Cellular Potts model report

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1 Introduction

In this report we present a proposed solutions for the "Cellular Potts model assignments" created by Alvaro Kohn-Luque on October 2019, which dives into some application of the Cellular potts model, namely: (1) "Cell sorting" in which we tackle the clustering behaviour of cells, (2) "Tumor growth" where we apply constrains to prevent uncontrollable cell growth and (3) "Networks" where we are asked to hypothesise which extra mechanisms were implemented in the already existing model proposed by Francois Graner and James A Glazier in 1994 [1] to essentially simulate vascular networks.
We answer all this questions, as well as implement our own vascular networks model, in order to validate our hypothesis on task (3).

2 Background theory

The Cellular Potts model is a computational model that describes the collective and singular behaviour of cells as they interact with each other. First introduced by Francois Graner and James A Glazier in 1994, it is capable of simulating the cell migration, clustering and growth by taking into account adhesive forces between both cell with cell interaction and cell with medium interactions, as well as cell size/volume constraints.
This is done by representing the cell as a lattice domain where each cell is a subset of lattice sites sharing the same cell ID. Thus allowing us to write our energy function with two distinctive components: one with the adhesive interaction in mind and the other with the size constraint

$$H = \underbrace{\sum_{interfaces} J_{xy}\,(1-\delta_{xy})}_{\text{total contact energy}} + \underbrace{\sum_{cells} \lambda_A (a_\sigma - A_\sigma)^2}_{\text{cells sizes}},$$

where $J_{x,y}$ is the contact energy between two cell ID x with y or with the same cell ID, δ a Kronecker-delta, λ the energy strength per area/volume of the volume/area constraint, a_σ the current cell area/volume of cell σ and A_σ the target area/volume of cell σ.
The actual cell evolution (movement) is determined and accepted by utilizing a modified Metropolis algorithm as a minimization function for the energy. Given as

$$P(\Delta H) = \begin{cases} 1 & \text{, if } \Delta H = H_{after} - H_{before} \leq 0 \\ e^{-\frac{\Delta H}{T}} & \text{, otherwise} \end{cases},$$

where T is referred to as the fluctuation energy.

In these exercises we will only be varying the contact energies $J_{x,y}$ and the temperature/fluctuation energy T.

3 Results

3.1 Cell sorting

In this task, we are asked to run a parameter sweep with Morpheus in order to displays a variety of cell sorting configurations by changing only two of the contact energies. Where the cell sorting configurations

in question, are attainable by considering the surface tension γ between two different cell types, defined as:

$$\gamma_{r,y} = J_{r,y} - \frac{J_{r,r} + J_{y,y}}{2} \tag{1}$$

$$\gamma_{r,m} = J_{r,m} - \frac{J_{r,r}}{2} \tag{2}$$

$$\gamma_{y,m} = J_{y,m} - \frac{J_{y,y}}{2} \tag{3}$$

where the subindex m, r and y signify medium, red cells and yellow cells respectively. The cell configurations are given as:

- Simple cell sorting ($\gamma_{r,y} > 0$, $\gamma_{r,m} = \gamma_{y,m} > 0$)
- Engulfment of red cells by yellow cells ($\gamma_{r,y} > 0$, $\gamma_{r,m} > \gamma_{y,m} > 0$)
- Mosaic cell ordering ($\gamma_{r,y} < 0$, $\gamma_{r,m} > 0$, $\gamma_{y,m} > 0$)
- Engulfment of yellow cells by red cells ($\gamma_{r,y} > 0$, $\gamma_{y,m} > \gamma_{r,m} > 0$)

As a solution for this problem, I have decided to consider changing red with red energy interaction $J_{r,r}$ and yellow with yellow energy interaction $J_{y,y}$ mainly due to the fact that by changing both variable, I am able to change the value of all three surface tensions defined above. With this in mind and the defined conditions/boundaries for each cell sorting configuration, we are therefore able to visualise the regions where each configuration occurs.
Figure 1 henceforth shows the expected $J_{r,r}$ and $J_{y,y}$ values required to obtain each of the desired cell configurations by representing them as different dot colours, while keeping the other interaction constants, namely $J_{r,y} = 16$ and $J_{r,m} = J_{y,m} = 12$.

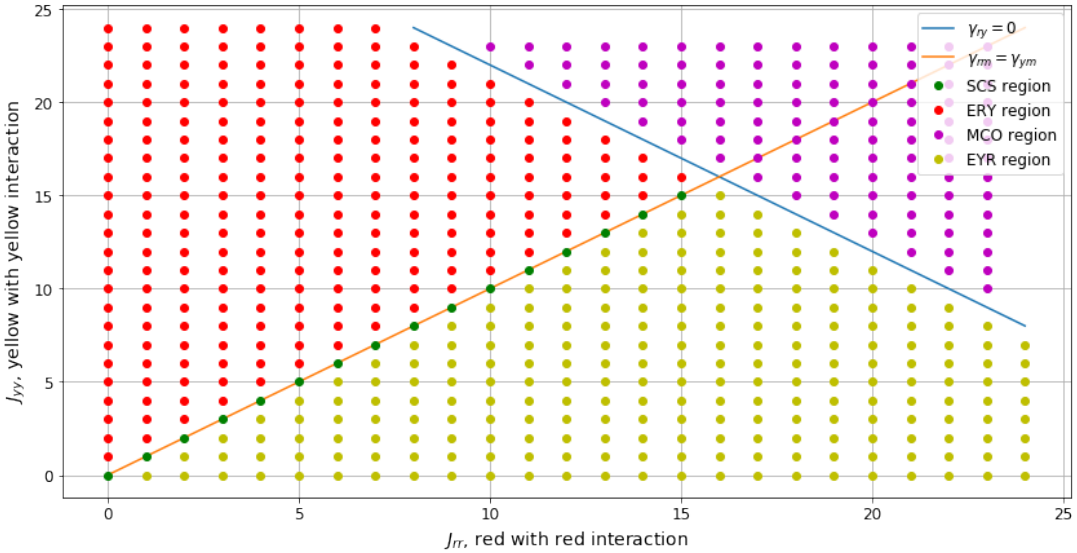


Figure 1: Illustration of Cell sorting phases, where the Single Cell sorting (SCS) region is represented as green, the Engulfment of red cells by yellow cells (EYR) region is represented as yellow, the Engulfment of yellow cells by red cells (ERY) region is represented as red and the Mosaic cell ordering (MCO) region is represented as purple. While the blue line shows when the surface tension between the red and yellow cells is zero and the orange line shows when the surface tension between the cells and the medium respectively, are equal to each other.

Given the results obtained from figure 1, we proceeded by merely picking values combinations that were relatively far from the lines/boundaries, with the main reason of having well defined cell configurations and not hybrids. Experimentation with temperature/fluctuation T was also done in order to observe its effect on the cell system, by simply running the same parameter sweep with a different temperature.

Table 1: Parameter sweep values combination used, as well as the different T values

Sweep parameters	Combinations
$J_{r,r}$	$[2, 2, 16, 16]$
$J_{y,y}$	$[2, 16, 22, 2]$
T values	5,6,7,8

The following figures, from 2 to 5, present the plots obtain from our combination. Where each column represents a specific timestep, from left to right, 100,10000 and 25000 respectively and each row a T value, from top to bottom, 5 to 8. While in each individual figure there are three plots, where the one to the left shows the red and yellow cells configuration, the middle one shows the numbers of cell interaction a single cell has with a different type cell and the right one shows interface between the two cell types.

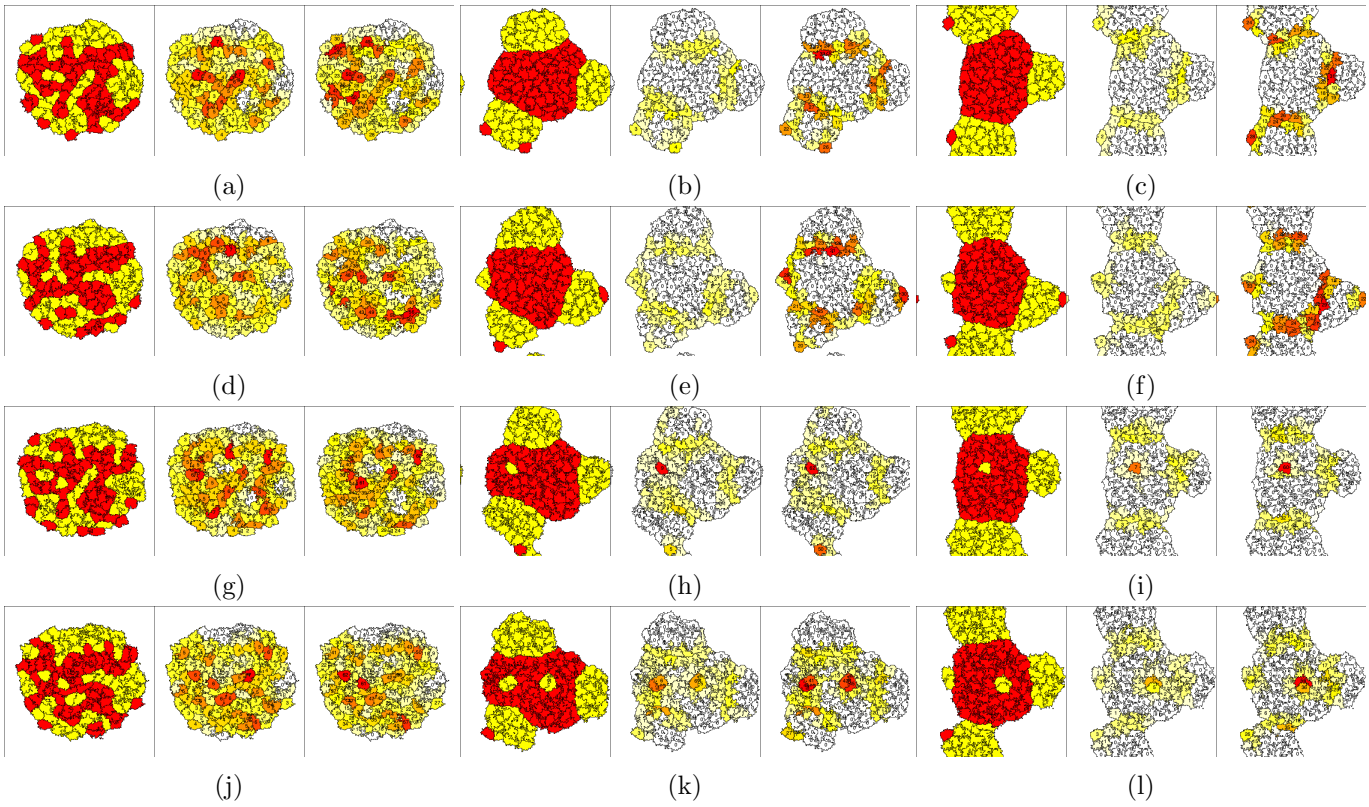


Figure 2: Single Cell Sorting, with $J_{r,r} = J_{y,y} = 2$. Where the top row results were obtained with $T = 5$, the second row with $T = 6$, the third with $T = 7$ and the last with $T = 8$

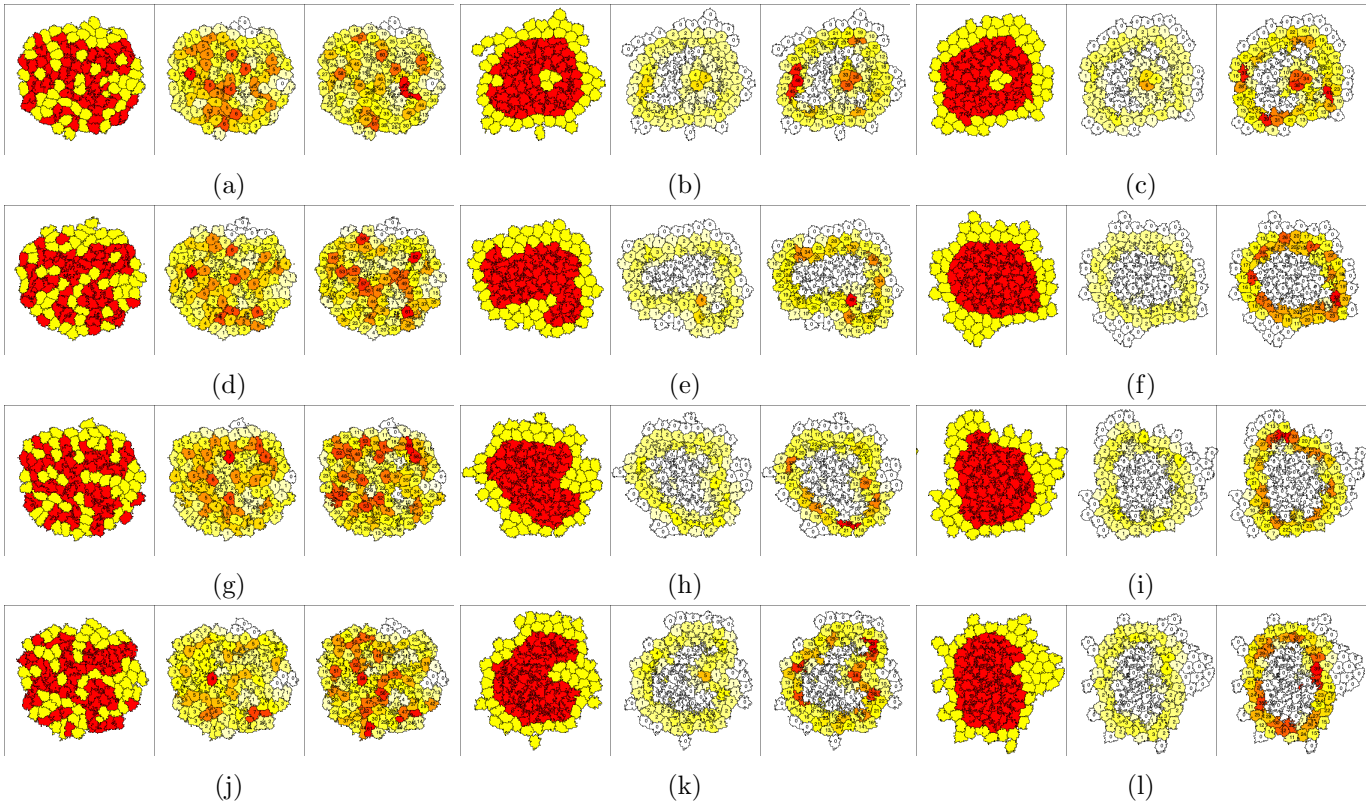


Figure 3: Engulfment of red cells by yellow cells, with $J_{r,r} = 2$ and $J_{y,y} = 16$. Where the top row results were obtained with $T = 5$, the second row with $T = 6$, the third with $T = 7$ and the last row with $T = 8$.

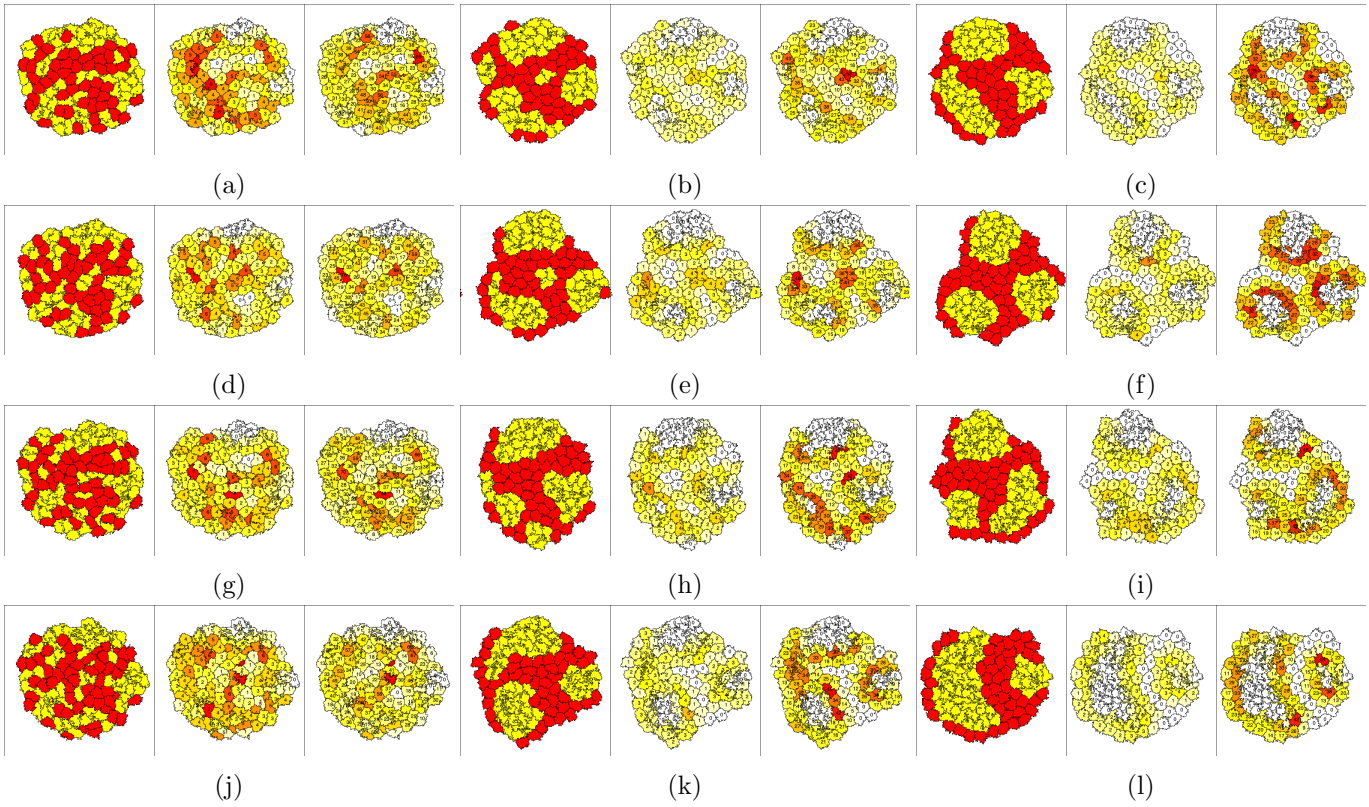


Figure 4: Engulfment of yellow cells by red cells, with $J_{r,r} = 16$ and $J_{y,y} = 2$. Where the top row results were obtained with $T = 5$, the second row with $T = 6$, the third with $T = 7$ and the last row with $T = 8$.

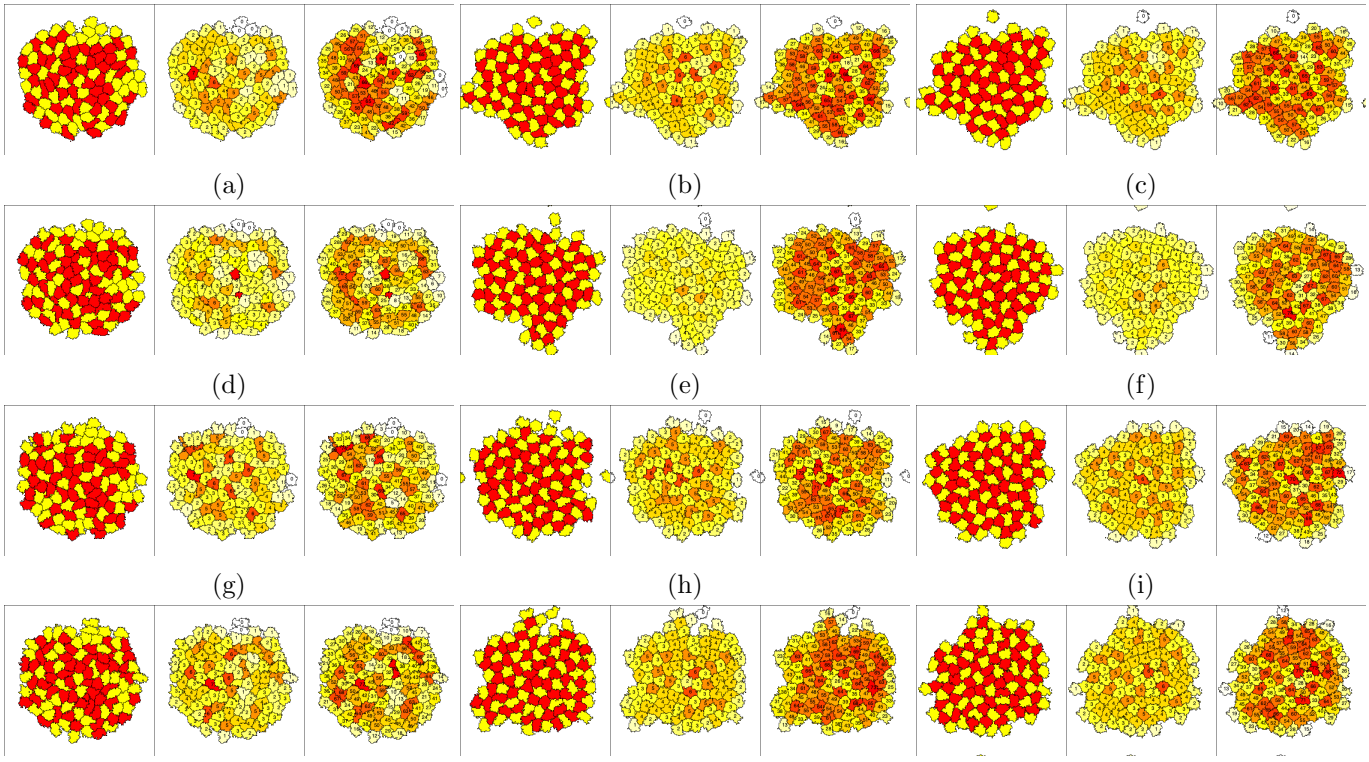
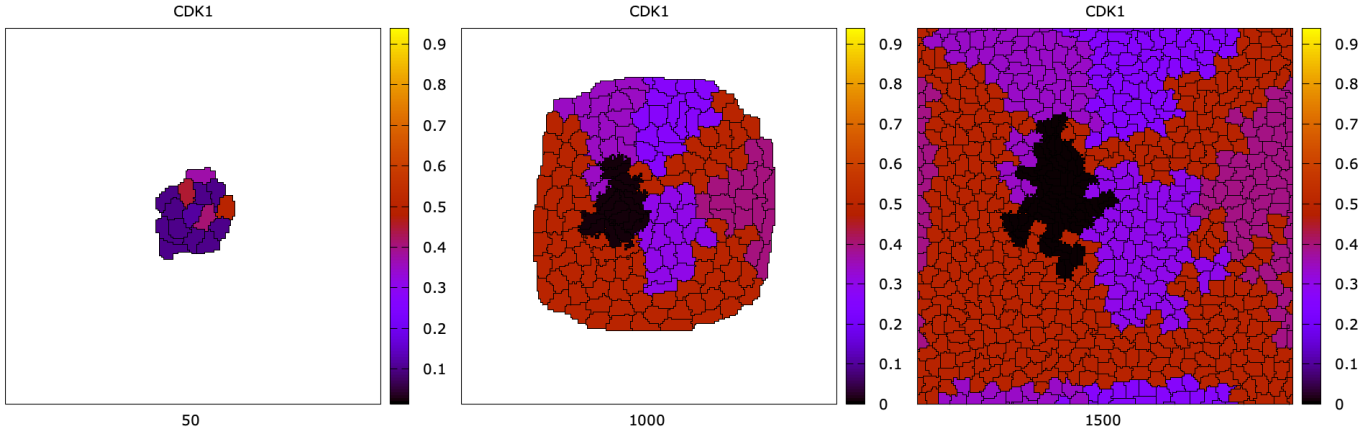


Figure 5: Mosaic cell ordering, with $J_{r,r} = 16$ and $J_{y,y} = 22$. Where the top row results were obtained with $T = 5$, the second row with $T = 6$, the third with $T = 7$ and the last row with $T = 8$.

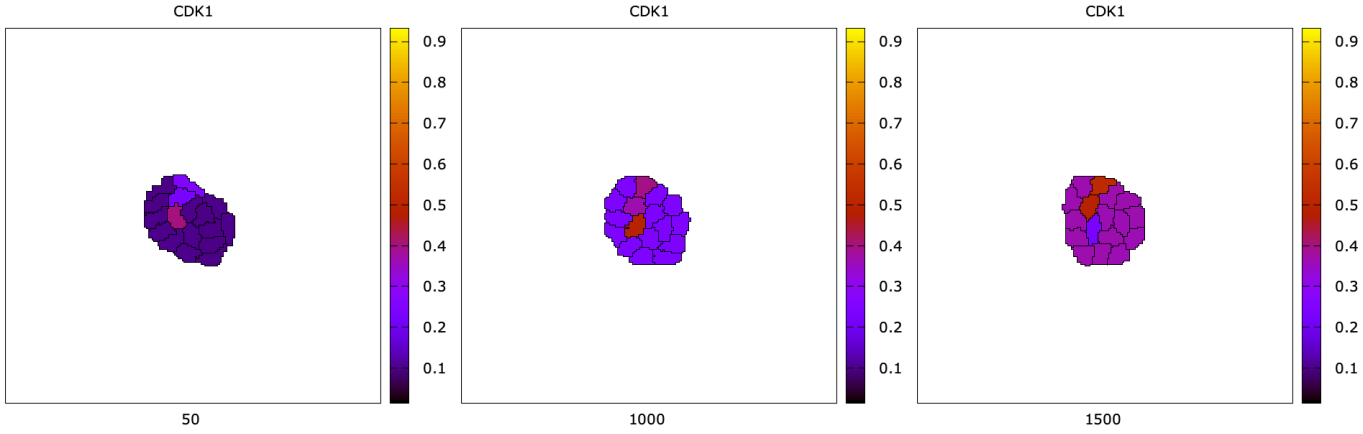
3.2 Tumor growth (not entirely correct, so look at Erin's report for the correct solution)

In this exercise we were asked to modify the tumor growth model that is given to us, such that the cells divide only when their current area is below 90% of their target area.
Here the solution is quite simple, we define a new property variable for the cell with the name Vt, as in volume target and set it as the target volume in the "VolumeConstraint" property in the cell. In the cell division section, where along side the condition for division we added an "and" condition stating that the cell current volume (cell.volume) should be lower then 90% of the target volume, if division is to occur.
Figure 7 clearly shows that we have prevented the cell from over exceeding its target area, while figure 6 shows the uncontrollable cell division behaviour.



(a) (b) (c)

Figure 6: Original tumor growth model results



(a) (b) (c)

Figure 7: Modified tumor growth model results

3.3 Networks

In this task we were asked to guess from the given **network.mp4** movie what are the extra mechanisms added to the 2D cell sorting model that we used on task 1, in order for it to show a vascular network.
The answer, again, is quite simple. Cell division is clearly present, as well as cell with medium interaction. So, all that is need is to delete the second cell from the 2D cell sorting model and add the cell division cycle, introduced in the tumor growth model.
All that we require to do now is to adjust the medium with cell interaction (so that the cells don't pile up into a ball) and add extra condition for cell division and cell death. After careful observation of frame by frame behaviour of the cells in the movie, the following is clear: Cell death occurs when a single cell enters in contact with more the 6 other cell and that division only occurs when a single less the 3 neighbours. Having this in mind we implemented a network model and run it with $T = 2$, $J_{m,c} = 6$ and $J_{c,c} = 3$.
As an end result, we were able to obtain a similar vascular network formation shown in the movie, thus giving us an indication the our hypothesis might not be entirely wrong.

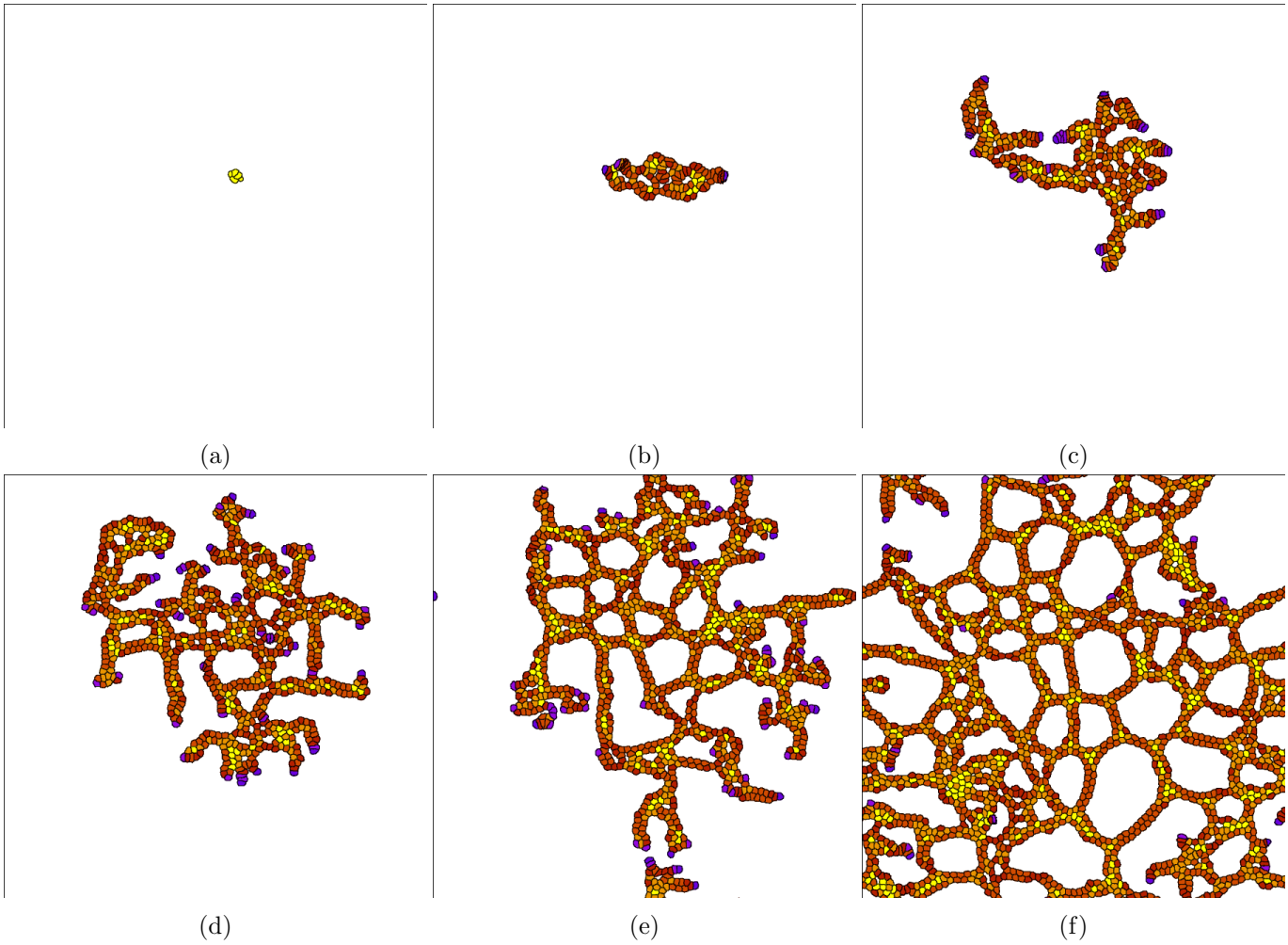


Figure 8: Implemented Vascular Network simulation evolution, where (a) shows the progress at timestep 50, (b) at 1000, (c) at at 3400, (d) at 9000, (e) at 18000 and (f) at 50000.

References

[1] François Graner and James Glazier. "Simulation of biological cell sorting using a two-dimensional extended Potts model". In: *Physical review letters* 69 (Oct. 1992), pp. 2013–2016. DOI: 10.1103/PhysRevLett.69.2013.