

# Characterizing evolutionary dynamics on a broader scale: a strain-space model for SARS-CoV-2

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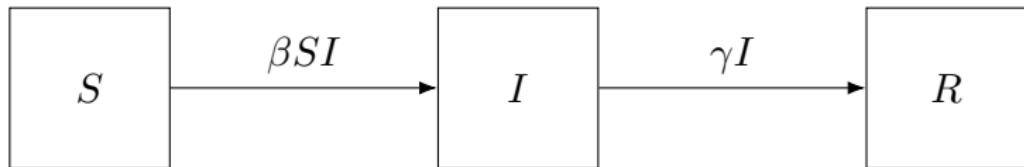
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July 12, 2022

# Infection spread with compartmental models



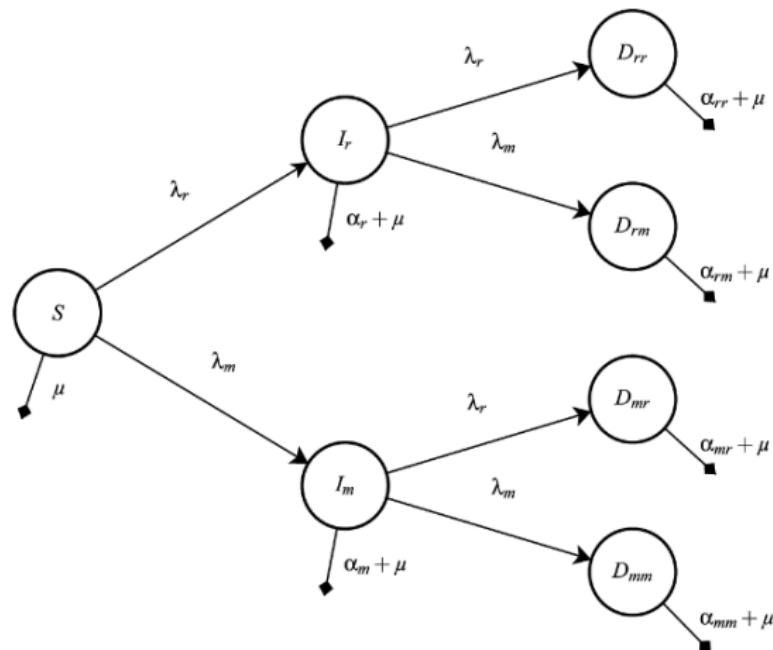
- $S(t)$  - fraction of susceptible hosts at  $t$
- $I(t)$  - fraction of infected hosts at  $t$
- $R(t)$  - fraction of recovered hosts at  $t$
- $1 = S(t) + I(t) + R(t)$  is constant

# Broad use of genomic data in dynamical epidemic models has been limited

	Continual Immune Selection	Weak or Absent Immune Selection	
		Tree shape controlled by non-selective population dynamic processes	
Idealized Phylogeny Shapes		Population size dynamics  Constant size 	Spatial dynamics <b>Strong spatial structure</b>  <b>Weak spatial structure</b> 
Examples	Human influenza A virus intra-host HIV	inter-host HIV inter-host HCV	Measles, rabies inter-host HIV
Tree Inferences	Detection of antigenic escape mutations	Estimation of population growth rates	Estimation of population migration rates

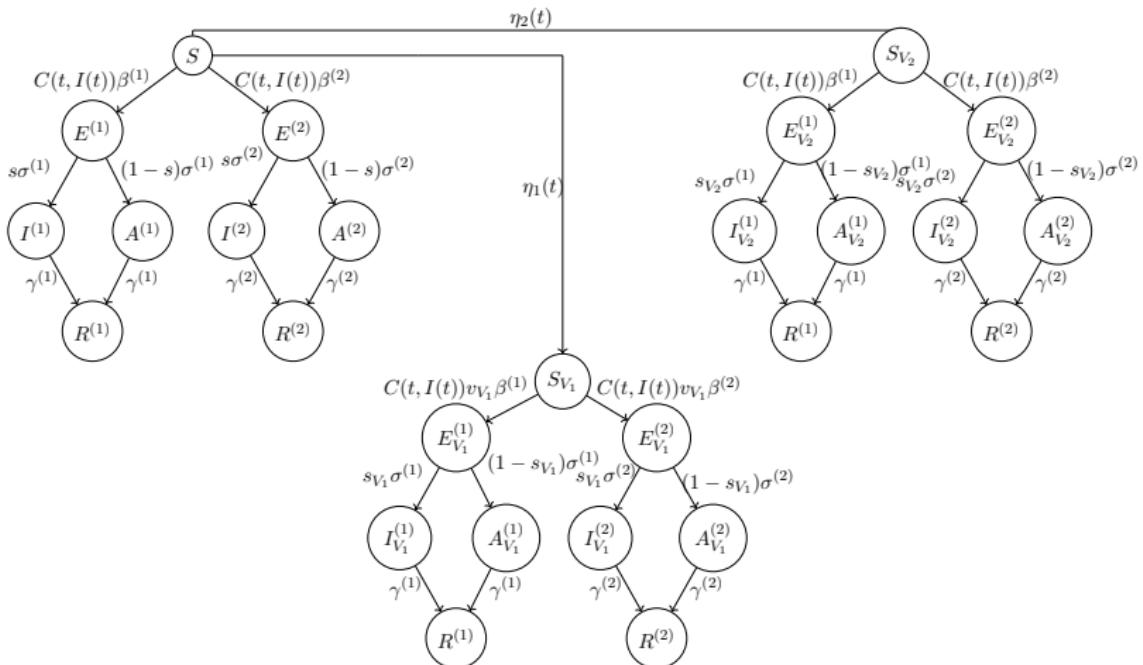
[Grenfell et al., 2004]

# Modeling multiple infections is challenging

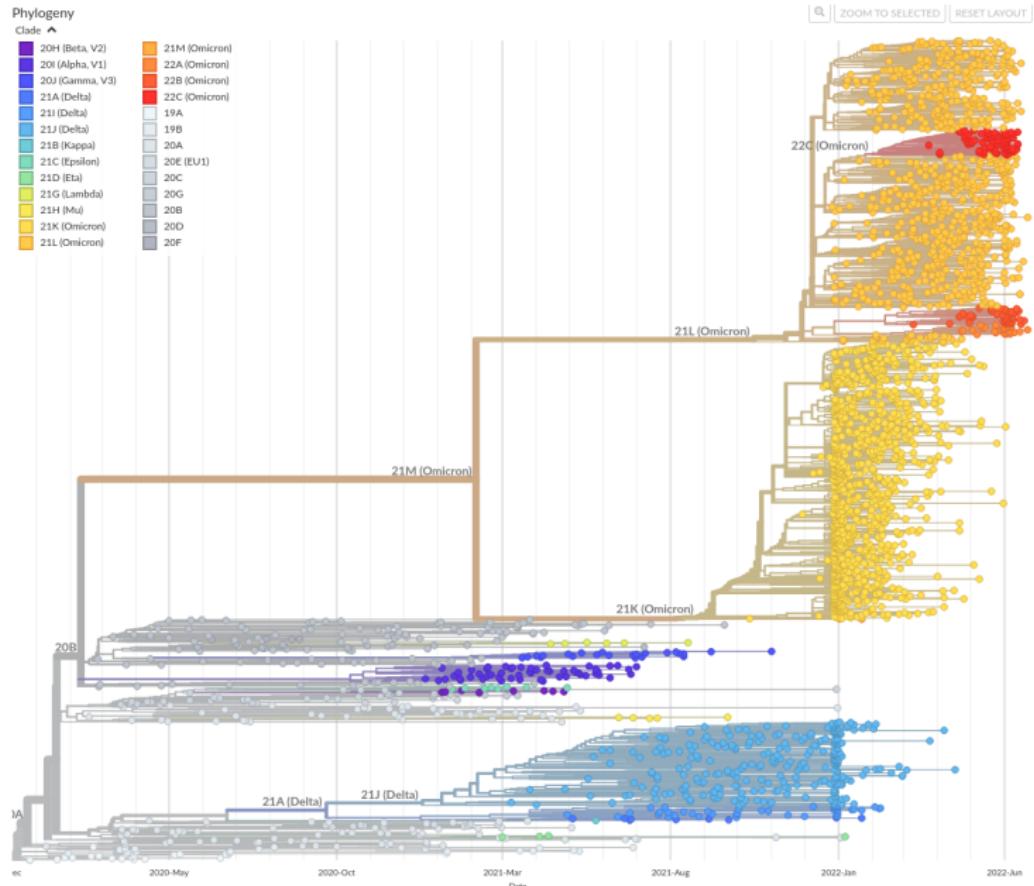


[Alizon and van Baalen, 2008]

# Complexity only increases with vaccination dynamics etc.



# How to incorporate more data?



# A useful approximation

RESEARCH ARTICLE | BIOLOGICAL SCIENCES | 

## Dynamics and selection of many-strain pathogens

Julia R. Gog and Bryan T. Grenfell [Authors Info & Affiliations](#)

December 12, 2002 | 99 (26) 17209–17214 | <https://doi.org/10.1073/pnas.252512799>

227 196 186    

**PNAS**  
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Abstract  
Derivation of the Model  
Application to Antigenic

**Abstract**  
Strain structure is of fundamental importance in the underlying dynamics of a number of pathogens. However, previous models have been too complex to accommodate many



J. Math. Biol. 44, 169–184 (2002)  
Digital Object Identifier (DOI):  
10.1007/s002850100120

## Mathematical Biology

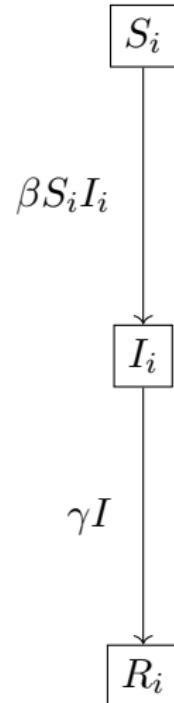
J.R. Gog · J. Swinton

## A status-based approach to multiple strain dynamics

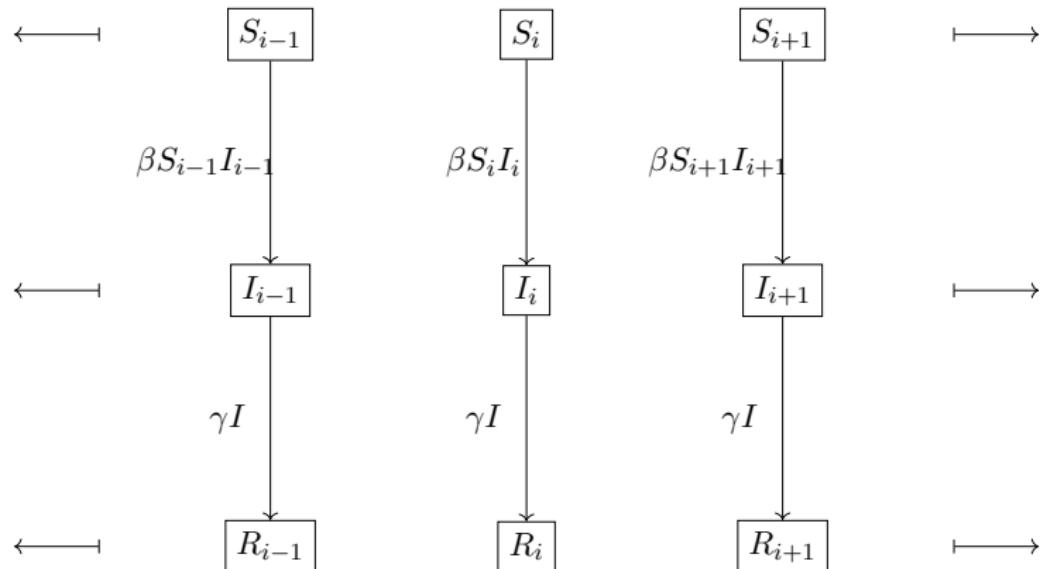
Received: 5 April 2000 / Revised version: 24 July 2001 /  
Published online: 8 February 2002 – © Springer-Verlag 2002

## Begin with SIR model

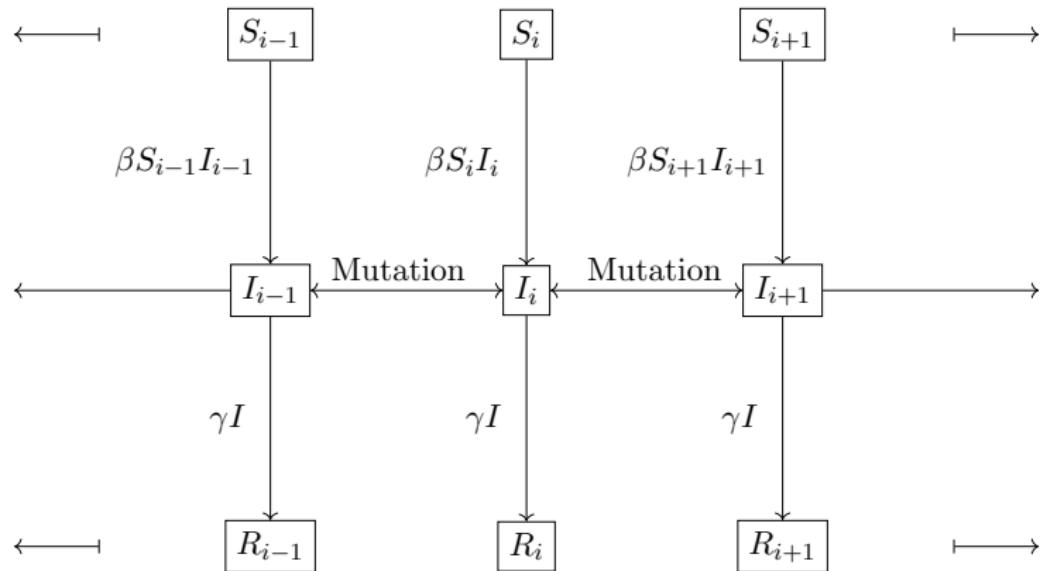
- Consider strains of a pathogen numbered  $i \in [1, N]$
- $S(t)$  - population of hosts susceptible to strain  $i$  at  $t$
- $I(t)$  - population of hosts infected with strain  $i$  at  $t$
- $R(t)$  - population of hosts recovered from strain  $i$  at  $t$



# Organize strains on a lattice



## Strains mutate into adjacent strains

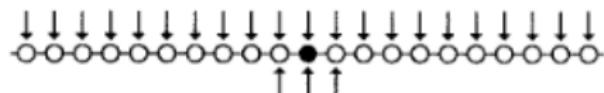


# Infections provide cross-immunity to nearby strains

$$\sigma_{ij} = e^{-(\frac{i-j}{d})^2}$$



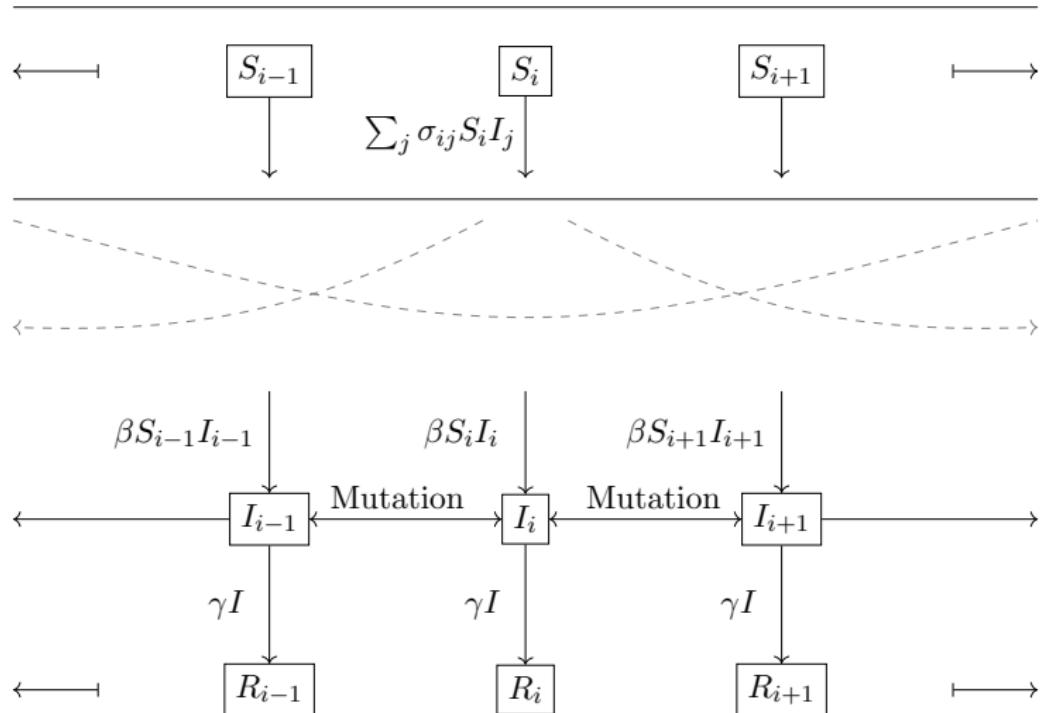
Cross-immunity to nearby strains



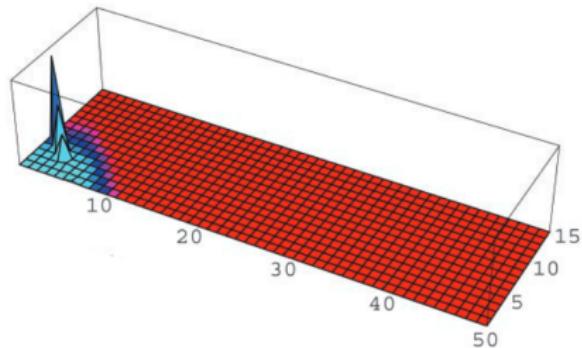
Mutation to adjacent strains

[Gog and Grenfell, 2002]

# Full strain lattice model in 1 dimension

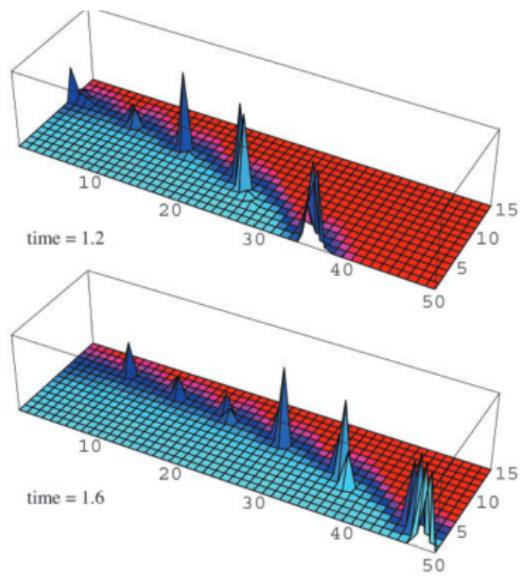
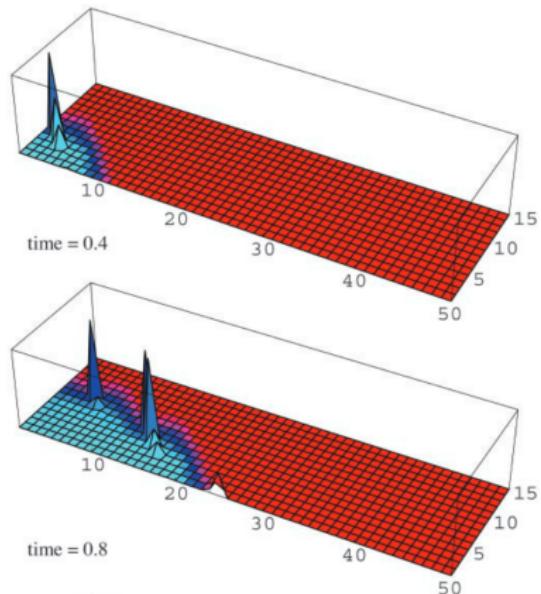


## Extending the strain lattice to 2 dimensions



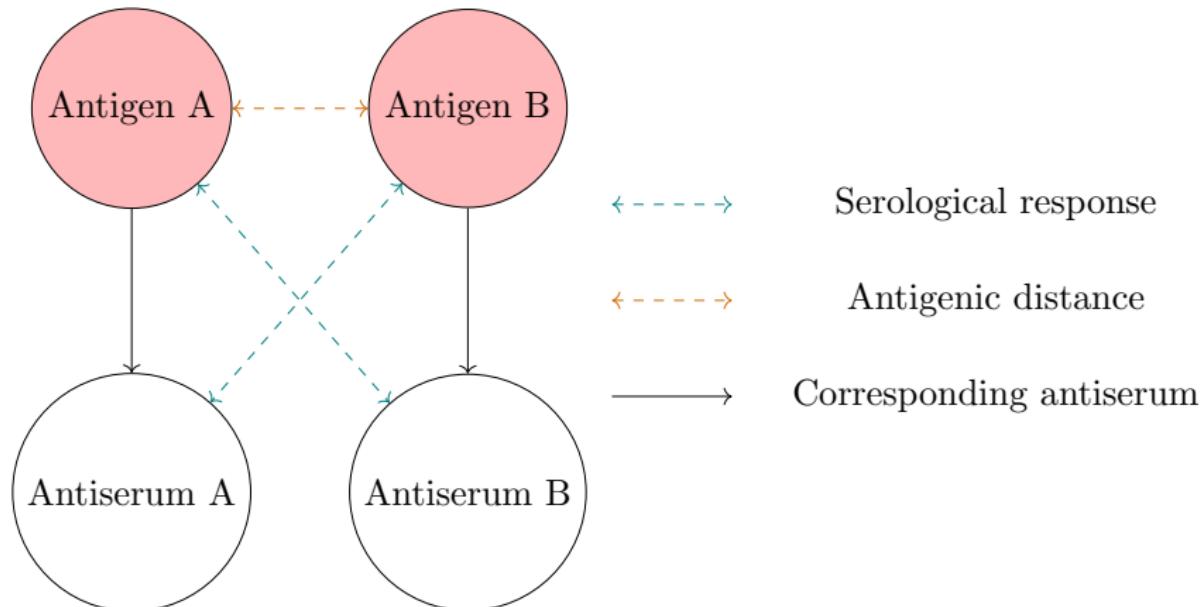
[Gog and Grenfell, 2002]

# Extending the strain lattice to 2 dimensions



[Gog and Grenfell, 2002]

# Quantifying antigenicity between viruses



Neutralization assays are used to estimate relative antibody titre

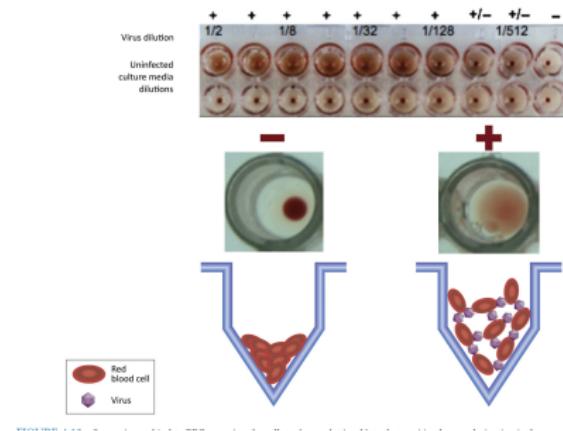
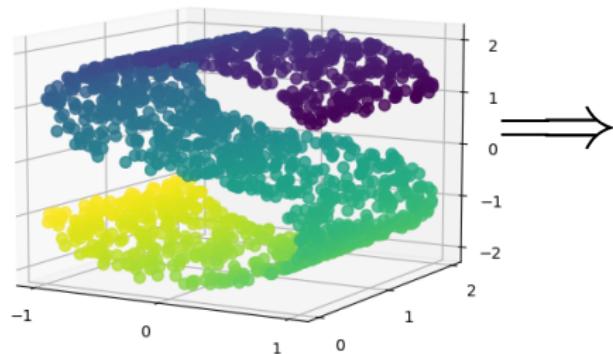


Illustration of mechanism behind hemagglutination assay

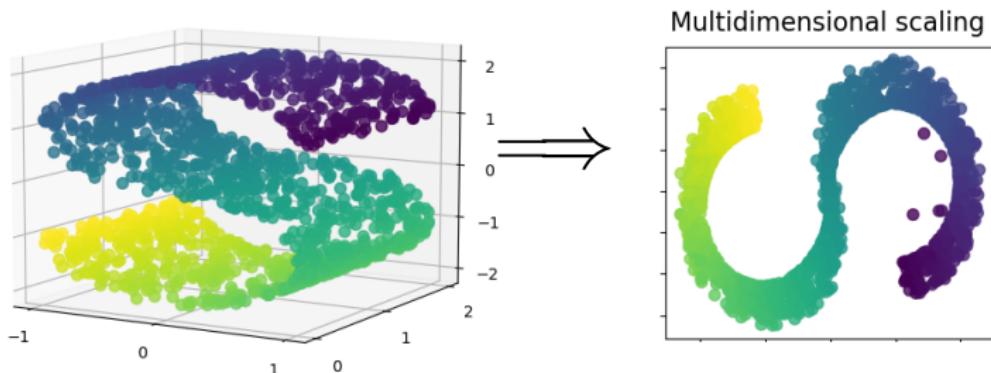
[Payne, 2017]

# Projecting points to low dimensions while preserving distances



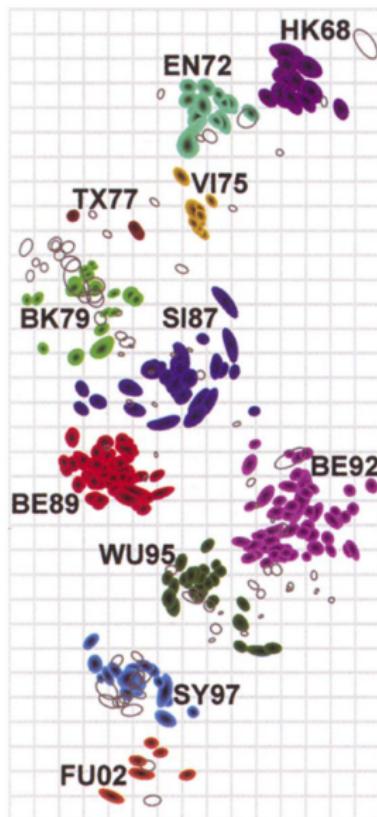
[Pedregosa et al., 2011]

# Projecting to low dimensions while preserving distances



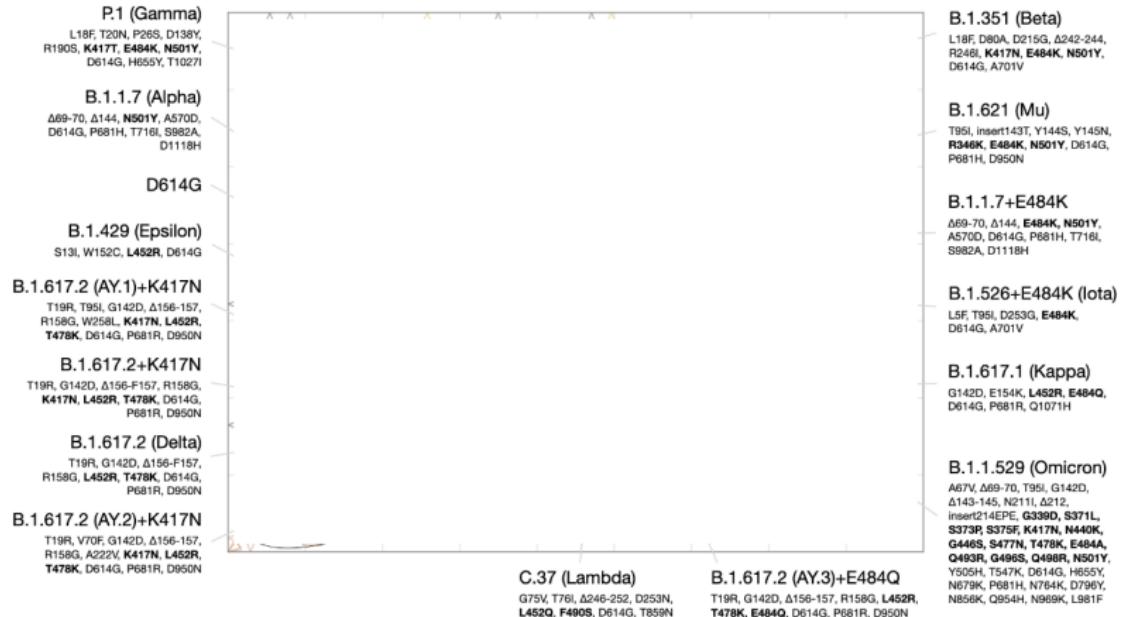
[Pedregosa et al., 2011]

# Approximating genomic data in 2 dimesions



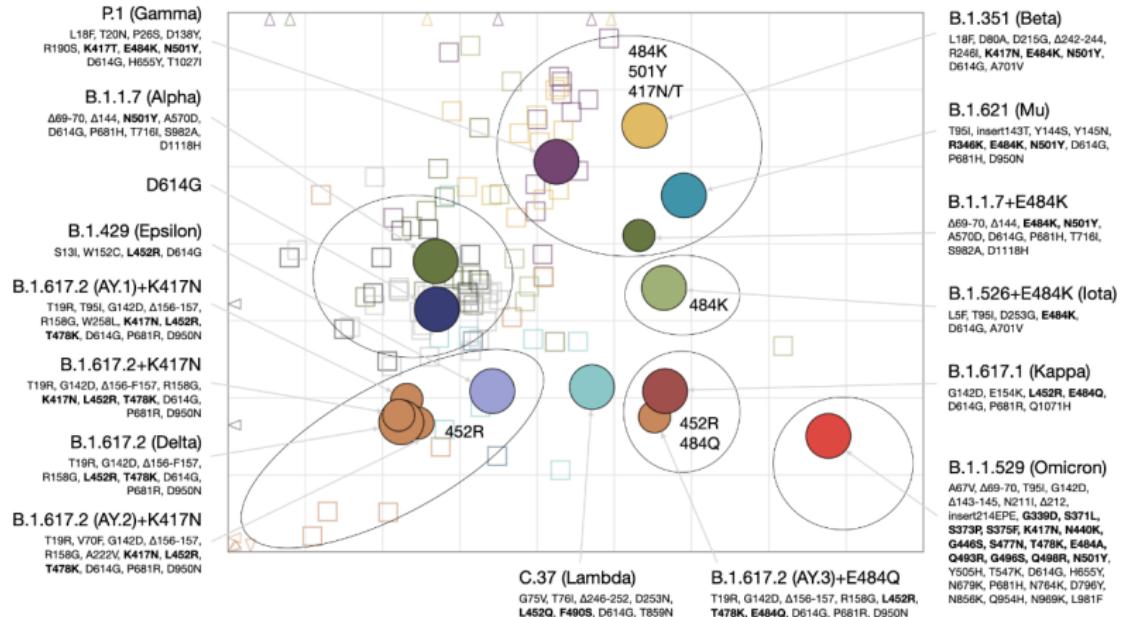
[Lapedes and Farber, 2001, Smith et al., 2004]

# Mapping SARS-CoV-2 in 2D



[Wilks et al., 2022]

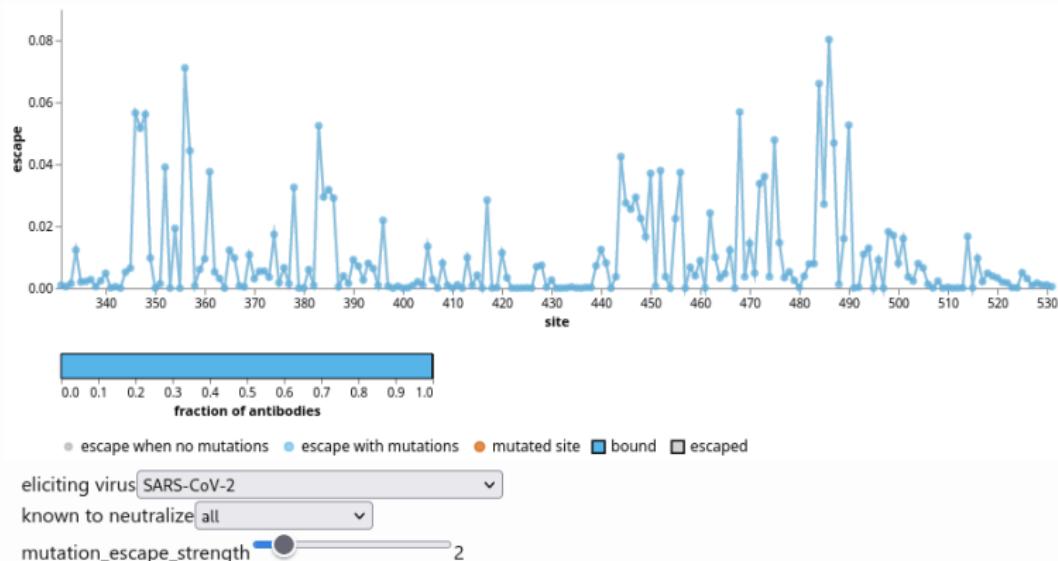
# Mapping SARS-CoV-2 in 2D



[Wilks et al., 2022]

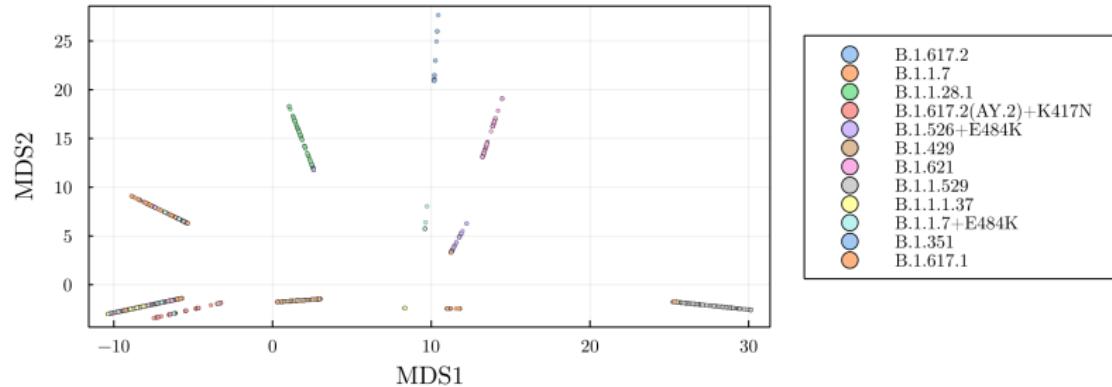
# Methods of adding more genomes: polyclonal antibody binding studies

## Escape calculator for SARS-CoV-2 RBD



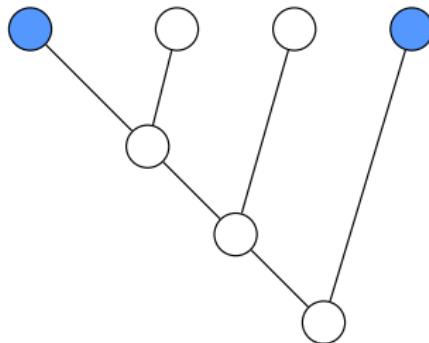
[Greaney et al., 2022]

# Antibody Binding map

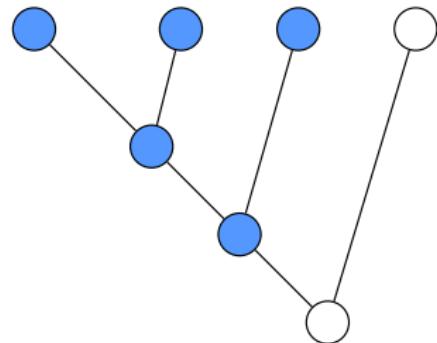


## Methods of adding more genomes: homoplastic sites

Homoplastic trait

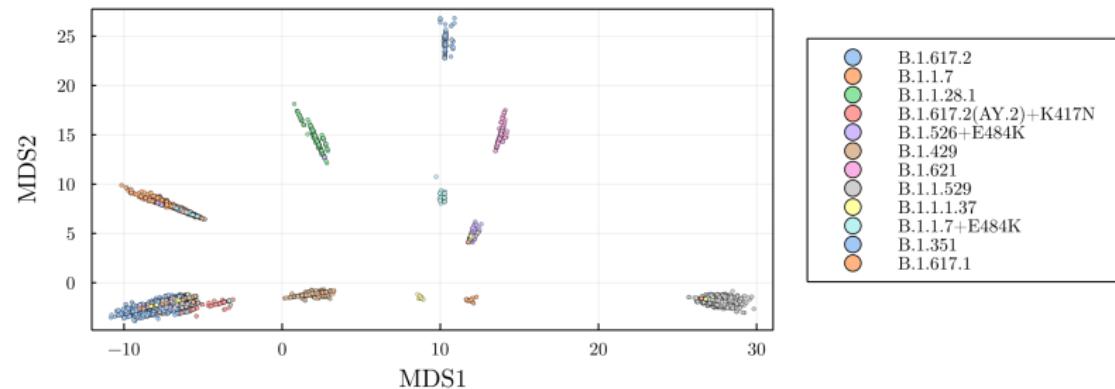


Homologic trait

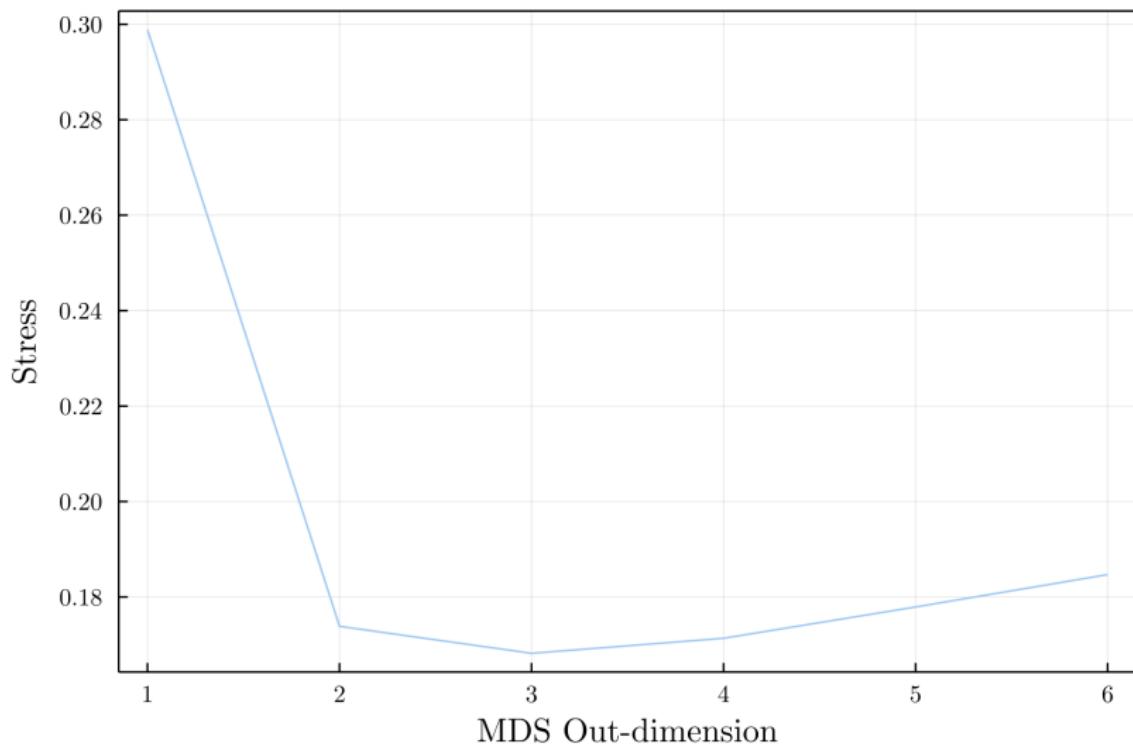


[Page and Holmes, 2009]

# Homoplasic mutations map



## Evaluating the MDS approximation



## Model parameters/variables

Symbol	Description
$N$	Size of variant grid
$K$	Total population
$S_{ij}$	Population susceptible to variant $(i, j) \in [0, N]^2$
$I_{ij}$	Population infected by variant $(i, j) \in [0, N]^2$
$R_{ij}$	Recovered/Immune to variant $(i, j) \in [0, N]^2$
$\sigma_{ijkl}$	Probability that exposure to variant $(i, j)$ causes immunity to variant $(k, l)$
$\beta_{ij}$	Transmission rate of variant $(i, j)$
$v(t)$	vaccination rate at time $t$
$s(t)$	stringency at $t$
$\xi$	Recovery rate of all strains
$\gamma$	Rate of immunity loss of all strains

Table of symbols for Model 2

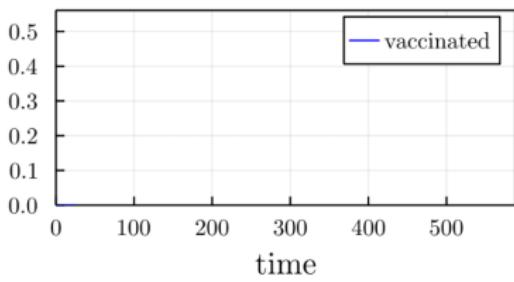
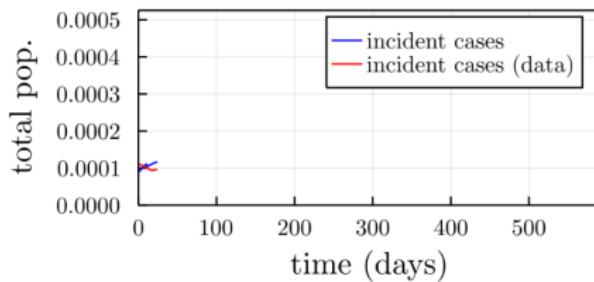
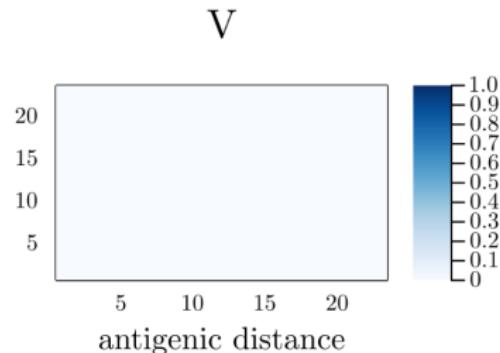
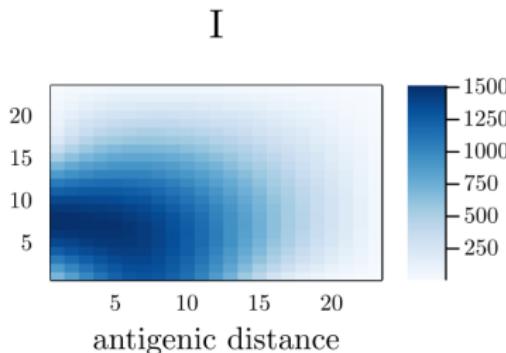
## Model Equations

$$\frac{S_{ij}}{dt} = -\frac{1}{K} \sum_{kl} s(t) \beta_{kl} \sigma_{ijkl} S_{ij} I_{kl} + \gamma(K - S_{ij} - I_{ij}) - V(t) S \quad (1)$$

$$\frac{I_{ij}(t)}{dt} = \frac{1}{K} s(t) \beta_{ij} S_{ij} I_{ij} - \xi I_{ij} + M (-4I_{ij} + I_{i-1,j} + I_{i+1,j} + I_{i,j-1} + I_{i,j+1}) \quad (2)$$

Boundary conditions:  $I_{0,j} = 0, I_{j,0} = 0, I_{N,j} = 0, I_{j,N} = 0$

# Model Dynamics



## Further work

- Differentiate between antigenic and genomic space
  - non-local diffusion
- Model fitting
- Applications
  - ▶ Simple inference on antigenic space
  - ▶ VoC-aware NPI usage and vaccination

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# Mutation homoplasy

