Evolving Morphogenetic Patterns with a Genetic Algorithm

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Abstract. In this paper is simulated the stable pattern generation and the evolution of the zebra skin models, composed of pigmented and non-pigmented cells The simulation experiments were carried out applying a genetic algorithm to the Young cellular automaton: a discrete version of the reaction-diffusion equations proposed by Turing in 1952.
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1 Introduction

One of the classical problems of morphogenesis, or the development of complex forms and patterns found in living organisms (Prusinkiewicz, [5]), is to explain how patterns of different animals (i.e., mammals, seashells, marine fishes) evolved resulting in a consolidated and stable pattern generation after generation. In 1952 Turing published a paper showing how patterns might grow from an initially nearly homogeneous state and how diffusion could drive to instability. A result of such instability is the emergence of 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 m_a and the inhibitor morphogen m_i), both diffusible but at different rates (d_a and d_i), can create patterns (D_A and D_I nonzero) on an initially homogeneous tissue by reacting in accordance with the nonlinear functions f and g:

$$\begin{cases} \frac{\partial m_a}{\partial t} = f(m_a, m_i) + d_a \Delta^2 m_a \\ \frac{\partial m_i}{\partial t} = g(m_a, m_i) + d_i \Delta^2 m_i \end{cases} \tag{1}$$

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

Twenty years after Turing's contribution, Gierer and Meinhardt ([2]) developed a model of pattern formation based on a short-range activator and

a long-range inhibitor which would promote the future development of simulation models by means of cellular automata. Cellular automata are discrete space and time models that have been used to model biological systems as a counterpart method to differential equations. A cellular automaton in two dimensions consists of a regular grid of cells, and each of them can be in one of a finite number of possible states, being updated synchronously in discrete time steps according to a local, identical interaction rule (Wolfram [6]). The state of each cell at the next time step t + 1 is determined by its present state at time t and the states of its surrounding neighbors. Depending on the pattern of initial cell states and transition rules, thus on how neighboring states influence the state of a particular cell, patterns of cell states in the checkerboard evolve over time and can propagate, interact, store and compute information ([6]).

Based on such an approach, Young ([7]) simulated Turing's reaction-diffusion model considering that cells lay out on a grid with two states, pigmented or nonpigmented, assuming that the pigmented cells produce activator m_a and inhibitor MI morphogens diffusing at different rates across the grid. The results obtained by Young were similar to those obtained with continuous reaction-diffusion equations.

In this paper, we simulate the evolution of two hypothetical morphogens, or proteins, that diffuse across a grid, using a modified Young model proposed by Gravan and Lahoz-Beltra [3]. The grid models an animal skin (as a zebra) in an embryonic state, composed of pigmented and nonpigmented cells. The simulation experiments were carried out applying a genetic algorithm to Young cellular automata searching for proper values of the diffusion distance and the field value: the two main features that define a morphogen like activator or inhibitor in Youngs model. In the biological realm, it is generally believed that zebras are dark animals, the white stripes being the areas where the pigmentation is inhibited. Such camouflage is an adaptation that prevents zebras from being seen by predators, confusing the zebras with most natural backgrounds. Murray ([4]) showed that the chevrons at the base of zebra limbs result from the overlapping of two reaction-diffusion systems, but in present it is still unknown how the zebra skin pattern is generated even when Turing's reaction-diffusion model could produce their characteristic stripe pattern ([3]).

The result of our simulation show that, under the assumption of the absence of predators ([4]), recombination is the genetic mechanism that plays the key role in morphogen evolution.

2 Cellular automata model of Turing's reaction diffusion system

The model proposed by Young ([7], [2]) 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 m_a which stimulates the transition from state 0 to

1 of nearby undifferentiated cells, as well as the inhibitor morphogen m_i promoting the opposite transition, thus from state 1 to 0, for nearby differentiated cells. When considered together, both morphogens define a morphogenetic field which is assumed to be circular and composed of two concentric rings. The morphogenetic field results from a short-range activation and long-range inhibition areas defined around a melanocyte cell located at the origin or center of the morphogenetic field. Once the pigmented cells are randomly distributed on a grid, the transition rules are applied to the pigmented and nonpigmented cells.

The cell automaton model proposed by Young consists of a regular grid of cells, and each of them can be in one of a two possible states, 0 and 1, when each cell R on the grid in position (i, j) receives influences of the morphogens produced by all pigmented cells R_p of the neighborhood in positions (i_0, j_0).

Consider $d(R, R_p)$ the Euclidean distance between R and R_p:

$$d(R, R_p) = |R - R_p| = \sqrt{(i - i_0)^2 + (j - j_0)^2}.$$

If the Euclidean distance $d(R, R_p)$ is less than or equal to radius R1 ($d(R, R_p) \leq r_1$), then the cell R located in position (i, j) receives the effect of the activator morphogen m_a, which is simulated by a positive field value k_1. Otherwise, if $r_1 < d(R, R_p) \leq r_2$ then the cell R in position (i, j) would receive the effect of the inhibitor morphogen m_i, which is given by a negative field value k_2. Finally, if for the cell R in position (i, j) we consider the composition of the effects of the morphogens produced by all nearby pigmented cells R_p in the neighborhood, then the future state of the cell R will be given by the sum of all the field values.

According to the model, the automaton transition rules for cells are given by the following rules:

1. If
$$\sum_{p:(|R-R_p|\leq r_1)} k_1 - \sum_{p:r_1<|R-R_p|\leq r_2} k_2 > 0$$
then the state of cell R at time t + 1 is pigmented (state 1).
2. If
$$\sum_{p:(|R-R_p|\leq r_1)} k_1 - \sum_{p:r_1<|R-R_p|\leq r_2} k_2 = 0$$
then the state of cell R at time t + 1 does not change and is equal to its state at time t (state 0 or 1).
3. If
$$\sum_{(p:|R-R_p|\leq r_1)} k_1 - \sum_{p:r_1<|R-R_p|\leq r_2} k_2 < 0$$
then the state of cell R at time t + 1 is not pigmented (state 0).

3 Evolving morphogenetic features with a genetic algorithm

In order to apply a genetic algorithm, we define a population of chromosomes simulated as strings of real values

$$Chromozome := (r_1, k_1, r_2, k_2)\,. \tag{2}$$

where the "genes" were defined by four real values modelling the diffusion distance r and the morphogenetic field value k of two different morphogen molecules, the activator m_1 and the inhibitor m_2. (Note that at the beginning of the simulation the two molecules are not defined as activator or inhibitor, both being candidates to be one or another type of morphogen during evolution.)

The implemented genetic algorithm uses one-point recombination and a population size of $p = 50$, testing recombination probability, as well as mutation probability values in different simulation experiments. Starting with a random population of chromosomes, reproduction, recombination and mutation were simulated, thus obtaining new generations of equal sizes. The initial population of chromosomes was obtained choosing arbitrary r_1 and r_2 in between 1 and 10, as well as k_1 and k_2 in between −5 and 5.

3.1 The fitness function

At each generation, the fitness f of each chromosome, thus the degree of the achievement of the M1 and M2 molecules in the morphogenic field, is defined as

$$f = max\{f_1, f_2\} \tag{3}$$

where

$$f_1 = C - (|\alpha - N_{ww}| + |\beta - N_{wb}| + |\gamma - N_{bb}|)$$
$$f_2 = C - (|\alpha - N_{bb}| + |\beta - N_{wb}| + |\gamma - N_{ww}|).$$

In the above functions, C is a constant (thus the total number of contacts among cells), fixed here at 2500, N_{ww}, N_{wb} and N_{bb} are the numbers of contacts between white-white, white-black and black-black cells, respectively, and (α, β, γ) are the parameters of the fitness functions whose values were set up as follows: $\alpha = 1500$, $\beta = 350$, $\gamma = 750$. The parameters α and β were obtained after some simulation experiments based on Youngs cellular automata model, simulations performed considering the values reported by Young: the activator morphogen m_a was a molecule with $r_1 = 2.30$, k_1= 1, and the inhibitor morphogen m_i a molecule with r_2=6.01, k_2=-1. Based on these values we generated 100 patterns , obtaining the average values of N_{ww}, N_{wb} and N_{bb}, labelled as α, β and γ.

In order to obtain the value of f is necessary to perform a simulation of the cellular automaton model, using the r_1, k_1, r_2 and k_2 values coded by each chromosome. The simulation begins assuming an initial random distribution, on a

rectangular lattice, of 95 percent of white cells (undifferentiated cells) and 5 percent of black cells (melanocytes or differentiated pigmented cells), updating the state of the cells with transition rules until the resulting pattern no longer changes. No more that five or six iterations were enough for convergence to a stable pattern and that the final pattern is not sensitive to the initial distribution of melanocytes or black cells, in the majority cases of our experiments. (However, in preliminary experiments we found unstable patterns!).

Once the chromosomes are evaluated, we select the mating pool of the next generation using the roulette wheel algorithm of parents selection (Davis [1]). This is a method for implementing reproduction simulating the Darwinian natural selection, by spinning a roulette wheel that assigns to each chromosome a slot whose arc size is proportional to its fitness value.

3.2 The crossover operator

Once a new generation of offspring chromosomes is obtained, a single point crossover proceeds with pairs of mates randomly selected. Since the first gene is linked with the second one and the third gene is linked with the fourth one, the crossover point is not randomly selected from a uniform distribution as is usual in a genetic algorithm. The crossover point is equal to 2 in the present simulations, just in the middle position of the chromosome. Finally, a single point crossover occurs when the segments of the two parent chromosomes i,j:

$$\begin{matrix}(r_1^i, k_1^i, r_2^i, k_2^i)\\(r_1^j, k_j^i, r_2^j, k_2^j)\end{matrix} \rightarrow \begin{matrix}(r_1^i, k_1^i, r_2^j, k_2^j)\\(r_1^j, k_j^i, r_2^i, k_2^i)\end{matrix} \tag{4}$$

3.3 The mutation operator

Mutation at a gene was simulated changing at random the value gene, choosing the mutated values of r or k from a uniform distribution with a similar range to those defined to obtain the initial population of chromosomes ($0 \leq r \leq 10$ and $-5 \leq k \leq 5$). Once again whether or not to change a gene value on a chromosome is decided on the basis of a Bernoulli trial, mutation being a success with a given probability (mutation probability) p_{mut}.

4 Simulation results and conclusions

Computer simulation experiments were performed using the population size, the morphogen diffusion distances and morphogenetic field values as described in Section 2 and 3: population $P = 50$, the morphogen diffusion distances $r_1 =$ 2.30, k_1= 0.6, r_2=6.00, k_2=-0.3 (determined by the Young [7]) coefficients) and $\alpha = 1500$, $\beta = 350$, $\gamma = 750$. The mutation operator was applied each $q = 2..5$ generations, with the probability $p_{mut} = 0.1$ and the number of generation was limited to $N = 25$.

Fig. 1. Representative stripe patterns obtained with the activator and inhibitor features obtained by decoding two chromosomes with maximum average fitness.

In Fig. 1 we show two representative stable patterns obtained by simulation.

An example of the unstable pattern skin development of a zebra is shown in Fig. 2.

Fig. 2. Unstable stripe patterns.

The simulation results are consistent with the general picture of pattern modelling and simulation based on Turings reaction-diffusion scheme ([4]). After a large number of simulations, the results indicate that the evolution of selected morphogens does not strongly depend on the initial configurations (almost all configurations become stable after a small number of cell automata iterations). The impact of mutation operator significative, similar results are obtained by varying the probability of mutation P_{mut} and the factor q. The result of our simulation show that (under the assumption of the absence of predators), the recombination operator is the genetic mechanism that plays the key role in morphogen evolution.

Acknowledgments

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