

D. Excitable Media

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Examples of Excitable Media

- Slime mold amoebas
- Cardiac tissue (& other muscle tissue)
- Cortical tissue
- Certain chemical systems (e.g., BZ reaction)
- Hodgepodge machine

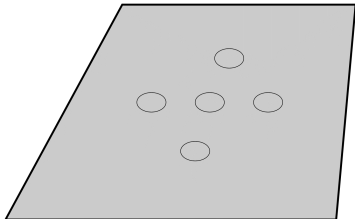
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Characteristics of Excitable Media

- Local spread of excitation
 - for signal propagation
- Refractory period
 - for unidirectional propagation
- Decay of signal
 - avoid saturation of medium

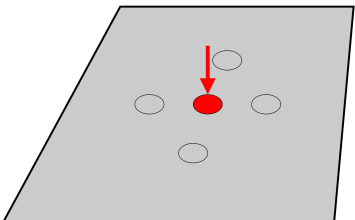
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Behavior of Excitable Media



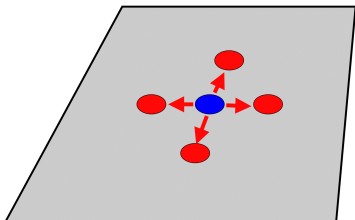
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Stimulation

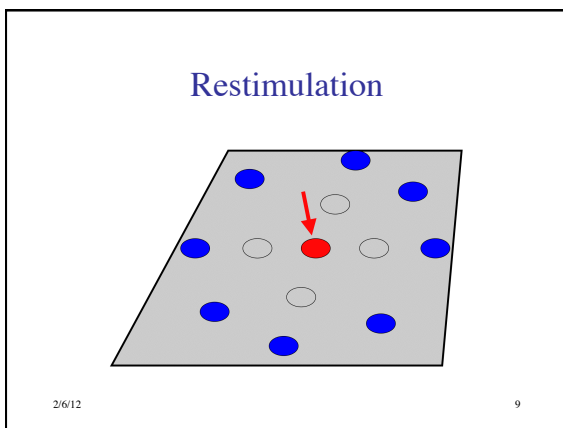
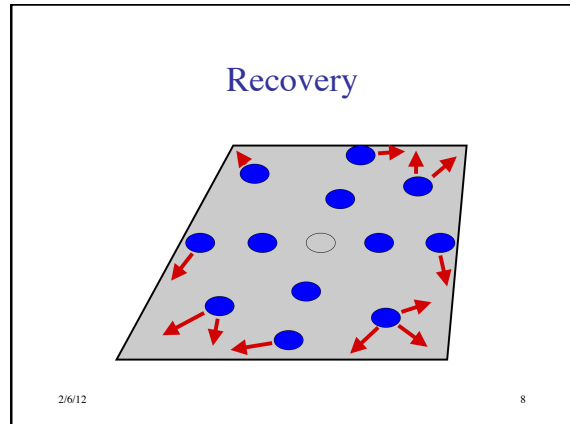
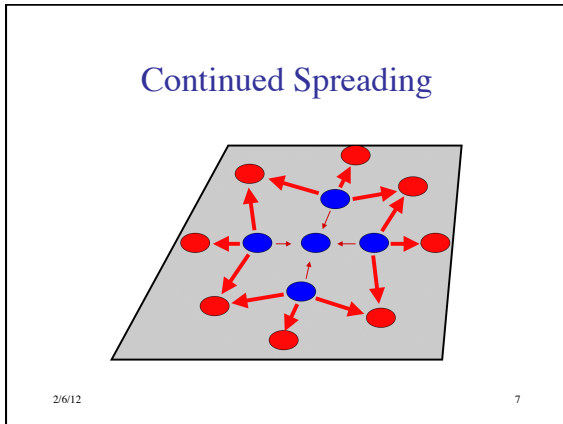


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Relay (Spreading Excitation)



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- ### Circular & Spiral Waves Observed in:
- Slime mold aggregation
 - Chemical systems (e.g., BZ reaction)
 - Neural tissue
 - Retina of the eye
 - Heart muscle
 - Intracellular calcium flows
 - Mitochondrial activity in oocytes
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- ### Cause of Concentric Circular Waves
- Excitability is not enough
 - But at certain developmental stages, cells can operate as pacemakers
 - When stimulated by cAMP, they begin emitting regular pulses of cAMP
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- ### Spiral Waves
- Persistence & propagation of spiral waves explained analytically (Tyson & Murray, 1989)
 - Rotate around a small core of non-excitable cells
 - Propagate at higher frequency than circular
 - Therefore they dominate circular in collisions
 - But how do the spirals form initially?
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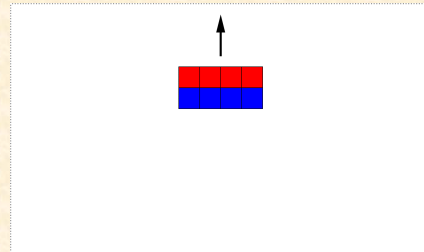
Some Explanations of Spiral Formation

- “the origin of spiral waves remains obscure” (1997)
- Traveling wave meets obstacle and is broken
- Desynchronization of cells in their developmental path
- Random pulse behind advancing wave front

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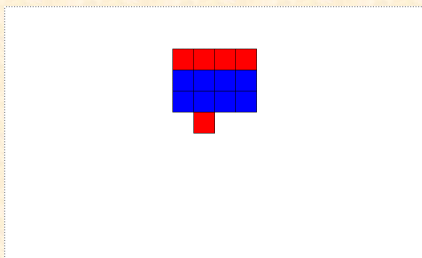
Step 0: Passing Wave Front



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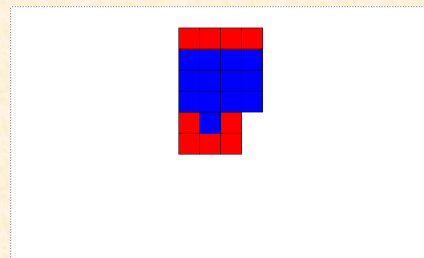
Step 1: Random Excitation



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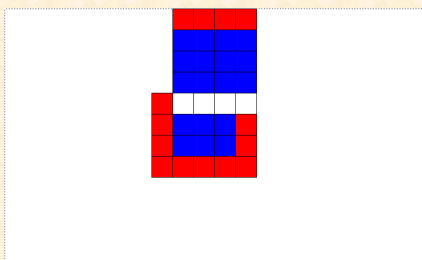
Step 2: Beginning of Spiral



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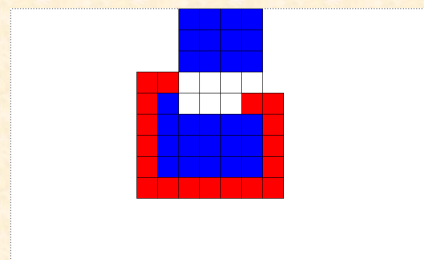
Step 3



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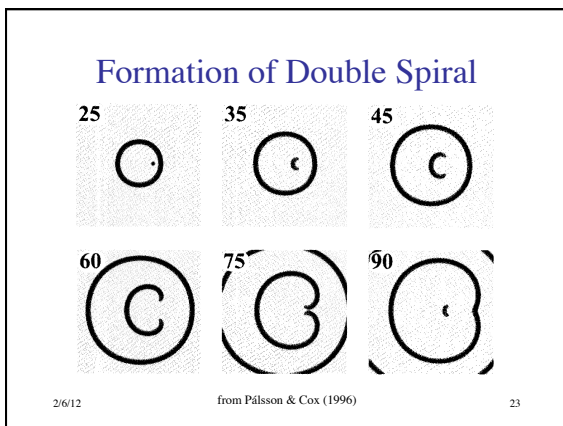
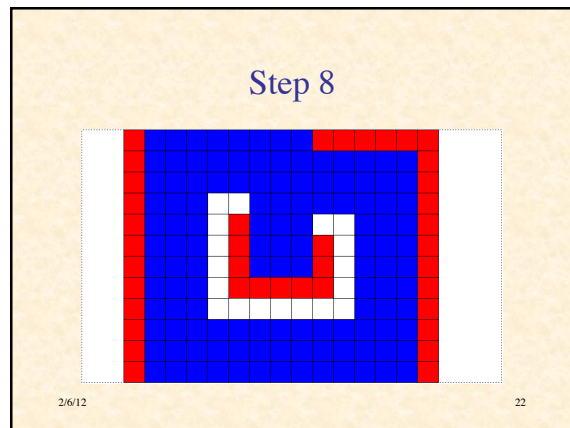
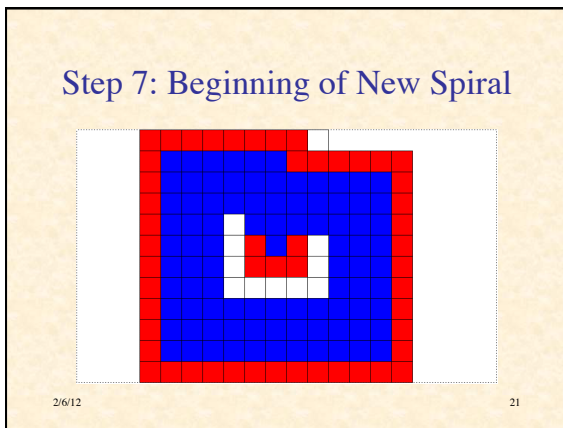
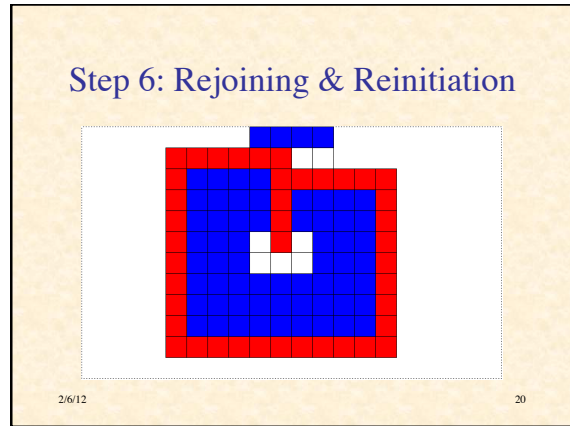
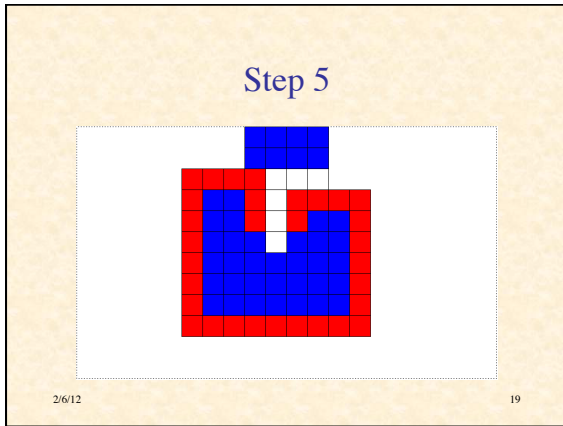
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Step 4



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**NetLogo Simulation
Of Spiral Formation**

- Amoebas are immobile at timescale of wave movement
- A fraction of patches are inert (grey)
- A fraction of patches has initial concentration of cAMP
- At each time step:
 - chemical diffuses
 - each patch responds to local concentration

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Response of Patch

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if patch is not refractory (brown) then
  if local chemical > threshold then
    set refractory period
    produce pulse of chemical (red)
  else
    decrement refractory period
    degrade chemical in local area
  
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Demonstration of NetLogo Simulation of Spiral Formation

[Run SlimeSpiral.nlogo](#)

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Observations

- Excitable media can support circular and spiral waves
- Spiral formation can be triggered in a variety of ways
- All seem to involve inhomogeneities (broken symmetries):
 - in space
 - in time
 - in activity
- Amplification of random fluctuations
- Circles & spirals are to be expected

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NetLogo Simulation of Streaming Aggregation

1. chemical diffuses
2. **if** cell is refractory (**yellow**)
3. **then** chemical degrades
4. **else** (it's excitable, colored white)
 1. **if** chemical > movement threshold **then**
take step up chemical gradient
 2. **else if** chemical > relay threshold **then**
produce more chemical (**red**)
become refractory
 3. **else** wait

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Demonstration of NetLogo Simulation of Streaming

[Run SlimeStream.nlogo](#)

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Typical Equations for Excitable Medium (ignoring diffusion)

- Excitation variable:

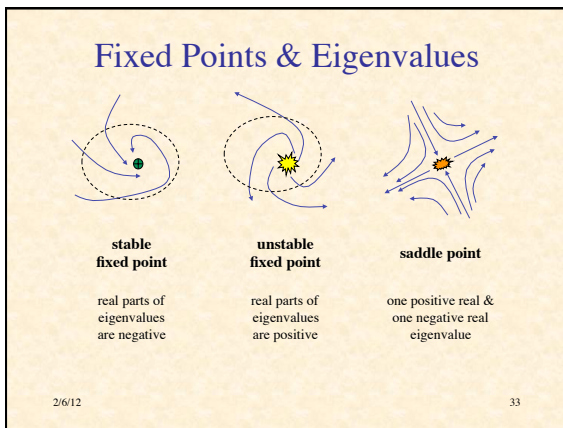
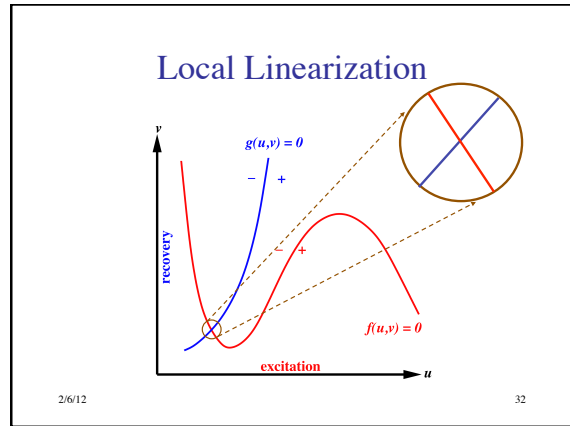
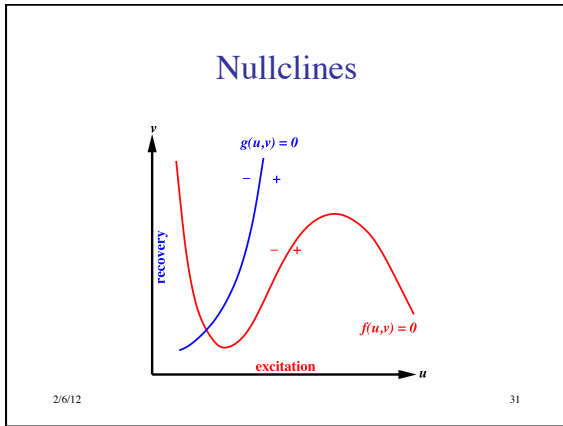
$$\dot{u} = f(u, v)$$

- Recovery variable:

$$\dot{v} = g(u, v)$$

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FitzHugh-Nagumo Model

- A simplified model of action potential generation in neurons
- The neuronal membrane is an excitable medium
- B is the input bias:

$$\dot{u} = u - \frac{u^3}{3} - v + B$$

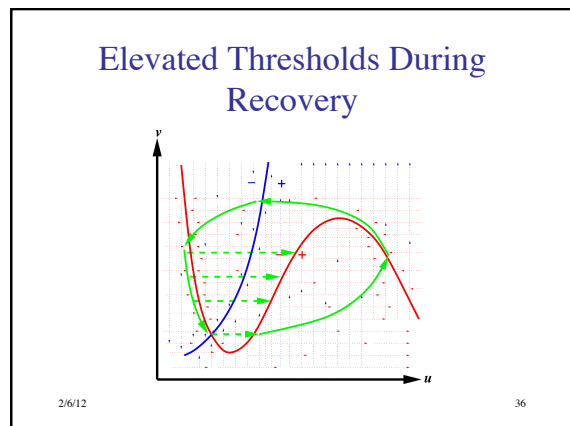
$$\dot{v} = \epsilon(b_0 + b_1 u - v)$$

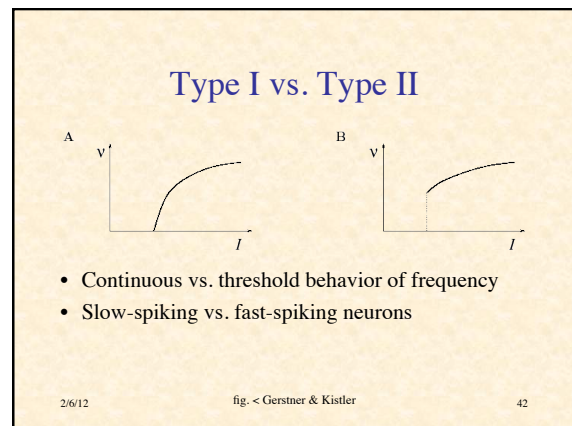
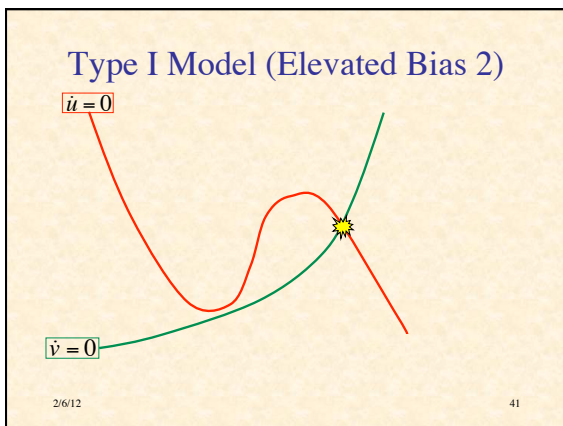
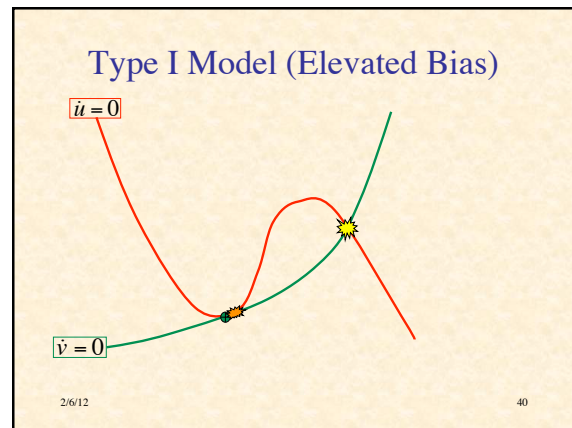
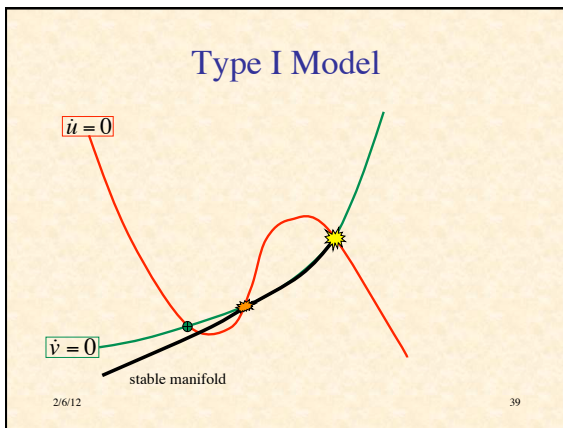
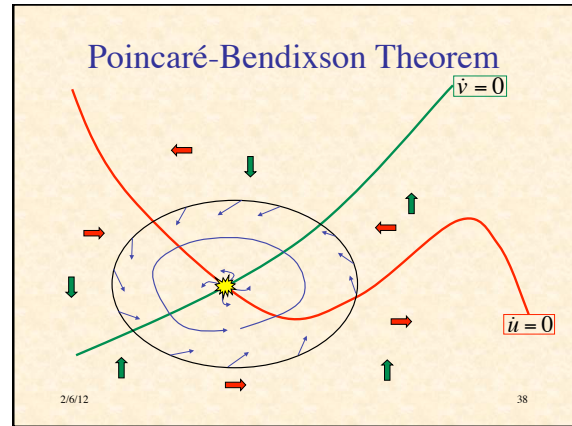
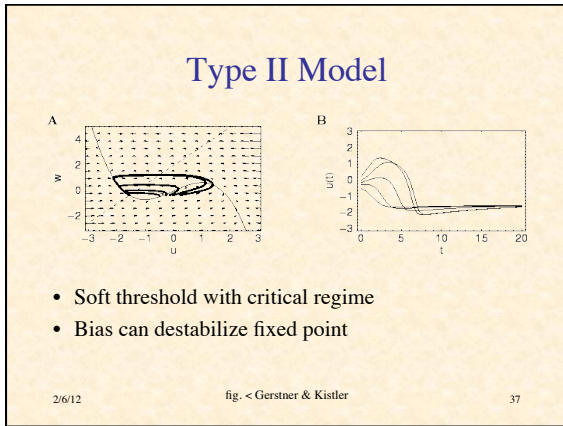
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NetLogo Simulation of Excitable Medium in 2D Phase Space

[\(EM-Phase-Plane.nlogo\)](#)

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Modified Martiel & Goldbeter Model for Dicty Signalling

Variables (functions of x, y, t):

- β = intracellular concentration of cAMP
- γ = extracellular concentration of cAMP
- ρ = fraction of receptors in active state



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Equations

$$\frac{d\beta(x,y,t)}{dt} = s\Phi(\rho, \gamma) - \beta k_i - \beta k_t \quad [1]$$

Rate of change in intracellular [cAMP] = Production of cAMP - Intracellular hydrolysis - Secretion of cAMP

$$\frac{d\gamma(x,y,t)}{dt} = \frac{k_r}{h}\beta - k_e\gamma + D\nabla^2\gamma \quad [2]$$

Rate of change in extracellular [cAMP] = Secretion of cAMP - Extracellular hydrolysis + Diffusion of cAMP

$$\frac{d\rho(x,y,t)}{dt} = f_2(\gamma)(1 - \rho) - f_1(\gamma)\rho \quad [3]$$

Rate of change in fraction of active receptor = Dephosphorylation of receptor - Phosphorylation of receptor

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Positive Feedback Loop

- Extracellular cAMP increases (γ increases)
- \Rightarrow Rate of synthesis of intracellular cAMP increases (Φ increases)
- \Rightarrow Intracellular cAMP increases (β increases)
- \Rightarrow Rate of secretion of cAMP increases
- (\Rightarrow Extracellular cAMP increases)

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Negative Feedback Loop

- Extracellular cAMP increases (γ increases)
- \Rightarrow cAMP receptors desensitize (f_1 increases, f_2 decreases, ρ decreases)
- \Rightarrow Rate of synthesis of intracellular cAMP decreases (Φ decreases)
- \Rightarrow Intracellular cAMP decreases (β decreases)
- \Rightarrow Rate of secretion of cAMP decreases
- \Rightarrow Extracellular cAMP decreases (γ decreases)

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Dynamics of Model

- Unperturbed \Rightarrow cAMP concentration reaches steady state
- Small perturbation in extracellular cAMP \Rightarrow returns to steady state
- Perturbation $>$ threshold \Rightarrow large transient in cAMP, then return to steady state
- Or oscillation (depending on model parameters)

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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.

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