Estimating non-homogeneous channel densities and synaptic activity from spatiotemporal dendritic voltage recordings

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Introduction

In estimation methods for neuronal properties, there is usually a tradeoff between biophysical realism and computational tractability [3].
If we have

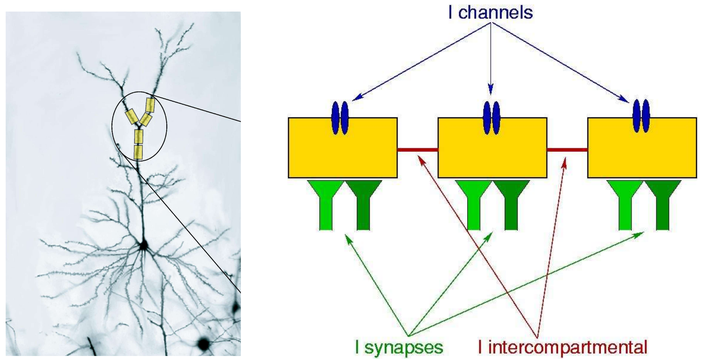
i) the spatiotemporal voltage signal (from voltage sensitive dyes)
ii) the exact branching structure of the neuron or piece of dendrite
iii) a description of channel kinetics

we can simultaneously infer

a) channel distribution
b) intracellular conductance
c) time-varying synaptic conductance distribution

This is possible because these parameters are coefficients in the voltage evolution equation and can be estimated by linear regression [see also 1, 2].

Method



The model equations

$$C\frac{dV_i}{dt} = I_i^{\text{channels}} + I_i^{\text{synapses}} + I_i^{\text{intercompartmental}}$$

$$I_i^{\text{channels}} = \sum_c \bar{g}_c g_c(t)(E_c - V_i(t))$$

$$I_i^{\text{synapses}} = \sum_s (\xi_s * k_s)(t)(E_s - V_i(t))$$

$$I_i^{\text{intercompartmental}} = \sum_a g_a \Delta V_a(t)$$

Solving the voltage evolution equation we find a simple linear regression for all parameters, e.g. for the channel densities:

$$\hat{\bar{\mathbf{g}}} = \arg\min_{\bar{\mathbf{g}}} (\dot{\mathbf{V}} - \bar{\mathbf{g}}\mathbf{M})^2$$

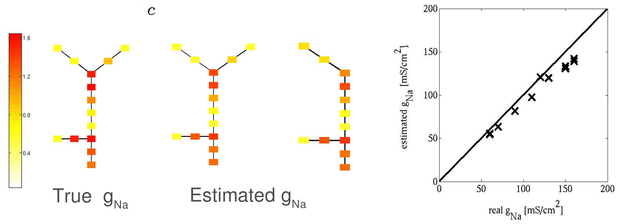
$$M_{ct} = g_c(t)(E_c - V(t))$$

NB: this is the ML solution under white Gaussian current noise.

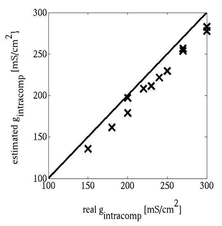
Individual estimates in a simple model

14 compartment model fitted with Hodgkin Huxley type channels. The estimation of the conductances shows a negative bias.

$$I_i^{\text{channels}} = \sum_c \bar{g}_c g_c(t)(E_c - V_i(t))$$

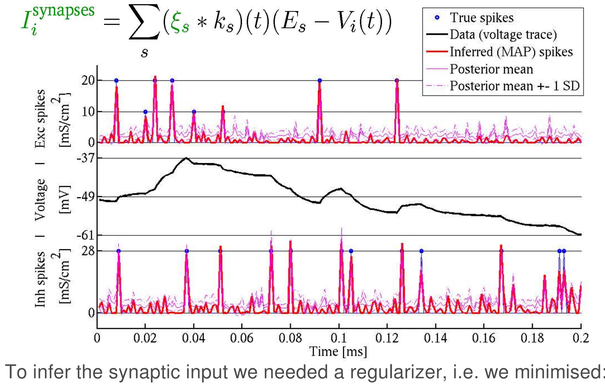


$$I_i^{\text{intercompartmental}} = \sum_a g_a \Delta V_a(t)$$



Single passive compartment with inhibitory and excitatory synaptic inputs

$$I_i^{\text{synapses}} = \sum_s (\xi_s * k_s)(t)(E_s - V_i(t))$$



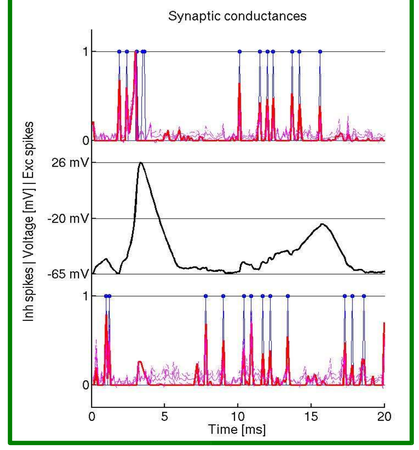
To infer the synaptic input we needed a regularizer, i.e. we minimised:

$$\hat{\boldsymbol{\xi}} = \arg\min_{\boldsymbol{\xi}} (\dot{\mathbf{V}} - \boldsymbol{\xi}\mathbf{M})^2 + \lambda\boldsymbol{\xi} \qquad M_{st} = \mathbf{K}_s(E_s - V(t))$$

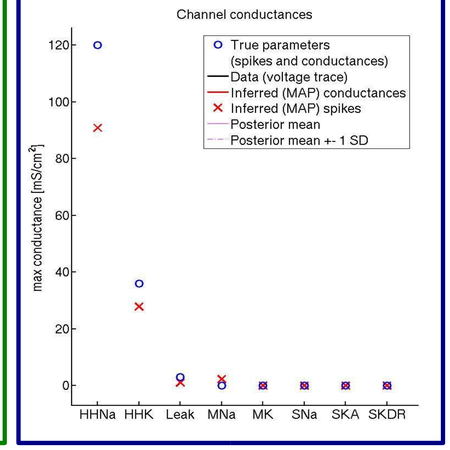
Joint estimation

Here we jointly estimated both presynaptic input and channel conductances. Presynaptic spikes are usually correctly identified, apart from when they occur during an action potential. The right panel shows that the conductances of channels not present during the generation of the voltage trace were mostly set to zero.

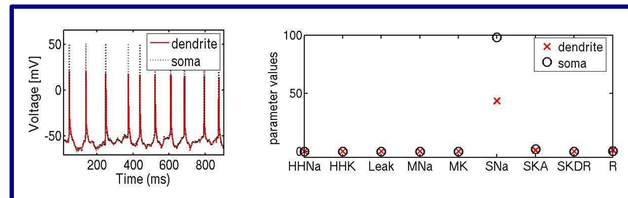
$$I_i^{\text{synapses}} = \sum_s (\xi_s * k_s)(t)(E_s - V_i(t))$$



$$I_i^{\text{channels}} = \sum_c \bar{g}_c g_c(t)(E_c - V_i(t))$$



Preliminary application: intracellular recording



Data [4] Dual recording of rat layer 5 pyramidal cell (soma & dendrite)
Model 2 compartments and 3 different Na and K kinetics

NB: One of our assumptions is violated (fully observed morphology). Parameter values are relative to membrane capacitance (100 ~ 100 mS/cm^2 under C = 1 μF/cm^2)

Discussion

- Calcium channels are ignored so far.
- Mistaken channel kinetics? But we can measure goodness of fit through likelihood.
- Voltage sensitive dyes may require a hidden variable formulation:
  high voltage noise,
  missing data due to partial sampling and missed dendrites.

References

[1] Wood, Gurney and Wilson (2004): Neurocomputing, 58-60: 1109-1116
[2] Morse, Davison and Hines (2001): Soc. Neurosci. Abstract
[3] Vanier and Bower (1999): J. Comp. Neurosci., 7(2): 149-171
[4] Data courtesy Mickey London, Wolfson Institute, UCL