56. Self-Organized Patterning: Principles, Mechanisms, and Applications

1 unit, Christopher Britten, November 18, 2025

Student preparation

Student are expected to read the following review:

1. **Ramos, R., Swedlund, B., Ganesan, A. K., Morsut, L., Maini, P. K., Monuki, E. S., Lander, A. D., Chuong, C.-M., & Plikus, M. V. (2024).** *Parsing patterns: Emerging roles of tissue self-organization in health and disease*. *Cell*.
   - Reviews current knowledge on the principles and mechanisms of self-organized patterning in embryonic tissues and explores how these principles and mechanisms apply to adult tissues that exhibit features of patterning. DOI: 10.1016/j.cell.2024.05.016

Useful as a primer for Agent Based Modeling in biology, but not required:

2. **Thorne, B.C., Bailey, A.M., & Peirce, S.M. (2007).** *Combining Experiments with Multi-Cell Agent-Based Modeling to Study Biological Tissue Patterning*. *Briefings in Bioinformatics*.
   - Explores the use of agent-based models in studying morphogenesis. DOI: 10.1093/bib/bbm024

Suggested reading for a historical perspective and more technical exposition on self-organized patterning, but not required and outside the scope of the course.

3. **Turing, A. M. (1952).** *The Chemical Basis of Morphogenesis*. *Philosophical Transactions of the Royal Society B: Biological Sciences*.
   - Foundational paper introducing reaction–diffusion models in pattern formation.
4. **Wolpert, L. (1969).** *Positional Information and the Spatial Pattern of Cellular Differentiation*. *Journal of Theoretical Biology*.
   - Introduces the concept of positional information in development.
5. **Koch, A.J., Meinhardt, H. (1994).** *Biological Pattern Formation: From Basic Mechanisms to Complex Structures*. *Science*.
   - Classic review on reaction–diffusion and self-organization in biological systems. DOI: 10.1126/science.1130088
6. **Kondo, S., & Miura, T. (2010).** *Reaction-Diffusion Model as a Framework for Understanding Biological Pattern Formation*. *Science*.
   - Discusses the application of reaction–diffusion models in biology. DOI: 10.1126/science.1179047
7. **Green, J. B. A., & Sharpe, J. (2015).** *Positional Information and Reaction–Diffusion: Toward a Quantitative Synthesis of Patterning*. *Development*.
   - Reviews the integration of positional information and reaction–diffusion theories. DOI: 10.1242/dev.114991

8. **Glen, C. M., Kemp, M. L., & Voit, E. O. (2019).** *Agent-based modeling of morphogenetic systems: Advantages and challenges*. *PLOS Computational Biology*.
   - Highlights the benefits and challenges of using ABMs in studying morphogenetic events. DOI: 10.1371/journal.pcbi.1006577
9. **Brassard J. A., Lutolf M.P. (2019).** *Engineering Stem Cell Self-organization to Build Better Organoids. Cell Stem Cell.* 2
   - Review of how self-organizing principles are leveraged for engineering stem cell systems. DOI: 10.1016/j.stem.2019.05.005

Course outline

Total time: 100 minutes

Learning Goals

By the end of this lecture, students should be able to:

- Explain fundamental principles of self-organized patterning.
- Distinguish between reaction–diffusion and positional information.
- Analyze examples from embryogenesis and disease.
- Distinguish between PDE and agent-based modeling approaches.
- Explain the basic concepts in agent-based modeling.
- Apply a conceptual model using agent-based model to understand a biological system.

1. Introduction & Context (5 min)

Core Concepts:

- Definition and significance of self-organized patterning in biological systems.

2. Fundamental Principles (10 min)

Core Concepts:

- Historical perspectives: Turing's reaction–diffusion models and Wolpert's positional information theory.
- Reaction–Diffusion Systems: Mechanisms by which molecular interactions lead to spatial patterns.
- Positional Information: How cells interpret spatial cues to determine their fate.
- Hybrid Models: Integration of reaction–diffusion and positional information to explain complex patterning.

3. Mechanistic Examples in development (10 min)

Core Concepts:

- Hair Follicle Spacing: Role of WNT/BMP signaling in pattern formation.
- Digit Formation: Morphogenetic processes in limb development.

4. Implications for disease (5 min)

Core Concepts:

- Tumor Heterogeneity: How misregulated patterning contributes to cancer progression.

5. Traditional Computational Models: Reaction–Diffusion and Positional Information (5 min)

Core Concepts: * **Reaction–Diffusion Models:** Mathematical frameworks explaining pattern formation. * **Positional Information Models:** How gradients influence cellular decisions.

6. Agent-Based Modeling (ABM) in morphogenetic systems (5 min)

Core Concepts:

- How ABM simulates individual cell behaviors to produce emergent patterns.
- Applications in morphogenesis, tissue engineering, and synthetic biology.
- Strengths vs. limitations compared to continuous models.

7. A technical introduction to ABM (10 mins):

Core concepts:

- Define concepts: agents and rule-based decisions
- Implementing probabilistic based rules
- General considerations simulating an ABM

Break for 10 minutes

Game based application of ABM (30 mins)

Key activities:

- Students will enact an ABM within the context of a role playing game.
- Students will be split into teams of ~5 students.

- Each team will run a probabilistic simulation using dice and a physical game board.

Demonstrate an ABM used to simulate an actual biological system (10 mins)

Core concepts:

- I will walk students either through an ABM from literature or from my own research.
- Demonstrate how to evaluate and draw inferences from an ABM in a research setting.