

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

Peter C. Jentsch, PhD <sup>1,4</sup>    Finlay Maguire, PhD <sup>3,5</sup>  
Samira Mubareka, MD, FRCPC <sup>1,2</sup>

<sup>1</sup>Sunnybrook Research Institute, Toronto, Canada

<sup>2</sup>University of Toronto, Toronto, Canada

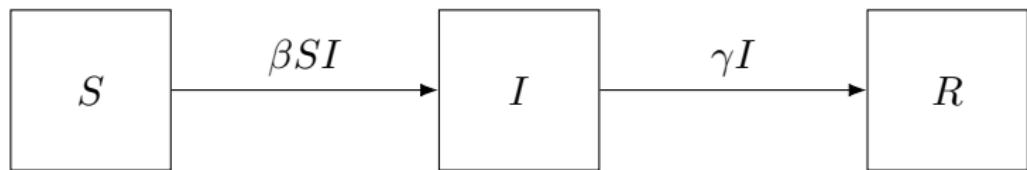
<sup>3</sup>Dalhousie University, Halifax, Canada

<sup>4</sup>Simon Fraser University, Burnaby, Canada

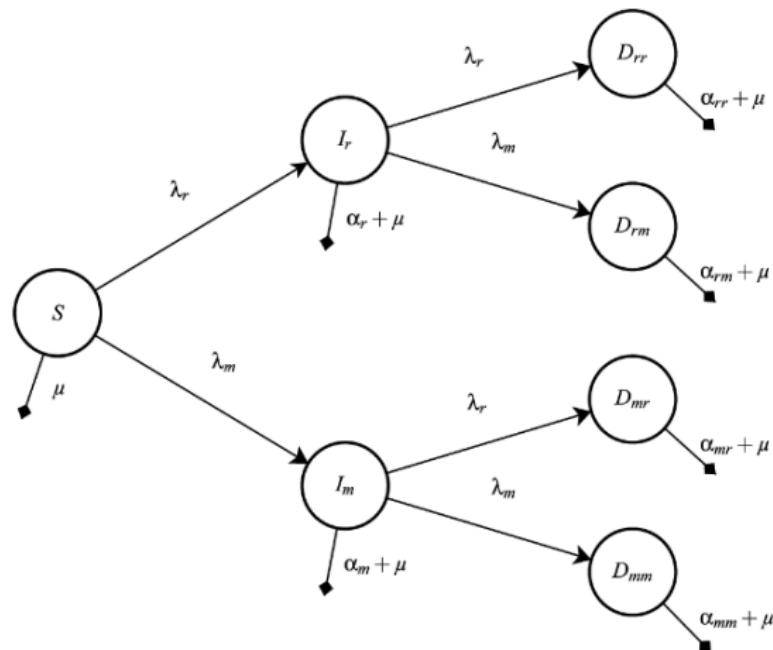
<sup>5</sup>Shared Hospital Laboratory, Toronto, Canada

July 11, 2022

# Infection spread with compartmental models

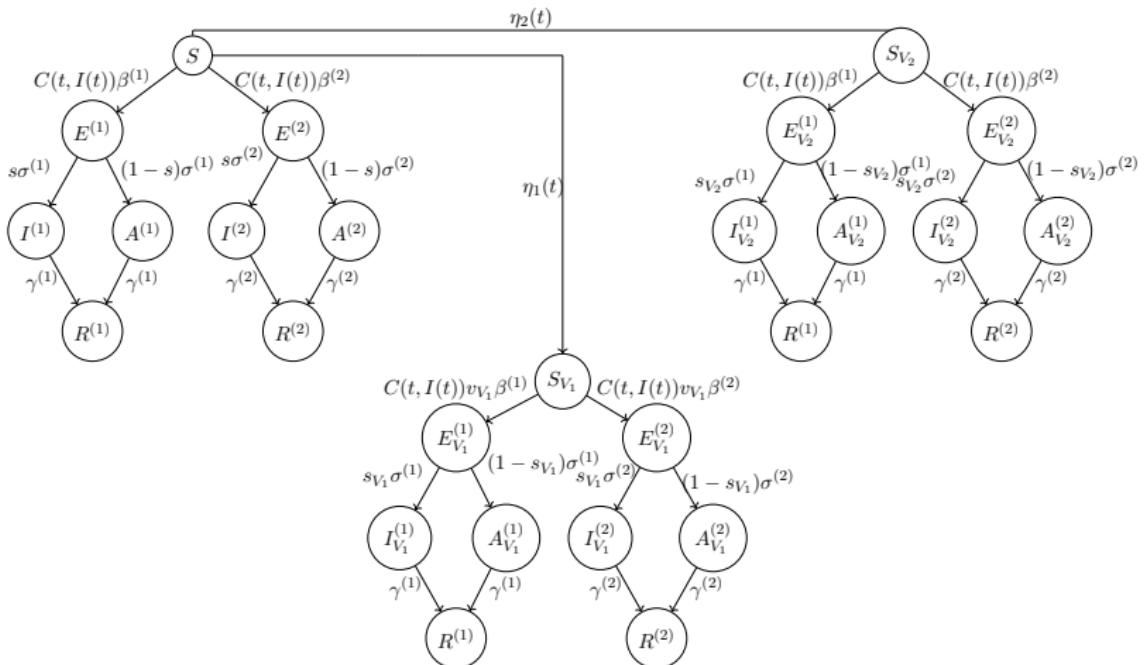


# Modeling multiple infections is challenging

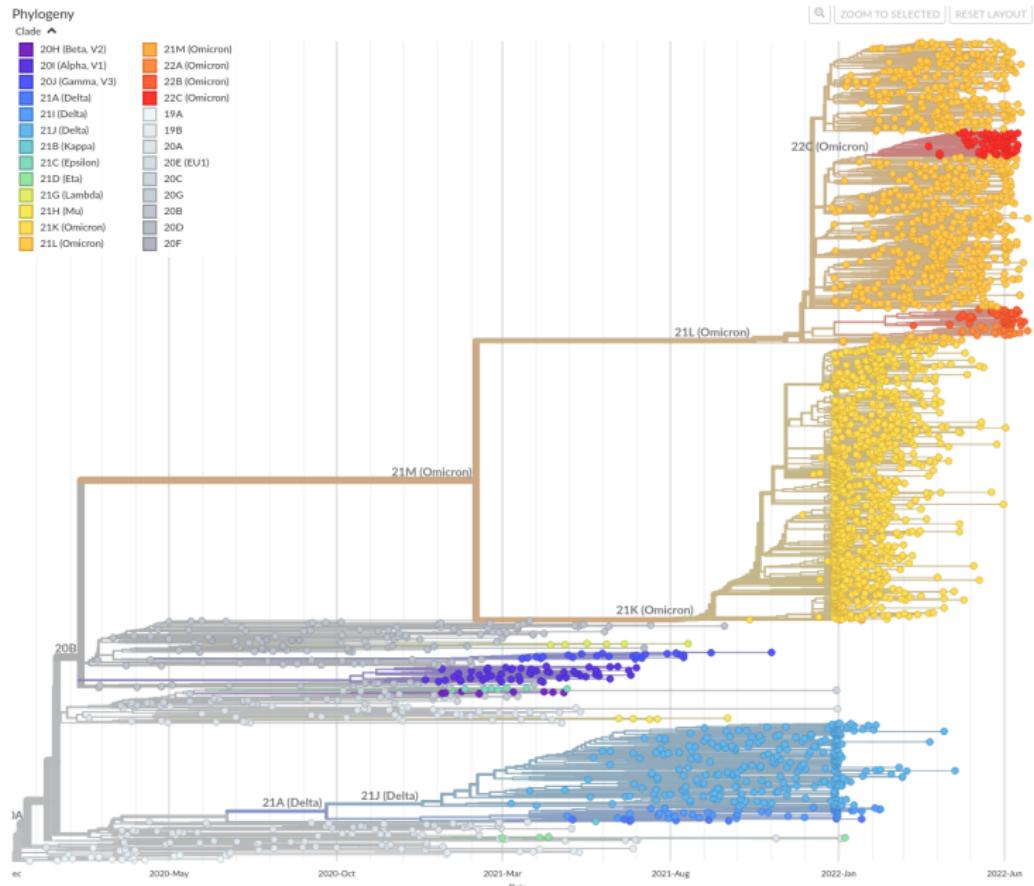


[Alizon and van Baalen, 2008]

# 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**  
Vol. 99 | No. 26

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

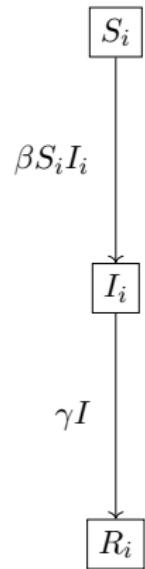
## Mathematical Biology

J.R. Gog · J. Swinton

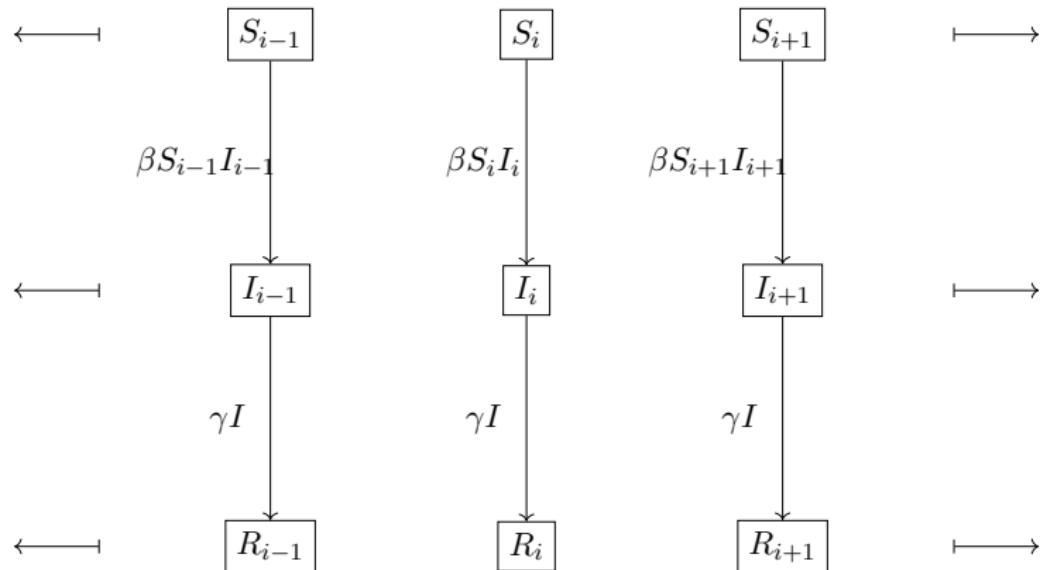
### A status-based approach to multiple strain dynamics

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

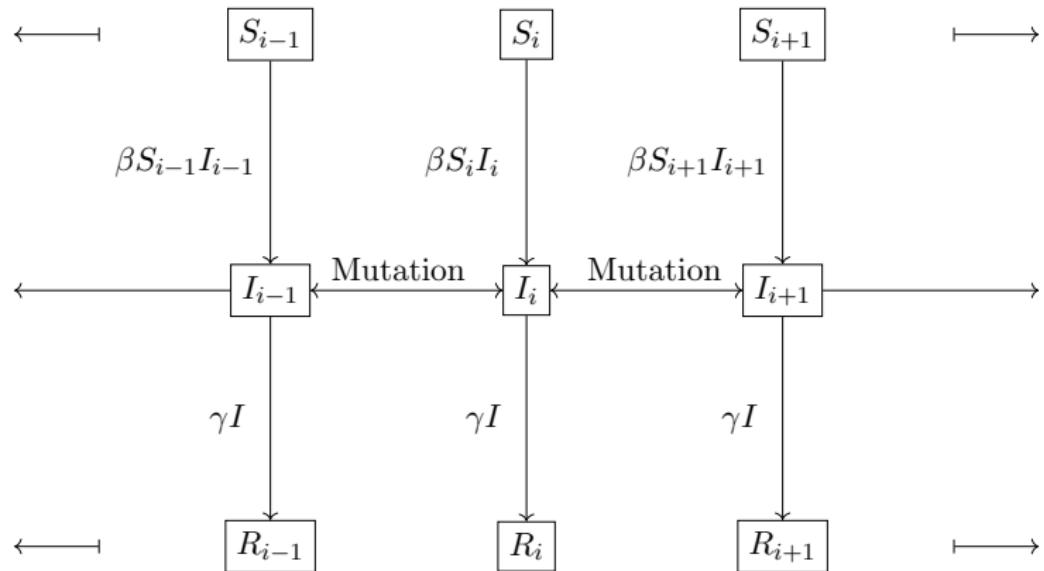
## Begin with SIR model



# Organize strains on a lattice



## Strains mutate into adjacent strains

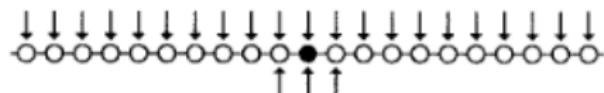


# Infections provide cross-immunity to nearby strains

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



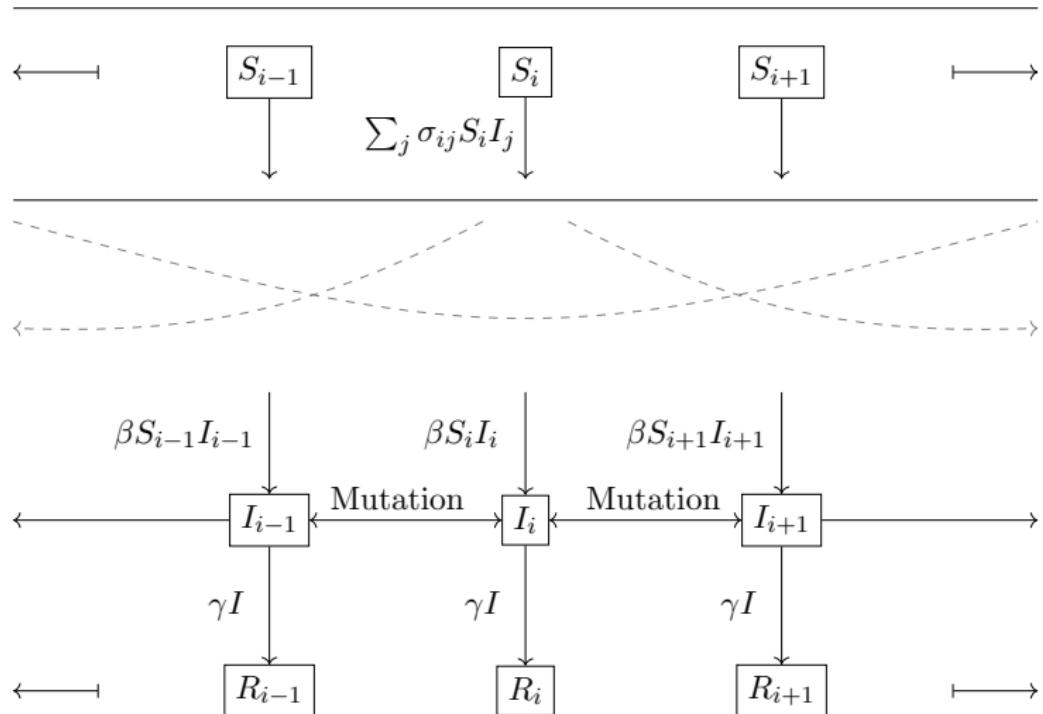
Cross-immunity to nearby strains



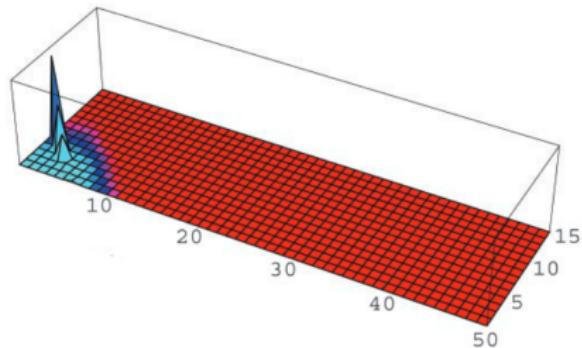
Mutation to adjacent strains

[Gog and Grenfell, 2002]

# Full strain lattice model in 1 dimension

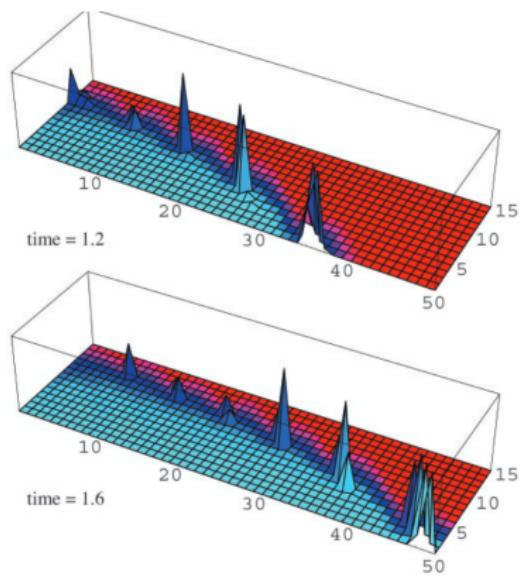
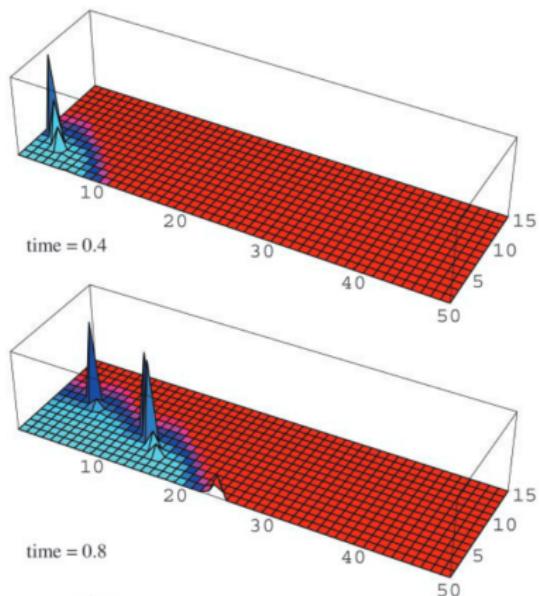


## Extending the strain lattice to 2 dimensions



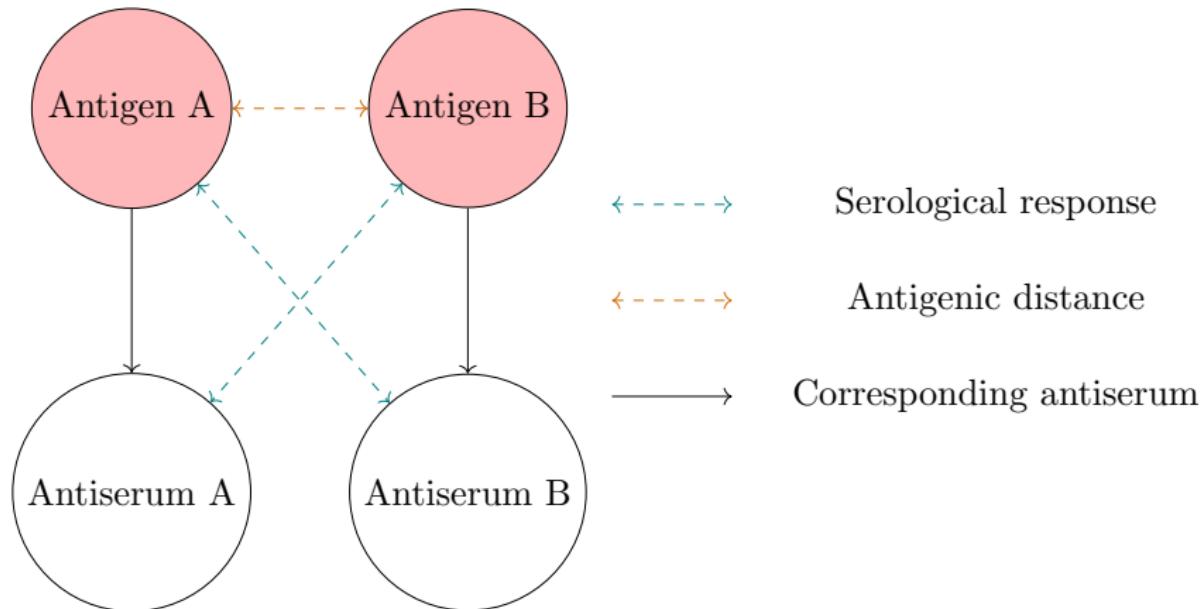
[Gog and Grenfell, 2002]

# Extending the strain lattice to 2 dimensions

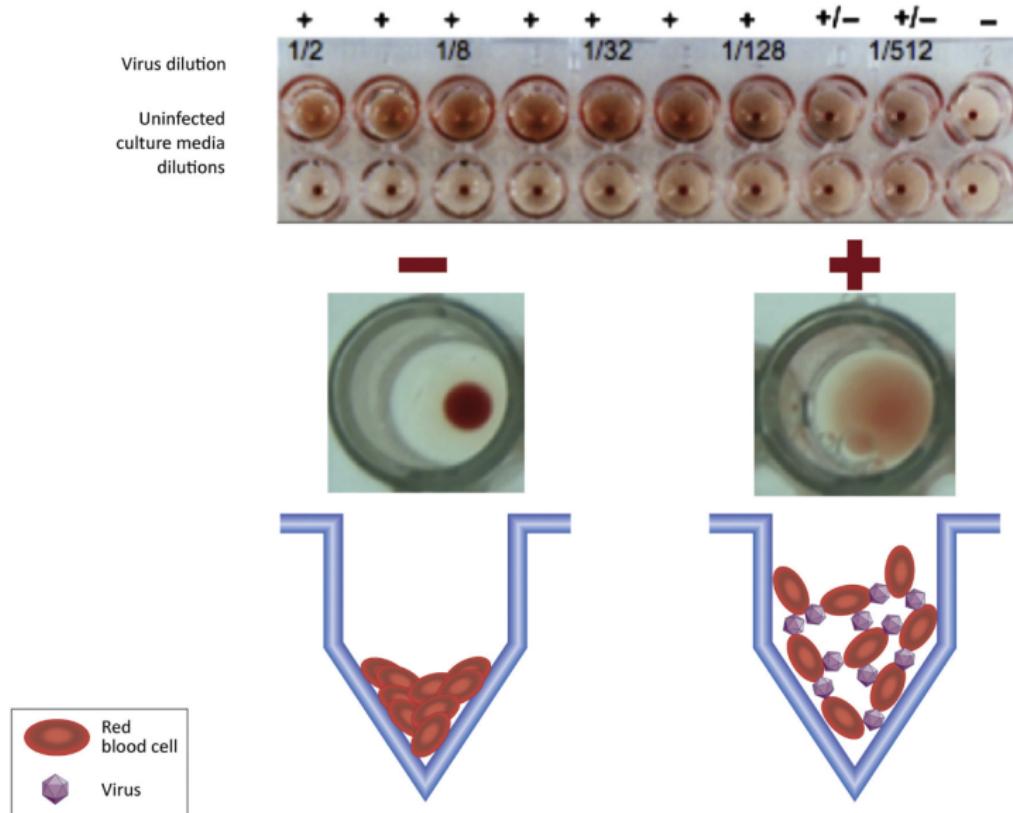


[Gog and Grenfell, 2002]

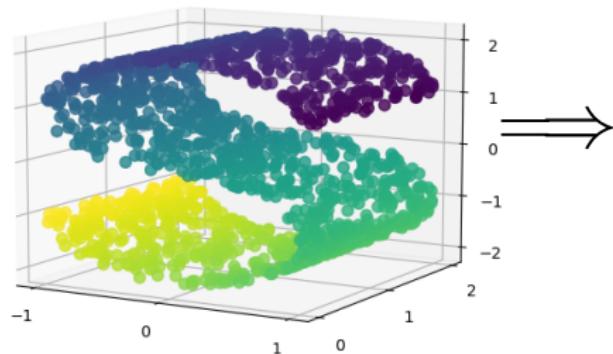
# Quantifying antigenicity between viruses



Neutralization assays are used to estimate relative antibody titre

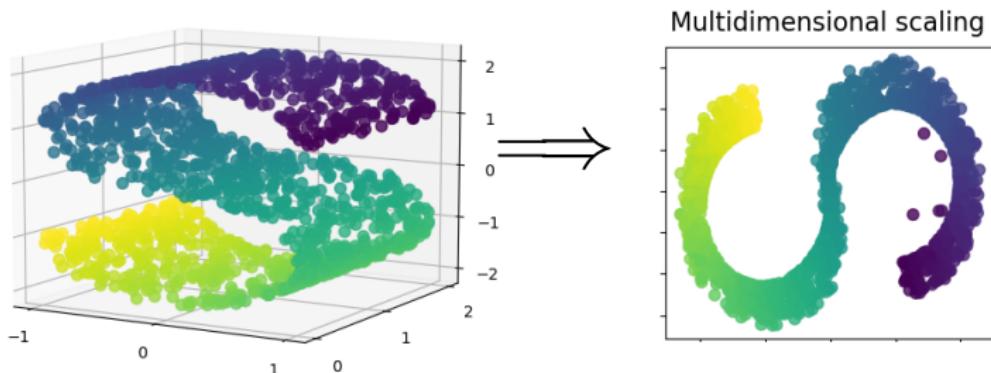


# Projecting points to low dimensions while preserving distances



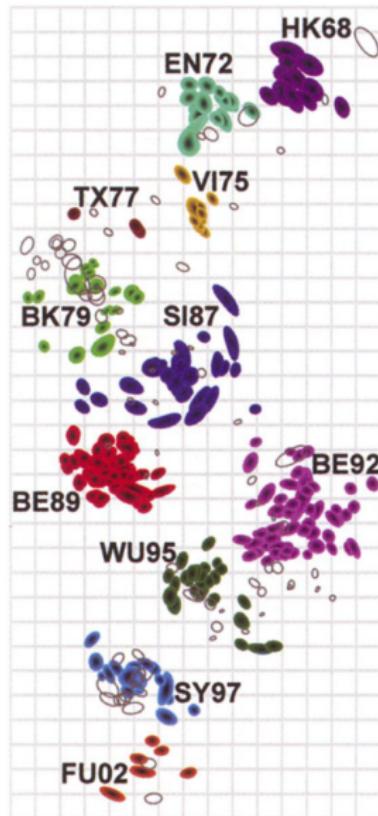
[Pedregosa et al., 2011]

# Projecting to low dimensions while preserving distances



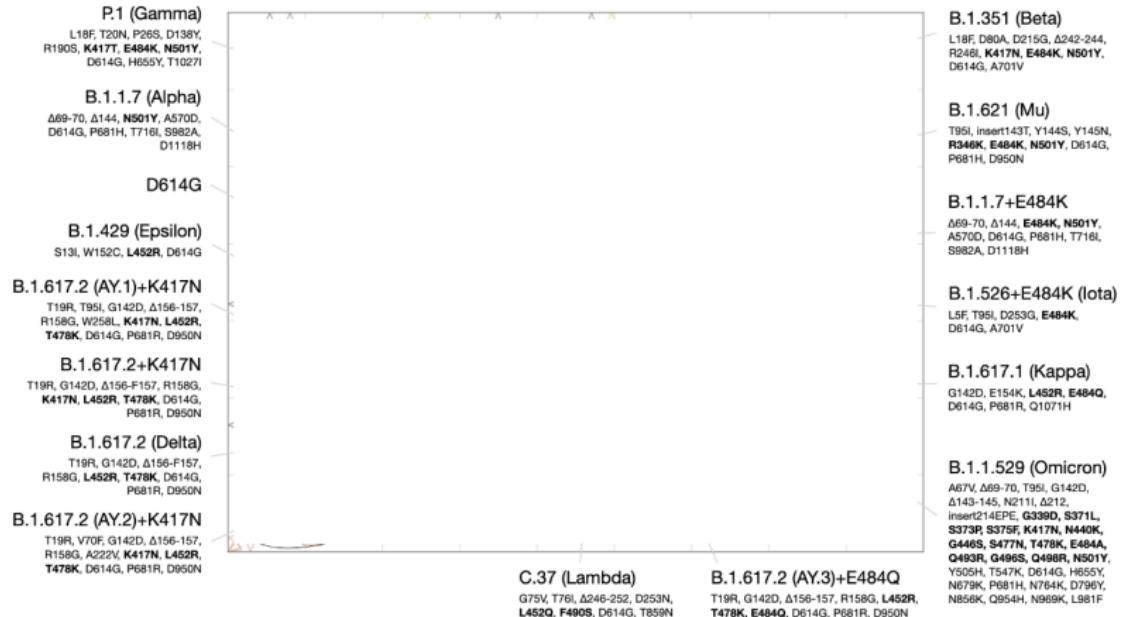
[Pedregosa et al., 2011]

# Approximating genomic data in 2 dimesions



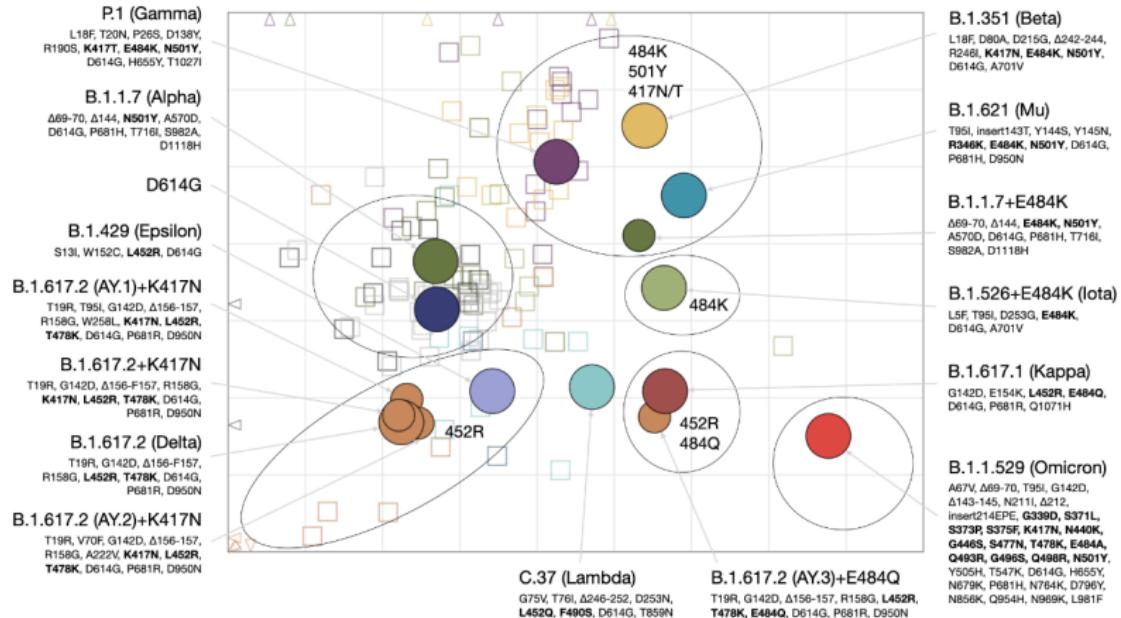
[Lapedes and Farber, 2001, Smith et al., 2004]

# Mapping SARS-CoV-2 in 2D



[Wilks et al., 2022]

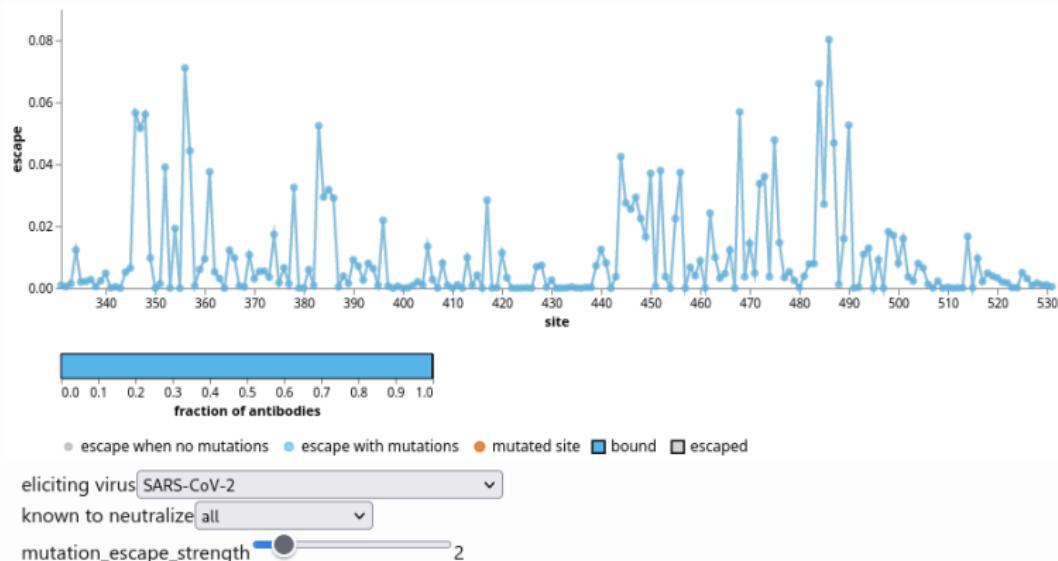
# Mapping SARS-CoV-2 in 2D



[Wilks et al., 2022]

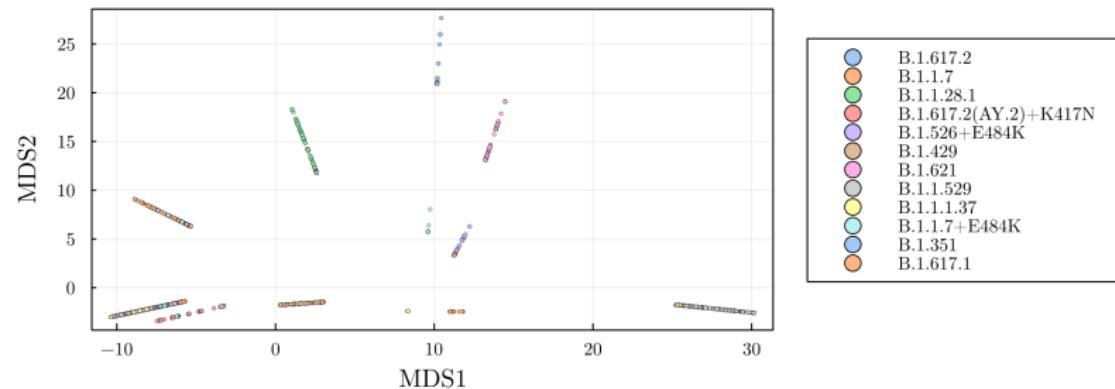
# Methods of adding more genomes: polyclonal antibody binding studies

## Escape calculator for SARS-CoV-2 RBD



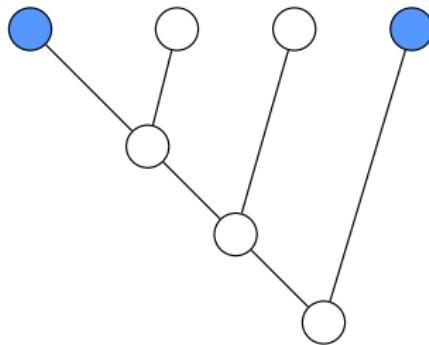
[Greaney et al., 2022]

# Antibody Binding map

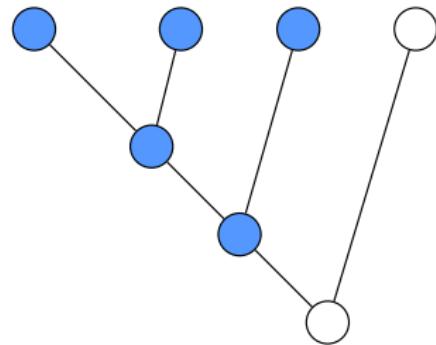


## Methods of adding more genomes: homoplastic sites

Homoplastic trait

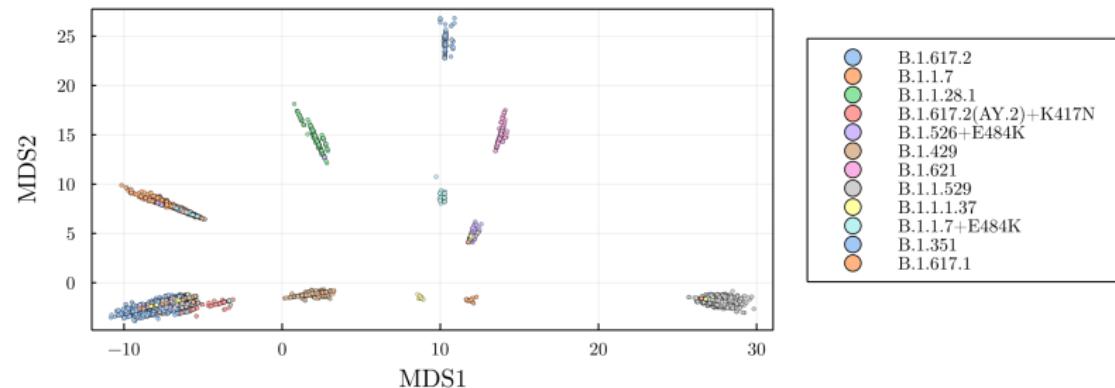


Homologic trait

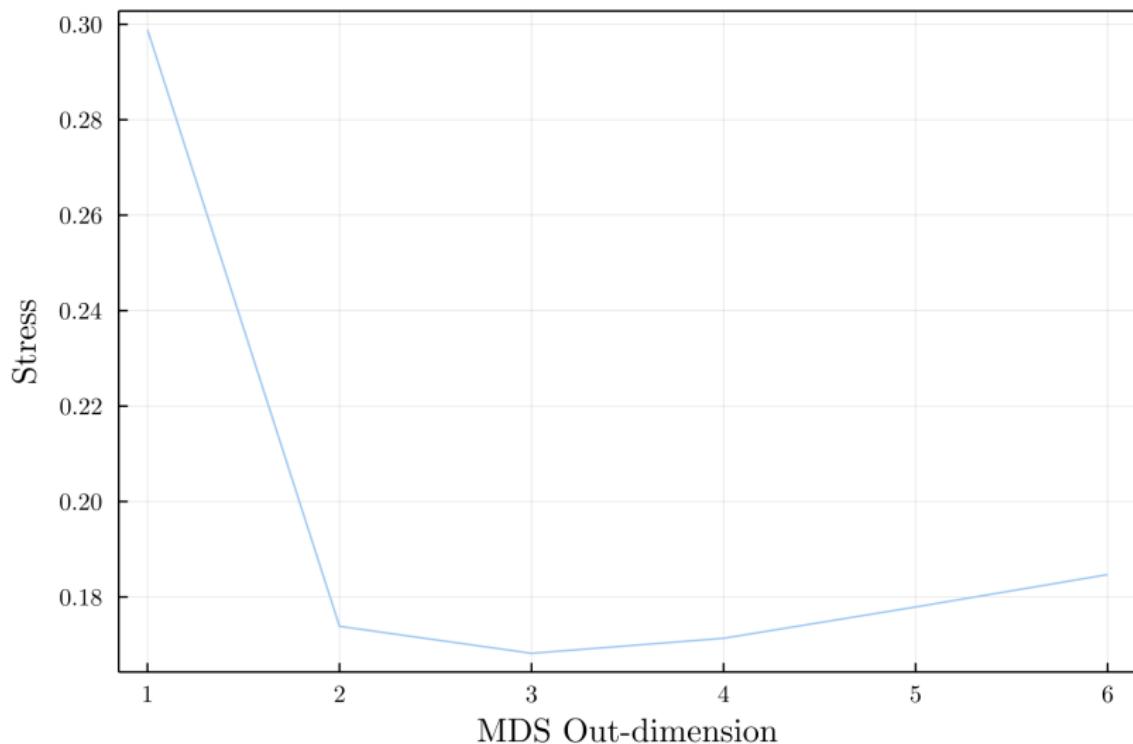


[Page and Holmes, 2009]

# Homoplasic mutations map



## Evaluating the MDS approximation



## Model parameters/variables

Symbol	Description
$N$	Size of variant grid
$S_{ij}$	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

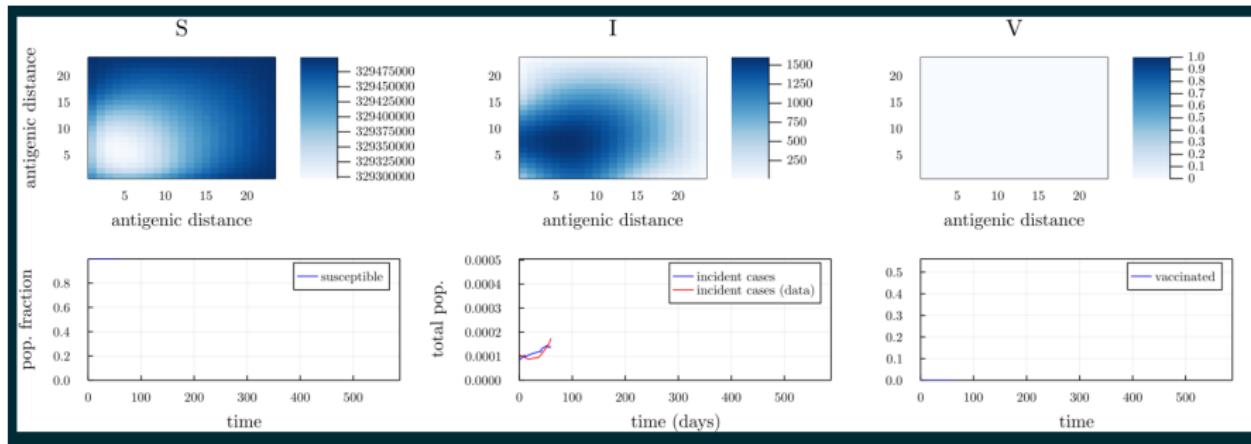
$$\frac{S_{ij}}{dt} = - \sum_{kl} s(t) \beta_{kl} \sigma_{ijkl} S_{ij} I_{kl} + \gamma R_{ij} - V(t) S \quad (1)$$

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

$$\frac{R_{ij}(t)}{dt} = \xi I_{ij} - \gamma R_{ij} + V(t) S \quad (3)$$

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

-  Alizon, S. and van Baalen, M. (2008).  
Multiple infections, immune dynamics, and the evolution of virulence.  
*The American Naturalist*, 172(4):E150–E168.
-  Gog, J. R. and Grenfell, B. T. (2002).  
Dynamics and selection of many-strain pathogens.  
*Proceedings of the National Academy of Sciences*, 99(26):17209–17214.
-  Greaney, A. J., Starr, T. N., and Bloom, J. D. (2022).  
An antibody-escape estimator for mutations to the sars-cov-2 receptor-binding domain.  
*Virus evolution*, 8(1):veac021.
-  Lapedes, A. and Farber, R. (2001).  
The Geometry of Shape Space: Application to Influenza.  
*Journal of Theoretical Biology*, 212(1):57–69.

- ❑ Page, R. D. and Holmes, E. C. (2009).  
*Molecular evolution: a phylogenetic approach.*  
John Wiley & Sons.
- ❑ Payne, S. (2017).  
*Viruses: from understanding to investigation.*  
Academic Press.
- ❑ Pedregosa, F., Varoquaux, G., Gramfort, A., Michel, V., Thirion, B., Grisel, O., Blondel, M., Prettenhofer, P., Weiss, R., Dubourg, V., Vanderplas, J., Passos, A., Cournapeau, D., Brucher, M., Perrot, M., and Duchesnay, E. (2011).  
Scikit-learn: Machine learning in Python.  
*Journal of Machine Learning Research*, 12:2825–2830.

- Smith, D. J., Lapedes, A. S., de Jong, J. C., Bestebroer, T. M., Rimmelzwaan, G. F., Osterhaus, A. D. M. E., and Fouchier, R. A. M. (2004).  
Mapping the Antigenic and Genetic Evolution of Influenza Virus.  
*Science*, 305(5682):371–376.
- Wilks, S. H., Mühlmann, B., Shen, X., Türeli, S., LeGresley, E. B., Netzl, A., Caniza, M. A., Chacaltana-Huarcaya, J. N., Daniell, X., Datto, M. B., Denny, T. N., Drosten, C., Fouchier, R. A. M., Garcia, P. J., Halfmann, P. J., Jassem, A., Jones, T. C., Kawaoka, Y., Krammer, F., McDanal, C., Pajon, R., Simon, V., Stockwell, M., Tang, H., van Bakel, H., Webby, R., Montefiori, D. C., and Smith, D. J. (2022).  
Mapping SARS-CoV-2 antigenic relationships and serological responses.  
Preprint, Immunology.

# Mutation homoplasy

