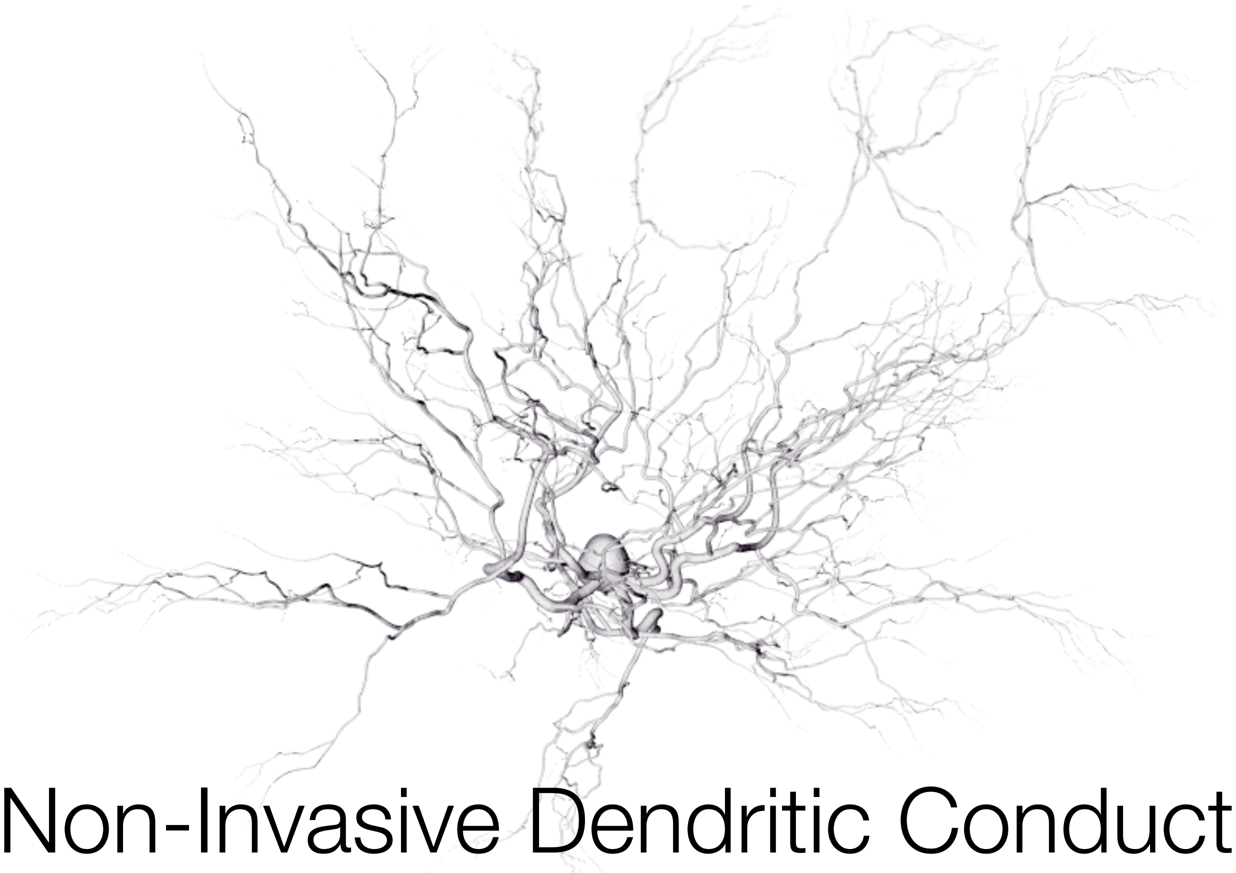
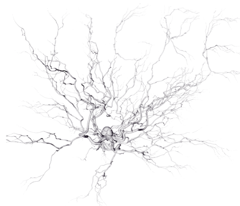


Non-Invasive Dendritic Conductance Recovery: A Spectral Method

Ryan George

July 14, 2010

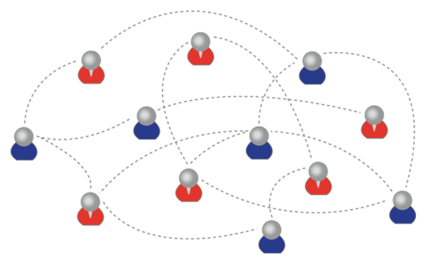
The defining feature of neural systems is plasticity.



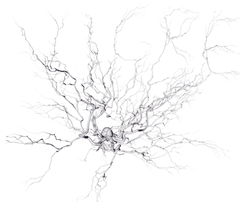
The defining feature of neural systems is plasticity.

Network

Neurotransmitters sent at synapses



synaptic plasticity



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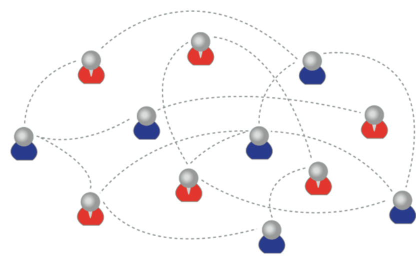
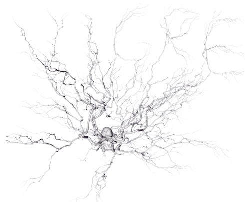


synaptic plasticity

Individual

Current passed along membrane

excitability



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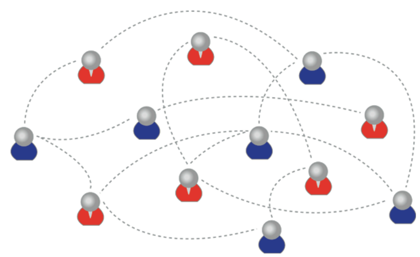
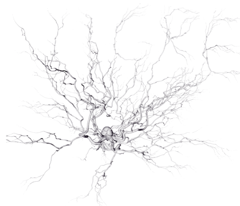


synaptic plasticity

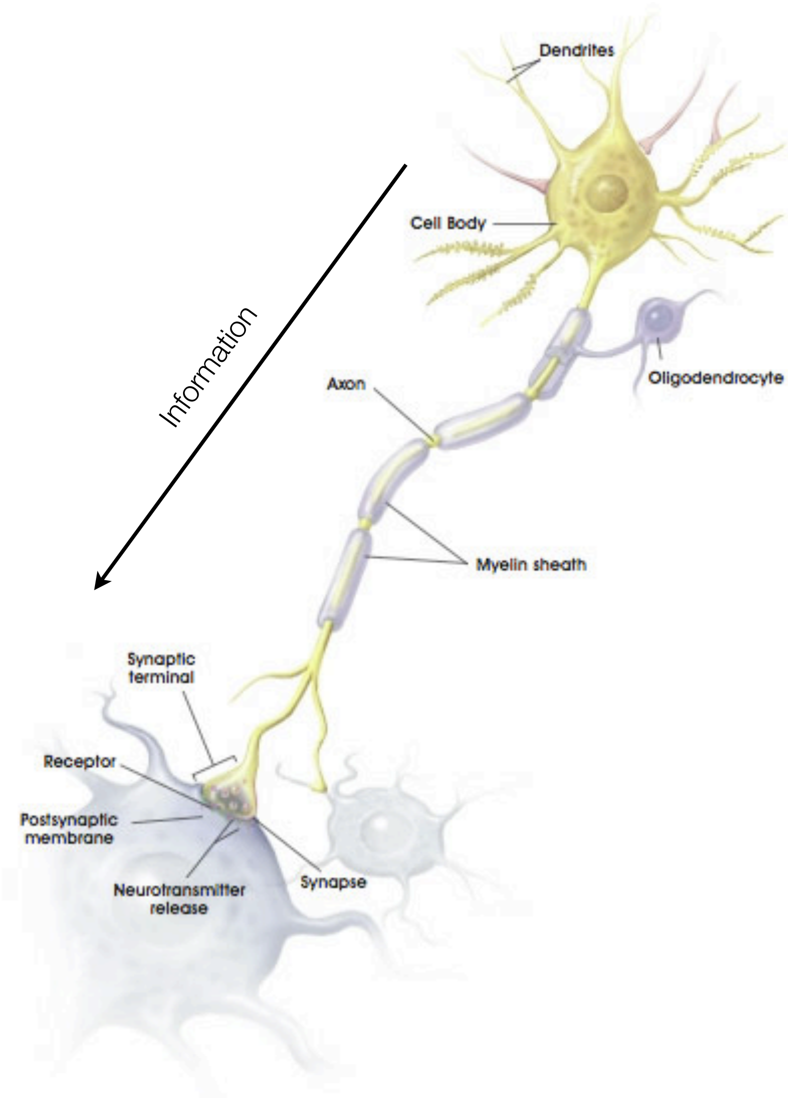
Internal

Current passed along membrane

excitability



Neuronal Structure

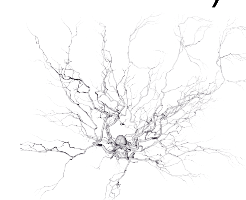


Our interest: dendrite ion channels, "conductance"

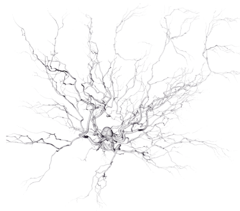
Conductance affects excitability

Non-uniform distribution

- Voltage Clamp (Hoffman et al.)
- Electron Microscopy (Lorincz et al.)

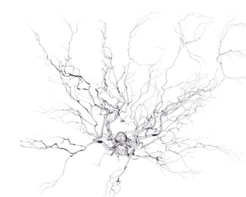


We want a non-invasive method for recovering the distribution of ion channels along a dendrite.



We want a non-invasive method for recovering the distribution of ion channels along a dendrite.

"non-invasive": only stimulating and recording voltage from the soma

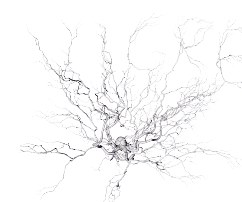


Overview

1. The Cable Equation

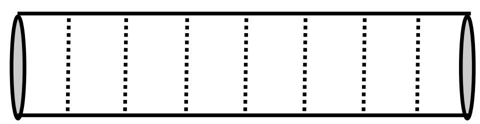
2. Dirichlet Series and Conductance Recovery

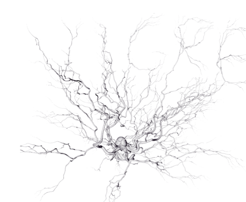
3. Expansion to trees



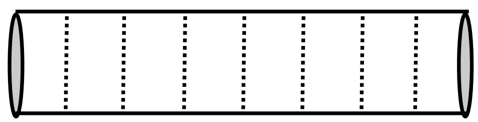
Modeling the Dendrite

Modeling the Dendrite



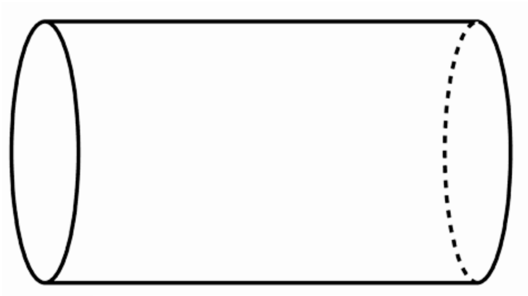


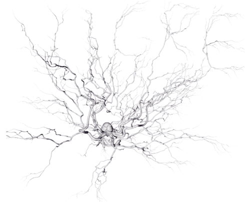
Modeling the Dendrite



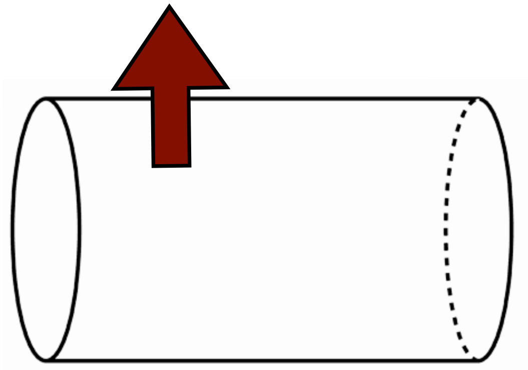
Transmembrane potential $v(x,t)$

Modeling the Dendrite: Current Balance



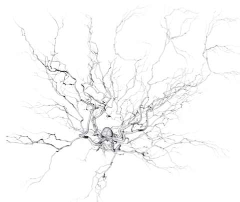


Modeling the Dendrite: Current Balance

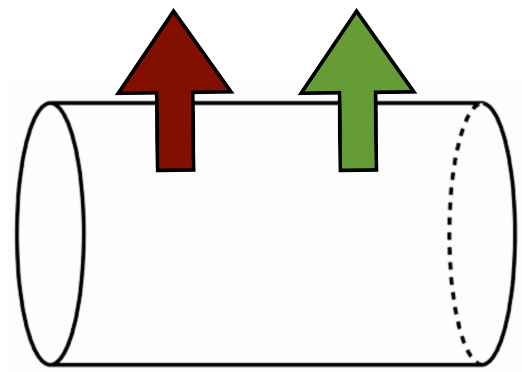


$$C_m \frac{\partial v}{\partial t}(x,t)$$

capacitive current



Modeling the Dendrite: Current Balance

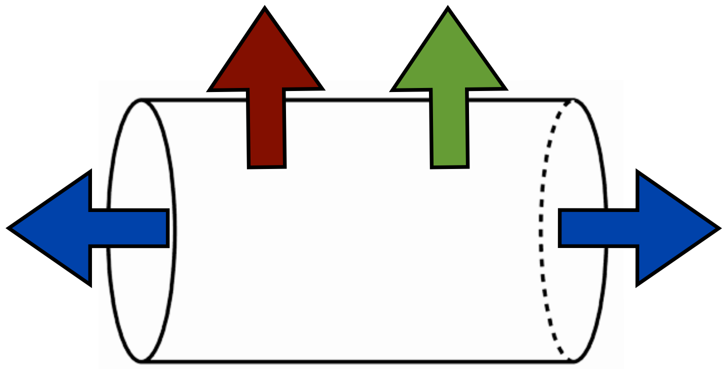


$$C_m \frac{\partial v}{\partial t}(x,t) + g_L(x)v(x,t)$$

capacitive current

leakage current

Modeling the Dendrite: Current Balance

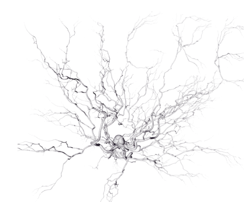


$$C_m \frac{\partial v}{\partial t}(x,t) + g_L(x)v(x,t) - \frac{a}{2R_a}\frac{\partial^2 v}{\partial x^2}(x,t) = 0$$

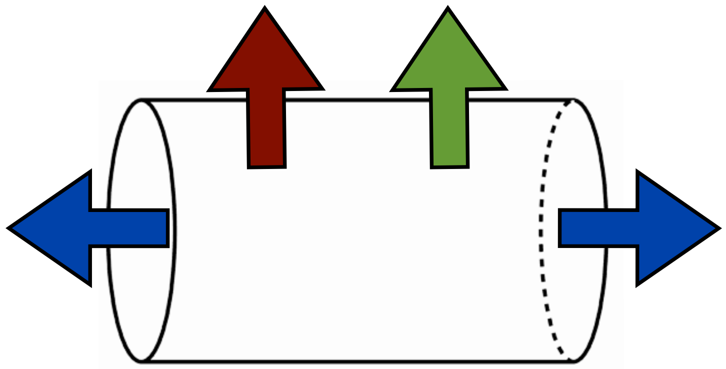
capacitive current

leakage current

axial current



Modeling the Dendrite: Current Balance



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capacitive current

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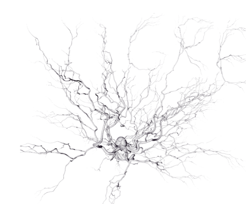


The Cable Equation

$$C_m \frac{\partial v}{\partial t}(x,t) + g_L(x) v(x,t) - \frac{a}{2R_a}\frac{\partial^2 v}{\partial x^2}(x,t) = 0$$

Boundary Conditions:

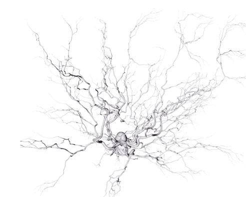
$$\frac{\partial v}{\partial x}(0,t) = -\frac{R_a}{\pi a^2} I_{\text{stim}}(t)$$

$$\frac{\partial v}{\partial x}(\ell,t) = 0$$

$$v(0,t) = v_{\text{obs}}(t)$$

Assume C_m, R_a, a known.

Seek $g_L(x)$.



The Eigenproblem

Separation of Variables: $v(x,t) = \sum_{n=0}^{\infty} q_n(x) p_n(t)$

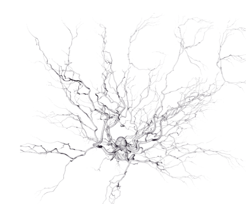
The space-dependent part must satisfy:

$$\frac{a}{2R_a} q_n''(x) = q_n(x)\left(\vartheta_n + g_L(x)\right)$$

$$q_n'(0) = q_n'(\ell) = 0$$

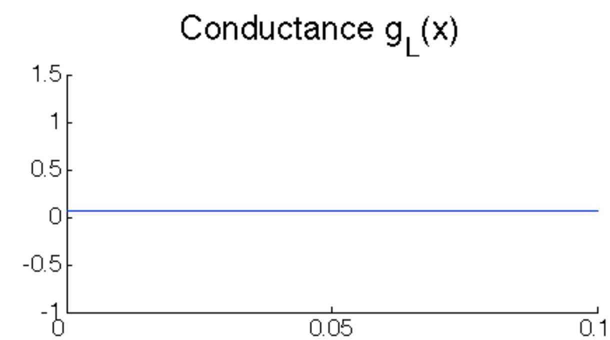
These are orthogonal in the sense:

$$\int_0^{\ell} q_m(x) q_n(x) \mathrm{d}x = \delta_{mn}$$



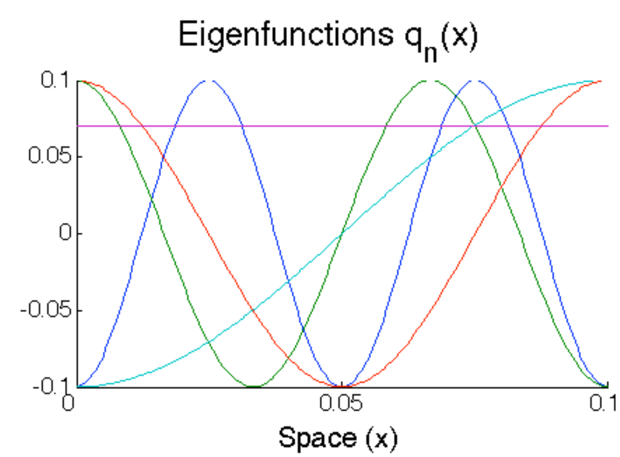
The Eigenfunctions

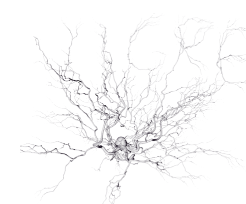
When $g_L(x) = g_0$,



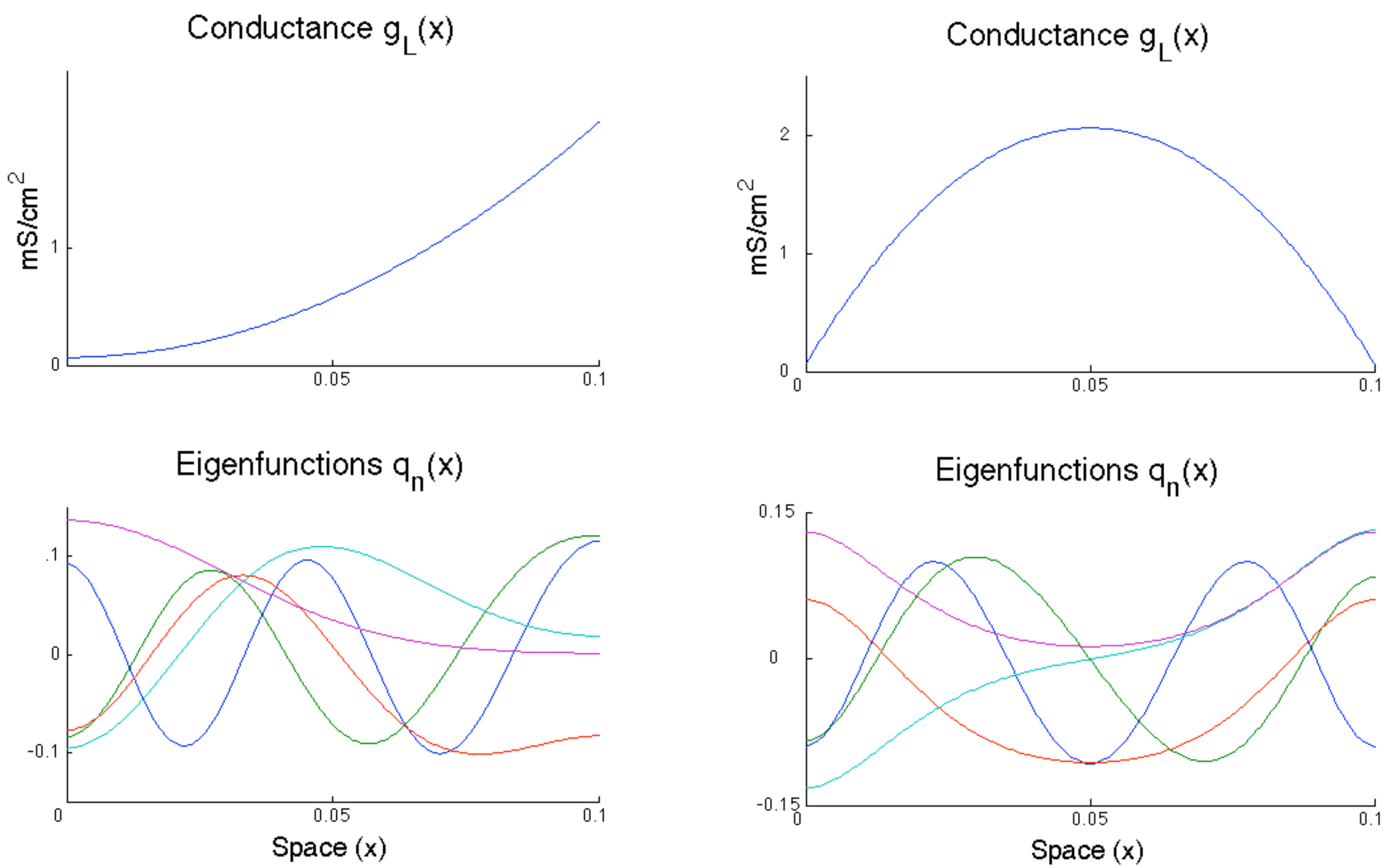
$$\vartheta_n = -\frac{an^2\pi^2}{2R_a\ell^2} - g_0$$

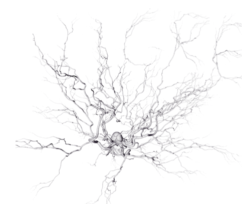
$$q_n(x) = \cos(n\pi x/\ell)$$





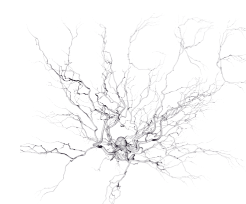
Examples of Eigenfunctions





Sketch of Time-Dependent Portion

Recall: $$v(x,t) = \sum_{n=0}^{\infty} q_n(x) p_n(t)$$

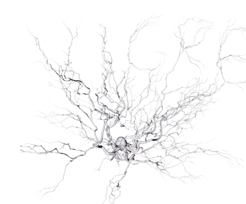


Sketch of Time-Dependent Portion

Recall: $$v(x,t) = \sum_{n=0}^{\infty} q_n(x) p_n(t)$$

Use orthogonality of q:

$$\int_0^l v(x,t) q_n(x) dx = p_n(t) \left(\int_0^l q_n(x) q_n(x) dx \right) = p_n(t)$$



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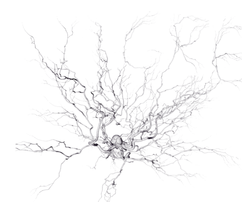
Differentiate and Substitute:

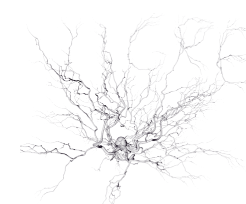
$$\begin{aligned} p_n'(t) &= \int_0^l \frac{\partial v}{\partial t}(x,t)q_n(x)dx \\ &= \int_0^l \frac{1}{C_m}\left(\frac{a}{2R_a}\frac{\partial^2 v}{\partial x^2} - g_L(x)v\right)q_n(x)dx \end{aligned}$$



Sketch of Time-Dependent Portion

Integrate by parts (not shown):

$$\int_0^{l_i} \frac{\partial^2 v}{\partial x^2}(x,t) q_n(x) dx = q_n(0) R_2 I_{stim}(t)/(\pi a^2) + \int_0^{l} q_n''(x) v(x,t) dx$$



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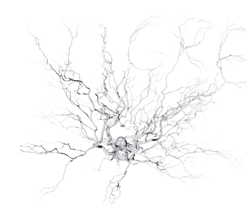
Use the identity:

$$\frac{a_i}{2R_a} \int_0^l q_n(x) q_m''(x) dx - \int_0^l q_n(x) q_m(x) g_L(x) dx - \theta_n \int_0^l q_n(x) q_m(x) dx = 0$$



Sketch of Time-Dependent Portion

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$$\int_0^{l_i} \frac{\partial^2 v}{\partial x^2}(x,t) q_n(x) dx = q_n(0) R_2 I_{stim}(t)/(\pi a^2) + \int_0^l q_n''(x) v(x,t) dx$$

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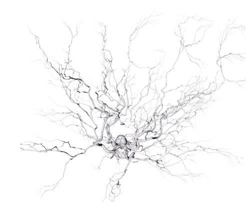
Arrive at:

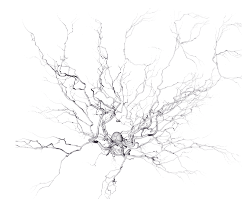
$$C_m p_t'(t) - \vartheta_n p(t) = q_n(0) I_{stim}(t)/(2\pi a)$$



General Solution

Solution to the time-dependent portion:

$$p_n(t) = \frac{q_n(0)}{2\pi a C_m} \int_0^t I_{stim}(s) e^{(t-s)\vartheta_n} ds$$



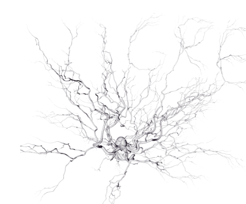
General Solution

Solution to the time-dependent portion:

$$p_n(t) = \frac{q_n(0)}{2\pi a C_m} \int_0^t I_{stim}(s) e^{(t-s)\vartheta_n} ds$$

Solution of cable equation:

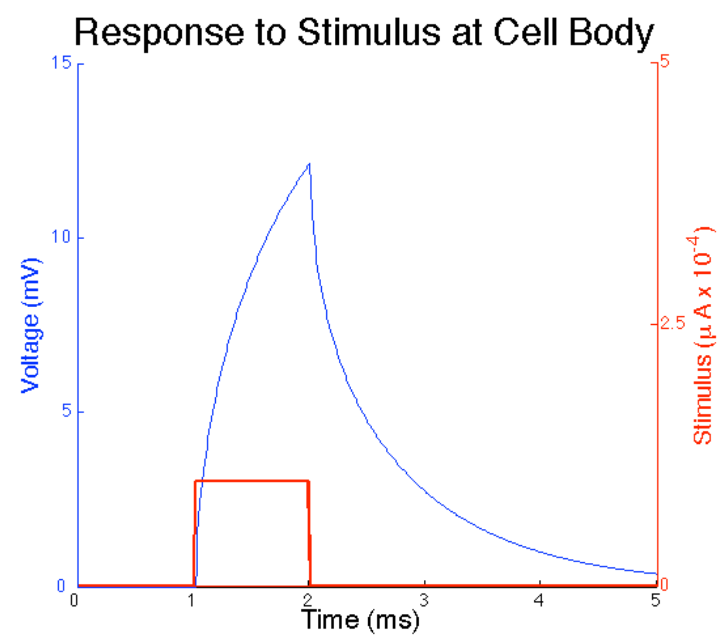
$$v(x,t) = \sum_{n=0}^{\infty} q_n(x) p_n(t) = \sum_{n=0}^{\infty} \frac{q_n(0) q_n(x)}{2 C_m a \pi} \int_0^t I_{stim}(s) e^{(t-s)\theta_n} ds$$



Dirichlet Series

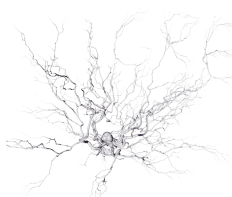
Set $x = 0$. This gives us voltage at the cell body:

$$v(0,t) = \sum_{n=0}^{\infty} \frac{q_n(0)^2}{2C_m a\pi} \int_0^t I_{stim}(s) e^{(t-s)\theta_n} ds$$



This solution is a Dirichlet series dependent on $\vartheta_n, q_n(0)^2$

(eigenvalues, norming constants)



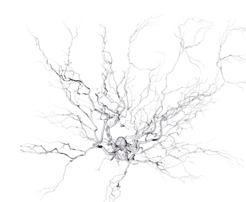
Dirichlet Series

A function has a unique Dirichlet Series representation.

If two representations: $$\sum_{n=1}^{\infty} a_n e^{\vartheta_n t} = v(0,t) = \sum_{n=1}^{\infty} b_n e^{\vartheta_n t}$$

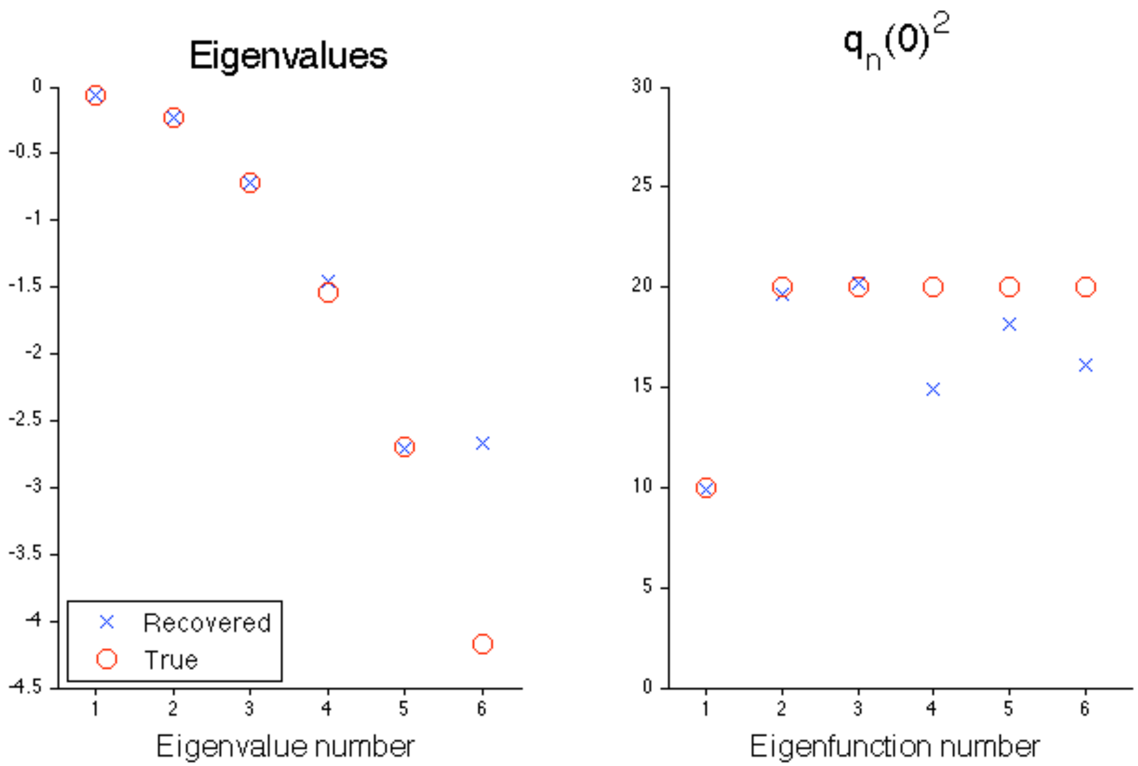
Then $$\sum_{n=1}^{\infty} (b_n - a_n) e^{\vartheta_n t} = 0 \qquad \text{for all } t$$

Thus for given $v(0,t)$ there is exactly one set $\{\vartheta_n, q_n(0)^2\}$.



Numerical Recovery of Eigenvalues

‘Peeling’ - Fit $\{\vartheta_n, q_n(0)^2\}$ to numerical solution.



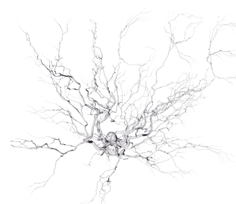
Eigenvalues to Coefficient

Inverse Sturm-Liouville Problem

Borg and Levinson's Theorem:

$$\{\vartheta_n, q_n(0)^2\} \iff g_L(x)$$

We recover conductance from eigenvalues and norming constants.



Method

1. Record (simulate) from soma

$$v(0,t)$$

$$\Downarrow$$

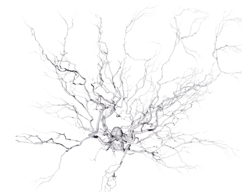
2. Find eigenvalues, norming constants

$$\{\vartheta_n, q_n(0)^2\}$$

$$\Downarrow$$

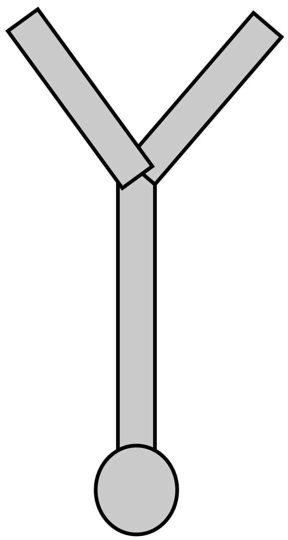
3. Recover Conductance

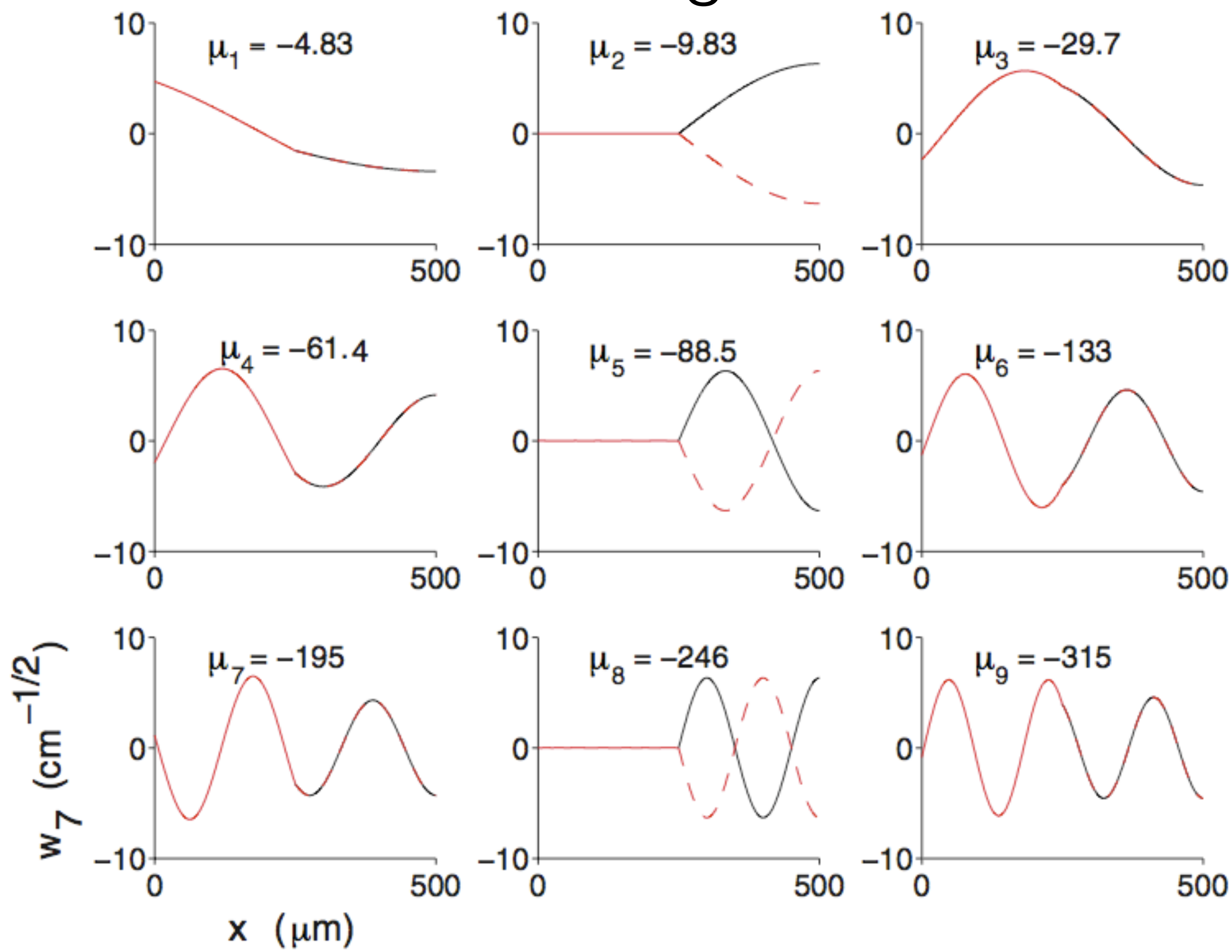
$$g_L(x)$$

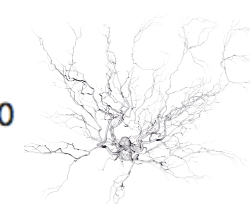


Expansion to Trees

Branched Eigenfunctions

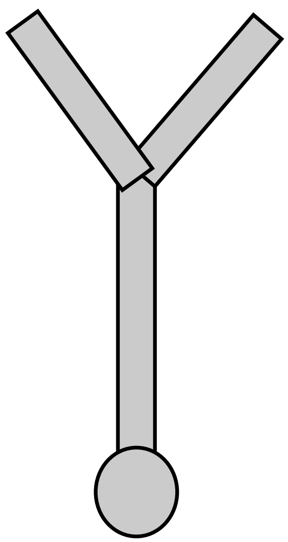


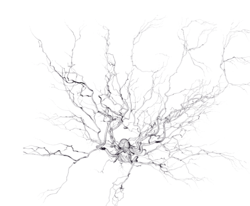




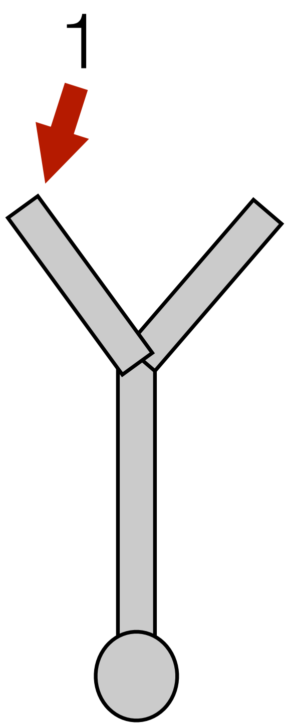
Expansion to Trees

Solution: three Dirichlet series.



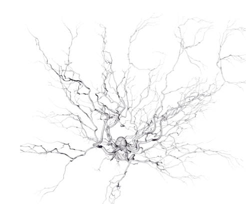


Expansion to Trees

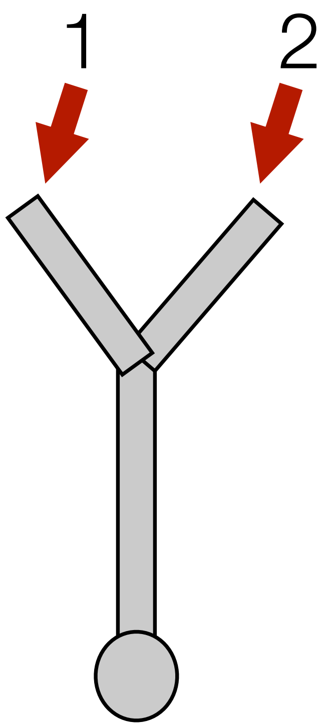


Solution: three Dirichlet series.

$$v_1(0,t) = \sum_{n=0}^{\infty} \frac{q_{n,1}(0)q_{n,3}(\ell_3)}{A_s h} \int_0^t I_{\text{stim}}(s) \exp((t-s)(\vartheta_n))ds$$



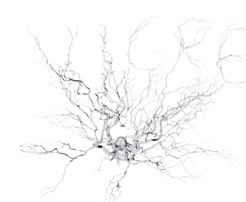
Expansion to Trees



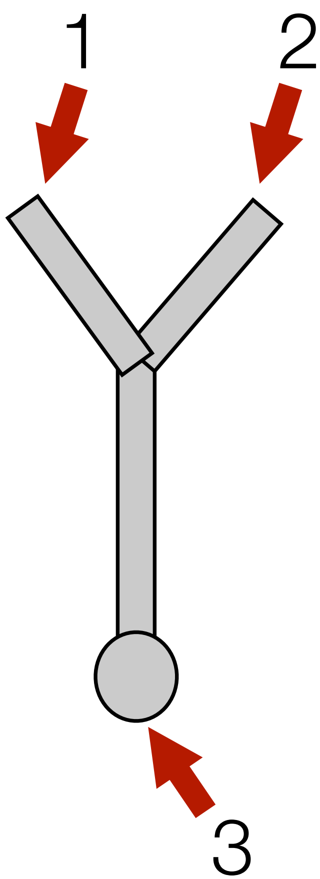
Solution: three Dirichlet series.

$$v_1(0,t) = \sum_{n=0}^{\infty} \frac{q_{n,1}(0) q_{n,3}(\ell_3)}{A_s h} \int_0^t I_{\text{stim}}(s) \exp((t-s)(\vartheta_n)) ds$$

$$v_2(0,t) = \sum_{n=0}^{\infty} \frac{q_{n,2}(0) q_{n,3}(\ell_3)}{A_s h} \int_0^t I_{\text{stim}}(s) \exp((t-s)(\vartheta_n)) ds$$



Expansion to Trees

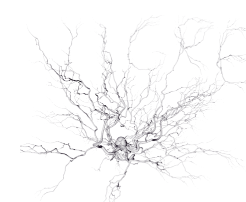


Solution: three Dirichlet series.

$$v_1(0,t) = \sum_{n=0}^{\infty} \frac{q_{n,1}(0)q_{n,3}(\ell_3)}{A_s h} \int_0^t I_{\text{stim}}(s)\exp((t-s)(\vartheta_n))ds$$

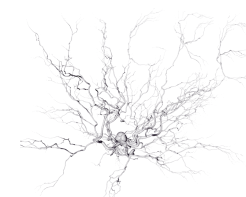
$$v_2(0,t) = \sum_{n=0}^{\infty} \frac{q_{n,2}(0)q_{n,3}(\ell_3)}{A_s h} \int_0^t I_{\text{stim}}(s)\exp((t-s)(\vartheta_n))ds$$

$$v_3(0,t) = \sum_{n=0}^{\infty} \frac{q_{n,3}(\ell_3)^2}{A_s h} \int_0^t I_{\text{stim}}(s)\exp((t-s)(\vartheta_n))ds$$



Conclusion

	Cable:	Tree:
1. Record (simulate) from soma and branches	$v(0,t)$	$v_i(0,t),\ i=1,...,N$
2. Find eigenvalues, eigenfunctions at 0	$\{\vartheta_n, q_n(0)^2\}$	$\{\theta_n, q_{n,1}, ..., q_{n,N}\}$
3. Recover Conductance	$g_L(x)$	$g_L^i(x),\ i=1,...,N$



Conclusion

	Cable:	Tree:
1. Record (simulate) from soma and branches	$v(0,t)$	$v_i(0,t),\ i=1,...,N$
	$\Downarrow$	$\Downarrow$
2. Find eigenvalues, eigenfunctions at 0	$\{\vartheta_n, q_n(0)^2\}$	$\{\theta_n, q_{n,1}, ..., q_{n,N}\}$
	$\Downarrow$	$\Downarrow$
3. Recover Conductance	$g_L(x)$	$g_L^i(x),\ i=1,...,N$

Thank you for your time.