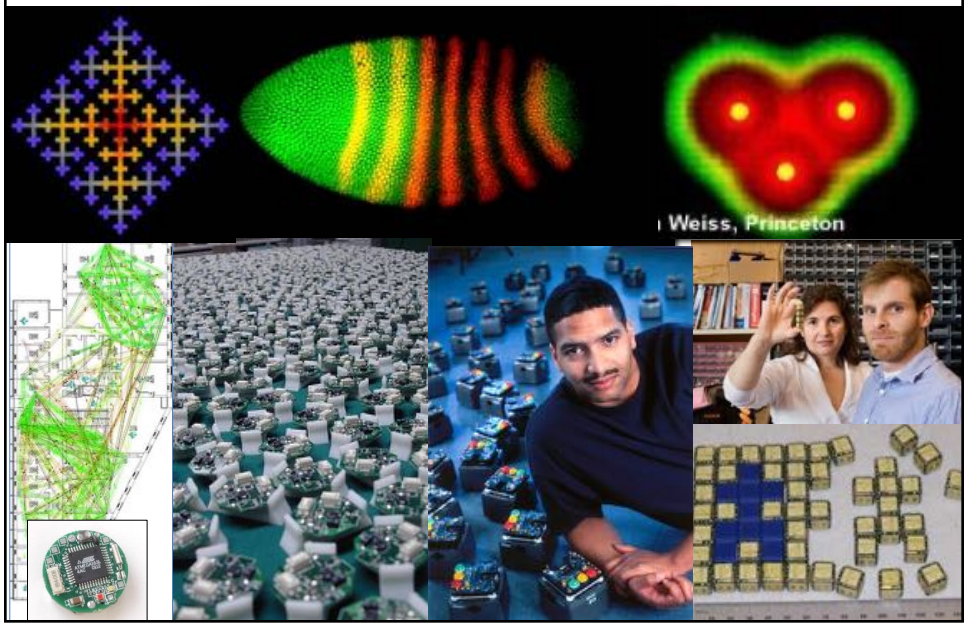
# Self-Assembly in Nature

## Turing Patterns, Morphogenesis, and Embryo Development

CS289

1

# “Spatial” Computation

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# 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

*3*

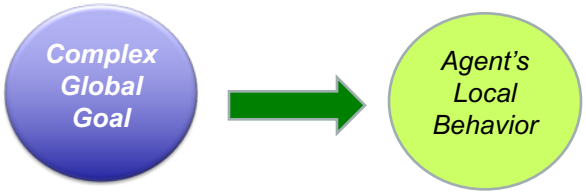
# New Topic: Cellular Computing

- Transition from “Swarm Intelligence” to “Multicellular Intelligence”
  - Insp
  - How
    *mo*
- Mode
  - D
  - V
  - Alan Turing, Turing patterns, 1952
  - Aristid Lindenmayer, L-systems, 1968
  - Lewis Wolpert, Embryo development, 1980s

- *Upcoming Lectures*
  - ***Biology (Today):*** *Multicellular models and inspiration*
  - ***Robotics:*** *Self-assembling “Cellular” Robotic Systems*
  - *Other: Cellular Automata Theory, DNA self-assembly, Synthetic Biology*

*4*

# New Theme: Global-to-Local



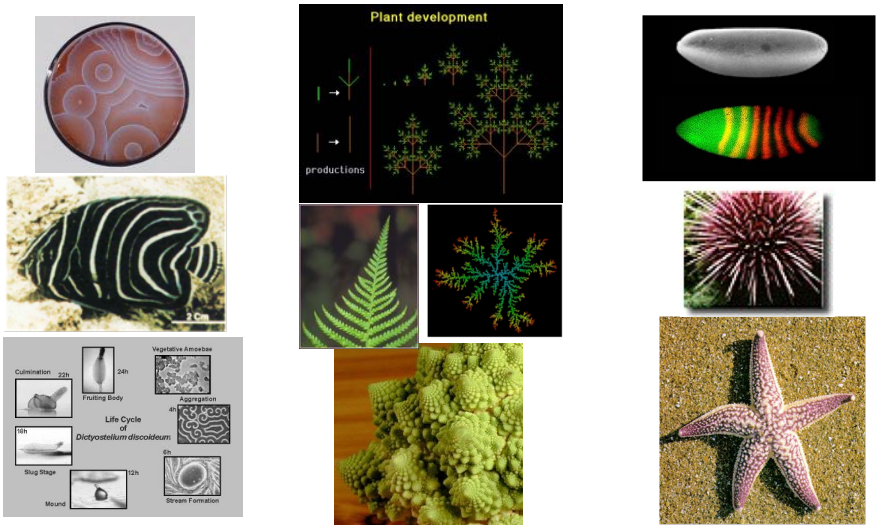

- Library of "local" algorithms inspired by cells
- How do we compose/derive "local" algorithms to achieve a more complex global goal?

Context: Self-organizing Complex Structure

5

# How do cells do it?

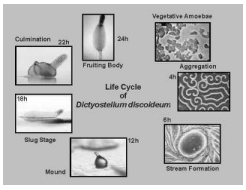
*Pattern* *Self-Assembly* *Structure*




6

# How do cells do it?

*Pattern*




Turing Patterns

7

# Turing's Question

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

8

## Turing's Question

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

9

## 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.

10

# Turing's Example

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

11

# Turing's Example

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

- Reaction-Diffusion Equations

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

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

12

# Turing's Example

- Suppose that we had two chemicals ("morphogens")
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- Reaction-Diffusion Equations

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

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

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

13

# 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

14

# 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
- 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 |

16

# 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<br>Y=1.02 | X=0.94<br>Y=0.98 |
| t=1 | X= ?<br>Y= ? | X= ?<br>Y= ? |

17

# 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= 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

18

# 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= 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)*

19

# Turing Patterns

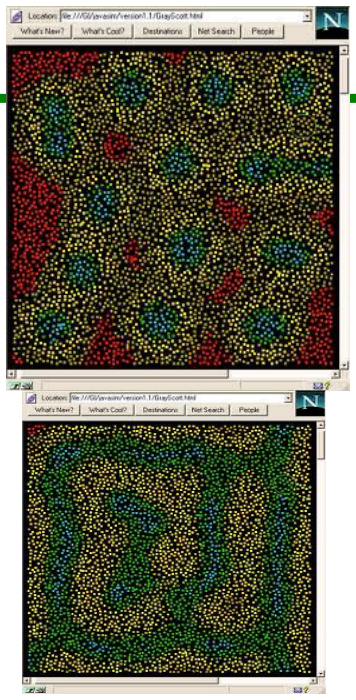
- What kinds of patterns can reaction-diffusion systems generate?

20

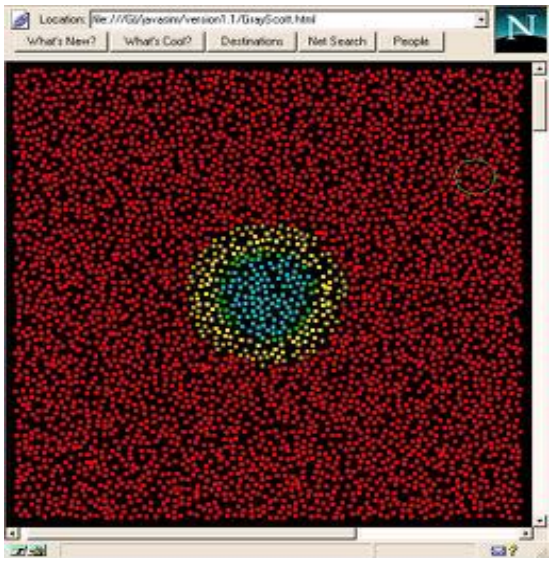
# Turing Patterns

- 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)

21



## Dots, Stripes & Bubbles!



22

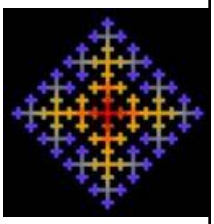
# Turing Patterns in Nature

- 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

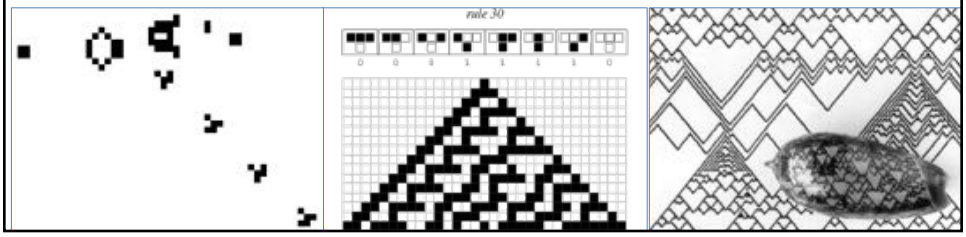
23

# Cellular Automata

- **Stanislaw Ulam and John von Neumann (1940s)**
  - Simulate "discrete" biology & physics;
  - Self-replicating machines



- Conway's Game of Life (1970s)
  - A simple intuitive rule….amazing dynamic patterns!
  - Turing Complete! (2002)
- Wolfram, A New Kind of Science, 2002
  - Systematic classification of *all* 1D two-state CA rules




24

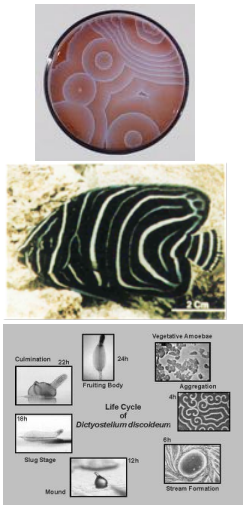
# Beyond spots and stripes?

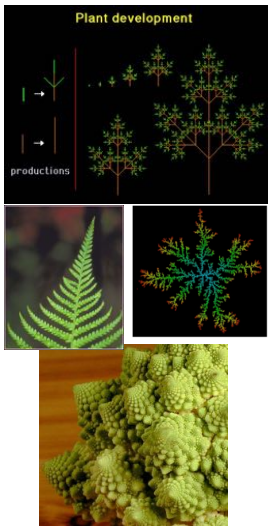
- Turing was wrong about embryogenesis
  - However his work had a significant impact on biology
  - Coined the word *"morphogen",* the notion of a chemical that directed cell fate. R&D eqns are commonly used
- But how do we move beyond spots and stripes?

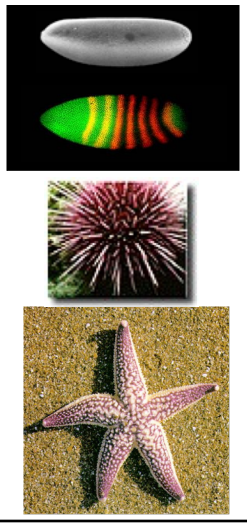
27

# How do cells do it?

*Pattern* *Self-Assembly* *Structure*



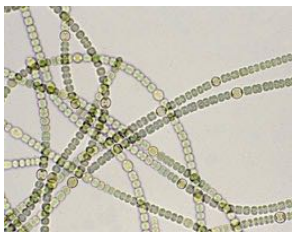



28

# 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*

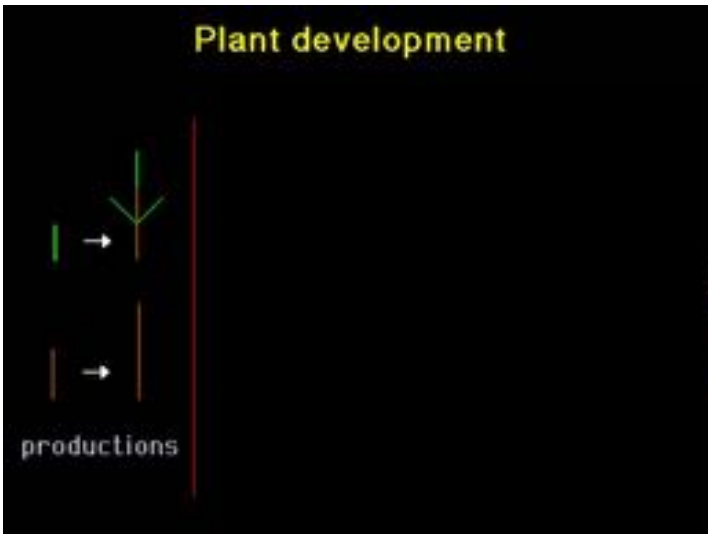
*A*
*n = 1ת: AB*
*n = 2ת: ABA*

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

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

29

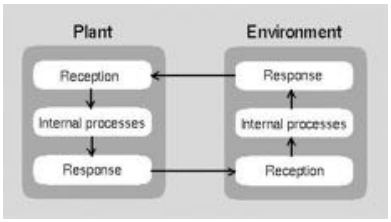
# Lindemayer and Grammars

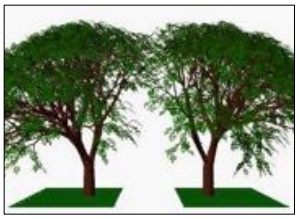


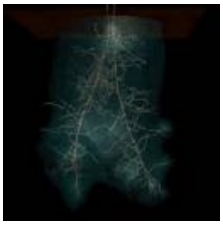

31

# 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



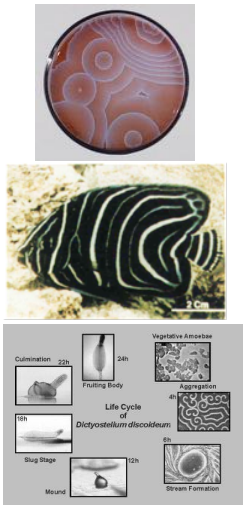



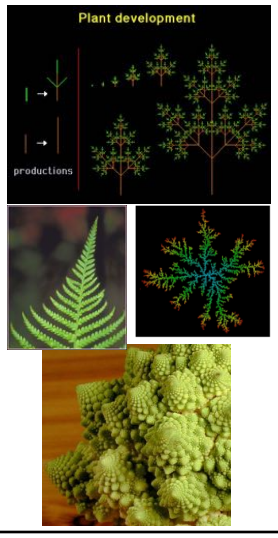


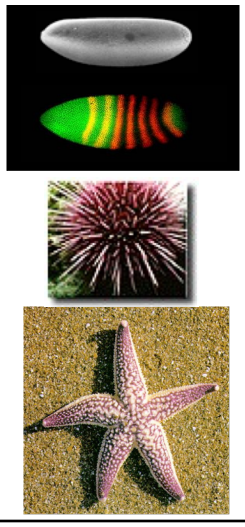
32

# How do cells do it?

*Pattern* *Self-Assembly* *Structure*

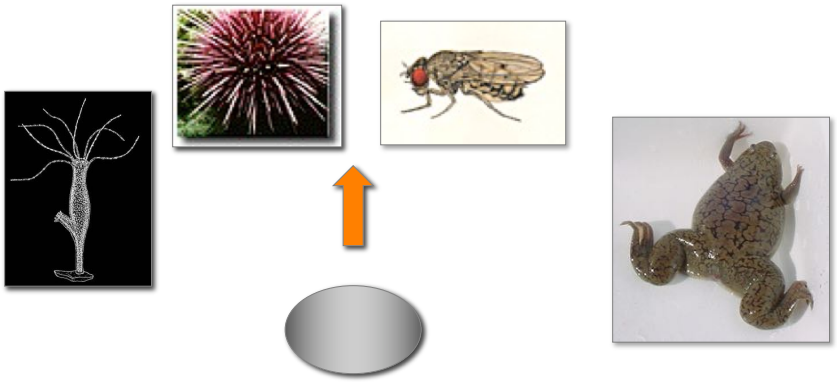


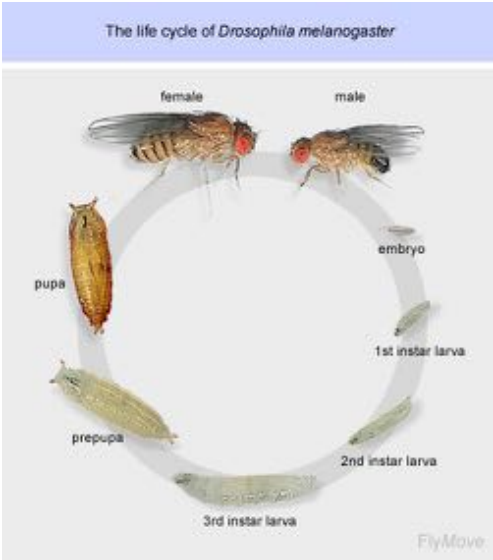
33

# Embryo Development



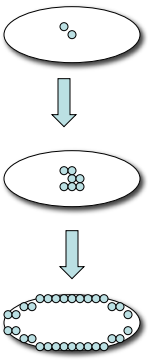
34

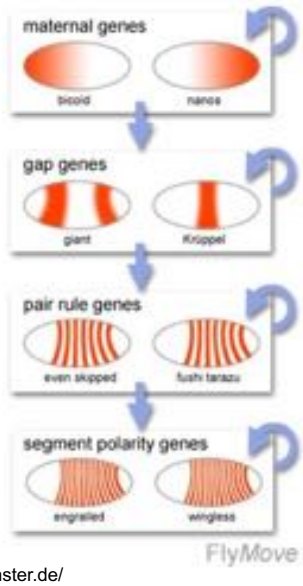
# Focus on One Example



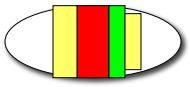

35

# Early Embryogenesis



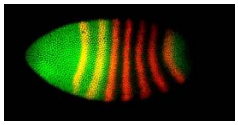



**GAP GENES**
(hunchback, giant, kruppel, knirps,..))

Gt|Kr|Kn|Gtt

**PAIR RULE GENES**
(even-skipped,runt, hairy, fushi tarazu, odd-skipped, (7 stripes))



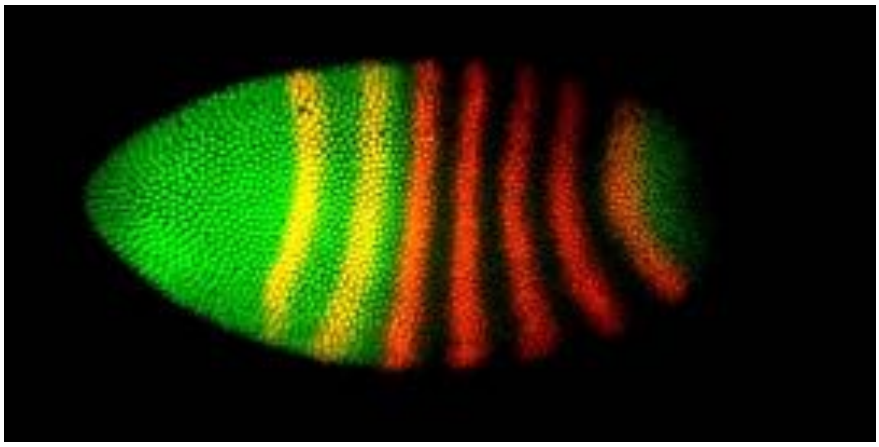
**SEGMENT POLARITY GENES**
(wingless, engrailed, (14 stripes))

**HOMEOTIC GENES**

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

38

## Morphogens and Positional Information!

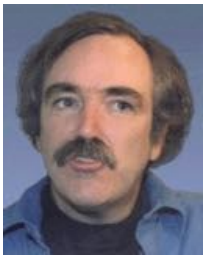


39

## 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".

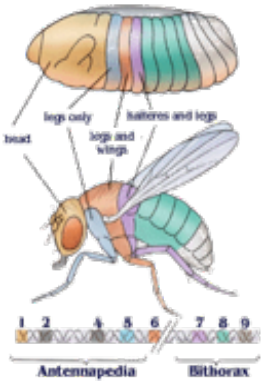




41

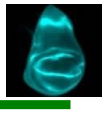
# Later Embryogenesis

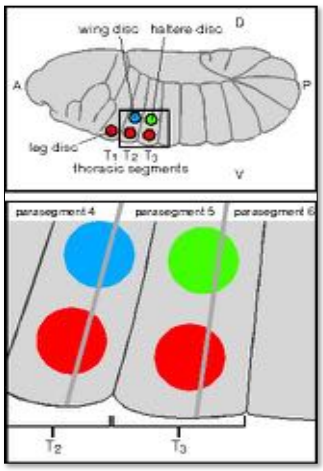
- How does one make a wing?

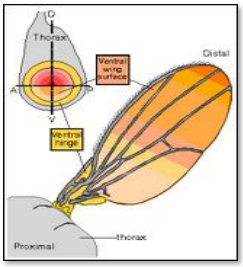



42

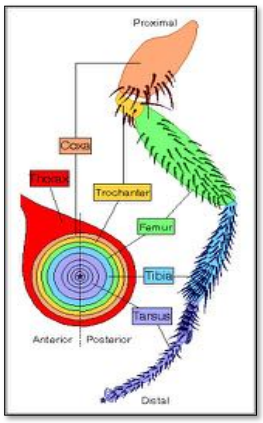
# Same Idea all over Again!





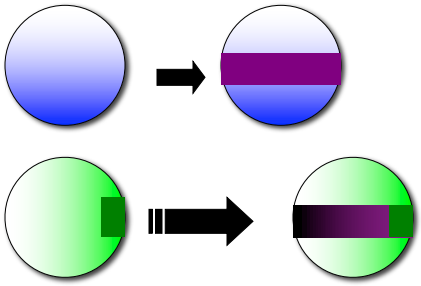





43

## and Again

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



44

## Common Design Principles

- Are there common design principles?

45

# Common Design Principles

- Catalog of Cell Strategies
  - Positional information and Morphogens
  - Cell Differentiation and Compartments
  - Lateral Inhibition, Induction
  - 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)
  - Modularity (e.g. imaginal discs as "subroutines")

46

# Common Design Principles

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

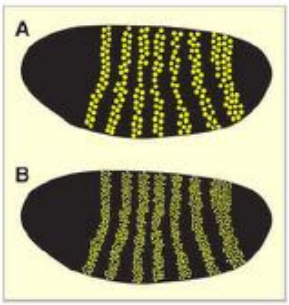
***High-Level Properties!***
- *Ability to be **Robust***
- *Ability to **Scale***
- *Ability to **Regenerate***
- *Ability to **Evolve***

- Higher-level S
  - Generative P
    - Patterns
    - Shape is encoded as a "construction" process
  - Structural Reuse (e.g "branching structures" in humans)
  - Modularity (e.g. imaginal discs as "subroutines")

47

# 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

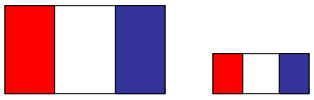



[See paper by Day and Lawrence]

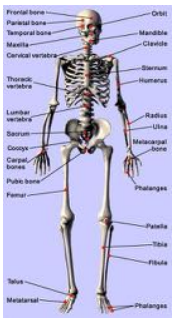
48

# Ability to Scale

- Similar structures occur at a wide variety of scales

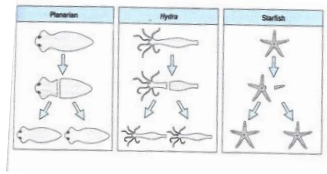


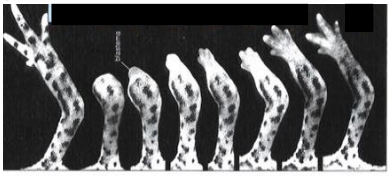
*[French Flag Problem: Lewis Wolpert]*

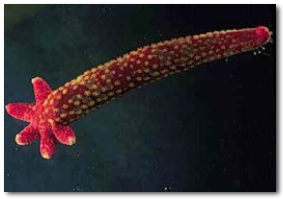


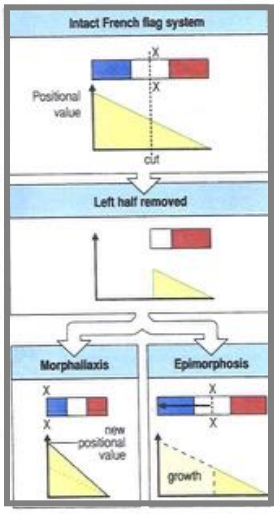
49

# Ability to Regenerate



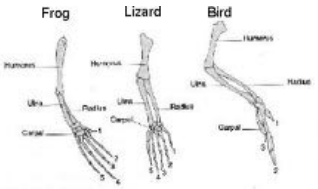


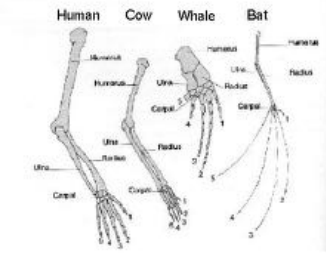


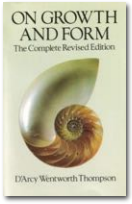

50

# 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?



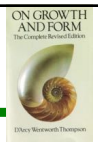



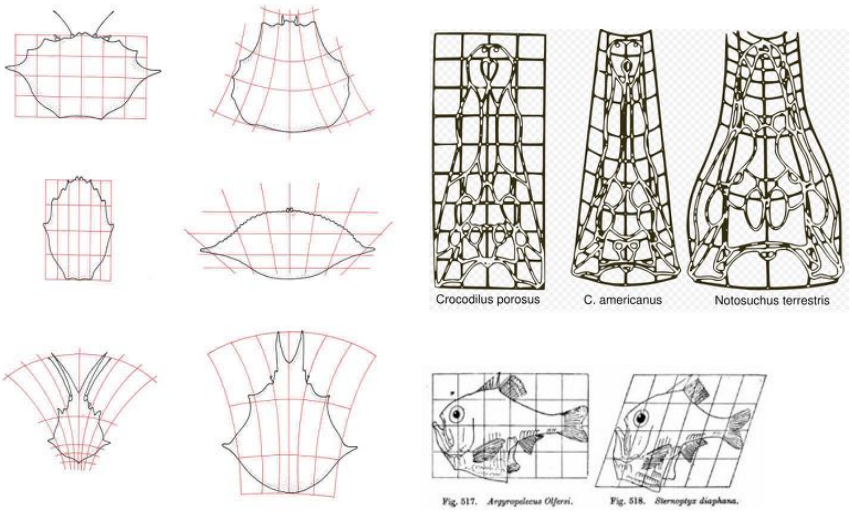




*D'Arcy Thompson (On Growth and Form, 1917) Proposed the idea of "coordinate transforms" to show that entire species can be related through simple transformations*

51

# Related Shapes



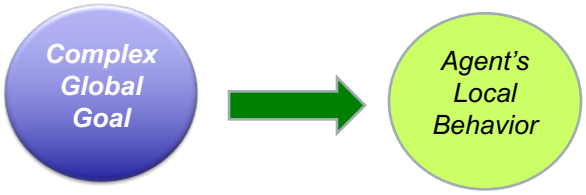

52

# Common Design Principles

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

53

# 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?

54