Self-Assembly in Nature

Turing Patterns, Morphogenesis, and Embryo Development

CS289, 2017

New Topic: Cellular Computing

- Transition from "Swarm Intelligence" to "Multicellular Intelligence"
  - Inspiration: Colonies of "Cells"
  - How has multicellular behavior, *in particular morphogenesis*, influenced new ways of thinking?
- Models of Morphogenesis ("form")
  - D'Arcy Thompson, On Growth and Form, 1917
  - Von Neumann and Ulam, Cellular Automata, 1940s
  - Alan Turing, Turing patterns, 1952
  - Aristid Lindenmayer and Prusinkiewicz, L-systems, 1968
  - Lewis Wolpert, Embryo development, 1980s

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- Mode
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- *Upcoming Lectures*
  - ***Biology:*** *Multicellular development*
  - ***CS:*** *Cellular Automata & Global2local Theory*
  - ***Robotics:*** *Self-assembling "Cellular" Robotic Systems*
  - *Other: DNA self-assembly, Synthetic Biology*

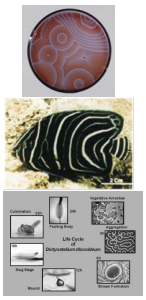
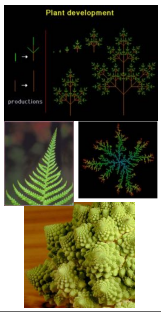
New Theme: Global-to-Local

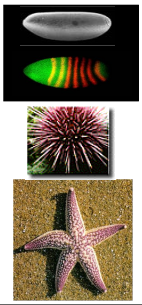
- How do we compose these "local" algorithms to achieve a more complex global goal?
- Can we automatically derive the "local agent rules" from the global goal?

Context: Self-organizing Complex Structure

How do cells do it?

Pattern *Self-Assembly* *Structure*



Turing Patterns

- Chemical/Physical
  - Belousov-Zhabotinsky (1951)
  - Synthetic Chemical Systems (Swinney et al, Nature1994)
- Animal Patterns
  - Seashells (Meinhardt, 1970s)
  - Animal Coats
  - Angelfish (Kondo & Asai1995)
- Multicellular Behavior
  - Slime mold
  - Bone patterning





Turing's Question

- How does one start with identical cells, but end up with a asymmetric, highly patterned organism?

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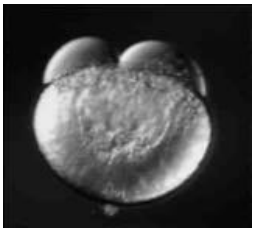

Turing's Question

- How does one start with identical cells, but end up with a asymmetric, highly patterned organism?
- Solution:
  - Nothing is ever "identical". There is always noise.
  - If a system could amplify this noise, then it could move from symmetry to asymmetry.

The Chemical Basis of Morphogenesis, A. M. Turing, Philosophical Trans. of the Royal Society of London, 1952.

Turing's Example

- Suppose that we had two chemicals ("morphogens")
  - X and Y
  - Reaction with each other
  - Diffuse in space

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- Reaction-Diffusion Equations

$$dX/dt = (5X - 6Y + 1) + R_x \nabla^2 X$$
$$dY/dt = (6X - 7Y + 1) + R_y \nabla^2 Y$$

where $R_x = 0.5$, $R_y = 4.5$

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- **Basic Idea:**
- Reaction or Diffusion by itself => steady state X=Y
- *But together, they can "amplify" X–Y …*

Turing's Example

- Reaction Part
  - dX/dt = (5X – 6Y + 1)
  - dY/dt = (6X – 7Y + 1)
  - Steady state, is when there is no more change (when dX/dt = dY/dt = 0)
  - Then, X=Y=1

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  - Steady state, is when there is no more change (when dX/dt = dY/dt = 0)
  - Then, X=Y=1
- Diffusion Part
  - Suppose I had two "cells" with different concentrations of X
  - Then net flow from high to low concentration
  - $dX/dt = R_x \nabla^2 X$ (Rx = 0.5)
  - dX/dt at Cell 1= 0.5 ($X_{cell2} - X_{cell1}$)

	Cell1	Cell 2
t=0	X=1.06	X=0.94
t=1	X=1.00	X=1.00

Turing's Example

- Reaction-Diffusion together
  - $dX/dt = (5X - 6Y + 1) + R_x \nabla^2 X$
  - $dY/dt = (6X - 7Y + 1) + R_y \nabla^2 Y$ $R_x = 0.5, R_y = 4.5$

	Cell1	Cell 2
t=0	X=1.06 Y=1.02	X=0.94 Y=0.98
t=1	X= ? Y= ?	X= ? Y= ?

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	Cell1	Cell 2
t=0	X=1.06 Y=1.02	X=0.94 Y=0.98
t=1	**X= 1.18** Y= 1.06	**X= 0.82** Y= 0.94

X Diffuses 1->2 by 0.06
Y Diffuses 1->2 by 0.18
BUT
X is created in Cell 1 by 0.18
Y is created in Cell 2 by 0.22

Turing's Example

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	Cell1	Cell 2
t=0	X=1.06 Y=1.02	X=0.94 Y=0.98
t=1	X= 1.18 Y= 1.06	X= 0.82 Y= 0.94
t=2	X= **1.54** Y= 1.18	X= **0.46** Y= 0.81

X Diffuses 1->2 by 0.06
Y Diffuses 1->2 by 0.18
BUT
X is created in Cell 1 by 0.18
Y is created in Cell 2 by 0.22

The difference keeps on growing…

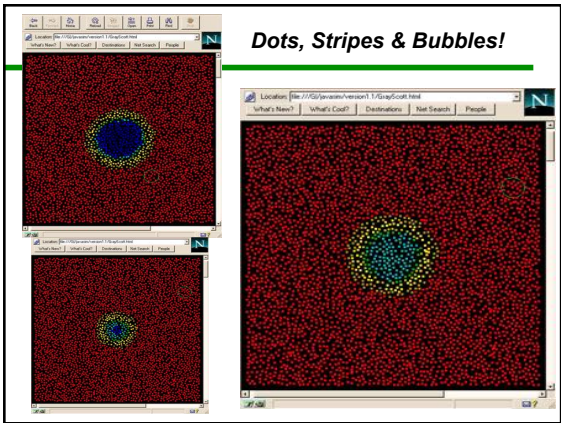
(non-uniform equilibrium)

Turing Patterns

- What kinds of patterns can reaction-diffusion systems generate?

Turing Patterns

- What kinds of patterns can reaction-diffusion systems generate?
- Activator-Inhibitor Model (Grier & Meinhardt, 1975)
  - Two morphogens U and V
  - U is an activator (creates itself)
  - U also creates its own inhibitor (V)
  - V diffuses much faster than U
  - (Grier, Meihardt, 1972, Activator-Inhibitor Model)
- Example: Gray Scott Equations
  - How does the system behave for different parameters?
  - (Amorphous Computer Simulation)



Dots, Stripes & Bubbles!

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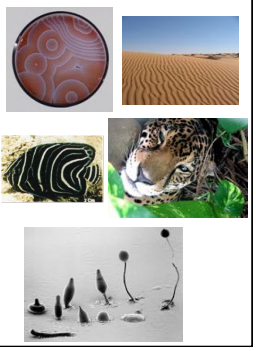
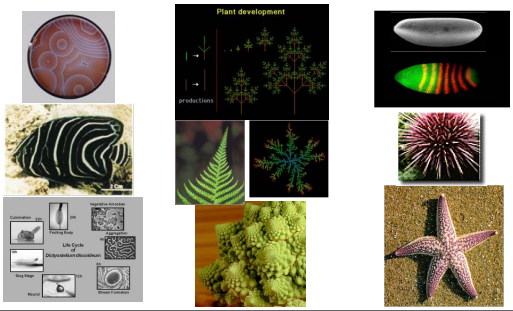


Beyond spots and stripes?

- Turing was wrong about embryogenesis
  - However his work had a significant impact on biology
  - Coined the word *"morphogen"*, the notion of a chemical that directed cell fate. R&D eqns are commonly used
- But how do we move beyond spots and stripes?

How do cells do it?

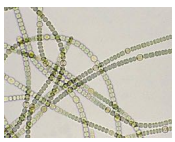
Pattern *Self-Assembly* *Structure*



Lindemayer and Grammars

Aristid Lindenmayer (November 17, 1925 – October 30, 1989)

Anabaena is a genus of filamentous cyanobacteria that exists as plankton. It is known for its nitrogen fixing abilities, and they form symbiotic relationships with certain plants, such as the mosquito fern.



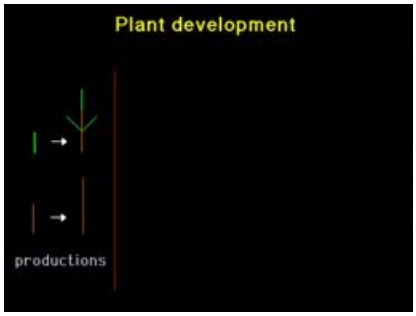
Anabaena Grammar 2 rules: A->AB B->A

A
n = 1ʌ: AB
n = 2ʌ: ABA

n = 3ʌ: ABAAB
n = 4ʌ: ABAABABA
n = 5ʌ: ABAABABAABAAB
n = 6ʌ: ABAABABAABAABABAABABA
n = 7ʌ: ABAABABAABAABABAABABAABAABABAABAAB

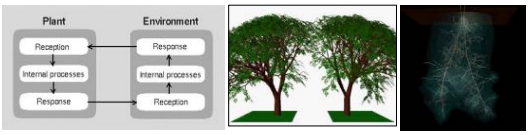
Aristid Lindenmeyer, "Mathematical models for cellular interaction in development." J. Theoret. Biology, 18:280--315, 1968.

Lindemayer and Grammars



Morphogenesis Language

- Use "Grammars" to capture self-assembly of predictable structures in plants
  - Prusinkiewicz and Lindemayer*, **Algorithmic Beauty of Plants** 1990
  - Influential in both biology and graphics
- Also incorporate more complex ideas:
  - Growth, environment, evolution
  - Fundamentally "different" from turing patterns



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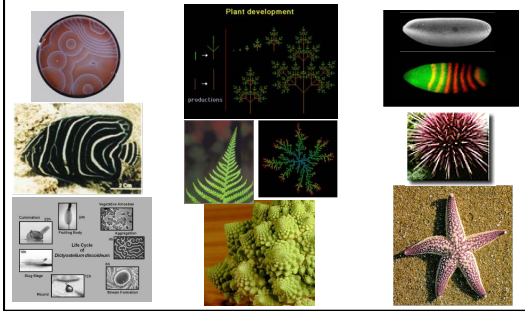
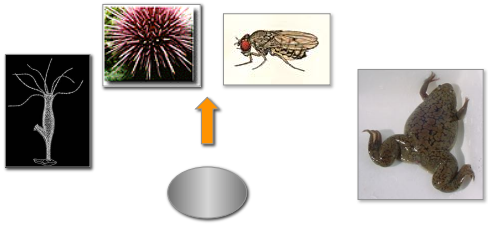
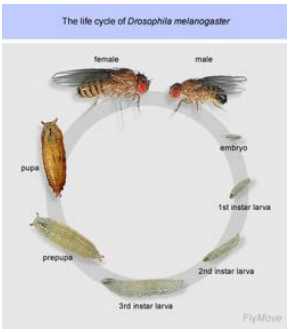


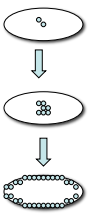
Embryo Development



Focus on One Example



Early Embryogenesis



COOL: http://flymove.uni-muenster.de/

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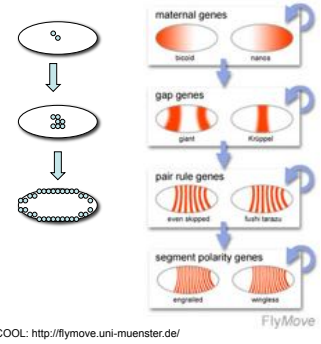

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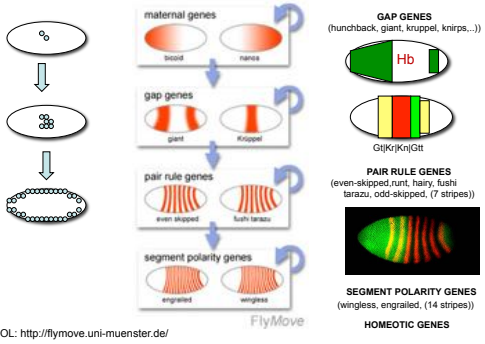

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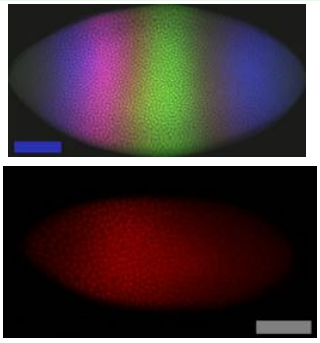
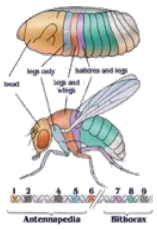


Nobel Prize, 1995

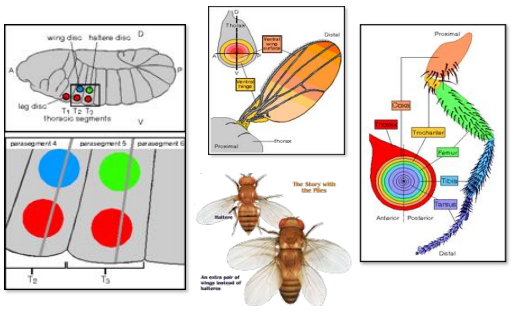
The Nobel Prize in Physiology or Medicine 1995
The Nobel Assembly at the Karolinska Institute in Stockholm, Sweden, has awarded the Nobel Prize in Physiology or Medicine for 1995 to Edward B. Lewis, Christiane Nusslein-Volhard and Eric Wieschaus for their discoveries concerning "the genetic control of early embryonic development".

Later Embryogenesis

- How does one make a wing?

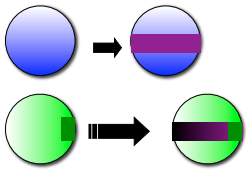


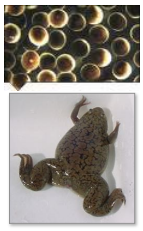
Same Idea all over Again!



and Again

- Frog (Xenopus) development
  - Animal-Vegetal Axis = Maternal Gradients
  - Dorsal-Ventral Axis = Spemann Organiser





Common Design Principles

- Are there common design principles?

Common Design Principles

- Catalog of Cell Strategies
  - Positional information and Morphogens
  - Cell Differentiation and Compartments
  - Lateral Inhibition, Induction
  - Sensing and feedback
  - Cell Death!!

Lewis Wolpert, 1970s, championed the idea of positional information in several seminal papers

- Higher-level Structural Principles
  - Generative Programs
    - Patterns are created and elaborated incrementally
    - Shape is encoded as a "construction" process
  - Structural Reuse (e.g "branching structures" in humans)
  - Structural Modularity (e.g. imaginal discs)

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High-Level Properties!
- *Ability to be **Robust***
- *Ability to **Scale***
- *Ability to **Regenerate***
- *Ability to **Evolve***

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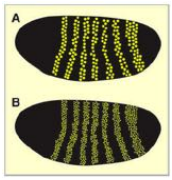
Ability to be Robust

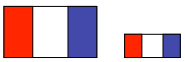
- Remarkably most processes can tolerate:
  - Temperature variation
  - Cell to cell variability
  - Mistakes like extra divisions
  - Cell Death and large damage
  - Variation in scale
- Still poorly understood



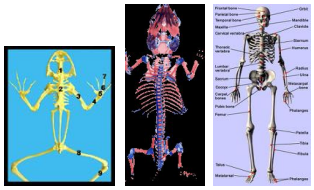
[See paper by Day and Lawrence]

Ability to Scale

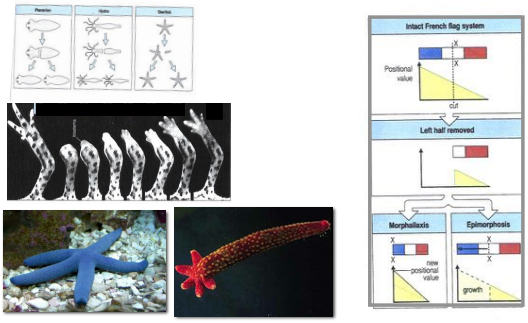
- Similar structures occur at a wide variety of scales



[French Flag Problem: Lewis Wolpert]

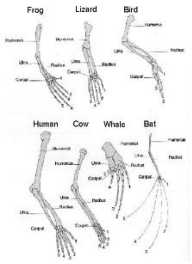


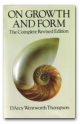
Ability to Regenerate



Ability to Evolve

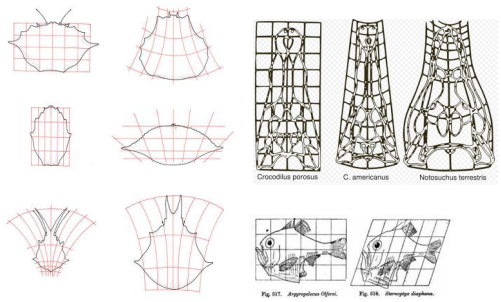
- Evolving Morphology
  - How is variation generated?
  - Can big structural changes arise simply from mutation?
  - How much is determined by genes vs the environment?





D'Arcy Thompson (On Growth and Form, 1917) Proposed the idea of "coordinate transforms" to show that entire species can be related through simple transformations

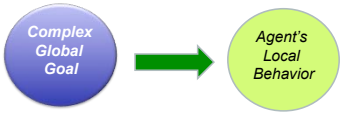
Related Shapes



Common Design Principles

- Are there common design principles?
  - Yes
- Can we capture these "principles" to design our own systems (complex shape, robustness, repair, modularity)

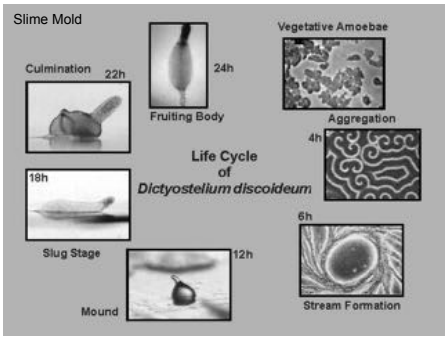
New Theme: Global-to-Local



- How do we compose these "local" algorithms to achieve a more complex global goal?
- Can we automatically derive the "local agent rules" from the global goal?

Lastly….

Multi-cellular Behavior



Multi-cellular Behavior