

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

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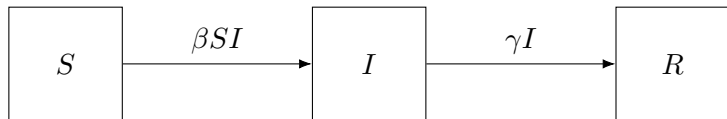
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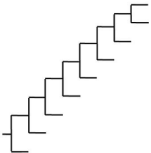
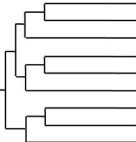
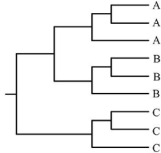
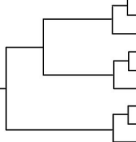
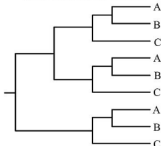
July 12, 2022

Infection spread with compartmental models



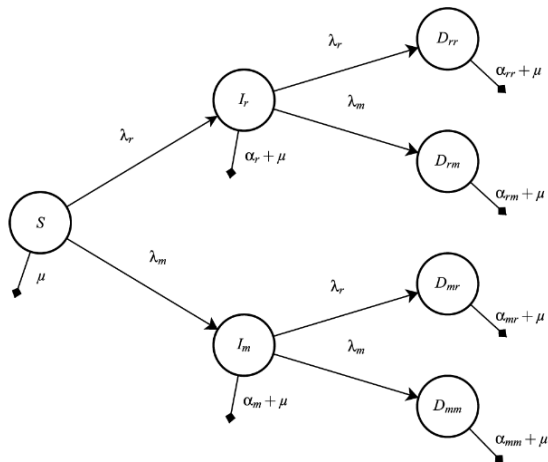
- $S(t)$ - fraction of susceptible hosts at t
- $I(t)$ - fraction of infected hosts at t
- $R(t)$ - fraction of recovered hosts at t
- $1 = S(t) + I(t) + R(t)$ is constant

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

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

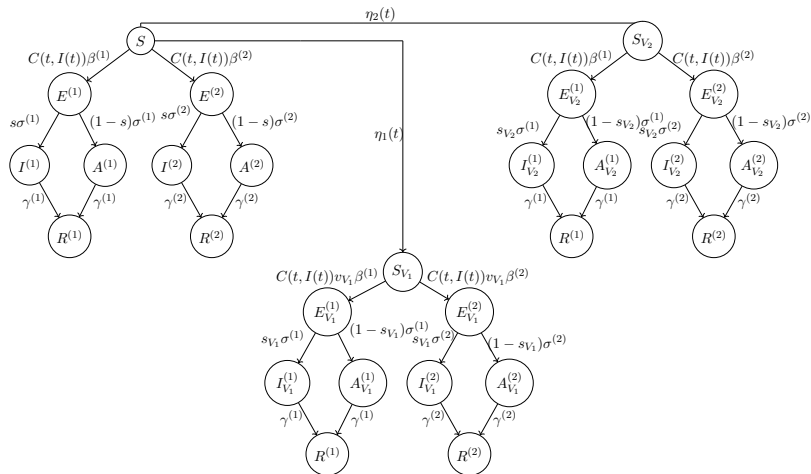
[Grenfell et al., 2004]

Modeling multiple infections is challenging

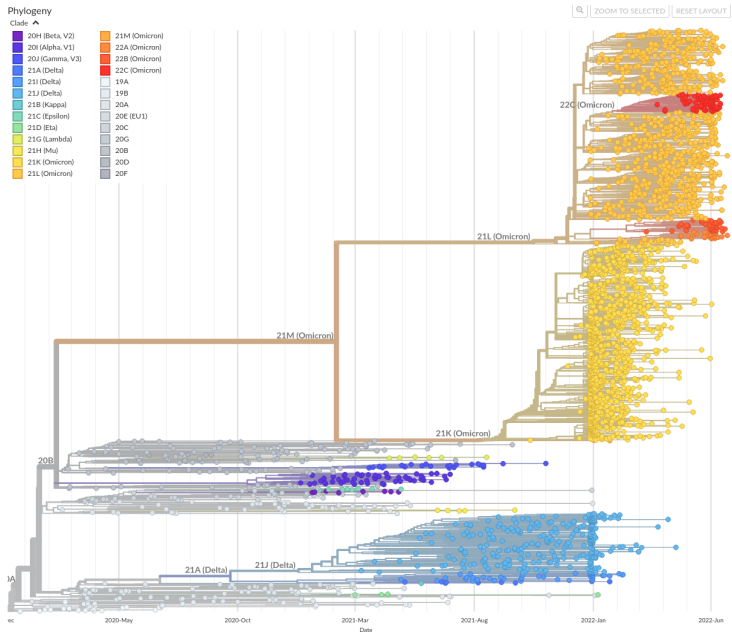


[Alizon and van Baalen, 2008]

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

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

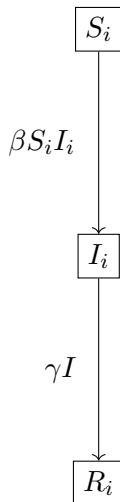
J.R. Gog · J. Swinton

A status-based approach to multiple strain dynamics

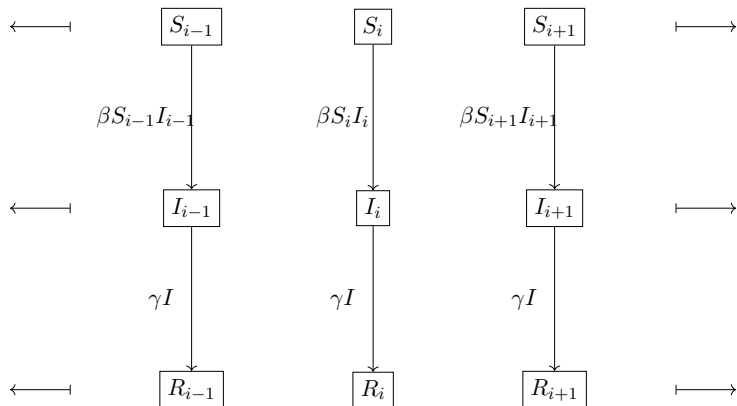
Received: 5 April 2000 / Revised version: 24 July 2001 /
Published online: 8 February 2002 – © Springer-Verlag 2002

Begin with SIR model

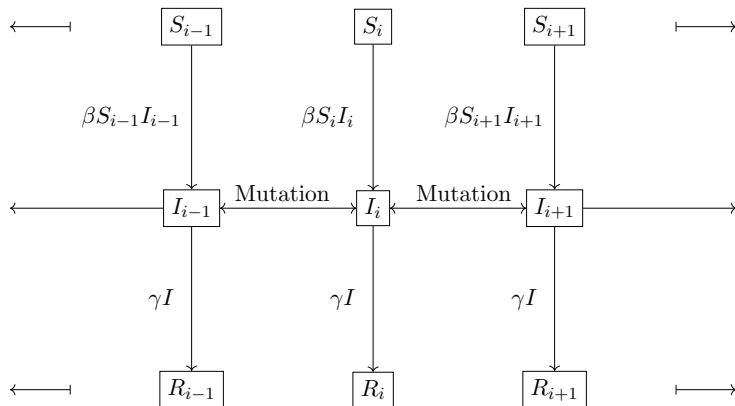
- Consider strains of a pathogen numbered $i \in [1, N]$
- $S(t)$ - population of hosts susceptible to strain i at t
- $I(t)$ - population of hosts infected with strain i at t
- $R(t)$ - population of hosts recovered from strain i at t



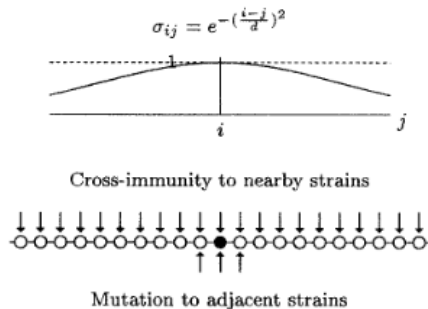
Organize strains on a lattice



Strains mutate into adjacent strains

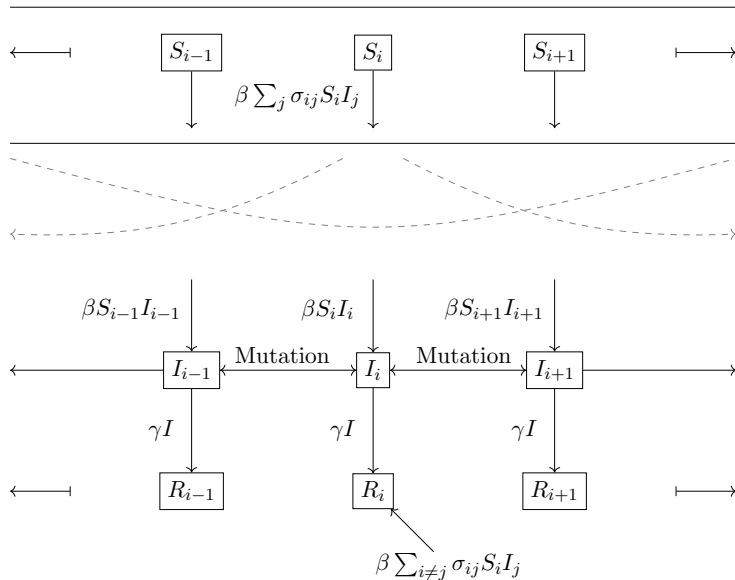


Infections provide cross-immunity to nearby strains

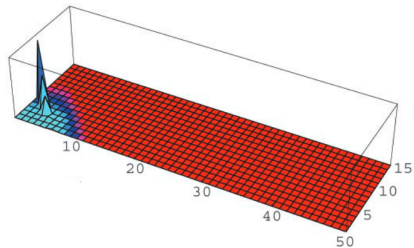


[Gog and Grenfell, 2002]

Full strain lattice model in 1 dimension

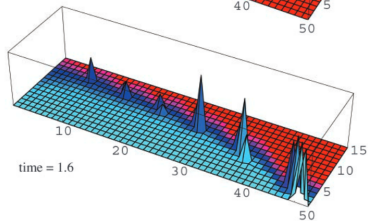
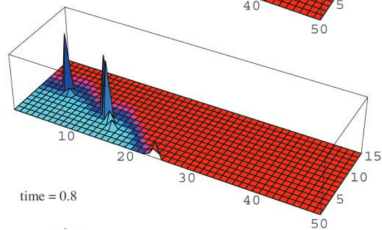
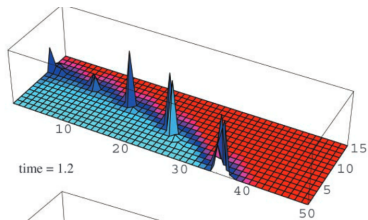
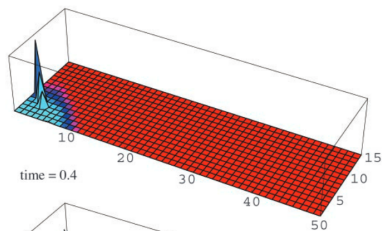


Extending the strain lattice to 2 dimensions



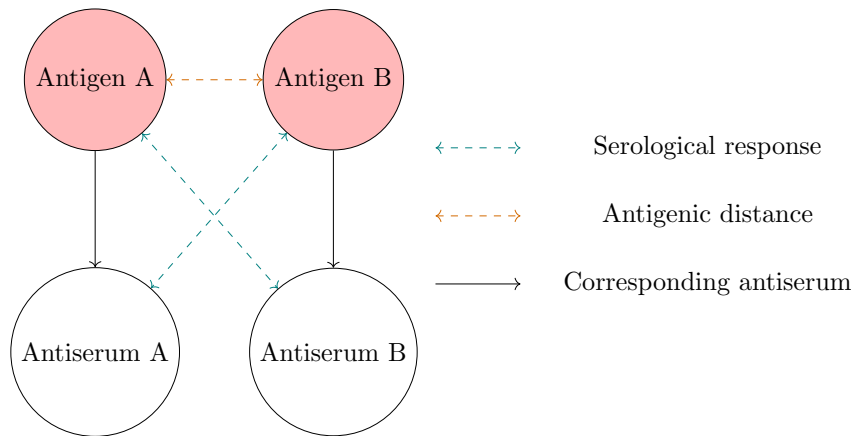
[Gog and Grenfell, 2002]

Extending the strain lattice to 2 dimensions

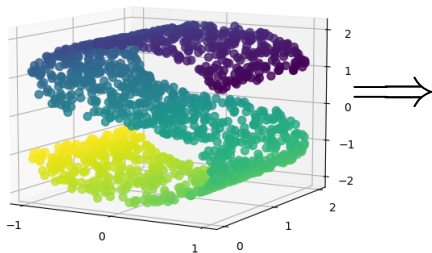


[Gog and Grenfell, 2002]

Quantifying antigenicity between viruses

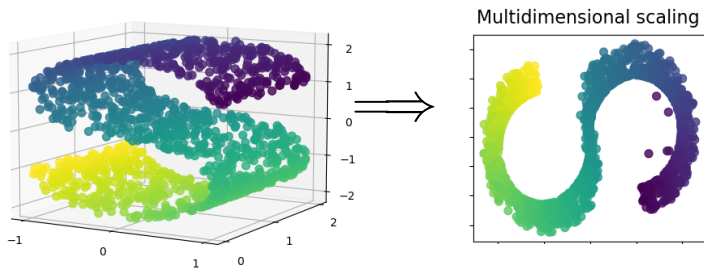


Projecting points to low dimensions while preserving distances



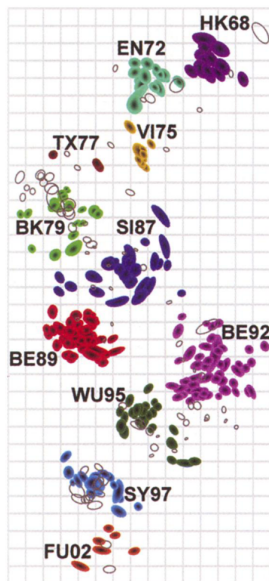
[Pedregosa et al., 2011]

Projecting to low dimensions while preserving distances

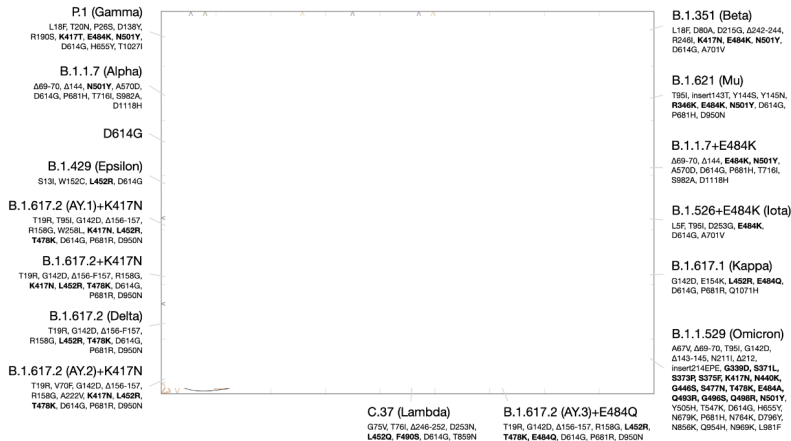


[Pedregosa et al., 2011]

Approximating genomic data in 2 dimesions

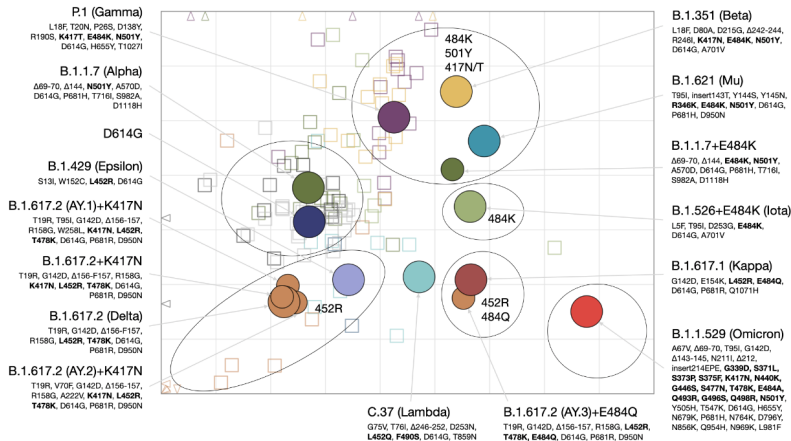


Mapping SARS-CoV-2 in 2D



[Wilks et al., 2022]

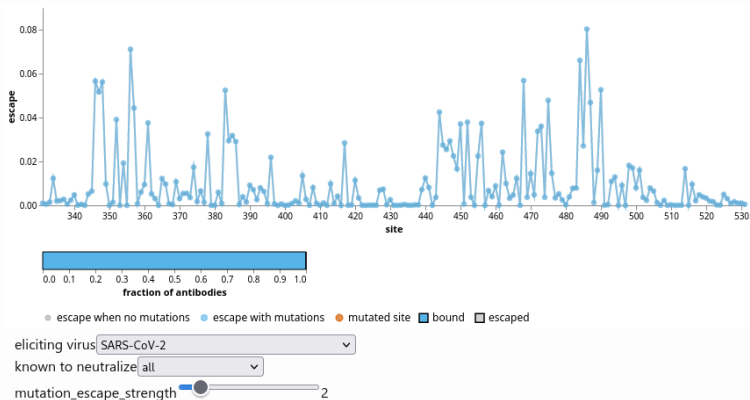
Mapping SARS-CoV-2 in 2D



[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 ($i \neq j$)

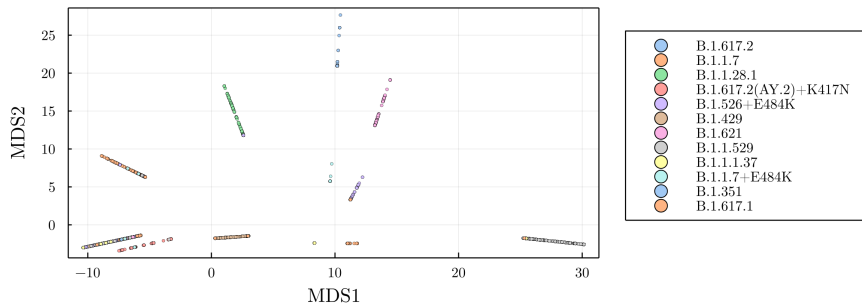
1. Find the closest lineages in existing antigenic map to g_i , and g_j , and corresponding points x_i and x_j
2. Determine difference in polyclonal binding affinity $B(g_i, g_j)$
3. Distance between g_i and g_j is $\|x_i - x_j\| + B(g_i, g_j)$
- 4.

Interpolating more data into antigenic map

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

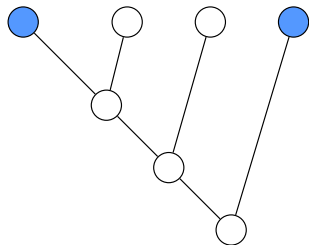
1. Find the closest lineages in existing antigenic map to g_i , and g_j , and corresponding points x_i and x_j
2. Determine difference in polyclonal binding affinity $B(g_i, g_j)$
3. Distance between g_i and g_j is $\|x_i - x_j\| + B(g_i, g_j)$
4. Use these distances as inputs to multidimensional scaling

Antibody Binding map

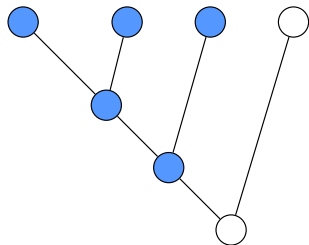


Methods of adding more genomes: homoplasious sites

Homoplasious mutation

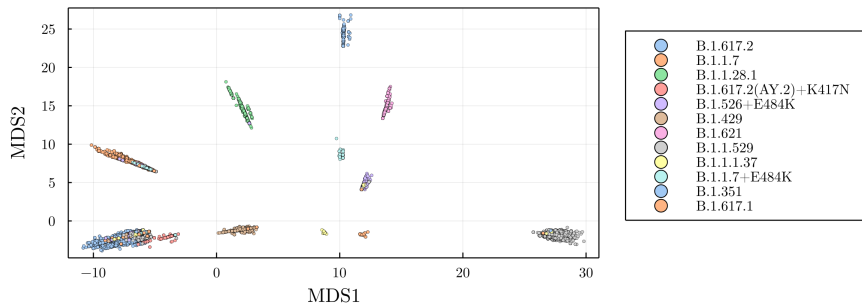


Homologous mutation

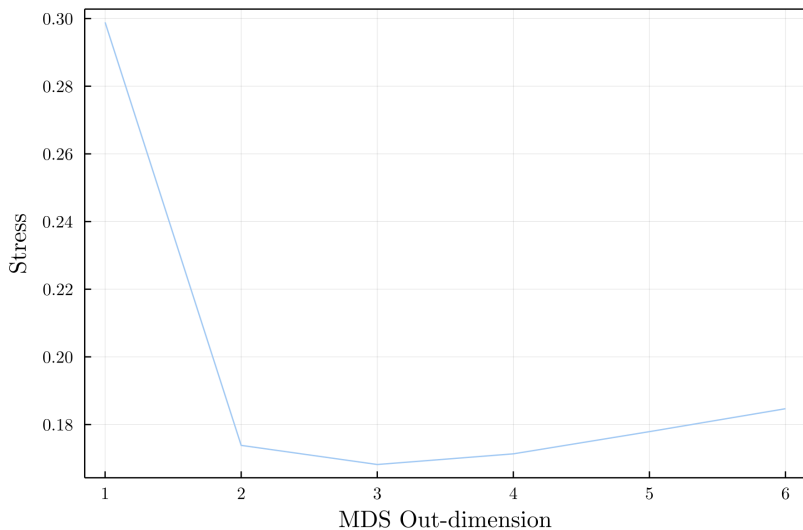


[Page and Holmes, 2009]

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

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

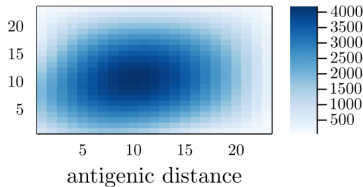
$$\frac{I_{ij}(t)}{dt} = s(t) \beta_{ij} S_{ij} I_{ij} - \xi I_{ij} + M(-4I_{ij} + I_{i-1,j} + I_{i+1,j} + I_{i,j-1} + I_{i,j+1}) \quad (2)$$

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

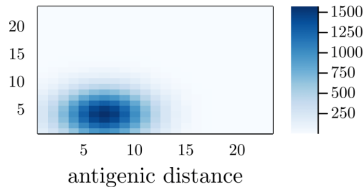
$$\frac{V_{ij}(t)}{dt} = v_{ij}(t)S - \gamma V_{ij} \quad (4)$$

Model Dynamics

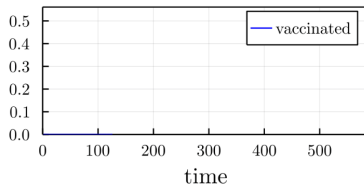
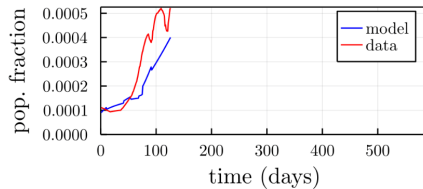
I



V



Incident (daily) cases



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

