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Towards an Efficient Algorithm for Calculating Membrane Response on Dendrites of Arbitrary Geometries

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Introduction

The brain consists of an extremely complex network of neurons, interconnected by interminable lengths of dendrites and through thousands of synaptic connections. The processing of neural spiking information is thought to be primarily due to the connectivity of neurons, with dendritic geometries and synaptic properties playing a major role. The development of an efficient computational framework for analysis of neuronal dynamics in large networks would therefore be extremely beneficial to our understanding of the computations that are implemented by neural networks and define our life processes.

Motivation

Numerical simulations allow the calculation of dendritic voltage in response to an injected current, on a branching tree of any geometry, by solving the passive cable equation:

$$\frac{\partial V}{\partial t} = D\frac{\partial^2 V}{\partial x^2} - \frac{V}{\tau} + I_{\text{app}}$$

However, numerical simulation is inefficient and thus, does not lend itself to the study of large neural networks, especially when analysing the system's behaviour with changing parameters, such as the chemical or electrical properties of synapses. Analytical solutions for the dynamics of voltage can be found in closed form on an infinite cable in the form of a Green's function.

$$G_{\infty}(x,t) = \frac{1}{\sqrt{4\pi Dt}} e^{-\frac{x^2}{\sqrt{4Dt}}} e^{-\frac{t}{\tau}}$$

Current can be injected at a specific time and location by convolving the Green's function with a term representing the current input, such as a delta or a rectangular pulse function:

$$H(x,t) = \int_0^t \int_{-\infty}^{\infty} G(x-x', t-t')\delta(x'-y)\sigma\Theta(t')\Theta(d-t')\mathrm{d}x'\mathrm{d}t'$$

Building the solution $H(x,t)$ to the passive cable equation with injected square pulse of current of strength σ and duration d at location $x = y$.

Theoretical Framework

It is possible to obtain a solution for the propagation of voltage on a branching structure of nontrivial geometry by adding boundary conditions to the system. The solution to the cable equation on a dendritic tree takes the form of an infinite sum, where each element is one of the possible paths for current to take on the structure.

$$G_{ij}(x,y,t) = \sum_{\text{paths}} A_{\text{path}} G_{\infty}(L_{\text{path}}, t)$$

Path coefficients are a function of the radii of the branches involved, and decrease exponentially with the number of interactions with branching nodes.
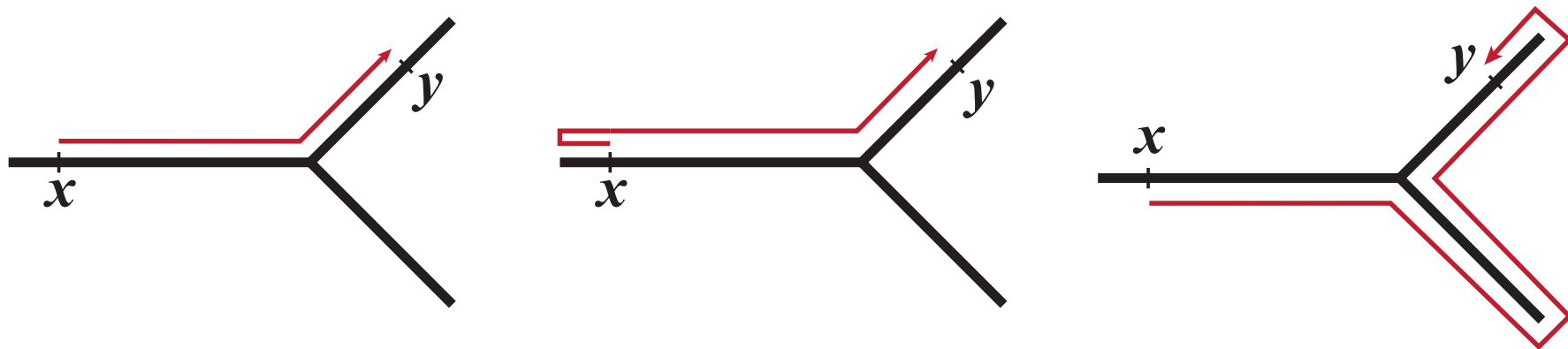

Three possible paths on a simple single-node system.

Any dendritic structure can be uniquely represented as a weighted digraph. Due to their bidirectional edges, there are infinite paths from the source to the target nodes on these trees. Using a heuristic search algorithm, it is possible to efficiently generate a list of simple paths with no repeated nodes or edges, from all pairwise combinations of sources and targets on the graph. From this basis, subpaths in the form of repeat edges and deviations may be added combinatorically to the paths to obtain a full list of paths under a certain threshold in length. In this way, a solution can be rapidly found to within an arbitrary convergence threshold.

Computational Efficiency

We considered a symmetrical system with six equal branches arranged around one central node, a caricature of the starburst amacrine cell, with injection in the form of a square pulse at the origin. Calculations took $0.05s$ on a single 3GHz core, compared with over sixty seconds on the same system using numerical simulation in NEURON.

Results
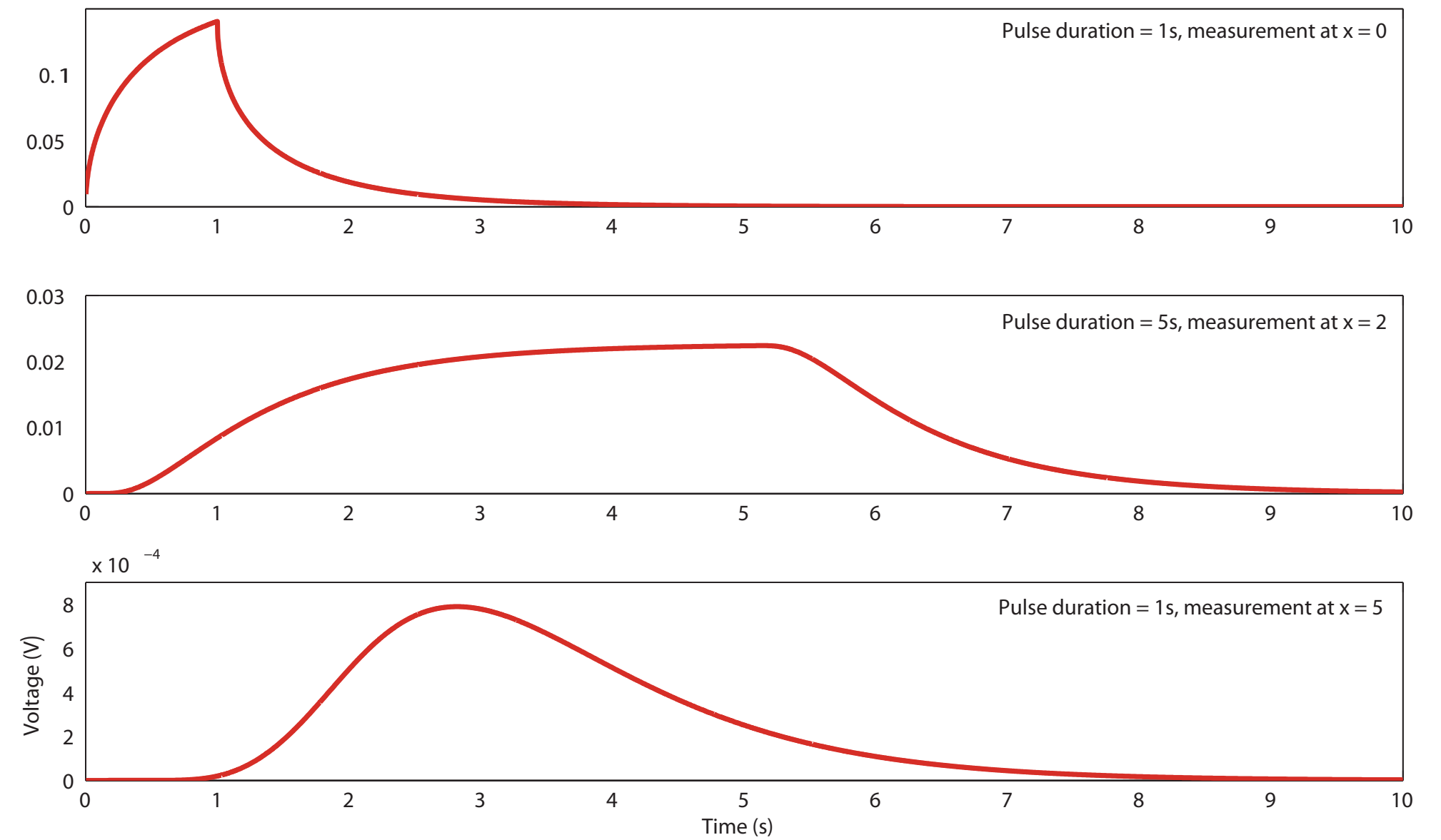
Application : directional selectivity in idealised cells

$$\frac{\partial V_n}{\partial t} = D\frac{\partial^2 V_n}{\partial x^2} - \frac{V_n}{\tau} + I_n(x,t)$$

$$0 \leq x \leq L, \ t > 0$$

Moving light stimulus $\quad t = (n-1)L/c$

Synaptic inhibition at $t = T_{n-1}$ (via threshold process)

The membrane voltage in cell n can be found as

$$V_n(x,t) = \int_0^t \int_0^L G_{0L}(x,x',t-s)I_n(x',s)\mathrm{d}x'\mathrm{d}s$$

where $G_{0L}(x,y,t)$ is the Green's function of a passive cable equation on a finite domain with closed boundary conditions.

$V_n(x,t) = W(x,t,L,c) - H(x,t,L,T_{n-1})$ can be found in closed form.

Ignoring indices and considering $(n-1)L/c - T_{n-1} = \Delta$,
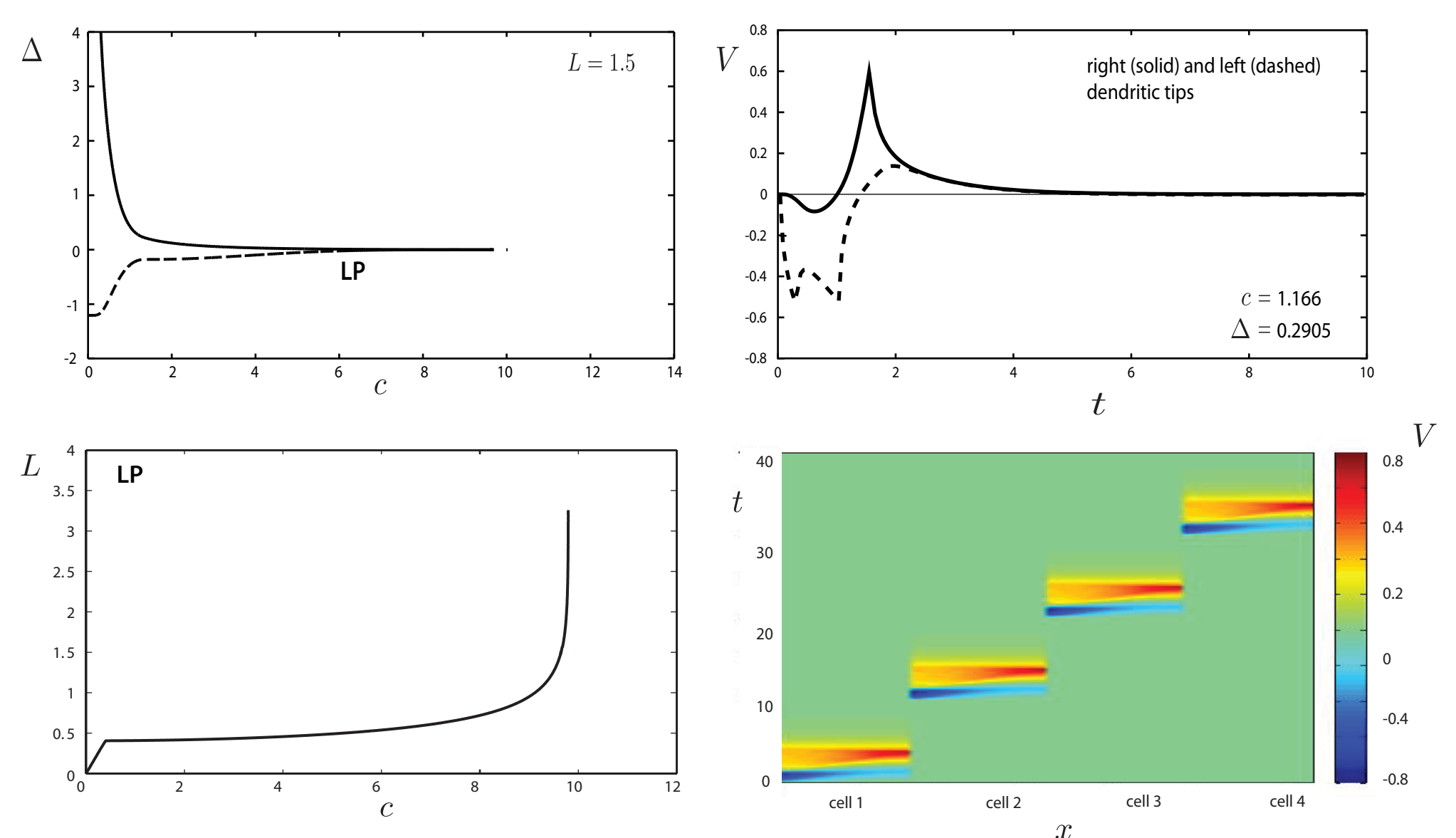we get $V(x,t) = W(x,t,L,c,\Delta) - H(x,t,L)$.

Time-locked solution

$$V(L,L/c) = h \qquad\qquad V(L,L/c-\Delta) = h$$

Preliminary Results

Some References :

- Abbott L. F., Fahri E., Gutmann S., *Biol. Cybern.* **66** (1991) 49–60
- Cao B. J., Abbott L. F., *Biophys. J.* **64** (1993) 303–313
- Coombes S., Timofeeva Y., Svensson C.-M., Lord G. J., Josić K., Cox S. J., Colbert C. M., *Biol. Cybern.* **97** (2007) 137–149
- Lee S., Zhou Z. J., *Neuron* **51** (2006) 787-799