

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

Peter C. Jentsch, PhD ^{1,4} Finlay Maguire, PhD ^{3,5}
Samira Mubareka, MD, FRCPC ^{1,2}

¹Sunnybrook Research Institute, Toronto, Canada

²University of Toronto, Toronto, Canada

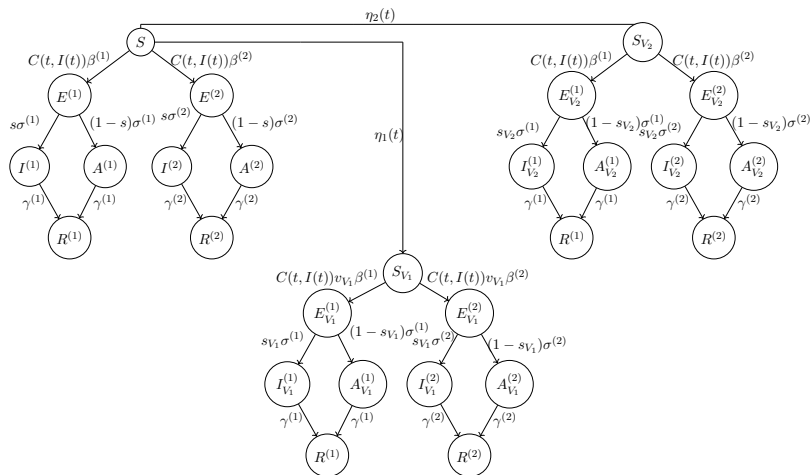
³Dalhousie University, Halifax, Canada

⁴Simon Fraser University, Burnaby, Canada

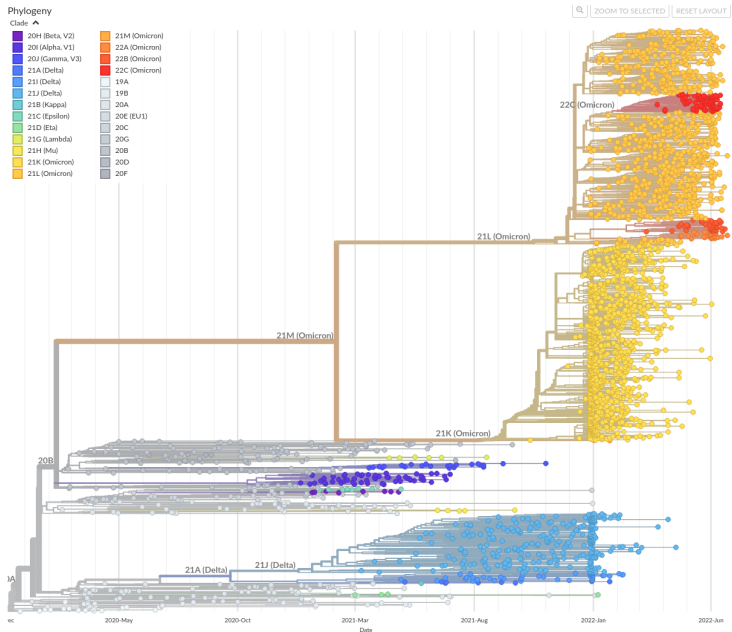
⁵Shared Hospital Laboratory, Toronto, Canada

July 8, 2022

Modeling multiple infections is challenging



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

PNAS

Vol. 99 | No. 26

Abstract

Derivation of the Model

Application to Antigenic

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

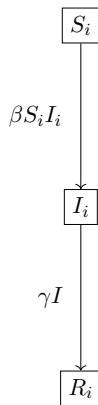
Mathematical Biology

J.R. Gog · J. Swinton

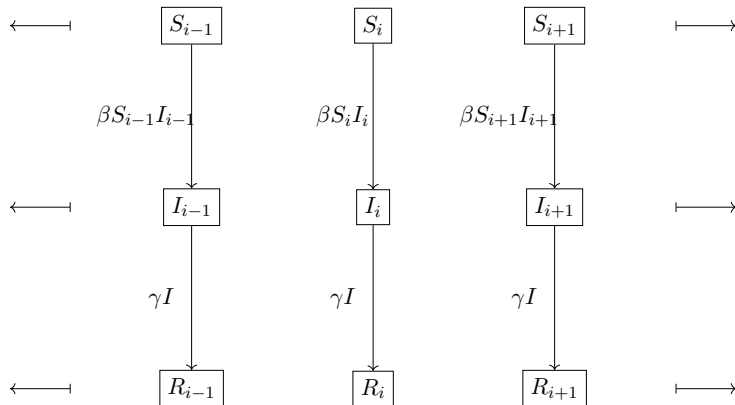
A status-based approach to multiple strain dynamics

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

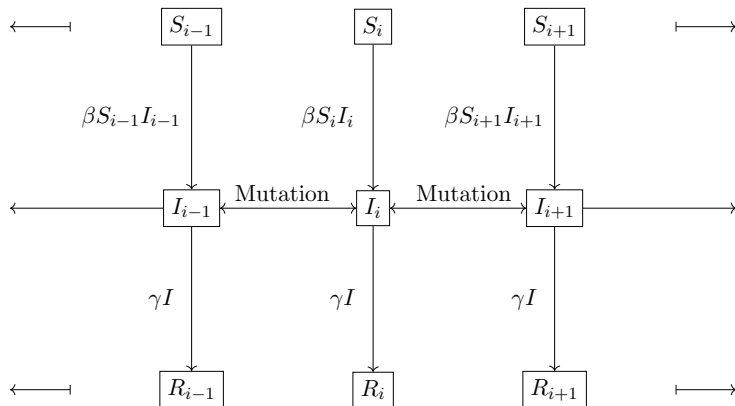
Begin with simple SIR model



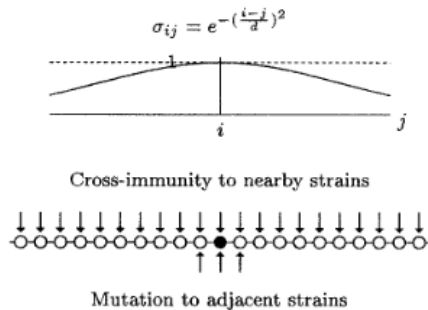
Organize strains on a lattice



Strains mutate into adjacent strains

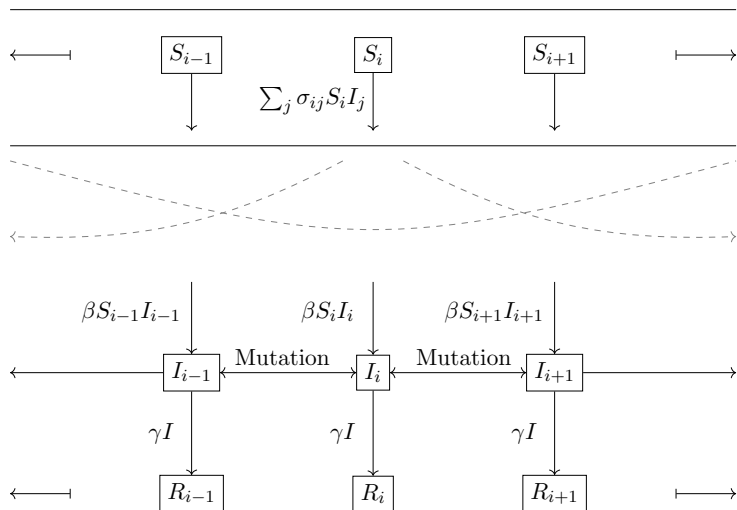


Infections provide cross-immunity to nearby strains

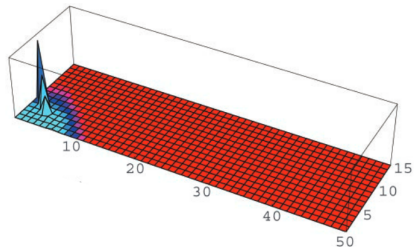


[Gog and Grenfell, 2002]

Full strain lattice model in 1 dimension

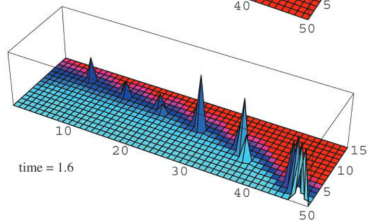
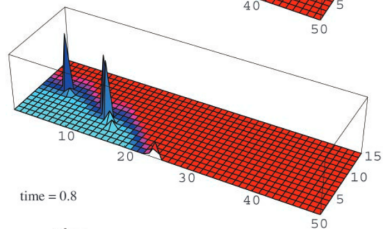
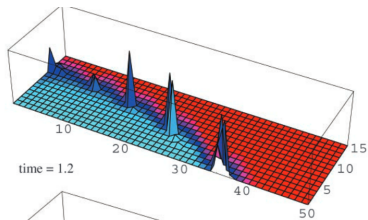
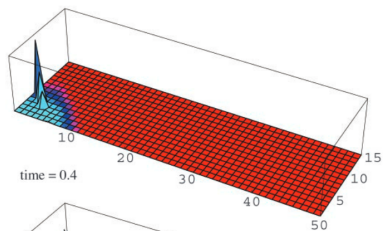


Extending the strain lattice to 2 dimensions



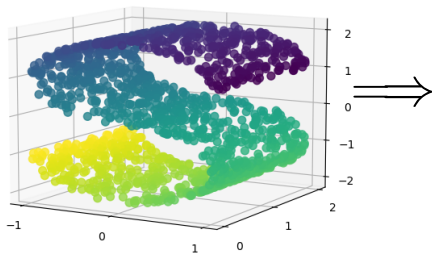
[Gog and Grenfell, 2002]

Extending the strain lattice to 2 dimensions



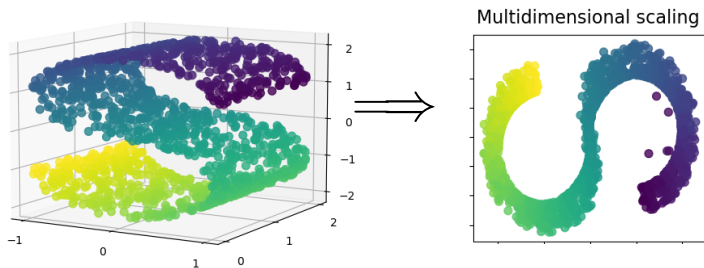
[Gog and Grenfell, 2002]

Projecting to low dimensions while preserving distances



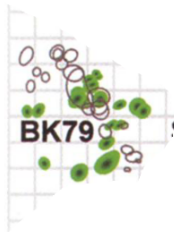
[Pedregosa et al., 2011]

Projecting to low dimensions while preserving distances

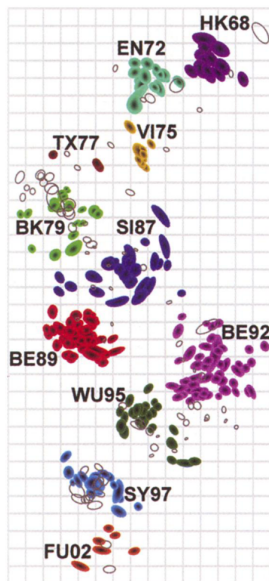


[Pedregosa et al., 2011]

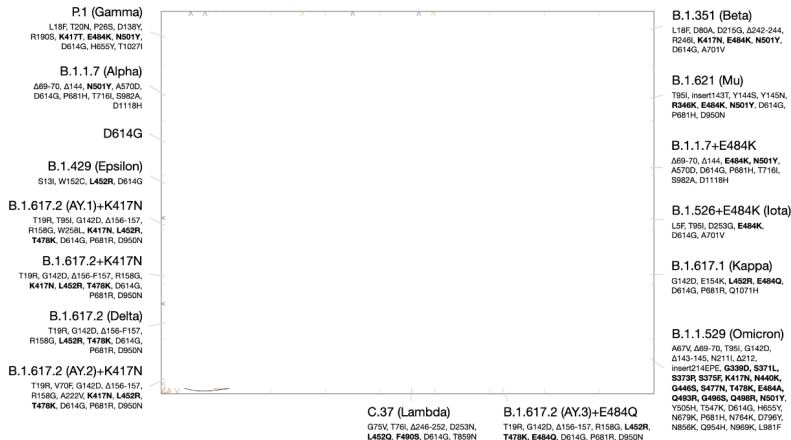
Approximating genomic data in 2 dimesions



Approximating genomic data in 2 dimesions

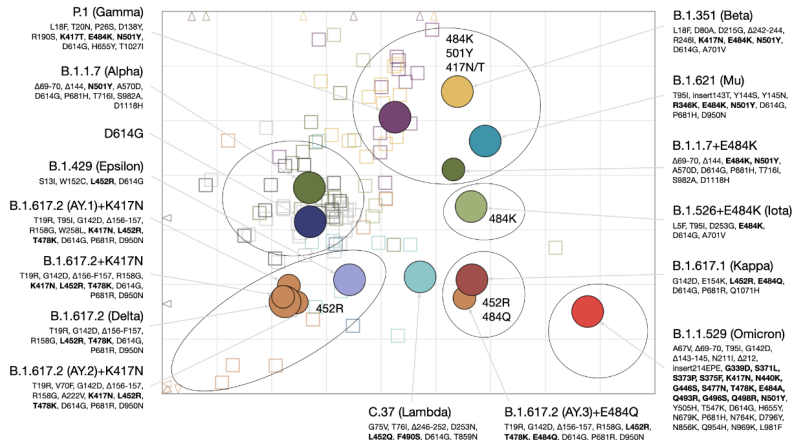


Mapping SARS-CoV-2 in 2D



[Wilks et al., 2022]

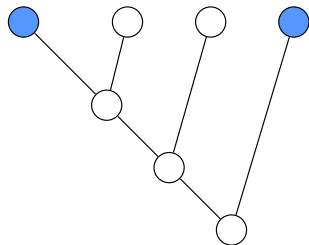
Mapping SARS-CoV-2 in 2D



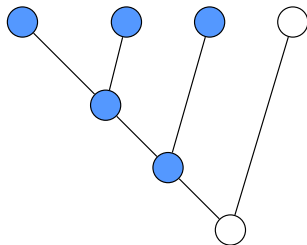
[Wilks et al., 2022]

Methods of adding more genomes: homoplasious sites

Homoplasious trait

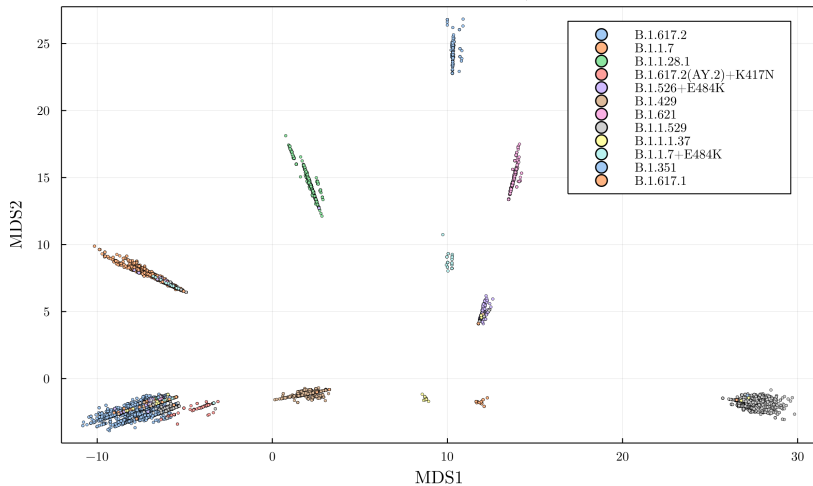


Homologous trait



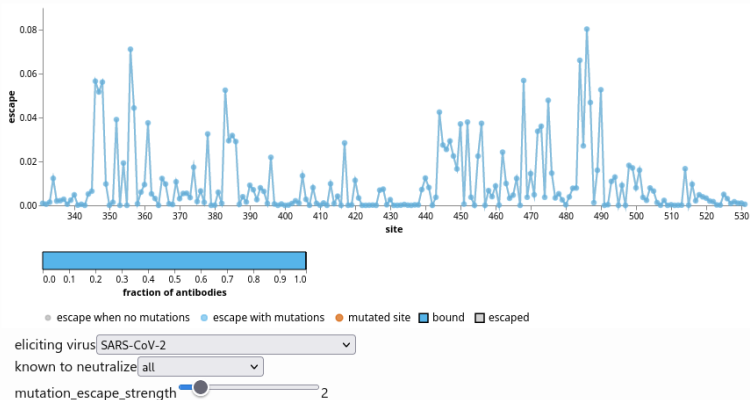
[Page and Holmes, 2009]

Homoplasic mutations map



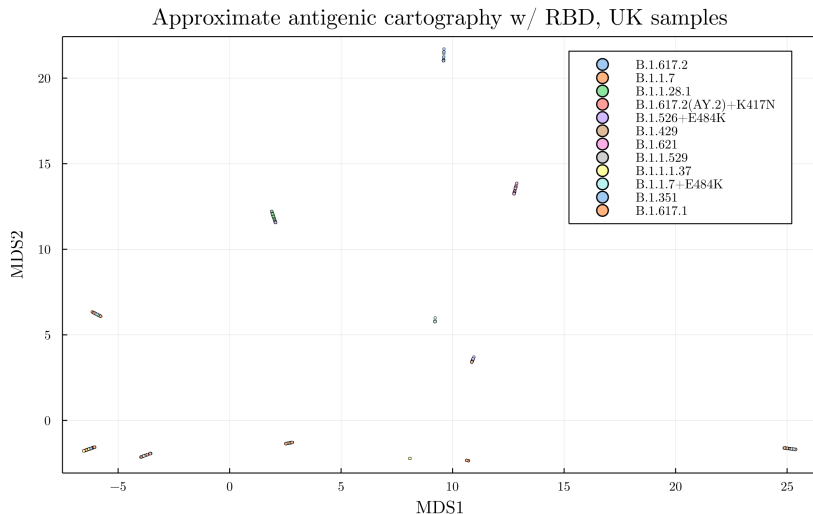
Methods of adding more genomes: polyclonal antibody binding studies

Escape calculator for SARS-CoV-2 RBD

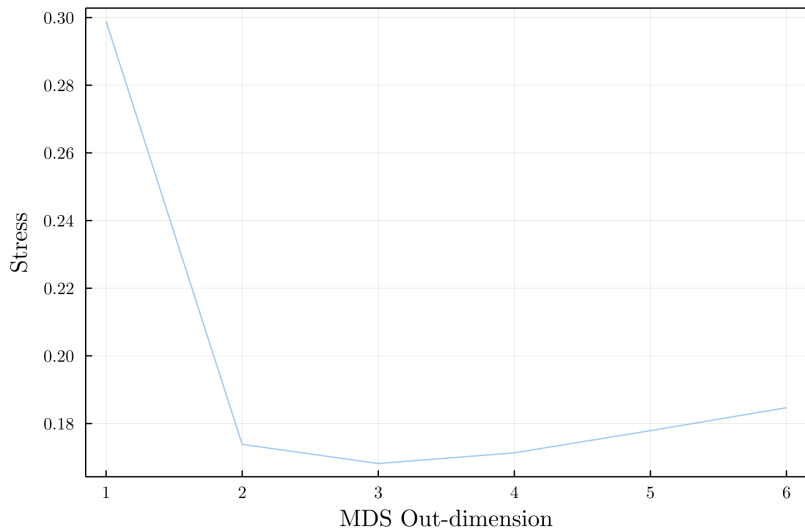


[Greaney et al., 2022]

Antibody Binding 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: $I_{0,j} = 0, I_{j,0} = 0, I_{N,j} = 0, I_{j,N} = 0$





Initial conditions computed from genomic data in GISAID



Model Dynamics

(gifs of 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

-  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., 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

