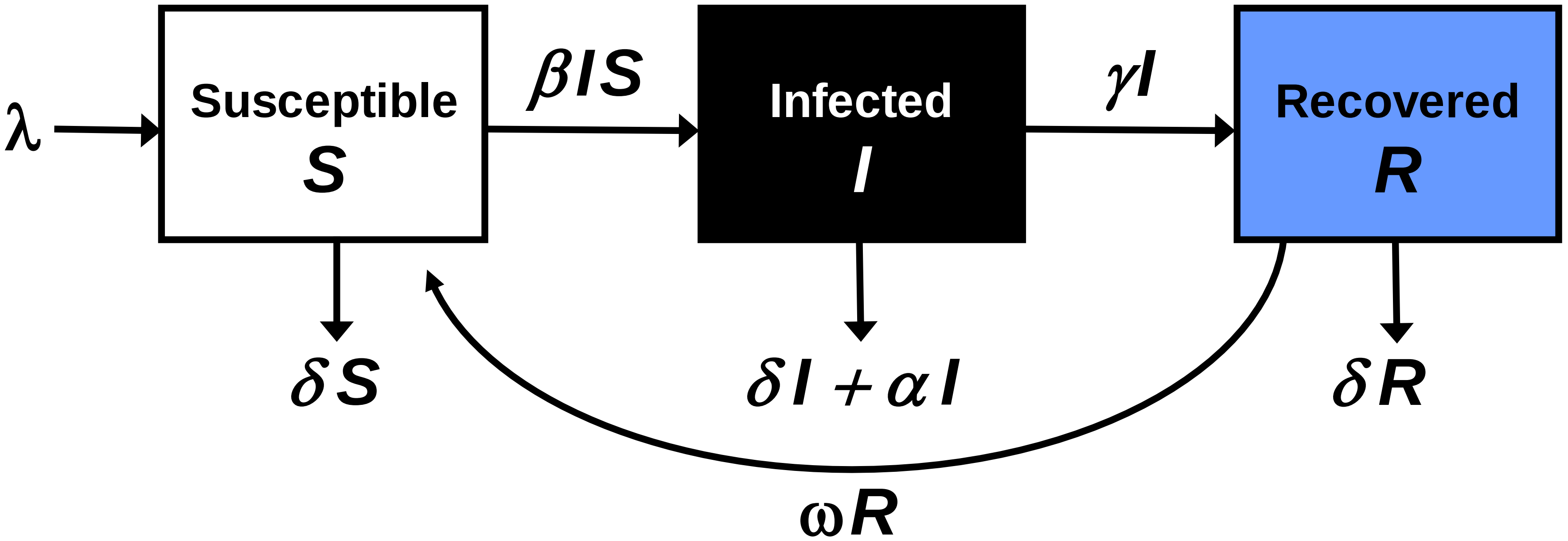
- **Evolution:**

  - both the parasite and its host can evolve

  - human intervention may affect evolution (virulence management)

Epidemiological models

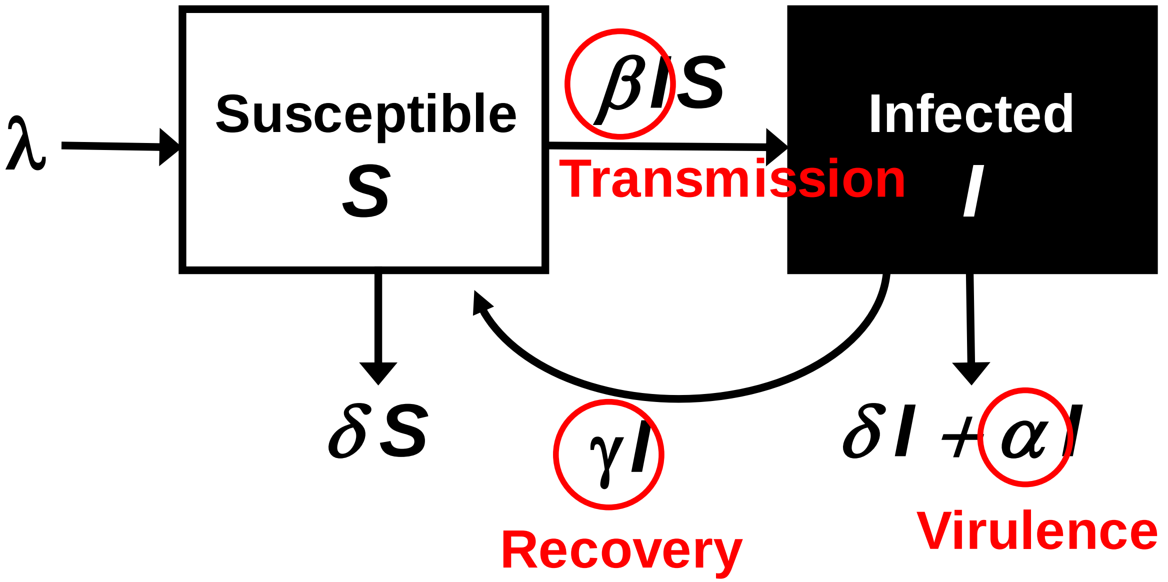
SIR



Childhood diseases
(measles, chickenpox, …)

Epidemiological models

SIS



SI epidemiological model

SIR

$$\frac{dS}{dt} = \lambda - \delta S - \beta IS + \omega R$$

$$\frac{dI}{dt} = \beta IS - (\delta + \alpha)I - \gamma I$$

$$\frac{dR}{dt} = \gamma I - \delta I - \omega R$$

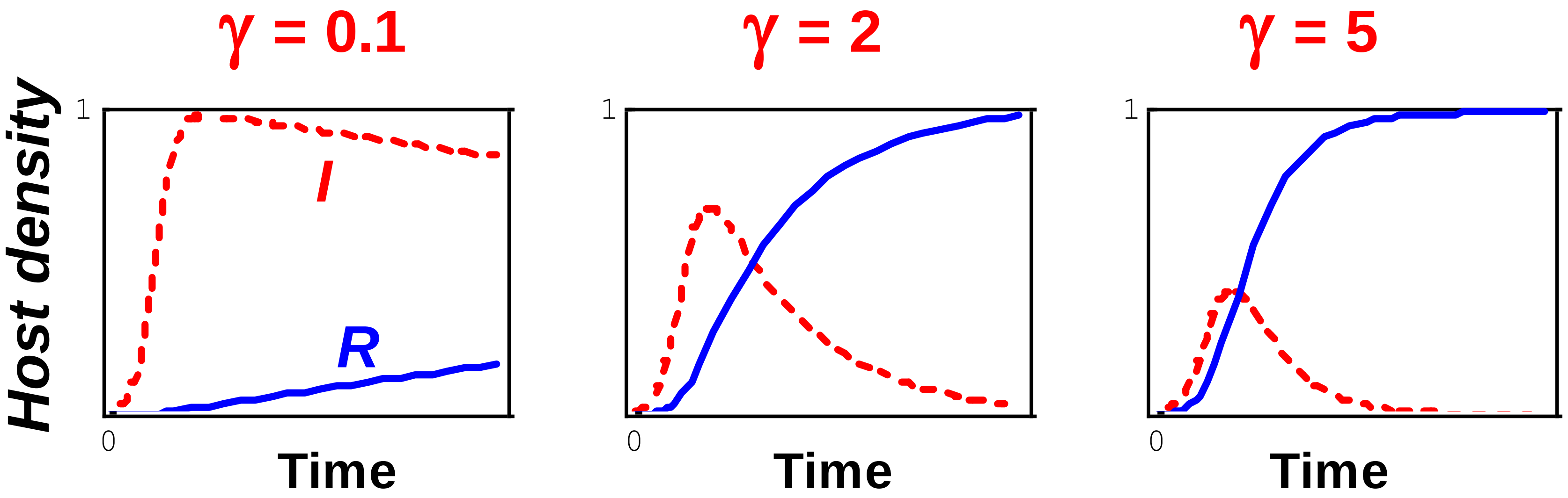
SIS

$$\frac{dS}{dt} = \lambda - \delta S - \beta IS + \gamma I$$

$$\frac{dI}{dt} = \beta IS - (\delta + \alpha)I - \gamma I$$

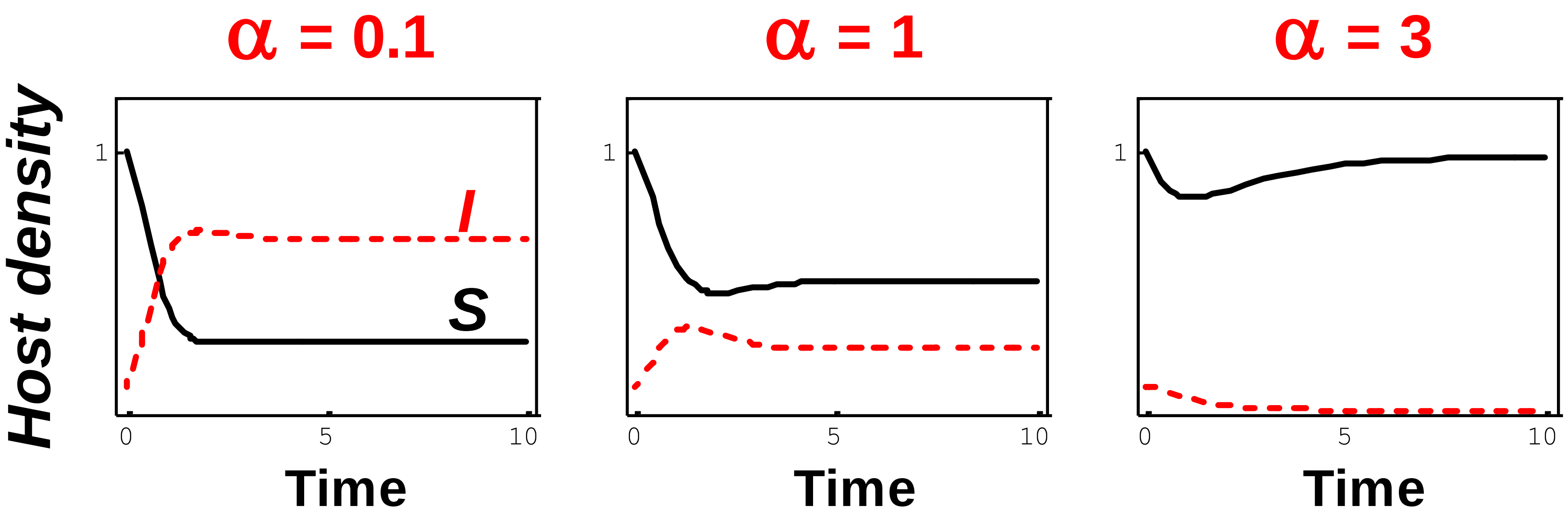
Simulations: SIR

$$\beta = 20, \lambda = 0, \alpha = 0, \delta = 0$$



Simulations: SIS

$$\beta = 4, \lambda = 1, \gamma = 0, \delta = 1$$



Equilibria

$$\frac{dS}{dt} = 0$$

$$\frac{dI}{dt} = 0$$

$$\begin{cases} S_0 = \lambda/\delta \\ I = 0 \end{cases}$$

$$\begin{cases} S_e = (\delta + \alpha + \gamma)/\beta \\ I_e = \dfrac{\lambda - \delta(\delta + \alpha + \gamma)/\beta}{\delta + \alpha} \end{cases}$$

Stability analysis of *S**, *I**

- First equilibrium: $S_0 = \lambda/\delta, \tilde{I} = \varepsilon$

$$\frac{dS}{dt} = \lambda - \delta S_0 - \beta \tilde{I} S_0 + \gamma \tilde{I}$$
$$= 0 - \varepsilon\left(\beta S_0 - \gamma\right)$$

$$\frac{dI}{dt} = \beta \tilde{I} S_0 - \left(\delta + \alpha\right)\tilde{I} - \gamma \tilde{I}$$
$$= \tilde{I}\underbrace{\left(\beta S_0 - \left(\delta + \alpha + \gamma\right)\right)}_{r_0}$$

Epidemic if:

$$\longrightarrow \boxed{\frac{\beta S_0}{\delta + \alpha + \gamma} > 1}$$

Stability analysis of *S**, *I**

$$\frac{dS}{dt} = f\left(S, I\right)$$

$$\frac{dI}{dt} = g\left(S, I\right)$$

$$\longrightarrow \mathbf{J} = \left.\begin{pmatrix} \partial f/\partial S & \partial f/\partial I \\ \partial g/\partial S & \partial g/\partial I \end{pmatrix}\right|_{S^*, I^*}$$

Stability if: **T**(**J**)<0 and **D**(**J**)>0

Disease free equilibrium $\{S_0, I_0\}$ unstable **if :** $\dfrac{\beta S_0}{\delta + \alpha + \gamma} > 1$

Endemic equilibrium $\{S_e, I_e\}$ **always** stable.

Interpretation: R_0

R_0 (the basic reproductive ratio) is the expected number of secondary infections due to a single infected host in a susceptible host population:

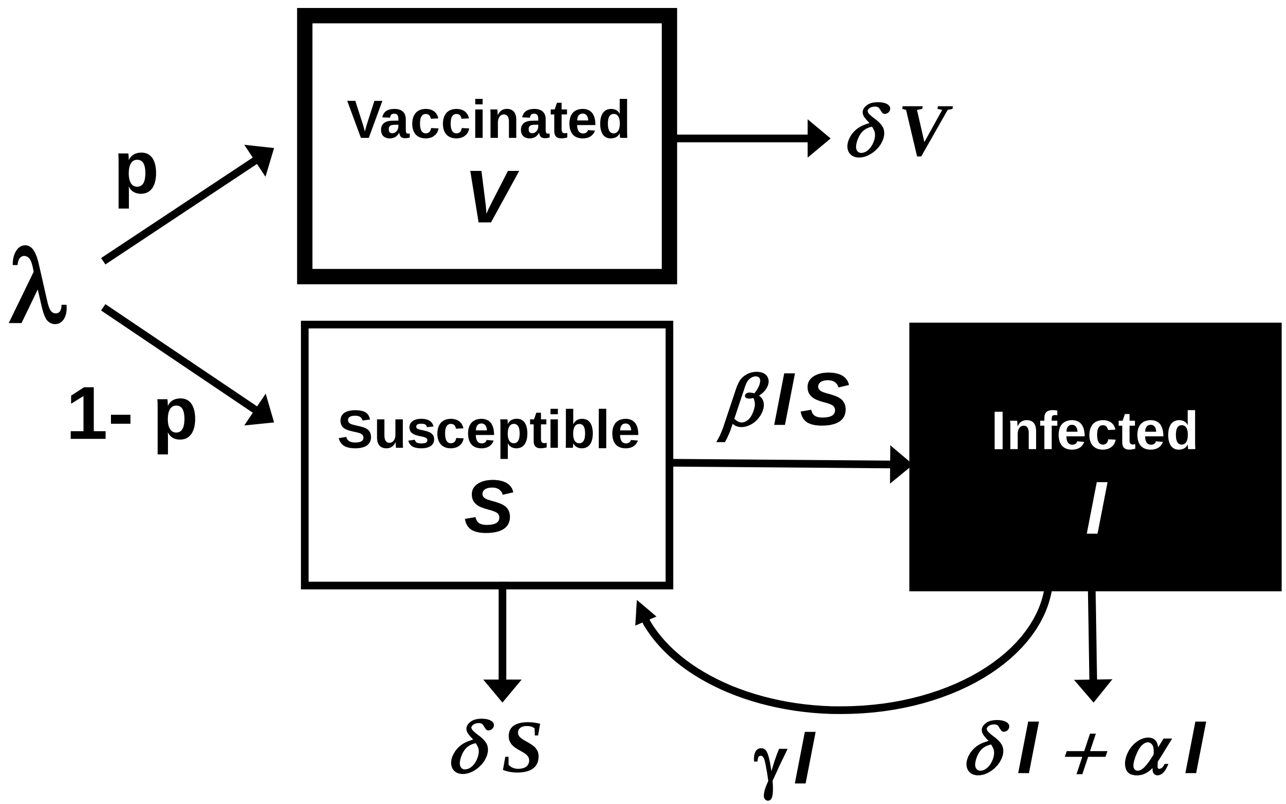
$$R_0 = \int_0^\infty l(a)\beta(a)S_0 \, da$$

Per generation (R_0) and instantaneous (r_0) growth rates:

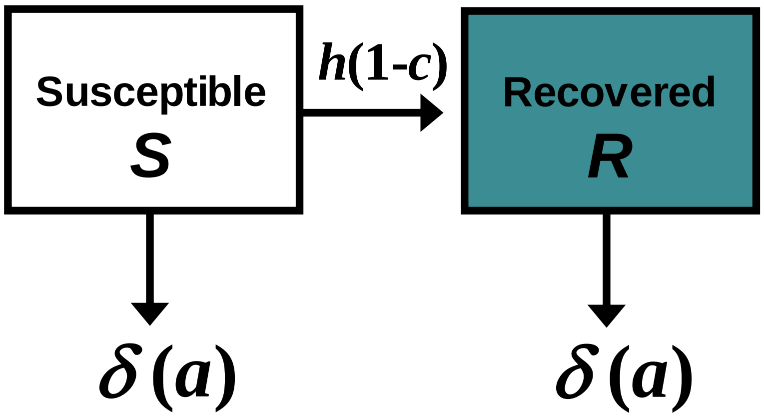
$$\begin{aligned}\frac{dI}{dt} &= \beta I S_0 - (\delta + \alpha + \gamma) I \\ &= (\beta S_0 - (\delta + \alpha + \gamma)) I \\ &= r_0 I\end{aligned}$$

$$\longrightarrow \quad R_0 > 1 \Leftrightarrow r_0 > 0$$

Modelling vaccination

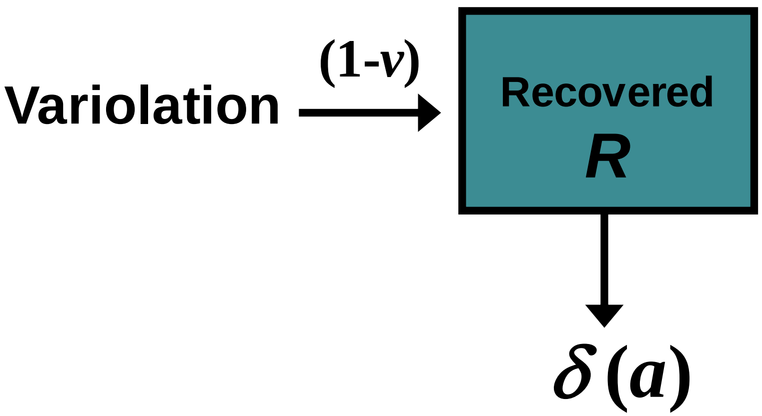


Bernoulli's model (1760)



Expected lifespan without variolation= 26.5 years

Bernoulli's model (1760)



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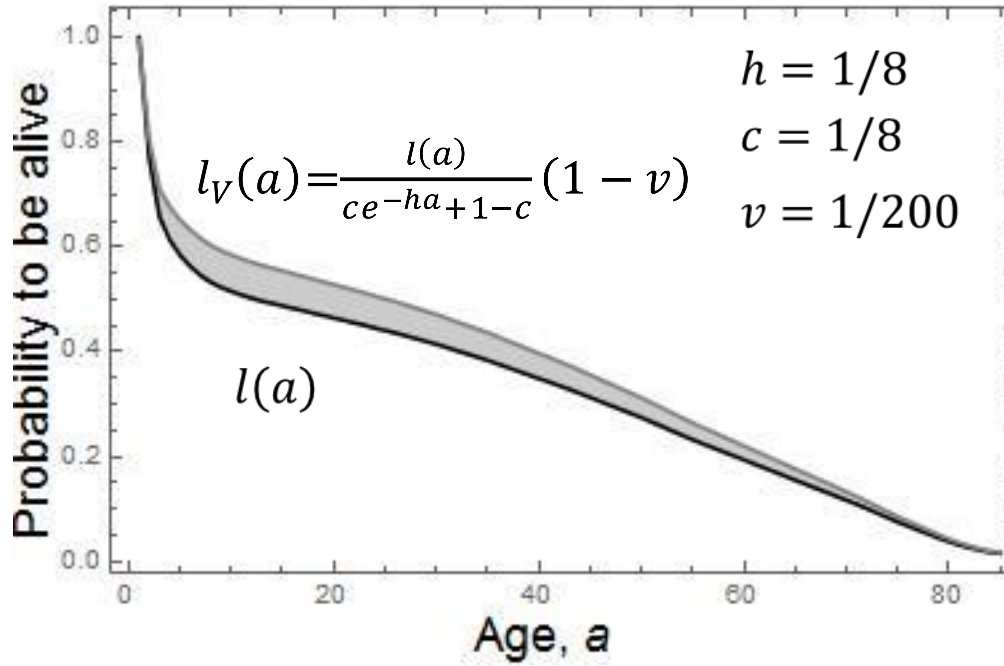
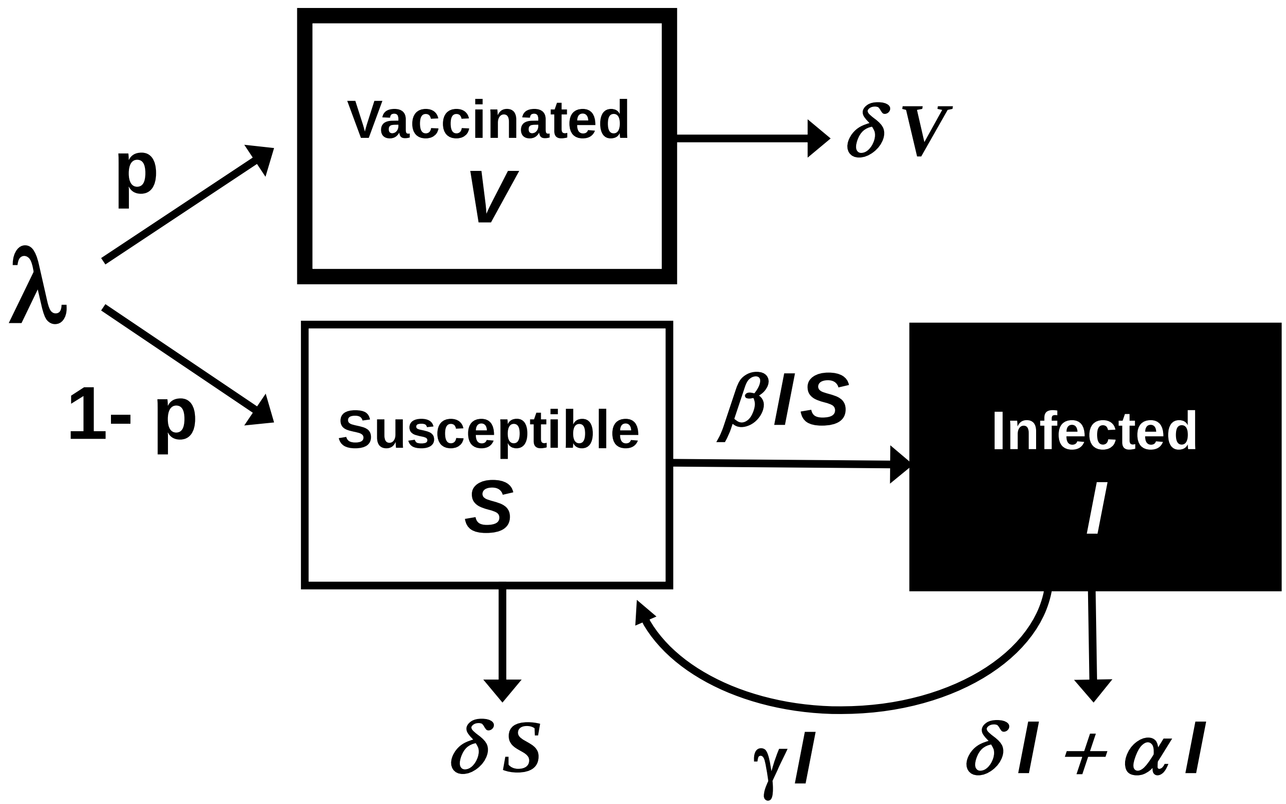


Expected lifespan without variolation= 26.5 years

Expected lifespan with variolation = 29.5 years

Modelling vaccination



Vaccination threshold

Before vaccination:

$$R_0 = \frac{\beta S_0}{\delta + \alpha + \gamma}$$

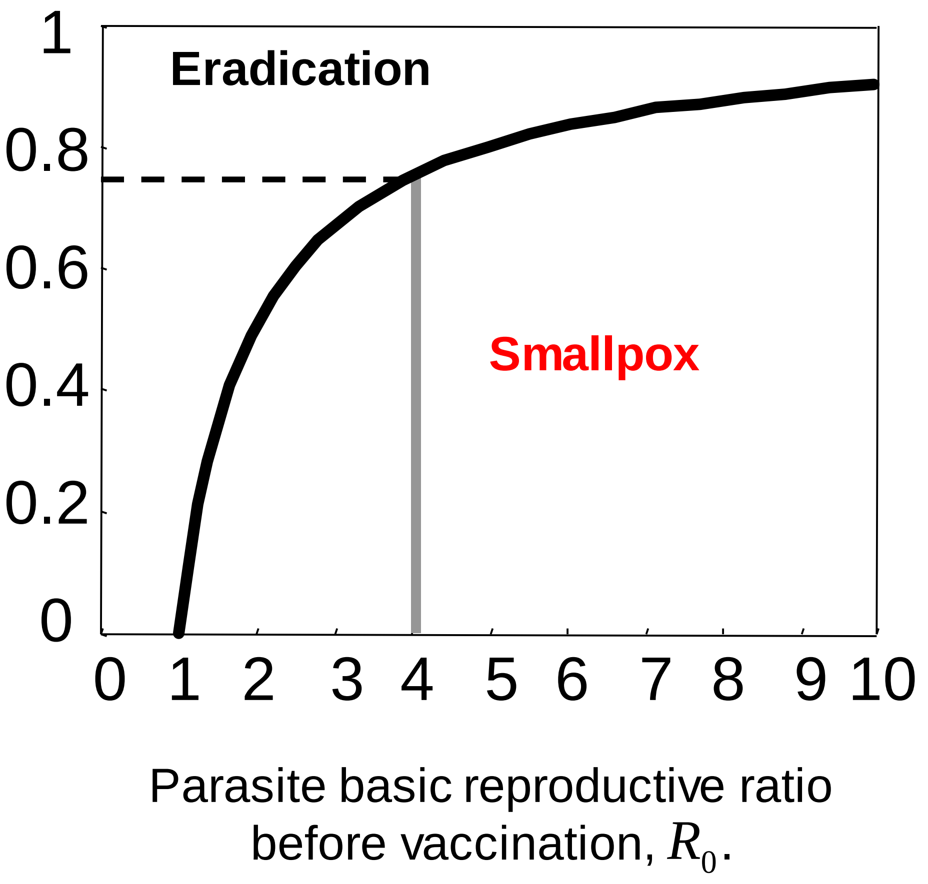
After vaccination:

$$R_0^V = \frac{\beta}{\delta + \alpha + \gamma} S_0 (1 - p)$$

Vaccination threshold ?: $p_c = 1 - 1/R_0$

Vaccination threshold

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



A guidebook for the derivation of R_0

1- Draw pathogen life cycle as a set of compartments

2- Write down epidemiological dynamics as a system of ODEs

3- What is the disease-free equilibrium: S_0?

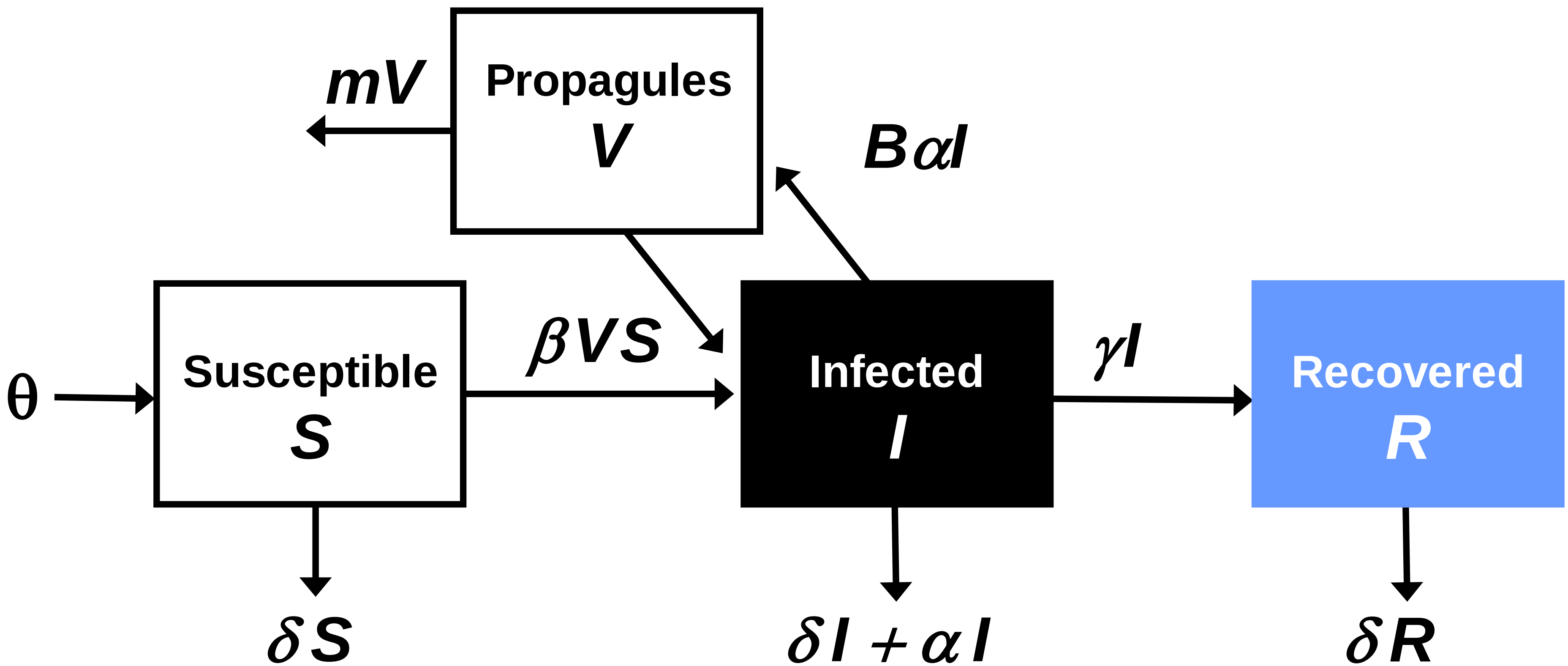
4- Is it possible to reduce dynamics in one dimention with a separation of time scale?

5- Matrix formulation:

- derivarion of instantaneous growth rate r_0
- derivation of per-generation growth rate R_0

A guidebook for the derivation of R_0

1- Draw pathogen life cycle as a set of compartments



A guidebook for the derivation of R_0

2- Write down epidemiological dynamics as a system of ODEs

$$\dot{S} = \theta - \delta S - \beta SV$$
$$\dot{I} = \beta VS - (\delta + \alpha + \gamma)I$$
$$\dot{V} = B\alpha I - mV - \beta SV$$
$$\dot{R} = \gamma I - \delta R$$

A guidebook for the derivation of R_0

2- Write down epidemiological dynamics as a system of ODEs

$$\begin{aligned}
\dot{S} &= \theta - \delta S - \beta SV \\
\dot{I} &= \beta VS - (\delta + \alpha + \gamma)I \\
\dot{V} &= B\alpha I - mV - \beta SV \\
\dot{R} &= \gamma I - \delta R
\end{aligned}$$

3- What is the disease-free equilibrium?

$$\dot{S} = 0 \qquad \Rightarrow \qquad S_0 = \frac{\theta}{\delta}$$

A guidebook for the derivation of R_0

4- Is it possible to reduce dynamics in one dimension with a separation of time scale?

$$\dot{V} = 0 \qquad \Rightarrow \qquad \hat{V} = \frac{B\alpha I}{m + \beta S}$$

The separation of time scale simplifies the dynamics:

$$\begin{aligned} \dot{S} &= \theta - \delta S - \beta S V \\ \dot{I} &= \beta \hat{V} S - (\delta + \alpha + \gamma) I \\ \dot{R} &= \gamma I - \delta R \end{aligned} \qquad \Rightarrow \; R_0 = \frac{\beta B \alpha}{(m + \beta S_0)(\delta + \alpha + \gamma)} S_0$$

A guidebook for the derivation of R_0

5- Matrix formulation: derivarion of instantaneous growth rate r_0

$$\dot{\mathbf{X}} = \mathbf{A}\,\mathbf{X}$$

$$\mathbf{T} = \begin{pmatrix} 0 & \beta S_0 \\ B\alpha & 0 \end{pmatrix}$$

$$\mathbf{\Sigma} = \begin{pmatrix} -(\delta + \alpha + \gamma) & 0 \\ 0 & -m - \beta S_0 \end{pmatrix}$$

$$\mathbf{A} = \mathbf{T} + \mathbf{\Sigma} = \begin{pmatrix} -(\delta + \alpha + \gamma) & \beta S_0 \\ B\alpha & -m - \beta S_0 \end{pmatrix}$$

$$r_0 = \frac{\delta + \alpha + \gamma + m + \beta S_0 + \sqrt{(\delta + \alpha + \gamma - m - \beta S_0)^2 + 4\beta S_0 B\alpha}}{2}$$

A guidebook for the derivation of R_0

5- Matrix formulation: derivarion of per-generation growth rate R_0

$$\dot{\mathbf{X}} = \mathbf{A}\,\mathbf{X}$$

$$\mathbf{T} = \begin{pmatrix} 0 & \beta S_0 \\ B\alpha & 0 \end{pmatrix}$$

$$\boldsymbol{\Sigma} = \begin{pmatrix} -(\delta+\alpha+\gamma) & 0 \\ 0 & -m-\beta S_0 \end{pmatrix}$$

$$\mathbf{K} = -\mathbf{T}\boldsymbol{\Sigma}^{-1} = \begin{pmatrix} 0 & \dfrac{\beta S_0}{m+\beta S_0} \\ \dfrac{B\alpha}{\delta+\alpha+\gamma} & 0 \end{pmatrix}$$

$$R_0 = \sqrt{\frac{\beta S_0 B\alpha}{(m+\beta S_0)(\delta+\alpha+\gamma)}}$$

Conclusion

- Compartments models are used to describe many different pathogen life cycles.

- R_0 is an important epidemiological quantity that summarizes the influence of many epidemiological parameters of both the pathogen and its host.

- When there is data, inference can be used to predict epidemiological dynamics.

- But these models assume that the pathogen population is monomorphic…

Definitions

- **R_0 (the basic reproductive ratio)**: expected number of secondary infections due to a single infected host in a virgin host population (i.e., where the parasite is absent)
- **Epidemiology**: study of the dynamics of diseases and other health related issues (e.g., infectious diseases, genetic diseases, pollutants)
- **Virulence**: (1) Induced host mortality *or* (2) ability to infect the host
- **Case mortality**: probability of dying once infected
  $$\chi = \alpha / (\alpha + \gamma)$$
- **Morbidity**: Incidence of disease in a population, including both fatal and nonfatal cases
- **Prevalence**: Proportion of infected hosts. In a SIR model:
  $$I/(S + I + R)$$
- **Force of infection**: Rate at which uninfected hosts become infected
  $$h = \beta I$$
- **Superinfection**: when a secondary infection occurs and when the new parasite strain does not coexist with the resident strain in the host
- **Multiple infection**: when a secondary infection occurs and when the new parasite strain coexists with the resident strain in the host