A Study of Sub-threshold Resonant Dendrites under Periodic Stimuli by Jamie Luo

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Motivation

- The dendritic trees of neurons act as complex networks of input branches conducting charge from other neurons to the soma.
- Understanding the response of dendrites to different stimuli has been the primary aim of this project.
- The focus has been on periodic inputs:
Chirp Experiments

- ‘Dendritic Resonance in Rat Neocortical Pyramidal Cells’ (2002) by Daniel Ullich (excerpt below)
- ‘The h Channel Mediates Location Dependence and Plasticity of Intrinsic Phase Response in Rat Hippocampal Neurons’ (2008) by Rishikesh Narayanan and Daniel Johnston

![Diagram of neuron with voltage and current traces]
Model: Quasi-active membrane

- The cell membrane of the is formed by a phospholipid bilayer dotted with ion-channels.
- The passive membrane model corresponds to the RC circuit containing only a resistance and capacitance element.
- Ion channels are incorporated as active non-linear elements ($g_L$).
- We linearise this non-linear circuit about some steady state to find our quasi-active membrane model, equivalent to an RLC circuit, with a resistance $r$ and inductance $L$ replacing the non-linear element ($g_L$).
The spatial component of the model is derived from cable theory.

Key assumption: only consider the variation along the long axis reducing the model from three dimensions to one.

From this one can derive the **standard cable equation**:\
\[
\frac{\partial V}{\partial t} = -\frac{V}{\tau} + D \frac{\partial^2 V}{\partial X^2}
\]

In the form of differential equations the **quasi-active membrane model**:

\[
C \frac{dV}{dt} = -\frac{V}{R} - \sum_{k=1}^{N} I_k + I_{inj}
\]

\[
L_k \frac{dI_k}{dt} = -\tau_k I_k + V
\]

One arrives at the complete system of differential equations by **coupling** the standard cable equation with resonant currents:

\[
\frac{\partial V}{\partial t} = -\frac{V}{\tau} + D \frac{\partial^2 V}{\partial X^2} - \frac{1}{C} \left[ \sum_{k=1}^{N} I_k - I_{inj} \right]
\]

\[
L_k \frac{dI_k}{dt} = -\tau_k I_k + V
\]
Laplace Transform Theory

CIRCUIT
(Differential Equation)

Input Signal → CIRCUIT → Output Signal

L.T. of Input Signal → Laplace transform of CIRCUIT → L.T. of Output Signal

Laplace transform of:

\[ f(\omega) = \int_{0}^{\infty} dte^{-\omega t} f(t) \]
Green’s function Solution

- L.T. of the CIRCUIT:
  \[-V_{xx}(x, \omega) + \gamma^2(\omega)V(x, \omega) = A\]

  \[\gamma^2(\omega) = \frac{1}{D}\left[\frac{1}{\tau} + \omega + \frac{1}{C}\sum_k \frac{1}{\tau_k + \omega L_k}\right]\]

  \[A(x, \omega) = \frac{1}{CD\gamma^2(\omega)}I_{\text{inj}}(x/y(\omega), \omega)\]

- Frequency domain Solution:
  \[V(X, \omega) = \int_0^\infty dYG_\infty(X - Y, \omega)I_{\text{inj}}(Y, \omega)/C\]

  \[G_\infty(X, \omega) = \frac{H_\infty(\gamma(\omega)X)}{D\gamma(\omega)}\]

  \[H_\infty(x) = \frac{e^{-|x|}}{2}\]

- Time domain solution:
  \[V(X,t) = \int_0^t ds \int_{-\infty}^\infty dYG_\infty(X - Y, t-s)I(Y,s)\]
Model Validity

Reconstructed geometry of a rat CA1 hippocampal pyramidal cell (396 branches)

**Dendritic** and **somatic** dual cell recording

Black curves - dendritic and somatic voltage responses from the model
Infinite Branch & a Single Input

- With a single input point the Frequency Domain Solution simplifies to become:

\[ V(X, \omega) = G_\infty(X - Y, \omega)I_{\text{inj}}(Y, \omega)/C \]

- Dimensionless simulations were run with both sine and chirp stimuli on Matlab using the DFT as a substitute for the L.T.

![Graph showing voltage over time for LRC circuit and nonlinear Ih current.](graph.png)
Observations: Resonance

$V(x,t)$ response for $x=0$
Observations: Phase Shift

$V(x,t)$ for $x=0,0.5,1$
Sine Plots

$V(x,t)$ response to a sine input for $x=0, 0.2, ..., 1$

$\mathbf{I}_{\text{inj}}(t) = \sin(\omega t), \; \omega = 2$
Sine Input & Impedance of RLC

Backward shift in $V(x,t)$ $x=0, 0.2, ..., 1$

Forward shift in $V(x,t)$ $x=0, 0.2, ..., 1$

$I_{inj}(t) = \sin(\omega t)$, $\omega = 2$

$I_{inj}(t) = \sin(\omega t)$, $\omega = 5$

No shift in $V(x,t)$ $x=0, 0.2, ..., 1$

$I_{inj}(t) = \sin(\omega t)$, $\omega = 3.1225$

Impedance plot

$z(i\omega) = \frac{1}{\gamma^2(i\omega)}$
Observed that under a sinusoidal input the phase difference between the input current and the voltage response were in phase at a critical frequency:

\[ \omega_c = \sqrt{\frac{L - Cr^2}{CL^2}} \]

Voltage Lead \( \omega < \omega_c \)

Voltage Lag \( \omega > \omega_c \)
Impedance/Transfer Function

- The Greens function is in fact the transfer function of the circuit

\[ V(X, \omega) = G_\infty (X - Y, \omega) I_{n, \in j} (Y, \omega)/C \]

- Theorem: Suppose a linear time invariant system is represented by a stable transfer function \( G(s) \) and the input has the form,

\[ A(sin(\omega t)) \]

then the steady state response has the form,

\[ B(sin(\omega t + \phi)) \]

where,

\[ B = A|G(i\omega)| \quad \& \quad \phi = \arg (G(i\omega)) \]

- Particularly:

\[
\phi = \arg(G(x, i\omega)) = -|x||y(i\omega)|\sin\left(\frac{\theta(\omega)}{2}\right) - \frac{\theta(\omega)}{2}
\]

\[
\theta(\omega) = \arg(y^2(i\omega))
\]
Simulation vs S.S. Solutions

Steady State Fits to $V(x,t)$ for $x=0, 0.2, ..., 1$

BLUE lines are simulated $V(x,t)$, GREEN lines are plots of:

$$A|G(x, i\omega)|\sin (\omega t + \phi)$$
Making a Chirp Envelope?

Attempts to construct a Chirp Envelope

Transience interferes and is often close to the experimental resonant frequency

RED lines are theoretically deduced maximal s.s. responses for the sine stimuli. BLUE lines are $V(x,t)$ plots under a Chirp stimulus for $x = 0, 0.3, 0.7, 1.0$. 
Generalisations & Comments

- Solution only describes the steady state and not the transient response.

- Predicting the profile of the response to a Chirp stimuli on an infinite branch based on analysis of the sine input is non-trivial due to transient effects. Although one can make qualitative statements about the profile of a Chirp response. The inverse problem could make for a useful scientific tool.

- Including more inductive branches in the model, representing more ion channels, should not affect the stability of the transfer function on the infinite branch and neither will designating one end of the branch a closed or open terminal.

- There exists a method for constructing the Green's function for an arbitrary branching structure.

- However the methods for deducing the steady state response are applicable only if the transfer function is stable and determining the stability of these transfer functions is non-trivial.
In the above paper the Green’s function for an arbitrary branching structure was constructed. The dynamics for a branch $i$ of the system are:

$$\frac{\partial V_i}{\partial t} = -\frac{V_i}{\tau} + \frac{\partial^2 V_i}{\partial X^2} - \frac{1}{C} \left[ \sum_{k=1}^{N} I_{k,i} - I_{inj,i} \right]$$

$$L_{k,i} \frac{d I_{k,i}}{dt} = -r_{k,i} I_{k,i} + V_i$$

$$\gamma_i^2(\omega) = \frac{1}{D_i} \left[ \frac{1}{\tau_i} + \omega + \frac{1}{C_i} \sum_{k} \frac{1}{r_{k,i} + \omega L_{k,i}} \right]$$

Branches

Nodes must satisfy continuity of potentials & conservation of current.

Terminals

Open end: $V_i(l_i, t) = 0$

Closed end: $\frac{\partial V_i(X, t)}{\partial X}|_{X=l_i} = 0$
Arbitrary Branching Structure 2

- As with the infinite resonant cable for each branch $i$:
  \[(1 - d_{xx})V_i = A_i\]

- General solution in frequency domain:
  \[V_i(x, \omega) = \sum_j \int_0^{l_j(\omega)} dy H_{ij}(x, y, \omega) A_j(y, \omega)\]

- where $H_{ij}(x, y, \omega)$ satisfies \[(1 - d_{xx})H_{ij}(x, y, \omega) = \delta_{ij} \delta(x - y)\] and the b.c.s.

- $H_{ij}(x, y, \omega)$ can be written in terms of $H_\infty(x) = \frac{e^{-|x|}}{2}$:
  \[H_{ij}(x, y, \omega) = \sum_{\text{trips}} A_{\text{trip}}(\omega) H_\infty(l_{\text{trip}})\]
  \[l_{\text{trip}} = l_{\text{trip}}(x_i, y_j, \omega)\]

- Coefficients of $A_{\text{trip}}(\omega)$
  \[p_k(\omega) = \frac{z_k(\omega)}{\sum_m z_m(\omega)}\]
  \[z_k(\omega) = \frac{\gamma_k(\omega)}{\tau_k}\]
Arbitrary Branching Structure 3

- How extendable is the sinusoid analysis to an arbitrary branching structure?

- Definitely applicable to the following special cases:

  Single infinite or semi-infinite branch

  Any number of semi-infinite branches connected at a single node if their membrane parameters (R, C, r and L) are identical

- Geometries still requiring investigation:

  Finite branches

  Branches with different membrane parameters
Two Semi-Infinite Branches

Two Semi Infinite Branches \( r = [0.5, 1], L = [3/7, 5] \)

\[
\begin{align*}
\mathbf{r} &= [0.5, 0.1] \quad \mathbf{L} = [5, 3/7] \\
\omega_c &= [0.4359, 1.5096]
\end{align*}
\]

Branch Parameters Reversed

\( I_{\text{inj}}(t) = \sin(\omega t), \; \omega = 1.5096 \)
References


• Rishikesh Narayanan and Daniel Johnston: ‘The h Channel Mediates Location Dependence and Plasticity of Intrinsic Phase Response in Rat Hippocampal Neurons’ The Journal of Neuroscience, May 28, 2008