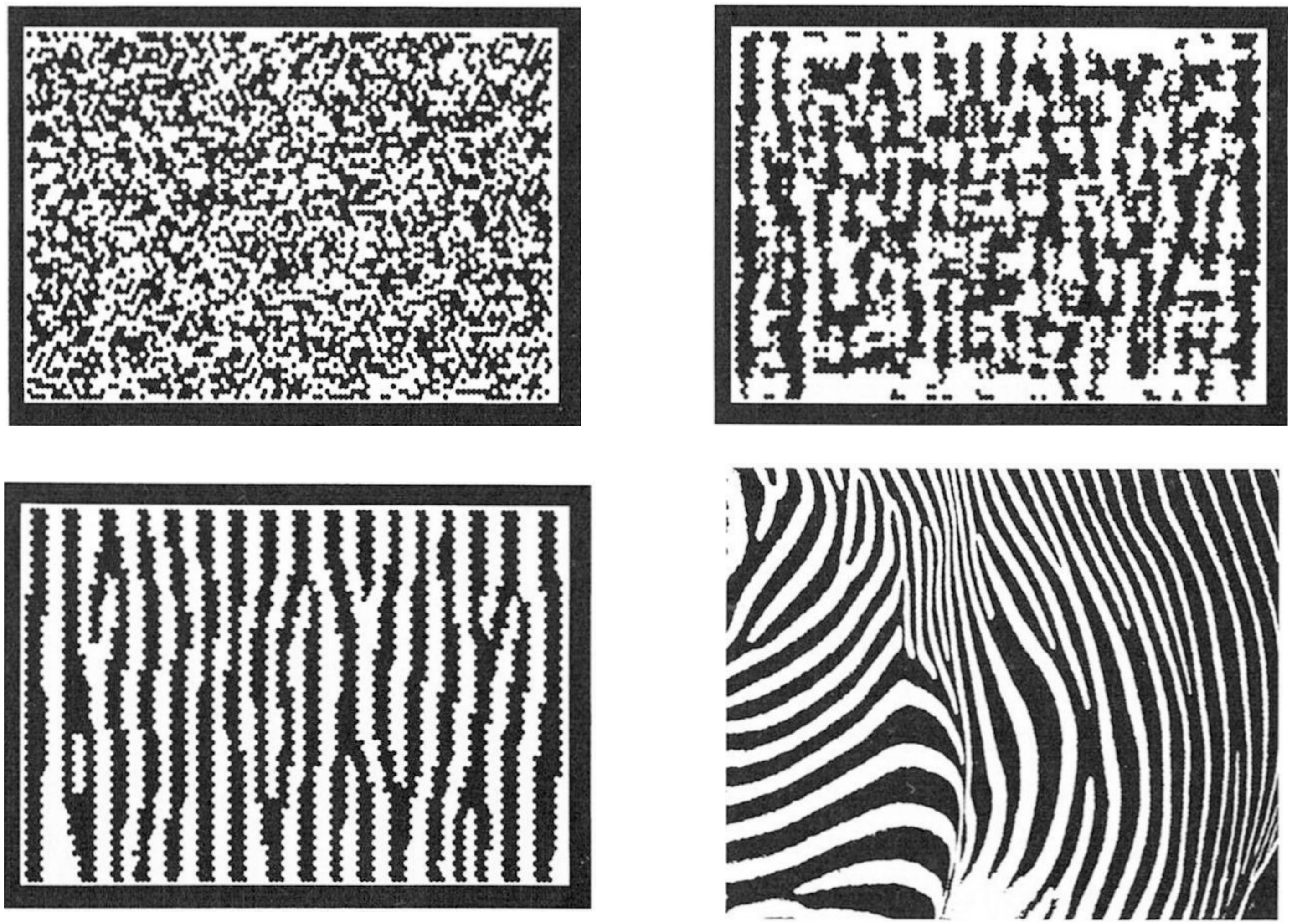
B.
Pattern Formation

Differentiation & Pattern Formation

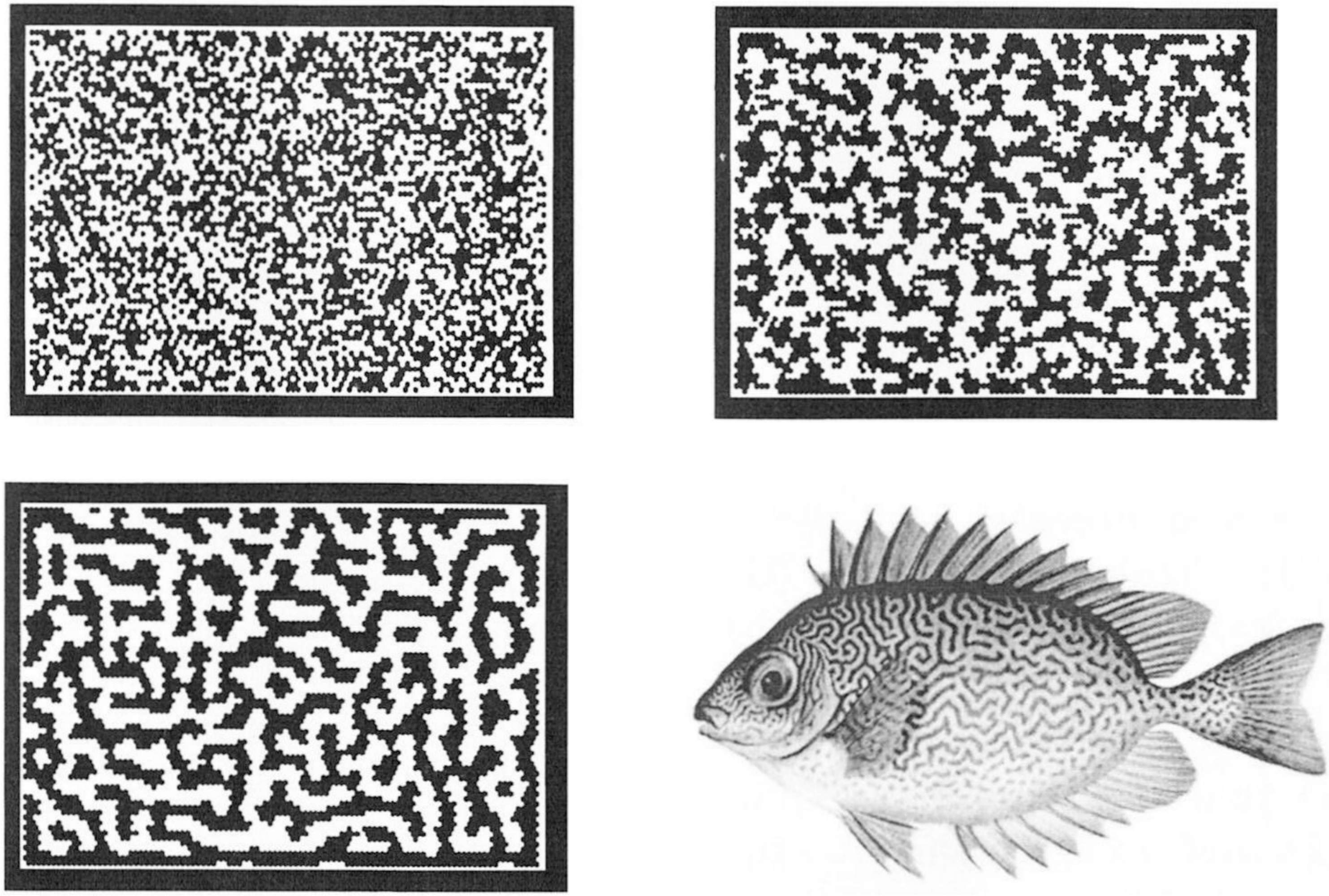
- A central problem in development: How do cells differentiate to fulfill different purposes?
- How do complex systems generate spatial & temporal structure?
- CAs are natural models of intercellular communication

Zebra



figs. from Camazine & al.: *Self-Org. Biol. Sys.*

Vermiculated Rabbit Fish

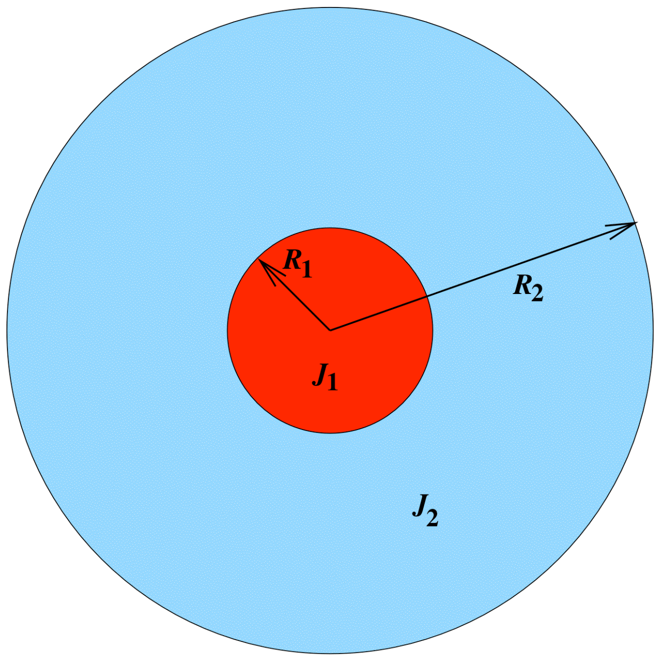


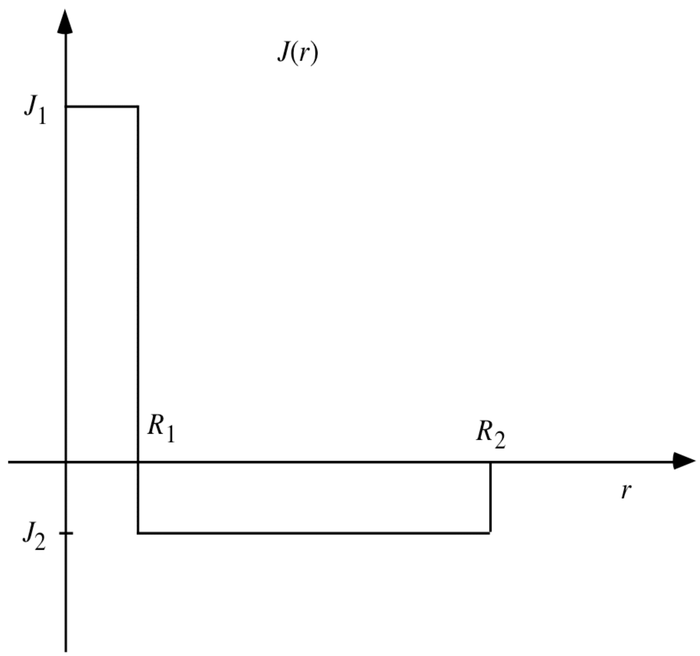
figs. from Camazine & al.: *Self-Org. Biol. Sys.*

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

Interaction Parameters





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

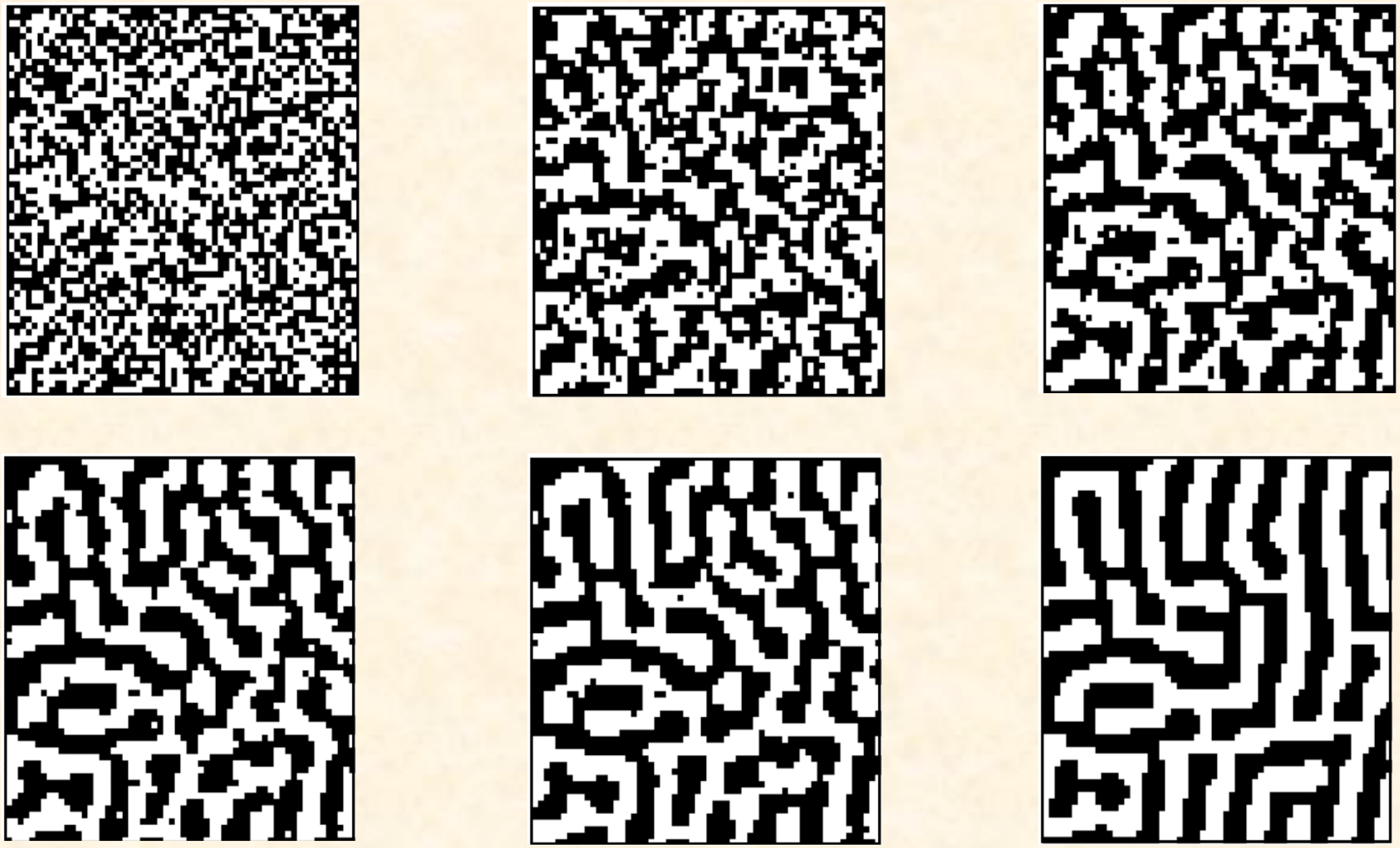
CA Activation/Inhibition Model

- 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:

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

Example

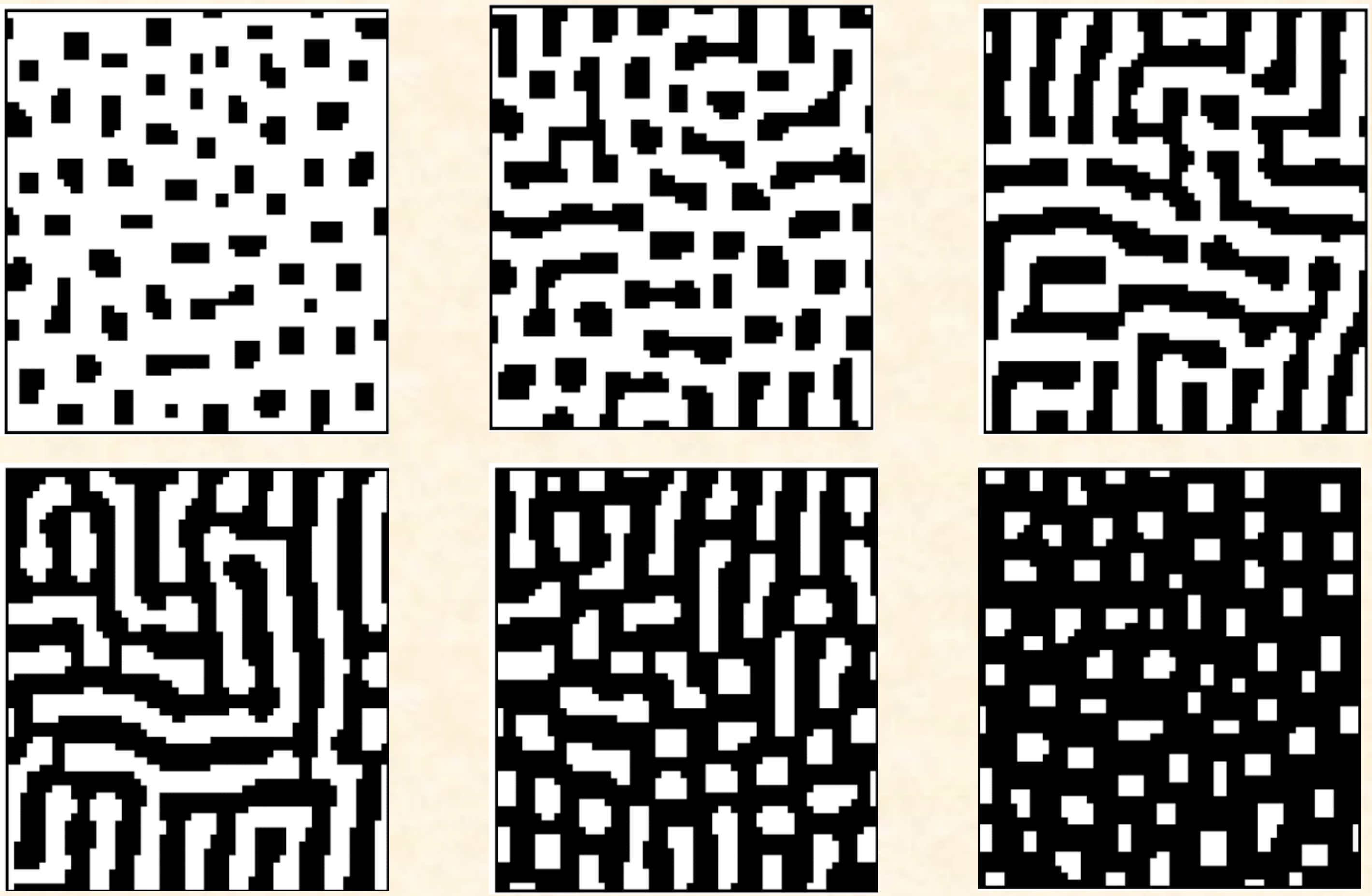
(R_1=1, R_2=6, J_1=1, J_2=–0.1, h=0)



figs. from Bar-Yam

Effect of Bias

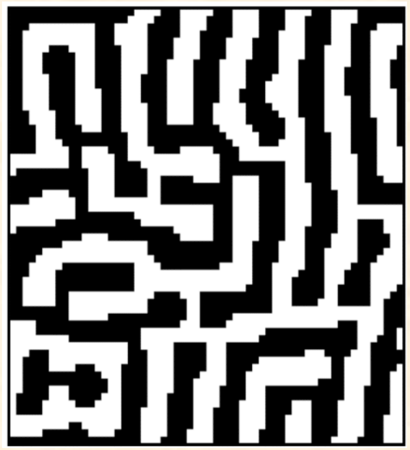
(h = –6, –3, –1; 1, 3, 6)



figs. from Bar-Yam

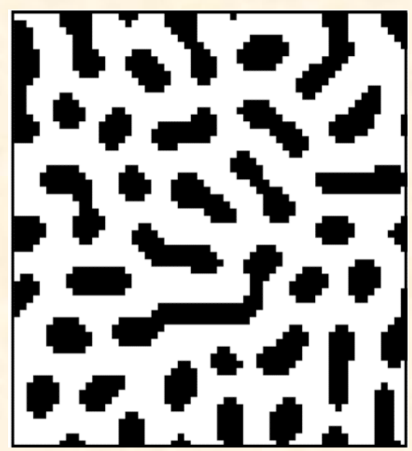
Effect of Interaction Ranges

$R_2 = 6$
$R_1 = 1$
$h = 0$



$R_2 = 8$
$R_1 = 1$
$h = 0$

$R_2 = 6$
$R_1 = 1.5$
$h = 0$



$R_2 = 6$
$R_1 = 1.5$
$h = -3$

figs. from Bar-Yam

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

RunAICA.nlogo

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)

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

Reaction-Diffusion System

diffusion

$$\frac{\partial A}{\partial t} = d_\mathrm{A}\nabla^2 A + f_\mathrm{A}(A,I)$$

$$\frac{\partial I}{\partial t} = d_\mathrm{I}\nabla^2 I + f_\mathrm{I}(A,I)$$

reaction

$$\frac{\partial}{\partial t}\begin{pmatrix} A \\ I \end{pmatrix} = \begin{pmatrix} d_\mathrm{A} & 0 \\ 0 & d_\mathrm{I} \end{pmatrix}\begin{pmatrix} \nabla^2 A \\ \nabla^2 I \end{pmatrix} + \begin{pmatrix} f_\mathrm{A}(A,I) \\ f_\mathrm{I}(A,I) \end{pmatrix}$$

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

Example: Activation-Inhibition System

- Let σ be some kind of threshold function
- Activator *A* and inhibitor *I* may diffuse at different rates in *x* and *y* directions
- Cell is "on" if activator + bias exceeds inhibitor

$$\frac{\partial A}{\partial t} = d_{\mathrm{Ax}} \frac{\partial^2 A}{\partial x^2} + d_{\mathrm{Ay}} \frac{\partial^2 A}{\partial y^2} + k_{\mathrm{A}} \sigma(A + B - I) A$$

$$\frac{\partial I}{\partial t} = d_{\mathrm{Ix}} \frac{\partial^2 I}{\partial x^2} + d_{\mathrm{Iy}} \frac{\partial^2 I}{\partial y^2} + k_{\mathrm{I}} \sigma(A + B - I) I$$

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

Demonstration of NetLogo Program for Activation/Inhibition Pattern Formation

Run Pattern.nlogo

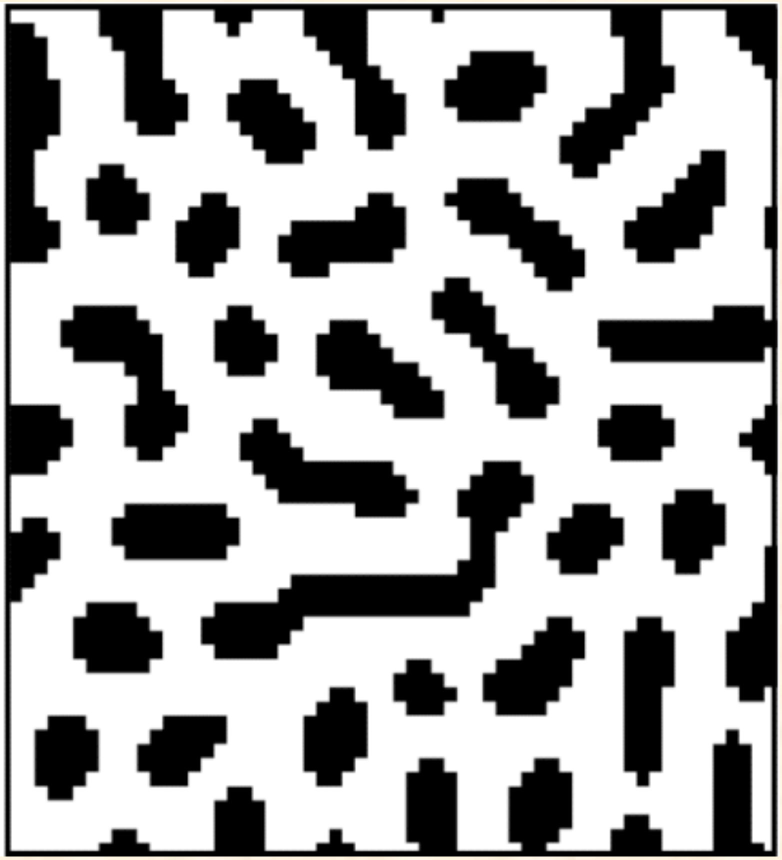
Turing Patterns

- 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*

Abstract Activation/Inhibition Spaces

- Consider two axes of cultural preference
  - E.g. hair length & interpersonal distance
  - Fictitious example!
- Suppose there are no objective reasons for preferences
- Suppose people approve/encourage those with similar preferences
- Suppose people disapprove/discourage those with different preferences
- What is the result?

Emergent Regions of Acceptable Variation



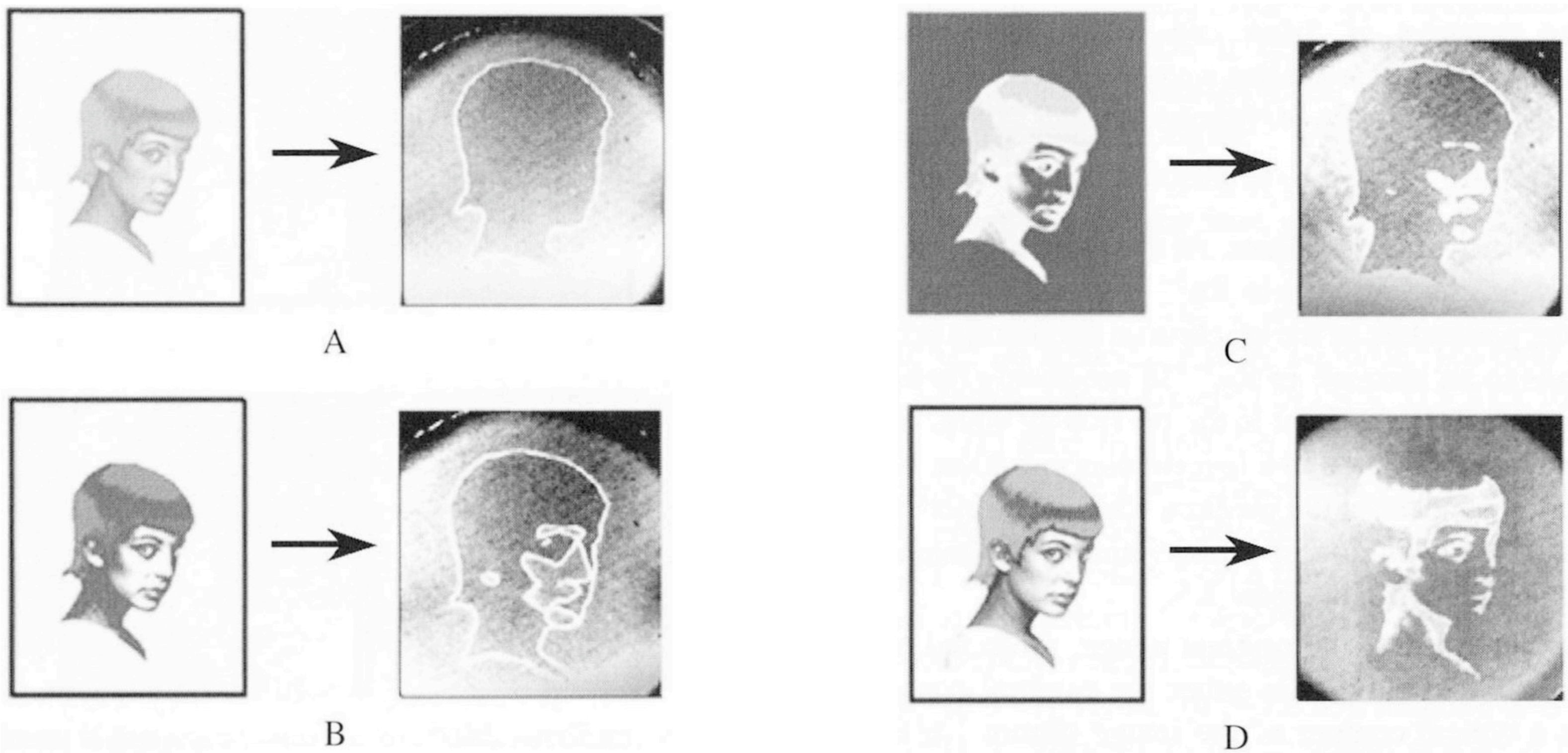
A Key Element of Self-Organization

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

Reaction-Diffusion Computing

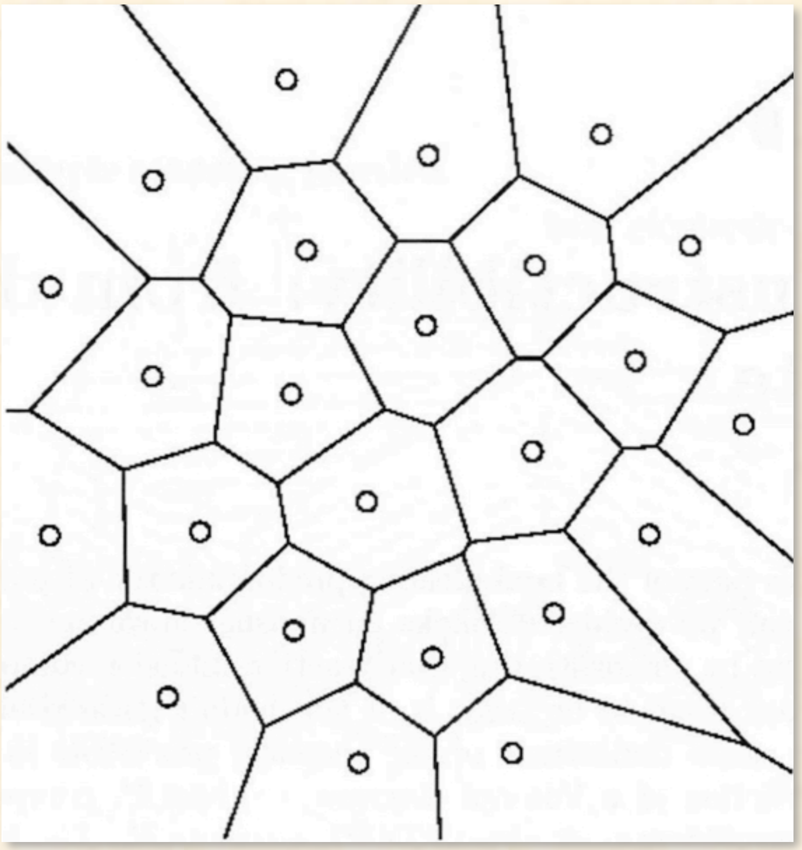
- Has been used for image processing
  - diffusion ⇒ noise filtering
  - reaction ⇒ contrast enhancement
- Depending on parameters, RD computing can:
  - restore broken contours
  - detect edges
  - improve contrast

Image Processing in BZ Medium



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

Voronoi Diagrams



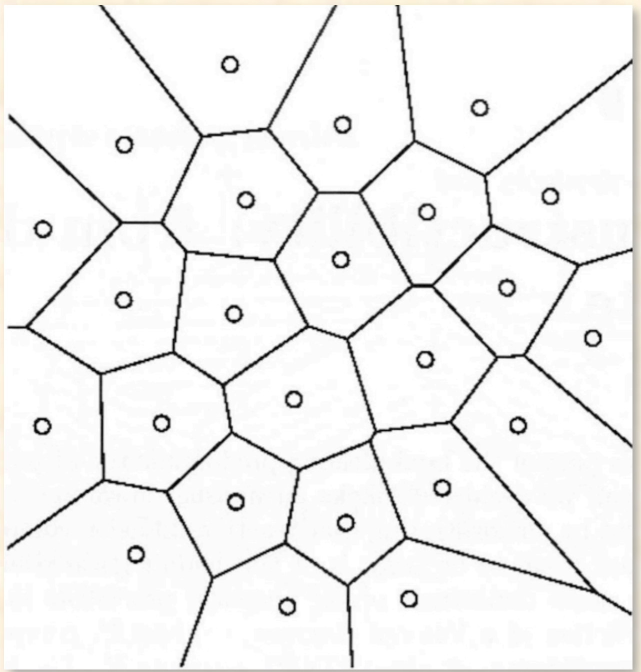
- Given a set of generating points:
- Construct polygon around each gen. point of set, so all points in poly. are closer to its generating point than to any other generating points.

Image < Adamatzky & al., *Reaction-Diffusion Computers*

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

Computation of Voronoi Diagram by Reaction-Diffusion Processor



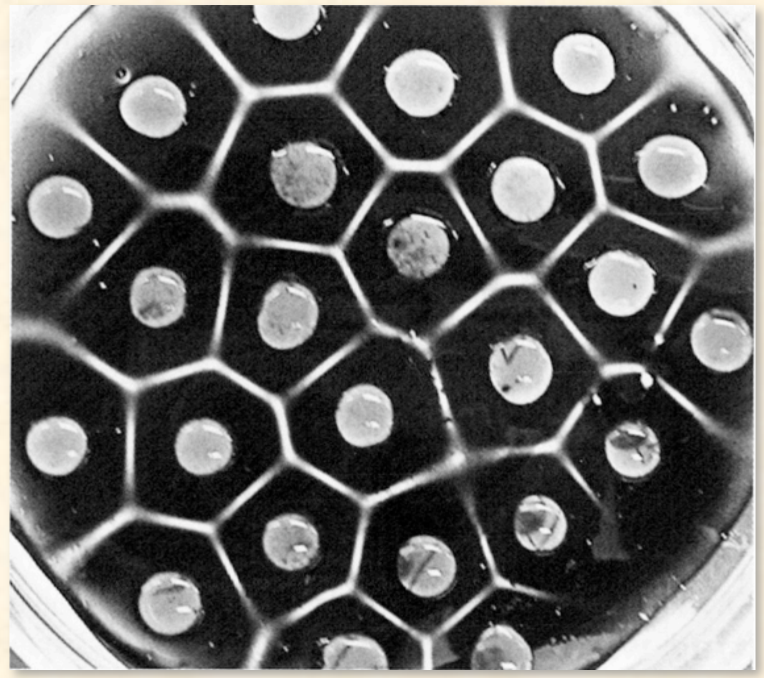


Image < Adamatzky & al., *Reaction-Diffusion Computers*

Mixed Cell Voronoi Diagram

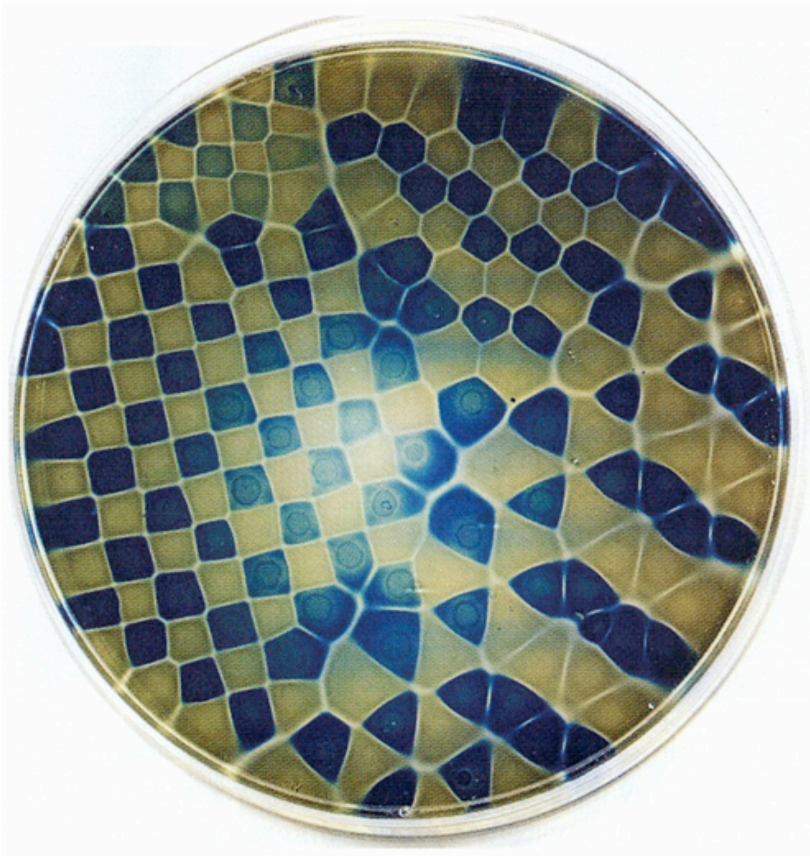


Image < Adamatzky & al., *Reaction-Diffusion Computers*

Path Planning via BZ medium: No Obstacles

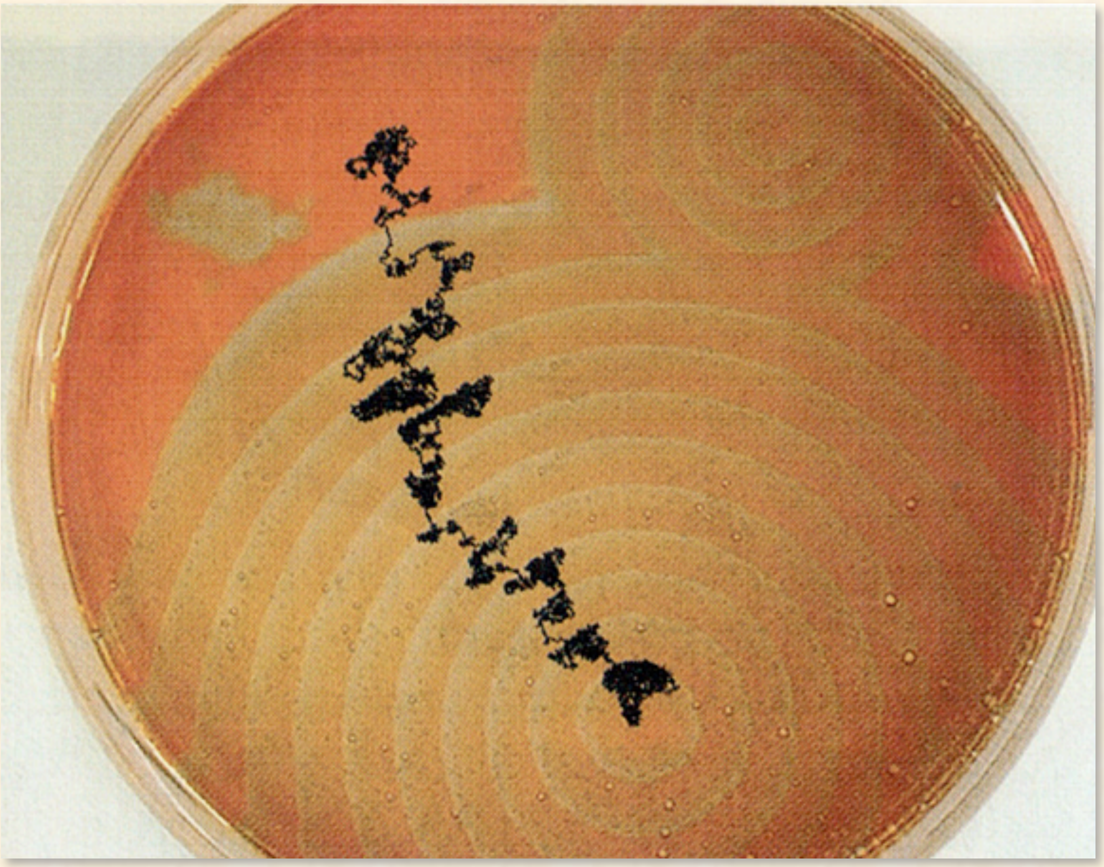


Image < Adamatzky & al., *Reaction-Diffusion Computers*

Path Planning via BZ medium: Circular Obstacles

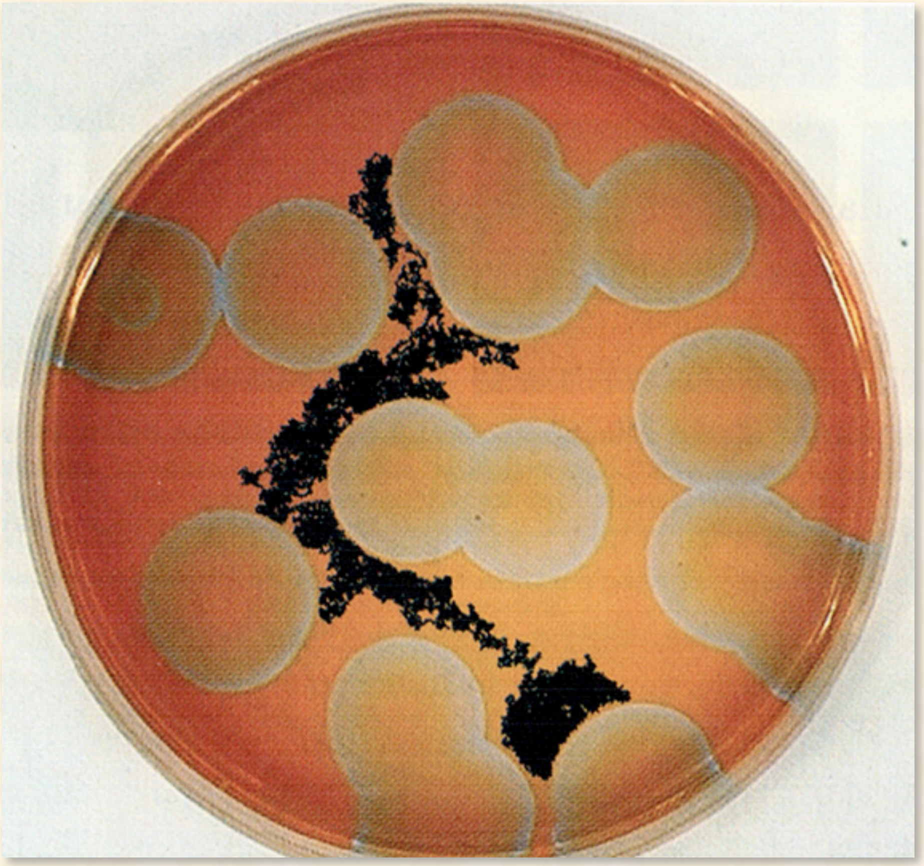


Image < Adamatzky & al., *Reaction-Diffusion Computers*

Mobile Robot with Onboard Chemical Reactor

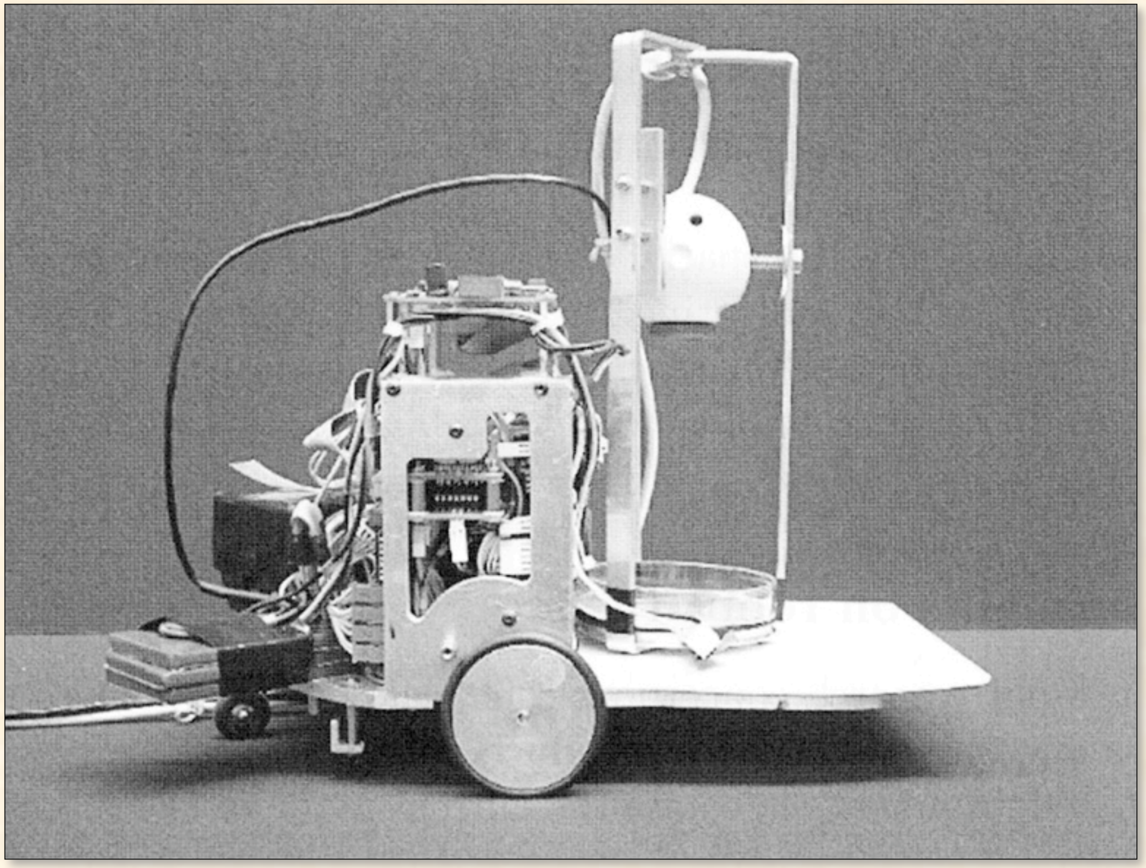


Image < Adamatzky & al., *Reaction-Diffusion Computers*

Actual Path: Pd Processor

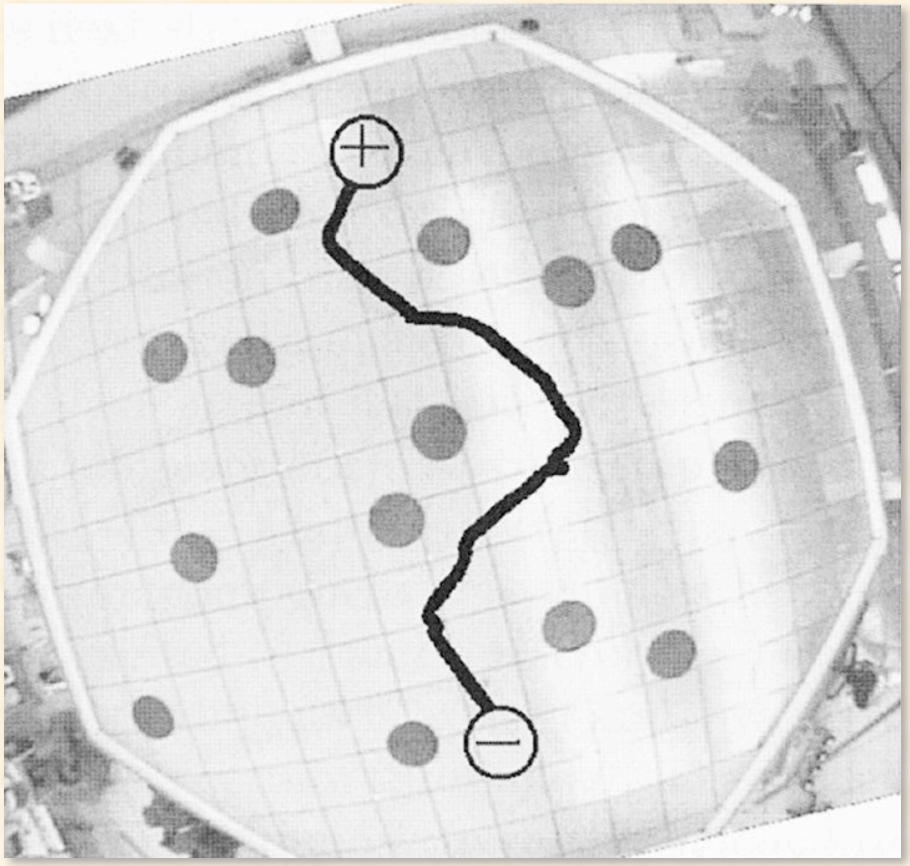


Image < Adamatzky & al., *Reaction-Diffusion Computers*

Actual Path: Pd Processor

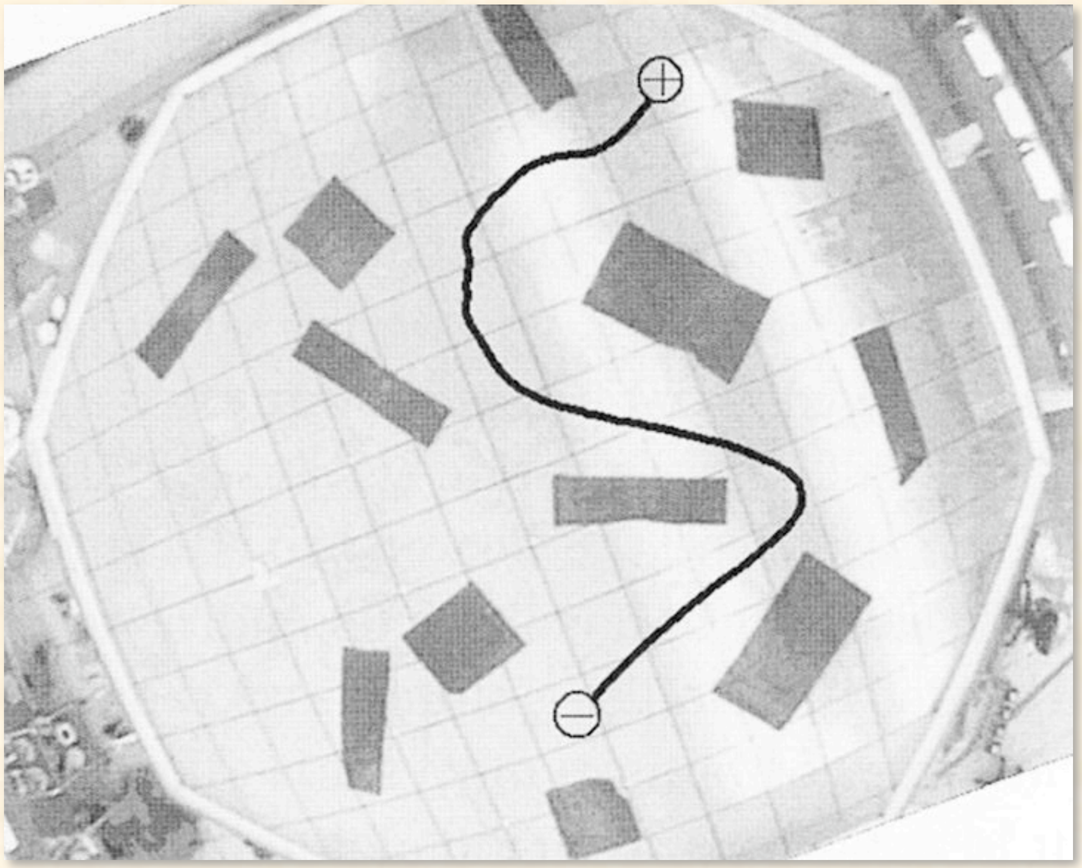


Image < Adamatzky & al., *Reaction-Diffusion Computers*

Actual Path: BZ Processor

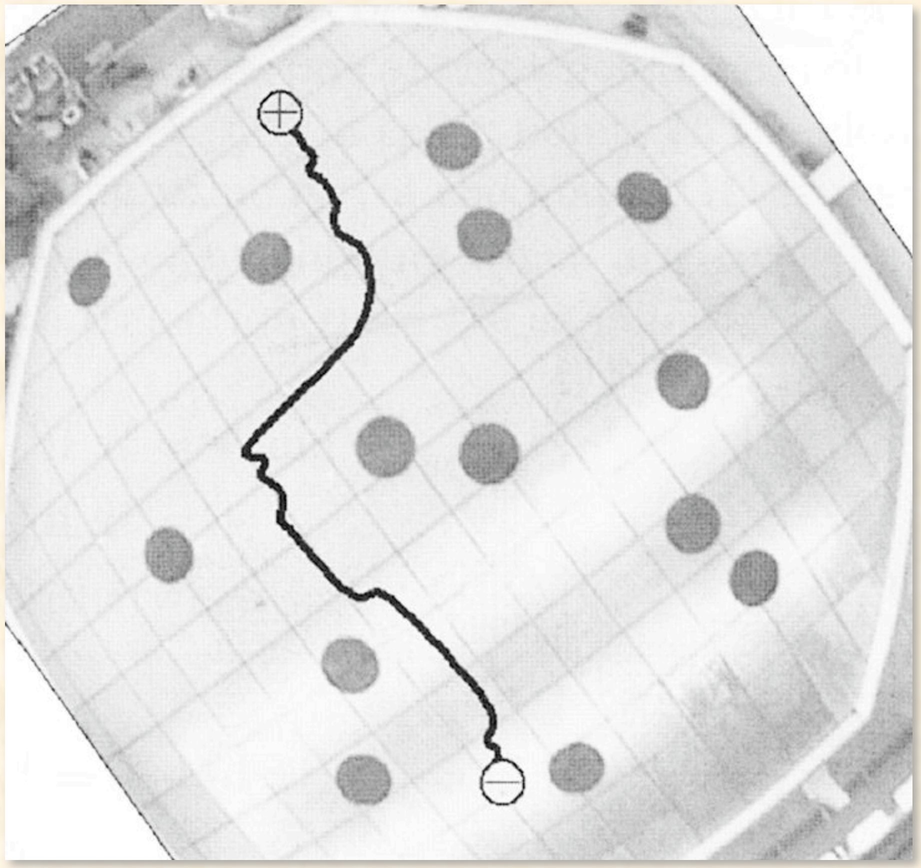


Image < Adamatzky & al., *Reaction-Diffusion Computers*

Bibliography for Reaction-Diffusion Computing

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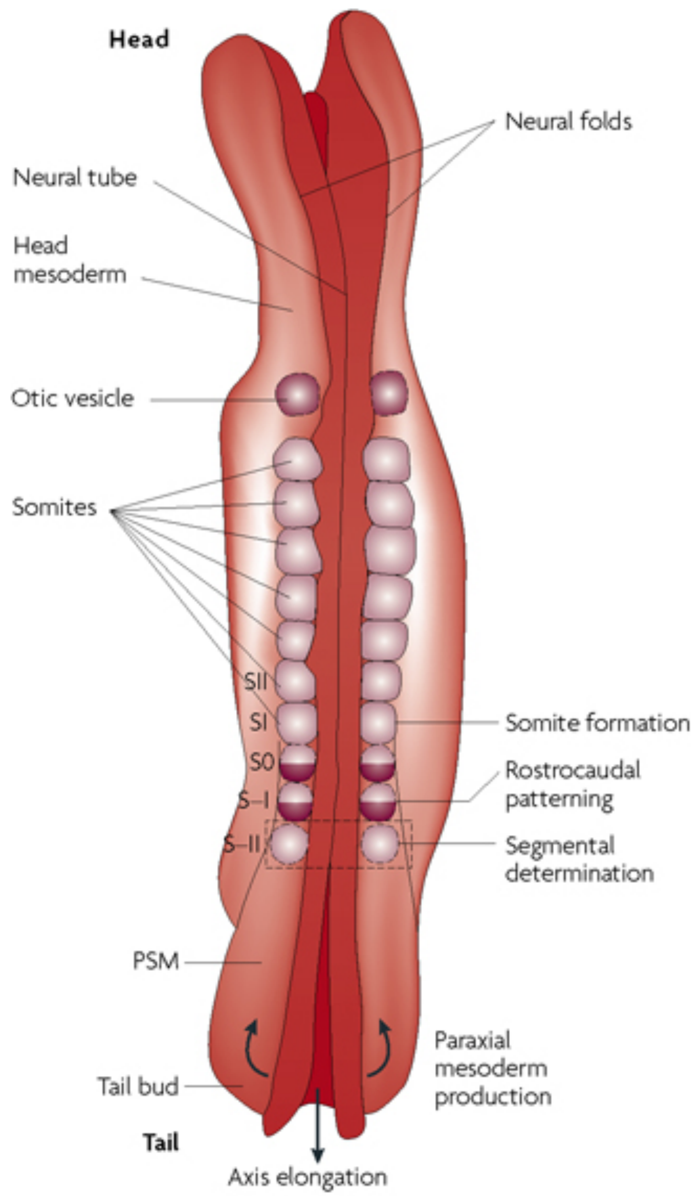
2. Adamatzky, Adam, De Lacy Costello, Ben, & Asai, Tetsuya. *Reaction Diffusion Computers*. Amsterdam: Elsevier, 2005.

Segmentation

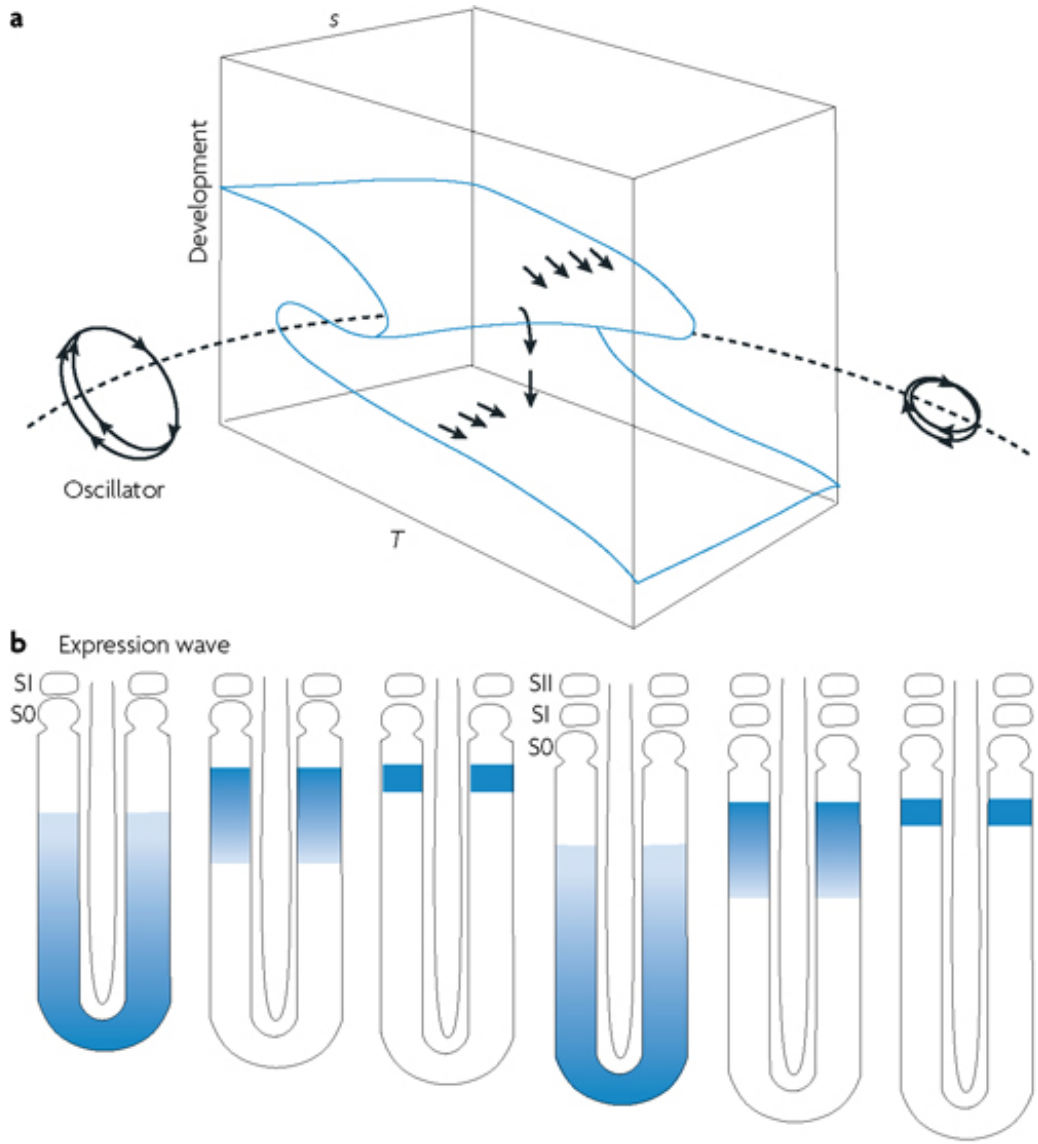
(in embryological development)

Vertebrae

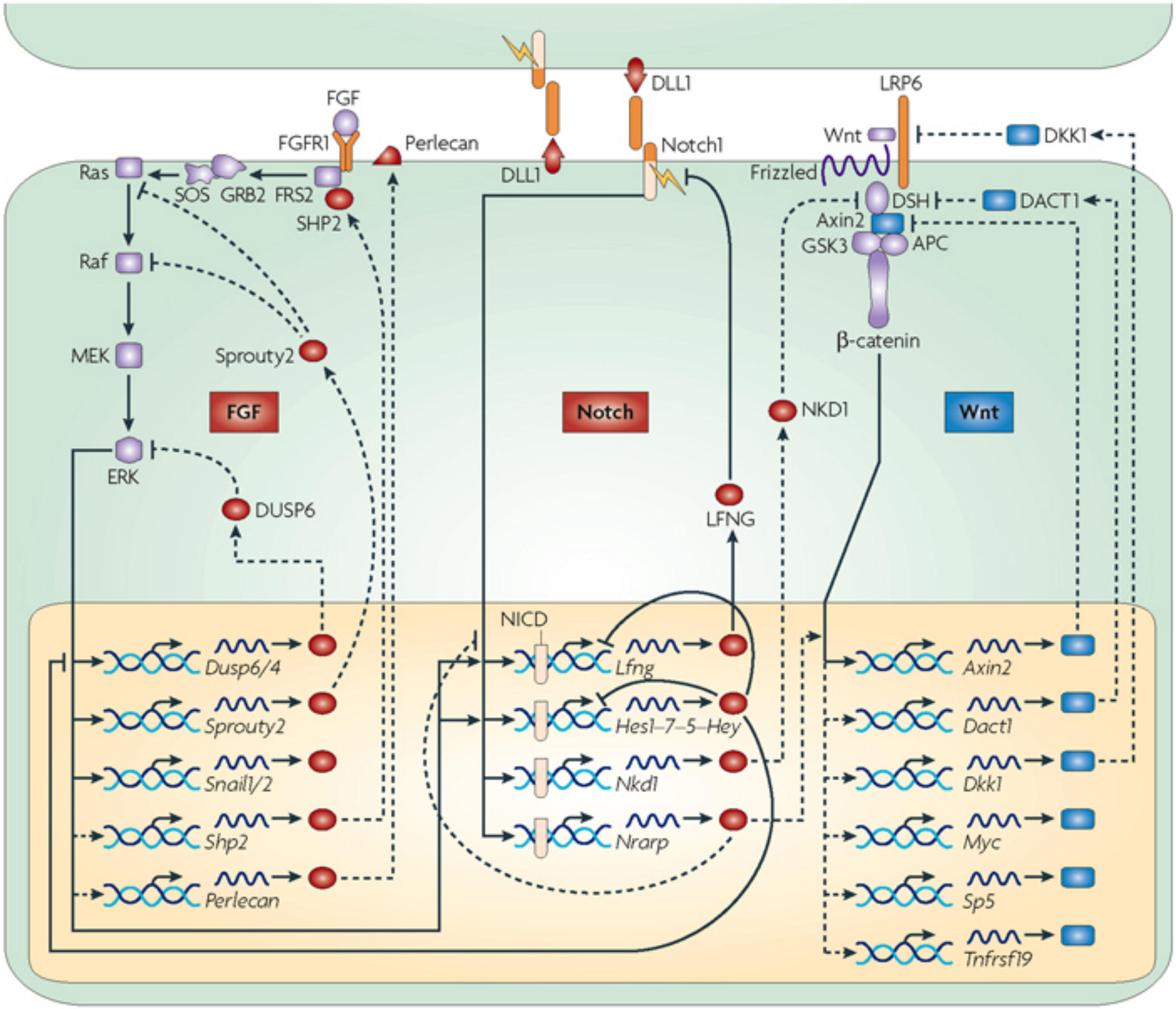
- Humans: 33, chickens: 55, mice: 65, corn snake: 315
- Characteristic of species
- How does an embryo "count" them?
- "Clock and wavefront model" of Cooke & Zeeman (1976).

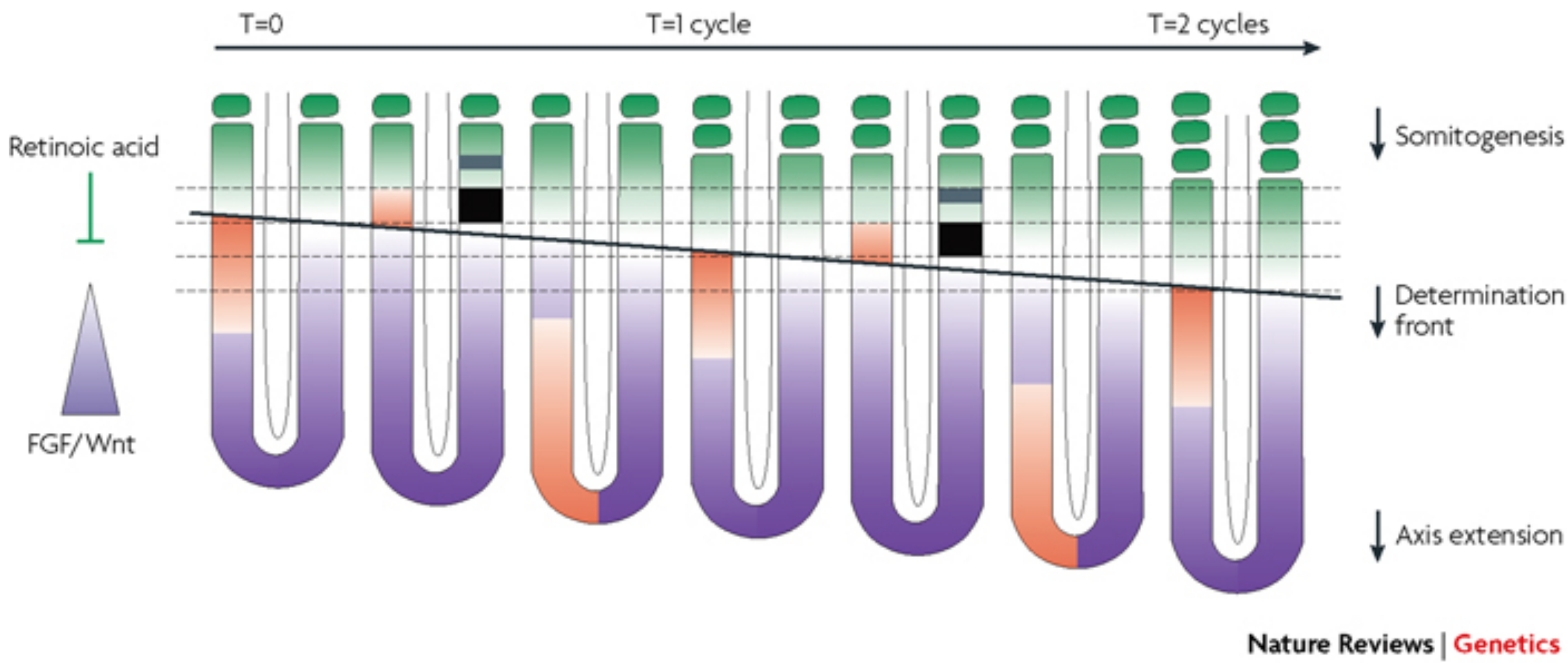


Nature Reviews | Genetics

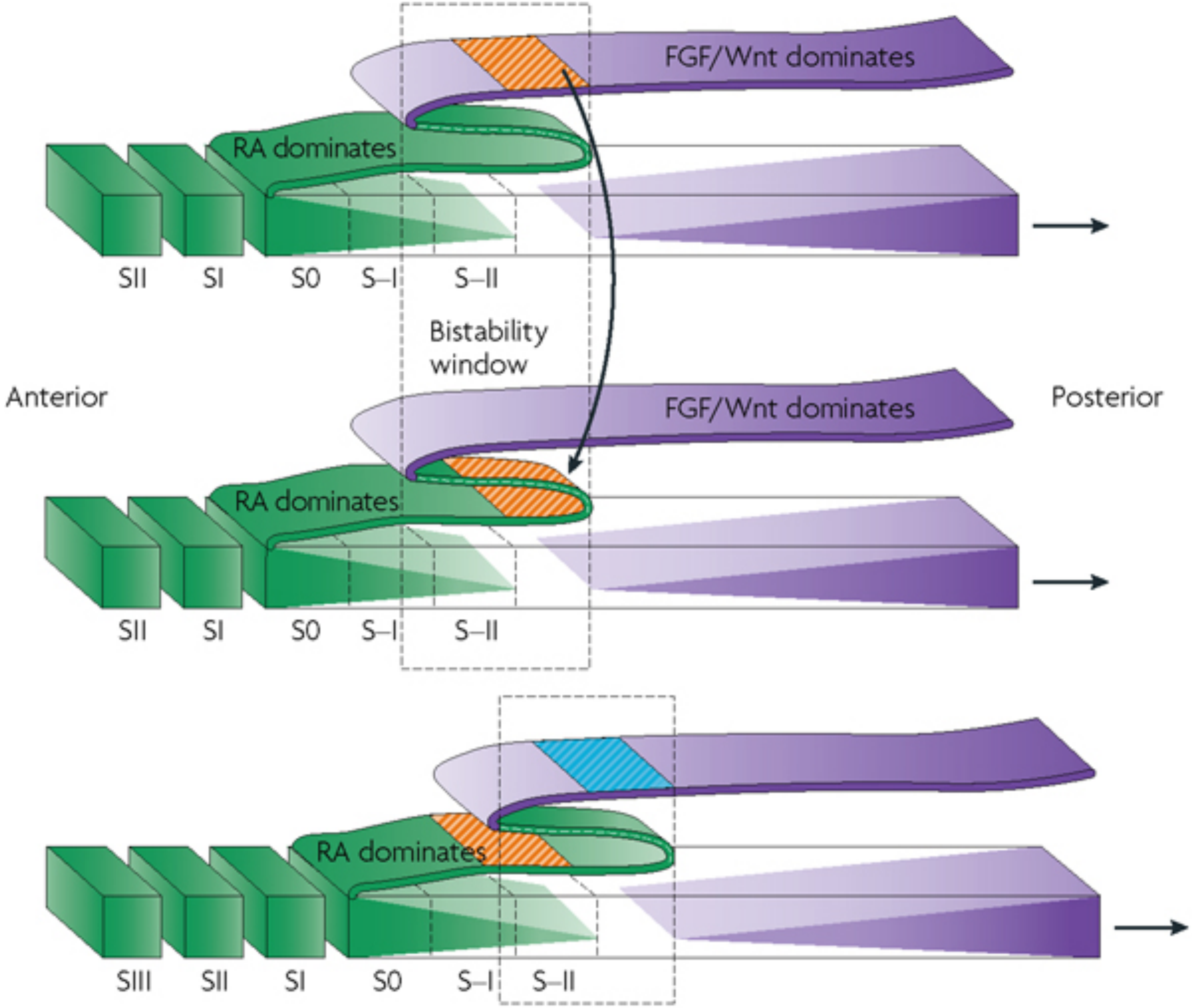


Nature Reviews | Genetics


FGF
FGFR1
Perlecan
DLL1
DLL1
Notch1
LRP6
Wnt
DKK1
Frizzled
Ras
SOS
GRB2
FRS2
SHP2
DSH
DACT1
Axin2
GSK3
APC
Raf
β-catenin
MEK
Sprouty2
FGF
Notch
NKD1
Wnt
ERK
DUSP6
LFNG
NICD
Dusp6/4
Sprouty2
Snail1/2
Shp2
Perlecan
Lfng
Hes1–7–5–Hey
Nkd1
Nrarp
Axin2
Dact1
Dkk1
Myc
Sp5
Tnfrsf19



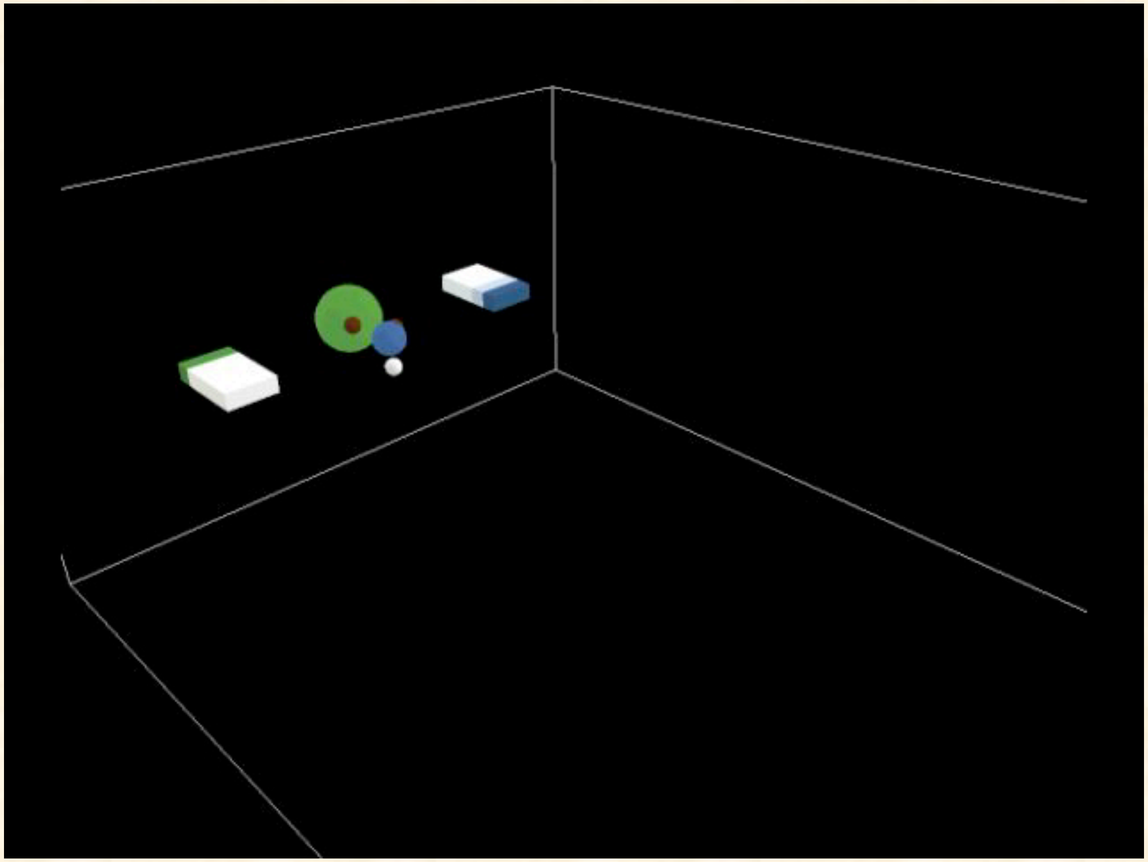
T=0
T=1 cycle
T=2 cycles
Retinoic acid
FGF/Wnt
Somitogenesis
Determination front
Axis extension
Nature Reviews | Genetics


FGF/Wnt dominates
RA dominates
SII
SI
S0
S–I
S–II
Bistability window
Anterior
FGF/Wnt dominates
Posterior
RA dominates
SII
SI
S0
S–I
S–II
RA dominates
SIII
SII
SI
S0
S–I
S–II

NetLogo Simulation of Segmentation

Run Segmentation.nlogo

Simulated Segmentation by Clock-and-Wavefront Process



Run Segmentation-cells-3D.nlogo

2D Simulation of Clock-and-Wavefront Process

Run Segmentation-cells.nlogo

Effect of Growth Rate

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.
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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.

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3. Tyson, J. J., & Keener, J. P. "Singular Perturbation Theory of Traveling Waves in Excitable Media (A Review)," *Physica D* **32** (1988): 327-61.
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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"