Parasite evolution in spatially structured populations

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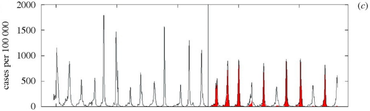
13 june 2016

MCEB 2016

Evolutionary epidemiology

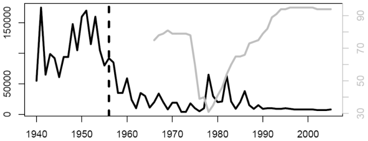
Applying ecological and evolutionary thinking to infectious diseases.

Population dynamics



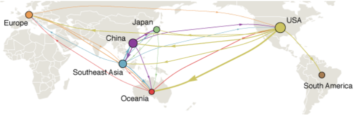
Koelle et al, *Interface*, 2010

Environmental change



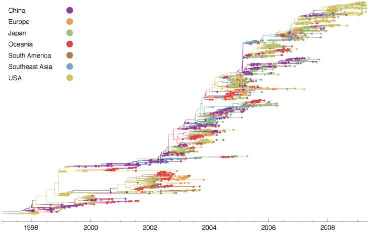
Rohani et al, 1999

Dispersal



↑ Bedford et al, *PLoS Pathogens*, 2010 →

Population genetics

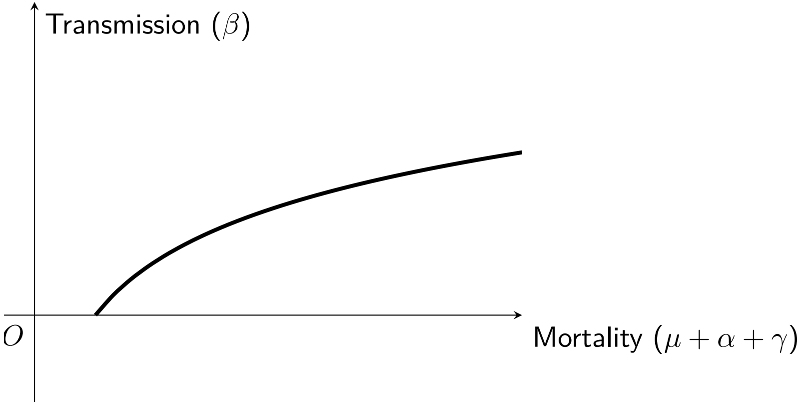


Basic questions

How do epidemiological dynamics affect the evolution of parasite life-history traits?

Specifically, how should a parasite allocate resources to reproduction (transmission) vs. survival?

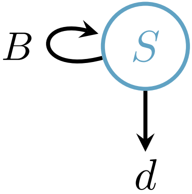
Transmission-virulence trade-off: $\beta(x)$, $\alpha(x)$



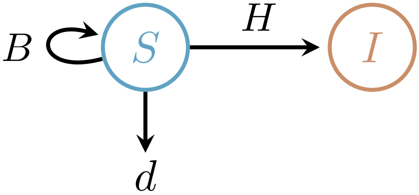
This talk

What is the impact of **host and parasite dispersal** on the evolution of parasite life-history traits?

An epidemiological model



An epidemiological model



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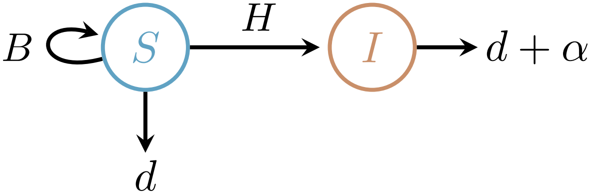
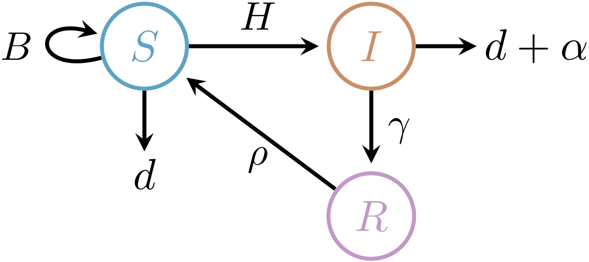


An epidemiological model



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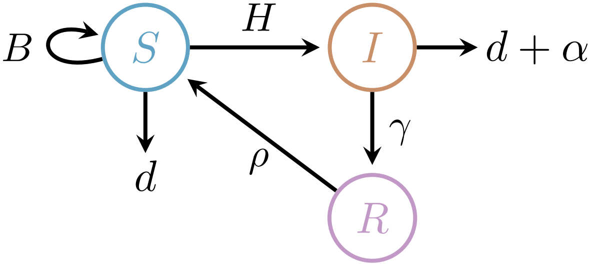
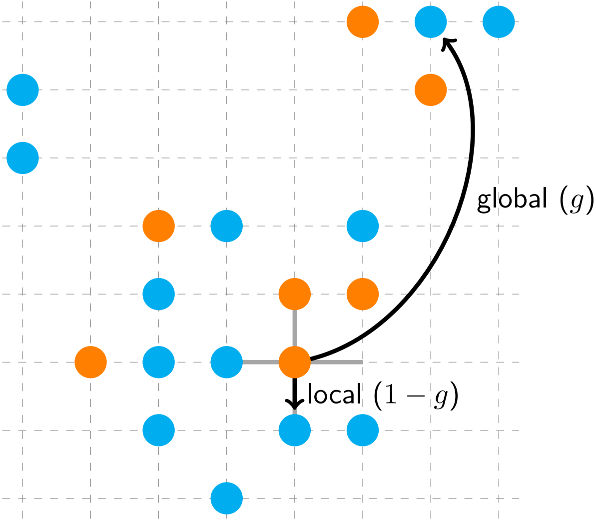


$$\begin{aligned}
\frac{dS}{dt} &= B(S, I, R) - dS + \beta SI + \gamma I \\
\frac{dI}{dt} &= \beta SI - (d + \alpha + \gamma)I \\
\frac{dR}{dt} &= \gamma I - \rho R
\end{aligned}$$

Parasite dispersal

M. Boots



p_S

$q_{S/I}$

Moment equations

Global dispersal ($g = 1$)

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

Moment equations

Global dispersal ($g = 1$)

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

Local dispersal ($g = 0$)

$$\begin{aligned}\frac{dI}{dt} &= \beta p_{SI} - (d + \alpha + \gamma) I \\ &= \beta q_{S|I} I - (d + \alpha + \gamma) I\end{aligned}$$

p_{SI} is the density of SI pairs.
The dynamics of p_{SI} in turns depend on the dynamics of other pair or triplet configurations...

Long-term evolution

From spatial dynamics to fitness

Dynamics of two parasite strains

$$\frac{dI}{dt} = \Big(\beta[S|I] - (d + \alpha + \gamma)\Big)I$$
$$\frac{dI'}{dt} = \Big(\beta'[S|I'] - (d + \alpha' + \gamma)\Big)I'$$

with

$$[S|x] = (1-g)q_{S/x} + gS$$

From spatial dynamics to fitness

Dynamics of two parasite strains

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with

$$[S|x] = (1-g)q_{S/x} + gS$$

Change in frequency

$$f = \frac{I'}{I+I'}$$

$$\frac{df}{dt} = f(1-f)\ \left[\underbrace{\beta'[S|I'] - \beta[S|I]}_{\text{transmission benefit}} \quad \underbrace{-(\alpha'-\alpha)}_{\text{virulence cost}}\right]$$

Invasion analysis

Weak selection: selection gradient

A rare mutant parasite invades when

$$\mathcal{S} = \frac{\partial v'}{v} + (1-g)\frac{\partial [S|I']}{[S|I]} > 0$$

where

$$v' = \frac{\beta'}{d+\alpha'} \quad \text{(reproductive value)}$$

- in a **well-mixed** population, selection acts to maximise the reproductive value of the parasite

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where

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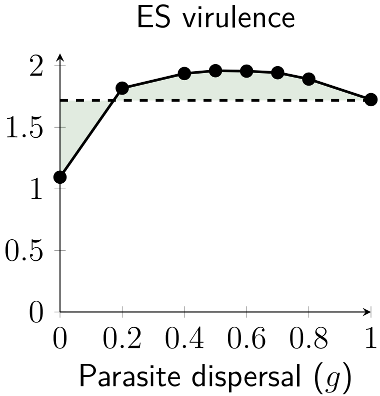
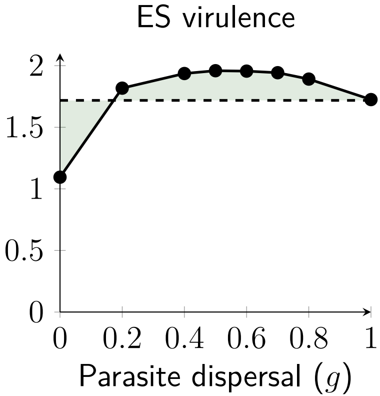
- in a **well-mixed** population, selection acts to maximise the reproductive value of the parasite
- **spatial structure** generates an additional selective pressure: local competition for susceptible hosts

Simulation results



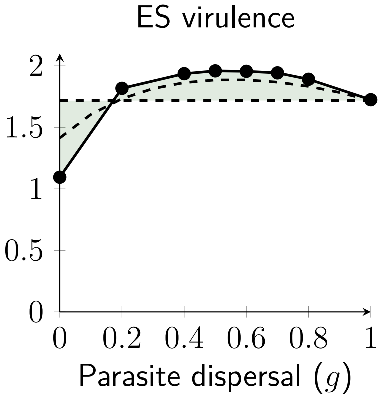
Simulation results



$$\underbrace{\mathbf{r}}_{\text{genetic structure (relatedness)}} > \underbrace{\bar{\phi} q_{S/SI} - q_{S/I}}_{\text{epidemiological structure}}$$

Lion & Boots *Ecol. Lett.* 2010

Simulation results



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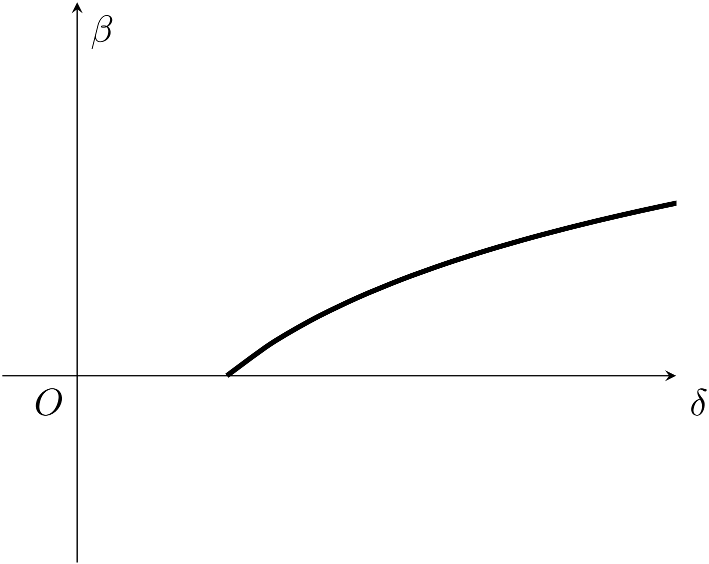
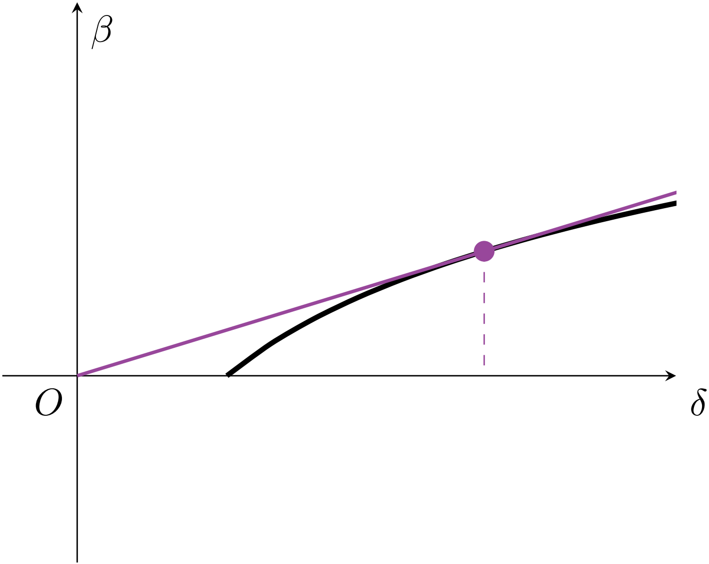
Graphical interpretation



Graphical interpretation



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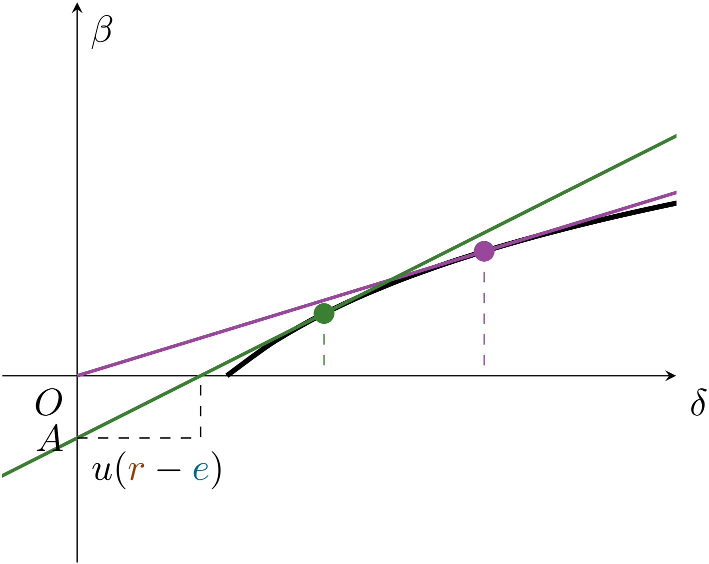

Kin competition

$$\mathcal{S} = \frac{\partial v'}{v} + (1-g)\frac{\partial [S|I']}{[S|I]} > 0$$

- As parasite dispersal becomes more local, parasites competing for susceptible hosts tend to be related.
- Local competition depends on **relatedness** between parasites.

Kin competition

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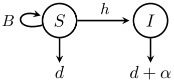
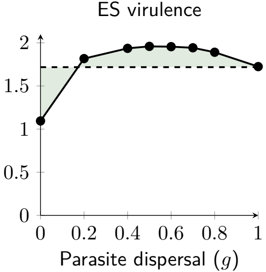
Epidemiological dynamics matter

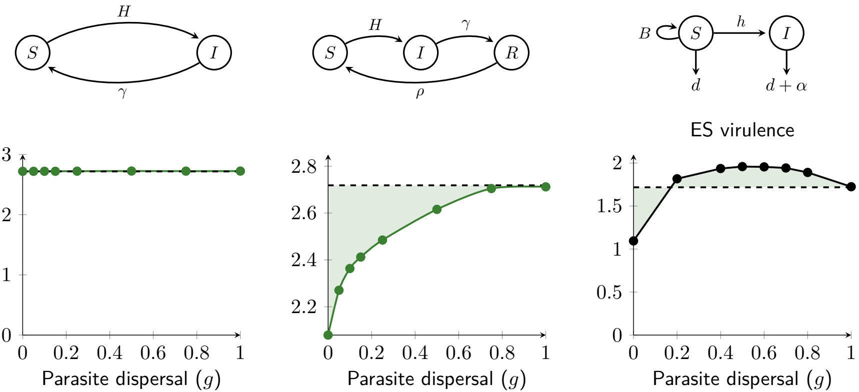




$$r > \bar{\phi} q_{S/SI} - q_{S/I}$$

Lion & Boots *Ecol. Lett.* 2010

Epidemiological dynamics matter



$$r > q_{I/I} - q_{I/R}$$

$$r > \bar{\phi} q_{S/SI} - q_{S/I}$$

Lion & Boots *Ecol. Lett.* 2010

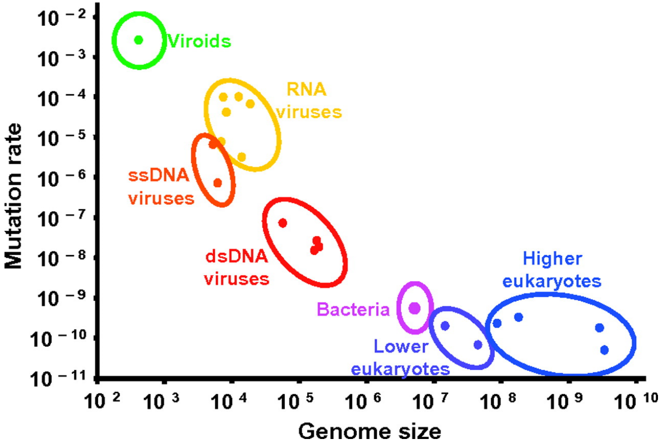
Summary so far...

- Interplay between spatial structuring and host heterogeneity may have potentially complex evolutionary consequences.

- Invasion analyses allow us to understand how selective pressures shape the **long-term evolution** of parasite life-history traits.

- However, invasion analyses assume a **separation of time scales between epidemiology and evolution**.
  For many parasites (e.g. viruses), this is unlikely to hold true.

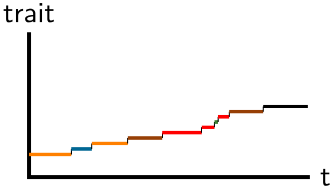
Rapid evolution in viruses



Gago et al, Science, 2009

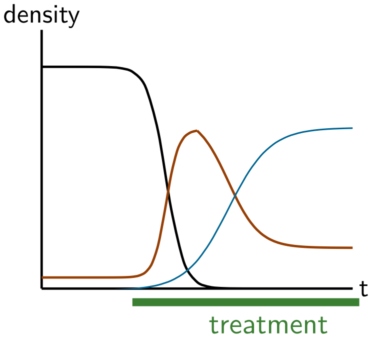
Time scales

Adaptive dynamics



- **Long-term** predictions
- **rare** mutations with **small phenotypic effects**

Evolutionary epidemiology



- **Short- and long-term** predictions
- genetic polymorphism

Another approach to theoretical evolutionary ecology

Ecological dynamics

Consider a population of N types. The dynamics of each type is

$$\frac{dn_i}{dt} = r_i(\mathbf{E})\, n_i \qquad \text{with} \qquad \mathbf{E} = \begin{pmatrix} \mathbf{n} \\ \mathbf{e} \end{pmatrix}$$

The dynamics of the total density is

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Evolutionary dynamics

Change in frequency $f_i = n_i/n$

$$\frac{df_i}{dt} = f_i \left(r_i(\mathbf{E}) - \overline{r_i(\mathbf{E})} \right)$$

Change in mean trait $\bar{z} = \sum_i z_i f_i$

$$\frac{d\bar{z}}{dt} = \mathsf{cov}_i(z_i, r_i(\mathbf{E})) + \text{mutation}$$

Evolutionary epidemiology

Per-capita growth rate of hosts infected by strain i

$$r_i(\mathbf{E}) = \beta_i S - (d + \alpha_i)$$

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Change in mean traits:

$$\frac{d}{dt}\begin{pmatrix}\bar{\alpha}_I \\ \bar{\beta}_I\end{pmatrix} = \underbrace{\mathbf{G}\begin{pmatrix}-1 \\ S\end{pmatrix}}_{\text{selection}} \underbrace{-\mu\begin{pmatrix}\bar{\alpha}_I - \bar{\alpha}_I^m \\ \bar{\beta}_I - \bar{\beta}_I^m\end{pmatrix}}_{\text{mutation}}$$

where

$$\mathbf{G} = \begin{pmatrix}\sigma_I^{\alpha\alpha} & \sigma_I^{\alpha\beta} \\ \sigma_I^{\beta\alpha} & \sigma_I^{\beta\beta}\end{pmatrix}$$

together with equations for epidemiological densities:

$$\frac{dS}{dt} = b - dS - \bar{\beta}_I S I$$

$$\frac{dI}{dt} = \bar{\beta}_I S I - (d + \bar{\alpha}_I) I$$

Day & Gandon, 2006; 2007

Spatial evolutionary epidemiology

S. Gandon

Per-capita growth rate of hosts infected by strain i

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Change in mean traits:

$$\frac{d}{dt}\begin{pmatrix}\bar{\alpha}_I \\ \bar{\beta}_I\end{pmatrix} = \mathbf{G}\begin{pmatrix}-1 \\ q_{S/I}\end{pmatrix} + \bar{\beta}_{IS} q_{S/I}\begin{pmatrix}\bar{\alpha}_{IS} - \bar{\alpha}_I \\ \bar{\beta}_{IS} - \bar{\beta}_I\end{pmatrix} - \mu\begin{pmatrix}\bar{\alpha}_I - \bar{\alpha}_I^m \\ \bar{\beta}_I - \bar{\beta}_I^m\end{pmatrix}$$

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$$\mathbf{G} = \begin{pmatrix}\sigma_I^{\alpha\alpha} & \sigma_{IS}^{\alpha\beta} \\ \sigma_I^{\beta\alpha} & \sigma_{IS}^{\beta\beta}\end{pmatrix}$$

Lion & Gandon, submitted

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where

$$\mathbf{G} = \begin{pmatrix}\sigma_I^{\alpha\alpha} & \sigma_{IS}^{\alpha\beta} \\ \sigma_I^{\beta\alpha} & \sigma_{IS}^{\beta\beta}\end{pmatrix}$$

Lion & Gandon, submitted

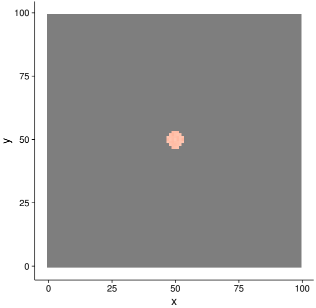
Application to transient dynamcis

A simple example

Let us consider the invasion dynamics of two parasite strains:

- a wild-type strain
- a mutant strain (lower R_0 but higher transmission and virulence)

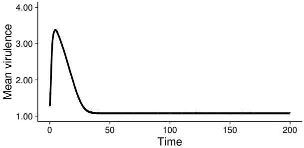
I will contrast two scenarios: global dispersal and local dispersal.
I will focus on the simpler SIS model (host fecundity $\rightarrow \infty$).

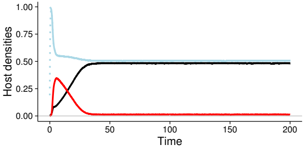


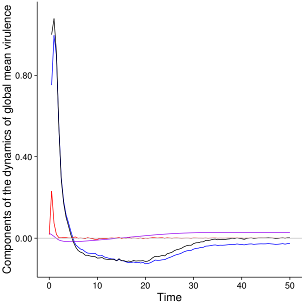
Change in mean virulence

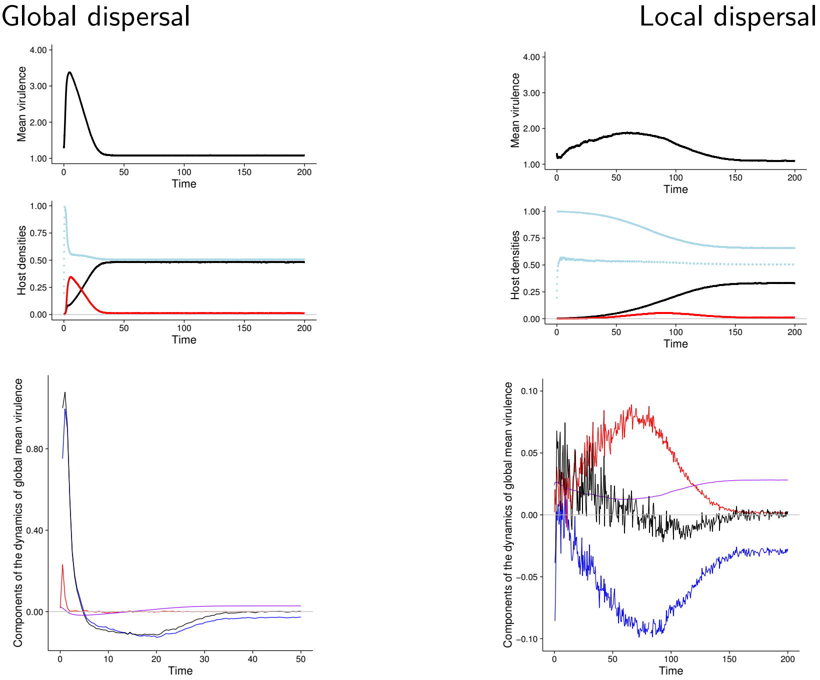
$$\frac{d\bar{\alpha}_I}{dt} = \underbrace{\left[q_{S/I}\sigma_{IS}^{\alpha\beta} - \sigma_I^{\alpha\alpha}\right]}_{\text{trade-off}} + \underbrace{\bar{\beta}_{IS}q_{S/I}(\bar{\alpha}_{IS} - \bar{\alpha}_I)}_{\text{spatial differentiation}} \underbrace{-\mu(\bar{\alpha}_I - \bar{\alpha}_I^m)}_{\text{mutation bias}}$$

Global dispersal

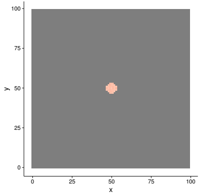




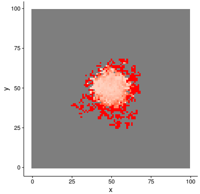



Global dispersal
Local dispersal
Mean virulence
4.00
3.00
2.00
1.00
Time
0
50
100
150
200
Host densities
1.00
0.75
0.50
0.25
0.00
Components of the dynamics of global mean virulence
0.80
0.40
0.00
0
10
20
30
40
50
0.10
0.05
0.00
−0.05
−0.10

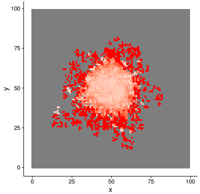
(a) $t = 0$



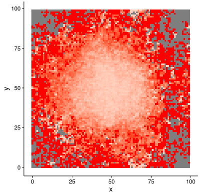
(b) $t = 10$



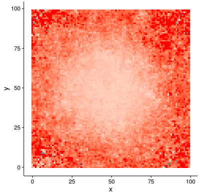
(c) $t = 20$



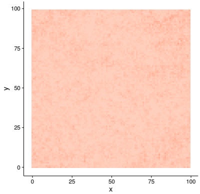
(d) $t = 50$



(e) $t = 70$



(f) $t = 150$



Dynamics of spatial differentiation

$$\frac{d(\bar{\alpha}_{IS}-\bar{\alpha}_I)}{dt} = \underbrace{\left(\bar{\phi} q_{S/SI}\sigma^{\alpha\beta}_{ISS} - \sigma^{\alpha\beta}_{IS} q_{S/I}\right) \quad -\sigma^{\alpha\beta}_{IS}\left(\phi + \bar{\phi} q_{I/SI}\rho_S\right)}_{\text{Transmission}}$$

$$\underbrace{-\left(\sigma^{\alpha\alpha}_{IS} - \sigma^{\alpha\alpha}_{I}\right) \quad +\sigma^{\alpha\alpha}_{I}\frac{q_{I/I}}{q_{S/I}}\rho}_{\text{Mortality}}$$

$$-\underbrace{\left[\bar{\beta}_{IS} q_{S/I} + \frac{d+\bar{\alpha}_{II}}{q_{S/I}}\right](\bar{\alpha}_{IS}-\bar{\alpha}_I)}_{\text{Mixing}}$$

$$-\underbrace{\mu\frac{N}{N-1}(\bar{\alpha}_{IS}-\bar{\alpha}_I)}_{\text{Mutation}}$$

Initial dynamics of spatial dynamics

Aim: understanding the build-up of spatial differentiation $\bar{\alpha}_{IS} - \bar{\alpha}_I$.

Starting from initial condition $\bar{\alpha}_{IS} - \bar{\alpha}_I \approx 0$, we can write the initial dynamics (neglecting mutation bias) as:

$$\frac{d(\bar{\alpha}_{IS} - \bar{\alpha}_I)}{dt} = \underbrace{\sigma_{IS}^{\alpha\beta}(\bar{\phi} q_{S/SI} - q_{S/I})}_{\text{Epidemiological effect}}$$

$$\underbrace{-\sigma_{IS}^{\alpha\beta}(\phi + \bar{\phi} q_{I/SI} \rho_S) + \sigma_I^{\alpha\alpha} \frac{q_{I/I}}{q_{S/I}} \rho}_{\text{Genetic effect}}.$$

where

$$\rho = \frac{\sum_i \sum_j \alpha_i \alpha_j f_{ij} - \bar{\alpha}_{II}^2}{\sigma_I^{\alpha\alpha}} \tag{1}$$

$$\rho_S = \frac{\sum_i \sum_j \alpha_i \beta_j f_{iSj} - \bar{\alpha}_{ISI} \bar{\beta}_{ISI}}{\sigma_{IS}^{\alpha\beta}} \tag{2}$$

Spatial differentiation at equilibrium

Scaling $\bar{\alpha}_{IS} - \bar{\alpha}_{I}$ by population variance, we obtain at equilibrium

$$\hat{D} = \frac{\frac{q_{I/I}}{q_{S/I}}\rho - \frac{\sigma^{\alpha\beta}_{IS}}{\sigma^{\alpha\alpha}_{I}}(\phi + \bar{\phi} q_{I/SI}\rho_{S}) - \frac{(\sigma^{\alpha\alpha}_{IS} - \sigma^{\alpha\alpha}_{I})}{\sigma^{\alpha\alpha}_{I}}}{\bar{\beta}_{IS} q_{S/I} + \frac{\bar{\alpha}_{II}}{q_{S/I}} + \mu\frac{N}{N-1}}. \tag{3}$$

Back to invasion analyses

Weak selection limit:

$$\frac{d\bar{\alpha}_I}{dt} = \sigma_I^{\alpha\alpha} \left[\left. \frac{d\beta}{d\alpha} \right|_{\alpha=\bar{\alpha}_I} q_{S/I} - 1 + \bar{\beta}_I q_{S/I} D \right]$$

where

$$D = \frac{\bar{\alpha}_{IS} - \bar{\alpha}_I}{\sigma_I^{\alpha\alpha}}$$

is a fast variable under weak selection.

Back to invasion analyses

Weak selection limit:

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where

$$D = \frac{\bar{\alpha}_{IS} - \bar{\alpha}_I}{\sigma_I^{\alpha\alpha}}$$

is a fast variable under weak selection.

Using a quasi-equilibrium approximation for D, we obtain:

$$\frac{d\bar{\alpha}_I}{dt} = \sigma_I^{\alpha\alpha} \left(1 - \frac{q_{I/I}\rho}{1 + q_{S/I}} \right) \left[\frac{d + \bar{\alpha}_I}{\bar{\beta}_I} \left. \frac{d\beta}{d\alpha} \right|_{\alpha=\bar{\alpha}_I} - 1 \right]$$

which is the result of Lion & Boots (2010) and Lion (in press).

Back to invasion analyses

Weak selection limit:

$$\frac{d\bar{\alpha}_I}{dt} = \sigma_I^{\alpha\alpha} \left[\left.\frac{d\beta}{d\alpha}\right|_{\alpha=\bar{\alpha}_I} q_{S/I} - 1 + \bar{\beta}_I q_{S/I} D \right]$$

where

$$D = \frac{\bar{\alpha}_{IS} - \bar{\alpha}_I}{\sigma_I^{\alpha\alpha}}$$

is a fast variable under weak selection.

Using a quasi-equilibrium approximation for D, we obtain:

$$\frac{d\bar{\alpha}_I}{dt} = \sigma_I^{\alpha\alpha} \left(1 - \frac{q_{I/I}\rho}{1 + q_{S/I}}\right) \left[\frac{d + \bar{\alpha}_I}{\bar{\beta}_I} \left.\frac{d\beta}{d\alpha}\right|_{\alpha=\bar{\alpha}_I} - 1 \right]$$

which is the result of Lion & Boots (2010) and Lion (in press).

Furthermore:

$$\bar{\beta}_{IS} q_{S/I} \frac{\bar{\alpha}_{IS} - \bar{\alpha}_I}{\sigma_I^{\alpha\alpha}} \approx \beta\, \partial[S|I'] \qquad \text{(kin competition term)}$$

Model with host demography

We can also write equations for the dynamics of mean traits when host fecundity is finite.

As in the SIS model, we can write under weak selection

$$\frac{d\bar{\alpha}_I}{dt} = \sigma_I^{\alpha\alpha} \left(1 - \frac{q_{I/I}\rho}{\kappa}\right) S$$

where

$$S = \left[1 - \omega \left(q_{I/I}\rho - \bar{\phi} q_{S/SI} + q_{S/I}\right)\right] \frac{d + \bar{\alpha}_I}{\bar{\beta}_I} \left.\frac{d\beta}{d\alpha}\right|_{\alpha = \bar{\alpha}_I} - 1$$

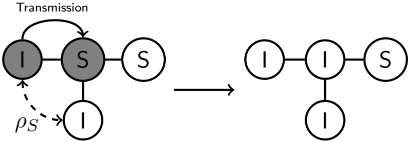
and we also recover the result discussed in the first part.

Take-home messages

- Spatial moment equations can be used to model the long- and short-term evolution of parasites.
- Long-term evolution can be studied using an extension of standard Adaptive Dynamics techniques.
- An AD approach cannot capture some features of infectious diseases biology (e.g. short-term dynamics, or out-of-equilibrium dynamics). In such cases, it is helpful to bridge the gap between QG and AD models.
- A key insight of both AD and QG approaches is that selection on parasite traits depends on measures of **epidemiological** and **genetic structure** (relatedness).

(a) Transmission

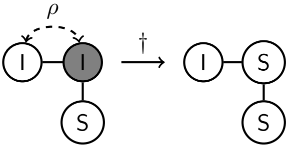
Effect on $\bar{\alpha}_{IS}$



↗ $+\,\bar{\phi} q_{S/SI} \sigma^{\alpha\beta}_{ISS}$

↘ $-\,(\phi + \bar{\phi} q_{I/SI} \rho_S) \sigma^{\alpha\beta}_{IS}$

(b) Mortality



↘ $-\,\sigma^{\alpha\alpha}_{IS}$

↗ $+\,\dfrac{q_{I/I}}{q_{S/I}} \rho \; \sigma^{\alpha\alpha}_{I}$