Biophysical cortical column model for optical signal analysis

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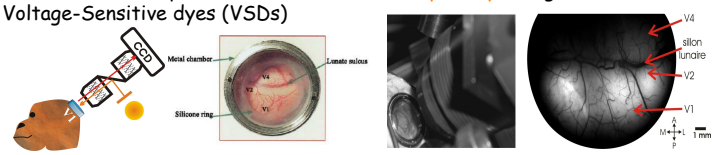
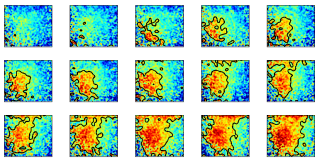
We propose a biological cortical column model, at a some mesoscopic scale, in order to better understand and start to interpret biological sources of voltage-sensitive dye imaging signal. The mesoscopic scale, corresponding to a micro-column, is about 50 µm. Simulations are done thanks to the NEURON and NEURONCONSTRUCT software. This model suggests that the OI signal is the result of an average from multiple components whose proportion changes with levels of activity and shows surprisingly that inhibitory cells, spiking activity and deep layers may well participate more to the signal than initially though.

Voltage-sensitive dye imaging (VSDI): Methods

- The membrane potential can be measured optically, using Voltage-Sensitive dyes (VSDs) — Slovin et al., 2002

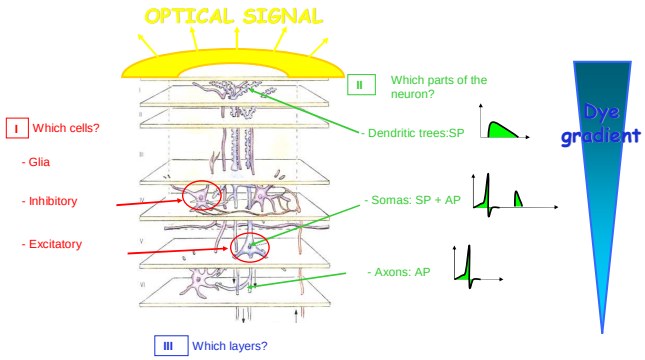


- The dye molecules act as molecular transducers that transform changes in membrane potential into optical signals — Reynaud et al., 2007
- Advantages of the method:
  - High spatial resolution: 50 µm
  - High temporal resolution: < ms

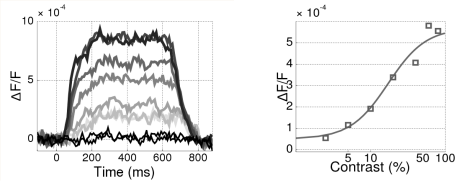


The optical signal, where is it coming from?

- The optical signal is the sum of many things:



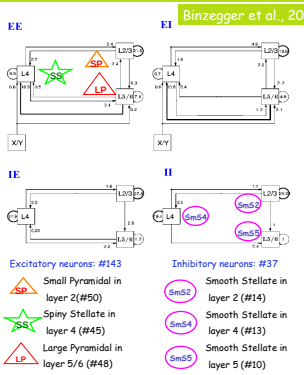
- Nature of the signal:
  - Locally proportional to the membrane potential of all neuronal components
  - Proportional to the excited membrane surface of all neuronal components
  - A simple gradient of VSD fluorescence depending on depth
- VSDI experiment on monkey: — Reynaud et al., 2007



→ **Modeling a bio-physical cortical column is a requirement**

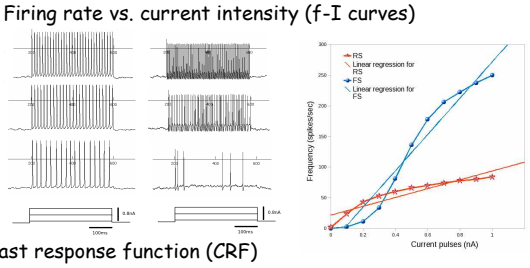
A compartmental model

- Specifications: 6 specific populations of neurons — Binzegger et al., 2004
  - 2 populations, Excitatory (E) and Inhibitory (I) neurons
    - **Compartmentalization**
    - **HH like membrane potential equation**
    - **Passive dendrites**
    - **AMPA receptors on the dendrites**
    - **GABA receptors on the somas**
  - 3 main layers (L2/3, L4, L5/6)
  - Independent synaptic bombardment on all cells (fluctuating conductances, Destexhe et al., 2001)
  - Connectivity ("a la" Binzegger)
  - X/Y: Thalamic input: random spike input with increasing strength (contrast input)
- Simulation: NEURON and NEURONCONSTRUCT software

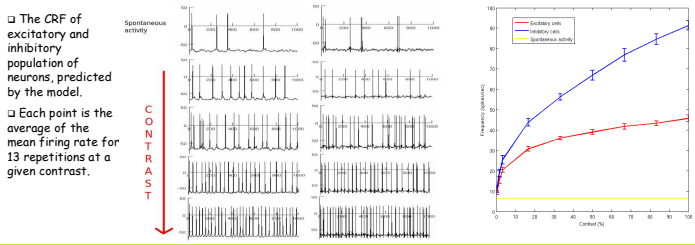


Model behaviour

- Single Neurons: Firing rate vs. current intensity (f-I curves)
  - Action potential responses to depolarizing current injection in the two main populations of respectively excitatory neurons and inhibitory neurons.
  - RS and FS cells are known to be respectively the great majority of excitatory and inhibitory cells in the neocortex.



- Network: Contrast response function (CRF)
  - The CRF of excitatory and inhibitory population of neurons, predicted by the model.
  - Each point is the average of the mean firing rate for 13 repetitions at a given contrast.



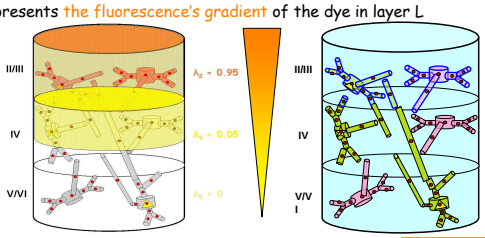
VSD signal computation

- For a given layer L, the OI signal computation is given by:

$$OI^L = \lambda^L * \sum_{i=1}^{N^L} V_i(0.5) * S_i$$

where

- N^L is the number of compartments in layer L
- S_i is the surface of the i^{th} compartment
- $V_i(0.5)$ is the membrane potential taken in the middle of the i^{th} compartment
- λ^L represents the fluorescence's gradient of the dye in layer L



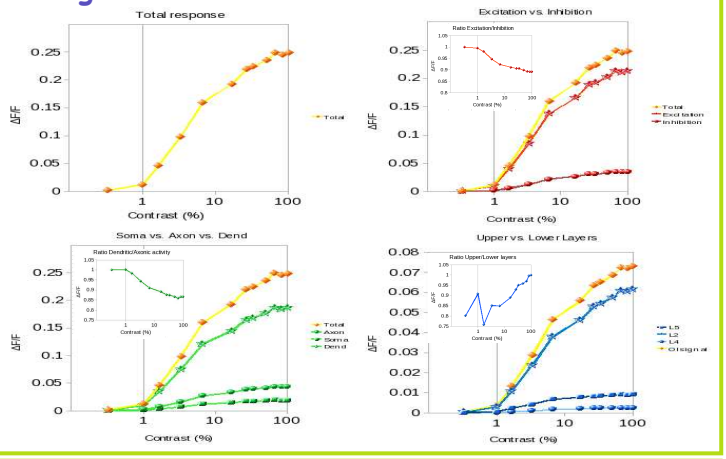
- The total VSD signal computation is given by:

$$OI = \sum_{L\in\{layers\}} OI^L$$

Lippert et al., 2007

$$OI = 0.95 * OI^{L2} + 0.05 * OI^{L4}$$

VSD signal contributions



Conclusion

- This model confirms and quantifies the fact that the VSD signal mainly reflects dendritic activity of excitatory neurons in superficial layers.
- However, the model also shows that inhibitory cells, spiking activity and deep layers are non-negligible and should be taken into account in the computation of the optical signal.

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