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Spatiotemporal modelling of immobilized cell growth

to predict emerging 3D cell architectures and individual-based behaviours

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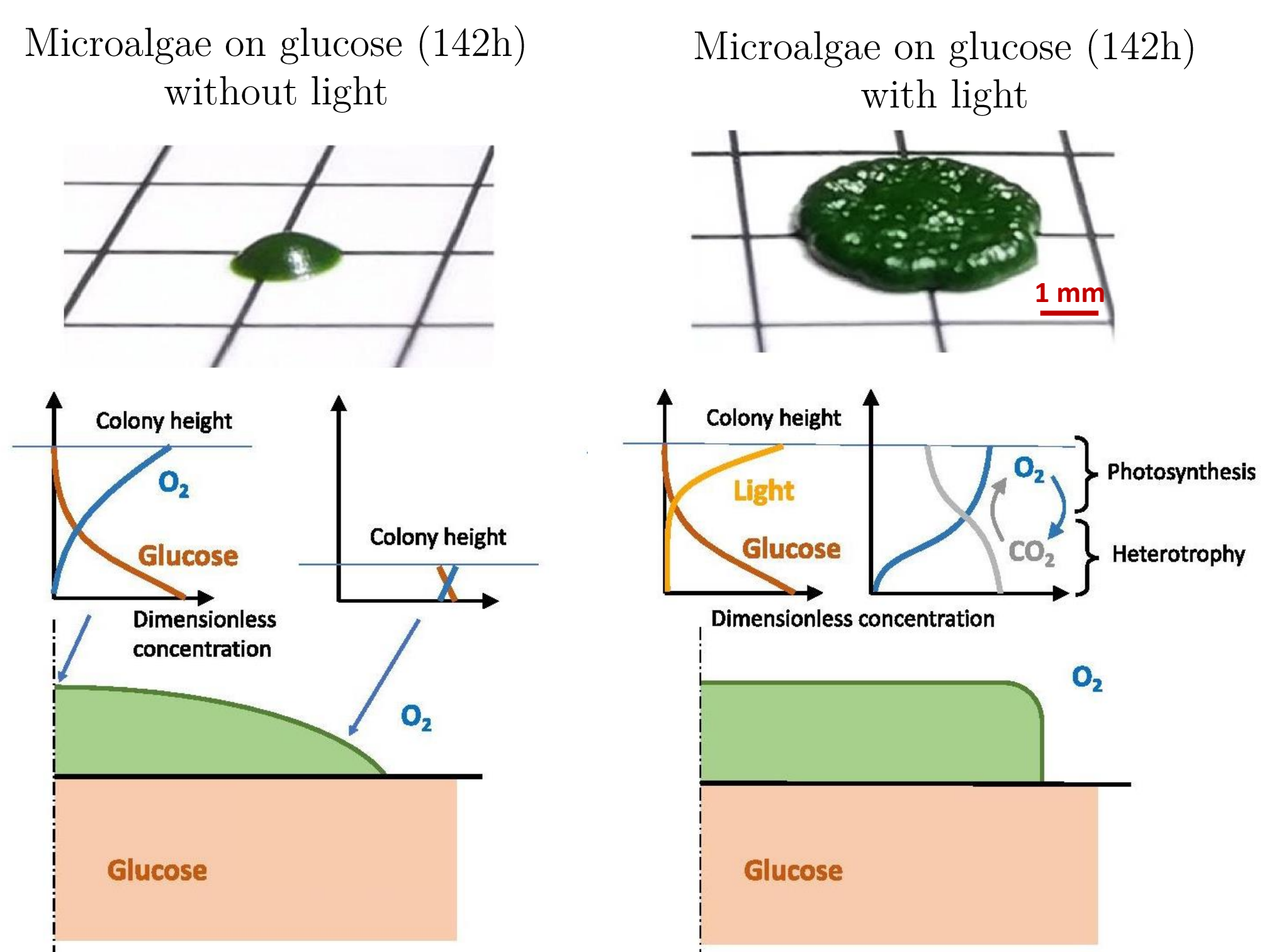


Context

Animal tissue engineering } Cell propagation on surfaces, with emerging properties
Microalgae biofilm culture }

Immobilized cultures:

- Stable gradients of growth conditions
- Local interactions prevail → Possibility of behaviour differentiation

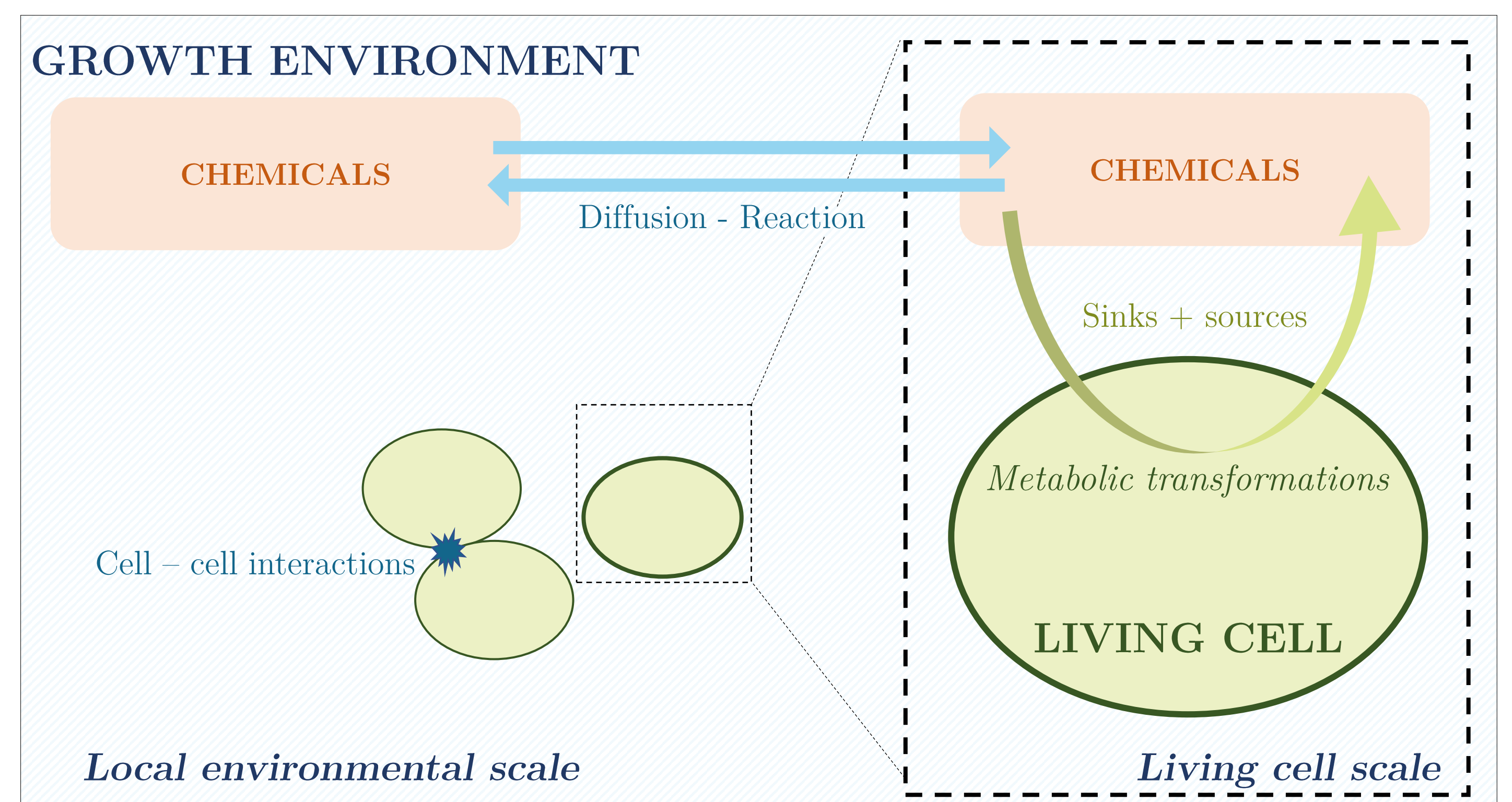


(top) Photos of microalgal colony morphology;
(bottom) Schematic diagram of the microenvironment and metabolism in the colony.
Figure adapted from Zhang and Perré, 2020¹

Behaviour emerges from interactions between:

- Diffusion and reaction of compounds in the growth environment
- Sinks and sources of compounds due to the biological behaviour of individual cells
- Local-range cell-to-cell interactions (mechanics, quorum sensing)

➤ Hybrid (continuous + discrete) modelling approach

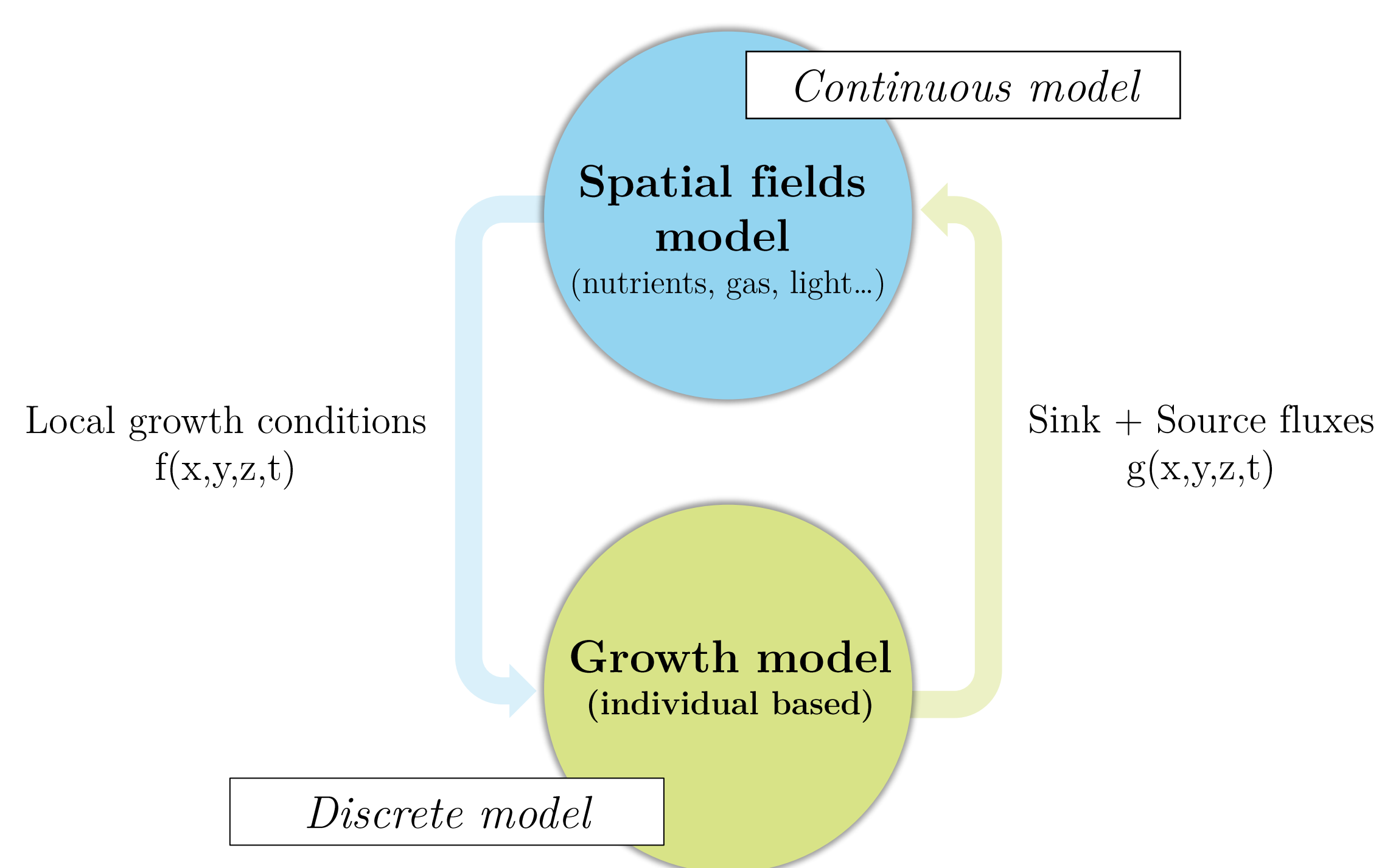


The phenomena leading to emerging behaviour happen at different scales

Theoretical approach

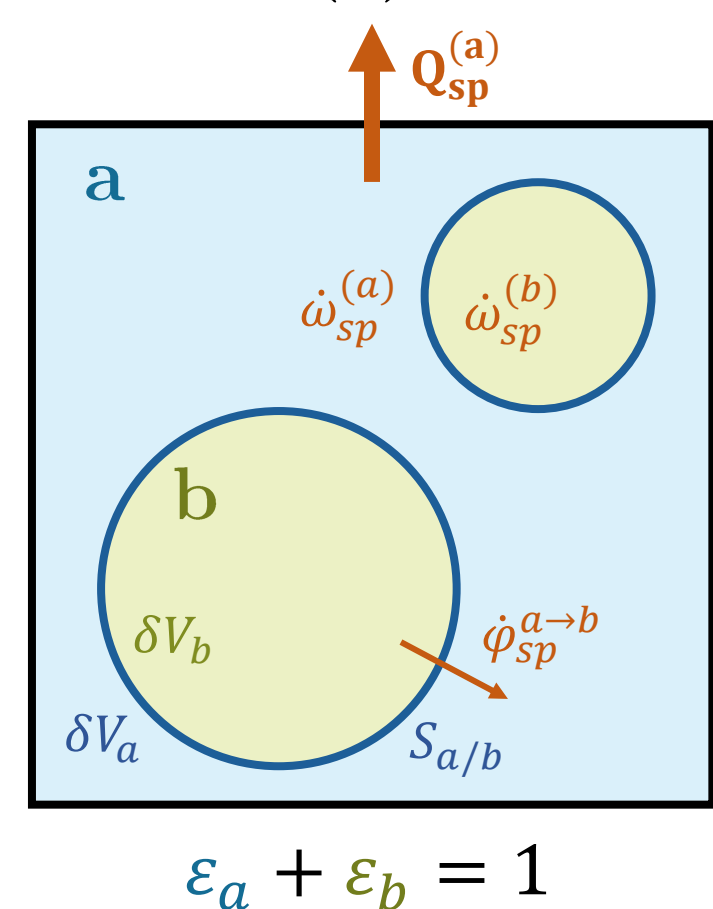
What description suits this situation best?

- Continuous model for environmental variables
- Individual-based (discrete) model for biological agents



Diffusion-reaction in a two-compartment system:

Abiotic phase (a)
Biotic phase (b): set of agents



For each chemical species sp considered:

$$\frac{\partial}{\partial t}(m_{sp}^{(a)}) + \delta V \nabla \cdot \mathbf{Q}_{sp}^{(a)} = \delta V \omega_{sp}^{(a)} + S_{a/b} \omega_{sp}^{b \rightarrow a}$$

$$\frac{\partial}{\partial t}(m_{sp}^{(b)}) + \delta V \nabla \cdot \mathbf{Q}_{sp}^{(b)} = \delta V \omega_{sp}^{(b)} + S_{a/b} \omega_{sp}^{a \rightarrow b}$$

$\mathbf{Q}_{sp}^{(a)} = \mathbf{j}_{sp}^{(a)}$ Advection is neglected in (a)
 $\mathbf{Q}_{sp}^{(b)} = \mathbf{j}_{sp}^{(b)}$ Advection and diffusion neglected in (b)
 $\omega_{sp}^{(a)} = 0$ No chemical transformation in (a)

$$\frac{\partial}{\partial t}(\varepsilon_a \rho_{sp}^{(a)}) + \nabla \cdot \mathbf{j}_{sp}^{(a)} = \Sigma_{a/b} \omega_{sp}^{b \rightarrow a}$$

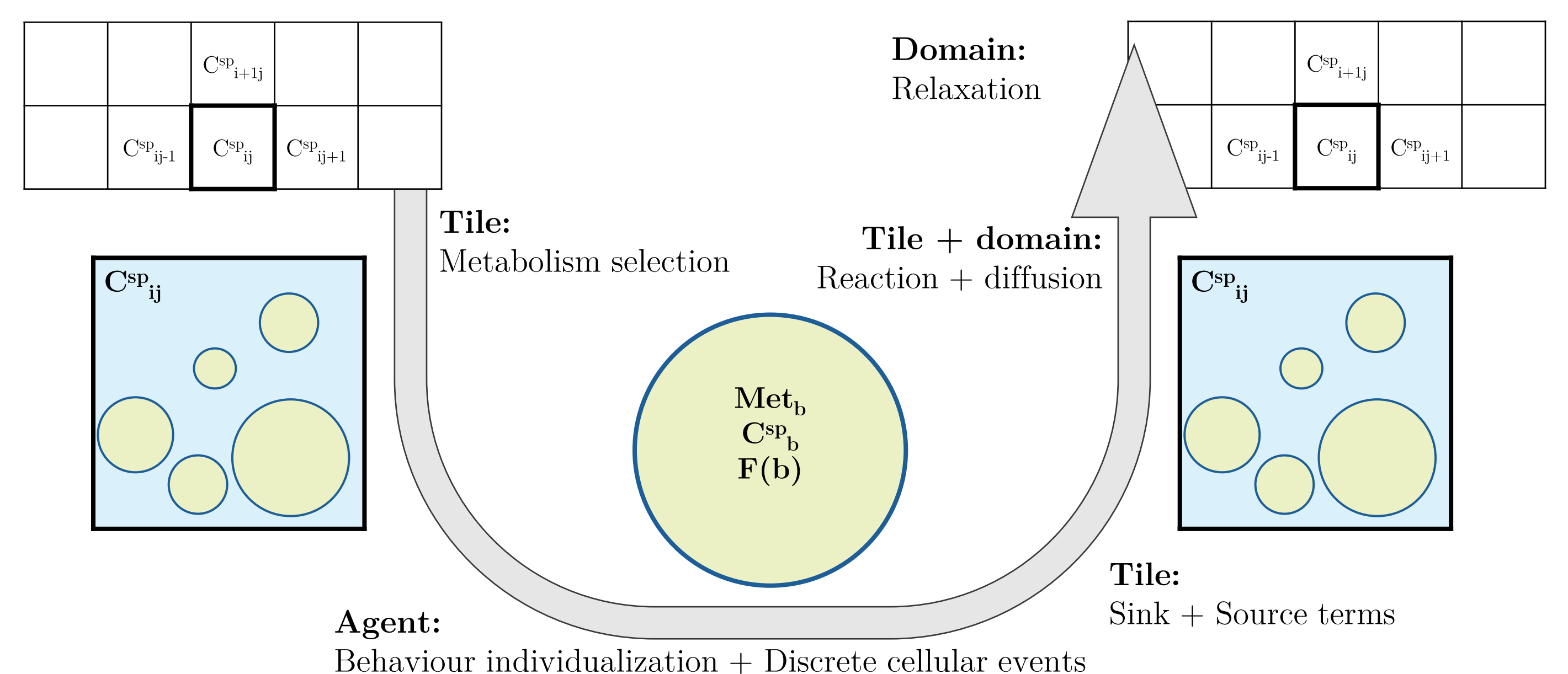
$$\frac{\partial}{\partial t}(\varepsilon_b \rho_{sp}^{(b)}) = \varepsilon_b \omega_{sp}^{(b)} - \Sigma_{a/b} \omega_{sp}^{b \rightarrow a}$$

With $S_{a/b} = \Sigma_{a/b} \cdot \delta V$

Algorithmic framework

How is the computer implementation carried out?

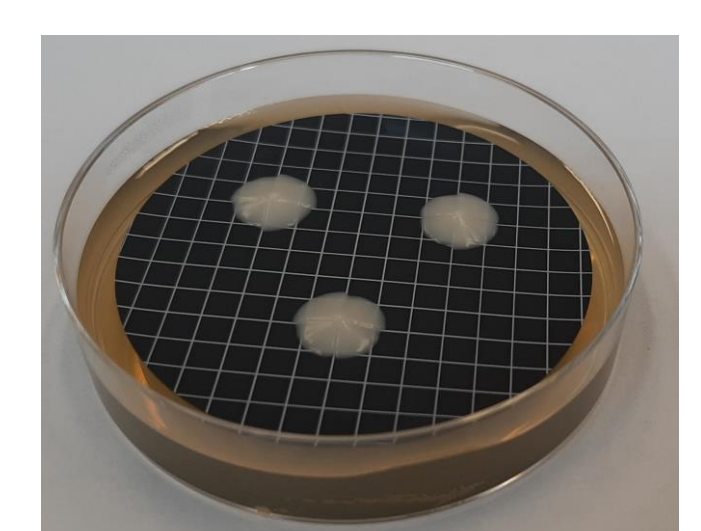
- Top-down identification of individual evolutionary laws
- Down-top update of tile and domain parameters



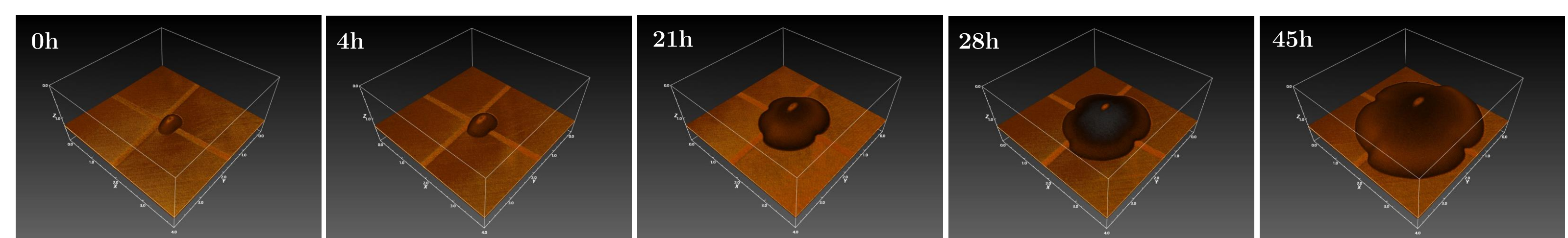
Experimental validation

What living tool and imaging strategy can be used for model calibration and refinement?

- *Saccharomyces cerevisiae*: microorganism extensively reviewed
- Optical Coherence Tomography (OCT) for non-destructive observation



Petri dish with *S. cerevisiae* colonies



3D OCT scans of an *S. cerevisiae* colony

Perspectives

Better understanding of the links between microscopic individual actions and macroscopic emerging observations

Synergy between experiments and model to gain new insight
Extension to other types of cells



Improving support matrix for animal tissue engineering
Improving support and media for biofilm culture