Module 6: Dictyostelium cluster formation & slug movement

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Aim

- this was planned as a one week project, students should develop a complex model
- teach them about biology: morphogenesis, cellular behavior, ...
- teach them about mathematics: CPM, PDE, coupling

Description

- good description on what has been done can be found in the report by the students (see section Papers)
- it's been two days of teaching:
    - first explain CPM and let them play with that a little (e.g. cell sorting)
    - explain PDE system we are going to use
        - I had to explain about phase plane analysis quite a bit
- then on day 3 start to couple PDE & CPM
    - start with coupling in one direction only
        - e.g. first give a fixed gradient and let CPM cells perform chemotaxis
        - then formulate a PDE where a substance is only produced where CPM cells are
    - then couple in both directions (implement the Savill model)
        - perform clustering and slug movement experiment

Paper

- Savill, N. J., & Hogeweg, P. (1997). Modelling morphogenesis: from single cells to crawling slugs. J. Theor. Biol, 184, 229-235. link
- Stan Marée (2002), From pattern formation to morphogenesis: multicellular coordination in *Dictyostelium discoideum* link
- Alberto Quintero, Mirko Myllykoski, Anna Igolkina, Alexandra Rohde O'Sullivan Freltoft, Nitya Dixit, Fabian Rost (2012), Morphogenesis and Dynamics of Multicellular Systems, link

Morpheus models

h ClusterFormation.xml |h

```
<?xml version='1.0' encoding='UTF-8'?>
```

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                <Condition boundary="y" type="constant"/>
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                <Condition boundary="-y" type="constant"/>
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    </Time>
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            <Property symbol="phase" value="0"/>
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                <Target value="20"/>
            </VolumeConstraint>
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                <Strength symbol-ref="mu"/>
            </Chemotaxis>
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                <Maximum symbol-ref="max_c"/>
            </PDEReporter>
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0)</Expression>
            </Equation>
            <Equation symbol-ref="phase" name="Rule_2_3">
```

```
                <Expression>if(phase == 1 and max_c > 0.1, 2,
if(phase == 2 and phaseTime>phase2duration, 3,
if(phase == 3 and max_c &lt; 0.05, 1,
phase
))) </Expression>
            </Equation>
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            </Function>
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        <Strength symbol-ref="mu"/>
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  </Disabled>  -->
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            <Contact type1="ameba" type2="medium" value="2"/>
            <Contact type1="ameba" type2="autoAmeba" value="4"/>
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        </Interaction>
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        </MetropolisKinetics>
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```

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                <Condition boundary="-y" value="0"/>
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            </DiffEqn>
            <DiffEqn symbol-ref="r">
                <Expression>alpha*epsilon*(3.5*c-b-r)</Expression>
            </DiffEqn>
            <Function symbol="epsilon">
                <Expression>if(c &lt; 0.0065, 0.5,
if(c &lt; 0.841, 0.0589,
0.5))</Expression>
            </Function>
            <Function symbol="f">
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if(c &lt; 0.841, -3*c+0.15,
15*(c-1)))</Expression>
            </Function>
            <Function symbol="alpha">
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            </Function>
        </System>
    </PDE>
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            </InitRectangle>
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                </ColorMap>
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            <Cells symbol-ref="cell.volume" min="15" max="25"/>
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    </Analysis>
</MorpheusModel>
```

- Movie: Cluster Formation & cAmp Spirals
- for the movie the system size was 500×500 with 4000 cells randomly placed, everything else was like in the example above

h CrawlingSlug.xml |h

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                <Condition boundary="-y" type="constant"/>
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    </Time>
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                <Strength symbol-ref="mu"/>
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                <Maximum symbol-ref="max_c"/>
            </PDEReporter>
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            <Equation symbol-ref="phaseTime">
                <Expression>if(phase == 2, phaseTime+MCStime,
0)</Expression>
            </Equation>
            <Equation symbol-ref="phase" name="Rule_2_3">
                <Expression>if(phase == 1 and max_c > 0.1, 2,
if(phase == 2 and phaseTime>phase2duration, 3,
if(phase == 3 and max_c &lt; 0.05, 1,
phase
))) </Expression>
            </Equation>
            <Property symbol="phase2duration" value="0.5"/>
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```
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      <Strength symbol-ref="mu"/>
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        <Property symbol="phase" value="0"/>
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  </CellTypes>
  <CPM>
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        <Contact type1="ameba" type2="autoAmeba" value="4"/>
        <Contact type1="autoAmeba" type2="medium" value="3"/>
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```
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        <System solver="euler" time-step="0.1">
            <DiffEqn symbol-ref="c">
                <Expression>alpha*(-f -r)</Expression>
            </DiffEqn>
            <DiffEqn symbol-ref="r">
                <Expression>alpha*epsilon*(3.5*c-b-r)</Expression>
            </DiffEqn>
            <Function symbol="f">
                <Expression>if(c &lt; 0.0065, 20*c,
if(c &lt; 0.841, -3*c+0.15,
15*(c-1)))</Expression>
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            <Function symbol="alpha">
                <Expression>if(cell.id != 0, 1, 0)</Expression>
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            <Function symbol="epsilon">
                <Expression>if(c &lt; 0.0065, 0.5,
if(c &lt; 0.841, 0.0589,
0.5))</Expression>
            </Function>
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```

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          <Dimensions size="5 5 0" center="55 50 0"/>
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  </CellPopulations>
  <Analysis>
      <Gnuplotter interval="10">
          <Terminal opacity="0.7" name="png"/>
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                  <Color value="-0.5" color="dark-violet"/>
                  <Color value="0" color="white"/>
                  <Color value="1.0" color="red"/>
              </ColorMap>
          </PDE>
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                  <Color value="3" color="red"/>
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              </ColorMap>
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        </Plot>
    </Logger>
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</MorpheusModel>
```

- Movie: Crawling Slug