

Meinhart simulations on an evolving line

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1 Mathematical support

1.1 Governing equations

Here, we simulate the boundary of a cell moving in response to an auto-activating internal machinery, biased by external chemoattractant signals. There are three constituent parts of the internal machinery- an autocatalytic local activator, a local inhibitor which destabilises regions of local activation, and a global inhibitor, through which distal patches of the local activator can compete (1). We move the boundary outward with a local force proportional to the concentration of the local activator, and retract the boundary normally to maintain a preferred cell size, allowing the cell to move. For a complete reference on this system, see (2). This particular implementation of the system was used in (3).

Our system evolves according to the following equations:

$$\partial_t a = D_a \Delta_\Gamma a + \frac{s(a^2/c + b_a)}{(k_M + b)(1 + s_a^2)} - d_a a, \quad (1)$$

$$\partial_t b = D_b \Delta_\Gamma b + k_b a - d_b b, \quad (2)$$

$$\partial_t c = \frac{r_c}{|\Gamma|} \oint_\Gamma a \, d\mathbf{x} - r_c c, \quad (3)$$

$$s(\mathbf{x}, t) = 1 + d_r \text{RND} + \left(\frac{C(\mathbf{x}, t)}{C(\mathbf{x}, t) + k_d} \right) \left(1 + d_r \text{RND} \right), \quad (4)$$

$$\partial_t \Gamma = (f_a a(\mathbf{x}, t) - \lambda(A - A_0)) \hat{\Gamma}(\mathbf{x}, t), \quad (5)$$

where a , b and c are the local activator, local inhibitor and global inhibitor, respectively, $s(\mathbf{x}, t)$ represents the stimulus strength in terms of external concentration C at position \mathbf{x} and time t , $\Gamma(\mathbf{x}, t)$ represents the boundary line of the cell, and $\hat{\Gamma}(\mathbf{x}, t)$ is the outward normal of $\Gamma(\mathbf{x}, t)$ at the point \mathbf{x} . $|\Gamma|$ is the total length of the boundary. RND introduces the noise required for symmetry-breaking, and is drawn from the interval $(0, 1)$, and d_r controls the magnitude of this noise.

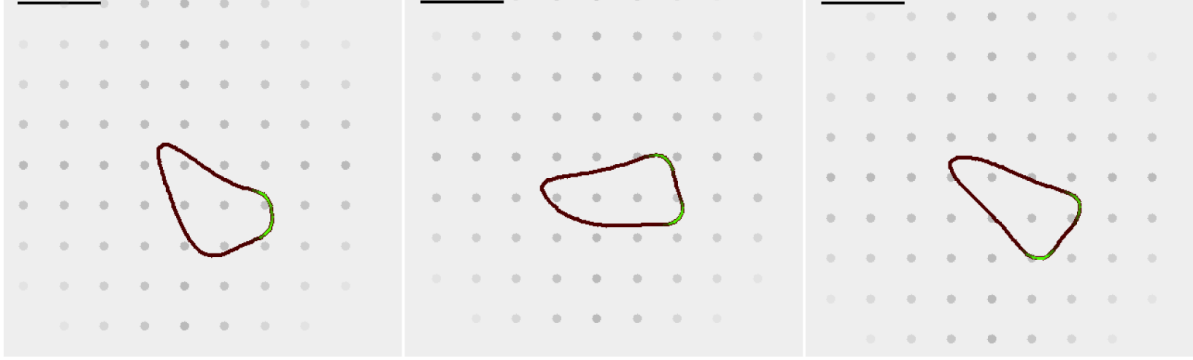


Figure S1: Example frames from a simulation run with argument “v true”. (A) Three stills of a running simulation are shown. The strength of the activator signal is displayed around the perimeter in green, and the value of the local inhibitor is used to decide on the redness of the outer line.

1.2 Running the simulation

Practically, the system is simulated using a central-space, forward-time finite differences model on an evolving line of finite element nodes. The value of d_r has been hard-coded to 0.05. The simulation is built in the executable file **MeinhardtCell.jar**. In Windows or OSX, double-clicking on the file will run the simulation, with a GUI enabling variation of parameters and a live window showing the current state of the simulated cell (see Fig. S1). In order to allow batches of simulations to be run, command-line execution is also available. On the command line, first change to the .jar file’s parent directory and issue the following command:

```
java -jar MeinhardtCell.jar
```

The values of parameters can be changed by inputting command-line arguments to the simulation. Each argument takes the form of a command key followed by a value, with all arguments separated by spaces. For example, if one wished to change the standard values for k_b and r_c , the birth rate of the local inhibitor and speed of the global inhibitor, respectively, one could use the following command:

```
java -jar MeinhardtCell.jar bB 0.004 GI_SPEED 0.05
```

The table below gives a full list of keys for command line specification of parameters.

Argument	function	Default value.
DURATION	The duration of the simulation, in arbitrary units	100000
ACTIN_FK	f_a , the constant of proportionality for outward force from the activator.	0.0015
GLSPEED	r_c , the response speed of the global inhibitor.	0.07
bB	k_b , the birth rate of the local inhibitor.	0.0028
dB	d_b , the death rate of the local inhibitor.	0.013
diffB	D_b , the diffusivity of the local inhibitor.	0.045
KM	k_M , a Michaelis-Menten-like constant for the local inhibitor.	0.16
sA	s_a , the variable controlling saturation of the local activator.	7.0E-5
BASAL_A	b_a , the basal activator production level.	0.1
diffA	D_a , the diffusivity of the local activator.	0.025
dA	d_a , the death rate of the local activator.	0.02
DIR_OUT	The output directory (relative to the built .jar file).	MeinhardtSimulation
v	Display the UI. Can be true or false .	true if run without arguments, false otherwise.

1.3 Output of simulations

The output of the simulation is placed in a folder relative to the .jar file, which can be specified using the DIR_OUT argument. The output consists of a file named **CONSTANTS.txt**, which records the parameters used in the simulation, and a subfolder containing several files. In all cases but one, the rows are recorded time points and the columns are the output values at each finite element node. The exception is the file **cellGI.csv**, which only takes a single value at each time point. A description of each file follows:

File name	description
cellGI.csv	The global inhibitor value.
cellLA.csv	The local activator concentration at each node around the boundary.
cellLI.csv	The local inhibitor concentration at each node around the boundary.
cellS.csv	The local value of $s(\mathbf{x}, t)$ at each node around the boundary.
cellX.csv	The x co-ordinate of each finite element node.
cellY.csv	The y co-ordinate of each finite element node.

Note that the number of finite element nodes used to represent the boundary is not constant, as nodes are added or removed from the list as their density on the evolving line changes. As the front expands, they will need adding in order to maintain accuracy, and as the rear retracts they become too dense and are removed. As such, boundary points are best interpreted as samples of an evolving surface at their respective locations, rather than as physical landmarks on the boundary that always represent the same fixed point.

References

- [1] Meinhardt H (1999) Orientation of chemotactic cells and growth cones: models and mechanisms. *J Cell Sci* **112**:2867-74.
- [2] Neilson MP *et al* (2011) Chemotaxis: A feedback-based computational model robustly predicts multiple aspects of real cell behaviour. *PLoS Biol* **9**:e1000618.
- [3] Tweedy L, Meier B, Stephan J, Heinrich D, Endres R G (2013) Distinct cell shapes determine accurate chemotaxis. *Sci. Rep.* 3:10.1038/srep02606.