

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

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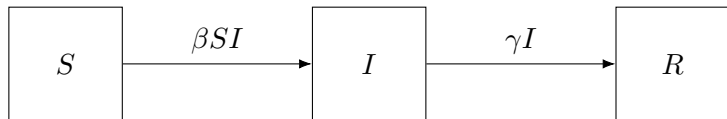
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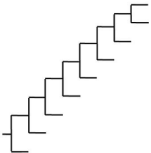
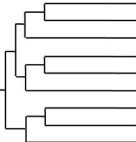
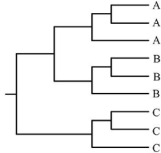
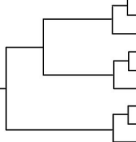
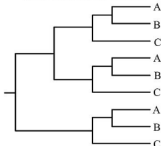
August 11, 2022

# Infection spread with compartmental models



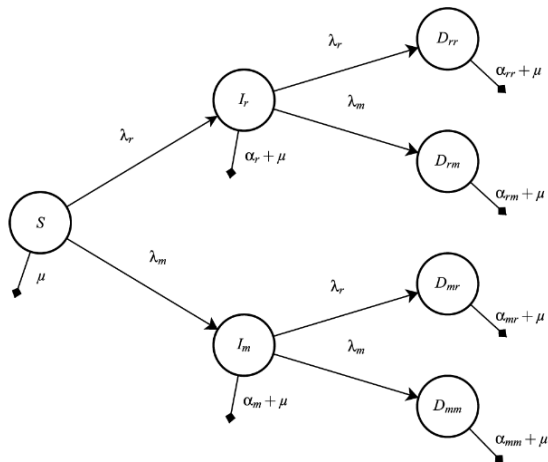
- $S(t)$  - fraction of susceptible hosts at  $t$
- $I(t)$  - fraction of infected hosts at  $t$
- $R(t)$  - fraction of recovered hosts at  $t$
- $1 = S(t) + I(t) + R(t)$  is constant

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

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

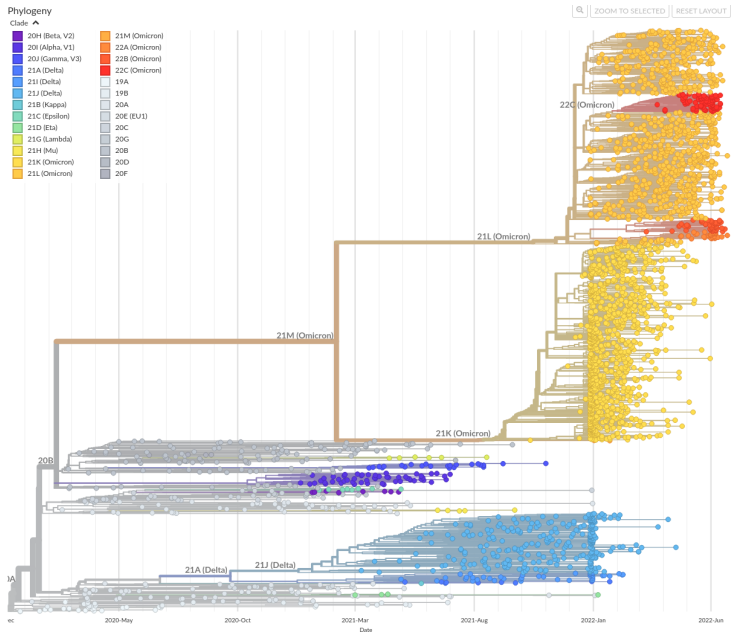
[Grenfell et al., 2004]

# Modeling multiple infections is challenging



[Alizon and van Baalen, 2008]

## 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

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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Abstract

Derivation of the Model

Application to Antigenic

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

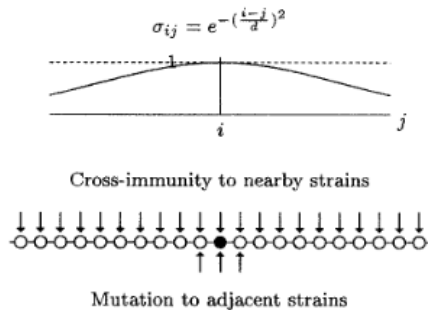
## Mathematical Biology

J.R. Gog · J. Swinton

## A status-based approach to multiple strain dynamics

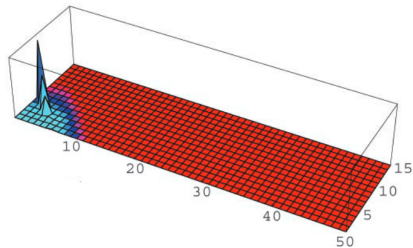
Received: 5 April 2000 / Revised version: 24 July 2001 /  
Published online: 8 February 2002 – © Springer-Verlag 2002

# Infections provide cross-immunity to nearby strains



[Gog and Grenfell, 2002]

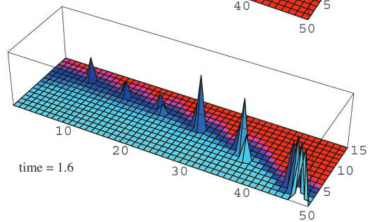
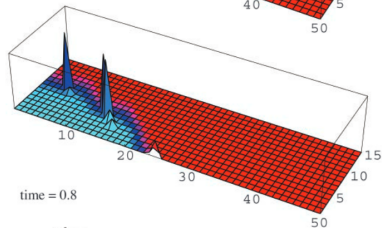
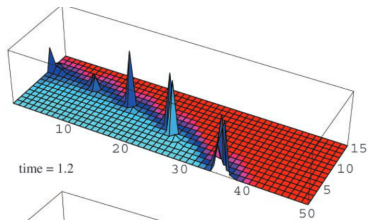
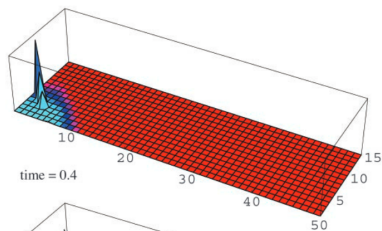
# Extending the strain lattice to 2 dimensions



[Gog and Grenfell, 2002]

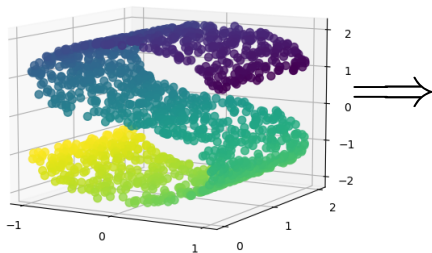


# Extending the strain lattice to 2 dimensions



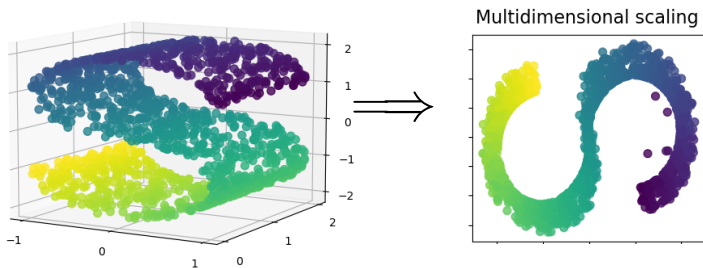
[Gog and Grenfell, 2002]

# Projecting points to low dimensions while preserving distances



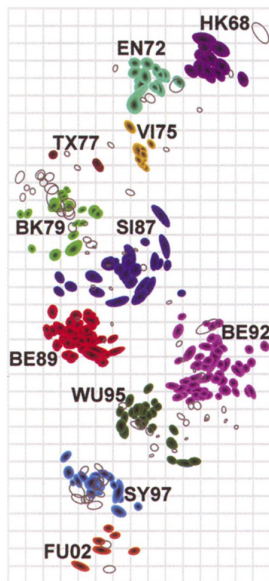
[Pedregosa et al., 2011]

# Projecting to low dimensions while preserving distances

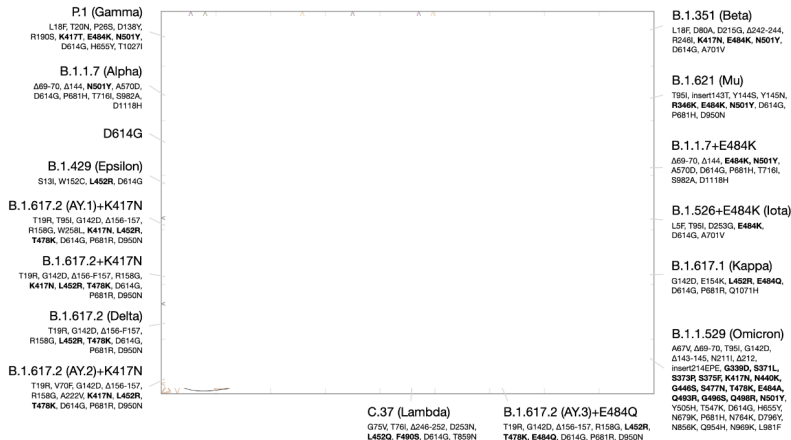


[Pedregosa et al., 2011]

# Approximating genomic data in 2 dimesions

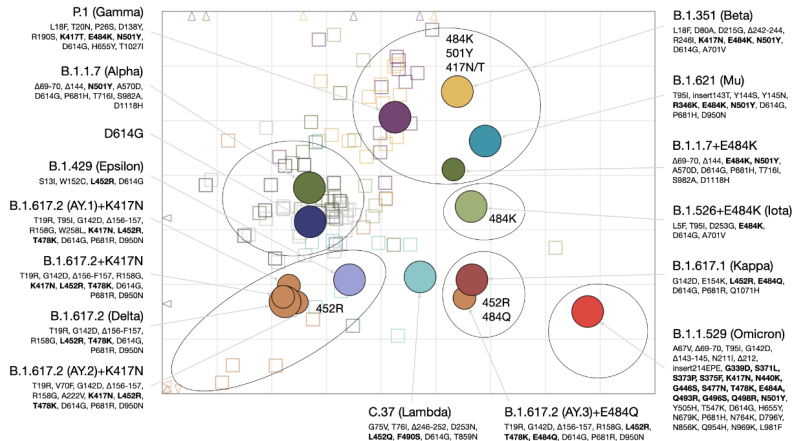


# Mapping SARS-CoV-2 in 2D



[Wilks et al., 2022]

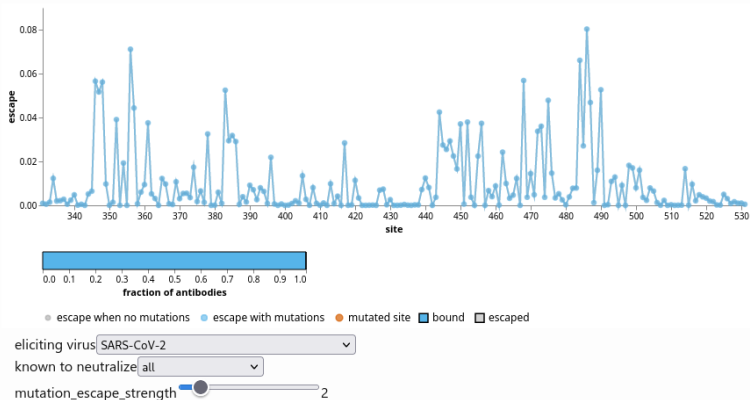
# Mapping SARS-CoV-2 in 2D



[Wilks et al., 2022]

# Methods of adding more genomes: polyclonal antibody binding studies

## Escape calculator for SARS-CoV-2 RBD



[Greaney et al., 2022]

# Interpolating more data into antigenic map

For each pair of genomes  $g_i$  and  $g_j$  ( $i \neq j$ )

1. Find the closest lineages in existing antigenic map to  $g_i$ , and  $g_j$ , and corresponding points  $x_i$  and  $x_j$
- 2.
- 3.
- 4.



# Interpolating more data into antigenic map

For each pair of genomes  $g_i$  and  $g_j$  ( $i \neq j$ )

1. Find the closest lineages in existing antigenic map to  $g_i$ , and  $g_j$ , and corresponding points  $x_i$  and  $x_j$
2. Determine difference in polyclonal binding affinity  $B(g_i, g_j)$
- 3.
- 4.

## Interpolating more data into antigenic map

For each pair of genomes  $g_i$  and  $g_j$  ( $i \neq j$ )

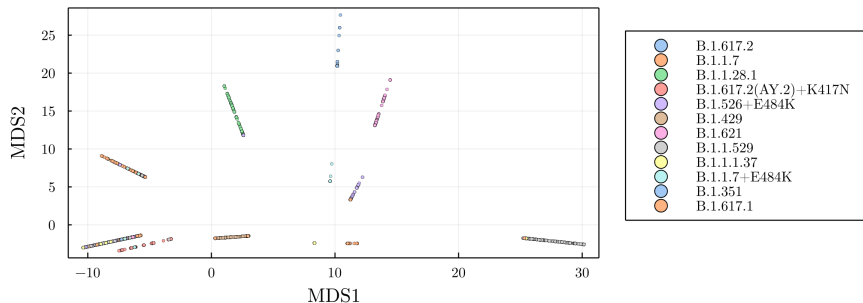
1. Find the closest lineages in existing antigenic map to  $g_i$ , and  $g_j$ , and corresponding points  $x_i$  and  $x_j$
2. Determine difference in polyclonal binding affinity  $B(g_i, g_j)$
3. Distance between  $g_i$  and  $g_j$  is  $\|x_i - x_j\| + B(g_i, g_j)$
- 4.

## Interpolating more data into antigenic map

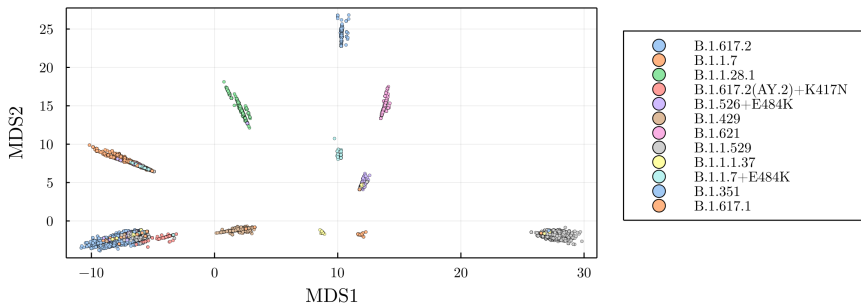
For each pair of genomes  $g_i$  and  $g_j$  ( $i \neq j$ )

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2. Determine difference in polyclonal binding affinity  $B(g_i, g_j)$
3. Distance between  $g_i$  and  $g_j$  is  $\|x_i - x_j\| + B(g_i, g_j)$
4. Use these distances as inputs to multidimensional scaling

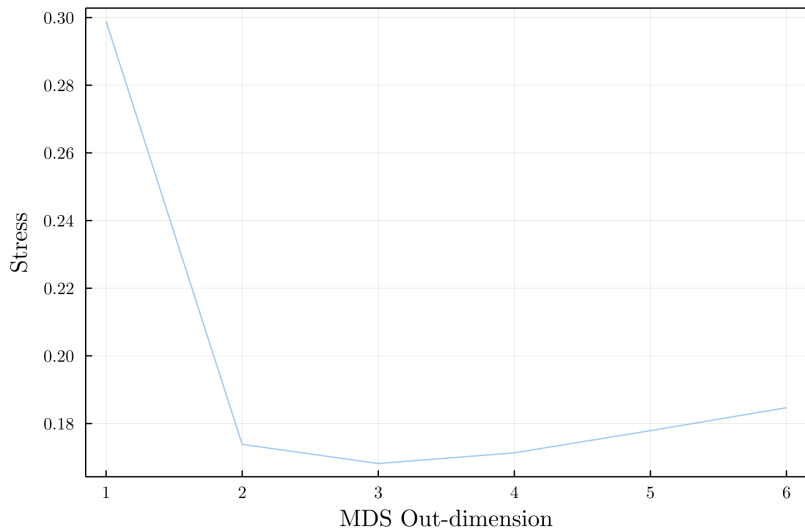
# Antibody Binding map



# 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 from variant $(i, j) \in [0, N]^2$
$V_{ij}$	Immune by vaccination 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 $(i, j)$
$v_{ij}(t)$	vaccination rate at time $t$ against variant $(i, j)$
$s(t)$	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

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

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

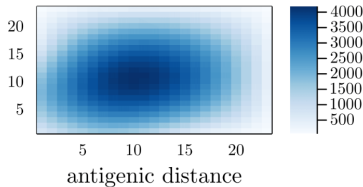
$$\frac{R_{ij}(t)}{dt} = \sum_{kl \neq ij} s(t) \beta_{kl} \sigma_{ijkl} S_{ij} I_{kl} + \xi I_{ij} - \gamma R_{ij} + v_{ij}(t)S \quad (3)$$

$$\frac{V_{ij}(t)}{dt} = v_{ij}(t)S - \gamma V_{ij} \quad (4)$$

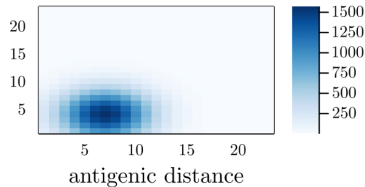


# Model Dynamics

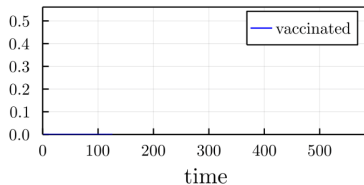
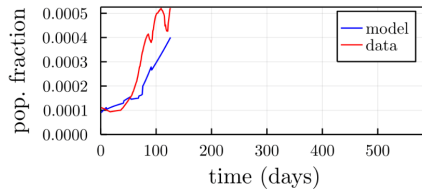
I



V



Incident (daily) cases



## Further work

- More detailed methods for interpolation of additional genome data
- 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

