Self-study exercise

Understanding the Cellular Potts Model

Handout for the *Natural Computing* lecture, January 30, 2025

In the lecture, we have discussed how CPMs can be powerful models to study self-organizing behaviour of cells. But how do we need to set our CPM parameters such that we get realistic cells?
In the following three self-study exercises, you will walk through the CPM using an interactive online implementation. Here, you will get a feel for how you can model cell behavior with a CPM by tuning the parameters that control the energy $\Delta\mathcal{H}$.
You do not need to hand in your answers to this assignment, but you will need the outcome of the third exercise to begin homework assignment 1. We therefore recommend you finish this self-study exercise before the work group for assignment 1.

Objectives of This Exercise

1. Understand how the various CPM parameters interact with each other to govern cell behavior.
2. Realize that it can be difficult to tune the parameters of a CPM.
3. Apply this knowledge to create different modes of cell migration in the CPM, and explain how this helps understand those migration modes.

Please go to http://computational-immunology.org/teaching/cpm/collective.html. This is an implementation of a special version of the Cellular Potts Model in which cells can migrate [1]. You can also use https://artistoo.net/explorables/Explorable-CPM.html as a reminder of the CPM dynamics.

Self-study exercises

Exercise .1 CPM basics

Make sure that the field is empty (hit refresh or "remove all cells"), and that the parameters have the following values:

$\text{Adhesion}_{\text{cell-matrix}}$	$\text{Adhesion}_{\text{cell-cell}}$	Volume	λ_V	Perimeter	λ_P	Max_{Act}	λ_{Act}	T	Framerate
20	0	500	50	340	0	0	0	20	1

We will now investigate how the basic CPM parameters for adhesion, cell volume, and cell perimeter influence behavior (you can ignore the λ_{Act} and Max_{Act} parameters for now). This exercise is meant to illustrate what the CPM parameters do, and the questions are to guide your thinking – you don't have to write everything down. Try to spend at most 30 minutes on this exercise.

1. Make sure all the parameters are set as in the table above, click "seed cell" and then "start". What do you see? What kind of motion does this cell have?
2. Now set the $\text{Adhesion}_{\text{cell-matrix}}$ to 0. What happens to the cell? Why do you think that happens? (Hint: look back to the description of the CPM and adhesion energy in the lecture...) Also try a negative value for $\text{Adhesion}_{\text{cell-matrix}}$. What is the meaning of positive or negative adhesion values here?
3. Return to the parameters in the table above. With these parameters, the cell is given an ideal volume (500 pixels), and a "level of importance" of this volume for the energy (λ_V). Try making the cell bigger or smaller (what parameter should you change?). How can you make the volume unimportant for the energy – and what happens then? What happens when you make λ_V really large (say, 1000)?
4. So far, we have considered $\Delta\mathcal{H}$ with only terms for adhesion and cell volume. We will now investigate the effect of the cell perimeter (circumference). The cell already has a target perimeter (340), but this is currently not taken into account in the calculation of $\Delta\mathcal{H}$. For that, we need to make λ_P non-zero. Try setting it to 2. What happens to the cell? Try making the cell "membrane" more or less ruffled. How would you do that?
5. Set the perimeter to 340 and λ_P to 2. Now change the $\text{Adhesion}_{\text{cell-matrix}}$ to 0 again. Does this have the same effect as it did in question 2? Why do you think that is?

Exercise .2 Cell migration: the Act model

We will explore the CPM extension that allows cell migration [1]. In this exercise, you will see the effect of the main Act-CPM parameters Max_{Act} and λ_{Act}. In particular, you will reproduce two different "modes" of migration: amoeboid and keratocyte-like (see lecture). Before you start, please refresh the page and set the CPM parameters as follows:

$\text{Adhesion}_{\text{cell-matrix}}$	$\text{Adhesion}_{\text{cell-cell}}$	Volume	λ_{Volume}	Perimeter	λ_{P}	Max_{Act}	λ_{Act}	T	Framerate
30	0	500	50	340	2	20	0	20	1

1. Seed a cell and click "start". You should now see colored pixels at the border of the cell, which indicate the "activity" that pixels remember (because we have set Max_{Act} to 20). Other than the color of the pixels, does the cell behave in a different way than with $\text{Max}_{\text{Act}} = 0$? Why/why not?
2. Set λ_{Act} to 100. Would you describe this movement as random or persistent?
3. *(Optional)* What happens when you set λ_{P} to 0 now? Why? (Reset it to 2 before you continue)
4. What happens when you increase λ_{Act} further? (Try steps of 100).
5. *(Optional)* If you increase λ_{Act} to very high values (eg 1000), the cell is prone to breaking in pieces. Can you fix that by altering some other CPM parameter again? (Note: you may have to increase λ_{Act} further when you have done this... Does that make sense to you?)
6. Reset λ_{Act} to 0, change Max_{Act} to 80, and repeat questions 1,2, and 4 above. What do you see?

Exercise .3 Collective migration

In this last exercise, we will investigate the "collective migration" arising when moving cells interact. Before starting, please refresh the page to clear the grid, and then ensure that the parameters have the following values:

$\text{Adhesion}_{\text{cell-matrix}}$	$\text{Adhesion}_{\text{cell-cell}}$	Volume	λ_{Volume}	Perimeter	λ_{P}	Max_{Act}	λ_{Act}	T	Framerate
20	0	200	50	180	2	20	200	20	5

Note: Sometimes it can take a couple of minutes for the cells to show interesting behaviors – allow the simulation to run for a while before you draw conclusions...

1. To seed multiple cells at once, click "+10 cells" a few times (this will take a while...). What do you see? How does the behavior change as the grid becomes more densely packed with cells? Try a nice range of densities, from a nearly empty space to a grid that is (nearly) full with cells. (You can also add cells in specific spots by clicking on the canvas).
2. Now, refresh the page, reset the parameters, increase Max_{Act} to 80, and repeat the previous exercise. What happens? How is this different from what you saw with $\text{Max}_{\text{Act}} = 20$? How full can you make the grid before the behavior really changes (if it ever does...)? If you're in doubt, change Max_{Act} back to 20 and compare what happens with a full grid versus a single cell at this parameter value...

References

[1] I. Niculescu, J. Textor, and R. J. de Boer. Crawling and Gliding: A Computational Model for Shape-Driven Cell Migration. *PLOS Computational Biology*, 11(10):1–22, 2015.