## Module 4: Vascular Patterning

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Aim:

- Learn to distinguish between alternative hypothesis/mechanisms explaning the same phenomenon
- When two different mechanisms can reproduce the same phenomenon, how can modeling help to distinguish between these mechanisms?

Description:

- Introduce problem and provide examples:
  - multiple mechanism, same result

- Introduce CPM/PDE hybrid/multiscale models
  - coupling model formalisms (through production + chemotaxis)

- Introduce vasculogenesis
  - Isolated cells into vascular network

- Provide two models: A.xml and B.xml that show the same behavior

- Assignment 1: What biological processes do these models reflect?
  - Autocrine model: angioblasts produce their own chemoattractant (VEGF)
  - Paracrine model: paracrine chemoattractant is bound to angioblasts-produced matrix molecules

- Assignment 2: How can you determine which one is more plausible?
  - Theoretically?
    - Explore differences in parameter sensitivity:
      - Sensitivity analysis: `ParamSweep` (see "parameter sweep" in FAQ)
  - Experimentally?
    - Explore how the models produce different predictions:
      - Inhibit VEGF binding (use nonbindnig isoform VEGF121)
      - Change cell densities
      - Administer fluorescent VEGF
  - Quantitative analysis?
    - Quantify parameters:
      - FRAP: diffusion
      - FRAP: rate of binding/unbindung
      - ELISA: decay
      - Microfluidic device: chemotactic strength

Paper:

- Köhn-Luque A, de Back W, Starruß J, Mattiotti A, Deutsch A, J-M Perez-Pomares, HA Hererro. (2011) Early Embryonic Vascular Patterning by Matrix-Mediated Paracrine Signalling: A Mathematical Model Study. PLoS ONE 6(9): e24175. link

Documents:

- Assignment (handout, pdf)
- Diff (handout, pdf)

Morpheus models:

- Example: Vascular patterning

- h A.xml (autocrine chemotaxis)|h

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<MorpheusModel version="1">
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            <Neighborhood>
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            </Neighborhood>
        </Lattice>
    </Space>
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        <StopTime value="4000"/>
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    </Time>
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            </Chemotaxis>
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            <Contact type1="Angioblasts" type2="Angioblasts"
value="160"/>
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                <Order>2</Order>
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            </Cells>
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```

```
                </ColorMap>
            </PDE>
        </Gnuplotter>
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- h B.xml (paracrine chemotaxis)|h

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    </Space>
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        <SaveInterval value="0"/>
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    </Time>
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                <Strength value="25"/>
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            </VolumeConstraint>
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            <Property symbol="s" value="2000" name="chemotactic
strength"/>
            <ConnectivityConstraint/>
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```

```
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    </CellTypes>
    <CPM>
        <Interaction default="0">
            <Contact type1="medium" type2="Angioblasts" value="80"/>
            <Contact type1="Angioblasts" type2="Angioblasts"
value="160"/>
        </Interaction>
        <MetropolisKinetics temperature="50" stepper="edgelist">
            <Neighborhood>
                <Order>2</Order>
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        </MetropolisKinetics>
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    </CPM>
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        <Layer symbol="v" name="ECM">
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        </Layer>
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            <Diffusion rate="1e-3" unit="µm²/s"/>
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                <Expression>gamma2*cell - alpha*u*v</Expression>
            </DiffEqn>
            <DiffEqn symbol-ref="w">
                <Expression>alpha*u*v</Expression>
            </DiffEqn>
        </System>
    </PDE>
    <CellPopulations>
        <Population size="0" type="Angioblasts">
            <InitRectangle cells="200" type="regular">
                <Dimensions size="200 200 0" origin="0 0 0"/>
            </InitRectangle>
        </Population>
    </CellPopulations>
    <Analysis>
        <Gnuplotter clean="true" interval="50" timename="false">
            <Terminal opacity="0.65" name="png"/>
```

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            <Cells flooding="true">
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                    <Color value="1" color="gray"/>
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                <ColorMap>
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                </ColorMap>
            </PDE>
        </Gnuplotter>
    </Analysis>
</MorpheusModel>
```

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