

# Why cross-feeding? Guidance from simple models

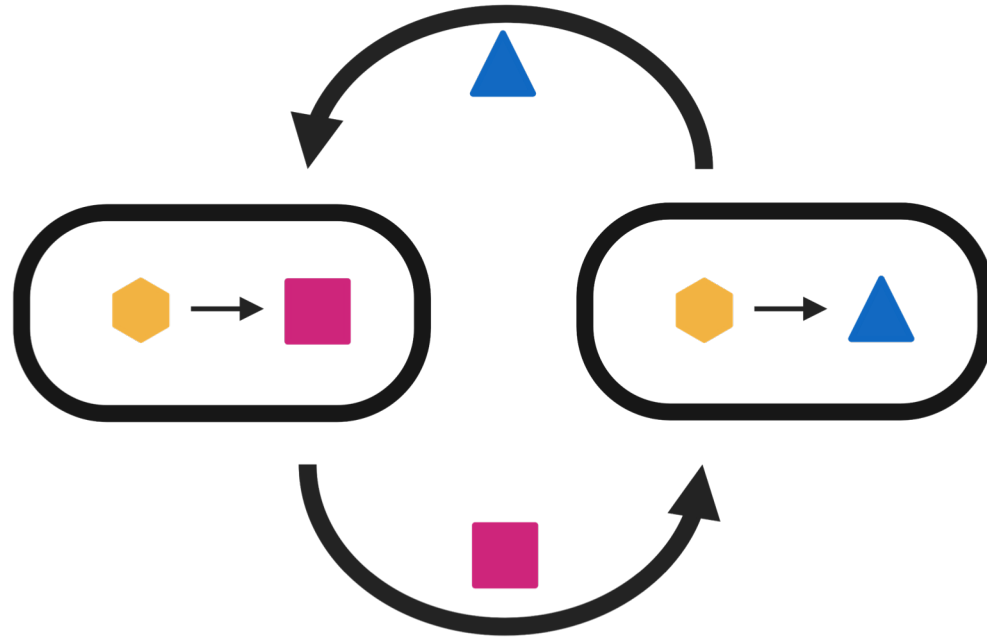
KITP Program on the Ecology and Evolution of  
Microbial Communities  
July 29, 2021

## Part II

Can noisy metabolism drive the evolution of microbial cross-feeding?

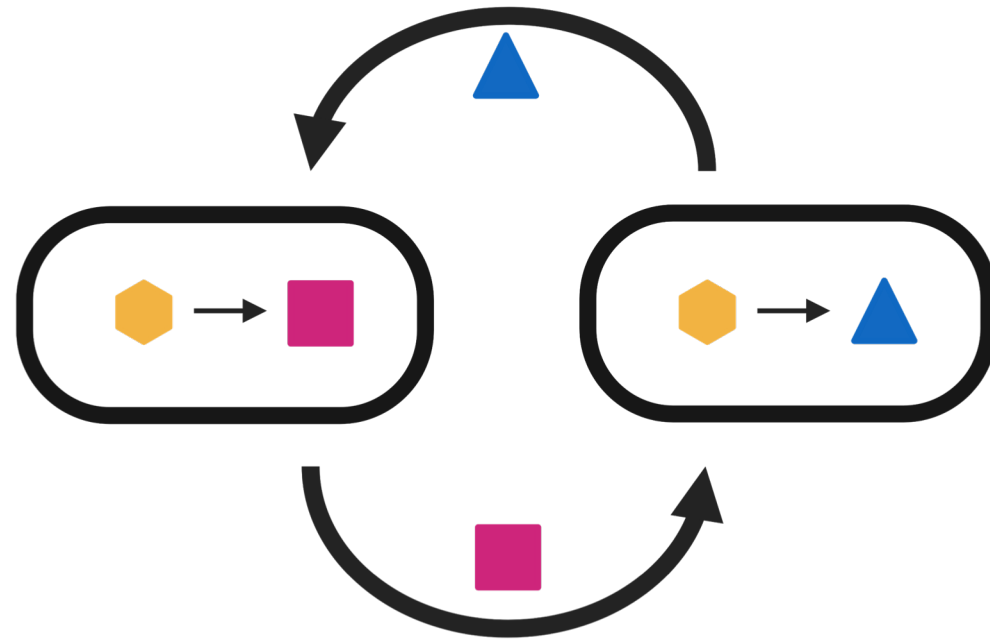
with Jaime Lopez

# Metabolite exchange is ubiquitous in microbial communities



Example: bacteria-bacteria and  
bacteria-algae vitamin exchange

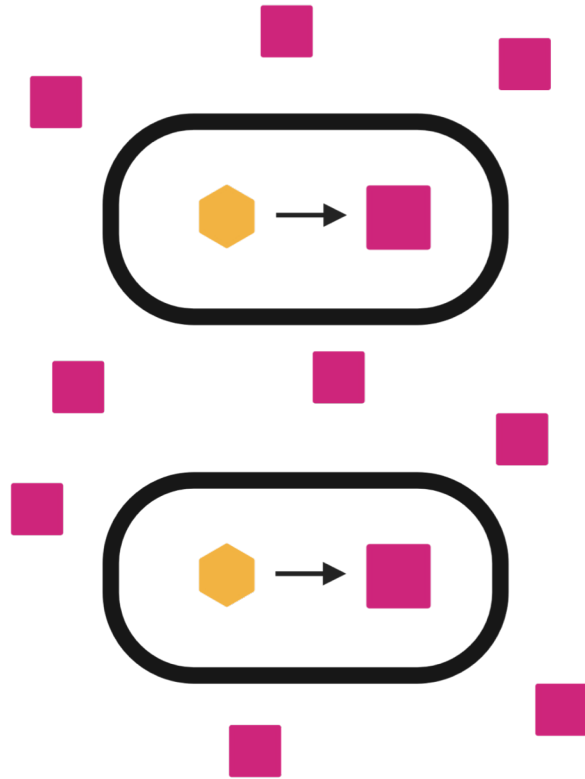
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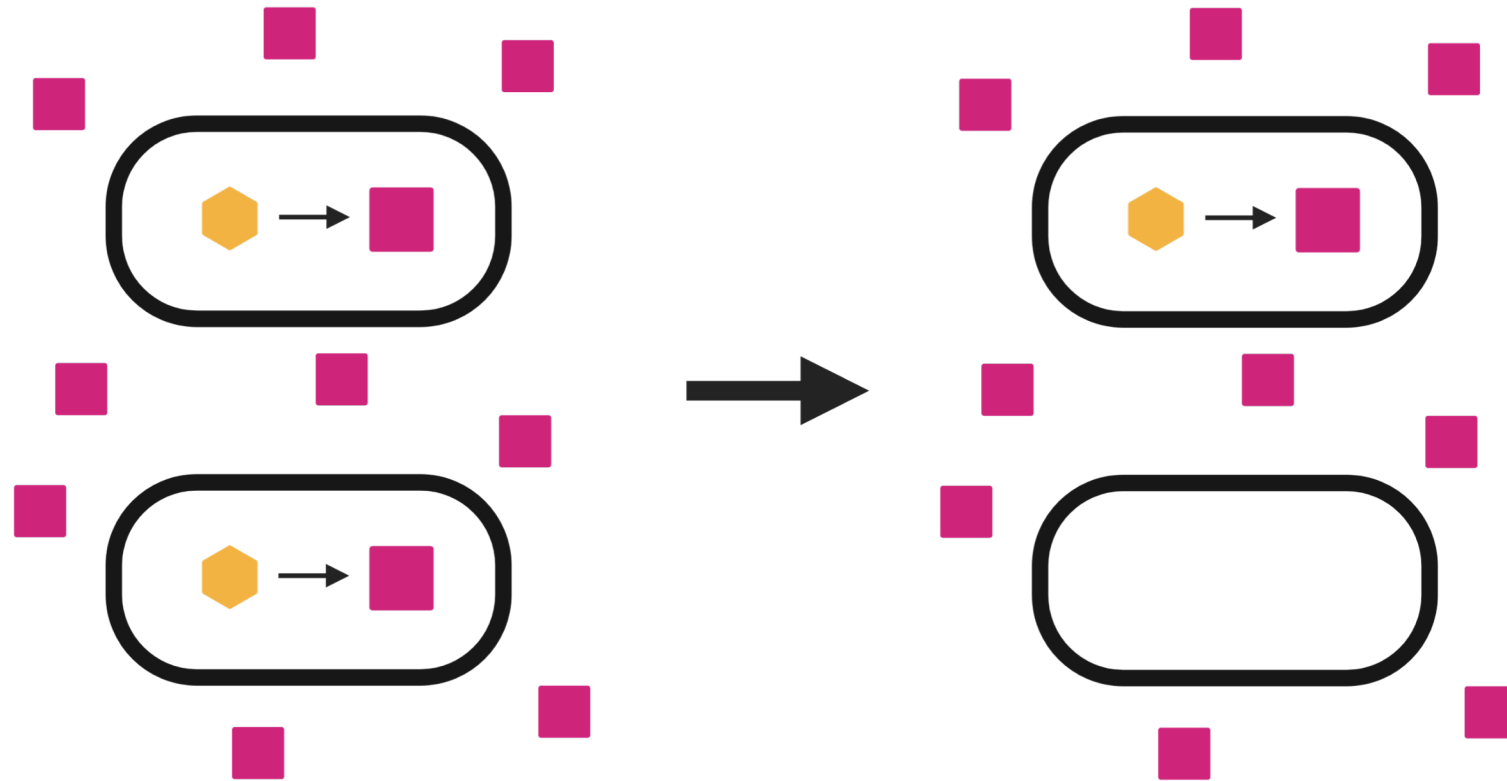
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How does this cooperation  
evolve?

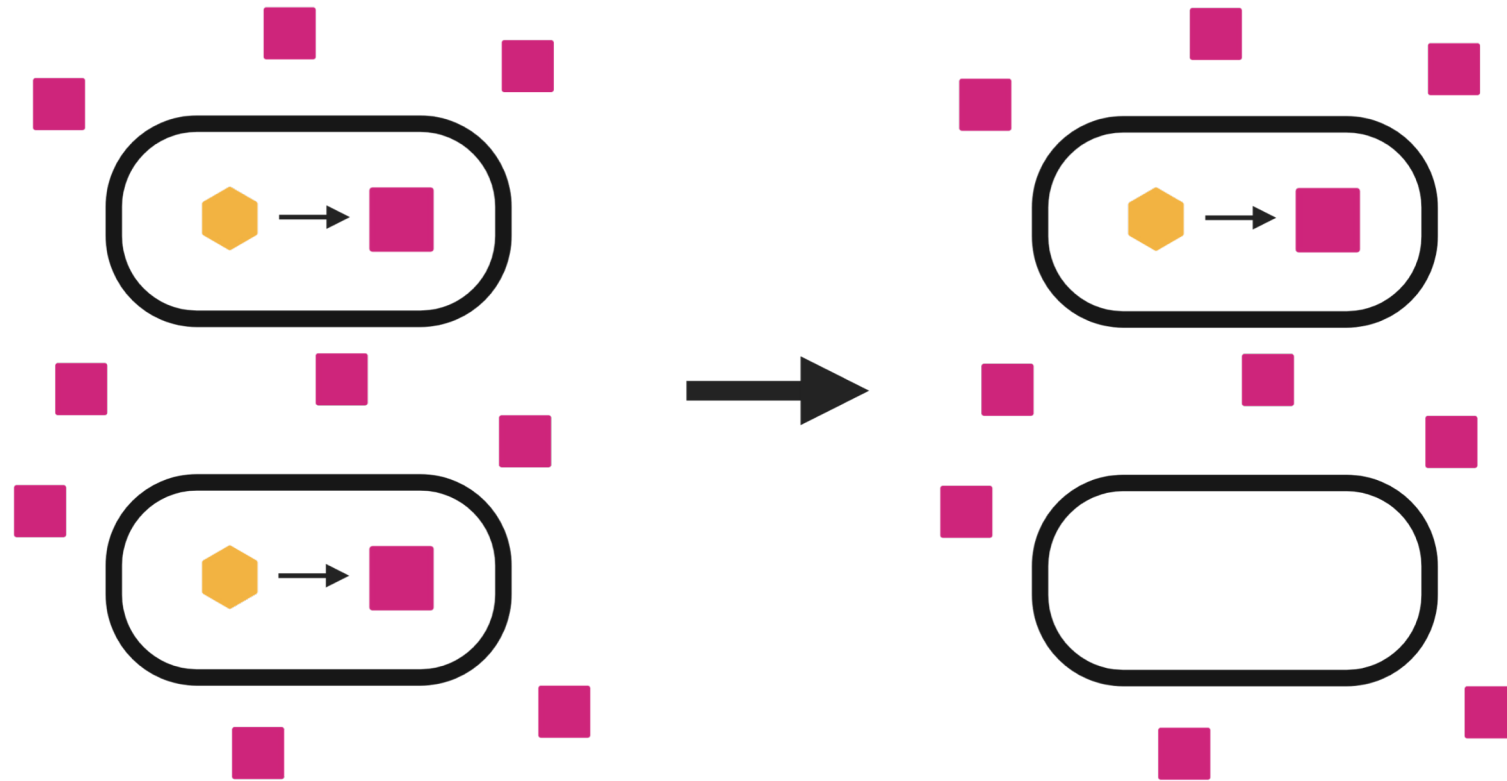
# The Black Queen Hypothesis (Morris 2012): leakage encourages cross-feeding



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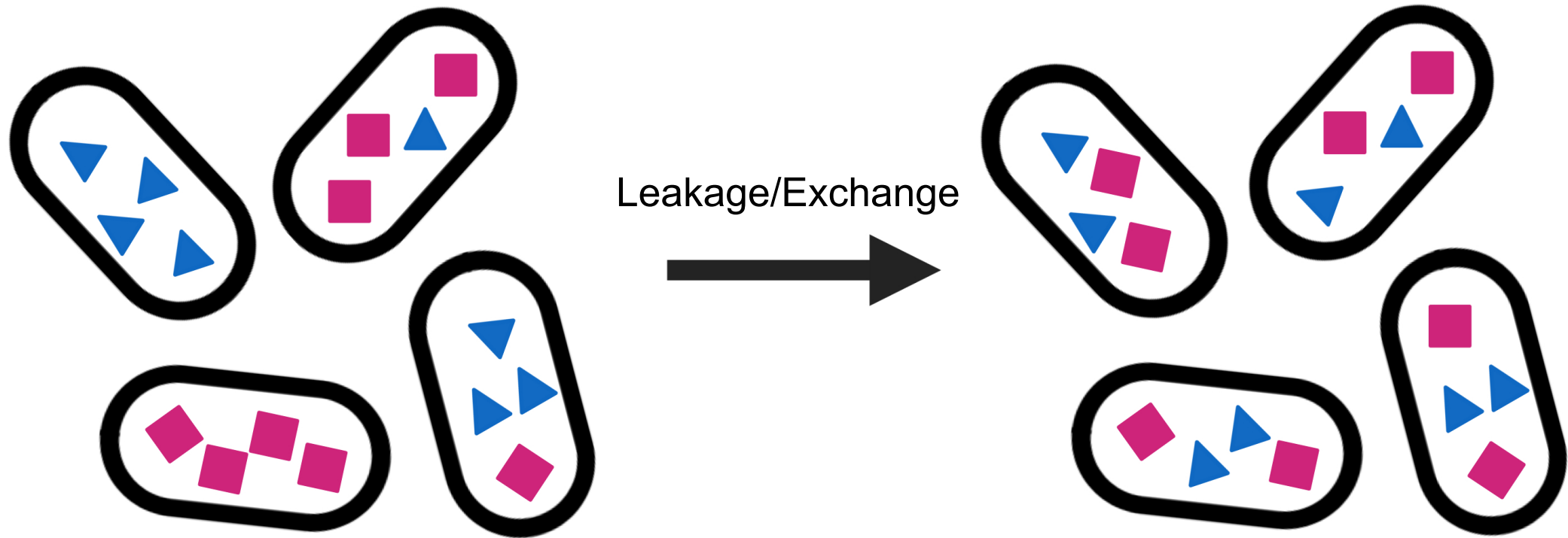
But how does the leakage evolve?

Metabolite noise could promote leakage to  
“average out” imbalances

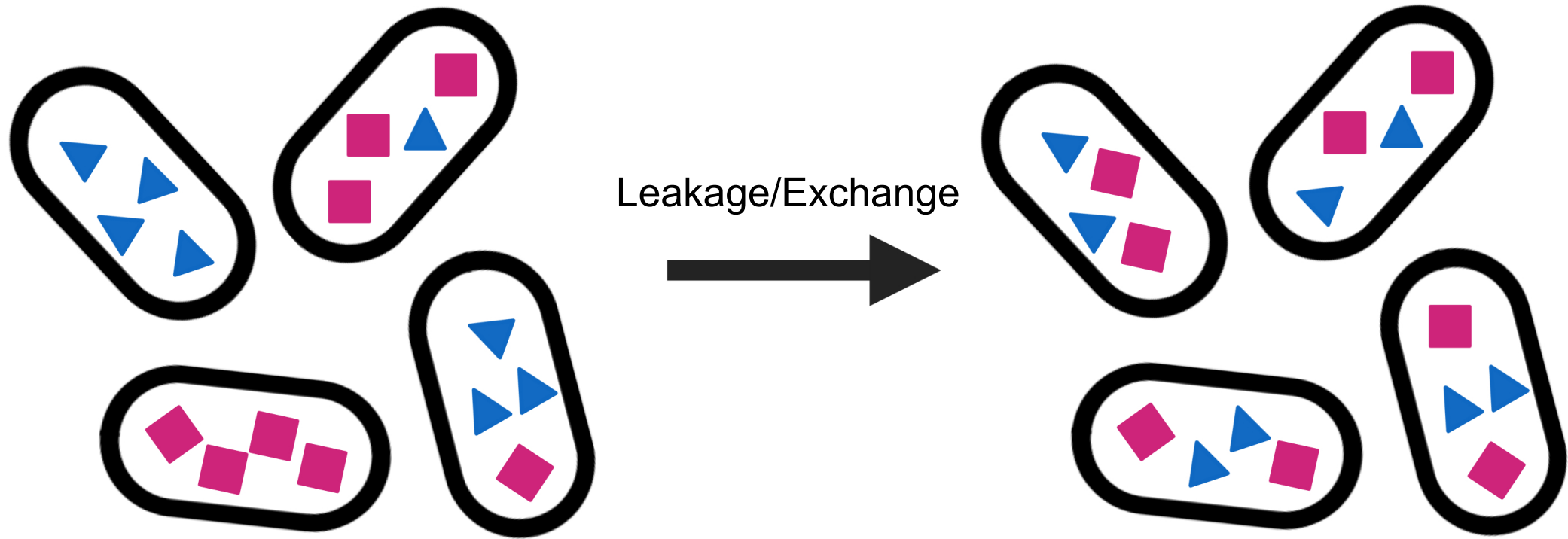




# Metabolite noise could promote leakage to 'average out' imbalances

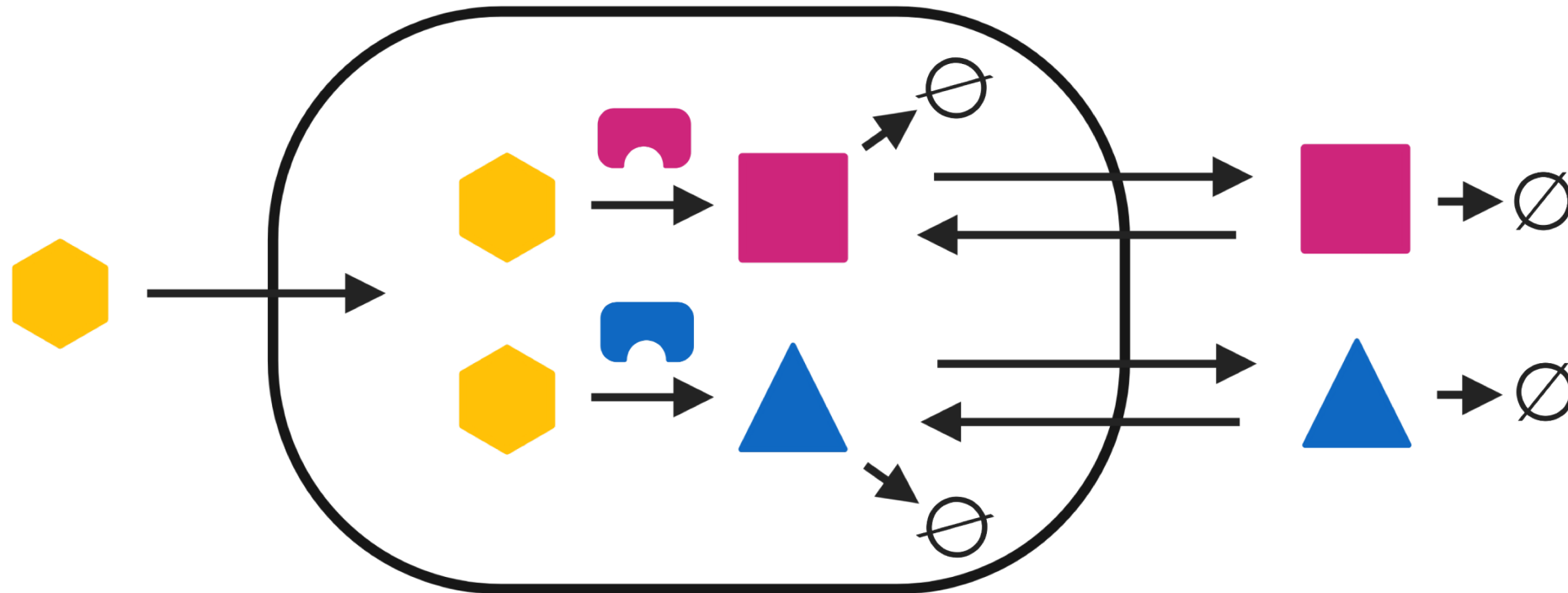


# Metabolite noise could promote leakage to 'average out' imbalances



Noise-averaging cooperation (NAC)

# Let's test this out in a simple model of cell metabolism



$$\text{Growth rate} \propto \text{Min}([\text{pink square}], [\text{blue triangle}])$$

# Metabolite dynamics

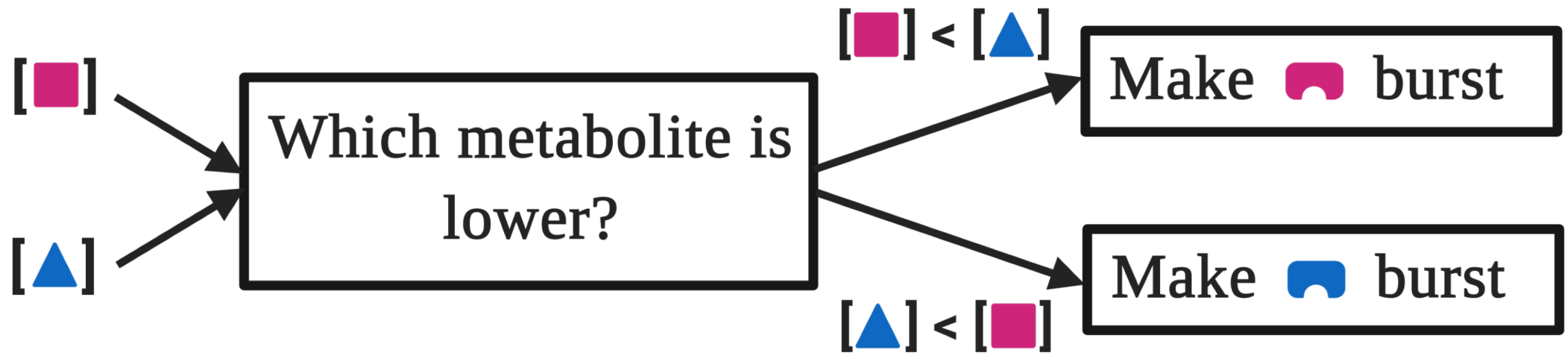
Intracellular

$$\frac{dm_i^{\text{int}}}{dt} = \overset{\text{Production}}{\boxed{\kappa E_i}} - \overset{\text{Growth}}{\boxed{\text{Min}_i(m_i^{\text{int}})}} + \overset{\text{Leakage}}{\boxed{P \cdot (m_i^{\text{ext}} / r_V - m_i^{\text{int}})}} - \overset{\text{Degradation}}{\boxed{\delta m_i^{\text{int}}}}$$

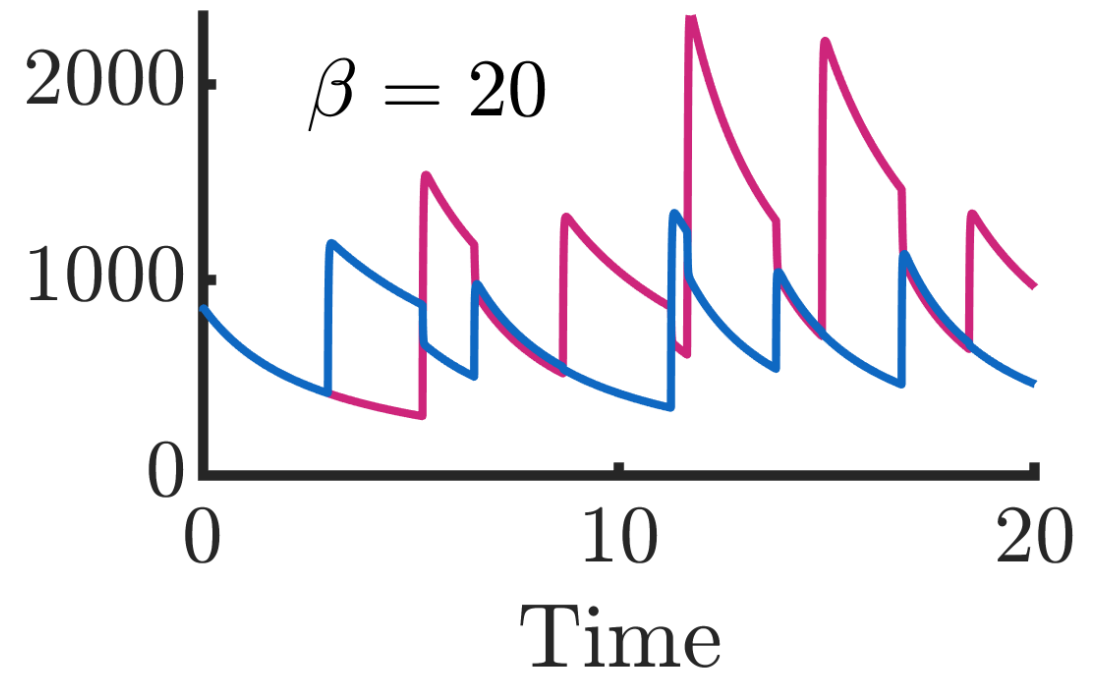
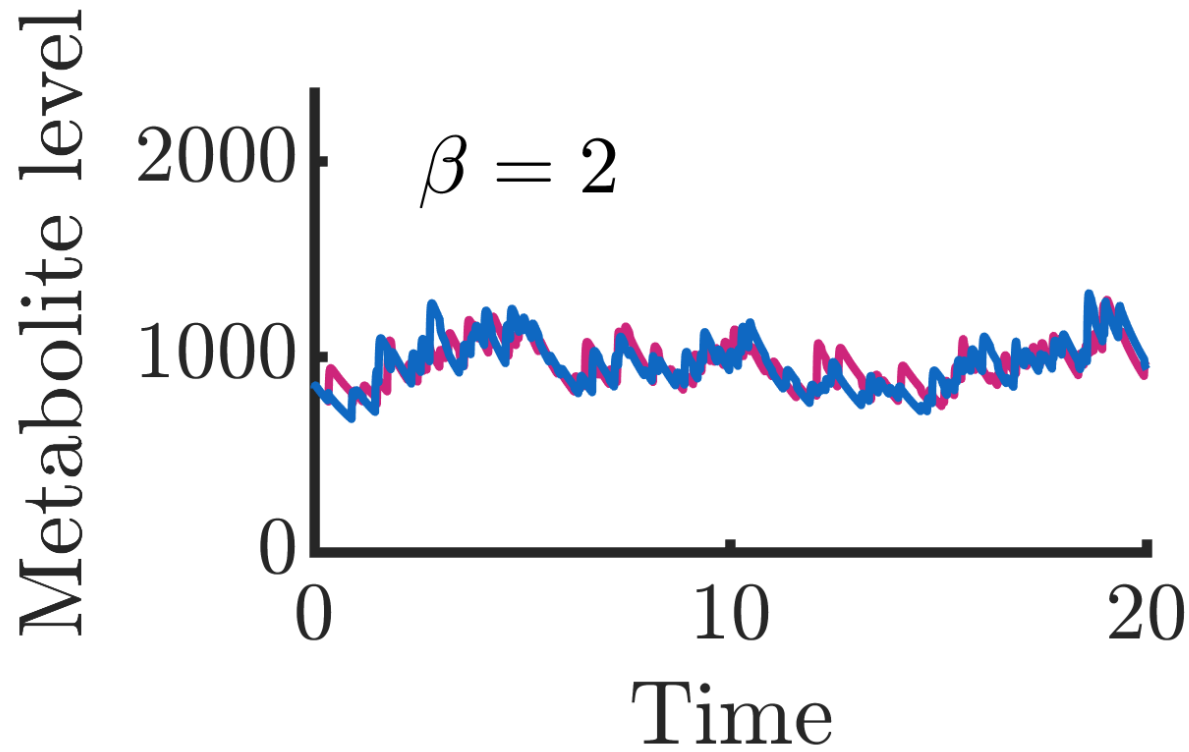
Extracellular

$$\frac{dm_i^{\text{ext}}}{dt} = \overset{\text{Leakage}}{\boxed{-P \cdot (m_i^{\text{ext}} / r_V - m_i^{\text{int}})}} - \overset{\text{Degradation}}{\boxed{\delta m_i^{\text{ext}}}}$$

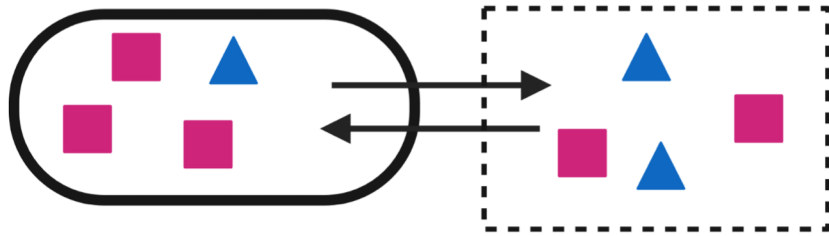
# Bang-bang enzyme regulation scheme



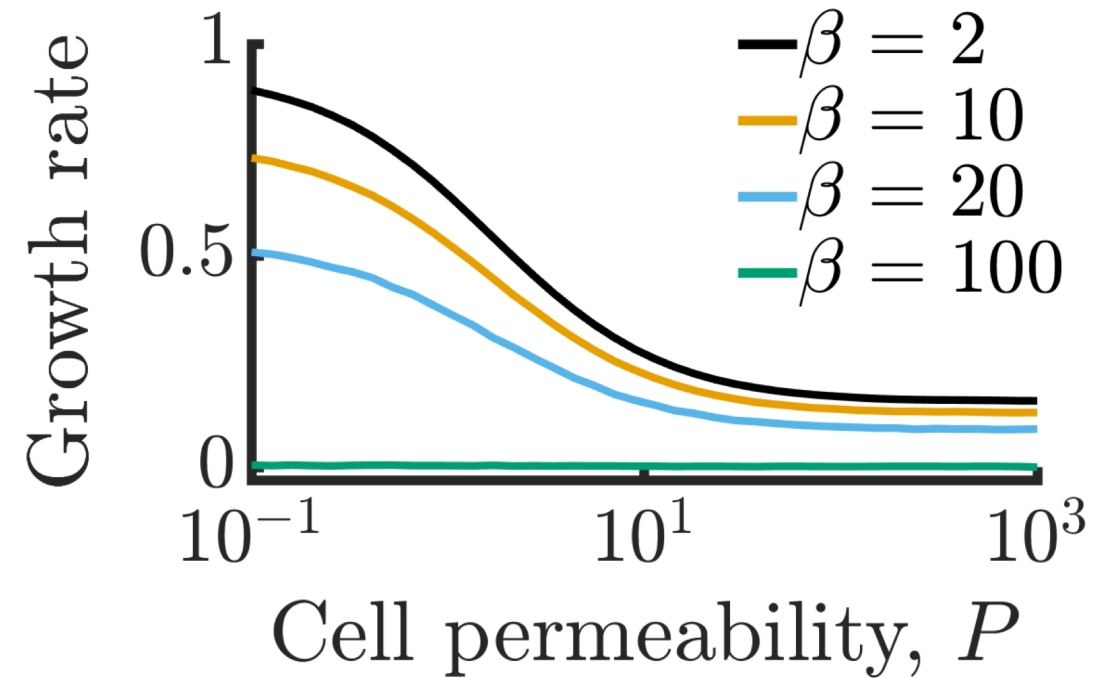
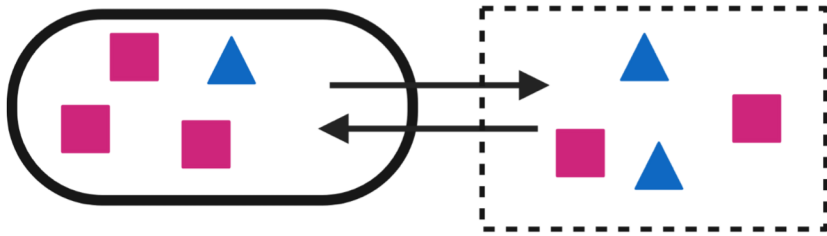
# Example of metabolite dynamics



# The control case: leakage from an isolated cell

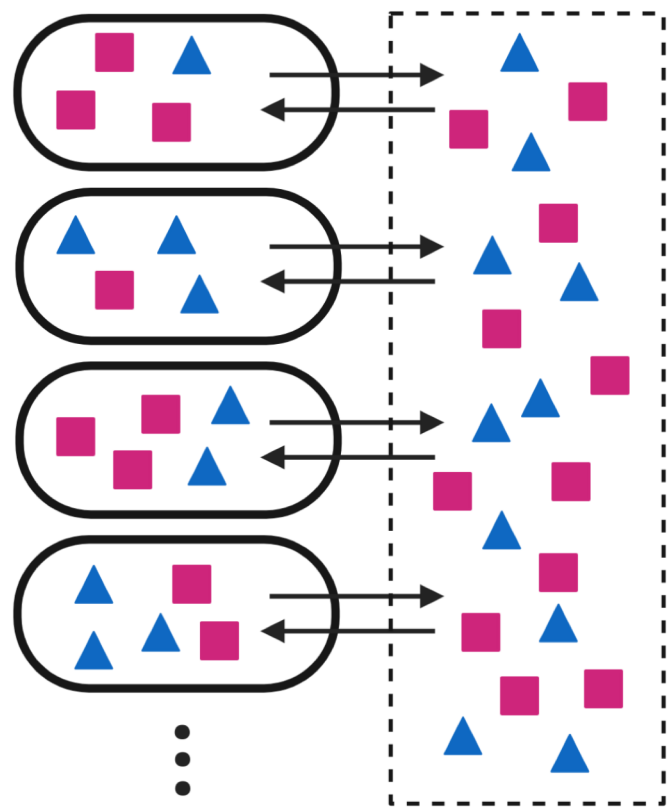


# The control case: leakage from an isolated cell

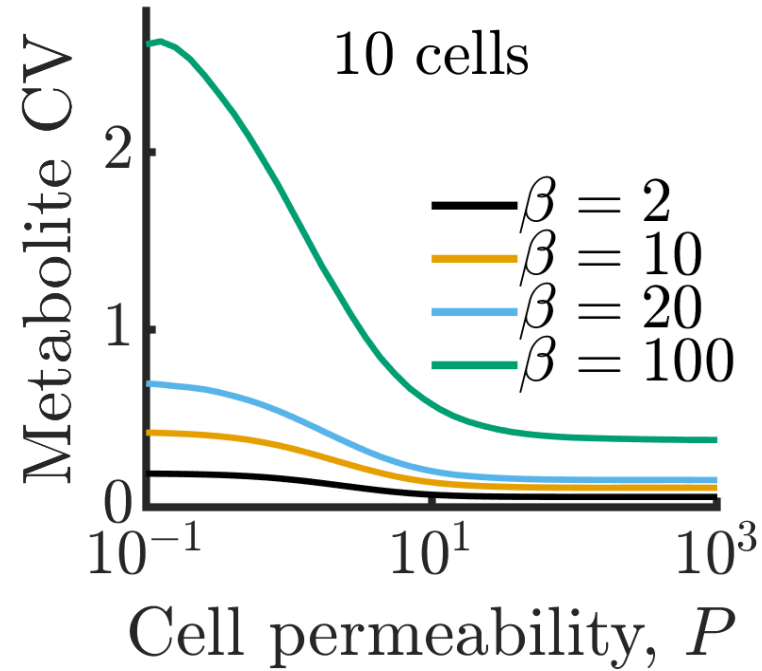
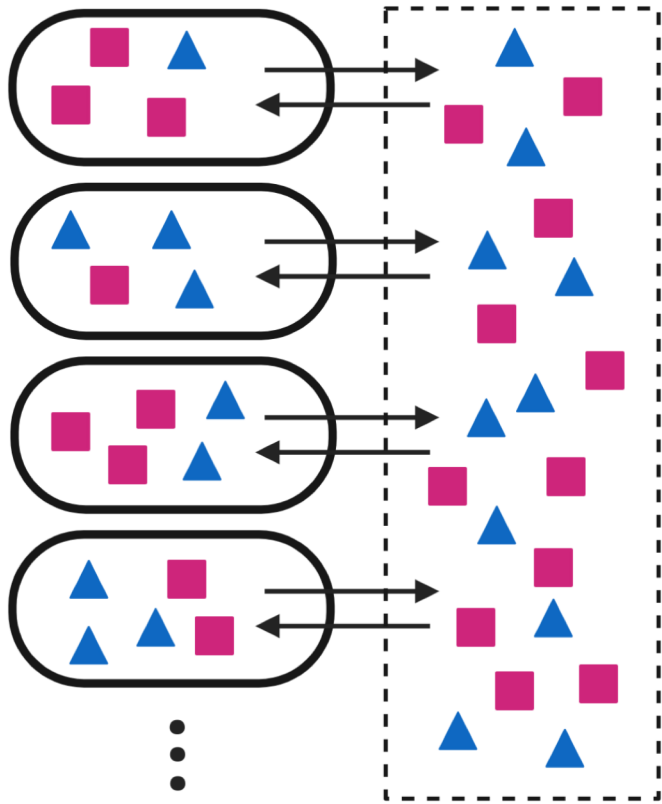




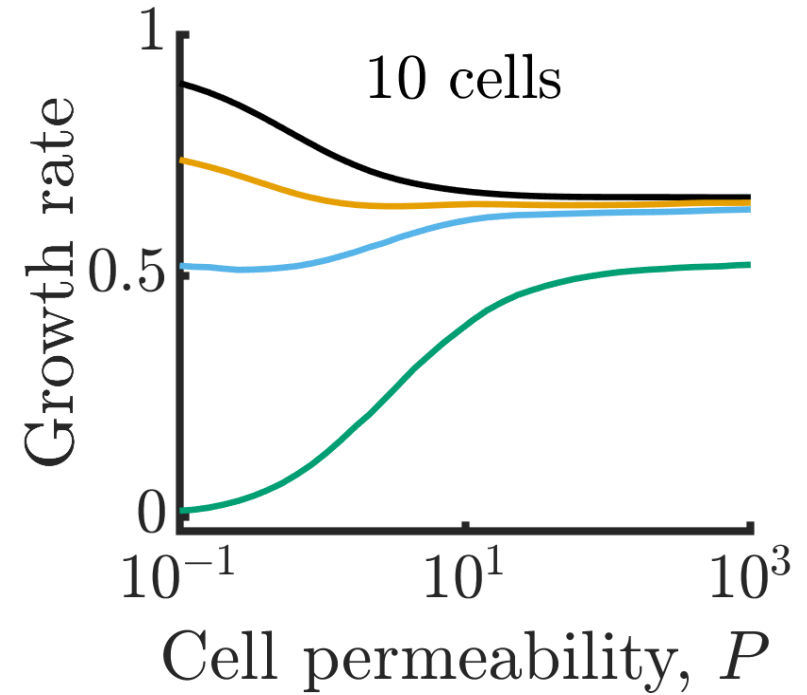
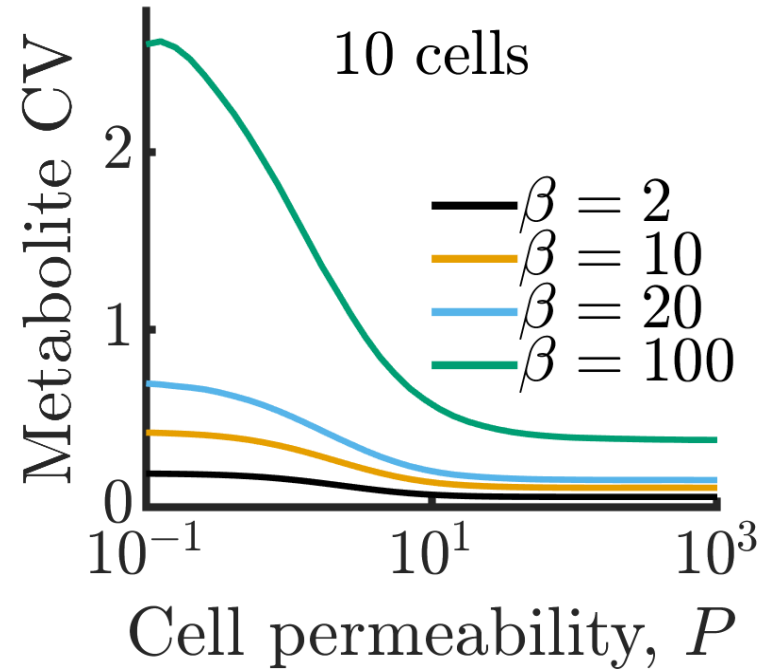
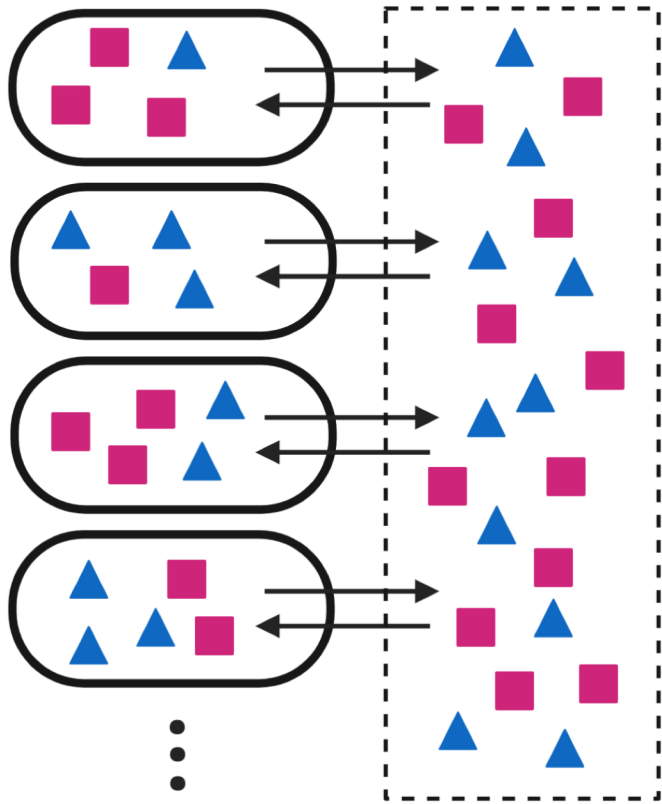
# What about leakage in a community?



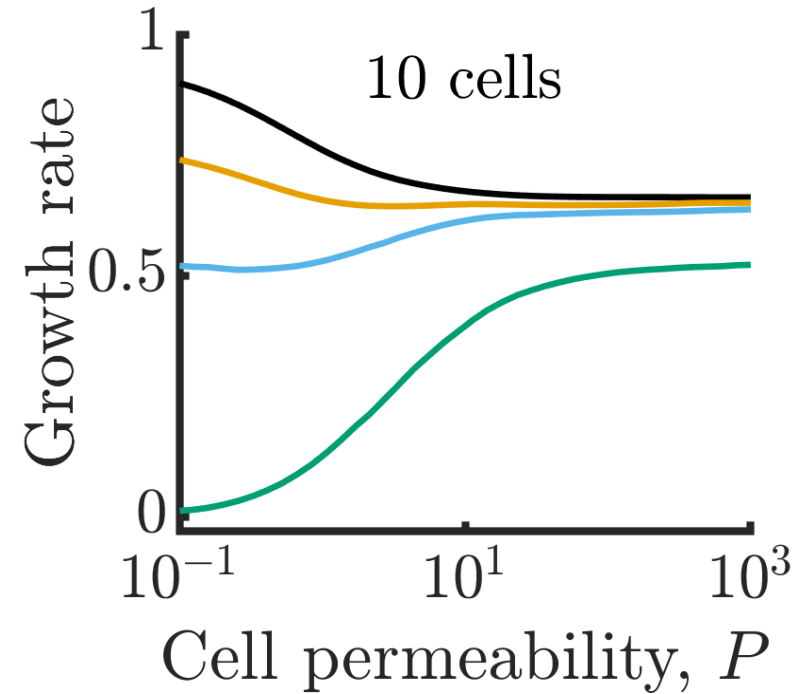
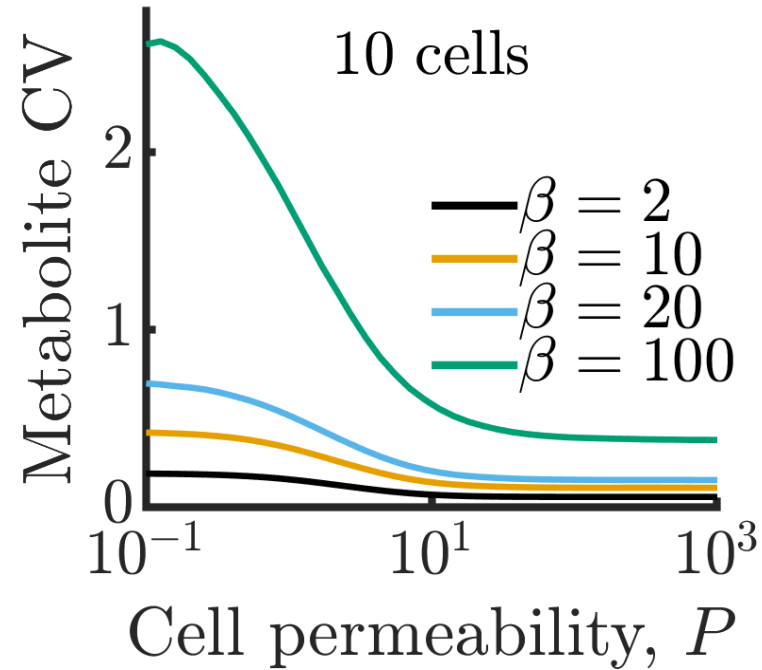
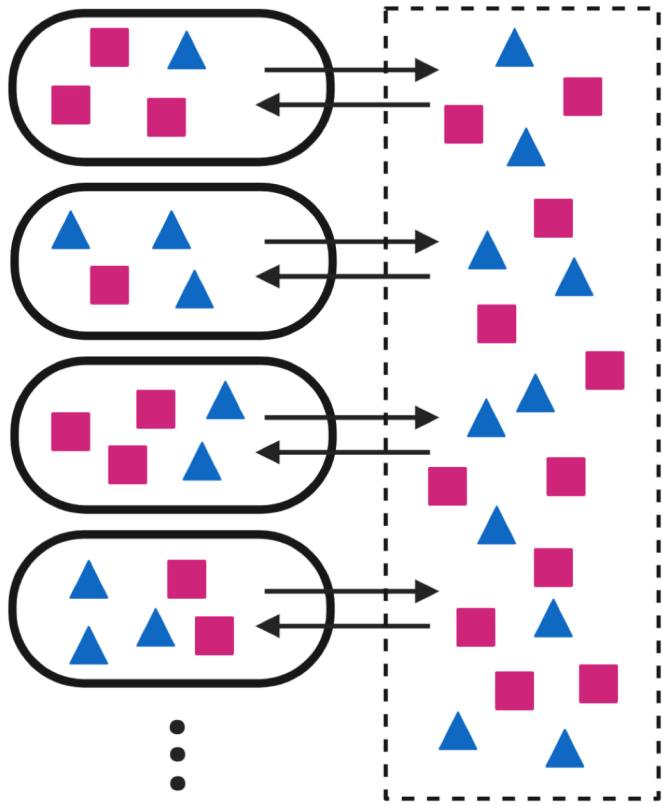
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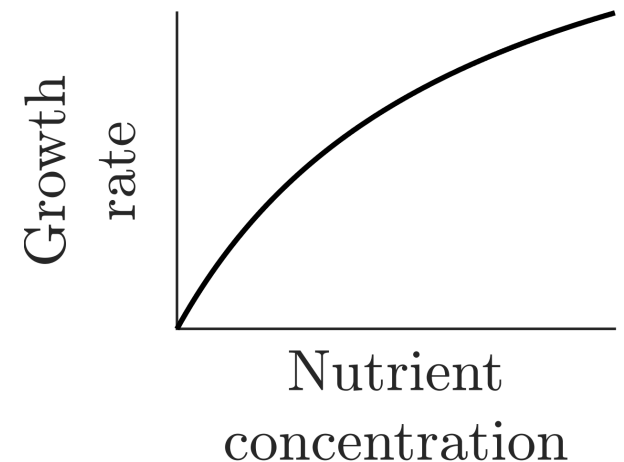
# What about leakage in a community?



$$\text{Metabolite CV} \propto \frac{1}{\sqrt{\text{Number of cells}}}$$

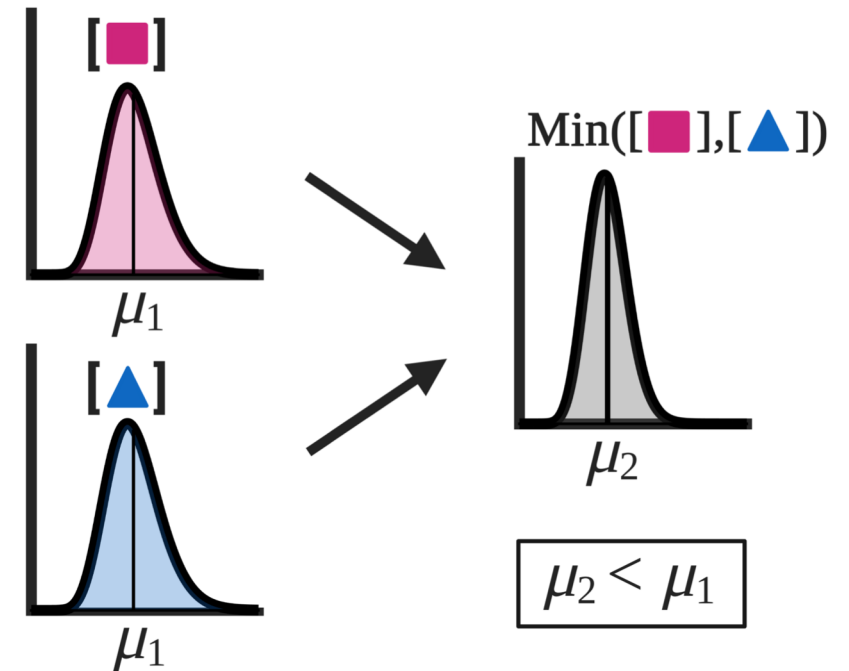
# Could this mechanism work outside of the simple model?

- For NAC to occur, the average growth must be lower than the growth at the average metabolite level
- By Jensen's Inequality, this means the growth function must be concave



# Are cells noisy enough for this mechanism to work?

- With empirical estimates of metabolite distributions, compute the distribution of growth rates given a growth function
- This gives us an estimate of whether NAC is potentially beneficial

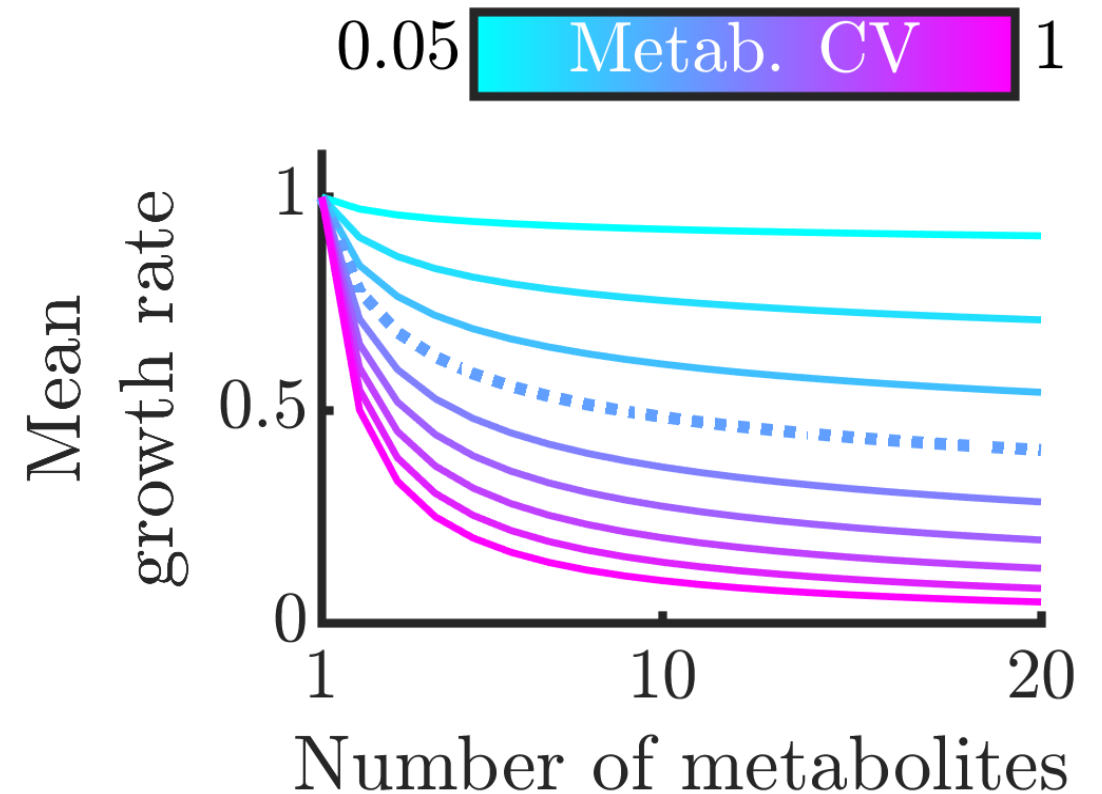


# Estimating noise-driven growth loss in *E. coli*

1. Empirical estimates of *E. coli* essential protein level distributions (Taniguchi 2011)
2. Assume metabolite noise primarily driven by enzyme noise
3. Compute growth for different numbers of limiting metabolites distributions assuming Liebig's law of the minimum

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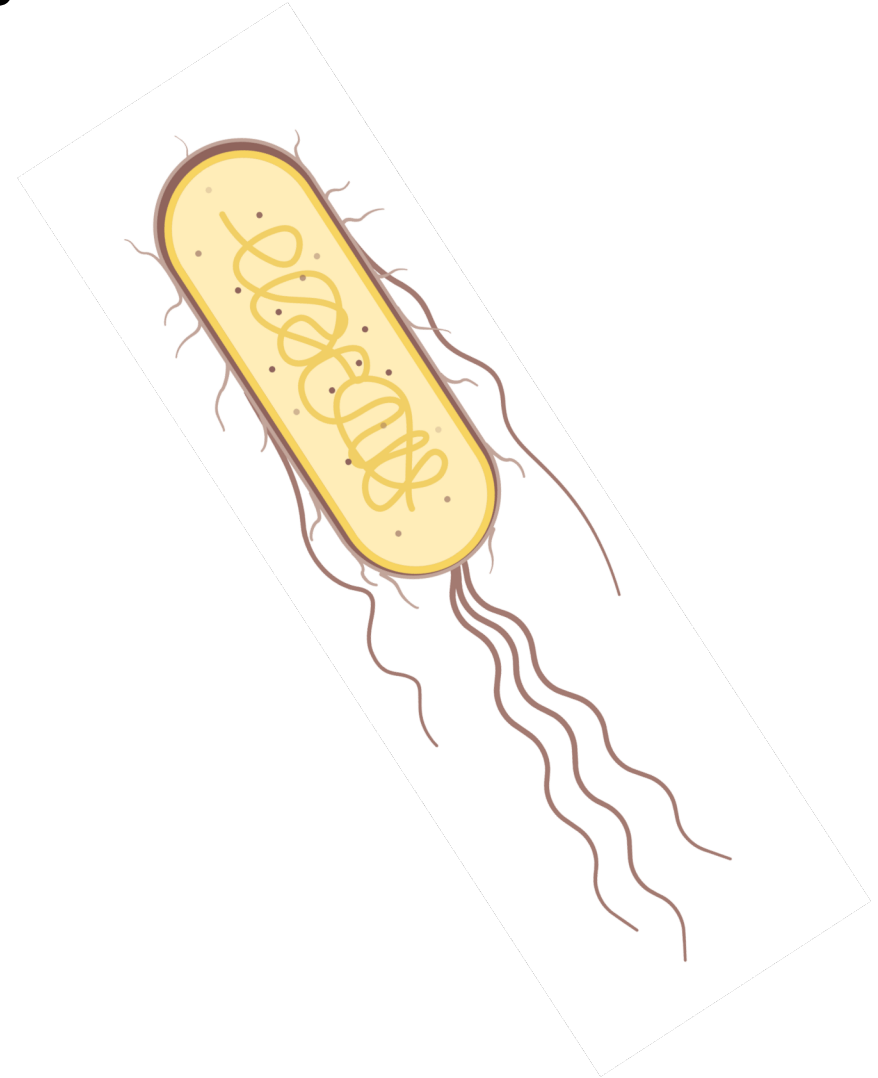
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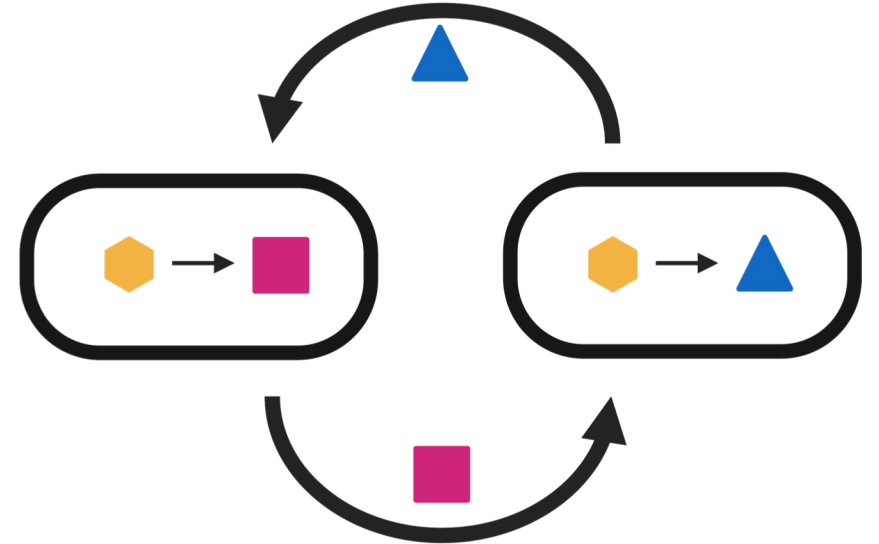
# Possible experimental ways to test for NAC

- Population-level measurements of growth rate at different densities
- Single-cell measurements of growth rate at varying densities



# Summary

- Metabolic noise can potentially promote metabolite leakage, setting the stage for cross-feeding evolution
- Whether leakage is favored depends on growth function shape, noise levels, and leakage costs
- This hypothesis is experimentally testable



# Thanks for listening!

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Center for the Physics  
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