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
• 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
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

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

\[ f(u,v) = 0 \]
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
Type II Model

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

fig. < Gerstner & Kistler
Poincaré-Bendixson Theorem

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

\[ \dot{\mathbf{v}} = 0 \]
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

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

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

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
  \((\gamma \text{ increases})\)
- \(\Rightarrow\) 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

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,
  then return to steady state
- Or oscillation (depending on model parameters)
Additional Bibliography


continue to “Part III”