CPM of Collective Migration

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1 Introduction

The purpose of this report was to investigate the effect of grids of obstacles on the collective migration pattern of cells in the Cellular Potts Model (CPM) by conducting a variety of experiments via simulations. To design the environment for our observations, we kept a few requisites in mind: we wanted to obtain an environment with multiple, evenly spaced obstacles, each the size of half a cell. To obtain such a layout, we first attempted to modify the existing "Microchannel" example, by reforming the microchannel into a blob shape. We were successful, but obtained one big obstacle, which was not satisfactory for our requirements. Next, we explored other existing aristoo simulations and came across one explorable that was well-suited to our experiment, you can view it at the bottom of this site. After adapting the size and number of cells we were able to start our observations. In the following sections of this report, we will explain what parameters we modified, and what behavior we were able to observe.

2 Background

A CPM is a complex cellular automaton used for modeling cells and tissues. In this report, we describe how we used CPM to investigate complex cell behaviour. In particular, how the introduction of obstacles impacted collective cell migration. CPM simulations rely on certain parameters that determine cell behavior. Tools like Aristoo allow users to set these parameters and observe the effects on their simulation in real time. For this experiment, we will set all parameters to a certain value as part of the environment setup, and we'll not modify them for our observations. We'll dive into the specific values the parameters were set to for this experiment in section 3.2. However, we will first build some intuition about what these parameters do. **Volume**: sets a size for the cell. Biologically this would be regulated for example by osmotic pressure and cytoskeletal tension. While Volume represents the target size of a cell, λ_v represents the constraint that controls how much a cell can deviate from this target. A lower λ_v value means cells will freely expand or shrink, while higher λ_v maintain a nearly constant size, resisting compression or expansion. **Perimeter**: represents the target value for cell rigidity. The constraint λ_p determines how much a cell's perimeter can deviate from this target. Low λ_p means the cells can take irregular, jagged shapes, while higher λ_p means cells will maintain a compact roundish shape. Adhesion is described by the parameter J. **Adhesion$_{\text{cell-matrix}}$**: This parameter defines how strongly cells interact with the extracellular matrix. Low $J_{\text{cell-matrix}}$ values means the cells stick more to the substrate, so their behavior will be more spread-out. Higher $J_{\text{cell-matrix}}$ values mean there is a weak adhesion to the substrate, so cells will be able to move more freely. **Adhesion$_{\text{cell-cell}}$**: describes the adhesive strength between neighboring cells. Low $J_{\text{cell-cell}}$ means there is a strong adhesion between cells, so cell clusters will likely form and tissue structures will be more compact. High $J_{\text{cell-cell}}$ values would cause cells to spread apart. **Max$_{\text{act}}$** sets a limit on persistence-driven mobility. It depends on how recently the cell has moved. Biologically, this would influence how long a cell continues to move into the same direction. Low Max_{act} values means cells will have more short-term directional movement, resulting in more random motion. High Max_{act} means cells maintain directional movement for longer. $\lambda_a ct$ defines how strongly a cell prefers to maintain movement, so low $\lambda_a ct$ means more random movement, and high $\lambda_a ct$ means movement

will be directional and sustained in time. Temperature T defines the stochasticity of Monte Carlo updates, affecting how often unfavorable moves are accepted. Biologically, it simulates random fluctuations in cell shape or movement due to noise. Low Temperature values means cells move more deterministically, with less noise. High Temperature means there are more random fluctuations in shape and movement. Cell Number determines how many cells are initialized in the simulation. Biologically, this would represent the cell population density, so Cell Number values affect crowding effects.

3 Methods

3.1 Experimental Design

Our main goal was to investigate how varying densities of obstacles impact the collective migration of cells in a two-dimensional cellular Potts model (CPM). Each simulation was run on a (250×250)-voxel grid, with a specific number of equally spaced circular obstacles introduced. By systematically modifying the number of obstacles we were able to explore a range of obstacle densities while preserving consistent cell parameters. This setup allowed us to answer the main question: "How do obstacles change the collective migration behavior of cells?"

In order to avoid confounding factors such as variable cell sizes or different temperature parameters, we held the principal CPM parameters fixed when increasing the obstacle density. We also introduced sufficient numbers of cells to ensure that collective migration effects were observable and not limited by the number of cells present.

3.2 Methodology and Implementation: CPM Setup

All simulations were performed in a 2 dimensional grid of size 250×250 with periodic boundary conditions ($\mathrm{torus} = [\mathrm{true}, \mathrm{true}]$). Table 1 summarizes the main CPM parameters used, including the target volume and perimeter constraints, adhesion energies, and activity parameters. For cell-kind 1 (the only migrating cell type), we set $\mathrm{Adhesion}_{\text{cell-matrix}} = 20$ and $\mathrm{Adhesion}_{\text{cell-cell}} = 0$. The volume constraint parameters ($Volume = 200$, $\lambda_{Volume} = 50$) and perimeter constraint parameters ($P = 180$, $\lambda_P = 2$) were chosen such that cells retain compact shapes while still exhibiting substantial motility.

Parameter	Value	Parameter	Value
$\mathrm{Adhesion}_{\text{cell-matrix}}$	20	$\mathrm{Adhesion}_{\text{cell-cell}}$	0
Volume	200	λ_{Volume}	50
Perimeter	180	λ_P	2
$\mathrm{Max}_{\text{act}}$	$20 \rightarrow 80$	λ_{Act}	200
T	20	Framerate	5
Cell Number	300	Obstacles $(n \times n)$	1, 3, 6, 9
Obstacle Radius	5		

Table 1: CPM Simulation Settings

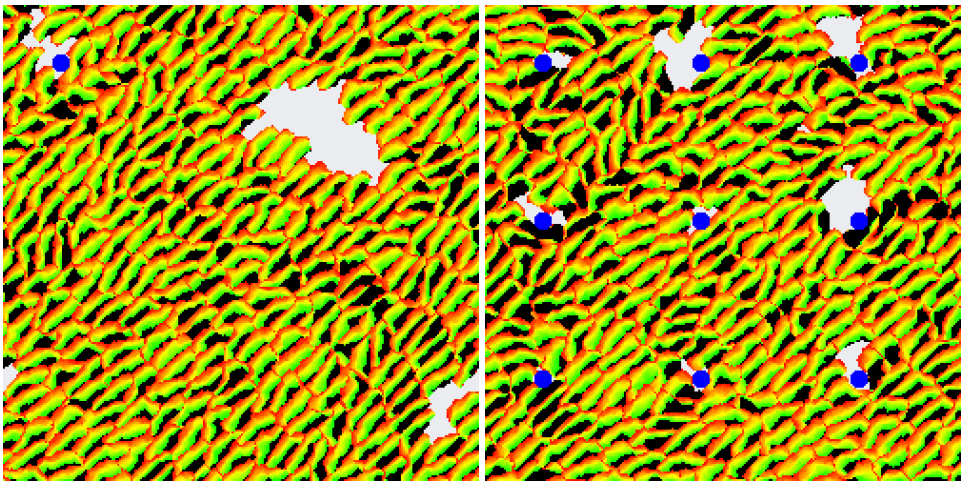
We used the $\mathrm{ActivityConstraint}$ with $\lambda_{\mathrm{act}} = 200$ and $\mathrm{MAX}_{\text{act}}$ ranging from 20 to 80. This ensures that cells with high past activity tend to remain active, contributing to persistent migration. The effective temperature was fixed at $T = 20$. Each simulation consisted of seeding 300 cells at random non-obstacle positions and letting the model evolve for a burn-in period, followed by the actual simulation. During this recorded phase images were output at every 5 steps (framerate 5 in Table 1). These image snapshots allowed us to make videos of the evolving cell configurations, which we will discuss in the results section.

Obstacle Implementation. We introduce obstacles by designating a fixed set of *barrier voxels* using $\mathrm{BorderConstraint}$. Each circular obstacle is centered at a regular interval in the grid, with a fixed radius of 5 voxels. We used up to $(n \times n)$ obstacle grids (where $n \in \{1, 3, 6, 9\}$), ensuring that obstacles are evenly spaced. We colored the obstacles blue so that they are easily visible in the resulting simulations.

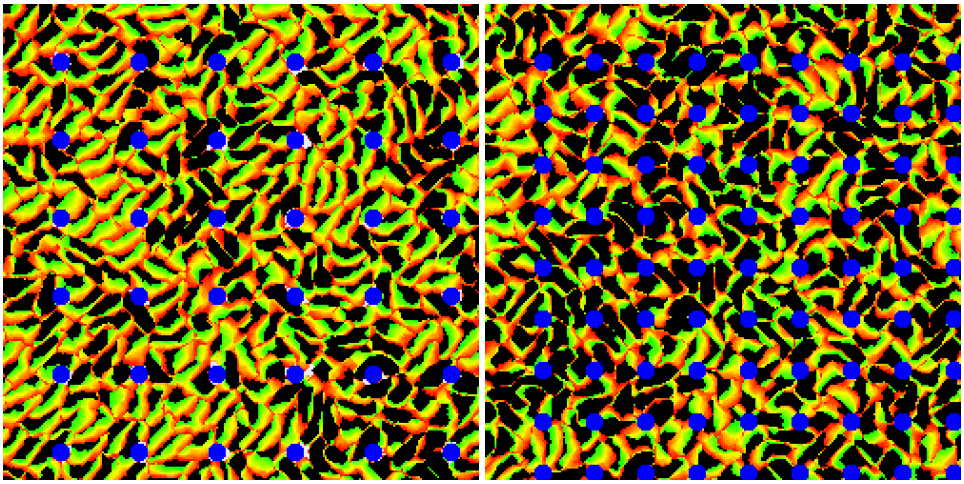
Cell Seeding and Burn-in. We seeded 300 cells into free voxels (voxels not marked as obstacles). This was done by randomly choosing a coordinate (x, y) outside the obstacle regions for each new cell and setting that pixel to a unique cell ID. A short burn-in phase was applied to relax initial shapes before recording the main simulations.

Temporal Updating and Output. Once the initial cell layout was generated, we ran each simulation for 15000 Monte Carlo steps at a temperature $T = 20$. The simulation loop proceeds by repeatedly calling `timeStep()`, which stochastically flips pixels according to CPM acceptance rules. The cells are colored based on local activity, allowing easy visual inspection and analysis of cell migration patterns.

4 Results



(a) 1 Obstacle (b) 3×3 grid of obstacles



(c) 6×6 grid of obstacles (d) 9×9 grid of obstacles

Figure 1: Collective migration patterns of the CPM model vs number of obstacles. Videos of the migration patterns can be found at this link for Youtube.

5 Discussion

The simulation paramters are found in table 1, several images of the migration pattern are seen in figure 1, along with a link to videos of the migration patterns. The simulation settings are identical to that of the original Exercise 3 of the Self Study Assignment, where Max_{act} has been increased from 20 to 80, causing the cells to move much quicker. The one other change that was introduced were the obstacles. Subfigure (a) of Figure 1 demonstrates unobstructed collective migration behavior, as there is only a single obstacle in the north-west corner of the image. One can see that all 300 cells seem to roughy be traveling in a collective mass towards the north west, with several white gaps. The red portions of the cell indicate those portions that are experiencing the most activity or movement, while black is the least. In the first figure the amount of black regions is relatively small, as cells are free to move. Considering figure (b) now, the collective migration is still observable with a grid of 3×3 obstacles, but there is noticeable obstruction and distortion of the pattern around the obstacles. Figure (c) and (d) at 6×6 and 9×9 demonstrate complete deterioration of the collective migration - there is no global movement of cells towards one region, and the percent of inactive cell has drastically increased, as shown by the amount of black pixels. This conforms with intuition as the introduction of obstacles effectively introduces "congestion" into the cell behavior, and it takes them more time to navigate around the obstacles. Taken to the extreme, it is expected that if even higher obstacle densities are introduced that cell movement would effectively come to a halt.

6 Conclusion

In this experiment, we could observe how the introduction of obstacles into a collective cell migration simulation results in slower, less organized movement, and how this change in behavior is directly proportional to the number of obstacles that are introduced.