

Immune escape:

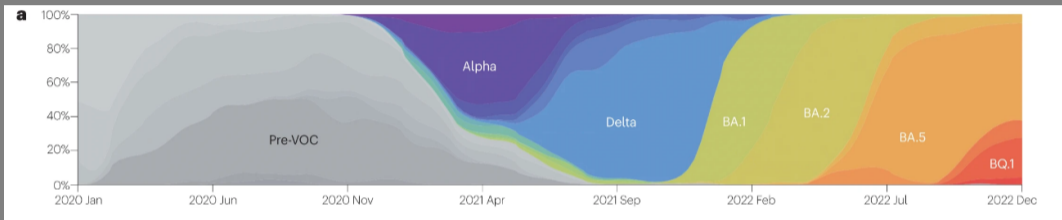
from individual differences to the population level

Maria A. Gutierrez and Julia R. Gog

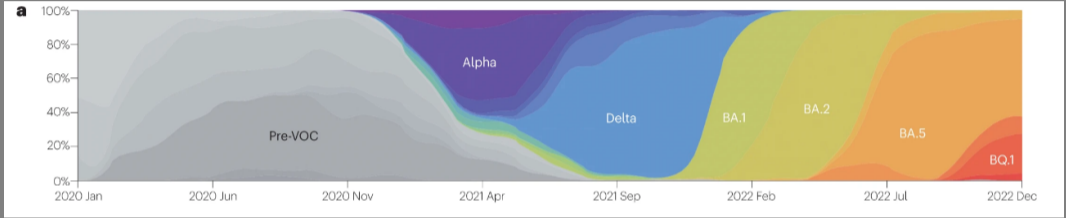
University of Cambridge, UK



Markov *et al*, Nature Reviews Microbiology 2023

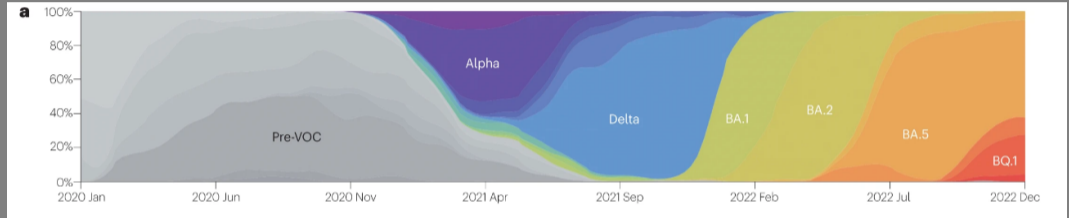


Markov *et al*, Nature Reviews Microbiology 2023

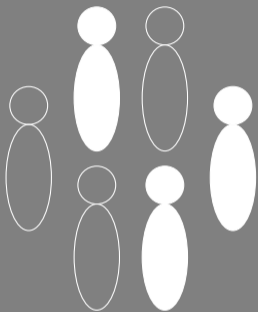


What drives evolution?

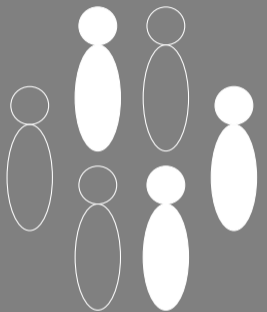
Markov *et al*, Nature Reviews Microbiology 2023



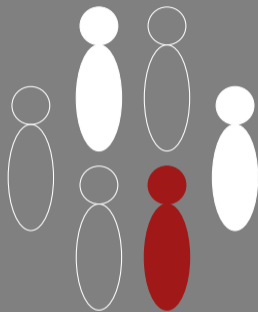
What drives evolution?
Impact of vaccination?



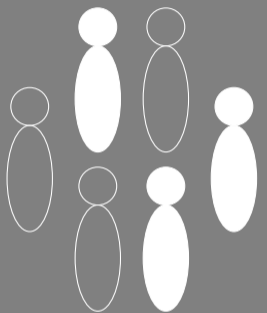
wildtype infections



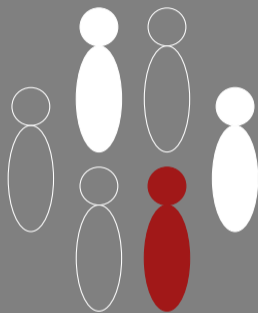
wildtype infections



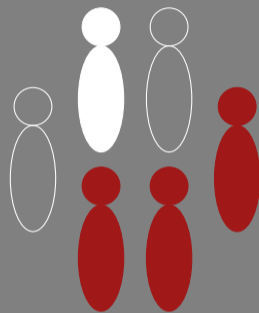
new strain *appears*



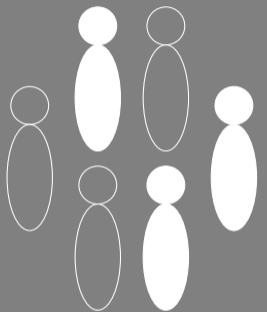
wildtype infections



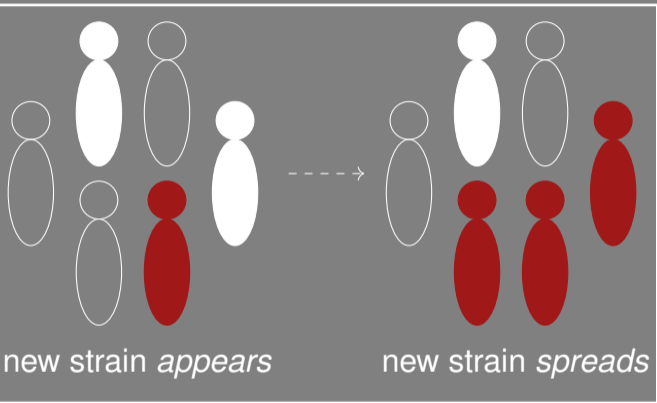
new strain *appears*



new strain *spreads*

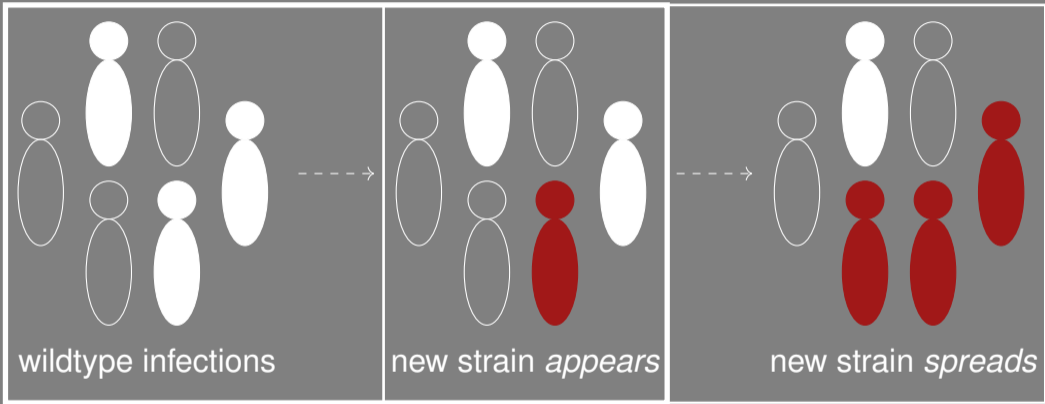


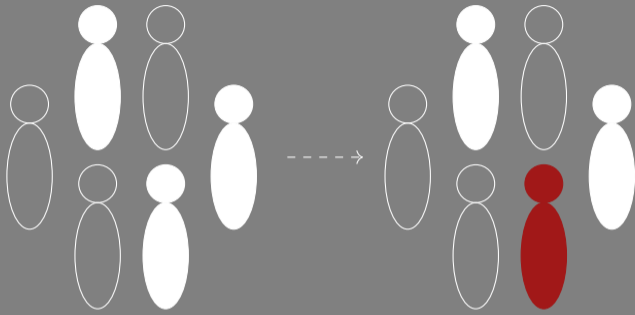
wildtype infections

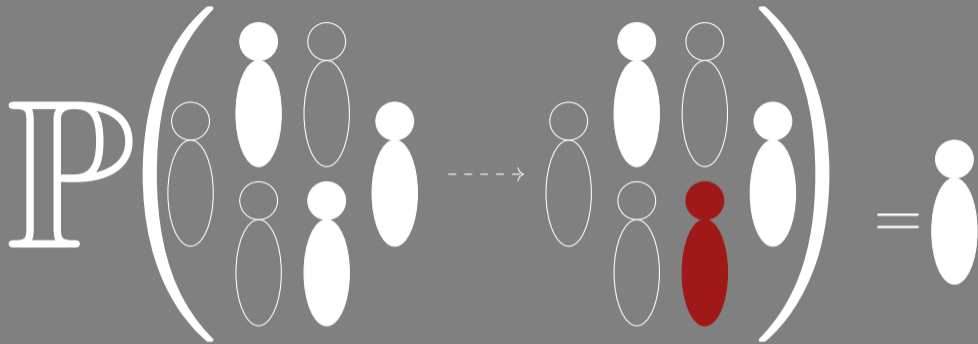


new strain *appears*

new strain *spreads*

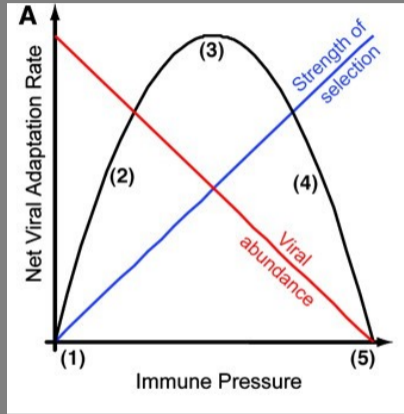
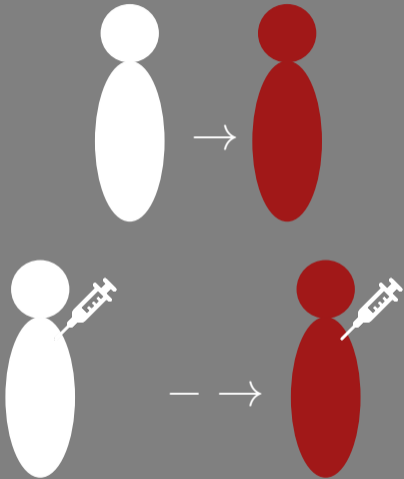






Escape pressure

Hartfield et al. 2014, Gog et al. 2021,
Rella et al. 2021, Saad-Roy et al. 2021



Grenfell *et al.*, Science 2004

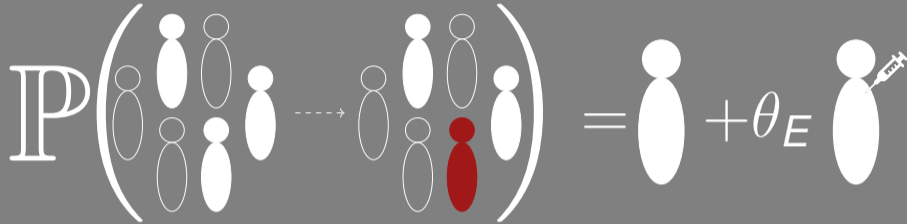
infections
in unvaccinated

$$\mathbb{P} \left(\begin{array}{c} \text{[Group of 7 unvaccinated people]} \\ \text{---} \\ \text{[Group of 7 people, 1 vaccinated]} \end{array} \right) = \text{[1 unvaccinated]} + \theta_E \text{[1 vaccinated]}$$

Escape pressure

infections
in vaccinated

infections
in unvaccinated



Escape pressure

infections

in vaccinated

$$P(t) = I_U(t) + \theta_E I_V(t)$$

Unvaccinated fraction $(1 - c)$



$$\dot{S}_U = -S_U\lambda(t)$$

$$\dot{I}_U = S_U\lambda(t) - I_U$$

$$S_U(0) = (1 - c)$$

Vaccinated fraction c



$$\dot{S}_V = -S_V\lambda(t)$$

$$\dot{I}_V = S_V\lambda(t) - I_V$$

$$S_V(0) = c\theta_S$$

$$\lambda = R_0(I_U + \theta_I I_V)$$

Unvaccinated fraction $(1 - c)$



$$\dot{S}_U = -S_U\lambda(t)$$

$$\dot{I}_U = S_U\lambda(t) - I_U$$

$$S_U(0) = (1 - c)$$

Vaccinated fraction c



$$\dot{S}_V = -S_V\lambda(t)$$

$$\dot{I}_V = S_V\lambda(t) - I_V$$

$$S_V(0) = c\theta_S$$

$$\lambda = R_0(I_U + \theta_I I_V)$$

$\forall t$

$$(1 - c)^{-1}(S_U, I_U, R_U) = (c\theta_S)^{-1}(S_V, I_V, R_V)$$

$$(S, I) := (1 - c)^{-1}(S_U, I_U) = (c\theta_S)^{-1}(S_V, I_V)$$

$$R_e = R_0(1 - c(1 - \theta_S\theta_I))$$

$$S(\infty) = -W(-R_e e^{-R_e}) / R_e \text{ (Lambert W-function)}$$

$$(S, I) := (1 - c)^{-1}(S_U, I_U) = (c\theta_S)^{-1}(S_V, I_V)$$

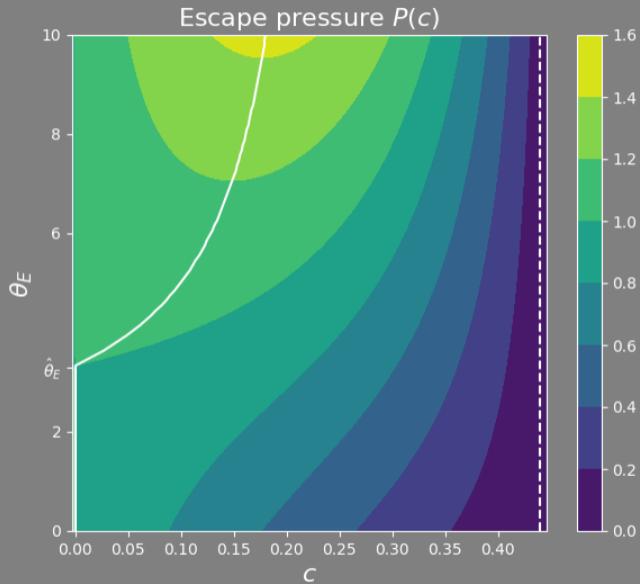
$$R_e = R_0(1 - c(1 - \theta_S\theta_I))$$

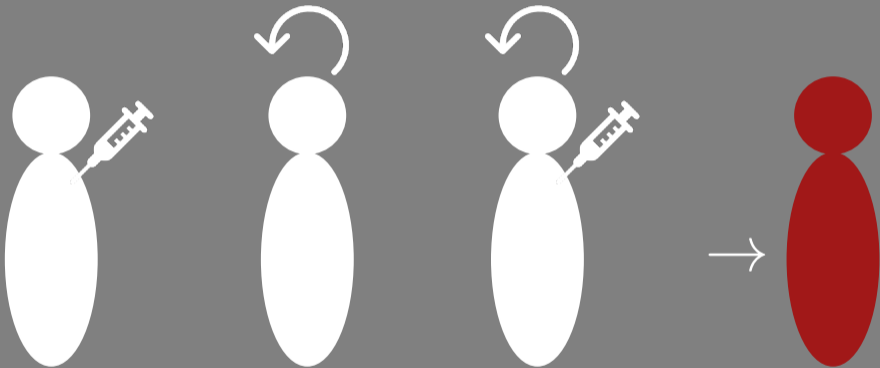
$$S(\infty) = -W(-R_e e^{-R_e}) / R_e \text{ (Lambert W-function)}$$

$$\int_0^\infty P(t) dt = \int_0^\infty (I_U + \theta_E I_V) dt$$

Cumulative escape pressure

$$P = (1 - c + \theta_S\theta_EC) \left(1 + \frac{1}{R_e} W(-R_e e^{-R_e}) \right)$$



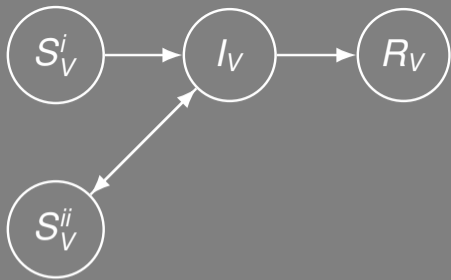
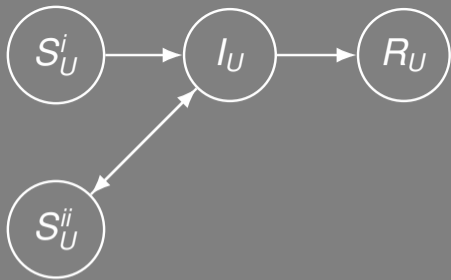


$$\mathbb{P}\left(\begin{array}{c} \text{[Group of 8 white people]} \\ \text{---} \\ \text{[Group of 8 people, 1 red, 1 with syringe]} \end{array}\right) = \text{[1 white person]} + \theta_E \text{[1 person with syringe]}$$

The diagram illustrates a probabilistic model. On the left, a large 'P' is followed by a large set of parentheses. Inside the parentheses, a dashed arrow points from a group of 8 white stylized human figures to a group of 8 stylized human figures, where one figure is red and one has a syringe. To the right of the parentheses is an equals sign, followed by a single white stylized human figure, a plus sign, the Greek letter θ_E , another plus sign, and a stylized human figure with a syringe.

$$\mathbb{P} \left(\begin{array}{c} \text{[Group of 7 white people]} \\ \text{--->---} \\ \text{[Group of 7 people, 1 red]} \end{array} \right) = \text{[1 white]} + \theta_E \text{[1 white with syringe]} + \theta_E \text{[1 white with arrow]} + \theta_E \text{[1 white with arrow and syringe]}$$

The diagram illustrates a probability distribution over a population of 7 individuals. On the left, a group of 7 white icons is shown with a dashed arrow pointing to a group of 7 icons where one is red. This is equated to a sum of four terms: a single white icon, and three terms each consisting of a white icon with a different attribute (syringe, arrow, or both) multiplied by the parameter θ_E .



$$\dot{S}_U^i = -S_U^i \lambda(t)$$

$$\dot{S}_U^{ii} = -S_U^{ii} \lambda(t) + \theta'_S I_U$$

$$\dot{I}_U = (S_U^i + S_U^{ii}) \lambda(t) - I_U$$

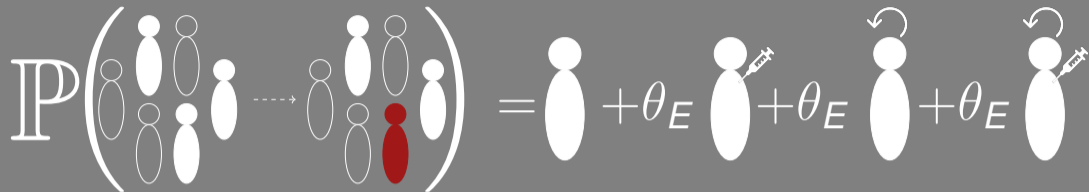
$$S_U^i(0) = 1 - c$$

$$\dot{S}_V^i = -S_V^i \lambda(t)$$

$$\dot{S}_V^{ii} = -S_V^{ii} \lambda(t) + \theta'_S I_V$$

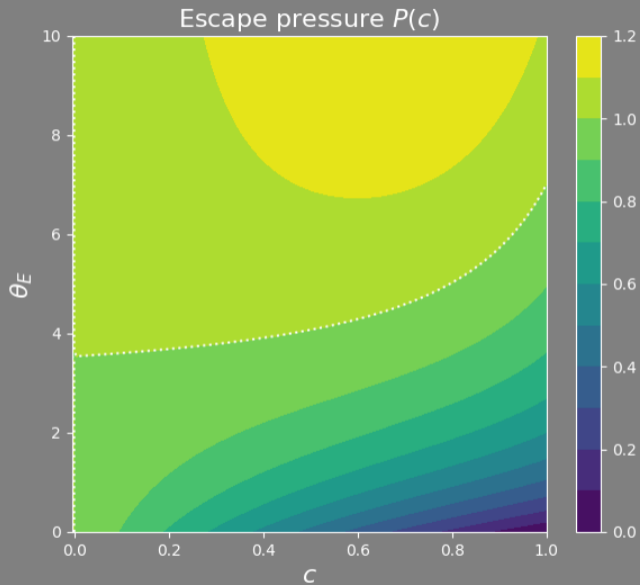
$$\dot{I}_V = (S_V^i + S_V^{ii}) \lambda(t) - I_V$$

$$S_U^{ii}(0) = c \theta_S$$

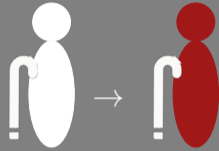


$$P = \left[1 - c + \theta_E \left(\frac{\theta'_S (1 - R_0^{-1}) + c(\theta_S - \theta'_S)}{1 - \theta'_S} \right) \right] \left(1 + \frac{W[-re^{-r}]}{r} \right)$$

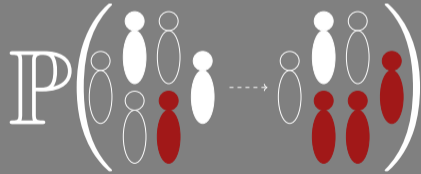
$$r = (R_e - \theta'_S) / (1 - \theta'_S)$$



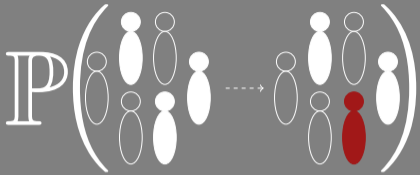
Immunocompromised hosts,
population heterogeneity,
vaccination strategies.



Stochastic extinction,
invasion dynamics.



Multiple waves, antigenic
evolution between waves.

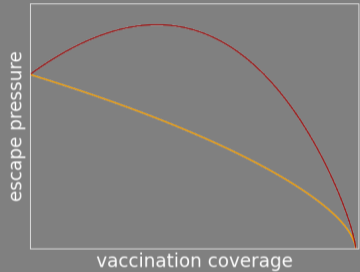


Escape pressure

depends on vaccination %:

unimodal or **decreasing**

... determined by θ_E !



Gutierrez and Gog 2023,
J. Theoretical Biology