

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

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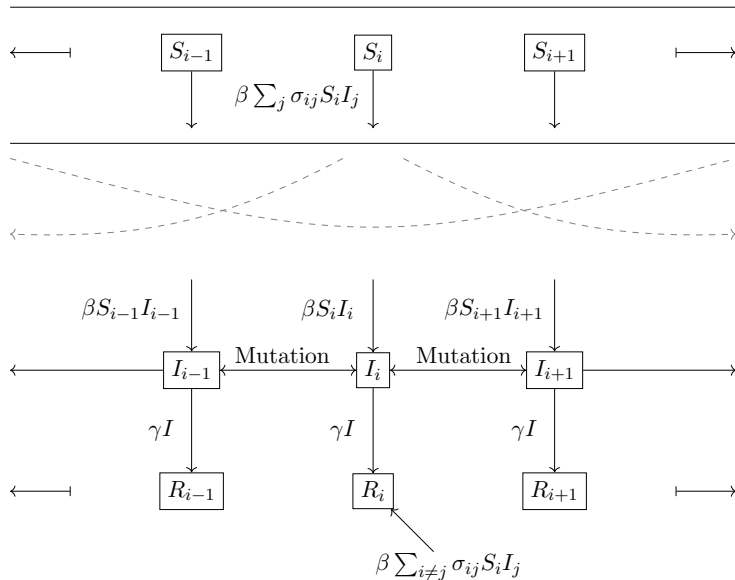
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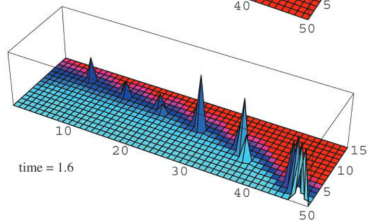
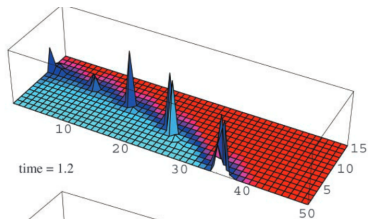
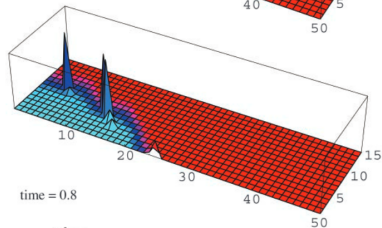
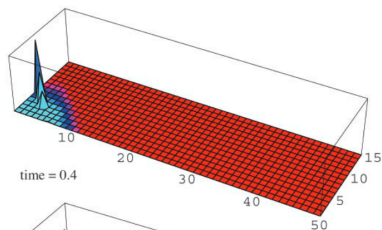
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Full strain lattice model in 1 dimension

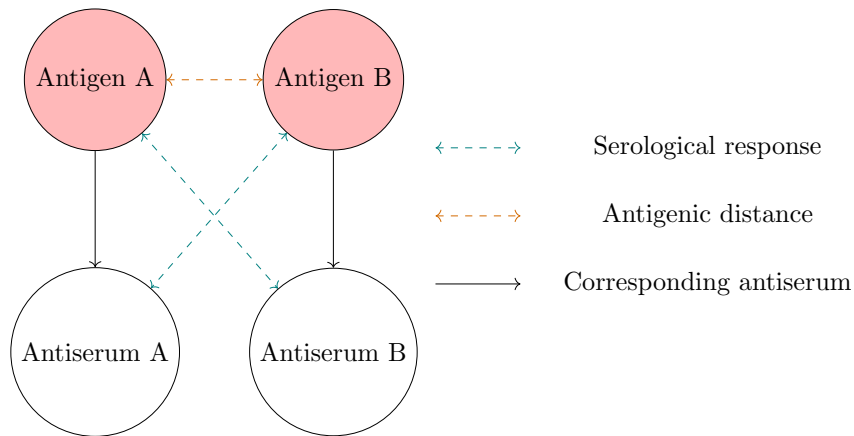


Extending the strain lattice to 2 dimensions

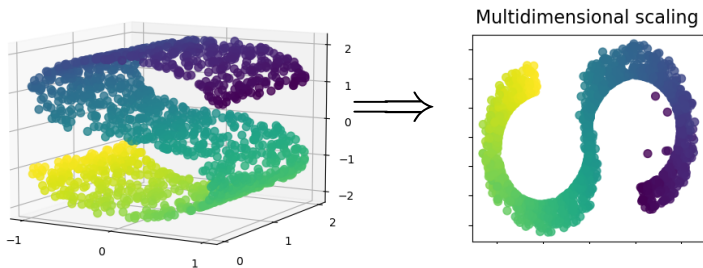


[Gog and Grenfell, 2002]

Quantifying antigenicity between viruses

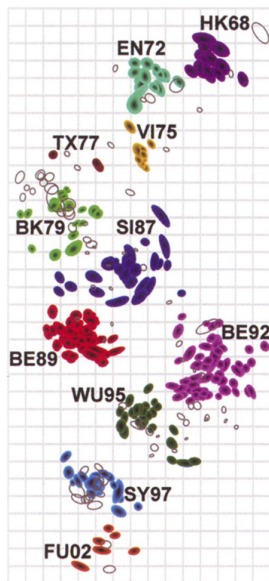


Projecting to low dimensions while preserving distances

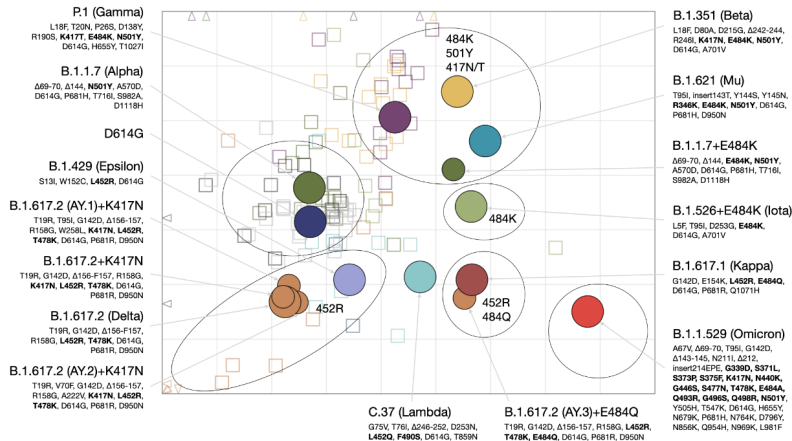


[Pedregosa et al., 2011]

Approximating genomic data in 2 dimesions



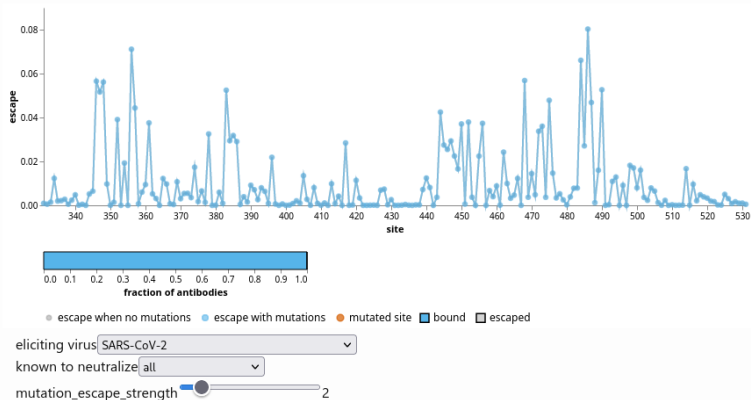
Mapping SARS-CoV-2 in 2D



[Wilks et al., 2022]

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.

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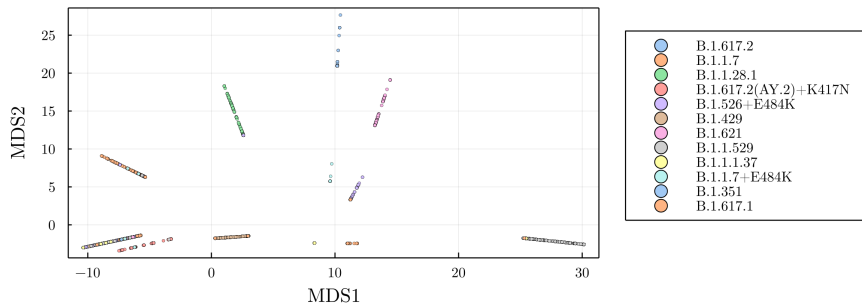
1. Find the closest lineages in existing antigenic map to g_i , and g_j , and corresponding points x_i and x_j
2. Determine difference in polyclonal binding affinity $B(g_i, g_j)$
3. Distance between g_i and g_j is $\|x_i - x_j\| + B(g_i, g_j)$
- 4.

Interpolating more data into antigenic map

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

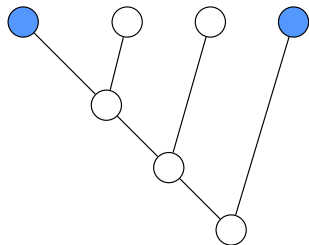
1. Find the closest lineages in existing antigenic map to g_i , and g_j , and corresponding points x_i and x_j
2. Determine difference in polyclonal binding affinity $B(g_i, g_j)$
3. Distance between g_i and g_j is $\|x_i - x_j\| + B(g_i, g_j)$
4. Use these distances as inputs to multidimensional scaling

Antibody Binding map

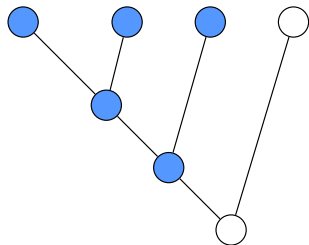


Methods of adding more genomes: homoplasious sites

Homoplasious mutation

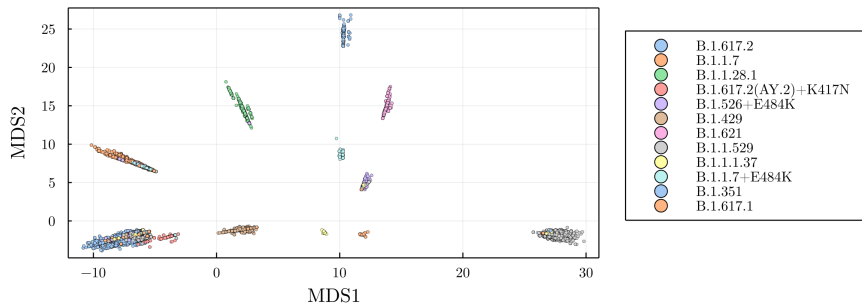


Homologous mutation

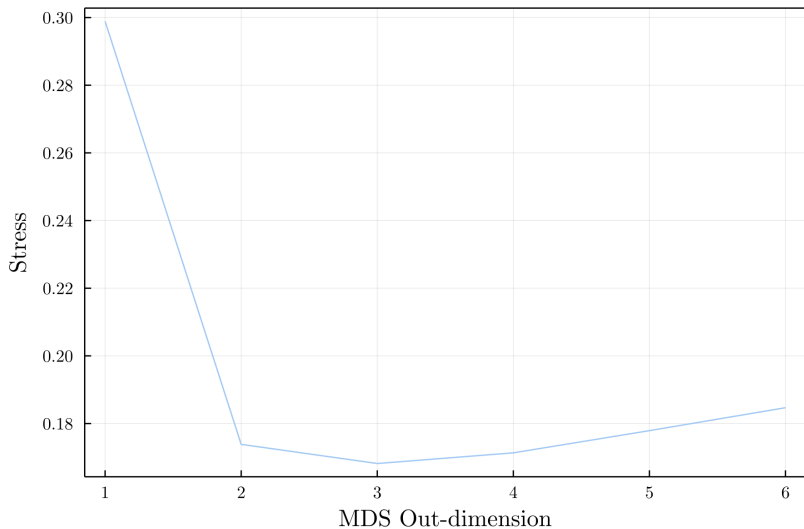


[Page and Holmes, 2009]

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

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

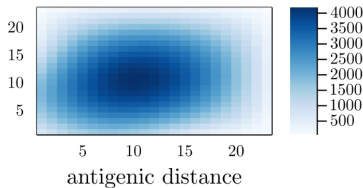
$$\frac{I_{ij}(t)}{dt} = s(t) \beta_{ij} S_{ij} I_{ij} - \xi I_{ij} + M(-4I_{ij} + I_{i-1,j} + I_{i+1,j} + I_{i,j-1} + I_{i,j+1}) \quad (2)$$

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

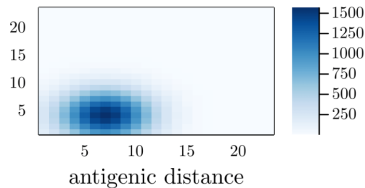
$$\frac{V_{ij}(t)}{dt} = v_{ij}(t)S - \gamma V_{ij} \quad (4)$$

Model Dynamics

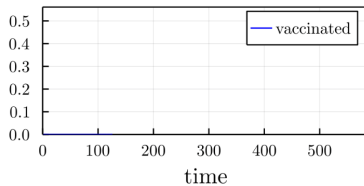
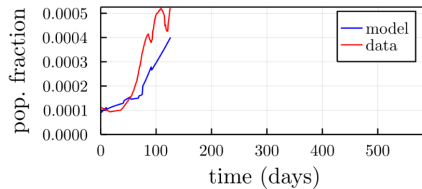
I



V









Incident (daily) cases



Case importation

- Evolution of Omicron represents a huge shift in antigenic space
- Intermediate steps not represented in data
- We add imports to solve this problem

-  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.

-  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., Mühlemann, B., Shen, X., Türel, 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

