An introduction to evolutionary epidemiology of infectious diseases

Part 2

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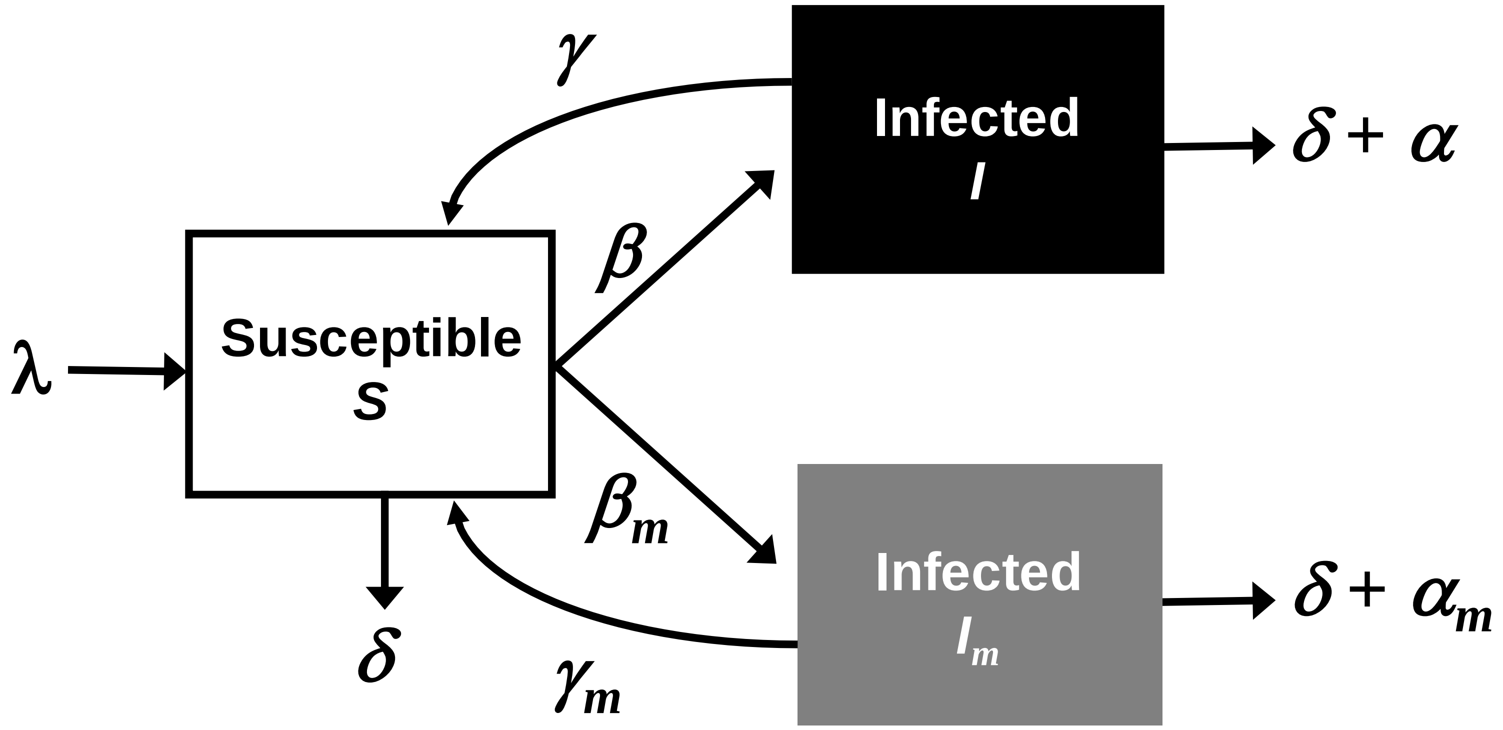
Epidemiology and evolution



Can the mutant parasite population invade?

Dynamics of the mutant

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

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

Dynamics of the mutant

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

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

$$\frac{dI_m}{dt} = \beta_m I_m S - (\delta + \alpha_m + \gamma_m) I_m$$

Dynamics of the mutant

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

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

$$\boxed{\frac{dI_m}{dt} = \beta_m I_m S_e - (\delta + \alpha_m + \gamma_m) I_m}$$

Fitness of the mutant

$$R_m = \frac{\beta_m}{\delta + \alpha_m + \gamma_m} S_e$$

$$r_m = \left(\beta_m S_e - \left(\delta + \alpha_m + \gamma_m\right)\right)$$

Fitness of the resident ?:

$$R = \frac{\beta}{\delta + \alpha + \gamma} S_e = 1$$

$$r = \left(\beta S_e - \left(\delta + \alpha + \gamma\right)\right) = 0$$

The mutant invades if:

$$R_m > R = 1$$

$$r_m > r = 0$$

Evolution maximises per-host transmission factor:

$$\boxed{\frac{\beta_m}{\delta + \alpha_m + \gamma_m}}$$

Maximisation of β_m

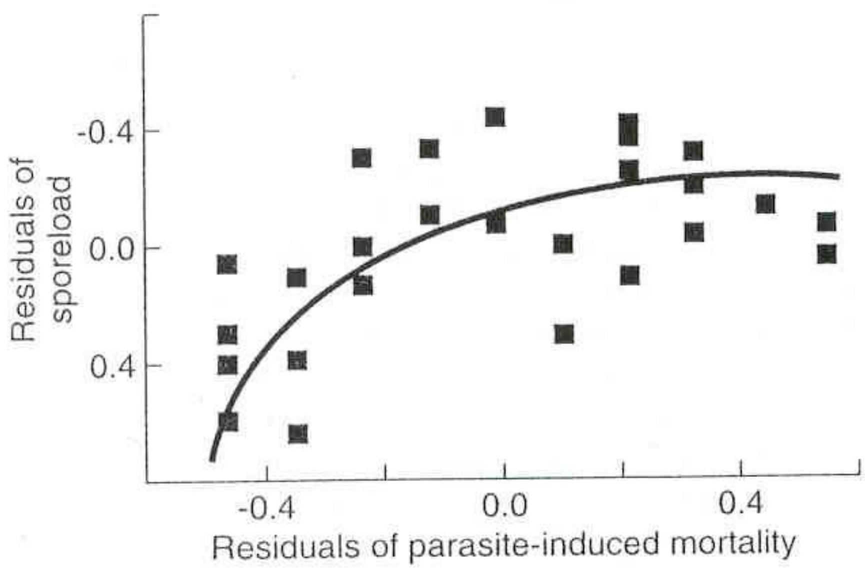
Minimisation of α_m

Minimisation of γ_m

Trade-offs

Between virulence and transmission :

- Within-host density affects transmission
- Within-host density affects virulence



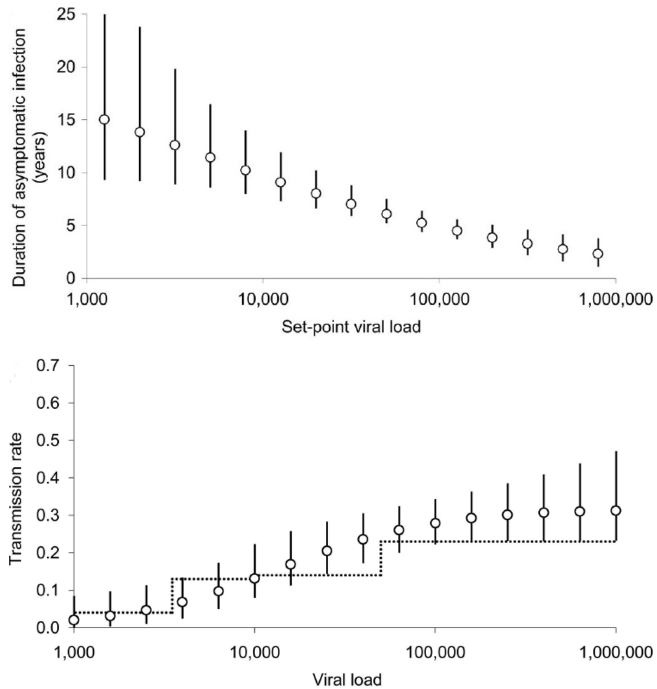
Microsporidia

Ebert & Herre 1996

Trade-offs

Between virulence and transmission :

- Within-host density affects transmission
- Within-host density affects virulence



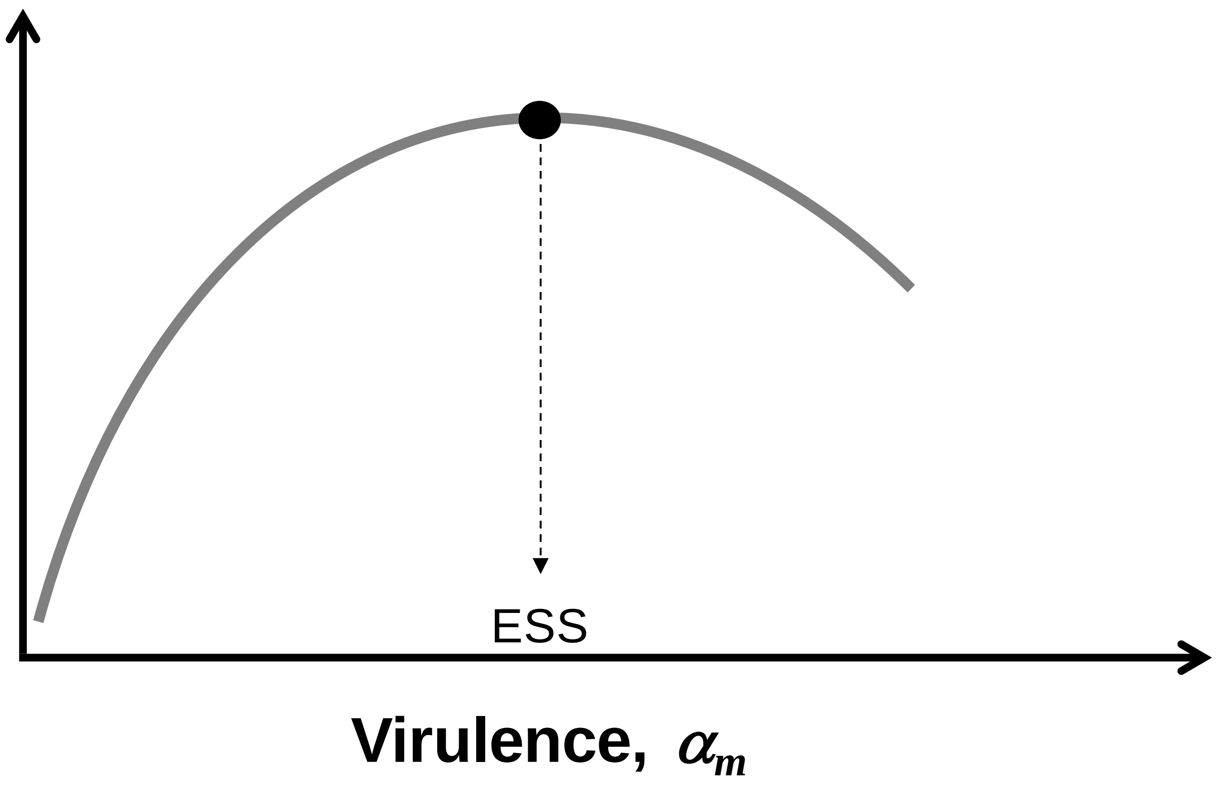
HIV

Fraser et al. 2007

With trade-offs

- Per-host transmission factor:

$$\frac{\beta_m}{\delta + \alpha_m + \gamma_m}$$



With trade-offs

Geometrical derivation of ESS:

$$\left.\frac{dR_m}{d\alpha_m}\right|_{\alpha=ESS} = 0$$

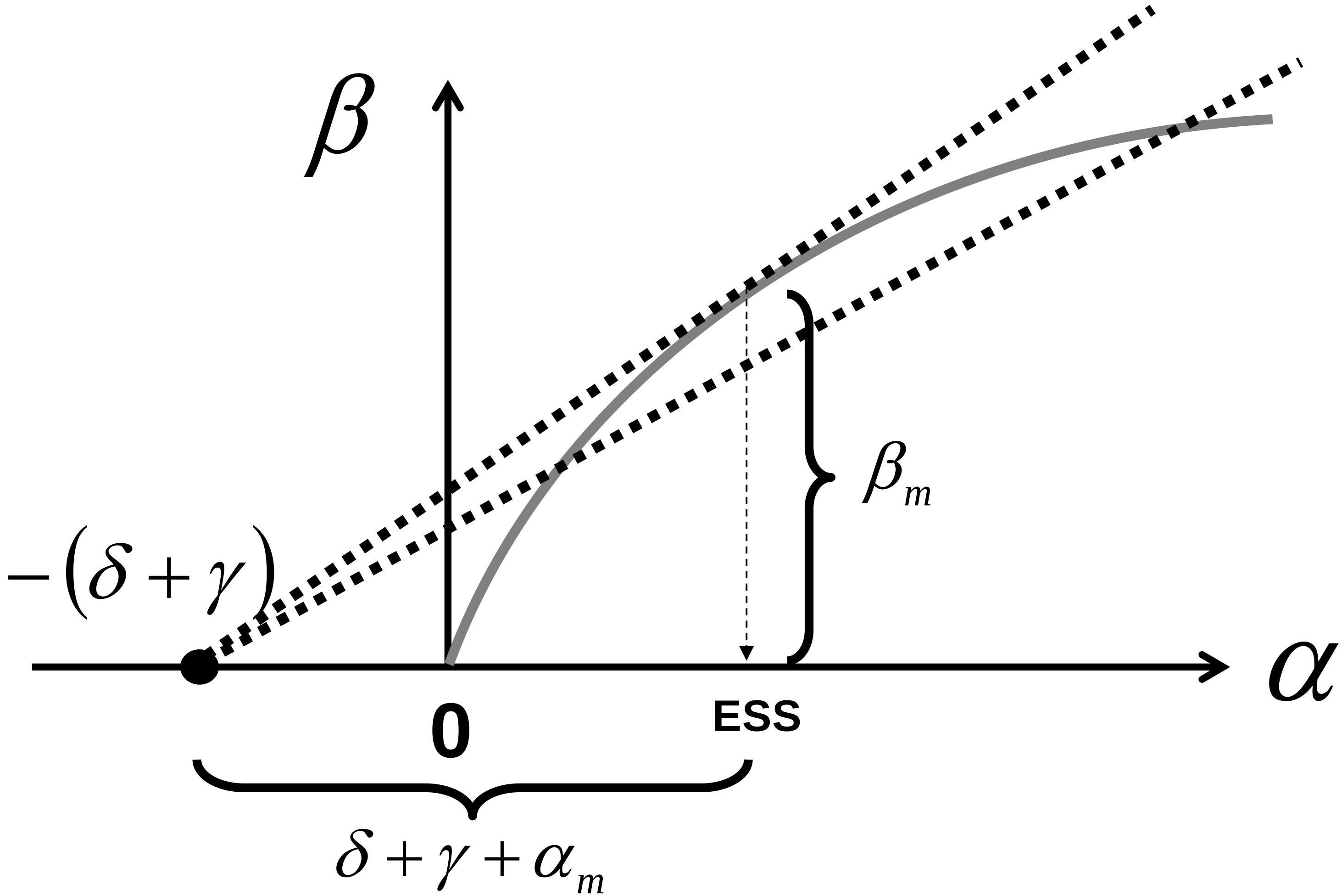
Trade-off:
Virulence
versus
Transmission

$$\frac{d\beta_m}{d\alpha_m} = \frac{\beta_m}{\delta + \gamma + \alpha_m}$$

With trade-offs

$$\frac{d\beta}{d\alpha} = \frac{\beta}{\delta + \gamma + \alpha}$$

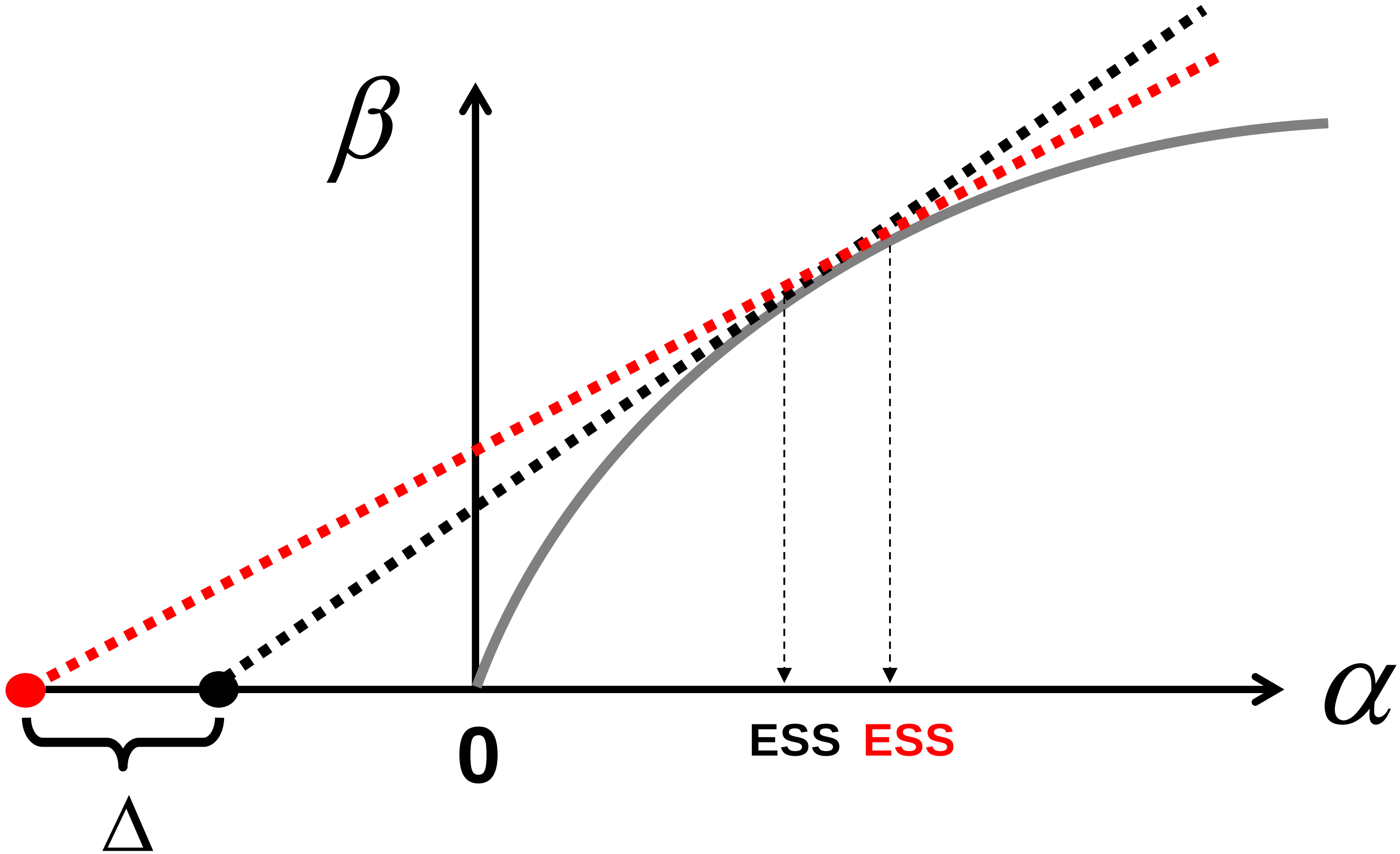
- Transmission *versus* virulence:



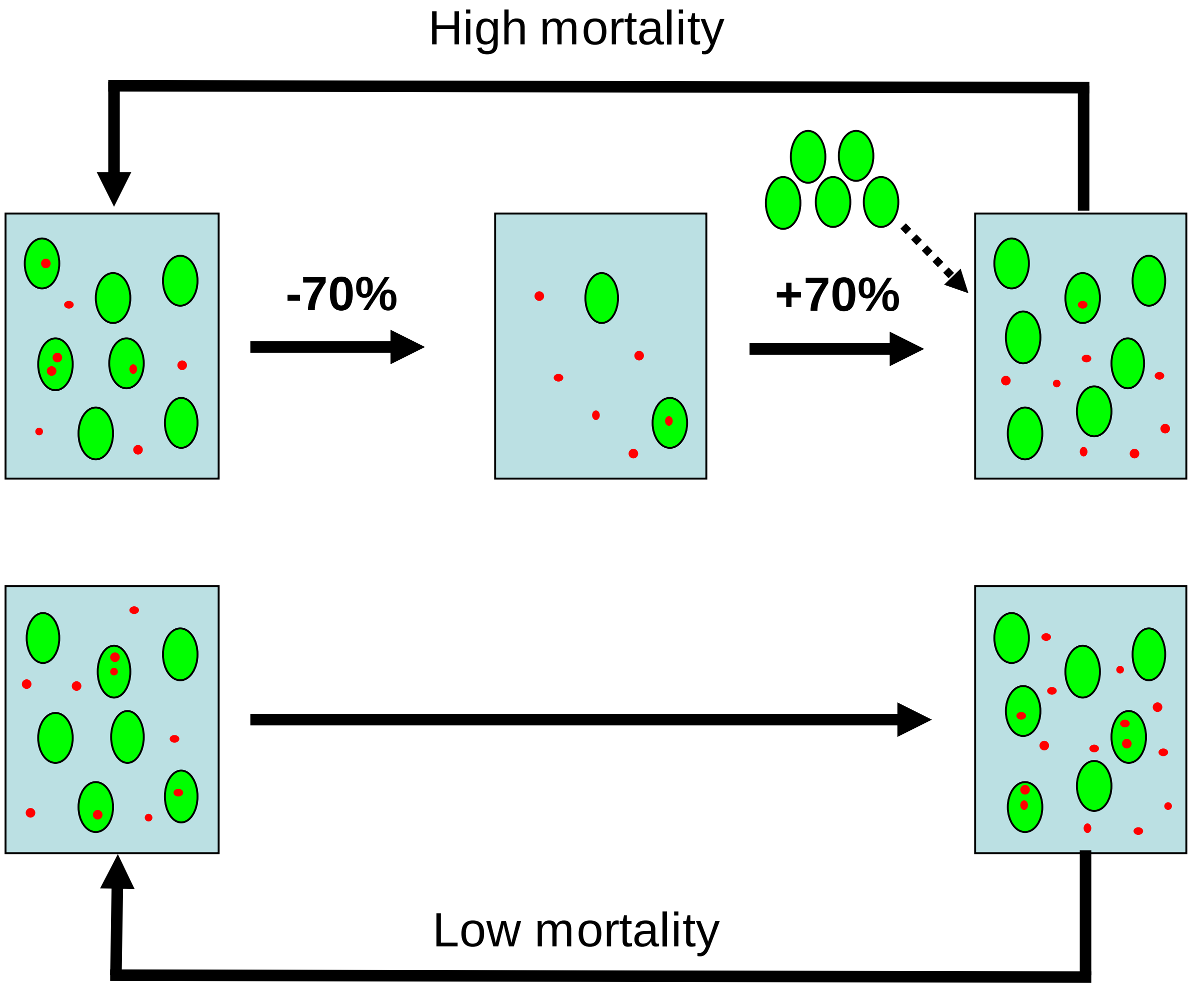
With trade-offs

$$\frac{d\beta}{d\alpha} = \frac{\beta}{\delta + \gamma + \alpha}$$

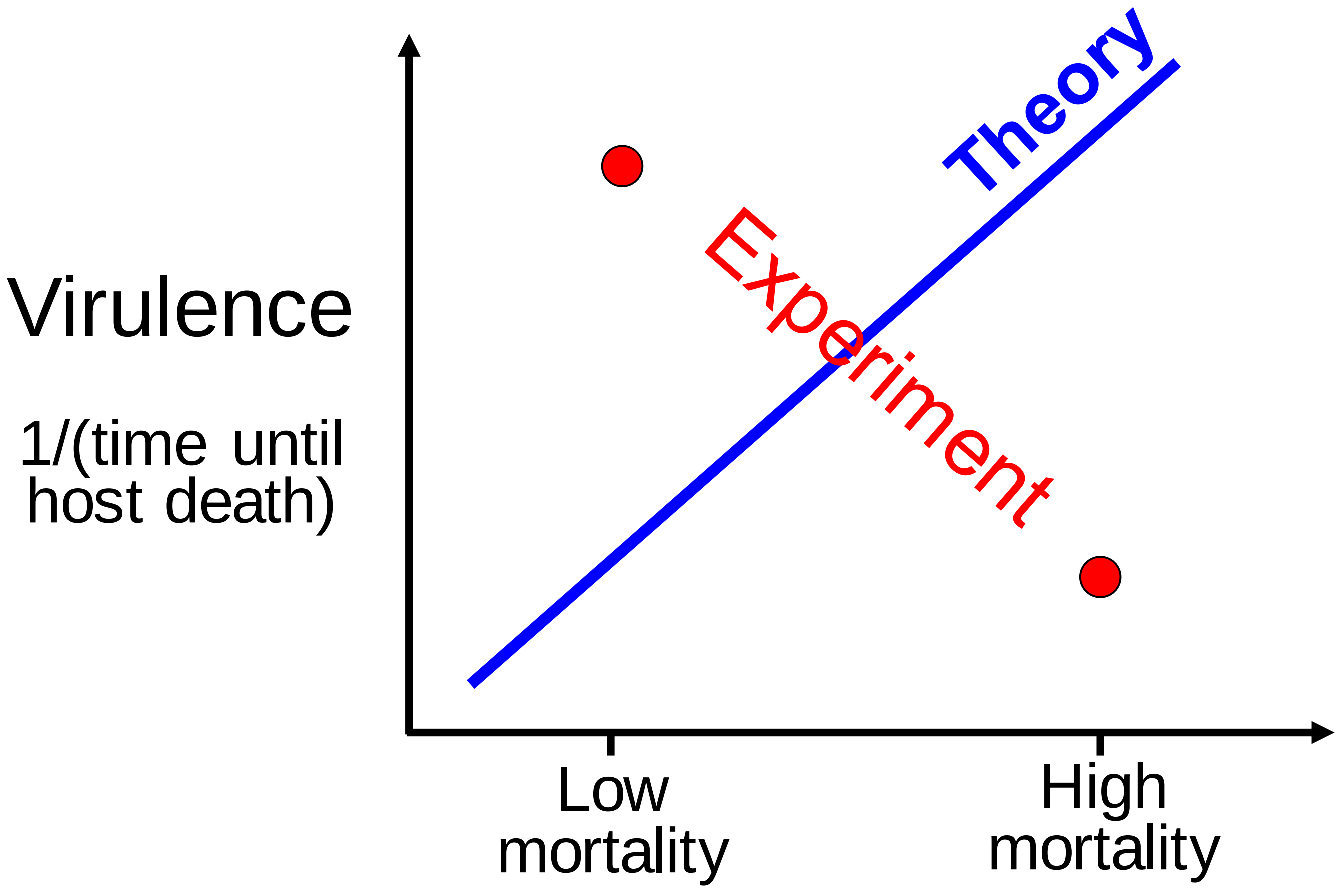
- Transmission *versus* virulence:



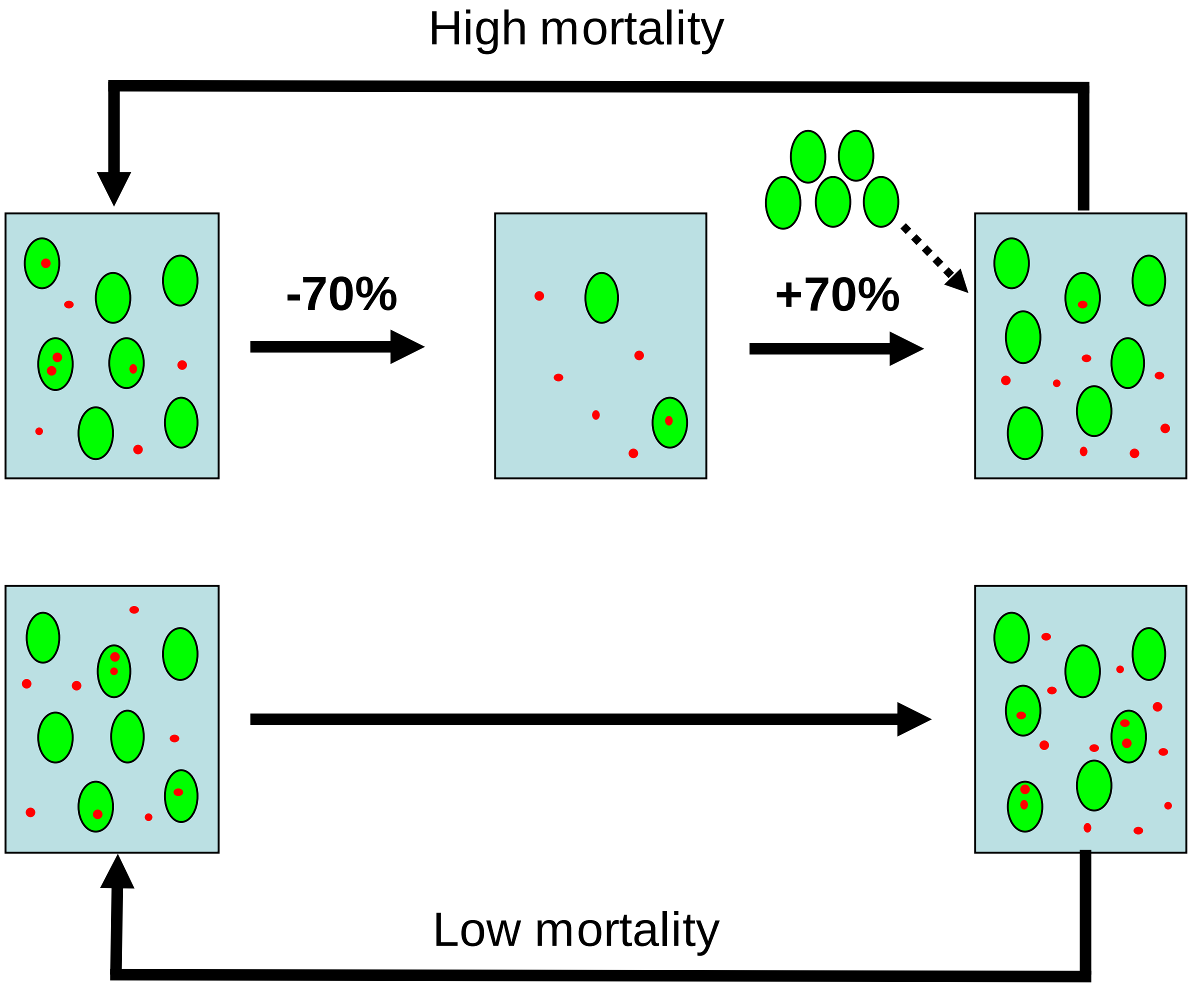
Ebert & Mangin, 1997



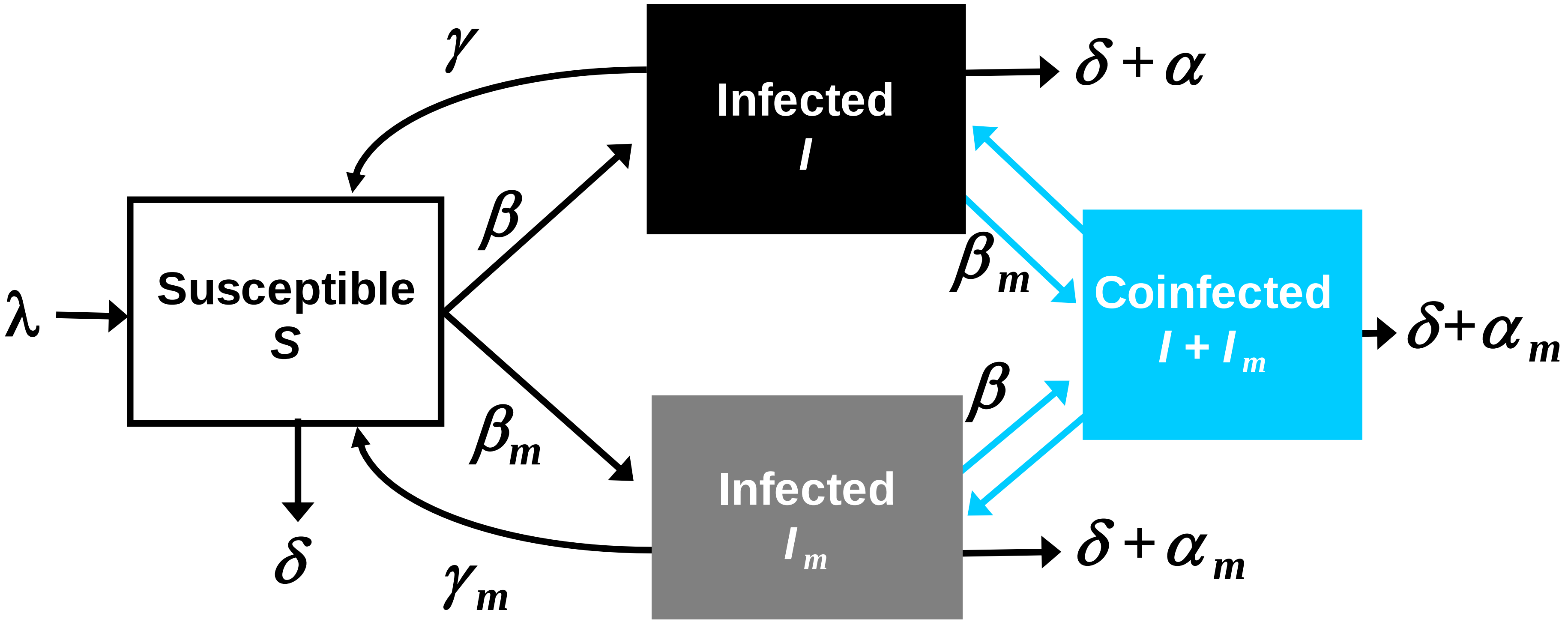
Ebert & Mangin, 1997



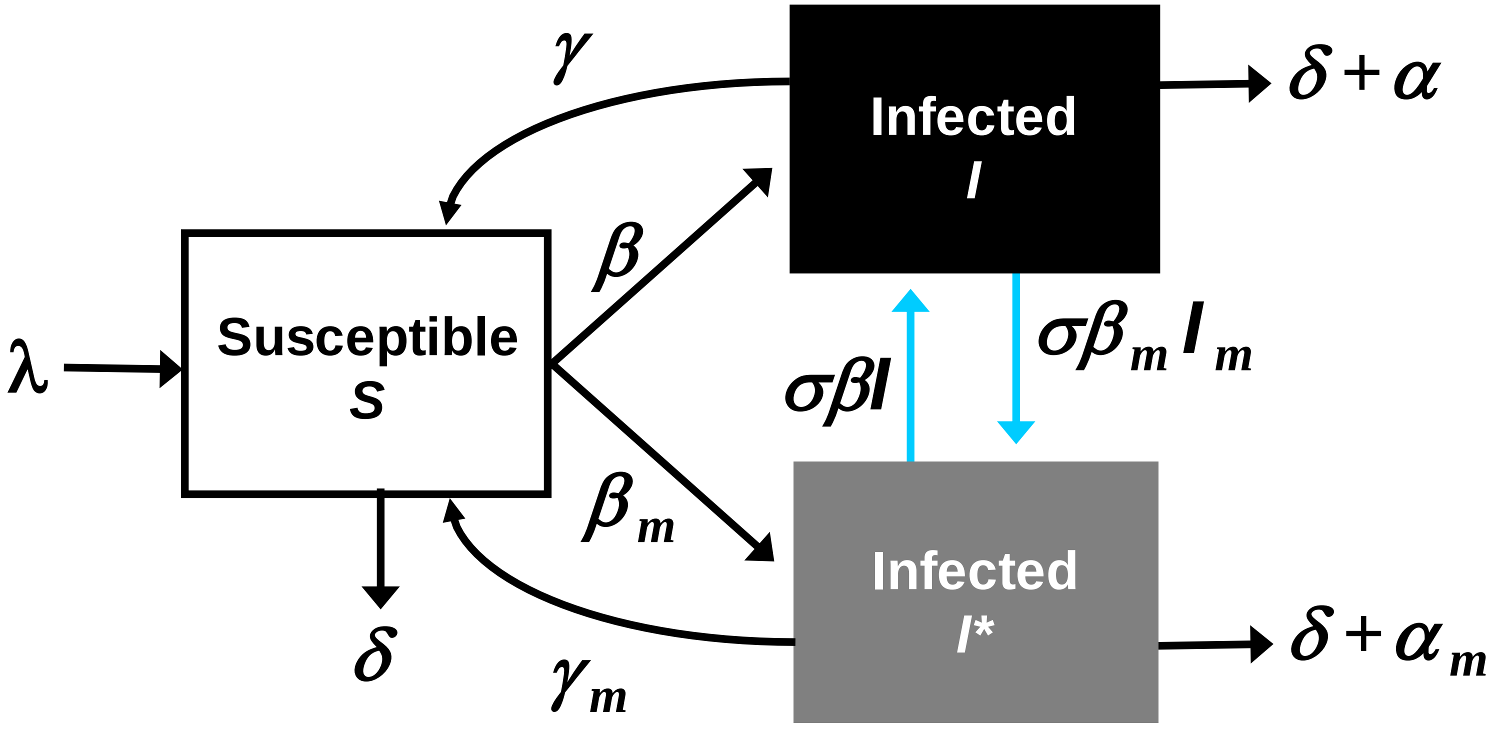
Ebert & Mangin, 1997



Within-host competition
multiple infection



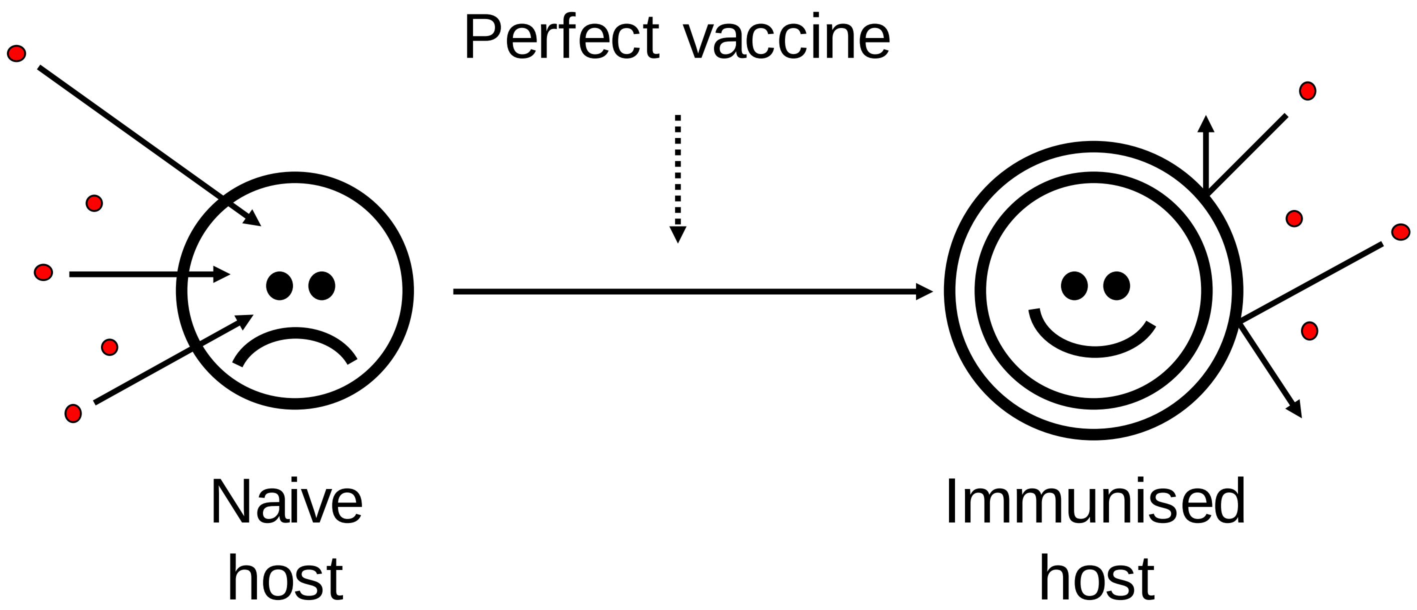
Within-host competition
superinfection



$$R[\alpha_m, \alpha] = \frac{\beta_m}{\delta + \alpha_m + \gamma_m + \sigma\, \beta I}$$

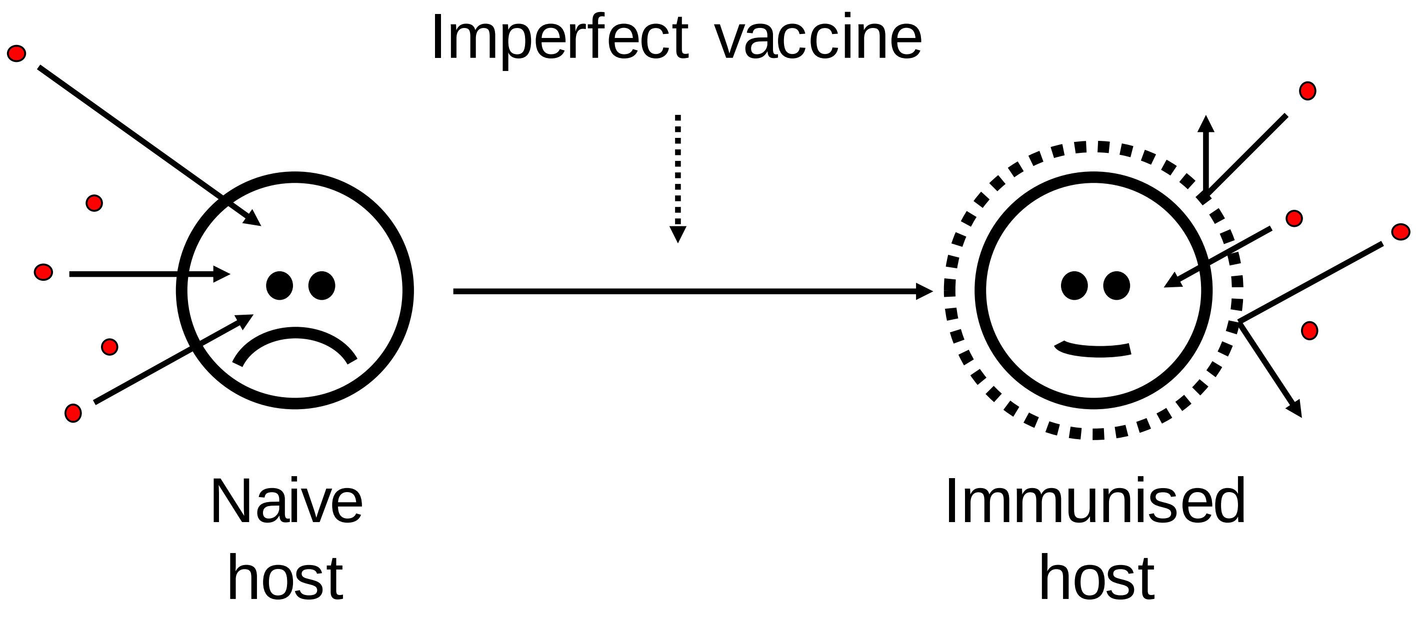
Virulence management

Imperfect vaccination and virulence evolution:



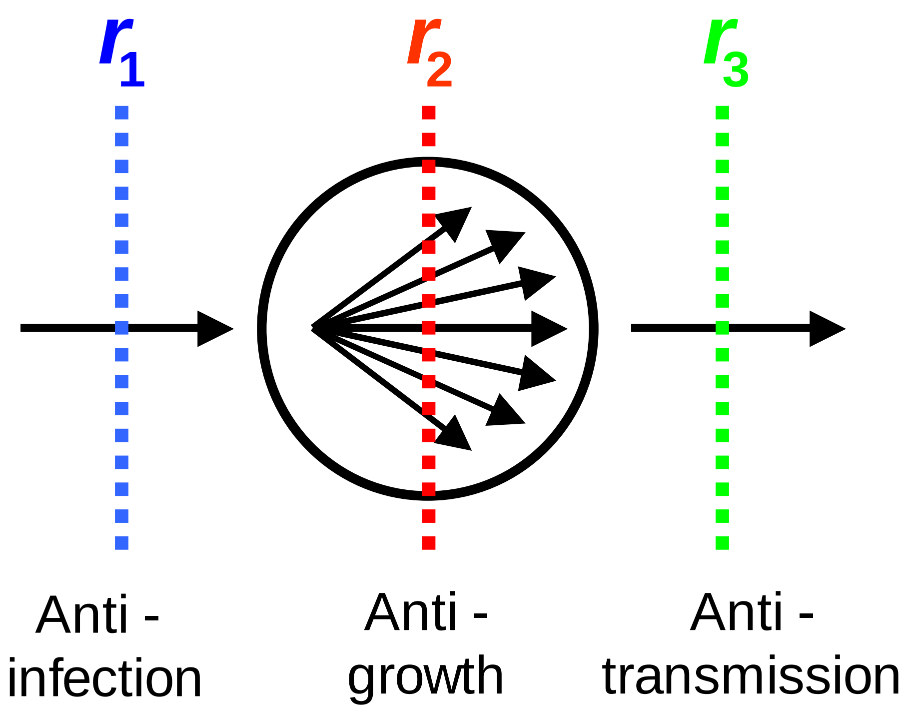
Virulence management

Imperfect vaccination and virulence evolution:



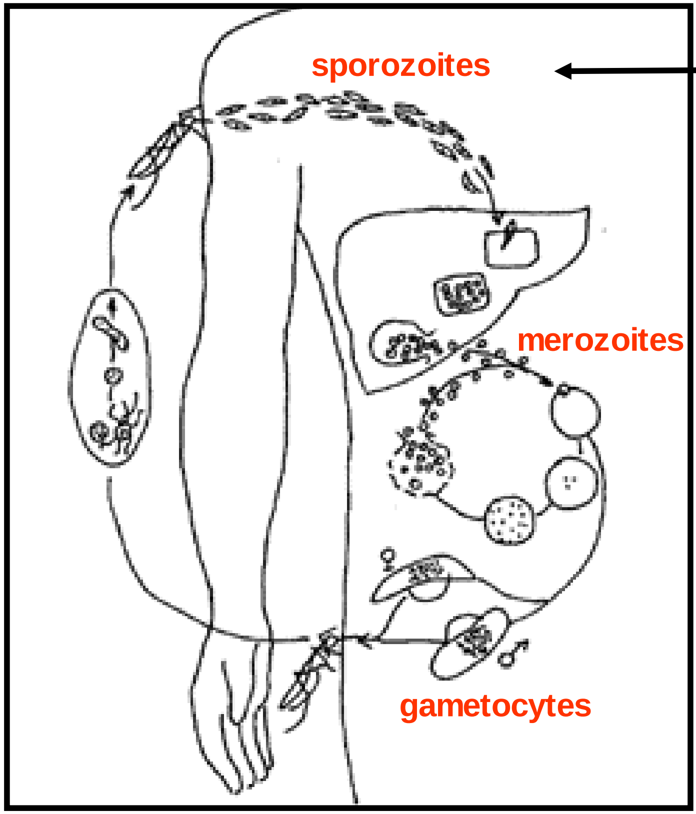
1. Semi-immunity

Host resistance may occur at different stages of the parasite life cycle



Malaria vaccines

Plasmodium falciparum life cycle



Anti-infection : $\boldsymbol{r_1}$.

Anti-growth : $\boldsymbol{r_2}$.

Anti-transmission : $\boldsymbol{r_3}$.

2. Modèle épidémiologique

$$dS/dt = (1-\boldsymbol{p})\lambda - (\delta + h)S$$

$$dI/dt = hS - (\delta + \alpha)I$$

Naive hosts

$$dS'/dt = \boldsymbol{p}\lambda - (\delta + h')S'$$

$$dI'/dt = h'S' - (\delta + \alpha')I'$$

Vaccinated hosts

$$h \equiv \beta I + \beta' I'$$

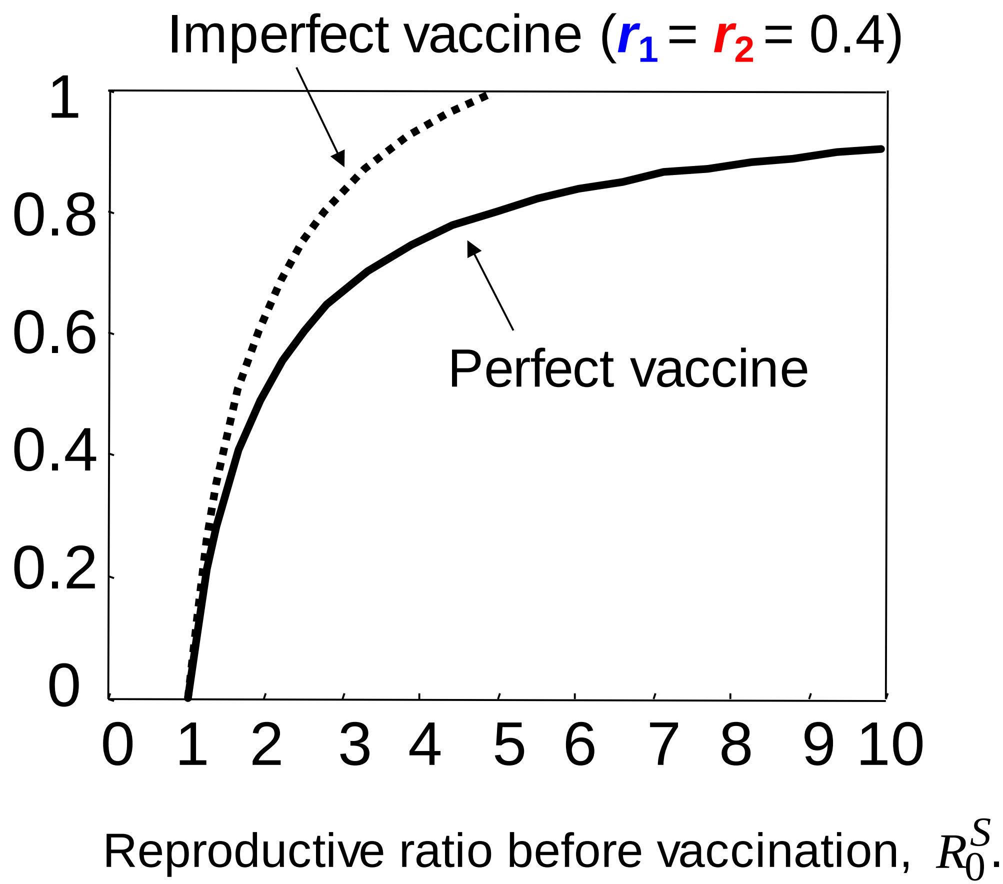
$$\boxed{\beta \equiv \beta[\alpha]} \longleftarrow \text{Trade off}$$

$$h' \equiv (1 - \boldsymbol{r_1})h \qquad \alpha' \equiv (1 - \boldsymbol{r_2})\alpha \qquad \beta' \equiv (1 - \boldsymbol{r_3})\beta[\alpha']$$

Vaccination et éradication

Vaccination threshold:

$$p_c = 1 - \frac{1 - R_0^V}{R_0^S - R_0^V}$$



3. Evolutionary consequences

- ***Antigenic*** **evolution**

- ***Life history*** **evolution:**

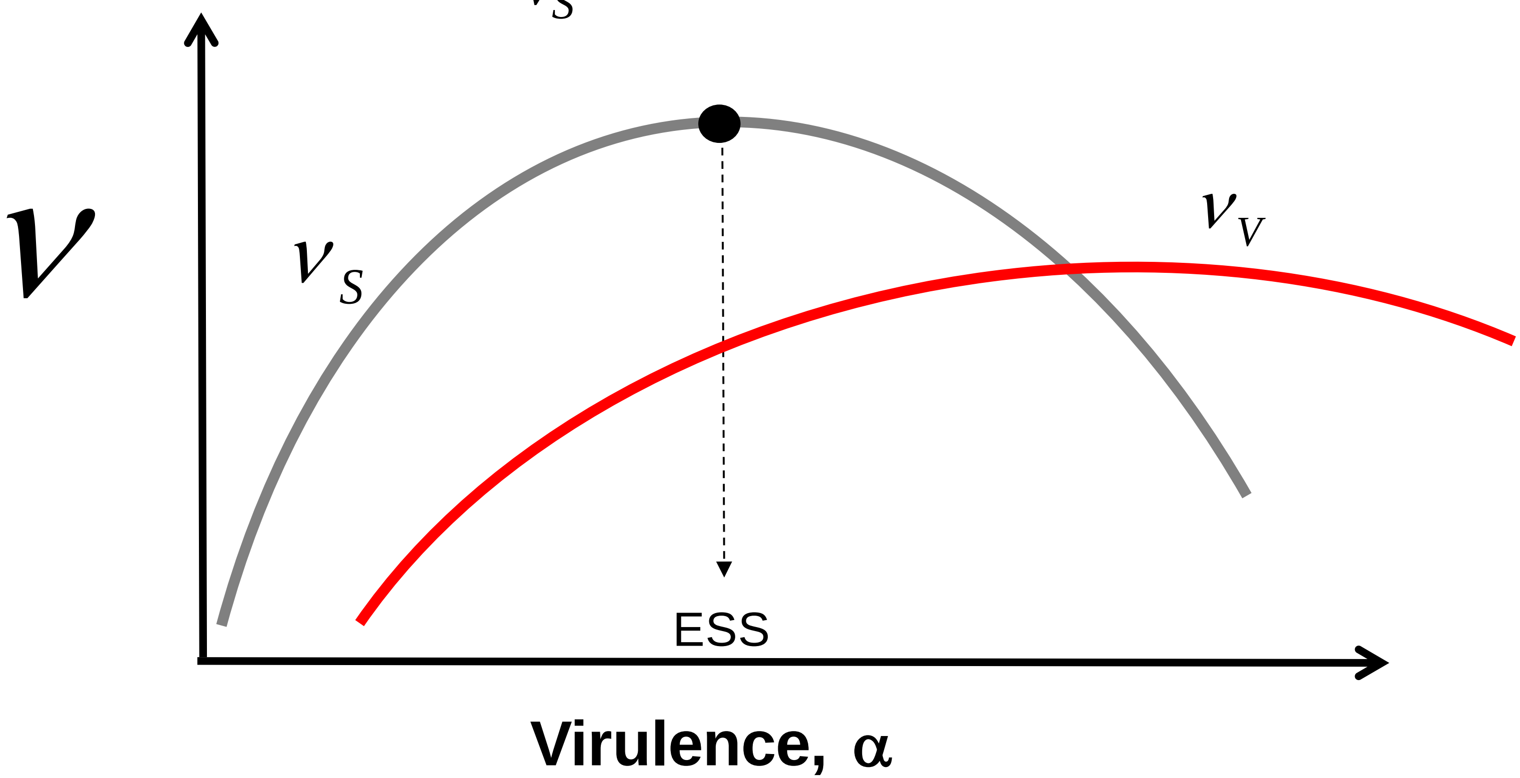
Exploitation strategy

Virulence: α
(on naive hosts)

Transmission: β

ESS virulence in a **heterogeneous** host populatiuon

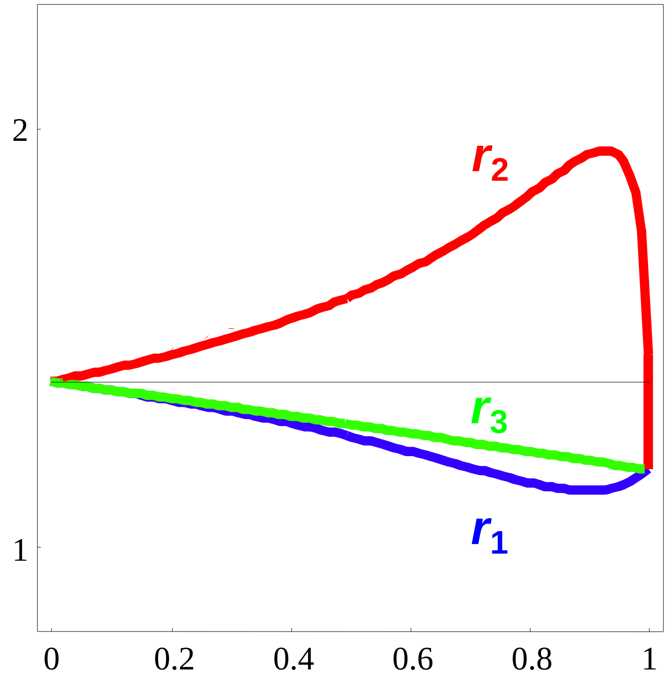
$$R_0[\alpha_m,\alpha] \equiv \frac{\beta[\alpha_m]}{\underbrace{\delta+\alpha_m+\sigma h}_{v_S}} N$$



Results

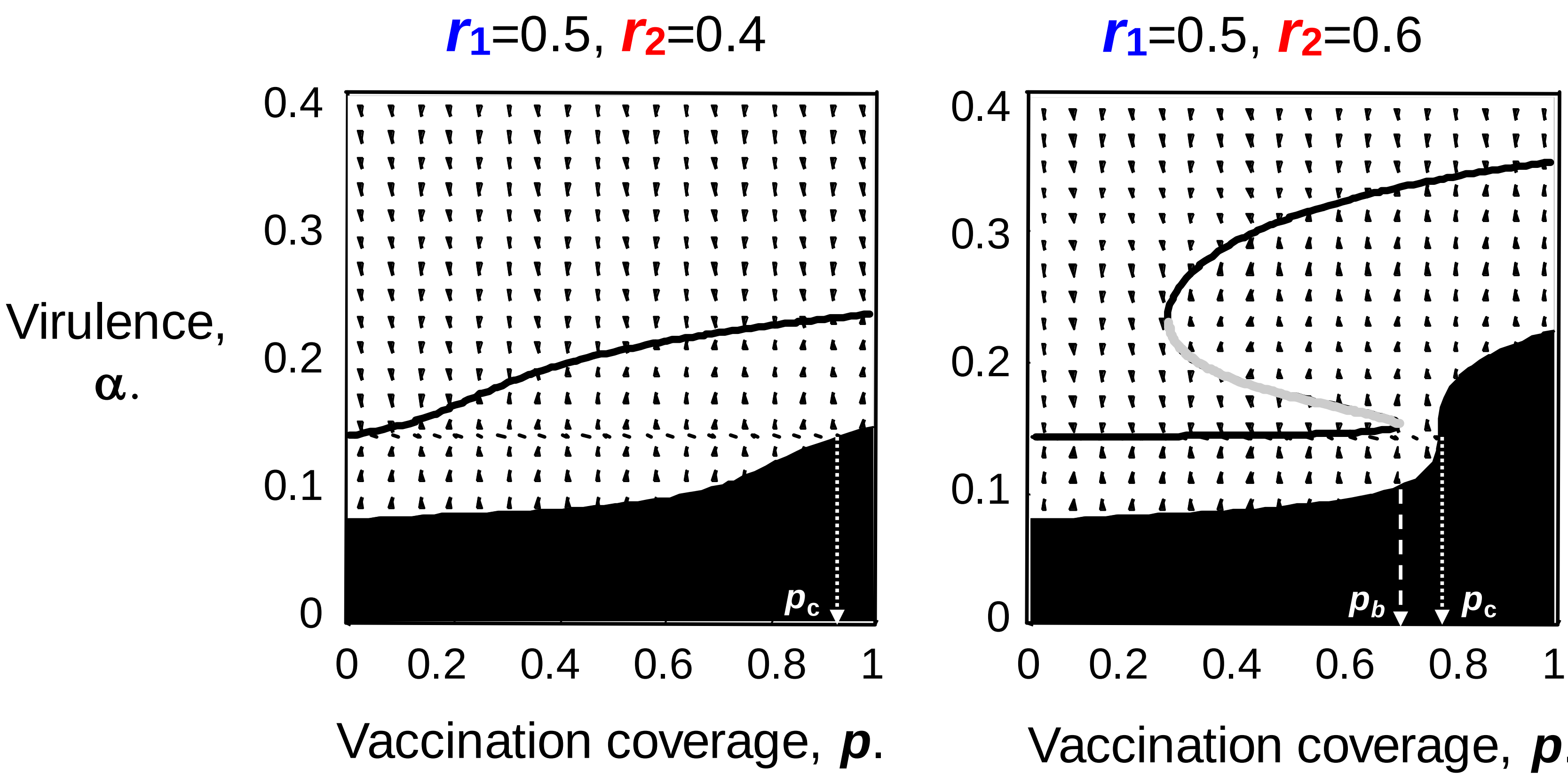
Different imperfect vaccines with ***p***=0.5

ESS, α*.

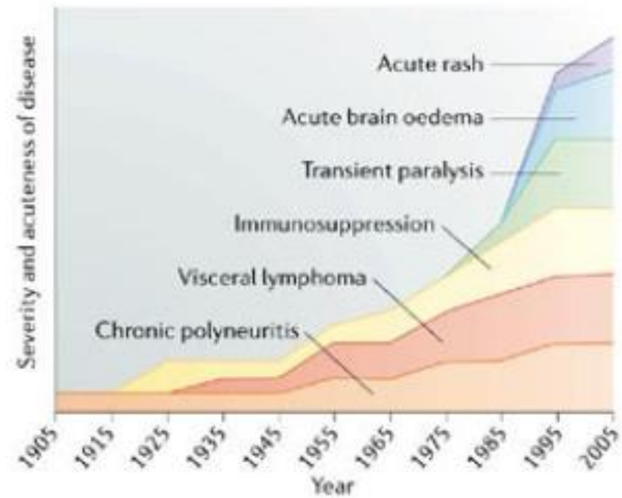


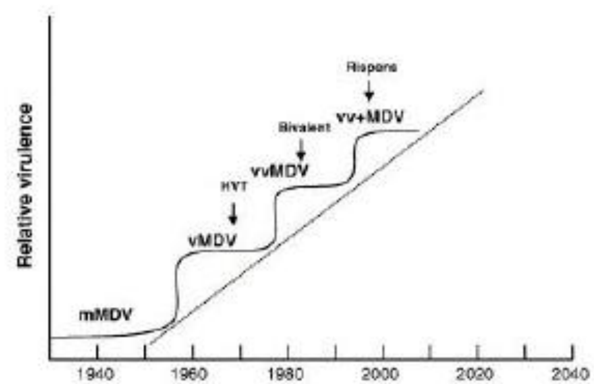
Vaccine efficacy

Virulence evolution and parasite eradication



Vaccine driven evolution
Marek's disease





Conclusion

Parasite evolution can erode the benefits of vaccination

- Increase of virulence (on naïve hosts)
- Eradication may become impossible

…but some vaccine properties (i.e., r_1) may limit these negative consequences.

A guidebook for adaptive dynamics

1- Draw pathogen life cycle as a set of compartments

2- Write down epidemiological dynamics as a system of ODEs

3- What is the endemic equilibrium: S_e?

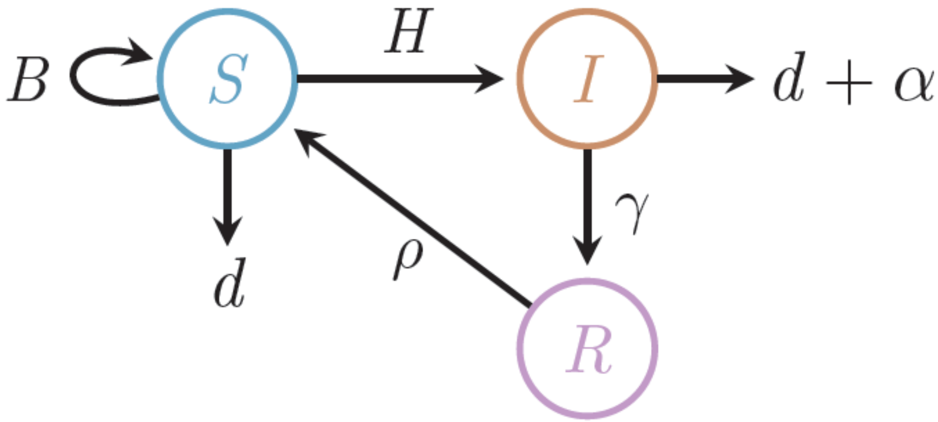
4- What is the dynamics of a rare mutant pathogen?

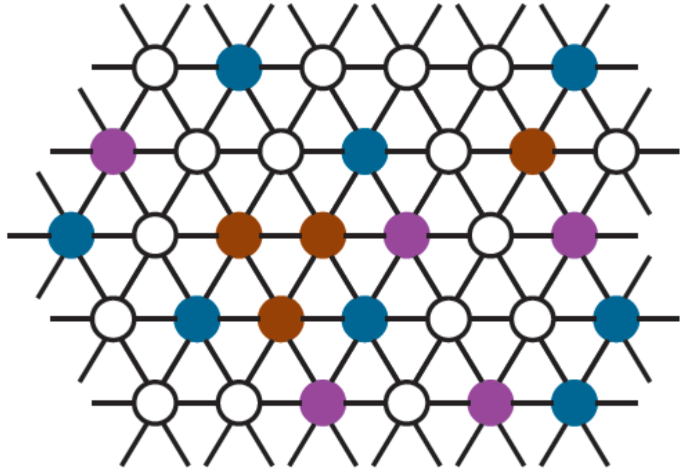
5- Is it possible to reduce dynamics in one dimension with a separation of time scale?

6- Matrix formulation?

- derivarion of instantaneous growth rate r_m
- derivation of per-generation growth rate R_m

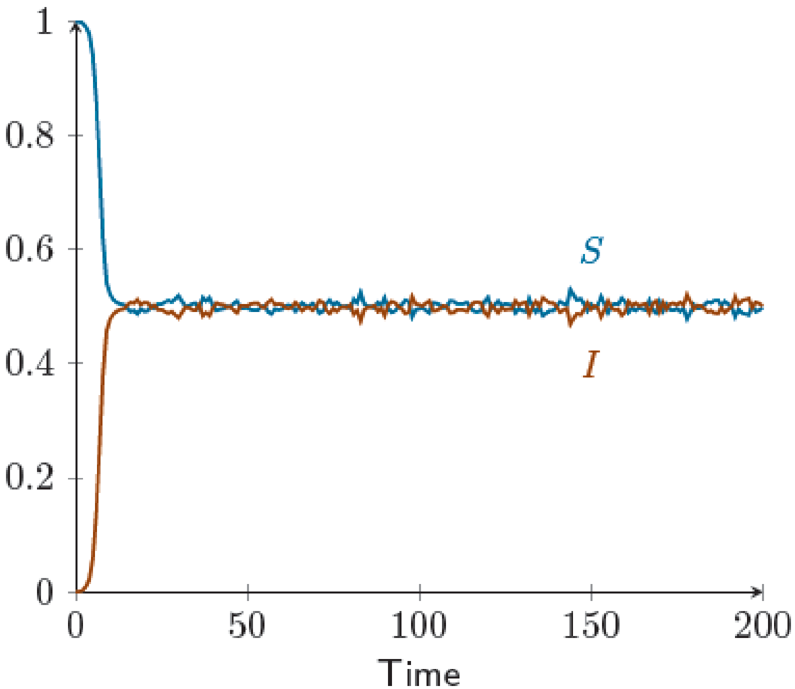
Spatial structure



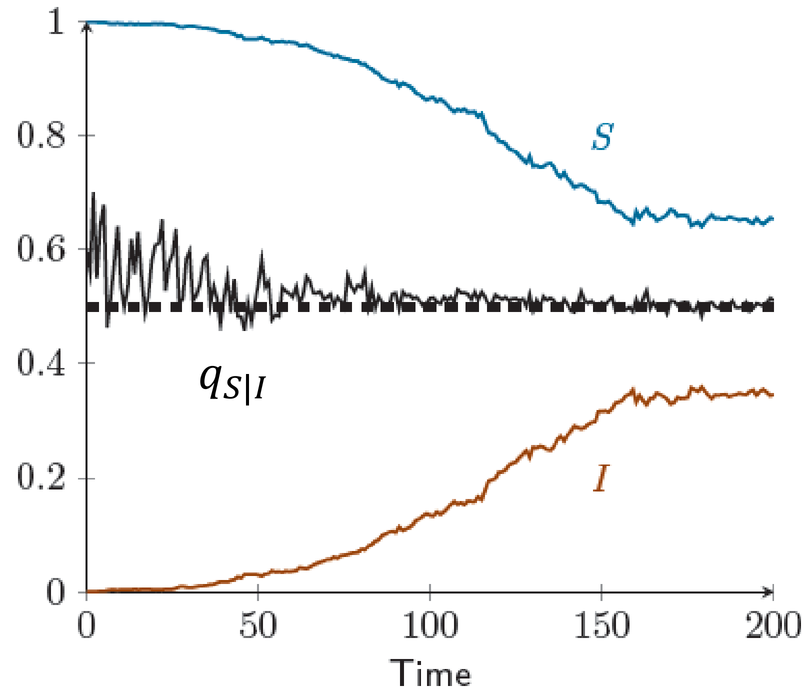


Spatial structure

Migration globale du parasite
g_P=1



Migration locale du parasite
g_P=0



Spatial structure

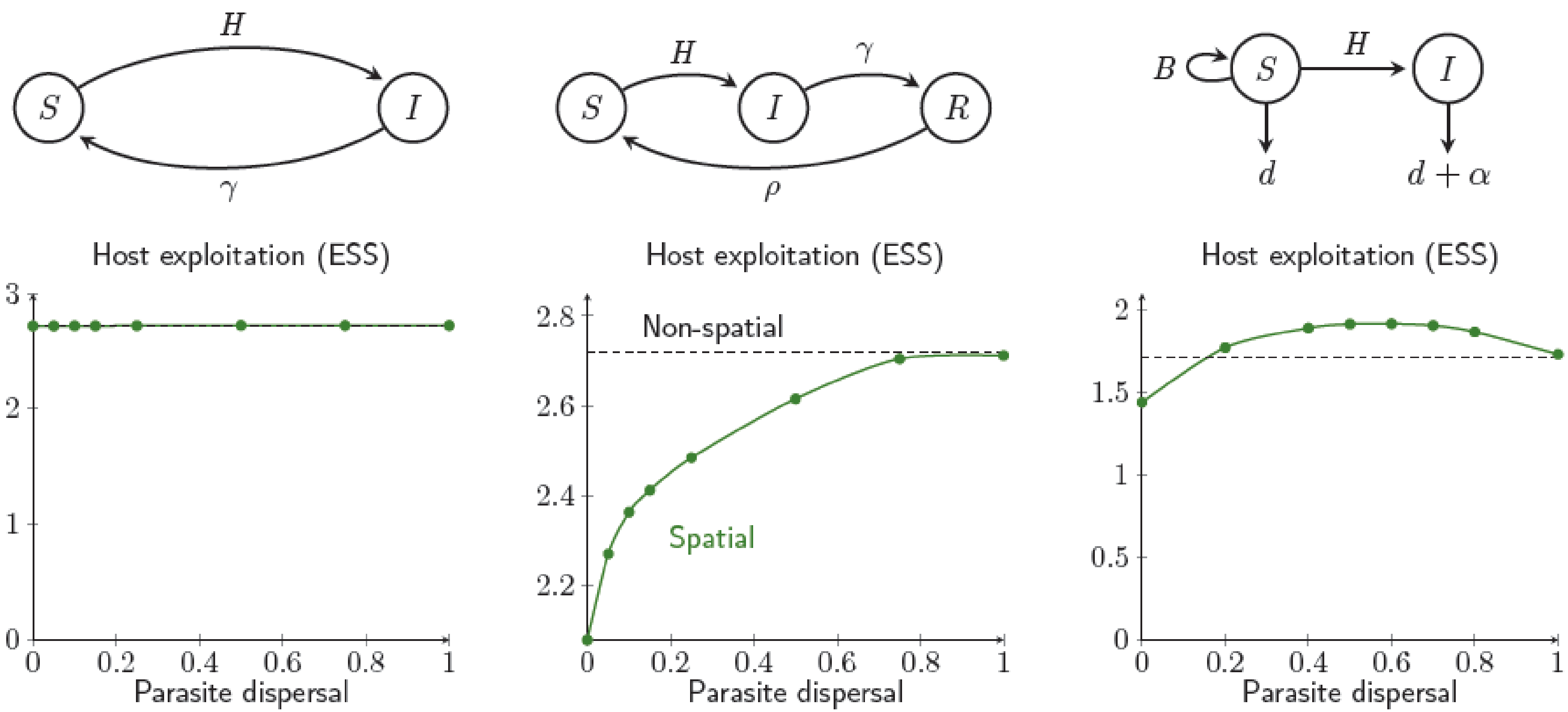
The mutant invades when:

Lion & Gandon 2015

$$R_m - R + (1 - g_P)\frac{\left(q_{S|I_m} - q_{S|I}\right)}{R_m R} > 0$$

Spatial structure

Lion & Boots 2010



Conclusion

- Small mutation rates allow to decouple epidemiological and evolutionary dynamics.

- Adaptative dynamics allows to identify ESS and long term evolutionary outcomes.

- This is very helpful to identify the effects of various environmental factors (host demography, vaccination, spatial structure…) on pathogen evolution.

- But difficult to generate short-term predictions…