Biophysical cortical column model for optical signal analysis

Sandrine Chemla, Frédéric Chavane and Thierry Viéville

Projet Odyssée, INRIA Sophia-Antipolis

Equipe DyVA, INCM

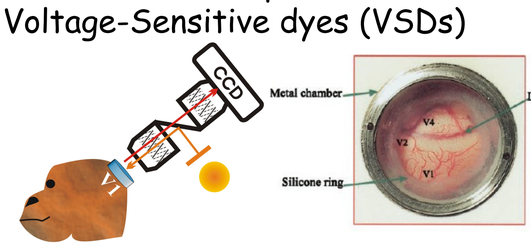
Contact: Sandrine.Chemla@sophia.inria.fr

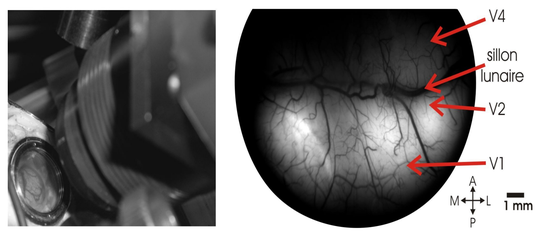
We propose a biological cortical column model, at a some mesoscopic scale, in order to better understand and start to interpret biological sources of voltage-sensitive dye imaging signal. The mesoscopic scale, corresponding to a micro-column, is about 50 µm. Simulations are done thanks to the NEURON 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 and spiking activity may well participate more to the signal than initially though.**

Voltage-sensitive dye imaging: Methods

- The membrane potential can be measured optically, using Voltage-Sensitive dyes (VSDs)

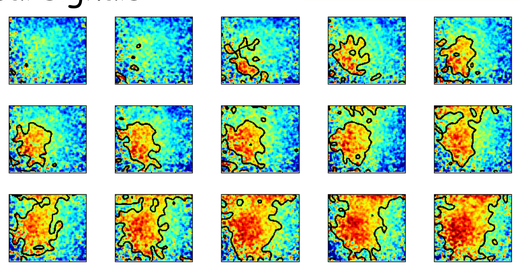
Slovin et al., 2002





- The dye molecules act as molecular transducers that transform changes in membrane potential into optical signals

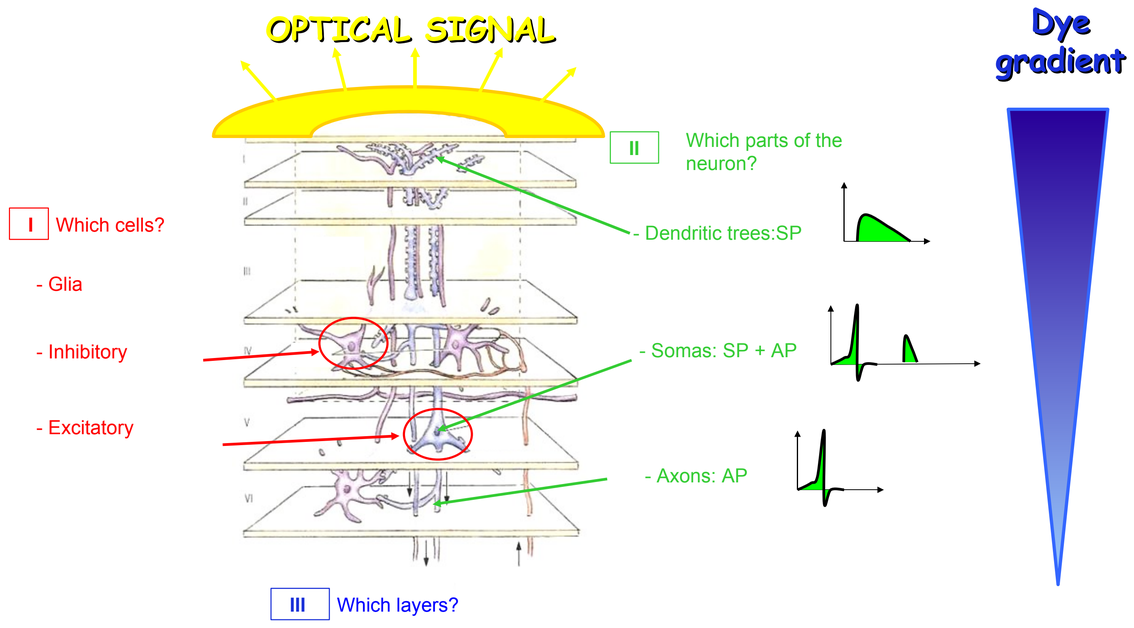
Reynaud et al., 2007



- Advantages of the method:
  - High spatial resolution: 50 µm
  - -High temporal resolution: < ms

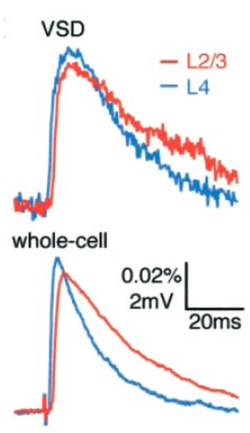
The optical signal, where is it coming from?

- The optical signal is the sum of many things:



- VSD signal/Membrane potential relationship
  - The amplitudes of the VSD signals are linearly correlated with both changes in membrane potential and the membrane area of the stained neuronal elements under each measuring pixel.
  - Whole cell voltage recordings, from Petersen, show a close correlation for individual neurons. What can we say for a population of neurons?
  - Several factors can influence this global linearity:
    - -Noise level
    - -Synchronization
    - -Inhibitory neurons' activity

Petersen et al., 2003



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

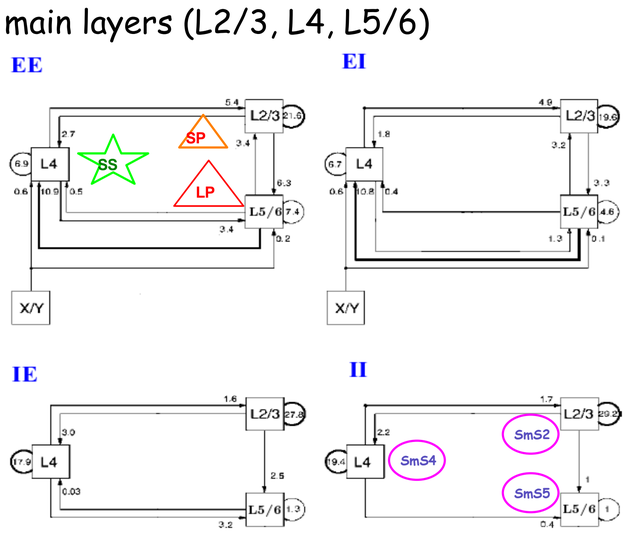
Cortical column paradigm

	Anatomical	OI pixel	Functional	Physico-fonctional	Cortical Area
Type of cortical column	Microcolumn or Minicolumn	Our Column	Orientation, ocular dominance column	Macrocolumn or Hypercolumn (V1)	Neural Mass
Spatial scale	40-50 µm	50-100 µm	200-300 µm	600 µm (and more)	10 mm
Number of neurons	80-100 neurons	200 neurons	Several minicolumns	60-100 minicolumns or 10000 neurons	100XThousand neurons of the same type (pyr, stellate,…)

Proposed model

- We choose a family of models based on a cortical microcircuit, whose synaptic connections are made only between six specific populations of neurons:
  - 2 populations, Excitatory (E) and Inhibitory (I) neurons
  - in 3 main layers (L2/3, L4, L5/6)

Binzegger et al., 2004



Excitatory neurons: #120
- SP: Small Pyramidal in layer 2 (#40)
- SS: Spiny Stellate in layer 4 (#20)
- LP: Large Pyramidal in layer 5/6 (#60)

Inhibitory neurons: #30
- SmS2: Smooth Stellate in layer 2 (#10)
- SmS4: Smooth Stellate in layer 4 (#5)
- SmS5: Smooth Stellate in layer 5 (#15)

- X/Y represents the thalamic inputs

NEURON simulation environment

Hines, Carnevale

Provides tools for constructing, exercising, and managing simplified up to biologically realistic models of electrical and chemical signaling in neurons and networks of neurons

Compartmentalization:

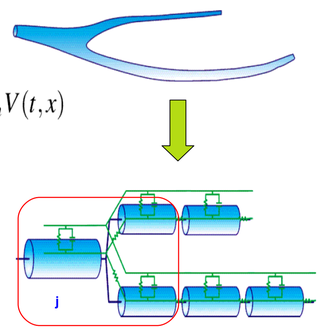
Continuous system (Cable equation)

$$g_{in}\frac{\partial^2 V(t,x)}{\partial x^2} = I_m(t,x) = C\frac{\partial V(t,x)}{\partial t} + g_m V(t,x)$$

Discontinuous system in space and in time

(Set of ordinary differential equations with first order derivatives in time and set of algebraic difference equations)

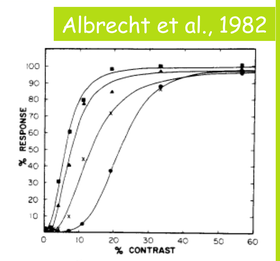
$$\sum_k g_{in\,jk}\left(V_k(t) - V_j(t)\right) = C_j\frac{dV_j(t)}{dt} + g_j(t)V_j(t)$$



Preliminary results

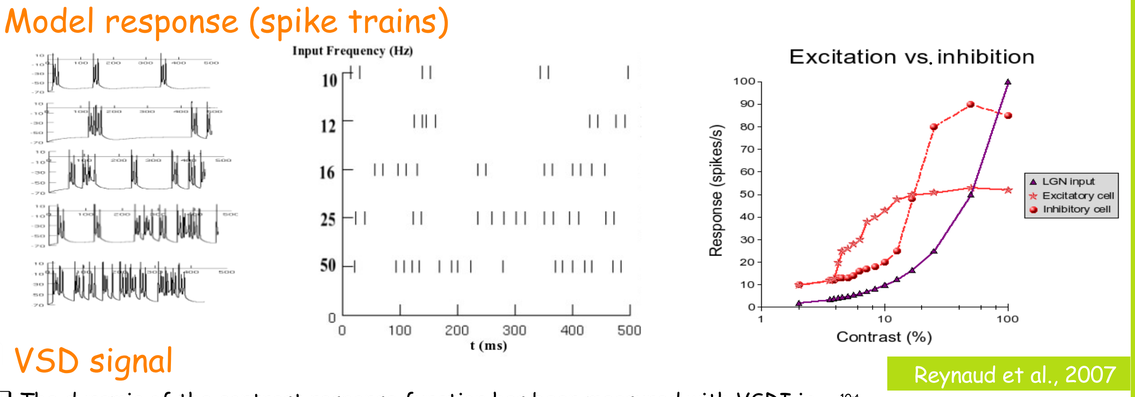
Albrecht et al., 1982

- Contrast response function
  - Cortical cells adjust non-linearly their response to an input with increasing strength, described by the contrast response function (see figure from Albrecht).
  - Nonlinearities in the CRF (compression and saturation) allow cortical cells to adjust the useful dynamic response to an operating range of contrast that can be modulated. This control is supposed to be adjusted by a dynamic balance between excitation and inhibition.



Contrast response functions of four striate cells (from monkeys and cats)

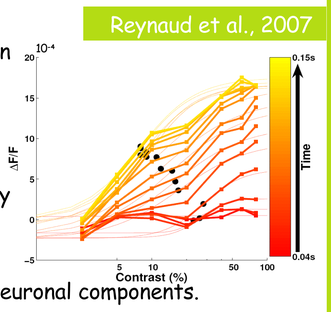
- Model response (spike trains)



- VSD signal

Reynaud et al., 2007

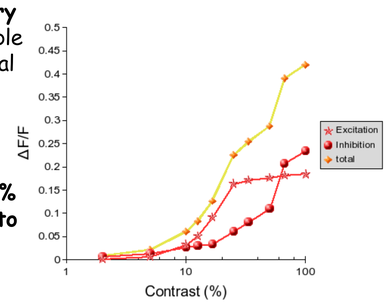
  - The dynamic of the contrast response function has been measured with VSDI in the monkey visual cortex: the dynamic range of the response decreases to lower contrast with time.
  - What are the participation of the various neuronal components to this population signal? In particular, are excitatory and inhibitory cells participating equally for different contrasts? Is the ratio between spiking and synaptic activity the same when the network is at low vs. high levels of activity? What are the respective participation of cells from lower vs. high layers?



  - VSD signal is simulated using a linear integration on the membrane surface of neuronal components. Our model can predict the different contributions of the VSD signal:

- Excitation vs. Inhibition

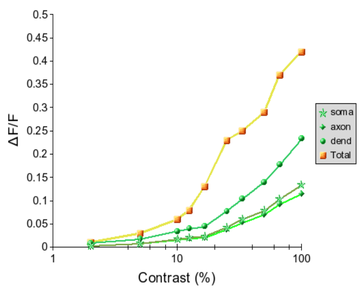
Globally, **excitatory cells** are responsible of **60%** of the total OI response. **Inhibitory cells** participation increases with contrast: from **32% at low contrasts to 55% at high contrasts**.



- Post-Synaptic vs. Action potential

Globally, **only 50% of the optical signal comes from dendritic post-synaptic activity.**

The ratio between spiking and synaptic activity increase (0.4 to 0.6) with contrast.



Partially supported by the EC IP project FP6-015879, FACETS

www.inria.fr