Morphogenetic Pattern Generation Using an Ultra-Discrete Reaction-Diffusion System

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Abstract. The paper present an alternative approach to the determination of a cellular automaton simulator for the stable patterns generation and the evolution of the mammals skin models. The proposed simulator uses the ultra-discrete version of an important reaction-diffusion systems arising from the bio-mathematics domain: the Thomas-Murray reaction-diffusion system.
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1 Introduction

The Reaction-Diffusion modeling and simulations, particularly in a sense of chemical computation or in the domain of biophysics, becomes a hot topic of computer science, physics and chemistry.

The Reaction Diffusion process is one in which a number of substances or morphogens can diffuse over a surface and react with each other to produce stable patterns on the surface. This mechanism has been studied by biologists as well as mathematicians as the system, which consists of a series of non-linear coupled partial differential equations, is thought to be responsible for pattern formation in nature, such as the patterns on an animal's coat. Work on reaction diffusion began when Alan Turing proposed a mechanism which could explain the development of animal embryos and the fact that they can be self-organizing.

The pattern generating reaction-diffusion systems are governed by a set of coupled partial differential equations as seen above. The problem with simulating a system such as this is that the equations are continuous. This means that the equation represents the entire solution space of the system which has an infinite number of values for time and space. The continuous nature of the system makes it very difficult to simulate on a computer which by nature cannot handle continuous systems.

We must therefore discretize these equations so that we can simulate the system on a grid or lattice which can be used in a computer. This discretization

is done on a lattice where the simulation takes place. The simulation method used is that of cellular automata.

In 2007 I proposed a very simple CA model that can simulate the zebra skin patterns formation (see [1]). This model was constructed beginning from the Yang discretization of Turing's system, following the approach of Gravan C. and Lahoz-Beltra R.([2]). The purpose of the present paper approach is to propose an alternative approach to construct a pattern generator simulation for mammals skin models (leopard, tiger or giraffe), obtained by a direct ultra-discretization procedure applied to the Thomas-Murray Reaction-Diffusion System, and to verify if the ultra-discretization method preserves the reaction-diffusion phenomena in this particular case.

2 The Thomas-Murray system (TMS)

In 1952 Turing ([8]) published a paper suggesting that, under certain conditions, some chemicals can react and diffuse from an initially nearly homogeneous state to create spatial stable patterns as a consequence of the breakdown of symmetry and homogeneity. Turing proposed that the temporal variation of the concentrations of two different chemicals, named by Turing as morphogens (the activator morphogen $\underline{u}$ and the inhibitor morphogen $\underline{v}$), both diffusible but at different rates (d_a and d_i), can create patterns on an initially homogeneous tissue by reacting in accordance with some nonlinear functions f and g:

The general form of Turing's Reaction-Diffusion systems is

$$\begin{cases} \frac{\partial u}{\partial t} = d_a \nabla u + f(u,v) \\ \frac{\partial v}{\partial t} = d_i \nabla v + g(u,v) \end{cases} \tag{1}$$

where d_a, d_i are diffusion constants, x, y are the spatial coordinates and u, v are functions of x, y and t.

In Turing's model, the activator morphogen u activates the production of itself and the production of the inhibitor v , whereas v inhibits the production of itself and decreases the activator u production.

More that twenty years later, Thomas ([6]) proposed a model of enzyme reaction, based on the Turing's Reaction Diffusion system. This particular system was largely studied by Murray ([4], [5] Chap.15) as the possible mechanism responsible for laying down most of the mammals coat spacing patterns. The model assumes the animal skin is formed by a uniform distribution of pigmented cells (black, state 1), differentiated by melanocytes, and undifferentiated cells (white, state 0). Melanocytes produce the activator morphogen u which stimulates the transition from state 0 to 1 of nearby undifferentiated cells, as well as the inhibitor morphogen v promoting the opposite transition, thus from state 1 to 0, for nearby differentiated cells. The time evolution of the concentrations of activator/inhibitor morphogenes is determined by the Thomas-Murray system (TMS):

$$\begin{cases} \frac{\partial u}{\partial t} = \nabla u + \gamma[a - u - h(u,v)] \\ \frac{\partial v}{\partial t} = d\nabla v + \gamma[\alpha(b - v) - h(u,v)] \\ h(u,v) = \frac{\rho \cdot uv}{1+u+Kv^2} \end{cases} \tag{2}$$

where *a,b,* α *,* γ and K are positive parameters, the ratio of diffusion coefficients $d = d_i/d_a$ is greater that one (normally take values greater that 12) and the scale factor γ is a measure of the domain and control only the dimension of patterns. (In the next we consider the parameters *a=b=* γ *=1.*)

In order to investigate the type of spatial pattern generated by the full nonlinear system (2) and to construct a pattern generator simulator, we must discretize this system until to a simulator cellular automaton witch simulate the nonlinear behavior of the (TMS).

A cellular automaton (Wolfram [9], Weimar [10]) provide a framework for a large class of discrete models with homogeneous interactions, characterized by the following properties:

- They consist of a regular discrete lattice of cells.
- The evolution takes place in discrete time steps.
- Each cell is characterized by a state taken from a finite set of states.
- Each cell evolves according to the same rule which depends only on the state of the cell and a finite number of neighboring cells.
- The neighborhood relation is local and uniform.

Cellular automata (CA) have been widely adopted in the sciences as simple but powerful models of the real world because the complex patterns produced by their long-time behaviors can mimic observations with tremendous accuracy.

In the particular case of mammalian coat patterns generation, a simple cellular automata model of Turing's system was succefully used by Gravan C. and Lahoz-Beltra R. ([2]) to simulate the patterns formation on the zebra's skin. In 2007 Boldea C. proposed (in [1]) a similar CA model, obtained using a genetic algorithm aproach. But these models are only empirical experiences, witch do not reflect correctly the nonlinear phenomena characterizing the Thomas Murray system. For this reason, we choused an ultra-discretization procedure that preserves the continuous nonlinear behavior of the system (2).

3 Discrete and ultra-discrete reaction diffusion system derived from the Thomas-Murray system

Cellular automata (CA) have been widely adopted in the sciences as simple but powerful models of the real world because the complex pat-terns produced by their long-time behaviors can mimic observations with tremendous accuracy ([9],[10]). However, the lack of mathematical tools makes prediction difficult in CA models. , think was by The work of Tokihiro et al. [7] developed a method to ultra-discretize continuous systems, based on a limit passing procedure and

confirmed that there are integrable, predictable, Cellular Automata obtained by this method.

First step to apply the method of Tokihiro et al. in order to obtain a discrete valuated, discrete time, discrete space variables system (ultra-discrete system) from equations (2), is to pass by a classical discrete version of this equation.

The discrete versions of the above (TM) system are obtained by replacing the time derivative

$$\frac{\partial u(x,y,t)}{\partial t} \to \frac{u(x,y,t+\Delta t)-u(x,y,t)}{\Delta t} \to u(x,y,t+1)-u(x,y,t) \tag{3}$$

and the space derivatives by

$$\frac{\partial u(x,y,t)}{\partial x} \to u(x+1,y,t)-u(x,y,t) \tag{4}$$

$$\frac{\partial u(x,y,t)}{\partial y} \to u(x,y+1,t)-u(x,y,t) \tag{5}$$

$$\begin{array}{l}\Delta u \to u(x+1,y,t)+u(x-1,y,t)+\\ +u(x,y+1,t)+u(x,y-1,t)-4u(x,t)\end{array} \tag{6}$$

By plugging these discretizations into the system (2), one obtain

$$\left\{\begin{array}{l} u(x,t+1)=u(x,y,t)+[u(x+1,y,t)+u(x-1,y,t)+\\ u(x,y+1,t)+u(x,y-1,t)-4u(x,t)]-\\ -[u(x,y,v)-1+h(u(x,y,t),v(x,y,t))]\\ \\ v(x,t+1)=v(x,y,t)+d[v(x+1,y,t)+v(x-1,y,t)+\\ +v(x,y+1,t)+v(x,y-1,t)-4v(x,t)]-\\ -[\alpha(u(x,y,t)-1)+h(u(x,y,t),v(x,y,t))]\end{array}\right. \tag{7}$$

Next, we apply the ultra-discretization procedure on the system (7): given a rational function in u and v, the ultra-discretization method requires that we introduce new variables U and V defined by $u = exp(U/å)$, $v = exp(V/å)$. After we take the limit å0+ of the equations using the identities:

$$\lim_{\varepsilon\to 0+} \varepsilon \log\left[e^{A/\varepsilon}+e^{B/\varepsilon}\right] = \max(A,B)$$

$$\lim_{\varepsilon\to 0+} \varepsilon \log\left[e^{A/\varepsilon}-e^{B/\varepsilon}\right] = Alt\max(A,B)$$

where

$$Alt\max(A,B) = \left\{\begin{array}{c} A,\ if\ A>B\\ 0,\ if\ A=B\\ -B,\ if\ A<B\end{array}\right.$$

is the alternate maximum function. Ultra-discrete equations are naturally posed on the max-plus semi-ring (defined in [3]).

The ultra-discretisation procedure transform the diffusion part of eq. (7)

$$\begin{cases} u(x,t+1) = u(x,y,t) + [u(x+1,y,t) + u(x-1,y,t) + \\ u(x,y+1,t) + u(x,y-1,t) - 4u(x,t)] \\ \\ v(x,t+1) = v(x,y,t) + d \cdot [v(x+1,y,t) + v(x-1,y,t) + \\ +v(x,y+1,t) + v(x,y-1,t) - 4v(x,t)] \end{cases} \tag{8}$$

into

$$\begin{cases} u_{x,y}^{t+1} = \max[u_{x,y}^t, Alt\max(u_{x+1,y}^t, u_{x,y}^t), Alt\max(u_{x-1,y}^t, u_{x,y}^t), \\ Alt\max(u_{x,y+1}^t, u_{x,y}^t), Alt\max(u_{x,y-1}^t, u_{x,y}^t)\} \\ v_x^{t+1} = \max[v_{x,y}^t, Alt\max(v_{x+1,y}^t, v_{x,y}^t) + \delta, Alt\max(v_{x-1,y}^t, v_{x,y}^t) \\ +\delta, Alt\max(v_{x,y+1}^t, v_{x,y}^t) + \delta, Alt\max(v_{x,y-1}^t, v_{x,y}^t) + \delta\} \end{cases} \tag{9}$$

where δ =[ln(d)] is a diffusion ratio parameter. The reaction part become:

$$\begin{cases} h(u,v) \rightarrow u_{x,y}^t + v_{x,y}^t - \\ \quad - Alt\max(\max(u_{x,y}^t, 2v_{x,y}^t + k), 1) + R \equiv H(u_{x,y}^t, v_{x,y}^t) \\ (u-1) + H(u,v) \rightarrow \max[Alt\max(u_{x,y}^t, 1), H(u_{x,y}^t, v_{x,y}^t)] \equiv \\ \quad \equiv \Psi_1(u_{x,y}^t, v_{x,y}^t) \\ \alpha(v-1) + h(u,v) \rightarrow \max[Alt\max(v_{x,y}^t, 1) + A, H(u_{x,y}^t, v_{x,y}^t)] \equiv \\ \quad \equiv \Psi_2(u_{x,y}^t, v_{x,y}^t) \end{cases} \tag{10}$$

where *R,A,k* are constants. (We used the operations $uv \rightarrow U+V$, $cv \rightarrow V+k$and $u+v \rightarrow max(U,V)$ in the ultra-discrete limit, with *k=⌊ln(c)⌋* for any positive constant *c*.)

The ultra-discrete version of Thomas-Murray system (2) will be:

$$\begin{cases} u_{x,y}^{t+1} = \max(u_{x,y}^t, u_{x+1,y}^t, u_{x-1,y}^t, u_{x,y+1}^t, u_{x,y-1}^t) \\ \quad - \Psi_1(u_{x,y}^t, v_{x,y}^t) \\ v_{x,y}^{t+1} = \max(u_{x,y}^t, u_{x+1,y}^t + \delta, u_{x-1,y}^t + \delta, u_{x,y+1}^t \\ \quad + \delta, u_{x,y-1}^t + \delta) - \Psi_2(u_{x,y}^t, v_{x,y}^t) \end{cases} \tag{11}$$

Note that a supplementary reset condition must be introduced in order to simulate the real physical phenomena: ux,yt+1 $u_{x,y}^t \leftarrow 0$, $v_{x,y}^t \leftarrow 0$ if the calculated values from (11) are negatives, corresponding to a negative concentration of a morphogene.

4 Simulation results and conclusions

The system (11) can be used to define a non-standard cellular bi-valuated automaton, according to each cell a pair of values $C_{x,y}(t) = (u_{x,y}^t, v_{x,y}^t)$, where

$x, y, t \in IN$, and $u^t_{x,y}, v^t_{x,y}$ are real functions. The pattern generator simulator is simply defined by

$$P^t_{i,j} = \begin{cases} 1, & if \ u^t_{i,j} > v^t_{i,j} \\ 0, & if \ u^t_{i,j} \leq v^t_{i,j} \end{cases} \tag{12}$$

for $i, j, t \in \Omega \subset IN$. Conventionally, we consider that *" 1"*is associated with colored cells, and *"0"* correspond to the "white" cells.

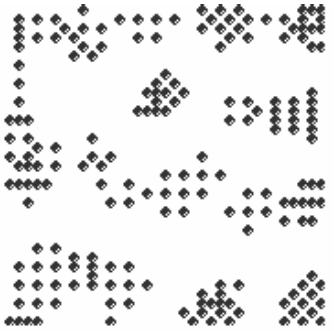

Fig. 1. Initial configuration of the cell automaton. Only the presence of activator is represented.

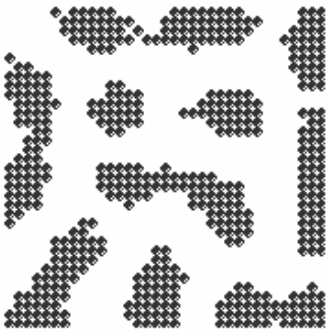

Fig. 2. Example of a generated pattern for δ =R=A=0

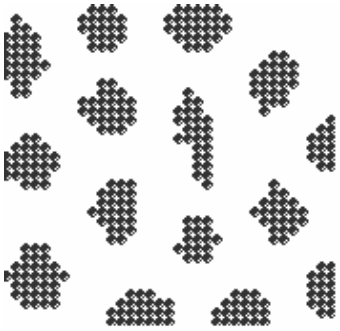

Fig. 3. Example of a generated pattern for δ =R=1

For the purpose of testing the reaction diffusion simulation we ran some simulations with different parameters to see what kinds of patterns would be produced. In the simulations we used two lattices for the initial values of $(u^t_{x,y}, v^t_{x,y})$ with equal concentrations of each morphogene. Each cell take the initial value $u^0_{x,y} \leftarrow 1$ with a certain probability p_a, and the initial value $v^0_{x,y} \leftarrow 1$, with a certain probability p_i, in rest any initial state become null (see Fig.1).

The more that 50 numerical experiments realized by the authors permit to remark that the CA model described by eqn. (11) is always superior limited by a maximum value and the generated patterns become stable after a certain time.

The Figures 2 and 3 shows the results of a reaction diffusion simulation which we carried out using a fluctuation of the parameters of the model.

In conclusion, the simulation results are consistent with the general picture of pattern modeling and simulation based on Turing's reaction-diffusion scheme. The cell automaton P from (12) present a similar nonlinear behavior like the full continuous Thomas-Murray system (2).

References

[1] **Boldea C.R.**, Evolving Morphogenetic Patterns with a Genetic Algorithm,Research Notes in Artificial Intelligence and Digital Communications, Vol. 107, 2007, 127-132.

[2] **Gravan C. and Lahoz-Beltra R.**, Evolving Morphogenetic Fields In The Zebra Skin Pattern Based On Turing'S Morphogen Hypothesis - Int. J. Appl. Math. Comput. Sci., Vol. 14, No. 3, 2004, pp. 351–361.

[3] **Joshi N. and Ormerod C**, The General Theory Of Linear Difference Equations Over The Max-Plus Semi-Ring, Studies in Applied Mathematics, Volume 118, Number 1, January 2007, pp. 85-97.

[4] **Murray J.D**, On Pattern Formation Mechanisms for Lepidopteron Wing Patterns and Mammalian coat markings, Philosophical Translations of the Royal Society B, Vol. 295, 1981, pp. 473-496.
[5] **Murray J.D**, Mathematical Biology, New York, Springer-Verlag, 1989.
[6] **Thomas D.**, Artificial enzyme membranes, transport, memory and oscillatory phenomena, in D. Thomas and J.-P. Kerneves (eds.) Analysis and Control of Immobilized Enzyme Systems, Berlin, Springer, 1975, pp. 223-254.
[7] **Tokihiro T., Takahashi D., Matsukidaira J. and Satsuma J.**, From soliton equations to integrable cellular automata through a limiting procedure Phys. Rev. Lett. 76, 1996 , pp. 3247–3250.
[8] **Turing A.**, The Chemical Basis of Morpho-genesis, Philosophical Translations of the Royal Society B, Vol. 237, 1952, pp. 37-72.
[9] **Wolfram S.**, New constructions in cellular automata Proceedings of the Conference Santa Fe NM 1998, New York, Oxford University Press, 2003.
[10] **Weimar J. R.**, Simulation with Cellular Automata, Braunschweig, 1996.