

Joint modeling of voltage-sensitive imaging data and laminar microelectrode recordings



H. Lindén¹, K.H. Pettersen¹, A. Devor^{2,3,4}, P. Tian², I.C. Teng², A.M. Dale^{2,3}, G.T. Einevoll¹

¹Mathematical Sci. and Technol., Norwegian Univ. of Life Sci., Aas, Norway;

²Dept. of Neurosciences, ³Dept. of Radiology, UCSD, La Jolla, CA; ⁴MGH, Harvard Med. Sch., Boston, MA



Introduction

- **Voltage-sensitive dye (VSD)** imaging measures average *transmembrane potentials* along cortical surfaces, but lacks depth resolution. VSD signal at each pixel represents weighted sum of transmembrane potentials with sensitivity decreasing with distance from cortical surface

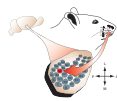
- **Local field potential (LFP)** reflects transmembrane currents [**current-source density (CSD)**] and can be measured throughout the cortical layers with linear (laminar) multielectrodes

- VSD and LFP signals represent complementary information for constraining candidate neural network models: *A successful model should account for results from both types of experiments simultaneously*

- Here: Presentation of mathematical modeling scheme to 'translate' results from neural-network models to VSD and CSD/LFP predictions

- Example system: Rat barrel cortex following stimulation by single whisker flicks

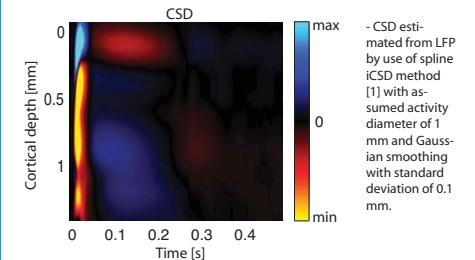
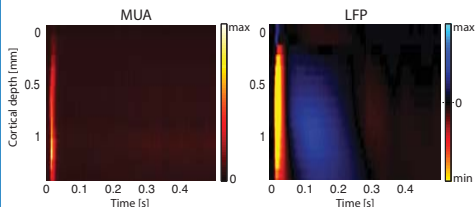
- Trial-averaged responses to single whisker flicks



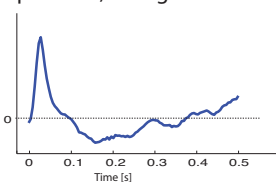
Experimental data

Example laminar-electrode data

- Local field potential (LFP): 0.1-500 Hz
- Multi-unit activity (MUA): >750 Hz, rectified



Example trace, voltage-sensitive dye (VSD)



- Summed VSD activity from disk with radius 1 mm, centered on earliest detectable response

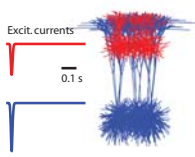
Model circuit

- Morphologically reconstructed layer-2/3 [2] and layer-5 pyramidal [3] cells (downloaded from *NeuroMorpho.Org* and *ModelDB* [4])

- Neurons placed randomly in columnar cylinder of diameter 0.4 mm

- All neurons receive fast basal excitation; in addition layer-5 neurons receive slow inhibition (basal, apical, or both) or apical excitation

- Simulations done in NEURON in combination with our own Python-based package LFPy



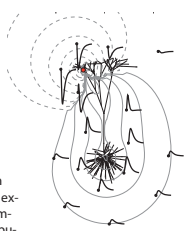
Forward model CSD/LFP

- Depth profile of current-source density (CSD) found by summing transmembrane currents at a particular depth from all dendrites of all neurons in the two neuronal populations

- Depth profile of local-field potential (LFP) $\Phi(r,t)$ found by use of fundamental formula for contribution from *N*-compartment neuron [5,6,7]:

$$\phi(r,t) = \frac{1}{4\pi\sigma} \sum_{n=1}^N \frac{I_n(t)}{|r - r_n|}$$

where $I_n(t)$ denotes transmembrane current in compartment *n* positioned at r_n , and σ is the extracellular conductivity. Total LFP found by summing over all neurons in the two neuronal populations



Example LFP from layer-5 neuron receiving apical excitatory synaptic input

Forward model VSD

- The contribution to the voltage-sensitive dye (VSD) signal from the *N*-compartmental neuron is modeled as

$$S_{VSD}(t) = \sum_{n=1}^N f(z_n) A_n V_n(t)$$

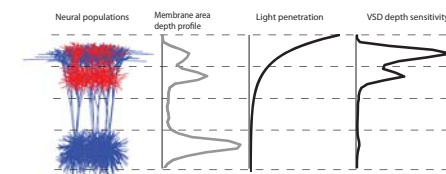
where A_n is area of compartment *n*, $f(z_n)$ is the depth sensitivity of the VSD signal, and $V_n(t)$ is the transmembrane potential in compartment *n* at time *t*

- Total signal found by summing over all neurons in both neuronal populations

- Presently we assume

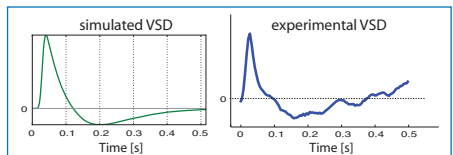
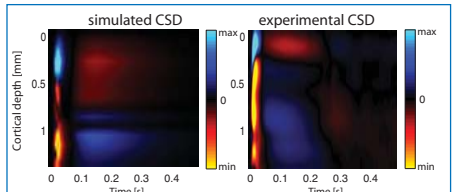
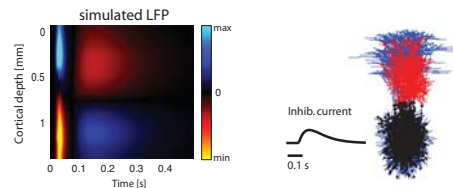
$$f(z) = f_0 e^{-z/\lambda_{VSD}}$$

λ_{VSD} is here set to 200 μ m



Model predictions

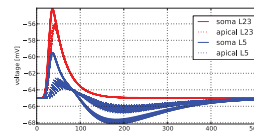
Scenario 1: slow basal inhibition



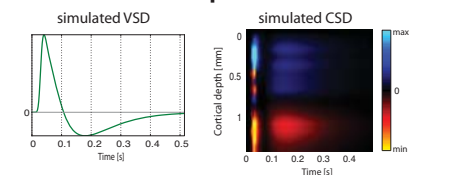
- Predicts qualitatively similar VSD as experiment
- Predicts CSD pattern with same polarity as experiment

Simulated membrane potentials:

- Note: Membrane potentials are qualitatively similar in somas and apical dendrites

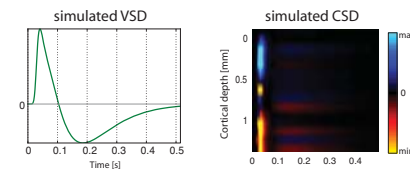


Scenario 2: slow apical inhibition



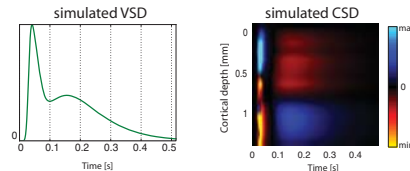
- Predicts qualitatively similar VSD profile as experiment
- Predicts CSD pattern with opposite polarity as experiment for late times

Scenario 3: slow basal+apical inhibition



- Predicts qualitatively similar VSD as experiment
- Predicts no clear CSD pattern at late times

Scenario 4: slow apical excitation



- Predicts positive VSD at all times, different from experiments
- Predicts CSD pattern with same polarity as experiment

Take-home message

- VSD and CSD are complementary measures of neural activity

- **Negative VSD (hyperpolarization) does not necessarily imply inhibitory currents in the upper layers (cf. scenario 1)**

- **Unlike CSD, VSD distinguishes situations with apical excitation from situations with basal inhibition (cf. scenarios 1 and 4)**

References

- [1] Pettersen KH et al, *J Neurosci Methods* (2006)
- [2] Wang Y et al, *Cereb Cortex* (2002)
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Acknowledgements

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