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-excitble 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 4
Step 5
Step 6: Rejoining & Reinitiation
Step 7: Beginning of New Spiral
Step 8
Formation of Double Spiral

from Pálsson & Cox (1996)
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

\[ g(u, v) = 0 \]

\[ f(u, v) = 0 \]
Local Linearization

\[ g(u,v) = 0 \]

\[ f(u,v) = 0 \]

recovery

excitation
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:

\[
\begin{align*}
\dot{u} &= u - \frac{u^3}{3} - v + B \\
\dot{v} &= \varepsilon (b_0 + b_1 u - v)
\end{align*}
\]
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

\[ \dot{u} = 0 \]

\[ \dot{v} = 0 \]
Type I Model

\[ \dot{u} = 0 \]

\[ \dot{v} = 0 \]

stable manifold
Type I Model (Elevated Bias)

\[ \dot{u} = 0 \]

\[ \dot{v} = 0 \]
Type I Model (Elevated Bias 2)

\[ \dot{u} = 0 \]

\[ \dot{v} = 0 \]
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 $x$, $y$, $t$):

$\beta =$ intracellular concentration of cAMP

$\gamma =$ extracellular concentration of cAMP

$\rho =$ fraction of receptors in active state
Equations

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

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

\[ \frac{d\gamma(x, y, t)}{dt} = \frac{k_t}{h} \beta - k_c \gamma + D \nabla^2 \gamma \]  \hspace{1cm} [2]

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

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

Rate of change in fraction of active receptor = Dephosphorylation of receptor - Phosphorylation of receptor
Positive Feedback Loop

- Extracellular cAMP increases
  \((\gamma \text{ increases})\)
- \(\Rightarrow\) Rate of synthesis of intracellular cAMP increases
  \((\Phi \text{ increases})\)
- \(\Rightarrow\) Intracellular cAMP increases
  \((\beta \text{ increases})\)
- \(\Rightarrow\) Rate of secretion of cAMP increases
- \((\Rightarrow\) Extracellular cAMP increases)
Negative Feedback Loop

• Extracellular cAMP increases
  \((\gamma \text{ increases})\)

• \(\Rightarrow\) cAMP receptors desensitize
  \((f_1 \text{ increases}, f_2 \text{ decreases}, \rho \text{ decreases})\)

• \(\Rightarrow\) Rate of synthesis of intracellular cAMP decreases
  \((\Phi \text{ decreases})\)

• \(\Rightarrow\) Intracellular cAMP decreases
  \((\beta \text{ decreases})\)

• \(\Rightarrow\) Rate of secretion of cAMP decreases

• \(\Rightarrow\) Extracellular cAMP decreases
  \((\gamma \text{ decreases})\)

See Equations
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)
Additional Bibliography


continue to “Part III”