# Natural Computing: Assignment 1 Report

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## 1 Introduction

The Cellular Potts Model (CPM) is an automaton for modeling cells and tissues. It consists of a pixel grid in which each pixel takes a particular state. Each state's value can represent either a type of cell or the background. The grid structure is represented as an undirected graph where nodes correspond to pixels and edges represent neighboring pixels. The model introduces the concept of global energy which consists of different terms (adhesion, volume, perimeter, etc.). The model's objective is to minimize the sum of all terms. We will introduce the different terms we experimented with in this study.

**Adhesion term:** The adhesion term is given by the following formula:

$$\mathcal{H} = \sum_{(i,j)\in E} J_{T_i,T_j} \left(1 - \delta_{ij}\right)$$

It represents the energy gain between two neighboring pixels. It depends on the adhesion coefficients $J_{T_i,T_j}$, the higher its value the higher the energy obtained when those two cells are neighboring each other. Therefore, pixels of cell types with higher adhesion coefficients will tend to repel each other while cells with low coefficient will be clustered together.

**Volume term:** The volume term is given by the following formula:

$$\mathcal{H} = \sum_{\sigma} \lambda_{V,\tau} \left(V_\sigma(t) - V_\tau\right)^2$$

As can be derived from the formula, the closer the volume of the cell (number of pixels clustered together) is to the target volume $V_\sigma(t)$, the less energy the system will have. Therefore, by modifying $\lambda_{V,\tau}$ and $V_\sigma(t)$ we can modify each cell's size.

**Perimeter term:** The perimeter term is analogous to the volume term but for each cell's perimeter.

The simulation then proceeds as follows:

1. It randomly selects a source and a target.
2. If the energy is reduced by copying the source to the target, then the target pixel state is changed to the source's type. If the copying increases the energy, there still is a $e^{-\frac{\Delta\mathcal{H}}{T}}$ chance of the copying occurring (where temperature $T$ is a tunable parameter).
3. This process is then repeated as many times as desired, making the system evolve in time.

Cell movement can be induced by introducing an activity term to the total energy. This term favors copy attempts from active pixels to inactive ones. This effect can be tuned by modifying $\lambda_{Act}$ and $\mathrm{Max}_{\mathrm{Act}}$. In this work, we will use the CPM to investigate how obstacles change collective cell motion on a crowded grid.

# 2 Methods

## 2.1 Simulation

All simulations of the cellular pots model were performed using Artistoo, a web-based framework for building interactive simulation models of cells.

### 2.1.1 Constant Simulation Parameters

The simulations were performed on a $300 \times 300$ pixels two-dimensional grid with periodic boundary conditions. We used a CPM with temperature $T = 20$. We defined three cell types: background, migrating cells and obstacles. In total, 400 migrating cells were used in each simulation. The adhesion, volume, perimeter and activity parameters were kept constant across all experiments.

### 2.1.2 Obstacle Design

**Obstacle Parameters** Obstacle cells were designed to behave as round, stationary structures. Therefore, we set the adhesion between obstacles and other cell types to a high value (100), while the adhesion among obstacle cells is set to 0. This penalizes the contact between obstacles and migrating cells, while making sure that obstacle cells stick together.

As required by the assignment, obstacle cells are set to half the target volume size of migrating cells, resulting in a target volume of obstacles of 100 pixels, compared to 200 pixels for migrating cells. The volume constraint strength of obstacles is set to a high value $\lambda_V = 100$, making sure that obstacles maintain a stable size.

The perimeter is closely related to the roundness of the obstacle and will be discussed in detail in the next part. The strength $\lambda_P$ for the obstacle is set to be high (50), forcing the obstacle to adhere to perimeter constraints. To prevent motion of obstacle cells, we set its $\mathrm{Max}_{\mathrm{Act}}$ to 0.

**Obstacle Roundness** The circle is the shape that minimizes the perimeter for a given area. Therefore, setting the target perimeter to be less than the perimeter of a circle with our target volume should force the system to produce circular shaped cells. However, the simulation is based on square pixels, its evolution and seed are stochastic, thus, the cells exhibit a polygon shape rather than a perfect circle. Increasing the temperature reduces this effect but requires changing a variable with global effects on the system. Ultimately, we set the target perimeter to be 40, as this value provided us with the roundest obstacles.

**Number of Obstacles** To place the obstacles with regular spacing, we designed a for loop that iterates over the grid and computes evenly spaced coordinates to seed obstacles. In this project, to investigate the effect of obstacle density on cell migration, we consider six obstacle densities in addition to a no-obstacle baseline. Specifically, we simulate environments containing 0, 16, 25, 49, 81, 100 and 144 obstacles.

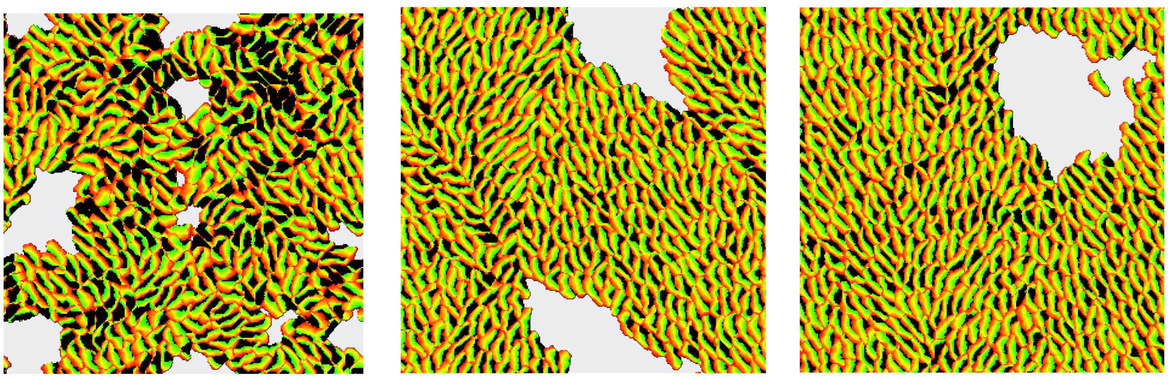
## 2.2 Analysis

To assess the effects of different obstacle numbers, we ran the differing simulations and visually assessed the effects. We describe the findings based on pictures of the simulations. Moreover, we verify our visually observed findings using quantitative measures. Specifically, we measured the mean speed of the migrating cells for the different numbers of obstacles. This was done by measuring the difference in cell centroids in both the x- and y-plane in each Monte Carlo time step (MCTS), and computing the Euclidean distance ($v = \sqrt{dx^2 + dy^2}$). The mean speed was computed over all cells for 1000 MCTSs after a burn-in period of 500 MCTSs.

# 3 Results

## 3.1 Visual Observations

### 3.1.1 Migrating Cells without Obstacles



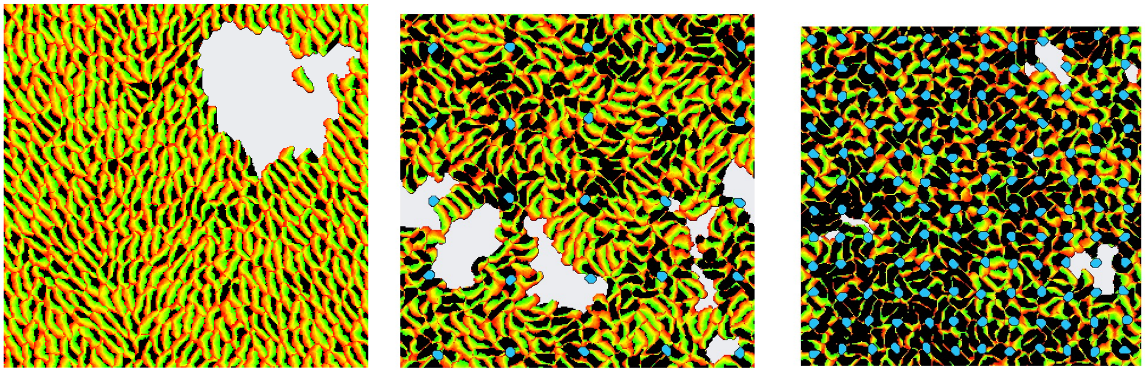
(a) Beginning phase (b) Middle phase (c) Long-term phase

Figure 1: Observations of Cell Migration Without Obstacles

Without obstacles on the grid, we observe the cells to display the following behaviors. In the beginning, the cells are moving in different directions at different speeds; after some time, cells are moving at the same speed. They then slowly start to form several streams. Within a stream, the cells are moving in the same direction, but between streams there are differences in directions. In the end, the cells all move together in the same direction.

The behaviors can be observed from the figures. In Figure 1a the cells have different areas of "blackness", showcasing that they are moving at different speeds; the red part in the front of each cell, which represents the direction they are moving, are very different per cell. In Figure 1b and 1c the black part of each cell has approximately the same volume, meaning that they move at the same speed. In Figure 1b the red part of the cells are still pointing to slightly different directions, but in Figure 1c they are all pointing to the left of the figure.

### 3.1.2 Migrating Cells with Obstacles



(a) Without obstacles

(b) With a few obstacles (25)

(c) With many obstacles (144)

Figure 2: Observations of Cell Migration With Obstacles

After placing obstacles on the grid, we observe the following cell behaviors. When a single migrating cell runs into an obstacle, it will get blocked, but after some time it will move by the obstacle and continue moving, and usually in a different direction from before it meets the obstacle. For cell groups in general, the obstacles slow down their migrating speed and also change their moving directions. Both effects become stronger as the number of obstacles increases.

Observing the figures, in Figure 2b with a few obstacles, the cells are moving slower than in 2a with no obstacles, showing larger black areas. The moving directions of the migrating cells in Figure 2b also differ more compared to the directions of the cells in 2a. However, there are still small streams of cells moving in the same direction as indicated by the red parts of the cells. In Figure 2c, with large amounts of obstacles on the grid, the cells are moving very slowly with black areas covering the major part of the grid; the red parts of the cells also point to completely different directions, suggesting different moving directions.

## 3.2 Quantitative Results

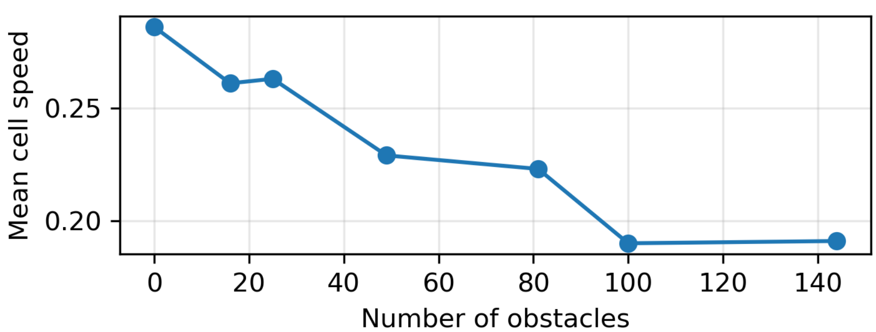



Figure 3: Curve visualizing the effect of obstacles on mean cell speed

Figure 3 demonstrates the effect of obstacle density on cell migrating speed. Without obstacles, the cells reach a mean speed of nearly 0.30. As the number of obstacles increases from 0 to 100, the mean cell speed gradually decreases to less than 0.20, which remains remains stagnant afterwards.

# 4 Discussion and Conclusion

In this experiment we explored how obstacles affect the collective cell behavior on the CPM. In particular, we experimented with different quantities of obstacles and measured the average cell speed for each configuration. We observed that with no obstacles, cells move relatively faster and will eventually move in the same direction. As the number of obstacles increases, the average cell speed decreases, but stagnates after the obstacle number reaches 100. As the number of obstacles increases, the cells' moving directions become more random.

Migrating cells do not stop moving after they run into obstacles since we set the adhesion between migrating cells and obstacles to a large number (100). Therefore, when both cells' edges meet, the system's energy increases, punishing edge overlap and causing cells to move away from the obstacles. During this phase, the cell's position circles around the obstacle, making the cell slower and potentially changing its direction.

In sum, as a single cell encounters an obstacle, it will slow down and change its direction. Therefore, when the obstacle density increases, more migrating cells encounter obstacles. Cells are then constantly redirected and slowed down, reducing the average speed and preventing the cells from following a moving pattern, as opposed to the case with no obstacles.