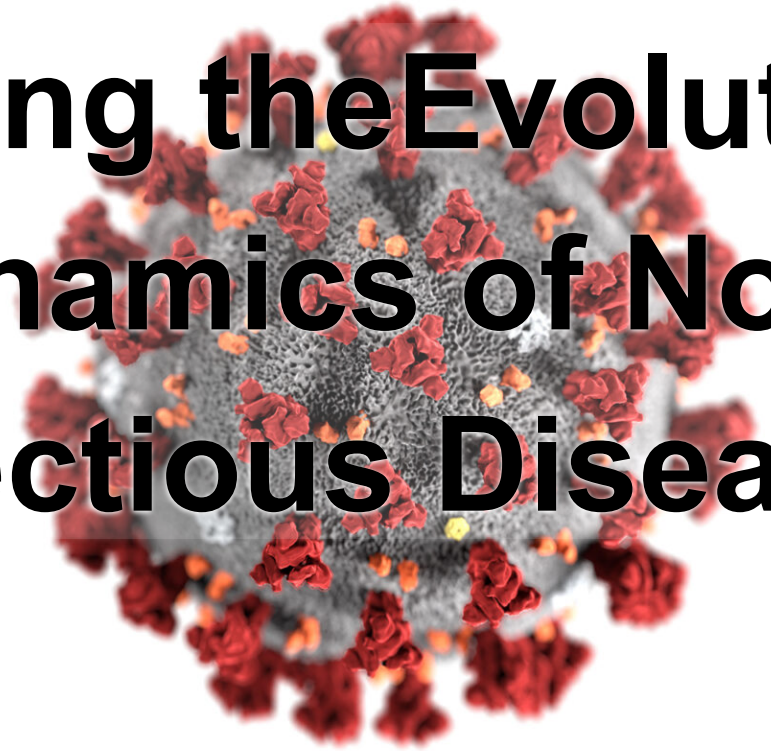
Modeling theEvolutionary Dynamics of Novel Infectious Diseases



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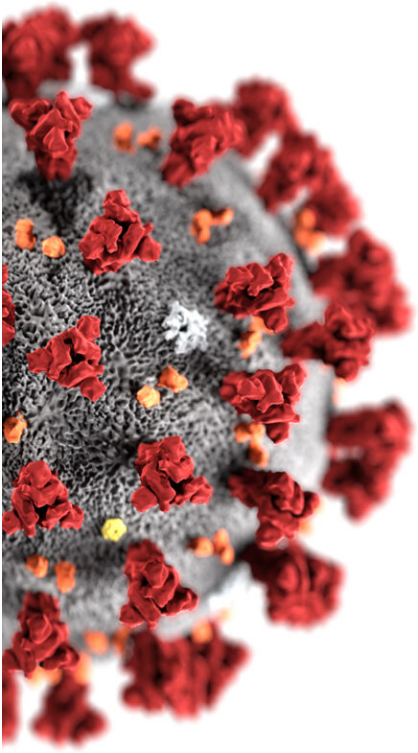
June 2023

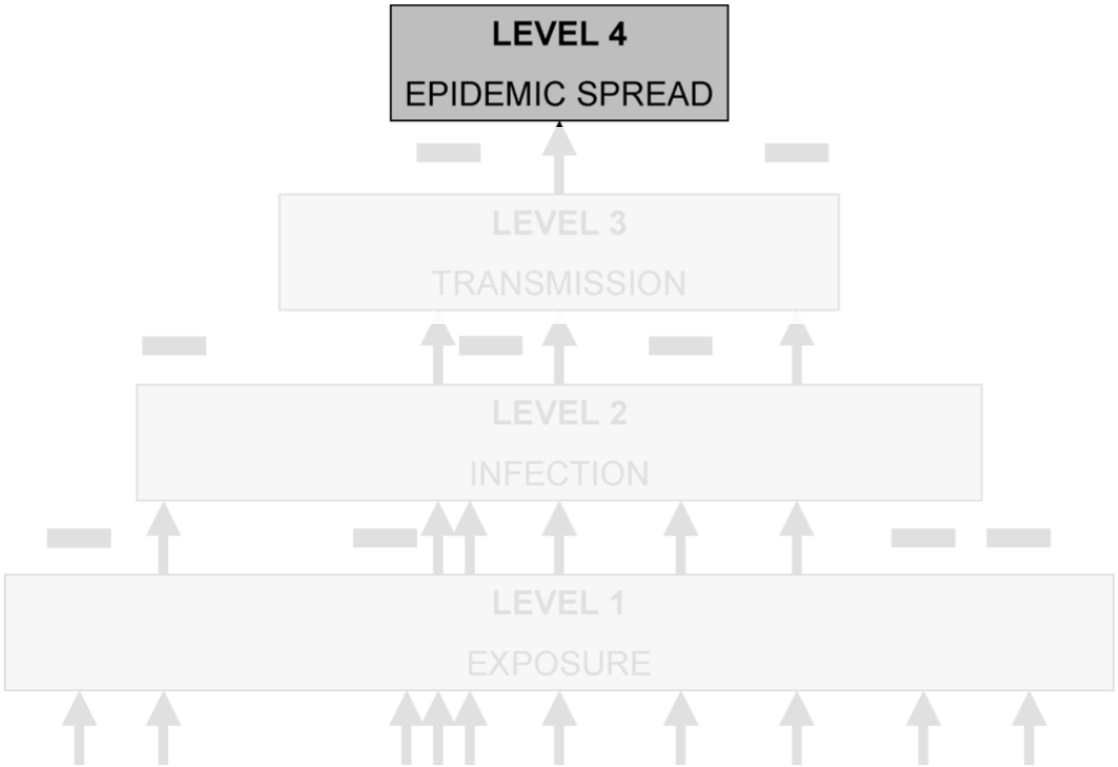


Outline

- Pathogen adaptation during epidemics
- Patterns of SARS-CoV-2 evolution
- Vaccination and pathogen evolution

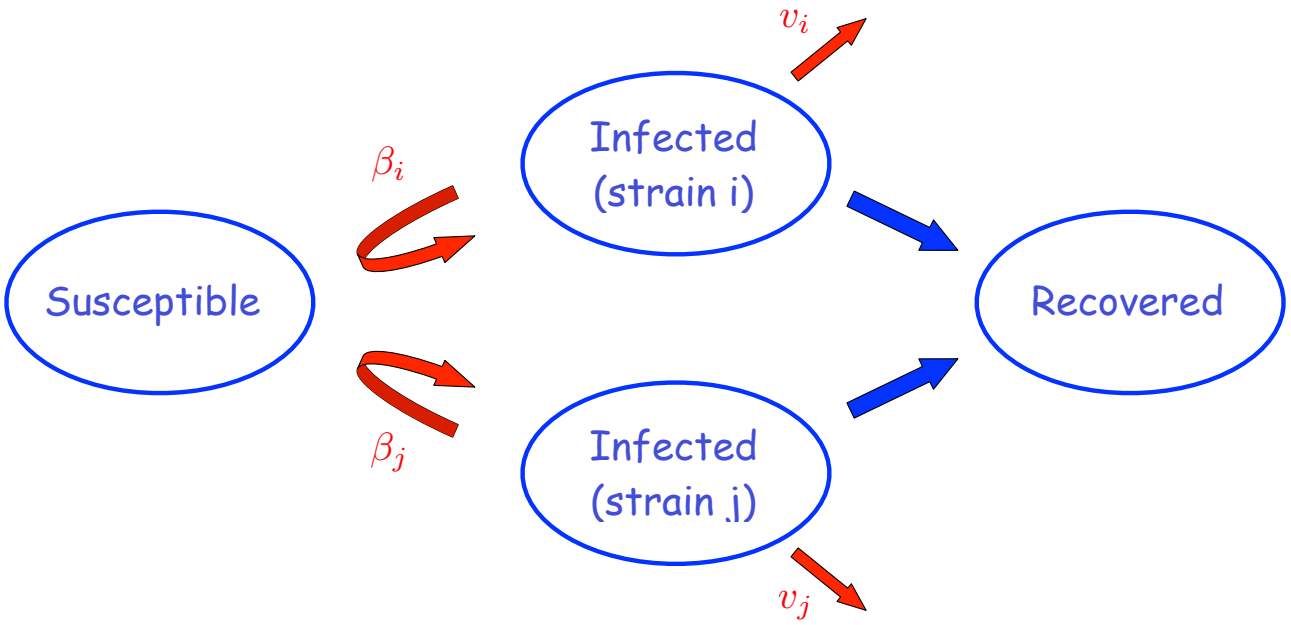
Queen's UNIVERSITY

The Emergence of Infectious Diseases



Wolfe et al. 2007. *Nature,* 447: 279; Woolhouse and Gaunt. 2007. *Critical Reviews in Microbiology*, 33:231

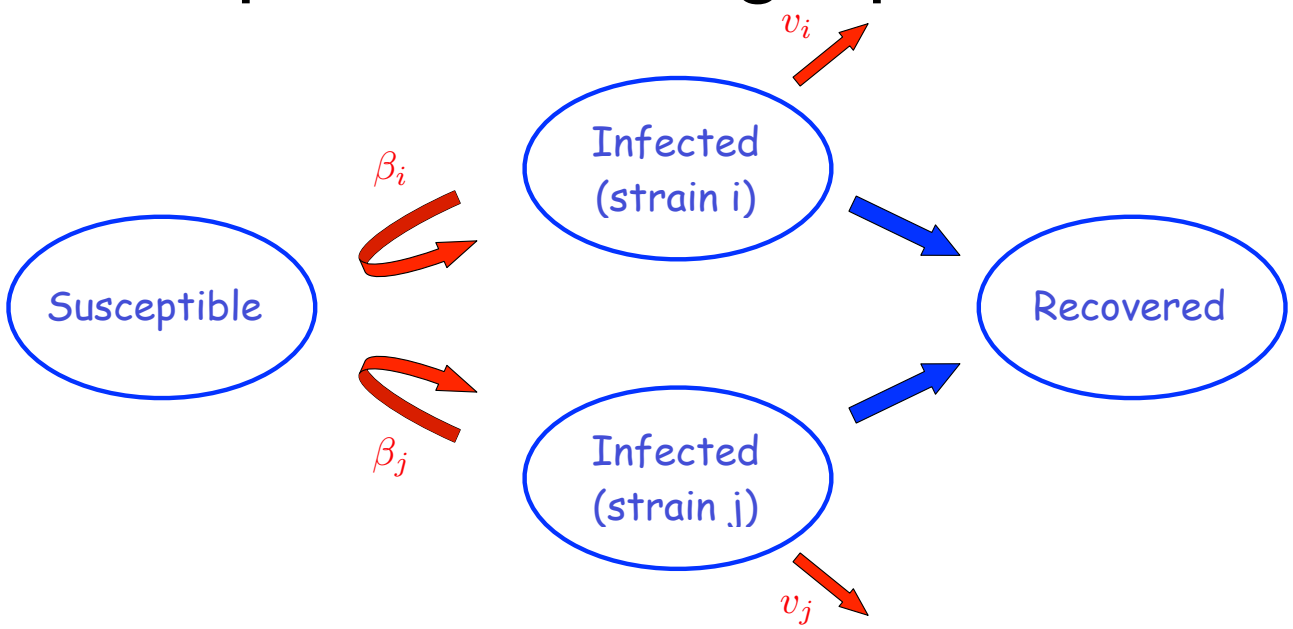
Adaptation During Epidemics



$$\frac{dS}{dt} = -S \sum_i \beta_i I_i$$

$$\frac{dI_i}{dt} = S\beta_i I_i - (v_i + c) I_i$$

Adaptation During Epidemics



$$\frac{dS}{dt} = -S\sum_i \beta_i I_i$$

$$\frac{dI_i}{dt} = S\beta_i I_i - (v_i + c)I_i$$

$$\frac{dS}{dt} = -S\bar{\beta}I \qquad I = \sum_i I_i$$

$$\frac{dI}{dt} = S\bar{\beta}I - (\bar{v} + c)I \qquad p_i = I_i/I$$

$$r_i = S\beta_i - (v_i + c)$$

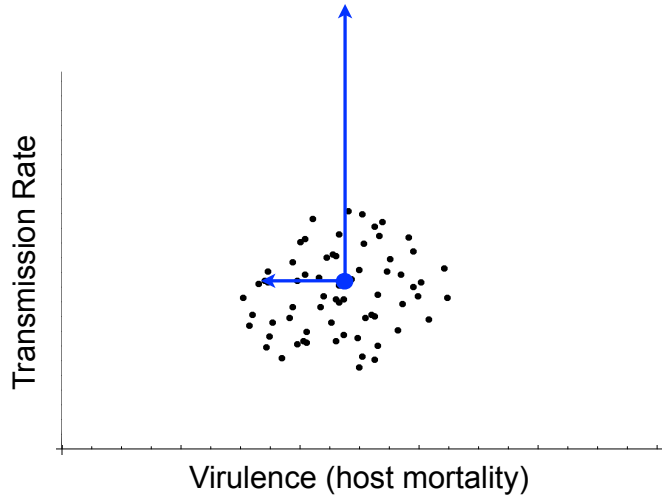
$$\frac{dp_i}{dt} = p_i(r_i - \bar{r}) \qquad \bar{x} = \sum_i x_i p_i$$

Transmission and Virulence Evolution

$$\frac{\mathrm{d}\bar{\beta}}{\mathrm{d}t} = \sigma_{\beta\beta} S - \sigma_{v\beta}$$

$$\frac{\mathrm{d}\bar{v}}{\mathrm{d}t} = \sigma_{v\beta} S - \sigma_{vv}$$

$$\begin{bmatrix} \mathrm{d}\bar{\beta}/\mathrm{d}t \\ \mathrm{d}\bar{v}/\mathrm{d}t \end{bmatrix} = \mathbf{G} \cdot \begin{bmatrix} S \\ -1 \end{bmatrix}$$

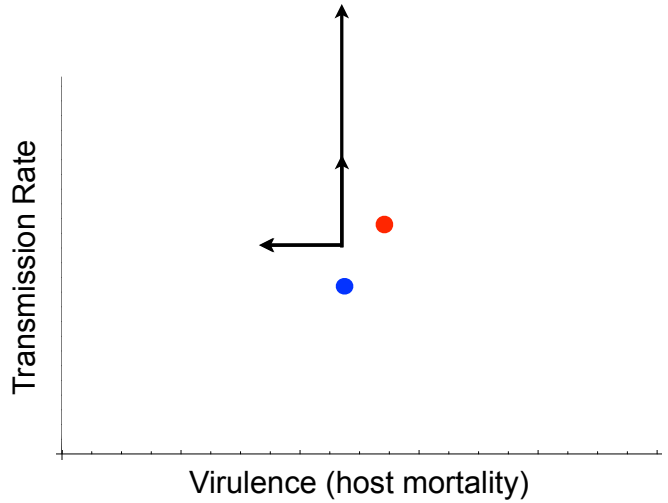


Day and Proulx. 2004. *Am Nat* 163:E40. Day and Gandon. 2005. In Disease Evolution: Models, Concepts, and Data Analysis Day and Gandon, 2007. *Ecology Letters* 10: 876

Transmission and Virulence Evolution

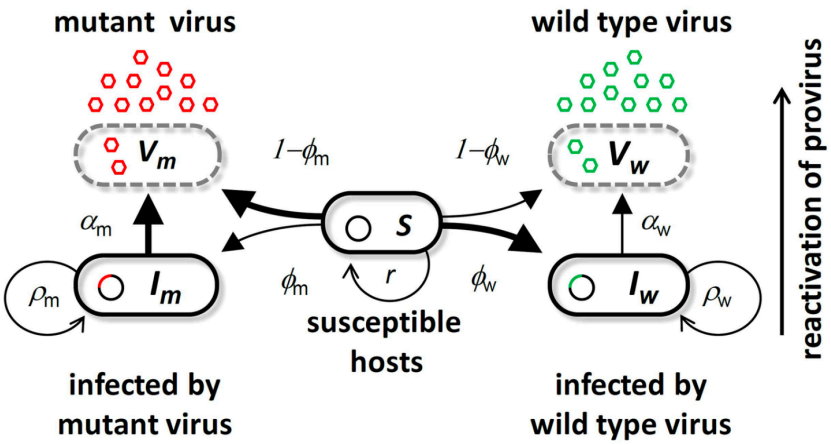
$$\frac{dp}{dt} = p(1-p)\Delta r$$

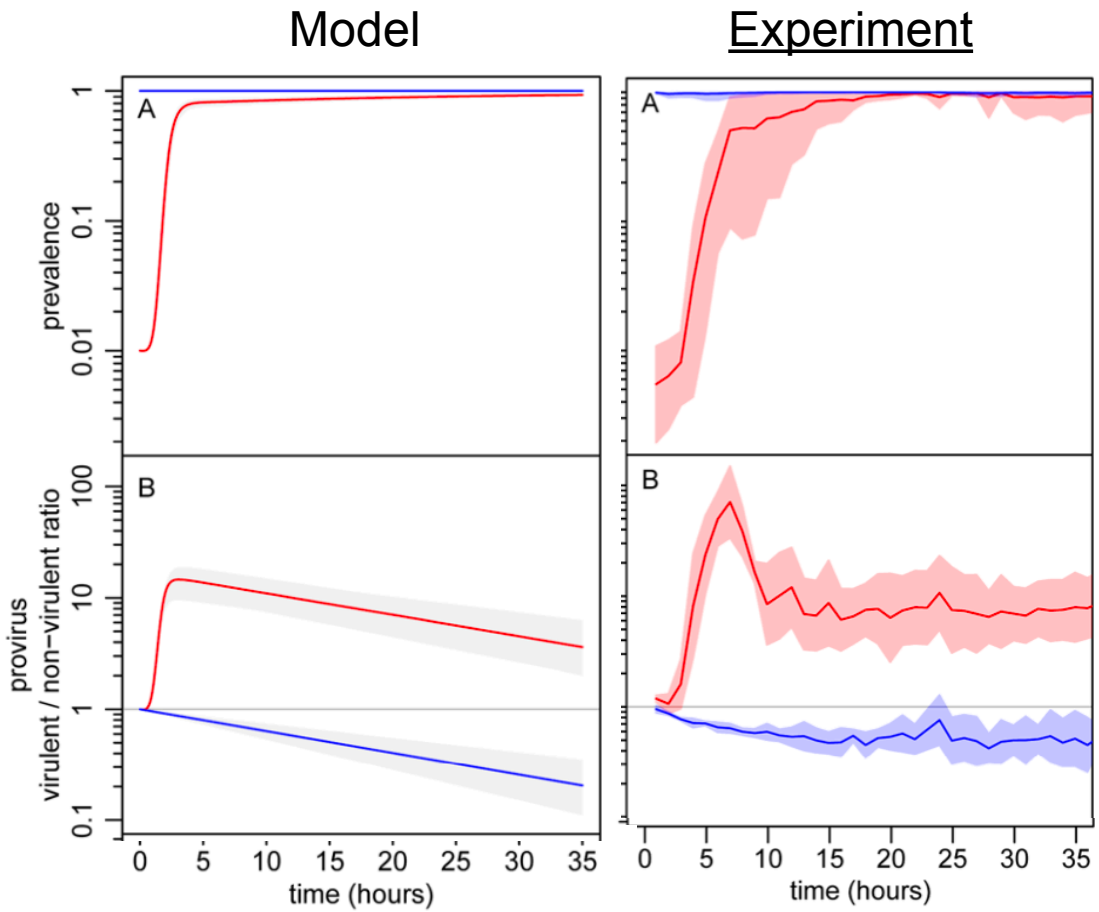
$$\begin{aligned}\Delta r &= r_1 - r_2 \\ &= \Delta\beta S - \Delta v\end{aligned}$$



Lenski and May. 1994. *JTB* 169:253; Frank. 1996. *Quart Rev. Biol*. 71:37; Day and Proulx. 2004. *Am Nat* 163:E40; Day and Gandon. 2005. In Disease Evolution: Models, Concepts, and Data Analysis; Day and Gandon, 2007. *Ecology Letters* 10: 876; Bull and Ebert 2008. *Evol App* 1:172

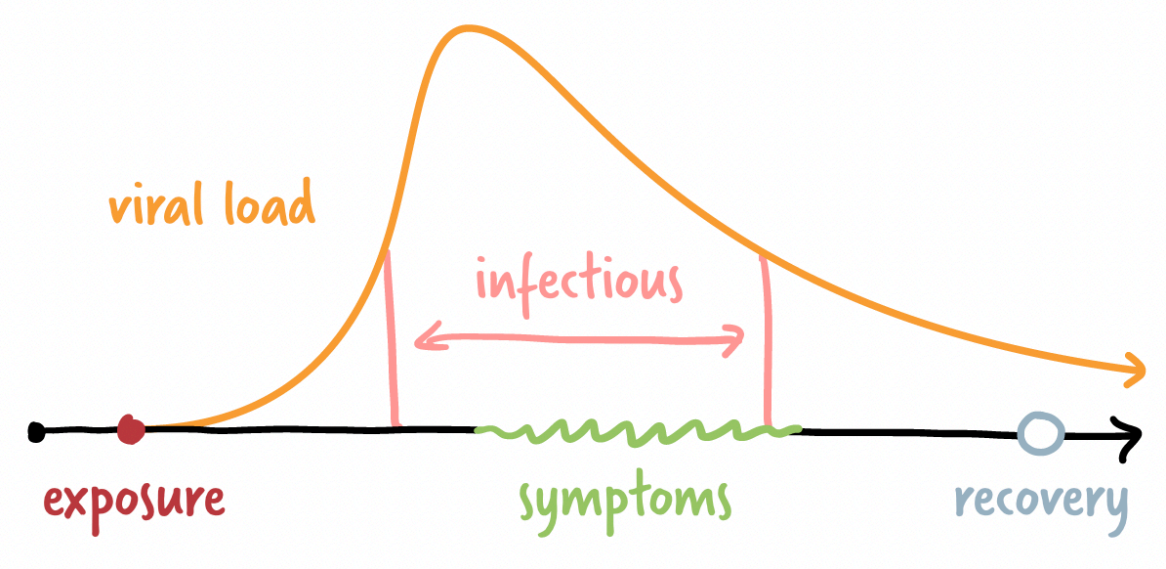
Lambda phage and *E. coli*





Berngruber et al. 2013. PLoS Pathogens 9:e1003209

What About Timing of Transmission and Virulence?



www.nytimes.com/interactive/2020/

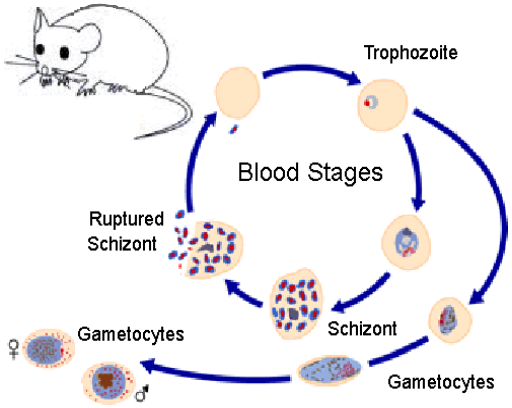
Transmission Rate Evolution

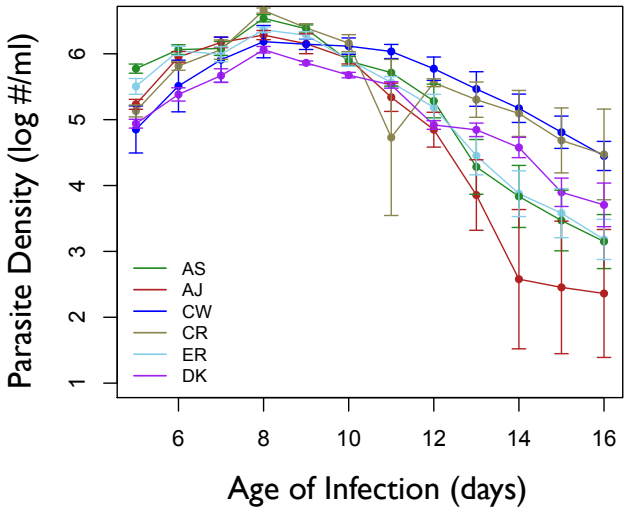
$$\dot{\bar{\beta}} \propto S\sigma_{\beta\beta}$$

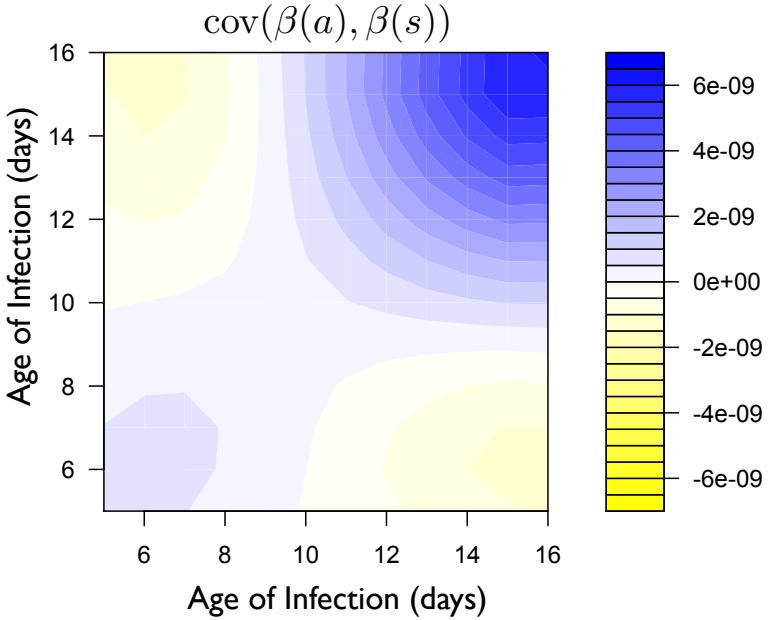
$$\dot{\bar{\beta}}(a) \propto S\int_0^\infty q(s)G_{\beta,\beta}(a,s)\mathrm{d}s$$

$$G_{\beta,\beta} = \mathrm{cov}(\beta(a),\beta(s))$$

$$q(s) = I(s)/\int I(a)\mathrm{d}a$$







Kirkpatrick & Heckman. 1989. *J Math Biol* 27:429; Mideo et al. 2008. *TREE* 23:511; Mideo et al. 2011. *Evolution* 65:3298; Day et al. 2011. *Evolution* 65:3448

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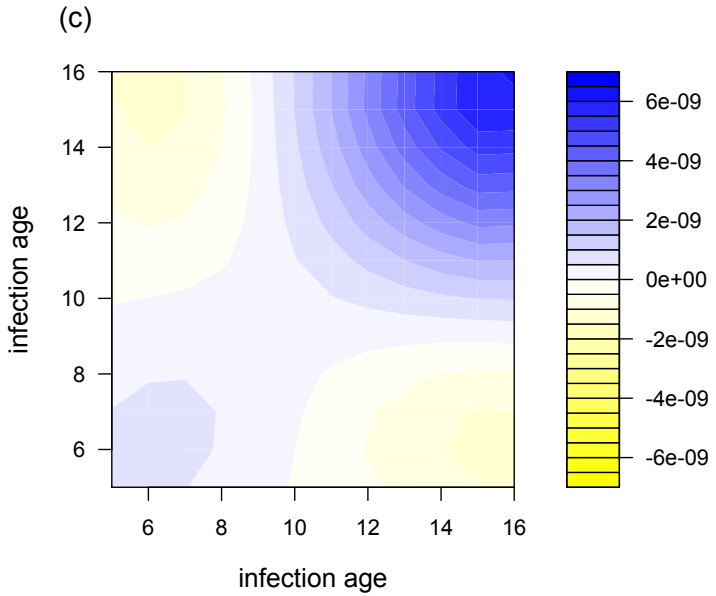
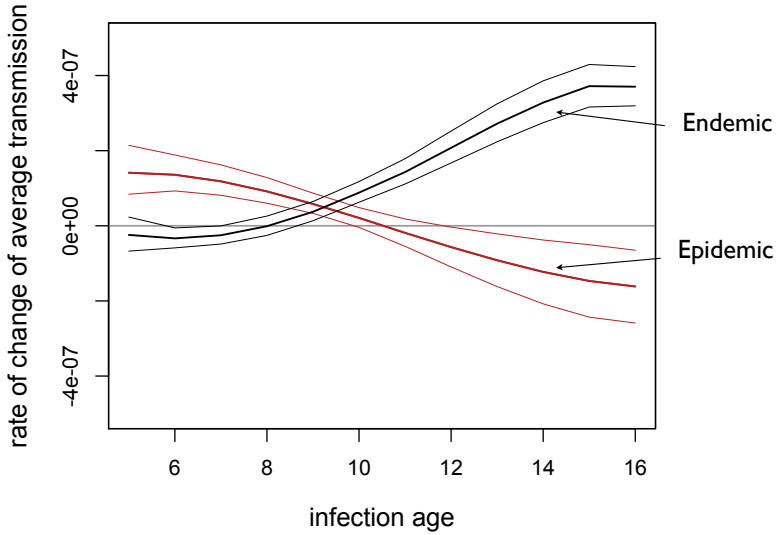
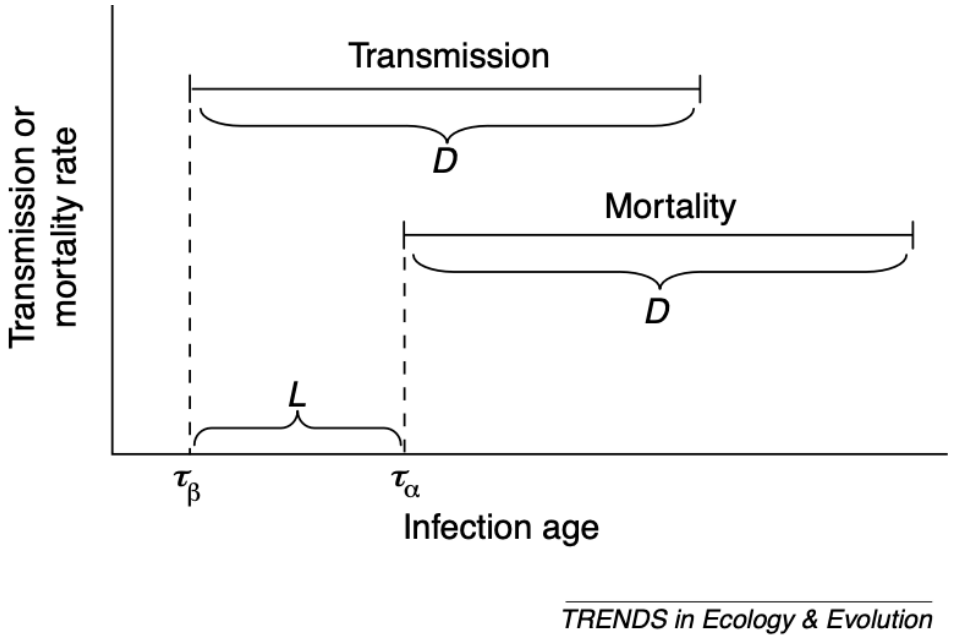


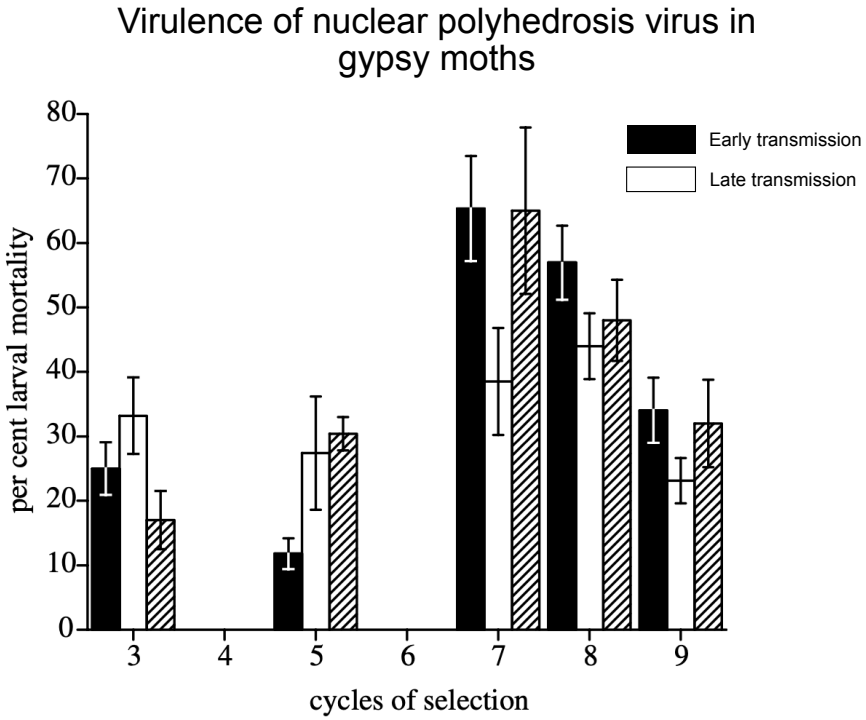


Mideo et al. 2011. *Evolution* 65:3298; Day et al. 2011. *Evolution* 65:3448

Virulence Evolution



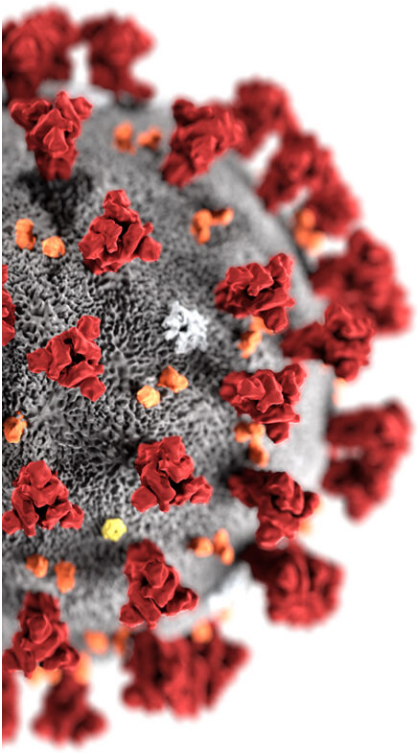
Day. 2003. *TREE* 18:113



Cooper, V.S. et al. 2002. *Proc R Soc Lond B* 269:1161

Adaptation During Epidemics
- General Predictions -

1. Strong selection for increased transmission rate during pandemic.
2. Strong selection for earlier transmission during a pandemic.
3. Weak selection against virulence if transmission occurs before symptoms.



Outline

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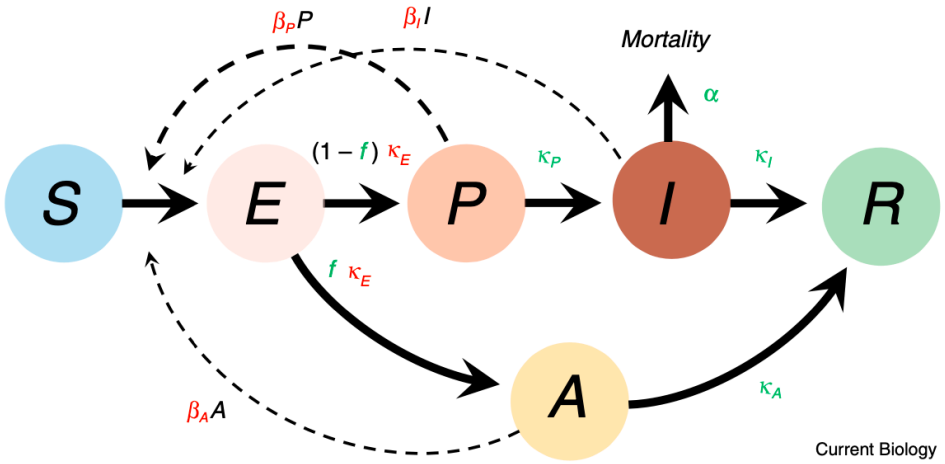
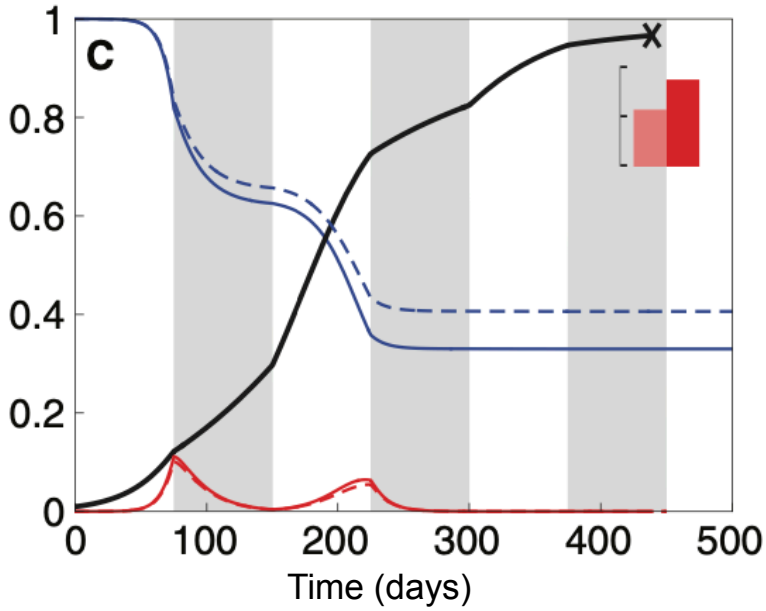
- Vaccination and pathogen evolution

Evolution in SARS-CoV-2



Transmission & Virulence



$$\frac{dp}{dt} = p(1-p)\Delta r$$

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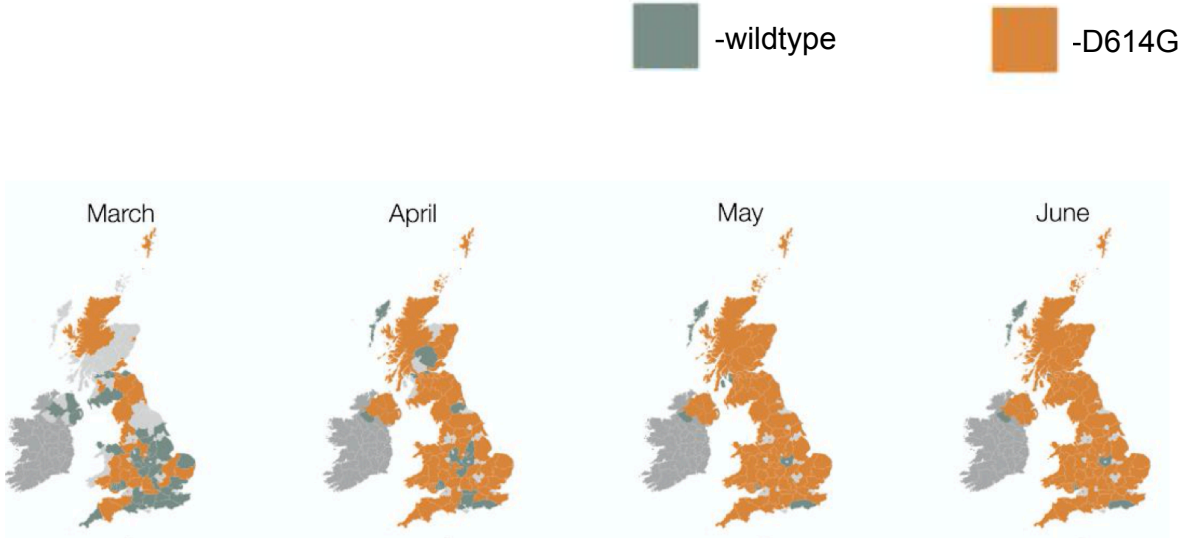
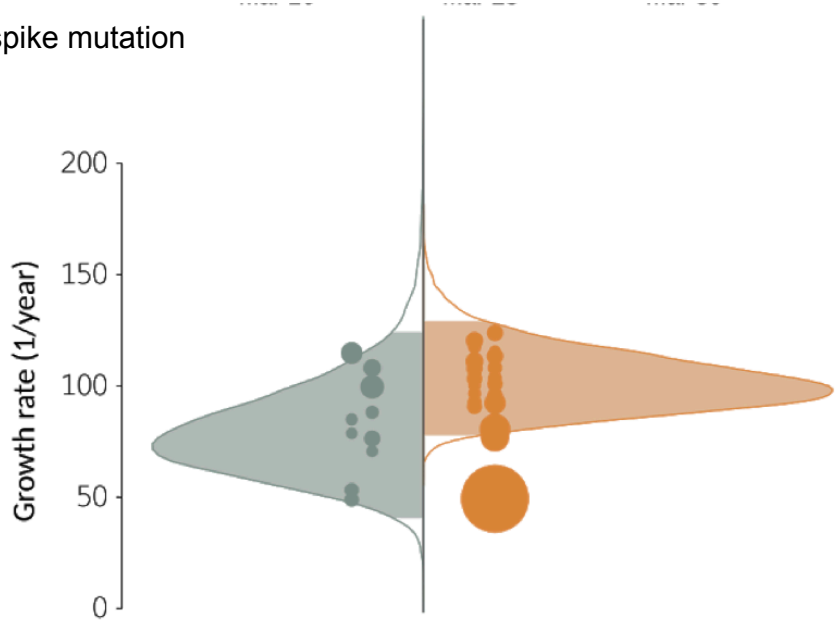
Day et al. 2020. *Current Biology* 30:R849

D614G Spike Mutation

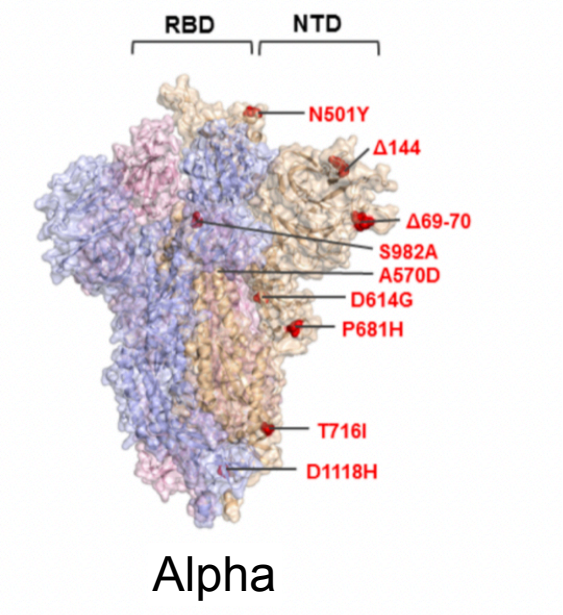




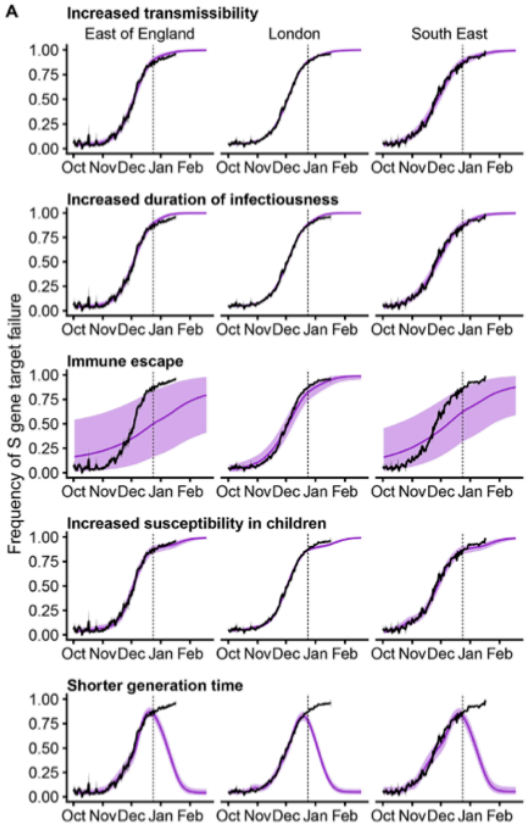
Evaluating the effects of SARS-CoV-2 Spike mutation D614G on transmissibility and pathogenicity

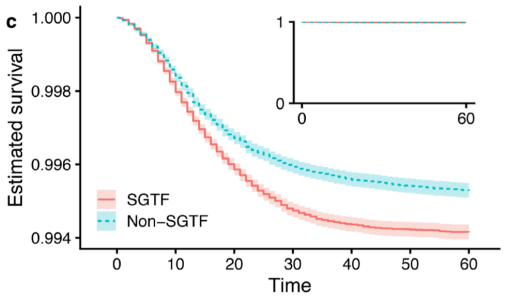
Authors:
Erik Volz*[1] , Verity Hill[2] , John T. McCrone[2], Anna Price[3], David Jorgensen[1], Áine O'Toole[2], Joel Southgate[3,4], Robert Johnson[1], Ben Jackson[2], Fabricia F. Nascimento[1], Sara M. Rey[4], Samuel M. Nicholls[5], Rachel M. Colquhoun[2], Ana da Silva Filipe[6], James Shepherd [6], David J. Pascall[7], Rajiv Shah[6], Natasha Jesudason[6], Kathy Li[6], Ruth Jarrett[6], Nicole Pacchiarini[4], Matthew Bull[4], Lily Geidelberg[1], Igor Siveroni[1], Ian Goodfellow[8], Nicholas J. Loman[5], Oliver G. Pybus[8,9], David L. Robertson[6], Emma C. Thomson[6], Andrew Rambaut*[2], Thomas R. Connor*[3,4,11], on behalf of the CoG-UK consortium[12]

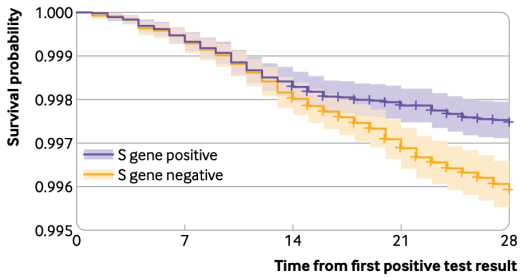
Transmission-Virulence Evolution in SARS-CoV-2



Alpha

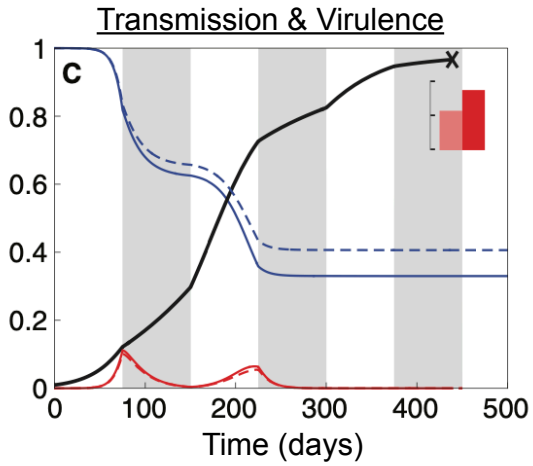






Davies et al. 2021. *Science 372:eabg3055*; Davies et al. 2021. *Nature 593:270*; Challen et al. *BMJ* 2021;372:n579 | doi: 10.1136/bmj.n579

Transmission-Virulence Evolution in SARS-CoV-2



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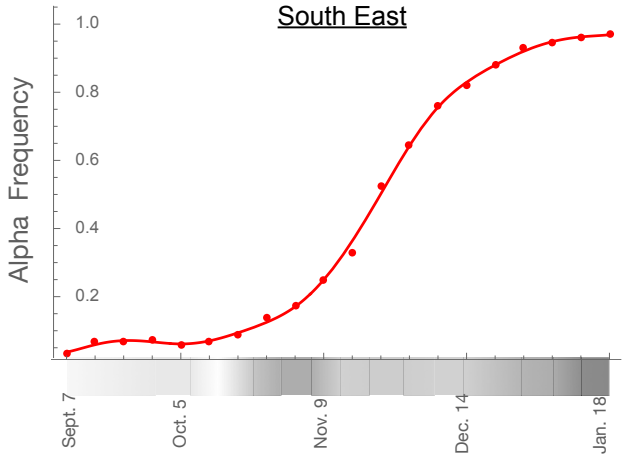
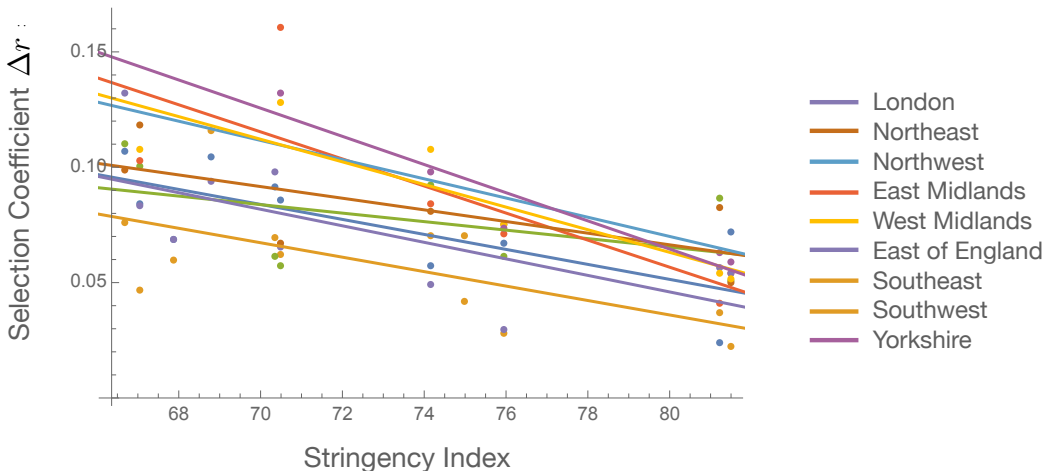
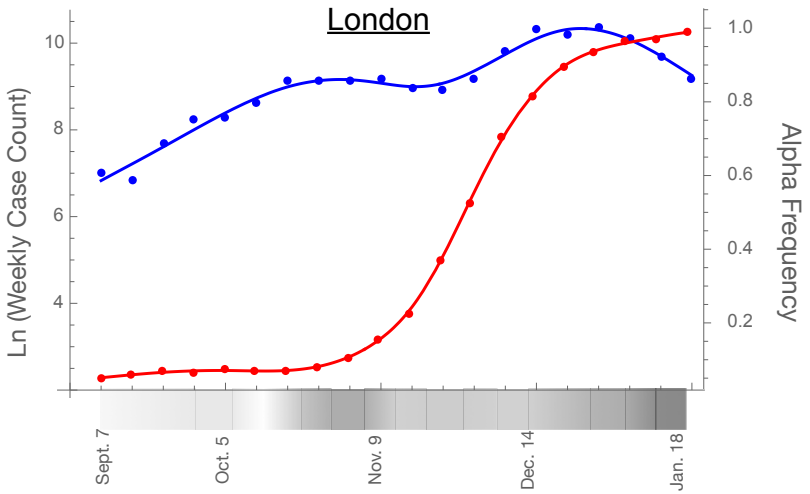




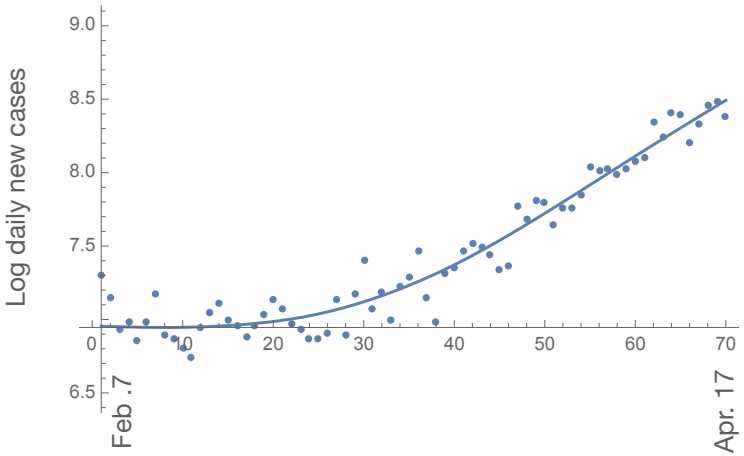
Day and Gandon, 2007. *Ecol. Lett.* 10: 876
Day et al. 2020. *Current Biology* 30:R849
Otto et al. 2021. *Current Biology* 31:R918

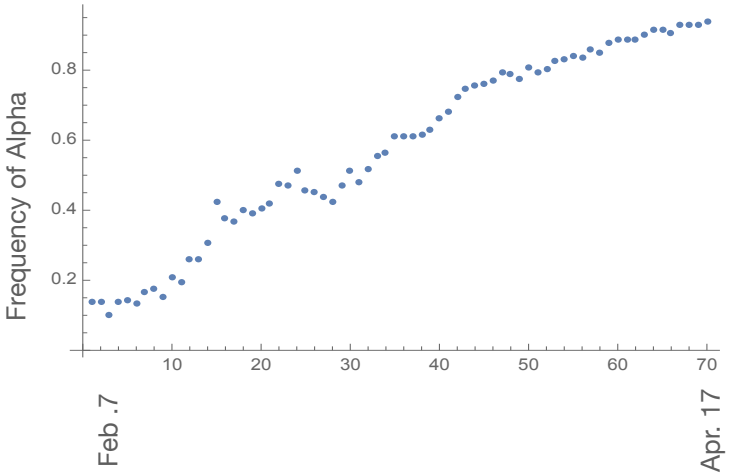
Fisher's Fundamental Theorem

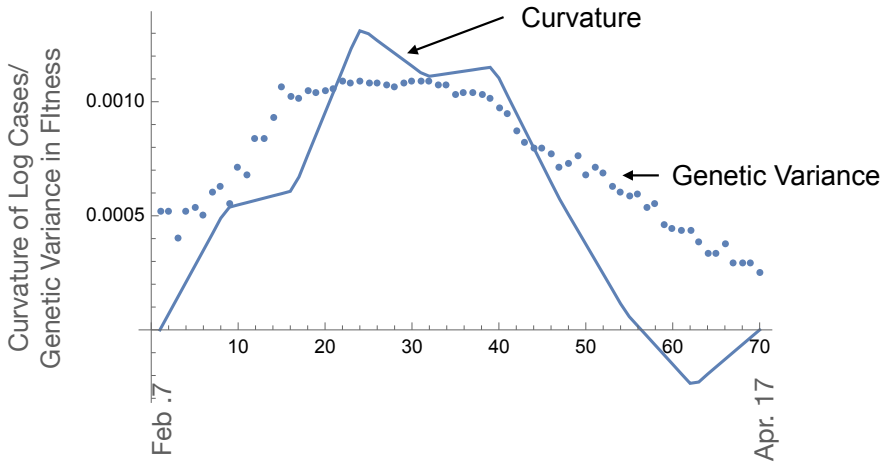


- (FFT) Rate of change of intrinsic growth rate *r* (curvature of blue plot) equals genetic variance in fitness
- In general, nth derivative equals nth cumulant of the distribution of fitness values

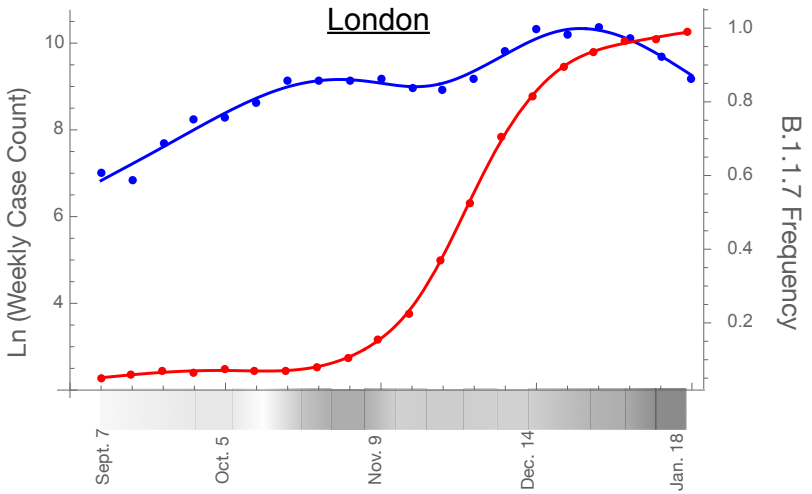
Ontario Data, 2021





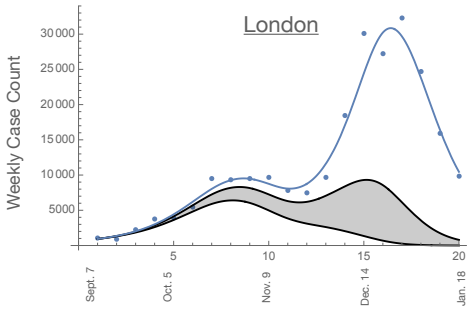


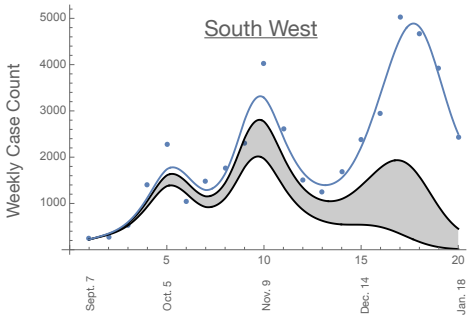
Quantifying the Epidemiological Effect of Evolution

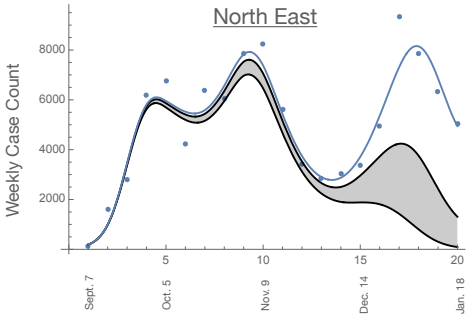


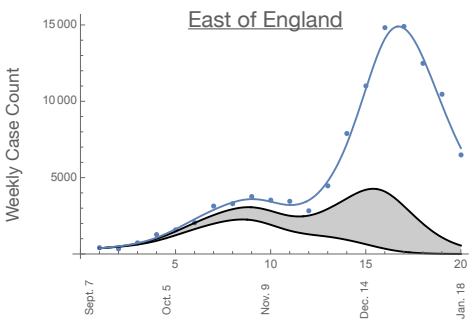
- What would have happened if there had been no evolution?
- Keep all interventions as they occurred but go back and “remove” evolution.

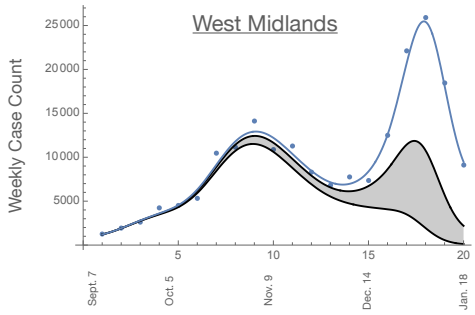
  -intrinsic growth rate is $r_{WT}(t) + s(t)\,p(t)$. Subtract $s(t)\,p(t)$ from slope at each point in time and integrate this “corrected” growth rate forward

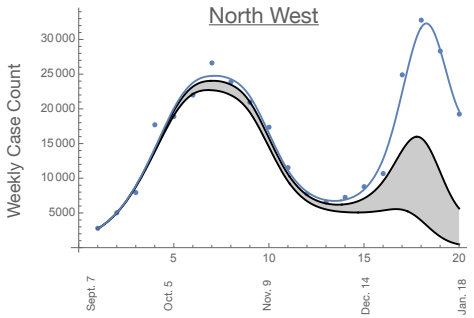

London
Weekly Case Count
30 000
25 000
20 000
15 000
10 000
5000
5
10
15
20
Sept. 7
Oct. 5
Nov. 9
Dec. 14
Jan. 18


South West
Weekly Case Count
5000
4000
3000
2000
1000
5
10
15
20
Sept. 7
Oct. 5
Nov. 9
Dec. 14
Jan. 18


North East
Weekly Case Count
8000
6000
4000
2000
5
10
15
20
Sept. 7
Oct. 5
Nov. 9
Dec. 14
Jan. 18


East of England
Weekly Case Count
15 000
10 000
5000
5
10
15
20
Sept. 7
Oct. 5
Nov. 9
Dec. 14
Jan. 18


West Midlands
Weekly Case Count
25 000
20 000
15 000
10 000
5000
5
10
15
20
Sept. 7
Oct. 5
Nov. 9
Dec. 14
Jan. 18


North West
Weekly Case Count
30 000
25 000
20 000
15 000
10 000
5000
5
10
15
20
Sept. 7
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Nov. 9
Dec. 14
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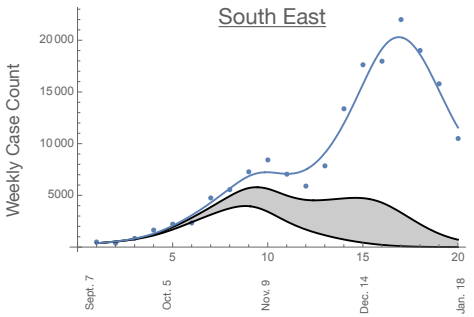
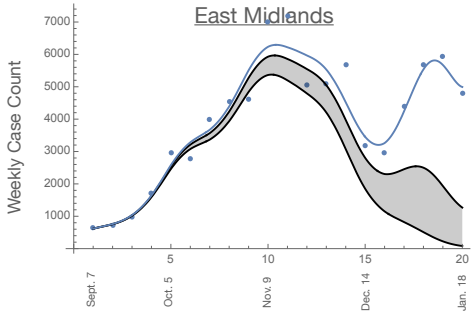
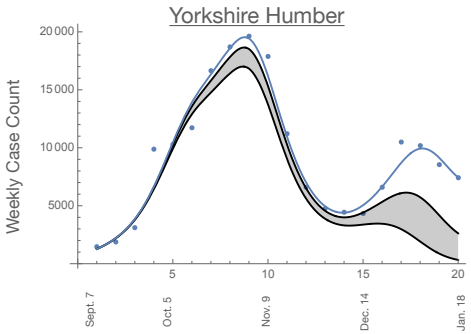
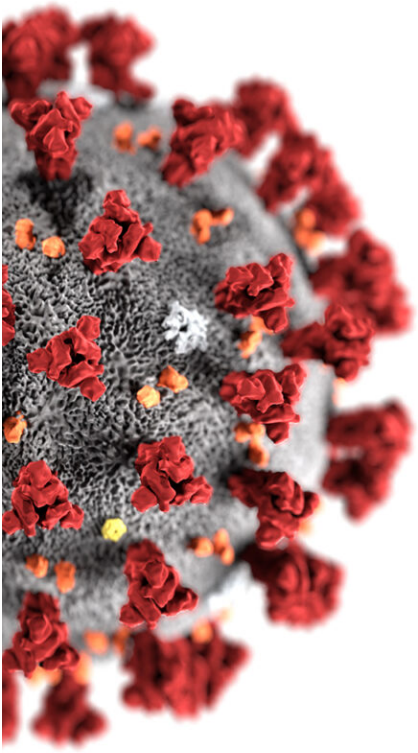

South East
Weekly Case Count
20 000
15 000
10 000
5000
5
10
15
20
Sept. 7
Oct. 5
Nov. 9
Dec. 14
Jan. 18


East Midlands
Weekly Case Count
7000
6000
5000
4000
3000
2000
1000
5
10
15
20
Sept. 7
Oct. 5
Nov. 9
Dec. 14
Jan. 18


Yorkshire Humber
Weekly Case Count
20 000
15 000
10 000
5000
5
10
15
20
Sept. 7
Oct. 5
Nov. 9
Dec. 14
Jan. 18



Outline

- Pathogen adaptation during epidemics
- Patterns of SARS-CoV-2 evolution
- Vaccination and pathogen evolution

Categorizing Vaccine-Adapted Variants

Fitness of variant *i* in **naive** hosts

1

Fitness of variant *i* in **vaccinated** hosts

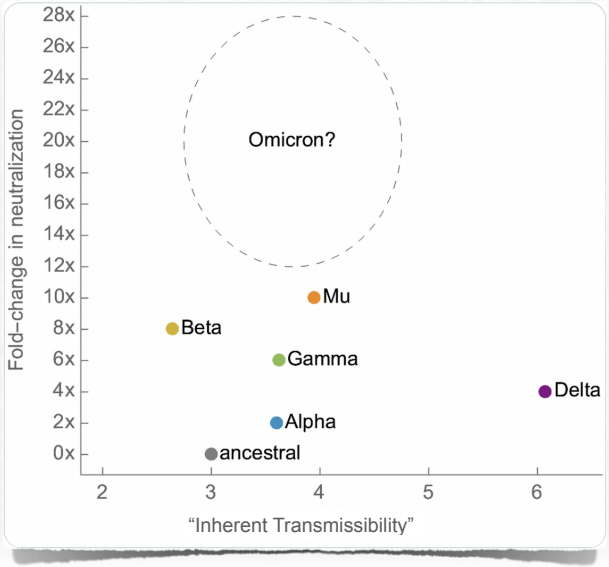
Fitness components (between host)

Infectivity σ_i | Transmission β_i | Infection duration $1/\gamma_i$

Fitness components (between host)

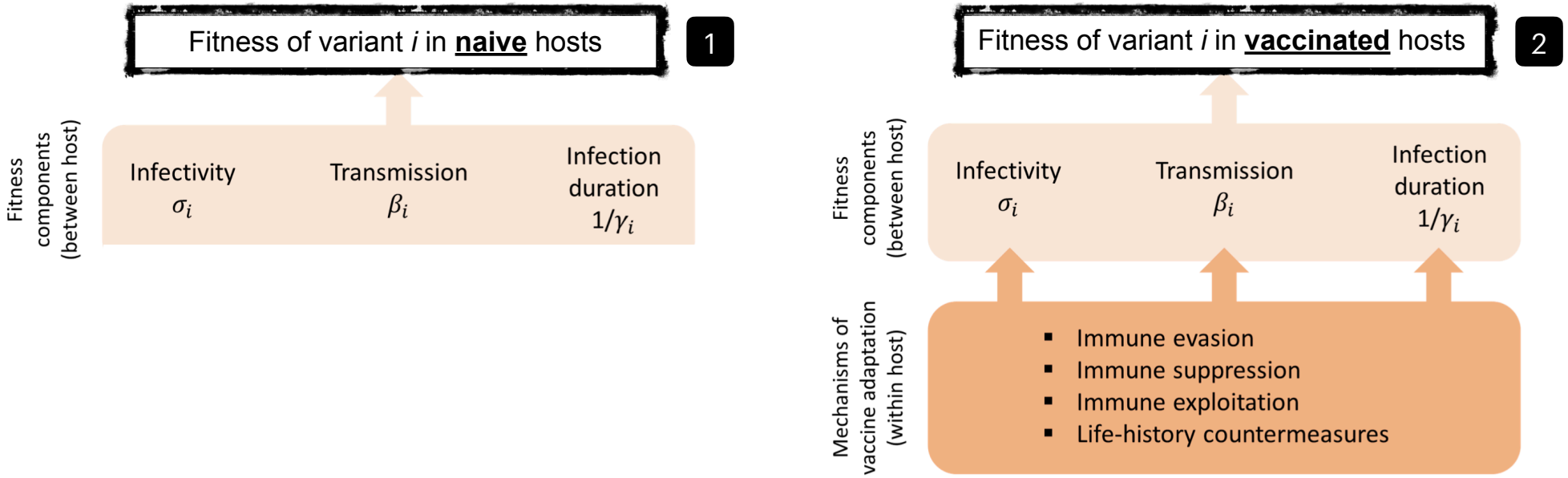
Infectivity σ_i | Transmission β_i | Infection duration $1/\gamma_i$

2



Day et al. 2022. Pathogen evolution under vaccination campaigns. PLoS Biology 20(9): e3001804

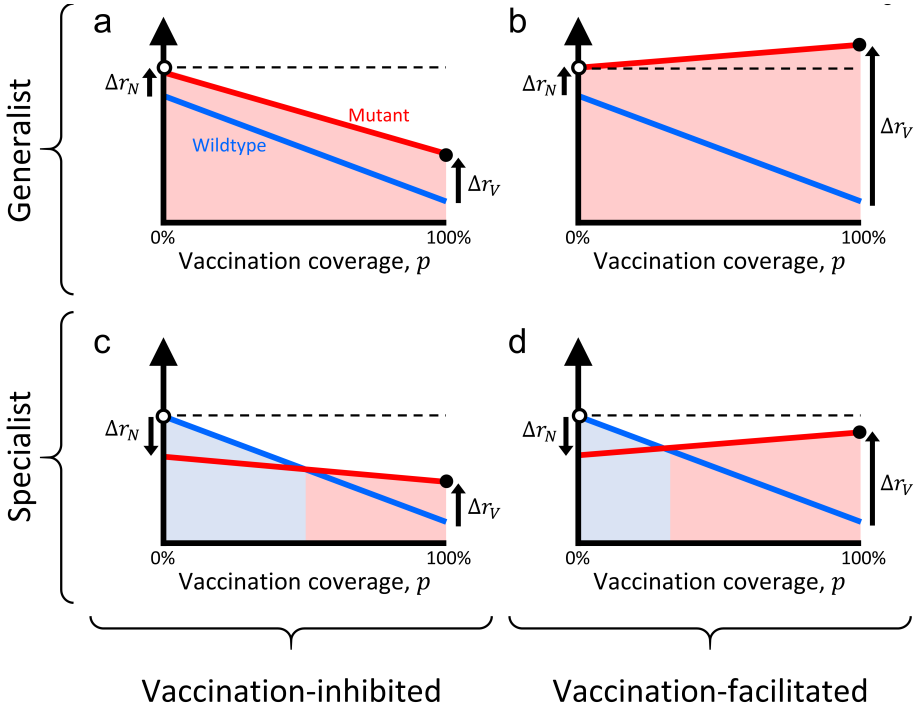
Categorizing Vaccine-Adapted Variants

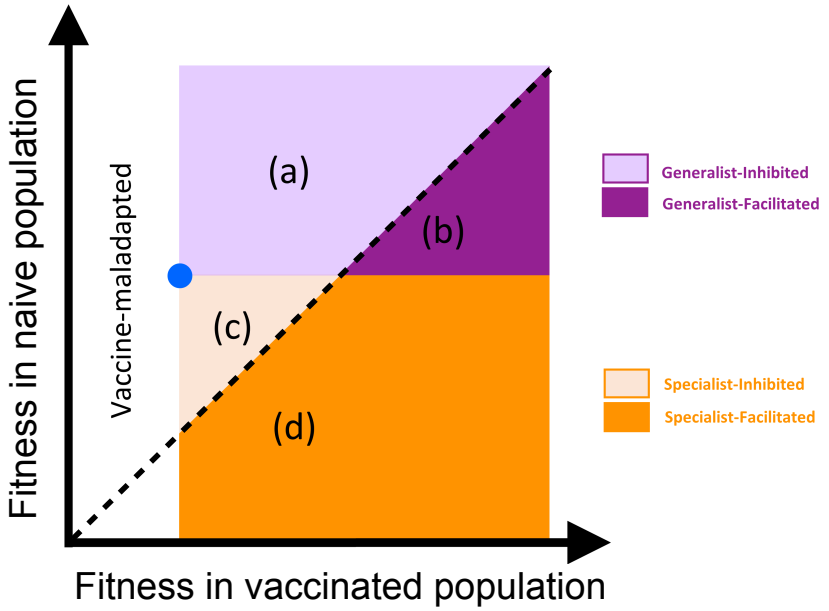


Day et al. 2022. Pathogen evolution under vaccination campaigns. PLoS Biology 20(9): e3001804

Categorizing Vaccine-Adapted Variants

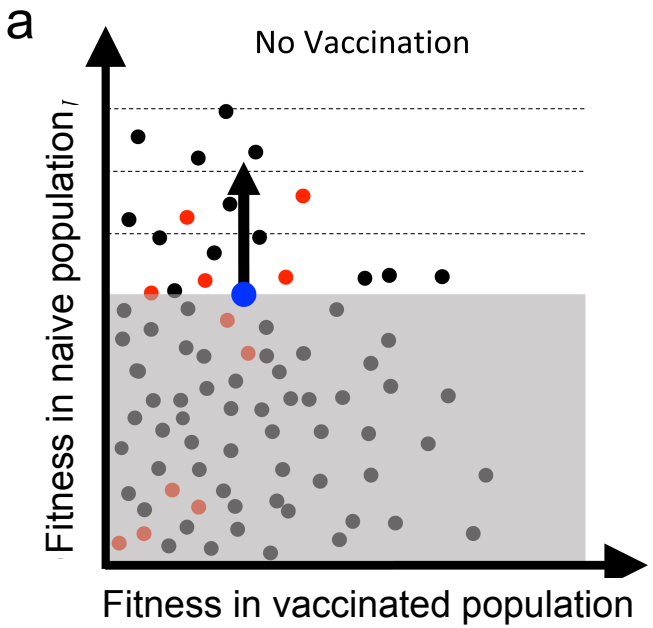
Two axes of categorization





Day et al. 2022. Pathogen evolution under vaccination campaigns. PLoS Biology 20(9): e3001804

Pathogen Evolution under Vaccination



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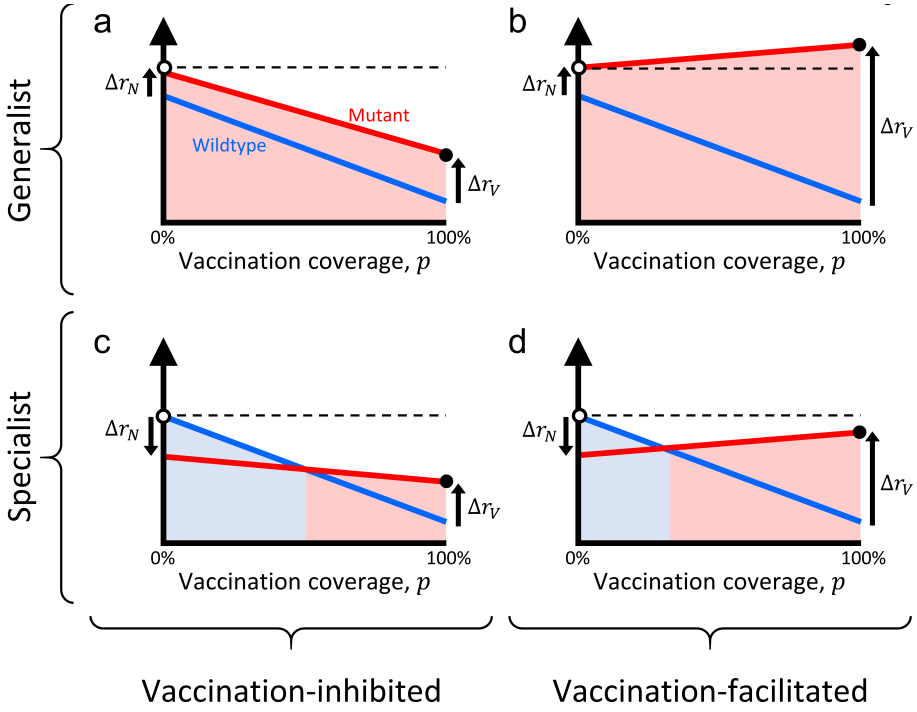
Pathogen Evolution under Vaccination

Two axes of categorization



- Successful variants tend to transition over time from generalist to specialists
- Predictions about inhibited/facilitated less clear

Day et al. 2022. Pathogen evolution under vaccination campaigns. PLoS Biology 20(9): e3001804

Evidence From Other Pathogens

Vaccine-driven pathogen evolution is relatively rare. Where it has occurred we typically have:

- Vaccines that are “leaky”.
- Vaccines that target a small number of epitopes.

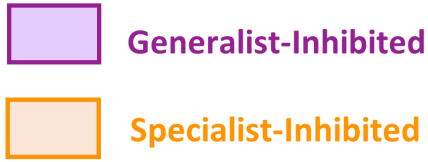
Both are true for SARS-CoV-2.

Kennedy DA, Read AF. Proc Roy Soc B: 2017;284:20162562.
Kennedy DA, Read AF. PNAS 2018;115: 12878

Evidence From Other Pathogens

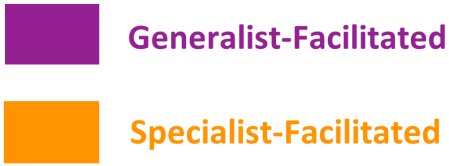
Tendency to go from generalist to specialist over time

- Malaria
- Hep B
- Bordetella pertussis
- Wildlife/agricultural
- Streptococcus pneumoniae
- Influenza (less clear)



Very few cases of vaccine-facilitation

- Marek's disease virus
- Myxoma virus?



Day et al. 2022. Pathogen evolution under vaccination campaigns. PLoS Biology 20(9): e3001804

SARS-CoV-2

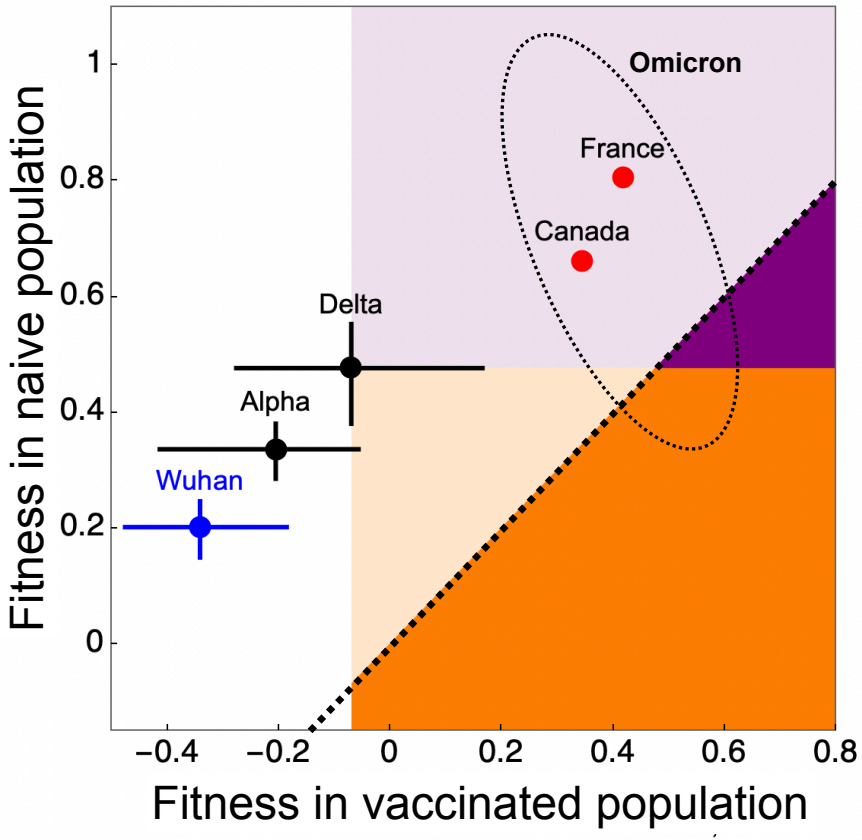
(Can use SARS-CoV-2 surveillance data to categorize VOCs in real time)

Generalist-Inhibited

Generalist-Facilitated

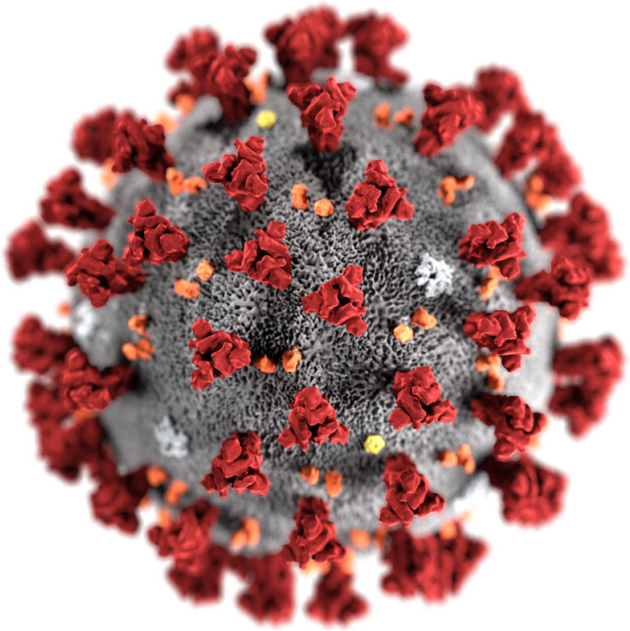
Specialist-Inhibited

Specialist-Facilitated



(TWO-DOSE Vaccinated)

Day et al. 2022. Pathogen evolution under vaccination campaigns.
PLoS Biology 20(9): e3001804



Summary

- Pathogen adaptation during epidemics
- Patterns of SARS-CoV-2 evolution
- Vaccination and pathogen evolution

Acknowledgements

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