Immune escape:

from individual differences to the population level

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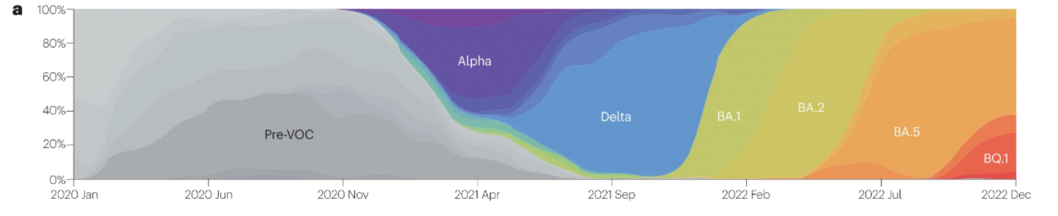
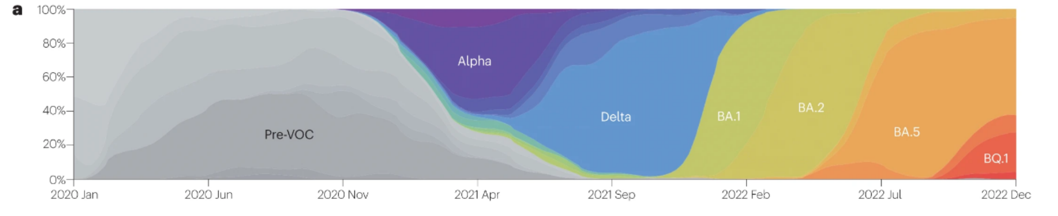
Markov *et al*, Nature Reviews Microbiology 2023

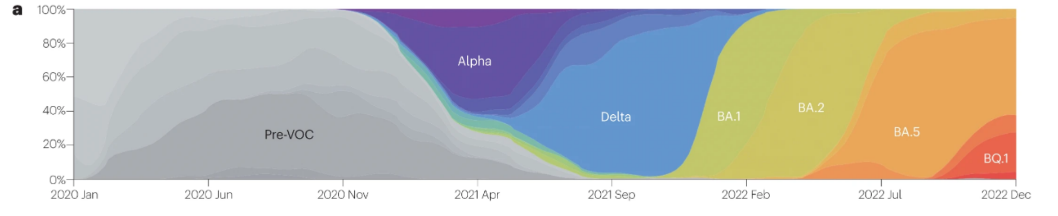


Markov *et al*, Nature Reviews Microbiology 2023

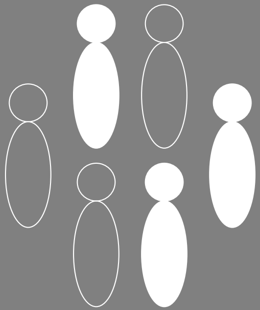


What drives evolution?

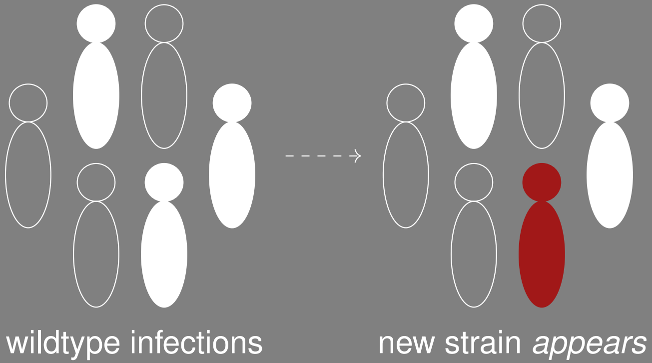
Markov *et al*, Nature Reviews Microbiology 2023

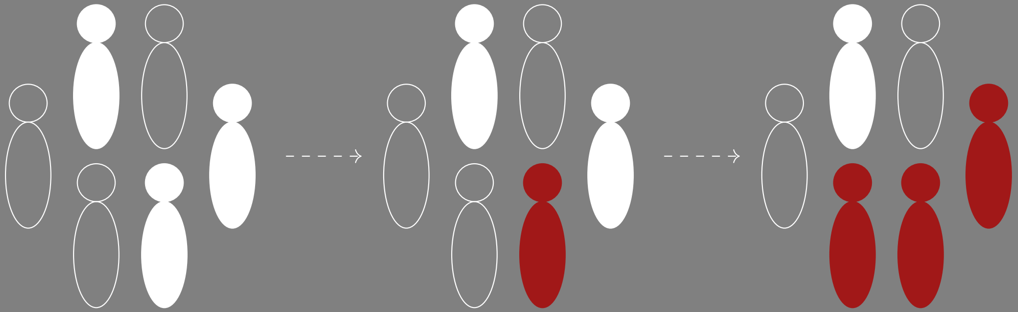


What drives evolution?
Impact of vaccination?

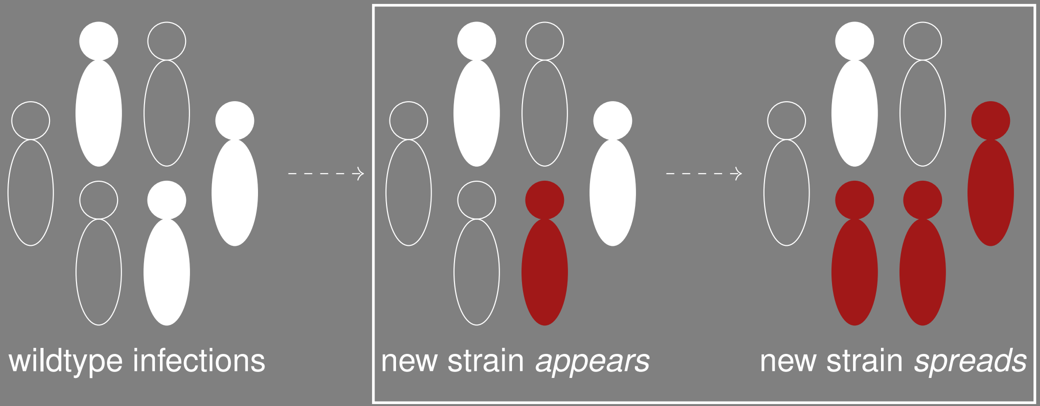


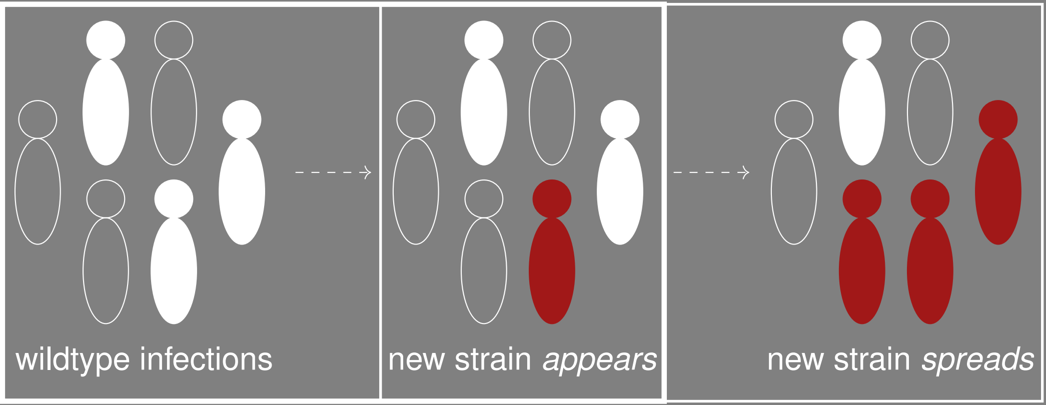
wildtype infections

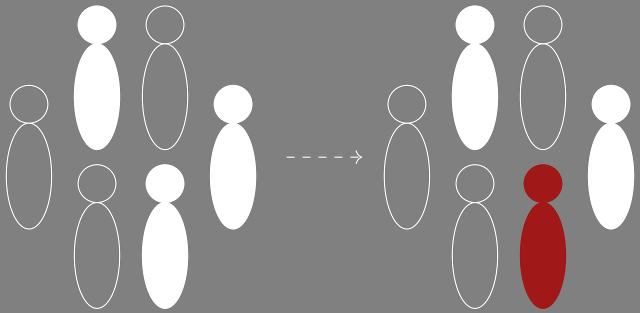

wildtype infections
new strain *appears*

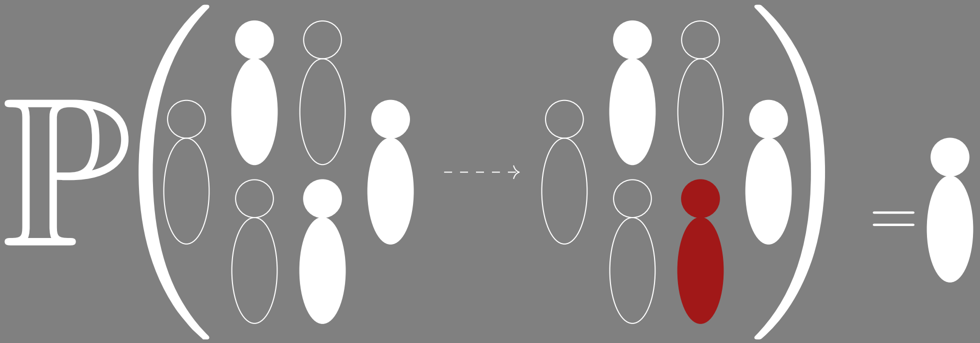


wildtype infections | new strain *appears* | new strain *spreads*


wildtype infections
new strain *appears*
new strain *spreads*

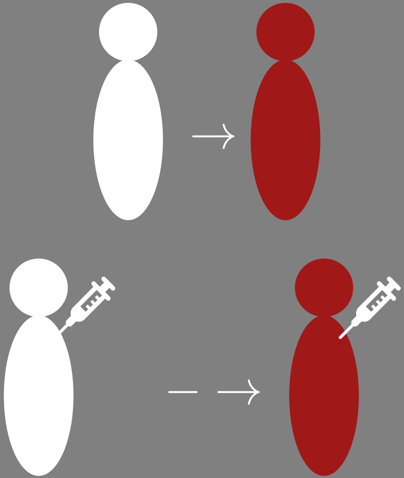

wildtype infections
new strain *appears*
new strain *spreads*

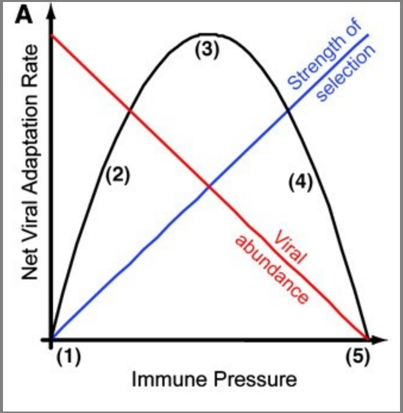




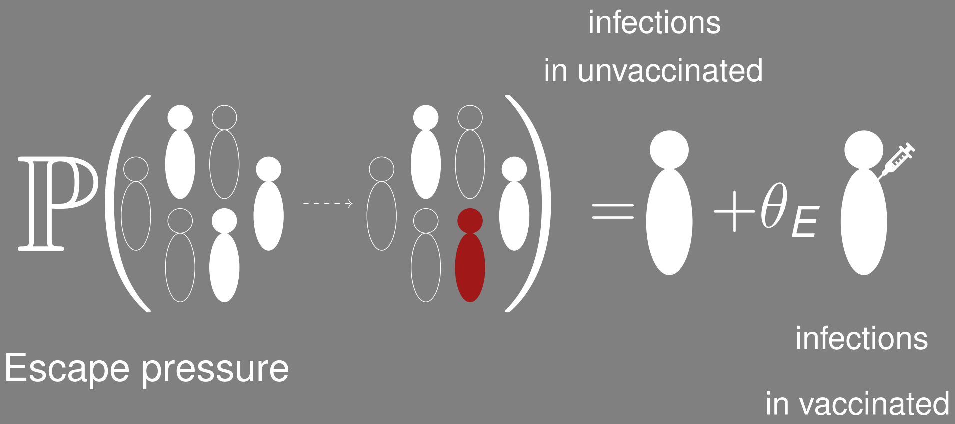
Escape pressure

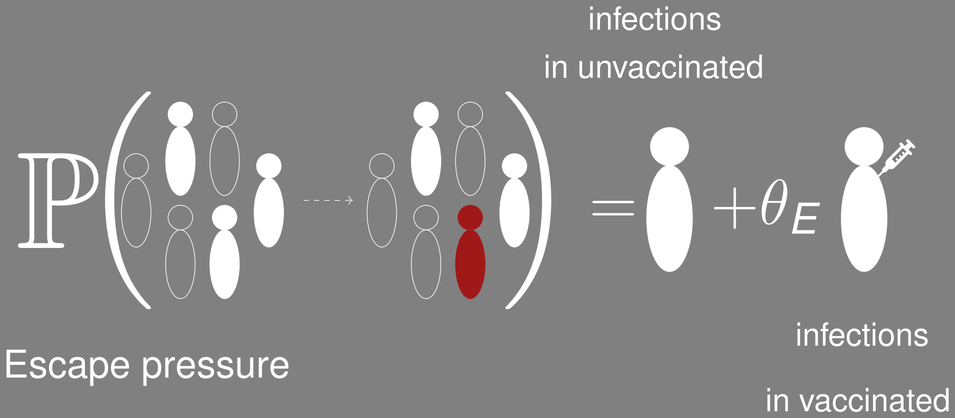
Hartfield et al. 2014, Gog et al. 2021,
Rella et al. 2021, Saad-Roy et al. 2021





Grenfell *et al.*, Science 2004


infections
in unvaccinated
$\mathbb{P}$
$= \quad + \theta_E$
infections
in vaccinated
Escape pressure



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

Unvaccinated fraction $(1 - c)$

Vaccinated fraction c

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

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

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

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

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

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

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

Unvaccinated fraction $(1-c)$

Vaccinated fraction c

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

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

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

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

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

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

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

$$\forall t$$

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

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

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

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

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

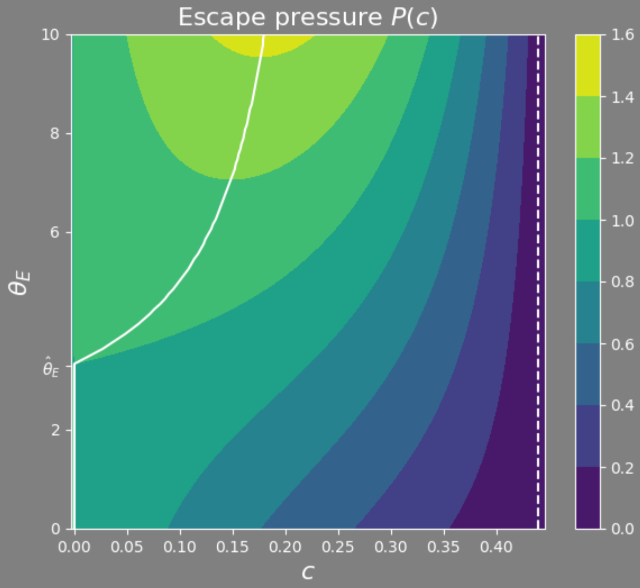
$$R_e = R_0(1 - c(1 - \theta_S \theta_I))$$

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

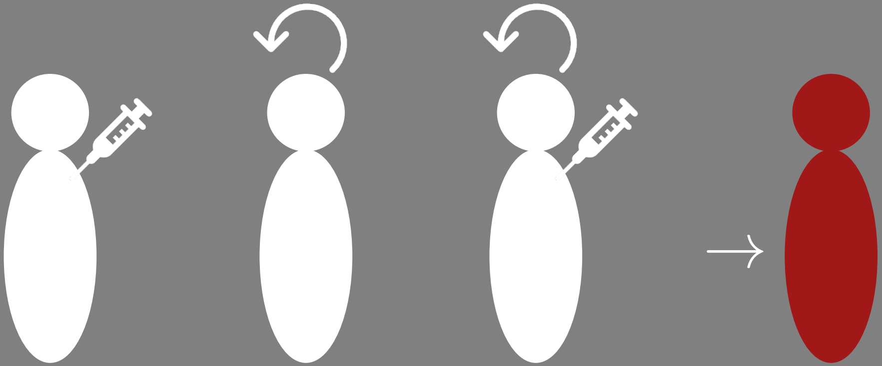
$$\int_0^\infty P(t)dt = \int_0^\infty (I_U + \theta_E I_V)dt$$

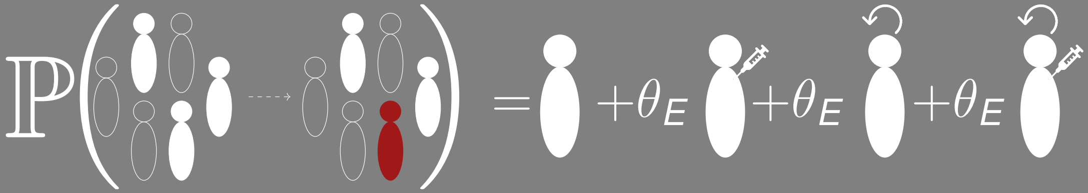
Cumulative escape pressure

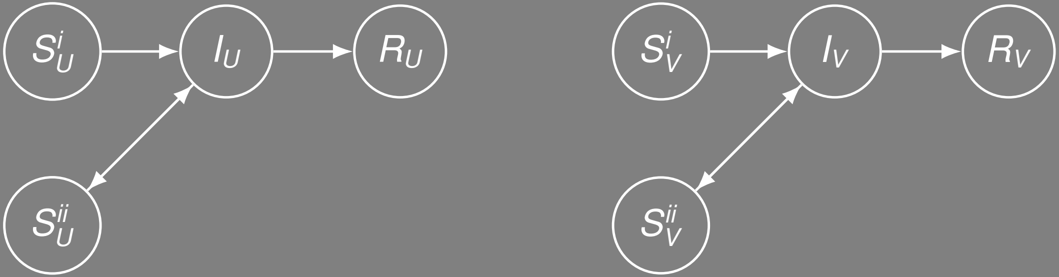
$$\boxed{P = (1 - c + \theta_S \theta_E c)\left(1 + \frac{1}{R_e} W\left(-R_e e^{-R_e}\right)\right)}$$



Escape pressure $P(c)$
θ_E
$\hat{\theta}_E$
10
8
6
2
0
0.00
0.05
0.10
0.15
0.20
0.25
0.30
0.35
0.40
c
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0




ℙ
=
+θE
+θE
+θE

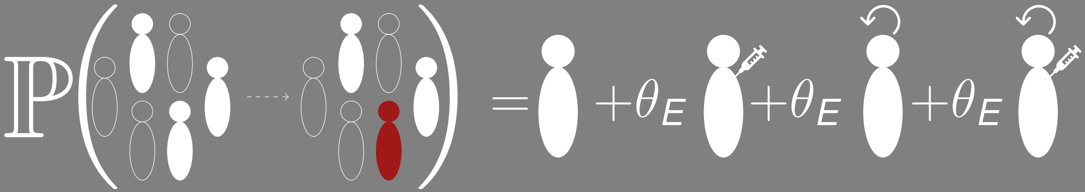


$$\dot{S}_U^i = -S_U^i\lambda(t) \qquad \dot{S}_V^i = -S_V^i\lambda(t)$$

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

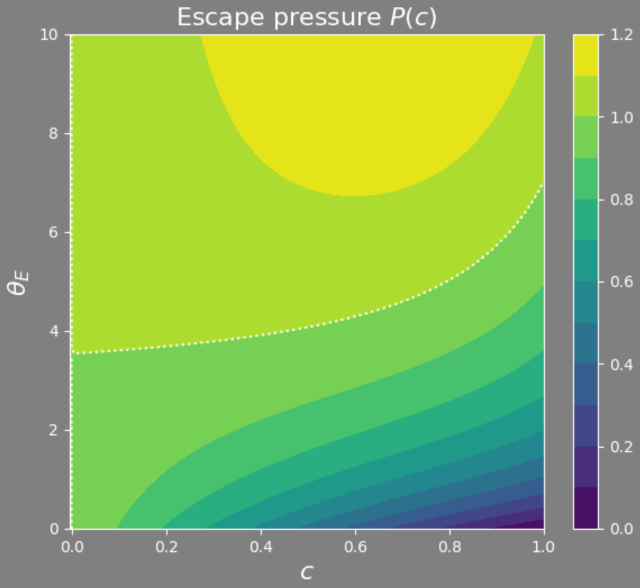
$$\dot{I}_U = (S_U^i + S_U^{ii})\lambda(t) - I_U \qquad \dot{I}_V = (S_V^i + S_V^{ii})\lambda(t) - I_V$$

$$S_U^i(0) = 1 - c \qquad S_U^{ii}(0) = c\theta_S$$



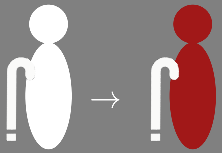
$$P = \left[1 - c + \theta_E\left(\frac{\theta'_S(1 - R_0^{-1}) + c(\theta_S - \theta'_S)}{1 - \theta'_S}\right)\right]\left(1 + \frac{W\left[-re^{-r}\right]}{r}\right)$$

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



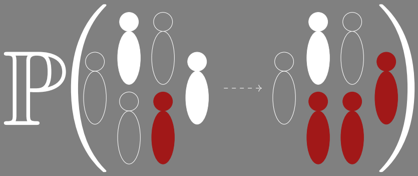
Escape pressure $P(c)$
θ_E
c
0
2
4
6
8
10
0.0
0.2
0.4
0.6
0.8
1.0
0.0
0.2
0.4
0.6
0.8
1.0
1.2

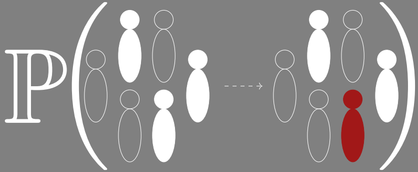
Immunocompromised hosts, population heterogeneity, vaccination strategies.



Stochastic extinction, invasion dynamics.

Multiple waves, antigenic evolution between waves.



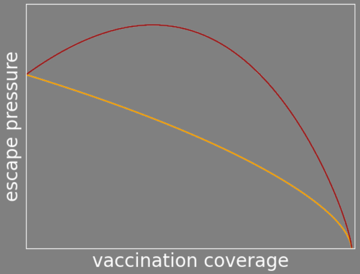


Escape pressure

depends on vaccination %:

unimodal or decreasing

...determined by θ_E!



Gutierrez and Gog 2023,
J. Theoretical Biology