

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

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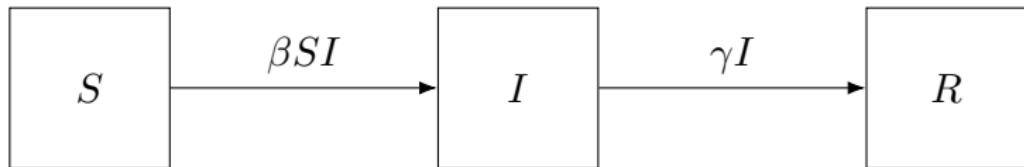
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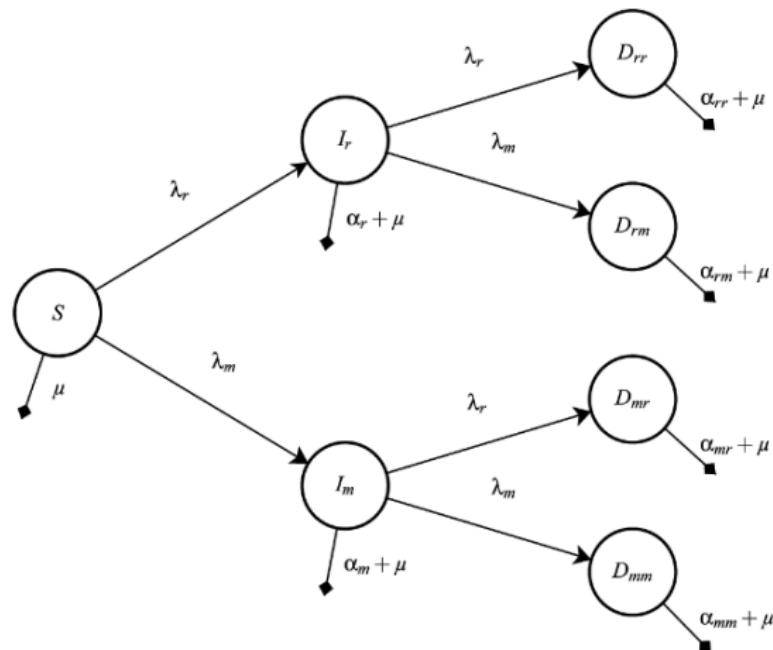
July 12, 2022

Infection spread with compartmental models



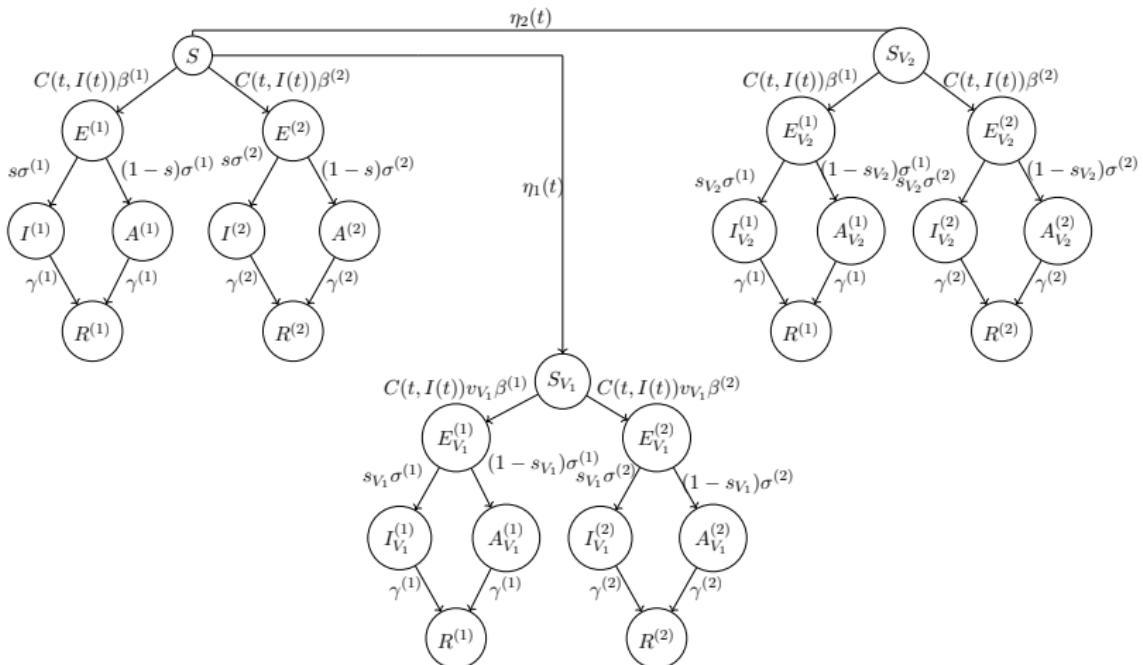
- $S(t)$ - fraction of susceptible hosts at t
- $I(t)$ - fraction of infected hosts at t
- $R(t)$ - fraction of recovered hosts at t
- $1 = S(t) + I(t) + R(t)$ is constant

Modeling multiple infections is challenging

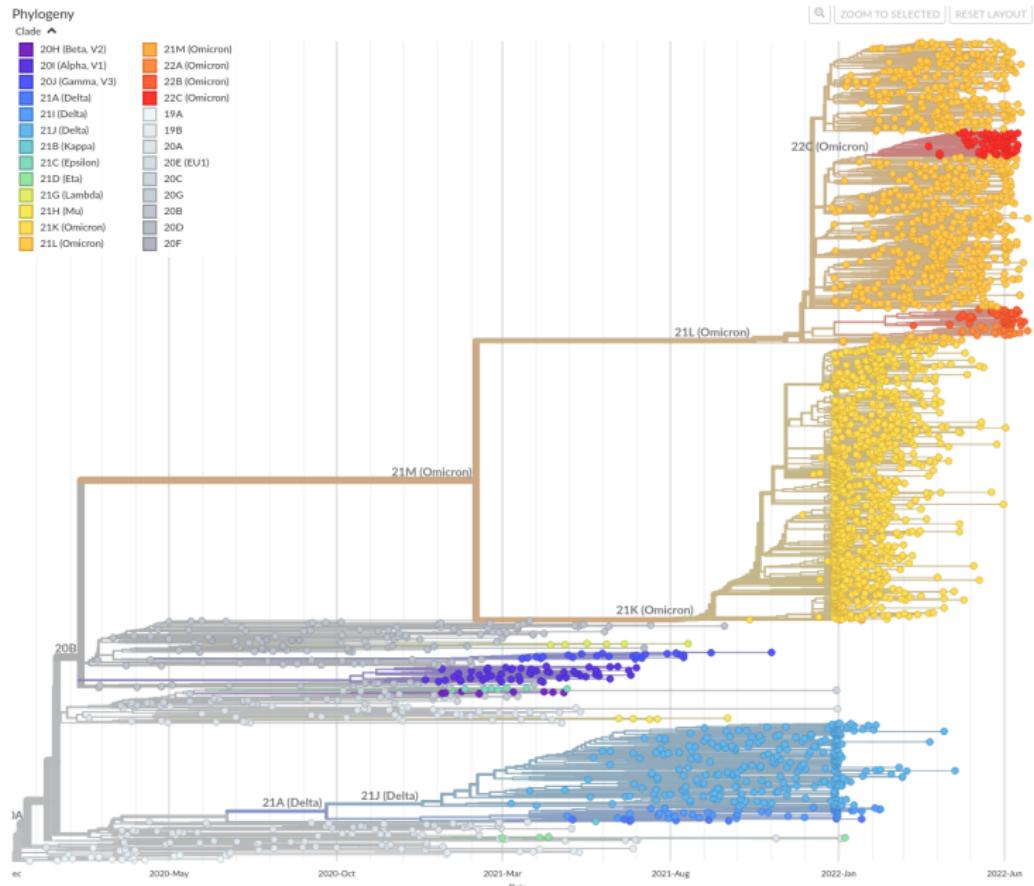


[Alizon and van Baalen, 2008]

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>

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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



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Mathematical Biology

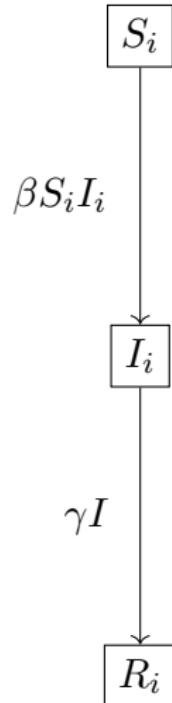
J.R. Gog · J. Swinton

A status-based approach to multiple strain dynamics

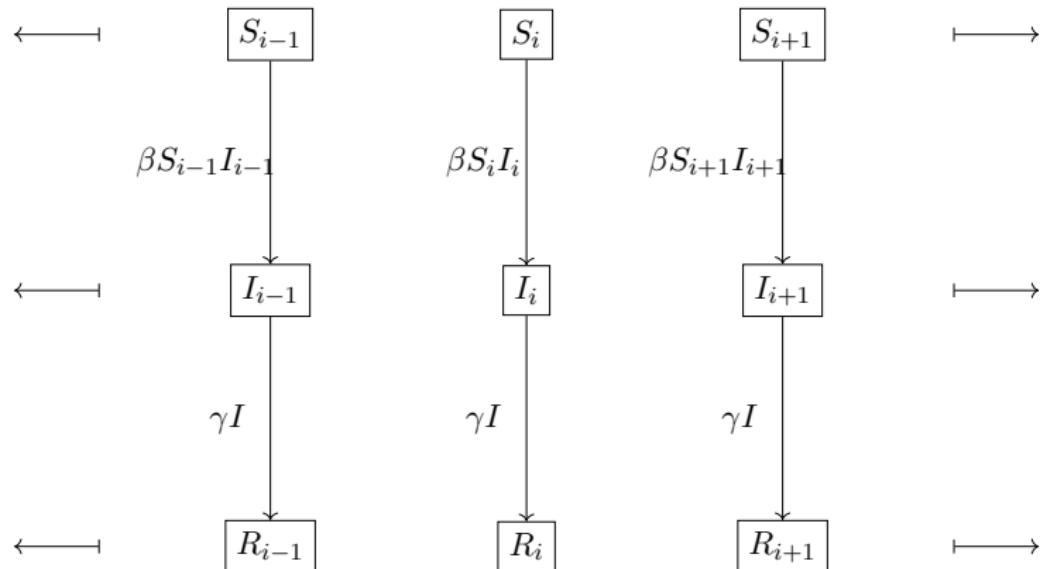
Received: 5 April 2000 / Revised version: 24 July 2001 /
Published online: 8 February 2002 – © Springer-Verlag 2002

Begin with SIR model

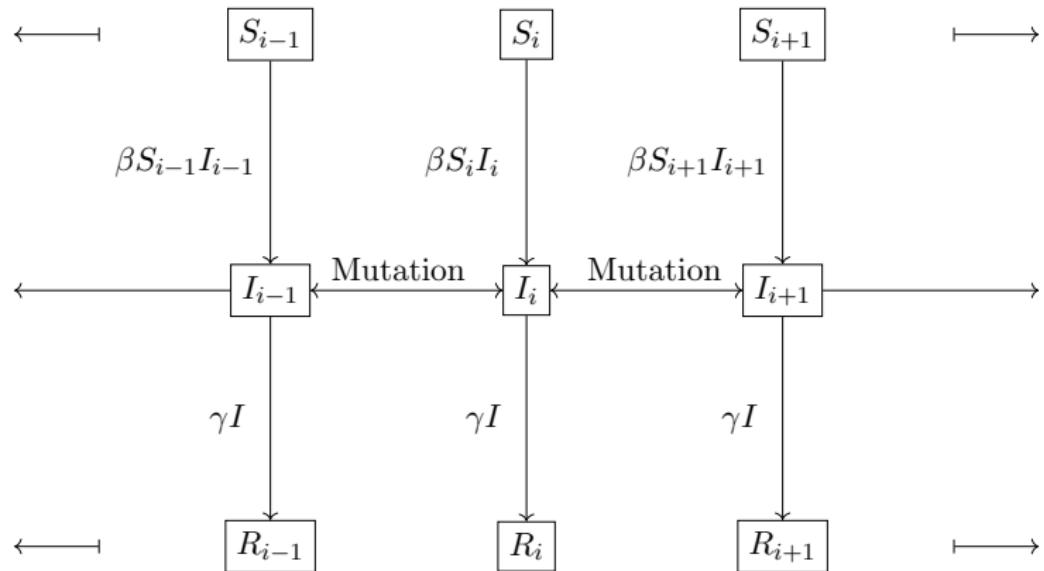
- Consider strains of a pathogen numbered $i \in [1, N]$
- $S(t)$ - population of hosts susceptible to strain i at t
- $I(t)$ - population of hosts infected with strain i at t
- $R(t)$ - population of hosts recovered from strain i at t



Organize strains on a lattice



Strains mutate into adjacent strains

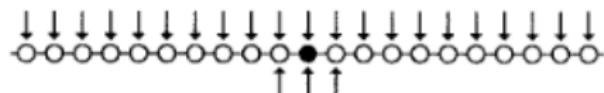


Infections provide cross-immunity to nearby strains

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



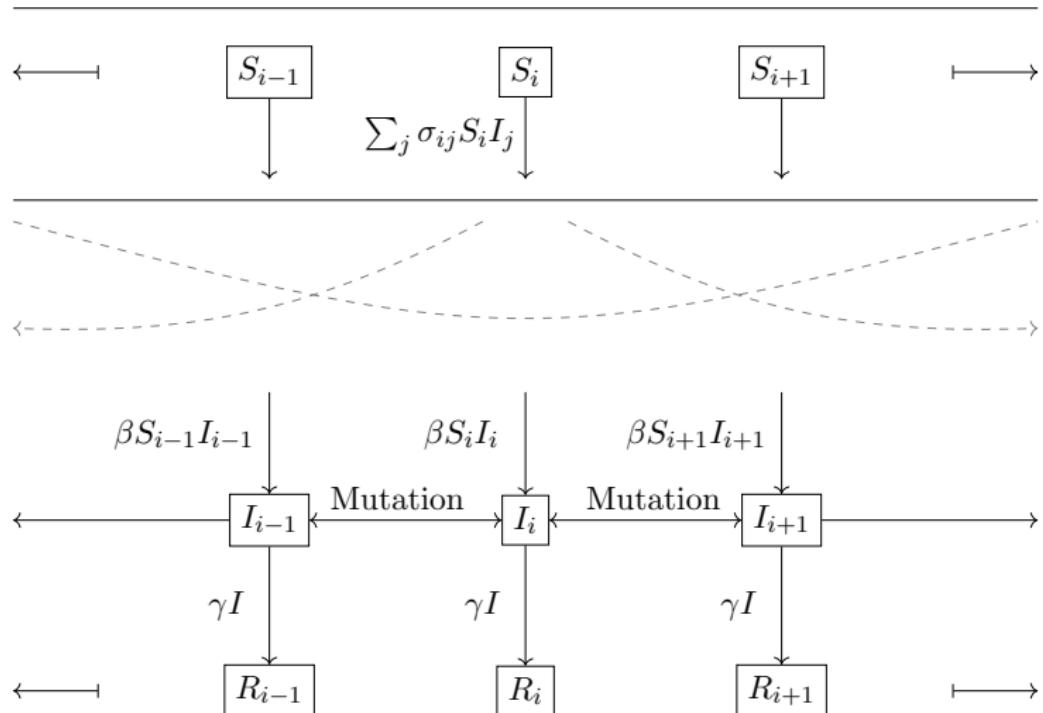
Cross-immunity to nearby strains



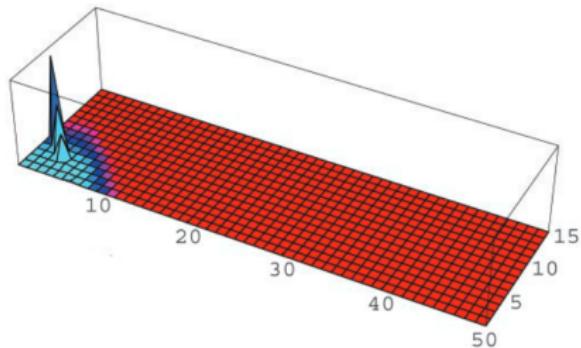
Mutation to adjacent strains

[Gog and Grenfell, 2002]

Full strain lattice model in 1 dimension

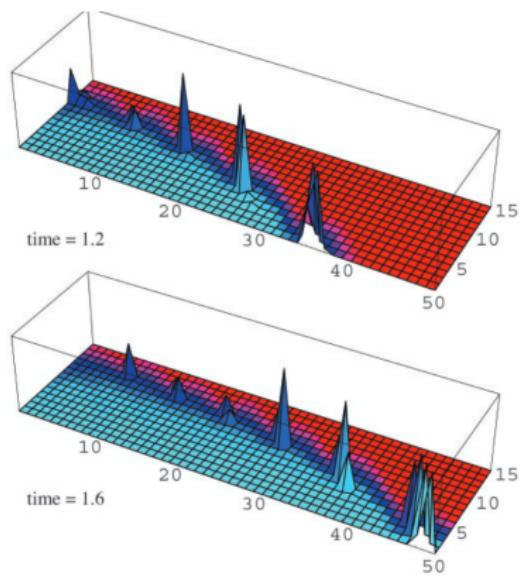
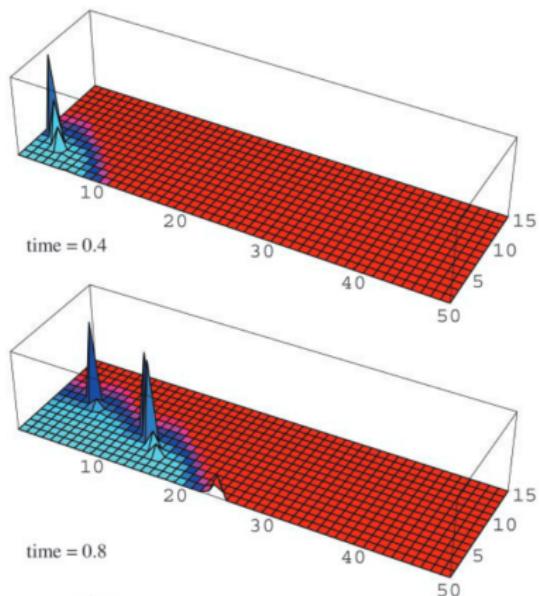


Extending the strain lattice to 2 dimensions



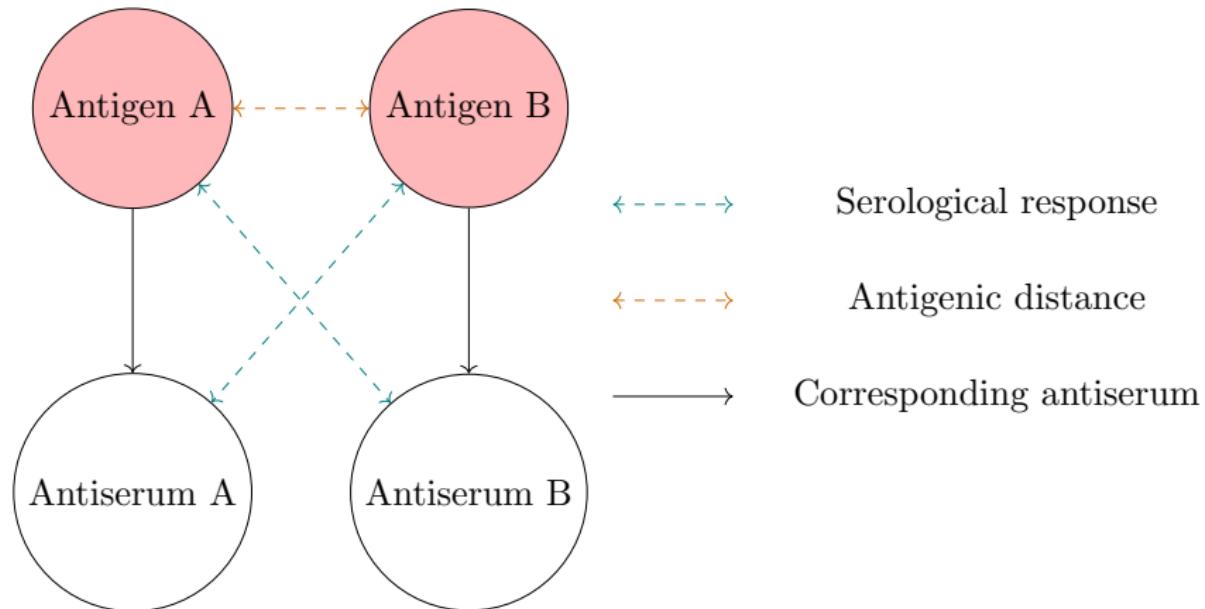
[Gog and Grenfell, 2002]

Extending the strain lattice to 2 dimensions



[Gog and Grenfell, 2002]

Quantifying antigenicity between viruses



Neutralization assays are used to estimate relative antibody titre

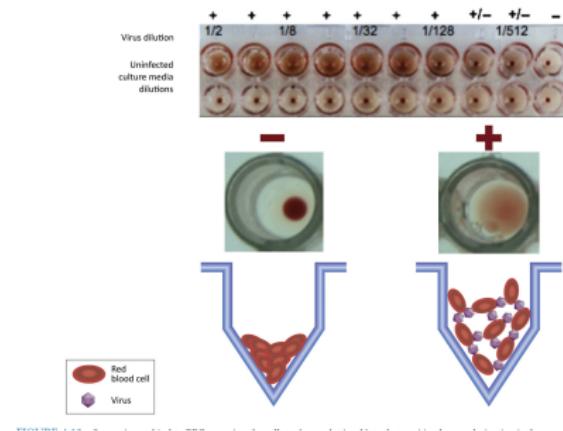
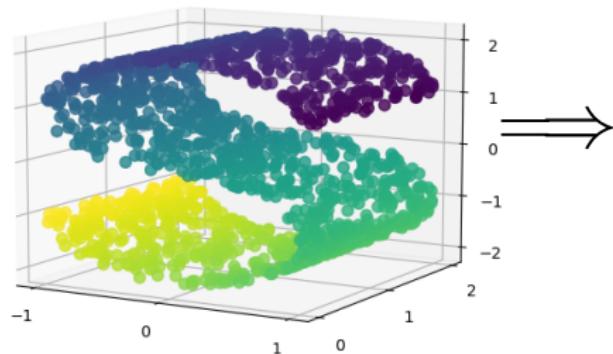


Illustration of mechanism behind hemagglutination assay

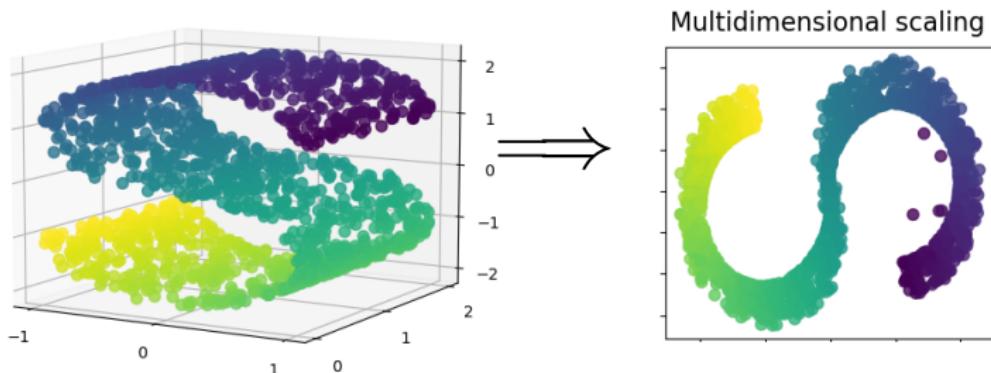
[Payne, 2017]

Projecting points to low dimensions while preserving distances



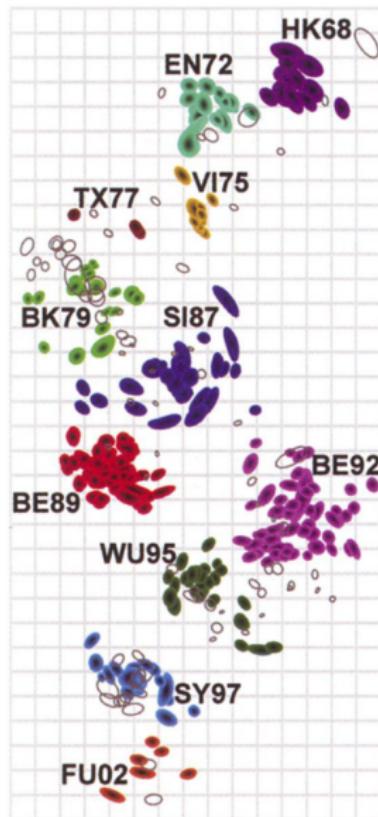
[Pedregosa et al., 2011]

Projecting to low dimensions while preserving distances



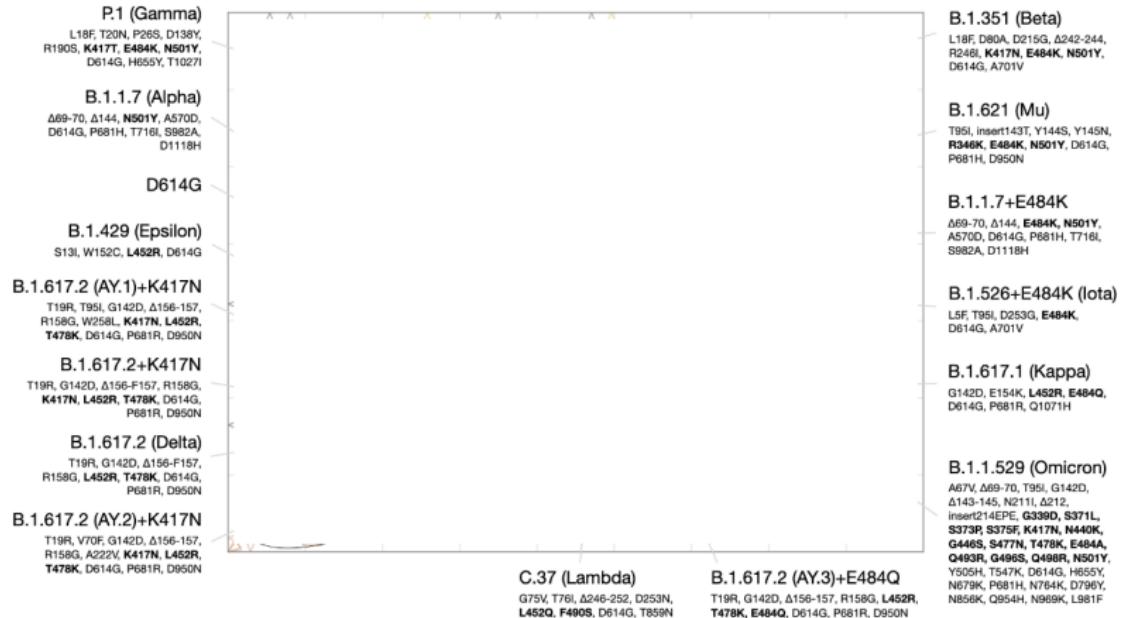
[Pedregosa et al., 2011]

Approximating genomic data in 2 dimesions



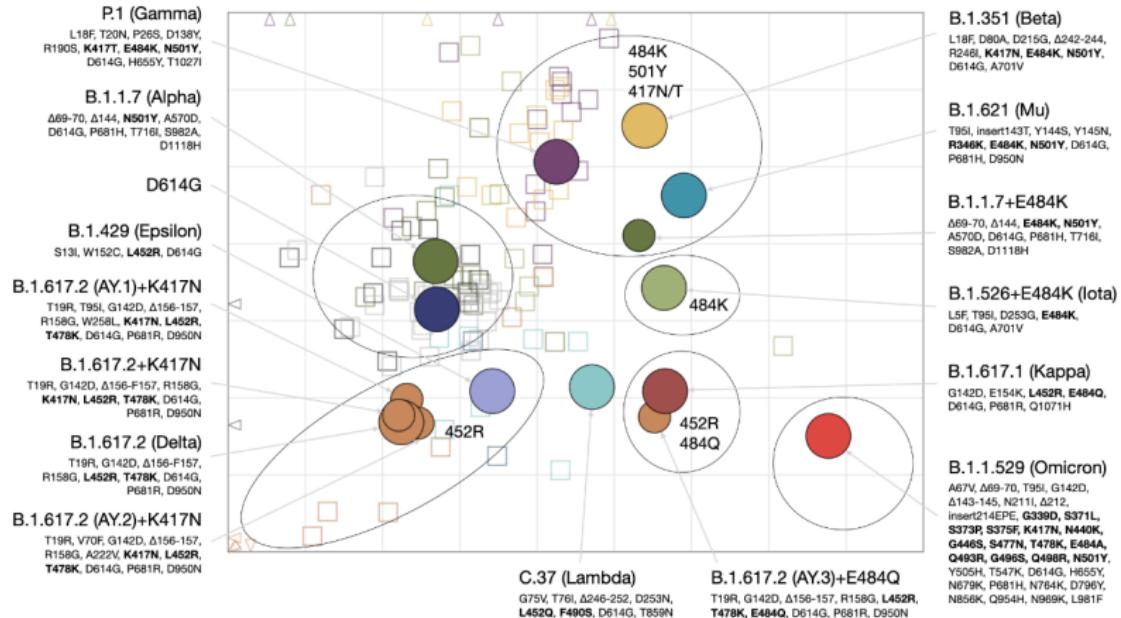
[Lapedes and Farber, 2001, Smith et al., 2004]

Mapping SARS-CoV-2 in 2D



[Wilks et al., 2022]

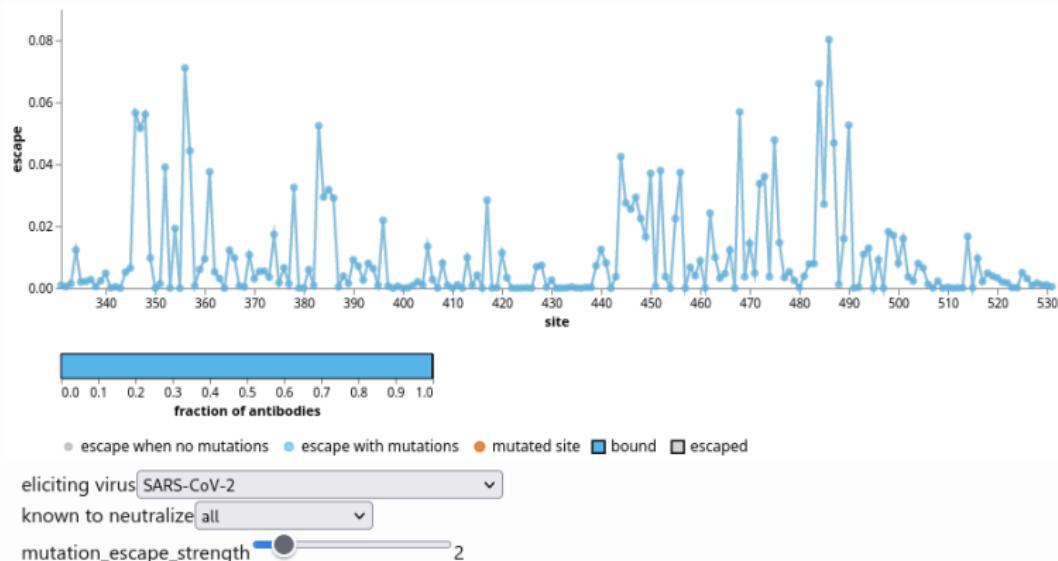
Mapping SARS-CoV-2 in 2D



[Wilks et al., 2022]

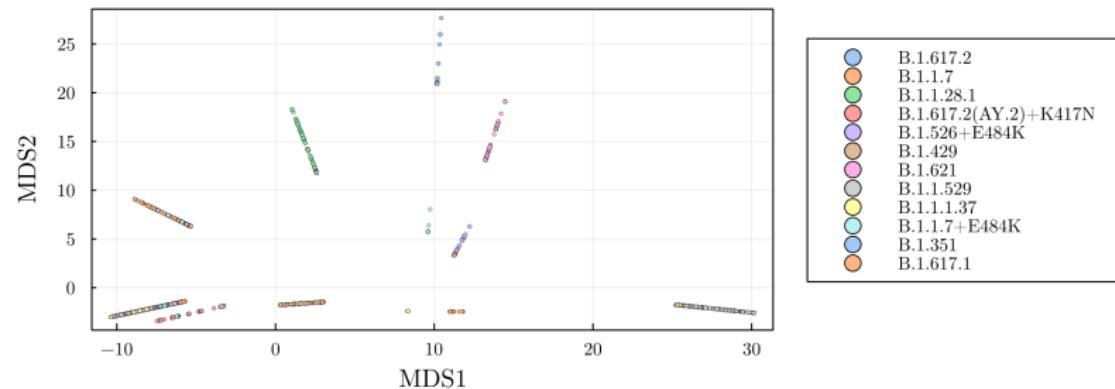
Methods of adding more genomes: polyclonal antibody binding studies

Escape calculator for SARS-CoV-2 RBD



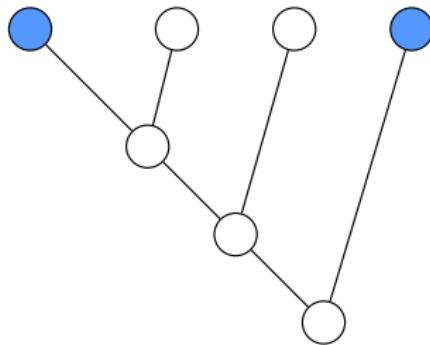
[Greaney et al., 2022]

Antibody Binding map

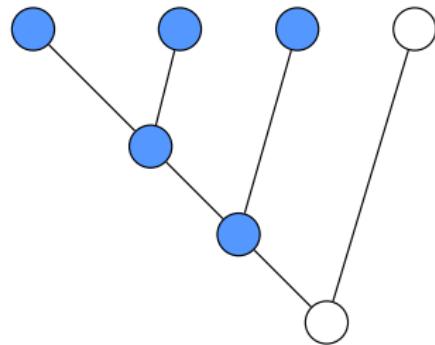


Methods of adding more genomes: homoplastic sites

Homoplastic trait

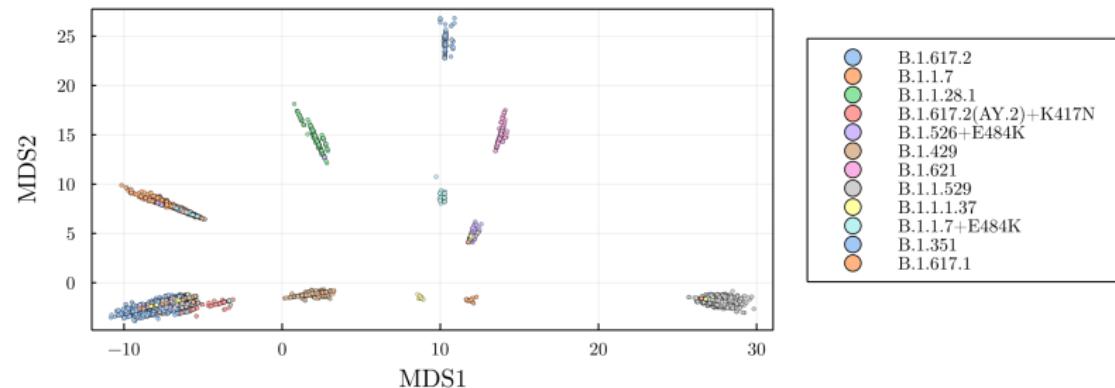


Homologic trait

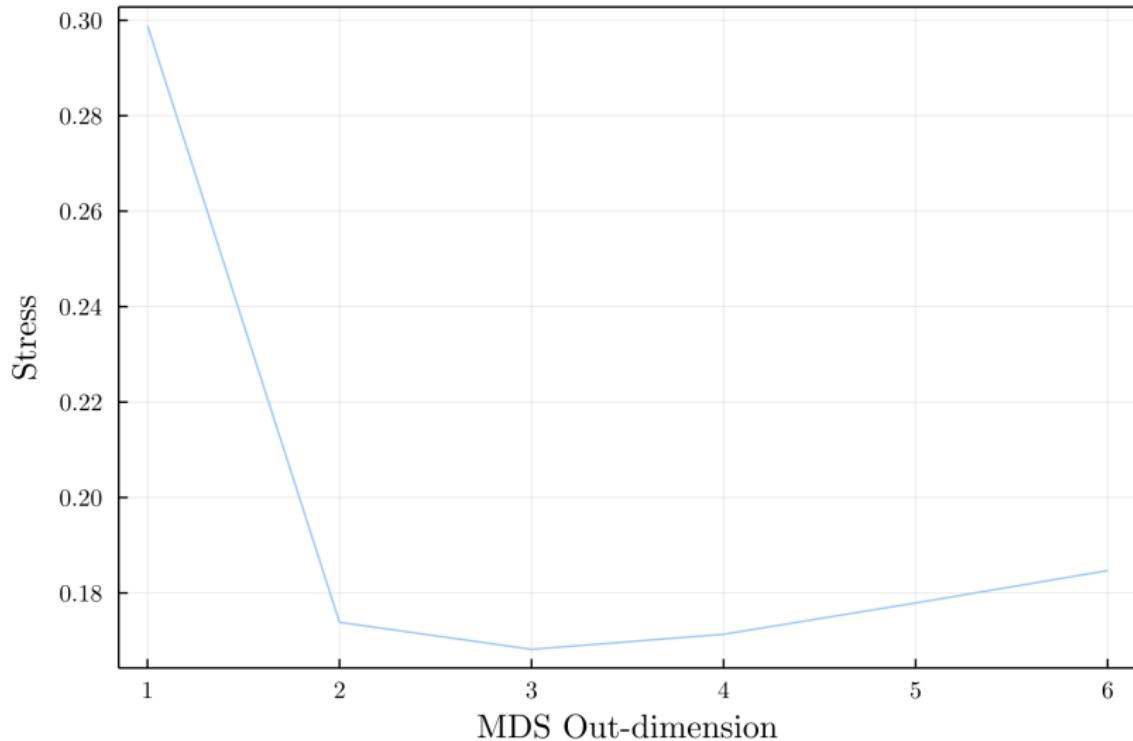


[Page and Holmes, 2009]

Homoplasic mutations map



Evaluating the MDS approximation



Model parameters/variables

Symbol	Description
N	Size of variant grid
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 $(i, j) \in [0, N]^2$
σ_{ijkl}	Probability that exposure to variant (i, j) causes immunity to variant (k, l)
β_{ij}	Transmission rate of variant (i, j)
$v(t)$	vaccination rate at time t
$s(t)$	stringency at t
ξ	Recovery rate of all strains
γ	Rate of immunity loss of all strains

Table of symbols for Model 2

Model Equations

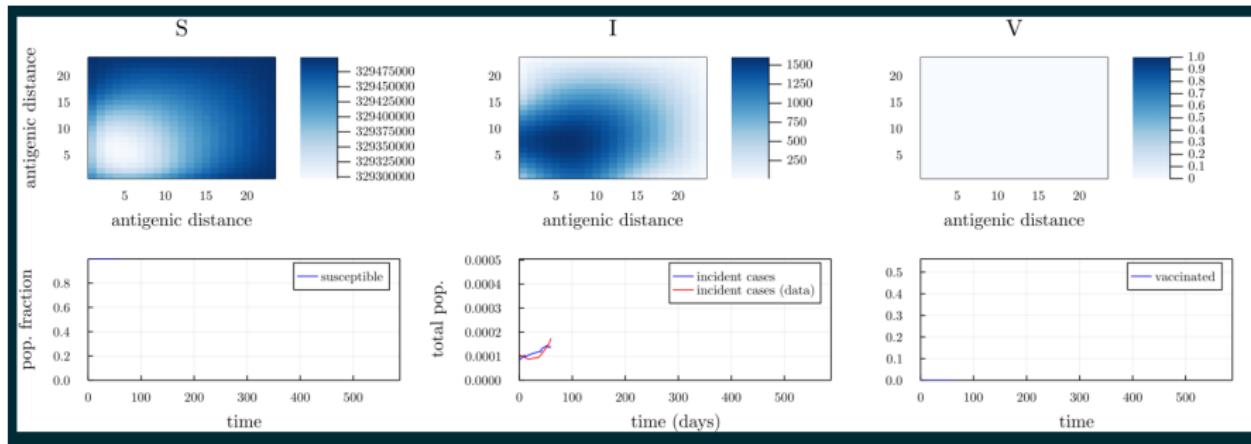
$$\frac{S_{ij}}{dt} = - \sum_{kl} s(t) \beta_{kl} \sigma_{ijkl} S_{ij} I_{kl} + \gamma R_{ij} - V(t) S \quad (1)$$

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

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

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

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Mutation homoplasy

