Journal of Bioinformatics and Computational Biology
Vol. 5, No. 4 (2007) 1–10

Imperial College Press
www.icpress.co.uk

A CELLULAR AUTOMATON TO MODEL THE DEVELOPMENT OF PRIMARY SHOOT MERISTEMS OF ARABIDOPSIS THALIANA

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Received
Revised
Accepted

Development of organisms is a very complex process in which a lot of gene networks of different cell types are integrated. Development of a cellular automaton (Ermentrout and Edelshtein-Keshet, *J Theor Biol* **160**:97–133, 1993) that models the morphodynamics of different cell types is the first step in understanding and analysis of the regulatory mechanisms underlying the functioning of developmental gene networks. A model of a cellular automaton has been developed, which simulates the embryonic development of shoot meristem in Arabidopsis thaliana. The model adequately describes the basic stages in development of this organ in wild and mutant types.

Keywords: Cellular automaton; mathematical model; development of shoot meristems; parameters of model; period of division.

1. Introduction

Postembryonic development of the above-ground part of higher plants depends on the functioning of the primary shoot apical meristem (SAM), a dynamic structure that forms leafage, flowers, and scape. The formation of the primary SAM occurs at the earliest stages of embryogenesis. Furthermore, the functioning of the promeristem triggers development of the germ layers and at that time a complex meristem structure is being formed (Fig. 1).[2]

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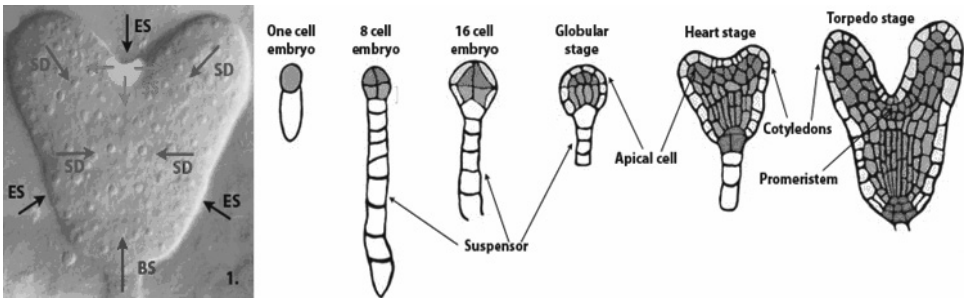

Fig. 1. (a) Directions of the model's hypothetical signal distributions in heart-stage embryo tissues: ES is External Signal, SS is Stem Signal, SD is Signal of Differentiation, and BS is Basal Signal. (b) Developmental stages of a plant embryo with the indication of organs and tissues significant to the model.

The cells of the apical and basal parts have different expression of different genes in a 16-cell embryo. No further development of embryos is possible without SAM, or at least their apical parts.[3]

Cellular automata have been extensively used to model a wide range of processes.[1,4] In general, a cellular automaton is loosely defined as a collection of cells with states that change their state depending on at least the states of neighboring cells. The positional relationship of von Neumann[5] cellular automaton is rectilinear in two dimensions; i.e. a two-dimensional (2D) grid, as formed by the intersection of two sets of mutually perpendicular lines, producing cells. The set of cells define a cell space, this space being of infinite size. The neighborhood (a grouping function) is part of the state-transition function, and defines for any cell, the set of other cells upon which the state of that cell depends. Biological systems are particularly suitable for analyzing by cellular automata.[1] In particular, cellular automata models have been used for a vascular tumour growth on a Voronoi lattice,[6] to simulate the immune dynamics of particular diseases,[7,8] to model shape-space interactions,[9] and finally for simulation of development of the multicellular organisms known as morphogenesis.[10] The literature on modeling morphogenesis is extensive. Held[11] provides a good summary. Most current models for morphogenesis are based on purely continuum approaches[12] or discrete cellular automata. Here, the authors introduce cellular automaton to model for development of the primary SAM in embryogenesis of the Arabidopsis thaliana. Modeling covers the initiation of SAM, the formation of the SAM complex structure and its further functioning. Here, the embryo is described as a 2D array of cells, the rates of division of which depend on the cellular environment. The cells in the model may receive and, depending on the cell type, produce signals that should be received by other cells in the model. The biological meaning of signals is the concentration of certain diffusing substances, or morphogenes, which provide a specific influence on the cell.

2. Methods and Algorithms

The model assumes that the stage and rates of division of an individual cell depend on the influence of signals that are coming from other cells of embryo. Under the model, four biologically meaningful signals, which unambiguously simulate the morphodynamics of cell tissues at the generally accepted level of abstraction, were selected (Fig. 1). They are the following: the External signal, the Basal signal, the Stem signal and the Signal of differentiation. The External signal is an equivalent of real substances produced by cells of epidermis. In the real embryo apical-basal pattern of development is controlled at the early step by a special organ, a suspensor. It is likely that the suspensor has an influence on the cells of embryo through certain signals; and in the model this influence is defined by the basal signal. The Stem signal formed in pluripotent cells of the meristem is a biological analog of the cytokinin hormone.[13] This signal influences on the rate of division. Lateral differentiated cells produce signal of differentiation. A biological analog of the differentiation signal influencing on the rate of division is such hormone as auxin.[13]

All the embryo cells in the model can be classified according to the type of the signal they produce:

(1) *Null*. These cells mean empty space that neither produce signals nor divide.
(2) *NullEx*. Cells of the epidermic layer. They produce External Signal (ES) and are represented around the entire perimeter of the embryo. They do not divide, but they are supposed to surround cell embryos in the model.
(3) *NullSus*. Cells of the suspensor. They produce Basal Signal (BS) and are confined to the lower part of the embryo. There are two NullSus cells in the model.
(4) *Lateral*. These cells imitate "differentiated" cells, which produce Signal of Differentiation (SD).
(5) *Promeristem*. Cells of the embryo meristems. These cells produce Stem Signal (SS) and are confined to the upper part of the embryo. During development, they change into L2meristem and L3meristem type cells.
(6) *Transit*. Cells near the meristem. They also produce SD, but have the highest rates of division.
(7) *L2meristem*. Cells of the meristem. They are situated in second layer from the epidermic layer of the upper part of the embryo. These cells produce SS.
(8) *L3meristem*. Cells located one layer down from the L2meristem type cells. These cells produce SS.

Each cell has a set of internal parameters to characterize its state:

(1) Type. Cell type.
(2) ES0, BS0, SS0, SD0 are the values of the signals produced by the cell.
(3) ES, BS, SS, SD are the values of the signals accepted by the cell.

(4) K_{ij} is the characteristic of cell state at position (i, j) calculated as the ratio of SS to SD. Each type of cell has own range of K. At the current point of time, the cell is influenced in the state characterized by the parameter:

$$K_{ij} = \frac{\text{StemSignal}_{ij}}{\text{DifferentSignal}_{ij}}.$$

(5) T_{ij} is the period of cell division, which depends on the current value of the characteristic K_{ij}.

(6) Tp_{ij} is the number of iterations after the last division of the cell at position (i, j).

We calculate the overall influence of all the cells on the cell at position (i, j) by the following formulas:

$$\begin{aligned}
\text{ExternSignal}_{ij} &= \alpha^E_{ij} \sum_{k,m} \text{ExternSignal0}_{km} e^{-n/R_E},\\
\text{BasalSignal}_{ij} &= \alpha^B_{ij} \sum_{k,m} \text{BasalSignal0}_{km} e^{-n/R_B},\\
\text{StemSignal}_{ij} &= \alpha^S_{ij} \sum_{k,m} \text{StemSignal0}_{km} e^{-n/R_S},\\
\text{DifferentSignal}_{ij} &= \alpha^D_{ij} \sum_{k,m} \text{DifferentSignal0}_{km} e^{-n/R_D}.
\end{aligned}$$

The summation is performed over all the cells of a particular tissue, including the epidermis layer and the suspensor; (k, m) is the position of the cell, the influence of which was taken into account; $n = abs(k-i)+abs(m-j)$, where i, j are the considered cell coordinates, k, m are the affected cell coordinates; R_E, R_B, R_S, R_D are the constants which characterize penetrance for ES, BS, SS, and SD, respectively. The model assumes that time in which a distribution of signals reaches steady state is much less than characteristic time of cell cycle. In this sense we can say that system reaches steady state instantly. Also this model assumes that while generated signal by the cell achieves to other cell located on the distance "n", this signal will lose part of the own power in each cells between them. In general it can be showed with this equation $\frac{d}{dn}S = -\lambda S$, where S is the concentration of the signal. Solution of the equation is $S = S_0 e^{-\lambda n}$ that we show in above formula, where λ replaces by $\lambda = 1/R$. $\alpha^E_{ij}, \alpha^B_{ij}, \alpha^S_{ij}, \alpha^D_{ij}$ are the constants which characterize the sensitivity of the cell to a certain type of signal. This constant expresses cells receptivity to signal, in other words the model assumes that signals have secondary transmitters that increase or decrease effect. This constant depends only on the type of the cell.

The qualitative behavior of the function T_{ij} is shown in the Fig. 2 according to the biological position:

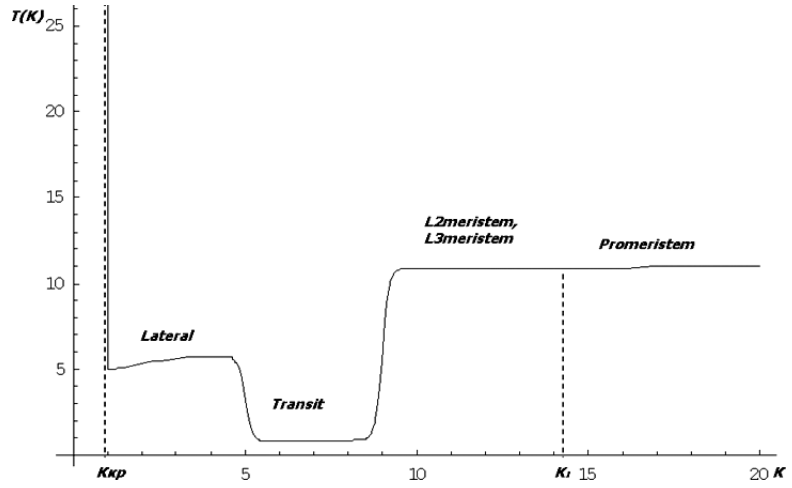

Fig. 2. Dependence of division periods on the parameter K for different cell types.

As can be seen from Fig. 2, the embryo meristem cells (Promeristem, L2meristem, L3meristem) in the tissue divide slower than the others; the Transit type cells divide very quickly; the rates of division of the Lateral type cells are medium. When the parameter K takes on the value $K_{\kappa p}$, the period of division becomes infinity and the cells will not divide anymore. When the parameter K takes on the threshold value K_1, the Promeristem type cells divide into L2meristem and L3meristem cells. This dependence was revealed by using the function:

$$f(x) = \frac{1}{1 + e^{\frac{x-\mu}{\sigma}}},$$

where x is a value of K_{ij}, μ is equals to critic values of K_{ij} and σ equals to 0.1. If T_{ij} is not an integer, the function T_{ij} is rounded in accordance with the standard rules of adjustment. To ascertain whether or not a cell is undergoing division, Tp_{ij} and T_{ij} are compared. At the next iteration, the value Tp_{ij} is increased by one for each non-dividing cell. If $Tp_{ij} > T_{ij}$, division into two daughter cells is ascertained. For each daughter cell, Tp_{ij} is equal to zero. Noteworthy, if T_{ij} increases more rapidly than Tp_{ij}, the cell will not divide. The model is used pseudo parallel simulation for calculation of signal concentration, selection of cell type and for selection of division direction, but directly procedure of division occurs in series and sequence of division is selected in a random way.

3. Results

The developed cellular automaton adequately describes the developmental morphodynamics of primary shoot meristem of *Arabidopsis thaliana* in embryogenesis (Fig. 3).

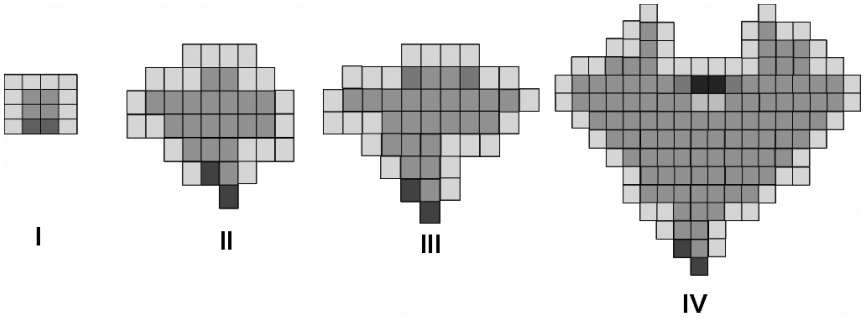

Fig. 3. Developmental stages of plant embryo modeled by the cell automaton: I — 16 cell embryo; II — globular stage; III — heart stage; IV — torpedo stage.

By varying the parameters of the cellular automaton, we have successfully modeled the following mutations described in the literature:

(a) the meristem forms but cannot cope with the auxin flowing in from the germ layers, and so it differentiates. This leads to formation of the joined germ layers and as a consequence to the stoppage of the plant development;[14]
(b) the meristem forms, and so do germ layers, but no regulation is exerted on the meristem cells population. As a result, the meristem cells differentiate and the meristem zone shrinks.[2,15]

Visualization of the cellular automaton (Fig. 4) was created that allows simulating of the process of development.

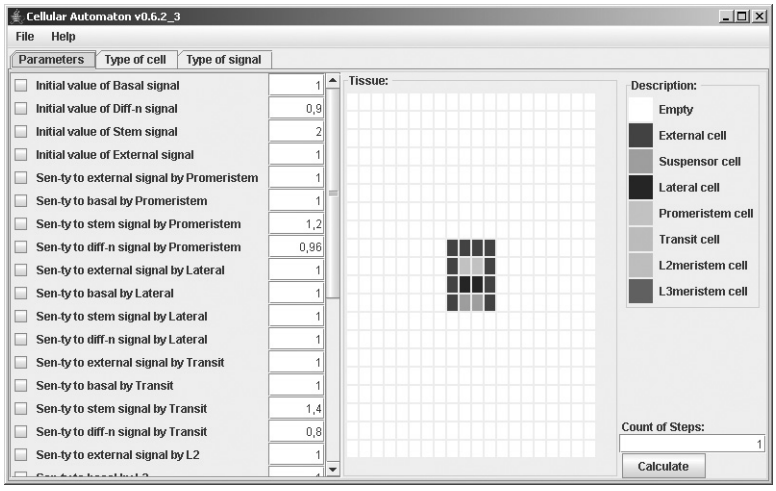

Fig. 4. Visualization of developed cellular automaton.

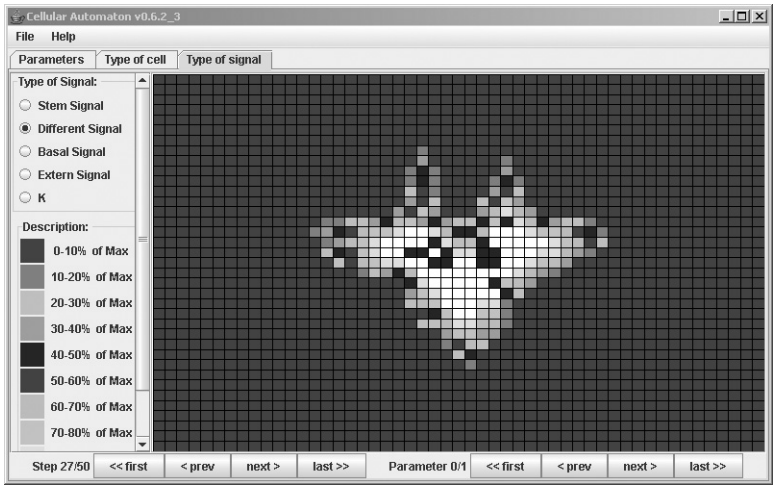

Fig. 5. Visualization of differentiation signals distribution.

Also, the visualization of cellular automaton model allows estimating distribution of four biologically meaningful signals, which unambiguously simulate the morphodynamics of the cell tissues (Fig. 5).

4. Discussion

Creation of a cellular automaton that imitates morphodynamics of embryo development by means of regulation of signals produced by different embryonic cells is a first step in modeling the process of development in general and in modeling the gene network for morphogenesis in particular.[16] The formation of plant meristems in embryogenesis is characterized by a combination of a violent development of differentiating tissue and a stable development of its stem cells. Both processes were modeled in the cellular automaton being reported. Not only is this automaton a tool for predicting the dynamics of the division process and the cell differentiation process which underway in the systems being considered, but also for the examination of how real mutations influence the system. As a progression of this work, we plan to develop a cellular automaton, which will enable modeling of various experimentally induced mutations. Sophistication of characteristic cell definitions will be added for a more adequate description. Also, in the future work, we plan to use the cellular automaton model introduced here to investigate the development of primary shoot meristem of the Arabidopsis thaliana in embryogenesis under different initial parameters of the model. It allows recognizing of significant parameters, which greatly influence on behavior of dynamic system and determining the stable state of this biological system by variation parameters. The created visualization of the model will be essential helper in decision of the problem and clear helper for biologists.

Acknowledgments

The authors are grateful to Eric Mjolsness for productive discussion of the model. This work was supported in part by INNOVATION PROJECT IT-CP.5/001 "Development of software for computer modeling and design in post genomic system biology (system biology in silico)" and US National Science Foundation (FIBR EF-0330786 Development Modeling and Bioinformatics). The work was supported in part by the Russian Foundation for Basic Research No 05-07-98012-p_06b_B, 05-07-9801204-01-00458, 05-07-98011 and by projects of the SB RAS Presidium No 10104-34/II-18/155-270/1105-06-001/28/2006-1 and "Computational modeling and experimental reconstruction of gene networks" and by the Russian Federal Agency for Science and Innovations (State contract No 02.467.11.1005), and also by interdisciplinary integration projects of fundamental study of the SB RAS No 34, No 115.

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