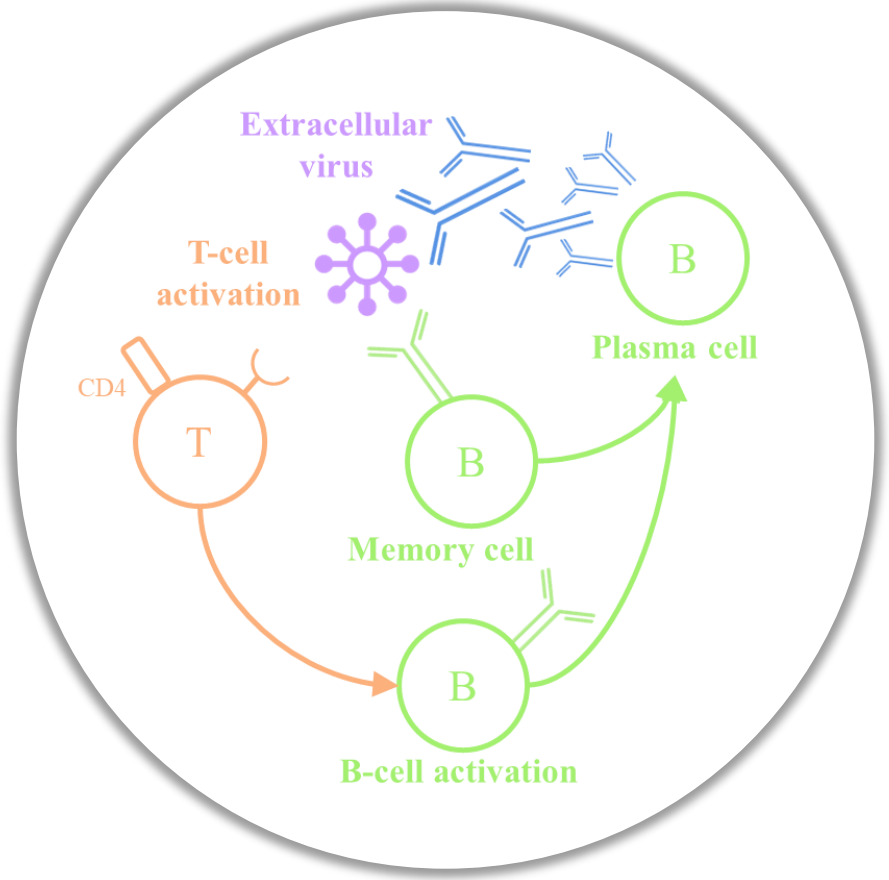
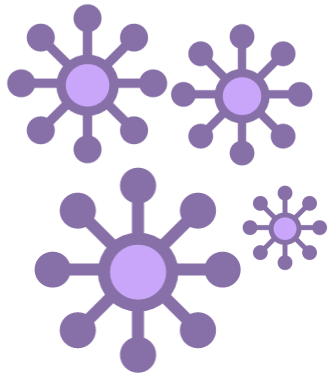
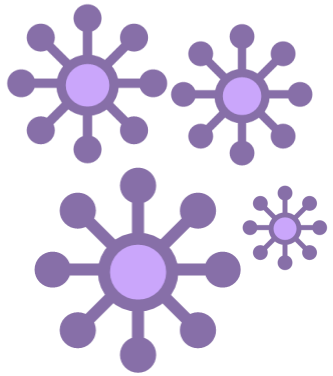


Generative modelling in Covid-19



Generative modelling in Covid-19

Dynamic causal modelling
Mean-field modelling
Applications to epidemiology
Applications to immunology



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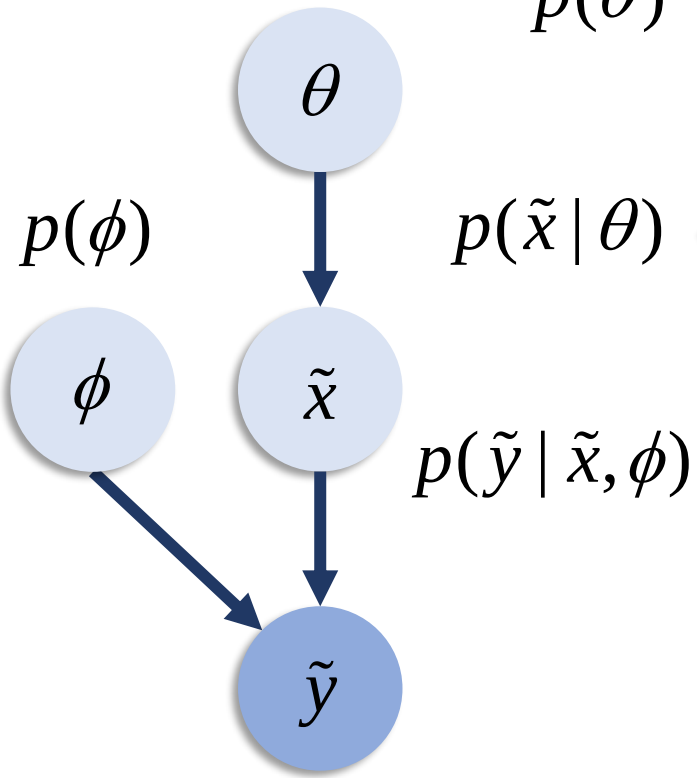
Dynamic causal modelling



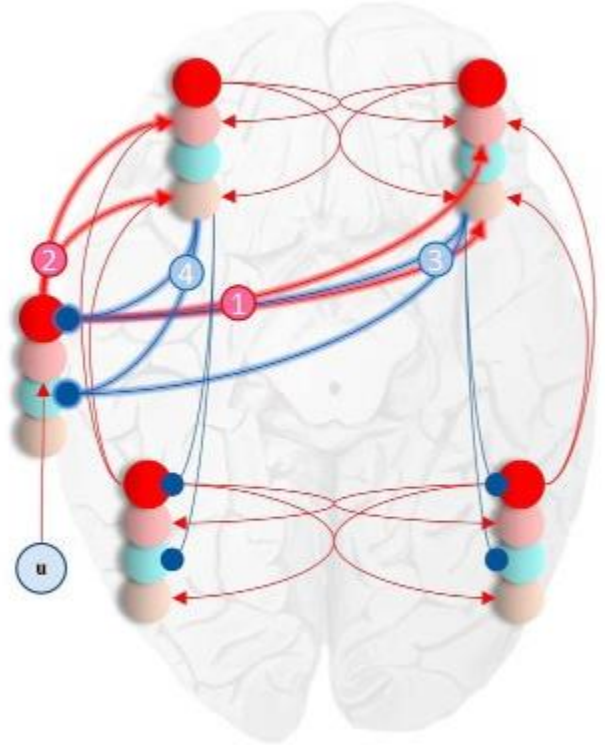
$p(\theta)$

$p(\phi)$

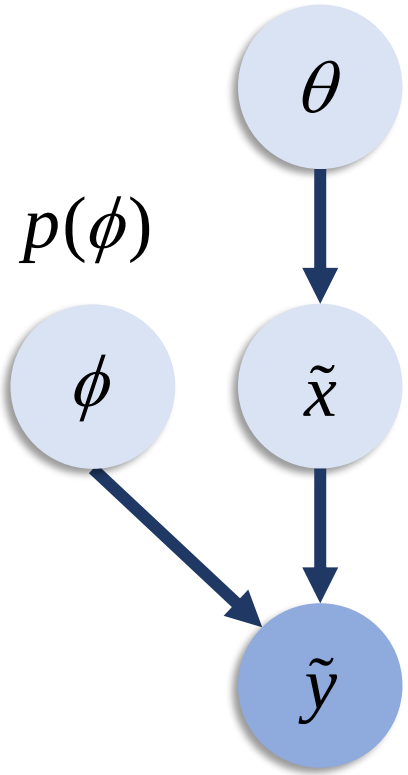
$p(\tilde{x} \mid \theta)$

$\dot{x} = f(x, \theta) + \omega$

$p(\tilde{y} \mid \tilde{x}, \phi)$



Dynamic causal modelling



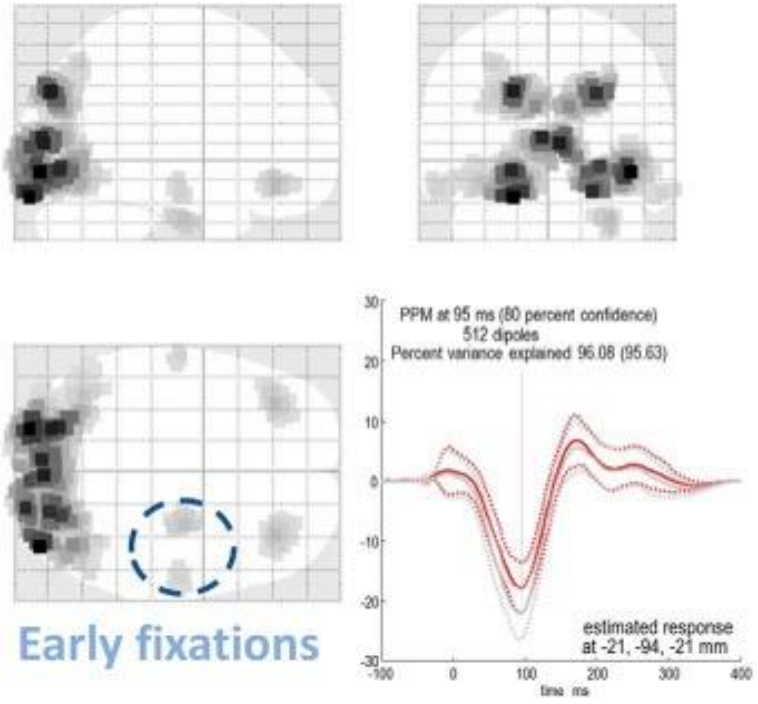
$p(\theta)$

$p(\phi)$

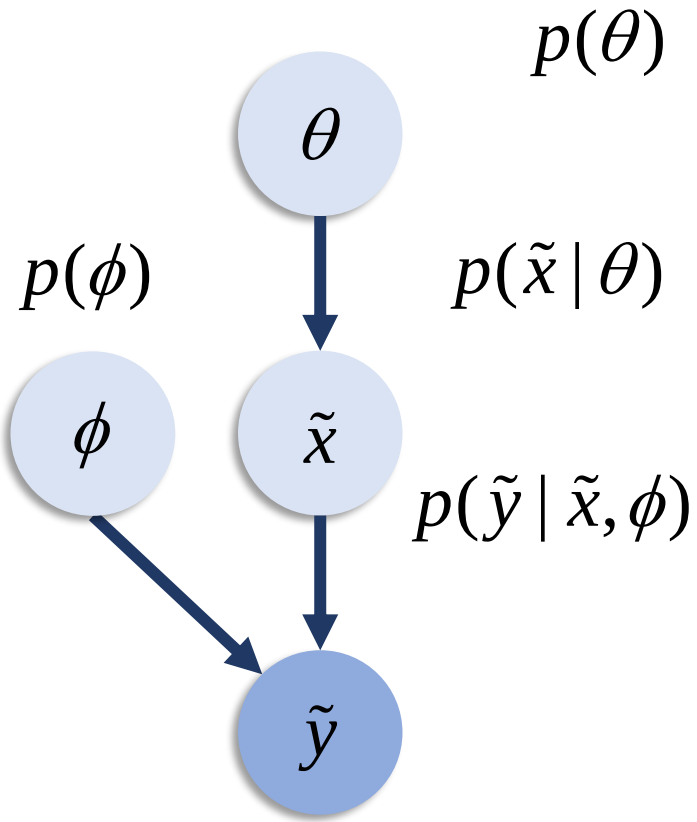
$p(\tilde{x} \mid \theta)$

$p(\tilde{y} \mid \tilde{x}, \phi)$

$\tilde{y} = g(\tilde{x}, \phi) + \zeta$



Dynamic causal modelling

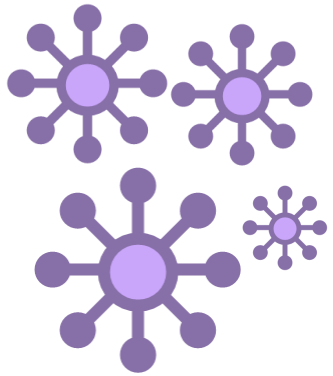


Variational Laplace

$$q(\theta,\phi) = \mathrm{N}\ (\mu,\Sigma)$$

$$F = \mathrm{E}_q\left[\ln q(\theta,\phi) - \ln\ p(\theta,\phi,\tilde{y})\right]$$

$$q(\theta,\phi) = \arg\min_q F;\ \ln\ p(\tilde{y}) \approx -\min_q F$$



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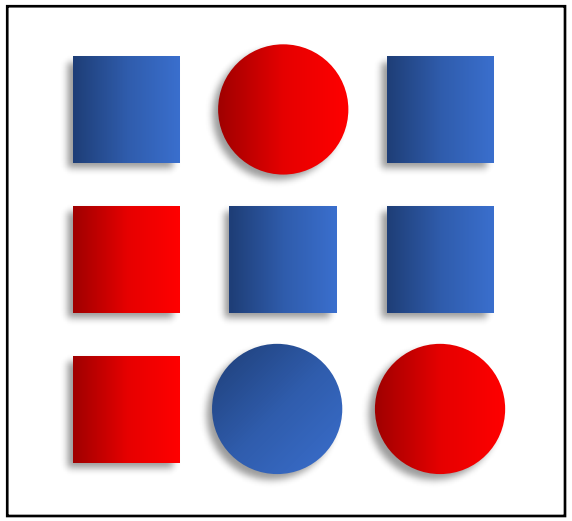
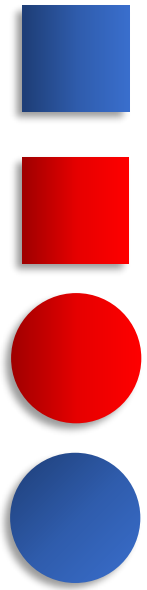
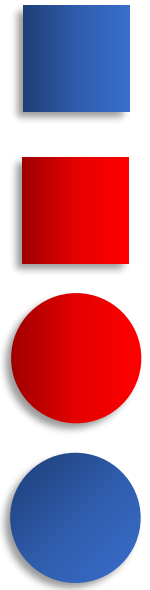
Mean-field modelling



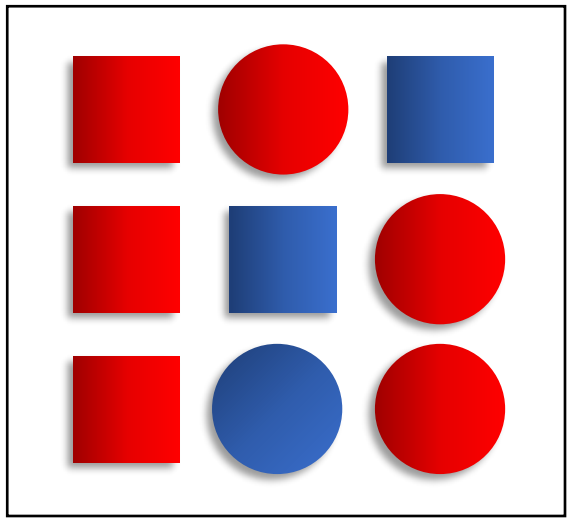


$$= \begin{bmatrix} \theta_{11} & \theta_{12} & \theta_{13} & \theta_{14} \\ \theta_{21} & \theta_{22} & \theta_{23} & \theta_{24} \\ \theta_{31} & \theta_{32} & \theta_{33} & \theta_{34} \\ \theta_{41} & \theta_{42} & \theta_{43} & \theta_{44} \end{bmatrix}$$



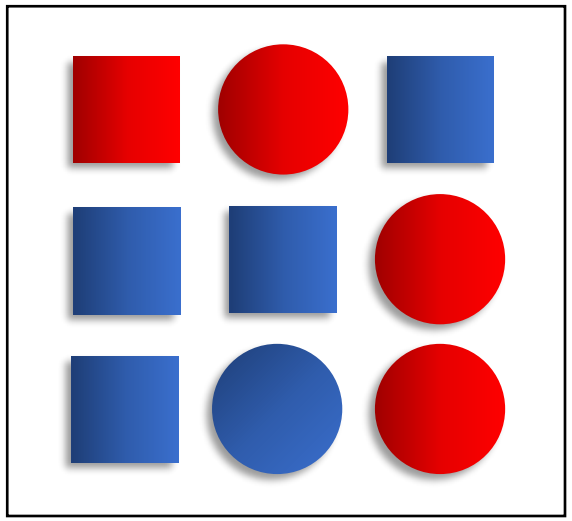
$\tau+1$

Mean-field modelling



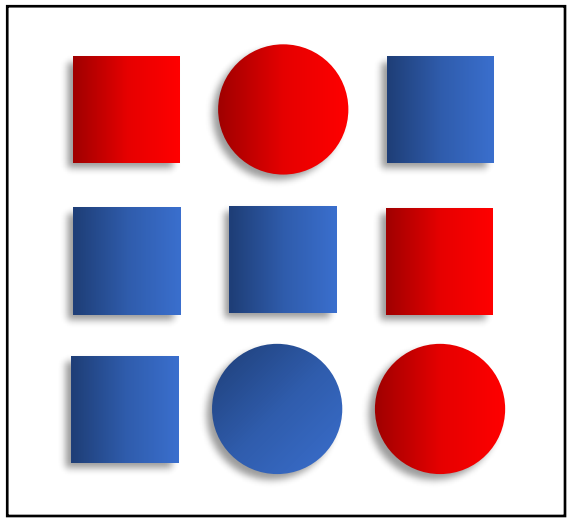
$$\begin{matrix} \\ \\ \\ \\ \tau+1 \end{matrix} = \begin{bmatrix} \theta_{11} & \theta_{12} & \theta_{13} & \theta_{14} \\ \theta_{21} & \theta_{22} & \theta_{23} & \theta_{24} \\ \theta_{31} & \theta_{32} & \theta_{33} & \theta_{34} \\ \theta_{41} & \theta_{42} & \theta_{43} & \theta_{44} \end{bmatrix} \begin{matrix} \\ \\ \\ \\ \tau \end{matrix}$$

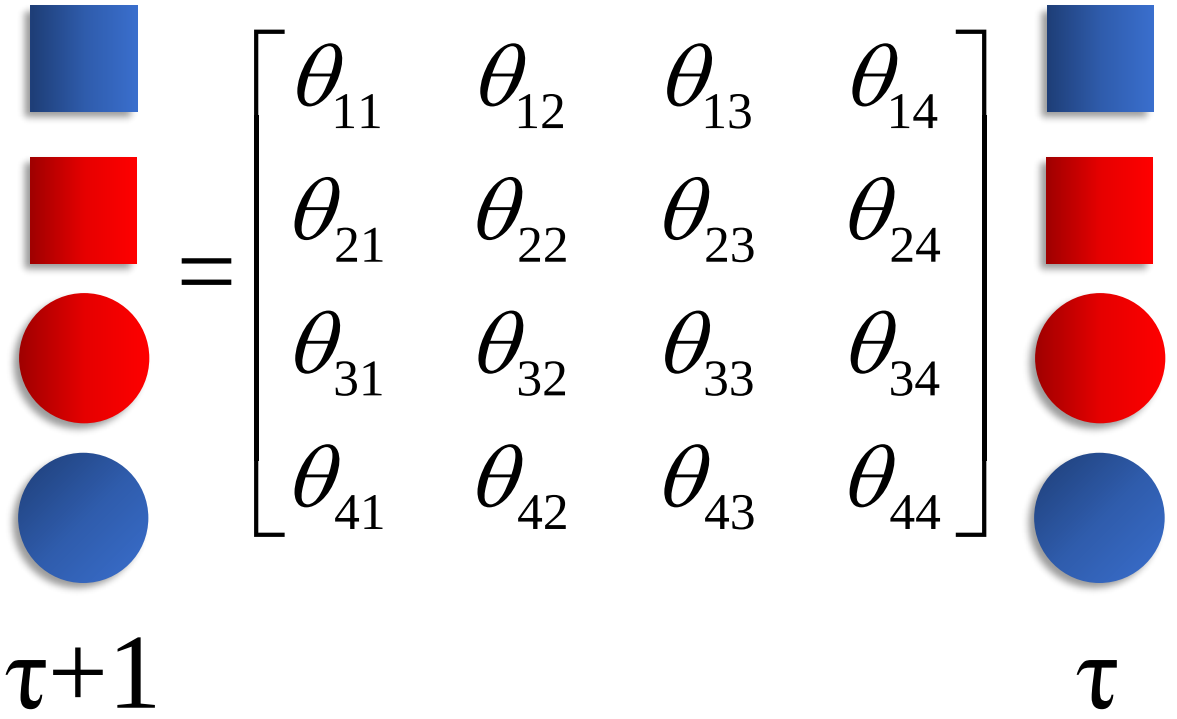
Mean-field modelling



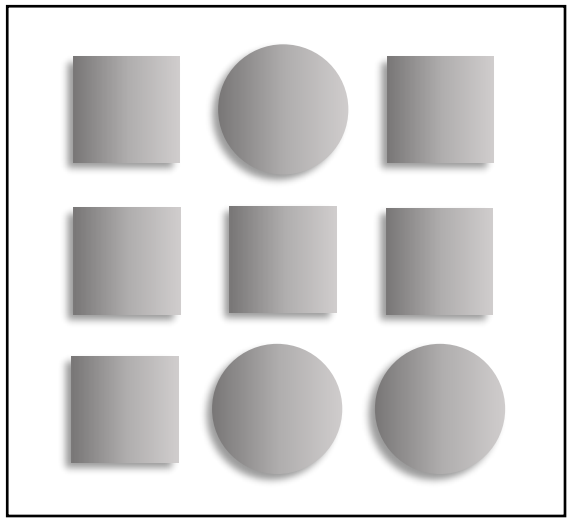
$$\begin{matrix} \\ \\ \\ \\ \tau+1 \end{matrix} = \begin{bmatrix} \theta_{11} & \theta_{12} & \theta_{13} & \theta_{14} \\ \theta_{21} & \theta_{22} & \theta_{23} & \theta_{24} \\ \theta_{31} & \theta_{32} & \theta_{33} & \theta_{34} \\ \theta_{41} & \theta_{42} & \theta_{43} & \theta_{44} \end{bmatrix} \begin{matrix} \\ \\ \\ \\ \tau \end{matrix}$$

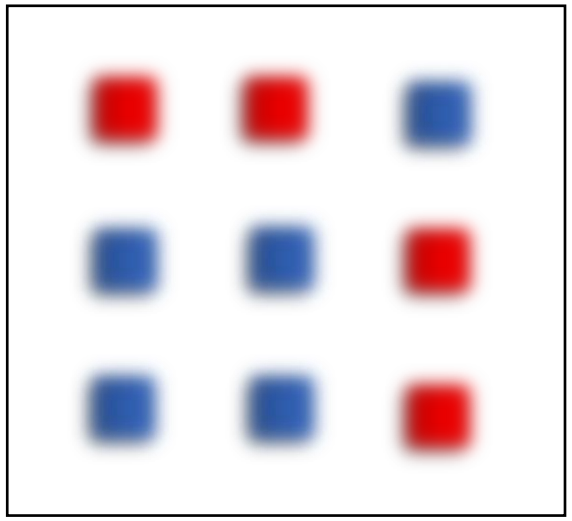
Mean-field modelling





Mean-field modelling





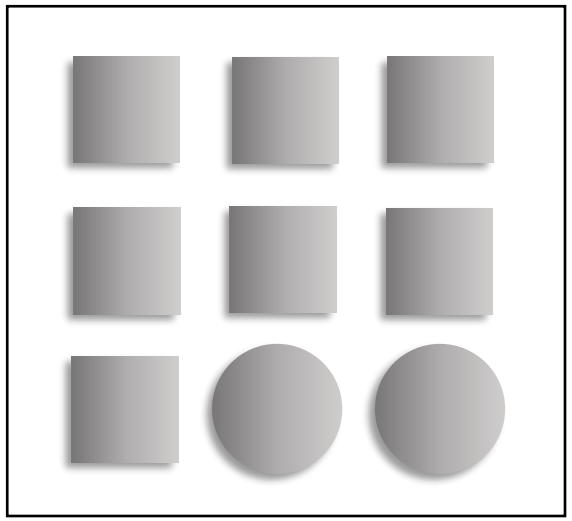
$$\begin{bmatrix} \theta_{11} & \theta_{12} & \theta_{13} & \theta_{14} \\ \theta_{21} & \theta_{22} & \theta_{23} & \theta_{24} \end{bmatrix}^{(1)}$$

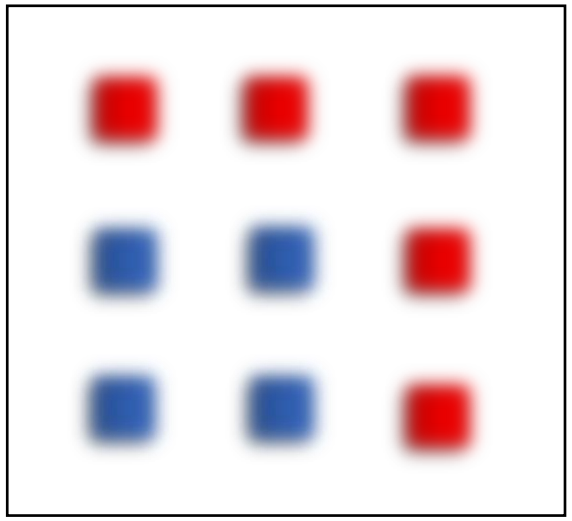
$$\begin{bmatrix} \theta_{11} & \theta_{12} & \theta_{13} & \theta_{14} \\ \theta_{21} & \theta_{22} & \theta_{23} & \theta_{24} \end{bmatrix}^{(2)}$$

$\tau+1$

τ

Mean-field modelling





$$\begin{bmatrix} \theta_{11} & \theta_{12} & \theta_{13} & \theta_{14} \\ \theta_{21} & \theta_{22} & \theta_{23} & \theta_{24} \end{bmatrix}^{(1)}$$

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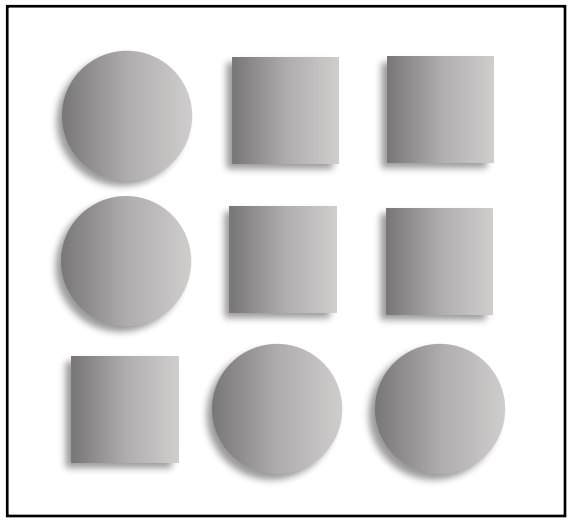
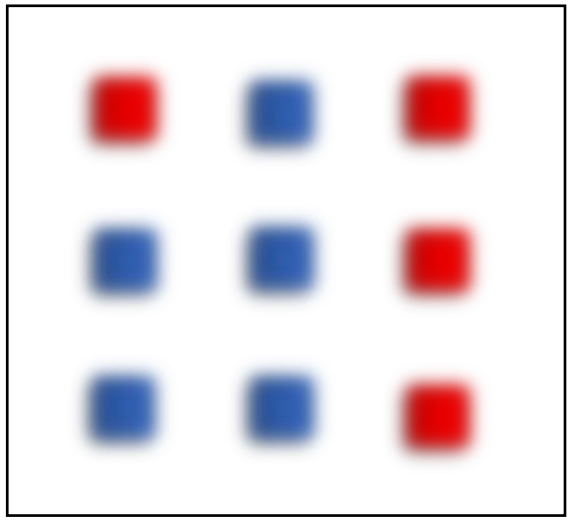
$\tau+1$

τ

Mean-field modelling





$$\begin{bmatrix} \theta_{11} & \theta_{12} & \theta_{13} & \theta_{14} \\ \theta_{21} & \theta_{22} & \theta_{23} & \theta_{24} \end{bmatrix}^{(1)}$$

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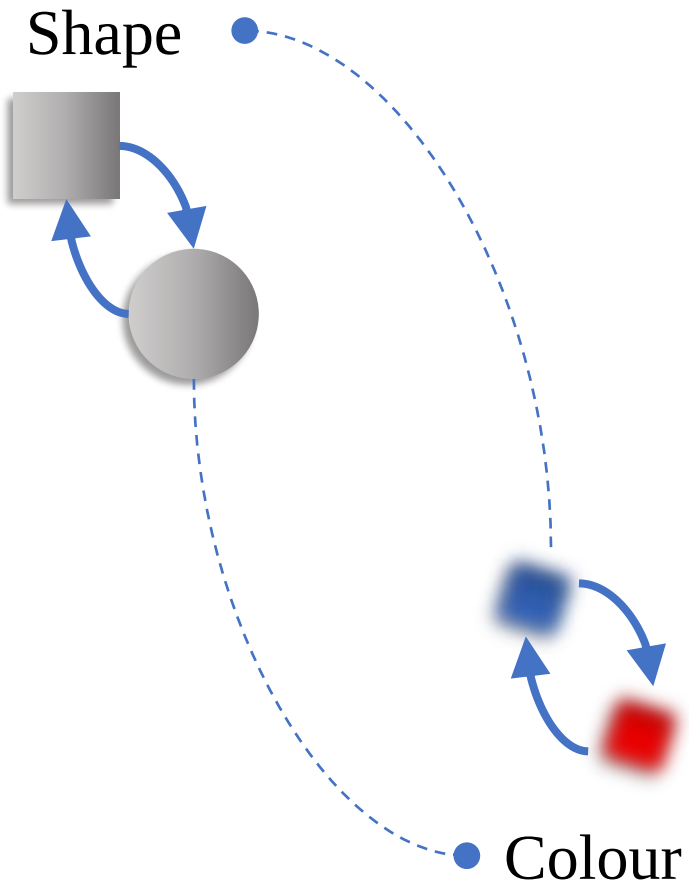
τ

Mean-field modelling



$$\begin{bmatrix} \theta_{11} & \theta_{12} & \theta_{13} & \theta_{14} \\ \theta_{21} & \theta_{22} & \theta_{23} & \theta_{24} \end{bmatrix}^{(1)}$$

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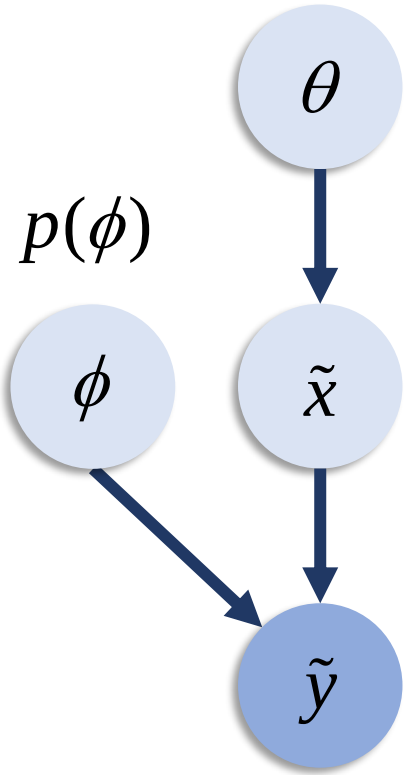
$\tau+1$

τ

Mean-field modelling



$p(\theta)$

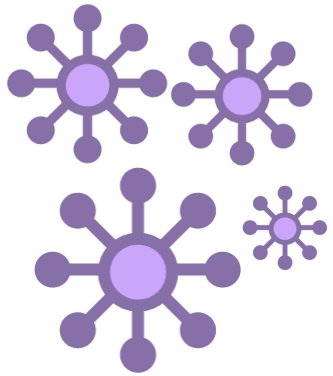
$p(\phi)$

$p(\tilde{x} \mid \theta)$

$\dot{x} = f(x, \theta)$

$p(\tilde{y} \mid \tilde{x}, \phi)$

$$\dot{x}_j^{(i)} = \sum_k \sum_l \sum_m \ldots A_{jklm\ldots}^{(i)}(\theta) x_k^{(1)} x_l^{(2)} x_m^{(3)} \ldots$$



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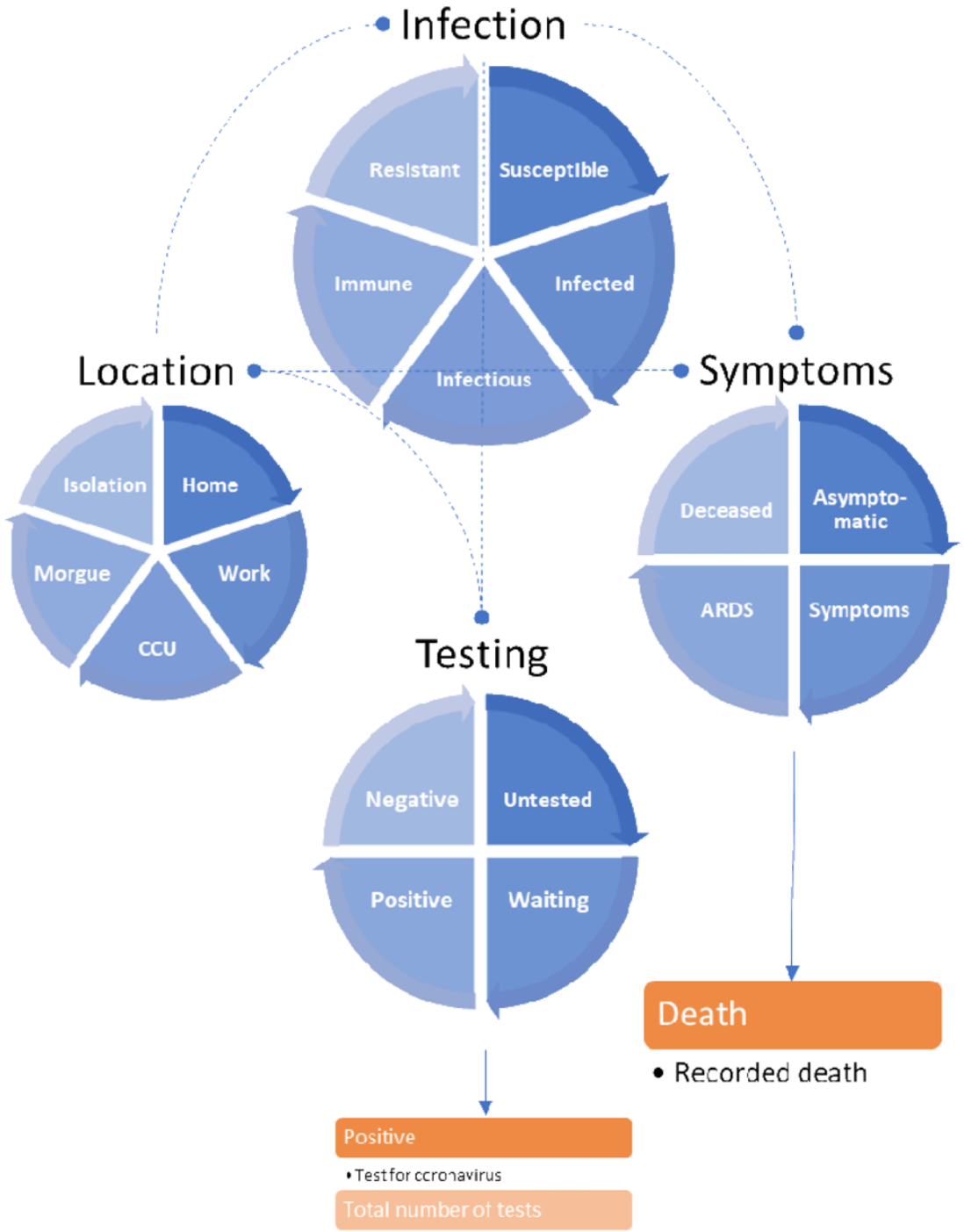
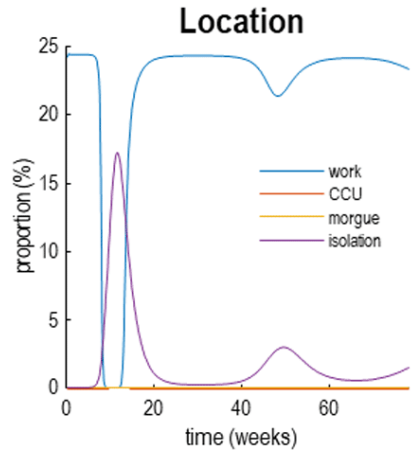
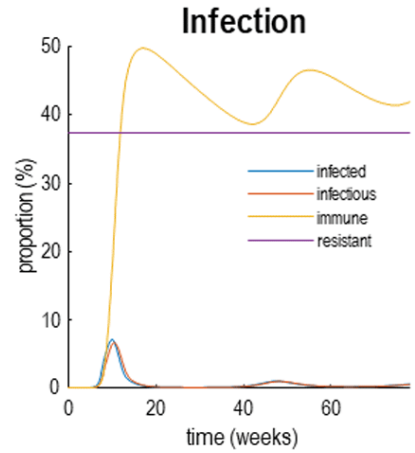
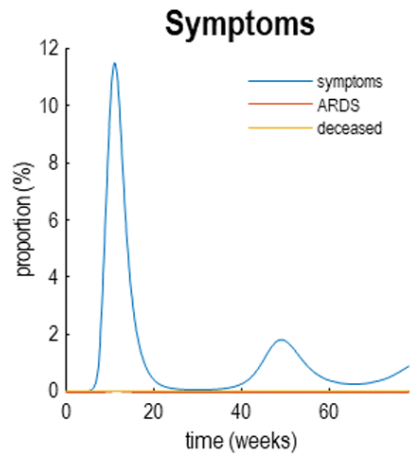
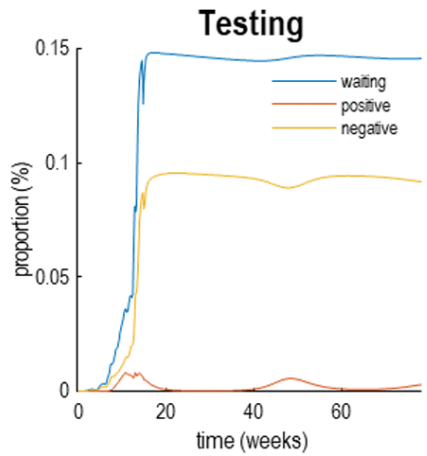

Infection
Resistant
Susceptible
Immune
Infected
Infectious
Location
Isolation
Home
Morgue
Work
CCU
Symptoms
Deceased
Asympto-matic
ARDS
Symptoms
Testing
Negative
Untested
Positive
Waiting
Death
• Recorded death
Positive
• Test for coronavirus
Total number of tests

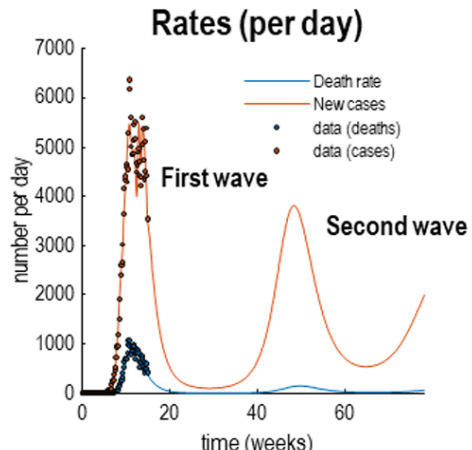

Location
proportion (%)
time (weeks)
work
CCU
morgue
isolation

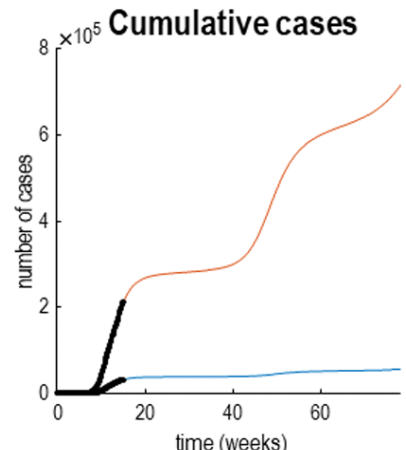

Infection
proportion (%)
time (weeks)
infected
infectious
immune
resistant

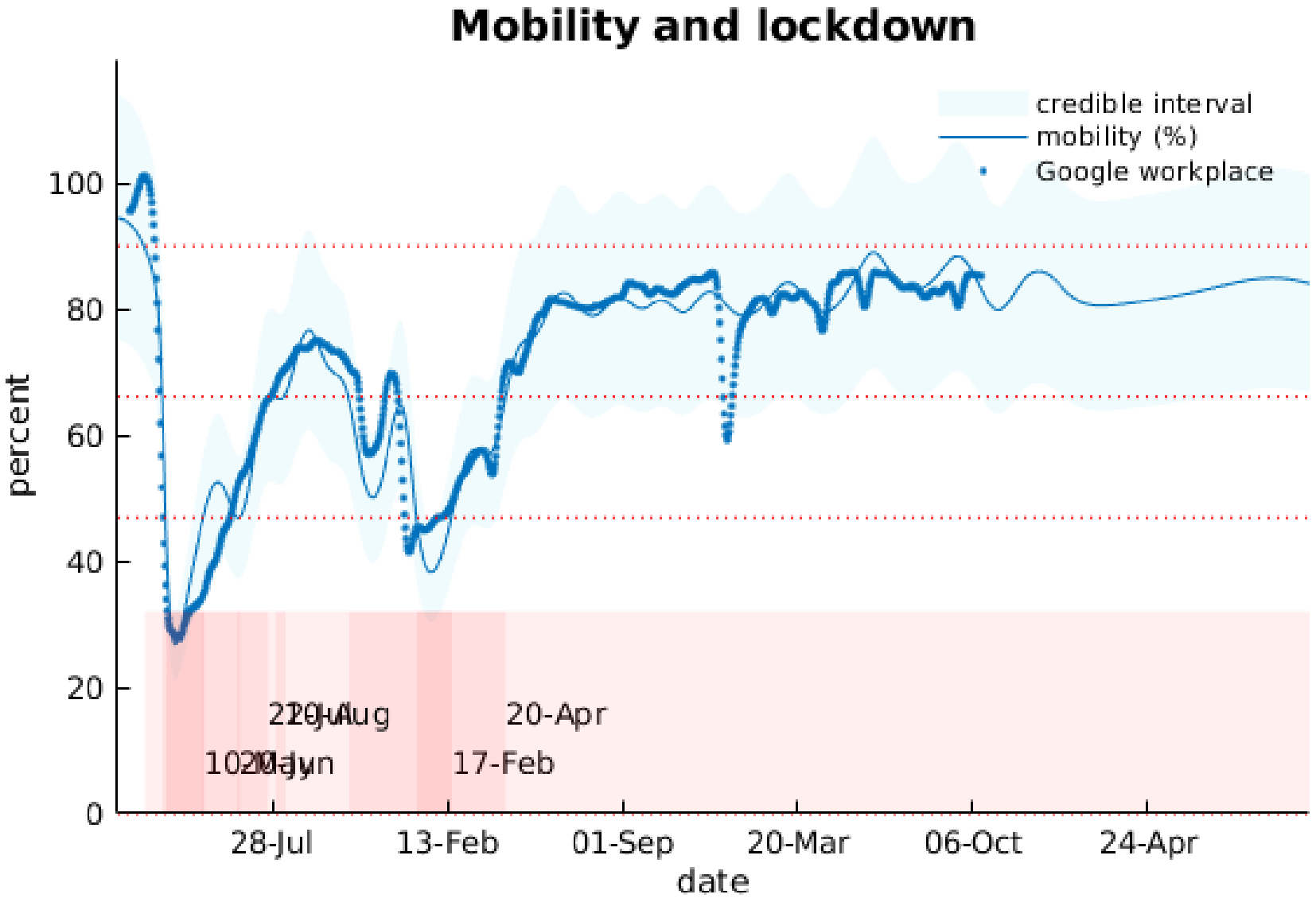
30


Symptoms
proportion (%)
time (weeks)
symptoms
ARDS
deceased

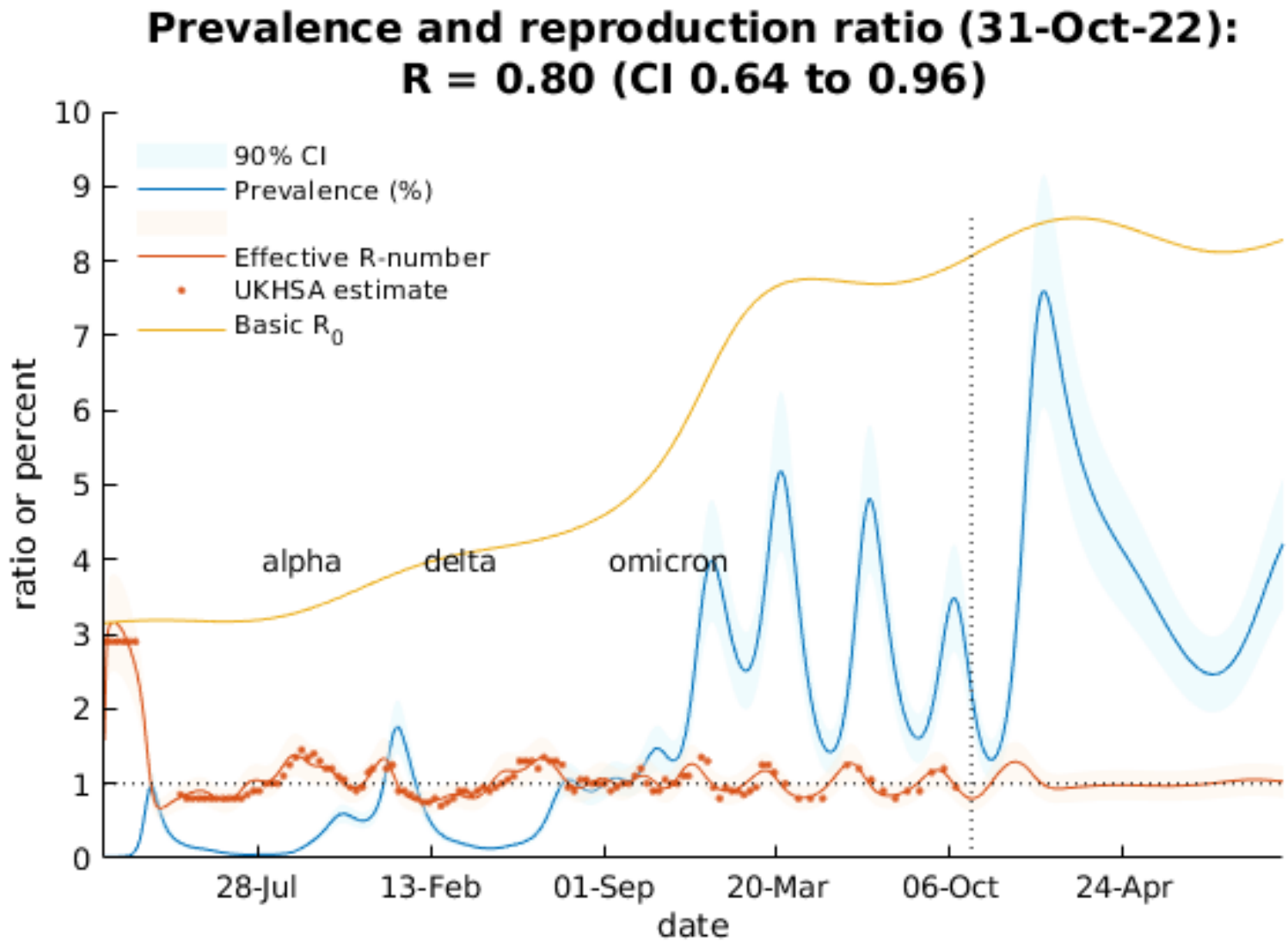

Testing
proportion (%)
time (weeks)
waiting
positive
negative


Rates (per day)
number per day
time (weeks)
Death rate
New cases
data (deaths)
data (cases)
First wave
Second wave


Cumulative cases
number of cases
time (weeks)



https://www.fil.ion.ucl.ac.uk/spm/covid-19/forecasting/



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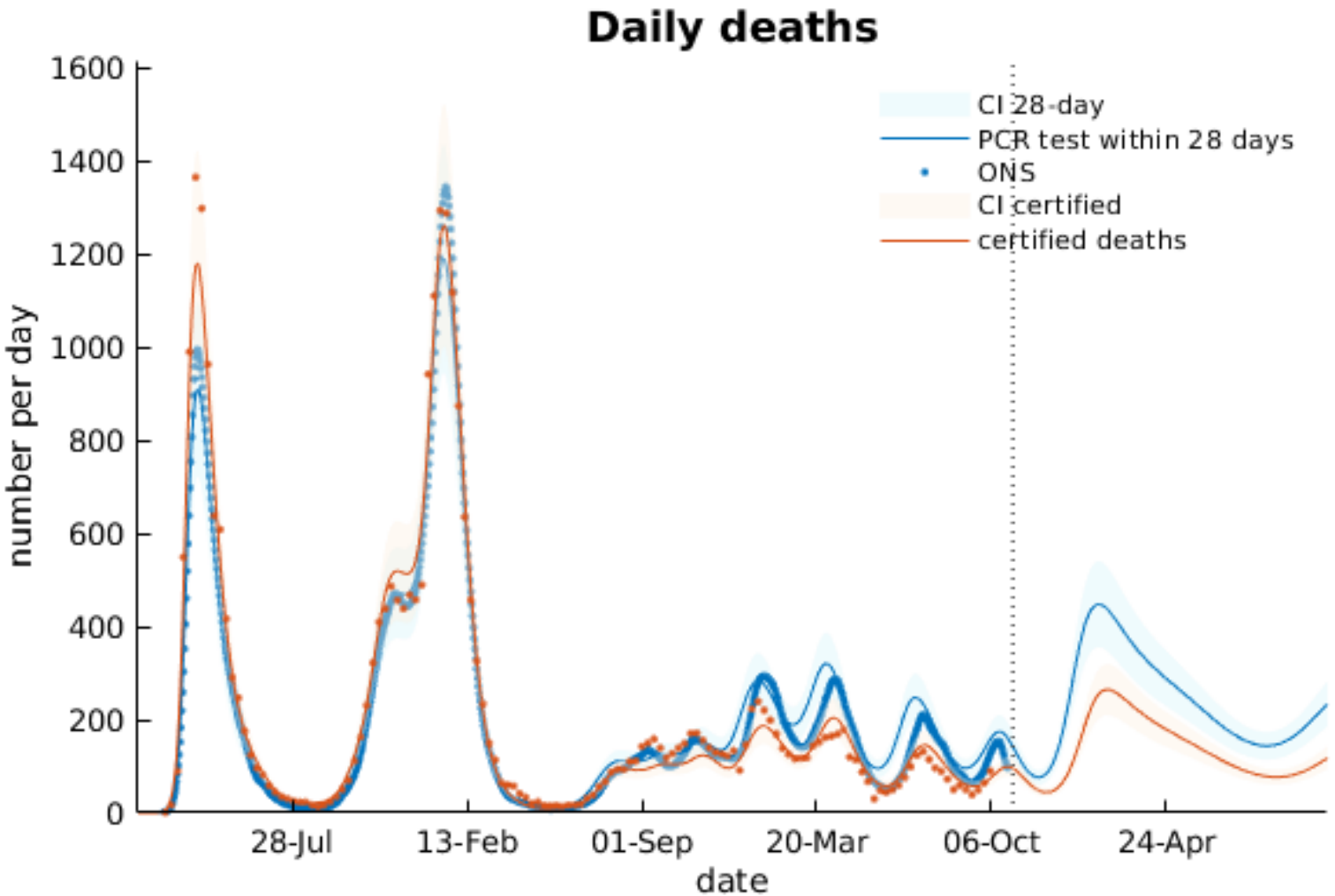
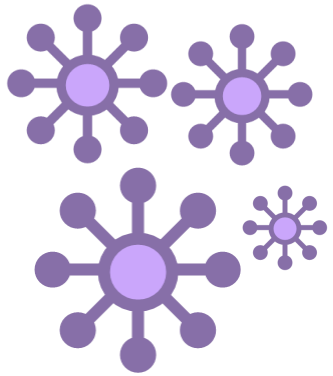


https://www.fil.ion.ucl.ac.uk/spm/covid-19/forecasting/



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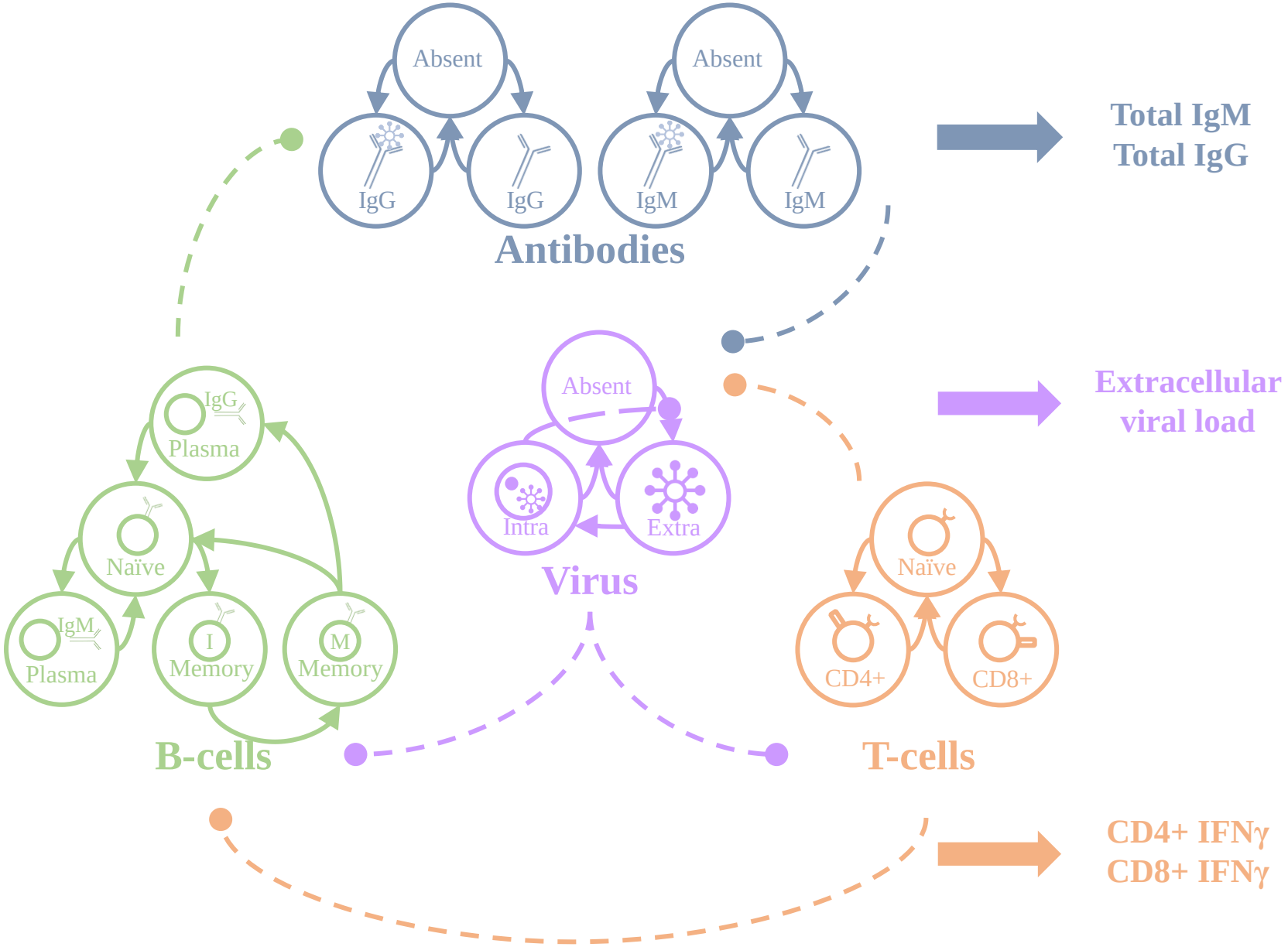
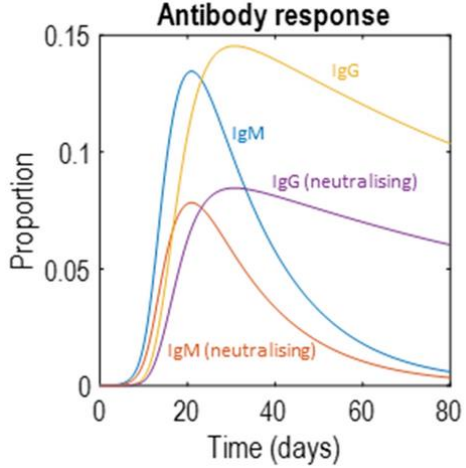
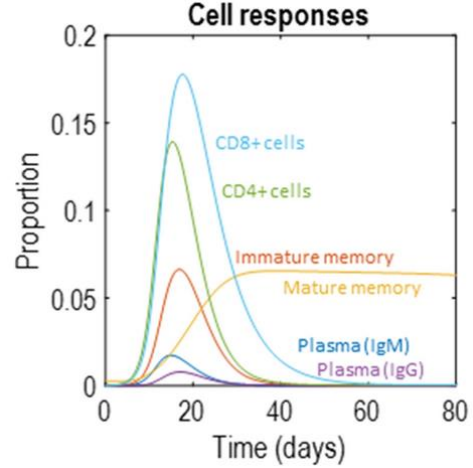
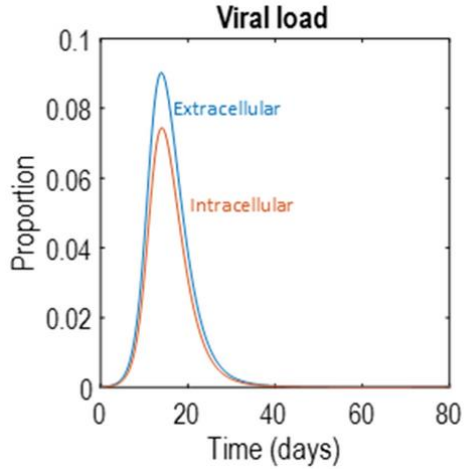
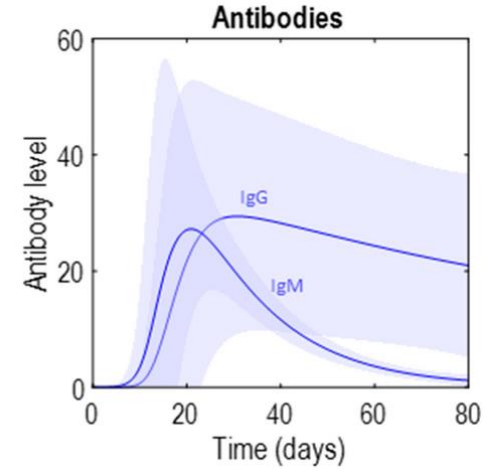
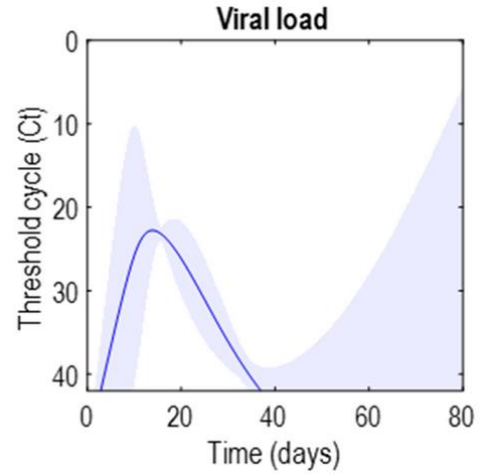

Absent
Absent
IgG
IgG
IgM
IgM
Antibodies
Total IgM
Total IgG
Absent
Intra
Extra
Virus
Extracellular
viral load
IgG
Plasma
Naïve
IgM
Plasma
I
Memory
M
Memory
B-cells
Naïve
CD4+
CD8+
T-cells
CD4+ IFNγ
CD8+ IFNγ

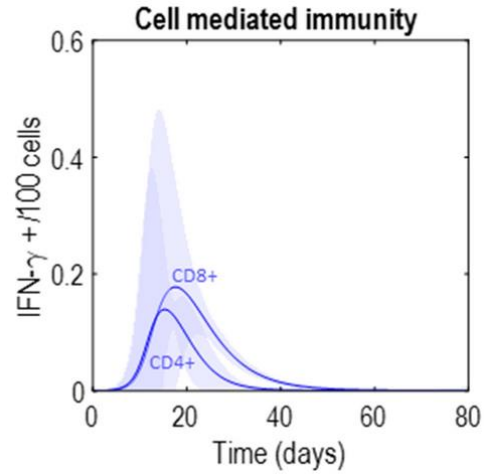

Antibody response
IgG
IgM
IgG (neutralising)
IgM (neutralising)
Proportion
Time (days)


Cell responses
CD8+ cells
CD4+ cells
Immature memory
Mature memory
Plasma (IgM)
Plasma (IgG)
Proportion
Time (days)


Viral load
Extracellular
Intracellular
Proportion
Time (days)

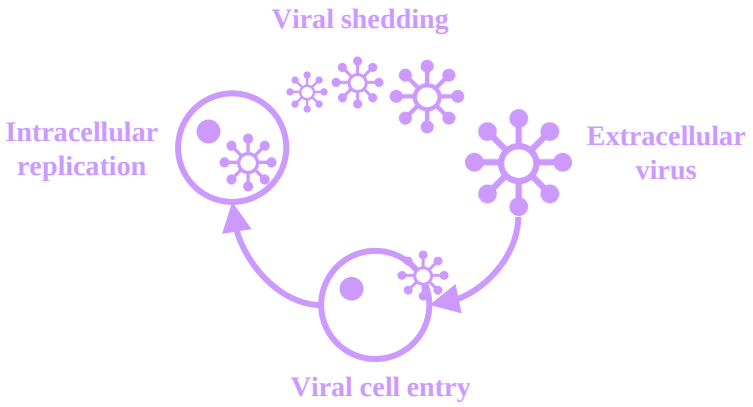

Antibodies
IgG
IgM
Antibody level
Time (days)

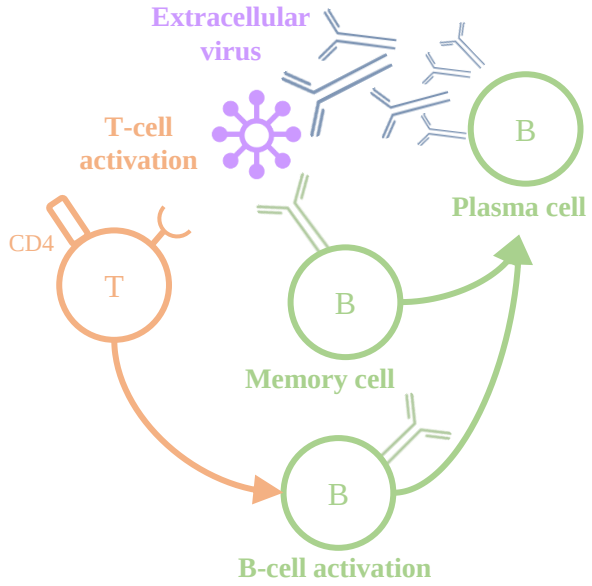

Viral load
Threshold cycle (Ct)
Time (days)


Cell mediated immunity
CD8+
CD4+
IFN-γ +/100 cells
Time (days)

Reduced cell entry

As viruses replicate inside cells, slower viral cell entry (e.g., with host receptor polymorphisms) reduces the effective viral replication rate.



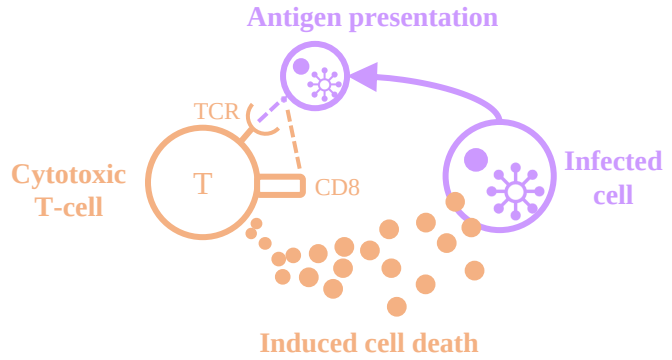


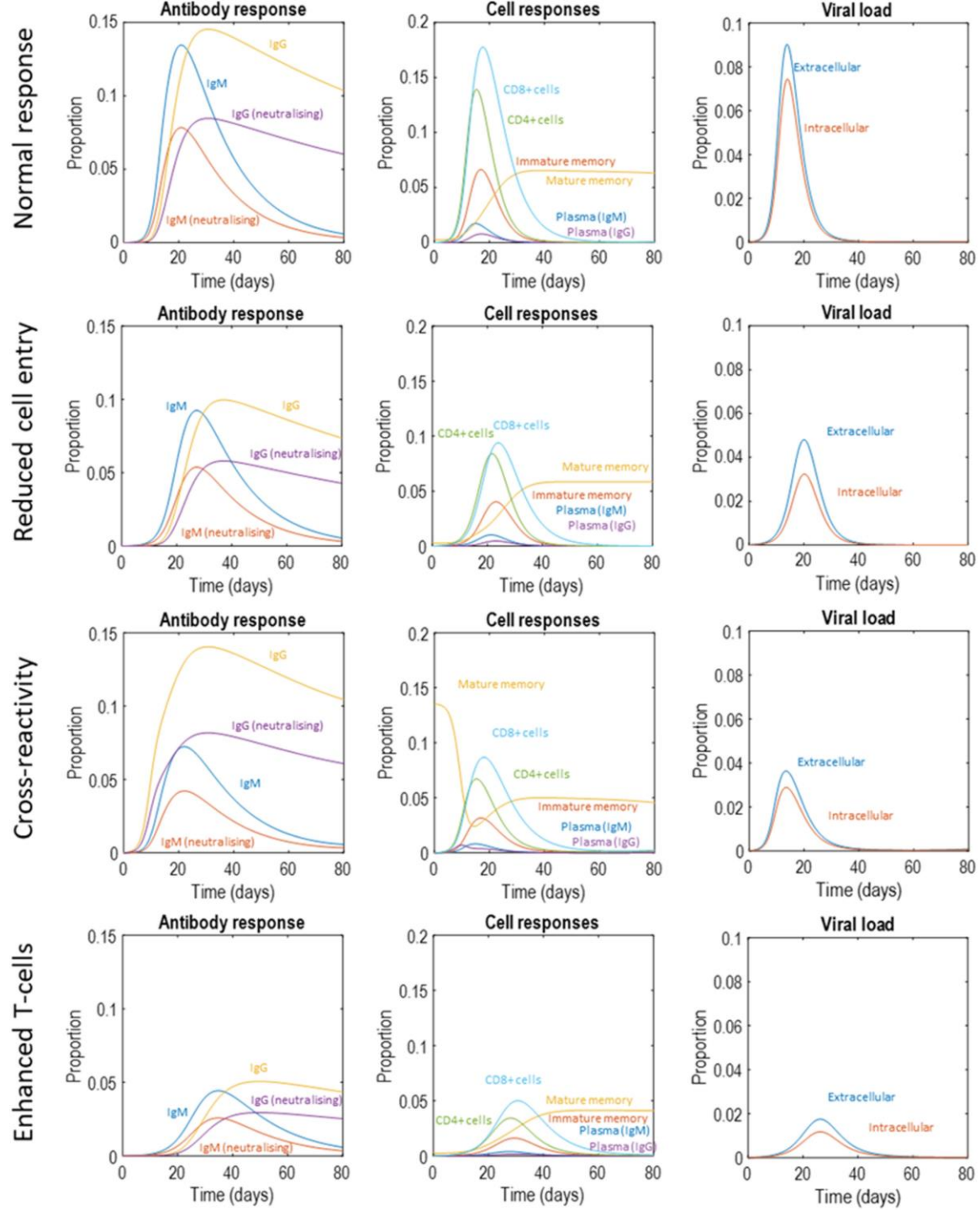
Memory B-cells

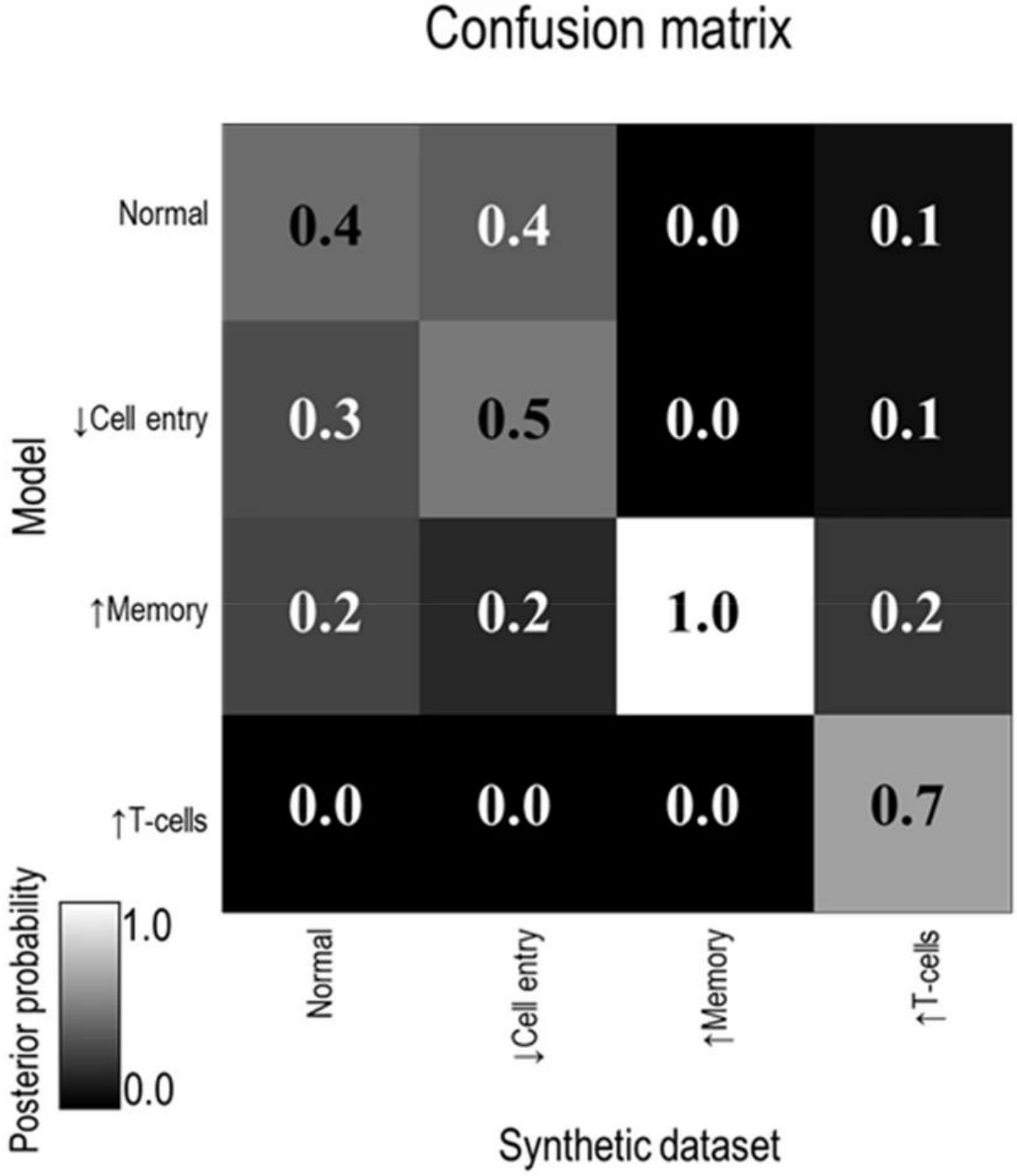
Previous exposure to similar antigens from other viruses could mean a larger memory cell population. These allow for a faster rise in antibody-producing plasma cells.

Enhanced T-cell activity

Increased T-cell mediated killing of infected cells reduces the amount of intracellular virus, with consequences for viral replication and shedding.




Normal response
Reduced cell entry
Cross-reactivity
Enhanced T-cells
Antibody response
Cell responses
Viral load
Proportion
Time (days)
IgG
IgM
IgG (neutralising)
IgM (neutralising)
CD8+cells
CD4+cells
Immature memory
Mature memory
Plasma (IgM)
Plasma (IgG)
Extracellular
Intracellular


Confusion matrix
Normal
↓Cell entry
↑Memory
↑T-cells
Model
0.4
0.4
0.0
0.1
0.3
0.5
0.0
0.1
0.2
0.2
1.0
0.2
0.0
0.0
0.0
0.7
Posterior probability
1.0
0.0
Normal
↓Cell entry
↑Memory
↑T-cells
Synthetic dataset

Resources

Wellcome Open Research

Wellcome Open Research 2021, 5:103 Last updated: 10 JUN 2

Check for updat

METHOD ARTICLE

REVISED Second waves, social distancing, and the spread of COVID-19 across the USA [version 3; peer review: 2 approved]

Previously titled: Second waves, social distancing, and the spread of COVID-19 across America

Karl J. Friston[1], Thomas Parr[1], Peter Zeidman[1], Adeel Razi[1,2], Guillaume Flandin[1], Jean Daunizeau[3], Oliver J. Hulme[4,5], Alexander J. Billig[6], Vladimir Litvak[1], Catherine J. Price[1], Rosalyn J. Moran[7], Christian Lambert[1]

Wellcome Open Research

Wellcome Open Research 2020, 5:89 Last updated: 10 JUN 2022

Check for updates

METHOD ARTICLE

REVISED Dynamic causal modelling of COVID-19 [version 2; peer review: 2 approved]

Karl J. Friston[1], Thomas Parr[1], Peter Zeidman[1], Adeel Razi[1,2], Guillaume Flandin[1], Jean Daunizeau[3], Ollie J. Hulme[4,5], Alexander J. Billig[6], Vladimir Litvak[1], Rosalyn I. Moran[7], Cathy I. Price[1], Christian Lambert[1]

Wellcome Open Research

Wellcome Open Research 2021, 5:144 Last updated: 10 JUN 2022

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METHOD ARTICLE

REVISED Testing and tracking in the UK: A dynamic causal modelling study [version 2; peer review: 1 approved, 1 approved with reservations]

Karl J. Friston[1], Thomas Parr[1], Peter Zeidman[1], Adeel Razi[1,2], Guillaume Flandin[1], Jean Daunizeau[3], Oliver J. Hulme[4,5], Alexander J. Billig[6], Vladimir Litvak[1], Cathy J. Price[1], Rosalyn J. Moran[7], Christian Lambert[1]

Wellcome Open Research

Wellcome Open Research 2020, 5:204 Last updated: 10 JUN 202

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METHOD ARTICLE

REVISED Effective immunity and second waves: a dynamic causal modelling study [version 2; peer review: 2 approved]

Karl J. Friston[1], Thomas Parr[1], Peter Zeidman[1], Adeel Razi[1,2], Guillaume Flandin[1], Jean Daunizeau[3], Oliver J. Hulme[4,5], Alexander J. Billig[6], Vladimir Litvak[1], Cathy J. Price[1], Rosalyn J. Moran[7], Anthony Costello[8], Deenan Pillay[9], Christian Lambert[1]

scientific reports

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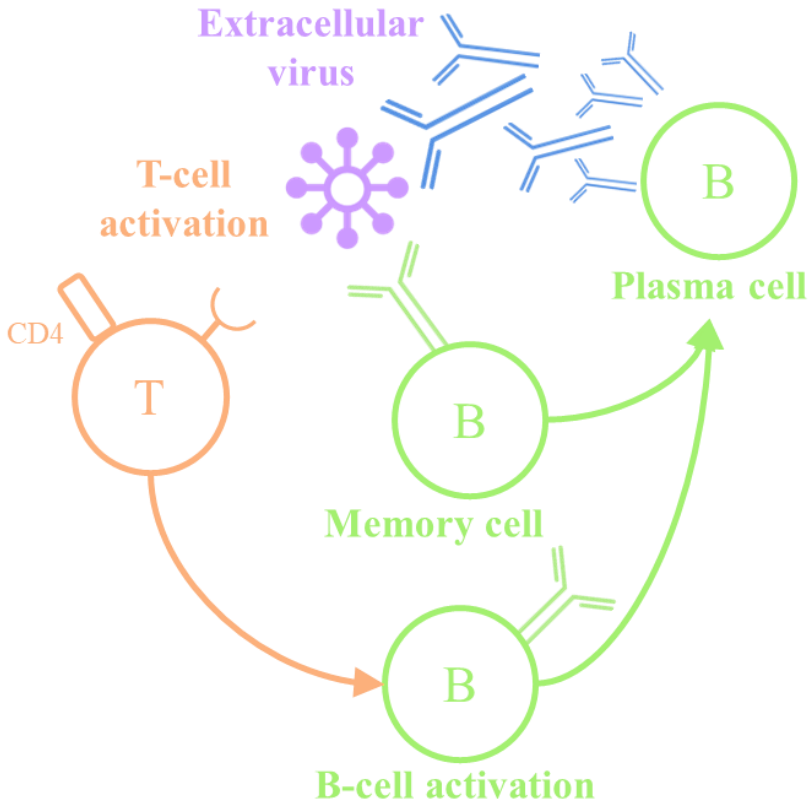
OPEN

Dynamic causal modelling of immune heterogeneity

Thomas Parr[1]✉, Anjali Bhat[1], Peter Zeidman[1], Aimee Goel[2], Alexander J. Billig[3], Rosalyn Moran[4] & Karl J. Friston[1]

https://www.fil.ion.ucl.ac.uk/spm/covid-19/



Thanks

Adeel Razi
Aimee Goel
Alexander Billig
Anjali Bhat
Cathy Price
Christian Lambert
Guillaume Flandin
Jean Daunizeau
Karl Friston
Oliver Hulme
Peter Zeidman
Rosalyn Moran
Vladimir Litvak
And many others