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
Part 2D: Excitable Media

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
Part 2D: 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-exitable 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
Part 2D: Excitable Media

Step 1: Random Excitation

Step 2: Beginning of Spiral
Part 2D: Excitable Media

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:
  \[
  \dot{u} = u - \frac{u^3}{3} - v + B
  \]
  \[
  \dot{v} = \varepsilon(b_0 + b_1u - v)
  \]
NetLogo Simulation of Excitable Medium in 2D Phase Space

(EM-Phase-Plane.nlogo)

Elevated Thresholds During Recovery
Part 2D: Excitable Media

Type II Model

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

Poincaré-Bendixson Theorem

\[ \dot{y} = 0 \]
\[ \dot{u} = 0 \]
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

fig. `< Gerstner & Kistler
Modified Martiel & Goldbeter Model for Dicty Signalling

Variables (functions of $x, y, t$):
\[ \beta = \text{intracellular concentration of cAMP} \]
\[ \gamma = \text{extracellular concentration of cAMP} \]
\[ \rho = \text{fraction of receptors in active state} \]

Equations

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

Rate of change in intracellular [cAMP]

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

Rate of change in extracellular [cAMP]

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

Rate of change in fraction of active receptor
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)

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)
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