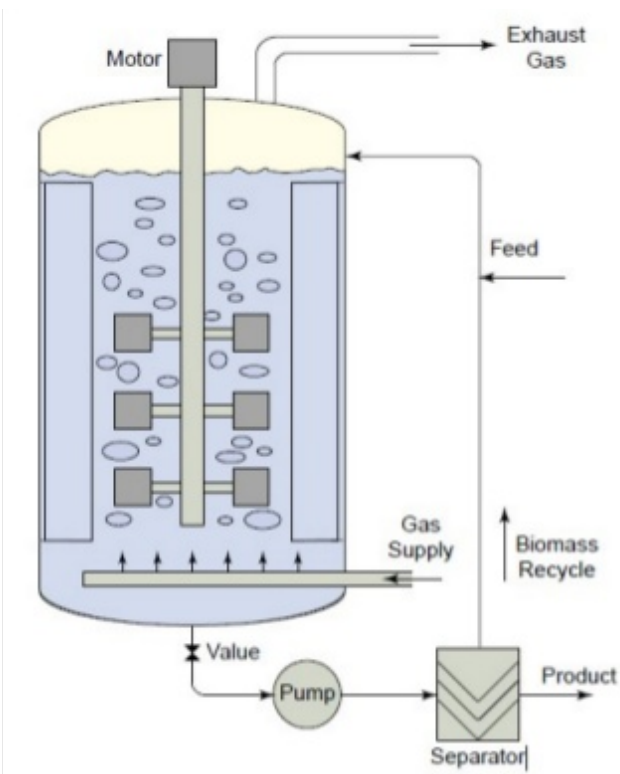
A multiscale mathematical model of bacterial nutrient uptake



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C1NET conference

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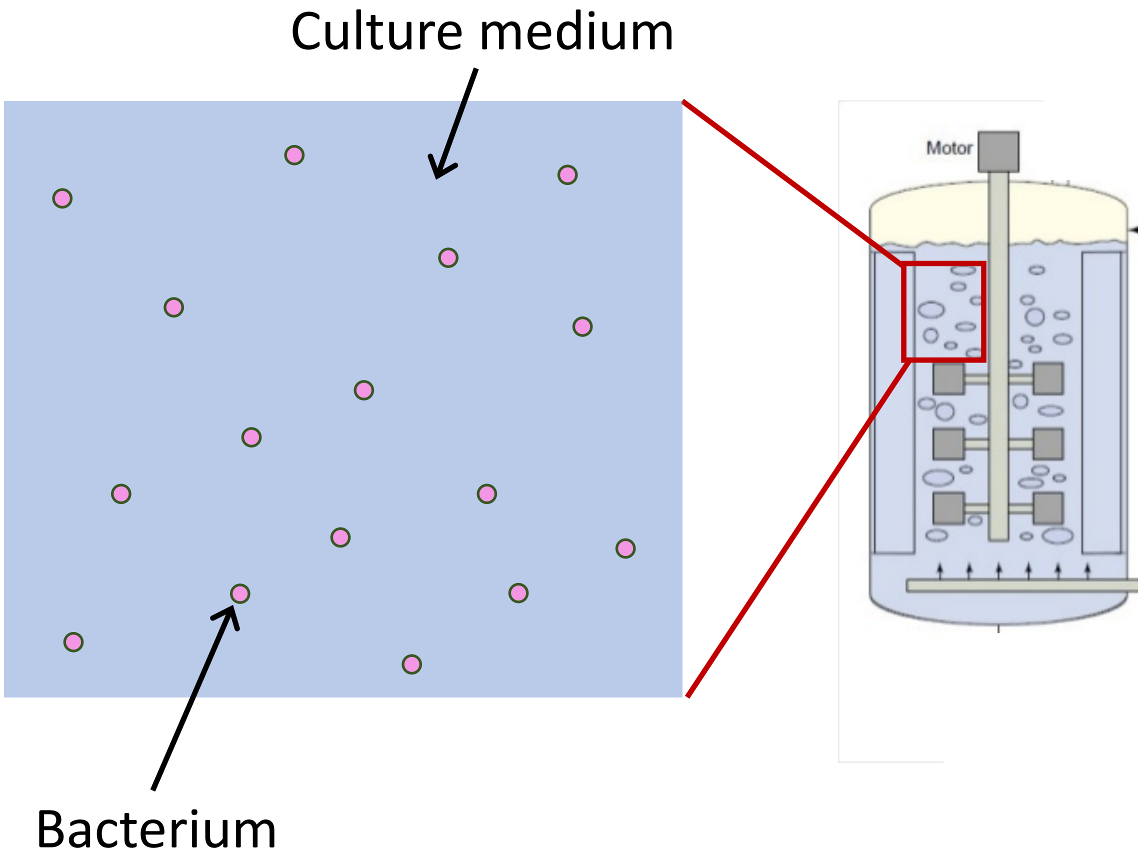
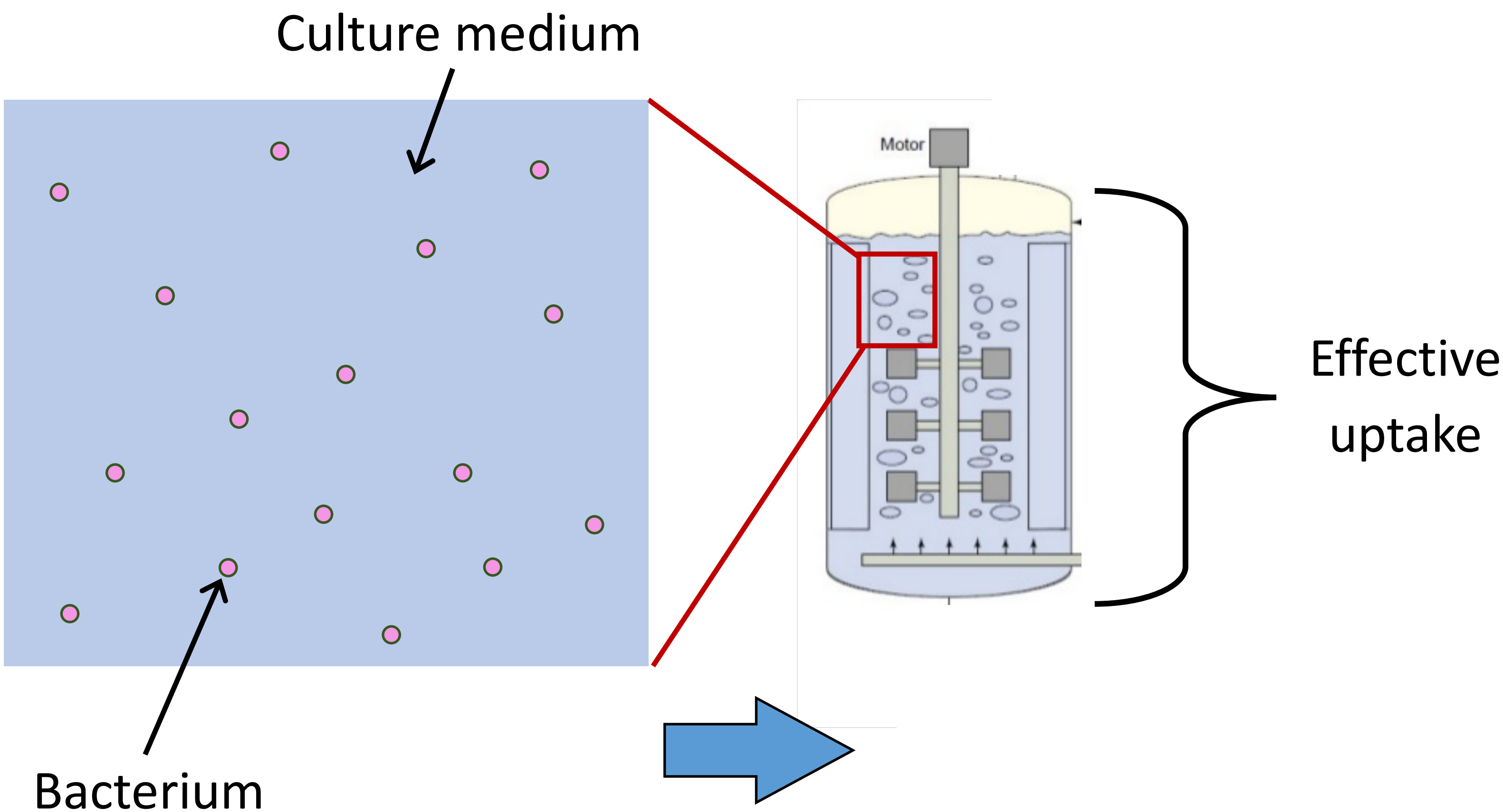
The University of Nottingham UNITED KINGDOM · CHINA · MALAYSIA

UNIVERSITY OF OXFORD Mathematical Institute

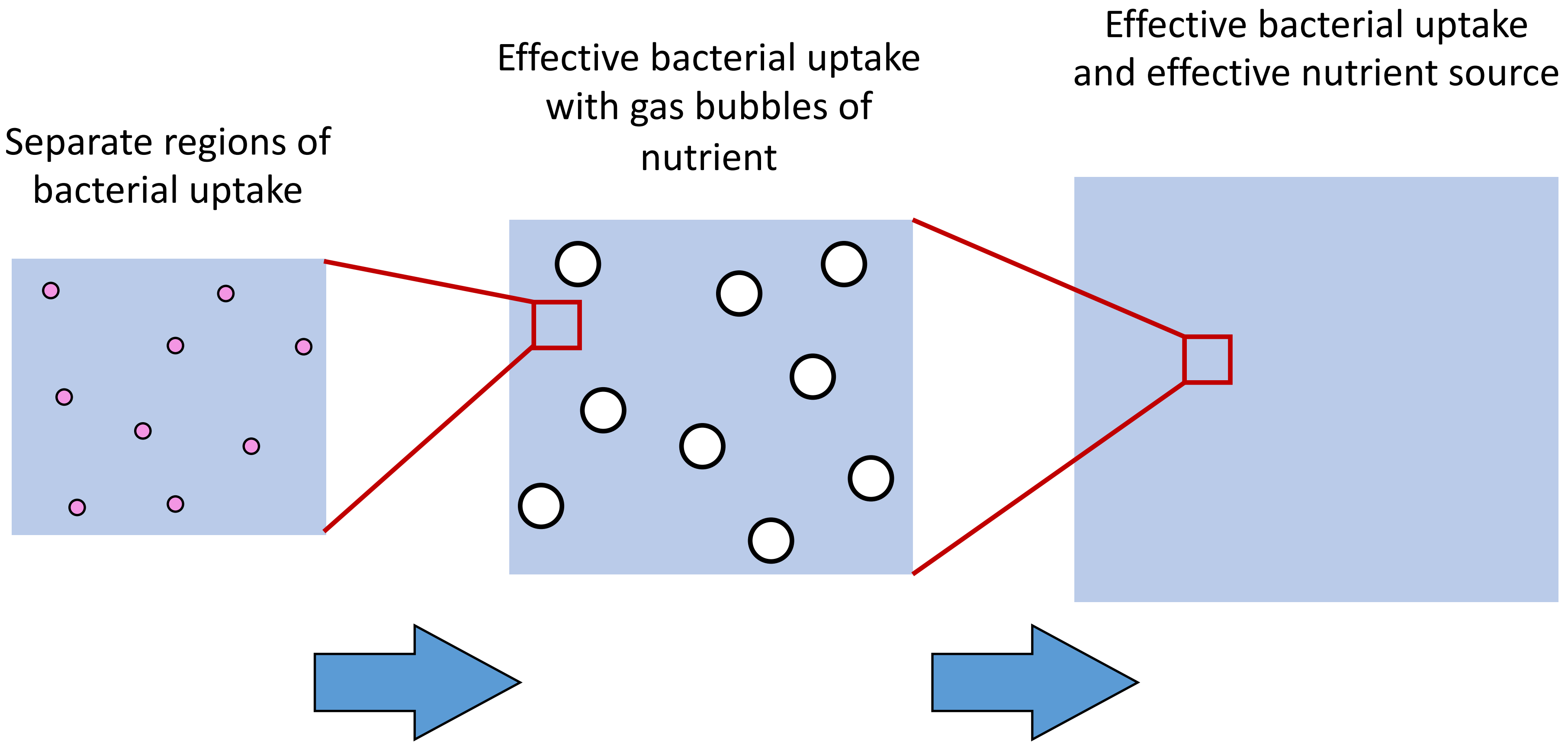
Bacterial factories



Effective nutrient uptake

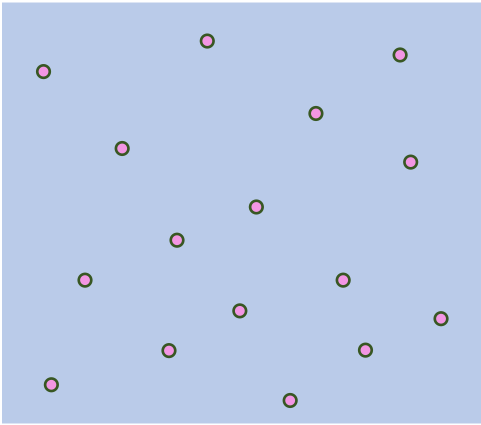


Multiscale modelling



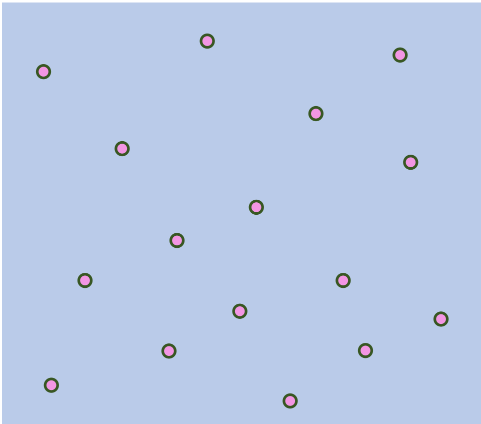
Key questions

- What form should the effective uptake take?



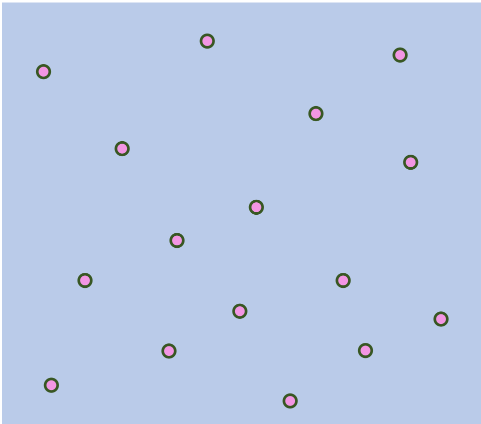
Key questions

- What form should the effective uptake take?
  - Scaling with surface area or volume?



Key questions

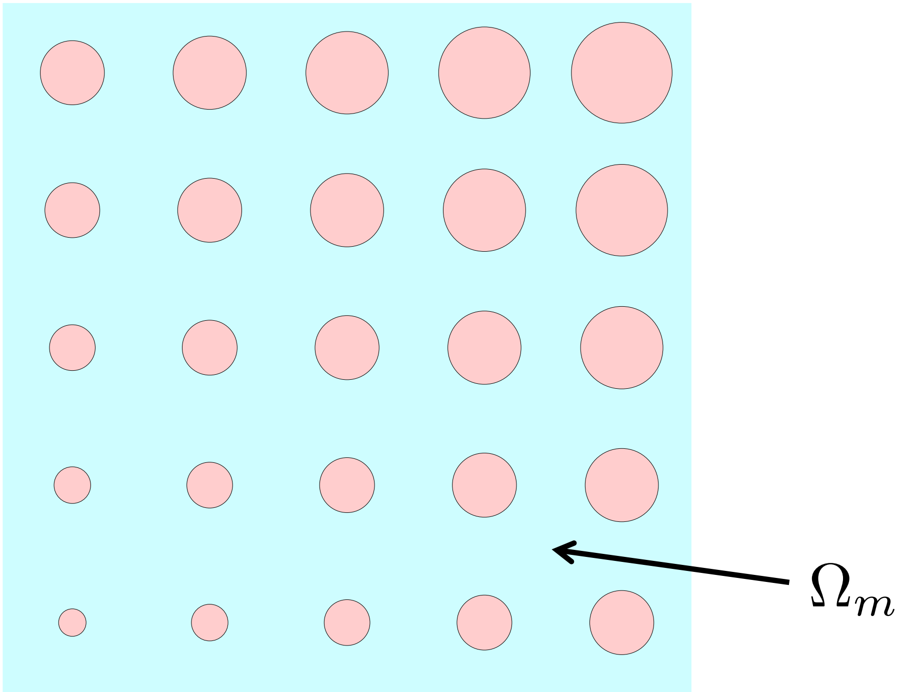
- What form should the effective uptake take?
  - Scaling with surface area or volume?
  - Can we determine how the transition between surface area and volumetric scaling occurs?



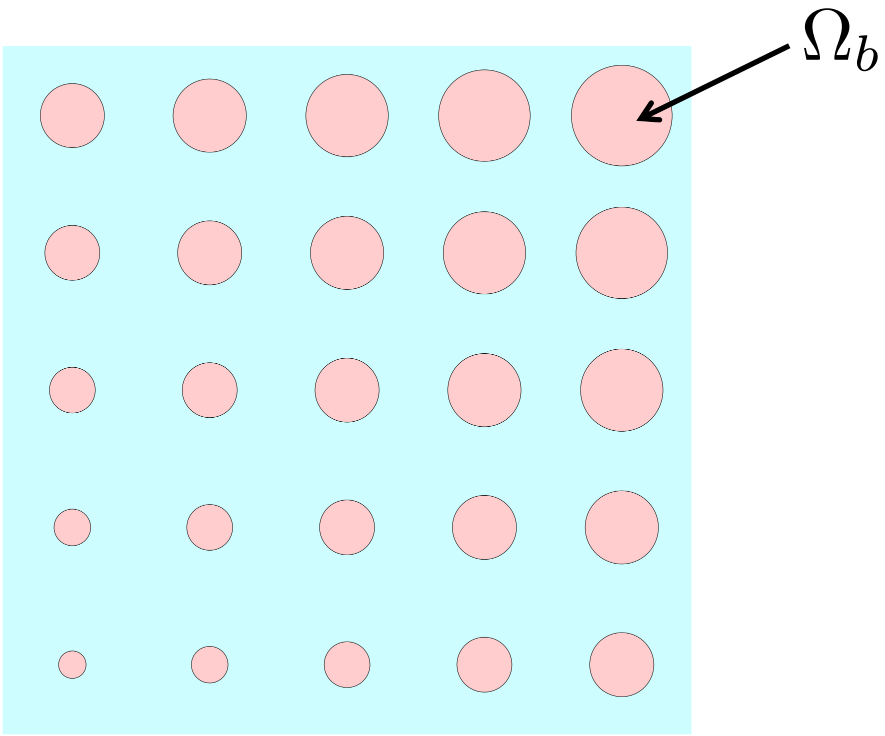
Model formulation

In culture medium

- Nutrient diffusion



Model formulation



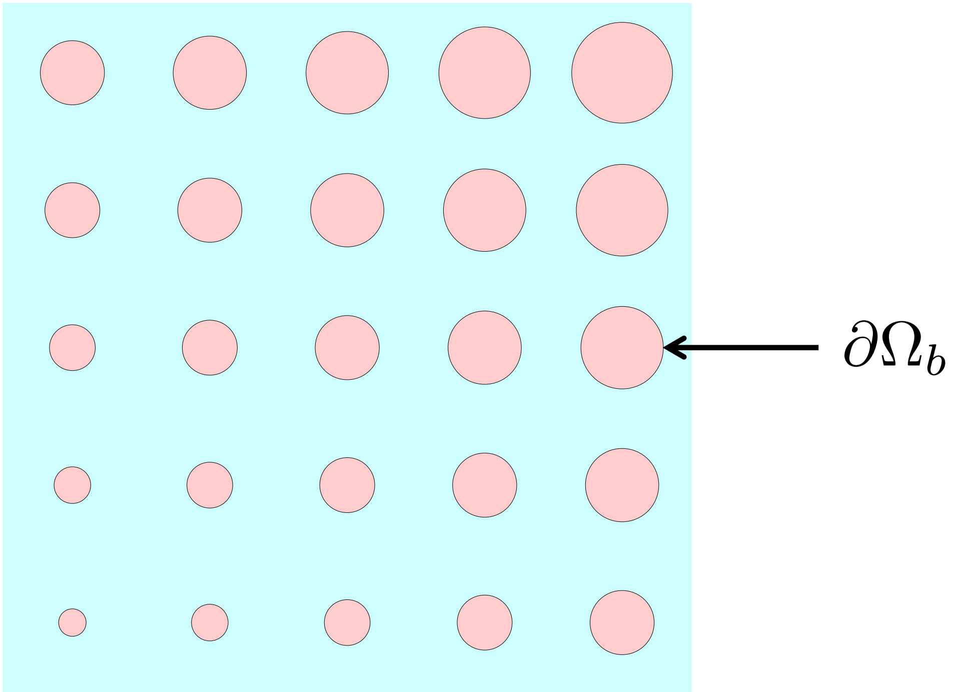
In culture medium

- Nutrient diffusion

In bacteria

- Nutrient diffusion
- Nutrient absorption

Model formulation



In culture medium

- Nutrient diffusion

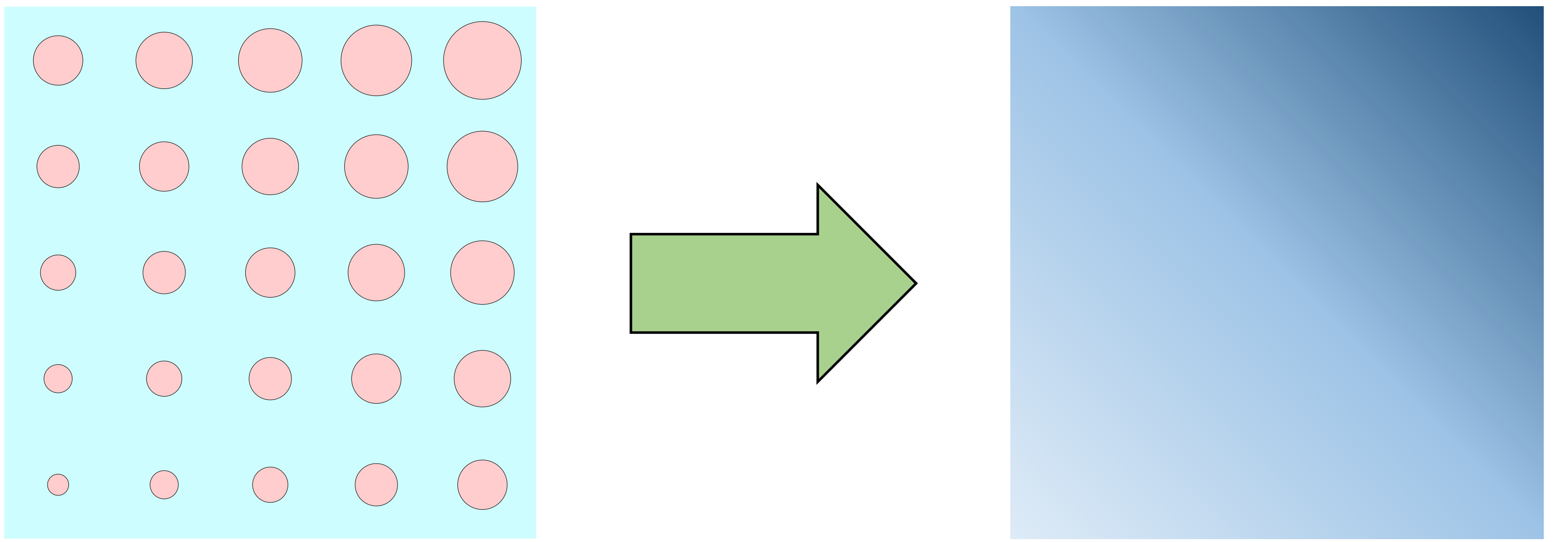
In bacteria

- Nutrient diffusion
- Nutrient absorption

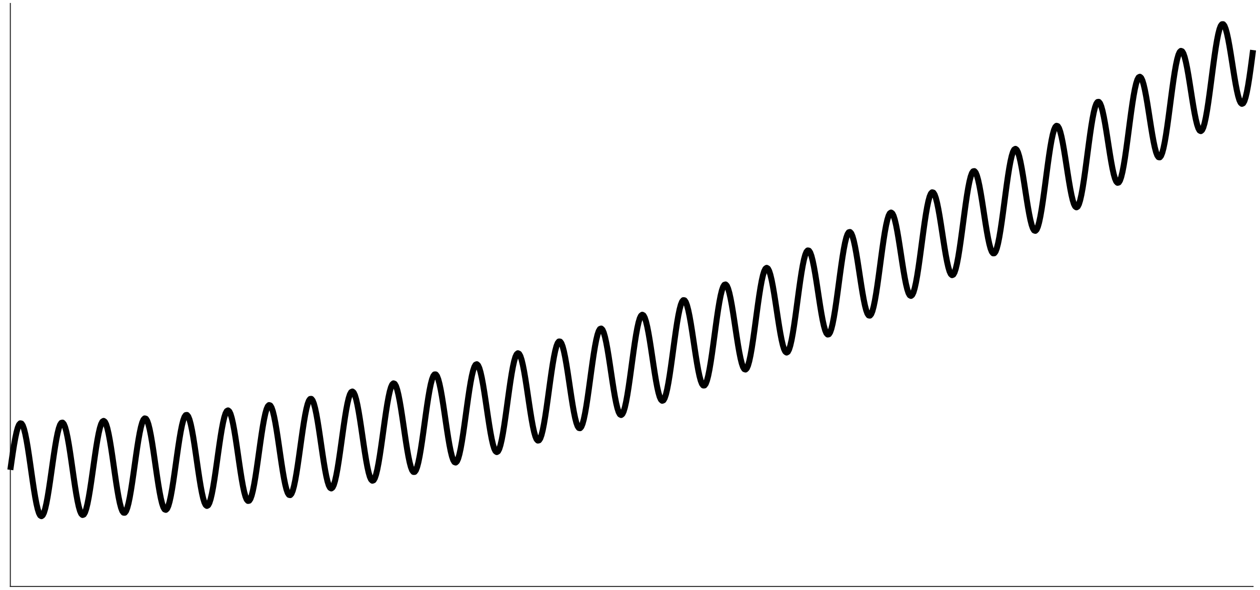
At bacterial membrane

- Nutrient flux is conserved
- Nutrient is maintained in local equilibrium

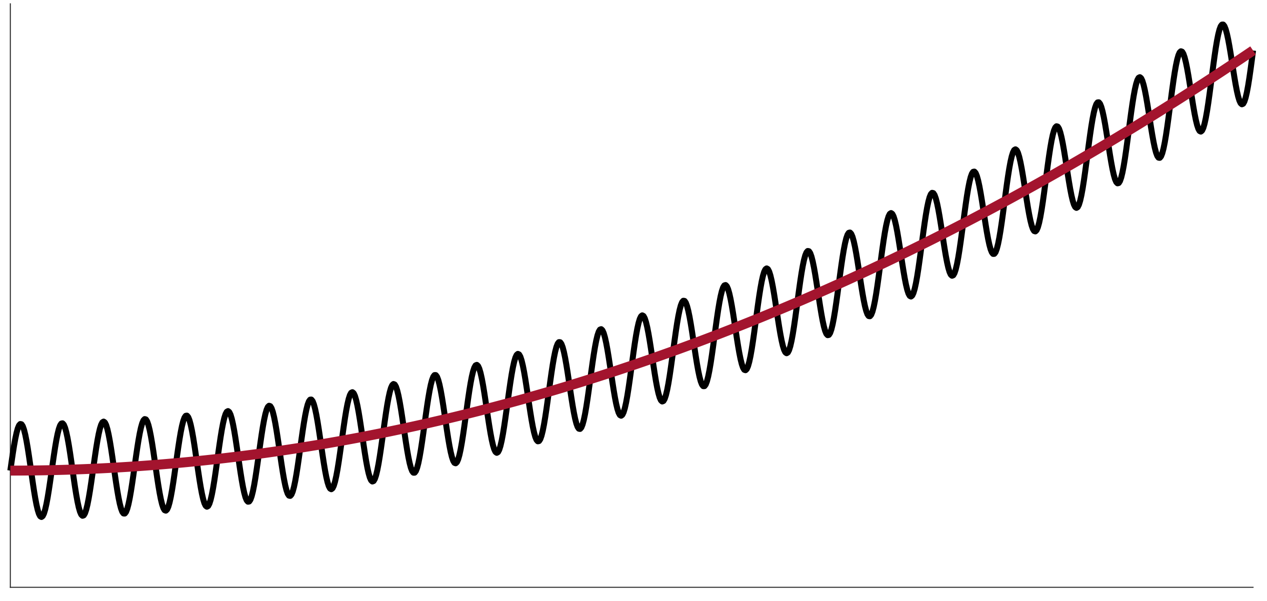
Mathematical homogenization



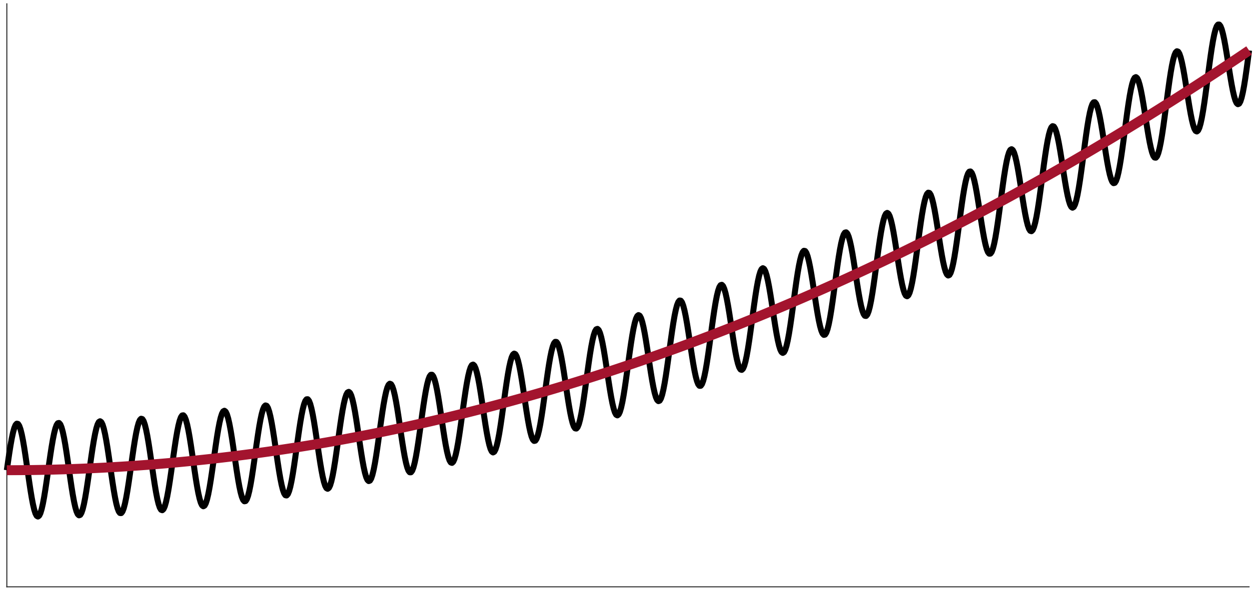
Mathematical homogenization



Mathematical homogenization

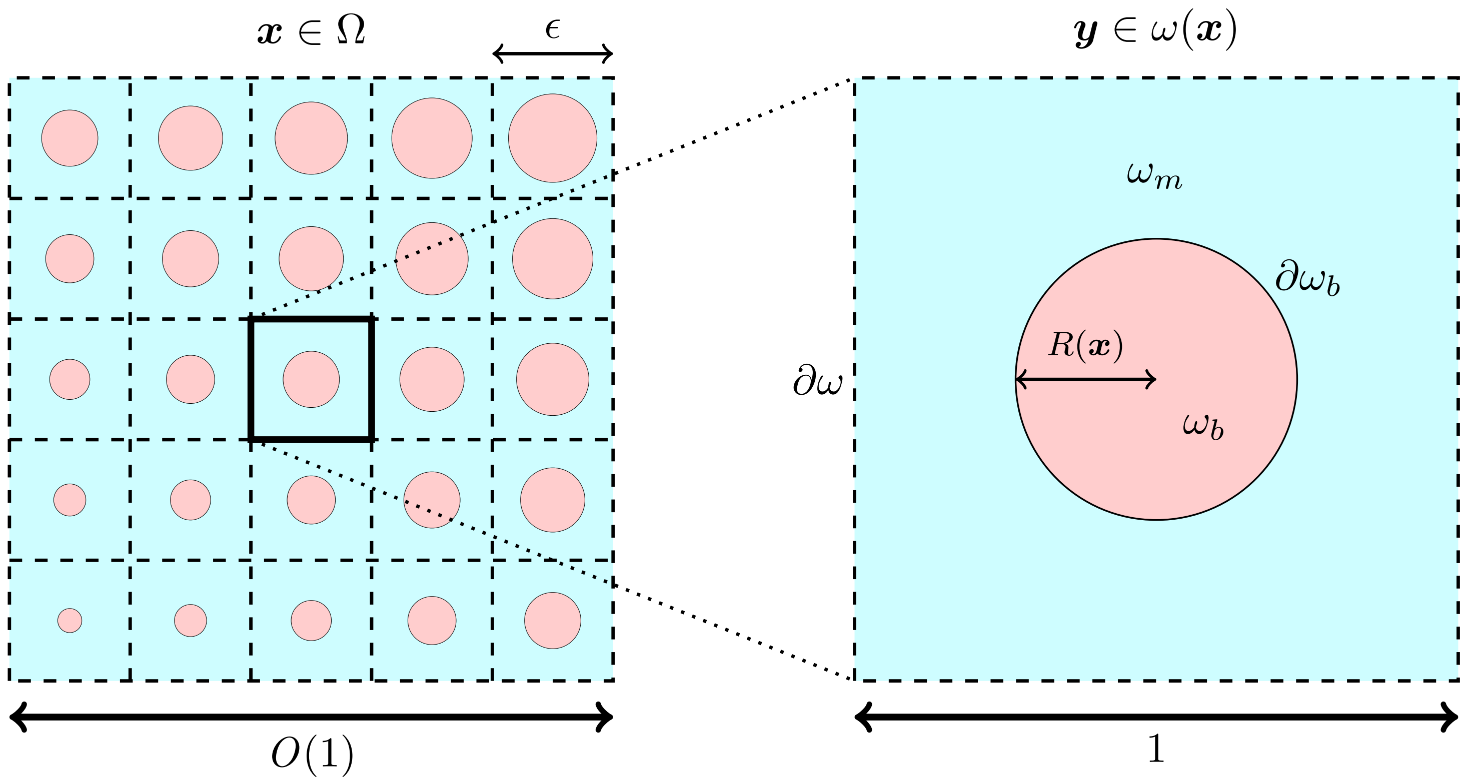


Mathematical homogenization



Goal: derive an equation for the local average from the full system

Mathematical homogenization



We want a governing equation for the locally-averaged concentration

Mathematical homogenization

$$\frac{\partial \widehat{c}}{\partial t} = \underbrace{\nabla \cdot \left(\overline{D} \nabla \widehat{c}\right)}_{\text{Effective diffusion}} - \underbrace{f\left[\widehat{c}\right]}_{\boxed{\text{Effective uptake}}}$$

Our main interest

$\overline{D}$ is an effective diffusion coefficient to be determined via homogenization

Three important cases

	Bact. diffusivity	Uptake strength	Bact. density
Case 1	Normal	Normal	Normal
Case 2	Very small	Normal	Normal
Case 3	Normal	Very large	Very sparse

Upscaling diffusion through first-order volumetric sinks: a homogenization of bacterial nutrient uptake
MP Dalwadi, Y Wang, JR King, NP Minton, *SIAM J Appl Math*, 78, pp. 1300–1329

Case 1

- This is the important problem for the effective diffusion

	Bact. diffusivity	Uptake strength	Bact. density
Case 1	Normal	Normal	Normal
Case 2	Very small	Normal	Normal
Case 3	Normal	Very large	Very sparse

Case 1

- This is the important problem for the effective diffusion
- The effective uptake scales with bacterial volume

	Bact. diffusivity	Uptake strength	Bact. density
Case 1	Normal	Normal	Normal
Case 2	Very small	Normal	Normal
Case 3	Normal	Very large	Very sparse

Case 2

- A ‘double-porosity’ model

	Bact. diffusivity	Uptake strength	Bact. density
Case 1	Normal	Normal	Normal
Case 2	Very small	Normal	Normal
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Case 2

- A 'double-porosity' model

- The effective uptake now has a memory property
  - The history of the problem is important until a steady state is reached.

	Bact. diffusivity	Uptake strength	Bact. density
Case 1	Normal	Normal	Normal
Case 2	Very small	Normal	Normal
Case 3	Normal	Very large	Very sparse

Case 2 (steady state)

$$\boxed{f[\widehat{c}] = 4\pi \hat{D} R \left(\sqrt{\hat{\mu}} R \coth \sqrt{\hat{\mu}} R - 1 \right) \widehat{c}}$$

$\hat{D}$ is bacterial diffusivity

R is bacterial radius

$\hat{\mu}$ is actual (pointwise) strength of uptake

Case 2 (steady state)

$$\boxed{f\left[\widehat{c}\right] = 4\pi \hat{D} R \left(\sqrt{\hat{\mu}} R \coth \sqrt{\hat{\mu}} R - 1 \right) \widehat{c}}$$

$f\left[\widehat{c}\right]$ scales with bacterial surface area for strong uptake

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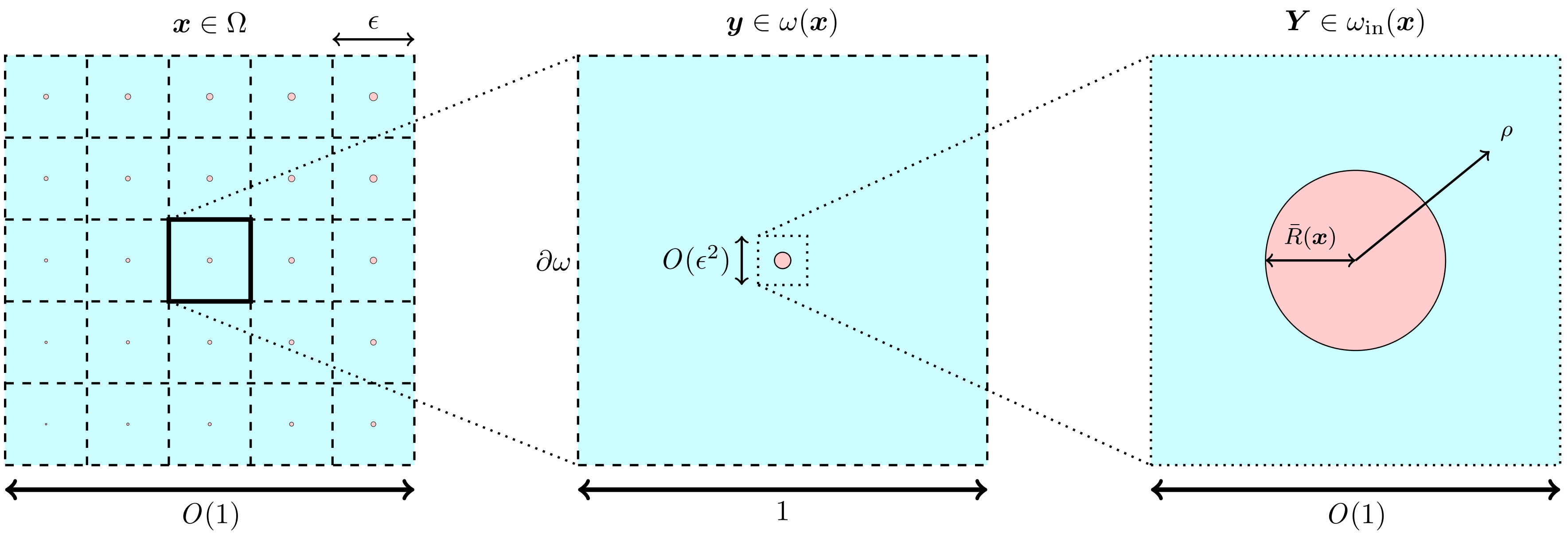
$$\boxed{f\left[\widehat{c}\right] = 4\pi \hat{D} R \left(\sqrt{\hat{\mu}} R \coth \sqrt{\hat{\mu}} R - 1 \right) \widehat{c}}$$

$f\left[\widehat{c}\right]$ scales with bacterial surface area for strong uptake

$f\left[\widehat{c}\right]$ scales with bacterial volume for weak uptake

Case 3



	Bact. diffusivity	Uptake strength	Bact. density
Case 1	Normal	Normal	Normal
Case 2	Very small	Normal	Normal
Case 3	Normal	Very large	Very sparse

Case 3

$$\boxed{f\left[\widehat{c}\right] = \frac{4\pi D\bar{R}\left(\sqrt{\bar{\mu}}\bar{R}\coth\sqrt{\bar{\mu}}\bar{R}-1\right)}{1+D\left(\sqrt{\bar{\mu}}\bar{R}\coth\sqrt{\bar{\mu}}\bar{R}-1\right)}\widehat{c}}$$

	Bact. diffusivity	Uptake strength	Bact. density
Case 1	Normal	Normal	Normal
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Case 3

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$f\left[\widehat{c}\right]$ scales with bacterial volume for weak uptake

Case 3

$$\boxed{f\left[\widehat{c}\right] = \frac{4\pi D\bar{R}\left(\sqrt{\bar{\mu}}\bar{R}\coth\sqrt{\bar{\mu}}\bar{R} - 1\right)}{1 + D\left(\sqrt{\bar{\mu}}\bar{R}\coth\sqrt{\bar{\mu}}\bar{R} - 1\right)}\widehat{c}}$$

$f\left[\widehat{c}\right]$ scales with bacterial volume for weak uptake

$f\left[\widehat{c}\right]$ scales with bacterial surface area for low diffusivity

Case 3

$$\boxed{f\left[\widehat{c}\right] = \frac{4\pi D\bar{R}\left(\sqrt{\bar{\mu}}\bar{R}\coth\sqrt{\bar{\mu}}\bar{R} - 1\right)}{1 + D\left(\sqrt{\bar{\mu}}\bar{R}\coth\sqrt{\bar{\mu}}\bar{R} - 1\right)}\widehat{c}}$$

$f\left[\widehat{c}\right]$ scales with bacterial volume for weak uptake

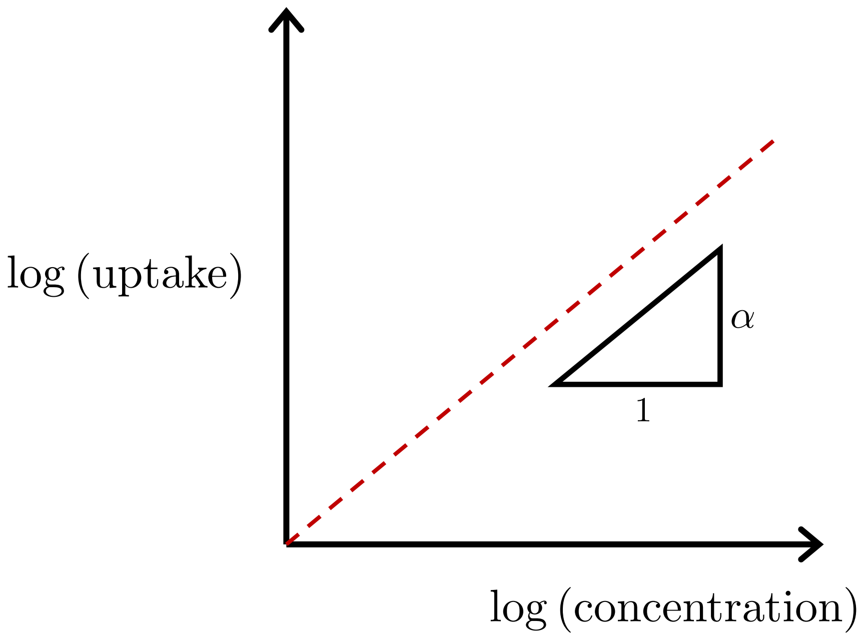
$f\left[\widehat{c}\right]$ scales with bacterial surface area for low diffusivity

$f\left[\widehat{c}\right]$ scales with bacterial radius for strong uptake

Extension to nonlinear uptake

(when the dissolved gas concentration is small)

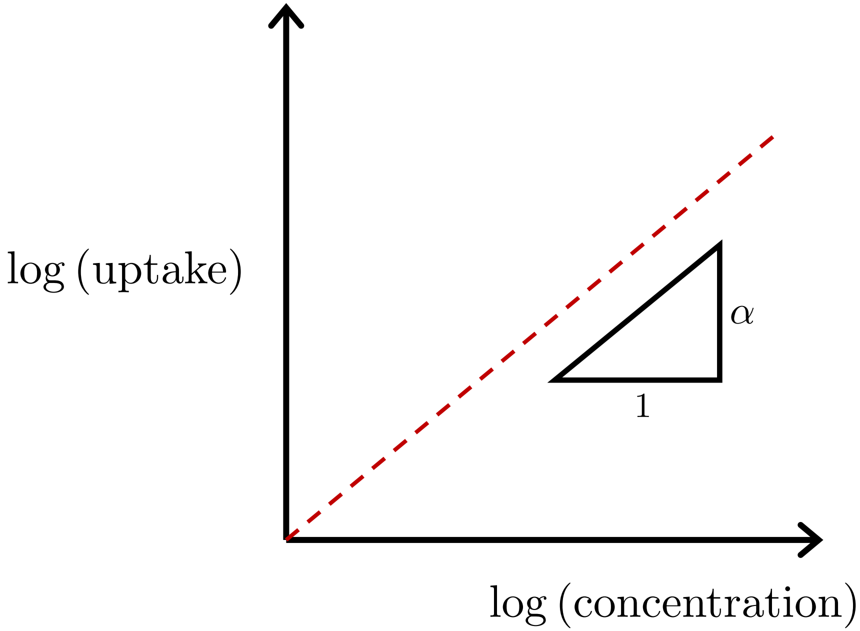
- Sub-linear uptake can be detected



Extension to nonlinear uptake

(when the dissolved gas concentration is small)

- Sub-linear uptake can be detected
- Measurements cannot discern between super-linear and linear uptake



Conclusions

- We systematically derived the effective uptake for nutrient diffusing through a colony of bacteria.
- We found how the effective uptake smoothly transitions between scaling with the bacterial radius, surface area, and volume.
- Our model allows us to determine *when* we will be able to deduce bacterial properties from experimental observation.

Acknowledgements

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