Module 1: Delta-Notch (ODE systems, ODEs on a grid)

Author: Fabian Rost

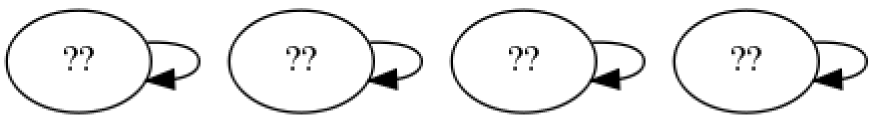
Aim

- learn about ODE models (dynamics in morpheus, steady states analytically)
- develop first models

Description

Basic ODEs

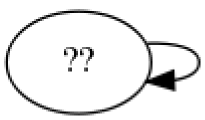
- get to know what students know about ODEs and adjust the module to the pre-knowledge
- give them very simple sketches of biomolecular models, which they should translate into ODEs, e.g.



- could be translated to the following ODEs:

$$\begin{align} \dot A &= k_1 \\ \dot A &= k_2 A \\ \dot A &= - k_3 A \\ \dot A &= k_4 - k_5 A \end{align}$$

- discuss those ODEs by
  - calculate steady state (do not calculate the stability, to complicated for biologists)
  - simulate in morpheus
- typical models for biochemistry/systems biology use hill kinetics:



$$\begin{align} \dot A &= \frac{\theta^n}{\theta^n + B^n} - k A \end{align}$$

Delta-Notch

- then discuss the delta-notch sketch with two species
  - start with the Collier model
  - let them simplify the Collier model sketch (remove the delta or notch species)
  - let them develop an ODE for this system (they should be able to do so from the above examples)

- they could come up with something like:

\begin{align} \dot A_1 &= \frac{\theta^n}{\theta^n + A_2^n} - A_1 \\ \dot A_2 &= \frac{\theta^n}{\theta^n + A_1^n} - A_2 \end{align}

- this system is bistable for certain parameter ranges, if the students are advanced they might find this out themselves
- bistable e.g. for $\theta=0.1$, $n=4$,
- if they have this system running in morpheus go spatial and let them simulate the system on a square and hexagonal grid
- then you could also move to shaped cpm cells or even moving cells

- students won't do so much on their own in this session, it is a lot teaching on ODEs (don't be theoretical here, not enough time!) and introducing morpheus

Paper:

- Joanne R. Collier, Nicholas A.M. Monk, Philip K. Maini, Julian H. Lewis, Pattern Formation by Lateral Inhibition with Feedback: a Mathematical Model of Delta-Notch Intercellular Signalling, Journal of Theoretical Biology, Volume 183, Issue 4, 21 December 1996, Pages 429-446, ISSN 0022-5193, http://dx.doi.org/10.1006/jtbi.1996.0233.

Morpheus models

```
<?xml version='1.0' encoding='UTF-8'?>
<MorpheusModel version="3">
    <Description>
        <Details></Details>
        <Title></Title>
    </Description>
    <Space>
        <Lattice class="linear">
            <Neighborhood>
                <Order>1</Order>
            </Neighborhood>
            <Size symbol="size" value="100, 0, 0"/>
        </Lattice>
        <SpaceSymbol symbol="space"/>
    </Space>
    <Time>
        <StartTime value="0"/>
        <StopTime value="5"/>
        <TimeSymbol symbol="time"/>
    </Time>
    <Global>
        <Constant symbol="k1" value="1.0"/>
        <Variable symbol="A" value="1.0"/>
```

```
        <System solver="heun" time-step="0.01">
            <DiffEqn symbol-ref="A">
                <Expression>k1 * A</Expression>
            </DiffEqn>
        </System>
    </Global>
    <Analysis>
        <Logger time-step="0.01">
            <Input>
                <Symbol symbol-ref="A"/>
            </Input>
            <Output>
                <TextOutput/>
            </Output>
            <Plots>
                <Plot time-step="5">
                    <Style style="points"/>
                    <Terminal terminal="png"/>
                    <X-axis>
                        <Symbol symbol-ref="time"/>
                    </X-axis>
                    <Y-axis>
                        <Symbol symbol-ref="A"/>
                    </Y-axis>
                </Plot>
            </Plots>
        </Logger>
    </Analysis>
</MorpheusModel>
```

LateralInhibition.xml

```
<?xml version='1.0' encoding='UTF-8'?>
<MorpheusModel version="3">
    <Description>
        <Details></Details>
        <Title></Title>
    </Description>
    <Space>
        <Lattice class="hexagonal">
            <Neighborhood>
                <Order>1</Order>
            </Neighborhood>
            <Size symbol="size" value="10,10,0"/>
            <BoundaryConditions>
                <Condition boundary="x" type="periodic"/>
                <Condition boundary="-x" type="periodic"/>
                <Condition boundary="x" type="periodic"/>
```

```
                <Condition boundary="-y" type="periodic"/>
            </BoundaryConditions>
        </Lattice>
        <SpaceSymbol symbol="space"/>
    </Space>
    <Time>
        <StartTime value="0"/>
        <StopTime value="50"/>
        <TimeSymbol symbol="time"/>
        <RandomSeed value="42"/>
    </Time>
    <CellTypes>
        <CellType class="biological" name="cells">
            <Property symbol="X" value="0.0"/>
            <Constant symbol="theta" value="0.1"/>
            <Constant symbol="n" value="6"/>
            <Property symbol="X_neighbour" value="0.0"/>
            <NeighborhoodReporter>
                <Input scaling="cell" value="X"/>
                <Output symbol-ref="X_neighbour" mapping="average"/>
            </NeighborhoodReporter>
            <System solver="heun" time-step="0.01">
                <DiffEqn symbol-ref="X">
                    <Expression>theta^n/(theta^n+X_neighbour^2)
- X</Expression>
                </DiffEqn>
            </System>
        </CellType>
    </CellTypes>
    <CellPopulations>
        <Population size="1" type="cells">
            <InitCellLattice/>
            <InitProperty symbol-ref="X">
                <!--    <Disabled>
        <Expression>if(cell.id == 1, 1, 0)</Expression>
    </Disabled>
-->
                <Expression>rand_uni(0, 0.01)</Expression>
            </InitProperty>
        </Population>
    </CellPopulations>
    <Analysis>
        <Gnuplotter time-step="50">
            <Plot>
                <Cells value="X"/>
            </Plot>
            <Terminal name="png"/>
        </Gnuplotter>
    </Analysis>
```

```
    <Global>
        <Constant symbol="X" value="0.0"/>
    </Global>
</MorpheusModel>
```