Introduction to Physiology

IV - Coupling and Propagation in Excitable Media

J. P. Keener

Mathematics Department
University of Utah
Spatially Extended Excitable Media

Neurons and axons
Spatially Extended Excitable Media

Mechanically stimulated Calcium waves
Conduction system of the heart

- Electrical signal originates in the SA node.
- The signal propagates across the atria (2D sheet), through the AV node, along Purkinje bers (1D cables), and throughout the ventricles (3D tissue).
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Spatially Extended Excitable Media

The forest fire analogy
Spatial Coupling

Conservation Law:

\[ \frac{d}{dt} (\text{stuff in } \Omega) = \text{rate of transport} + \text{rate of production} \]

\[\frac{d}{dt} \int_{\Omega} u dV = \int_{\partial \Omega} J \cdot n ds + \int_{\Omega} f dv \]

becomes

\[ \frac{\partial u}{\partial t} = \nabla \cdot (D \nabla u) + f(u) \]
Question: Can anything interesting happen with coupled cells that does not happen with a single cell?
Coupled Cells

Normal cell and cell with slightly elevated potassium - uncoupled
Normal cell and cell with slightly elevated potassium - coupled
Coupled Cells

Normal cell and cell with moderately elevated potassium - uncoupled
Coupled Cells

Normal cell and cell with moderately elevated potassium - coupled

Who could have guessed? – p.8/22
Normal cell and cell with greatly elevated potassium - uncoupled
Normal cell and cell with greatly elevated potassium - coupled
From Ohm’s law

\[ V_i(x+dx) - V_i(x) = -I_i(x) r_i dx, \quad V_e(x+dx) - V_e(x) = -I_e(x) r_e dx, \]

In the limit as \( dx \to 0 \),

\[ I_i = - \frac{1}{r_i} \frac{dV_i}{dx}, \quad I_e = - \frac{1}{r_e} \frac{dV_e}{dx}. \]
The Cable Equation

From Kirchhoff’s laws

\[ I_i(x) - I_i(x + dx) = I_t dx = I_e(x + dx) - I_e(x) \]

In the limit as \( dx \to 0 \), this becomes

\[ I_t = -\frac{\partial I_i}{\partial x} = \frac{\partial I_e}{\partial x}. \]
Combining these

\[ I_t = \frac{\partial}{\partial x} \left( \frac{1}{r_i + r_e} \frac{\partial V}{\partial x} \right), \]

and, thus,

\[ C_m \frac{\partial V}{\partial t} + I_{ion} = I_t = \frac{\partial}{\partial x} \left( \frac{1}{r_i + r_e} \frac{\partial V}{\partial x} \right). \]

This equation is referred to as the **cable equation**.
Cardiac Tissue -

The Bidomain Model:

- At each point of the cardiac domain there are two comingle domains, the extracellular and the intracellular domains with potentials $\phi_e$ and $\phi_i$, and the transmembrane potential $\phi = \phi_i - \phi_e$. 
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- These potentials drive currents, $i_e = -\sigma_e \nabla \phi_e$, $i_i = -\sigma_i \nabla \phi_i$, where $\sigma_e$ and $\sigma_i$ are conductivity tensors.
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- These potentials drive currents, $i_e = -\sigma_e \nabla \phi_e$, $i_i = -\sigma_i \nabla \phi_i$, where $\sigma_e$ and $\sigma_i$ are conductivity tensors.
- Total current is

$$i_T = i_e + i_i = -\sigma_e \nabla \phi_e - \sigma_i \nabla \phi_i.$$
Kirchhoff’s laws:

- Total current is conserved: $\nabla \cdot (\sigma_i \nabla \phi_i + \sigma_e \nabla \phi_e) = 0$
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- Transmembrane current is balanced:

\[
\chi \left( C_m \frac{\partial \phi}{\partial t} + I_{ion} \right) = \nabla \cdot (\sigma_i \nabla \phi_i)
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surface to volume ratio,
Kirchhoff’s laws:

- Total current is conserved: \( \nabla \cdot (\sigma_i \nabla \phi_i + \sigma_e \nabla \phi_e) = 0 \)

- Transmembrane current is balanced:

\[
\chi \left( C_m \frac{\partial \phi}{\partial r} + I_{ion} \right) = \nabla \cdot (\sigma_i \nabla \phi_i)
\]

- surface to volume ratio, capacitive current,
Kirchhoff’s laws:

- Total current is conserved: \( \nabla \cdot (\sigma_i \nabla \phi_i + \sigma_e \nabla \phi_e) = 0 \)
- Transmembrane current is balanced:

\[
\chi \left( C_m \frac{\partial \phi}{\partial \tau} + I_{ion} \right) = \nabla \cdot (\sigma_i \nabla \phi_i)
\]

surface to volume ratio, capacitive current, ionic current,
Kirchhoff’s laws:

- Total current is conserved: \( \nabla \cdot (\sigma_i \nabla \phi_i + \sigma_e \nabla \phi_e) = 0 \)
- Transmembrane current is balanced:

\[
\chi \left( C_m \frac{\partial \phi}{\partial \tau} + I_{ion} \right) = \nabla \cdot (\sigma_i \nabla \phi_i)
\]

surface to volume ratio, capacitive current, ionic current, and current from intracellular space.
Kirchhoff’s laws:

- Total current is conserved: \( \nabla \cdot (\sigma_i \nabla \phi_i + \sigma_e \nabla \phi_e) = 0 \)

- Transmembrane current is balanced:

\[
\chi \left( C_m \frac{\partial \phi}{\partial t} + I_{\text{ion}} \right) = \nabla \cdot (\sigma_i \nabla \phi_i)
\]

- Boundary conditions:

\[ n \cdot \sigma_i \nabla \phi_i = 0, \quad n \cdot \sigma_e \nabla \phi_e = I(t, x) \]

and \( \int_{\partial \Omega} I(t, x) \, dx = 0 \) on \( \partial \Omega \).
Traveling Waves

\[
\frac{\partial u}{\partial t} = D \frac{\partial^2 u}{\partial x^2} + f(u)
\]

with \( f(0) = f(a) = f(1) = 0 \), \( 0 < a < 1 \).

- There is a unique traveling wave solution \( u = U(x - ct) \),
- The solution is stable up to phase shifts,
- The speed scales as \( c = c_0 \sqrt{D} \),
- \( U \) is a homoclinic trajectory of \( DU'' + cU' + f(U) = 0 \).
Gap junctional coupling

Calcium Release through CICR Receptors
Discrete Effects

Discrete Cells

\[
\frac{dv_n}{dt} = f(v_n) + d(v_{n-1} - 2v_n + v_{n-1})
\]

Discrete Calcium Release

Discrete Release Sites

\[
\frac{\partial u}{\partial t} = D \frac{\partial^2 u}{\partial x^2} + g(x) f(u)
\]
Suppose a diffusible chemical $u$ is released from

- a long line of evenly spaced release sites;
- Release of full contents $C$ occurs when concentration $u$ reaches threshold $\theta$.

\[
\frac{\partial u}{\partial t} = D \frac{\partial^2 u}{\partial x^2} + \sum_n Source(x - nh)\delta(t - t_n)
\]
Recall that the solution of the heat equation with $\delta$-function initial data at $x = x_0$ and at $t = t_0$ is

$$u(x, t) = \frac{1}{\sqrt{4\pi(t - t_0)}} \exp\left(-\frac{(x - x_0)^2}{4D(t - t_0)}\right)$$
Suppose known firing times are $t_j$ at position $x_j = jh$, $j = -\infty, \cdots, n - 1$. Find $t_n$. At $x = x_n = nh$,

$$u(nh, t) = \sum_{j=-\infty}^{n-1} \frac{C}{\sqrt{4\pi(t - t_j)}} \exp\left(-\frac{(nh - jh)^2}{4D(t - t_j)}\right)$$

$$\approx \frac{C}{\sqrt{4\pi(t - t_{n-1})}} \exp\left(-\frac{h^2}{4D(t - t_{n-1})}\right) = \frac{C}{h} f\left(\frac{D\Delta t}{h^2}\right)$$
Solve the equation

\[ \frac{\theta h}{C} = f\left(\frac{D \Delta t}{h^2}\right) \]

This is easy to do graphically:

Conclusion: Propagation fails for \( \frac{\theta h}{C} > \theta^* \approx 0.25 \) (i.e. if \( h \) is too large, \( \theta \) is too large, or \( C \) is too small.)
Including recovery variables

\[ \frac{\partial v}{\partial t} = D \frac{\partial^2 v}{\partial x^2} + f(v, w), \quad \frac{\partial w}{\partial t} = g(v, w) \]

Solitary Pulse
Periodic Waves
Skipped Beats
On a Ring
Periodic Ring

Wolff Parkinson White