

# Within- and between-host processes of phenotype dynamics of zoonotic pathogens

Modelling phenotypic evolution across species

Henrik Sjödin, Umeå University, Sweden



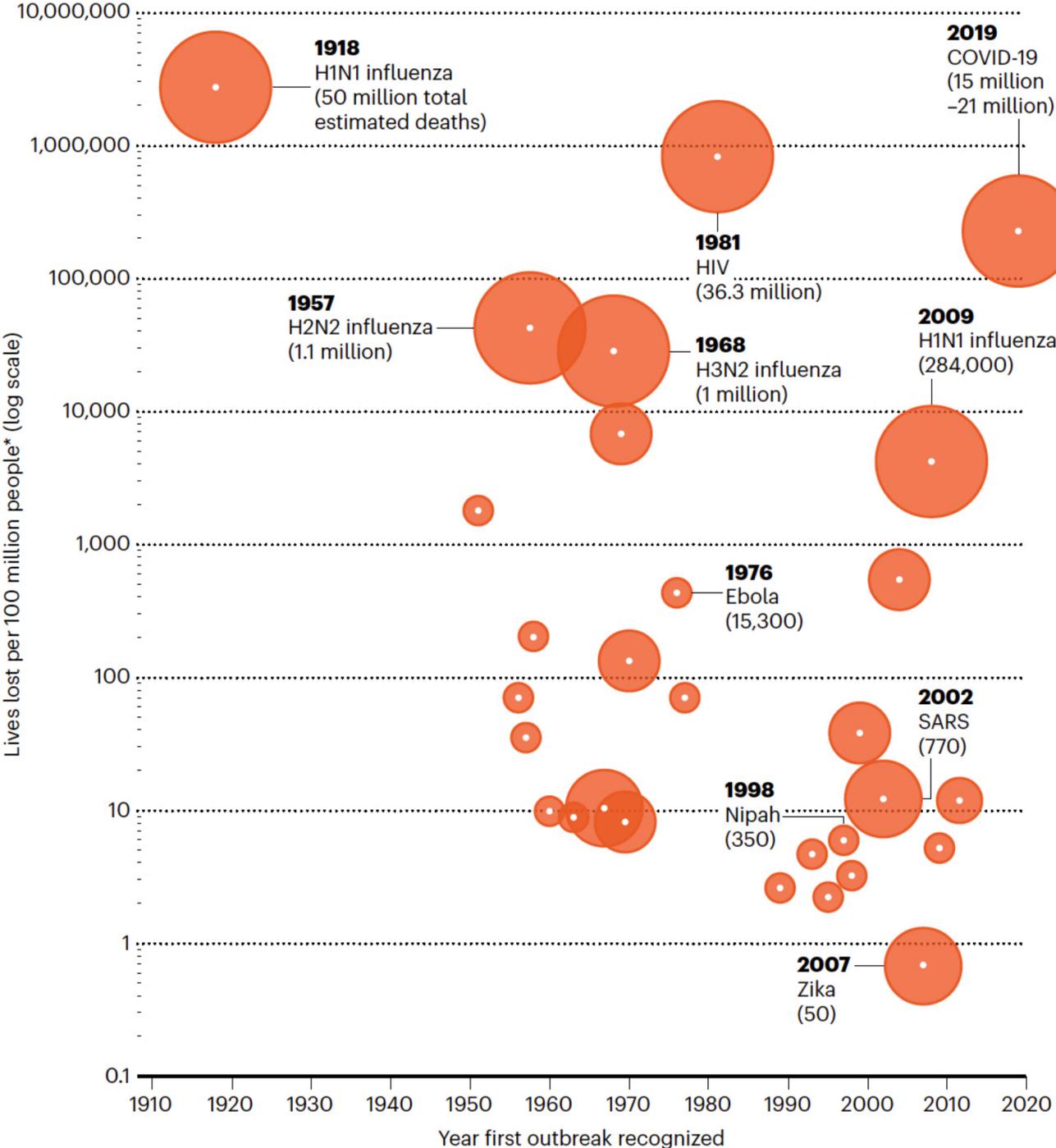
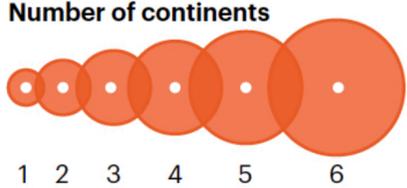
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UNIVERSITY



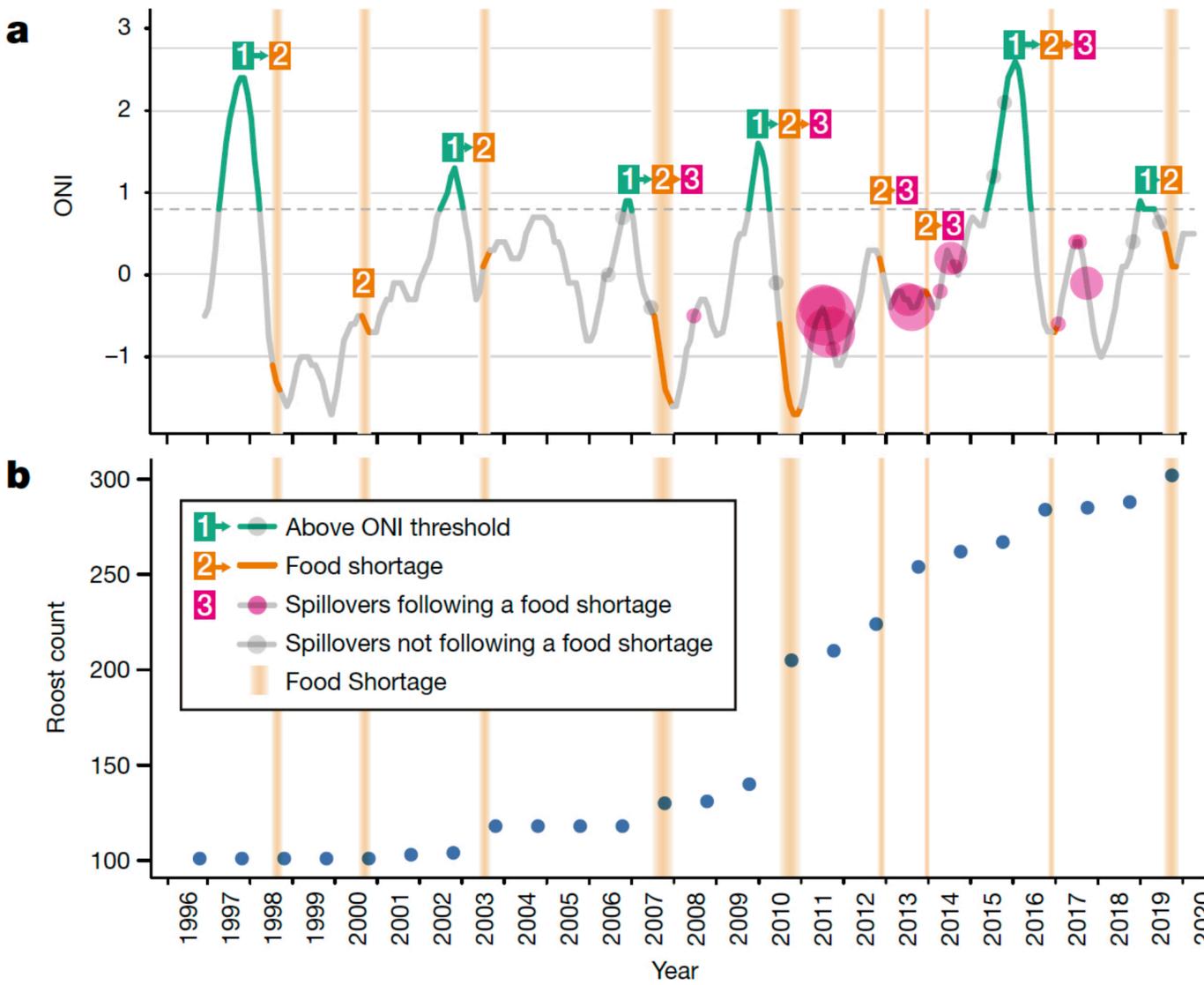
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# SPILLOVERS: A GROWING THREAT

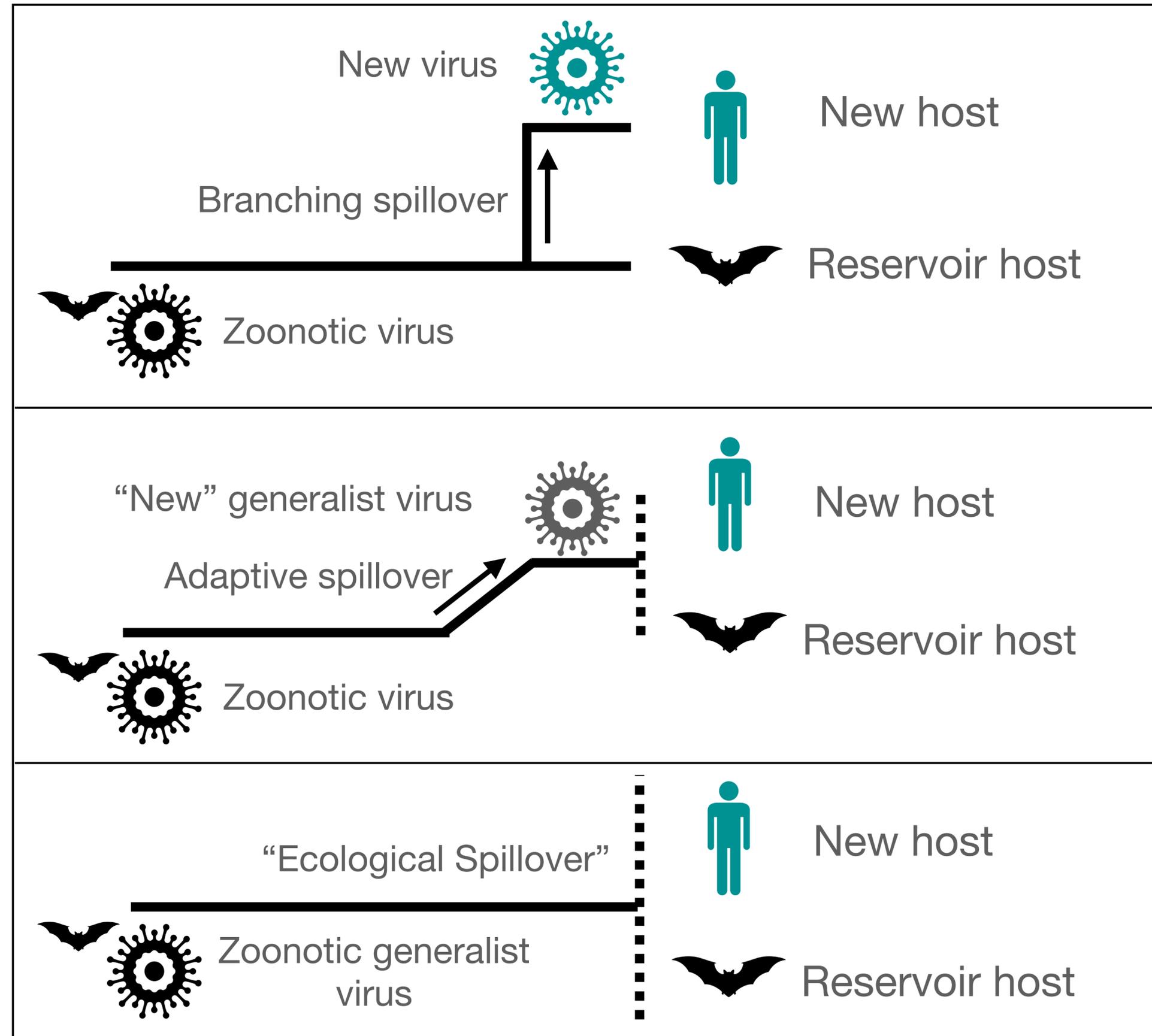
Deforestation and other changes have increased the likelihood of animal viruses jumping into people, with globalization and a higher density of human populations having increased the chance that such spillover events will be catastrophic. The annual economic loss from viral zoonoses since 1918 is US\$212 billion.



\*Data are from viral outbreaks of zoonotic origin that resulted in ten or more deaths; figures in parentheses are total estimated deaths spread over multiple years (and over multiple outbreaks, in some instances) rounded to the nearest ten.



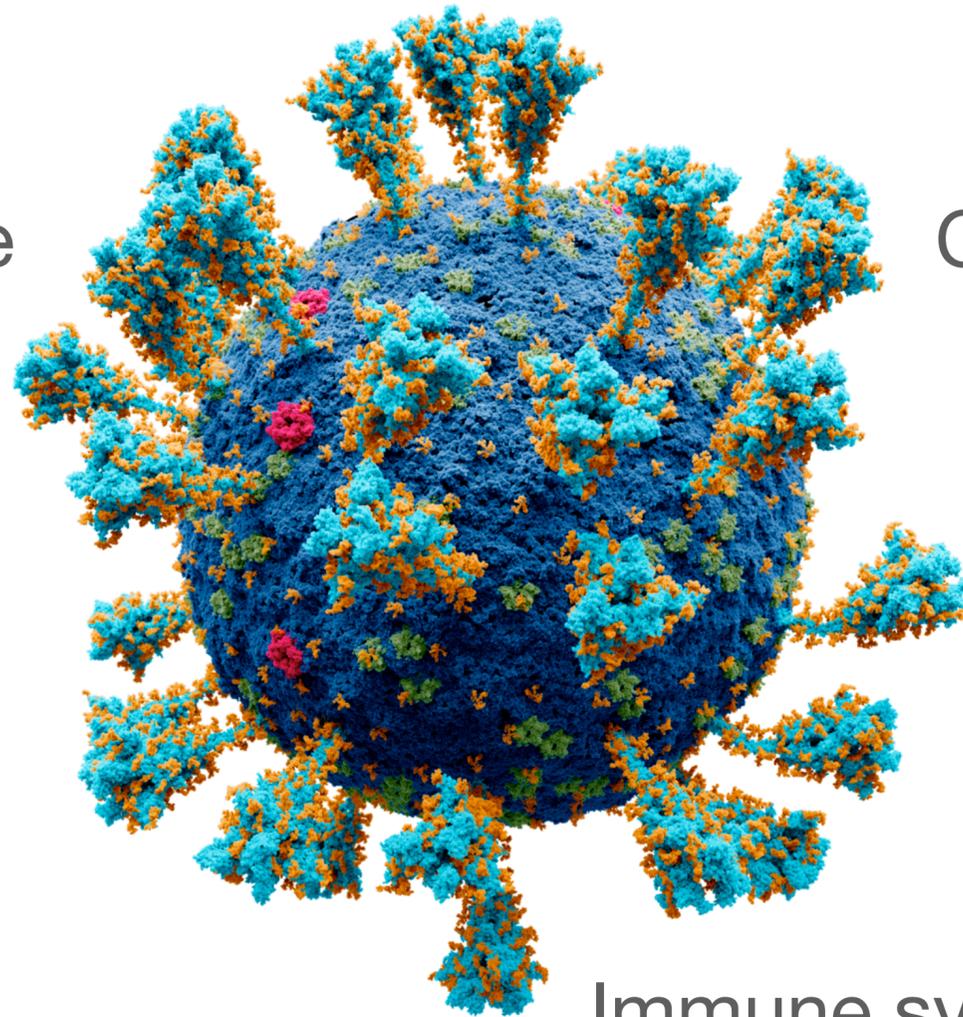
# Three categorical cases of spillover



# The virion as the unit of selection

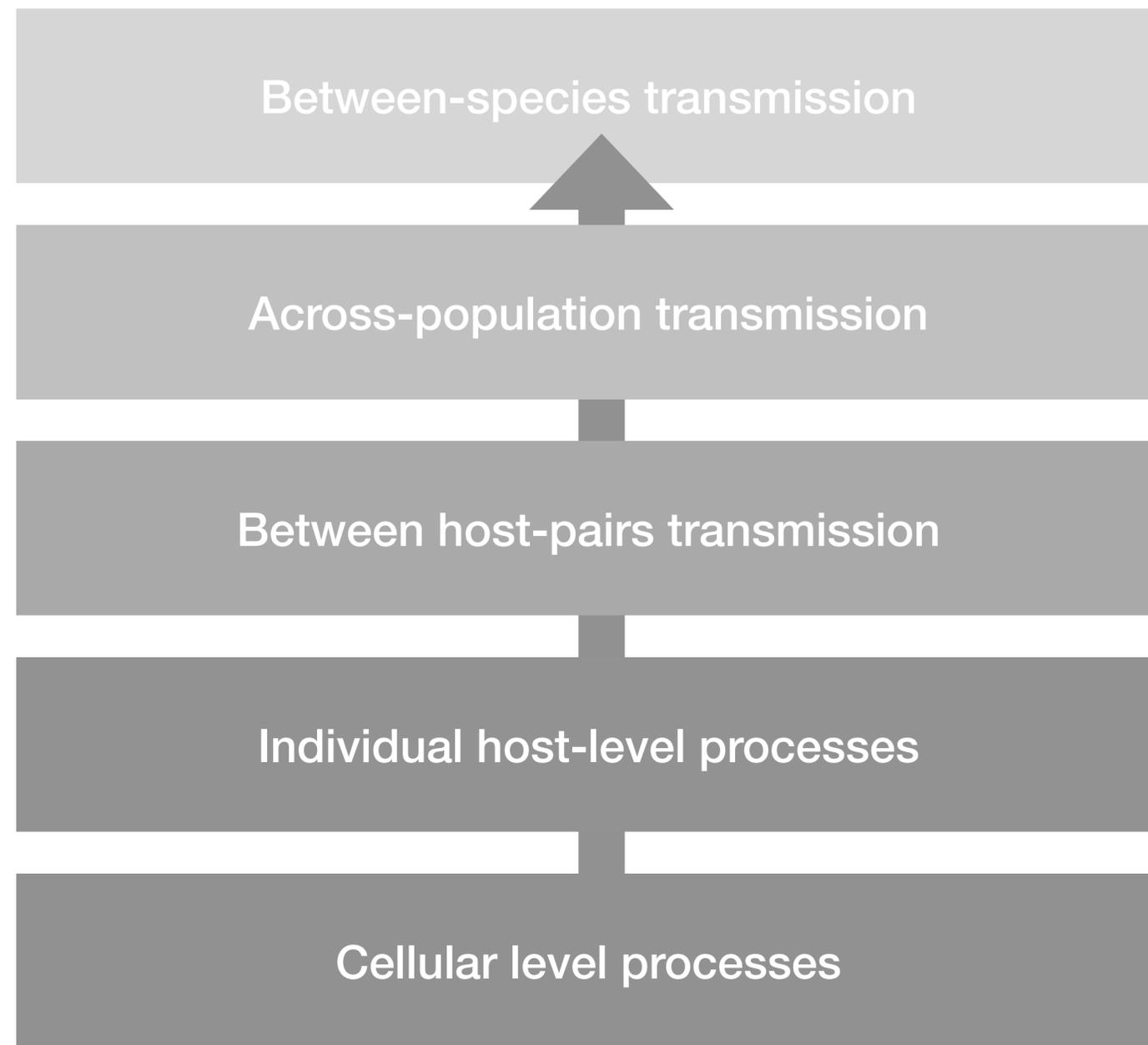
Replication rate

Cell infection rate



Immune system processes

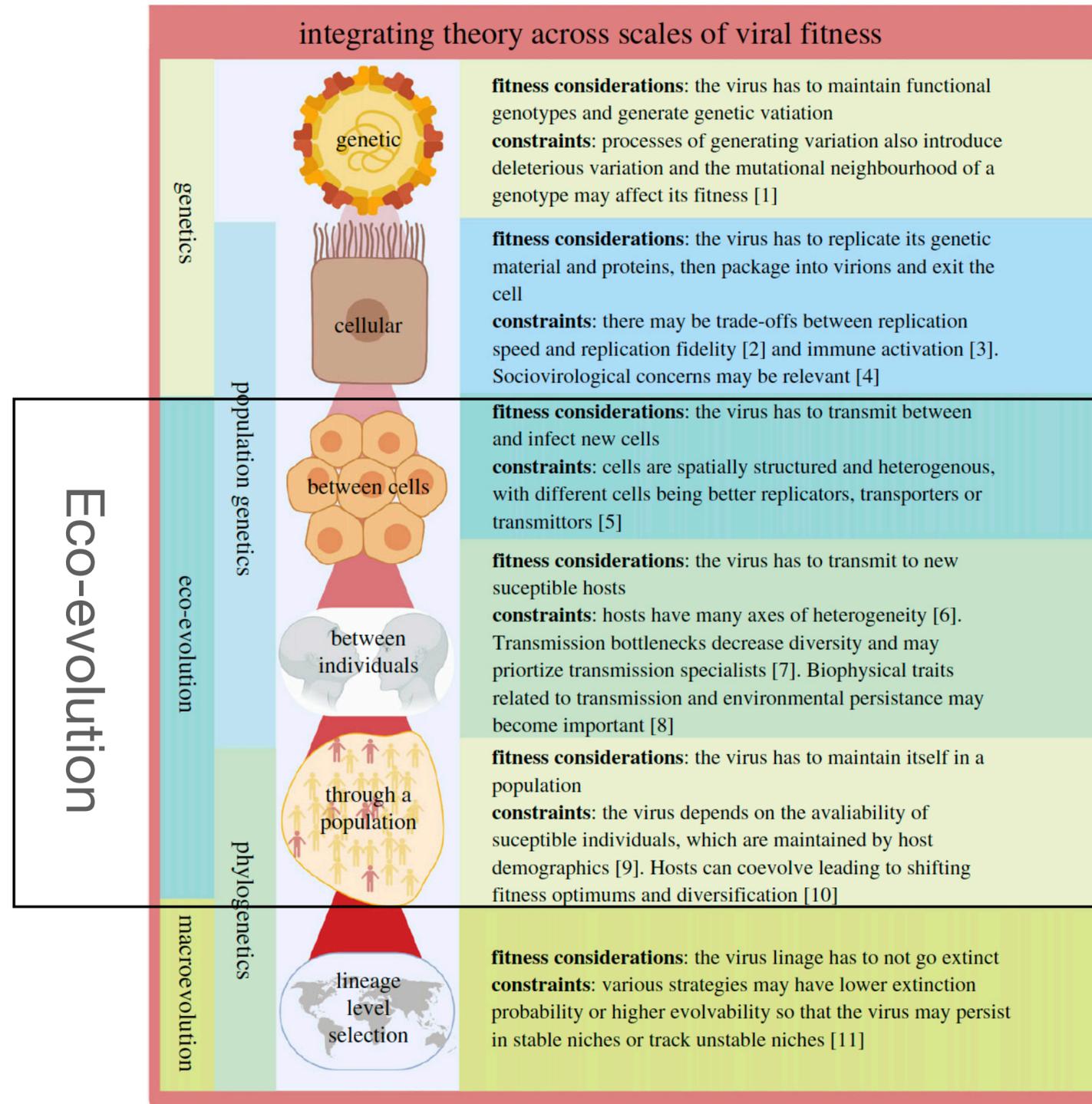
# Process scales



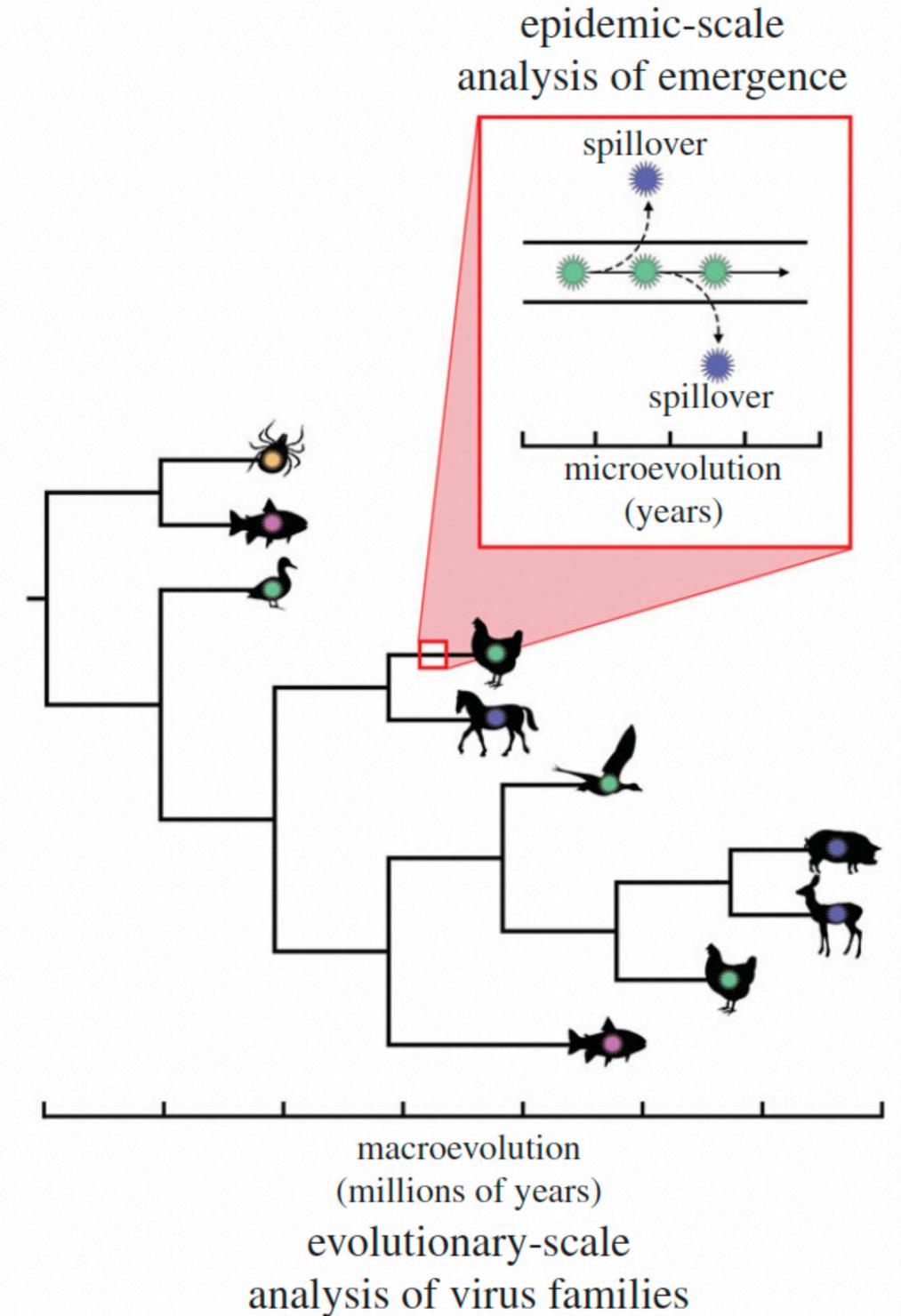
Evolution

- Host specificity
- Species contact structures
- Host adaptation
- Cost to generalism
- ...

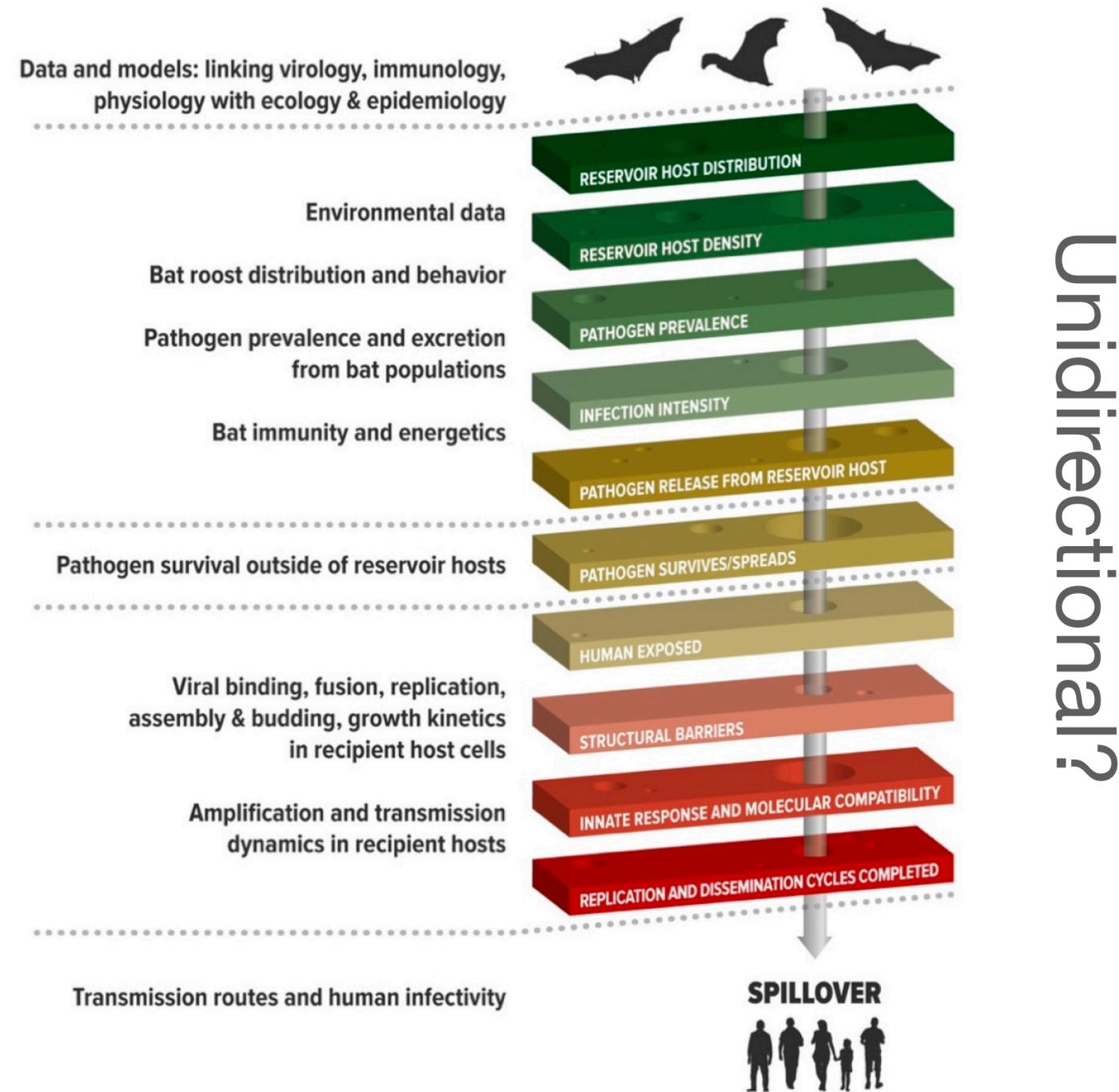
# Process scales



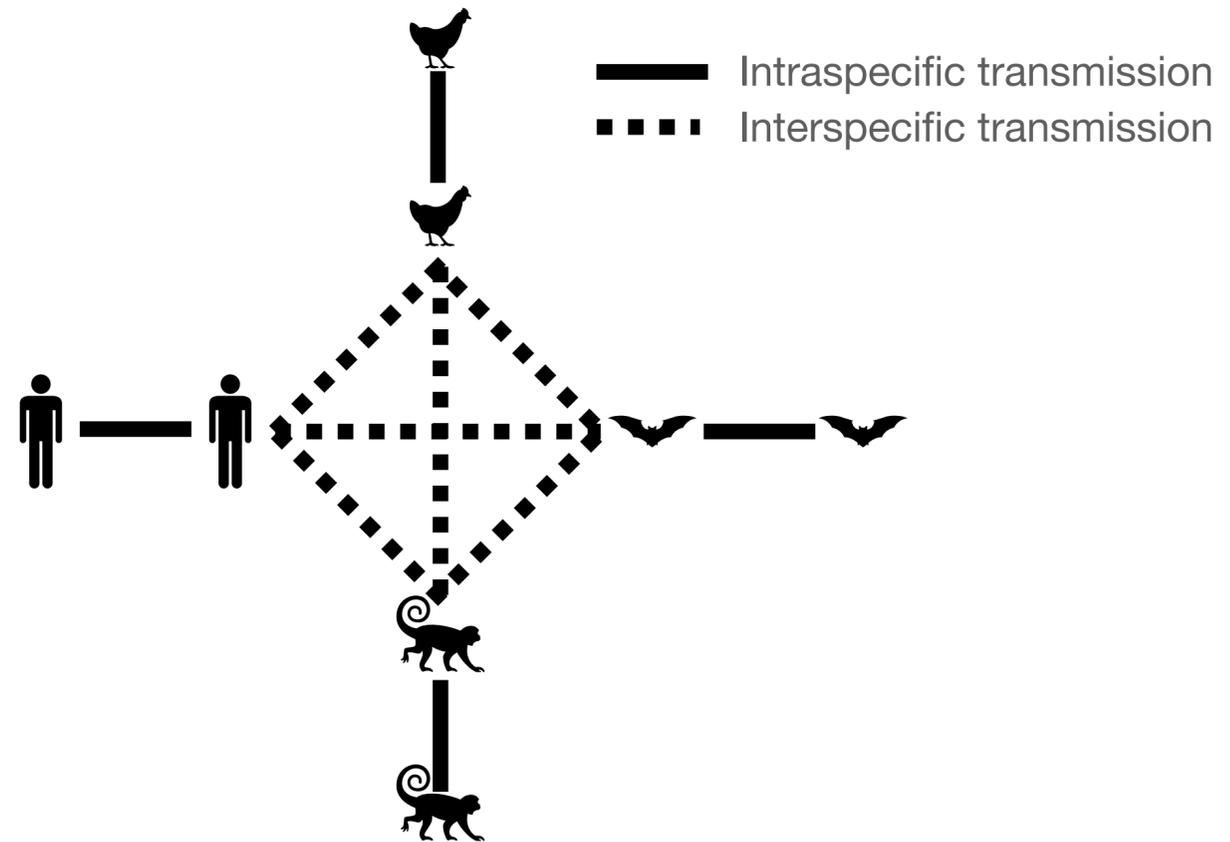
**Figure 1.** Integrating theory across scales of viral fitness. 1, [44]; 2, [45]; 3, [46]; 4, [47]; 5, [48]; 6, [21]; 7, [49]; 8, [50]; 9, [51]; 10, [10]; 11, [52]. Created with Biorender.com. (Online version in colour.)



# Mechanisms of spillover



**Figure 1.** Biological data needed to understand and predict spillover (**left**) aligned to the key mechanisms of spillover (**right**). In addition, epidemiology and social sciences are employed to understand human exposure. Adapted from Plowright et al. [1].





Intraspecific transmission

$$\dot{S} = -\frac{\beta SI}{N} + \gamma I, \quad \dot{I} = \frac{\beta SI}{N} - \gamma I, \quad \lambda = \frac{\beta I}{N}$$

1. With implicit within-host processes

$$R_0 = \frac{\beta S_0}{\gamma N} = \frac{\beta}{\gamma}$$

$$R'_e = \frac{\beta' S^*}{\gamma' N} = \frac{\beta' \gamma}{\beta \gamma'} = \frac{R'_0}{R_0}$$

2. With explicit within-host processes

$$\beta = \boxed{c \tau} \rightarrow c \tau(s) = \beta(s)$$

$$\gamma \rightarrow \gamma(s)$$

$$R_e(s', s) = \frac{\beta(s') S^*(s)}{\gamma(s') N} = \frac{\beta(s') \gamma(s)}{\beta(s) \gamma(s')}$$

Across-population transmission

But what is  $s$ ?

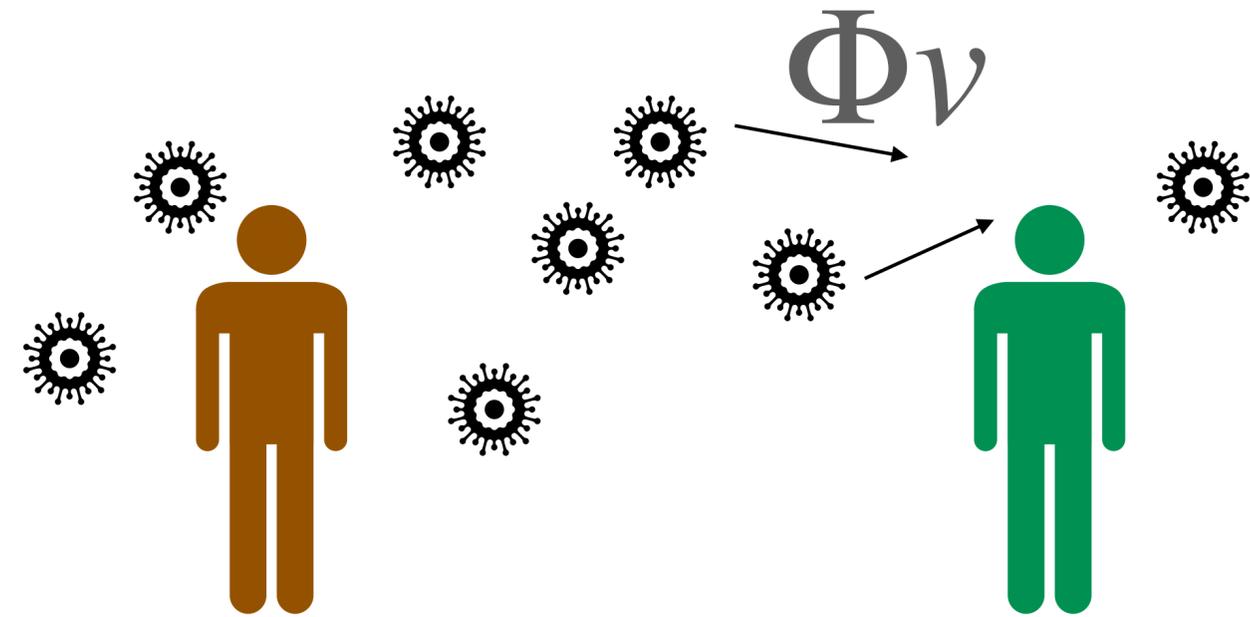


Intraspecific transmission

$$\beta = c \tau \rightarrow \beta(v) = c \tau(v)$$

$$\beta = c \tau \rightarrow \beta(i, r, a) = c \tau(i, r, a)$$

Between host-pairs transmission



Donor

Recipient

## Within-host dynamics

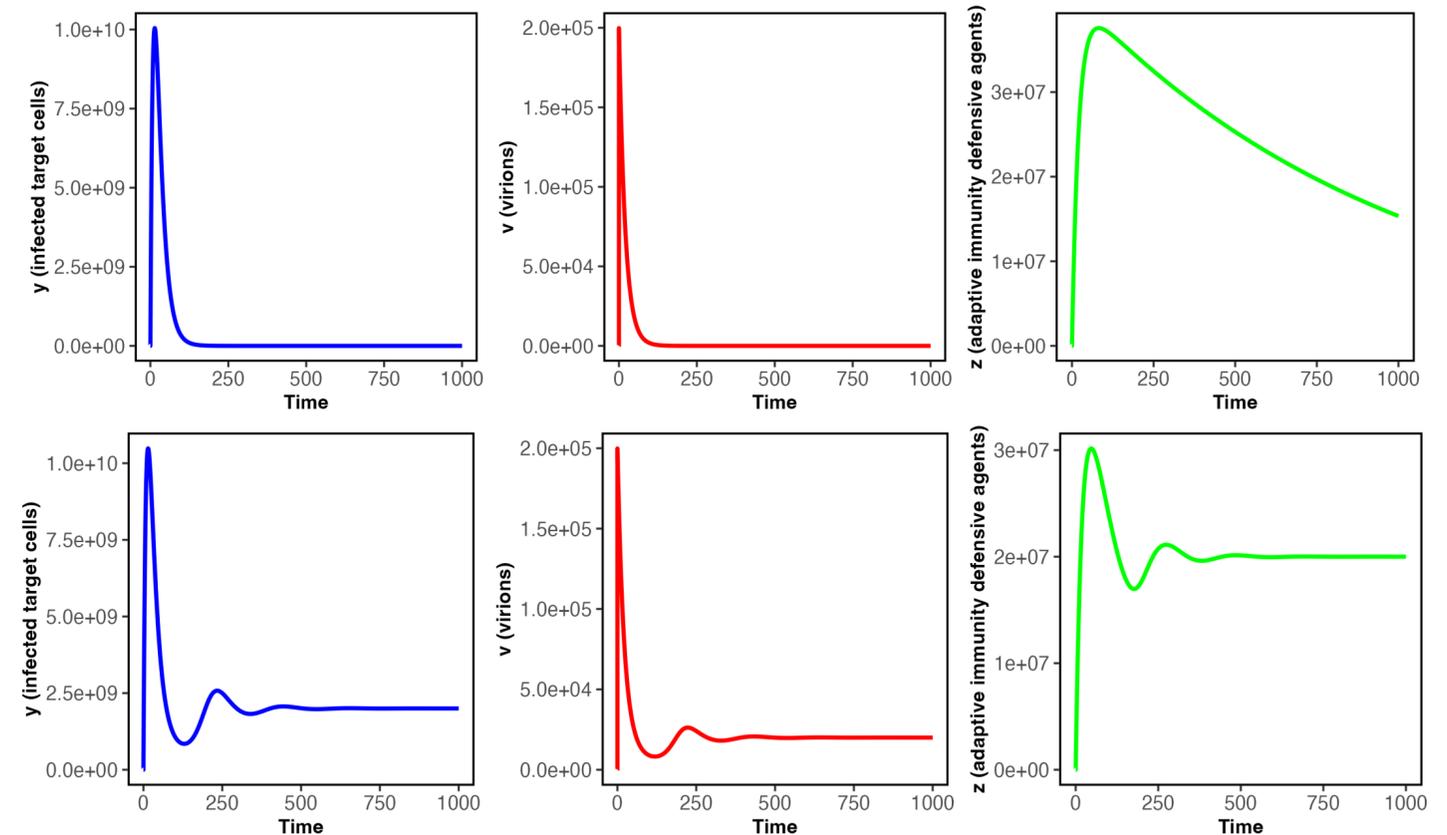
Cells :  $\dot{c} = \Lambda - d_c c - icv$

Infected cells :  $\dot{y} = icv - d_y y$

Virions :  $\dot{v} = ry - mf(a)zv$

Antibodies :  $\dot{z} \propto v$

Cellular level processes

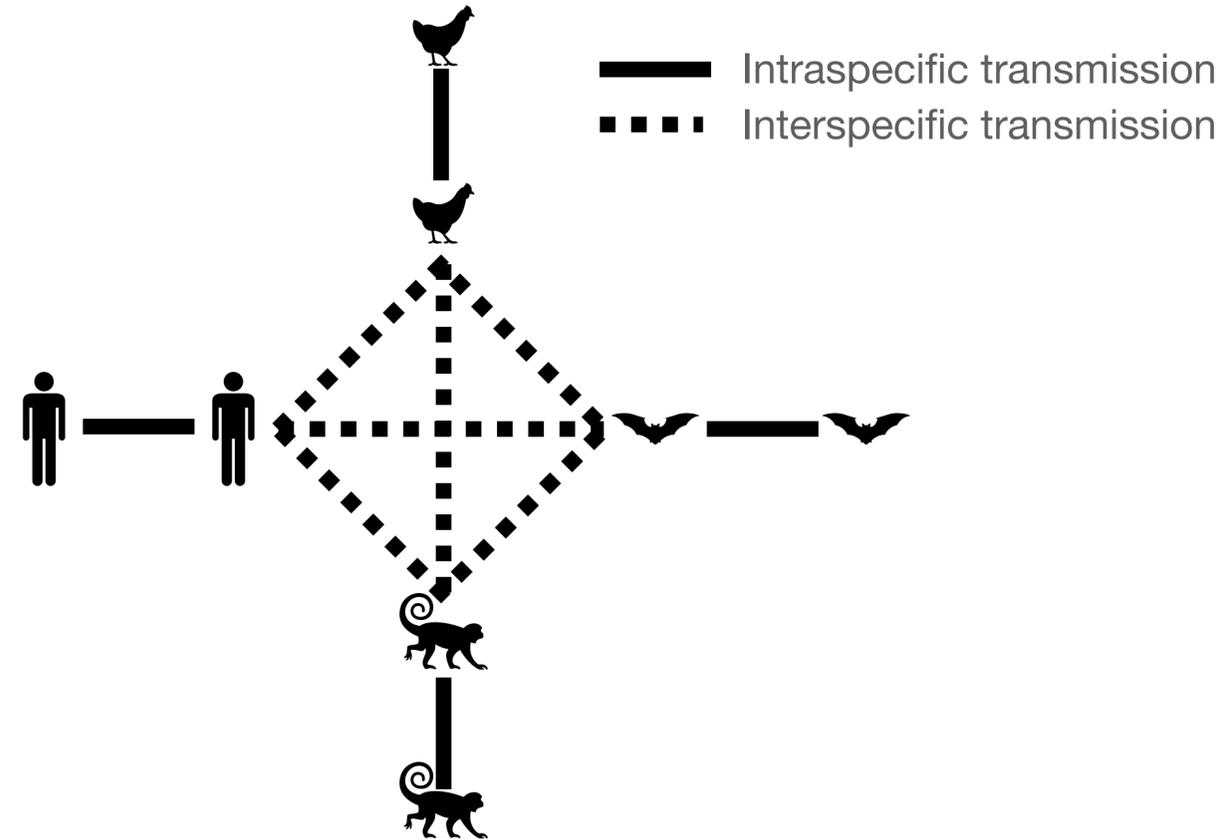


# Multi-species ( $n$ ) and multi-pathogen ( $m$ ) SIS

$$\dot{S}_j = -S_j \sum_{k=1}^n \sum_{i=1}^m \lambda_{jki}(s_i) + \sum_{i=1}^n \gamma_{ji}(s_i) I_{ji}(s_i)$$

$$\dot{I}_{ji} = S_j \sum_{k=1}^n \lambda_{jki}(s_i) - \gamma_{ji}(s_i) I_{ji}(s_i)$$

Species contact structure where we can define for instance “species overlap”



Basic reproduction number ( $R_0$  or  $R'_e$ ) given by the spectral radius of the next-generation matrix:

$$R_0 = \rho \left( -T\Sigma^{-1} \right)$$

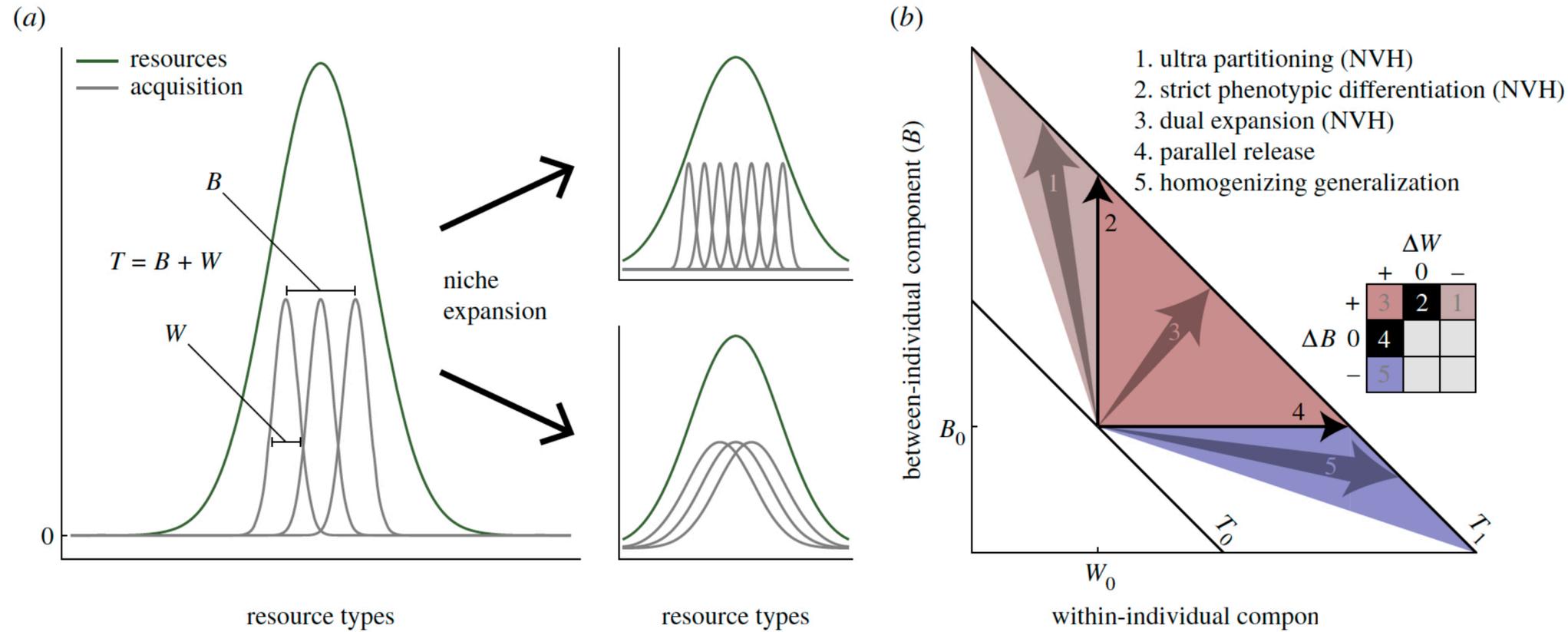
Between-species transmission

# Deterministic approximation of evolutionary dynamics

$$\frac{ds_i}{dt} \propto \frac{dR_e(s_i, \hat{S})}{ds_i}$$

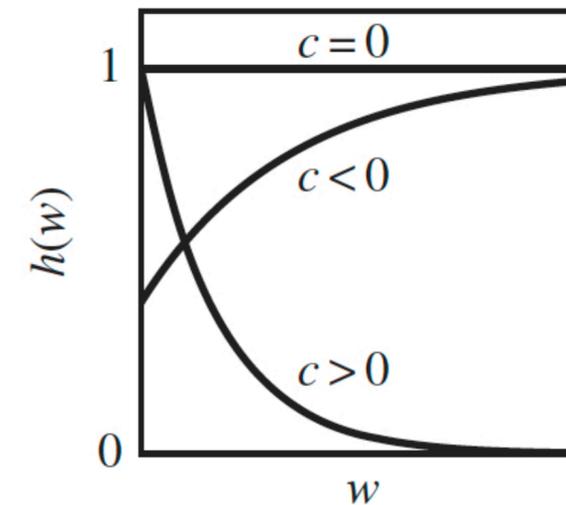
Evolution

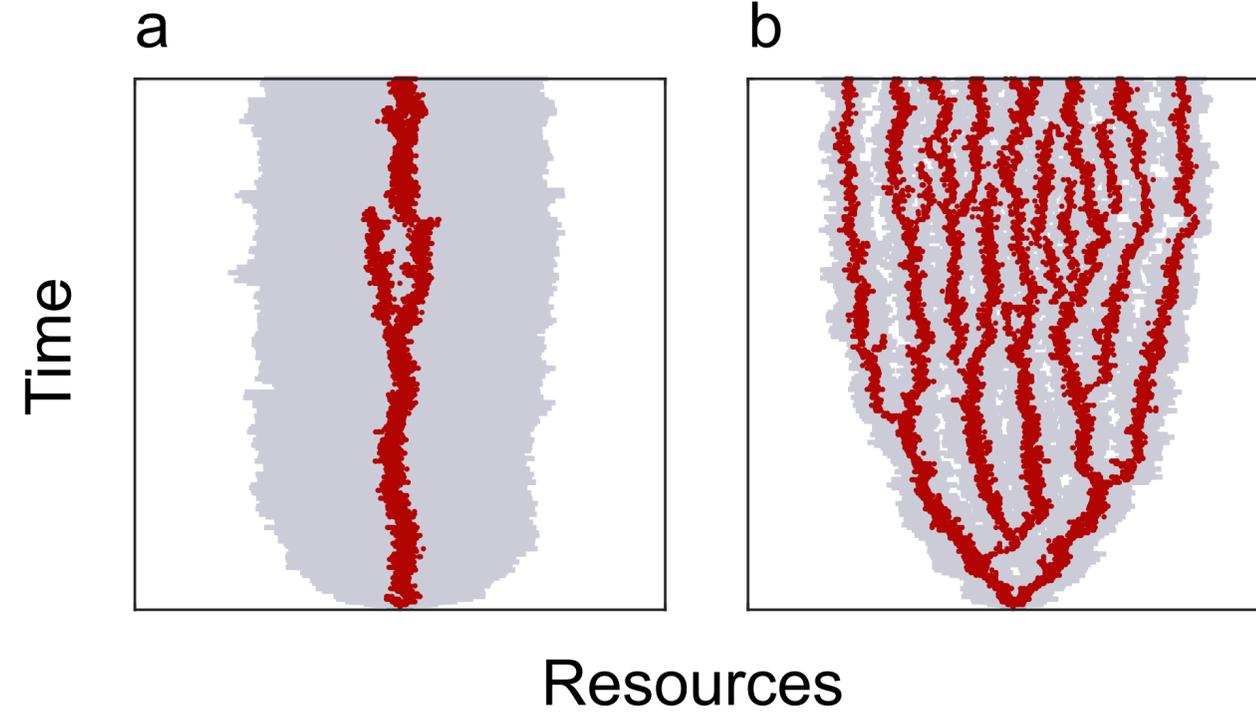
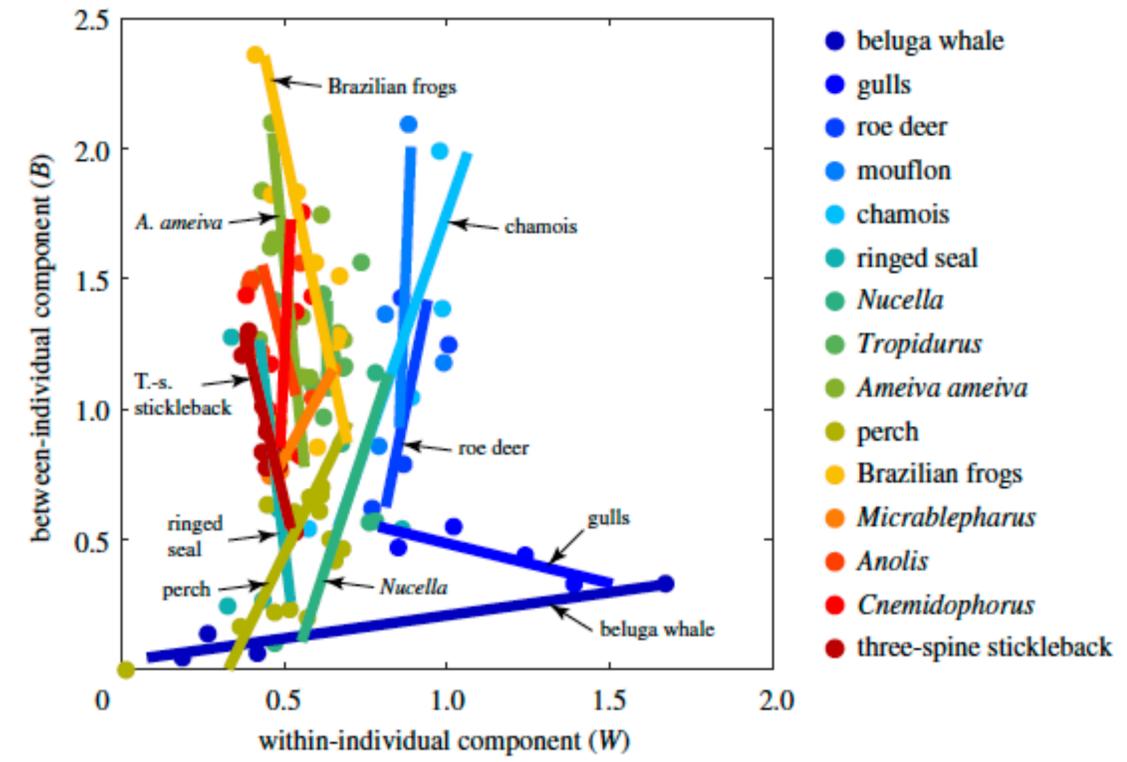
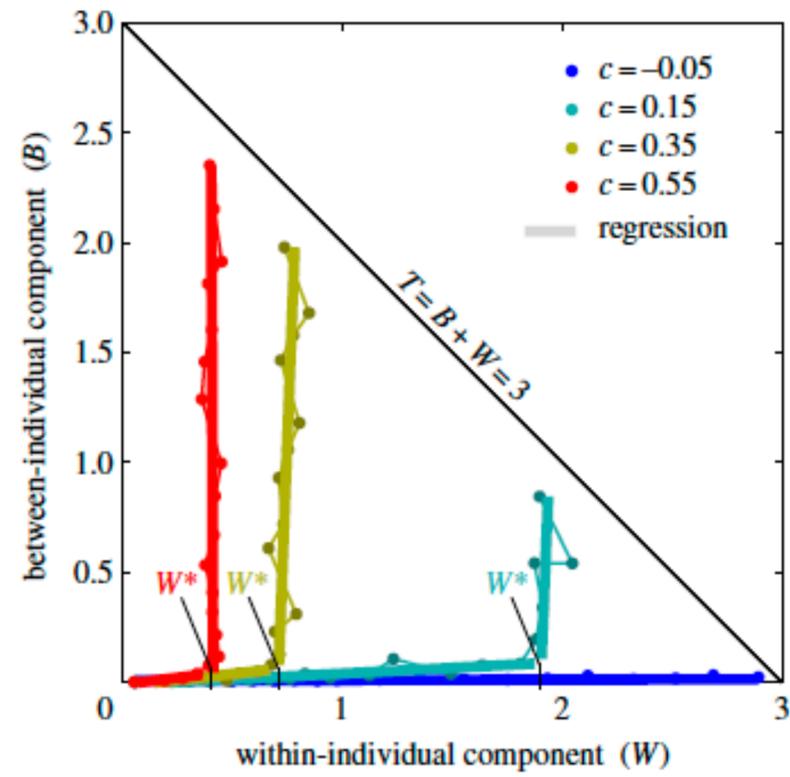
# Host adaptation: niche evolution

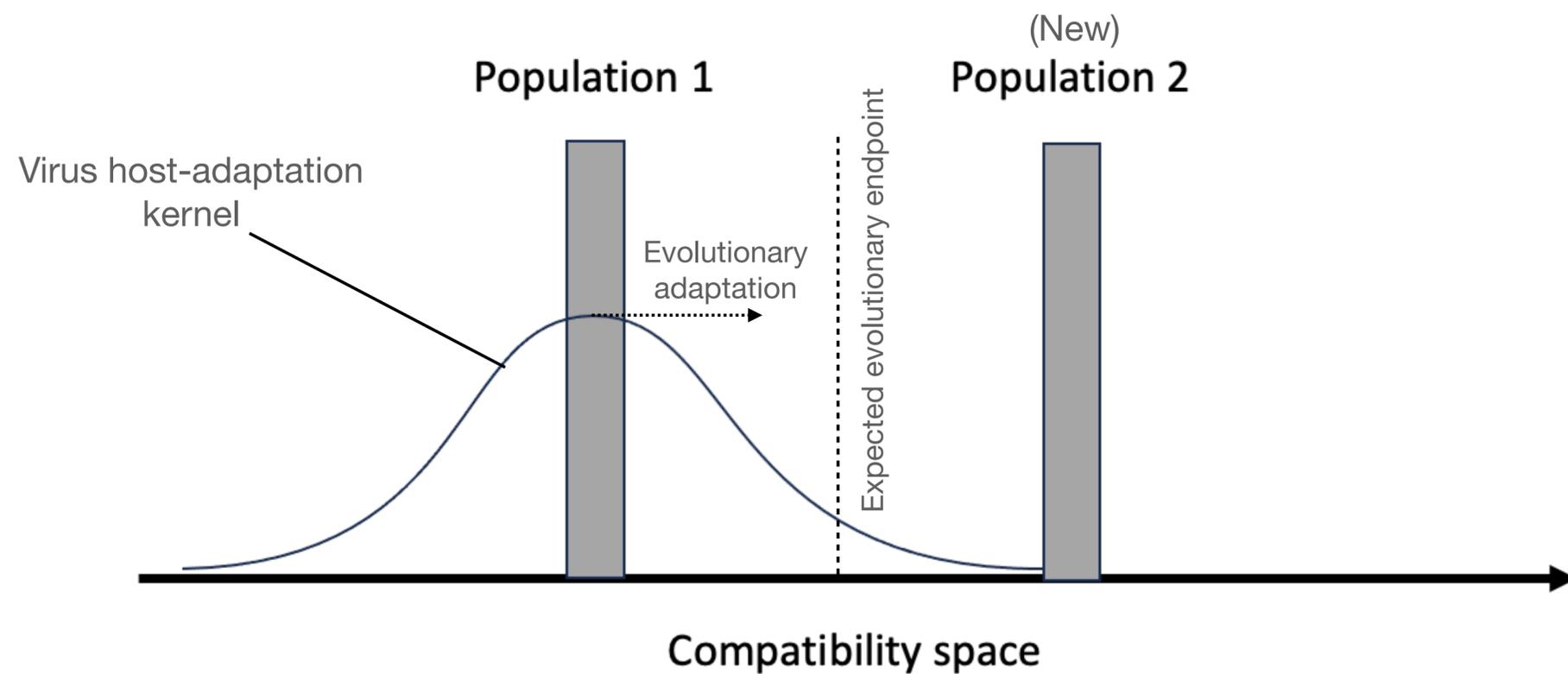


$$a(x, u, w) = \frac{h(w)}{\sqrt{2\pi w}} \exp\left(-\frac{(x-u)^2}{2w^2}\right),$$

$$f(u_i, w_i) = q\left(b \int_x a(x, u_i, w_i) R^*(x) dx - m\right),$$



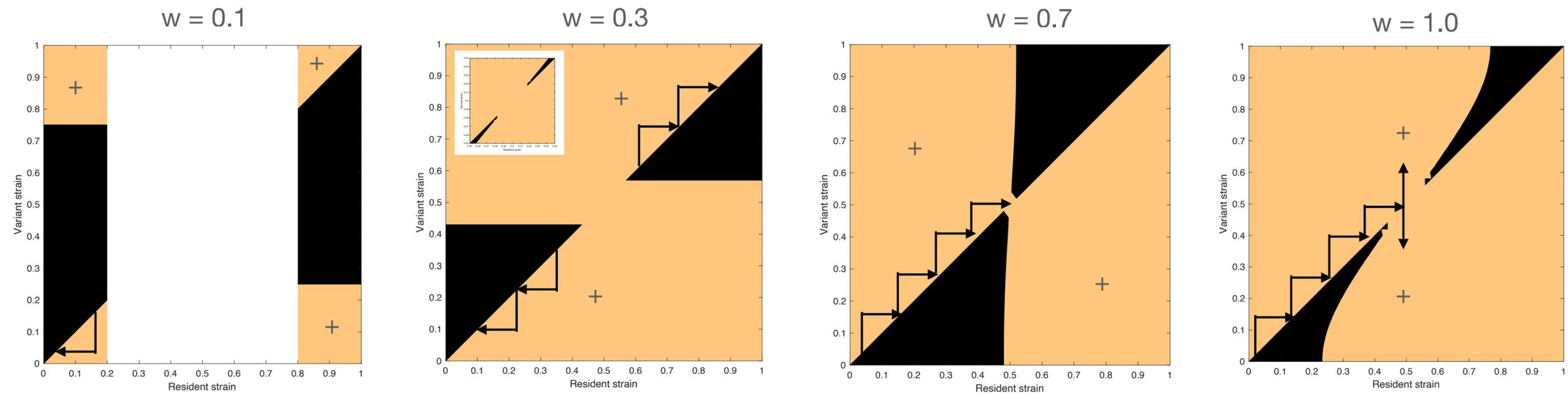




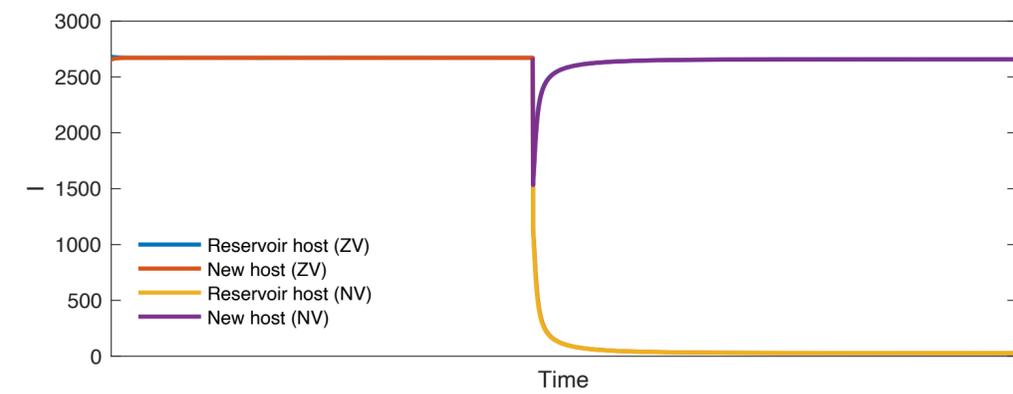
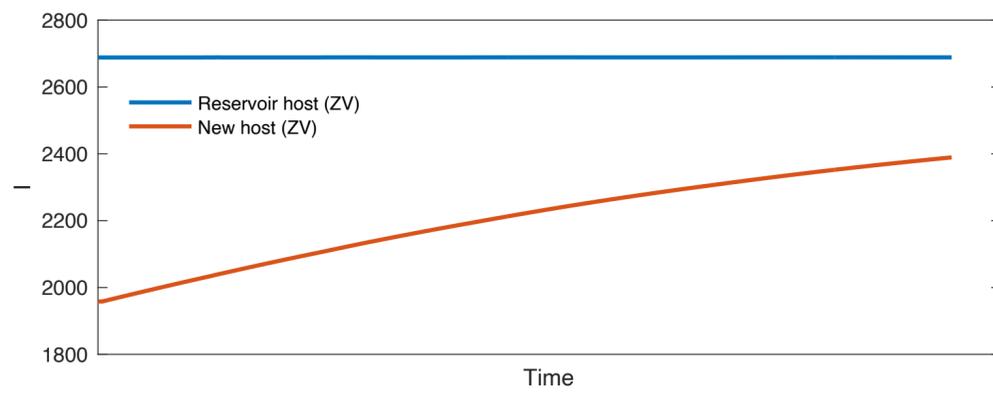
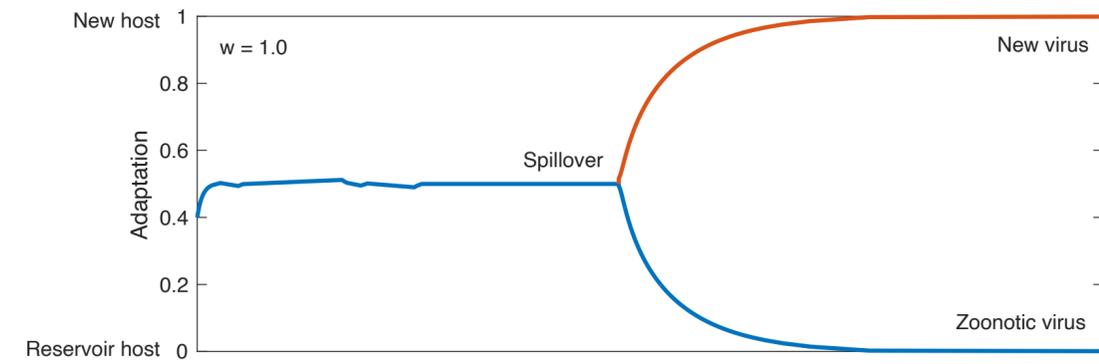
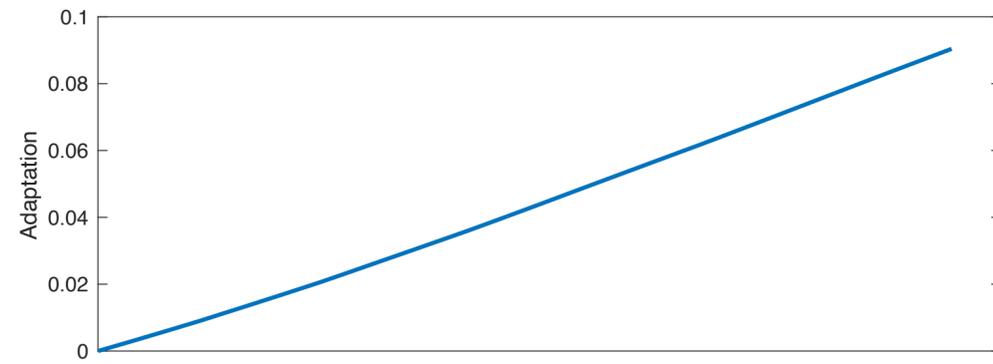
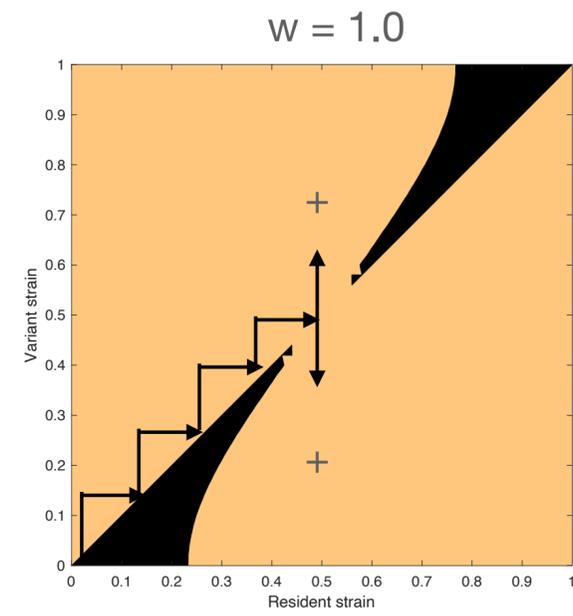
- Population 1 and 2 has a 0.01 overlap.
- All parameters are fixed except of niche position.
- Neutral cost to generalism.
- (1) Degree of host specificity?
- (2) Degree of cross-species interaction?

# Example: Pairwise invisibility plots

$w$  = “host breadth“ or “host-adaptation width”

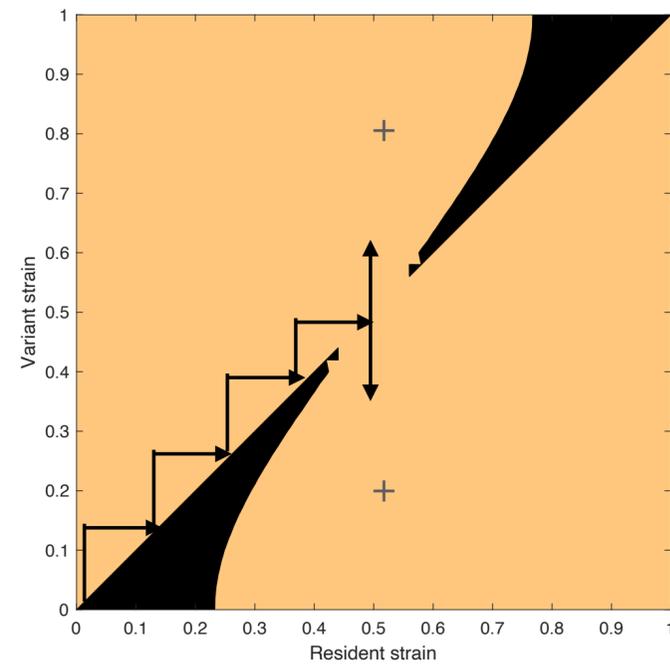


# Spillover

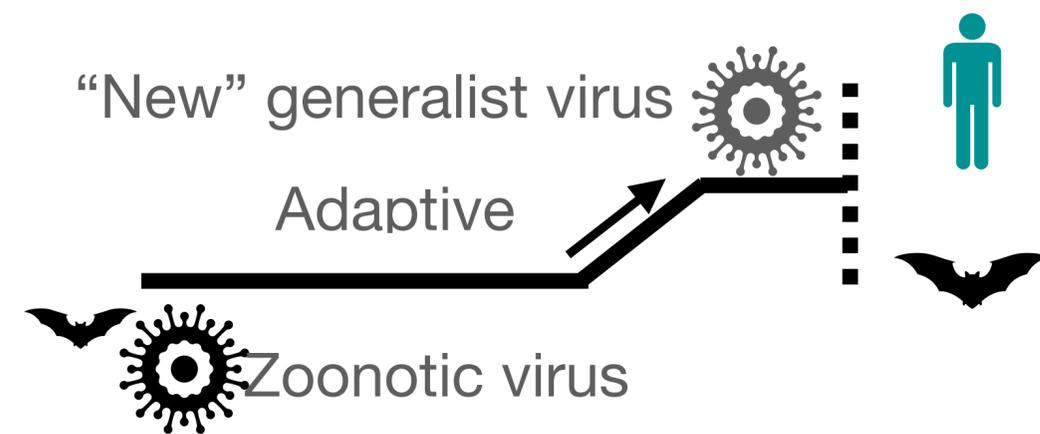
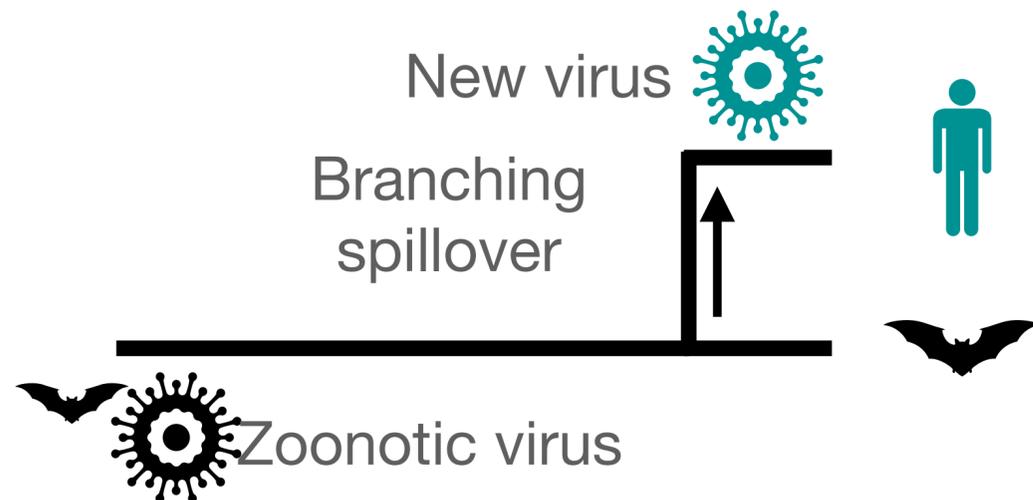
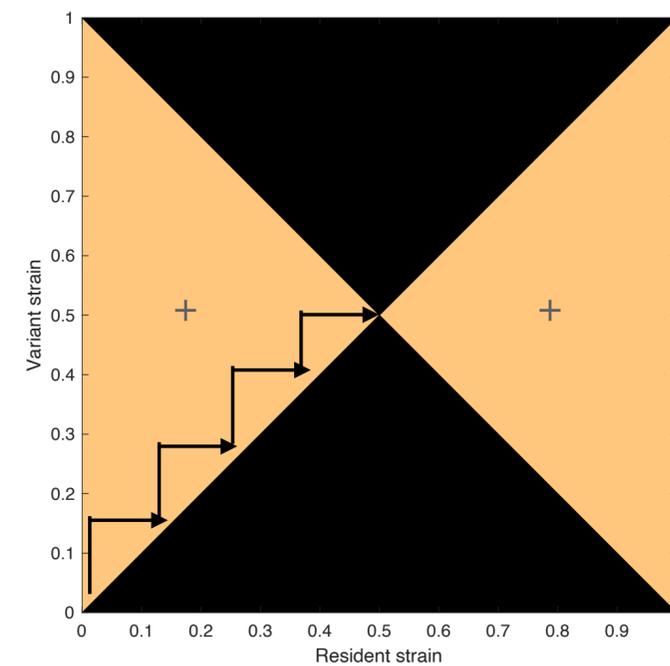


# Spillover

Species overlap = 0.01



Species overlap = 0.5



- Host width can evolve
- Replication- and cell-infection rates can evolve
- Antigenic drift/adaptation (Willian Silva)
- Virulence feedback to contact rates (Willian Silva)
- Explicit network-based species contact structure (Peter Fransson)
- Phylogenetic pathogen-host compatibility space (Peter Fransson)