Digital Hormone Models for Self-Organization

Wei-Min Shen, Cheng-Ming Chuong, and Peter Will
University of Southern California, 4676 Admiralty Way, Marina del Rey, CA 90292, USA
shen@isi.edu, chuong@pathfinder.usc.edu, will@isi.edu

Abstract

How do multiple elements/agents self-organize into global patterns based on local communications and interactions? This paper describes a theoretical and simulation model called "Digital Hormone Model" (DHM) for such a self-organization task. The model is inspired by two facts: complex biological patterns are results of self-organization of homogenous cells regulated by hormone-like chemical signals (Jiang *et al.* 1999), and distributed controls can enable self-reconfigurable agents to performance locomotion and reconfiguration (Shen, Salemi, & Will 2000; Shen, Lu, & Will 2000; Salemi, Shen, & Will 2001). The DHM is an integration and generalization of reaction-diffusion model (Turing 1952) and stochastic cellular automata (Lee *et al.* 1991). The movements of agents (or cells) in DHM are computed not by the Turing's differential equations, nor the Metropolis rule (Kirkpatrick & Sorkin 1995), but by stochastic rules that are based on the concentration of hormones in the neighboring space. Experimental results have shown that this model can produce results that match and predict the actual findings in the biological experiments of feather bud formation among uniform skin cells (Jiang *et al.* 1999). Furthermore, an extension of this model may be directly applicable to self-organization in multi-agent systems using simulated hormone-like signals.

Introduction

This paper is to develop a general computational model for self-organization in multi-agent systems. In particular, we describe the Digital Hormone Model (DHM) that is generalized from an existing distributed control system for self-reconfigurable agents (Shen, Salemi, & Will 2000; Shen, Lu, & Will 2000; Salemi, Shen, & Will 2001). The model is inspired by the fact that many complex patterns in biological systems appear to be the results of self-organization among homogenous cells regulated by hormones, and self-organization is based on local interactions among cells rather than super-imposed and pre-determined global structures (Jiang *et al.* 1999; Chuong *et al.* 2000). The paper describes the model in detail, reports the experimental results in simulating feather buds formation among homogeneous skin cells, and finds a number of correlations between individual hormone diffusion profiles and the features of final patterns. These results match the findings in the actual biological experiments and predict cases that have yet been observed in biological experiments but consist with the expected behaviors of hormone-regulated self-organization.

Computational Models for Self-Organization

Throughout the history of science, there have been many computational models for self-organization. Perhaps one of the earliest is Turing's reaction-diffusion model (Turing 1952), in which he analyzed the interplay between the diffusions of reacting species and concluded that their nonlinear interactions could lead to the formation of spatial patterns in their concentrations. Turing's model uses a set of differential equations to model the periodic pattern formation in a ring of discrete cells or continuous tissues that interact with each other through a set of chemicals he called "morphogens". Assuming that there are $r = (1, \ldots N)$ cells in the ring, and two morphogens X and Y among these cells, and letting the concentration of X and Y in cell r be X_r and Y_r, the cell-to-cell diffusion rate of X and Y be u and v, and the increasing rate of X and Y caused by chemical reactions be $f(X, Y)$ and $g(X, Y)$, respectively, Turing modeled the dynamics of this ring as the following set of $2N$ differential equations:

$$\begin{aligned} dX_r/dt &= f(X_r, Y_r) + u(X_{r+1} - 2X_r + X_{r-1}), \\ dY_r/dt &= g(X_r, Y_r) + v(Y_{r+1} - 2Y_r + Y_{r-1}). \end{aligned}$$

By analyzing the solutions of these equations, Turing illustrated that a given ring of cells, which initially has the uniform concentration of Y and X, can self-organize through random fluctuations, chemical reactions, and diffusion, into a ring of periodic patterns in the concentration of Y. Two important conditions for Turing stability are: (1) between X and Y, one must be the inhibitor and the other activator, and (2) the inhibitor must have a greater diffusion rate than the actuator.

Turing's reaction-diffusion model was startlingly novel, and it has been supported both mathematically (Murray 1989) and experimentally (Ouyang & Swinney 1991), and many applications are described in (Meinhardt 1982). Interestingly, Witkin and Kass (1991) extended the traditional reaction-diffusion systems by allowing anisotropic and spatially non-uniform diffusion, as well as multiple competing directions of diffusion. They use these models to synthesize textures with different patterns.

Cellular Automata (CA) (Gutowitz 1991; Toffoli 2000), especially those that have stochastic characteristics (Lee *et al.* 1991), are another important modeling technique for self-organization. Perhaps the most famous illustration of self-organization using CA is the Game of Life, where randomly distributed cells on a space of grids will live or die based on a set of very simple and deterministic rules. Life is a deterministic CA, but when rules of a CA have stochastic characteristics, then they could also be capable of modeling random fluctuations in the environment, and that may be a critical element in simulating interactions among many autonomous elements that perceive and react to local information in the environment. In fact, the Digital Hormone Model to be proposed here is essentially an integration of stochastic CA, reaction-diffusion models, and network-like diffusion space with dynamic topology.

The Digital Hormone Model

The Digital Hormone Model (DHM) is designed for simulating, understanding, and controlling self-organization in large-scale multi-agent systems. In this model, agents are simulated as cells that secrete hormones, and hormones diffuse and influence the behaviors of other cells. The Digital Hormone Model consists of a space (we use grids in this paper) and a set of moving cells. The term "cell" here can stand for any type of autonomous and intelligent elements, such as agents, agents, unmanned vehicles, mobile sensors, network nodes, or weapons. Among the grids, cells can live, evolve, migrate, or die as time passes. Each living cell occupies one grid at a time and a cell can secrete chemical hormones (or communication signals in general), which diffuse into its neighboring grids to influence other cells' behaviors. Hormones may have different types and diffusion functions. Two types of hormones are most common: an *activator* hormone that will encourage certain cell actions, while an *inhibitor* hormone will prohibit certain cell actions. We assume that hormones may react to each other (summation, subtraction, or modification), and may diffuse to the neighboring grids according to certain functions. Similar to the extensions used in Witkin and Kass (1991), we allow anisotropic and spatially non-uniform diffusion. Cells are autonomous and intelligent agents that can react to hormones and perform actions such as *migration, secretion, differentiation, proliferation, death,* or *adhesion.*

At any given time, a cell selects and executes one or more actions according to a set of internal behavior rules. These rules can be deterministic or probabilistic. We assume that the rules are given and will not cause a cell to select conflicting actions. Given the grids, cells, hormones, actions, and rules, the DHM works as follows:

1. All cells select actions by their behavior rules;
2. All cells execute their selected actions;
3. All grids update the concentration of hormones;
4. Go to Step 1.

To illustrate the above definitions, let us consider a simple DHM_0 in Figure 1, where cells (shown as black dots in the grids) migrate on a space of N^2 grids. The space is a torus in the sense that the leftmost and rightmost columns are neighbors, and the topmost and bottommost rows are neighbors. Cells in DHM_0 have only two actions: secretion and migration, and the former is a constant action that always produces two hormones: the activator A and the inhibitor I. The diffusion rates for A and I secreted from a cell at the grid (a, b) to its surrounding grids are characterized by Guassian distributions:

$$\begin{aligned} f_A(x,y) &= (2\pi\sigma^2)^{-1} exp\{[(x-a)^2+(y-b)^2]/2\sigma^2\} \\ f_I(x,y) &= -(2\pi\rho^2)^{-1} exp\{[(x-a)^2+(y-b)^2]/2\rho^2\}, \end{aligned}$$

where $\sigma < \rho$ in order to satisfy Turing's stability condition. Notice that the activator A has the positive value and the inhibitor I has the negative value. Because $\sigma < \rho$, A has a sharper and narrower distribution then I. We assume that the two hormones react to each other so that the concentration of hormones in any given grid can be computed by summing up all present "A"s and "I"s in the grid. In Figure 1, we have illustrated in the grids the combined hormones around a single cell and around two nearby cells. Since the grids are discrete, the rings around the cells are shown as squares instead of circles.

In this simple model DHM_0, two simple rules govern the cell's actions. One rule states that "secrete A and I for every step", and this means that each cell secretes these hormones at every step. The second rule states that "migrate to an immediate neighbor grid based on the hormone distribution in these neighbors". More specifically, the probability for a cell to migrate to a particular neighboring grid (including the grid it is currently occupying) is proportional to the concentration of A and inversely proportional to the concentration of I in that grid. This rule is fundamentally stochastic, so that the selection of migrating grid is non-deterministic. To implement this rule, let the hormone value in the occupying grid be h_0 and let the values in the eight immediate

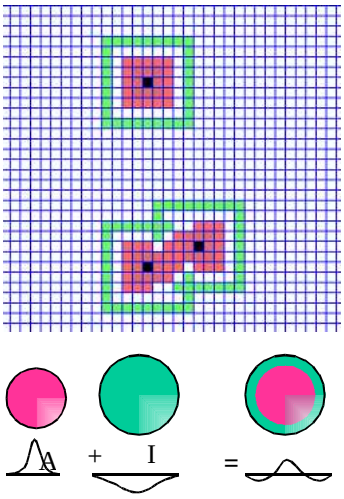

Figure 1: The simple DHM_0

neighbors be h_1, h_2, h_3, h_4, h_5, h_6, h_7, and h_8, respectively. Based on their signs, these values are grouped into three groups: $G1$, $G2$, and $G3$, where the members in $G1$ all have positive values (say sum to P_{G1}), those in $G2$ have zero values, and those in $G3$ have negative values. To decide which group to migrate to, a random number x is generated in the range of $(0, 100P_{G1}+10|G2|+|G3|]$. If $0 < x <= 100P_{G1}$, then the cell will migrate to $G1$. If $100P_{G1} < x <= 100P_{G1} + 10|G2|$, then the cell will migrate to $G2$. Otherwise, the cell will migrate to $G3$. The decision ensures that a cell will migrate to $G1$ with the highest probability, to $G2$ with lower probability, and to $G3$ with the lowest probability. After a group is selected, we then select a grid from the group with a similar procedure. For example, to select a grid from $G1$, a random number will be generated in the range of $(0, h_{i1} + h_{i2} + h_{i3} + \ldots + h_{i|G1|}]$, where h_{ij} are individual values in $G1$ ($h_{ij} > 0$), and a grid will be selected depending on where the number falls in the range. This ensures that grids with higher concentrations of the activator hormone will be selected with higher probabilities. To select a grid from $G2$, we order the grids in the group $g_1, g_2, \ldots, g_{|G2|}$ (note that all these grids have zero hormone values), and a random number y is generated in the range of $(0, |G2|]$, and the grid of g_y is selected. To select a grid from $G3$, a random number will be generated in the range of $(0, (-h_{j1})^{-1} + (-h_{j2})^{-1} + (-h_{j3})^{-1} + \ldots + (-h_{j|G3|})^{-1}]$, where h_{ij} are individual values in $G3$ ($h_{ij} < 0$), and a grid will be selected depending on where the number falls in this range. This ensures that grids with lower concentrations of the inhibitor hormone will be selected with higher probabilities.

Notice that the above rule for selecting migration direction is different from the Metropolis rules used in simulated annealing (Kirkpatrick & Sorkin 1995), which first randomly selects a neighbor without considering the concentration of hormones, and then makes a go or no-go decision based on the energy difference and the current temperature. In the Digital Hormone Model, the notion of temperature is embedded in the decision rules described above. Interestingly, our experiments show that the Metropolis rule does not allow cells to converge into patterns in this model no matter what temperature is set.

Since all movements are local and synchronized, there may be a chance where multiple cells "collide" in the same grid. The collision of cells is solved in a simple manner. All cells first "virtually" move to the grids they selected. If there are multiple cells in the same grid, then the extra cells will be randomly distributed to those immediate neighboring grids that are empty. This is an environmental function, not a cellular action. But this action will ensure that no grid is hosting more than one cell at any time.

The Experimental Results of the DHM

Using the digital hormone models, we hope to learn valuable detailed computational knowledge about how hormones and receptors affect the result of self-organization in a large system with many autonomous elements. In particular, the initial research issues we would like to investigate are as follows: Will the proposed Digital Hormone Model enable cells to self-organize into patterns at all? Will the size of final patterns be invariant to the cell population density? Will the hormone diffusion profiles affect the size and shape of the final patterns? Will an arbitrary hormone diffusion profile enable self-organization and pattern formation?

To find solutions for these questions, we ran two sets of experiments using the simplified digital hormone model DHM_0 described above. In the first set of experiments, we set the hormone diffusion profile to approximate the standard distributions. For any single isolated cell, let the cell's n^{th} ring of neighbors be the neighboring cells at a distance of n cells away from the cell. Using this definition, we define the concentration level of the activator hormone at the cell's surrounding grids as follows: 0.16 for the 0^{th} ring (i.e., the occupying grid), 0.08 the 1^{st} ring, 0.04 the 2^{nd} ring, 0.02 the 3^{rd} ring, and 0 the 4^{th} and beyond. For the inhibitor hormone, the concentration levels for the 0^{th} through the 4^{th} rings of neighbors are: -0.05, -0.04, -0.03, -0.02, and -0.01, respectively, and 0.0 for the 5^{th} ring and beyond. Thus the combined concentration levels of hormones at the 0th through 4th rings are: 0.11, 0.04, 0.01, 0, and -0.01, respectively, and 0.0 for the 5^{th} ring and beyond. We assume that the concentrations of hormones secreted by a cell at grids beyond the 4^{th} ring are so insignificant that they can be practically ignored.

Given this fixed hormone diffusion profile, we have

run a set of simulations on a space of 100 × 100 grids with different cell population densities ranging from 10% through 50%. Starting with cells randomly distributed on the grids, each simulation runs up to 1,000 action steps, and records the configuration snapshots at steps of 0, 50, 500, and 1,000. As we can see from the results in the upper part of Figure 2, cells in all simulations indeed form clusters with approximately the same size. These results demonstrate that the digital hormone model indeed enables cells to form patterns. Furthermore, the results match the observations made in the biological experiments. The size of the final clusters does not change with cell population density, but the number of clusters does. Lower cell densities result in fewer final clusters, while higher densities form more clusters.

In the second set of experiments, we started with the same cell population density, but varied the hormone diffusion profiles. We wanted to observe the effects of different hormone profiles on the results of pattern formation. As we can see from the results shown in the lower part of Figure 2, when a balanced profile of activator and inhibitor is given (see the second row), the cells will form final patterns as in the first set of experiments. As the ratio of activator over inhibitor increases (see the third row), the size of final clusters also increases. These results are an exact match with the findings in the reported biological experiments (Jiang *et al.* 1999).

When the ratio of A/I becomes so high that there are only activators and no inhibitors (see the fourth row), then the cells will form larger and larger clusters, and eventually become a single connected cluster. On the other hand, when the ratio is so low that there is only inhibitor and no activator, then the cells will never form any patterns (see the first row), regardless of how long the simulation runs. This shows that not all hormone profiles enable self-organization. These results are yet to be seen in biological experiments, but they are consistent with the principles of hormone-regulated self-organization and thus qualified as meaningful predictions of cell self-organization by hormones.

The results presented in Figure 2 not only demonstrate that the proposed digital hormone model is indeed an effective tool for simulating and analyzing self-organization phenomena, but that it is also capable of producing results that match the actual findings in the biological experiments and can predict the possible outcomes for new biological experiments. The results show that hormones play a critical role in self-organization, and they enable many autonomous elements to form globally interesting patterns based on only their local information and interactions. This provides a departure point for new hypotheses, theories, and experiments for self-organization. Since the model is mathematically adjustable, it is much more economic and efficient for scientists, including biologists, to design new experiments

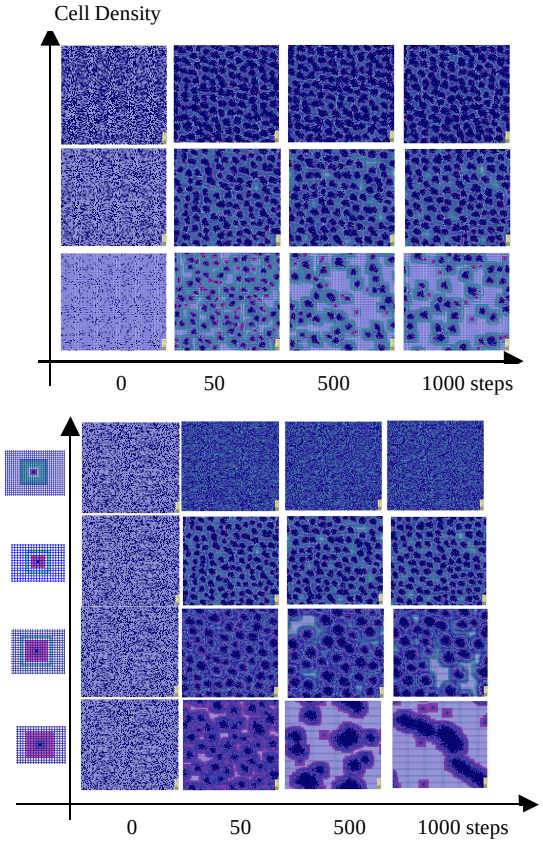

Figure 2: Two sets of experimental results on DMH_0

and to hypothesize new theories.

In addition to changing the ratio of activator and inhibitor hormones, we also have also varied the shape of hormone diffusion profiles and observe their effects on the features of the final patterns. For example, we have observed that if the profile is a narrow and long sandwich with the same orientation (the activator is in the middle and the inhibitors are on the outside), then cells will form striped patterns. This shows that given the proper hormone diffusion profiles, the DHM will allow cells to form patterns with different shapes.

Furthermore, we have also experimented with different mechanisms for decision making when selecting the migration direction, including the random procedure and the Metropolis rule. Experimental results have shown that Metropolis rule does not enable cells to aggregate into groups no matter what temperature setting is used. This is a bit unexpected, but one possible reason is that Metropolis rule first randomly selects a neighbor without considering the concentration of hormones, and then makes a go or no-go decision based on probability. This does not reflect the true distribution of hormone concentration in the neighboring grids. Similarly, and as expected, the random procedure for selecting migrating directions does not produce any interesting results ei-

ther.

Acknowledgments

We are grateful that this reserach is in part supported by the AFOSR contract F49620-01-1-0020 and the DARPA contract DAAN02-98-C-4032. The second author is supported by NSF IBN 9808874 and NIH AR 42177.

References

Chuong, C.-M.; Chodankar, R.; Widelitz, R.; and Jiang, T. X. 2000. Evo-devo of feathers and scales: Building complex epithelial appendages. *Current Opinion in Development and Genetics* 10:449–456.

Gutowitz, H., ed. 1991. *Cellular Automata — Theory and Experiment*. Cambridge, MA: MIT Press.

Jiang, T.-X.; Jung, H. S.; Widelitz, R. B.; and Chuong, C.-M. 1999. Self organization of periodic patterns by dissociated feather mesenchymal cells and the regulation of size, number and spacing of primordia. *Development* 126:4997–5009.

Kirkpatrick, S., and Sorkin, G. 1995. Simulated annealing. In Arbib, M., ed., *The Handbook of Brain and Neural Networks*. Cambridge, MA: MIT Press.

Lee, Y.; Qian, S.; Jones, R.; Barnes, C.; Flake, G.; O'Rouke, M.; Lee, K.; Chen, H.; Sun, G.; Zhang, Y.; Chen, D.; and Giles, G. 1991. Adaptive stochastic cellular automata: theory and experiment. In Gutowitz, H., ed., *Cellular Automata*. Cambridge, MA: MIT Press. 159–188.

Meinhardt, H. 1982. *Models of Biological Pattern Formation*. London: Academic Press.

Murray, J. 1989. *Mathematical Biology*. New York: Springer-Verlag.

Ouyang, Q., and Swinney, H. 1991. Transition from a uniform state to hexagonal and striped Turing patterns. *Nature* 352:610–612.

Salemi, B.; Shen, W.-M.; and Will, P. 2001. Hormone-controlled metamorphic agents. In *Proc. International Conference on Agentics and Automation*.

Shen, W.; Lu, Y.; and Will, P. 2000. Hormone-based control for self-reconfigurable agents. In *Proc. International Conference on Autonomous Agents*.

Shen, W.; Salemi, B.; and Will, P. 2000. Hormones for self-reconfigurable agents. In *Proc. 6th International Conference on Intelligent Autonomous Systems*.

Toffoli. 2000. Cellular automata. In Arbib, M., ed., *The Handbook of Brain Science*. Cambridge, MA: MIT Press.

Turing, A. 1952. The chemical basis of morphogenesis. *Philos. Trans. R. Soc. London B* 237:37–72.

Witkin, A., and Kass, M. 1991. Reaction-diffusion textures. *Computer Graphics* 25(3). also Proc. Siggraph 91.

References

Chuong, C.-M.; Chodankar, R.; Widelitz, R.; and Jiang, T. X. 2000. Evo-devo of feathers and scales: Building complex epithelial appendages. *Current Opinion in Development and Genetics* 10:449–456.

Gutowitz, H., ed. 1991. *Cellular Automata — Theory and Experiment*. Cambridge, MA: MIT Press.

Jiang, T.-X.; Jung, H. S.; Widelitz, R. B.; and Chuong, C.-M. 1999. Self organization of periodic patterns by dissociated feather mesenchymal cells and the regulation of size, number and spacing of primordia. *Development* 126:4997–5009.

Kirkpatrick, S., and Sorkin, G. 1995. Simulated annealing. In Arbib, M., ed., *The Handbook of Brain and Neural Networks*. Cambridge, MA: MIT Press.

Lee, Y.; Qian, S.; Jones, R.; Barnes, C.; Flake, G.; O'Rouke, M.; Lee, K.; Chen, H.; Sun, G.; Zhang, Y.; Chen, D.; and Giles, G. 1991. Adaptive stochastic cellular automata: theory and experiment. In Gutowitz, H., ed., *Cellular Automata*. Cambridge, MA: MIT Press. 159–188.

Meinhardt, H. 1982. *Models of Biological Pattern Formation*. London: Academic Press.

Murray, J. 1989. *Mathematical Biology*. New York: Springer-Verlag.

Ouyang, Q., and Swinney, H. 1991. Transition from a uniform state to hexagonal and striped Turing patterns. *Nature* 352:610–612.

Salemi, B.; Shen, W.-M.; and Will, P. 2001. Hormone-controlled metamorphic agents. In *Proc. International Conference on Agentics and Automation*.

Shen, W.; Lu, Y.; and Will, P. 2000. Hormone-based control for self-reconfigurable agents. In *Proc. International Conference on Autonomous Agents*.

Shen, W.; Salemi, B.; and Will, P. 2000. Hormones for self-reconfigurable agents. In *Proc. 6th International Conference on Intelligent Autonomous Systems*.

Toffoli. 2000. Cellular automata. In Arbib, M., ed., *The Handbook of Brain Science*. Cambridge, MA: MIT Press.

Turing, A. 1952. The chemical basis of morphogenesis. *Philos. Trans. R. Soc. London B* 237:37–72.

Witkin, A., and Kass, M. 1991. Reaction-diffusion textures. *Computer Graphics* 25(3). also Proc. Siggraph 91.