B.
Pattern Formation

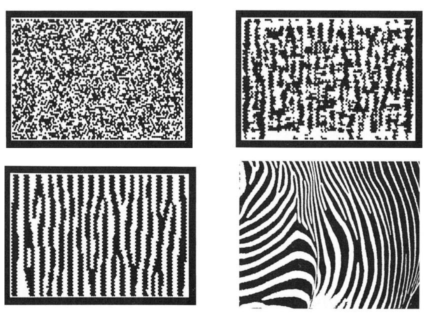
1/25/12 1

Differentiation & Pattern Formation

- A central problem in development: How do cells differentiate to fulfill different purposes?
- How do complex systems generate spatial & temporal structure?
- CAs are natural models of intercellular communication

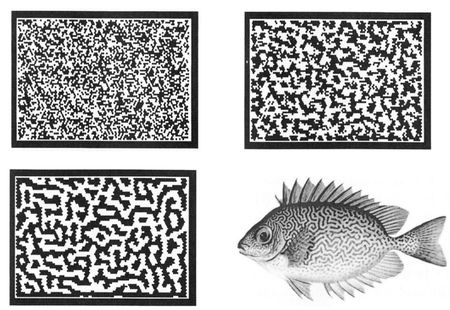
1/25/12 photos ©2000, S. Cazamine 2

Zebra



1/25/12 figs. from Camazine & al.: *Self-Org. Biol. Sys.* 3

Vermiculated Rabbit Fish



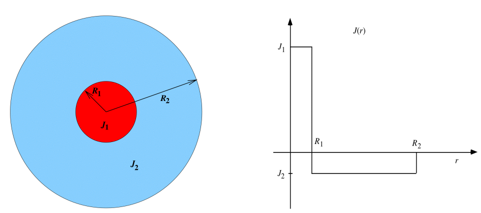
1/25/12 figs. from Camazine & al.: *Self-Org. Biol. Sys.* 4

Activation & Inhibition in Pattern Formation

- Color patterns typically have a characteristic length scale
- Independent of cell size and animal size
- Achieved by:
  - short-range activation ⇒ local uniformity
  - long-range inhibition ⇒ separation

1/25/12 5

Interaction Parameters



- R_1 and R_2 are the interaction ranges
- J_1 and J_2 are the interaction strengths

1/25/12 6

CA Activation/Inhibition Model

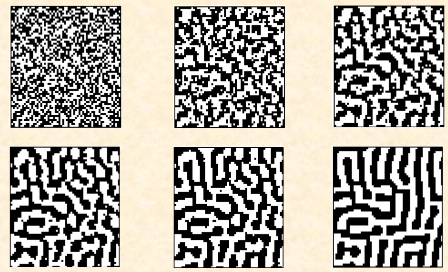
- Let states $s_i \in \{-1, +1\}$
- and h be a bias parameter
- and r_{ij} be the distance between cells i and j
- Then the state update rule is:

$$s_i(t+1) = \text{sign}\left[h + J_1 \sum_{r_{ij} < R_1} s_j(t) + J_2 \sum_{R_1 \le r_{ij} < R_2} s_j(t)\right]$$

1/25/12 7

Example

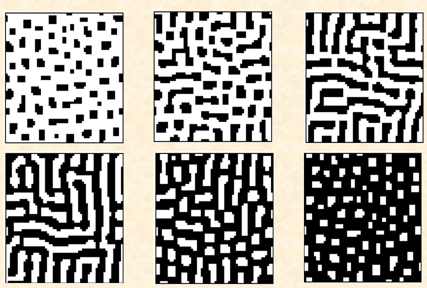
(R_1=1, R_2=6, J_1=1, J_2=–0.1, h=0)



1/25/12 figs. from Bar-Yam 8

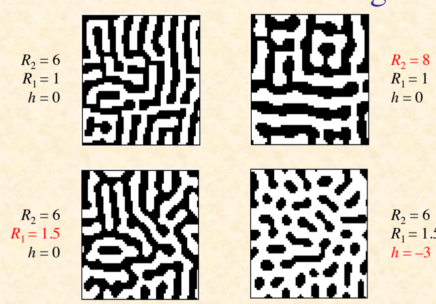
Effect of Bias

(h = –6, –3, –1; 1, 3, 6)



1/25/12 figs. from Bar-Yam 9

Effect of Interaction Ranges



1/25/12 figs. from Bar-Yam 10

Demonstration of NetLogo Program for Activation/Inhibition Pattern Formation: Fur

RunAICA.nlogo

1/25/12 11

Differential Interaction Ranges

- How can a system using strictly local interactions discriminate between states at long and short range?
- E.g. cells in developing organism
- Can use two different *morphogens* diffusing at two different rates
  - activator diffuses slowly (short range)
  - inhibitor diffuses rapidly (long range)

1/25/12 12

Digression on Diffusion

- Simple 2-D diffusion equation:

$$\dot{A}(x,y) = c\nabla^2 A(x,y)$$

- Recall the 2-D Laplacian:

$$\nabla^2 A(x,y) = \frac{\partial^2 A(x,y)}{\partial x^2} + \frac{\partial^2 A(x,y)}{\partial y^2}$$

- The Laplacian (like 2nd derivative) is:
  - positive in a local minimum
  - negative in a local maximum

1/25/12 13

Reaction-Diffusion System

diffusion | reaction

$$\frac{\partial A}{\partial t} = d_A \nabla^2 A + f_A(A,I)$$
$$\frac{\partial I}{\partial t} = d_I \nabla^2 I + f_I(A,I)$$

$$\frac{\partial}{\partial t}\begin{pmatrix} A \\ I \end{pmatrix} = \begin{pmatrix} d_A & 0 \\ 0 & d_I \end{pmatrix}\begin{pmatrix} \nabla^2 A \\ \nabla^2 I \end{pmatrix} + \begin{pmatrix} f_A(A,I) \\ f_I(A,I) \end{pmatrix}$$

$$\dot{\mathbf{c}} = \mathbf{D}\nabla^2 \mathbf{c} + \mathbf{f}(\mathbf{c}), \text{ where } \mathbf{c} = \begin{pmatrix} A \\ I \end{pmatrix}$$

1/25/12 14

Continuous-time Activator-Inhibitor System

- Activator A and inhibitor I may diffuse at different rates in x and y directions
- Cell becomes more active if activator + bias exceeds inhibitor
- Otherwise, less active

$$\frac{\partial A}{\partial t} = d_{Ax}\frac{\partial^2 A}{\partial x^2} + d_{Ay}\frac{\partial^2 A}{\partial y^2} + k_A(A + B - I)$$
$$\frac{\partial I}{\partial t} = d_{Ix}\frac{\partial^2 I}{\partial x^2} + d_{Iy}\frac{\partial^2 I}{\partial y^2} + k_I(A + B - I)$$

1/25/12 15

NetLogo Simulation of Reaction-Diffusion System

1. Diffuse activator in X and Y directions
2. Diffuse inhibitor in X and Y directions
3. Each patch performs:

stimulation = bias + activator – inhibitor + noise
if stimulation > 0 then
    set activator and inhibitor to 100
else
    set activator and inhibitor to 0

1/25/12 16

Demonstration of NetLogo Program for Activator/Inhibitor Pattern Formation

Run Pattern.nlogo

1/25/12 17

Demonstration of NetLogo Program for Activator/Inhibitor Pattern Formation with Continuous State Change

Run Activator-Inhibitor.nlogo

1/25/12 18

Turing Patterns

- Alan Turing studied the mathematics of reaction-diffusion systems
- Turing, A. (1952). The chemical basis of morphogenesis. *Philosophical Transactions of the Royal Society* **B 237**: 37–72.
- The resulting patterns are known as *Turing patterns*

1/25/12 19

A Key Element of Self-Organization

- Activation vs. Inhibition
- Cooperation vs. Competition
- Amplification vs. Stabilization
- Growth vs. Limit
- Positive Feedback vs. Negative Feedback
  - Positive feedback creates
  - Negative feedback shapes

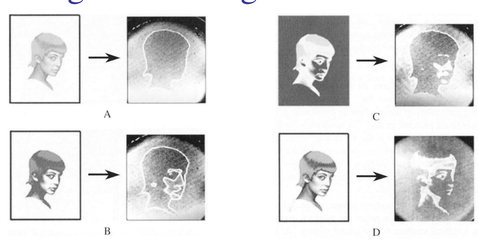
1/25/12 20

Reaction-Diffusion Computing

- Has been used for image processing
  - diffusion ⇒ noise filtering
  - reaction ⇒ contrast enhancement
- Depending on parameters, RD computing can:
  - restore broken contours
  - detect edges
  - improve contrast

1/25/12 21

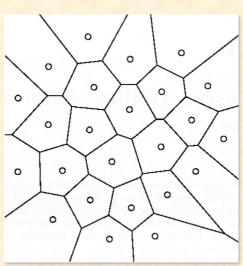
Image Processing in BZ Medium



- (A) boundary detection, (B) contour enhancement, (C) shape enhancement, (D) feature enhancement

1/25/12 Image < Adamatzky, *Comp. in Nonlinear Media & Autom. Coll.* 22

Voronoi Diagrams



- Given a set of generating points:
- Construct a polygon around each generating point of set, so all points in a polygon are closer to its generating point than to any other generating points.

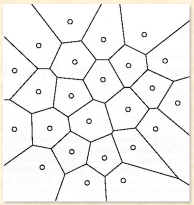
1/25/12 Image < Adamatzky & al., *Reaction-Diffusion Computers* 23

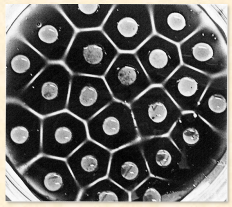
Some Uses of Voronoi Diagrams

- Collision-free path planning
- Determination of service areas for power substations
- Nearest-neighbor pattern classification
- Determination of largest empty figure

1/25/12 24

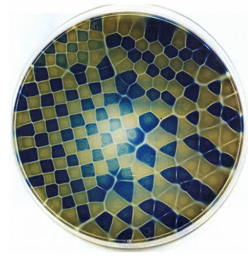
Computation of Voronoi Diagram by Reaction-Diffusion Processor





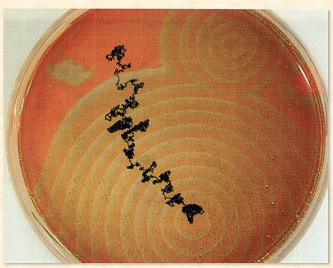
1/25/12 Image < Adamatzky & al., *Reaction-Diffusion Computers* 25

Mixed Cell Voronoi Diagram



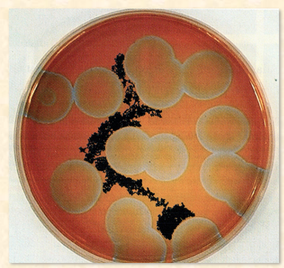
1/25/12 Image < Adamatzky & al., *Reaction-Diffusion Computers* 26

Path Planning via BZ medium: No Obstacles



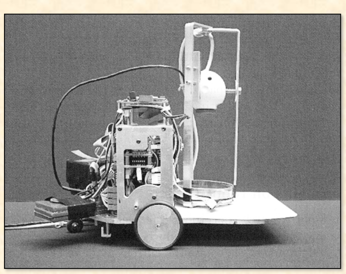
1/25/12 Image < Adamatzky & al., *Reaction-Diffusion Computers* 27

Path Planning via BZ medium: Circular Obstacles



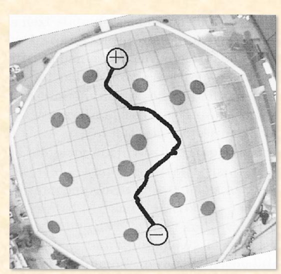
1/25/12 Image < Adamatzky & al., *Reaction-Diffusion Computers* 28

Mobile Robot with Onboard Chemical Reactor



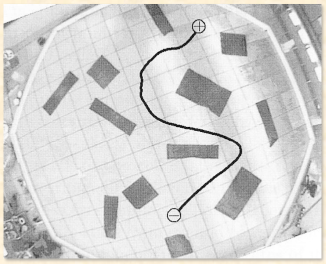
1/25/12 Image < Adamatzky & al., *Reaction-Diffusion Computers* 29

Actual Path: Pd Processor



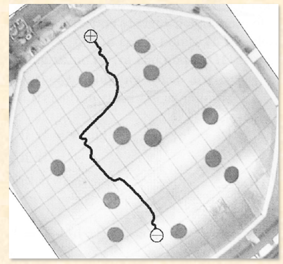
1/25/12 Image < Adamatzky & al., *Reaction-Diffusion Computers* 30

Actual Path: Pd Processor



1/25/12 Image < Adamatzky & al., *Reaction-Diffusion Computers* 31

Actual Path: BZ Processor



1/25/12 Image < Adamatzky & al., *Reaction-Diffusion Computers* 32

Bibliography for Reaction-Diffusion Computing

1. Adamatzky, Adam. *Computing in Nonlinear Media and Automata Collectives*. Bristol: Inst. of Physics Publ., 2001.
2. Adamatzky, Adam, De Lacy Costello, Ben, & Asai, Tetsuya. *Reaction Diffusion Computers*. Amsterdam: Elsevier, 2005.

1/25/12 33

Segmentation

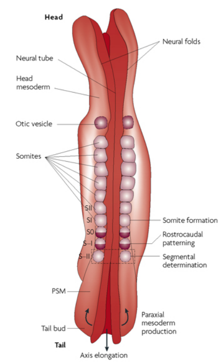
(in embryological development)

1/25/12 34

Vertebrae

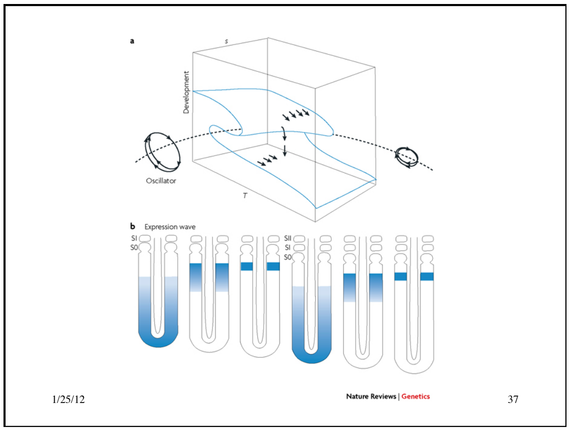
- Humans: 33, chickens: 55, mice: 65, corn snake: 315
- Characteristic of species
- How does an embryo "count" them?
- "Clock and wavefront model" of Cooke & Zeeman (1976).

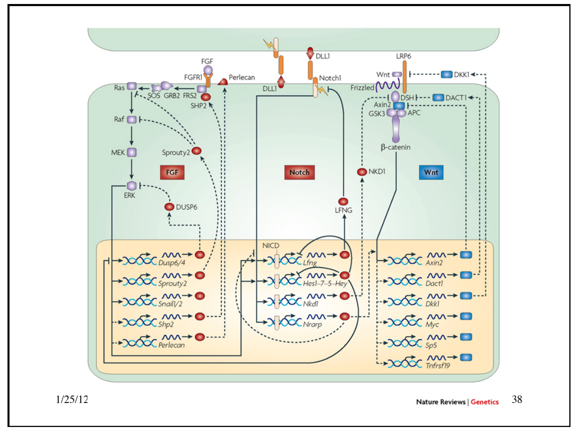
1/25/12 35

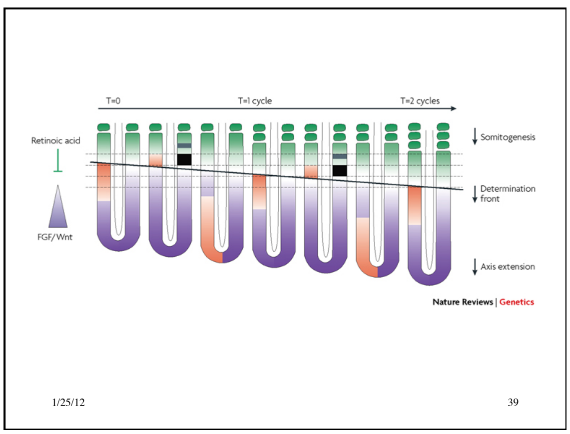


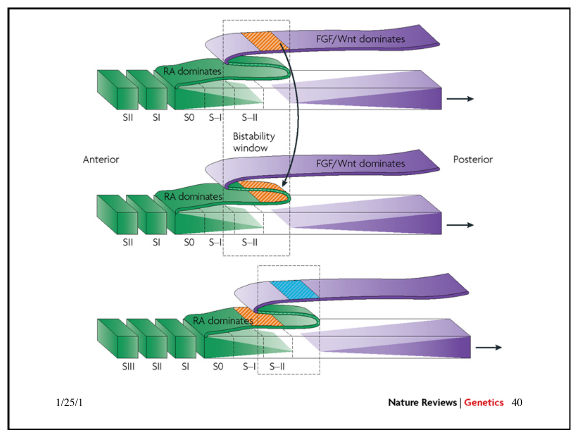
Nature Reviews | Genetics

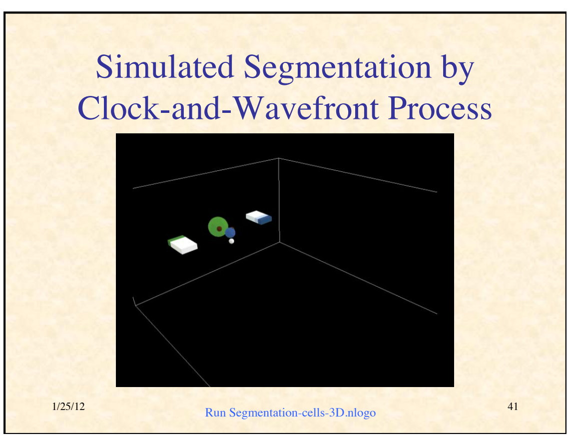
1/25/12 36

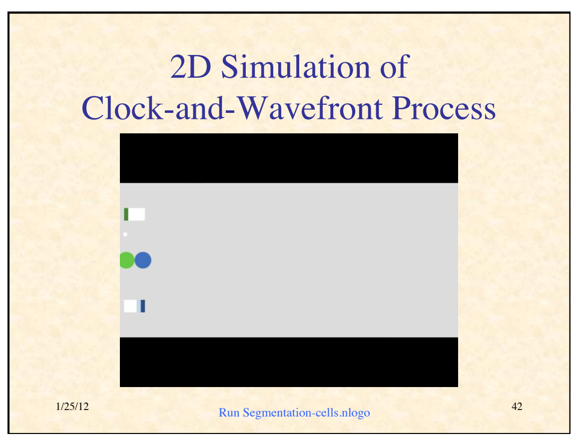

a
Development
Oscillator
T
b
Expression wave
1/25/12
Nature Reviews | Genetics
37

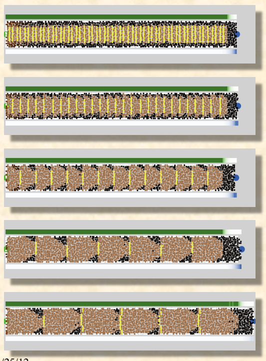

FGF
Notch
Wnt
1/25/12
Nature Reviews | Genetics
38


T=0
T=1 cycle
T=2 cycles
Retinoic acid
FGF/Wnt
Somitogenesis
Determination front
Axis extension
Nature Reviews | Genetics
1/25/12
39


FGF/Wnt dominates
RA dominates
SII SI S0 S–I S–II
Bistability window
Anterior
Posterior
SIII SII SI S0 S–I S–II
1/25/1
Nature Reviews | Genetics 40


Simulated Segmentation by
Clock-and-Wavefront Process
1/25/12
Run Segmentation-cells-3D.nlogo
41


2D Simulation of
Clock-and-Wavefront Process
1/25/12
Run Segmentation-cells.nlogo
42



Effect of Growth Rate

NetLogo Simulation of Segmentation

Run Segmentation.nlogo

Segmentation References

1. Cooke, J., & Zeeman, E.C. (1976). A clock and wavefront model for control of the number of repeated structures during animal morphogenesis. *J. Theor. Biol.* **58**: 455–76.
2. Dequéant, M.-L., & Pourquié, O. (2008). Segmental patterning of the vertebrate embryonic axis. *Nature Reviews Genetics* **9**: 370–82.
3. Gomez, C., Özbudak, E.M., Wunderlich, J., Baumann, D., Lewis, J., & Pourquié, O. (2008). Control of segment number in vertebrate embryos. *Nature* **454**: 335–9.

Additional Bibliography

1. Kessin, R. H. *Dictyostelium: Evolution, Cell Biology, and the Development of Multicellularity*. Cambridge, 2001.
2. Gerhardt, M., Schuster, H., & Tyson, J. J. "A Cellular Automaton Model of Excitable Media Including Curvature and Dispersion," *Science* **247** (1990): 1563-6.
3. Tyson, J. J., & Keener, J. P. "Singular Perturbation Theory of Traveling Waves in Excitable Media (A Review)," *Physica D* **32** (1988): 327-61.
4. Camazine, S., Deneubourg, J.-L., Franks, N. R., Sneyd, J., Theraulaz, G.,& Bonabeau, E. *Self-Organization in Biological Systems*. Princeton, 2001.
5. Pálsson, E., & Cox, E. C. "Origin and Evolution of Circular Waves and Spiral in *Dictyostelium discoideum* Territories," *Proc. Natl. Acad. Sci. USA*: **93** (1996): 1151-5.
6. Solé, R., & Goodwin, B. *Signs of Life: How Complexity Pervades Biology*. Basic Books, 2000.

continue to "Part 2C"