Pattern Formation: Gene Regulatory Network Study

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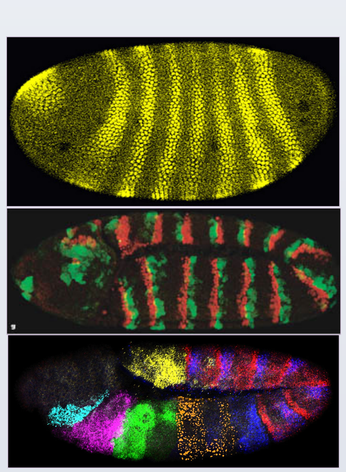
Pattern Formation

Generally pattern formation refers to principles behind self-organization process. In the process of self-organization, an initially disordered system forms a global coordination. This order is a result of local interactions between the components of the system. Studying visual ordered results of self-organization is called pattern formation. Genes play a major role in pattern formation.

Gene Regulatory Networks

Network Modeling. Biological systems consist of the huge number of components with complicated interactions among them. Network modeling is a powerful tool to represent living systems. These networks use nodes and edges to model a system. Nodes denote all components in the system and edges represent processes and interactions among the components.

Gene Regulatory Network. It is a specified type of network models. In general, nodes indicate genes, mRNAs, and proteins, whereas edges show transcription, translation, transcriptional regulation or protein-protein interactions. Edges can be directed to determine the orientation of interactions between nodes. The interactions are positive or negative, which show activation and inhibition respectively.



(a) Expression of hairy (yellow) in the cellular blastoderm [1].

(b) Expression of segment polarity genes, wingless (wg; green) and engrailed (en; red) [1].

(c) Expression of seven Hox genes at the extended germ band stage [1].

Figure 1. Examples of pattern formation in the process of developing from a single-celled egg into a multi-cellular embryo [1].

***Drosophila* Segment Polarity Gene Network.** It is a great instance. Figure 1 illustrates examples of gene expression in *Drosophila* embryos. These patterns arise during development and are a consequence of genetic regulatory networks that operate within cells and that respond to communication between cells [1].

Boolean Networks

This poster discuss Boolean networks that model gene regulatory networks. Boolean networks represent sets of expressed or non-expressed genes that are regulated by other genes using logic functions [1]. Nodes, which denote genes, can be in two states ON or OFF. ON or OFF respectively mean nodes have values of 1 or 0 and indicate gene expression or non-expression. Edges in Boolean networks are Boolean functions that are usually denoted by logic operators AND, OR, and NOT.

Attractors. Figure 2 (A, B) is an example of a Boolean network. The state of each node will be updated based on a logic function and its current state. The value of a cell changes each time the state of each node updates. Therefore, the cell will eventually settle into a set of states called a attractor. Attractors describe the long-time behavior of the cell.. Figure 2 (C) also shows the attractors of the network. In Figure 3, segment polarity genetic regulatory network and its attractors are illustrated in the different stages of the growth of the *Drosophila* embryo.

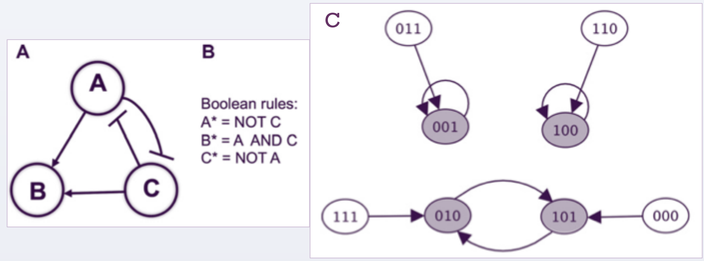


Figure 2. A simple Boolean network and its attractors. (A) A Boolean network with three nodes. The edge ⟶ or ⊣ denotes activation or inhibition. (B) Boolean rules regarding the network. (C) Attractors. The binary digits from left to right represent the state of each node. The gray states are fixed points [2].

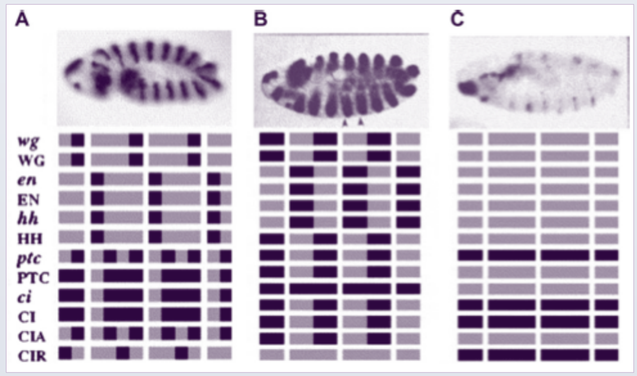


Figure 3. Gene expression in the *Drosophila* segment polarity genetic regulatory network. The vertical axis shows the genes and proteins. (A), (B), and (C) Attractors obtained by the Boolean models in the different stages of the growth of the embryo [2].

Methods

Intracellular Boolean Network. In this work, all cells have an identical intracellular Boolean network that were generated randomly, so that the number of nodes and their initial states follow a uniform distribution. The number of inputs to each node in Boolean networks can be 1, 2, 3. This makes networks with different domains called: ordered, critical, chaotic respectively.

Intercellular Network. A network of a two dimensional grid of cells is implemented. The intercellular signaling configuration is the edge connects the output of one gene in a cell to an input of a Boolean function of one or more of its neighbors [1]. The number of communicating genes is called the signaling bandwidth.

Signaling Configurations. Two kinds of signaling configurations are implemented: (1) Symmetric, where each cell contains a gene that receives inputs from all four neighbors [1]. (2) Orthogonal, where two adjacent cells signal directionally (North-South, East-West) [1].

Results

Figure 4. illustrates the outcome of apply the methods described in the previous section. Each image shows a pattern formation. Each network runs long enough to let cells get settled into attractors. Each color indicates a unique attractor.

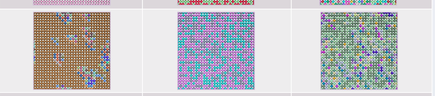
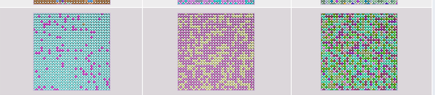
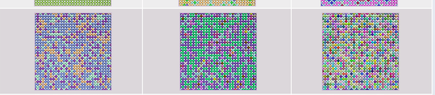
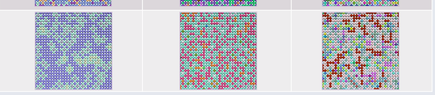
Comm.	BW	Domain	Patterns
orth.	5	ordered	
orth.	6	critical	
orth.	8	chaotic	
sym.	6	ordered	
sym.	5	critical	
sym.	7	chaotic	

Figure 4. Patterns from different Boolean networks with random initial states showing the intercellular signaling configuration (Comm.: orthogonal, symmetric), the bandwidth (BW: the number of communication genes), and the domain (ordered, critical, chaotic) of the intracellular network.

Conclusions

This poster presented a tutorial to gene regulatory network and random patterns generated by applying Boolean models on the grid of cells. The results show that the intercellular signaling configuration, the bandwidth, and the domain of the intracellular network have considerable influence on the generated patterns. Patterns with orthogonal signaling and in ordered or critical domains are more complex. Low information patterns are emerged from networks in chaotic domain or with symmetric signaling.

References

[1] Flann, Nicholas S., Hamid Mohamadloun, and Gregory J. Podgorski. "Kolmogorov complexity of epithelial pattern formation: The role of regulatory network configuration." *Biosystems (2013)*

[2] Saadatpour, Assieh, and Réka Albert. "Boolean Modeling of Biological Regulatory Networks: A Methodology Tutorial." *Methods (2012)*.