# Interacting MESC cells

1. Place cells randomly on a lattice. Could also be according to some pre-defined distribution (e.g. energy minimization), or purely randomly. Choose cell number and dimension to match some initial density.
   1. Which initial distribution best matches experimental settings? Look into NND distribution in stem cells.
   2. Idea: link g(r), density of states at distance r, to a way of distributing the cells.
2. Simulate dynamics using cellular automaton.
3. We observe that cells at low densities tend to aggregate together. Cell motility also needs to be taken into account.
4. It might help to calculate the signalling strength. This can be done as follows: (1) estimate from the number density approach, or (2) calculate exactly.

Differentiation process

1. Stem cells -> mesendoderm / neuro-ectoderm. Irreversible process; no spontaneous reversal.
2. Differentiation process driven by signalling molecules (LIF, WNT, FGF).
3. Density has influence on signalling molecule concentration.
4. Other forms of signalling might also play a role.

## Building the model

Density-dependent survival

1. Cellular automaton for randomly placed cells.
   1. Randomly place cells.
   2. Update rules.
   3. Visualization.
2. Analyse dynamics
   1. NND distribution
   2. Spatial order.
   3. Statistics on survival rates.
   4. Mean field approach seems possible. Analytical framework?
3. Stochastic survival rate.

Cell differentiation

1. Differentiation process for a single cell.
2. Cellular automaton + differentiation.
   1. Add more molecules (Wnt, FGF)

Additional features / comments

1. Cell motility.
   1. Mechanism = chemotaxis?
2. First take only signalling molecules into account, no juxtacrine signalling. This way we can see whether with only autocrine and paracrine signalling this might work. If not a good match, add other signalling methods.

## Key questions and quantities to look for

Density-dependent survival

* Density-dependent survival: can it be explained by the effect of a single signalling molecule?
* Characteristics of surviving cells vs. dead cells.
  + NND
  + Higher order neighbour distances?
* Predict survival rate of population.
* Clustering index.
* If not a good match with data, try altering characteristics:
  + Hard disks -> overlapping cells allowed.
  + Non-random initial distribution (think about how to implement).
* A

Collective cell differentiation

* Is cell differentiation mainly an autonomous effect or a collective effect?
* Percentage of differentiated cells (as function of time)

### Interesting parameters

Closed boundaries

Many cells switch off, but not all

L = 2;

R = 0.02; % disc radius

n = 10; % nmax = L/R (square packing)

K = 16;

S = 8;

All cells switch off, but slowly: n=9

All cells stay alive: n=12 (very hard to obtain with random sampling, 245917 rejections)

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