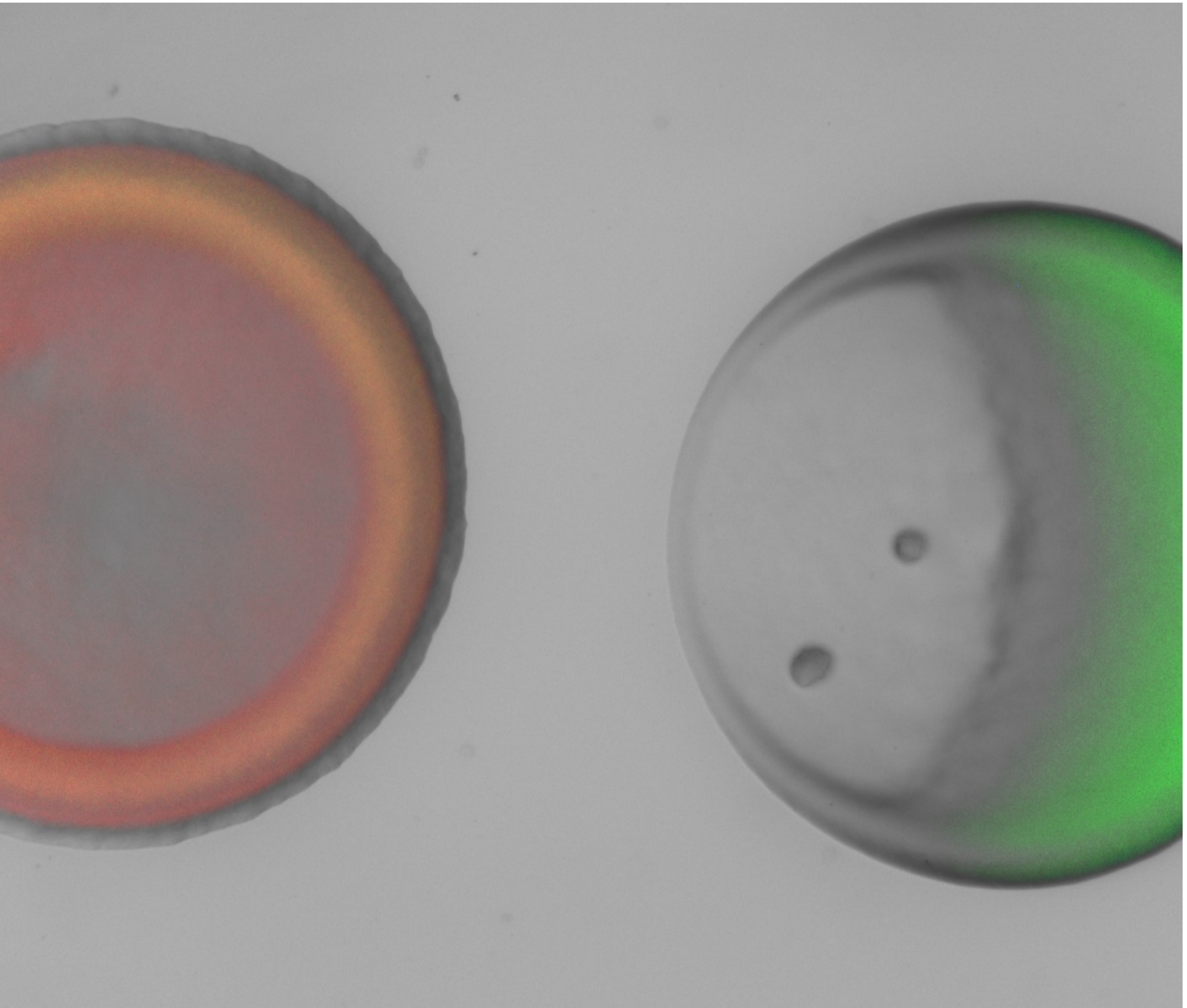

Computational design of synthetic microbial communities

Alex J H Fedorec
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University College London
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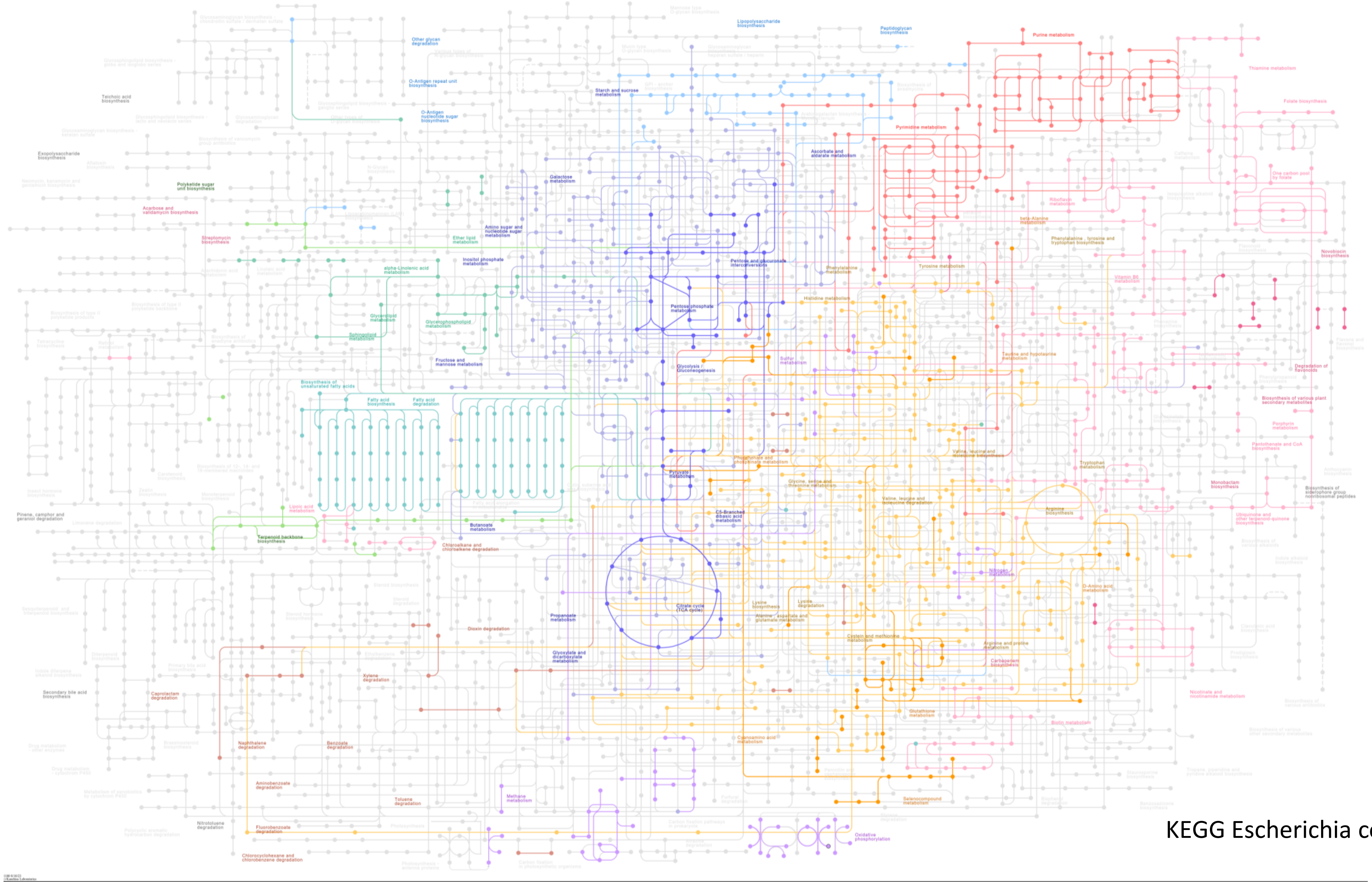
Why am I interested in microbial communities?

Sakurako Gibo

Microbes are (nearly) everywhere

Puri Lopez-Garcia

That makes them a great tool for engineering



KEGG Escherichia coli K-12 MG1655

plugandplaytechcenter.com

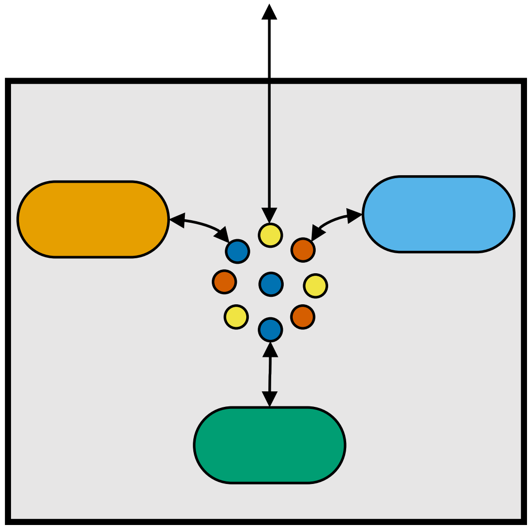
But it means there will be competition wherever we go


onetravel.com
Even in a sterile environment, microbes have limitations

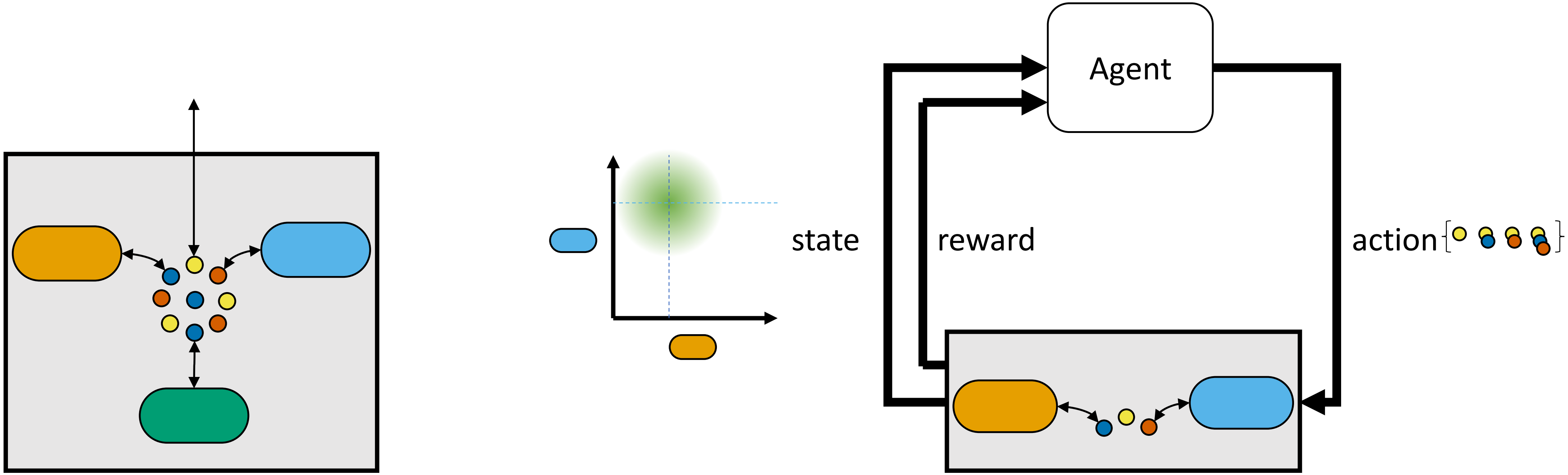
Therefore, creating synthetic communities *might* be useful

Synthetic microbial ecology

Cell-environment interactions

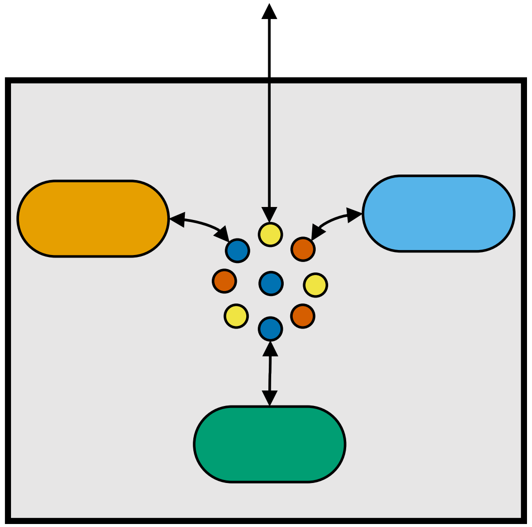


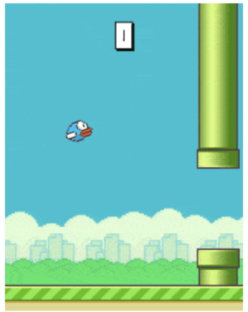
Synthetic microbial ecology – RL control

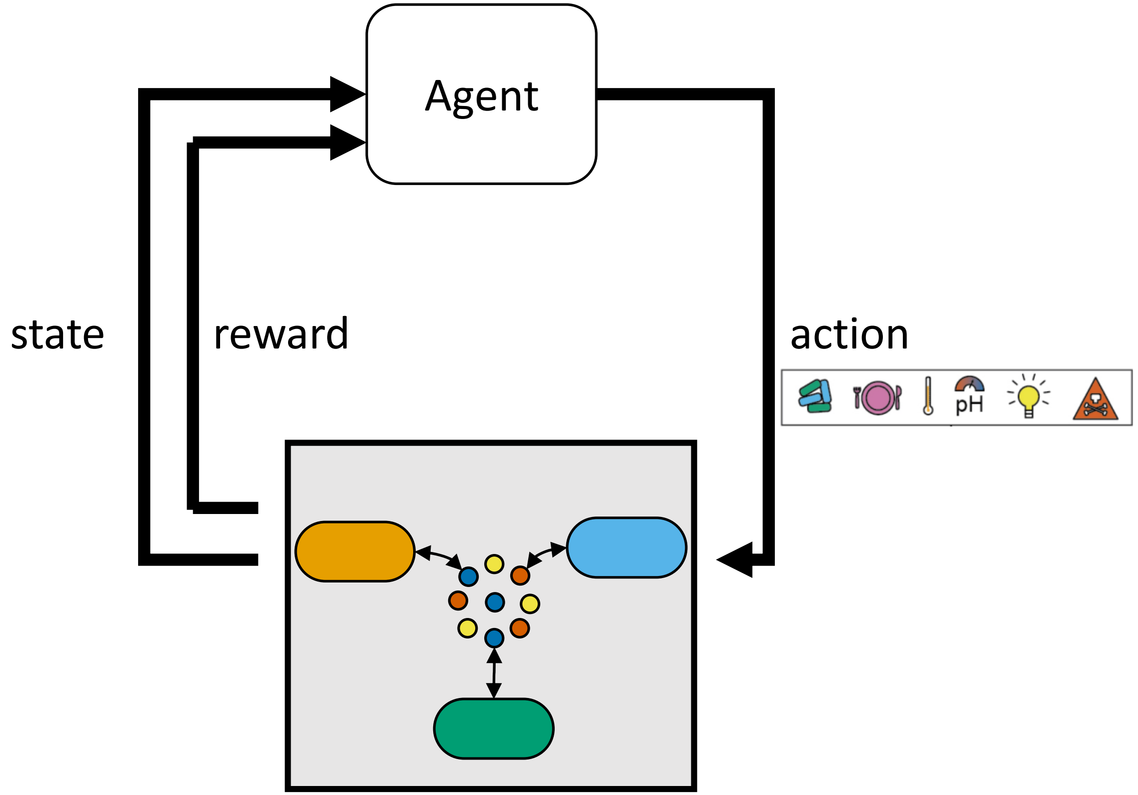


Treloar et al., PLOS Comp Biol, 2020

Synthetic microbial ecology – RL control

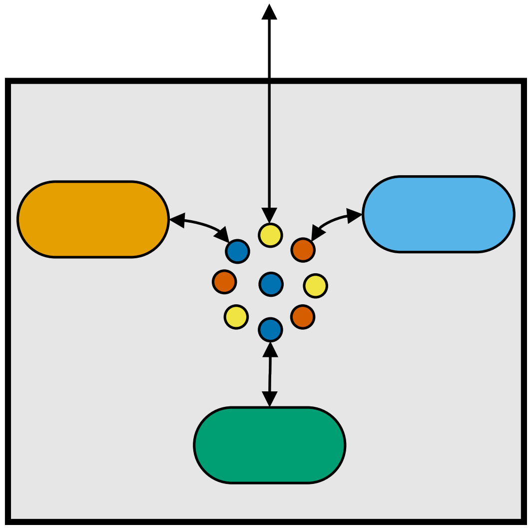




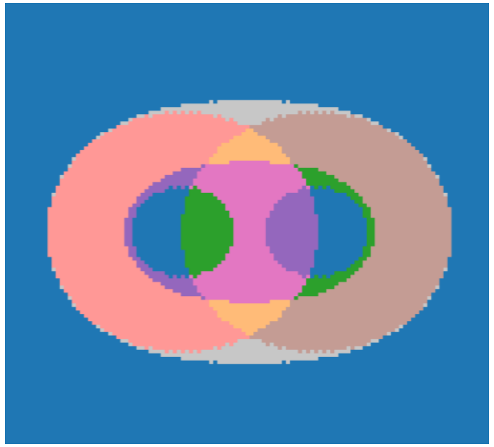


Synthetic microbial ecology

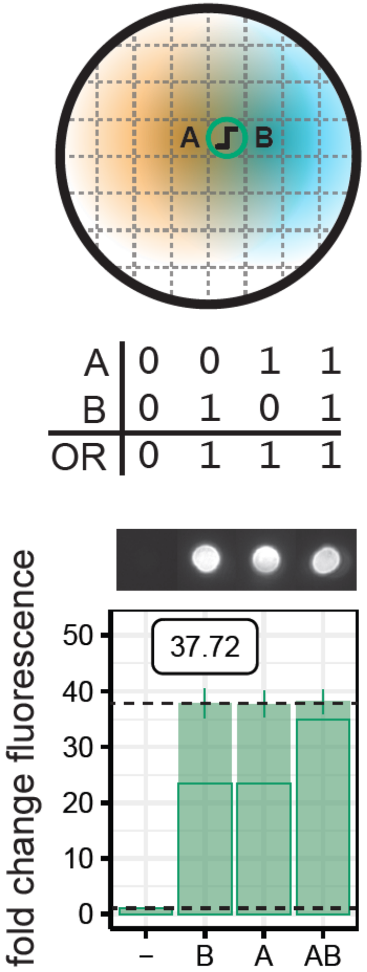
Cell-environment interactions



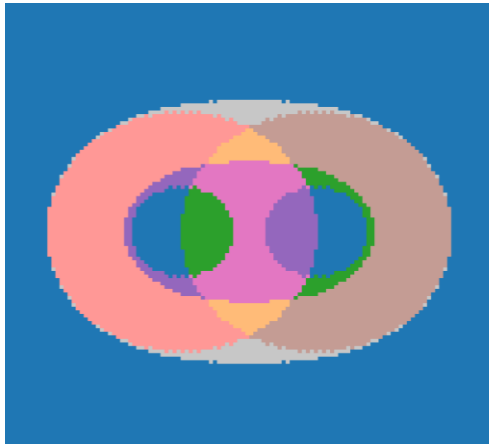
Spatial organisation



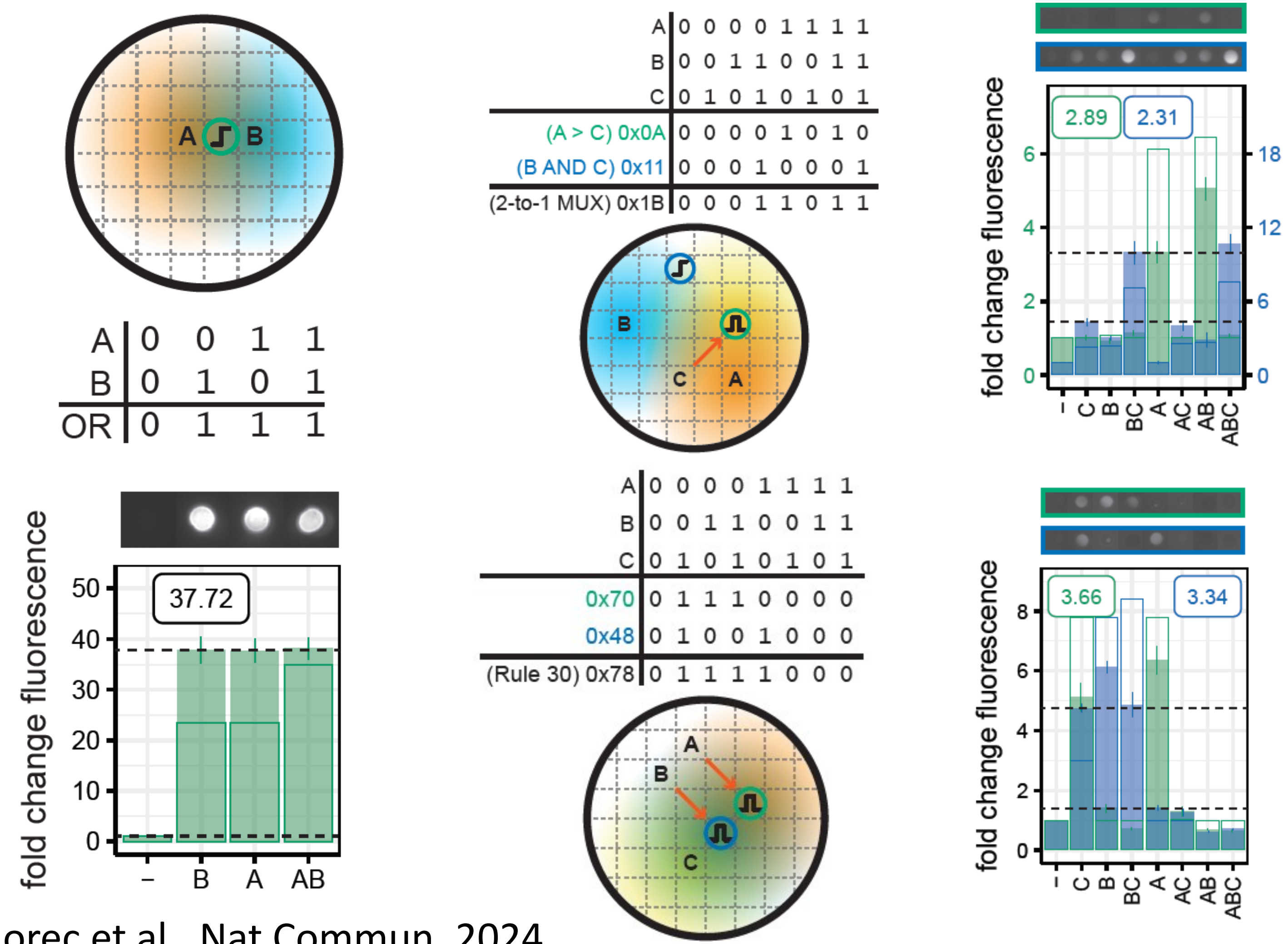
Synthetic microbial ecology – computational biofilms

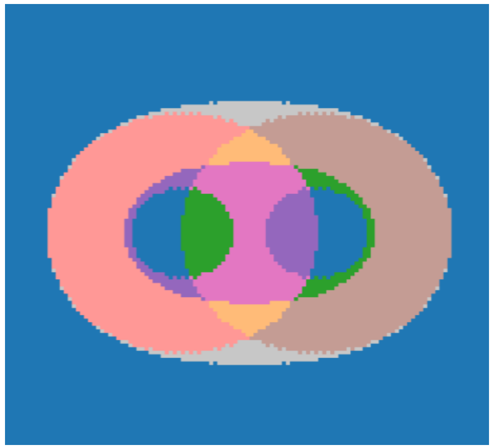


Fedorec et al., Nat Commun, 2024



Synthetic microbial ecology – computational biofilms

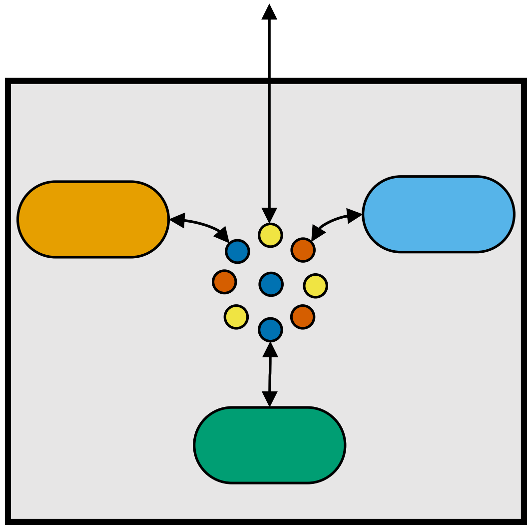




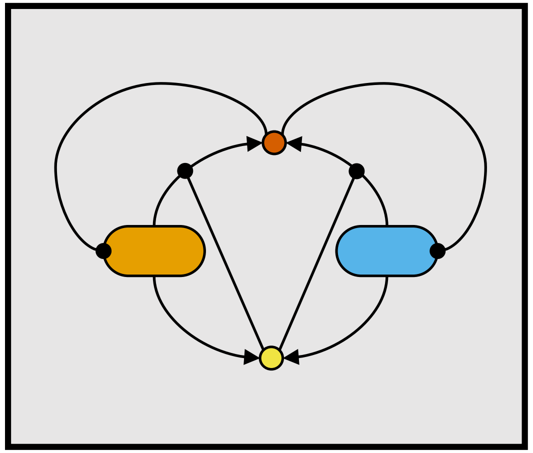
Fedorec et al., Nat Commun, 2024

Synthetic microbial ecology

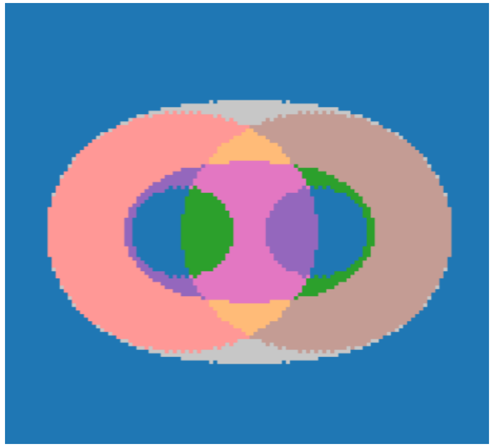
Cell-environment interactions



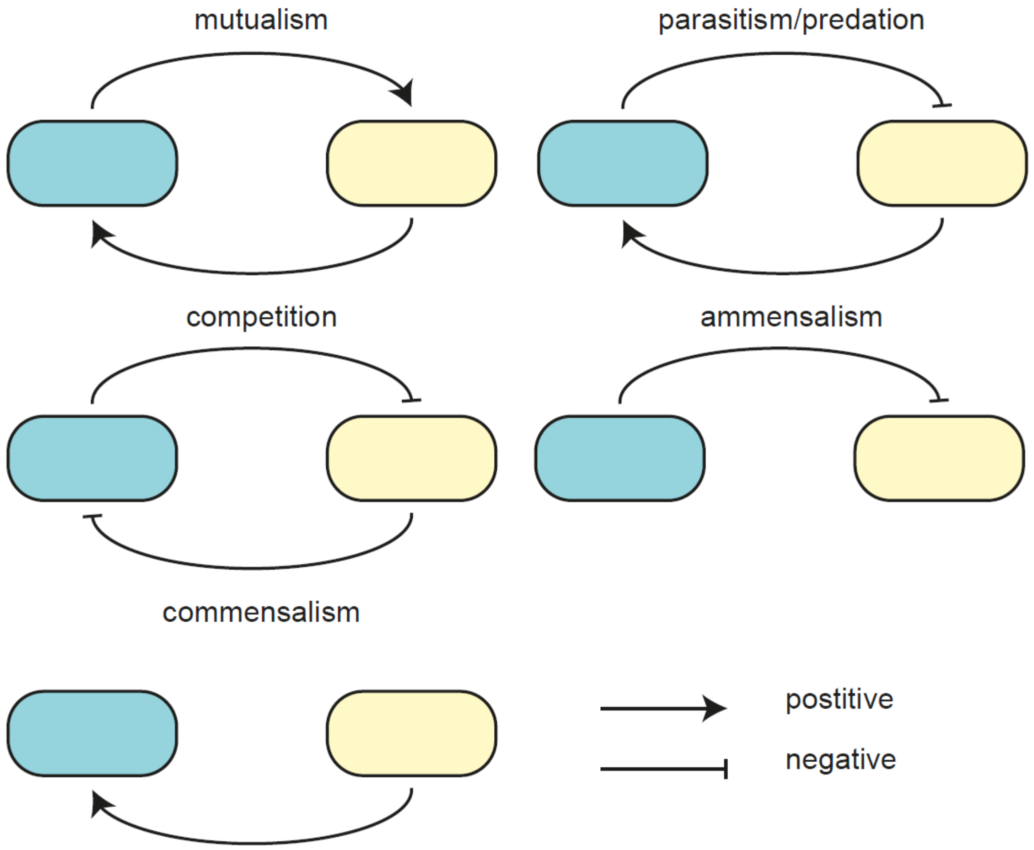
Cell-cell interactions



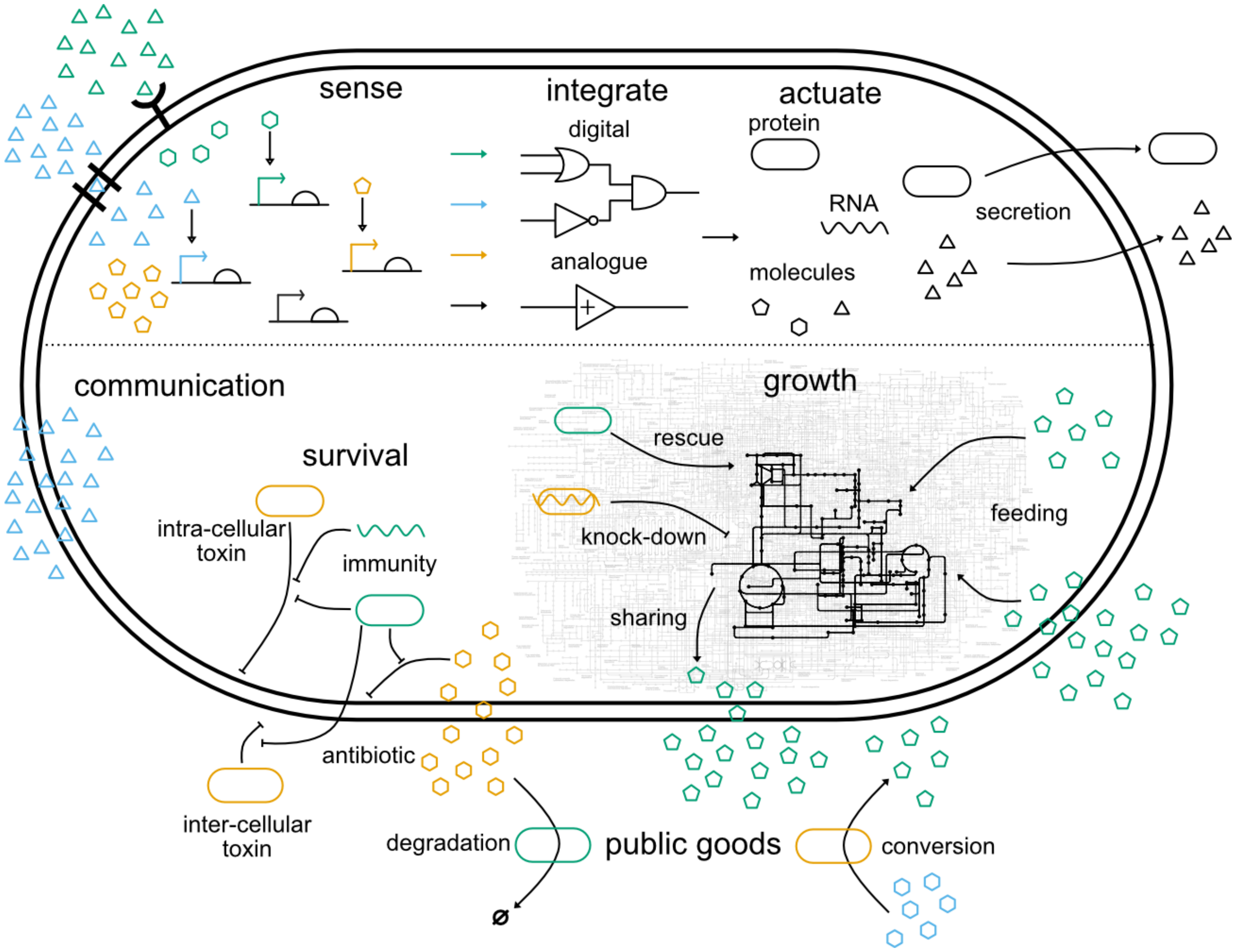
Spatial organisation/ computation



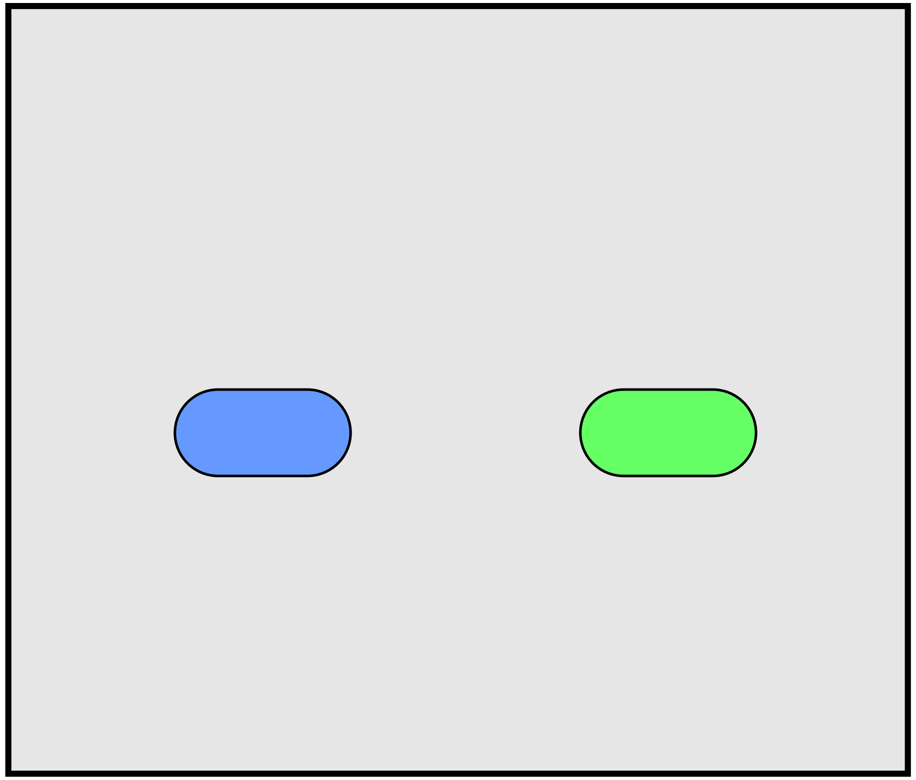
Interactions shape communities



Synthetic biology allows us to engineer interactions



We can build new communities by engineering interactions



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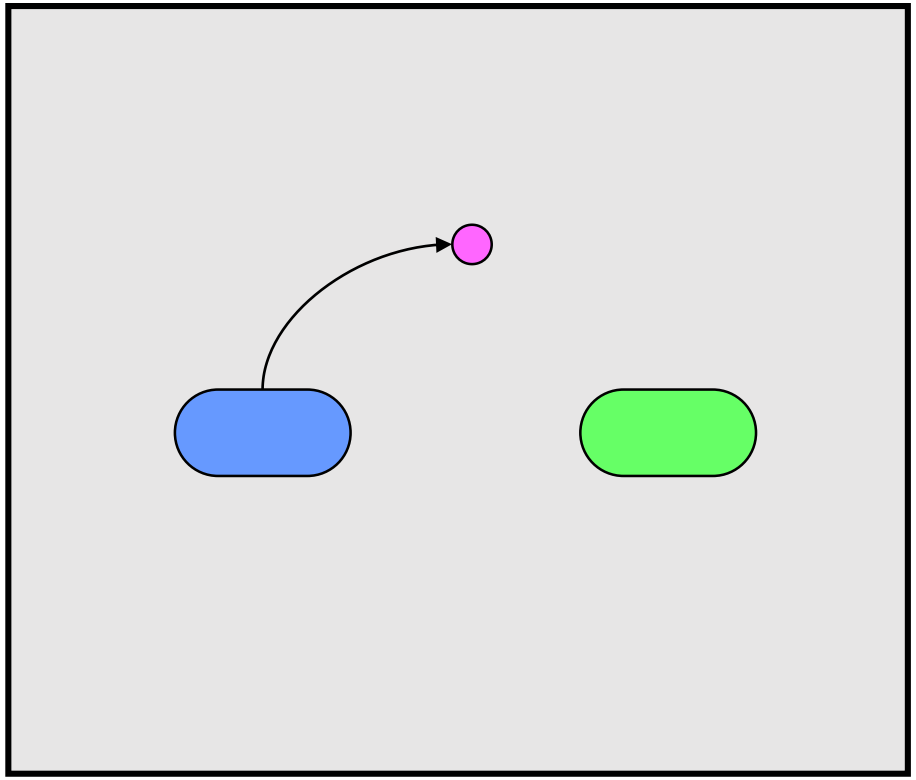

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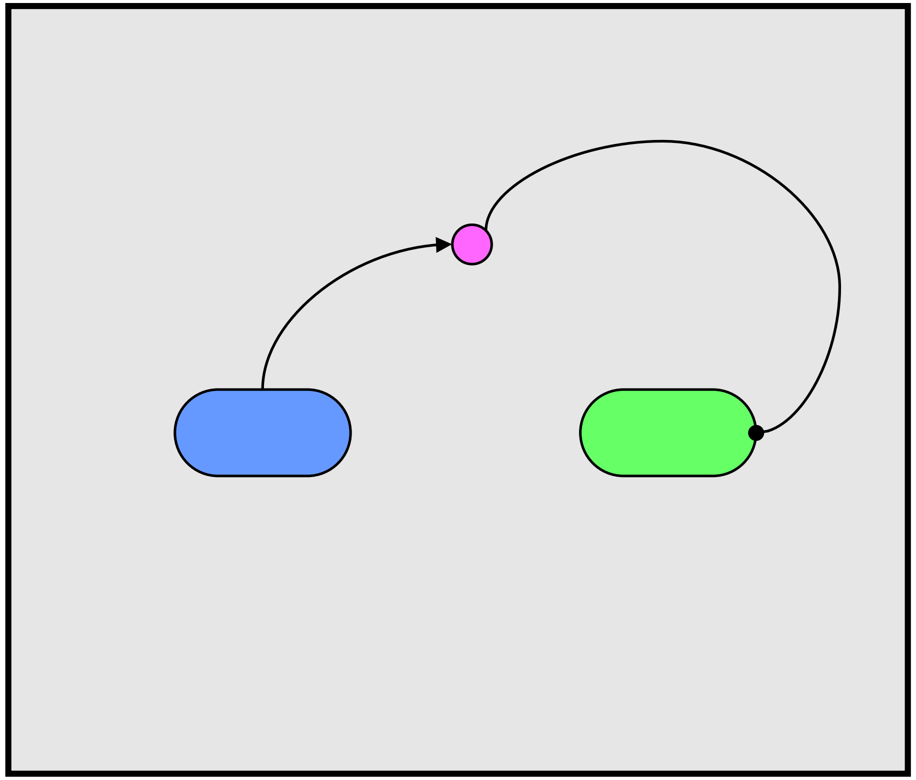

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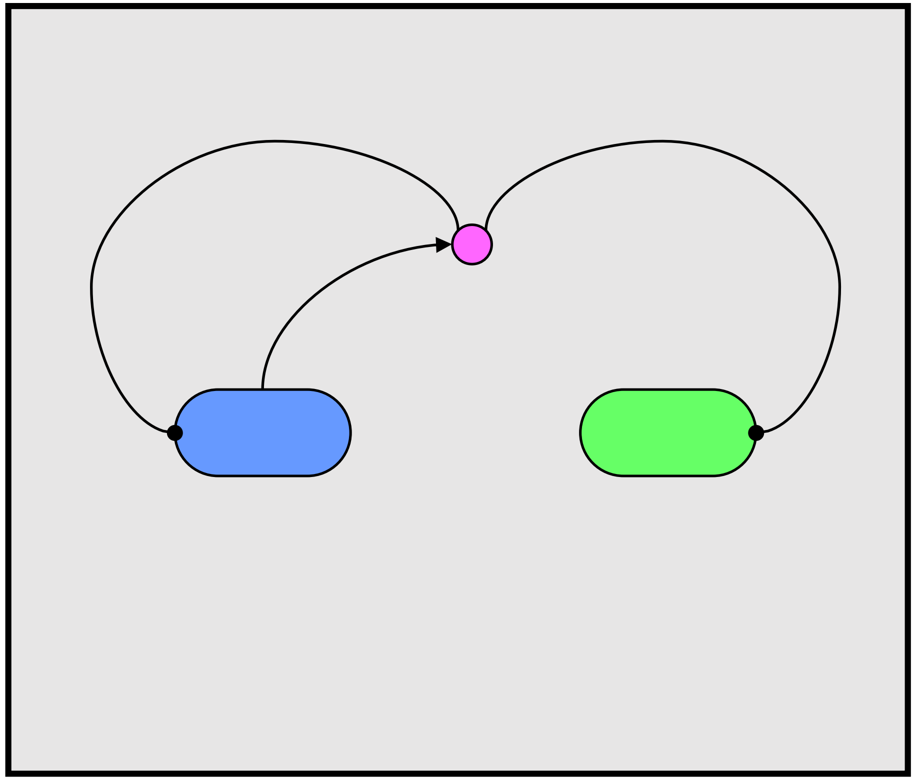

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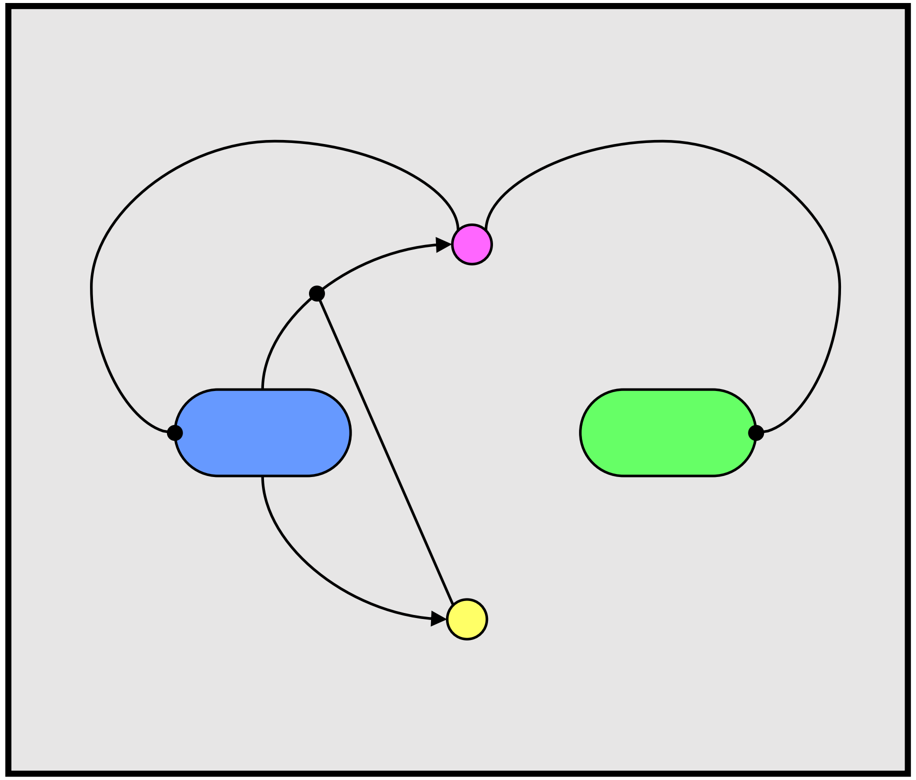

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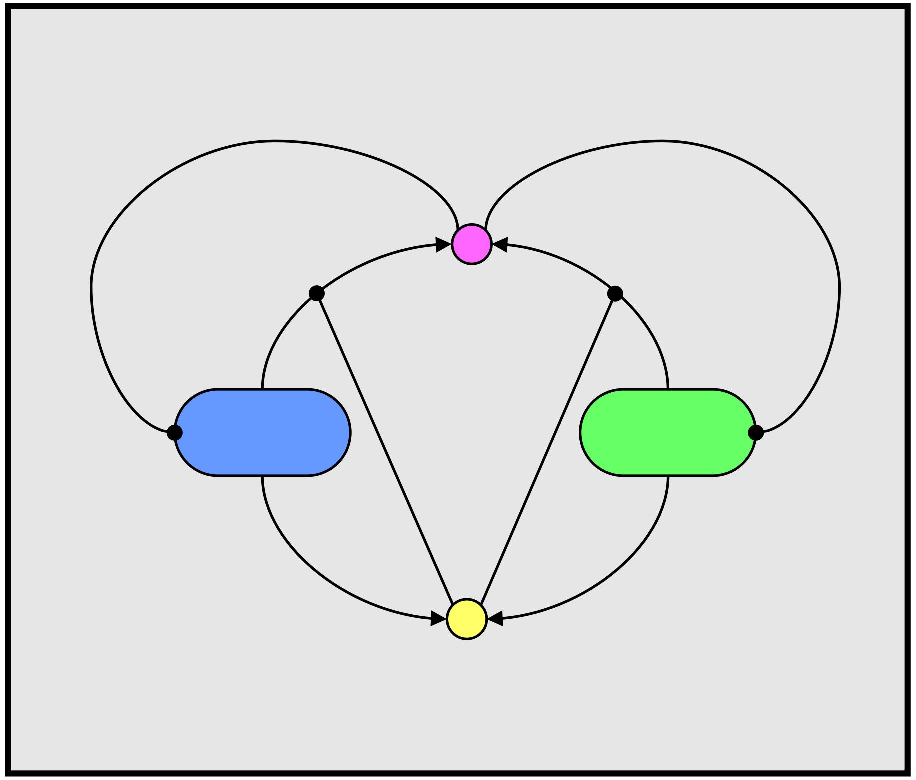
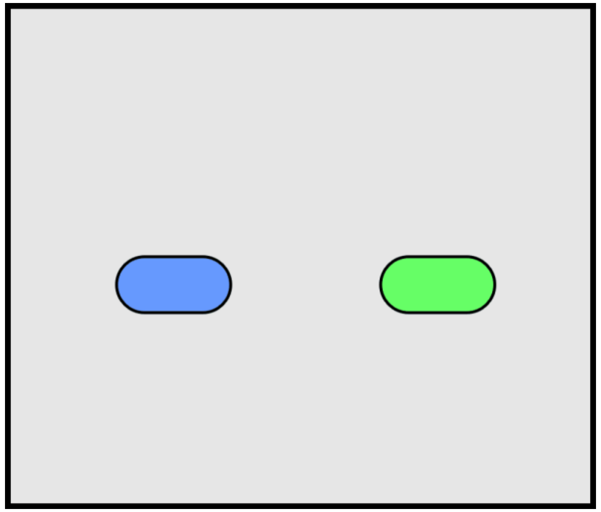


How do we know what to build?

For: 2 strains
1 extra-cellular molecule
1 signal molecule

15 unique topologies



How do we know what to build?

For: 2 strains
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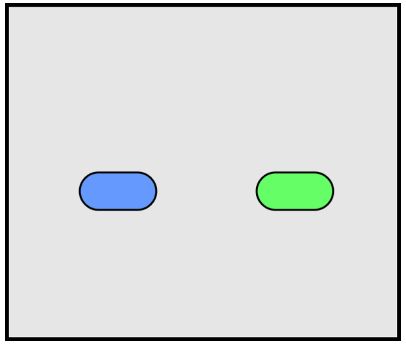
15 unique topologies

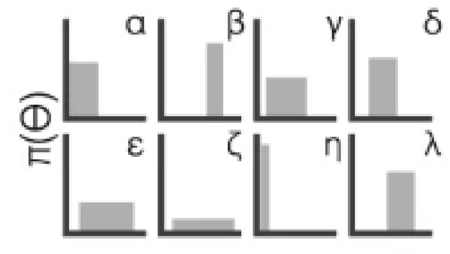
$$
\begin{aligned}
\frac{dX_i}{dt} &= \mu_i X_i - \omega_i X_i - D X_i \\
\frac{dA_j}{dt} &= D(A_{j_0} - A_j) + \sum_i \rho_{ij} X_i - \sum_i \frac{\mu_i X_i}{\gamma_{A_{ij}}} \\
\frac{dT_k}{dt} &= D(T_{k_0} - T_k) + \sum_i \rho_{ik} X_i - \sum_i \frac{\omega_i X_i}{\gamma_{T_{ik}}} \\
\frac{dS_m}{dt} &= D(S_{m_0} - S_m) + \sum_i k_{S_{im}} X_i \\
\mu_i &= \mu_{\max_i} \prod_j \frac{A_j}{K_{A_{ij}} + A_j} \\
\omega_i &= \sum_k \omega_{\max_{ik}} \frac{T_k}{K_{T_{ik}} + T_k} \\
\rho_{iz} &= \sum_m \left((k_{\max_{izm}} - k_{\min_{izm}}) \frac{S_m}{K_{izm} + S_m} + k_{\min_{izm}} \right)
\end{aligned}
$$

Inputs

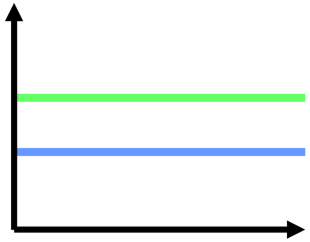
Model space



Parameter space



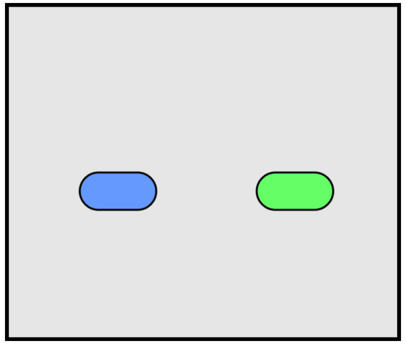
Desired behaviour



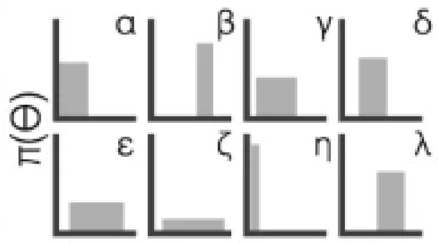
Karkaria et al., Nat Commun, 2021
Karkaria et al., PLOS Comp Biol, 2022

Inputs

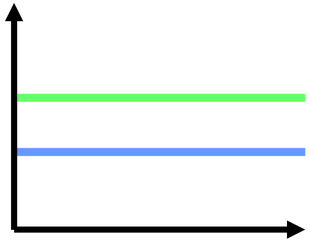
Model space



Parameter space

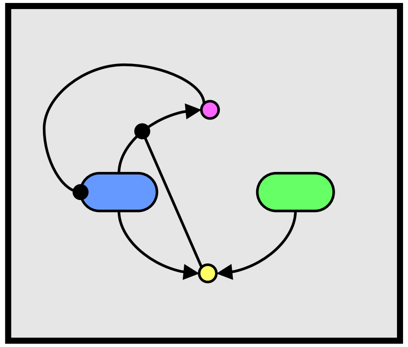


Desired behaviour

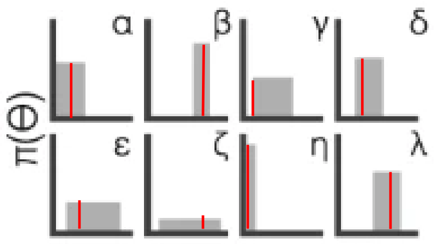


ABC

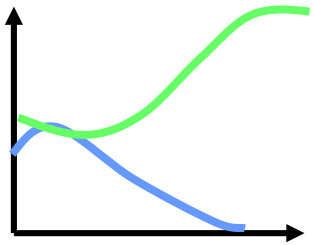
Sample a model



Sample parameters



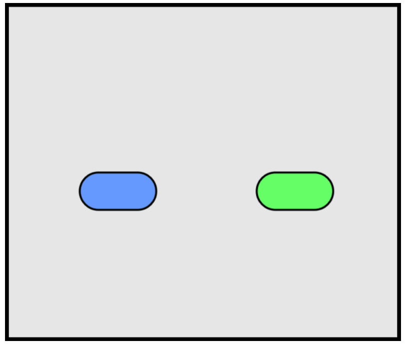
Simulate model and compare to desired behaviour



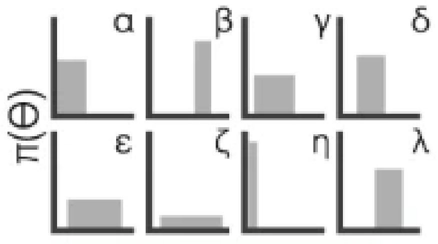
Karkaria et al., Nat Commun, 2021
Karkaria et al., PLOS Comp Biol, 2022

Inputs

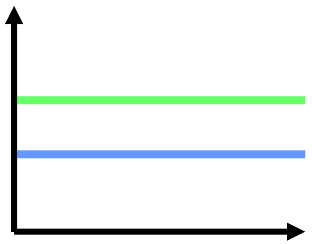
Model space



Parameter space

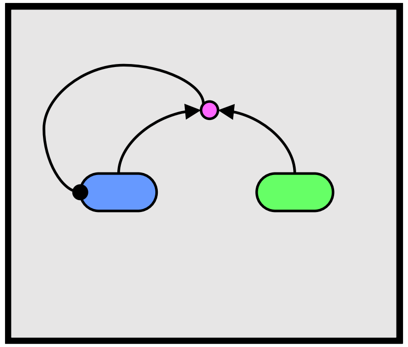


Desired behaviour

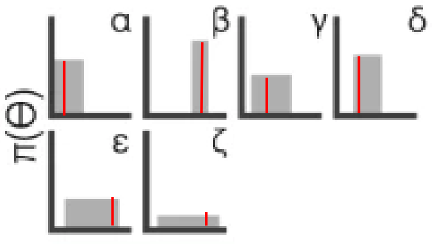


ABC

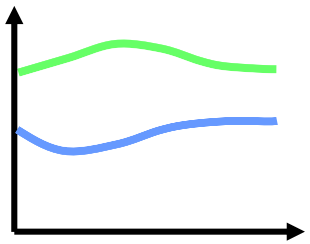
Sample a model



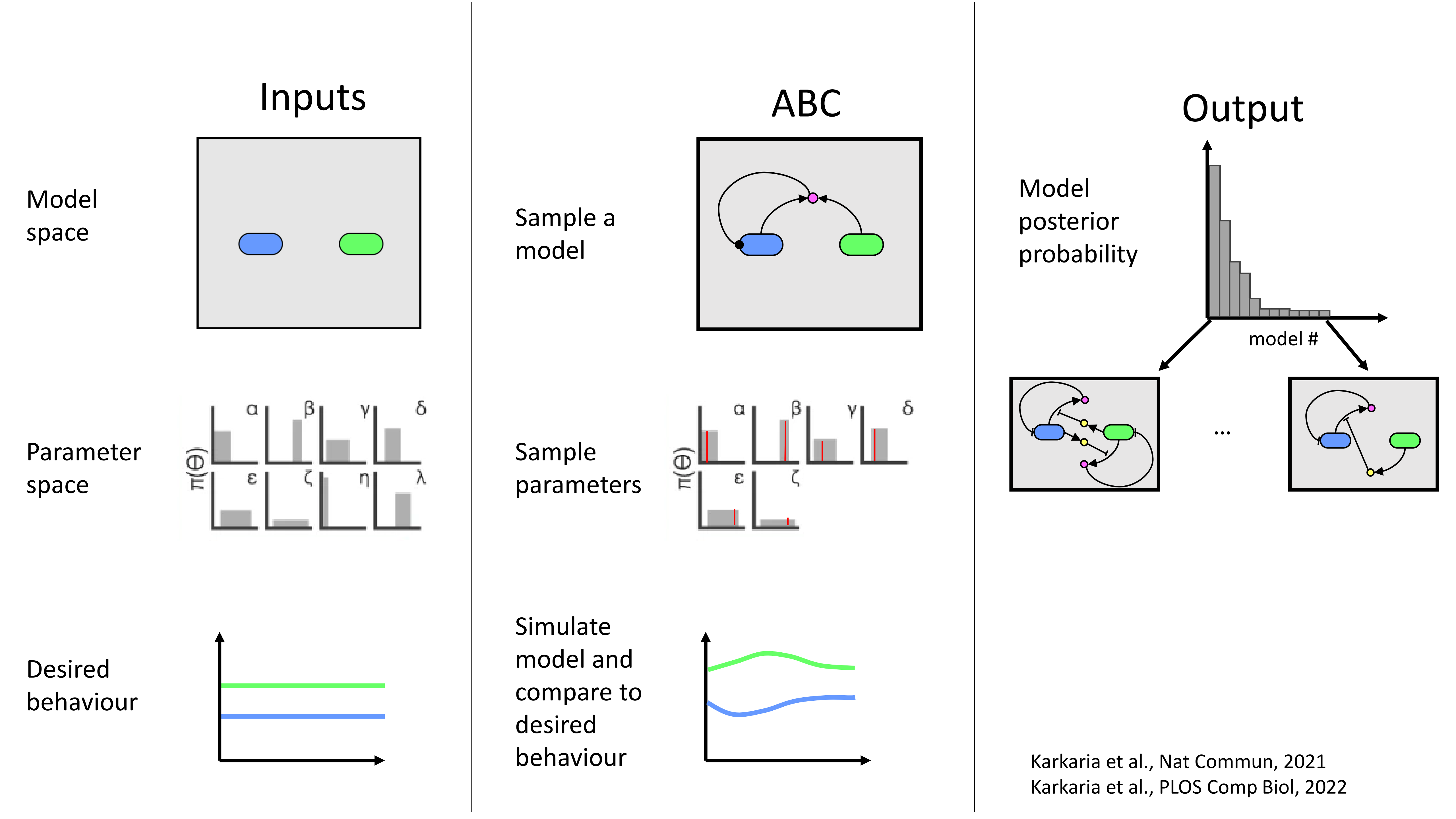
Sample parameters

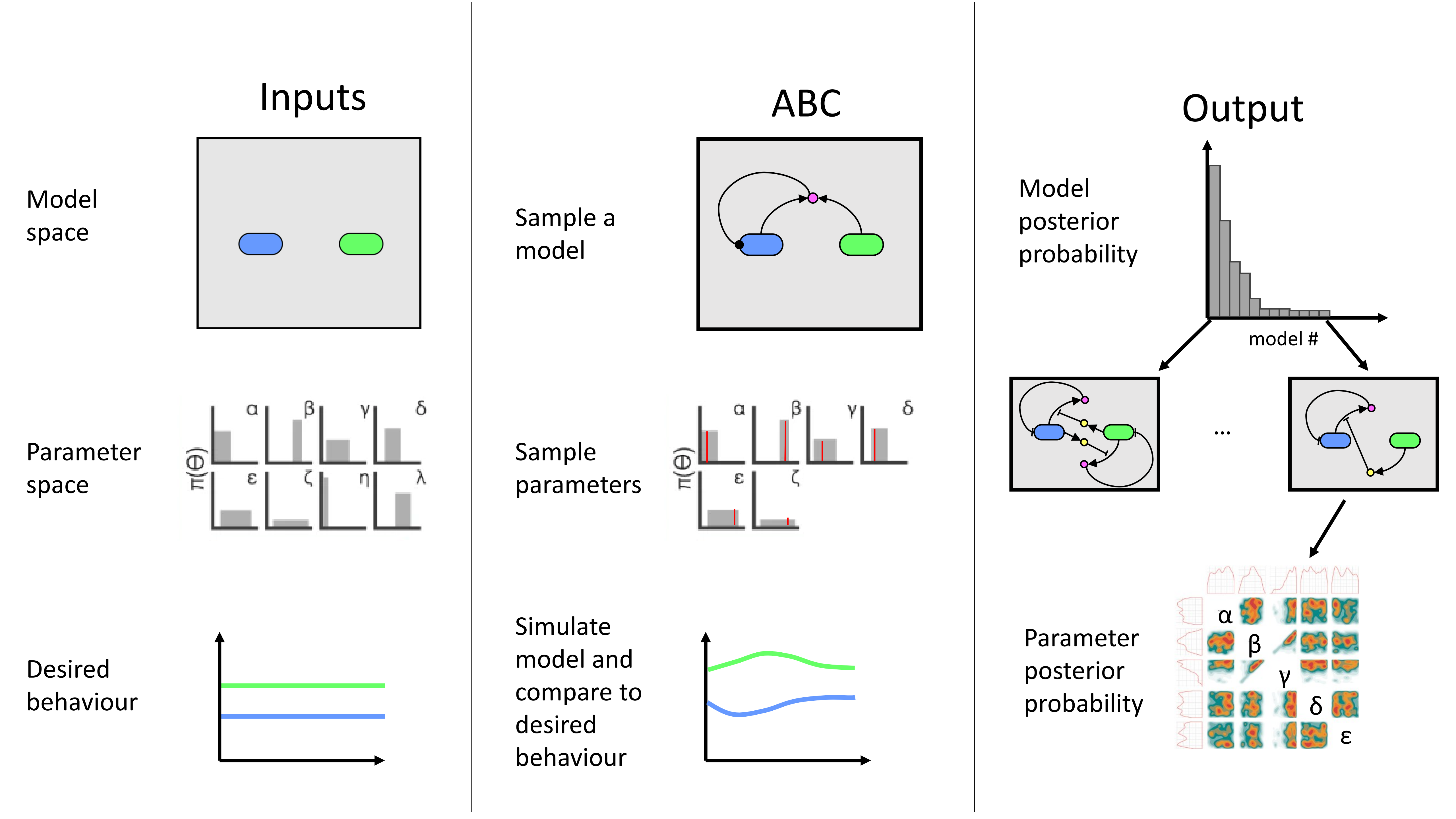


Simulate model and compare to desired behaviour



Karkaria et al., Nat Commun, 2021
Karkaria et al., PLOS Comp Biol, 2022


Inputs
Model space
Parameter space
π(Θ)
α
β
γ
δ
ε
ζ
η
λ
Desired behaviour
ABC
Sample a model
Sample parameters
π(Θ)
α
β
γ
δ
ε
ζ
Simulate model and compare to desired behaviour
Output
Model posterior probability
model #
...
Karkaria et al., Nat Commun, 2021
Karkaria et al., PLOS Comp Biol, 2022


Inputs
Model space
Parameter space
π(Θ)
α
β
γ
δ
ε
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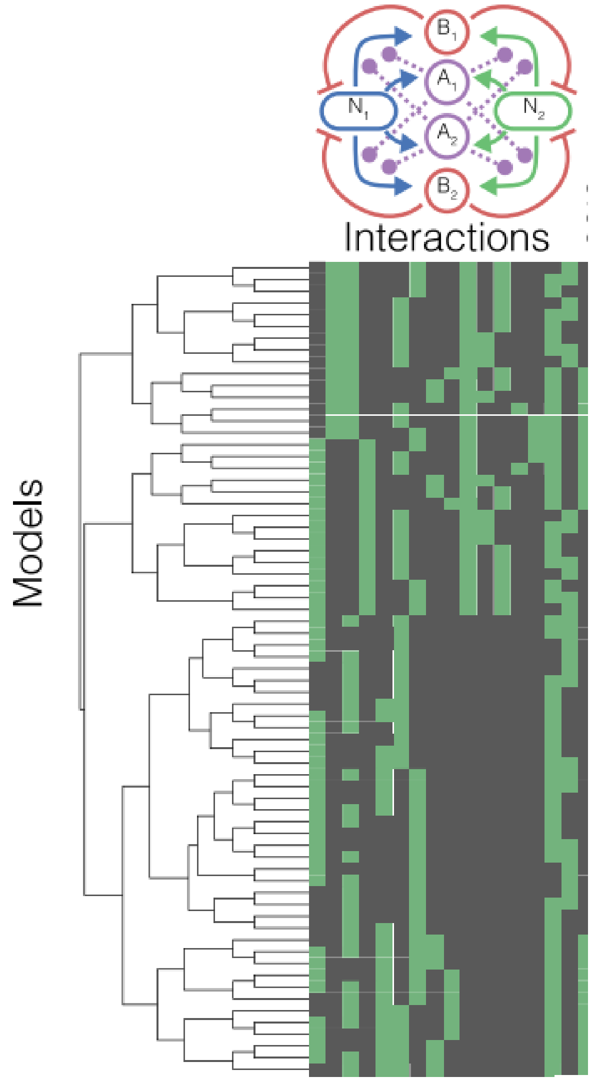
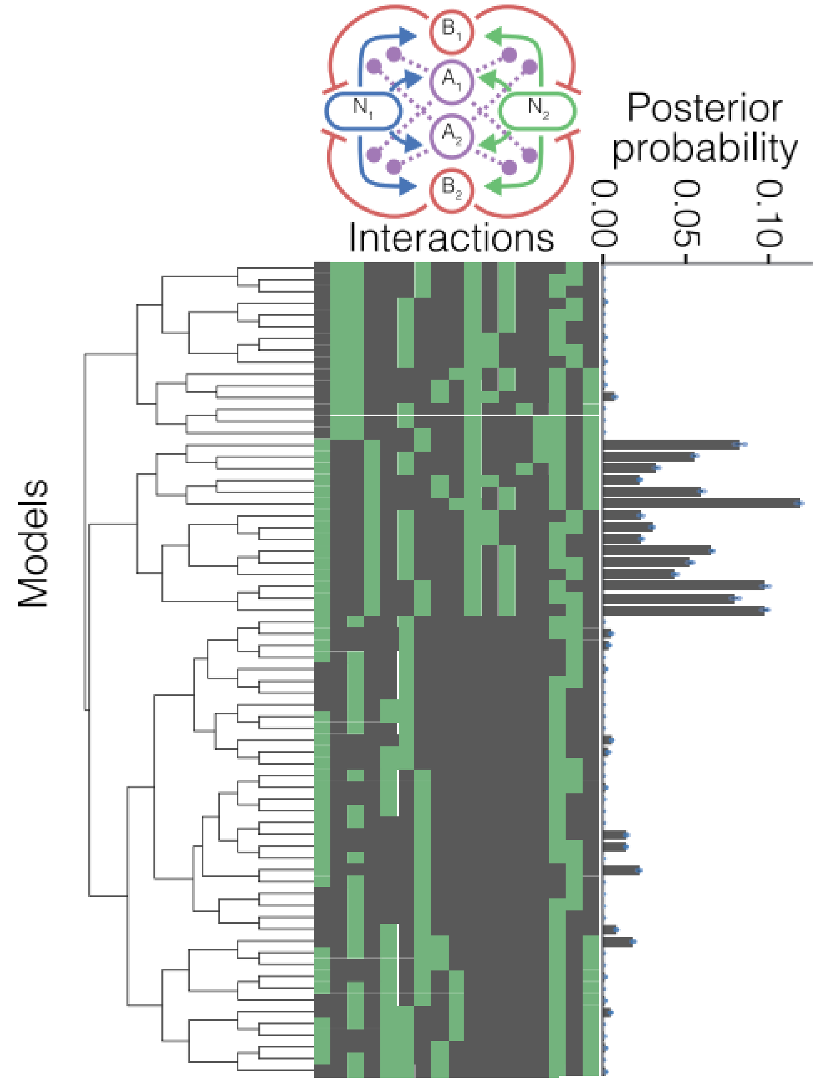
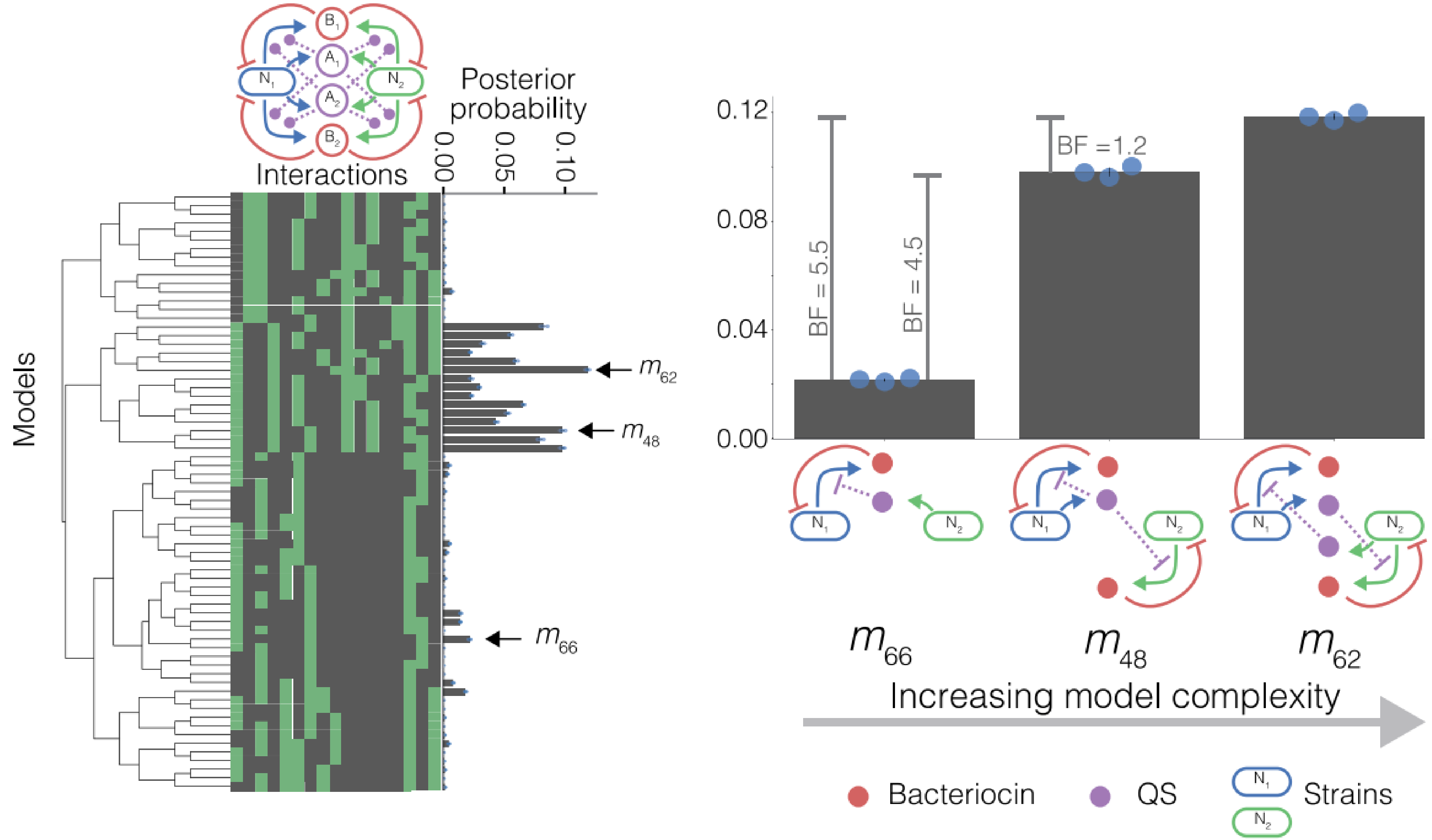
model #
...
Parameter posterior probability
α
β
γ
δ
ε



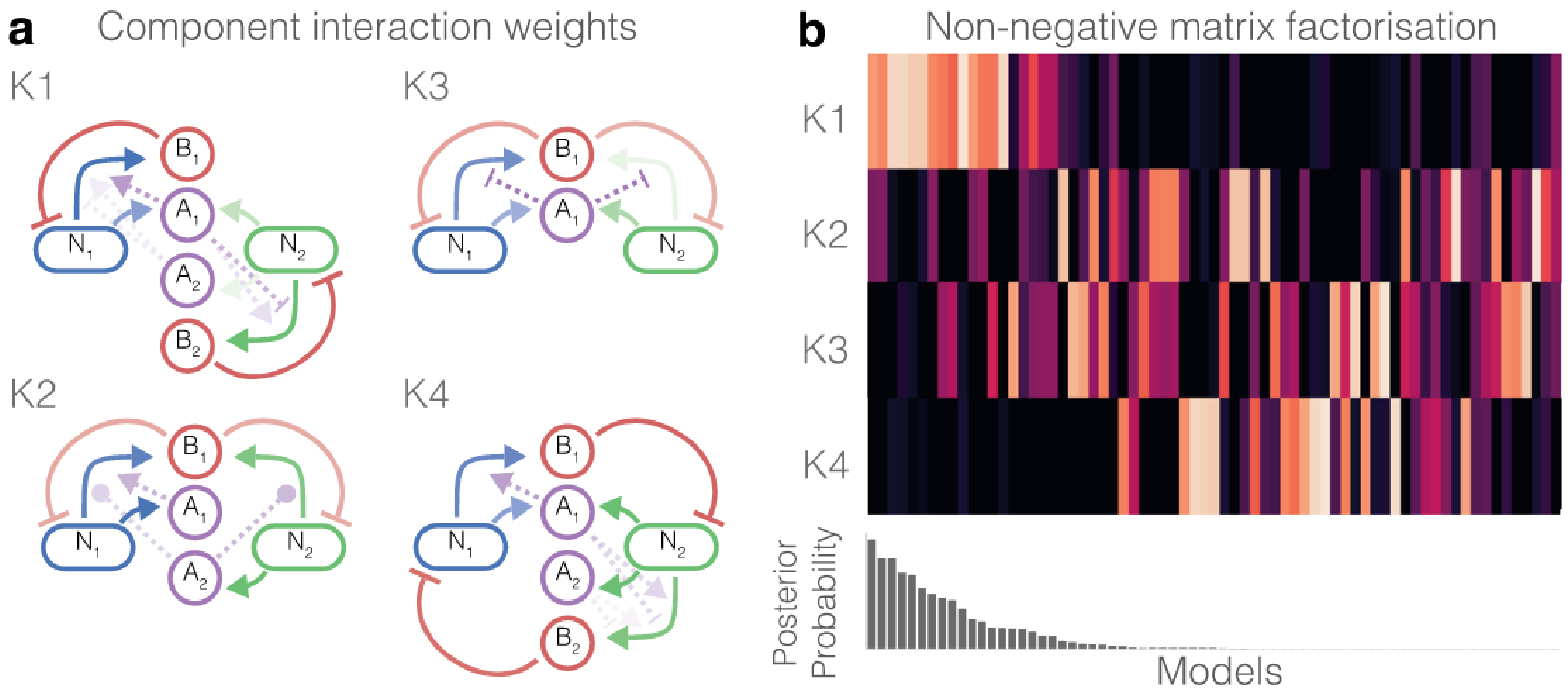
B1
A1
N1
N2
A2
B2
Interactions
Models


B1
B2
A1
A2
N1
N2
Interactions
Posterior probability
0.00
0.05
0.10
Models

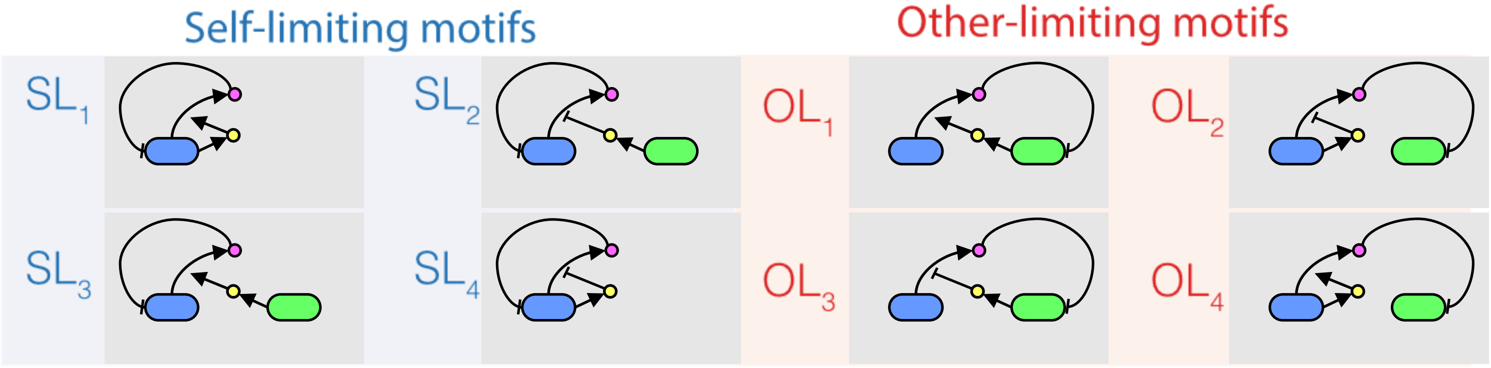


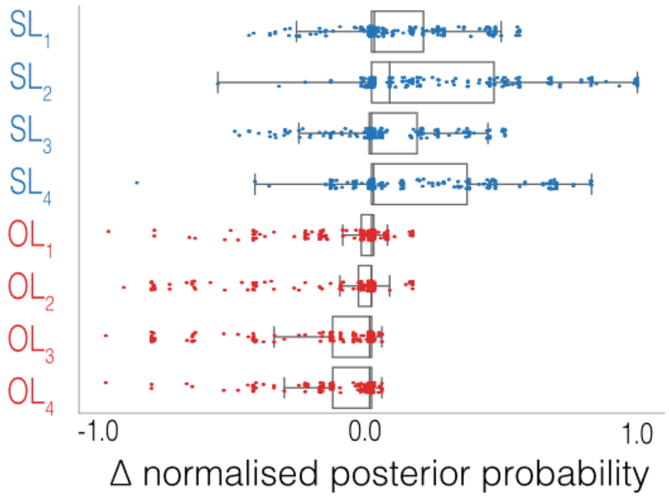
Interactions
Posterior probability
0.00
0.05
0.10
Models
m_{62}
m_{48}
m_{66}
0.12
0.08
0.04
0.00
BF = 5.5
BF = 4.5
BF =1.2
m_{66}
m_{48}
m_{62}
Increasing model complexity
Bacteriocin
QS
Strains

Are there general rules that I can follow?

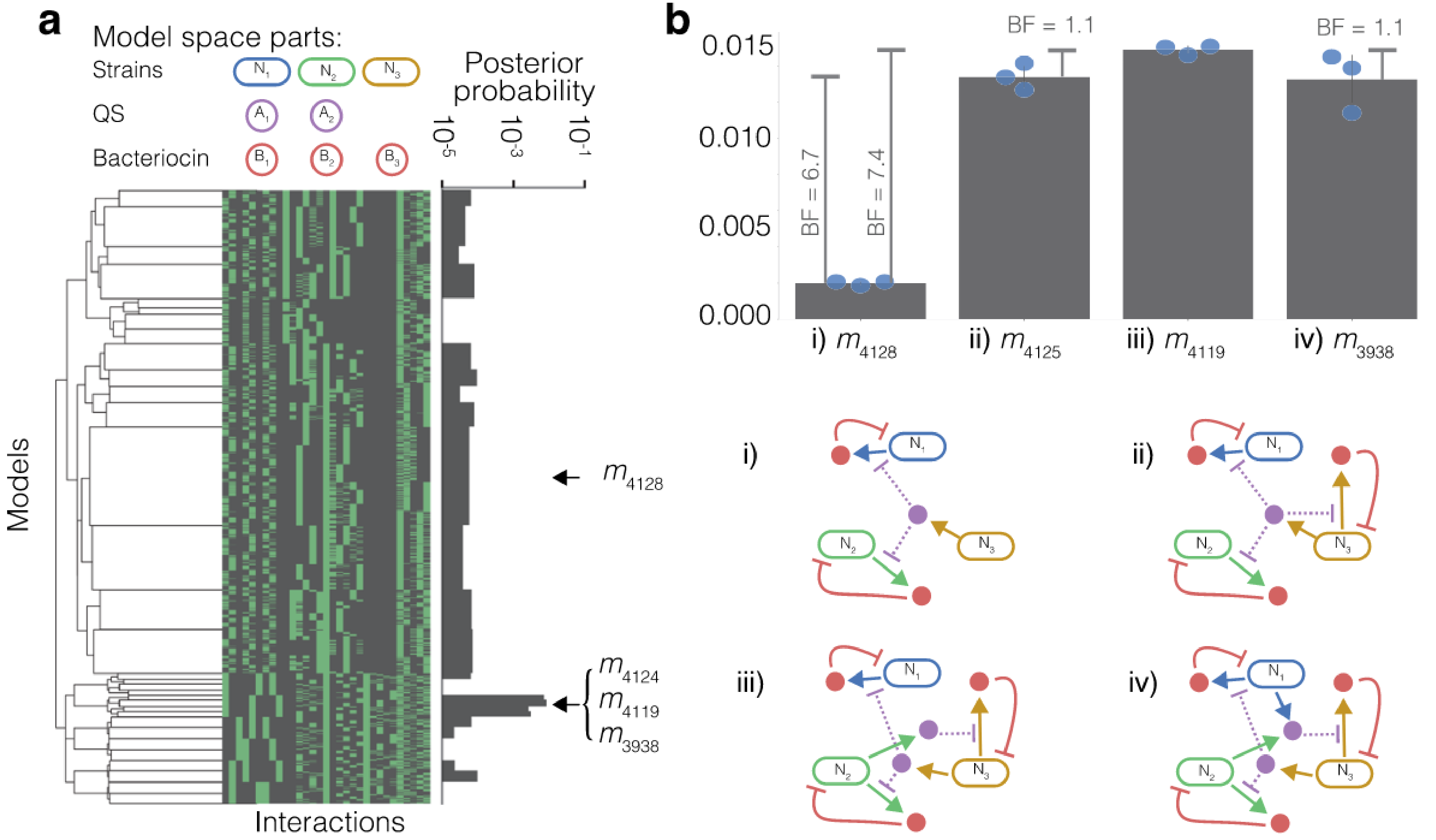


Are there general rules that I can follow?





Karkaria et al., Nat Commun, 2021


a
Model space parts:
Strains
QS
Bacteriocin
Posterior probability
Models
Interactions
b
BF = 6.7
BF = 7.4
BF = 1.1
BF = 1.1
0.015
0.010
0.005
0.000
i)
ii)
iii)
iv)

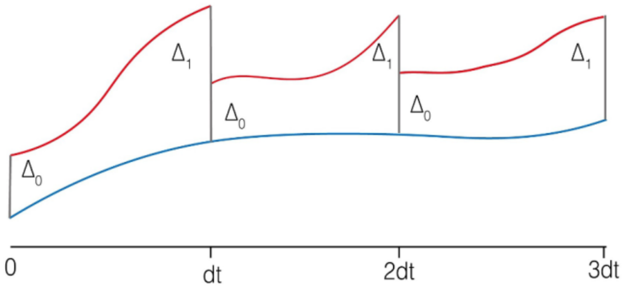
Using ABC to find rare behaviours (chaos)

Generalised Lotka-Volterra

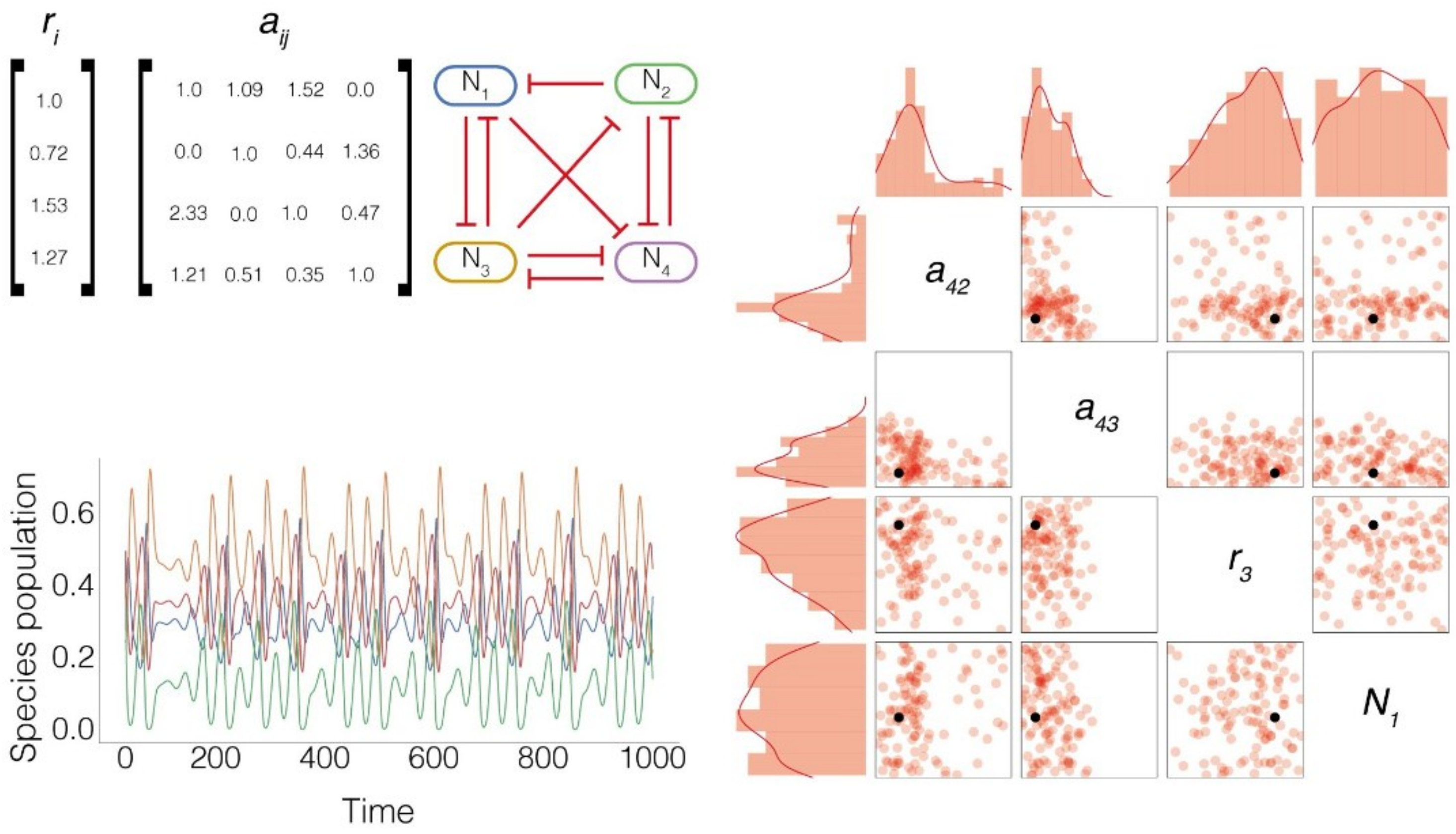
$$\frac{dX_i}{dt} = X_i\left(\mu_i + \sum_j \alpha_{i,j}\, X_j\right)$$

Distance function:

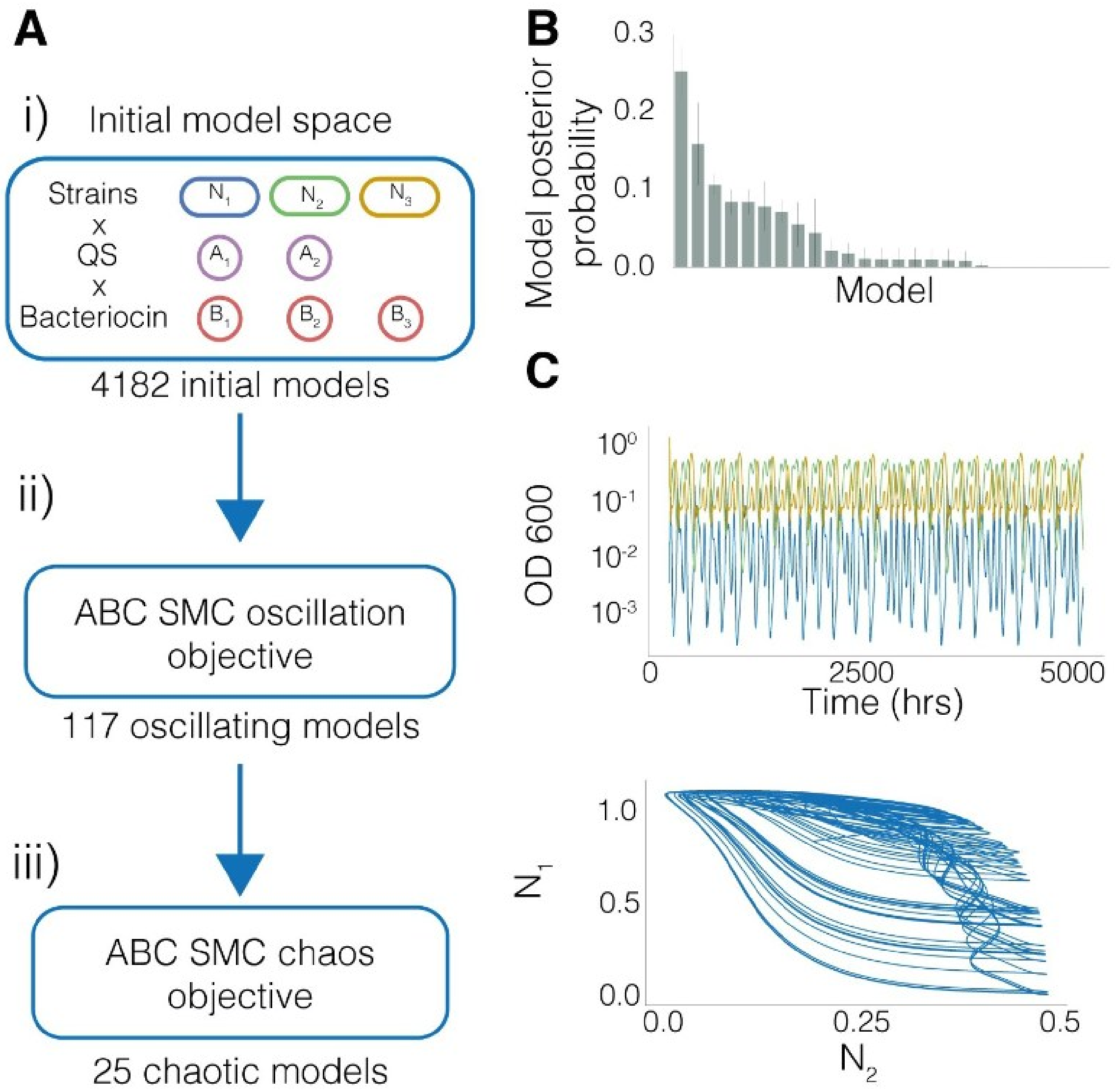
$d_1 = {}^{1}/_{(1+\lambda_1)}$ for $\lambda_1 > 0$



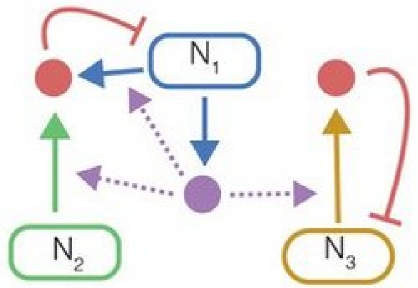
Sprott JC. Chaos and Time-Series Analysis; 2003

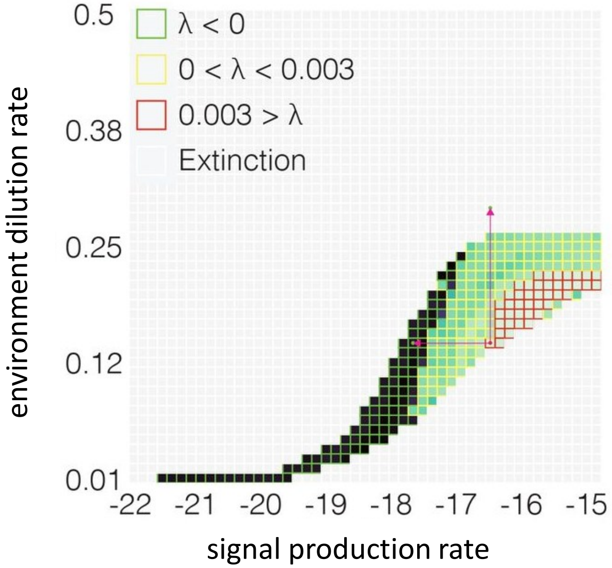


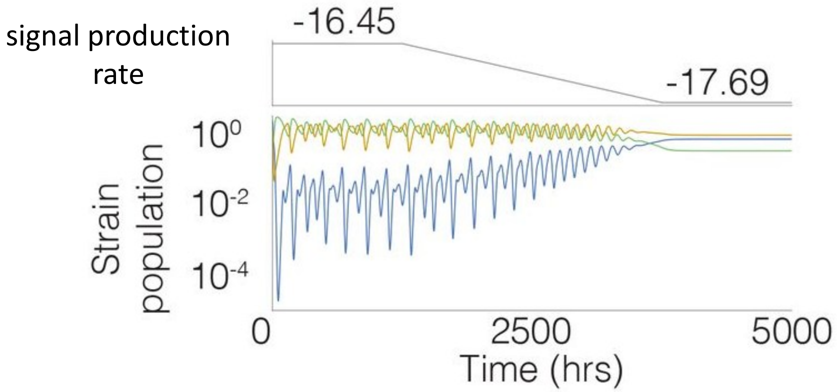
Oscillations as a route to chaos

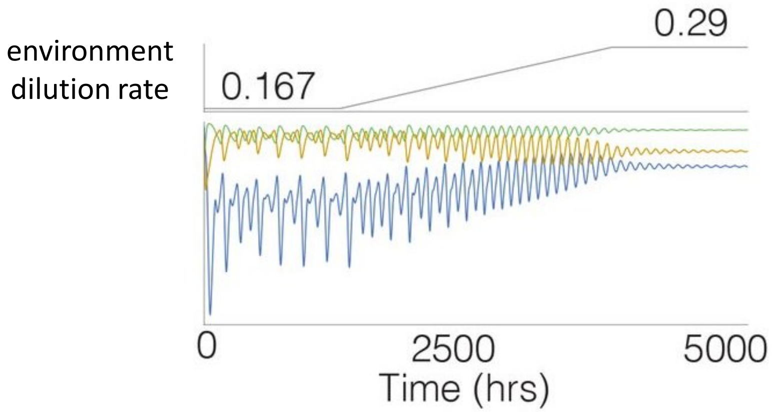


Moving from chaos to stability

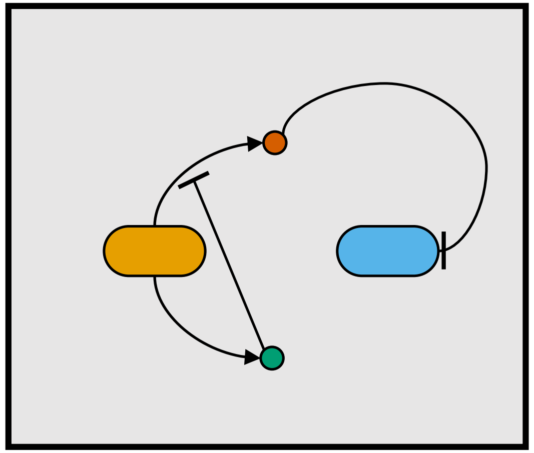


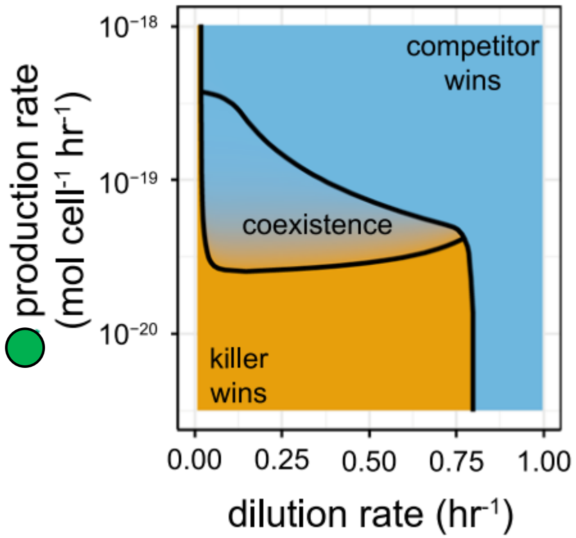


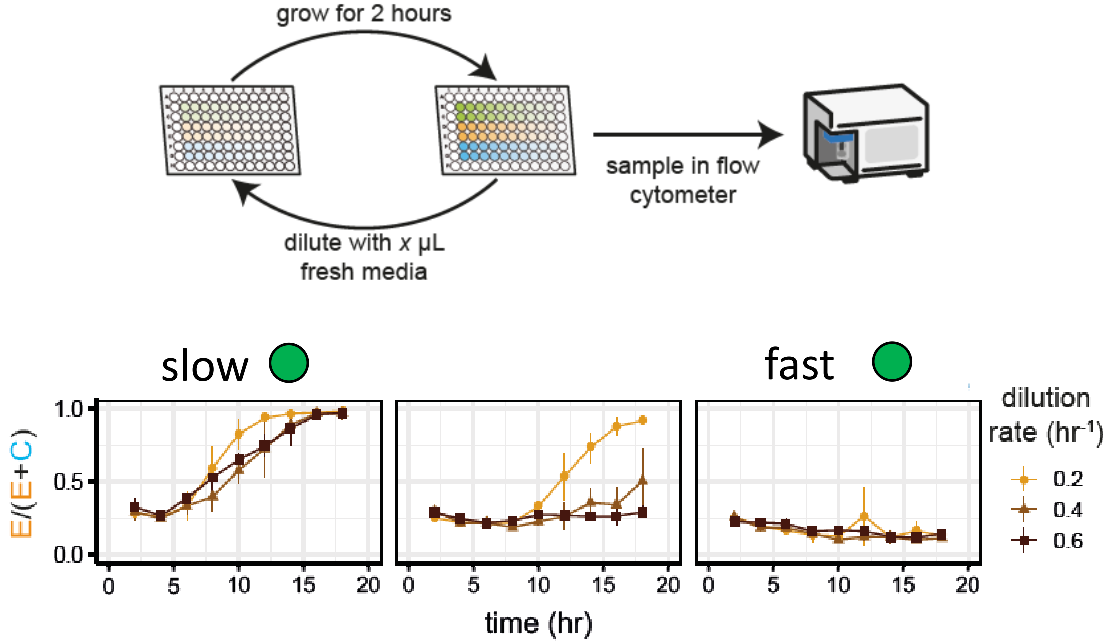




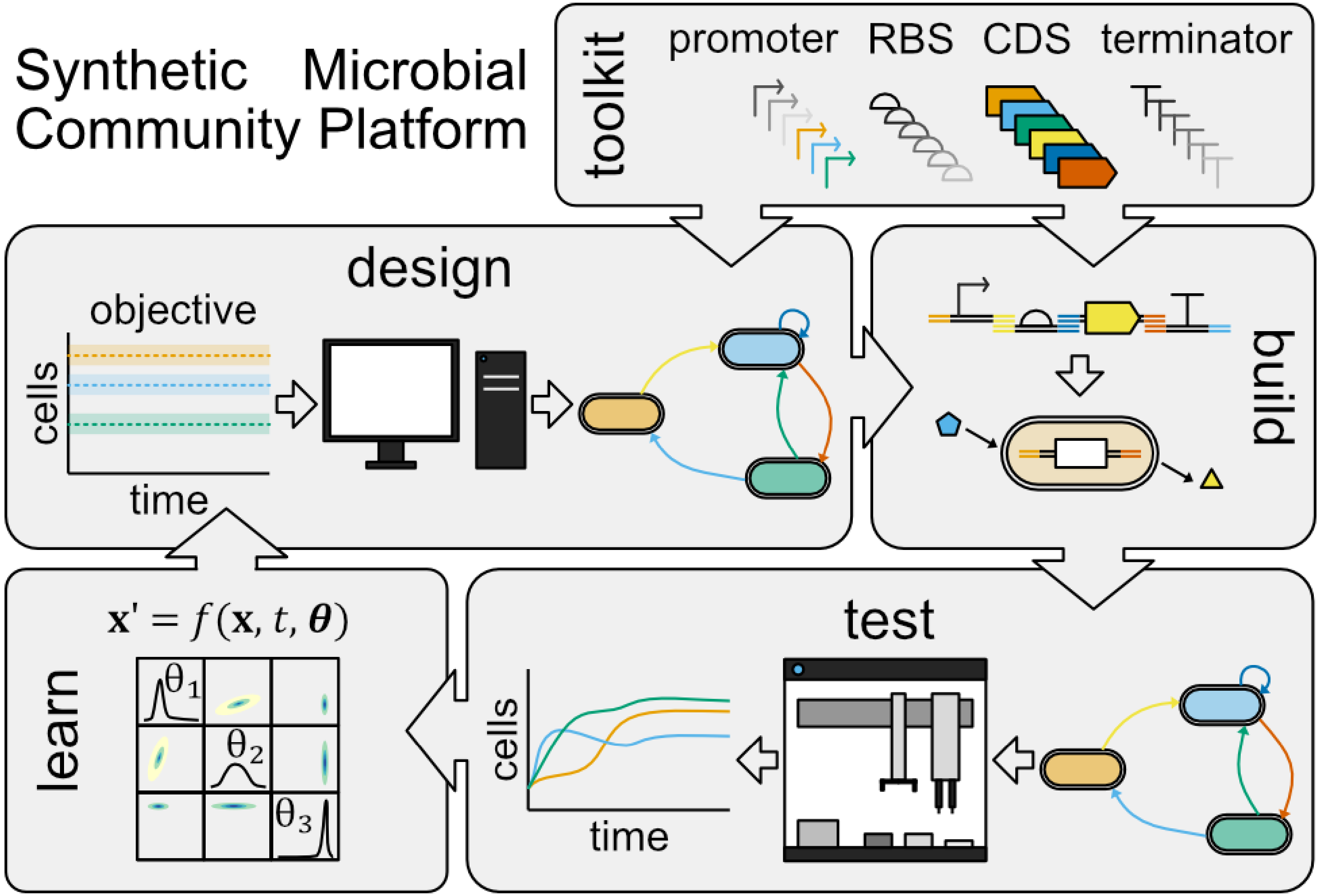
So that we can rapidly build and test communities







Fedorec et al., Nat Commun, 2021



I’m hiring postdocs for this work!

Acknowledgements

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Brian Ingalls

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UKRI Engineering and Physical Sciences Research Council

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