Self-Organization of a Virtual Multicellular Organism by Adding a Shape Model in the Cellular Potts Model

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Abstract

The Cellular Potts Model (CPM) is a cellular automaton (CA) allowing to model the morphogenesis of living cells. It characterizes a cell by its volume, surface and type. The CPM has already been used to simulate several models of cell self-organization. However, the cell shape is under-constraint $i.e.$ it does not implies a unique shape. We propose a definition and an implementation of the cell shape in the CPM, that can target a unique shape. The results of our simulations show that this target shape can structure and maintain the cellular tissue since the beginning of its growth and during its life.

I Introduction

The Cellular Potts Model (CPM) is a cellular automaton (CA) made by Glazier and Graner (Graner and Glazier, 1992). It has been often used to model and simulate phenomena occurring in the morphogenesis and embriogenisis. (Cickovski et al., 2005; Marée, 2000). The CPM is an extension of the Potts Model developed by Potts in 1952 which generalizes the Ising Model as described in (Wu, 1982). The dynamics of these models are based on a minimization of energy. In the discrete case, the CPM consists of a grid where a set of cells fills each site of the grid. The entities of the system are called cells and are characterized by a volume, surface and type. They are in interaction via contact energies and restricted access to grid sites.

The first model used to illustrate the CPM is the cell sorting. It shows how simple local interactions allow self-organization of the biological cells. At the cellular automata level the self-organization has already been done in more abstract phenomena like the Game of Life developed by John Conway (Gardner, 1970) or the Langton's Ant (Langton, 1984).

Since this first model several extensions of CPM have been done (Anderson et al., 2007). However, the cell shape is not defined in a more specific way. Indeed, in the basic CPM, the shape is characterized only by a target volume and surface. So several shapes can verify a same target volume and surface. In this paper we propose to add an energy that allows the cells to emerge towards a unique and defined shape. This energy comes from a set of springs which provides the cell a elastic shape .

We use the cell shape to structure the shape tissue via the cell self-organization. To test and show the characteristics of the cell shape we simulate a model which comes from an extended CPM. This model allows the cell to self-align and to build a coherent cellular tissue $i.e$ with a recognizable shape and a dynamical tissue renewal.

This paper is organized as follows. A formalization of the CPM is given in section II. In section III we describe the MorphoPotts which represents a cell defined in the CPM to which we add the elastic shape in section IV and other cell behaviors. Using the MorphoPotts, in section V, we simulate a model of tissue formation from which a stability of the cellular tissue and a dynamical tissue renewal emerge. Finally, we conclude in section VI.

II Presentation of the CPM

In this part we recall the formalism of CPM explained in (Graner and Glazier, 1992; Glazier and Graner, 1993). The first part describes the necessary notations to the comprehension of this paper. The second part describes the strong notions of this formalism (see Figure 1), $i.e.$ the state of the system and the transition function thanks to the transition probability, the energy function and the neighborhood function.

Notation. A grid is denoted by Sx and a site of this grid is denoted by (i, j). The value of a site (i, j) is denoted by $sx_{i,j}$. A cell is denoted by C_σ^t with $\sigma \in [1, N]$ where N is the number of cells and t the type of cell. The number 0 is reserved for the medium. A cell C_σ^t has a target volume (resp. surface) $V\sigma_t$ (resp. $S\sigma_t$) and current volume $V\sigma$ (resp. $S\sigma$). The target volumes and target surfaces of the cell are the volumes and surfaces to which the cell tends. The contact energies are recorded in a matrix T such that $T_{\sigma,\sigma'}$ (resp. $T_{t,t'}$) is the contact energy between the cell C_σ^t and the cell $C_{\sigma'}^{t'}$ (resp. between the cells of type t and t').

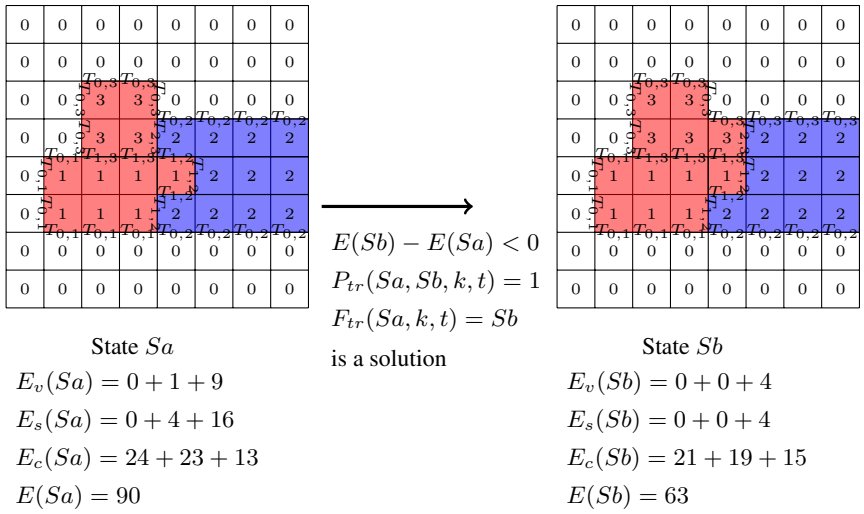


Figure 1: Example of a transition in the CPM. A state Sx is a grid 8x8 where to each site (i, j) we associate a value $sx_{i,j}$. So we have four cells ($\sigma \in [0, 3]$): one cell for the medium (C_0^m), two cells of red type (C_1^r, C_3^r) and one cell of blue type (C_2^b). The cells of the red type have the following characteristics: $V_{target} = 7$, $S_{target} = 12$, and the cell of blue type the following characteristics: $V_{target} = 10$, $S_{target} = 11$. In the state Sa the cell C_1^r (resp. C_2^b, C_3^r) has a volume $V1 = 7$ (resp. $V2 = 11$, $V3 = 4$) and a surface $S1 = 12$ (resp. $S2 = 13$, $S3 = 8$). In the state Sb the cell C_1^r (resp. C_2^b, C_3^r) has a volume $V1 = 7$ (resp. $V2 = 10$, $V3 = 5$) and a surface $S1 = 12$ (resp. $S2 = 11$, $S3 = 10$). The cell for the medium does not have volume and surface constraints. The matrix (symmetric) of contact energy (given) is defined as: $T_{0,1} = T_{0,3} = 2$, $T_{0,2} = 1$, $T_{1,2} = T_{2,3} = 3$, $T_{1,3} = 0$. Since the cell C_1^r and the cell C_3^r are of the same type $T_{1,?} = T_{?,3}$.

State of the System. The CPM is composed of a grid Sx[1] of D dimensions (here $D = 2$). Each site (i, j) is filled by a particle of cell C_σ^t, *i.e.* the value $sx_{i,j}$ of site (i, j) in the state Sx is equal to σ. So a cell C_σ^t is equal to $\{(i, j) \in Sx | sx_{i,j} = \sigma\}$ the set of sites whose value is σ.
Finally a state of system is a grid Sx where each $sx_{i,j}$ is equal to an integer $\sigma \in [0, N]$.

Transition Function. Let $F_{tr}(Sa, k, t) = Sb$ the transition function of the CPM between the State Sa and Sb according to k and t. Let Sc be the state Sa where the value of a site has been replaced by the value of a neighbor site. If the probability of transition P_{tr} between the states Sa and Sc is accepted, then $Sb = Sc$, otherwise $Sb = Sa$.

$$\begin{aligned} F_{tr}(Sa, k, t, p) = Sb \Leftrightarrow \exists (i', j') \in neighbor(i, j)(\\ (sc_{i,j} = sa_{i',j'}) \wedge \\ (Sc - sc_{i,j} = Sa - sa_{i,j}) \wedge (p = rand(]0, 1])) \wedge \\ (p \leq P_{tr}(Sa, Sc, k, t) \Rightarrow Sb = Sc) \wedge \\ (p > P_{tr}(Sa, Sc, k, t) \Rightarrow Sb = Sa)) \end{aligned}$$

where $rand(E)$ returns a random element of the set of E, $neighbor(i, j)$ is the set of neighbor sites of (i, j) and P_{tr} the probability of transition.
We can observe that only one site of the grid can change and since several sites can be candidates to change, the dynamics is asynchronous and non-deterministic.

Probability of Transition. The Probability of transition used is the Monte Carlo probability following a temperature t. Let $P_{tr}(Sa, Sb, k, t) = p$, the probability of transition between the states Sa and Sb according to k and t.

$$\begin{aligned} P_{tr}(Sa, Sb, k, t) = p \Leftrightarrow \\ t > 0 \wedge (E(Sb) - E(Sa)) \leq 0 \Rightarrow p = 1 \\ t > 0 \wedge (E(Sb) - E(Sa)) > 0 \Rightarrow \\ p = \exp\left((E(Sb) - E(Sa))/kt\right) \\ t = 0 \wedge (E(Sb) - E(Sa)) < 0 \Rightarrow p = 1 \\ t = 0 \wedge (E(Sb) - E(Sa)) = 0 \Rightarrow p = 0.5 \\ t = 0 \wedge (E(Sb) - E(Sa)) > 0 \Rightarrow p = 0 \end{aligned}$$

where $E(S)$ is the function of energy.
This probability promotes the transitions which lead to a lower energy state.

Energy Function. Let $E(S) = e$ the energy function of the state S. This function characterizes the state of the system. In the CPM, a basic function depends on the volume and surface of each cell and on the contact energies between two cells. $E(S)$ can be defined as:
$E(S) = \lambda_c * E_c(S) + \lambda_v * E_v(S) + \lambda_s * E_s(S)$ with
$E_c(S) =$

$$\sum_{(i,j) \in S} \sum_{(i',j') \in neighbors(i,j)} {}^2T_{s_{i,j}, s_{i',j'}} * (1 - \delta_{s_{i,j}, s_{i',j'}})$$

where λ_c, λ_v, λ_s are constants, $T_{x,x'}$ is a matrix of contact

[1] Here the environment is discrete but the continuous case is also defined (Glazier and Graner, 1993).

[2] In our simulations the neighbors are the nearest on a 3D square lattice.

energy between the type t and t' respectively of C_x^t and $C_{x'}^{t'}$. If $x = x'$ then $\delta_{x,x'} = 1$ otherwise 0.

$$E_v(S) = \sum_{\sigma \in [1,N]} (V\sigma_t - V\sigma)^2$$

$$E_s(S) = \sum_{\sigma \in [1,N]} (S\sigma_t - S\sigma)^2.$$

III MorphoPotts

To model biological phenomena in a more realistic way, we have proposed in (Tripodi et al., 2010) an multi-agent approach of CPM and a cell called MorphoPotts. The MorphoPotts is an extension of the cell defined in the CPM by adding the following behaviors: secretion and consumption of molecules, transformation of molecules into energy, migration on a gradient of molecules, cell division and cell differentiation. The MorphoPotts is very close to MorphoBlock (Ballet et al., 2009) compared to secretion of molecules and the migration under a gradient of molecules. But the core of MorphoBlock is a pixel whereas the core of MorphoPotts is a cell defined in the CPM. At CPM level, the closest work to MorphoPotts is probably Compucell3D (Cickovski et al., 2007), a software which implements the CPM and other behaviors. In this section, we describe fristly the MorphoPotts, and secondly a step of simulation of CPM-MorphoPotts couple.

Description of MorphoPotts

A MorphoPotts C_σ^t is based on the properties of the cell defined in section II, but it also has an internal energy E. This energy results from the consumption of molecules found in the environment. The MorphoPotts can perceive and modify the environment beyond their neighborhood boundaries defined in section II.

The behaviors of the MorphoPotts are described in Table 1. We assume that the secretion creates a gradient because the diffusion of molecules is faster than cell migration and the secretion is continuous. For the same reasons we assume that the consumption of molecules creates a "well" ($i.e.$ inverse effect of secretion). In this paper, the energy of the MorphoPotts is used as a criterion for MorphoPotts division and MorphoPotts death.

Step of Simulation

The step of the simulation which combines the CPM and the MorphoPotts is following:

1. Let i equals to 0 and n equal to the membrane size of all MorphoPotts.
2. While i is lower than n
   (a) One transition function of the CPM is applied.
   (b) If the criterion of division of the chosen MorphoPotts during the transition is verified, they divide.
   (c) i is incremented by 1
3. All MorphoPotts execute their method of maintenance.
4. All MorphoPotts execute their method of secretion.
5. All MorphoPotts (the scheduling is random to delete the artefacts) execute their method of consumption.
6. If the internal energy of the cells is lower than 0, they die.

The step of simulation can, for each cell, modify each membrane site before calling to methods of maintenance, secretion, consumption and death. This allows to synchronize every MorphoPotts and so to delete some artefacts due to asynchronicity of the CPM. Indeed, in reality, the cells move at the same time and not one after another.

Proposition of a cell shape energy

In the previous section we have built a model of cell called MorphoPotts. However, the cell shape is not strongly defined. A volume and a surface do not entirely characterize a geometric shape. The goal of this section is to constraint the cell to keep a certain rigidity of the shape. The cell shape is an important feature. It can lead to different functions and properties, $i.g.$ the spherical shape of red blood cells adapts perfectly to their role in transport from the bloodstream, the spindle-shaped muscle cells allows them to contact and realizes a close fit between them, thus facilitating the simultaneous contraction of muscle tissue.
Several propositions have already been done to target the cell shape, like cell elongation (Merks et al., 2006), but to our knowledge, none can target all forms. The idea is to give an elastic shape to the cell. For this we add a set of springs to the cell like described in Figure 2. In this section, we describe fristly the formalism , and secondly the implementation.

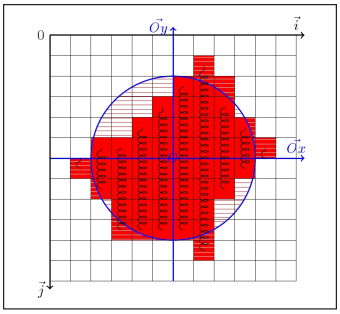


Figure 2: Example of elastic shape. We have one red cell C_2^r with an elastic shape where the distribution $sL0_p^s$ of springs R_p^s is given by the function of a circle of center O and radius 4, represented by the blue circle. The energy of this elastic shape is the sum of distance power 2 between the sites with the lines and the circle blue. The sites with white lines are sites of extension and the sites with red lines are sites of compression.

Behavior	Description
Secret a gradient of arg molecules Y	If the site (i,j) contains n molecules Y then, after the secretion, the site will contain a number of molecules Y equal to the integer closest to $n + \frac{arg}{\sqrt{(i-gx)^2+(i-gy)^2}}$ where (gx, gy) is the center of gravity of MorphoPotts.
Consume a gradient of arg molecules Y	If the site (gx, gy) contains n molecules Y and the site (i,j) contains n', the number of molecules Y in (i,j) is modified such that the new value is 0 if $n' < \frac{min(n,arg)}{\sqrt{(i-gx)^2+(j-gy)^2}}$ otherwise the new value is the integer closest to $n' - \frac{min(n,arg)}{\sqrt{(i-gx)^2+(j-gy)^2}}$
Migrate to the molecules	The energy function of the CPM is modified by adding a new energy $E_{migr} = -arg * \sum_{(i,j)\in M_\sigma} nbMolecules((i,j),Y)$ where $nbMolecules((i,j),Y)$ is the number of molecules Y on the site (i,j).
Transform the consumed molecules in energy	In this paper for each consumed molecule the energy is incremented by 1.
Differentiate	The probability that the MorphoPotts changes its types is equal to $\frac{arg}{\sum_{Y'\neq Y} arg'}$ where arg is the probabilty associated to the type Y cell.
Divide	A MorphoPotts can divide in two axes (vertical or horizontal). A new MorphoPotts is created according to the probability of differentiation. The energy of the new MorphoPotts is equal to E' and the energy of the old MorphoPotts is equal to E (internal energy of the MorphoPotts) minus E' minus $cost$ the cost of the MorphoPotts division.
Maintain	The energy of the MorphoPotts is decremented by arg, representing the costs of the maintenance.
Die	The MorphoPotts dies if its internal energy is equal to 0. The death means that the MorphoPotts looses all its abilities and it does not generate energy in the CPM.

Table 1: Abilities of the MorphoPotts

Formalisation of the elastic cell

To constraint the cell to keep a 3D shape in the CPM formalism, we define in this section a function of energy $E\sigma_{sp}$. $E\sigma_{sp}$ is null if the shape is reached by the Cell C_σ. $E\sigma_{sp}$ is the sum of energies provided by the springs given to the cell. The energy of one spring R at the position p, p' (the position of these extremities) for a cell C_σ is defined like:

$$\sum_{s_a=\sigma} \begin{cases} 1/2 * k * dist(a,R)^2 & \text{if this spring is the closest to site } a \text{ according to criterion } C(R,a) \text{ and } dist(a,R) = min(|\overrightarrow{ap}|, |\overrightarrow{ap'}|) \\ 0 & \text{otherwise.} \end{cases}$$

where k is the constant force of the spring.
The disposition of the springs depends on the model and several shapes can be given to one cell. In this paper the springs are parallel. For this:

- we add a Cartesian coordinate system (O, Ox, Oy, Oz) where O is a point in the grid. The axis Oy gives the direction of the springs.

- we add a set of springs perpendicular to the plan defined by the axes Ox and Oz, i.e the springs $R\sigma_p^s$ where $s \in \{+1, -1\}$ whose two extremities are in position (p_x, p_y, p_z) and $(p_x, s * L0_p^s + p_y, p_z)$, $L0_p^s$ being the rest length of spring. The distribution of $R\sigma_p^s$ and the length $L0_p^s$ depend on the desired shape (see Figure 2).

To compute $E\sigma_{sp}$ we define in this paper the following criterion C:
"$R\sigma_p^s$ is the closest spring to the site (i,j,l) if a spring $R\sigma_{p_x,y',p_z}^s$ such that $dist((i,j,l), R\sigma_p^s) > dist((i,j,l), R\sigma_{p_x,y',p_z}^s)$ does not exist"
So $E\sigma_{sp}$ in this paper is defined like:

$$E\sigma_{sp} = 1/2 \sum_{R\sigma_p^s} \sum_{s_a=\sigma \wedge C(R\sigma_p^s,a)} k_p^s * dist(a, R\sigma_p^s)^2$$

Implementation of the elastic cell

The implementation of the elastic cell can be done by the computation of the intersection between a cell and a line (the axis of the springs). A naive implementation could be to browse all sites of the cell and to build the set of sites which are crossed by the spring. The problem is that it will take too long simulation time.

In one simulation step of the CPM, only one site value $s_{i,j,l}$ changes, modifying the cells $C_\sigma, C_{\sigma'}$. So we have:
$\Delta E\sigma_{sp} = 1/2 * ($
$z(j, L0_p^s) * k_p^s * dist((i,j,l), R\sigma_p^s)^2 -$
$z(j, L0_{p'}^{s'}) * k_{p'}^{s'} * dist((i,j,l), R\sigma_{p'}^{s'})^2)$
C_σ is the cell which increases, C'_σ is the cell which decreases and (i,j,l) the site added or deleted. $C(R\sigma_p^s, (i,j,l))$ and $C(R\sigma_{p'}^{s'}, (i,j,l))$ are verified.
$z(j, L0_p^s) = 1$ if $p_j \leq j \leq s * L0_p^s + p_j$ (compression) otherwise -1 (extension).

Also to compute $\Delta_{E\sigma_{sp}}$, we store in a table for each site p of the shape, the static following informations: $z(p_j, R_p^s)$,

$L0_p^s$ and k_p^s, in the coordinate system of the shape.
So $\Delta_{E\sigma_{sp}}$ returns to compute one translation and one rotation (to find the position of the changed site in the coordinate system of the shape) and an access to the table. The cost is constant and does not significantly modify the simulation time.

Rotation and Translation of the elastic shape

We saw in the previous part that the definition of the cell shape uses a target shape. However, the shape is located at a specific coordinate. This causes the cell does not move in the environment. In this part we show how we consider the rotation and the translation of the shape according to the adding or deleting sites

Rotation of the elastic shape This part describes how the shape turns in the environment. For example, if a cell is attracted to a direction due to a gradient of molecules, the sites which are closed to the source of the gradient have a higher probability to be added to the cell. This behavior can turn the cell in the direction of the gradient.

We construct a function named $rotation(m, p, C_\sigma)$ which returns a vector of angle. The size of this vector is equal to the number of dimension. The angle corresponds to the rotation of the cell (C_σ) shape after adding the site s_p if $m = +$ or the deleting of the site s_p if $m = -$. The shape rotation is made by the rotation of its coordinate system compared with the coordinate system of the environment.

Here, $rotation(m, p, C_\sigma) = \alpha/V_\sigma * (arcant2(p_y, p_x), arcant2(p_z, p_y), arcant2(p_x, p_z))$.
This function means that the rotation angle is the angle between the axis Oy, the origin and the point p in the coordinate system of the shape. The angle value is normalized by the volume of the cell and the value is increased or decreased by α.

Translation of the elastic shape We construct a function $translation(C_\sigma)$ which returns a vector. This vector is used to translate the shape after adding or deleting a site of the cell C_σ.

Here, $translation(C_\sigma) = \beta * \Delta\vec{G}_\sigma$ where ΔG_σ is the variation of the gravity center of the cell C_σ during a simulation step of the CPM. β can favour or not the translation of the shape.

Rotation and Translation in the simulation step The rotation and translation of the shape is possible because environmental or internal conditions can add or delete sites of the cell in specific directions. However if the translation and the rotation are made at each step of the simulation, an undesirable $perpetuum\ mobile$ is possible.

Indeed, if the translation is realized towards a direction, the sites in this direction will be added to the cell that implies a new translation in this same direction and etc ... The translation and rotation are not done when the transition is accepted thanks to the energy provided by the springs, $i.e.$ when the variation of the energy is negative. The shape has to be reached before doing a new translation or rotation.

IV Validation of the elastic shape

To validate and show the interest of the elastic shape we test 2 models of MorphoPotts. The first model proposes to test the energy of the shape without cell translation and rotation, the second to test the cell translation and rotation by simulating the formation of a tissue via cell self-organization.

Example of the elastic shape

In this part, we test the elastic shape. For this, thanks to our tool we can draw a 3D shape and automatically store the informations described in section IV (see figure 3(a)).

The model used for the simulation consist of 4 MorphoPotts: one MorphoPotts to model the exterior medium to the cells and three MorphoPotts to test the same shape. The coordinate system of the shape of the middle MorphoPotts is rotated by $\pi/2$ on the axis $0x$ (see Figure 3(a)). A vertical section of the shape is given in Figure 3(a). The visible springs on the horizontal axis have the parameters $k = 10$. The springs of length null, complete the horizontal axis with $k = 10^6$ to avoid a growth of the cell along this axis. In this model, the parameter α (resp. β) of the rotation (resp. translation) is $null$. We just test the target shape. No contact, volume and surface energy are taken into account in this Model.

The results of the simulation are given in the Figure 3. The Figure 3(a) shows the initial state. The Figure 3(b) is a picture of the shape being built. The Figure 3(c) shows the MorphoPotts having reached the target shape and also validate our implementation of the elastic shape.

V Cell Self-organization

In this section we present a simulation of a model which test both the translation and rotation of the shape, and the cell self-organization to build a coherent tissue (a recognizable shape and a dynamical tissue renewal). After a description of model, we discuss the parameters before showing the results of the simulations.

Presentation of the model To show the interest and the properties of the rotation and the translation of the shape, we made a model allowing to simulate the generation and the life of a cellular tissue. This model consists of three type MorphoPotts:

- the first type of MorphoPotts models the exterior medium.
- the second type of MorphoPotts produces molecules in the medium.
- the third type of MorphoPotts consumes the produced molecules by the second type and divides. This type has a elastic shape and is used to build the tissue.

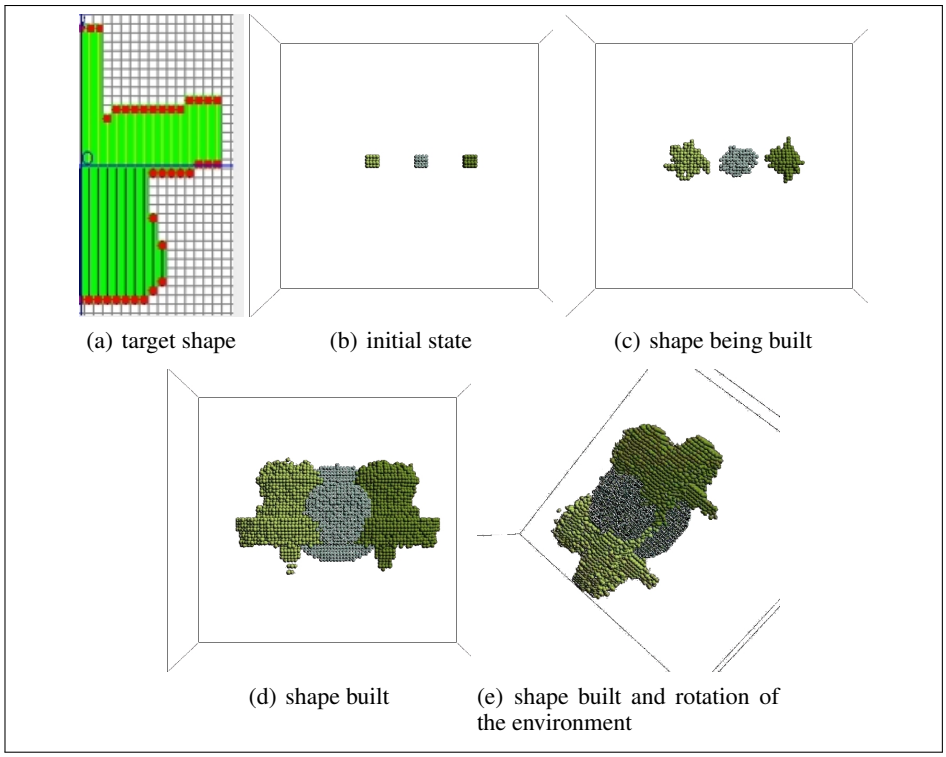


Figure 3: Example of elastic shape

The interactions between the MorphoPotts are:

- a direct interaction. A negative energy of contact (means that the MorphoPotts which stay together do not use energy) is set between the MorphoPotts of type 3 . A positive energy of contact is set between the MorphoPotts of type 3 and 2
- an indirect interaction. The MorphoPotts of type 2 provides molecules to MorphoPotts of type 3. If the MorphoPotts of type 3 does not found the molecules, it dies.

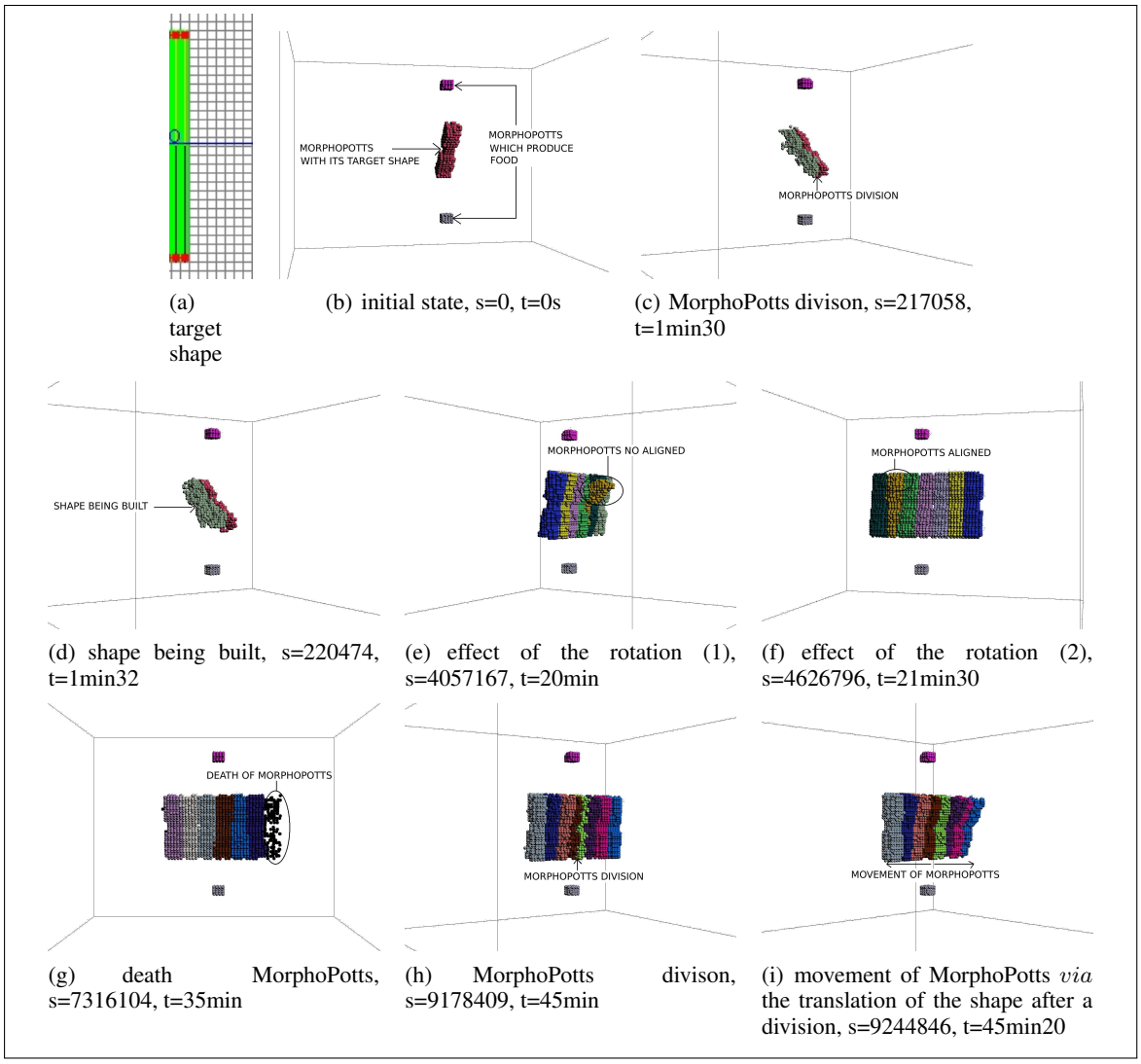
We show with this model that the cell shape and the contact energy can structure the cellular tissue. The competition of the MorphoPotts to consume the molecules allows a finite growth of cellular tissue like described in (Laforge et al., 2005) and a dynamical tissue renewal.

Parameters analysis We have defined 4 types of MorphoPotts. The parameters of these MorphoPotts are given in Table 1.

The energies of contact verify that $5 * T_{1,3} + T_{3,3} < 0$. When two MorphoPotts of type 3 are in contact thanks to the adding of a site, $\Delta E_c < 0$. The adding of this site is favored by energies of contact.
The concentration of the molecule 1 (produced by MorphoPotts of type 2) decreases with the distace from the source. If the MorphoPotts of type 3 are at a too long distance from a MorphoPotts of type 2, they have not enough molecules to survive (higher than 52 pixels).
The MorphoPotts of type 3 can divide if its energy is higher than 20000 (experimental value).

The shape described in Figure 4(a) is given to the MorphoPotts of type 3. The volume and the surface are each equal to 328,64. So the target volume and surface can fill the shape. 21 extra sites have to be added to the MorphoPotts of type 3 to verify the target volume and surface. The visible springs in Figure 4(a) on the horizontal axis have the parameters $k = 10^7$ to force the MorphoPotts to reach its shape. The springs of length null complete the horizontal axis with $k = 10^5$ to avoid a growth of the cell along this axis. In this model, the parameter α (resp. β) of the rotation (resp. the translation) is 10 (resp. 75). The rotation and the translation are possible only on the axis Oz because we model the construction of a cellular tissue along one direction. The α and β have been calibrated by dichotomy.

The parameters kt of the CPM is equal to 1, so the probability of transition is equal to $e^{-\Delta E}$. The transitions with $\Delta E > 0$ have a weak chance to be accepted. The constant λ_c (resp. λ_v, λ_s) is equal to 1 (resp. 10000, 10000). These constant values allow the MorphoPotts not to oversize their target volume.



(a) target shape

(b) initial state, s=0, t=0s

(c) MorphoPotts divison, s=217058, t=1min30

(d) shape being built, s=220474, t=1min32

(e) effect of the rotation (1), s=4057167, t=20min

(f) effect of the rotation (2), s=4626796, t=21min30

(g) death MorphoPotts, s=7316104, t=35min

(h) MorphoPotts divison, s=9178409, t=45min

(i) movement of MorphoPotts *via* the translation of the shape after a division, s=9244846, t=45min20

Figure 4: Cell Self-organization. This simulation shows how the cell shape can structure and maintain the cellular tissue since the beginning of its growth and during its life. t is the time of simulation and s is the number of CPM steps. The pc used used for this simulation is a Pentium Quad 2.8Ghz and the language is JAVA.

type	target volume	target surface	Energy of Contact	Secretion	Consumption	Division	Maintenance
1 (exterior medium)	_	_	$T_{1,3}$=100	_	_	_	_
2 (producer of molecules)	_	_	_	secr(310000,1)	_	_	_
3 (producer of molecules)	350	350	$T_{3,1}$=100 $T_{3,3}$=-10000	_	cons(1000,1)	div({E>20000, E/2,0}, 3)	main(600)

Table 2: MorphoPotts Parameters. The symbol _ means that the parameter is not taken into account. $cons(1000, 1)$ ($resp.$ secr(310000,1)) means that the MorphoPotts consumes ($resp.$ produced) a gradient, 1000 ($resp.$ 310000) molecules of type 1 in the center. div({E>20000, E/2,0}, 3) means that if the internal energy of the MorphoPotts is higher than 20000, it divides and gives half of its energy to newly born MorphoPotts and the cost of the division is null. main(600) means that the maintenance cost 600.

Discussion of the results The Figure 4 shows the results of the simulation[3]. The initial state (see Figure 4(b)) consists of one MorphoPotts of type 3 being attained its shape. The MorphoPotts of type 2, which produce the molecules, are also present. The MorphoPotts of type 1, which models the exterior medium, is invisible and occupies the empty environment. The environment is a 3D matrix 100x100x100.

Between Figure 4(b) and 4(c) the MorphoPotts of type 3 consumes enough molecules to have an energy allowing its division (on the axis Oy) in Figure 4(c). In Figure 4(d) the shape of the MorphoPotts of type 3 is being built. In the same time the two MorphoPotts of type 3 self-align thanks to the energies of contact. In figure 4(e) and 4(f) we observe the effects of the rotation of the shape. A MorphoPotts is not aligned with the other, the energy of contact favors the sites which are in contact with the other MorphoPotts to be added. So the shape is rotated in this direction. In figure 4(g), the MorphoPotts on right in the figure is too far (a distance higher than 52), and dies. This keeps a finite width of the cellular tissue. Figure 4(e) and 4(f) show the effects of the translation of the shape. After a MorphoPotts division at the center of the tissue, the MorphoPotts are compressed. This implies a translation of the MorphoPotts towards the exterior of the tissue.

The rotation of the shape and the energy of contact allow a self-alignment of the MorphoPotts. The translation of the shape and the competition between the MorphoPotts allow a finite growth of cellular tissue. During the simulation, the MorphoPotts divide at the center of tissue, move towards the exteriors and die at the extremities of the tissue. The shape of the tissue emerges thanks to the shape of the MorphoPotts.

VI Conclusion

We have defined a virtual cell called MorphoPotts. This MorphoPotts is based on the cell defined in the Cellular Potts Model. The MorphoPotts keeps the properties of this cell and the cell behaviors that have been added. In the CPM, the cell shape is represented only by a target volume and surface. We have proposed and implemented a target shape. Therefore, a set of springs is given to the MorphoPotts to build the shape. These springs provide an energy which is used to build a new function of energy in the CPM.

We have tested the target shape in two simulations. The first one shows that it is possible, with this target shape, to give a complex form to the MorphoPotts. The second simulation shows that this target shape allows to structure the cellular tissue. Combined with the energy of contact, the target shape allows the MorphoPotts to self-align. By adding the notion of the internal energy, available in the notion of the MorphoPotts, the second simulation shows that the MorphoPotts self-organize to form a cellular tissue. This tissue has a recognizable shape and a dynamical tissue renewal.

[3]The video of this simulation is available at
http://pagesperso.univ-brest.fr/~tripodi/private/ALIFE12/

Acknowledgements

We thank the Region Bretagne for its financial contributions.

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