C. 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)
Typical Equations for Excitable Medium (ignoring diffusion)

- Excitation variable:
  \[ \dot{u} = f(u, v) \]

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

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NetLogo Simulation of Excitable Medium in 2D Phase Space

(E.M-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

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

\[
\frac{d\beta(x,y,t)}{dt} = s\Phi(x,y) - \beta \Phi_1 - \beta \Phi_2 \quad [1]
\]

\[
\frac{d\gamma(x,y,t)}{dt} = \frac{k_2}{k_3} \beta - k_4 \beta + D \nabla^2 \gamma \quad [2]
\]

\[
\frac{d\rho(x,y,t)}{dt} = f_2(\gamma) (1 - \rho) - f_1(\gamma) \rho \quad [3]
\]
Part 2C: Excitable Media 9/9/08

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
  ($\gamma$ increases)
- $\Rightarrow$ cAMP receptors desensitize
  ($f_1$ increases, $f_2$ decreases, $\rho$ decreases)
- $\Rightarrow$ Rate of synthesis of intracellular cAMP decreases
  ($\Phi$ decreases)
- $\Rightarrow$ Intracellular cAMP decreases
  ($\beta$ decreases)
- $\Rightarrow$ Rate of secretion of cAMP decreases
- $\Rightarrow$ Extracellular cAMP decreases
  ($\gamma$ decreases)

See Equations

Dynamics of Model

- Unperturbed
  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)

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 of non-
  excitatable 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

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

from Pálsson & Cox (1996)
Response of Patch

\[
\text{if patch is not refractory (brown) then} \\
\text{if local chemical > threshold then} \\
\quad \text{set refractory period} \\
\quad \text{produce pulse of chemical (red)} \\
\text{else} \\
\quad \text{decrement refractory period} \\
\quad \text{degrade chemical in local area}
\]

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

Demonstration of NetLogo Simulation of Spiral Formation

Run SlimeSpiral.nlogo

Demonstration of NetLogo Simulation of Streaming Aggregation

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

Demonstration of NetLogo Simulation of Aggregation (Spiral & Streaming Phases)

Run SlimeStream.nlogo

Run SlimeAggregation.nlogo