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Nordic Institute for Theoretical Physics

The evolution of infectious diseases: connecting within- and between-host processes

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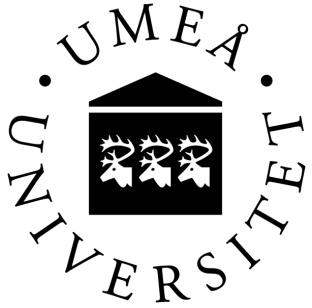


Introduction

What drives pathogen evolution?

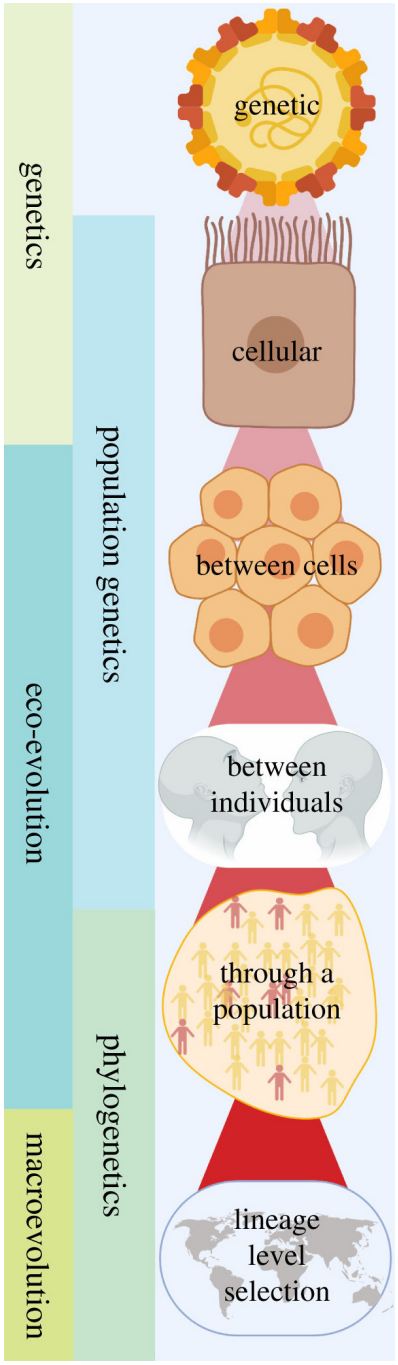
- *Changes in processes that occur at many different levels.*

How are different biological levels connected during pathogen evolution?

- *Via collective processes that span across different physical and temporal levels.*

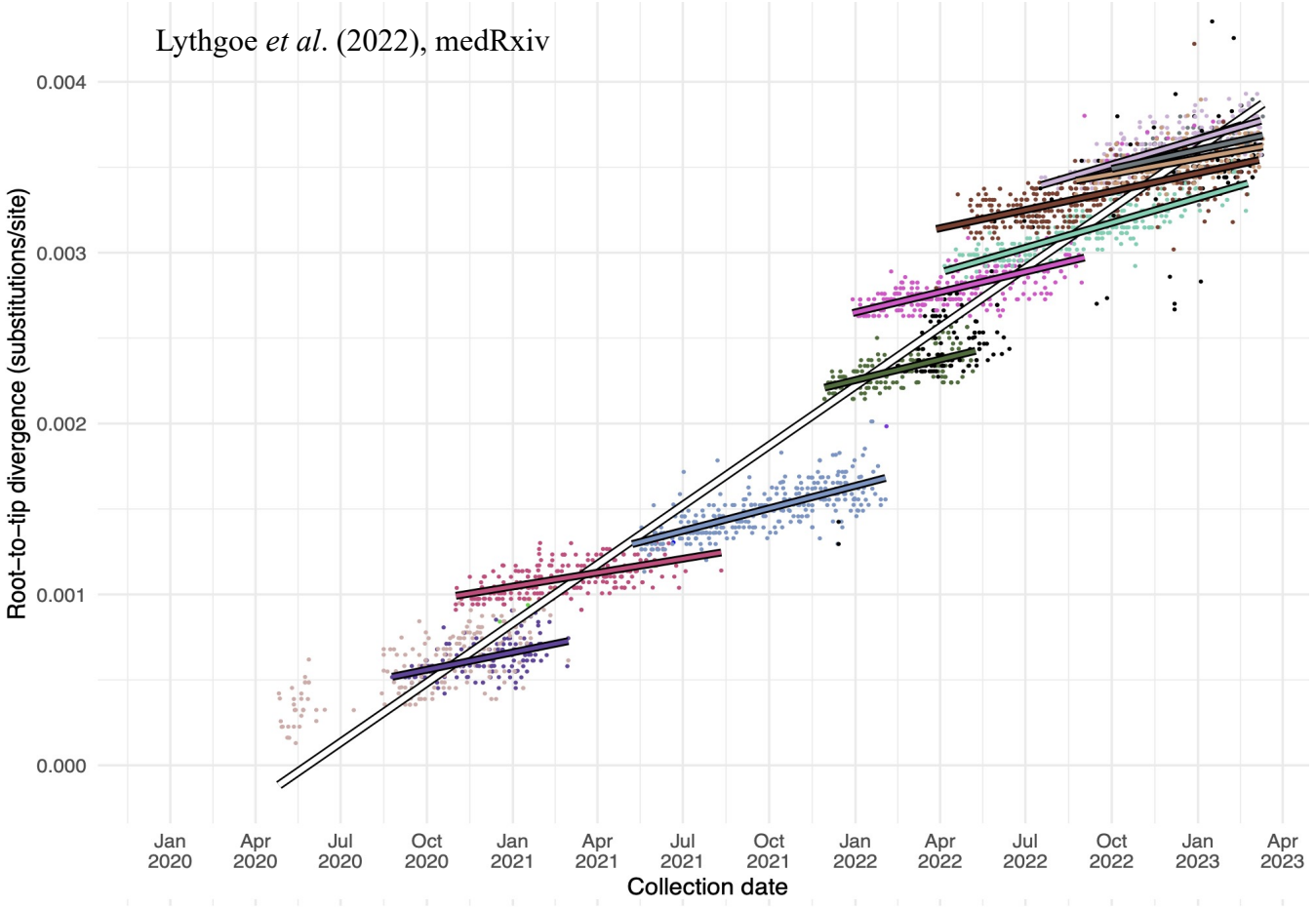
What makes a pathogen successful?

- *Variation in the pathogen's ability to spread and the availabibity of resources (susceptible individuals).*



Modified from Visher and Boots (2020). DOI: 10.1098/rspb.2020.1230

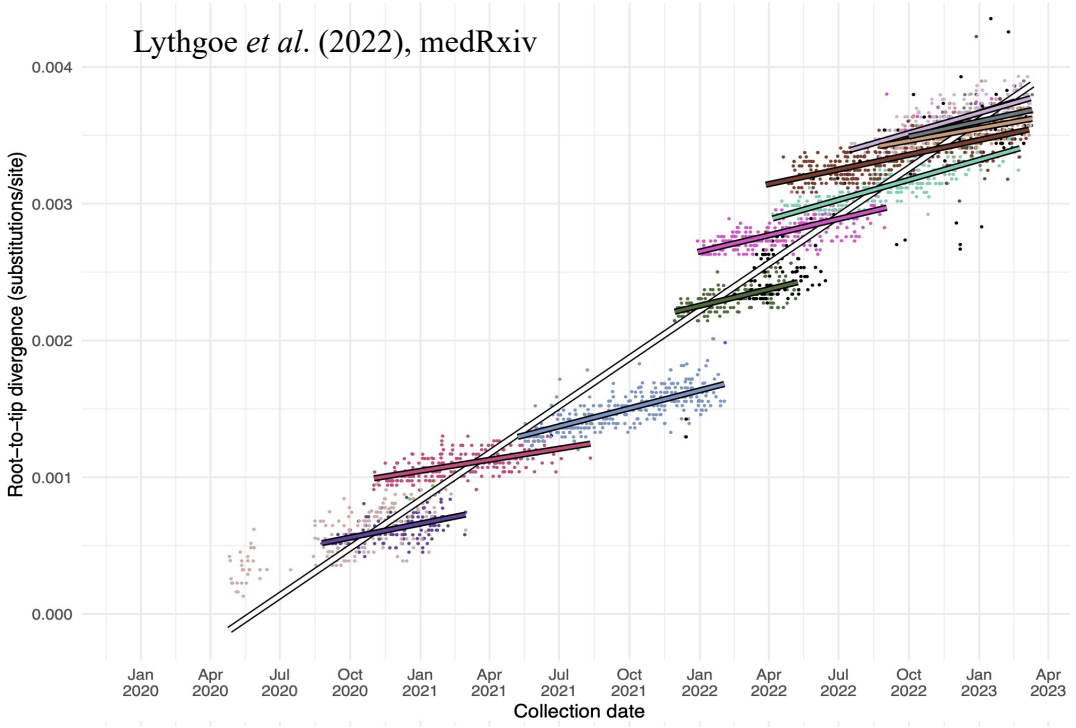
Introduction



Introduction

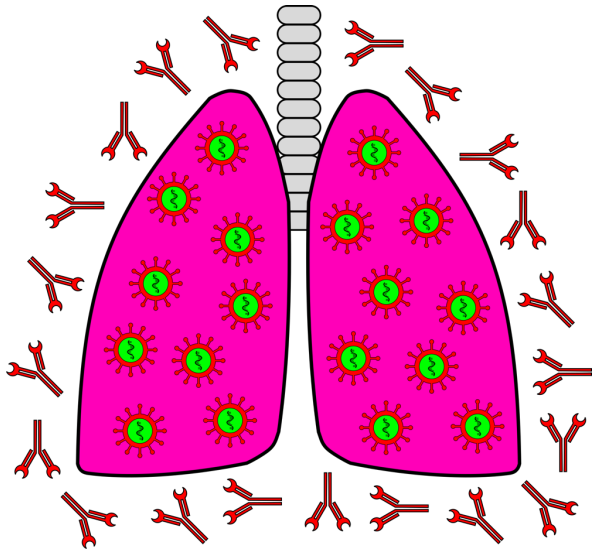
The observed evolutionary pattern is a consequence of

- Changes in processes that occur at many different levels.
- Collective processes that span across different physical and temporal levels.
- Variation in the pathogen's ability to spread and the availabibity of resources (susceptible individuals).

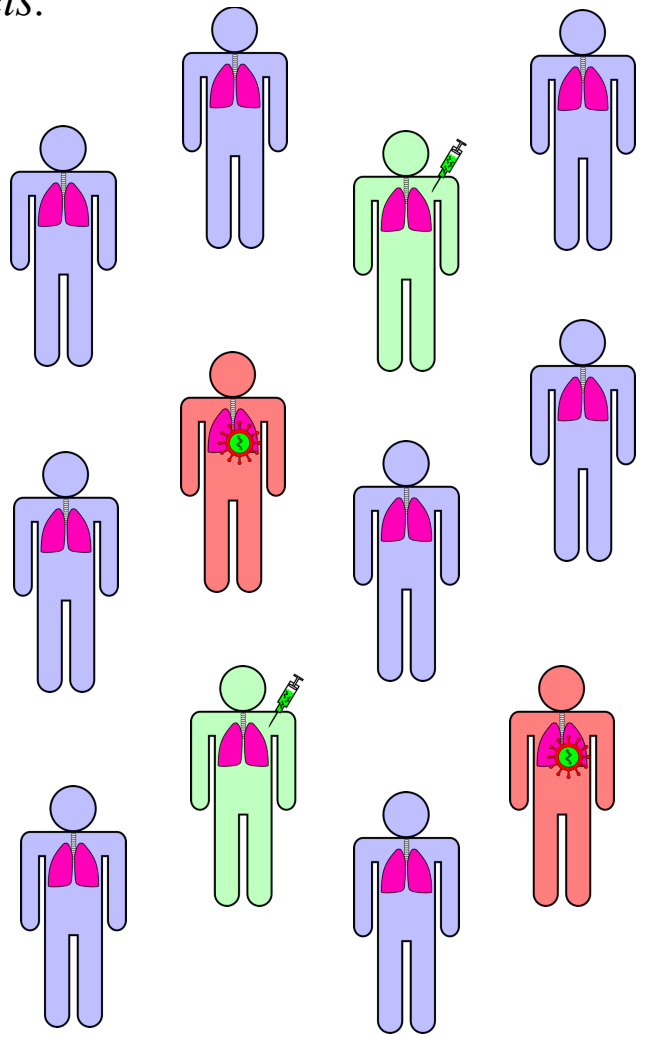


Introduction

- *Processes at different biological levels.*
- *Collective processes spanning across biological levels.*
- *Trait variation and availability of resources.*

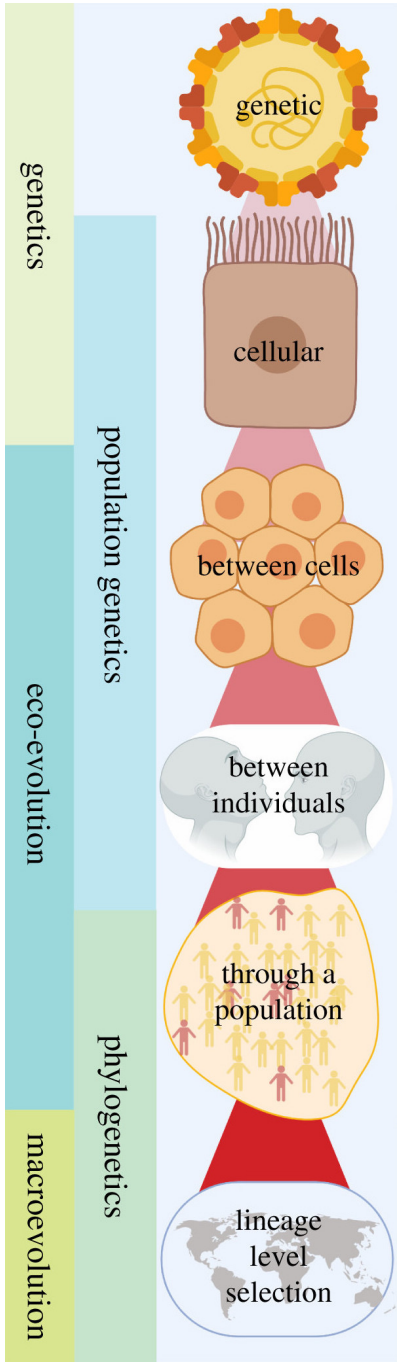


Within-host dynamics



Between-host dynamics

Introduction

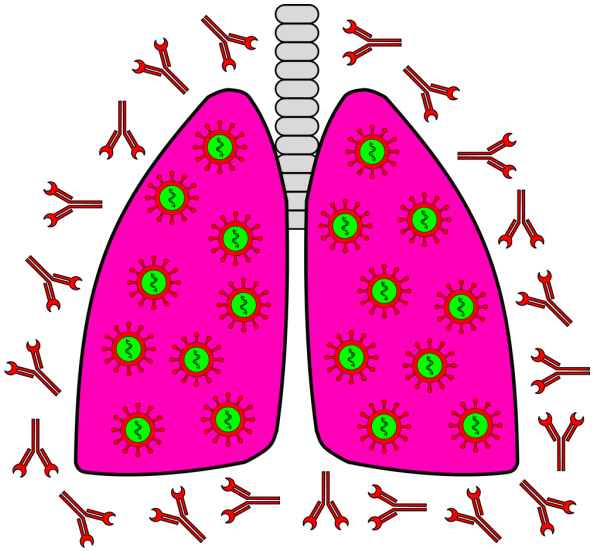


Modified from Visher and Boots (2020). DOI: 10.1098/rspb.2020.1230

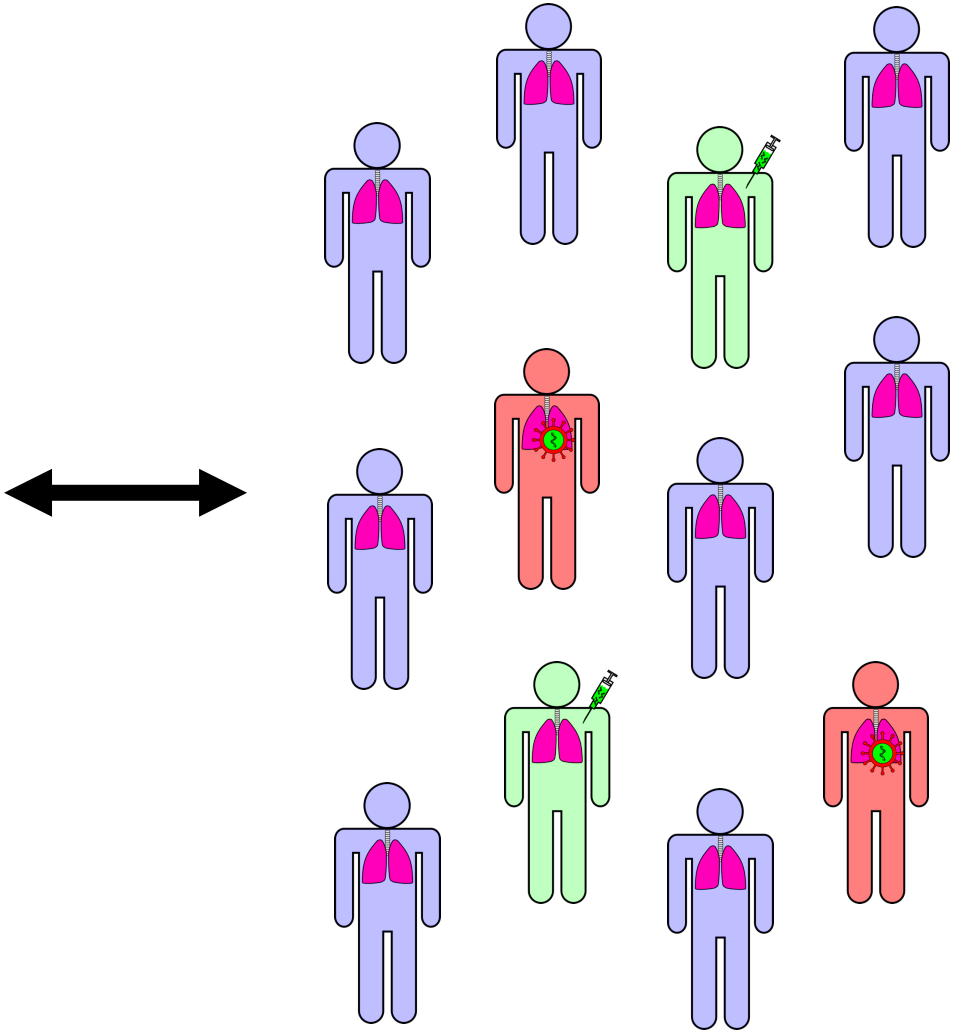
Within-host evolution:
Selection pressure to maximize within-host fitness (viral load).

Between-host evolution:
Selection pressure to maximize between-host fitness (transmission).

Introduction

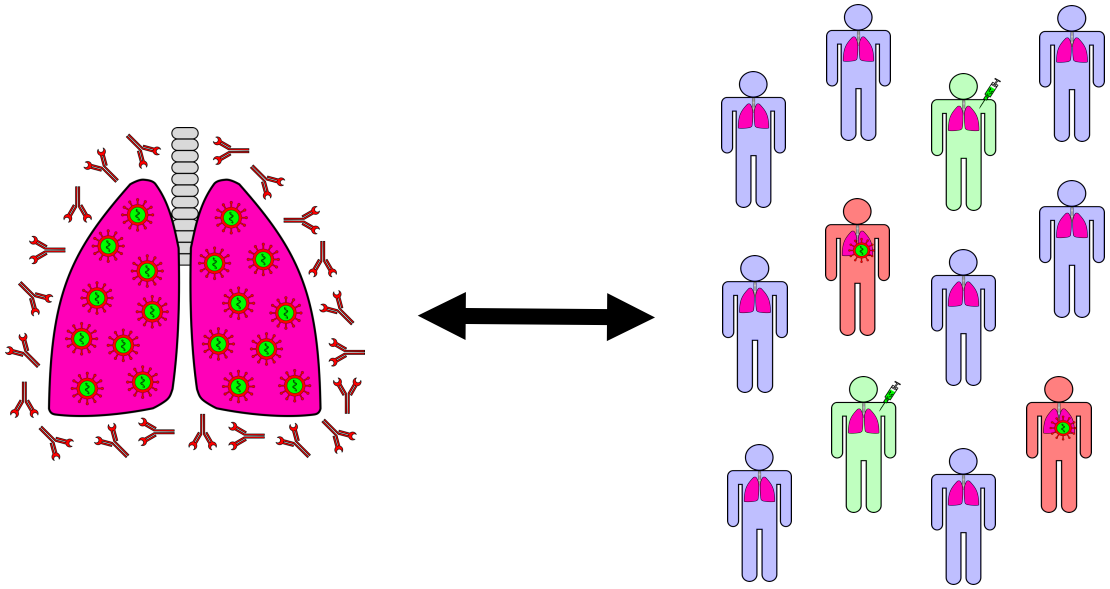


Within-host dynamics



Between-host dynamics

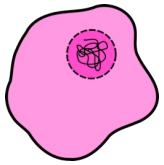
Introduction



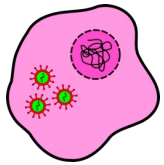
How does individual immunity due to vaccination and/or previous infections affect epidemiological dynamics and virus evolution?

What causes the patterns of variant substitution and saltational evolution that we observe in empirical data?

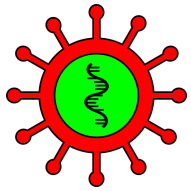
Within-host dynamics



$$\frac{du}{dt} = \lambda - d \cdot u(t) - i_j \cdot v_j(t) \cdot u(t)$$

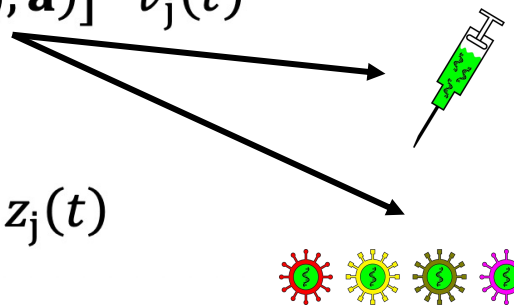


$$\frac{dy_j}{dt} = i_j \cdot v_j(t) \cdot u(t) - \omega \cdot y_j(t)$$

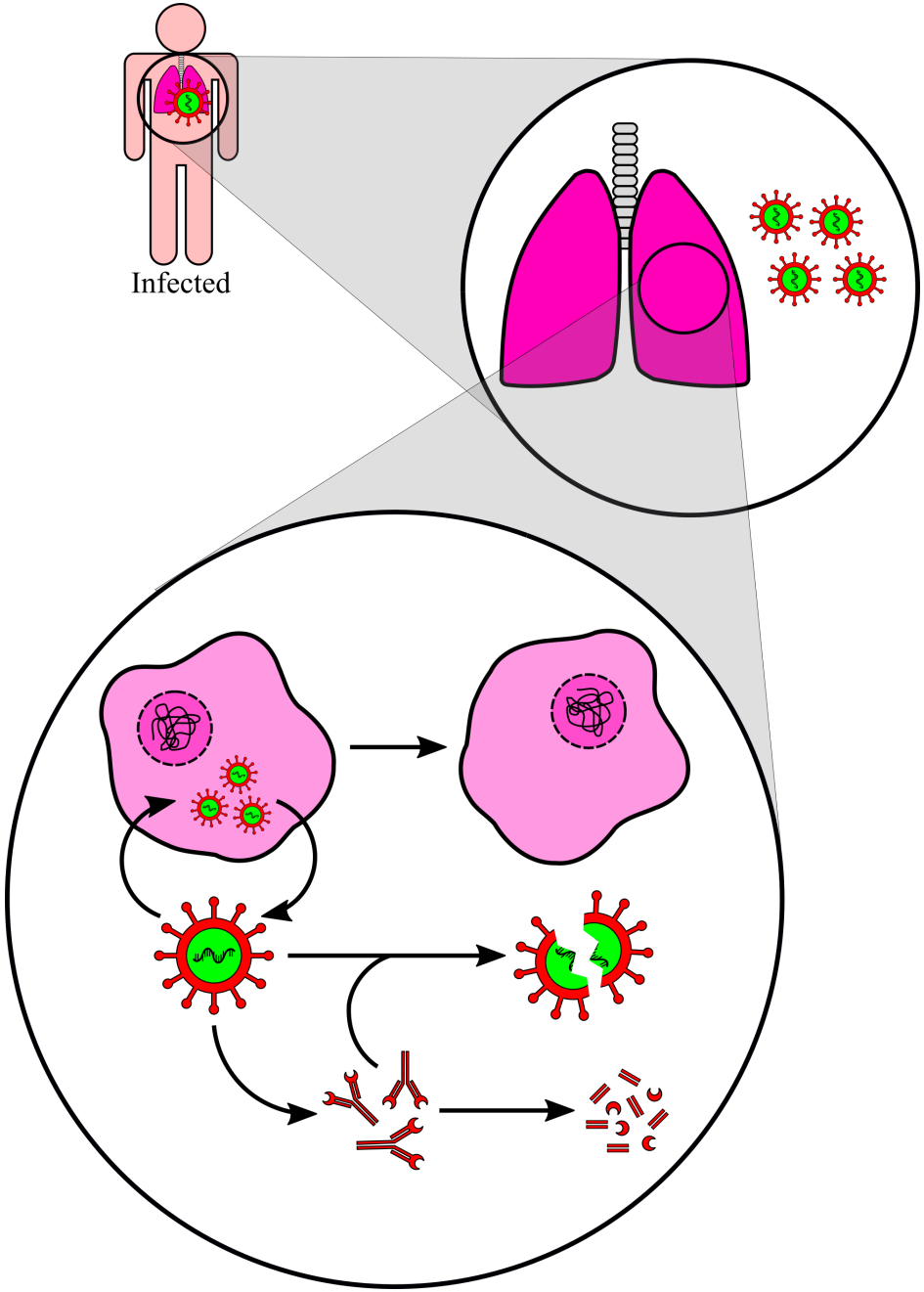


$$\frac{dv_j}{dt} = r_j \cdot y_j(t) - \left[m + \alpha_j(\mathbf{z}(t), \mathbf{a})\right] \cdot v_j(t)$$

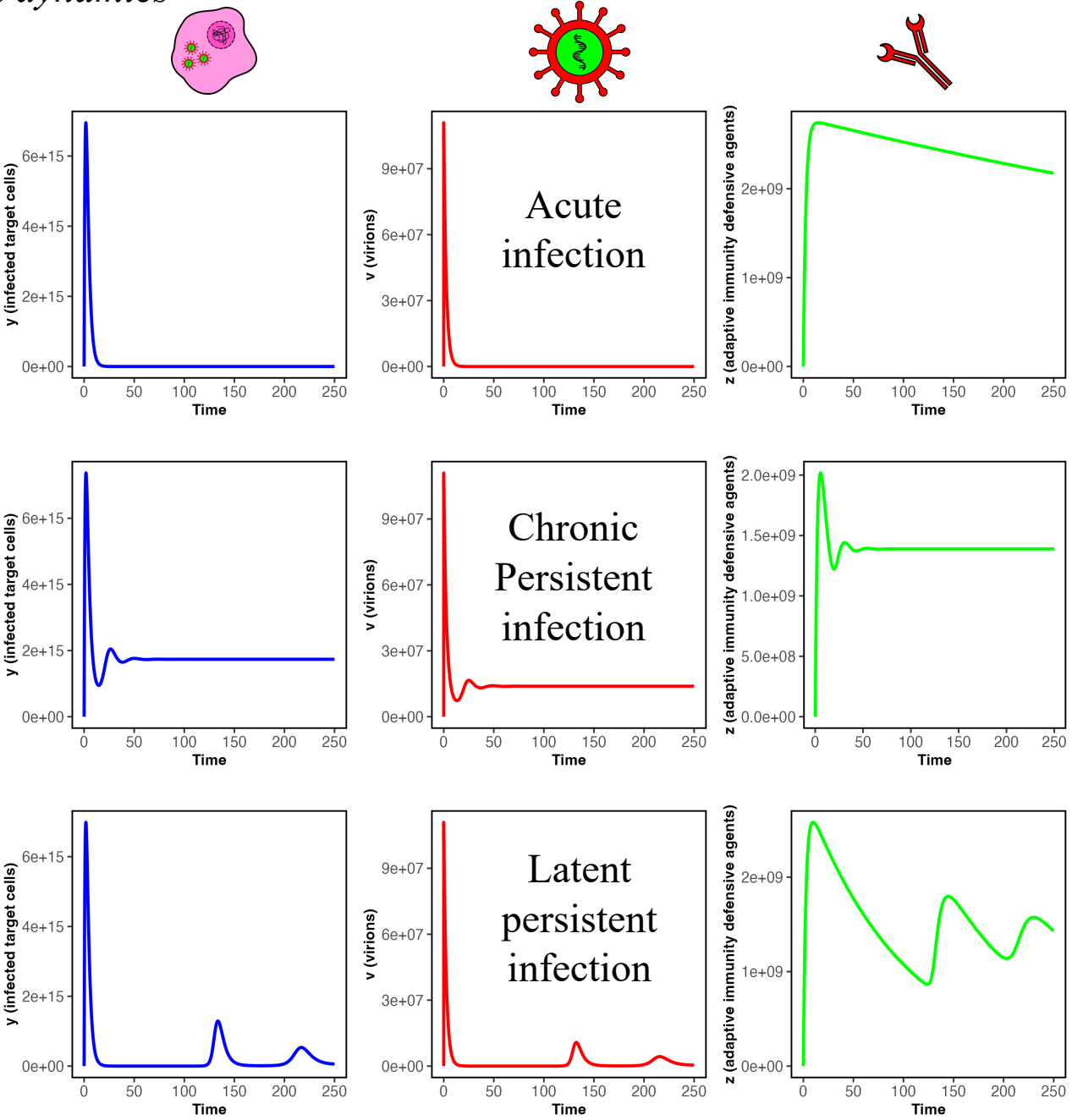
$$\frac{dz_j}{dt} = \zeta(a_j) \cdot v_j(t) - \eta \cdot z_j(t)$$



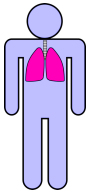
Within-host dynamics



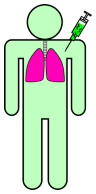
Within-host dynamics



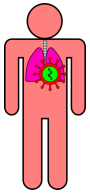
Between-host dynamics



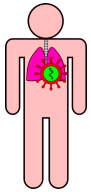
$$\frac{dS}{dt} = -\beta_{SS}(c,\tau_{SS}) \cdot S(t) \cdot I_S(t) - \beta_{VS}(c,\tau_{VS}) \cdot S(t) \cdot I_V(t)$$



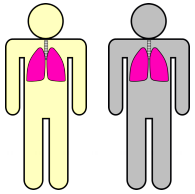
$$\frac{dV}{dt} = [h_S - \beta_{SV}(c,\tau_{SV}) \cdot V(t)] \cdot I_S(t) + [h_V - \beta_{VV}(c,\tau_{VV}) \cdot V(t)] \cdot I_V(t)$$



$$\frac{dI_S}{dt} = [\beta_{SS}(c,\tau_{SS}) \cdot S(t) - \gamma_S(\mu_S) - \theta(\bar{\mu}) - h_S] \cdot I_S(t) + \beta_{VS}(c,\tau_{VS}) \cdot S(t) \cdot I_V(t)$$

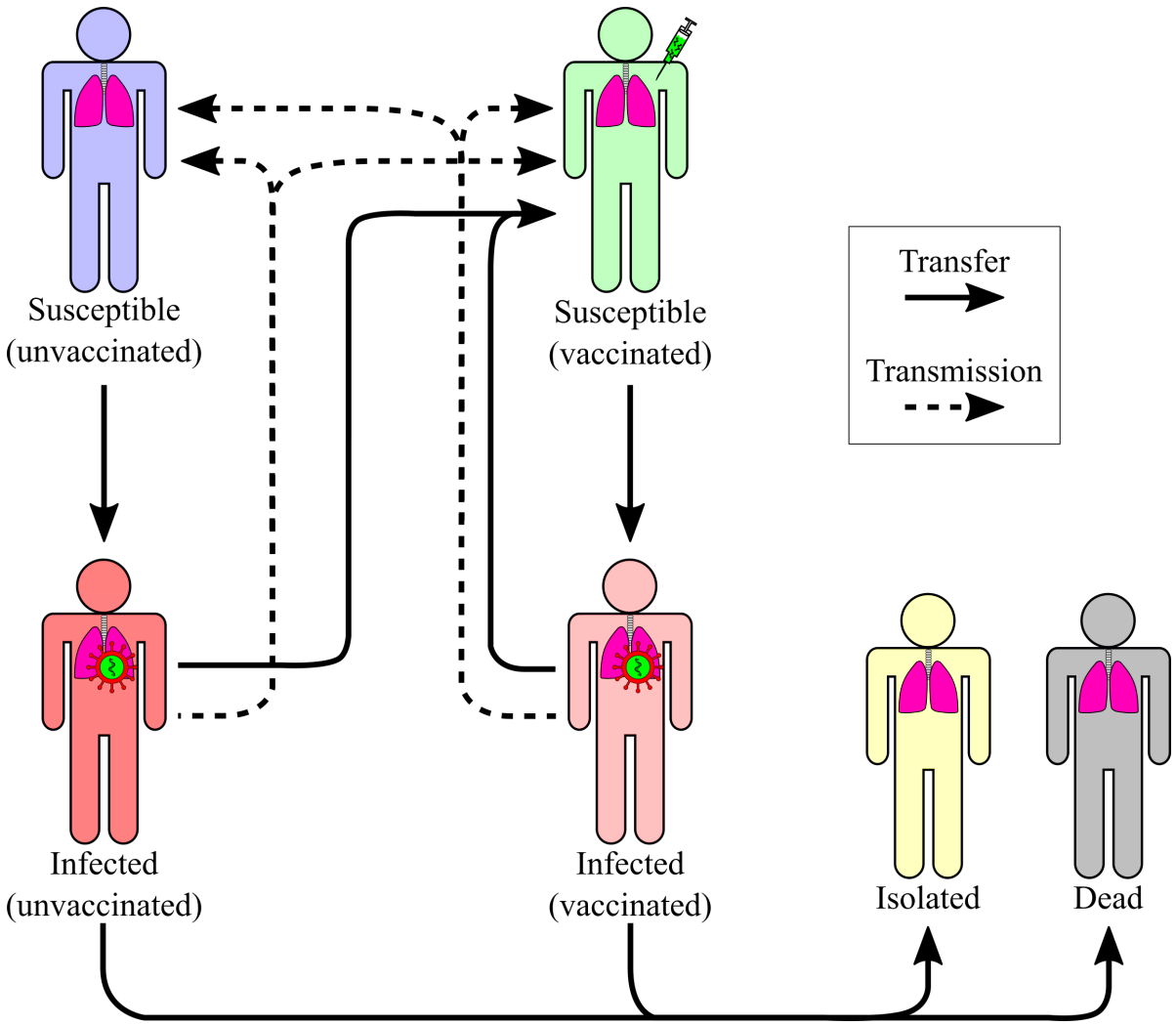


$$\frac{dI_V}{dt} = [\beta_{VV}(c,\tau_{VV}) \cdot V(t) - \gamma_V(\mu_V) - \theta(\bar{\mu}) - h_V] \cdot I_V(t) + \beta_{SV}(c,\tau_{SV}) \cdot V(t) \cdot I_S(t)$$

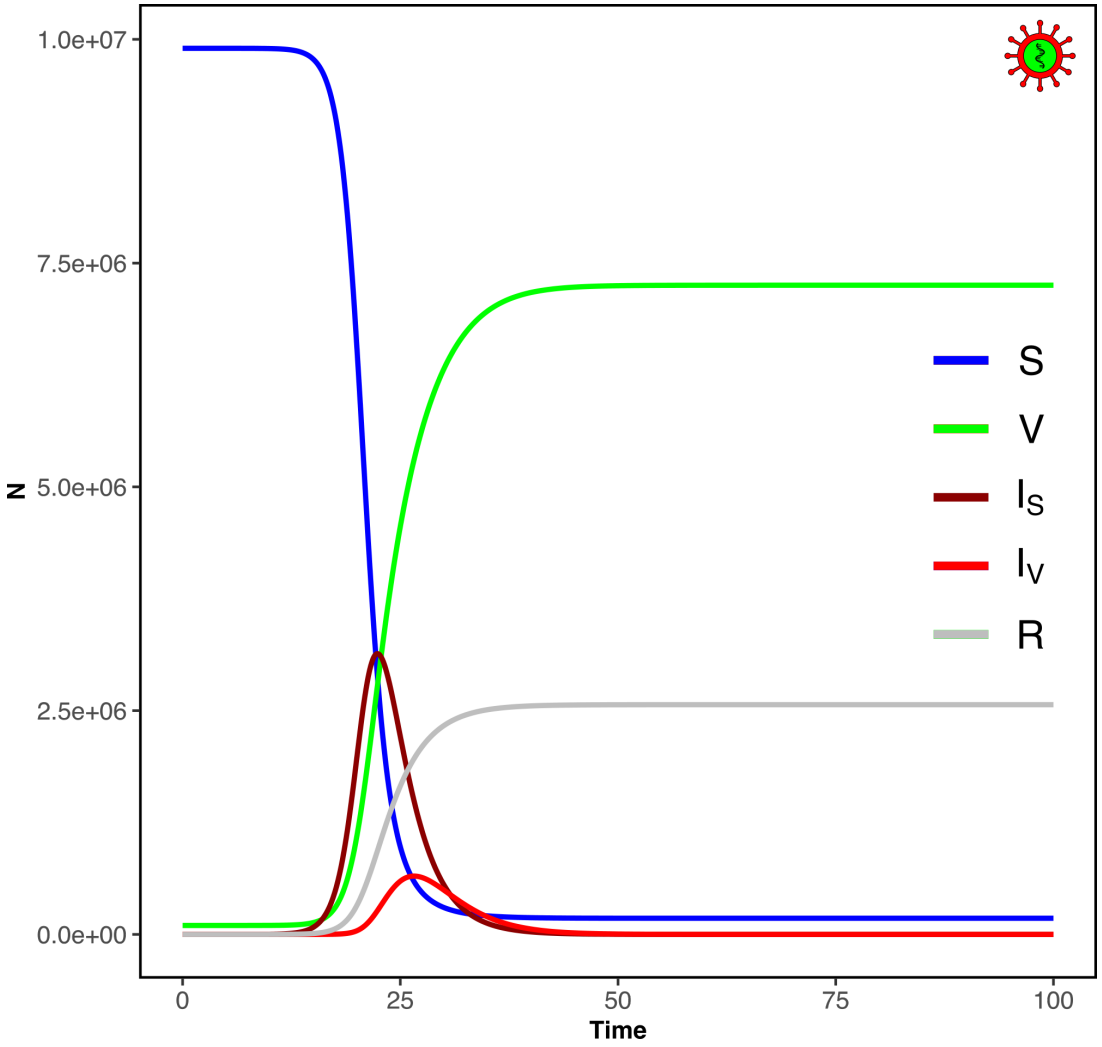


$$\frac{dR}{dt} = [\gamma_S(\mu_S) + \theta(\bar{\mu})] \cdot I_S(t) + [\gamma_V(\mu_V) + \theta(\bar{\mu})] \cdot I_V(t)$$

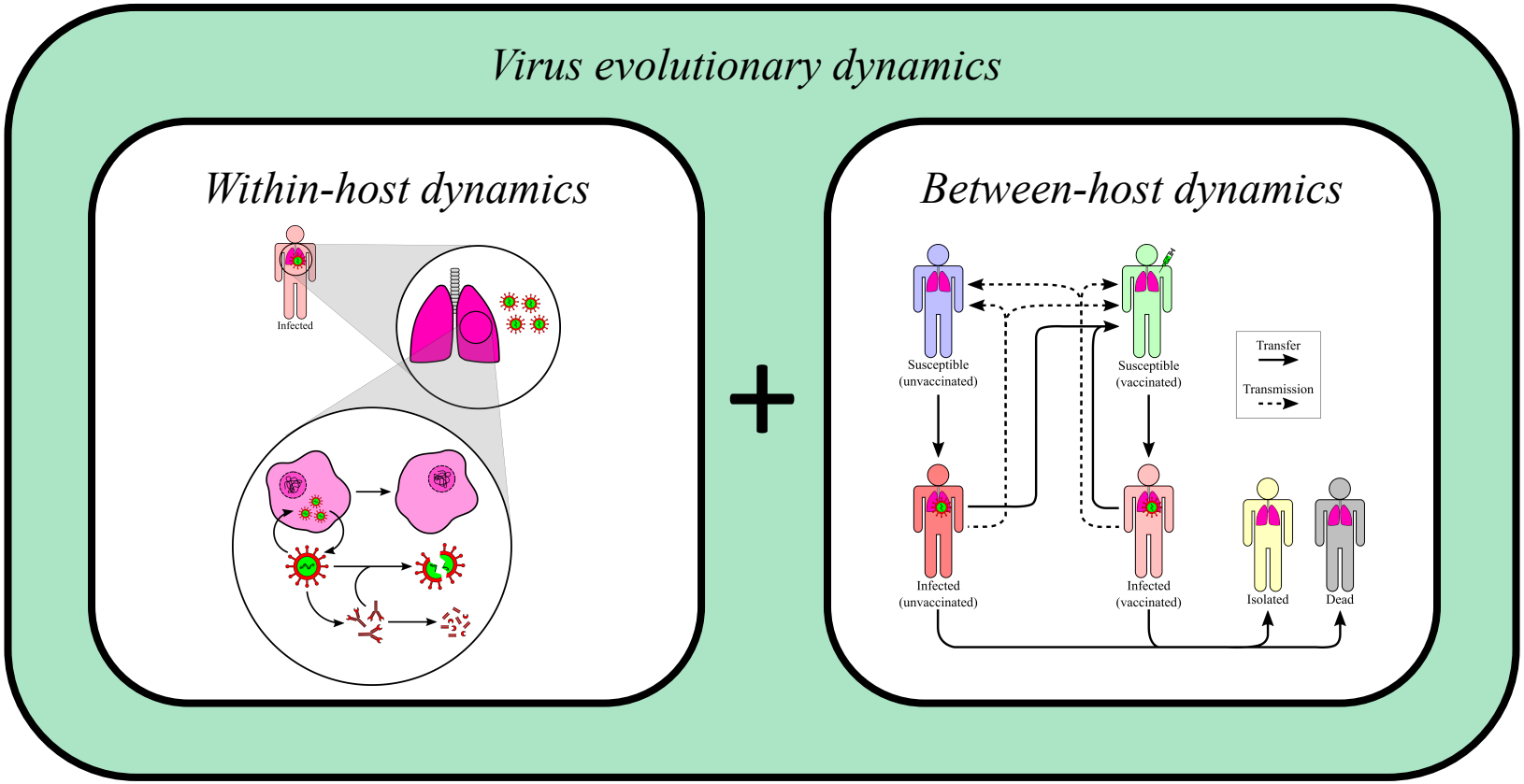
Between-host dynamics



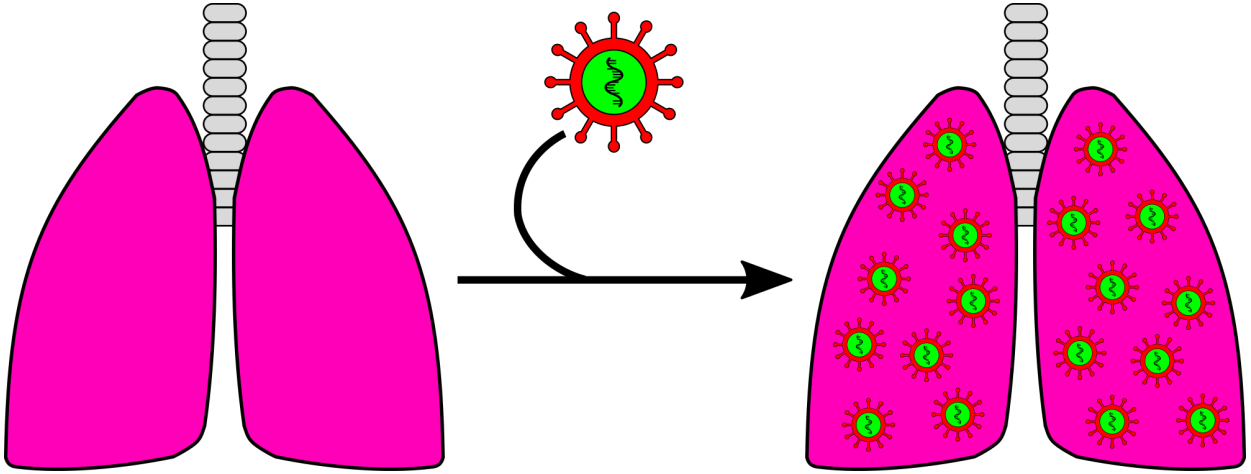
Between-host dynamics



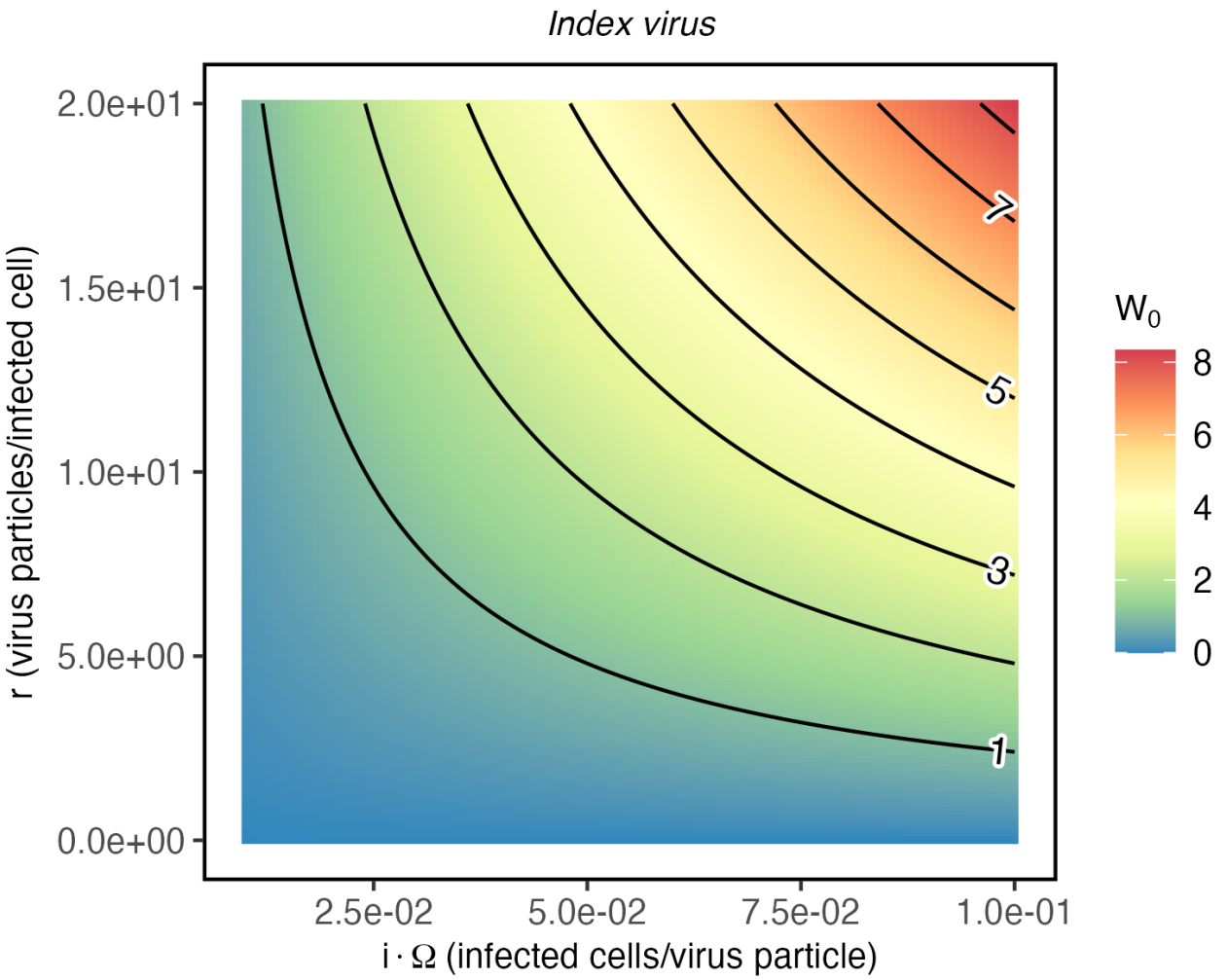
Virus evolutionary dynamics



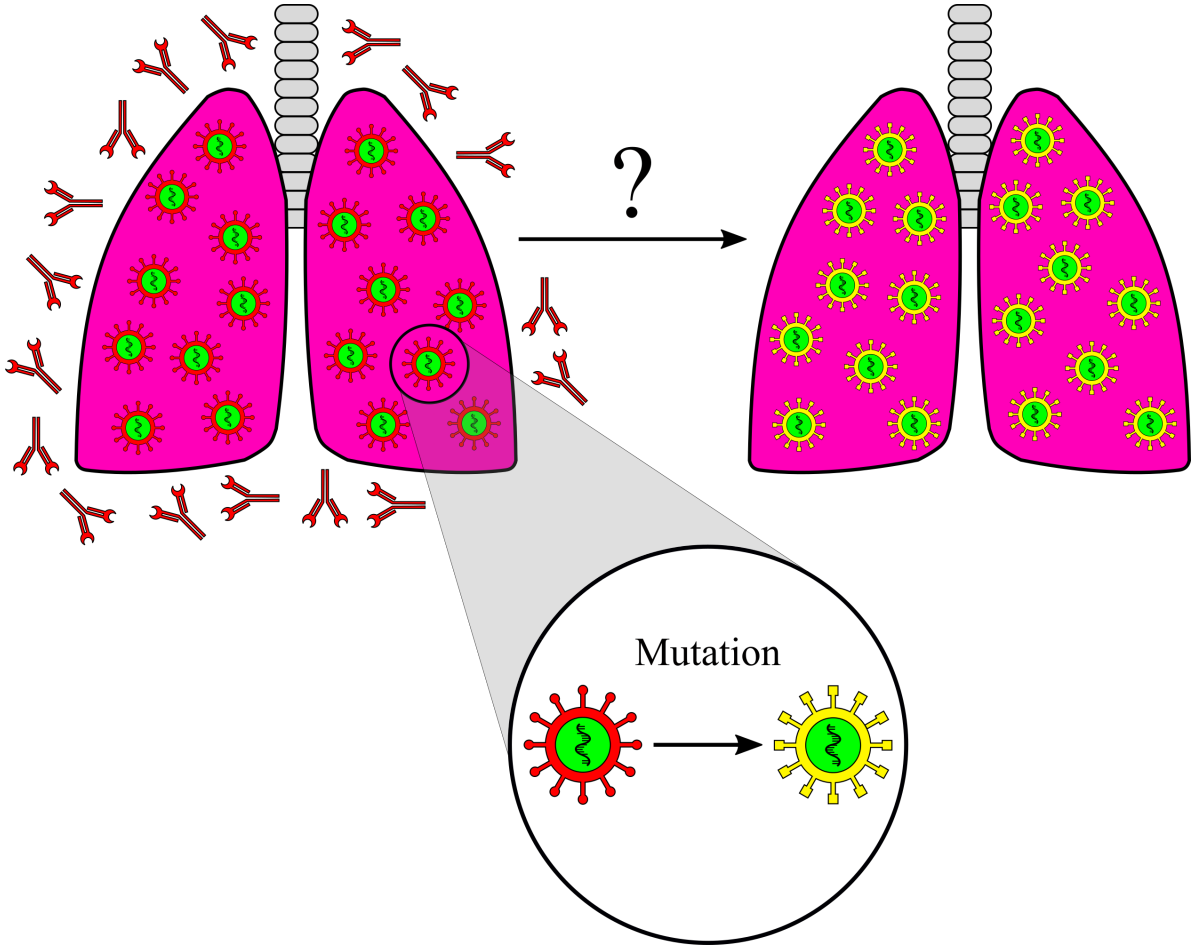
Within-host evolutionary dynamics



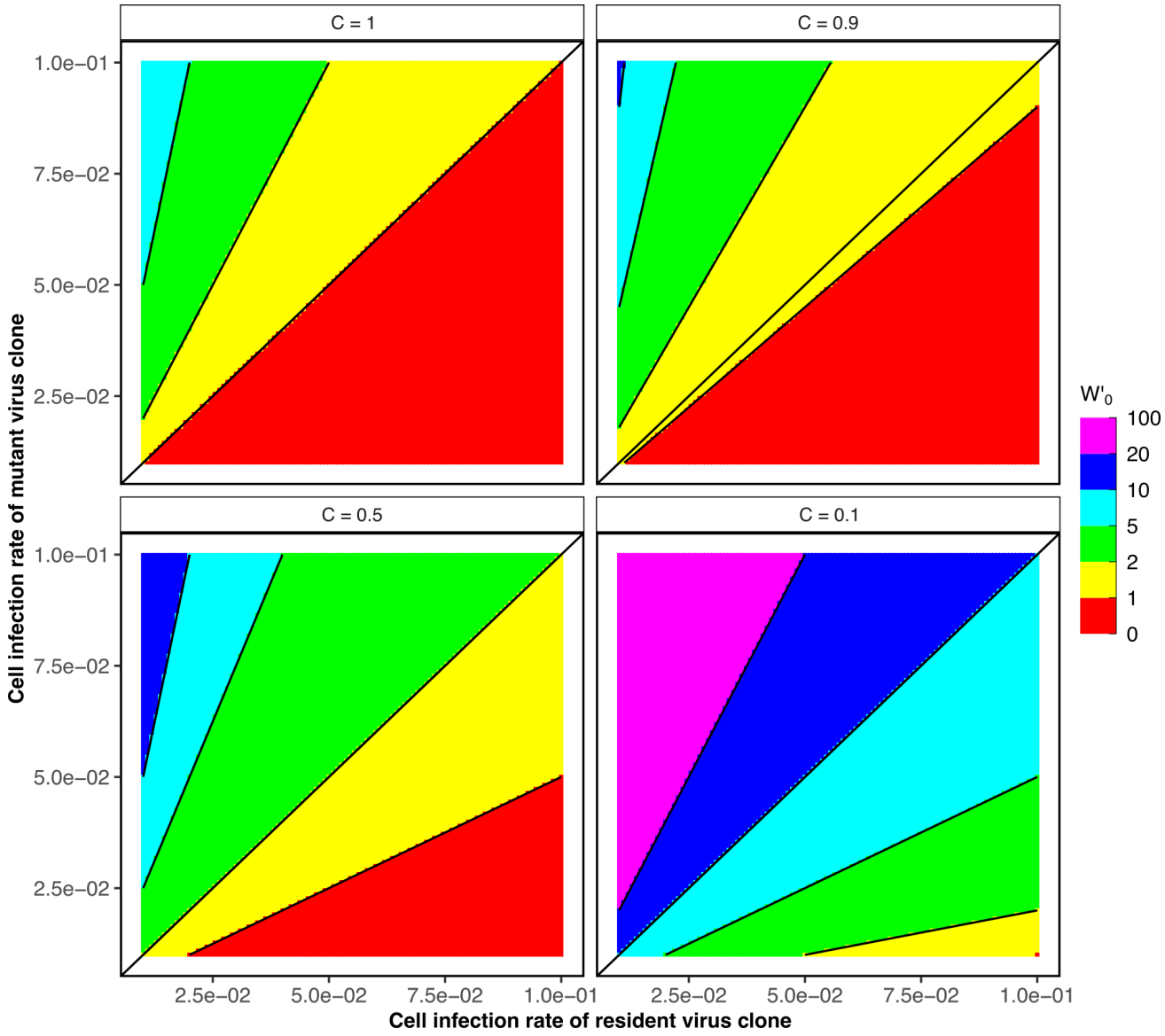
Within-host evolutionary dynamics



Within-host evolutionary dynamics



Within-host evolutionary dynamics

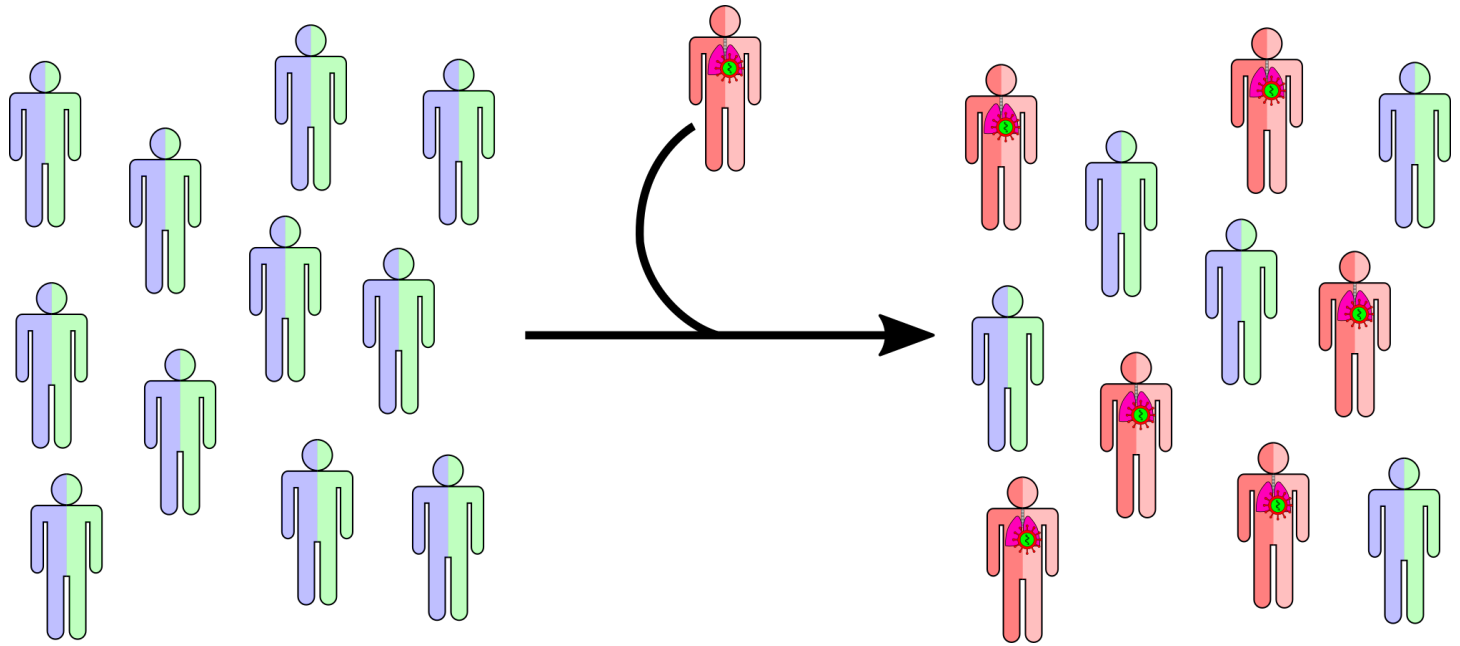


Between-host dynamics

$$R_{0_j} = \left| \frac{S_0 \cdot \beta_{SS}(c,\tau_{SS}) \cdot [\gamma_V(\mu_V) + \theta(\bar{\mu}) + h_V] + V_0 \cdot \beta_{VV}(c,\tau_{VV}) \cdot [\gamma_S(\mu_S) + \theta(\bar{\mu}) + h_S] + \sqrt{\sigma_1}}{2 \cdot [\gamma_S(\mu_S) + \theta(\bar{\mu}) + h_S] \cdot [\gamma_V(\mu_V) + \theta(\bar{\mu}) + h_V]} \right|$$

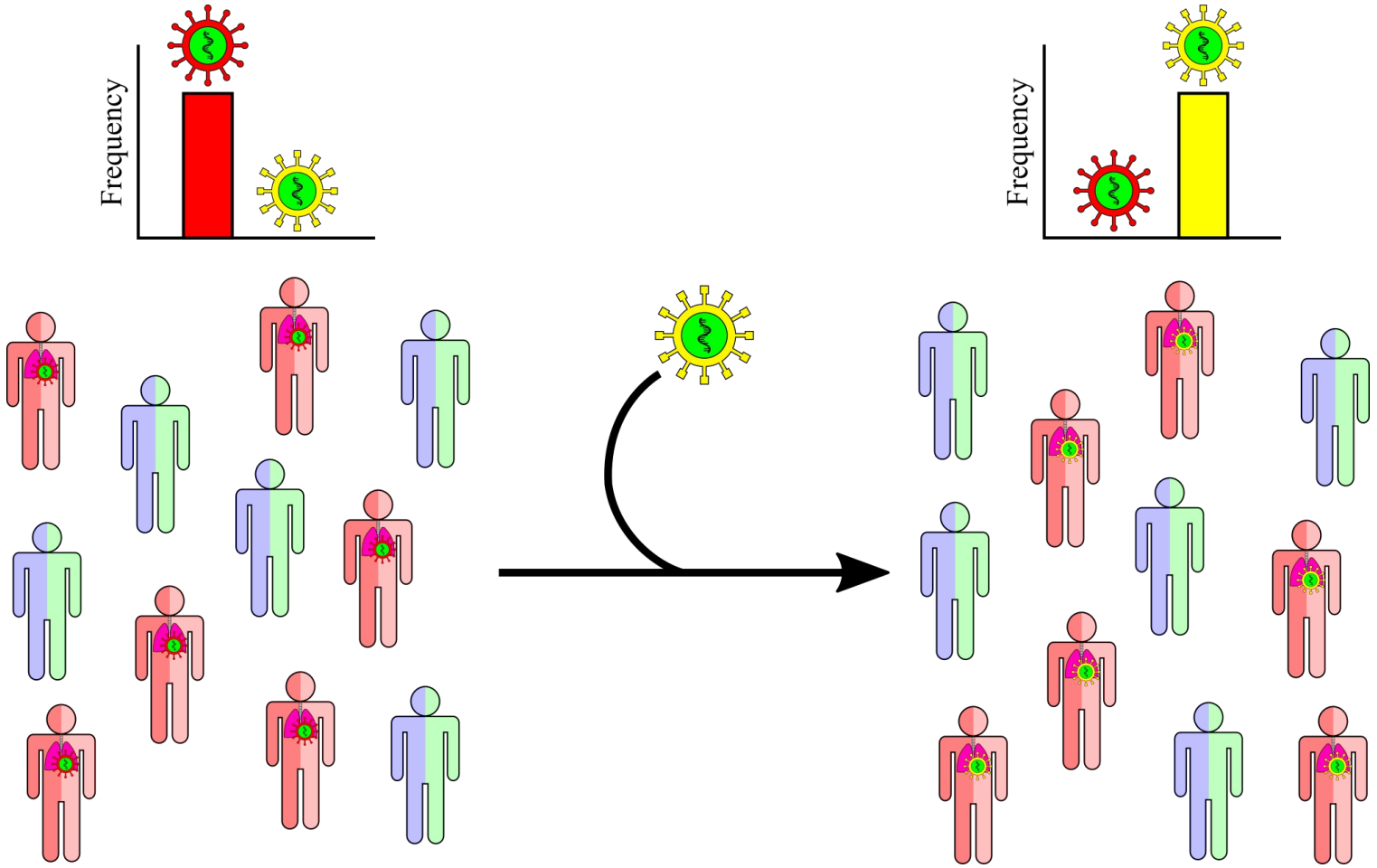
where

$$\begin{aligned} \sigma_1 = {} & [V_0 \cdot \beta_{VV}(c,\tau_{VV}) \cdot (\gamma_S(\mu_S) + \theta(\bar{\mu}) + h_S)]^2 \\ & + [S_0 \cdot \beta_{SS}(c,\tau_{SS}) \cdot (\gamma_V(\mu_V) + \theta(\bar{\mu}) + h_V)]^2 + 2 \cdot S_0 \cdot V_0 \\ & \cdot [2 \cdot \beta_{SV}(c,\tau_{SV}) \cdot \beta_{VS}(c,\tau_{VS}) - \beta_{SS}(c,\tau_{SS}) \cdot \beta_{VV}(c,\tau_{VV})] \\ & \cdot [\gamma_S(\mu_S) + \theta(\bar{\mu}) + h_S] \cdot [\gamma_V(\mu_V) + \theta(\bar{\mu}) + h_V] \end{aligned}$$



Between-host evolutionary dynamics

$$R_0(\mathbf{x}, \mathbf{x}', t_e) = R_0|_{\beta_{kl}=\beta'_{kl}}$$



Within-host evolutionary dynamics

$$W_e(\mathbf{x}', \mathbf{z}(t_\mathrm{m}), \mathbf{a}')$$

Between-host evolutionary dynamics

via

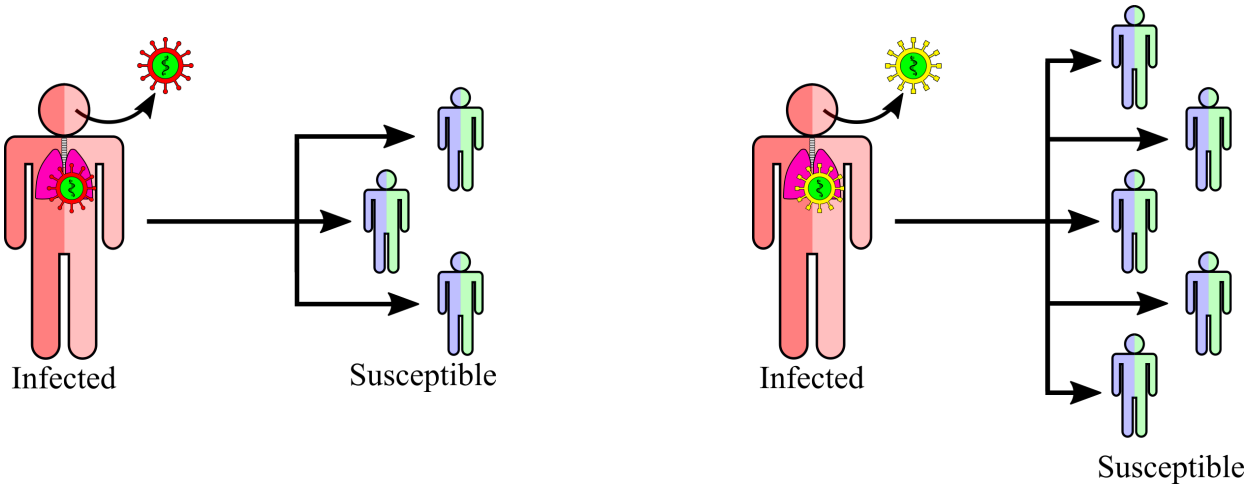
$$\beta_{\mathrm{kl}}(c, \tau_{\mathrm{kl}}) = c(\bar{\mu}(t)) \cdot \tau_{\mathrm{kl}}\left(\mathbf{x}^{\mathrm{k}}, \mathbf{z}^{\mathrm{l}}(t), \mathbf{a}^{\mathrm{l}}, \phi, \mathbf{n}^{\mathrm{k}}\right)$$

Between-host evolutionary dynamics

$$\beta_{kl}(c,\tau_{kl}) = c(\bar{\mu}(t)) \cdot \tau_{kl}\left(\mathbf{x}^k, \mathbf{z}^l(t), \mathbf{a}^l, \phi, \mathbf{n}^k\right)$$

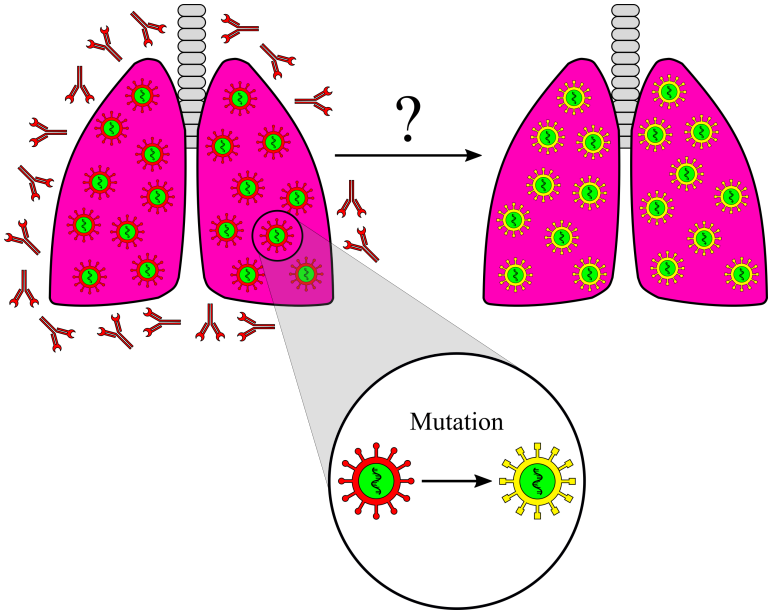
$$\downarrow$$

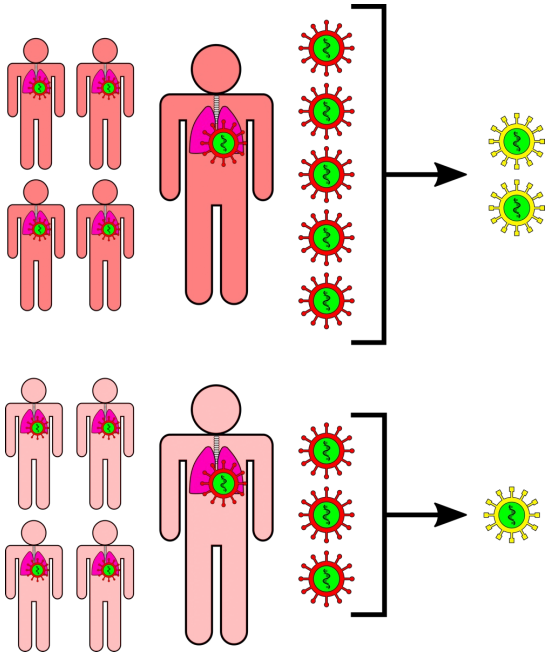
$$R_0(\mathbf{x}, \mathbf{x}', t_e) = R_0|_{\beta_{kl}=\beta'_{kl}}$$

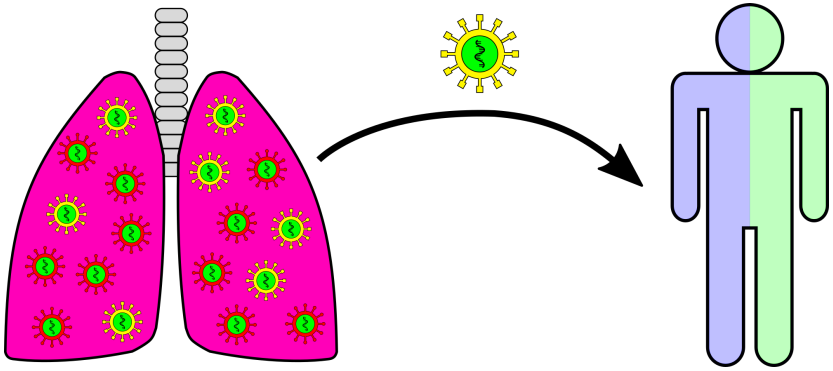


$$c(\bar{\mu}(t)) = c_0 + c_1 \cdot \exp\left(-c_2 \cdot \bar{\mu}(t) \cdot \frac{R(t)}{N_{pop}}\right)$$

Virus evolutionary dynamics

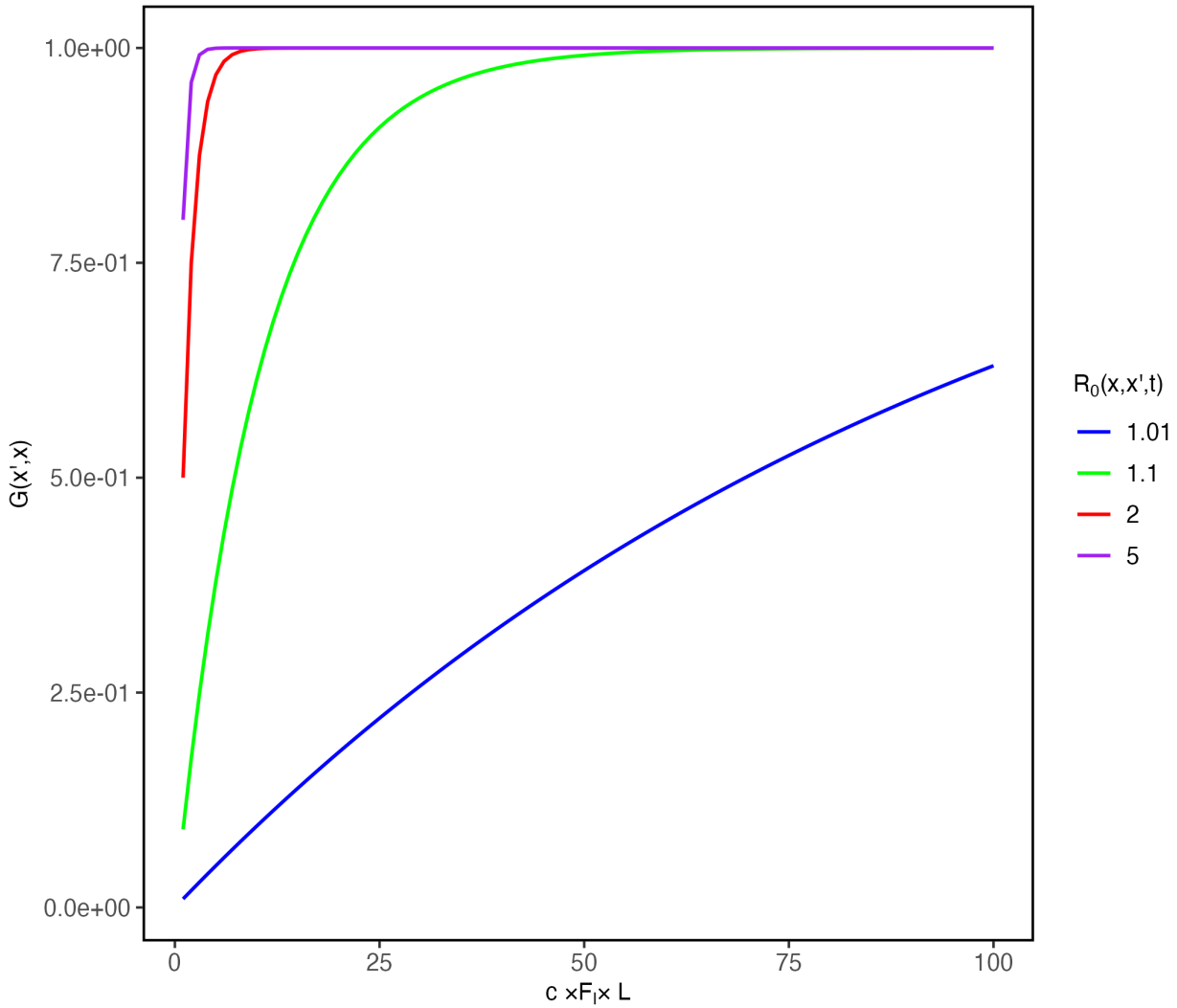




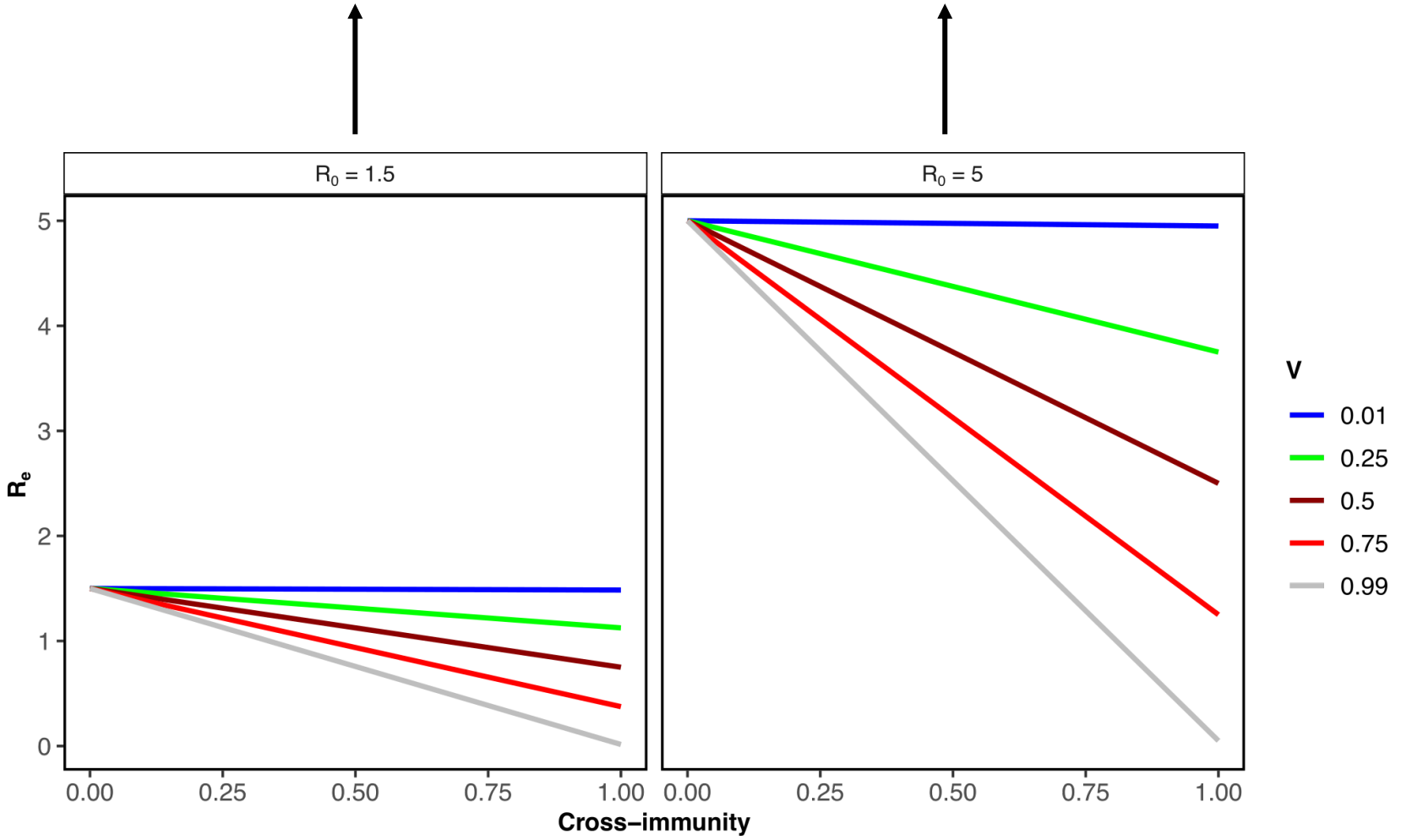


$$G(\mathbf{x}',\mathbf{x}) = 1 - \left(\frac{1}{R_0(\mathbf{x},\mathbf{x}',t_e)}\right)^{c(\bar{\mu}(t))\cdot F_I(t)\cdot\langle L\left(\mathbf{x}',\mathbf{x},t_I,\psi(t_I,X^I)\right)\rangle}$$

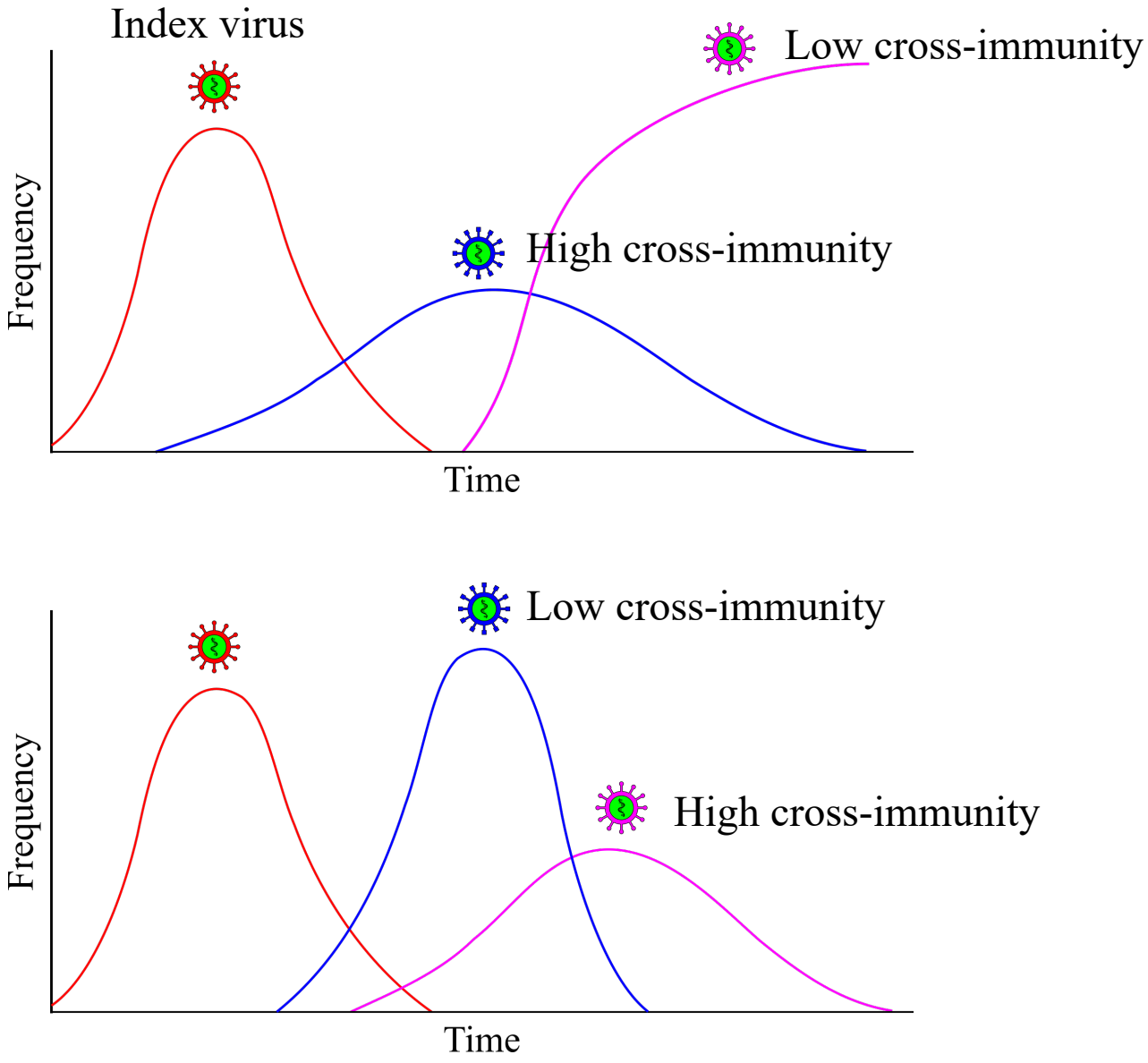
Virus evolutionary dynamics



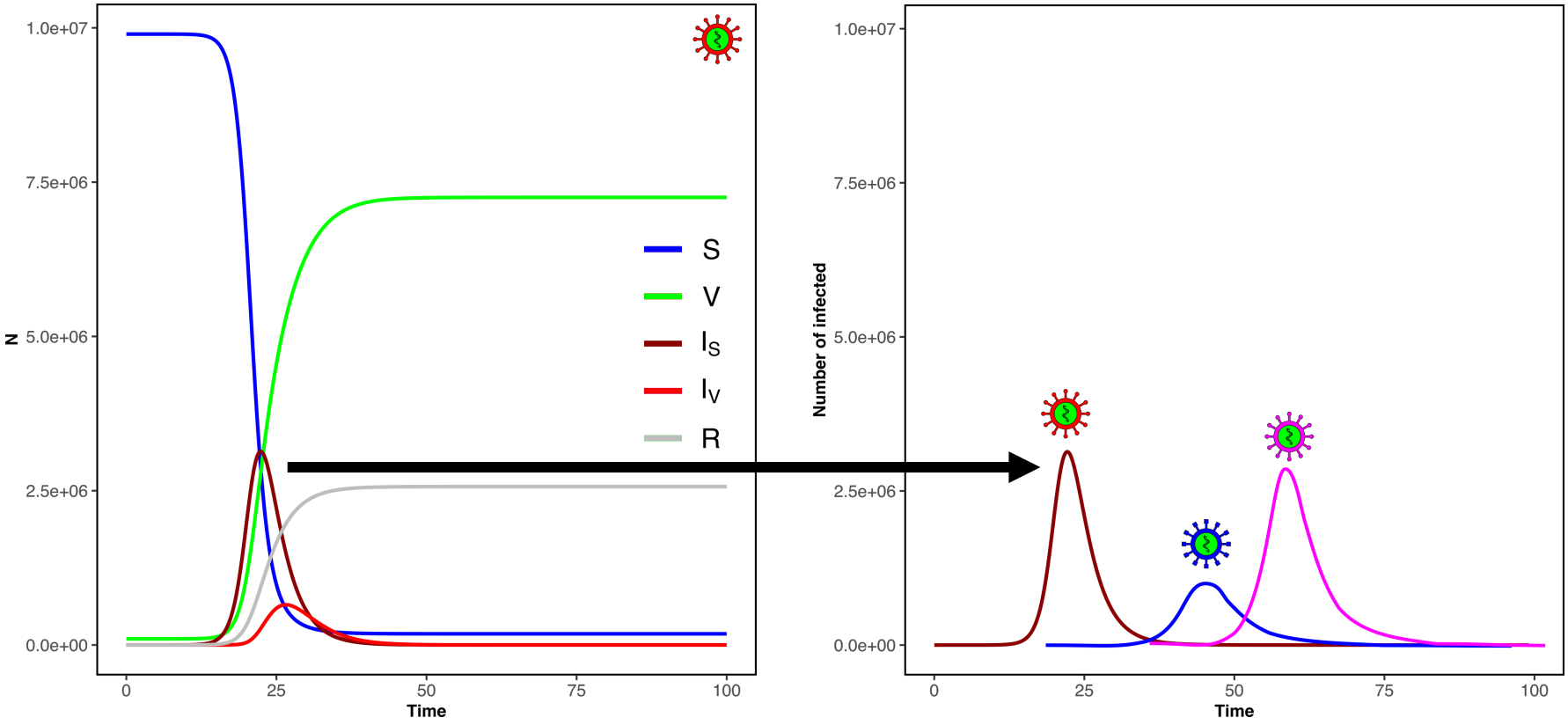
R_0 in a completely naive population (C=0)



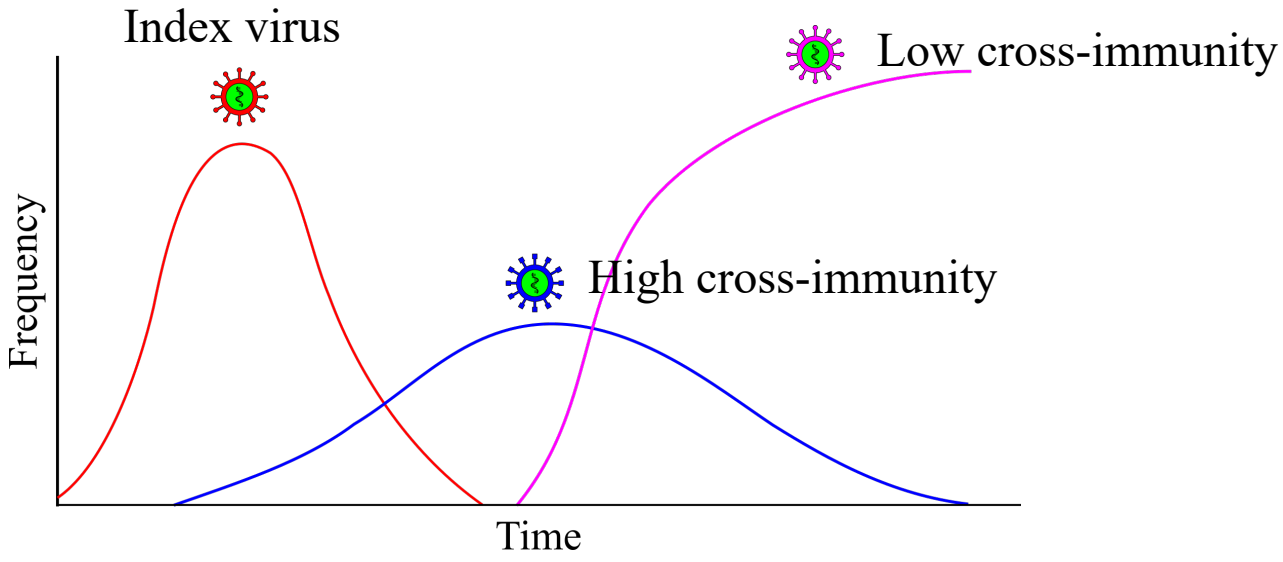
Virus evolutionary dynamics

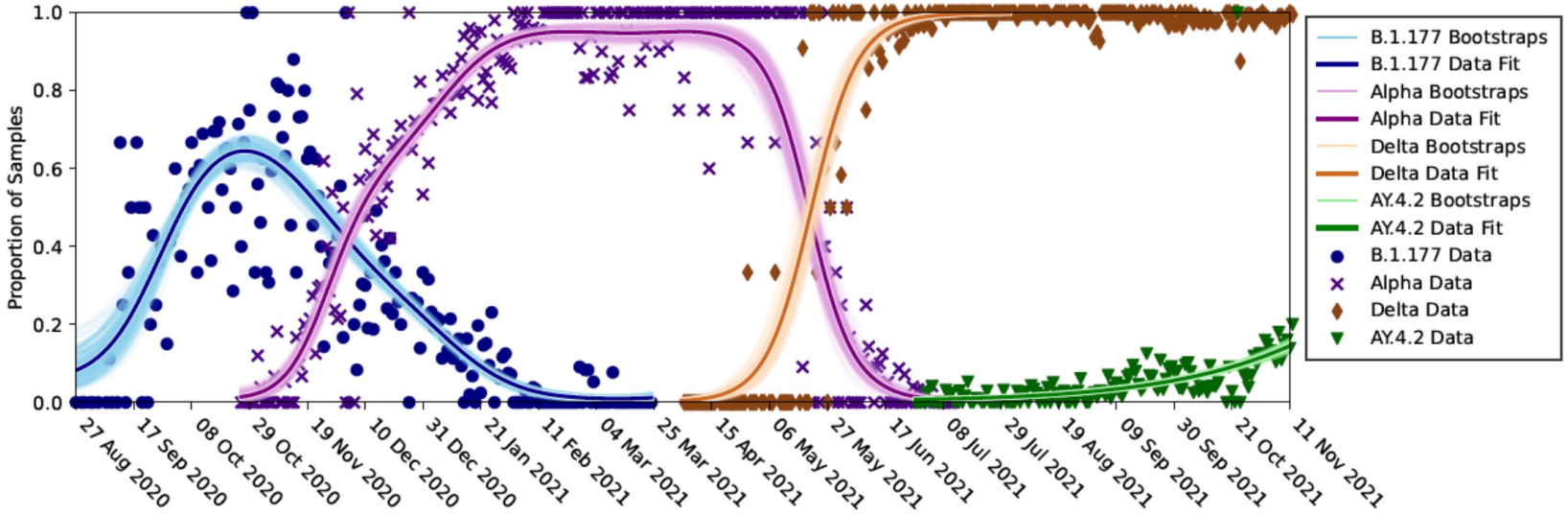


Virus evolutionary dynamics



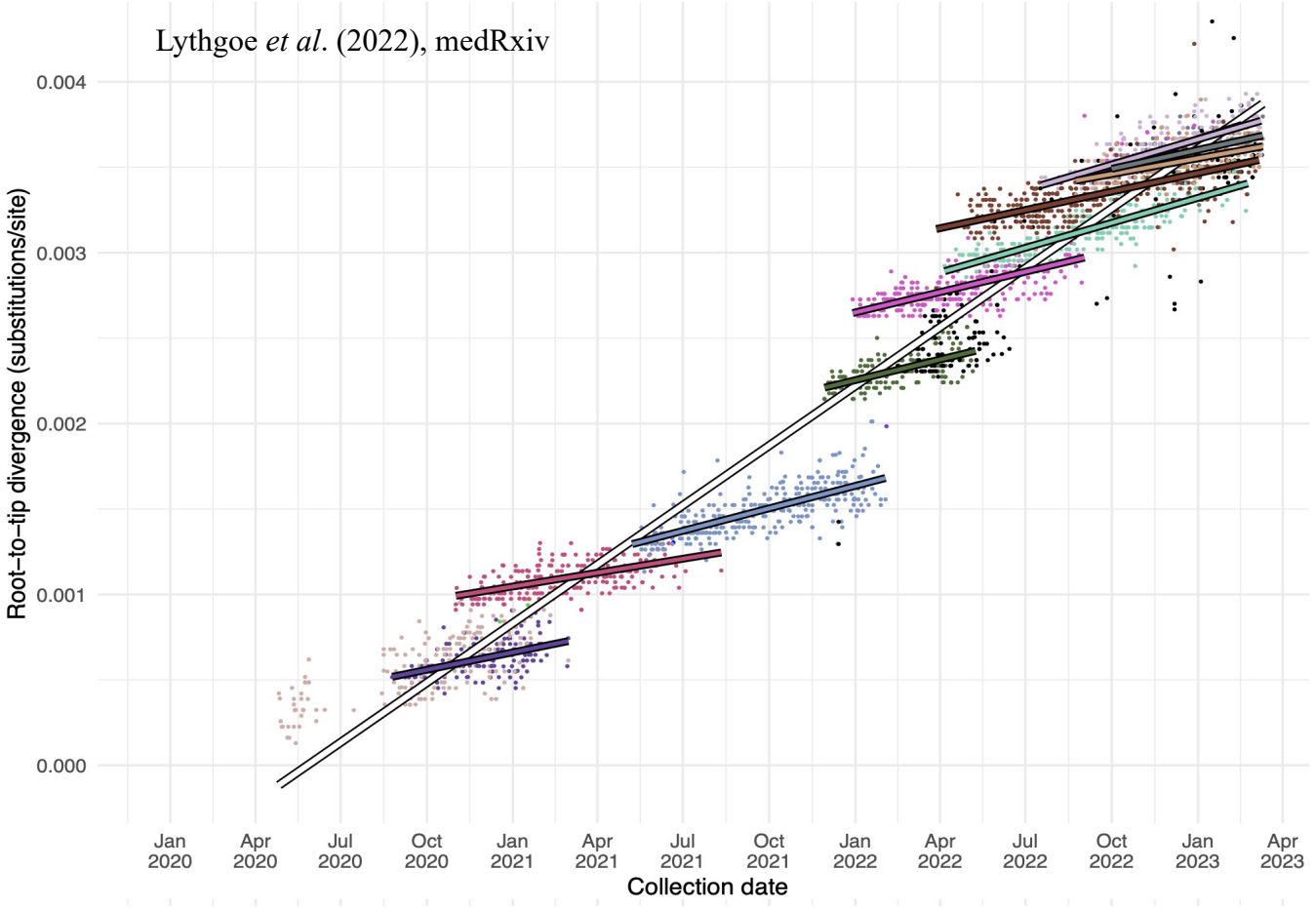
Virus evolutionary dynamics



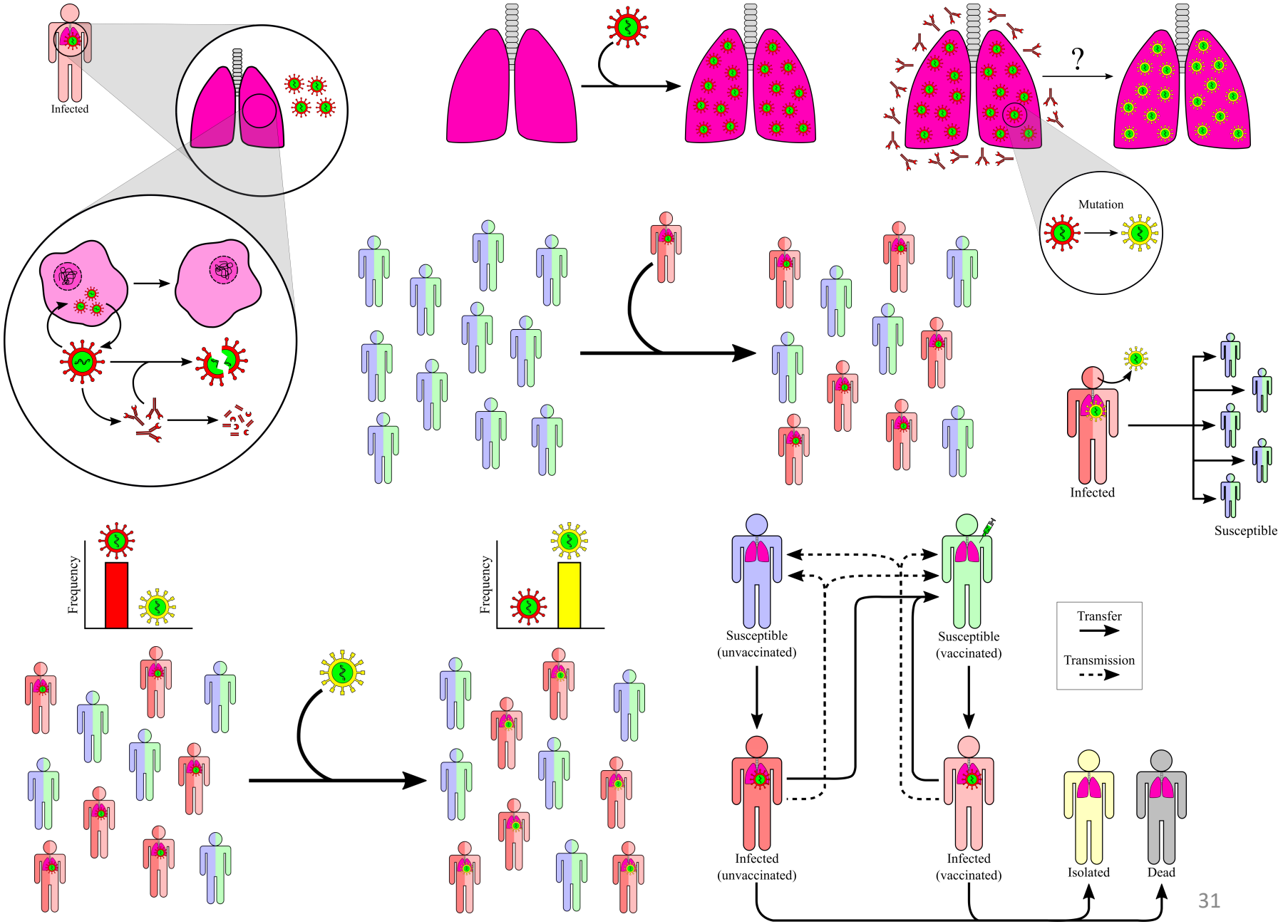


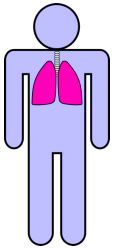
Lythgoe *et al*. (2022), medRxiv

Virus evolutionary dynamics



Summary


Infected
?
Mutation
Infected
Susceptible
Frequency
Frequency
Susceptible (unvaccinated)
Susceptible (vaccinated)
Transfer
Transmission
Infected (unvaccinated)
Infected (vaccinated)
Isolated
Dead



Thanks!

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