Introduction to Physiology IV - Coupling and Propagation in Excitable Media

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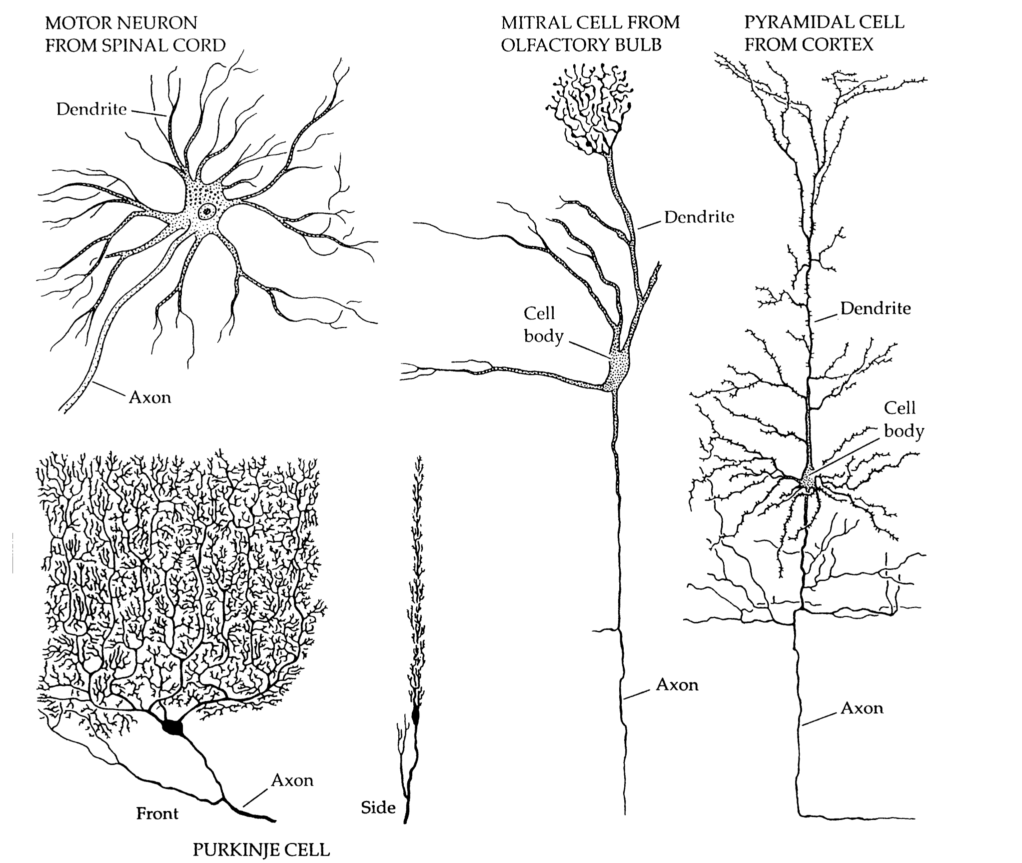
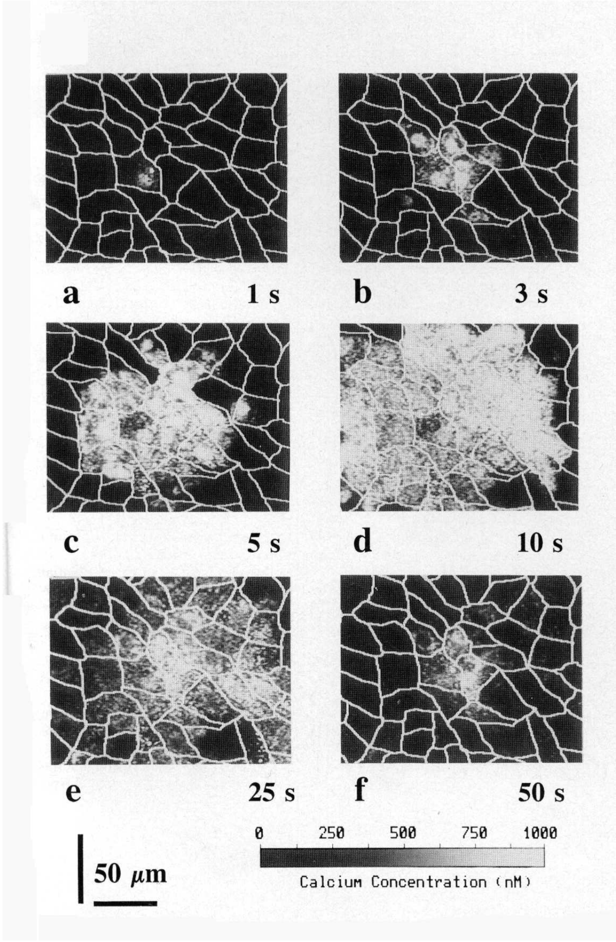
Spatially Extended Excitable Media



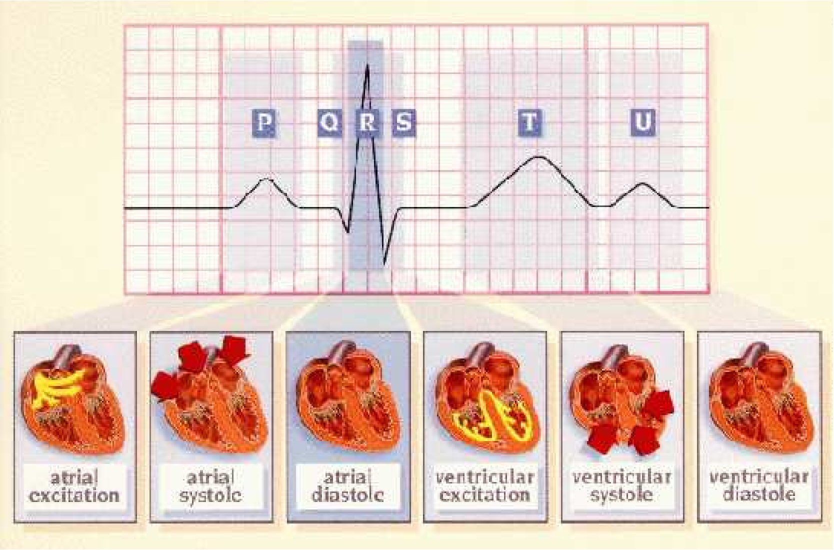
Neurons and axons

Spatially Extended Excitable Media



Mechanically stimulated Calcium waves

Conduction system of the heart



Imagine the Possibilities

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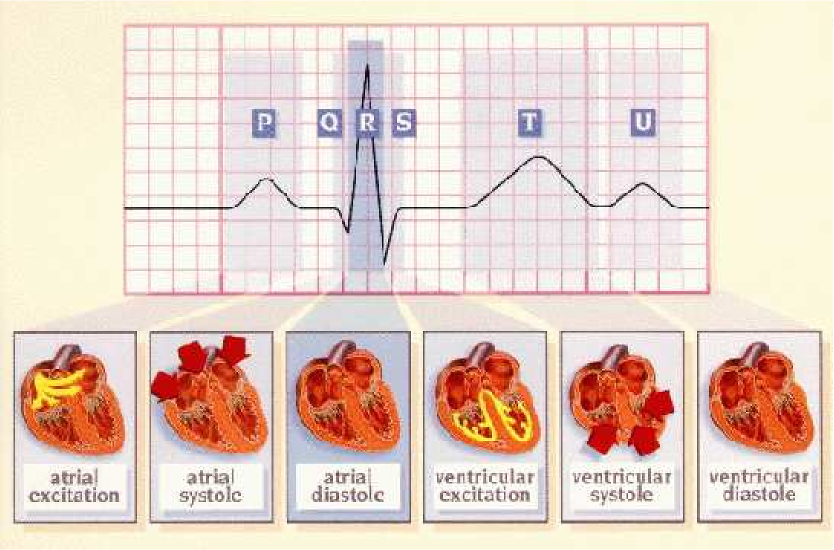
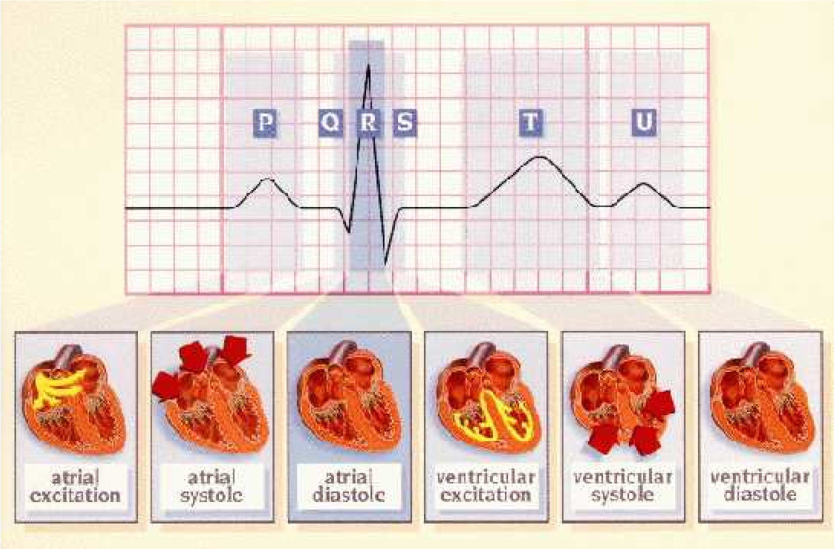
Conduction system of the heart



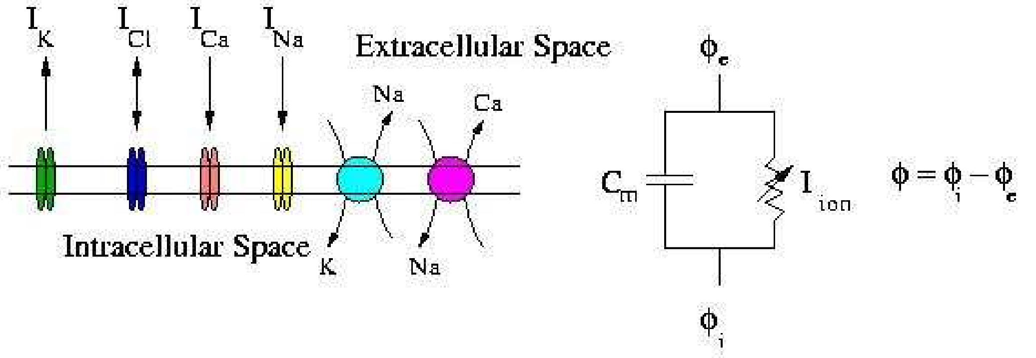
- Electrical signal originates in the SA node.

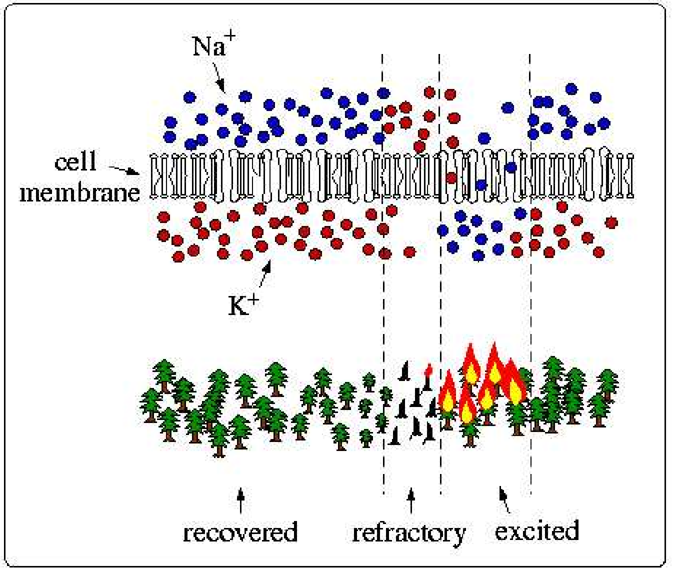
Conduction system of the heart



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

Spatially Extended Excitable Media





The forest fire analogy

Spatial Coupling

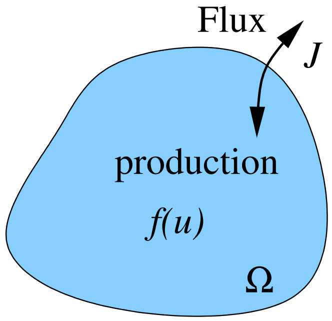
Conservation Law:

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

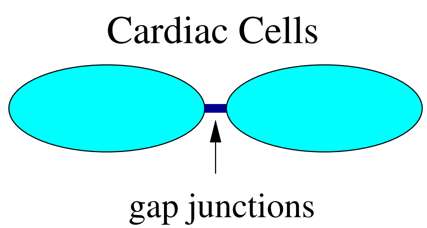
$$\frac{d}{dt}\int_{\Omega} u dV = \int_{\partial\Omega} J \cdot n ds + \int_{\Omega} f dv$$

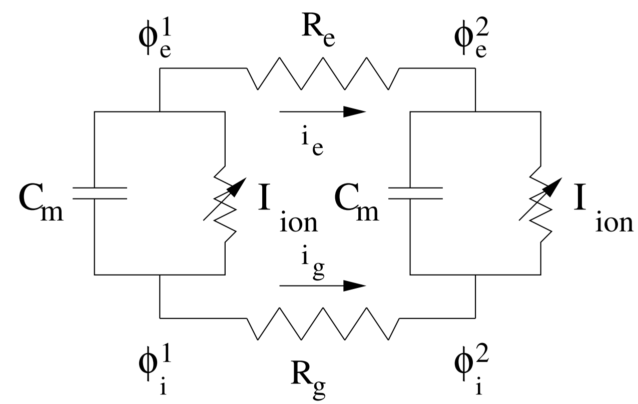
becomes

$$\frac{\partial u}{\partial t} = \nabla \cdot (D \nabla u) + f(u)$$



Coupled Cells





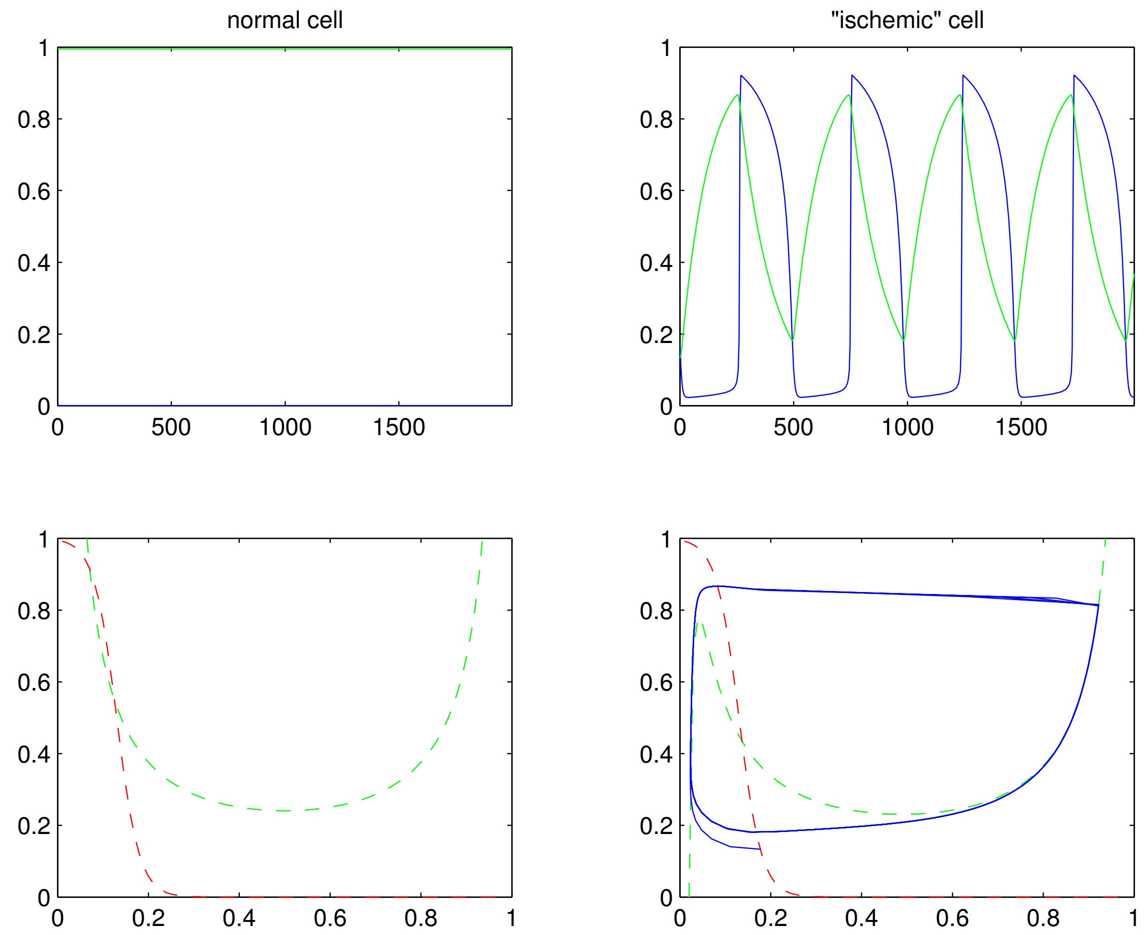
$$C_m \frac{d\phi^1}{dt} + I_{ion}(\phi^1, w) = -i_i = \frac{1}{R_e + R_g}(\phi^2 - \phi^1)$$

$$C_m \frac{d\phi^2}{dt} + I_{ion}(\phi^2, w) = i_i = \frac{1}{R_e + R_g}(\phi^1 - \phi^2)$$

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



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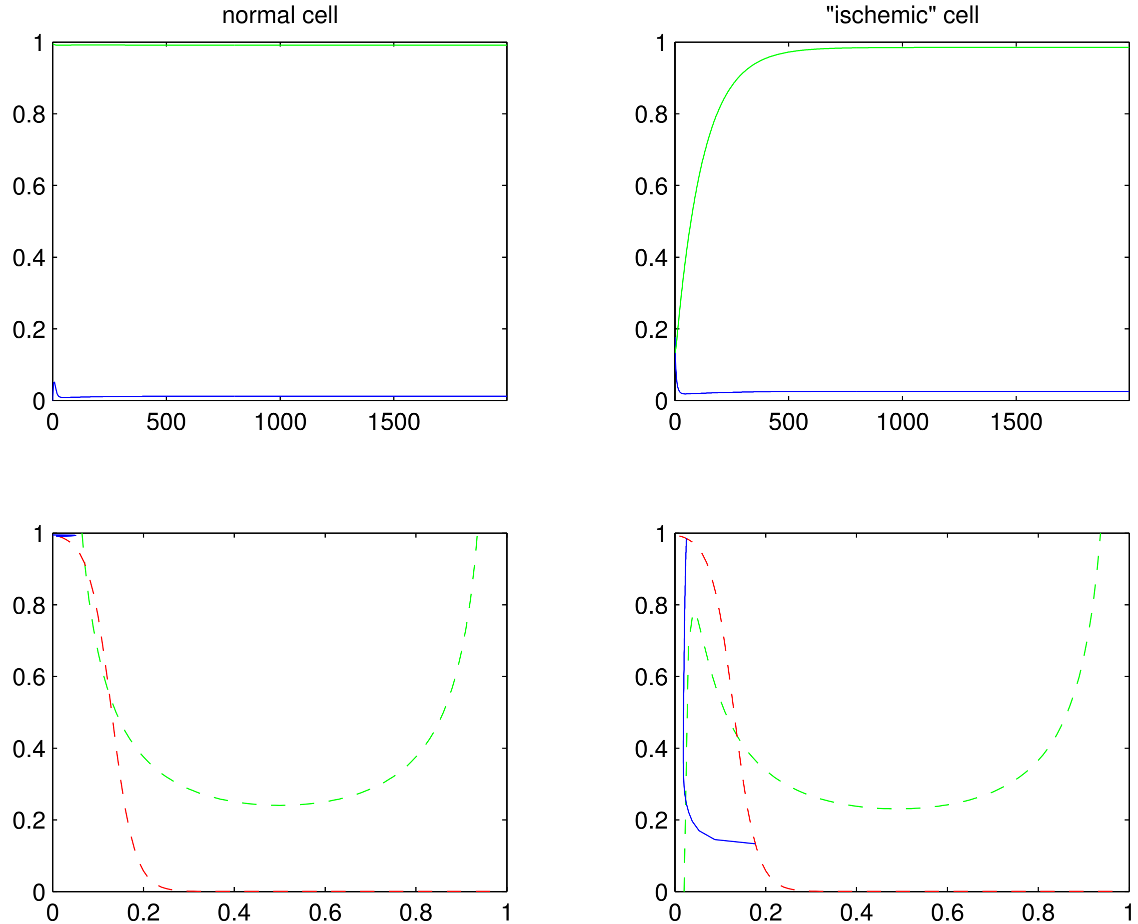
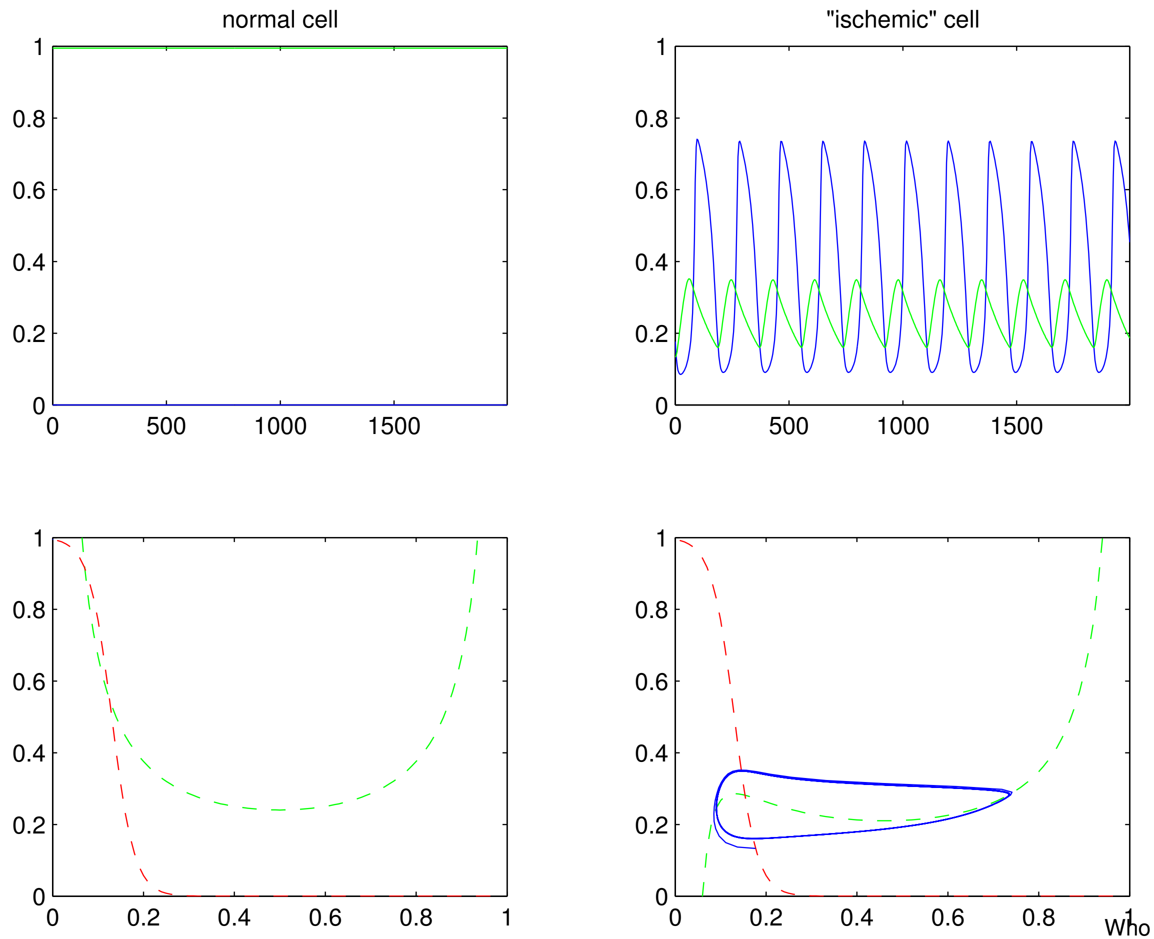


Coupled Cells

Normal cell and cell with moderately elevated potassium - uncoupled



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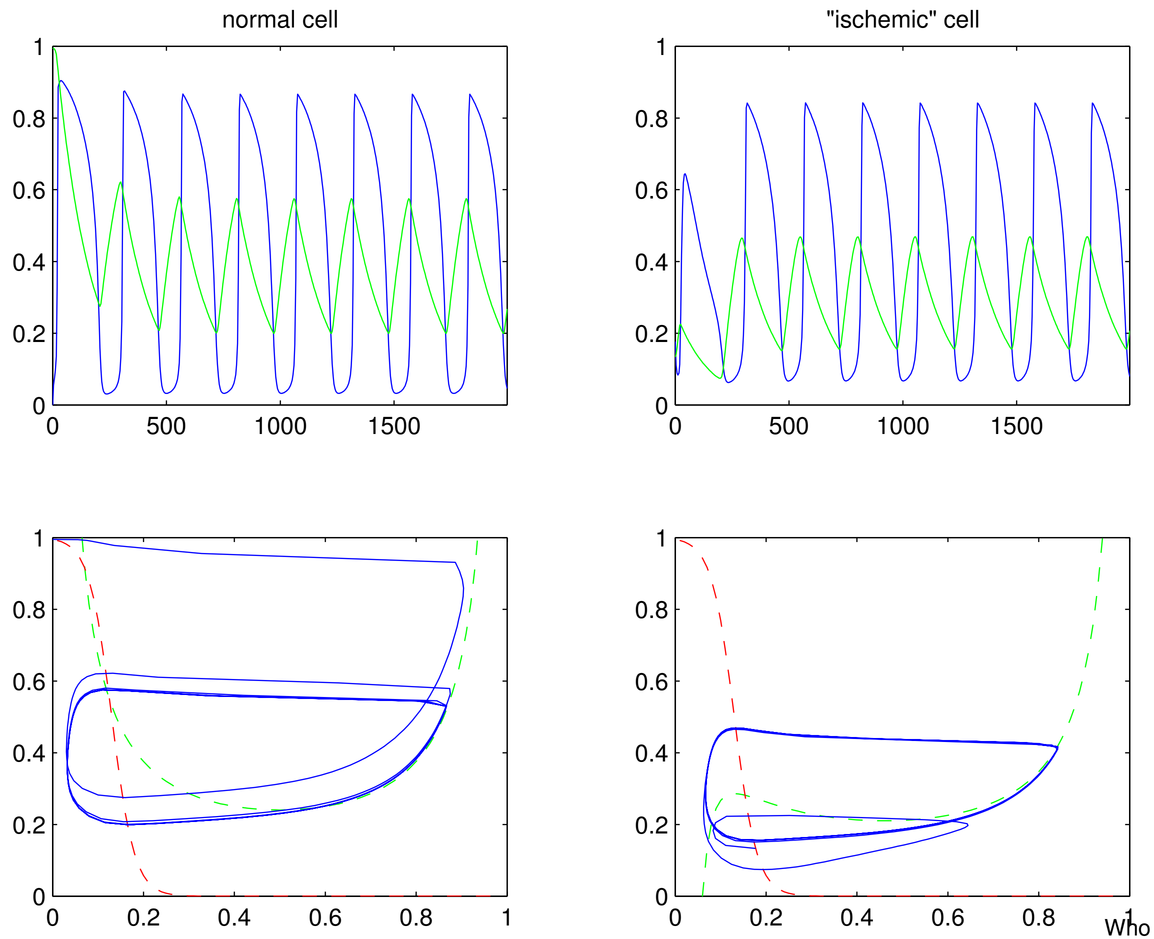
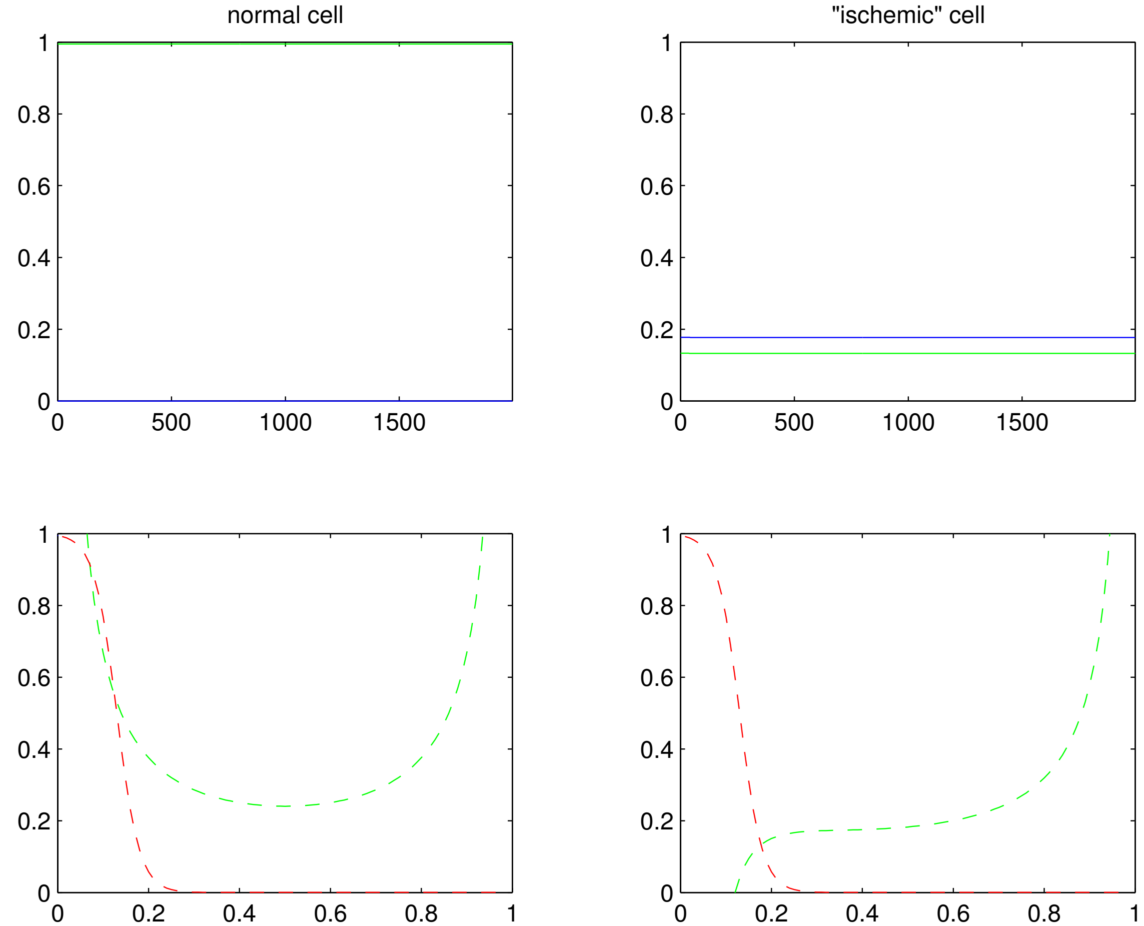


Coupled Cells

Normal cell and cell with greatly elevated potassium - uncoupled



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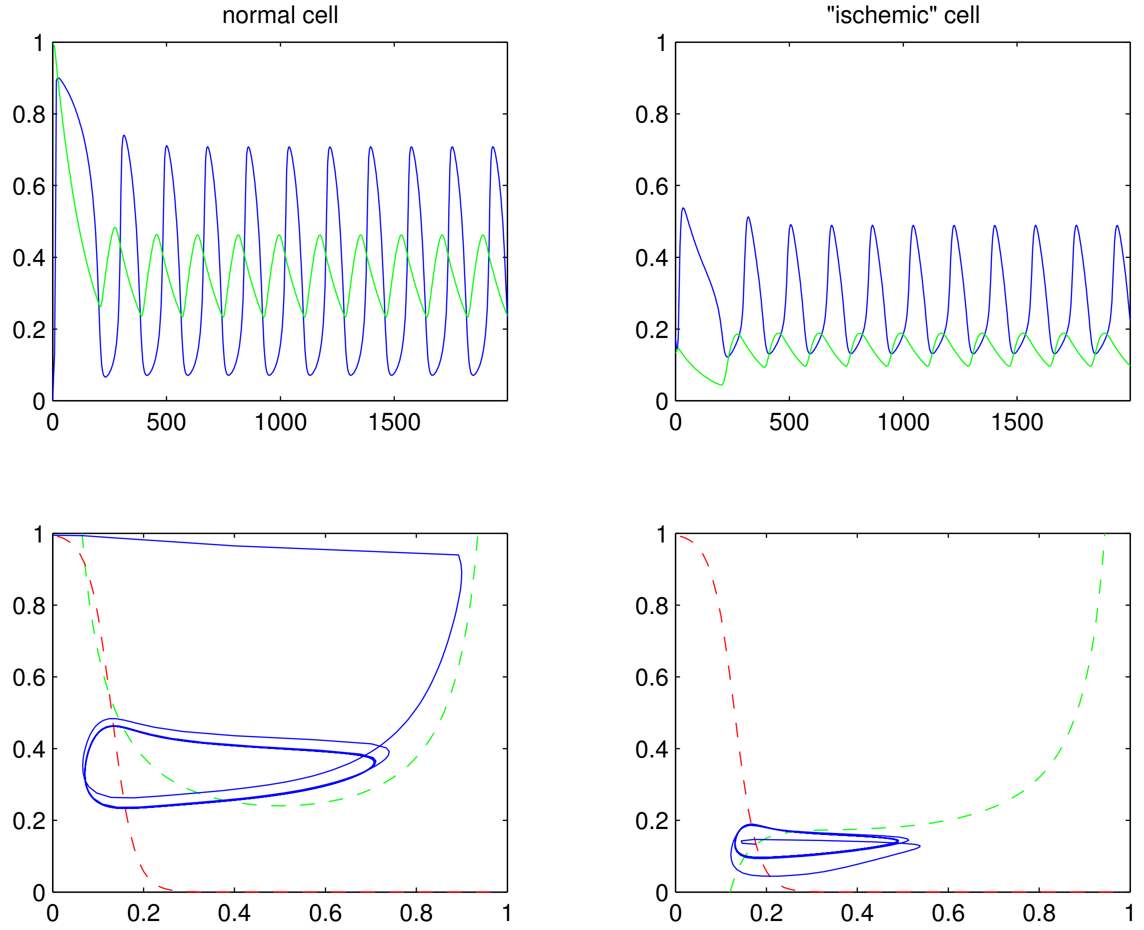
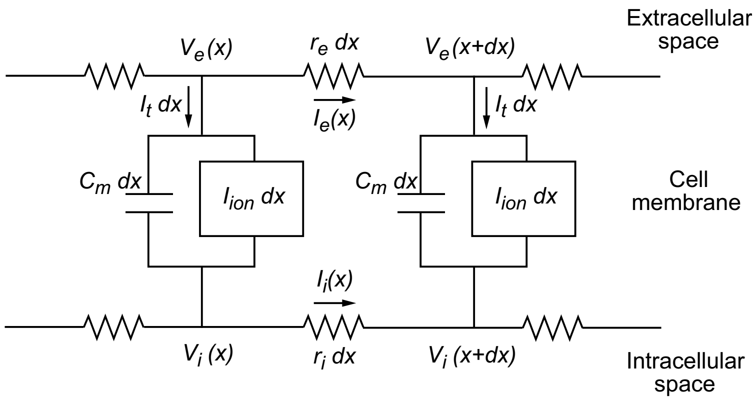


Axons and Fibers



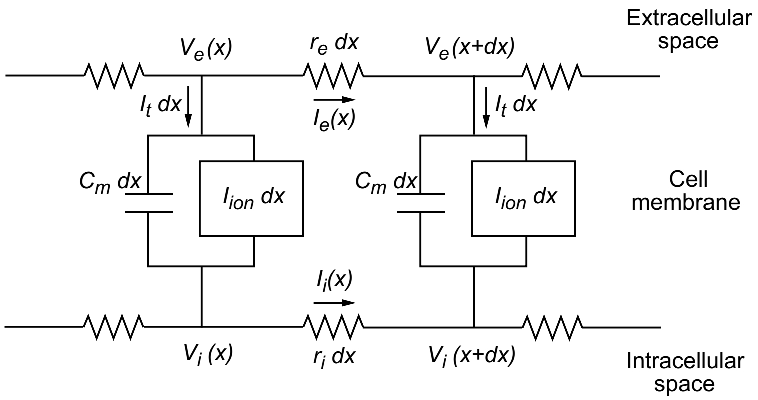
From Ohm's law

$$V_i(x+dx)-V_i(x) = -I_i(x)r_i dx, \;\; V_e(x+dx)-V_e(x) = -I_e(x)r_e dx,$$

In the limit as $dx \to 0$,

$$I_i = -\frac{1}{r_i}\frac{dV_i}{dx}, \qquad I_e = -\frac{1}{r_e}\frac{dV_e}{dx}.$$

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

$$I_t = -\frac{\partial I_i}{\partial x} = \frac{\partial I_e}{\partial x}.$$

The Cable Equation

Combining these

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

and, thus,

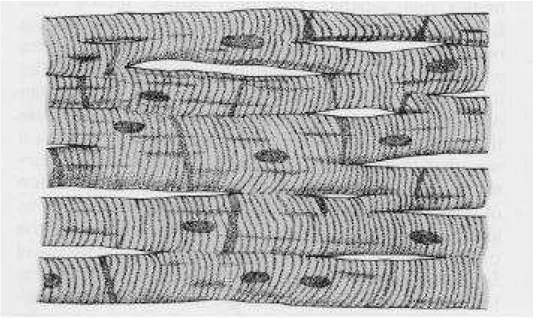
$$C_m \frac{\partial V}{\partial t} + I_{ion} = I_t = \frac{\partial}{\partial x}\left(\frac{1}{r_i + r_e}\frac{\partial V}{\partial x}\right).$$

This equation is referred to as the cable equation.

Modelling Cardiac Tissue

Cardiac Tissue -

The Bidomain Model:



- At each point of the cardiac domain there are two comingled regions, the extracellular and the intracellular domains with potentials ϕ_e and ϕ_i, and transmembrane potential $\phi = \phi_i - \phi_e$.

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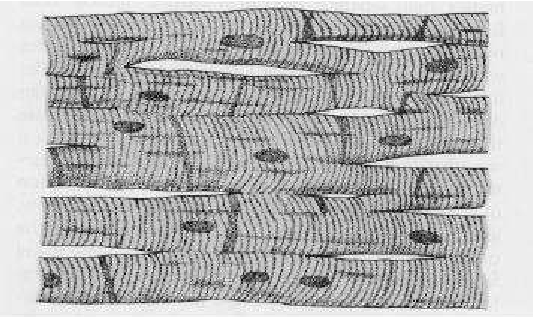
Modelling Cardiac Tissue



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- These potentials drive currents, $i_e = -\sigma_e \nabla \phi_e$, $i_i = -\sigma_i \nabla \phi_i$, where σ_e and σ_i are conductivity tensors.

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Modelling Cardiac Tissue

Cardiac Tissue -

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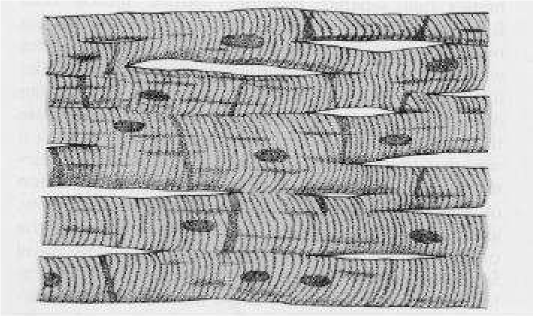

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- These potentials drive currents, $i_e = -\sigma_e \nabla \phi_e$, $i_i = -\sigma_i \nabla \phi_i$, where σ_e and σ_i are conductivity tensors.
- *Total current* is

$$i_T = i_e + i_i = -\sigma_e \nabla \phi_e - \sigma_i \nabla \phi_i.$$

Kirchhoff's laws:

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

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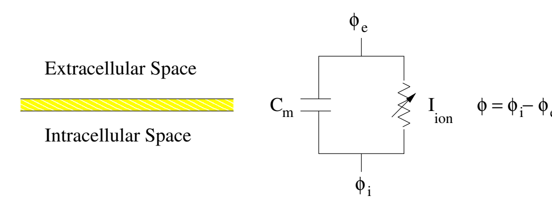
$$\chi \left(C_m \frac{\partial \phi}{\partial \tau} + I_{ion} \right) = \nabla \cdot (\sigma_i \nabla \phi_i)$$



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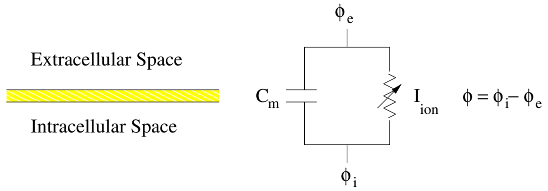

surface to volume ratio,

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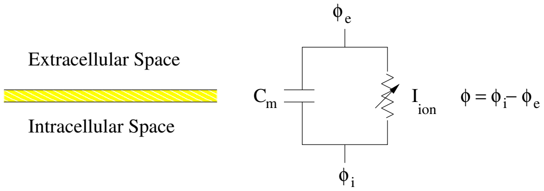

surface to volume ratio, capacitive current,

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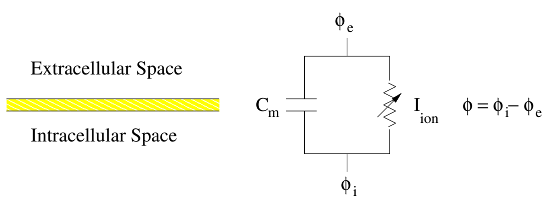

surface to volume ratio, capacitive current, ionic current,

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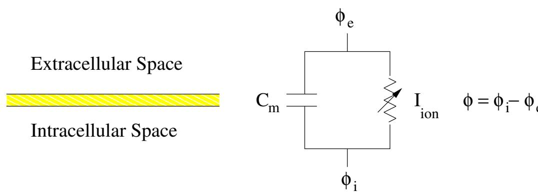

surface to volume ratio, capacitive current, ionic current, and current from intracellular space.

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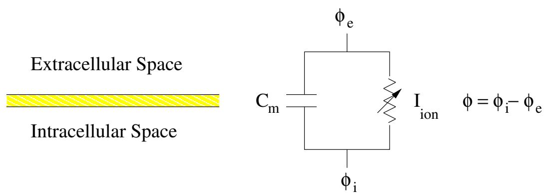
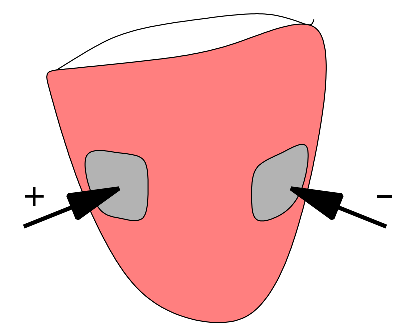


surface to volume ratio, capacitive current, ionic current, and current from intracellular space.

- Boundary conditions:

$$\mathrm{n} \cdot \sigma_i \nabla \phi_i = 0, \qquad \mathrm{n} \cdot \sigma_e \nabla \phi_e = I(t, x)$$

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

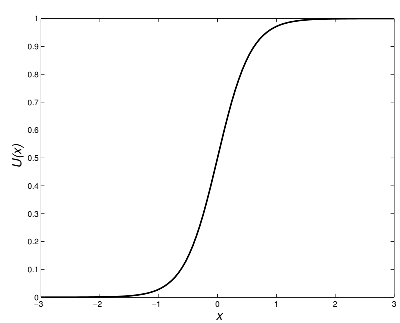


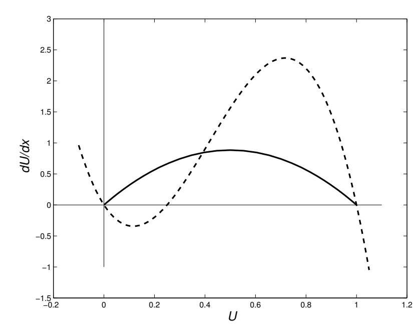
Traveling Waves

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

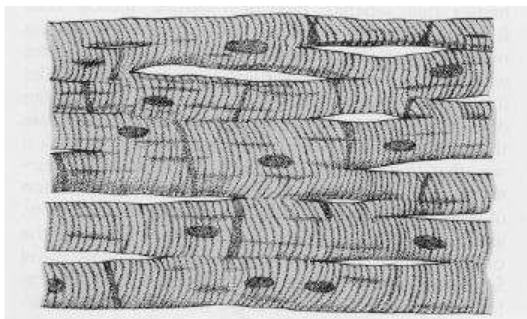
with $f(0) = f(a) = f(1) = 0$, $0 < a < 1$.

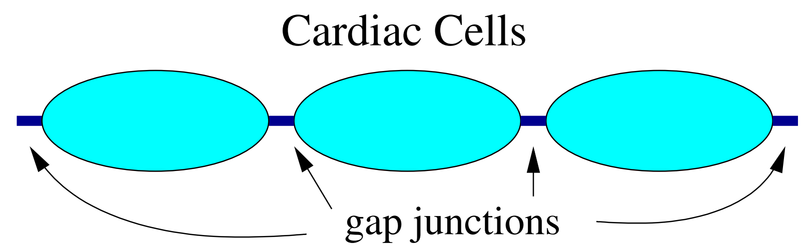
- There is a unique traveling wave solution $u = U(x - ct)$,
- The solution is stable up to phase shifts,
- The speed scales as $c = c_0\sqrt{D}$,
- U is a homoclinic trajectory of $DU'' + cU' + f(U) = 0$



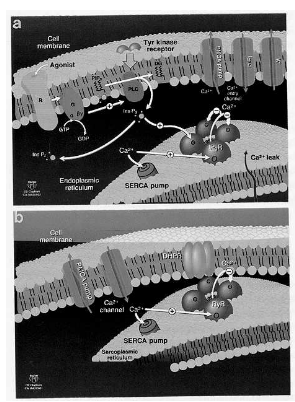


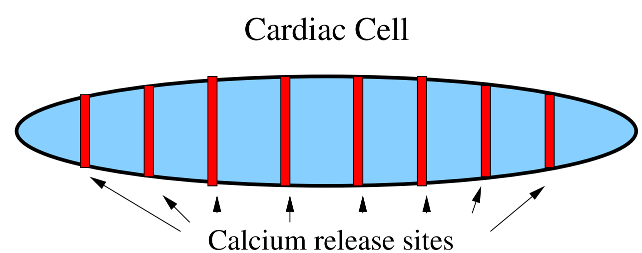
Discreteness





Gap junctional coupling





Calcium Release through CICR Receptors

Discrete Effects

Discrete Cells

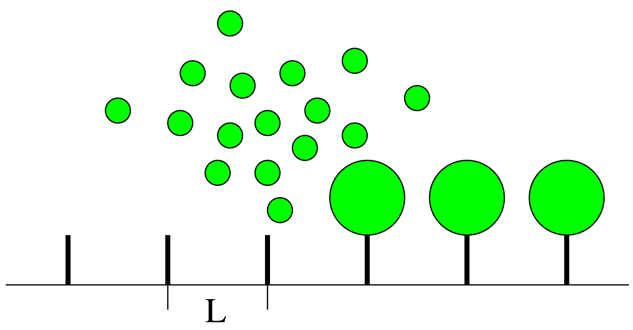
$$\frac{dv_n}{dt} = f(v_n) + d(v_{n-1} - 2v_n + v_{n-1})$$

Discrete Calcium Release

Discrete Release Sites

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

Fire-Diffuse-Fire Model



Suppose a diffusible chemical u is released from

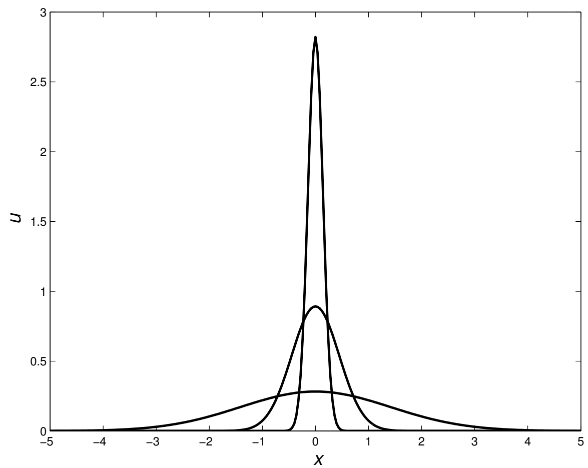
- a long line of evenly spaced release sites;
- Release of full contents C occurs when concentration u reaches threshold θ.

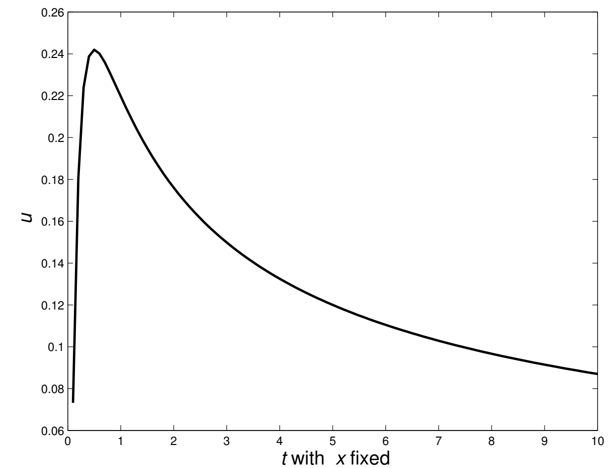
$$\frac{\partial u}{\partial t} = D\frac{\partial^2 u}{\partial x^2} + \sum_n Source(x - nh)\delta(t - t_n)$$

Fire-Diffuse-Fire-II

Recall that the solution of the heat equation with δ-function initial data at $x = x_0$ and at $t = t_0$ is

$$u(x,t) = \frac{1}{\sqrt{4\pi(t-t_0)}} \exp\left(-\frac{(x-x_0)^2}{4D(t-t_0)}\right)$$

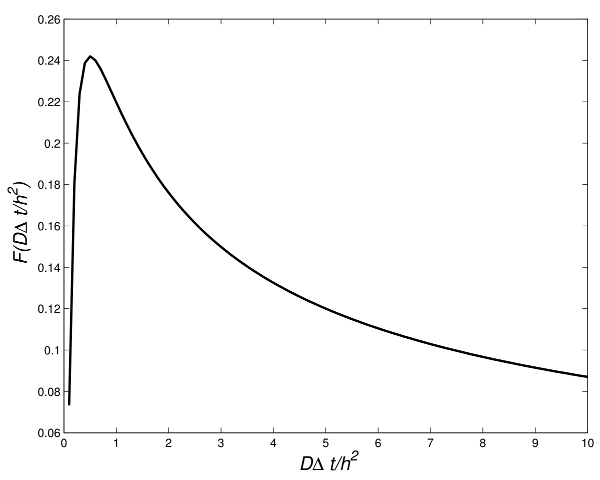




Fire-Diffuse-Fire-III

Suppose known firing times are t_j at position $x_j = jh$, $j = -\infty, \cdots, n-1$. Find t_n. At $x = x_n = nh$,

$$
\begin{aligned}
u(nh,t) &= \sum_{j=-\infty}^{n-1} \frac{C}{\sqrt{4\pi(t-t_j)}} \exp\left(-\frac{(nh-jh)^2}{4D(t-t_j)}\right) \\
&\approx \frac{C}{\sqrt{4\pi(t-t_{n-1})}} \exp\left(-\frac{h^2}{4D(t-t_{n-1})}\right) = \frac{C}{h} f\left(\frac{D\Delta t}{h^2}\right)
\end{aligned}
$$

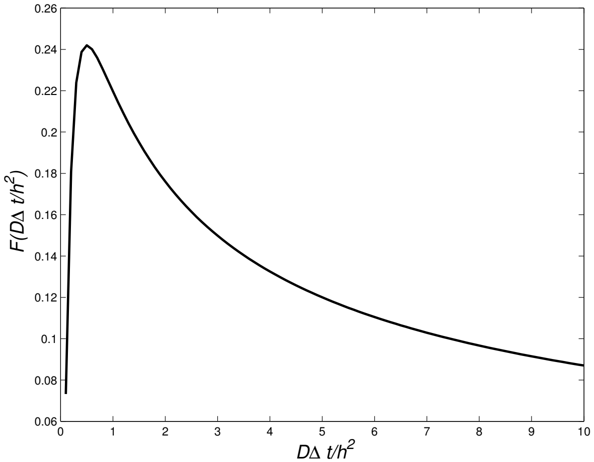


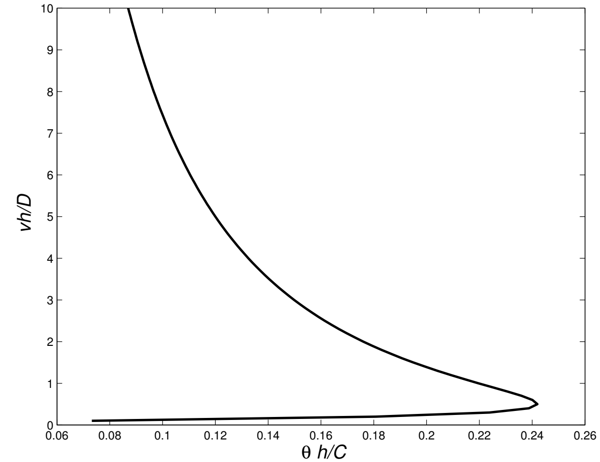
Fire-Diffuse-Fire-IV

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, θ is too large, or C is too small.)

With Recovery

Including recovery variables

$$\frac{\partial v}{\partial t} = D\frac{\partial^2 v}{\partial x^2} + f(v,w), \qquad \frac{\partial w}{\partial t} = g(v,w)$$

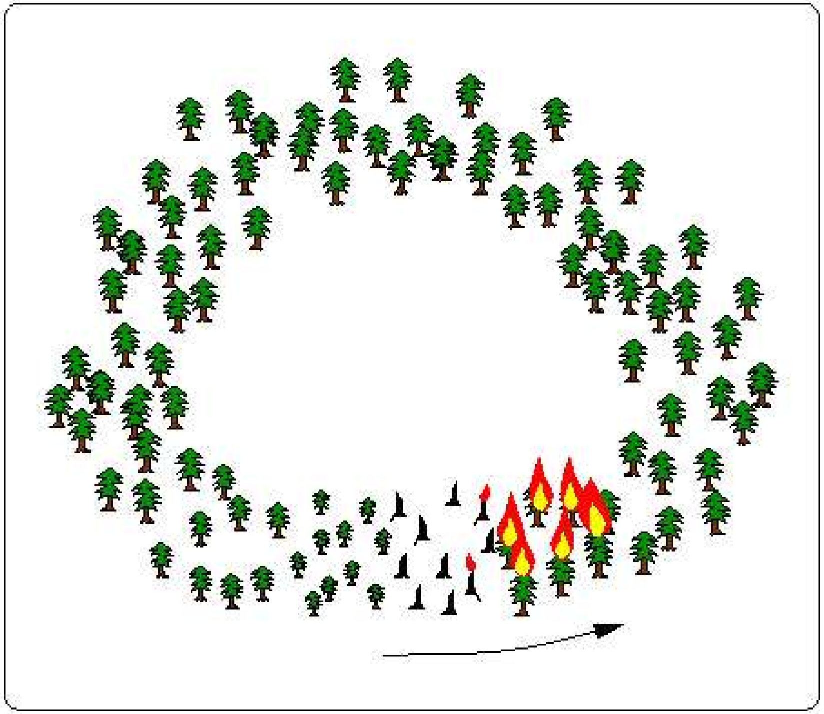
Solitary Pulse

Periodic Waves

Skipped Beats

On a Ring

Periodic Ring



Wolff Parkinson White