

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

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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:

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

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



$$\dot{A} = \frac{\theta^n}{\theta^n + B^n} - k A$$

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:

$$\begin{aligned} \dot{A}_1 &= \frac{\theta^n}{\theta^n + A_2^n} - A_1 \\ \dot{A}_2 &= \frac{\theta^n}{\theta^n + A_1^n} - A_2 \end{aligned}$$

- 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"/>
  </Global>
</MorpheusModel>
```

```

    <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>

```

LaterallInhibition_2cell.xml

```

<?xml version='1.0' encoding='UTF-8'?>
<MorpheusModel version="3">
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    <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="8"/>
<TimeSymbol symbol="time"/>
</Time>
<Global>
  <Variable symbol="A" value="0.51"/>
  <Variable symbol="A_neighbour" value="0.5"/>
  <System solver="heun" time-step="0.01">
    <DiffEqn symbol-ref="A">
      <Expression>theta^n / (theta^n + A_neighbour^n)
- k * A</Expression>
    </DiffEqn>
    <DiffEqn symbol-ref="A_neighbour">
      <Expression>theta^n / (theta^n + A^n)
- k * A_neighbour</Expression>
    </DiffEqn>
  </System>
  <Constant symbol="theta" value="0.1"/>
  <Constant symbol="n" value="6"/>
  <Constant symbol="k" value="1.0"/>
</Global>
<Analysis>
  <Logger time-step="0.1">
    <Input>
      <Symbol symbol-ref="A"/>
    </Input>
    <Output>
      <TextOutput/>
    </Output>
    <Plots>
      <Plot time-step="8">
        <Style style="points"/>
        <Terminal terminal="png"/>
        <X-axis>
          <Symbol symbol-ref="time"/>
        </X-axis>
        <Y-axis>
          <Symbol symbol-ref="A"/>
          <Symbol symbol-ref="A_neighbour"/>
        </Y-axis>
      </Plot>
    </Plots>
  </Logger>
</Analysis>
</MorpheusModel>
```

Laterallnhibition_space.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="y" 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>
```

From: <https://imc.zih.tu-dresden.de/wiki/morpheus/> - **Morpheus**

Permanent link: <https://imc.zih.tu-dresden.de/wiki/morpheus/doku.php?id=documentation:course:module1&rev=1510585848>

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