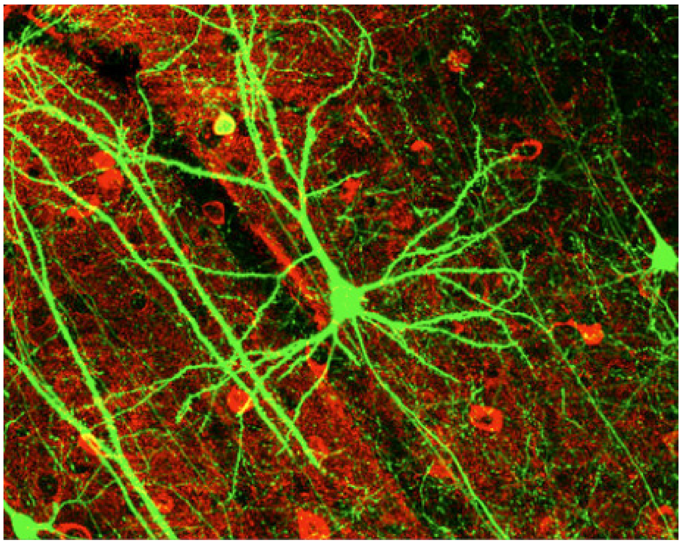
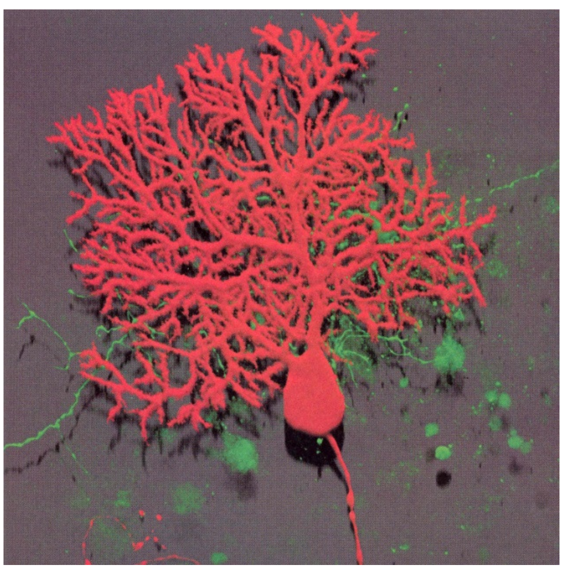
Neuronal Cable Theory on Dendritic Trees

Jon Bell

UMBC



(Pyramidal cell from mouse cortex; by Santiago Ramon)



(Purkinje cells, fluorenscent dyed; Technology Review, Dec. 2009)

Talk Outline

Introduce cable theory on metric tree graph: simple dynamics

Comparison principle leads to threshold conditions

Traveling wave (front) solutions and bounds on wave speed

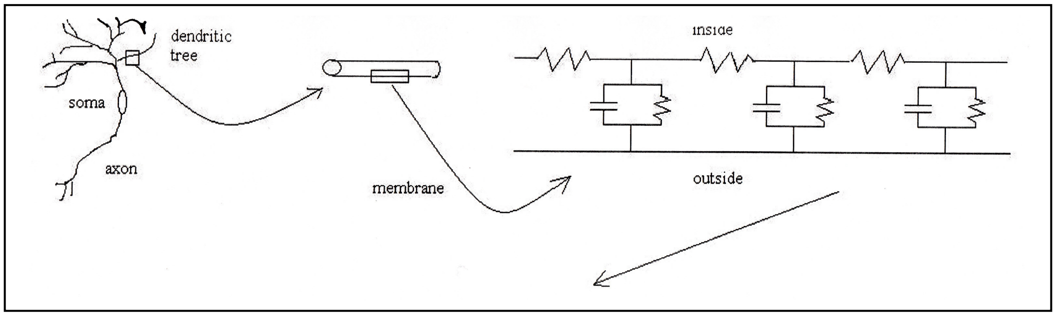
Conduction block on a star graph

Initial consideration of relevant systems on tree graph

Propagation and Conduction Block

Inverse problem: recovering a conduction parameter on a branch and extending approach to a tree graph

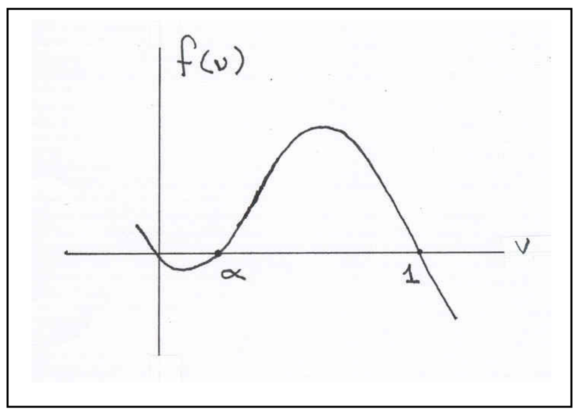
Neuronal Cable Theory: simplest current-voltage relation



$$\frac{a}{2R_i}\frac{\partial^2 u}{\partial x^2} = C_m \frac{\partial u}{\partial t} + I_{ion}(u,\ldots) = C_m \frac{\partial u}{\partial t} + \begin{cases} \sum_{ion-j} g_j(\underline{w})(u - E_j) \\ \dfrac{u}{R_m} \end{cases}$$

Example dynamics for this talk: bistable equation

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



$$H_f := \begin{cases} f \in C^1[0,A] & A > 1 \\ f(0) = f(1) = 0 & \\ f(u) < 0 & for \quad 0 < u < \alpha \\ f(u) > 0 & for \quad \alpha < u < 1 \\ \int_0^1 f(s)ds > 0 & \end{cases}$$

$\Omega = E \cup V$

$E = \{e_1, e_2, ..., e_N\}, V = \{v_{1,} v_2, ..., v_M\}$

$\partial\Omega = \{v \in V \mid index(v) = 1\} = \{\gamma_1, \gamma_2, ..., \gamma_m\}$

$V \setminus \partial\Omega = \{v \in V \mid index(v) > 2\}$

$\Omega =$ metric graph if every edge $e_j \in E$ is identified with an interval of the real line with positive length ℓ_j.

$\Omega =$ tree graph if there are no cycles.

Problem: (1) $\dfrac{\partial u}{\partial t} = r\dfrac{\partial^2 u}{\partial x^2} + f(u)$ on $\{\Omega \setminus V\} \times (0, T)$

(2) $u = 0$ on $\Omega \times \{0\}$

(3) $\sum_{j, e_j \sim v} c_j \partial u_j(v, t) = 0$ for $v \in V \setminus \{\gamma_1\}$ (Kirchhoff-Neumann)

u is continuous at v. ($c_j \propto r_j^2$)

(4) $-\partial u_1(\gamma_1, t) = I(t) > 0$ for $t \in [0, T]$

$\Omega^T = \Omega \times [0, T], \quad \Omega^0 = \cup_j e_j \times (0, T]$

Proposition: Let $f_1 \in C^1(\Re)$, $f_2 \in C(\Re)$, and $f_1(u) \geq f_2(u)$ on $\Re$. Assume there are constants α_0, ε_0 such that $\dot{f}_1(u) < \alpha_0 - \varepsilon_0$. Suppose $u, v \in C(\Omega^T) \cap C^{2,1}(\Omega^0)$ such that the following are satisfied for $t \in (0, T]$, for any $T > 0$:

(i) $u_{jt} - r_j u_{jxx} - f_1(u_j) \geq v_{jt} - r_j v_{jxx} - f_2(v_j)$ in $\Omega_j^T = e_j \times (0, T], \quad j = 1, ..., N$

(ii) $u_j \geq v_j \quad on \quad e_j \times \{0\}$

(iii) $K(u, t; \gamma) \geq K(v, t; \gamma)$ for all $\gamma \in V$

Then $u \geq v$ in Ω^T.

Threshold Behavior

Assume

H_{f1}: There exists $u_0, f_0 > 0$ such that for $0 \le u \le u_0$,

$f(u) \le -f_0 u$.

From the comparison principle,

Theorem: f satisfies H_f, H_{f1}; let $u \in Z_T := C(\Omega^T) \cap C^{2,1}(\Omega^{oT})$ satisfy, for any $T > 0$, and $t \in (0, T]$,

(1) $u_{jt} = r_j u_{jxx} + f(u_j) \quad in \quad \Omega_{jT}$

(2) $-u_{1x}(\gamma_0, t) = I(t) = \begin{cases} I_0 & for \quad 0 < t < t_0 \\ I_1 e^{-\delta(t-t_0)} & for \quad t \ge t_0 \end{cases}$

(3) $K(u,t;\gamma) = 0 \quad for \quad \gamma \in V \setminus \{\gamma_0\}$

(4) $u_j = 0 \quad in \quad \Omega_{j0} = e_j \times \{0\}$.

Here $I_0 \ge I_1 > 0, \quad 0 < \delta < f_0$. Then $\lim_{t\to\infty} u_j(x,t) = 0$ for all $x \in e_j$, all $j = 1,\ldots,N$.

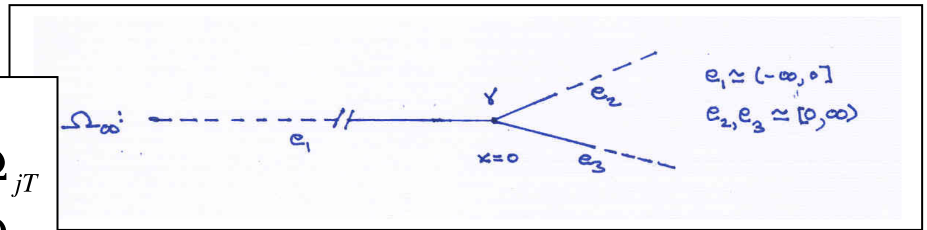
Assume

H_{f2}: for some $f_b > 0$, $f(u) \ge -f_b u$ for $u \ge 0$.

Theorem: Let f satisfies H_f, H_{f2} . Let $u \in Z_T$ solve (1)-(4) with $I(t)$ replaced by $\mu I^*(t)$, where $I^*(t) \ge 0$, I^* not identically zero. Then there exists a μ_0 such that if $\mu > \mu_0$, for each j, $u_j(x,t) \ge w_j(x,t)$ and $\lim_{t\to\infty} w_j(x,t) = 1$.

Bounds on the Speed of Propagation: IVP example

Consider the problem in $\Omega_\infty \times (0,\infty)$:



(IVP) =

$$\begin{cases} u_{jt} = r_j u_{jxx} + f(u_j) & in \quad \Omega_{jT} \\ u_j = \phi_j & in \quad \Omega_{j0} \\ K(u,t;\gamma) = 0 & for \quad t > 0 \end{cases}$$

Assume u is a solution to (IVP) such that

(*) $\lim_{t\to\infty} u_j = 1$ in $\Omega_\infty \times (0,\infty)$

Write $f(u) = f'(0)u + g(u) = -\alpha u + g(u)$, g is smooth, $g(u) = O(u^2)$ as $u \to 0$. $\sigma := \sup_{0<u<1}\{g(u)/u\} > 0$.

$$\mathcal{L}u_j := u_{jt} - r_j u_{jxx} + \alpha u_j - \sigma u_j = g(u_j) - \sigma u_j \le 0 \quad .$$

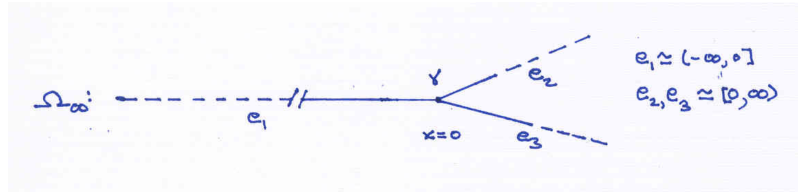
Assume $0 \le \phi_j \le 1, \quad j = 1,2,3$. Then (by another comparison argument) $0 \le u_j \le 1$.

Theorem: Suppose u is a solution to (IVP) satisfying (*). Let ϕ have bounded $\operatorname{supp}\phi \subset e_1$. If $\theta > \bar{\theta} := 2\sigma/\sqrt{\alpha+\sigma}$, then for each j, each $x \in e_j$,

$$\lim_{t\to\infty} u_j(x + \theta t, t) = 0 \quad .$$

Theorem: Suppose (IVP) admits a positive steady state solution $s(x)$ for $a \le x \le b < 0$, with $s(a) = s(b) = 0$. Suppose the only nonnegative global steady state τ of (IVP) with $\tau_1(x) \ge s(x)$ on $[a,b]$ is $\tau \equiv 1$. Let u be a solution to (IVP) with $\phi_1(x) \ge s(x)$ on $[a,b]$. Then there is a $\underline{\theta} > 0$ such that for $0 < \theta < \underline{\theta}$, for any x, any $\varepsilon > 0$, there is a $T > 0$ such that for $t > T$, $u_j(x + \theta \cdot t, t) \ge 1 - \varepsilon, \quad j = 1,2,3$.

Traveling Wave Fronts



Single branch e_1: $u_1(x,t) = \varphi_1(z)$, $z = x - \theta_1 t$: $r_1\ddot{\varphi}_1 + \theta_1\dot{\varphi}_1 + f(\varphi_1) = 0$

$$\begin{cases} \dot{\varphi}_1 = \psi \\ \dot{\psi} = -\dfrac{1}{r_1}\left(\theta_1\psi + f(\varphi_1)\right) \\ \lim\limits_{z\to-\infty}\varphi(z) = 1, \lim\limits_{z\to\infty}\varphi(z) = 0 \end{cases}$$

$$f(\varphi) = \varphi(1-\varphi)(\varphi-\alpha), \alpha \in (0,1/2)$$

$$\theta^* = \sqrt{2r_1}\left(\frac{1}{2} - \alpha\right)$$

$$\varphi(z) = \frac{1}{1 + e^{z/\sqrt{2r_1}}}$$

There exists a unique $\theta_1 = \theta^* > 0$ such that

There is trajectory $(\varphi_1, \psi) : (1,0) \to (0,0)$.

(If l_1 = finite length, $\varphi_1(z)$ is restricted to $z + \theta_1 t \in [0, l_1]$)

For star graph Ω_∞, continuity at $\gamma \in V_r$ implies $\varphi_1(-\theta_1 t) = \varphi_j(-\theta_j t)$, j = 2,3

$$\frac{\theta_1}{\theta_j} = \frac{\sqrt{r_1}}{\sqrt{r_j}} \qquad j = 2,3$$

$z = -\theta_2 t$, $\varphi_2(z) = \varphi_1(\dfrac{\theta_1}{\theta_2}z)$; similarly, $\varphi_3(z) = \varphi_1(\dfrac{\theta_1}{\theta_3}z)$. So TWF solution for Ω_∞

determined by $\varphi_1(\cdot)$, θ_1, with $\theta_j = \theta_1\sqrt{r_j / r_1}$.

By KN at $\gamma \in V_r$, $u_{jx}(\gamma, t) = (\theta_1/\theta_j)\dot{\varphi}_1(\theta_1 z/\theta_j)$, which implies

$$c_1 u_{1x} = c_2 u_{2x} + c_3 u_{3x} \Rightarrow c_1\dot{\varphi}_1 = c_2\dot{\varphi}_2 + c_3\dot{\varphi}_3 \Rightarrow c_1 = c_2\sqrt{\frac{r_1}{r_2}} + c_3\sqrt{\frac{r_1}{r_3}} \Rightarrow$$

$$\left(c_j \propto r_j^2\right) \Rightarrow \; r_1^{3/2} = r_2^{3/2} + r_3^{3/2}$$

Rall's equivalent cylinder condition for eliminating reflections
(Rall, 1962)

Conduction Block

Idea: TWF $u_1 = \varphi_1(z) \in (0,1)$ moving left-to-right, speed $\theta_1 > 0$

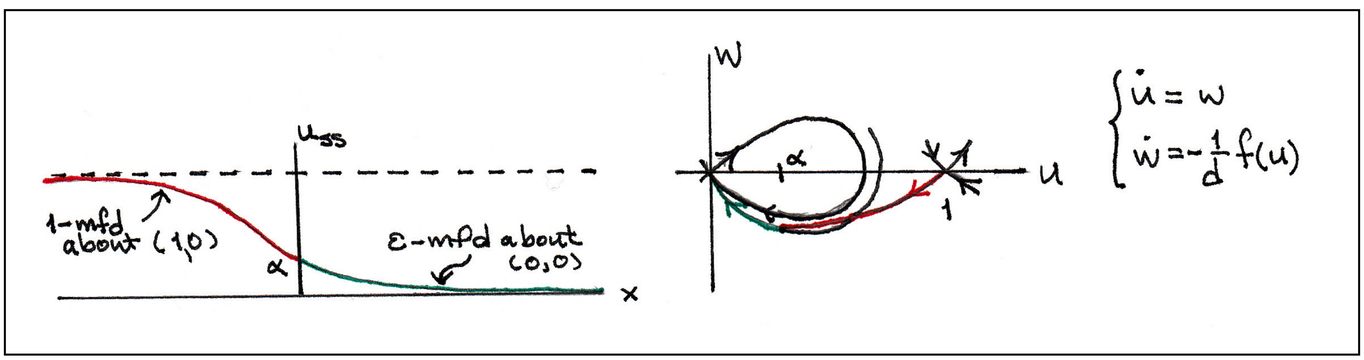
Construct a steady state solution $u_{ss}(x)$, with $\lim_{x \to -\infty} u_{ss}(x) = 1$ in e_1, and in a neighborhood of $x = 0$, $\lim_{x \to \infty} u_{ss}(x) = 0$ along e_2 and e_3. If $u(x,0) \le u_{ss}(x)$, $u = \varphi_1(z)$ will be blocked from propagating along branches away from γ.

Rescale $r_1 = 1$: $K(u,t;\gamma) = u_{1x}(0-,t) - r_2^2 u_{2x}(0+,t) - r_3^2 u_{3x}(0+,t)$

Let $z = \begin{cases} x & for \quad x \in e_1 \\ x / r_2^2 & for \quad x \in e_2 \\ x / r_3^2 & for \quad x \in e_3 \end{cases}$

$u_{jt} = d(z) u_{jzz} + f(u_j), \quad j = 1,2,3 \qquad K(u,t;\gamma) = u_{1z}(0-,t) - u_{2z}(0+,t) - u_{3z}(0+,t)$

$d(z) = \begin{cases} 1 & for \quad z \in e_1 \\ \beta\varepsilon & for \quad z \in e_2 \\ \varepsilon & for \quad z \in e_3 \end{cases} \qquad \beta := (r_3 / r_2)^3, \quad \varepsilon := 1 / r_3^3 < 1$ (the fatter branch)



Systems on Graphs

Example 1: FitzHugh-Nagumo (FHN)

$$\frac{\partial u}{\partial t} = r\frac{\partial^2 u}{\partial x^2} + f(u) - w$$ f satisfies H_f

$$\frac{\partial w}{\partial t} = \sigma u - \eta w$$ $r, \sigma, \eta > 0$ are constants

Example 2: Morris-Lecar (ML)

$$\frac{\partial u}{\partial t} = r\frac{\partial^2 u}{\partial x^2} - m_\infty(u)(u-1) - 2w(u+0.7) - g_l(u+0.36)$$

$$\frac{\partial w}{\partial t} = (w_\infty(u) - w)/\tau(u)$$

m_∞, w_∞ (resp. τ) depend on *u* in a shifted tanh (resp. sech) way

Example 3: More generally

$$\frac{\partial u}{\partial t} = r\frac{\partial^2 u}{\partial x^2} + F(u,W)$$

$$\frac{\partial w_1}{\partial t} = G_1(u,W)$$

……..

$$\frac{\partial w_m}{\partial t} = G_m(u,W)$$

FitzHugh-Nagumo on a Tree Graph

$$\frac{\partial u_j}{\partial t} = r_j \frac{\partial^2 u_j}{\partial x^2} + f(u_j) - w_j \qquad \text{in} \quad \Omega_j^T = e_j \times (0,T]$$

$$\frac{\partial w_j}{\partial t} = \sigma u_j - \eta w_j \qquad \text{and} \quad u_j = 0 = w_j \quad \text{in} \quad e_j \times \{0\}$$

$$K(u,t;\nu) = \sum_{j, e_j \sim \nu} c_j \partial u_j(\nu,t) = 0, \qquad u,\ w \text{ continuous at } \nu \in V \setminus \{\gamma_1\}$$

$$-\partial u_1(\gamma_1, t) = I(t) \qquad \text{for} \quad t \in [0,T]$$

$$f(u) = u(1-u)(u-\alpha), \quad \alpha \in (0, 1/2)$$

$$F(u) = \int_0^u f(s)ds = -u^2\left[\frac{u^2}{4} - \frac{1+\alpha}{3}u + \frac{\alpha}{4}\right] \text{ so } \begin{array}{ll} F(u) < 0 & \text{for} \quad 0 < u < a_1, \\ F(u) > 0 & \text{for} \quad a_1 < u < a_2, \quad \alpha < a_1 < 1 < a_2 \end{array}$$

$$E_1(t) = \sum_{j=1}^N \int_0^{l_j} \left\{ \frac{kr_j}{2}\left(\frac{\partial u_j}{\partial x}\right)^2 - kF(u_j) + \frac{d}{2}(u_j)^2 + \frac{k}{2}(u_j + w_j)^2 + \frac{K}{2}(u_j^2 + w_j^2) \right\} dx$$

Lemma: There are k, d, K such that, if for some $t_0 \ge 0$, every $j = 1, \ldots, N$, $\sup_{x \in e_j} |u_j(x, t_0)| < \alpha$, $\sqrt{E_1(t_0)} < \alpha$, then $\lim_{t \to \infty} (u_j(x,t), w_j(x,t)) = (0,0)$.

$$E_2(t) = \sum_{j=1}^N \int_0^{l_j} \left\{ \frac{r_j}{2}\left(\frac{\partial u_j}{\partial x}\right)^2 - F(u_j) + BL(u_j, w_j) \right\} dx, \quad BL(u,w) = \frac{1}{2}\left(Au^2 - 2Buw + Cw^2\right)$$

By proper choice of A, B, C, $BL(u_j, w_j) \ge 0$, for a j, and for solution (u,w), $dE_2 / dt \le 0$. Then

Lemma: Assume $\eta^2 \ge \sigma > 0$, and for some $t_0 \ge 0$, $E_2(t_0) < 0$. Then $E_2(t_0) < 0$ for all $t \ge t_0$, and this implies that for every $t \ge t_0$, there is a $k \in \{1, \ldots, N\}$, $x = x_k(t)$ such that $u_k(x_k(t), t) > a_1 > \alpha$.

Conduction and Conduction Block for FHN and ML Systems

Conduction: $\begin{cases} u_t = ru_{xx} + F(u,w) \\ w_t = G(u,w) \end{cases}$ on $\Omega_\infty \times \Re^+$

Single branch e_1: $u_1(x,t) = \varphi_1(z), \quad w_1(x,t) = \psi_1(z), \quad z = x - \theta_1 t$

$\lim\limits_{z\to-\infty}(\varphi_1(z),\psi_1(z)) = \lim\limits_{z\to\infty}(\varphi_1(z),\psi_1(z)) = (u_0,w_0)$, $\quad (u_0,w_0) =$ *rest state*

$$\begin{cases} \dot{\varphi}_1 = \zeta_1 \\ \dot{\zeta}_1 = -\dfrac{1}{r_1}\left(\theta_1\zeta_1 + F(\varphi_1,\psi_1)\right) \\ \dot{\psi}_1 = -\dfrac{1}{\theta_1}G(\varphi_1,\psi_1) \end{cases}$$

On the star graph…same as in scalar case

Continuity gives $\begin{cases} \varphi_j(z) = \varphi_1(\dfrac{\theta_1}{\theta_j}z) \\ \psi_j(z) = \psi_1(\dfrac{\theta_1}{\theta_j}z) \end{cases}$ and $\begin{cases} \theta_j = \theta_1\sqrt{r_j/r_1} \\ j = 2,3 \end{cases}$

KN requires $r_1^{3/2} = r_2^{3/2} + r_3^{3/2}$

Work in Progress: Conduction Block for FHN and ML Systems

No comparison principle, but there is a conditional comparison principle, say for our star graph Ω_∞^T: $BC(\overline{\Omega}_\infty^T) =$bounded, continuous functions on $\Omega_\infty \times [0,T]$, $Nu := u_t - d(x)u_{xx} - F(u,x)$, F smooth

$u_-, u, u_+ \in BC(\overline{\Omega}_\infty^T) \cap C^{2,1}(\Omega_\infty^T)$ such that

a. If $u_- \le u \le u_+ \quad on \quad [0,T] \Rightarrow Nu_- \le Nu \le Nu_+ \quad for \quad t \in (0,T]$

Let U_1= bounded neighborhood of γ (left boundary at $x = \alpha$); $x \in \Omega_{\infty,\alpha} \rightarrow$ $x \in U_1 \quad or \quad x \in e_2 \cup e_3$.

b. $u_- < u < u_+ \quad for \quad x \in \Omega_{\infty,\alpha}, t = 0$

c. $u_- \le u \le u_+ \quad for \quad x = \alpha, t > 0$

d. $K(u_-,t;\gamma) \le K(u,t;\gamma) \le K(u_+,t;\gamma) \quad for \quad t \in [0,T]$

Then $u_-(x,t) < u(x,t) < u_+(x,t) \quad in \quad \Omega_{\infty,\alpha}^T$.

$u(x,0) = \overline{u}(x), \quad w(x,0) = \overline{w}(x)$

$(\overline{u}, \overline{w}) \in V = \{(r,s) \mid r,s \in BC(\Re), s$ is Holder continuous on $\Re$, $(r(x),s(x)) = (0,0)$ for x in a neighborhood of γ and for $x \in e_j, j = 2,3, \|(r,s)\|_{\Omega_\infty^T} \le C \}$

For $(\overline{u}, \overline{w}) \in V$, if $\varphi_1, \varphi_2 \in C(\Omega_\infty \rightarrow \Re)$ are such that $\varphi_1 \le u(\cdot,t;\overline{u}) \le \varphi_2 \quad on \quad \Omega_\infty \quad \forall t \ge 0$, $\{\varphi_1, \varphi_2\}$ = **trap for *V*** (Pauwelussen, 1982). For i.c. $(\overline{u}, \overline{w}) \in V$, a solution is blocked if there is a trap $\{\varphi_1, \varphi_2\}$ for V such that $\|\varphi_j\| \le \rho(\varepsilon), j = 1,2, \quad \rho(\varepsilon) \rightarrow 0 \quad as \quad \varepsilon \rightarrow 0$.

A. Such a trap can be constructed for FHN on Ω_∞

$$u_t = d(x)u_{xx} + u(1-u)(u-a) - w, \quad w_t = \sigma u - \eta w$$

if $\sigma < a\eta$ by generalizing work of Pauwelussen.

B. Such a trap can be constructed for ML on Ω_∞

$$u_t = d(x)u_{xx} + m_\infty(u)(1-u) - 2w(0.7+u) - 0.5(0.36-u), \quad w_t = [w_\infty(u) - w]/\tau(u)$$

$$m_\infty(u) = 0.5\left\{1 + \tanh\left(\frac{u+0.01}{0.15}\right)\right\}, \quad w_\infty(u) = 0.5\left\{1 + \tanh\left(\frac{u-0.1}{0.145}\right)\right\}, \quad \tau(u) = \operatorname{sec}h\left(\frac{u-0.1}{0.29}\right)$$

by generalizing work of Zhou, Bell, 1992.

Inverse Problem: Recover a Spatially-Distributed Conduction Parameter

$$C\frac{\partial v}{\partial t} + g(x)(v - E) = r\frac{\partial^2 v}{\partial x^2} \quad \Rightarrow$$

Problem: $\frac{\partial u}{\partial t} + q(x)u = \frac{\partial^2 u}{\partial x^2}$ in $\{\Omega \setminus V\} \times (0,T)$ (1)

(**KN**) $\sum_{e_j \sim v} \partial u_j(v,t) = 0$ for $v \in V \setminus \partial\Omega$, and $t \in [0,T]$ (2)

$u(\cdot,t)$ is continuous at each vertex, for all $t \in [0,T]$

$\partial u = f$ on $\partial\Omega \times [0,T]$ $\quad f \in F^T := L^2([0,T], R^m)$ (3)

$u|_{t=0} = 0$ in Ω (4)

Response operator for system: $R^T = \{R_{ij}^T\}_{i,j=1}^m$ defined by

$$\left(R^T f\right)(t) = u^f(\cdot,t)_{|\partial\Omega} \qquad f \in F^T := L^2([0,T], R^m)$$

Spectral Data(SD): $\{\lambda_n, \varphi_n \mid \partial\Omega\}$ Let $\varphi = \varphi^f(x,\lambda)$ be the solution to

$L\varphi = -\frac{d^2\varphi}{dx^2} + q(x)\varphi = \lambda\varphi$ in $\{\Omega \setminus V\}$; φ satisfies KN condition at $V \setminus \partial\Omega$, $\partial\varphi(\gamma_j,\lambda) = f_j$, $\gamma_j \in \partial\Omega \rightarrow$ Spectrum $\{\lambda_n\}$ is real, discrete,

$\{\varphi_n\} =$ ON basis in $L^2(\Omega)$

IP: Recover $q(x)$ from the response operator $R^T = \{R_{ij}^T\}_{i,j=1}^m$

R^T, $\forall T > 0$ $\leftrightarrow$ Fourier-Laplace transform $\leftrightarrow$ $M(\lambda)$

Titchmarsh-Weyl (TW) matrix function: $\varphi^f\,|_{\partial\Omega} = M(\lambda) f$

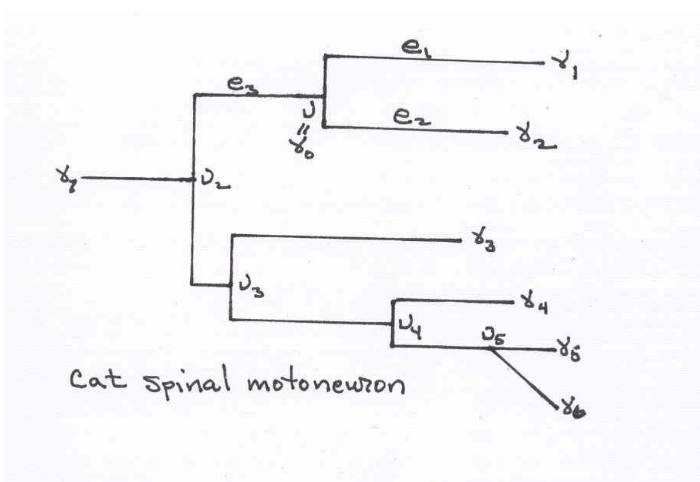
$$\varphi^f(x,\lambda) = \sum_{n=1}^{\infty} \frac{< f, \varphi_n\,|_{\partial\Omega} >}{\lambda_n - \lambda} \varphi_n(x) \quad \rightarrow$$

$$M(\lambda) = \left(M_{ij}(\lambda)\right), \quad M_{ij}(\lambda) = \sum_{n \geq 1} \frac{\varphi_n(\gamma_i)\varphi_n(\gamma_j)}{\lambda_n - \lambda}$$

Tree Graph Algorithm: Using $M(\lambda)$ and R^T

Idea: Use boundary data TW-function to determine q on boundary edges, then prune tree to smaller tree, recomputed $M(\lambda)$ for the smaller tree, and continue to "prune" edges until have IP on single interval.

(Single edge case theory in Avdonin, Bell, 2012)



Suppose conductance already found on e_1, e_2. Denote $\tilde{M}(\lambda)$ the M matrix for reduced graph $\tilde{\Omega} = \Omega \setminus \{e_1, e_2\}$. Rename $\nu = \gamma_0$ the "new" boundary vertex for $\tilde{\Omega}$. $\tilde{M}_{i0}$, $\tilde{M}_{0i}$, $\tilde{M}_{00}$ are matrix entries related to $\nu = \gamma_0$. Other entries $\tilde{M}_{ij}$ are the same as the corresponding M_{ij} of the original matrix M (for Ω).

These slides are on my website at the bottom of the page at

www.math.umbc.edu/~jbell/recent_presentation

under the title

Neuronal Cable Theory on Dendritic Trees