

# Textures in Simulations of Biological Cell Growth

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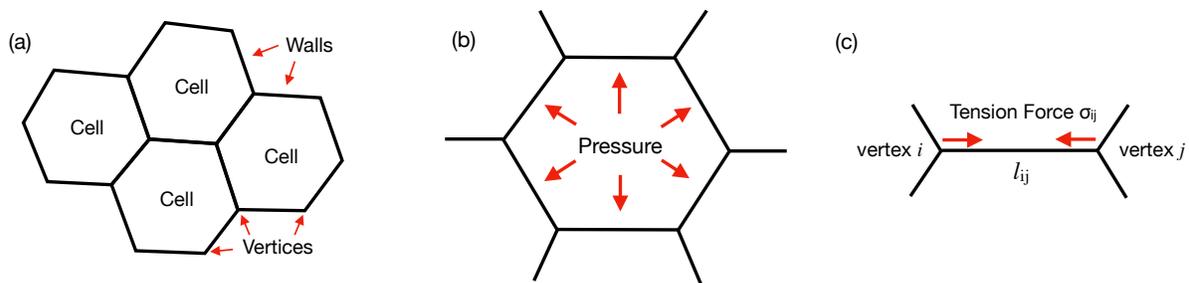
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## Abstract

We present botanically-inspired simulations of cell growth and division. The simulations abstract cells as polygons with visco-elastic cell walls that confine a pressurized fluid. Cell growth and division depends on the concentration of a growth hormone that is produced in a set of prescribed cells and diffuses throughout the system. We present a variety of patterns and textures in the resulting cell formations.

## Introduction

The simulations presented in this paper model the growth and division (mitosis) of plant cells. Unlike animal cells, plant cells do not move relative to one another after they divide. Once a plant cell divides, the two daughter cells will remain next to each other indefinitely, connected by a shared cell wall. The aim of this paper is to explore a biologically motivated model of cell growth to see what types of patterns and textures are made possible by abstract rules of cell division and growth. This paper was also inspired by the work of Hart [2], who created remarkably life-like plant forms from simple rules that operate on triangulated graphs. However, unlike his work, we focus more on cellular textures and patterns that emerge on a smaller scale. If his 3D models grow life-like virtual plants, our 2D models grow microscopic specimens in a virtual petri dish.



**Figure 1:** (a) Cell walls are modeled as two-dimensional polygons. Neighboring cells share a common wall. (b) Cells contain a fluid medium that exerts an outward pressure on the cell walls. (c) Cell walls act like visco-elastic springs that supply a restoring force when compressed or stretched.

## Cell Wall Dynamics

We adopt the “vertex dynamics” approach used by a number of biophysics groups [1, 4, 5] to model cell mechanics in 2D. Cells are composed of straight-edged walls that meet at vertices. The walls that bound each cell form a non-self-intersecting polygon. Each vertex is the point of intersection of two or more walls (see

Figure 1). The vertices are treated as point masses that move in response to forces applied by the elastic cell walls and to pressure forces exerted by the fluid medium within each cell.

An equation of motion for each vertex may be obtained using Newton's second law and by assuming each vertex has a constant mass  $m$ :

$$m \frac{d^2 \vec{r}_i}{dt^2} = \sum_j \vec{F}_{\text{elastic},ij} + \frac{1}{2} \sum_{\alpha,j} \vec{F}_{\text{pressure},\alpha ij} - \vec{F}_{\text{drag},i}, \quad (1)$$

where  $\vec{r}_i$  is the position vector of the  $i^{\text{th}}$  vertex. The terms on the r.h.s of the equation will be described below.

The cell walls are treated as a visco-elastic material that acts like an ideal spring for small displacements, but exhibits irreversible "creep" when stretched or compressed too far. Let  $l_{ij}$  be the length of a wall segment between vertices  $i$  and  $j$  and let  $l_{0,ij}$  be the resting length of the wall. The force on vertex  $i$  due to the elastic wall connected to vertex  $j$  is

$$F_{\text{elastic},ij} = -\frac{E}{l_{0,ij}} (l_{ij} - l_{0,ij}), \quad (2)$$

where  $E$  is elasticity of the material.

When the cell wall is stretched beyond its elastic limit, it yields to the applied force and the rest length increases. This behavior is often referred to as a plastic deformation. Biologists refer to this property as the "extensibility" of the cell and mechanical engineers refer to this behavior as "creep." Lockhart [3] first described this inelastic behavior of cells. We follow his approach and model the rest length of each cell wall as

$$\frac{1}{l_{0,ij}} \frac{dl_{0,ij}}{dt} = \begin{cases} 0 & \text{if } F_{\text{elastic},ij} < Y \\ \mu (F_{\text{elastic},ij} - Y) & \text{if } F_{\text{elastic},ij} \geq Y \end{cases} \quad (3)$$

where  $Y$  is the yield stress of the wall material.

Each cell is imagined to be filled with a fluid medium that exerts an outward pressure  $P_\alpha$ , where  $\alpha$  is an index that identifies a given cell (see Figure 1). The pressure force on a given wall is equal to the product of the pressure and the wall length:  $P_\alpha l_{ij}$ . This force is divided equally between the vertices  $i$  and  $j$ :

$$F_{\text{pressure},\alpha ij} = \frac{1}{2} P_\alpha l_{ij}. \quad (4)$$

The pressure force vector points outward, perpendicular the the wall.

We assume the fluid pressure is inversely proportional to the area of the 2D cell  $A_\alpha$

$$P_\alpha = c_1 M_\alpha / A_\alpha, \quad (5)$$

where  $M_\alpha$  is the fluid mass in cell  $\alpha$  and  $c_1$  is a constant. The mass  $M_\alpha$  may be thought of as the mass of the fluid inside the cell, while the sum of the vertex masses  $m_i$  may be thought of as the mass of the cell walls.

Each cell is "inflated" by increasing the fluid mass  $M_\alpha$  according to

$$\frac{dM_\alpha}{dt} = \gamma, \quad (6)$$

where the  $\gamma$  is a parameter that can, in general, depend on the concentration of a growth hormone (see below).

The final term in Equation 1 is a damping term. If  $\vec{v}_i$  is the velocity vector of a given vertex, then the damping force is given by

$$\vec{F}_{\text{drag},i} = -b\vec{v}_i, \quad (7)$$

where  $b$  is the drag coefficient.

Equations 1-7 define the cell dynamics in the absence of cell division and growth hormones. Model parameters are given in Table 1 at the end of the paper. This model assumes the dynamics are dominated by wall tension forces and cell pressure forces, i.e. it treats the system as being close to equilibrium where the inertia of a given cell is negligible. This system of equations, combined with the cell division methods described below were numerically integrated using a simple Eulerian scheme implemented in Python.

### Cell Division

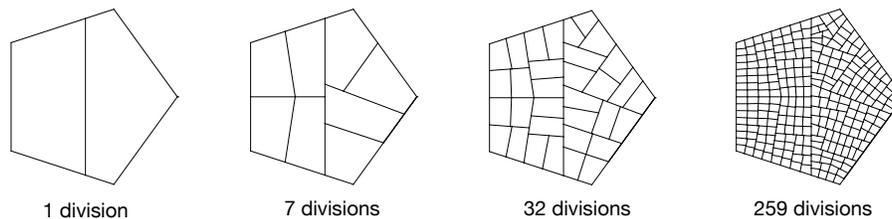
Cell division (mitosis) rules were first proposed in 1863 and remain an active area of research and debate in biology [1]. We explore two rules inspired by plant cell models.

- **Mitosis Rule #1:** The dividing wall takes the shortest path across the cell while passing through the cell's centroid. Cell division occurs when the area  $A_\alpha$  exceeds a threshold value  $\eta_{\text{mitosis}}$ .
- **Mitosis Rule #2:** The dividing wall is oriented as in rule #1, but cell division is initiated when both its area exceeds  $\eta_{\text{mitosis}}$  and the growth hormone concentration (see below) is exceeds a threshold  $\theta_1$ .

We are interested in exploring the range of textures and forms produced by these cell dynamics and division rules.

### Cell Division without Dynamics

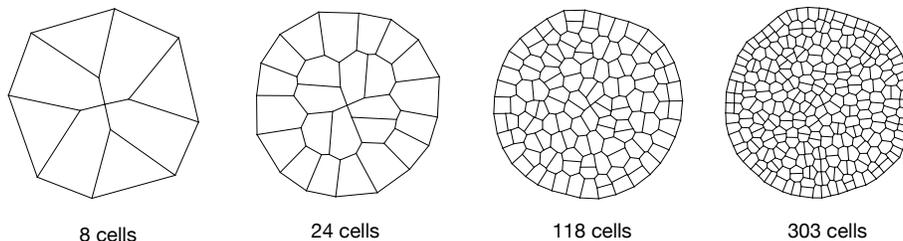
We first apply mitosis rule #1 to a fixed geometry (a pentagon) to see its affect in the absence of the dynamics. Figure 2 shows a pentagon that is successively divided by splitting each daughter cell using the rule described above. The dynamics in this simulation have been turned off: cell boundaries remain fixed throughout the division process. As the division process progresses, domains of closely aligned cells become apparent. However, the cell arrangement bears little resemblance to the organic patterns found in biological cells.



**Figure 2:** Cell mitosis rule #1 applied to a pentagon. Cell walls do not move once they are created. The cell division area threshold  $\eta_{\text{mitosis}}$  is lowered with each iteration to produce finer and finer divisions.

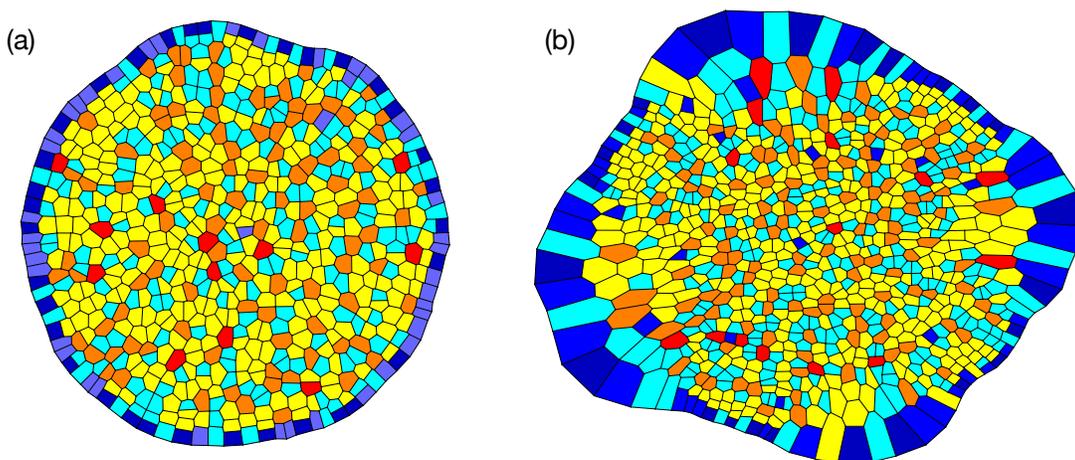
### Cell Division with Uniform Expansion

We now “turn on” the dynamics and apply Equations 1-7 to the initial configuration shown in the left-hand diagram in Figure 3. Each cell is inflated at a uniform rate. When a given cell's area exceeds a threshold value  $\eta_{\text{mitosis}}$ , it undergoes cell division. The dividing wall is created in a state of zero strain, i.e. the wall's rest length  $l_0$  is set equal to its current length  $l$ . As the cell continues to expand, the newly formed wall will lengthen and will be in a state of greater and greater tension. As the cell walls seek a minimum energy configuration, the wall tensions gradually converge and the angles between the walls at a vertex start to equalize. Thus, vertices with three intersecting walls tend to meet at  $120^\circ$ . Where the wall is relatively “young,” or where the cell has not expanded in the direction parallel to the wall, the wall tension will be low and the wall will intersect the other two walls at  $90^\circ$ . These effects are visible in Figure 3.



**Figure 3:** Cell mitosis rule #1 in which the growth rate is constant for every cell.

Figure 4(a) shows a snapshot of the same simulation in which the color of each cell is determined by the number of neighboring cells, i.e. by the local topology of the connectivity graph between cells. In biology, such connections are important because they affect how hormones and other chemicals diffuse from cell-to-cell. Aesthetically, I chose bright colors for  $n = 5-8$  that shimmer against the dark-blue  $n = 2-4$  polygons that border the edges.



**Figure 4:** Cell formations colored by the number of neighbors of each cell. Shades of dark blue have  $n = 2-4$ ; cyan has  $n = 5$ ; yellow has  $n = 6$ , orange has  $n = 7$ ; shades of dark red have  $n = 8-11$ . (a) Uniform growth rate using mitosis rule #1. (b) Growth rate set by the hormone level produced by four active cells on the periphery using mitosis rule #2.

### Diffusion of Hormones

We introduce a hormone  $H_\alpha$  (such as auxin) that is produced in a set of specified cells. The hormone diffuses between cells according to

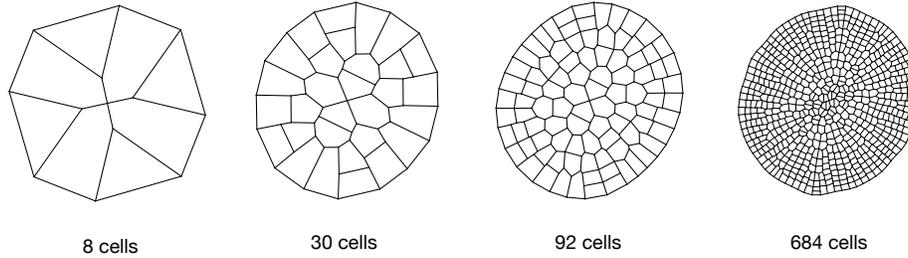
$$\frac{\partial H_\alpha}{\partial t} = -D\nabla^2 H_\alpha \quad (8)$$

where  $D$  is a diffusion coefficient and the Laplacian operator is approximated by transferring discrete parcels of hormones across cell walls.

We follow [4] in defining three stages of cell development. When the hormone concentration exceeds a threshold  $\theta_1$ , the cell will grow at a rate  $\gamma_1$  and undergo mitosis. As the hormone concentration drops due to diffusion and cell expansion, the cell enters the expansion phase where the cell grows at a rate  $\gamma_0$  but does

not divide. Finally, when the hormone concentration drops below  $\theta_0$ , the cell enters a maturation phase and neither expands nor divides.

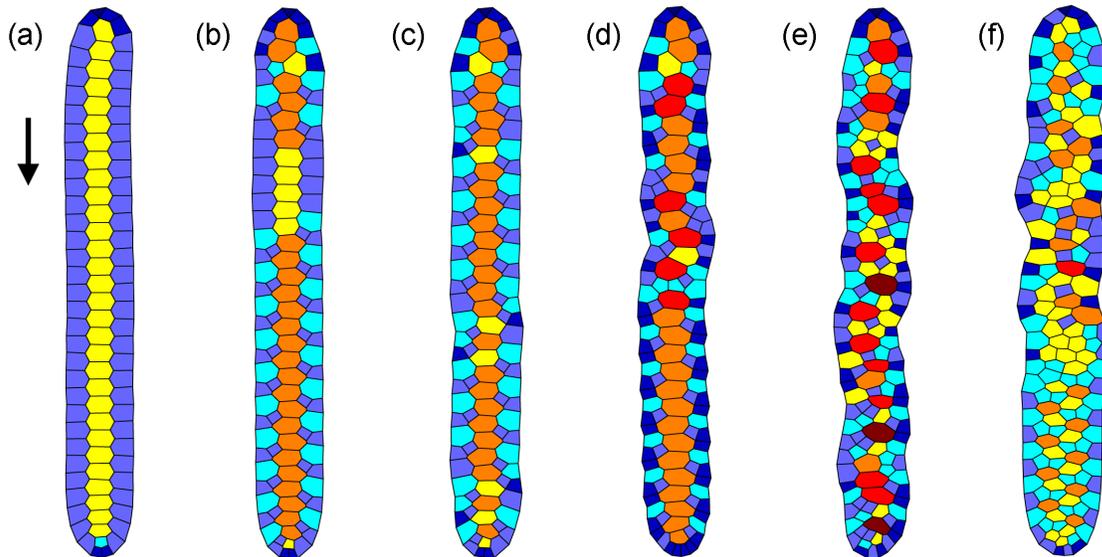
$$\frac{dM_\alpha}{dt} = \begin{cases} 0 & \text{if } H_\alpha < \theta_0 & \text{maturation phase} \\ \gamma_0 & \text{if } \theta_0 \leq H_\alpha < \theta_1 & \text{expansion phase} \\ \gamma_1 & \text{if } H_\alpha \geq \theta_1 & \text{mitosis phase} \end{cases} \quad (9)$$



**Figure 5:** Cell mitosis rule #2 based on a growth hormone that is produced by cells on the periphery.

Figure 5 shows a simulation with the same initial conditions as Figure 3, but which includes a hormone that is produced in cells on the outer periphery of the form. The combination of parameters causes growth to occur mainly in the outward, radial direction. The result is that cells form in files that radiate outward from the center of the form, much like cells within an annual growth ring in a tree cross-section.

In Figure 4(b), only four cells on the periphery produce the hormone. These cells are located in the NW, NE, SW, and SE corners of the form as indicated by the smaller cell size in those locations. The four blue “lobes” are regions where the cells are in the expansion phase of development and are correspondingly larger than those in the mitosis phase.



**Figure 6:** Cell formations with the same color pallet as in Figure 4. In each simulation, a single active cell produces the growth hormone. The formations grow down the page. In each trial,  $\theta_1 = 1.1\theta_0$ , where (a)  $\theta_0 = 0.16$ , (b)  $\theta_0 = 0.144$ , (c)  $\theta_0 = 0.138$ , (d)  $\theta_0 = 0.1365$ , (e)  $\theta_0 = 0.13$ , (f)  $\theta_0 = 0.1$ .

**Table 1: Model Parameters**

Parameter	Value(s)	Description
$m_i$	1	Vertex mass
$E$	1	Cell wall elasticity
$\mu$	40	Cell wall extensibility coefficient
$Y$	0.1	Cell wall yield stress
$c_1$	0.1	Pressure coefficient
$b$	0.3	Drag coefficient
$\gamma$	0.003-0.2	Cell inflation parameter
$\eta_0$	3	Area threshold for mitosis
$\theta_0$	0.01-2	Hormone threshold for cell maturation phase
$\theta_1$	0.01-2	Hormone threshold for cell mitosis
$D$	0.01	Hormone diffusion coefficient

### Linear Growth

Figure 6 shows the evolution of a cell system in which only a single cell produces the growth hormone. The active cell is constrained to move in a straight line down the page. When the threshold  $\theta_0$  is small, only a few cells have high enough hormone concentrations to undergo mitosis. Thus, the formation is only a few cells wide. The lowest threshold value shown in Figure 7(a) produces a highly-organized chain of cells with uniform topologies. In the simulations shown in Figures 7(b), 7(d) and 7(f), transient dynamics give way to regular, periodic patterns as the “organism” evolves down the page. The question of whether all patterns produced with this rule will eventually settle into a periodic pattern is presently unclear. Longer simulation runs of the patterns in Figures 7(c) and 7(e) appear to exhibit aperiodicity after hundreds of cell divisions.

### Summary and Future Work

We have presented a mechanical model of cell dynamics as a means of exploring biologically-inspired pattern formation. The vertex-model approach allows cell shapes and topological connectivity with neighboring cells to be studied. We introduced a diffusive growth hormone in the system that influences cell growth and division. In the future we hope to explore how hormone-based, reaction-diffusion processes can further affect pattern formation.

### References

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