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NSERC USRA Report
Simulating The Interactions And Migration Of Multicellular Tissues
And
Synthetic Image Generation

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1 Background

This summer I worked with Dr. Leah Edelstein-Keshet, MSc student Dhananjay Bhaskar, and PhD student Cole Zmurchok on two major projects: simulating GTPase dynamics in cells, and generating synthetic images of cells based on real microscopy cell images. Results from both projects will be submitted for publication in the near future. In this report I will give a brief overview of both projects, describe the technical work that I had done, and present some of the results we obtained. More detailed descriptions of these projects are available at request through `mohan_z@hotmail.com`.

2 Simulating The Interactions And Migration Of Multicellular Tissues

2.1 Introduction

Rac and Rho GTPases are signalling proteins that control cellular processes such as cell shape and cell polarity. In particular, high levels of Rac causes cell protrusion, while high levels of Rho causes cell contraction. It is known that mechanical feedback from the cell directly influences GTPases activities; in [2], Weiner et al. observed that mechanical tension inhibits Rac GTPase activity. Our group is interested in studying the behaviour of cells when their mechanical tensions are coupled with GTPase activities. Ordinary Differential Equation (ODE) models have been proposed for both 1D and 2D environments; part of my work this summer was focused on building simulation for the 2D model using CHASTE (Cancer, Heart, and Soft Tissue Environment), an open-source computational biology simulation software developed at Oxford. It is available at `http://www.cs.ox.ac.uk/chaste/`.

2.2 Methods

For our simulations, we adapted the vertex-based model from cell-based CHASTE. Cells in the vertex based model are represented by polygons whose vertices are free to move; their movements are governed by various forces, which could be modelled either explicitly or using a potential energy formulation. In Figure 1 some sample cells from a vertex-based simulation are shown.

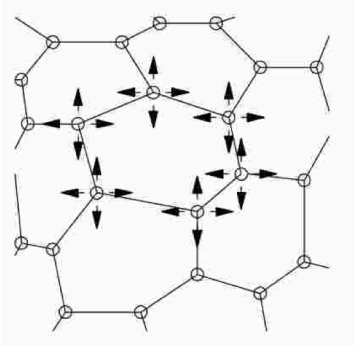

Figure 1: Sample cells in a vertex-based simulation (Adapted from [3])

Dhananjay and I built the simulations through coupling the 2D ODE model with cell area and tuning different simulation parameters, including sampling rate, mesh size, and adhesion energies.

2.3 Results

Our simulations showed waves of contraction and expansion of cells, as predicted by the ODE model. We discovered that in a vertex-based model, while adhesion energies do not change the overall pattern of GTPase activities in the cells, they affect the amplitude at which GTPase concentrations in the cells oscillate. Figure 2 shows some snapshots from the medium-adhesion simulation, in which cell-cell adhesion is set to be equal to cell-boundary adhesion.

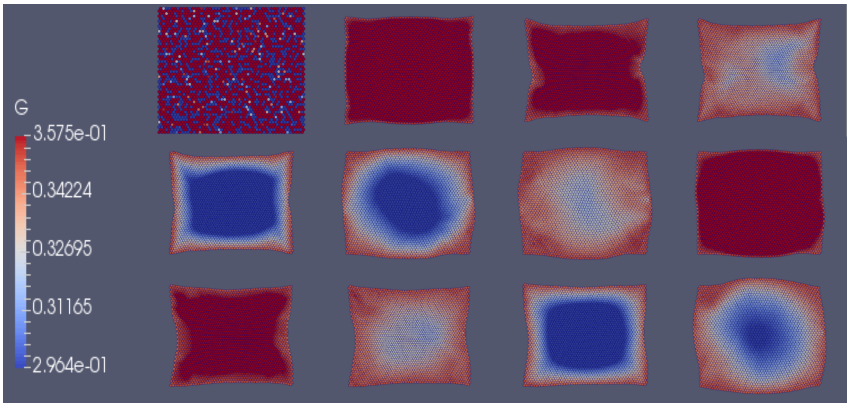

Figure 2: Snapshots of medium adhesion simulation with 2500 cells

3 Synthetic Image Generation

3.1 Introduction

The availability of large amounts of data in biological sciences has led to the emergence of quantitative biology as an exciting field of research. While supervised machine learning algorithms, including deep neural networks, have been shown to outperform other algorithms in quantitative analysis tasks, they require a large labelled/annotated training data set. Manually annotating data is tedious, costly, susceptible to user error and bias. To facilitate research in the area, we have developed a pipeline to generate synthetic images of cell shapes based on existing data sets, automatically annotating the new data in the process.

3.2 Methods

Dhananjay and I designed the procedure based on the existing literature. I was then tasked with implementation and sorting out the details needed to have the pipeline running. I achieved this through performing extensive research, coding, and testing. The final pipeline developed is as follows:

1. Data Pre-processing: Manually selecting representative cells from the four morphological clusters (elliptical, circular, elongated, protrusive) identified by our clustering algorithm, which was implemented as part of Dhananjay Bhaskar's Master thesis project.
2. Sampling of Boundary Points Based On Equal Arc Length
3. Extraction of Normalized Fourier Shape Descriptors
4. Generation and Visualization of Cell Shapes

3.3 Results

Synthetic cells generated for each morphological cluster are shown in Figure 3.

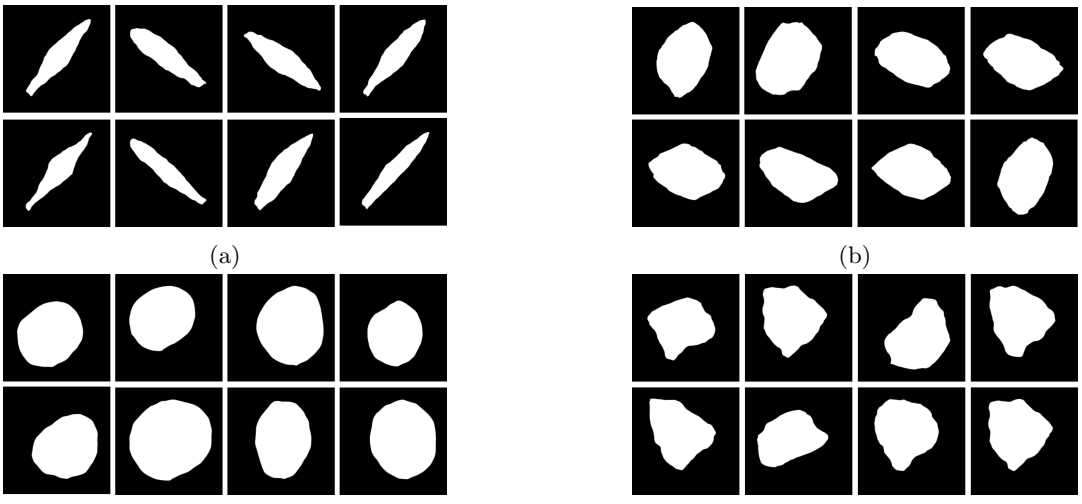

Figure 3: Sample synthetic cell images from the four morphological clusters identified by clustering algorithm. (a) Elongated Cluster, (b) Elliptical Cluster, (c) Circular Cluster, (d) Protrusive Cluster

4 Acknowledgements

I would like to thank Dhananjay Bhaskar for directing these projects and setting project goals, Dr. Leah Edelstein-Keshet for her supervision of the projects, Cole Zmurchok for his help in the GTPase project, and all members of the Leah Keshet Research Group for their support during my NSERC USRA work term.

References

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