Radboud Universiteit

Cellular Potts Model: Collective Cell Migration

Freek Hens s1033509
Guido Klein s1021586
Floris Rossel s1010794

1 Research question

How do obstacles affect collective cell motion in a Cellular Potts Model?

2 Hypotheses

This study posits three hypotheses:

1. The speed of cell movement will be negatively correlated with the amount of obstacles in the environment.
2. The speed of cell movement will be negatively correlated with the total number of cells.
3. There will be an interaction effect between the amount of cells and the amount of obstacles. Specifically, we expect the speed of cell movement to decrease more than the sum of the negative effects of both the amount of cells and the amount of obstacles combined.

3 Methods

The research question was investigated using the Cellular Potts Model (CPM) that is implemented in the "Artistoo" framework.

Two implementation of the obstacles were considered. There is a barrier function in the framework. However, this does not allow the user to modify the cell's parameters, which was specified in the assignment. Therefore, it was decided to implement the obstacles as a different cell type (henceforward referred to as the "obstacle cell").

The initialization of the cells can be found in Table 1. The obstacle cell does not interact with other cells or the background, and is half the size of a regular cell. The obstacle cell is penalized heavily for changing its perimeter, which renders it static. The regular cell is initialized such that they are "predisposed" to move actively without disintegrating.

	T	$\text{Adhesion}_{\text{Cell-Cell}}$	$\text{Adhesion}_{\text{Cell-Matrix}}$	V	λ_V	P	λ_P	Max_{Act}	λ_{Act}
Cell	20	10	10	400	20	300	0	50	500
Barrier	20	0	0	200	200	10	50	0	0

Table 1: Initialization of the cells

The grid is a 200 × 200 pixels square. The obstacle cells are seeded evenly spaced on this grid. This is done by a nested for-loop, in which the first one loops over all the rows and the second one over all the columns. Whenever both the column and the row modulo are equal to 1, then an obstacle cell is seeded at 10 pixels down and 10 pixels to the right. The regular cells are seeded randomly on the grid. Each simulation is averaged over 2 runs, to reduce the impact of the initialization of the grid. This is necessary, as the barrier cells are not perfectly round, and the regular cells are seeded randomly.

We simulate several obstacle densities together with several cell densities to assess their mutual influence as described in the hypotheses. We will simulate 0, 9, 16, 25, 49, and 100 obstacles together with 1, 10, 20, 30, 40, 50 cells in a factorial design. The results are shown in table 2. Four examples are shown in figure 3. A 15-second clip of a run is uploaded to Brightspace, together with this assignment, where 50 cells are simulated together with 25 obstacles.

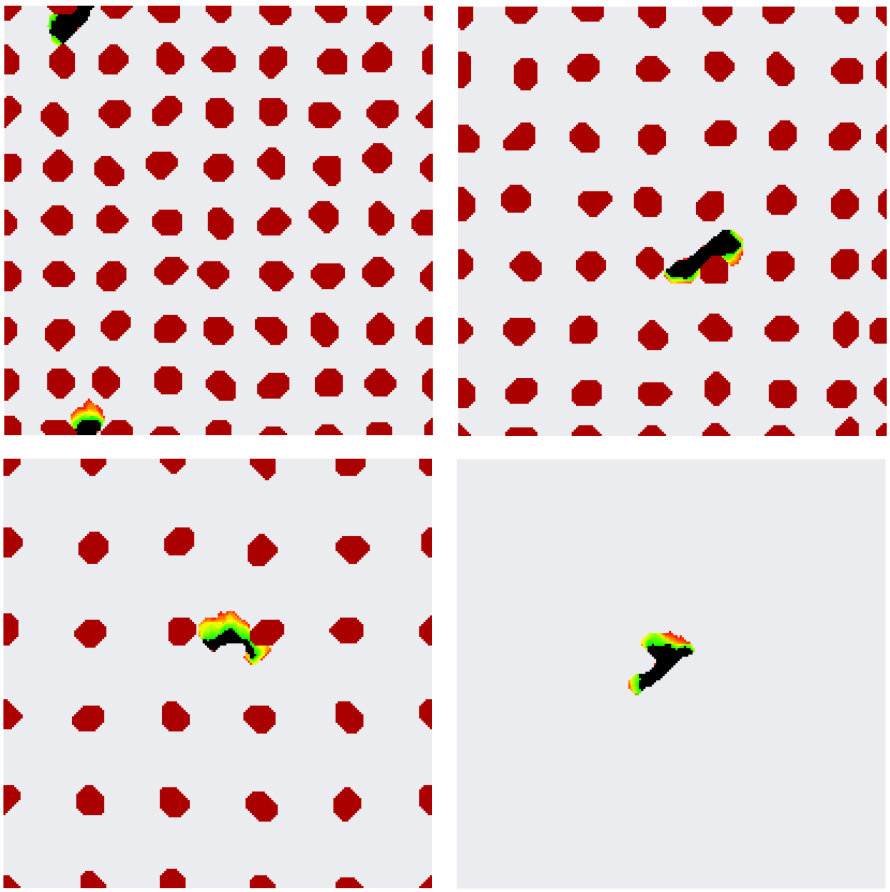

Figure 1: The environments for four obstacle densities, together with one cell. The obstacles are colored dark red and the cell is black, with the active parts colored in a gradient to show the time since last activation attempt. From top-left to bottom-right, there are: 64, 49, 25, and 0 obstacles. The obstacles on the edge of the field are wrapped around to the opposite side due to the torus option.

To assess the cell movement, we decided to calculate the average movement of the cells per time step. This is done by calculating the Euclidean change of position of the centroids of the cells over 10 time steps and dividing the average change in position of all cells to get an average velocity in pixels per second over all cells. This average is computed every 10 time steps and logged in the browser. A running average is also computed, which is reset after the first 200 time steps to account for the fact that it takes some time for the cells to settle after starting the model (see the run video on Brightspace). This means that the first 200 time steps are discarded, as it takes some time for the cells to settle at the start.

Since we have a torus enabled in our environment (meaning, the cells continue on the other side when they hit the side of the environment), the computation of centroids needs to be altered. The Artistoo framework has an option for this, but a bug was still found in which the velocity of certain cells was very high (due to their high displacement by the torus). Therefore we manually checked if the centroid of a cell was changing by a large amount, which we computed using the field size, and accounted for it in the computation of the average velocity of the cells.

The experimental setup chosen was a factorial design, which should be able to test the two main effects (hypotheses 1 and 2) and the interaction effect (hypothesis 3). The control condition for all hypothesis is the condition in which there is the lowest amount of cells and obstacles. In this case, this is 1 cell and 0 obstacles. The factorial design that is implemented can be seen in Table 2.

The code of our implementation can be found on Gitlab, more specifically, we worked in the file `CPM/examples/html/tutorial.html`.

4 Results

4.1 Data

		Number of Obstacles					
		0	9	16	25	49	100
Number of Cells	1	0.96	1.38	2.37	1.30	1.58	0.22
	10	1.51	1.46	1.76	1.81	1.49	0.64
	20	1.77	1.96	1.82	1.66	1.48	0.16
	30	1.94	1.71	1.64	1.63	1.41	0.18
	40	1.80	1.61	1.73	1.78	1.26	0.08
	50	1.44	1.69	1.41	1.52	1.21	0.06

Table 2: Factorial design of the experiment. Values represent average speed over 800 time steps averaged over 2 trials. These results are also depicted in figure 2.

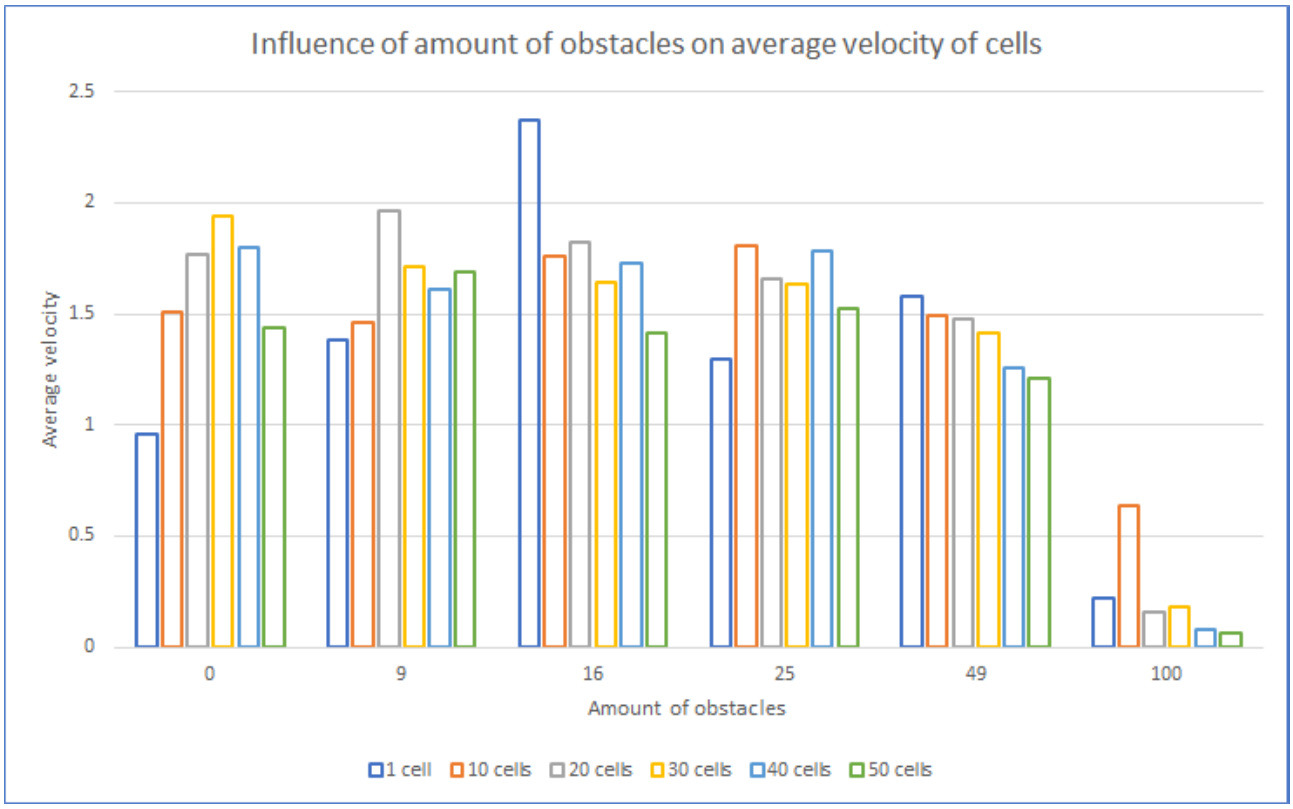

Figure 2: The results from our simulations. The amount of obstacles and the amount of cells were varied, and the average velocity of all cells, over 800 time steps is reported, in pixels per time step.

4.2 Observations

In trials with 100 obstacles, the movement of cells quickly goes down. Moreover, some cells are unable to move at all. This is effect is drastically reduced in trials with 49 obstacles, as can be seen in the last two columns of Table 2.

5 Discussion

Based on the results presented in Table 2 and Figure 2, we can observe that the highest collective cell velocities occur with 10 to 50 cells and 0 to 25 obstacles. Notably, there is an exceptional cell velocity in the case of 1 cell and 16 obstacles. However, as the number of obstacles increases to 49 and above, the cell speed begins to decline, suggesting that the movement of cells is inhibited by the available space. Since the difference in velocities is quite large from 49 to 100 obstacles, we will perform additional analyses with 64 and 81 obstacles.

Based on these results, it can be concluded that hypothesis 1 is likely true. Hypothesis 2 is likely false, as there seems to be a non-linear correlation between the cell movement speed and the total number of cells, which seems to have a peak around 9 to 25 obstacles. We are unable to speculate about hypothesis 3 based on this preliminary experiment, as there is too little data to do a two-way ANOVA significance test on this interaction. However, based on the current data, there might be an interaction effect, as the optimal number of obstacles appears to be different based on the amount of cells.

Based on these findings, we hypothesize that the amount of free space is the primary determinant of average cell speed, rather than the number of cells or obstacles, which indirectly affect the amount of free space available. We will test this hypothesis in following research, and also incorporate statistical tests such as variance of average cell displacement velocities over multiple runs and perform longer runs.

In summary, the results suggest that free space plays a critical role in determining the average cell speed, and the number of obstacles may be less important than previously thought.