

Group 16

Introduction

Collective cell migration is emergent behavior arising from local interactions between cells and their environment rather than from some sort of centralized control. Observations show that in dense tissues, cells often maintain coordinated motion despite strong crowding. We can reproduce this behavior in silico using the Cellular Potts Model (CPM). Previous CPM simulations show that collective migration can persist even under strong crowding, but real biological environments aren't homogeneous and contain immobile obstacles, and it is unclear how such obstacles can affect the collective migration in crowded systems.

This report uses a CPM to investigate the effects of obstacles on collective cell migration. Here, obstacles are modelled as immobile cell-like structures placed evenly on a crowded grid.

Methodology

In our experiments, simulations were performed using a CPM on a 2D lattice. Each lattice site carries a cell type "tau", allowing us to distinguish between cells and their characteristics ("lambda_act," "volume"...). We establish a baseline where cells remain highly motile and collectively migrating at high density, and perform all further experiments relative to this baseline. Obstacles are implemented as a distinct cell type from the migrating cells, and were made immobile by setting "lambda_act," the parameter that's responsible for the importance of strength in the Hamiltonian function, to zero. We also give very high values to "lambda_p" and "lambda_v," effectively making the obstacle shape robust and stable. Obstacles were assigned a fixed size approximately half that of a typical motile cell. We place the obstacles on the lattice in a regular spatial arrangement, allowing for easier visualization and behavior study.

Through this framework, we investigate the following questions: (1) how can we make an obstacle round and (2) what is the effect of obstacles on the motility of the cells, specifically under different density regimes?

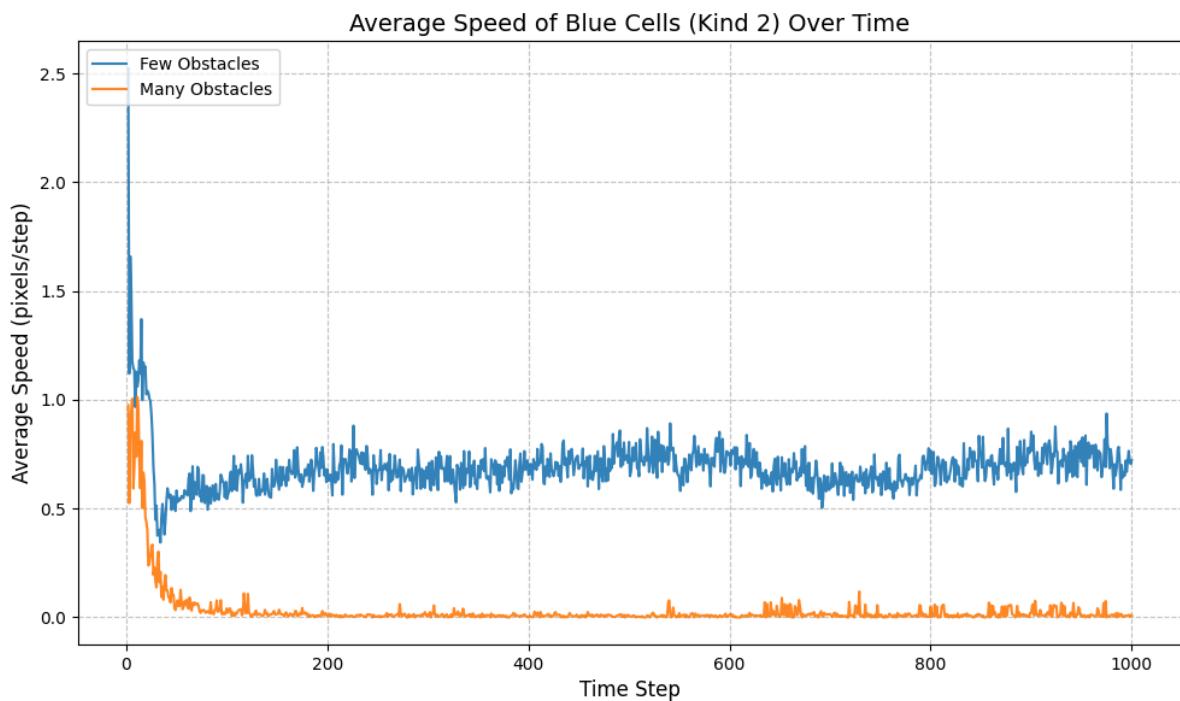
Results

Visual observation of the simulations showed clear differences between the two conditions. With few obstacles (spacing=50), migrating cells continuously moved throughout the simulation, successfully navigating around the sparse obstacles. In contrast, with many obstacles (spacing=10), cells became trapped between obstacles after an initial period of activity and remained largely immobilized for the rest of the simulation.

Figure 1 shows the analysis of average cell speed over time for both conditions. Both simulations began with an initial spike in activity (1.0-2.5 pixels/step) as cells adjusted their shape and position. After approximately 100 time steps, the two conditions diverged dramatically. In the few obstacles condition (blue line), cells stabilized to a consistent average speed of approximately 0.6-0.7 pixels/step, which was maintained throughout the entire 1000-step simulation with only minor fluctuations. In the many obstacles condition (orange line), average speed dropped to near zero (< 0.1 pixels/step) by time step 100 and remained at this minimal level for the remainder of the simulation. Occasional small spikes in the orange line represent rare instances where individual cells briefly shifted position before becoming re-trapped.

Cells in the sparse obstacle environment moved about 7 times faster than cells surrounded by many obstacles (0.7 vs 0.1 pixels/step), showing that more obstacles significantly slow down cell movement.

Figure 1: Average Speed of Type 2 Cells



Discussion

Modeling obstacles in the CPM

Obstacles were modeled as a second cell type with specific parameter settings that prevented movement and deformation. By setting `lambda_act` to zero, obstacles had no active motility. High values for `lambda_p` and `lambda_v` made the obstacle shape robust and stable, maintaining their approximately circular form. The high adhesion values ($J=500$) between obstacles and both background and migrating cells ensured that obstacles acted as

impenetrable barriers that migrating cells could not overlap with. This approach effectively created stationary, round obstacles without requiring any special model modifications.

Effect of obstacles on cell migration

When obstacles were placed between cells at low density, cells continued to move. The sparse obstacle distribution (spacing=50) allowed cells to maintain robust collective migration, suggesting they could efficiently navigate around isolated barriers. However, when the number of obstacles increased significantly (spacing=10), cell migration was dramatically reduced. The dense obstacle network created a crowded environment where cells became confined to small regions and could no longer sustain directional movement.

How obstacles change collective migration behaviour

The results clearly demonstrate that obstacles change collective migration behavior in a density-dependent manner. At low obstacle density, the system behaves similarly to obstacle-free conditions with persistent cell movement. However, beyond a critical obstacle density threshold, the migration system undergoes a transition to an immobilized state.

The strong adhesion between cells and obstacles ($J=500$) made the obstacles act like solid walls that cells couldn't pass through. Even though the cells had the ability to move, the dense arrangement of obstacles created a maze that was impossible to navigate. This shows that the physical layout of barriers in tissue can be the main factor that stops cells from migrating together, no matter how good the cells are at moving on their own.

Conclusion

This study demonstrates that obstacles profoundly affect collective cell migration in a density-dependent manner. Obstacles change collective migration behavior by creating physical barriers that, when sufficiently dense, fragment the available space and trap cells in isolated regions, effectively halting collective migration. With sparse obstacles, cells maintain robust migration, but dense obstacles cause a dramatic transition to immobilization. This suggests that the spatial organization of the extracellular environment is a critical determinant of whether cells can successfully migrate collectively through tissue, with implications for understanding cancer invasion and designing tissue engineering scaffolds.