Lecture 8

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

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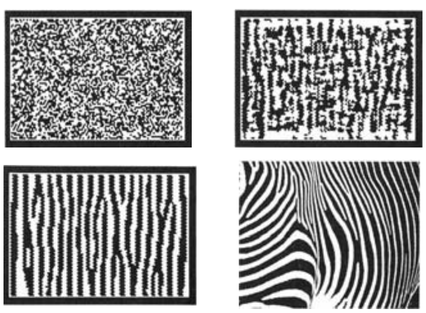
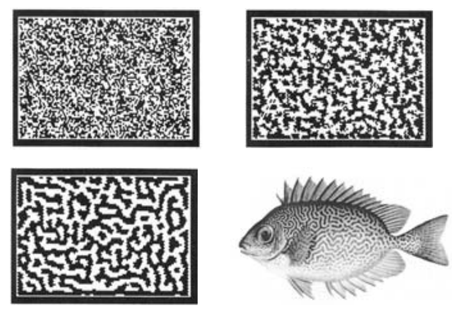
Zebra



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

Vermiculated Rabbit Fish

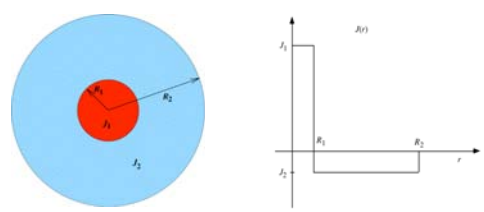


 figs. from Camazine & al.: *Self-Org. Biol. Sys.*

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:

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

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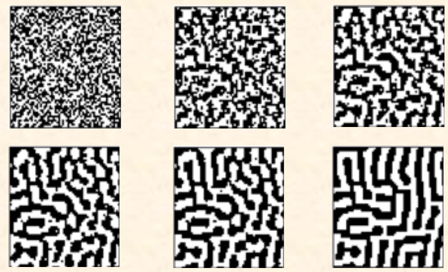
Example

(R_1=1, R_2=6, J_1=1, J_2=–0.1, h=0)



figs. from Bar-Yam

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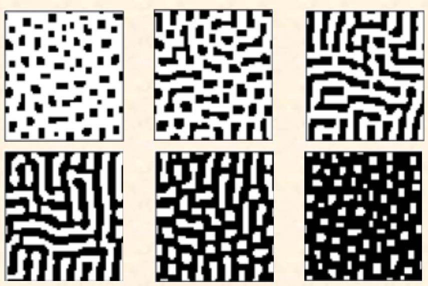
Effect of Bias

(h = –6, –3, –1; 1, 3, 6)



figs. from Bar-Yam

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Effect of Interaction Ranges

figs. from Bar-Yam

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

[Run Fur.nlogo]

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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)

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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

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Reaction-Diffusion System

diffusion

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

reaction

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

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

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Example: Activation-Inhibition System

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

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

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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

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Demonstration of NetLogo Program for Activation/Inhibition Pattern Formation

Run Pattern.nlogo

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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?

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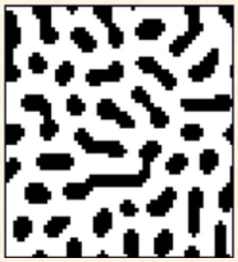
Emergent Regions of Acceptable Variation



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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

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Simple Example: Reaction-Diffusion System

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- Many natural patterns can be explained by reaction-diffusion equations
- $\partial \mathbf{c} / \partial t = D\nabla^2 \mathbf{c} + \mathbf{F}(\mathbf{c})$
- where **c** is a vector of concentrations, and D is a diagonal matrix of diffusion rates, and **F** is a nonlinear vector function

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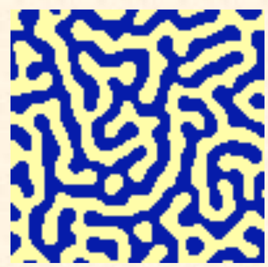
Equal X & Y Rates, No Bias



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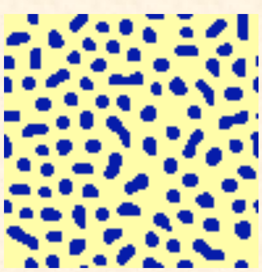
Equal X & Y Rates, Positive Bias



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Inhibitor Y Rate >> X Rate

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Example: Double Activation-Inhibition System

- Two independently diffusing activation-inhibition pairs
- May have different diffusion rates in X and Y directions
  - In this example, $I_{1y} >> I_{1x}$ and $I_{2x} >> I_{2y}$
- Colors in simulation:
  - green = system 1 active
  - red = system 2 active
  - yellow = both active
  - black = neither active

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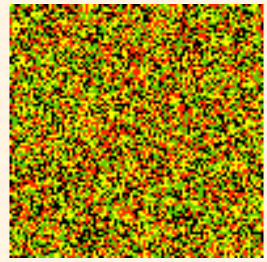
Random Initial State



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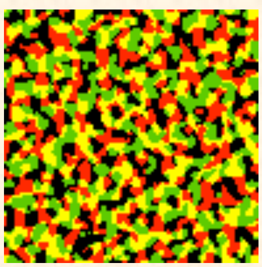
$T = 1$



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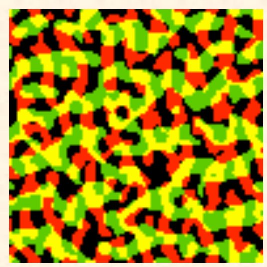
$T = 2$



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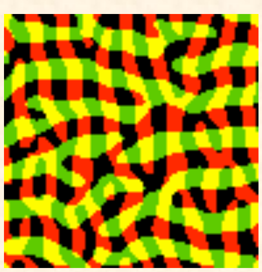
$T = 10$



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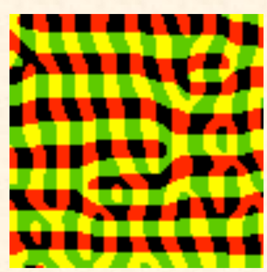
Stable Pattern ($T = 209$)



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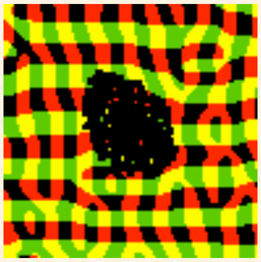
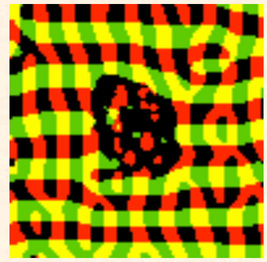
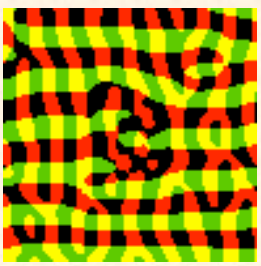
Damaged Pattern



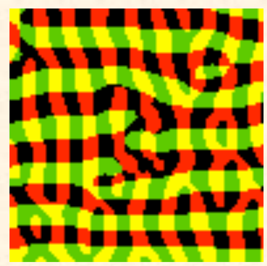
T = damage + 1



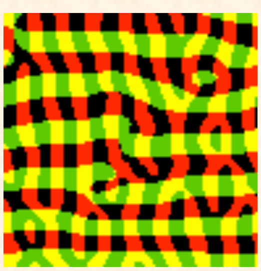
T = damage + 2



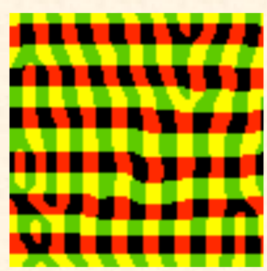
T = damage + 3



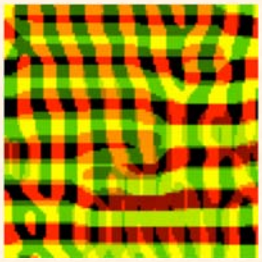
T = damage + 4



Stable (T = damage + 168)



Comparison to Original



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Example of Reorganization

- Exchange inhibitor diffusion rates for systems 1 & 2
- Vertical stripes (red) become horizontal
- Horizontal stripes (green) become vertical

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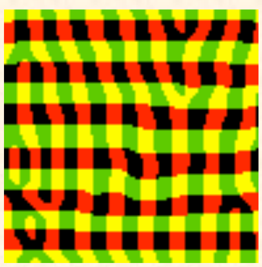
Stable Pattern Before Parameters Changed



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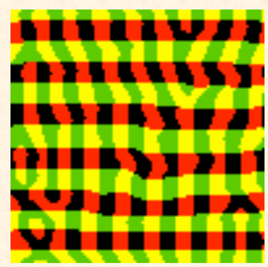
T = change + 1



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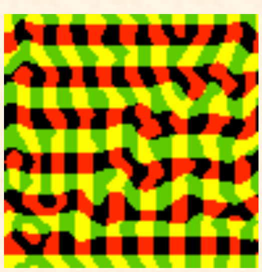
T = change + 2



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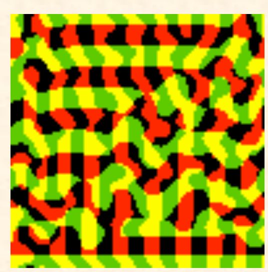
T = change + 3



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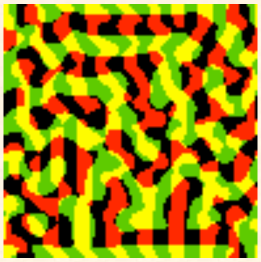
T = change + 4



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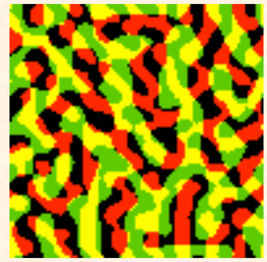
T = change + 6



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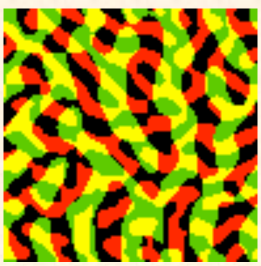
T = change + 9



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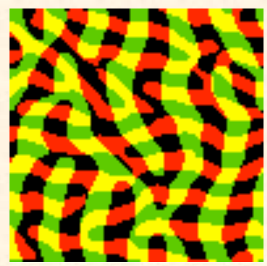
T = change + 18



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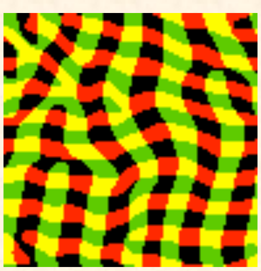
T = change + 34



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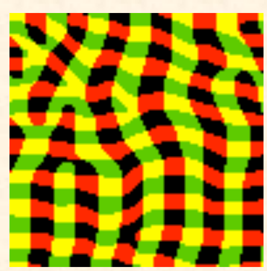
Stable (T = change + 85)



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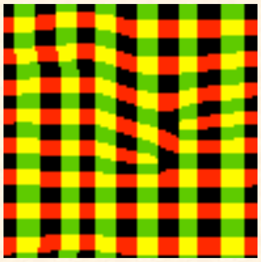
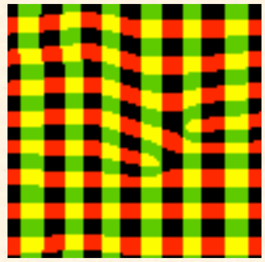
Introduction of Annealing Noise



Stability After Noise Eliminated



Additional Bibliography

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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.
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