

D.

Excitable Media

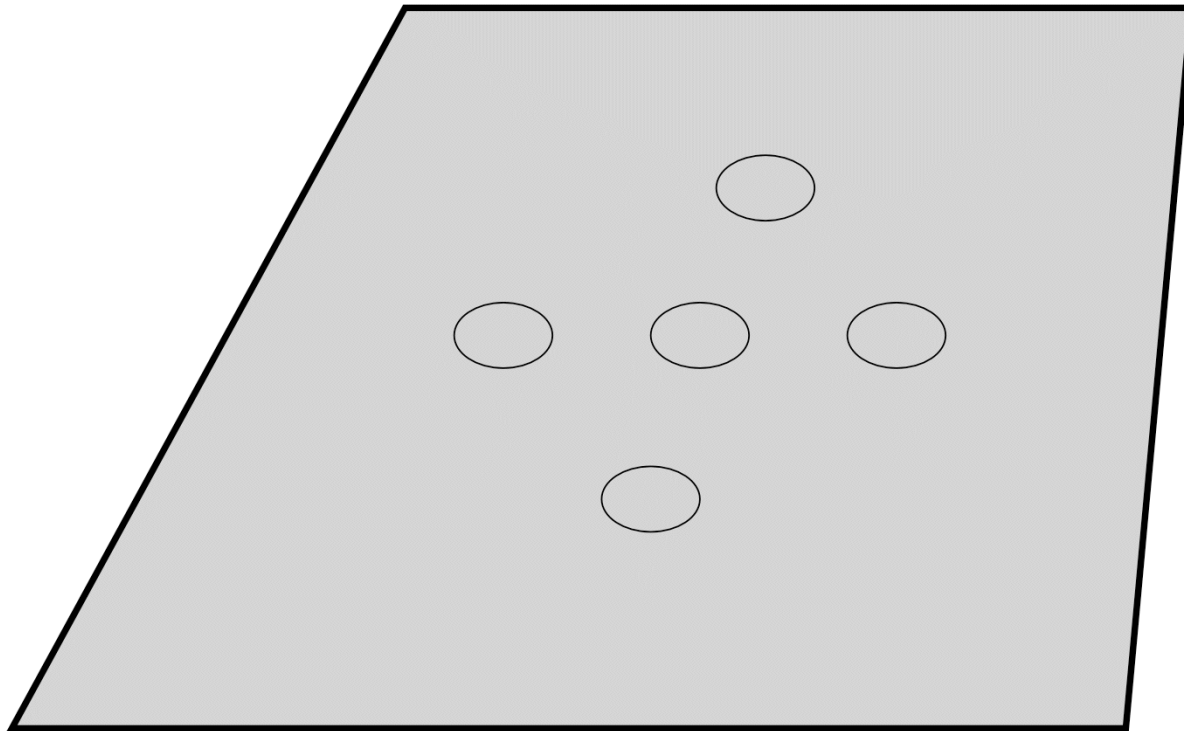
Examples of Excitable Media

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

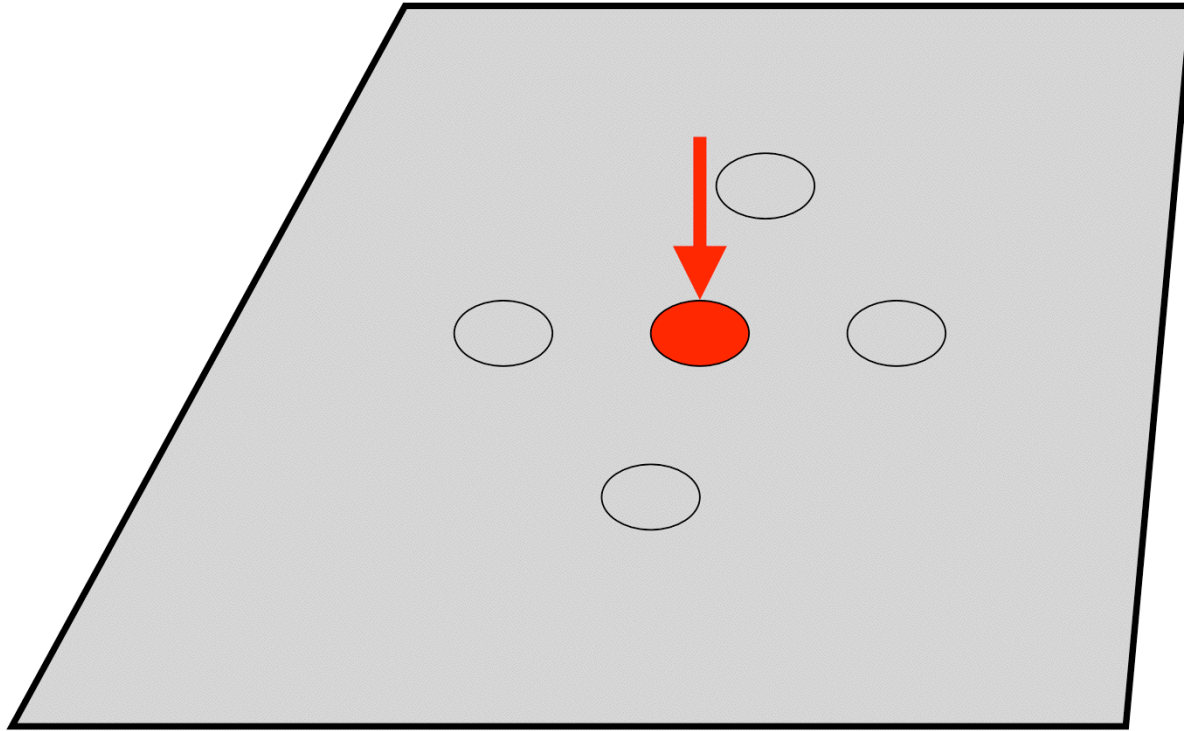
Characteristics of Excitable Media

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

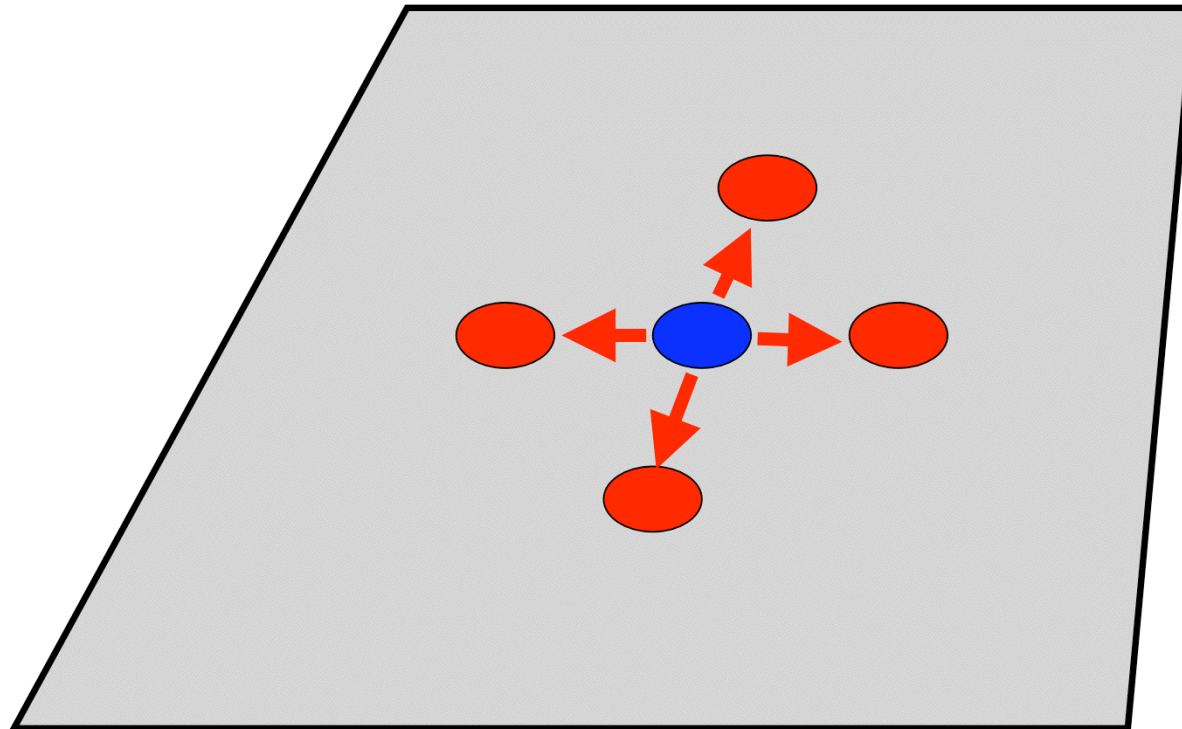
Behavior of Excitable Media



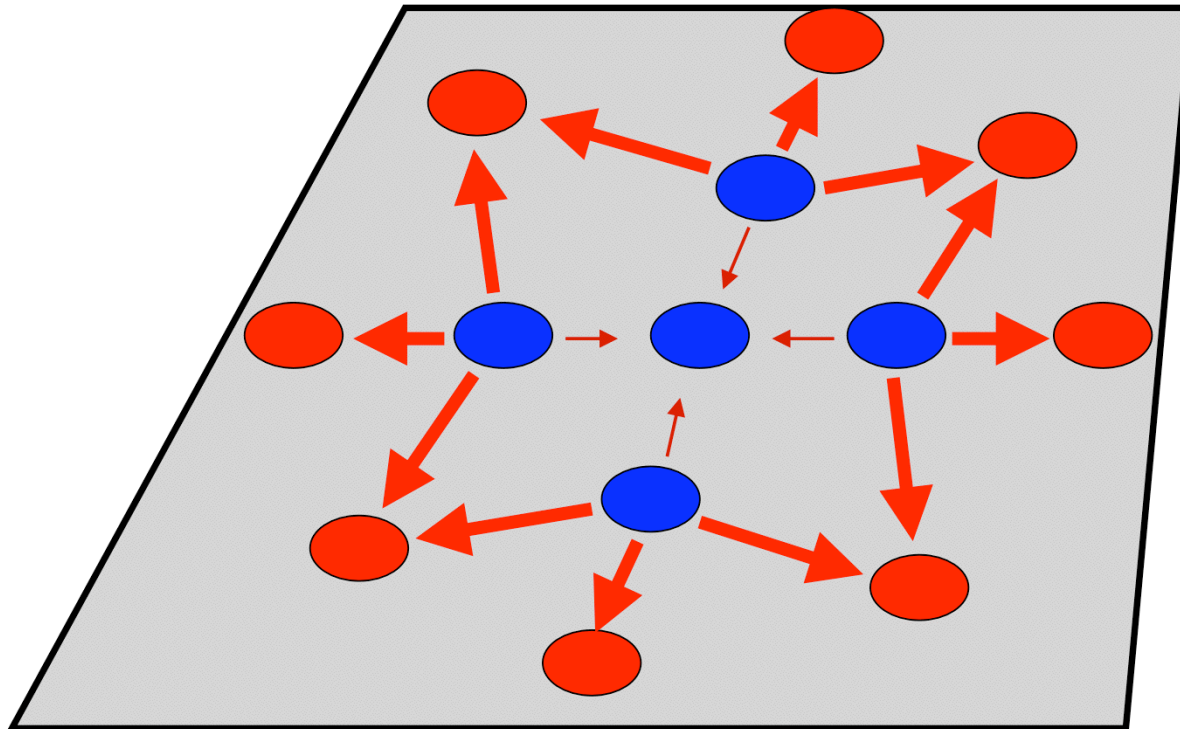
Stimulation



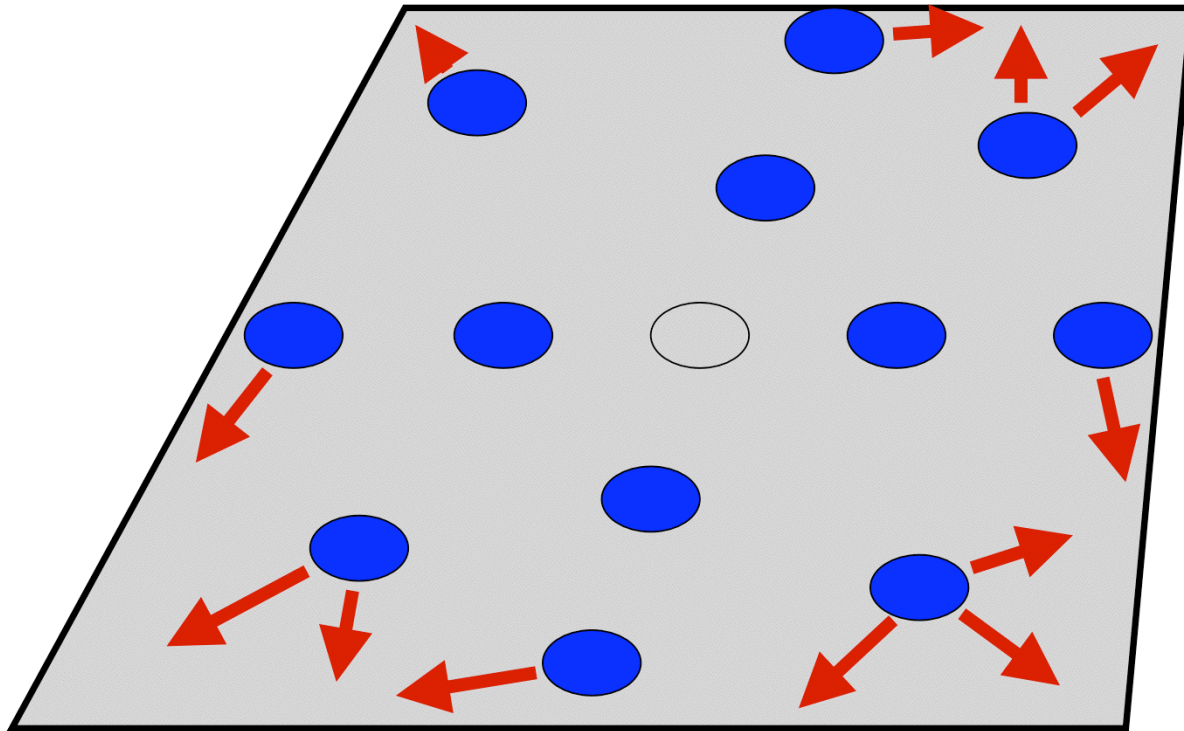
Relay (Spreading Excitation)



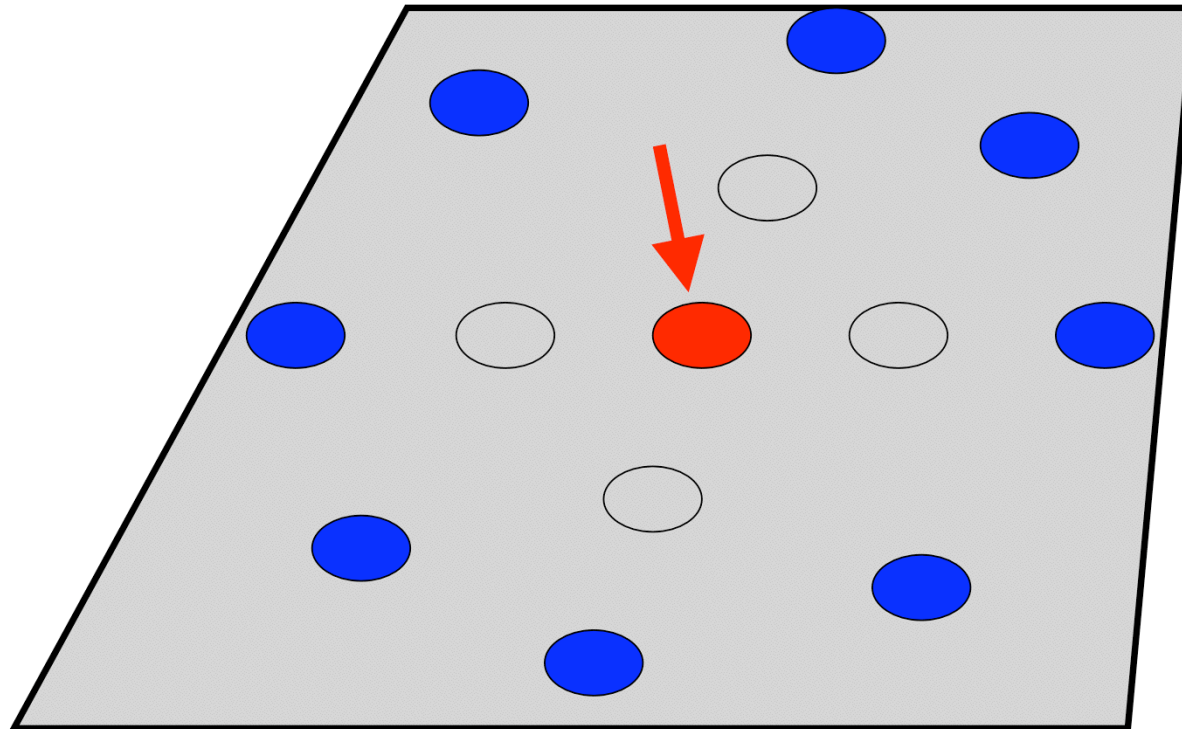
Continued Spreading



Recovery



Restimulation



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

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

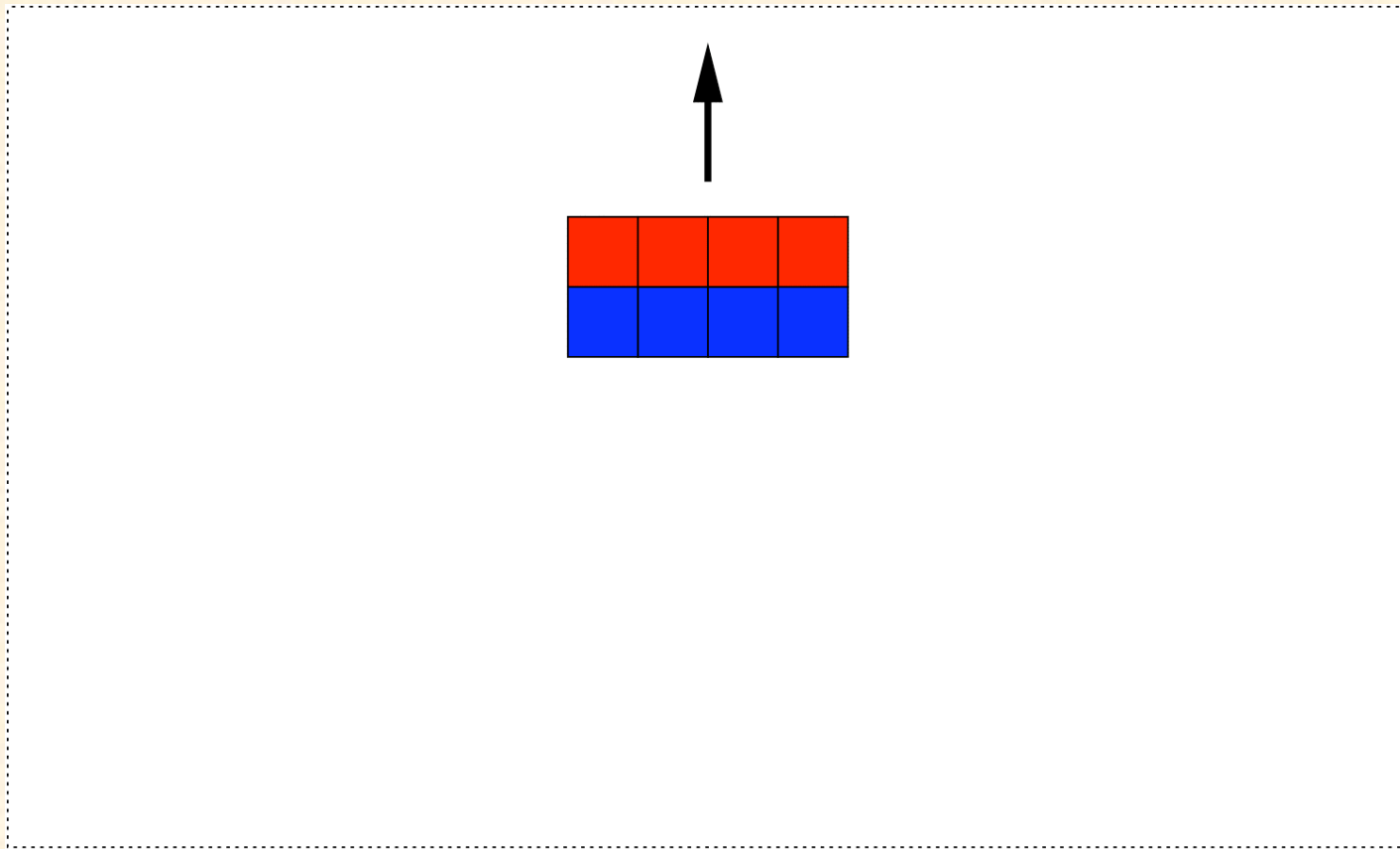
Spiral Waves

- 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?

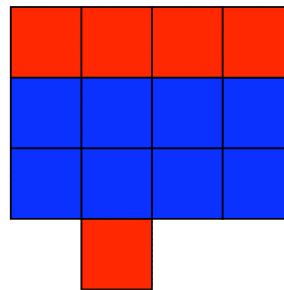
Some Explanations of Spiral Formation

- “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

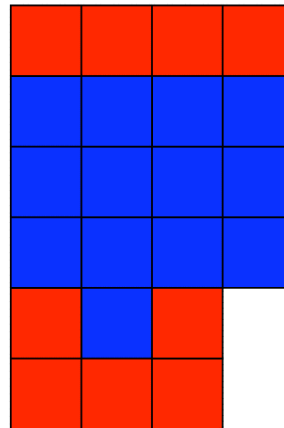
Step 0: Passing Wave Front



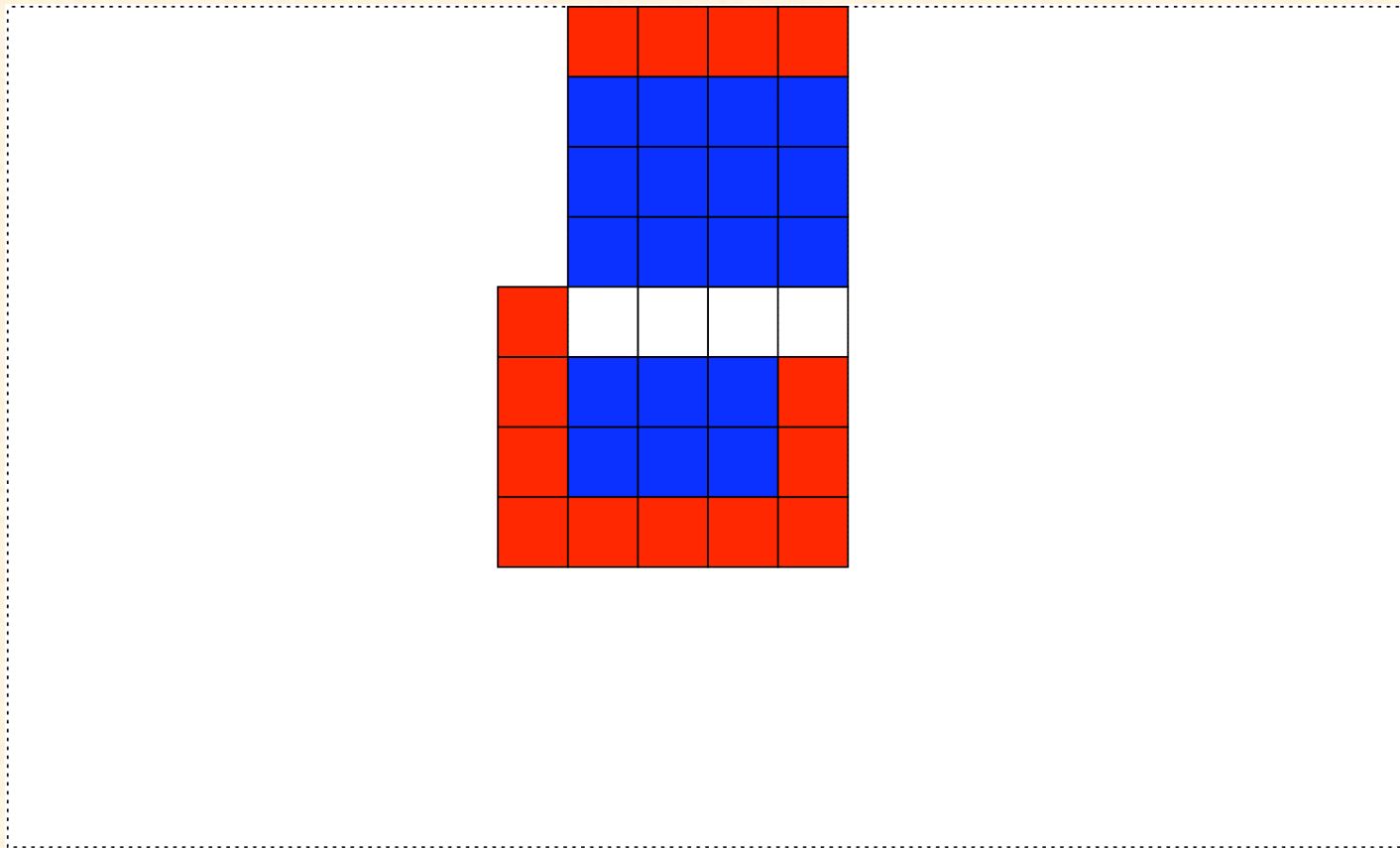
Step 1: Random Excitation



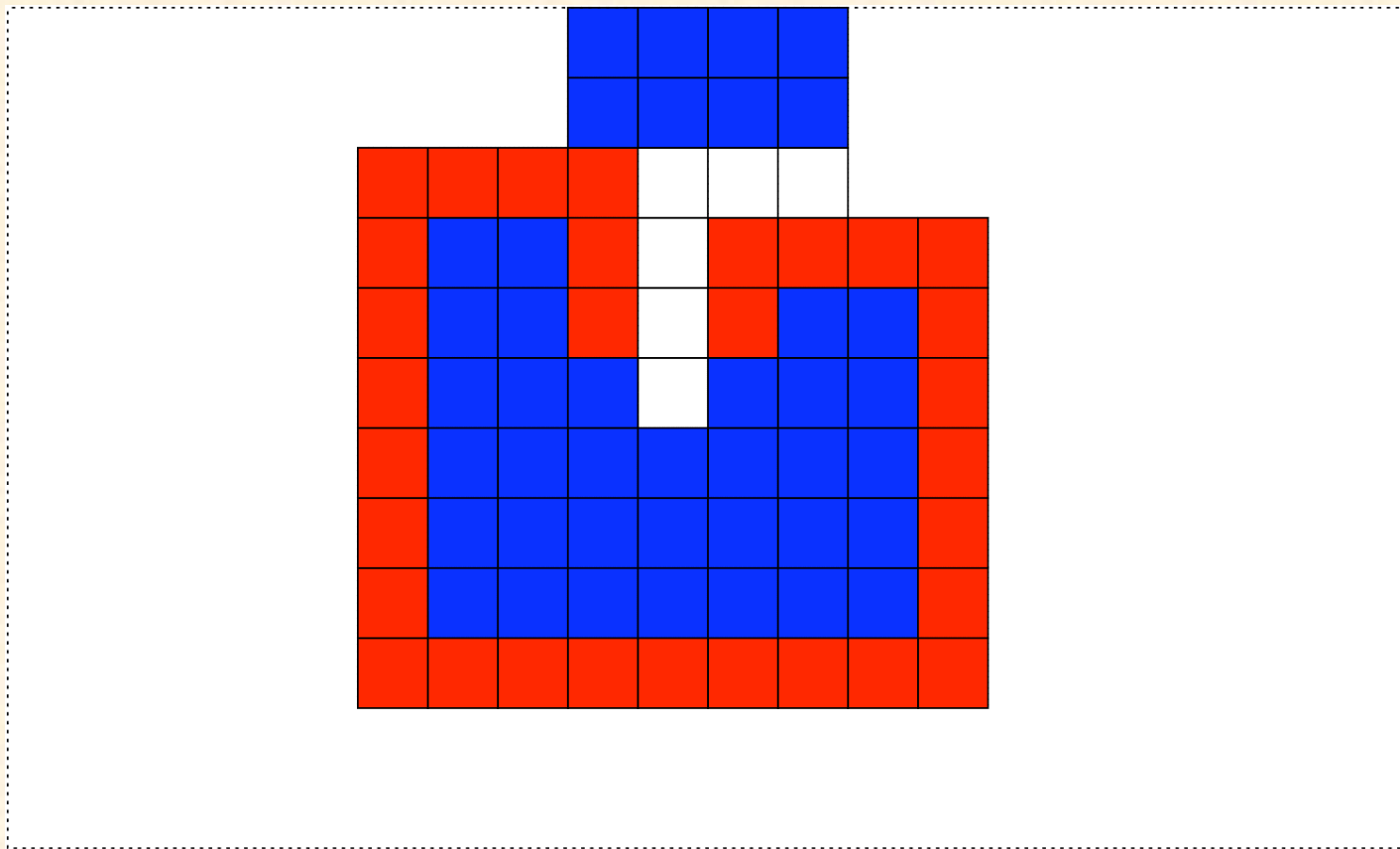
Step 2: Beginning of Spiral



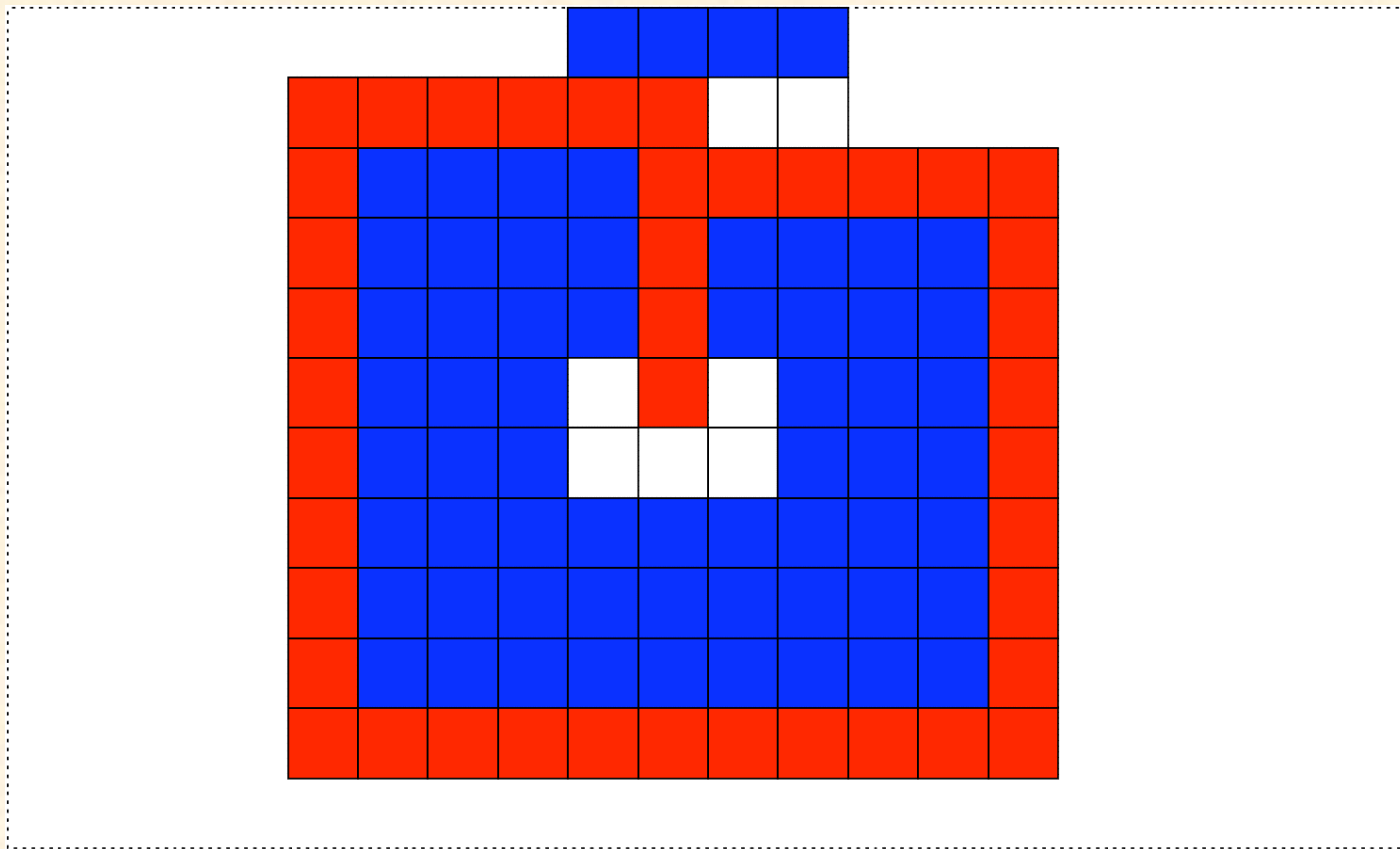
Step 3



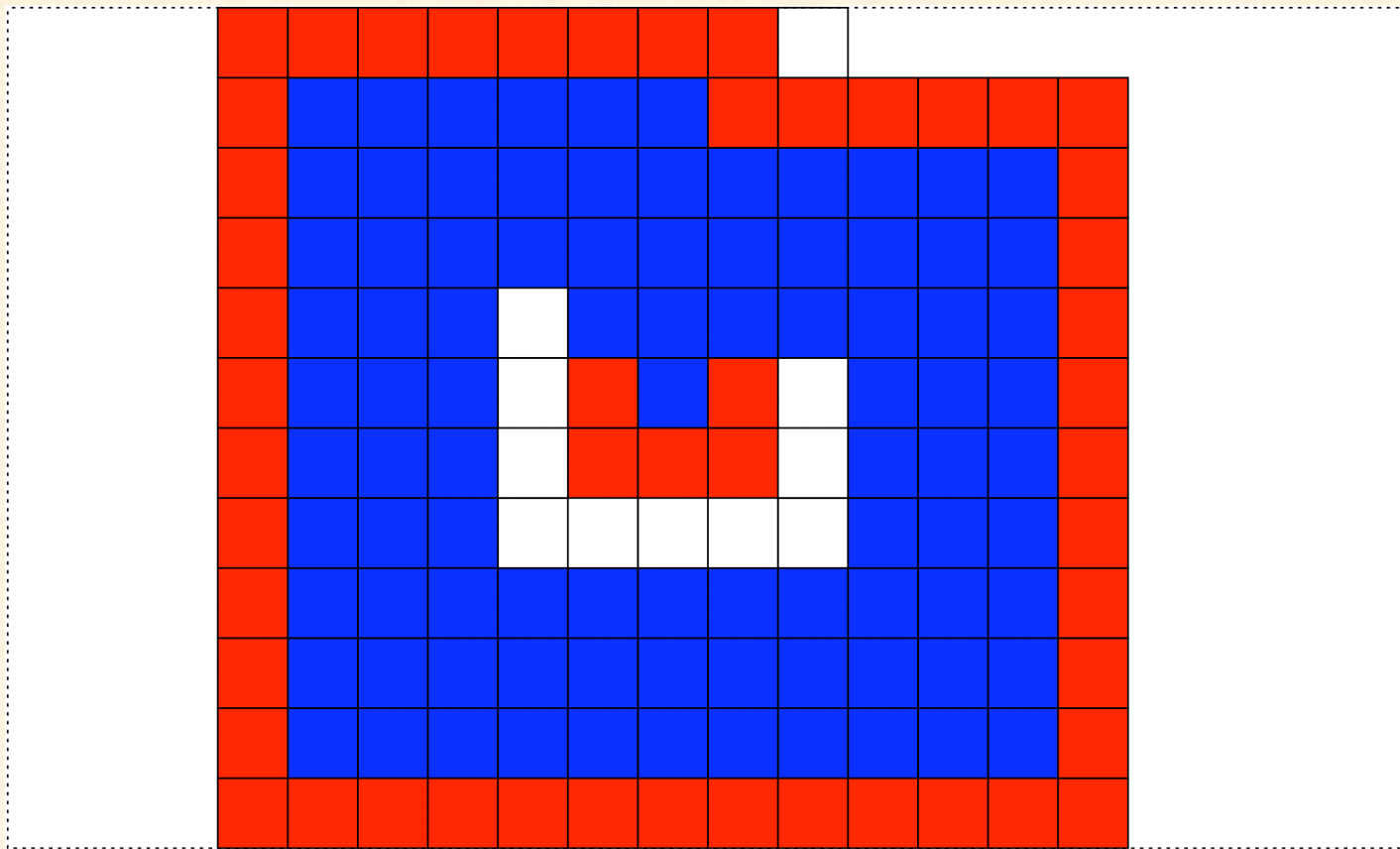
Step 5



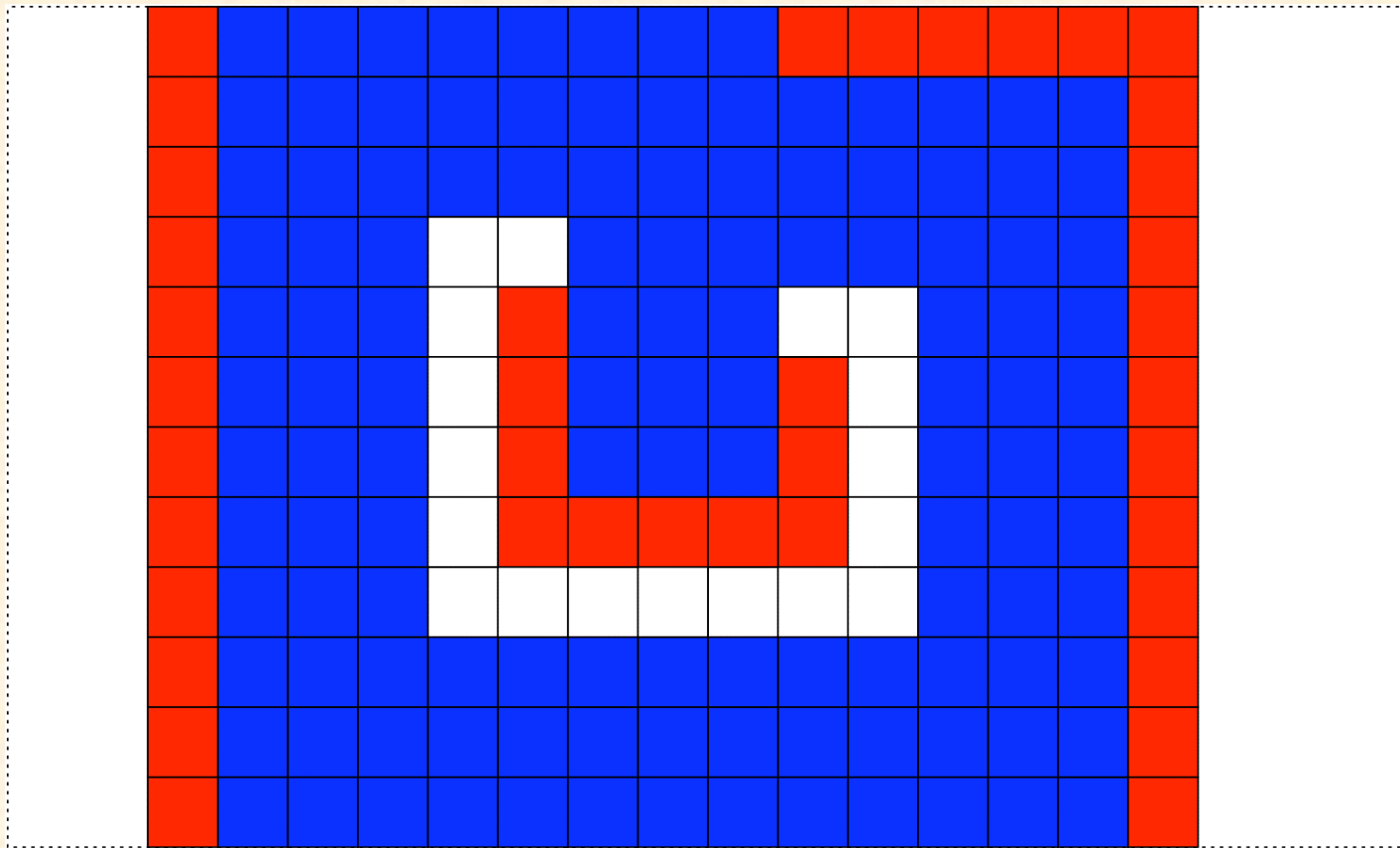
Step 6: Rejoining & Reinitiation



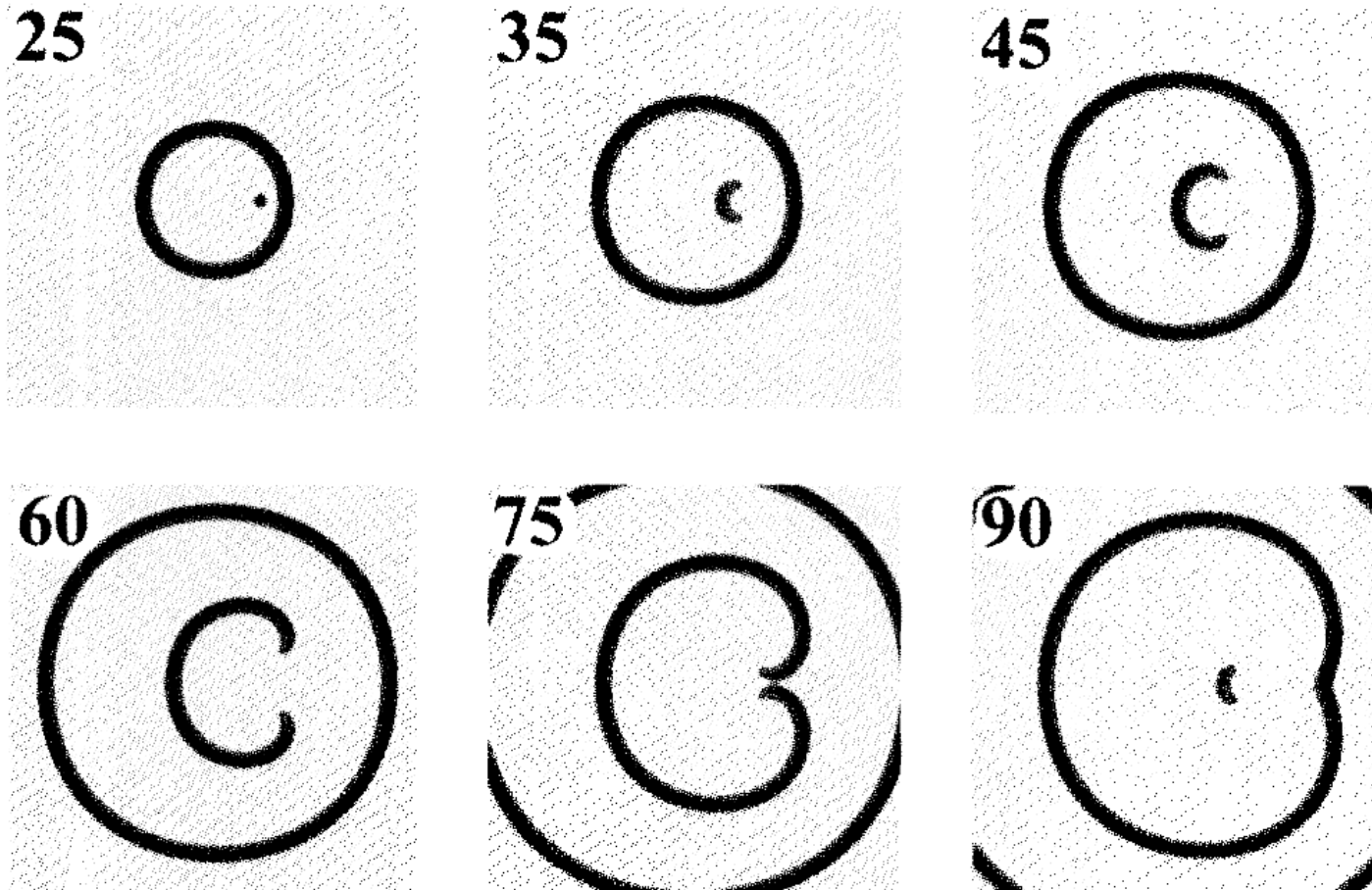
Step 7: Beginning of New Spiral



Step 8



Formation of Double Spiral



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

Response of Patch

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

Demonstration of NetLogo Simulation of Spiral Formation

[Run SlimeSpiral.nlogo](#)

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

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

Demonstration of NetLogo Simulation of Streaming

[Run SlimeStream.nlogo](#)

Typical Equations for Excitable Medium (ignoring diffusion)

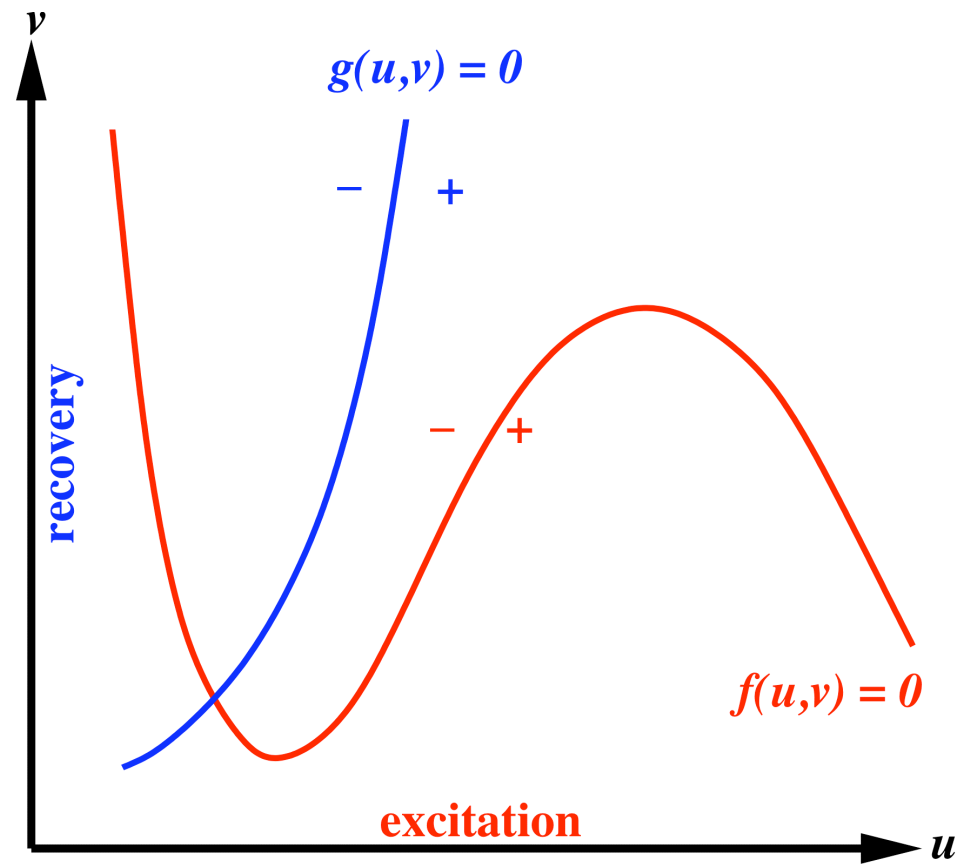
- Excitation variable:

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

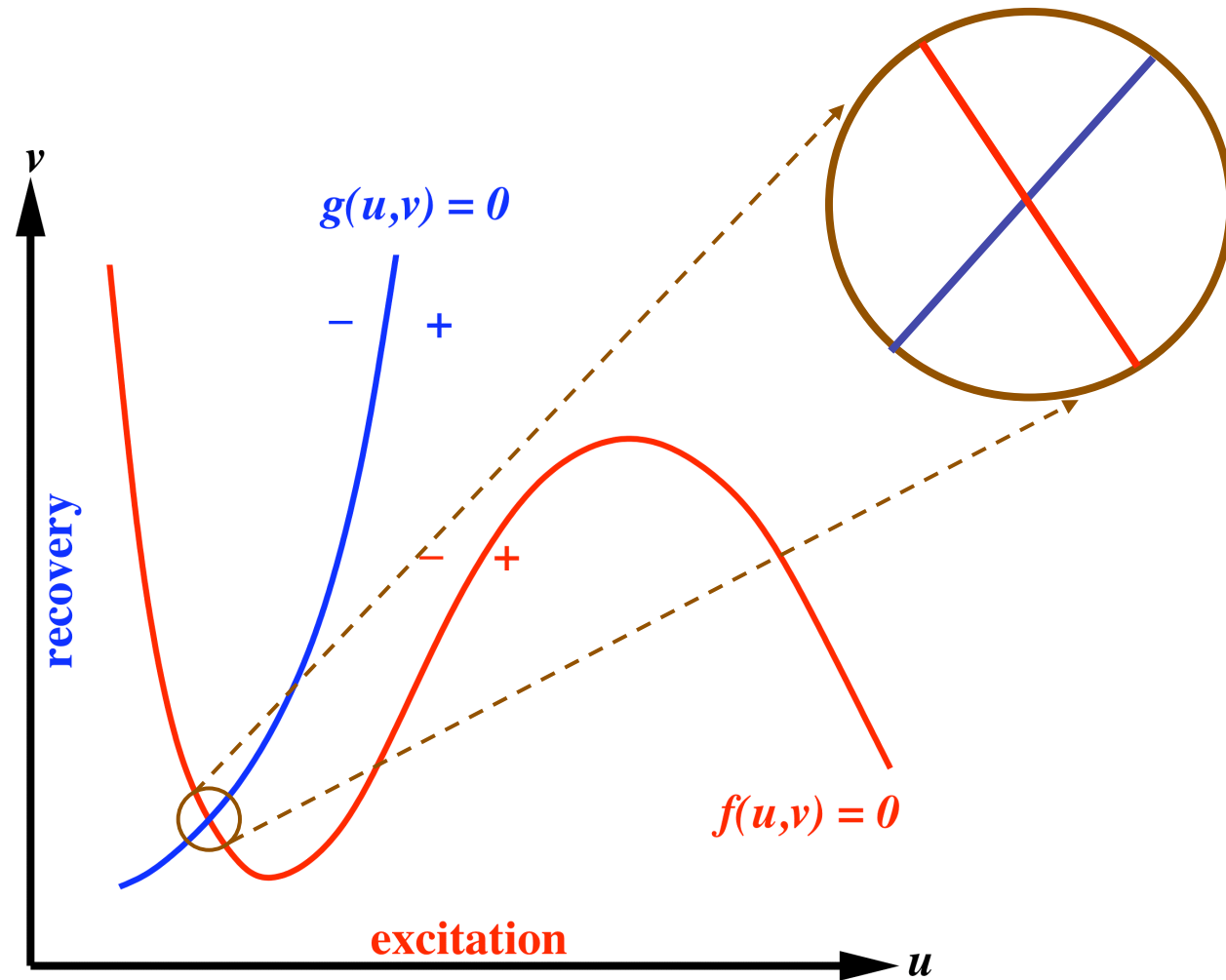
- Recovery variable:

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

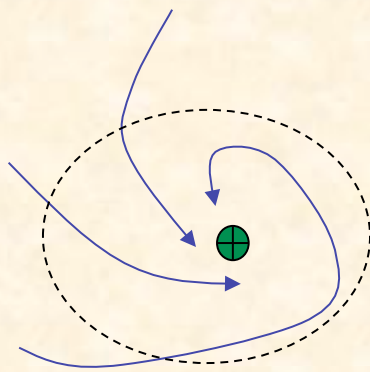
Nullclines



Local Linearization

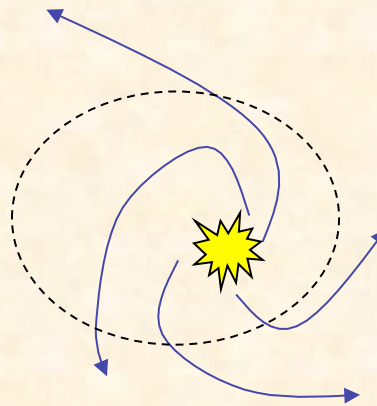


Fixed Points & Eigenvalues



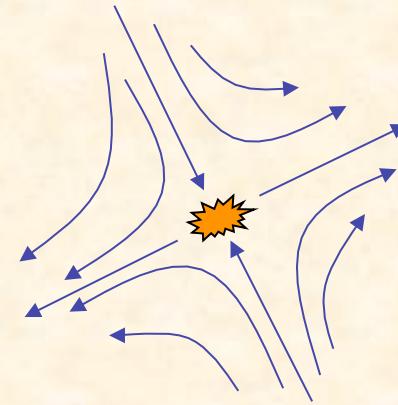
**stable
fixed point**

real parts of
eigenvalues
are negative



**unstable
fixed point**

real parts of
eigenvalues
are positive



saddle point

one positive real &
one negative real
eigenvalue

FitzHugh-Nagumo Model

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

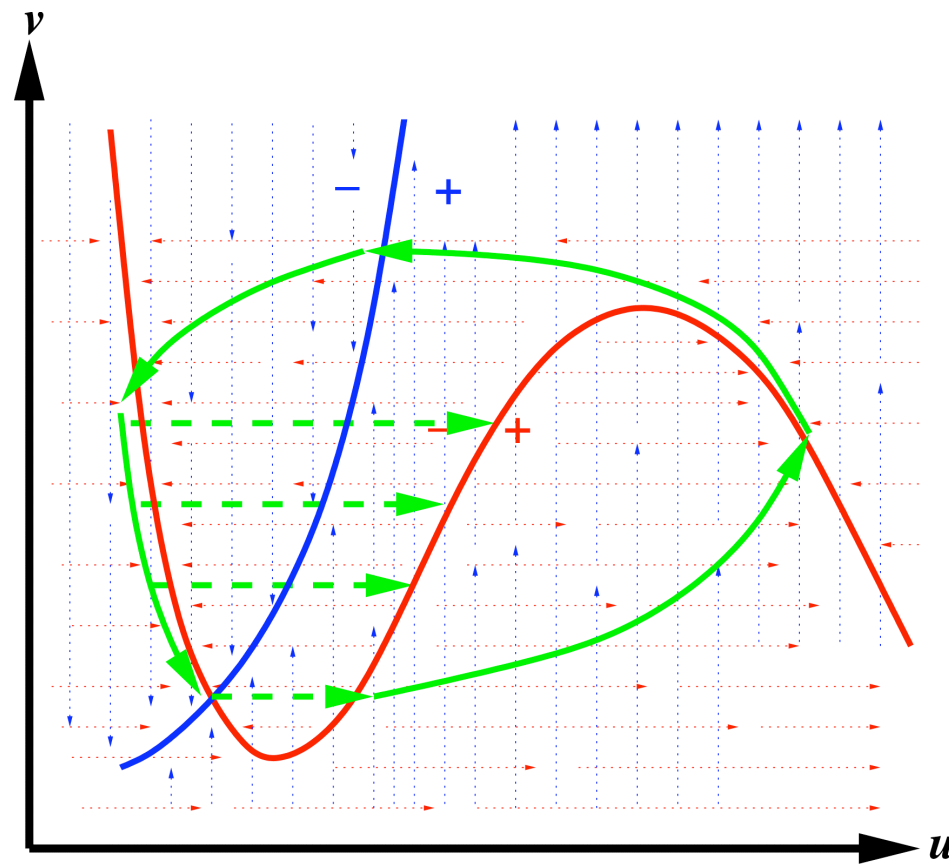
$$\dot{u} = u - \frac{u^3}{3} - v + B$$

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

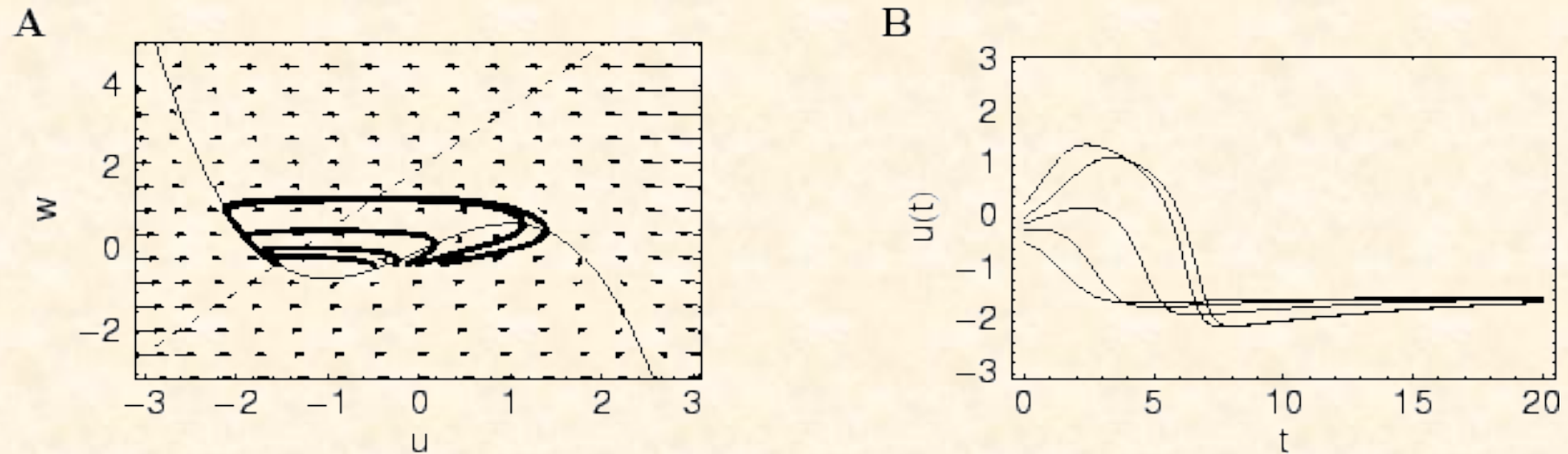
NetLogo Simulation of
Excitable Medium
in 2D Phase Space

(EM-Phase-Plane.nlogo)

Elevated Thresholds During Recovery

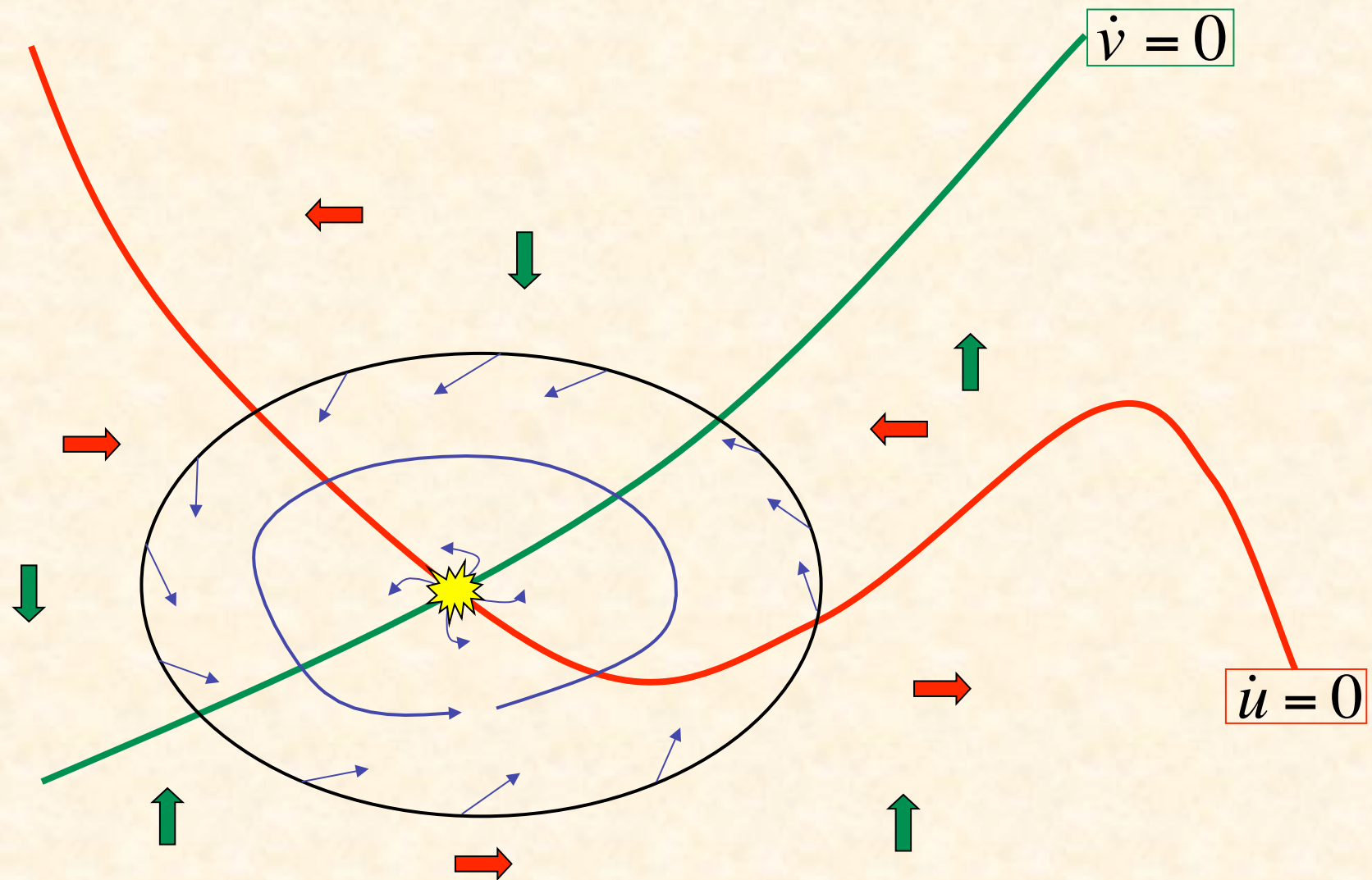


Type II Model

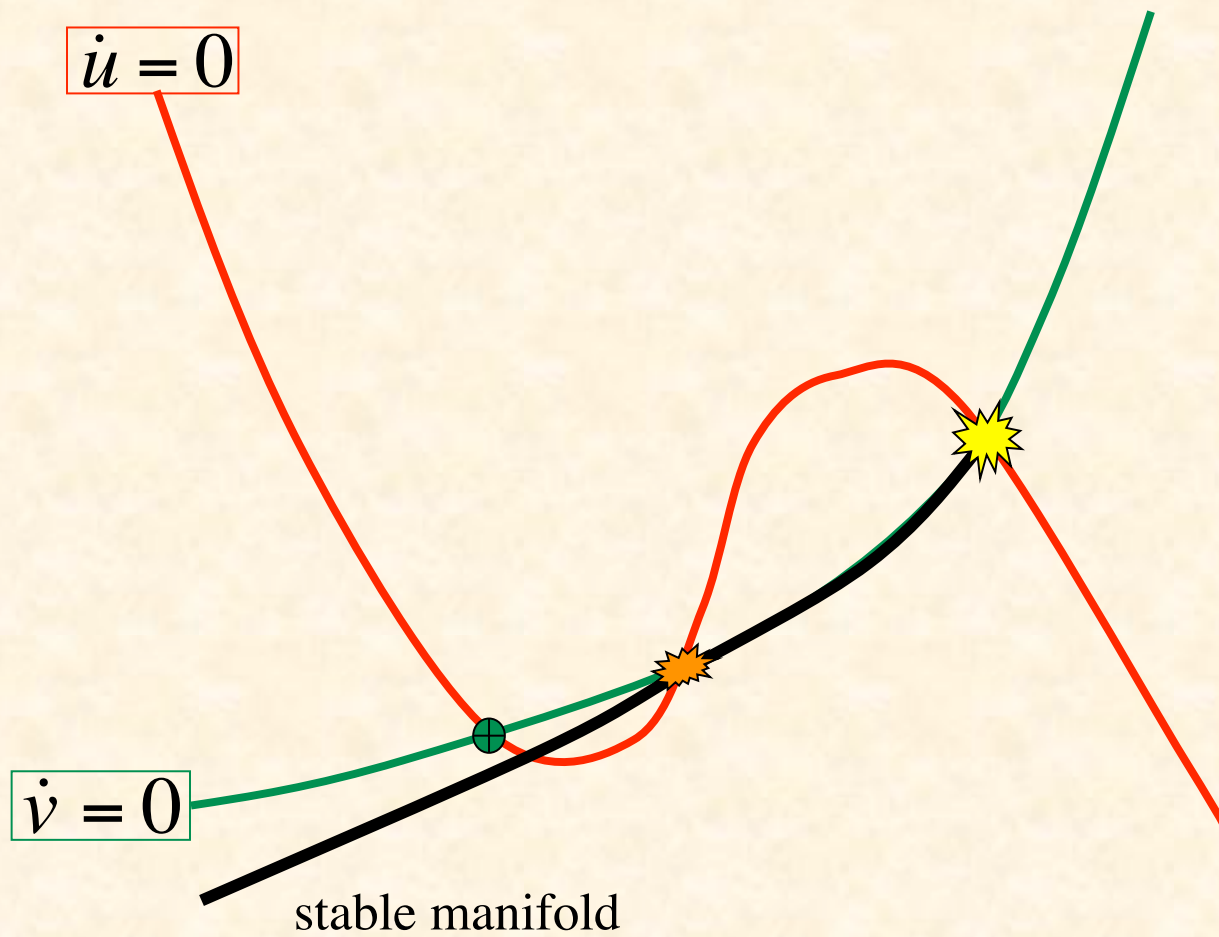


- Soft threshold with critical regime
- Bias can destabilize fixed point

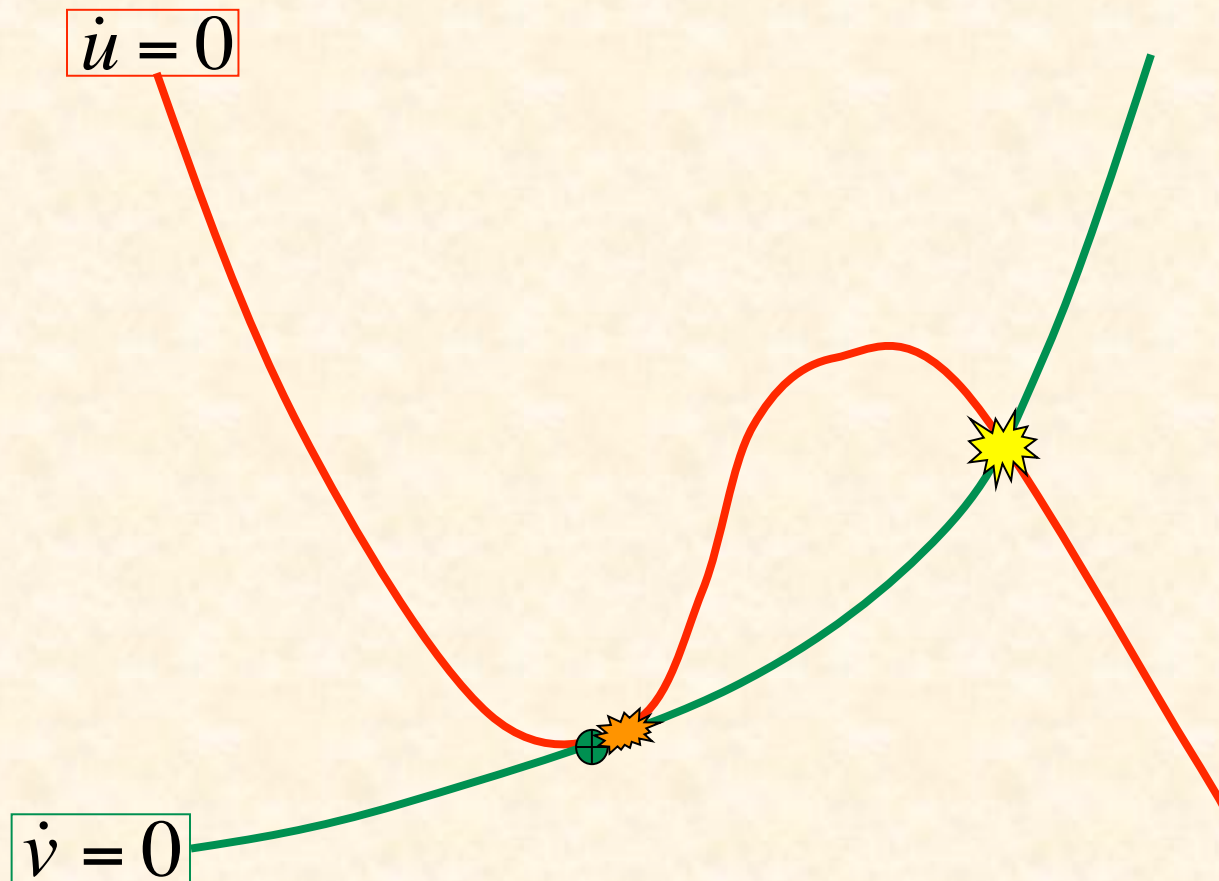
Poincaré-Bendixson Theorem



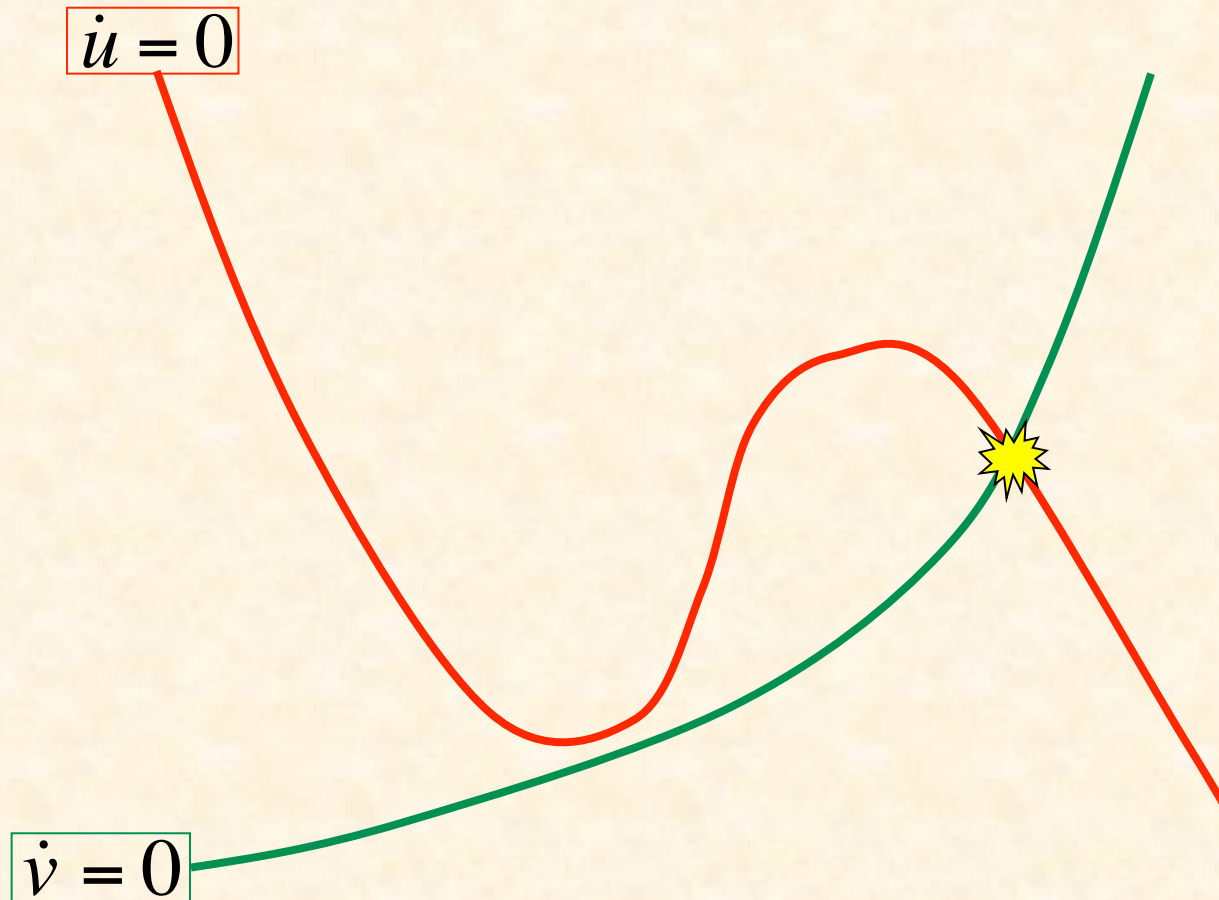
Type I Model



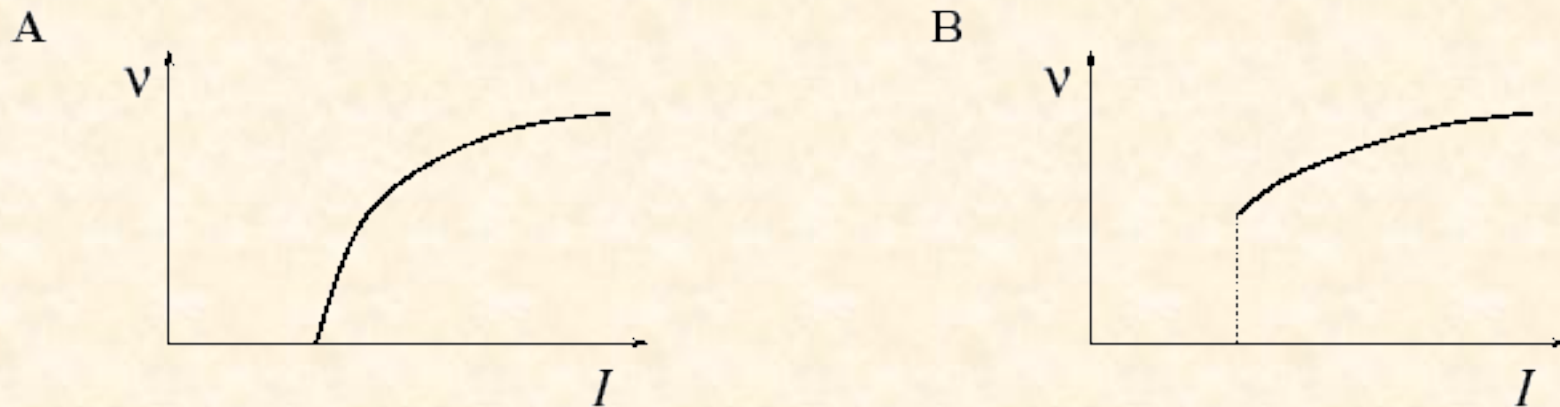
Type I Model (Elevated Bias)



Type I Model (Elevated Bias 2)



Type I vs. Type II



- Continuous vs. threshold behavior of frequency
- Slow-spiking vs. fast-spiking neurons

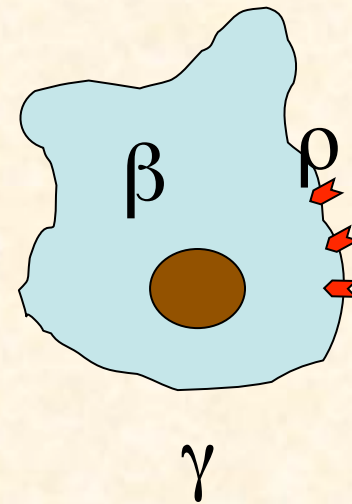
Modified Martiel & Goldbeter Model for Dicty Signalling

Variables (functions of x, y, t):

β = intracellular concentration
of cAMP

γ = extracellular concentration
of cAMP

ρ = fraction of receptors in active state



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

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

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

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)

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)

Dynamics of Model

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

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.