MSc Computational Science
joint programme UvA/VU

MODELLING DIFFUSIVE SIGNALLING IN *ASPERGILLUS* SPP. GERMINATION INHIBITION

INTERMEDIATE PRESENTATION - APRIL

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April 4, 2025

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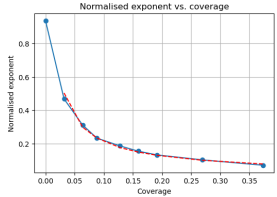
OUTLINE

INTRODUCTION

Effect of spore clusters on inhibitor decay

- Previously the **high-resolution model** showed that
  - the number of neighbours influences the inhibitor decay from the spore wall,
  - the distance between neighbours did not influence the inhibitor decay from the spore wall.
- The latter result was likely due to the **tight spatial constraint** (large high-resolution lattices are hard to compute).
- Furthermore, the high-resolution model uses an **implicit solver**, while the low- and medium-resolution models use an **explicit solver**.
- The cluster effect needs to be **verified across all model resolutions**.



OUTLINE

CLUSTERS ACROSS MODEL SCALES

Implicit vs. explicit solving

- The implicit method (backward Euler) [1] updates the lattice concentrations by solving a system of linear equations (matrix operations).
  - **unconditionally stable**
  - **first-order accurate** (the global error scales linearly with the simulation timestep Δt)
  - **large time steps** are possible, leading to shorter simulation time
  - **small time steps** may cause changes smaller than the computer accuracy, leading to simulations standing still
- The explicit method (forward Euler) [1] updates the lattice concentrations by "depositing" concentrations from a lattice node to its neighbours.
  - only **stable for small enough simulation timesteps**
  - **first-order accurate** (the global error scales linearly with Δt).
  - **large time steps** are not possible due to stability issues
  - **small time steps** may cause standstill of simulations

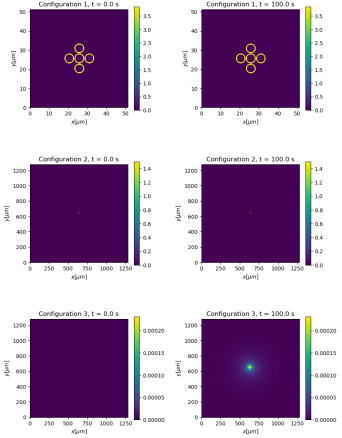
$$\frac{\partial c}{\partial t} = D\nabla^2 c \quad (1)$$

CLUSTERS ACROSS MODEL SCALES

Comparison setup

- Clusters of 2, 3, 6 and 7 spores are simulated with
  - spore-to-spore distance $2R < d < 5R$ in **high-resolution** simulations;
  - spore-to-spore distance $4R < d < 40R$ in **medium-resolution** simulations;
  - spore-to-spore distance $8R < d < 40R$ in **low-resolution** simulations;
- Measuring the exponent α in the inhibitor decay relationship

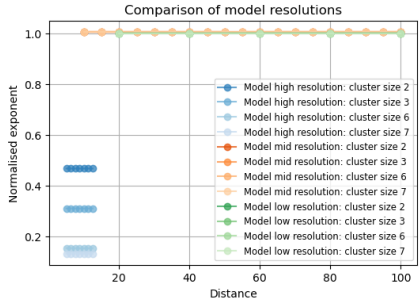
$$c_{\text{in}}(t) = c_0 e^{-\alpha \frac{t}{\tau}}, . \tag{2}$$



CLUSTERS ACROSS MODEL SCALES

Comparison results

- The blocking effect of neighbours is not detectable beyond $d > 4R$ using the **explicit method** (medium and low resolution).
- In contrast, the blocking effect is persistent over the range $2R < d < 5R$ using the **implicit method** (high resolution).
- Despite being stable at large timesteps, the **error** of the implicit error might be high and the **narrow boundary** of the high-resolution lattice may bias the results.

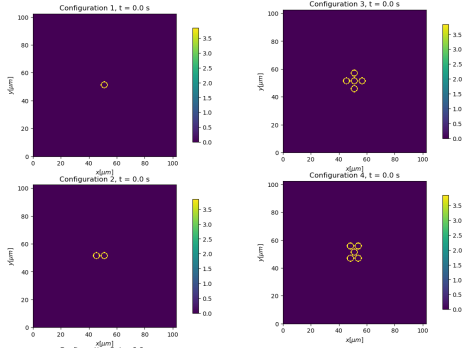


OUTLINE

ADJUSTMENT OF THE HIGH-RESOLUTION MODEL

Overview of adjustment

- Examining the potential errors in the high-resolution model, a step is made to bridge its gap toward the medium-resolution model.
- The spatial subdivision is changed from $\Delta x = 0.2\ \mu$m to $\Delta x = 0.4\ \mu$m.
- Clusters of size 1, 2, 7 and 13 are simulated using both an **implicit** method and an **explicit** method with varying spore-to-spore distance.
- Pending results: the goal is to confirm whether the **neighbour-blocking effect persists at longer ranges**.



OUTLINE

NEXT STEPS

Putting together a universal model

- If a spore is surrounded by adjacent neighbours, the effective cell wall area for inhibitor permeation is reduced by a factor α.
- The characteristic time for inhibitor permeation is

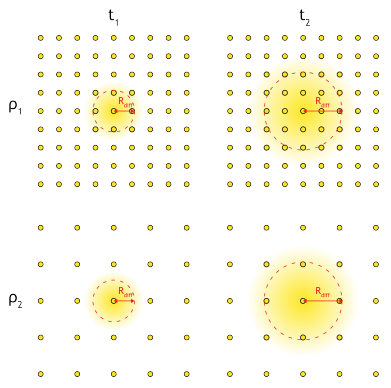
$$\tau = \frac{P_s A_{\text{eff}}}{V} = \frac{P_s A_{\text{spore}}}{V\alpha}. \tag{3}$$

- The inhibitor concentration in the spore is

$$c_{\text{in}}(t) = (c_0 + c_{\text{out}})\, e^{-\frac{t}{\tau}}, \tag{4}$$

where, at a moderate spore density ρ_s,

$$c_{\text{out}} = \rho_s \frac{A P_s c_0}{4\pi D^{3/2}} \int_0^{R_{\text{diff}}} dr\, r^2 \int_0^t t'^{-3/2} e^{\left(\tau t' - \frac{r^2}{4Dt'}\right)} dt'. \tag{5}$$



NEXT STEPS

To do

1. Verify the dependence of the decay exponent α on the number of spore neighbours.
2. Identify whether α only applies for close or adjacent neighbours.
   - If it does, the neighbour-blocking of cell wall permeation can be **decoupled** as a phenomenon from the effect of the general inoculum density ρ_s.
   - If it doesn't, then the two phenomena could potentially be **reduced** to a single relationship.
3. Refine the formula for c_{out} so it becomes valid for higher spore densities.
4. Fit combinations of ρ_s, P_s and $\langle N_{\text{neighbours}} \rangle$ to empirical data.
5. Interpret what the fitted P_s means in terms of molecular properties.

BIBLIOGRAPHY I

[1] Michael T. Heath and Eric M. Munson. “Scientific Computing: An Introductory Survey”. In: 1996. URL: https://api.semanticscholar.org/CorpusID:267834859.