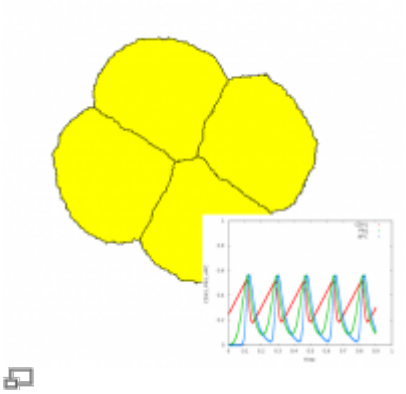
Multiscale models

ODEs in CPM cells: Cell cycle and proliferation



Cells divide according to an oscillatory ODE model representing the early cell cycle in Xenopus.

Introduction

This multiscale model example shows

1. how to define a coupled system of continuous ODEs in discrete CPM cells
2. how to specify and change time scales between these model formalisms

Model description

This model specifies an oscillatory ODE model representing the cell cycle in Xenopus oocytes using three components (CDK1, Plk1, APK) (Ferrell et al., Cell, 2011) (see `CellTypes→CellType→System`). This ODE model is coupled to 2D shaped CPM cells that perform divide based on the concentration of these components (see `CellTypes→CellType→Proliferation→Condition`). As in the early Xenopus cell cleavage, this leads to exponential growth of the number of cells, without increase of total cell volume.

Time scales

Time scales are defined in the following fashion:

- The so-called global time scheme is defined in `Time` and here runs from `0` to `1` arbitrary time units. All models and plugins specify their updating scheme in terms this global time scheme (e.g. `Analysis→Gnuplotter→interval`).
- The CPM time scale for cell motility and behaviors is defined in `CPM→MCSDuration`. This specifies the time that a single Monte Carlo step in the CPM lasts, in terms of the 'global time'. Here, the `MCSDuration` is $1.0\cdot10^{-4}$ which means the CPM is executed 10.000 times during this simulation.
- For setting time of ODEs, one has to distinguish the (1) how often the ODEs are evaluated from (2) controlling the time scale of the ODE dynamics:
    1. The time scale of the ODE dynamics can be changed using `System→time-scaling`. When larger or smaller than 1.0, this speeds up or slows down make the dynamics,

without influencing the accuracy of the approximation.
2. The accuracy of the numerical approximation (and is equal to the Δt of the numerical solver) is controlled using `System→time-step` (and is automatically rescaled according to the time scale).

Things to try

- Change the CPM time scale, relative to the ODE dynamics: Change `CPM→MCSDuration` to $1.0\cdot10^{-3}$ or decrease to $1.0\cdot10^{-5}$. This makes cells to have less resp. more motility/relaxation in between cell divisions.
- Change the time scale of the ODE dynamics, relative to the CPM by altering `System→time-scaling`.

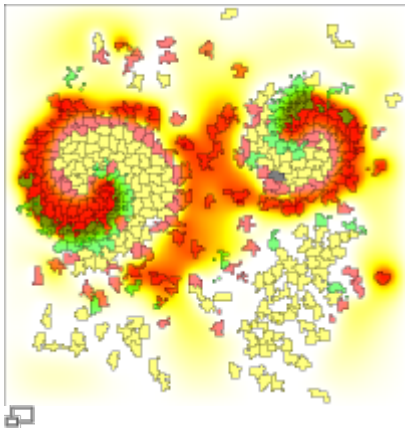
Model

h CellCycle.xml |h

```
extern>
http://imc.zih.tu-dresden.de/morpheus/examples/Multiscale/CellCycle.xml
```

In Morpheus GUI: `Examples → Multiscale → CellCycle.xml`

Dictyostelium



Aggregation of amoebas through chemotaxis towards waves of cAMP.

Video

Introduction

This model show chemotactic aggregation of Dictyostelium. It was constructed by students attending the ECMI modeling week 2012 in Dresden.

Model description

This model shows an interesting coupling between CPM cells and reaction-diffusion PDE. Cell state depends on the perceived concentration of cAMP, and determines whether a cell produces cAMP and whether it performs chemotaxis. The PDE is governed by a Fitzhugh-Nagumo-like model of an excitable medium, which causes traveling waves upon excitation. Chemotaxis through those waves causes cell aggregation.

Background colors indicate the cAMP concentration. Cells are color-coded according to their phase: excitable/resting (yellow), excited/chemotactic (green), refractory/resting (red).

Model

h Dictyostelium.xml |h

```
extern>
http://imc.zih.tu-dresden.de/morpheus/examples/Multiscale/Dictyostelium.xml
```

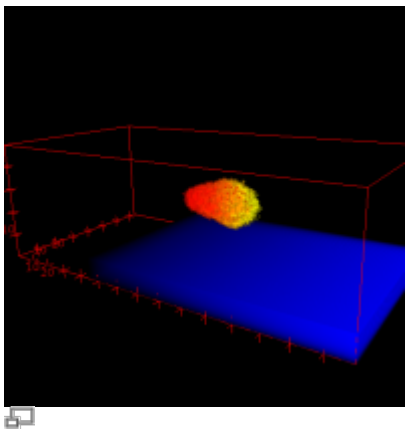
In Morpheus GUI: `Examples → Multiscale → Dictyostelium.xml`

References

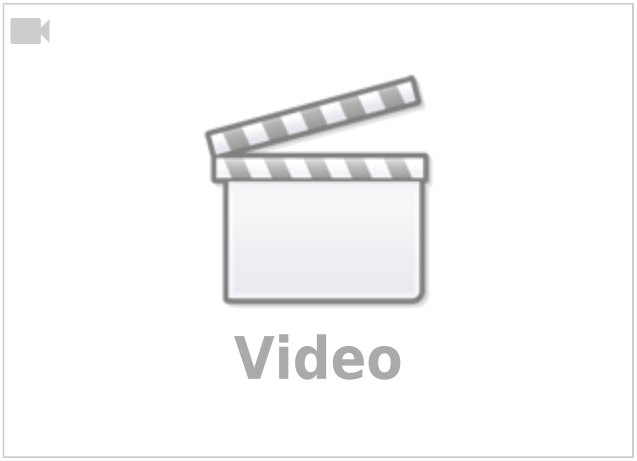
- Rost F, Quintero A, Myllykoski M, Igolkina A, Rohde O'Sullivan Freltoft A, Dixit N, Morphogenesis and Dynamics of Multicellular Systems. *ECMI Newsletter*, 52, 2012.
- Savill N and Hogeweg P. Modelling morphogenesis: from single cells to crawling slugs. *J. Theor. Biol*, 184:229–235, 1997.

MembraneProperties: Cell polarization and chemotaxis

Note: MembraneProperties are not available in public version of Morpheus.



Cell dynamically re-polarizes in response to switching external gradient



Introduction

This model of cell polarity shows the coupling of three model formalisms:

- A cellular Potts model
- A PDE model, solved on the membrane of the cell
- And an external gradient.

The cell membrane polarizes in response to the external gradient. Chemotactic cell motility depends on the polarity of the cell and the external gradient.

Description

This example implements two models of cell polarity: Meinhardt's substrate-depletion model and Edelstein-Keshet's wave-pinning model. The user can switch polarity model by `Disabling`/`Enabling` the relevant `System`.

The model defines a one-dimensional reaction-diffusion system (`MembraneProperty`) representing membrane-bound molecules, and is mapped to a cellular Potts model defining a discrete shaped cell. An external gradient, specified in a PDE, provides a signal for the polarization of the cell. In turn, the polarity of the cell influences its `chemotaxic` behavior.

After a switch in direction of the gradient, the cell re-polarizes in the new direction and starts to move up the gradient, iff the wave pinning model has been selected.

Model

h CellPolarity.xml |h

```
extern>
http://imc.zih.tu-dresden.de/morpheus/examples/Multiscale/CellPolarity.xml
```

Note: This model is not available in Morpheus GUI.

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