Help me I'm stuck - Obstacles interactions in Cellular Pott Models

Viktor Doychev, Philipp Küppers, Clara Periago Serrano
Donders Centre for Cognition
Radboud University
Thomas van Aquinostraat 4 6525 GD NIJMEGEN
philipp.kueppers@ru.nl

1 Introduction

Cell migration is an interesting phenomena to study, as its an important pillar of many biological processes such as tumor metastatsis and organ development. Furthermore, it can aid in solving computational problems, such as avoiding congestion in crowd dynamics. One potential application, could be information flow in neural networks. A commonly used framekwork to study cell migration `in silico` is the cellular Potts modeling (CPM) framekwork. Due to the use of a Hamiltonian function for guiding the model, almost any behaviour can be modelled by adding terms to the Hamiltonian. In this report we investigate how obstacles change change the collective migration behaviour of cells and how to mitigate the slow down of cells in such an environment.

2 Methods

2.1 Cellular Potts Modeling Framekwork

The CPM updates its states using Metropolis Hastings Sampling with the Hamiltonian

$$\Delta H = \Delta H_{adhesion} + \Delta H_{volume} + \Delta H_{perimeter} + \Delta H_{act}$$

To model active movement, we use an Act-CPM. This is modelled by adding a new term to the global energy equation

$$\Delta H_{act}(p_s \to p_t) = -\frac{\lambda_{act}}{\max_{act}}(GM_{act}(p_s) - GM_{act}(p_t))$$

Where the tunable parameters $\max_{act}$ and λ_{act} model the protrusive activity and strenght of the energetic reward respectively. In self-study exercise 1.3 we saw that the cells keep moving at large densities if we increase $\max_{act}$ to high values such as 80 and are stuck together in place for low values.

2.2 Obstacles

We model obstacles through a new cell type. In order to make the obstacle round and be non-moving obstacles, we only need to define a volume which is sufficiently enforced. We choose the obstacle volume to be half that of our cell size $V^{\text{obs}} = \frac{V}{2}$ and $\lambda_V^{\text{obs}} = 100$. Furthermore, we need to set λ_p to a moderately high value such as 50, while the perimeter p, can be zero or some other low value. For higher values of p, we loose the round static shape, as the obstacle tries to maximize its perimeter by leaving gaps in its area.

2.3 Experiments

We design the following experiments to investigate the effect of obstacles. In experiment 1, we have 16 evenly spaced obstacles that occupy most of the grid. We then evaluate the cell movement of 6 or

40 cells. The detailed CPM config can be found in Table 1. The CPM temperature was left to the default of 20 to simplify analysis.

Experiment	#cells	Adhesion J	λ_V	V	P	λ_P	λ_{ACT}	$\max_{ACT}$
1	[6,40]	$\begin{bmatrix} 0 & 0 & 0 \\ 0 & 20 & 500 \\ 0 & 0 & 0 \end{bmatrix}$	$\begin{bmatrix} 0 \\ 50 \\ 100 \end{bmatrix}$	$\begin{bmatrix} 0 \\ 500 \\ 250 \end{bmatrix}$	$\begin{bmatrix} 0 \\ 300 \\ 100 \end{bmatrix}$	$\begin{bmatrix} 0 \\ 1 \\ 50 \end{bmatrix}$	$\begin{bmatrix} 0 \\ 750 \\ 0 \end{bmatrix}$	$\begin{bmatrix} 0 \\ 25 \\ 0 \end{bmatrix}$

Table 1: Parameters used for the evaluated Cellular Pott Model.

3 Results

We first reproduced the baseline collective migration behaviour using the Act-CPM model in the absence of obstacles. At high cell density and low activity memory values (e.g. $\max_{act} = 20$), cells exhibited limited rearrangements and frequently became jammed, forming relatively static clusters. In contrast, increasing the activity memory to higher values (e.g. $\max_{act} = 80$) resulted in sustained collective motion even at high densities. Cells continuously changed shape and position and the tissue remained dynamic over long simulation times.

3.1 Experiment 1

To investigate the effect of obstacles, we introduced a second, non-migratory cell type representing obstacles into the simulation. Obstacles were smaller than migrating cells, remained static due to the absence of activity terms and were placed on the grid with regular spacing. We first studied the behaviour of six cells. Despite the lack of any avoidance mechanism, migrating cells were able to adapt their trajectories and navigate around the obstacles; since this is what minimizes our Hamiltonian energy function 2.1. Occassionally, the cells get stuck near an obstacle but then unstuck after some time. This can happen either by random chance, or more likely via another cell bumping into it and 'pushing' it. We observe that over time, cells getting stuck in between obstacles becomes more likely, but they eventually manage to get unstuck. Interestingly, increasing the number of cells to 40 and keeping the remaining parameters the same, results in the grid being fully covered by cells. Now, cells no longer get stuck for a longer time, but almost immediately are pushed away by other cells and keep moving. Instead of increasing the number of cells, we also evaluated a grid with more densly placed obstacles. Here, 6 cells get stuck most of the time and very rarely escape the obstacle before getting stuck again.

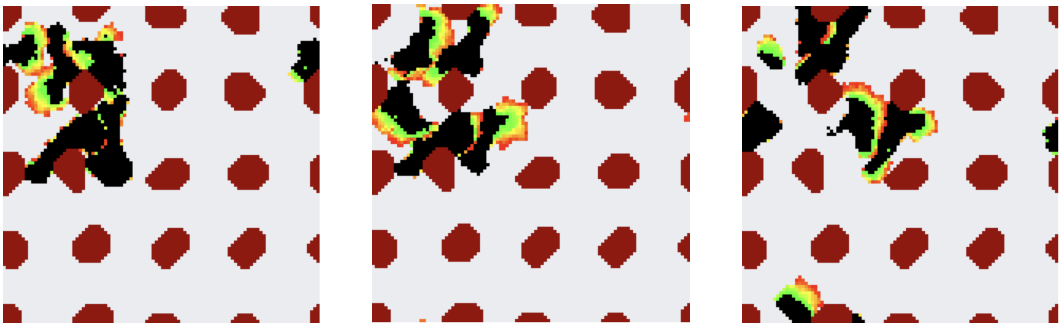

Figure 1: Behaviour in experiment 1 with 6 cells. **Left**: Two cells are stuck in the middle obstacle row. **Middle**: Collision with the upper group of cells disturbs the balance and gets the rightmost cell unstuck. **Right**: both cells are now unstuck, happily migrating together.

4 Discussion & Conclusion

In our experiments we evaluated the impact of obstacles on the migration of cells and how to mitigate the slow down caused by obstacles. It seems that for a small number of cells, obstacles can slow

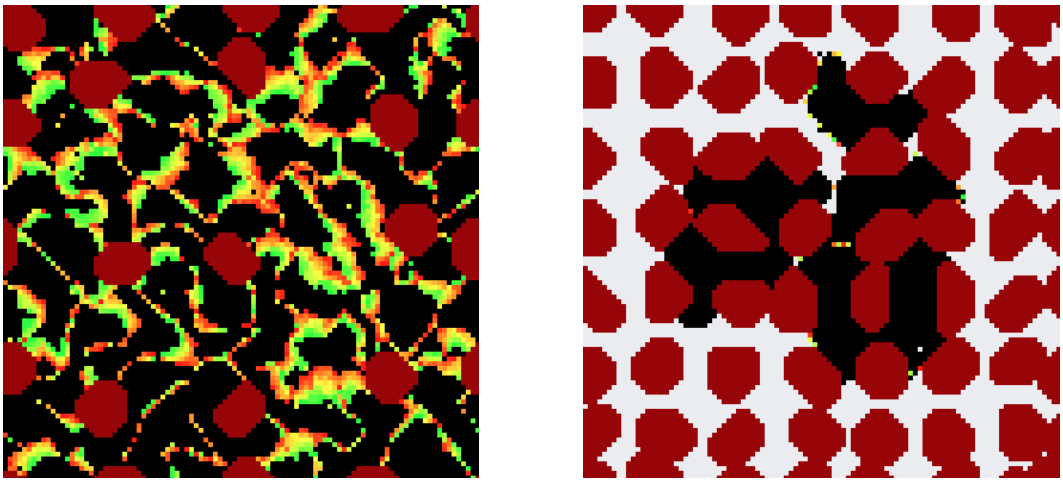

Figure 2: **Left**: Cell migration in a 100 by 100 grid with evenly spaced obstacles and 40 cells covering the whole grid. **Right**: 6 cells getting stuck when increasing the number of obstacles

down cell migration and cause them to get stuck. However, when most of the grid is covered in cells, they always have a neighbour behind them that is pushing them forward, preventing slow down. It also seemed weird to us, that when using 40 cells, some of the obstacles get pushed away or dont appear. It can be debated whether this behaviour is wanted or whether we should rather evaluate this experiment again with a different placement behaviour. In any case, it is clear, that we need a more systematic and structured approach, covering many more experiment settings in order to generalise our conclusions. Zooming out from the discussion of hyperparameters, we are unsure about how to investigate which simulations are biologically plausible. For instance, cell slowdown in our first experiment might never occur in nature, as there is never that much space between cells. Our hypothesis is instead, that the grid is always covered with cells or obstacles.