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
Part 5D: Excitable Media

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 4
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

Demonstration of NetLogo
Simulation of Spiral Formation (a closer look)

Run SlimeSpiralBig.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
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

\[
\frac{d\beta(x,y,t)}{dt} = \Phi(\rho, \gamma) - \beta k_1 - \beta k_t \quad [1]
\]

\[
\frac{d\gamma(x,y,t)}{dt} = \frac{k_1}{h} \beta - k_2 \gamma + D \gamma \quad [2]
\]

\[
\frac{d\rho(x,y,t)}{dt} = f_1(\gamma(1 - \rho)) - f_3(\gamma) \rho \quad [3]
\]

Positive Feedback Loop

- Extracellular cAMP increases ($\gamma$ increases)
- $\Rightarrow$ Rate of synthesis of intracellular cAMP increases ($\Phi$ increases)
- $\Rightarrow$ Intracellular cAMP increases ($\beta$ increases)
- $\Rightarrow$ Rate of secretion of cAMP increases
- $\Rightarrow$ Extracellular cAMP increases

See Equations
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, and then return to steady state
  - or oscillation (depending on model parameters)

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

- **Nullclines**
  - $g(u,v) = \theta$
  - $f(u,v) = \theta$

- **Local Linearization**
  - $g(u,v) = \theta$
  - $f(u,v) = \theta$

- **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
Neural Impulse Propagation

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

\[ \begin{align*}
\frac{\partial u}{\partial t} &= f(u, v, B) \\
\frac{\partial v}{\partial t} &= g(u, v, B) \\
\frac{\partial u}{\partial x} &= h(u, v, B) \\
\frac{\partial v}{\partial x} &= i(u, v, B)
\end{align*} \]

Hodgkin-Huxley equations

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

\[ \dot{u} = 0 \]

\[ \dot{v} = 0 \]

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

Additional Bibliography