

From generation to publication of simulated data in a large-scale model of thalamo-cortical loop

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of experimental biology

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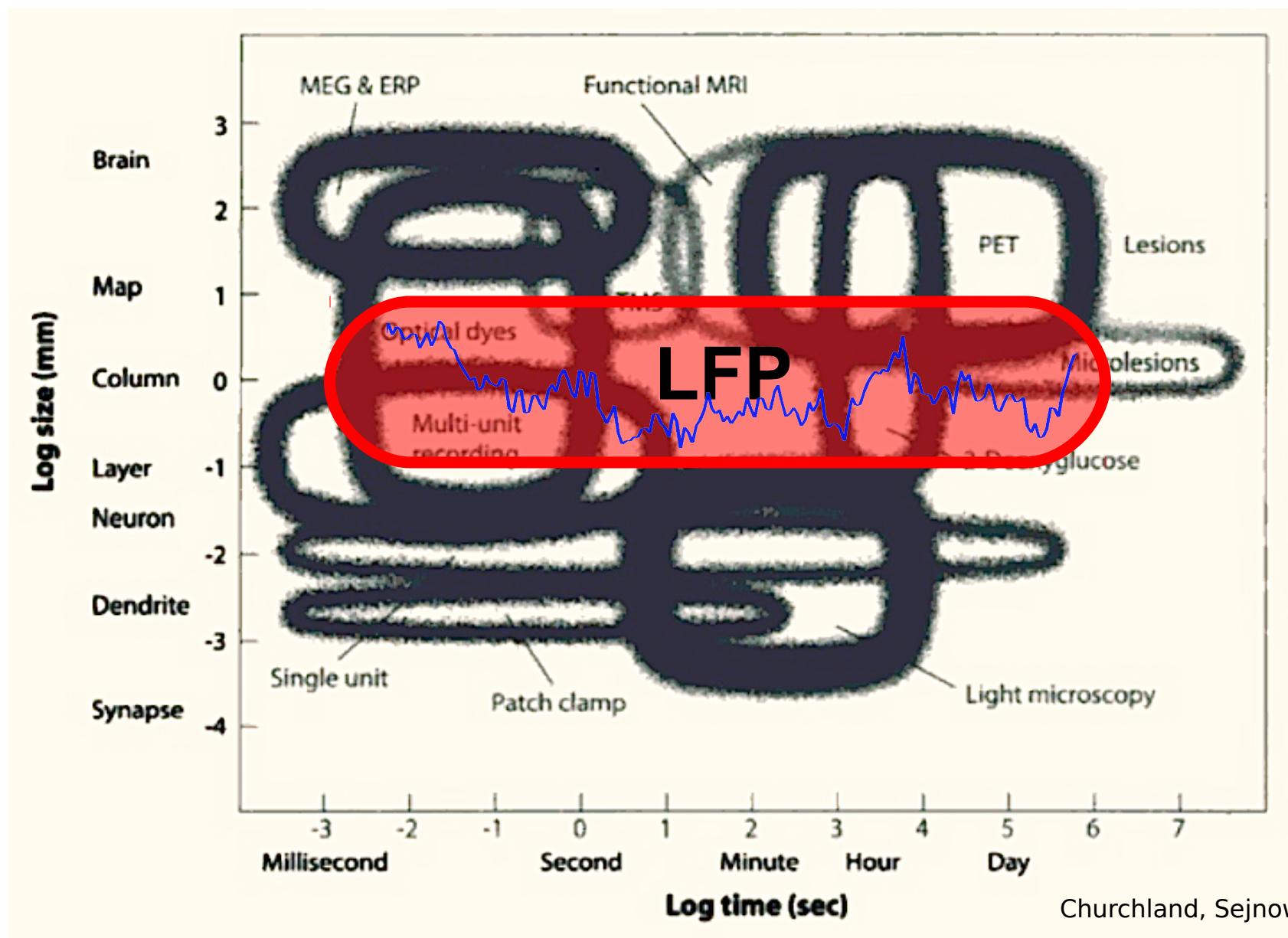


Neuroscience

- Experiment
- Measurement

Techniques to study brain function

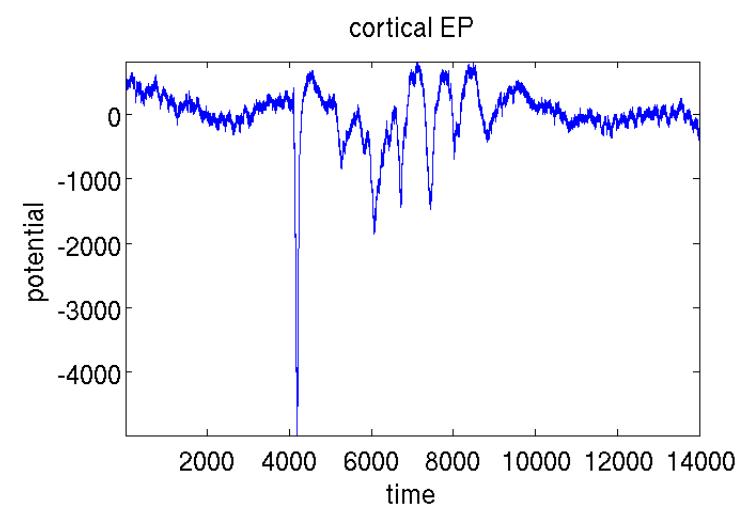
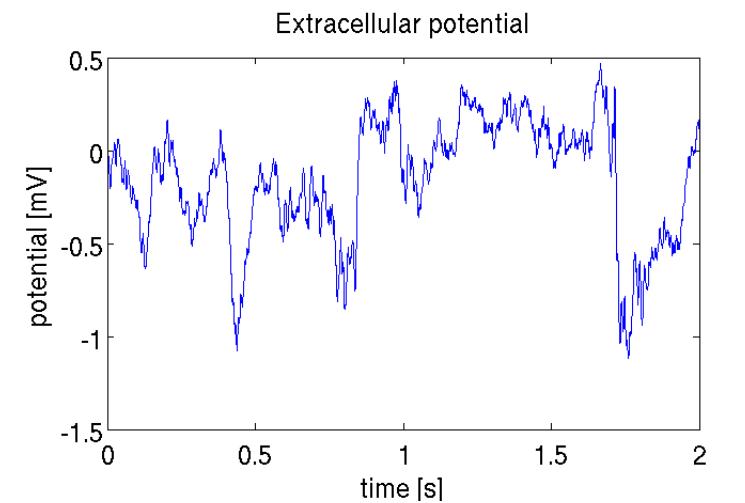
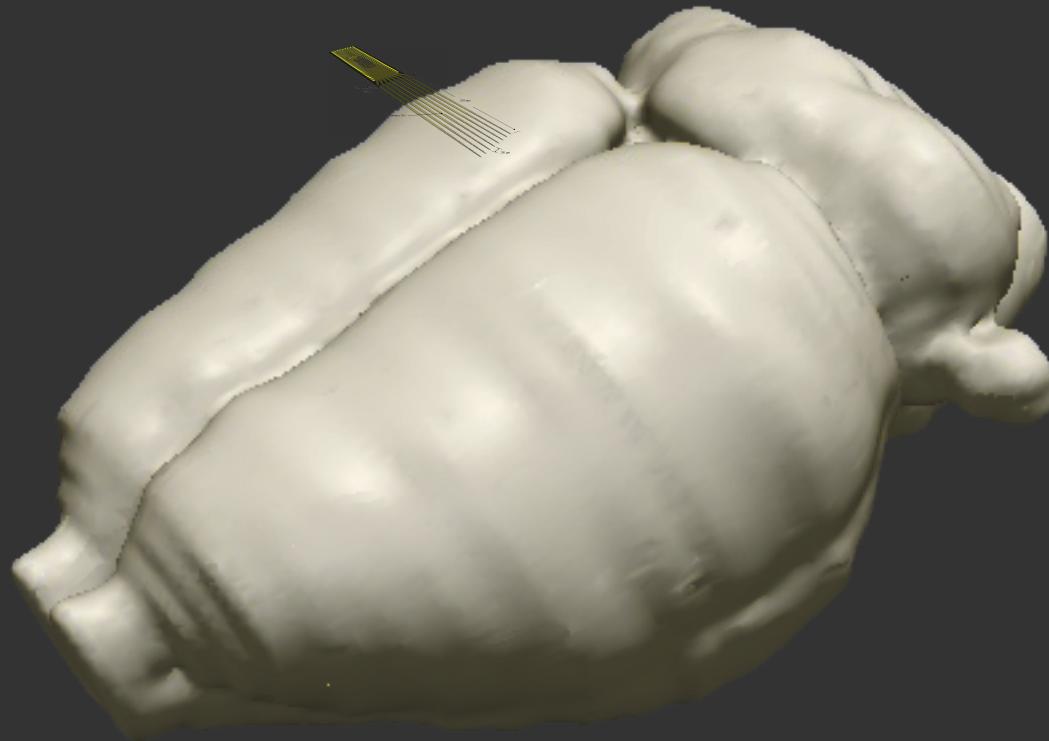
Temporal and spatial scales

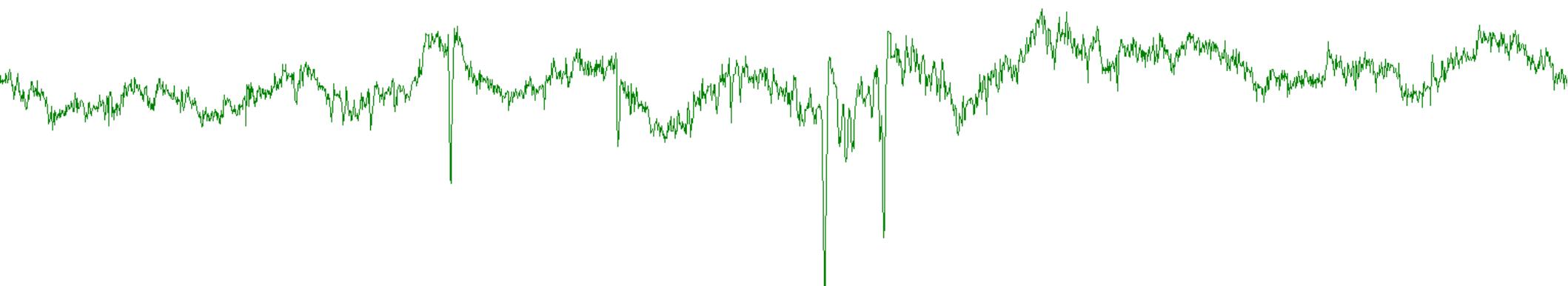


Churchland, Sejnowski 2000

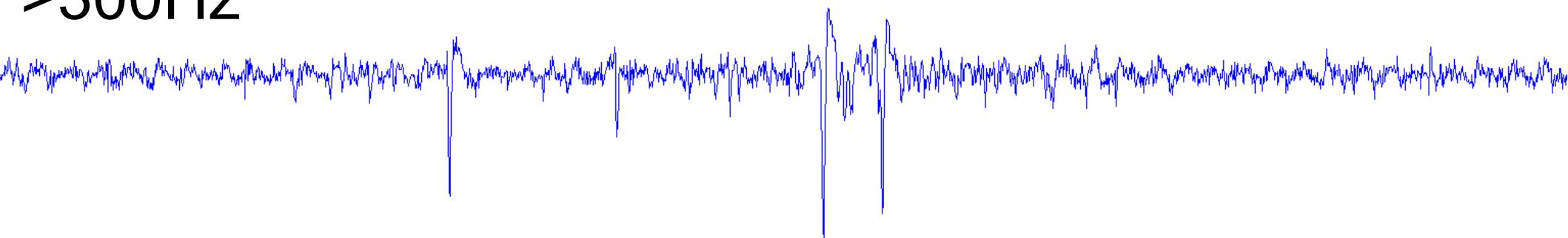
Electric potential in the brain

Mark Hunt





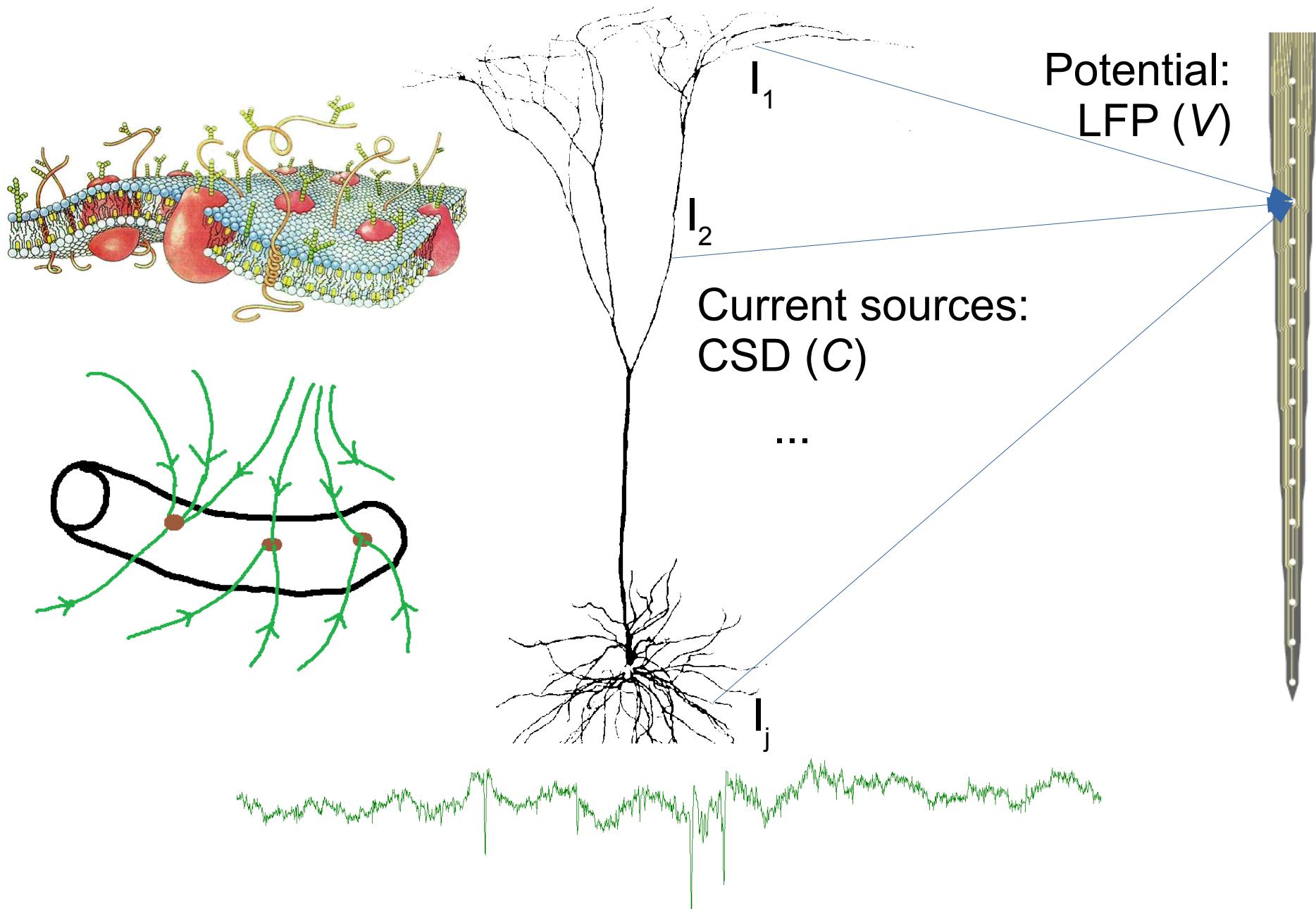
>300Hz



<300Hz – LFP



Electric potential in the brain



Current Source Density

$$V(\vec{r}, t) = \frac{1}{4\pi\sigma} \int \frac{\mathcal{C}(\vec{r}^0, t)}{|\vec{r} - \vec{r}^0|} d^3 r^0$$

$$\mathcal{C} = -\sigma \Delta V$$

\mathcal{C} – current source density

σ – conductivity tensor; here: a constant
(homogeneous and isotropic medium)

How to deal with LFP?

How to deal with LFPs?

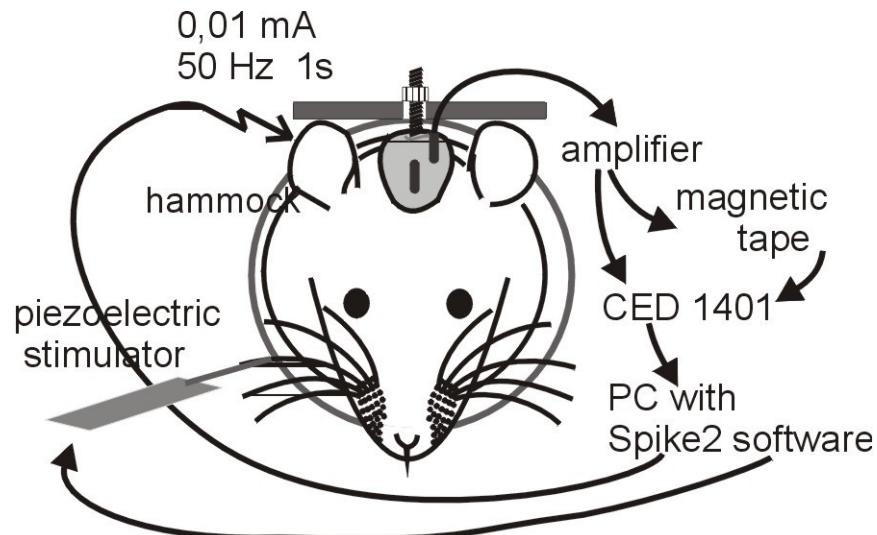
- Forward modeling:

Find out LFPs in a model and connect them with network activity

- Inverse modeling:

Find the sources of the potentials from data
Current Source Density analysis [CSD]

Experimental paradigm:



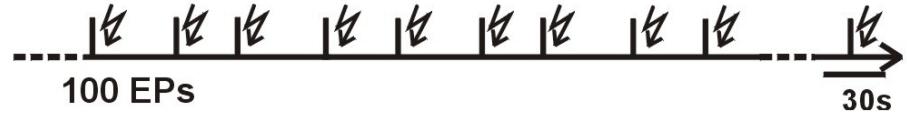
habituation sessions (H1, H2, H3...)



first session with reinforcement (C1)

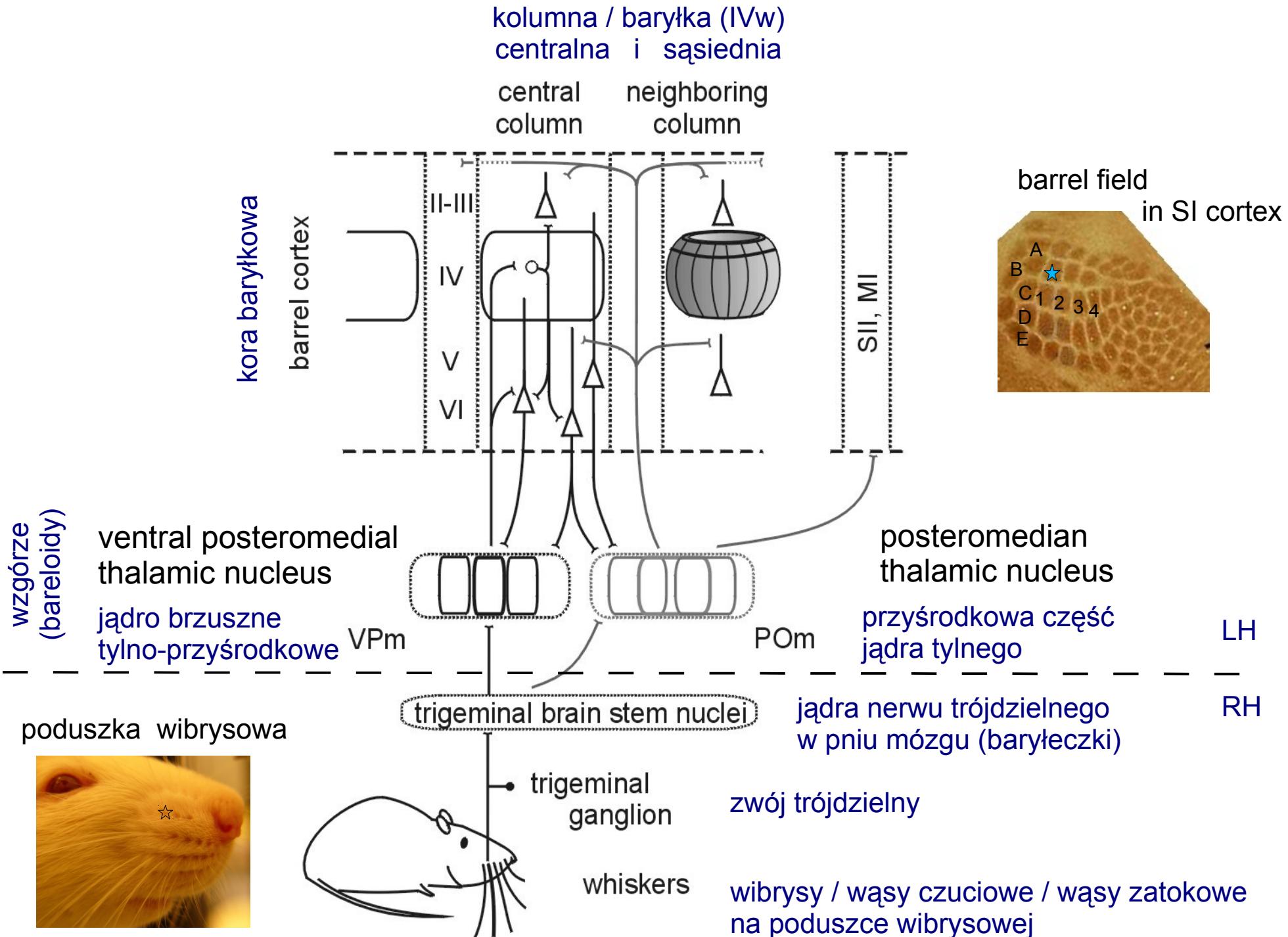


consecutive conditioning sessions (C2, C3 ...)



Vibrissa – barrel system of the rat

E. Kublik

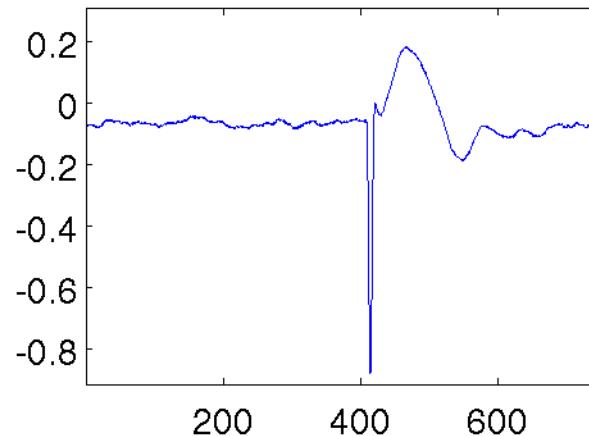


Data: evoked potentials

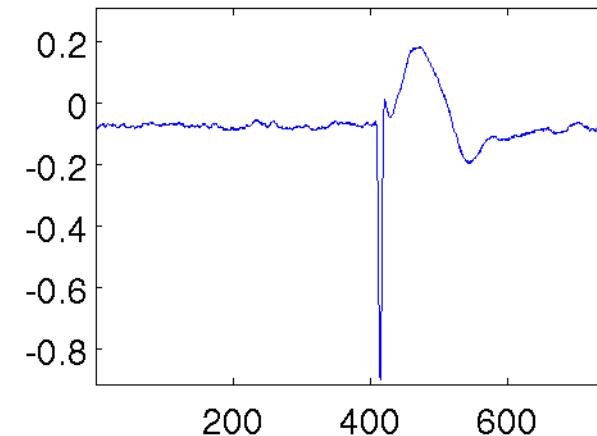
cortex

thalamus

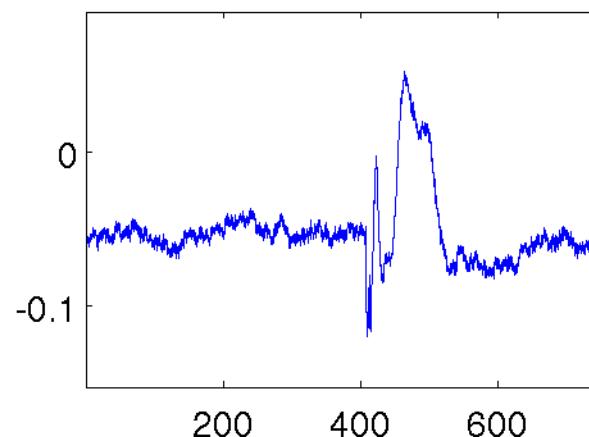
Cortex



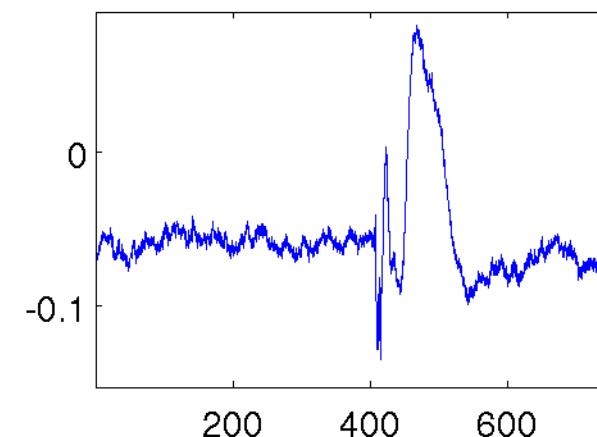
cortex, aroused



thalamus

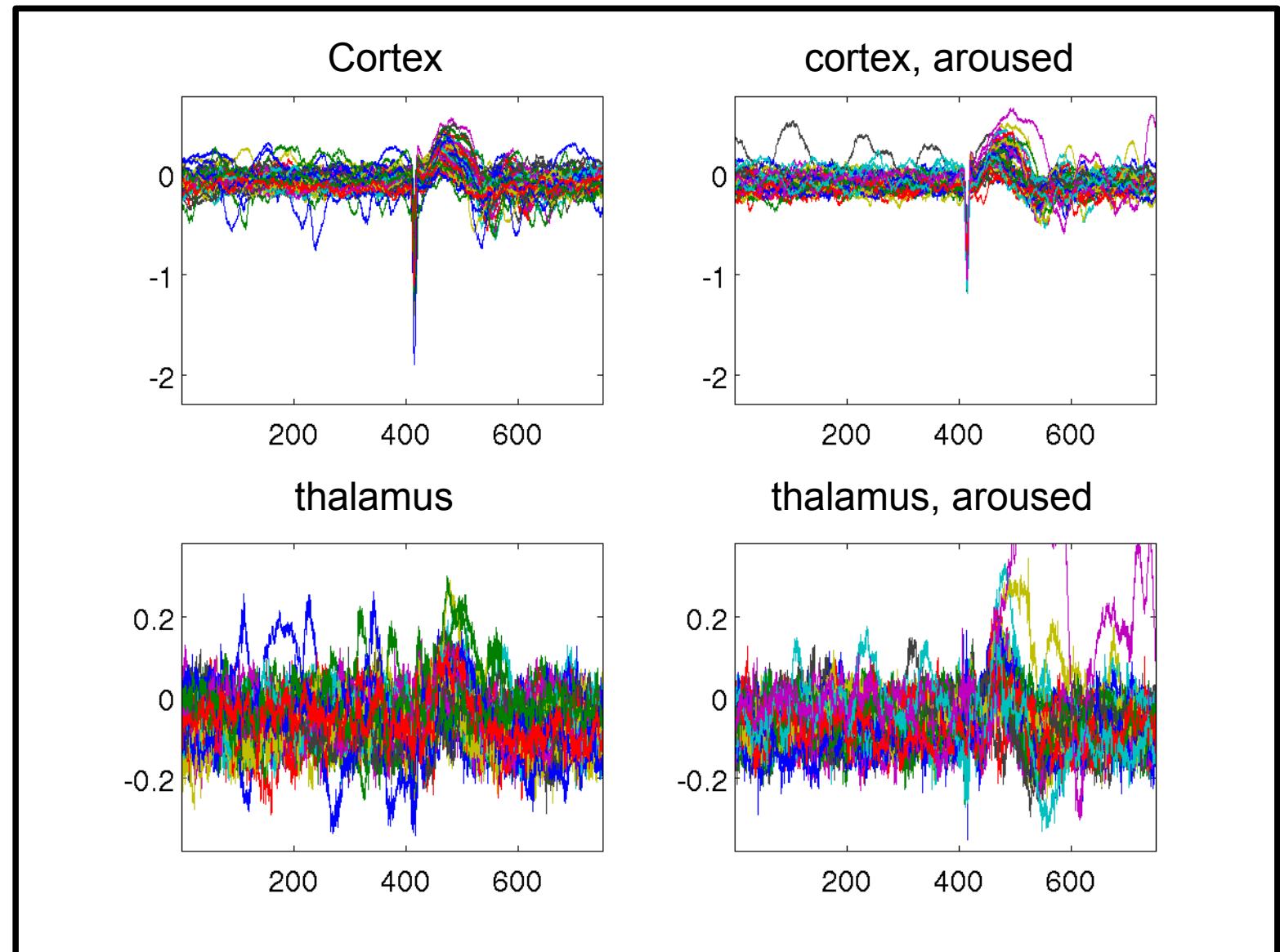


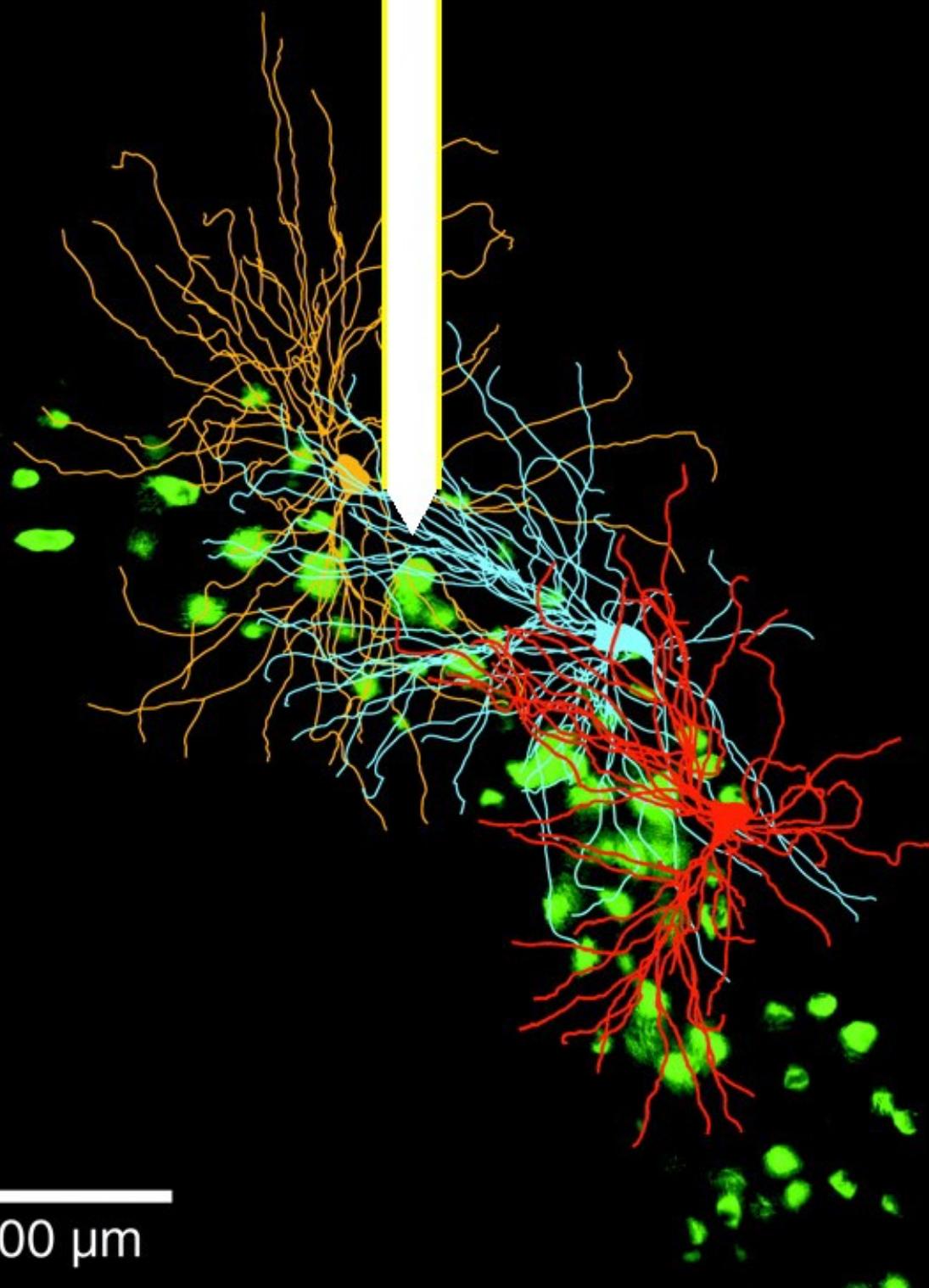
thalamus, aroused



Data: evoked potentials

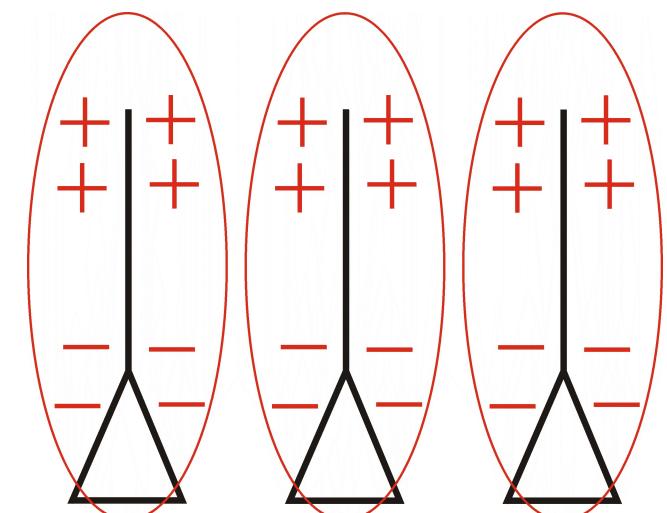
cortex



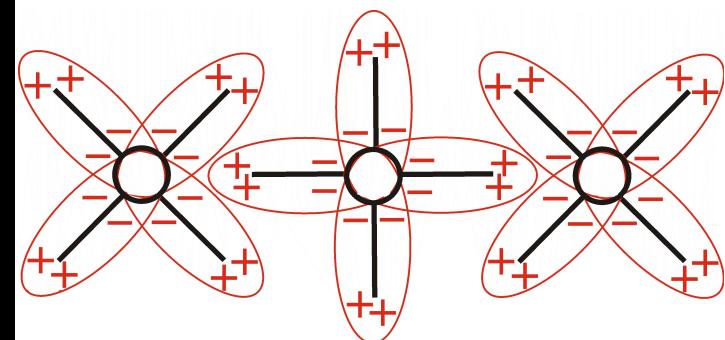


100 μ m

from Varga et al (2002) modified

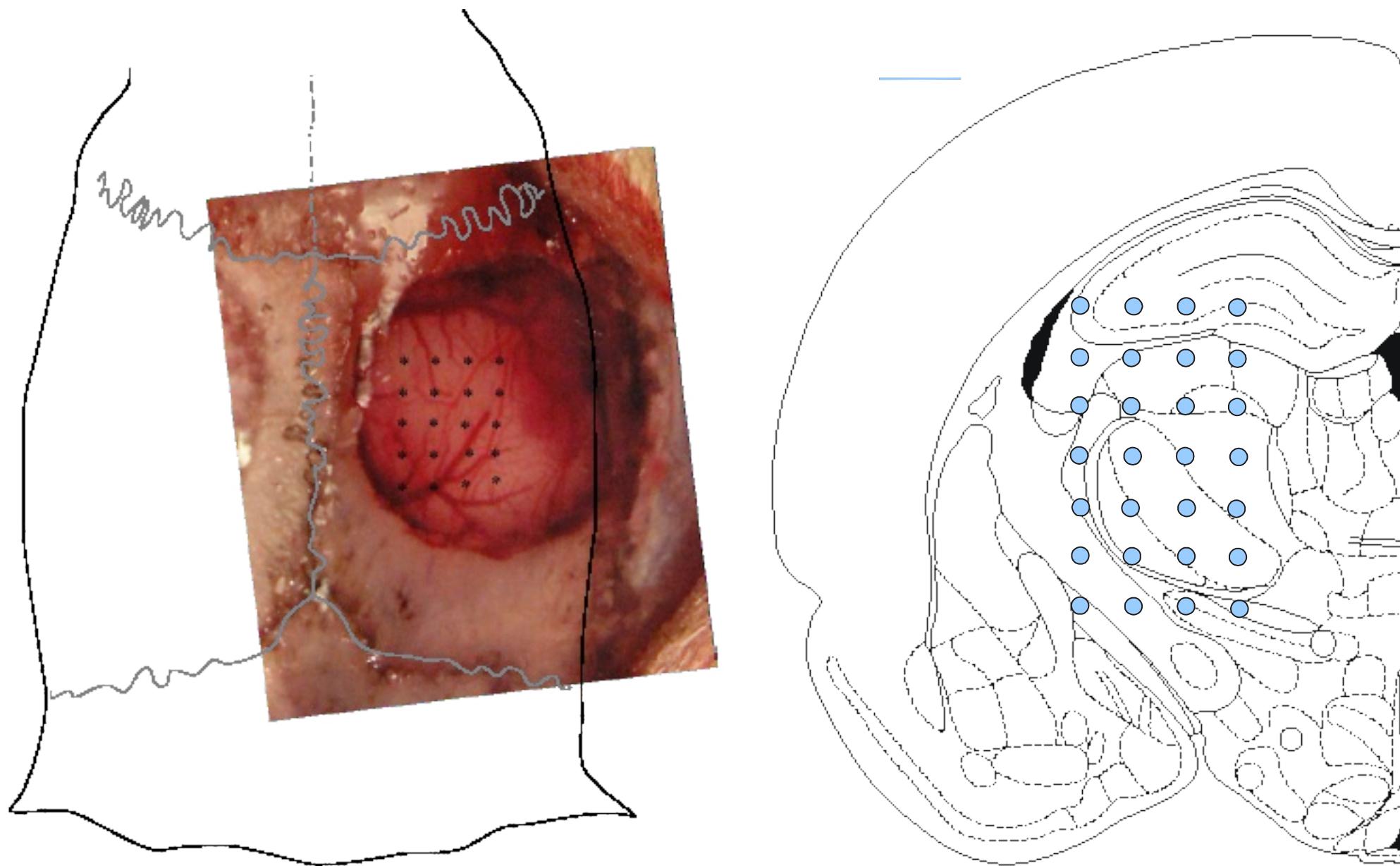


Open field



Closed field

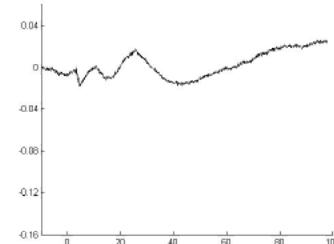
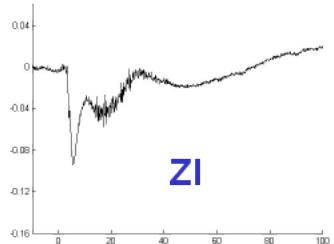
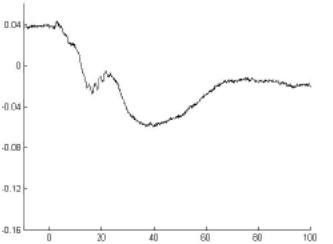
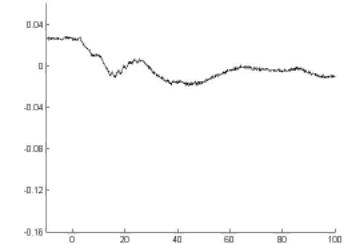
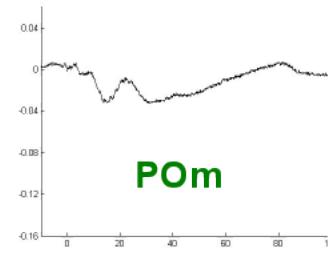
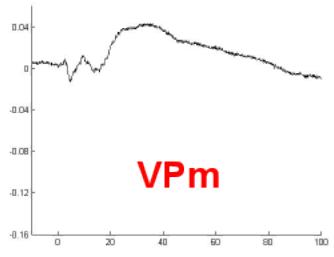
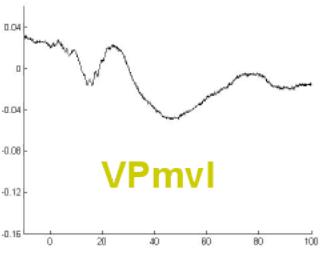
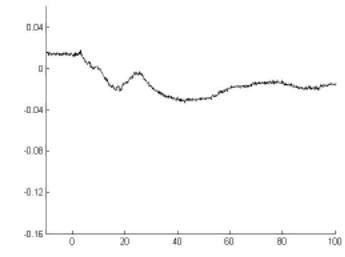
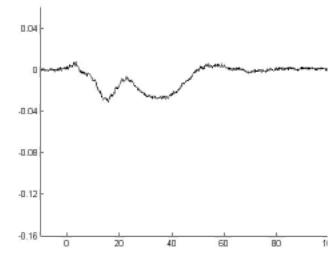
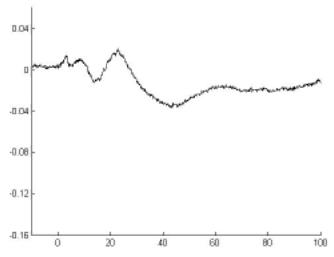
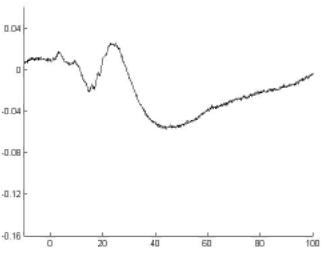
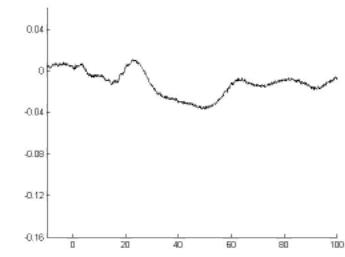
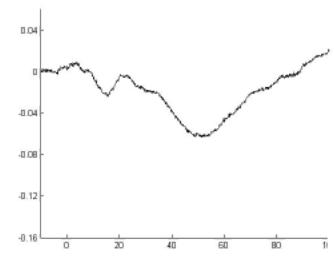
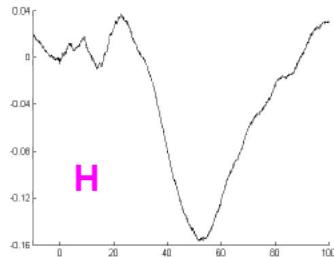
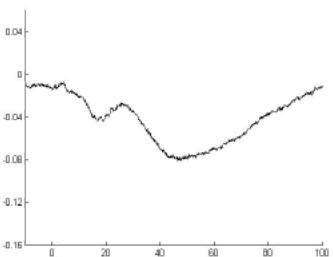
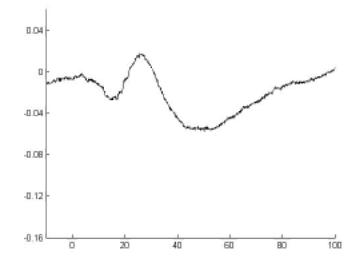
Experimental setup



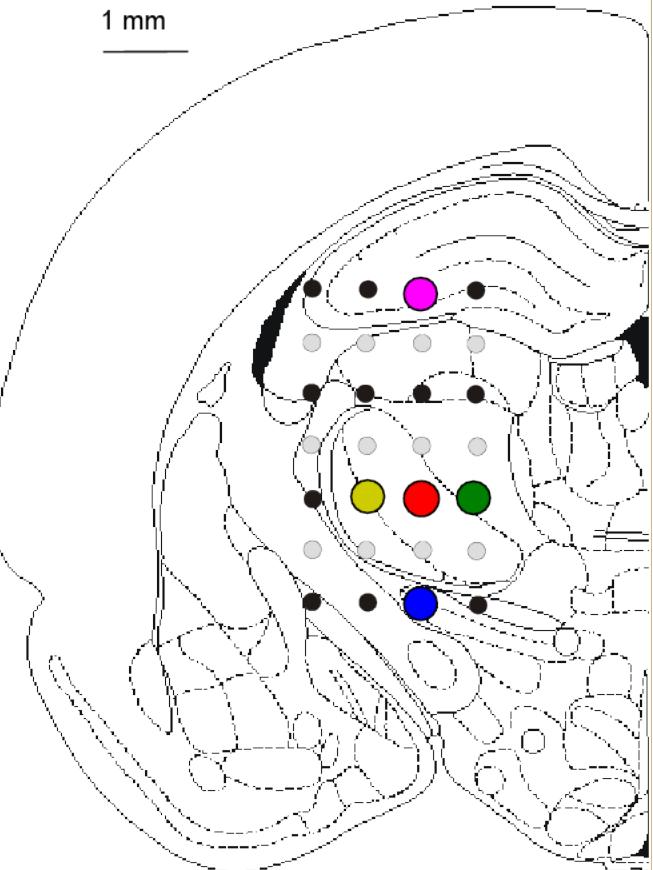
Example local field potentials recorded in the rat forebrain

D. Świejkowski

mV



1 mm



ms

CSD reconstruction methods

- Traditional CSD method

Pitts, W.H. (1952) Investigations on synaptic transmission. In *Cybernetics*
Freeman, J. A., & Nicholson, J. *Neurophysiol. C.* (1975), 38(2), 369–382.
Mitzdorf, U. *Physiol. Rev.* (1985), 65, 37

- iCSD (inverse CSD method)

Pettersen et al., *J.Neurosci. Methods* (2006)154(1–2), 116–133

Łęski et al., *Neuroinformatics* (2007) 5, 207-222

Łęski et al., *Neuroinformatics*(2011) Doi:10.1007/s12021-011-9111-4

- kCSD (kernel CSD method)

Potworowski et al., *Neural Computation* (2012)24:541-575

Traditional CSD

$$\textcolor{red}{C} = -\nabla \cdot [\sigma \nabla \textcolor{green}{V}]$$

- Numerical second derivative in 1D
(three-point formula)

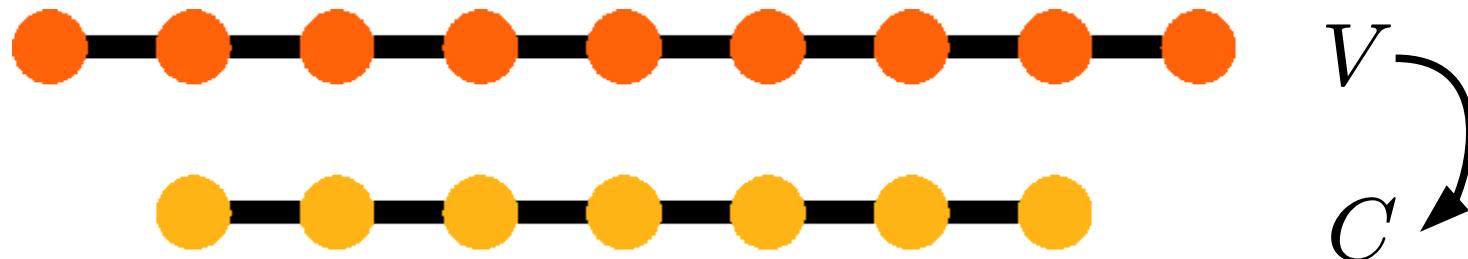
$$\frac{\partial^2 f}{\partial x^2} \simeq \frac{f(x + h) - 2f(x) + f(x - h)}{h^2}$$

- Problems:
 - Assumes homogeneity in y, z
 - Difficult to adapt to specific situation
 - Can't use at the boundary

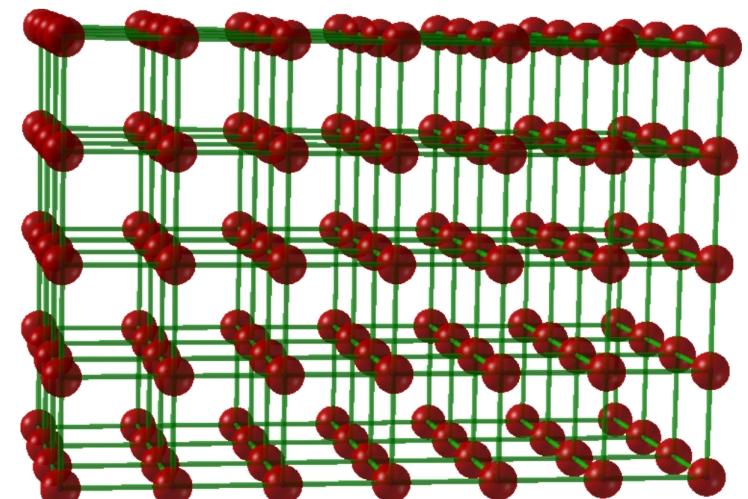
“Traditional” CSD method

$$C = -\sigma \frac{\partial^2 V}{\partial x^2} \approx -\sigma \frac{V(x+h) - 2V(x) - V(x-h)}{h^2}$$

In “traditional” CSD we lose points on the boundary:



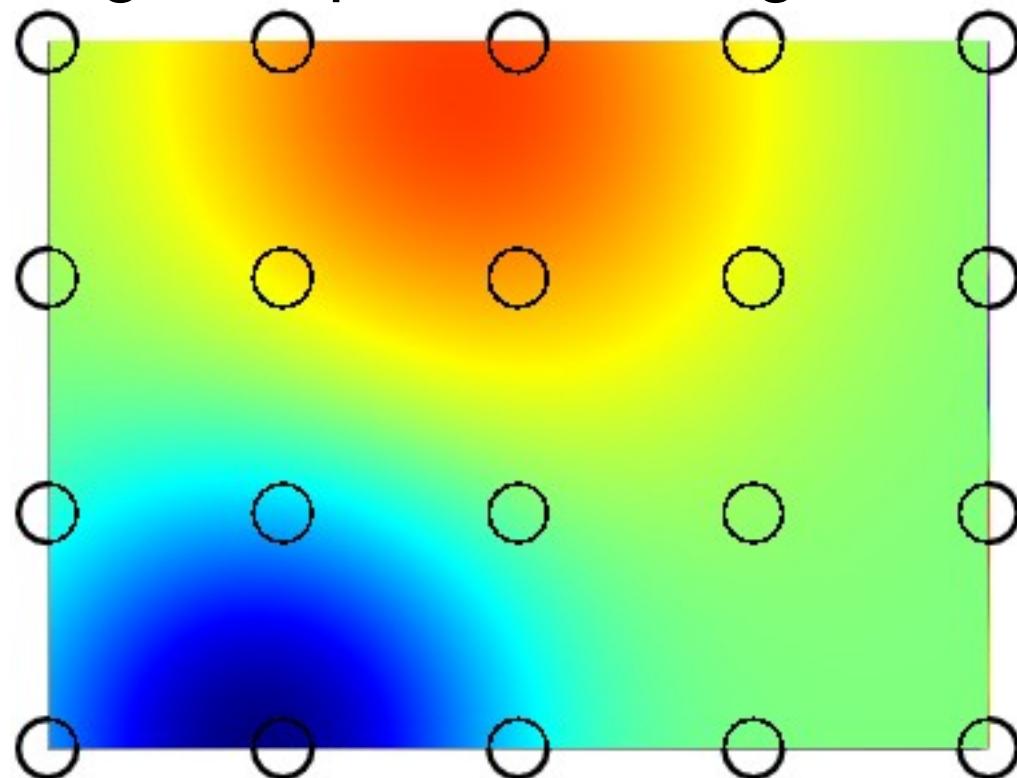
In 3D setup we considered (4x5x7)
one would lose 110 out of 140 points



Inverse current source density (iCSD)

- Assume N-parameter model of CSD
e.g. interpolated on a grid

Pettersen et al 2006
Łęski et al 2007



$$CSD(x) = \sum_{i=1}^N a_i \tilde{b}_i(x)$$

$$V_j = \sum_i \tilde{K}_{ji} a_i$$

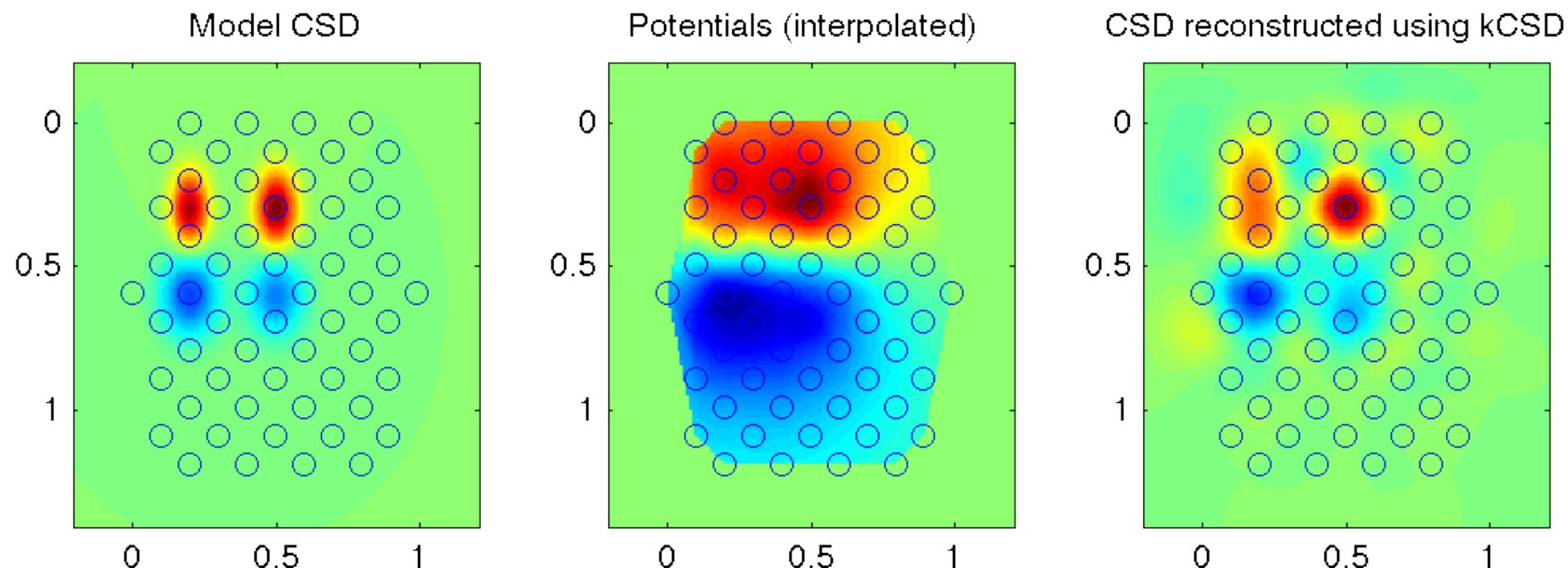
$$\vec{a} = (\tilde{K})^{-1} \vec{V}$$

- Evaluate potentials on the grid by forward modeling
 V at grid points = $F[N$ parameters of CSD]
- Invert F
 N parameters of CSD = $F^{-1}[V$ at grid points]

Kernel Current Source Density: kCSD

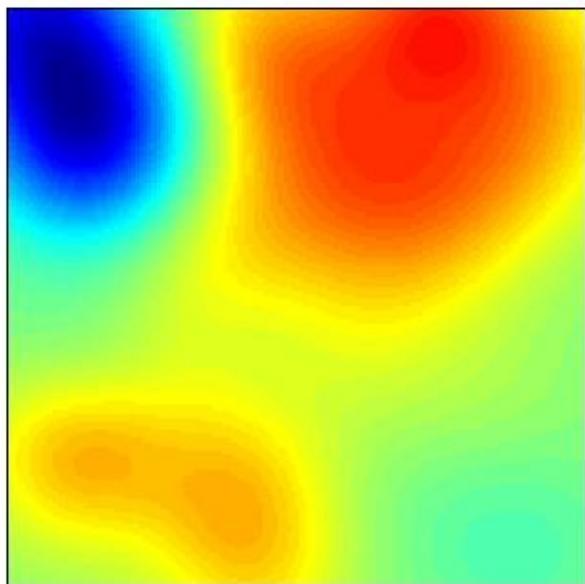
Potworowski et al., Neural Computation, 2012

- Nonparametric method (overcomplete bases)
- Arbitrary distribution of contacts
- Correction for noise



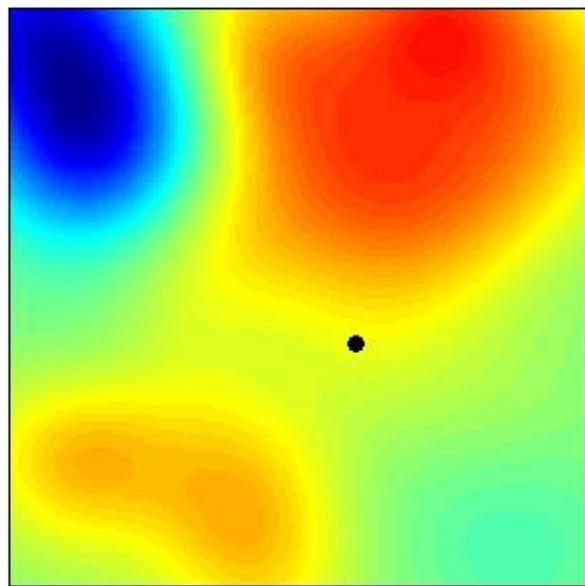
Kernel Current Source Density

CSD in the tissue



Kernel Current Source Density

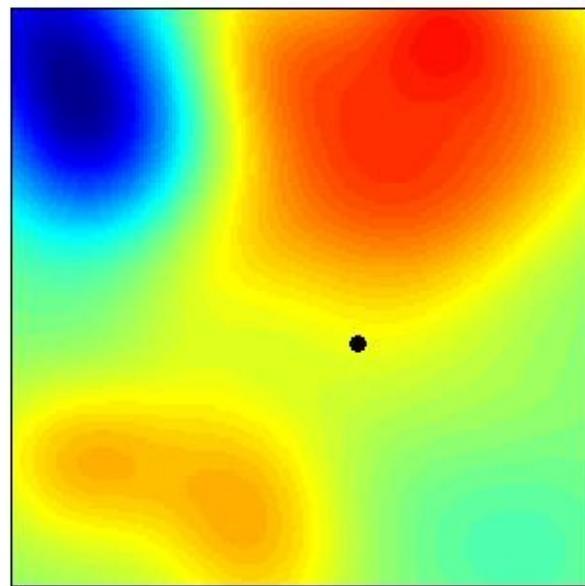
CSD in the tissue



1 electrode

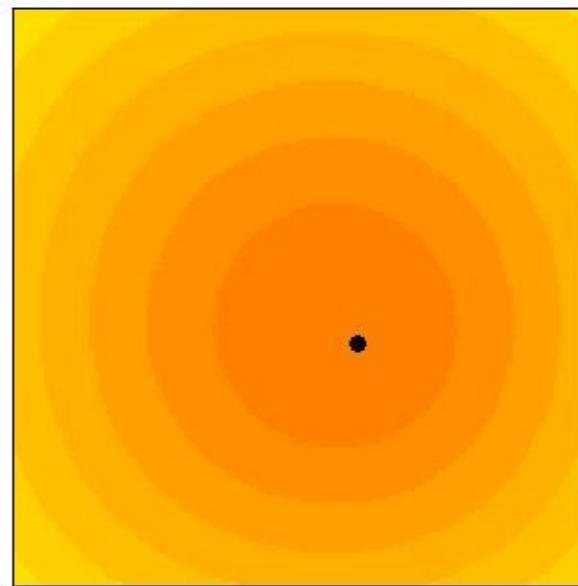
Kernel Current Source Density

CSD in the tissue



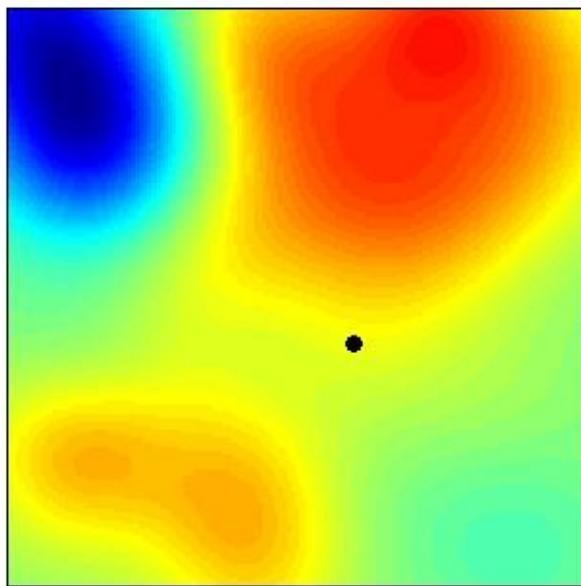
1 electrode

Interpolated potential



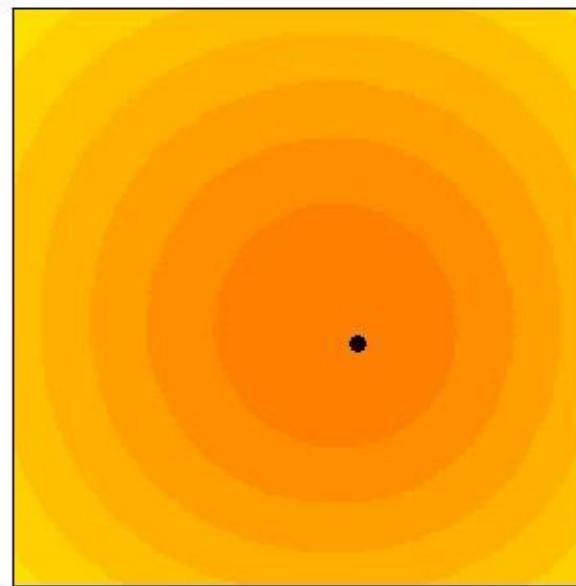
Kernel Current Source Density

CSD in the tissue

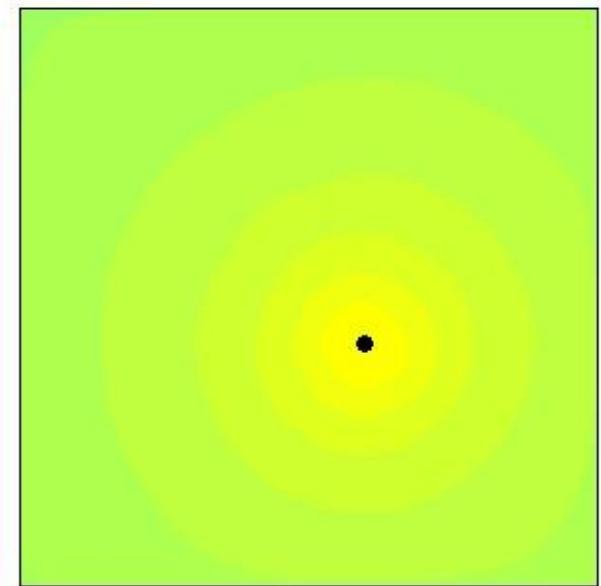


1 electrode

Interpolated potential

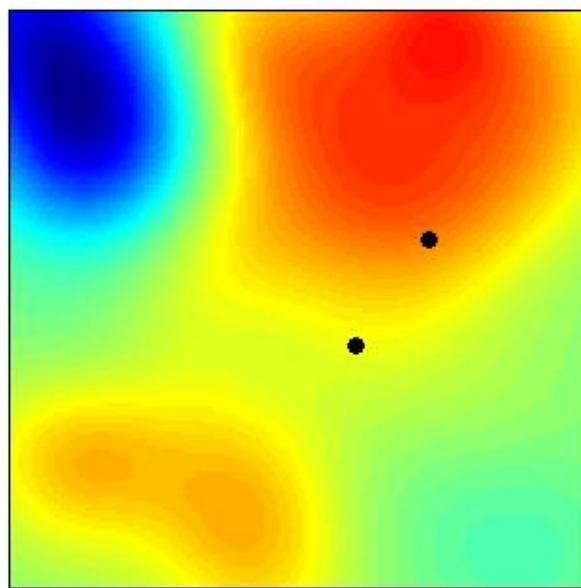


Reconstructed CSD



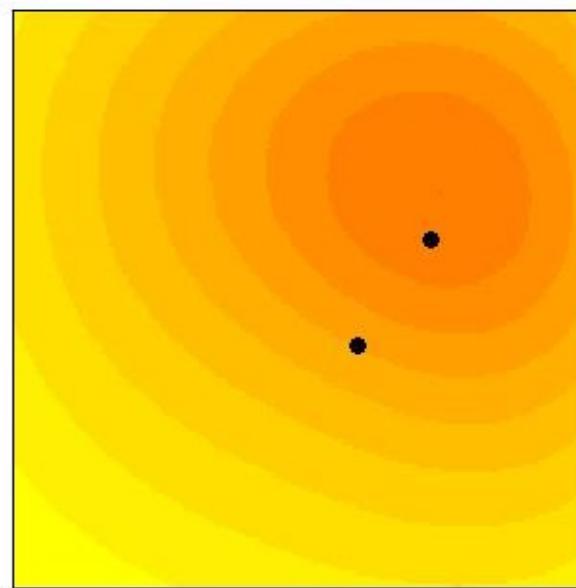
Kernel Current Source Density

CSD in the tissue

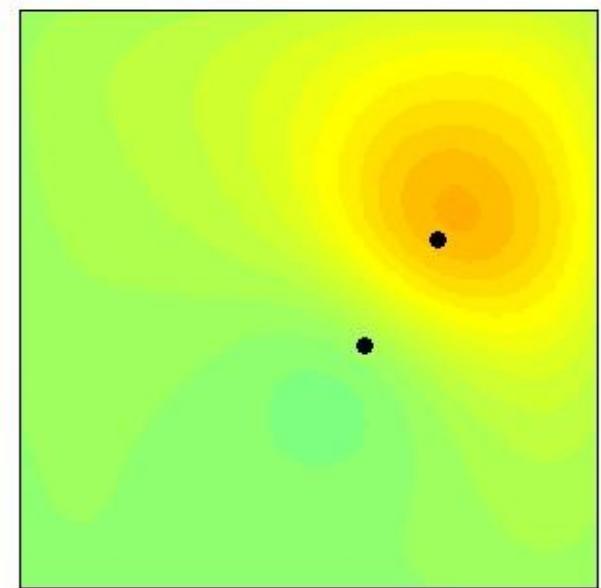


2 electrodes

Interpolated potential

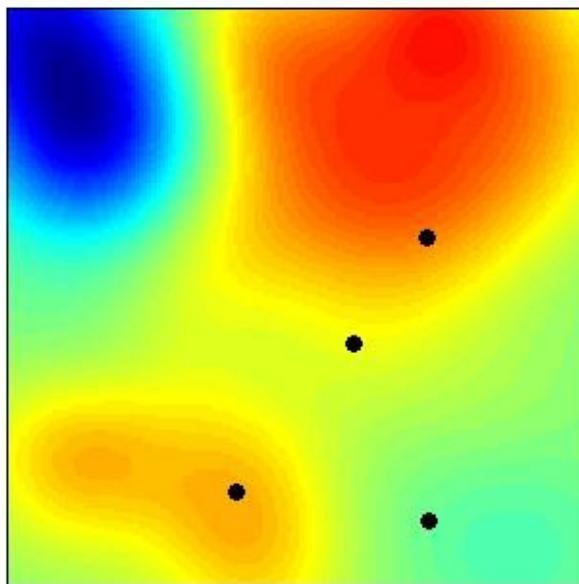


Reconstructed CSD

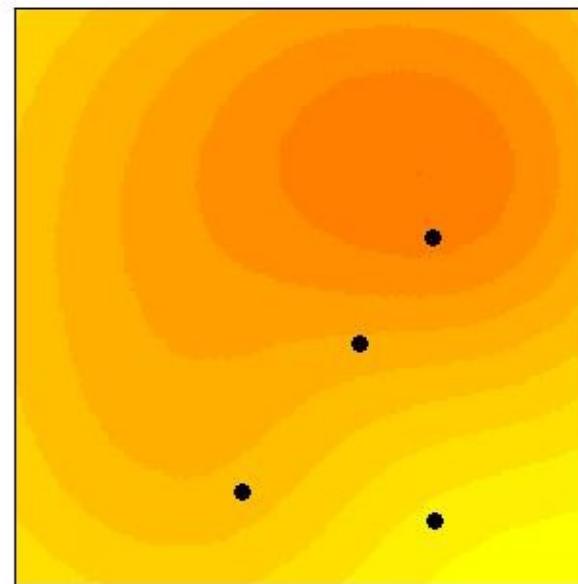


Kernel Current Source Density

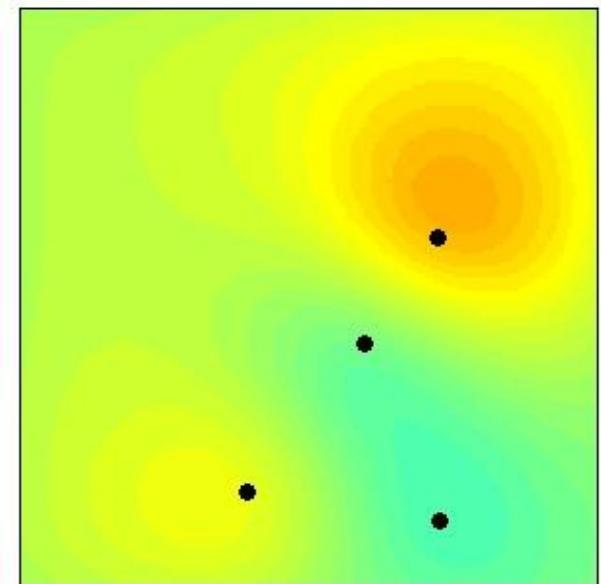
CSD in the tissue



Interpolated potential



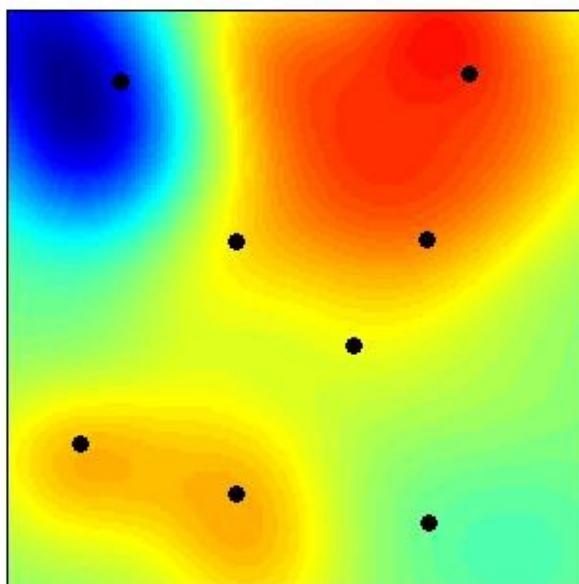
Reconstructed CSD



4 electrodes

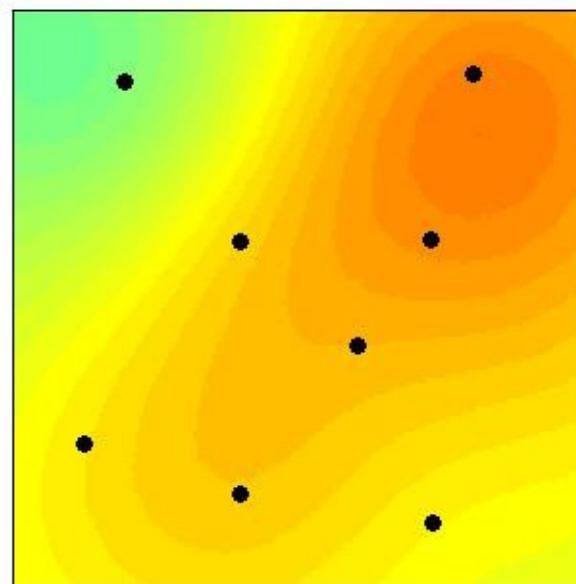
Kernel Current Source Density

CSD in the tissue

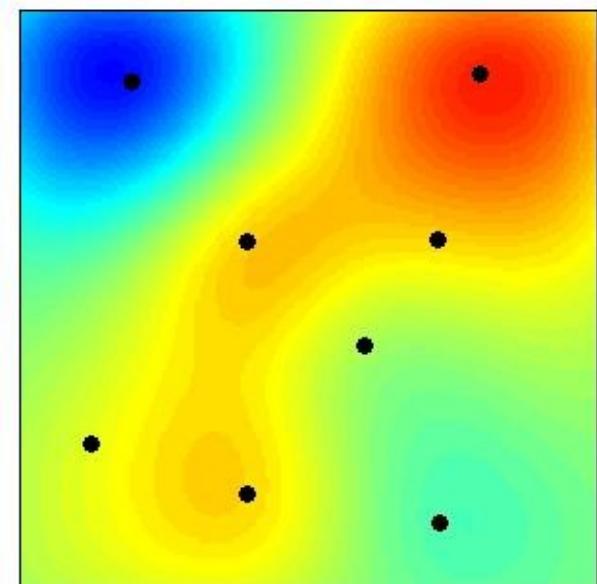


8 electrodes

Interpolated potential

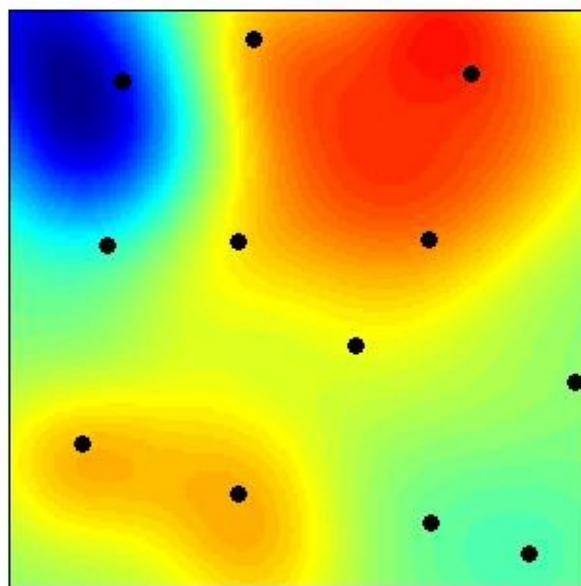


Reconstructed CSD

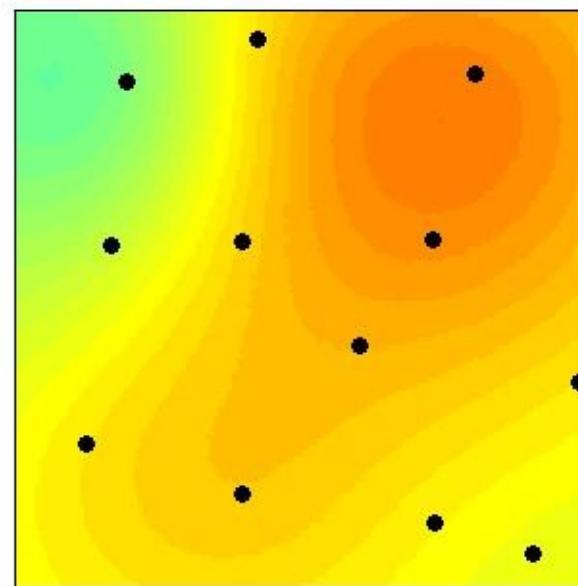


Kernel Current Source Density

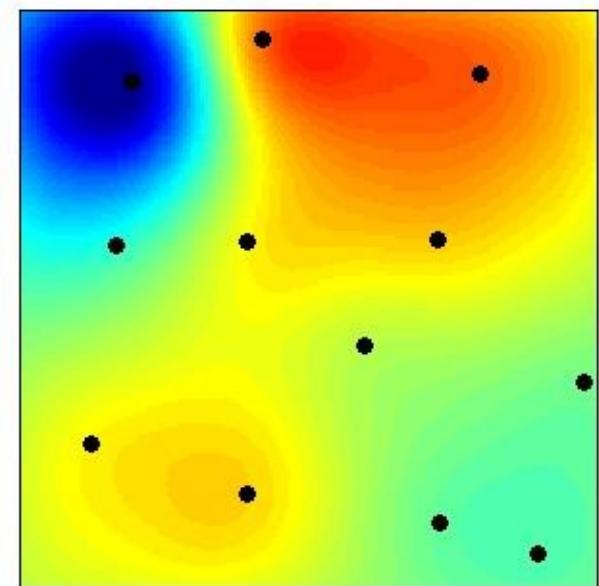
CSD in the tissue



Interpolated potential



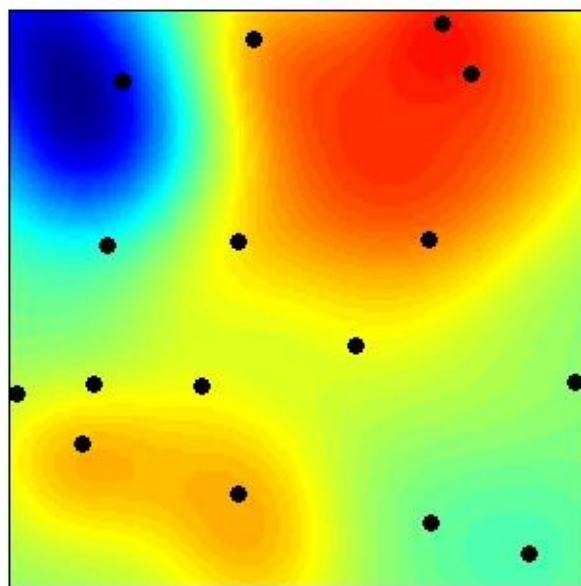
Reconstructed CSD



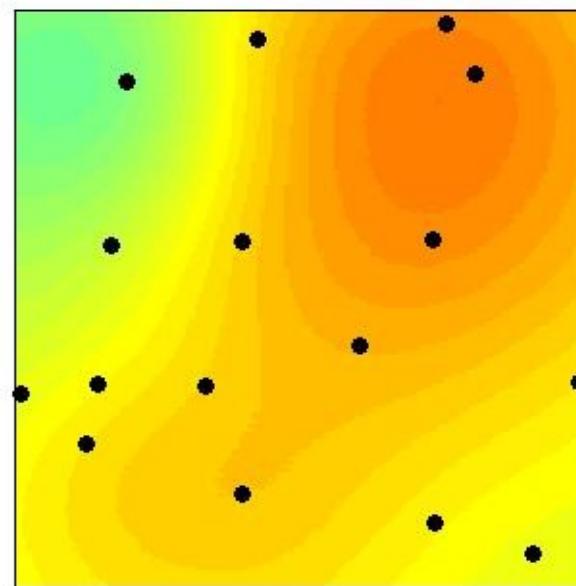
12 electrodes

Kernel Current Source Density

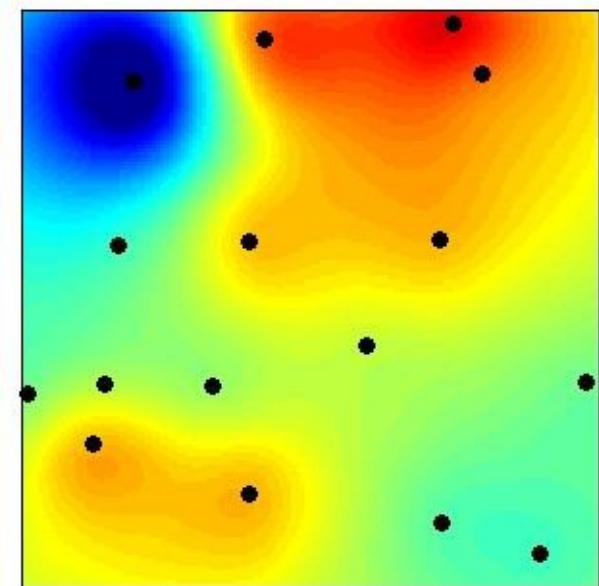
CSD in the tissue



Interpolated potential



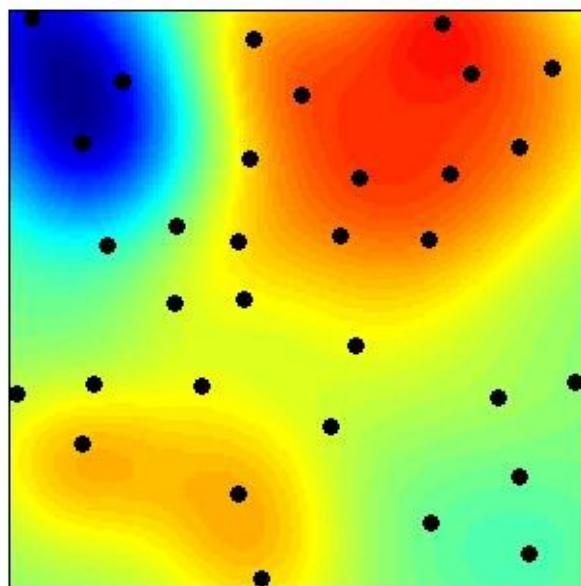
Reconstructed CSD



16 electrodes

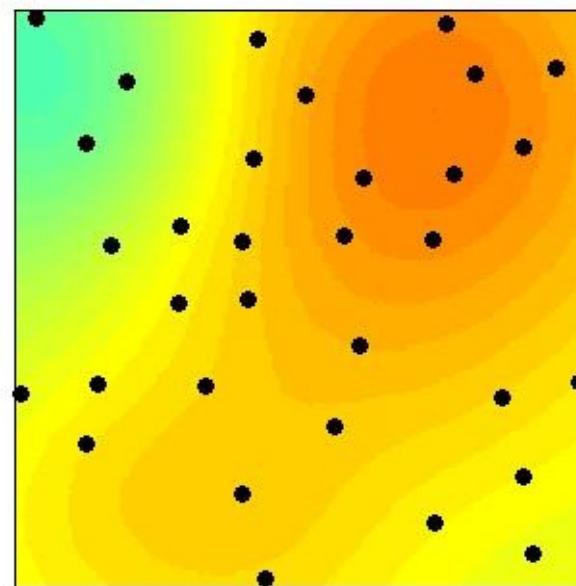
Kernel Current Source Density

CSD in the tissue

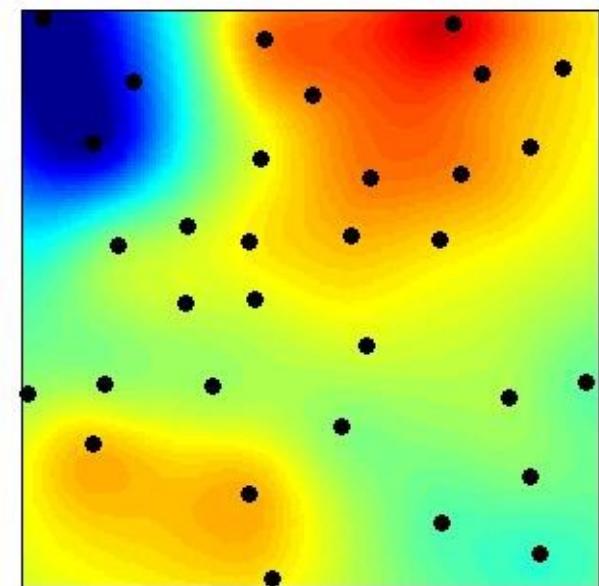


32 electrodes

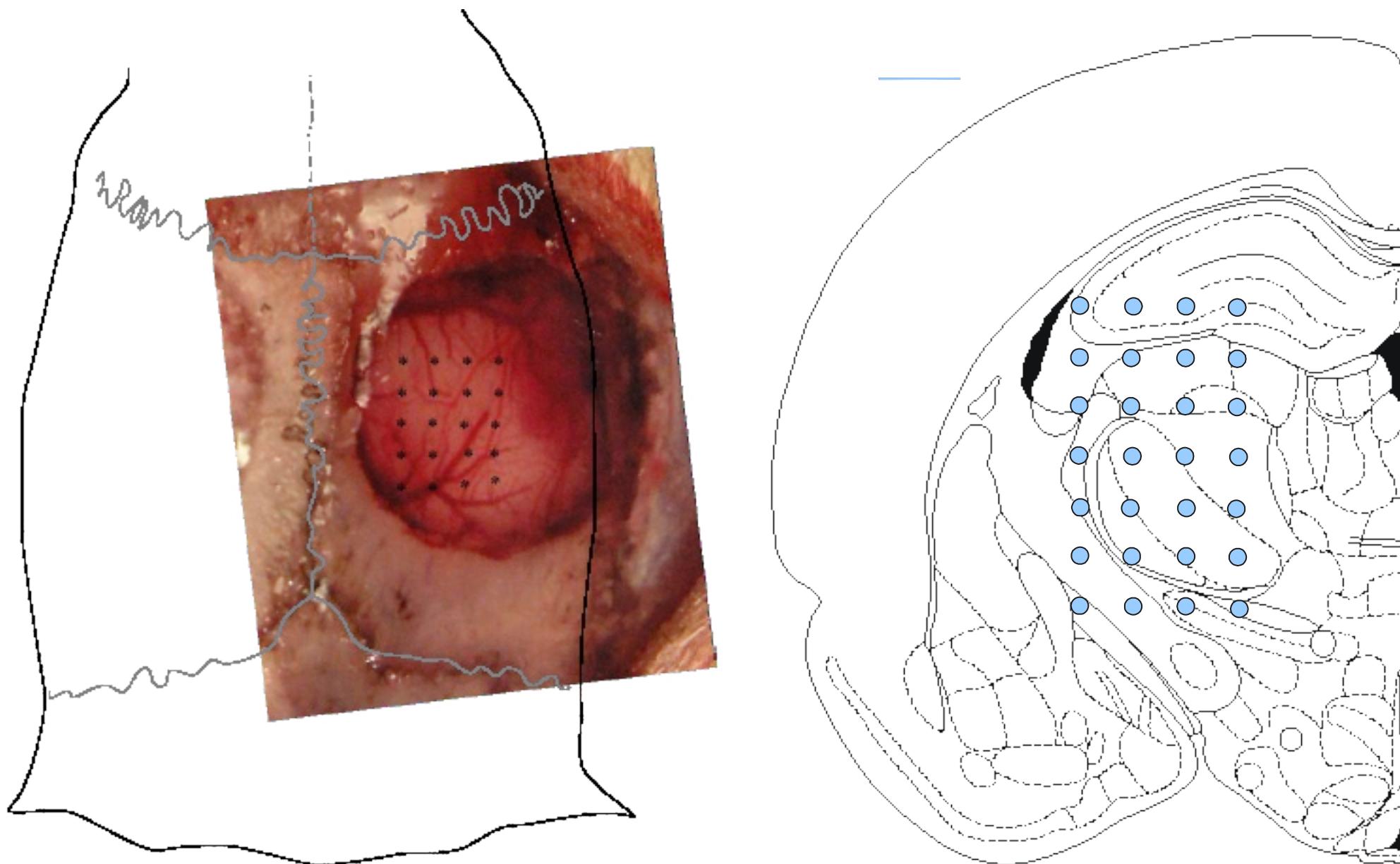
Interpolated potential



Reconstructed CSD

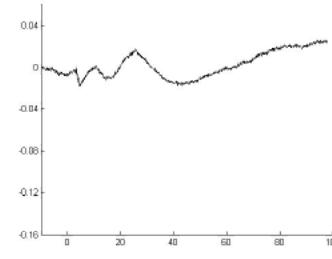
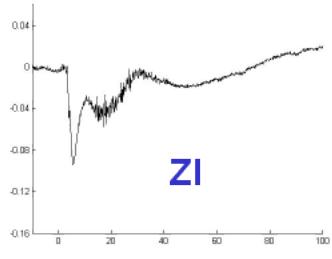
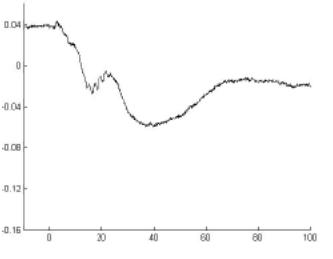
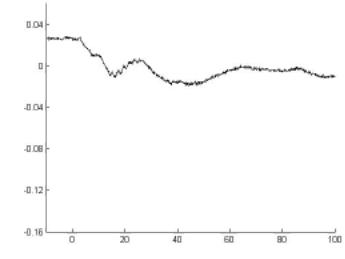
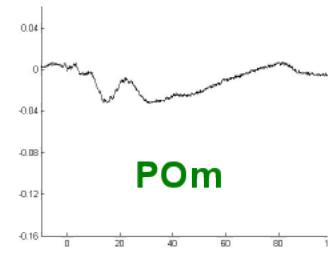
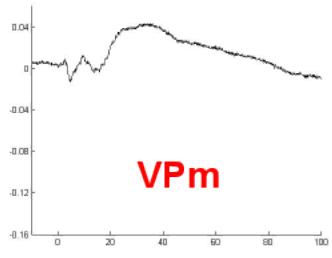
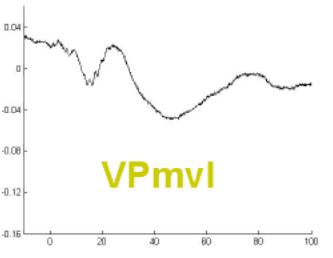
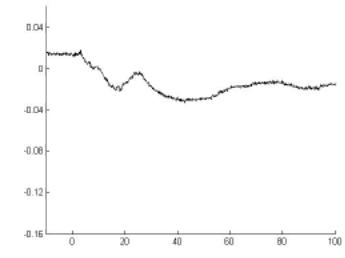
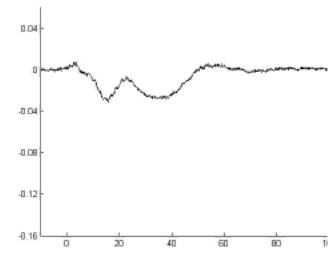
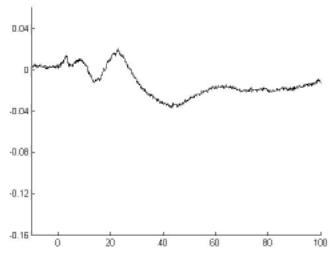
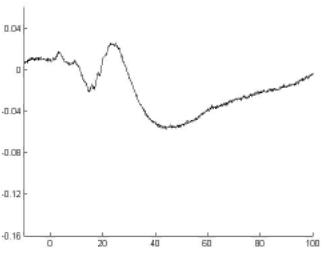
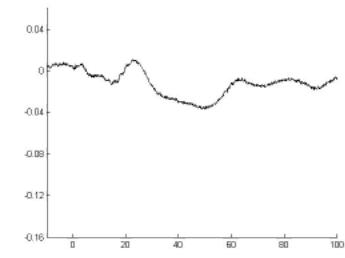
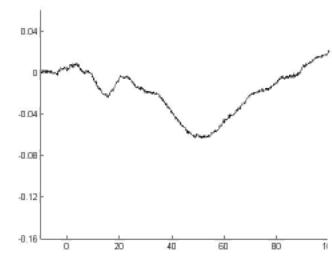
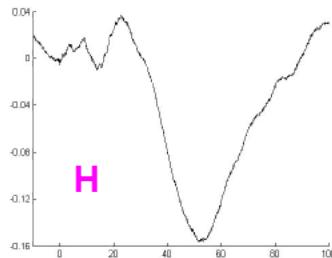
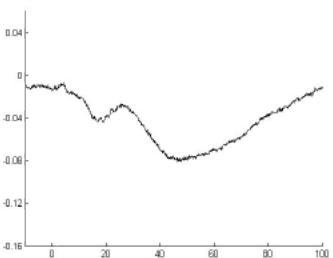
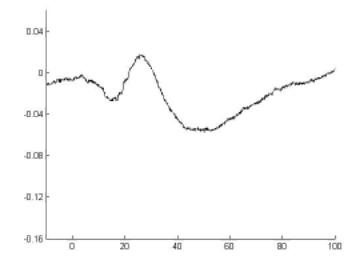


ICSD 3D: Experimental setup

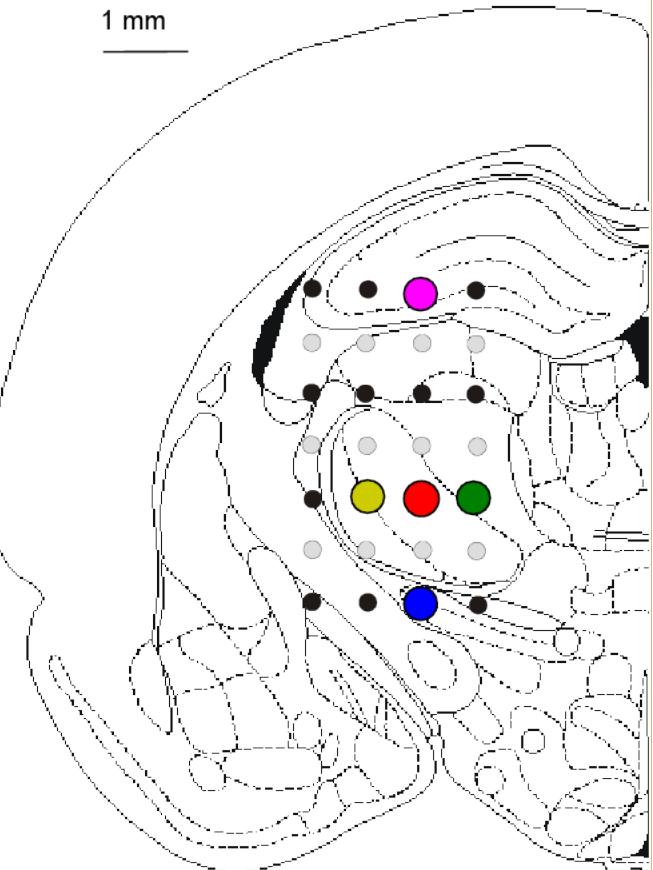


ICSD 3D: Example local field potentials recorded in the rat forebrain

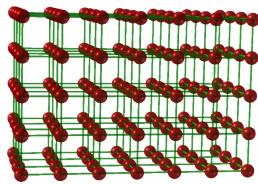
mV



1 mm



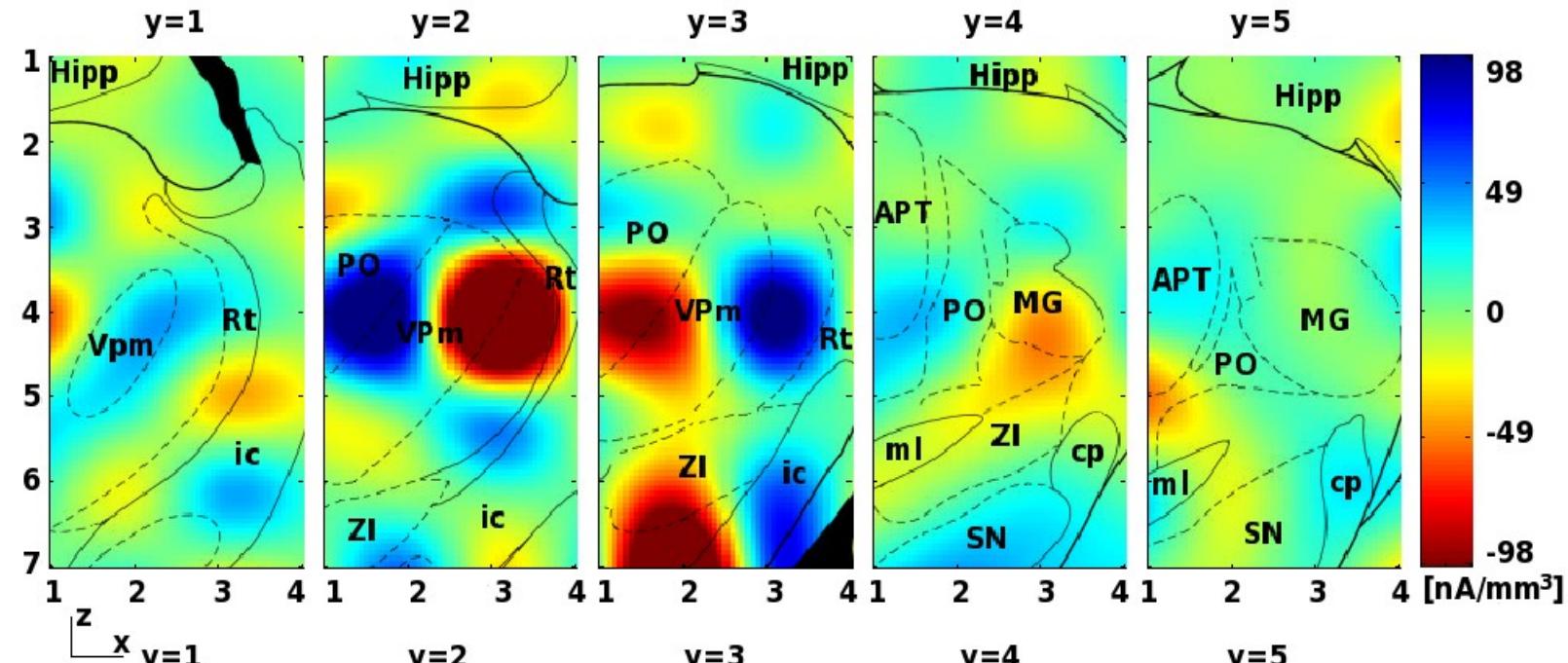
bregma -3.3 mm



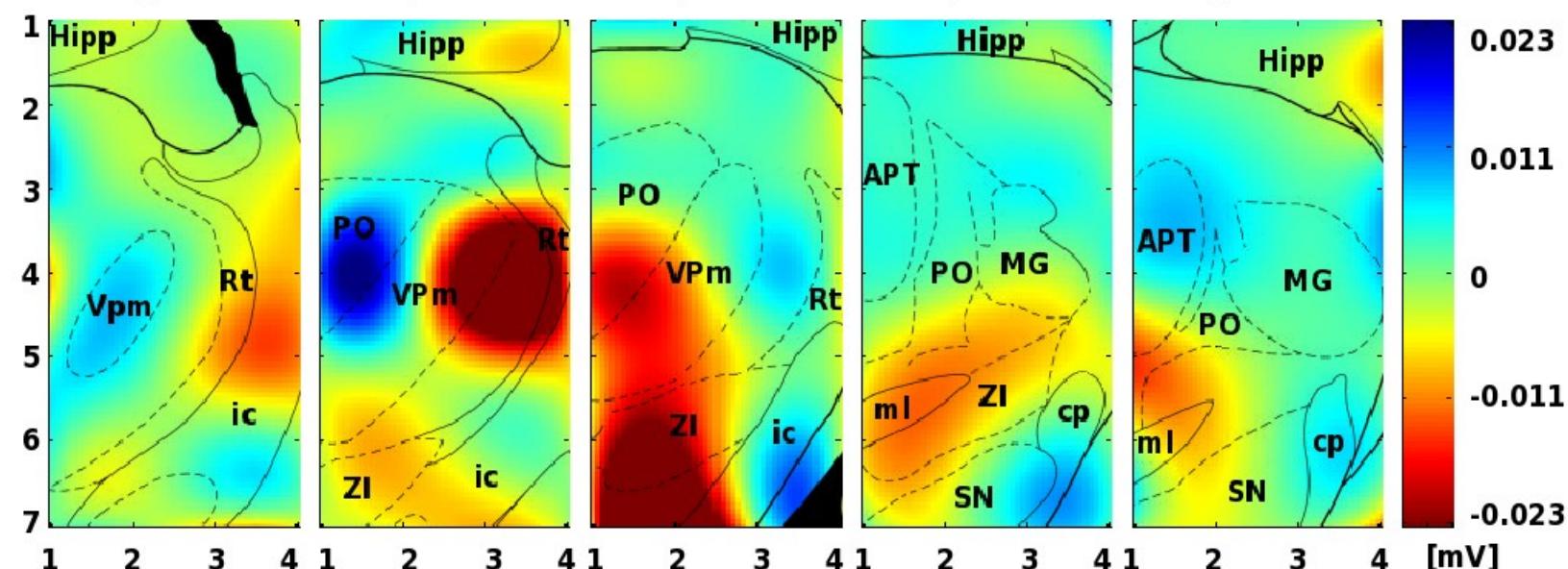
iCSD in 3D

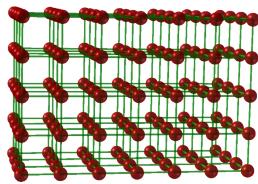
Daniel Świejkowski, Ewa Kublik, Andrzej Wróbel

**Current
Source
Density**



**Interpolated
field potential**

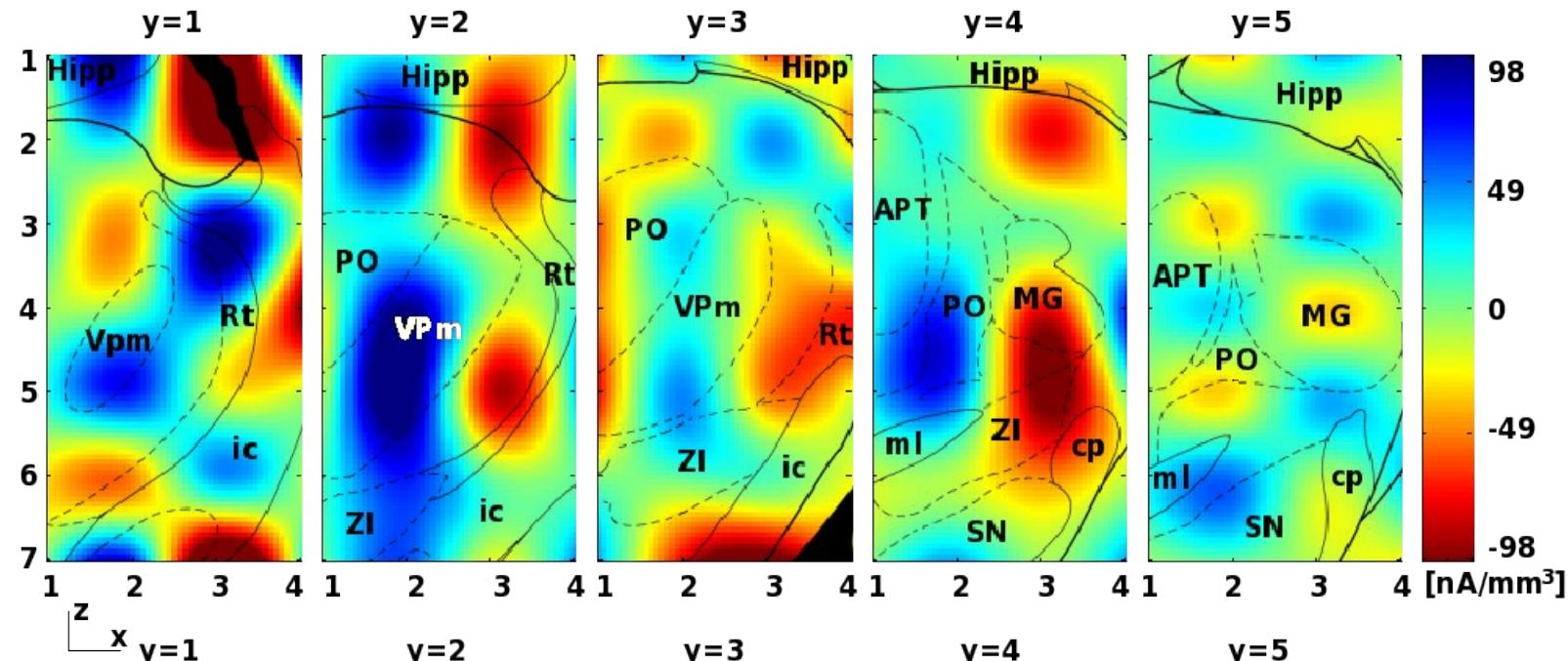




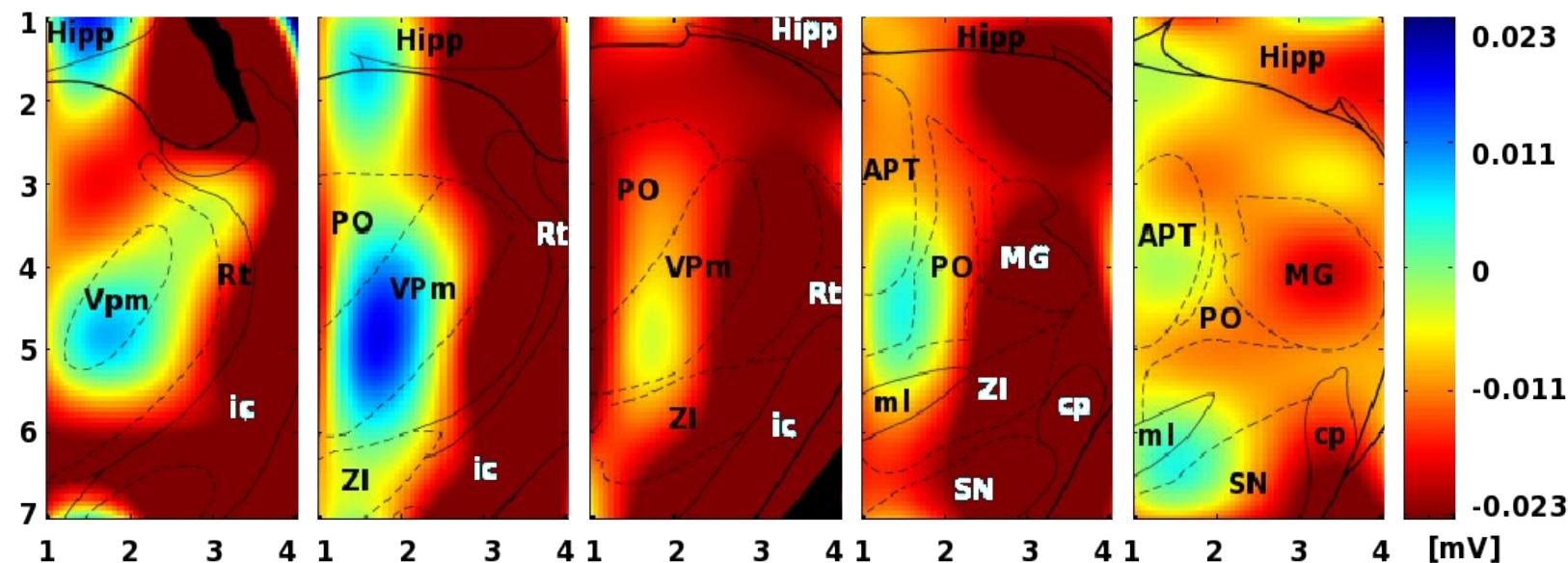
iCSD in 3D

Daniel Świejkowski, Ewa Kublik, Andrzej Wróbel

**Current
Source
Density**



**Interpolated
field potential**



Difficulties in analyzing LFP

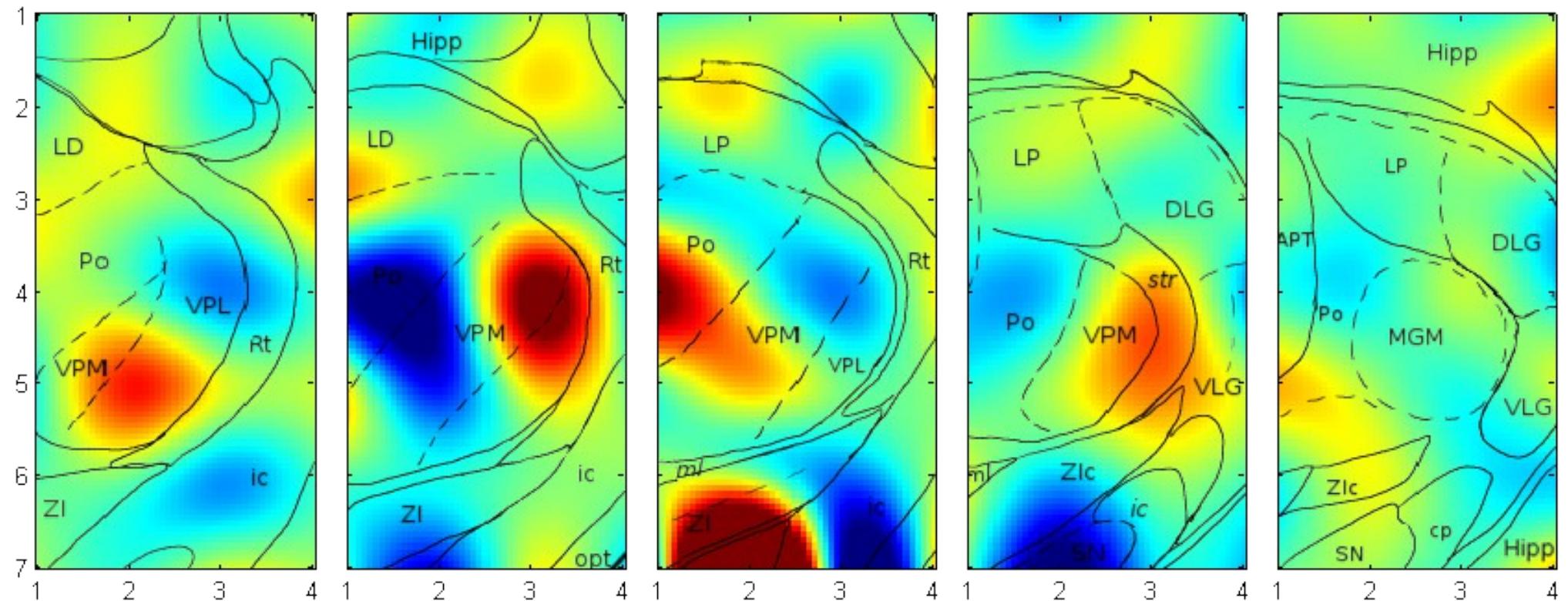
- Electric field propagation
(spatial blurring) → CSD
- Multiple populations overlapping
→ methods for identifying components

$$F(x, t) = \sum_i S_i(x) T_i(t)$$

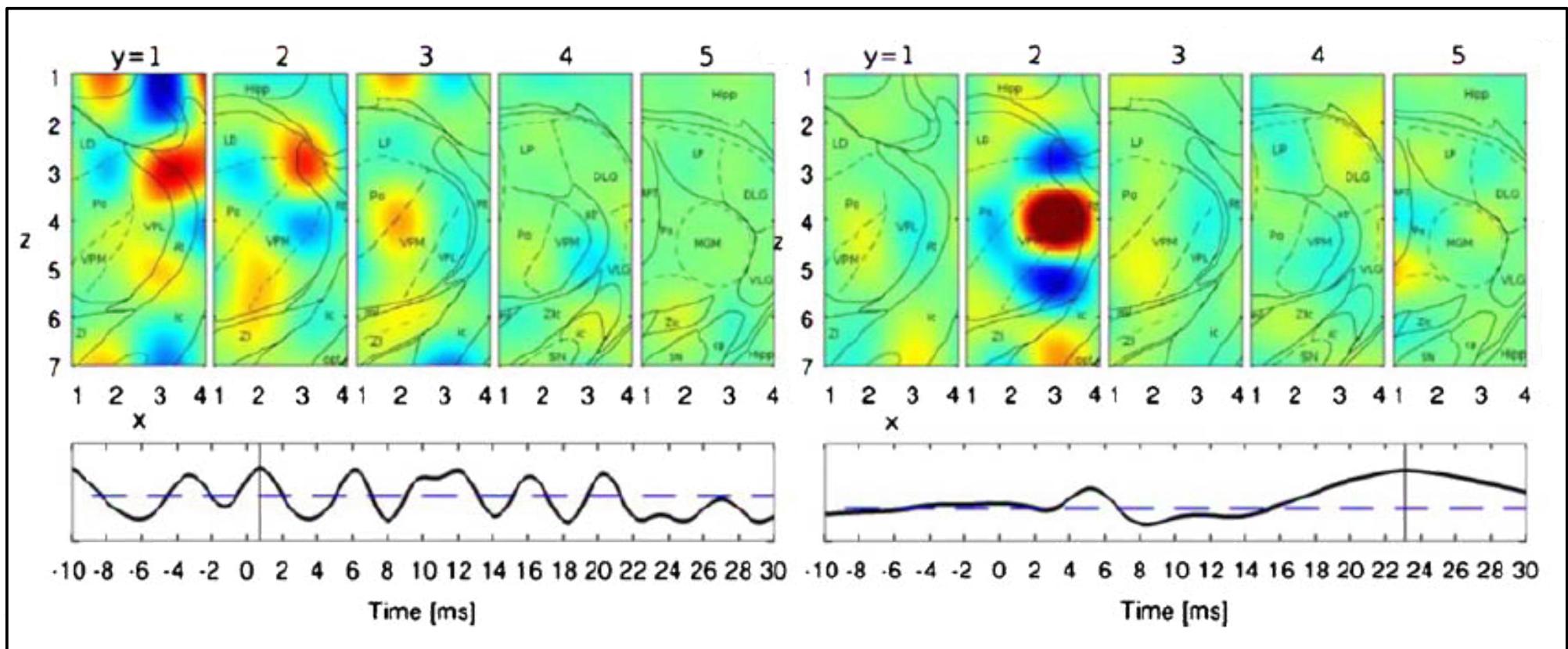
Extracting functional components of neural dynamics with ICA and iCSD

Multiple populations possible
in the same place

cocktail party problem – ICA



Temporal vs. spatial ICA (experimental data)

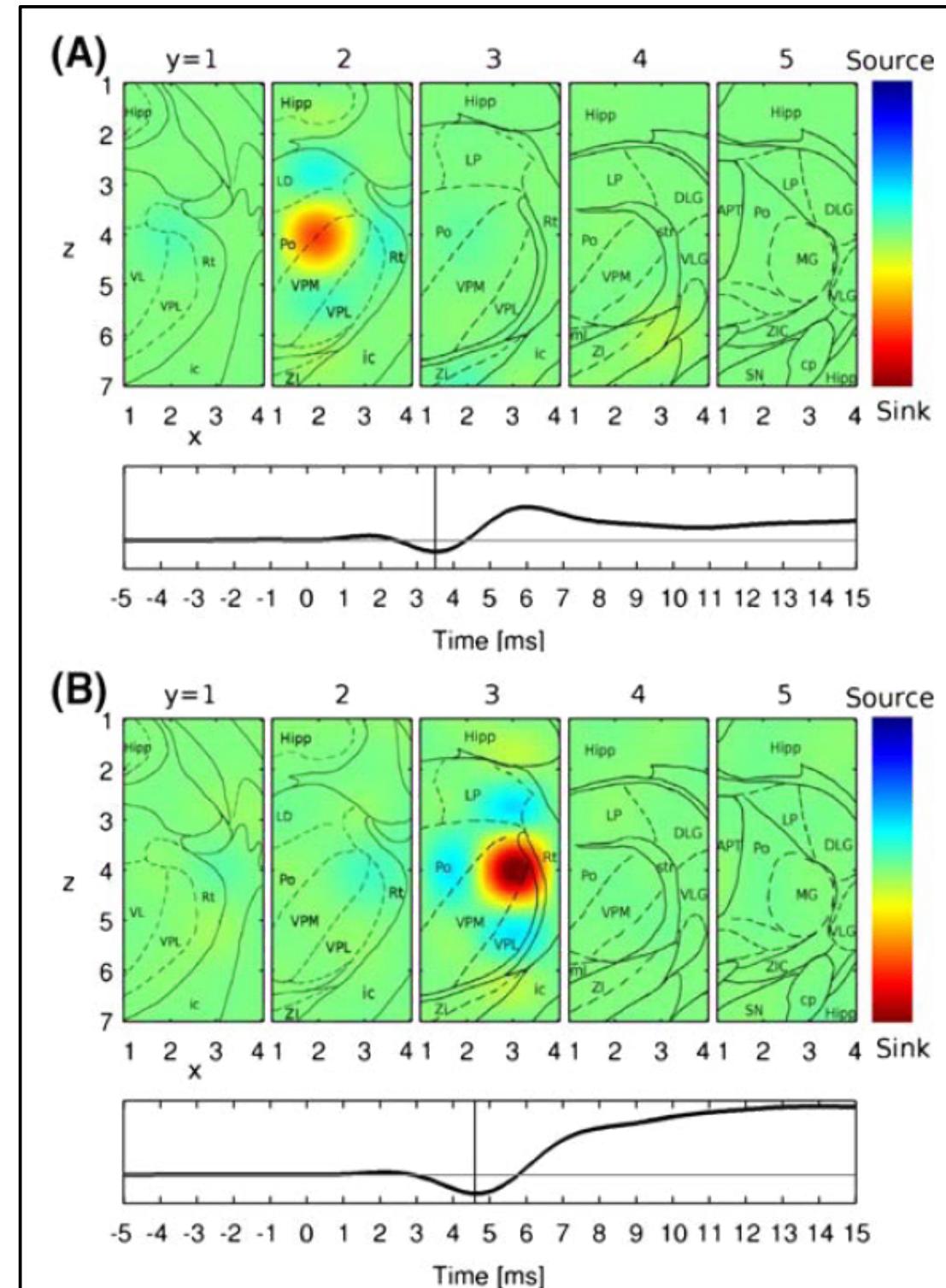


Temporal ICA

Spatial ICA

Experimental results

- Two components corresponding to two distinct pathways (single- and multi-whisker input)
- Delay of ~ 1ms
- Reliable localization in 5 out of 7 rats



Can we trust it?

In attempts to extract biophysically relevant information from laminar multielectrode LFP recordings, a number of previous efforts have employed principal component analysis (PCA; Di et al., 1990) and independent component analysis (ICA; Leski et al., 2009; Makarov et al., 2010).

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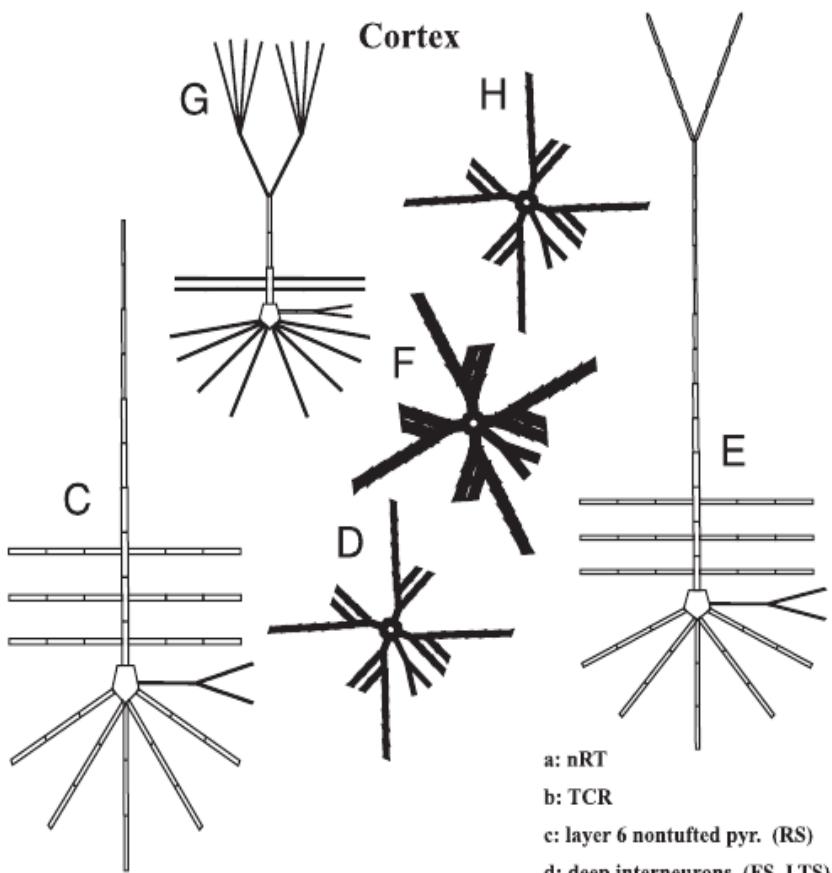
Gratiy, Devor, Einevoll, Dale; Front. In Neuroinf (2011) art. 32

Forward modeling
An example:

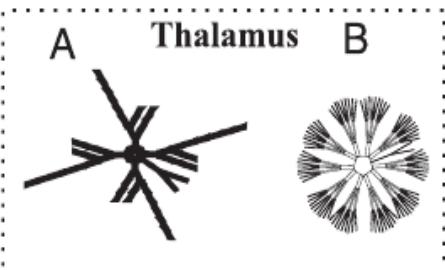
Traub's model of thalamocortical loop

Forward modeling in Traub's model

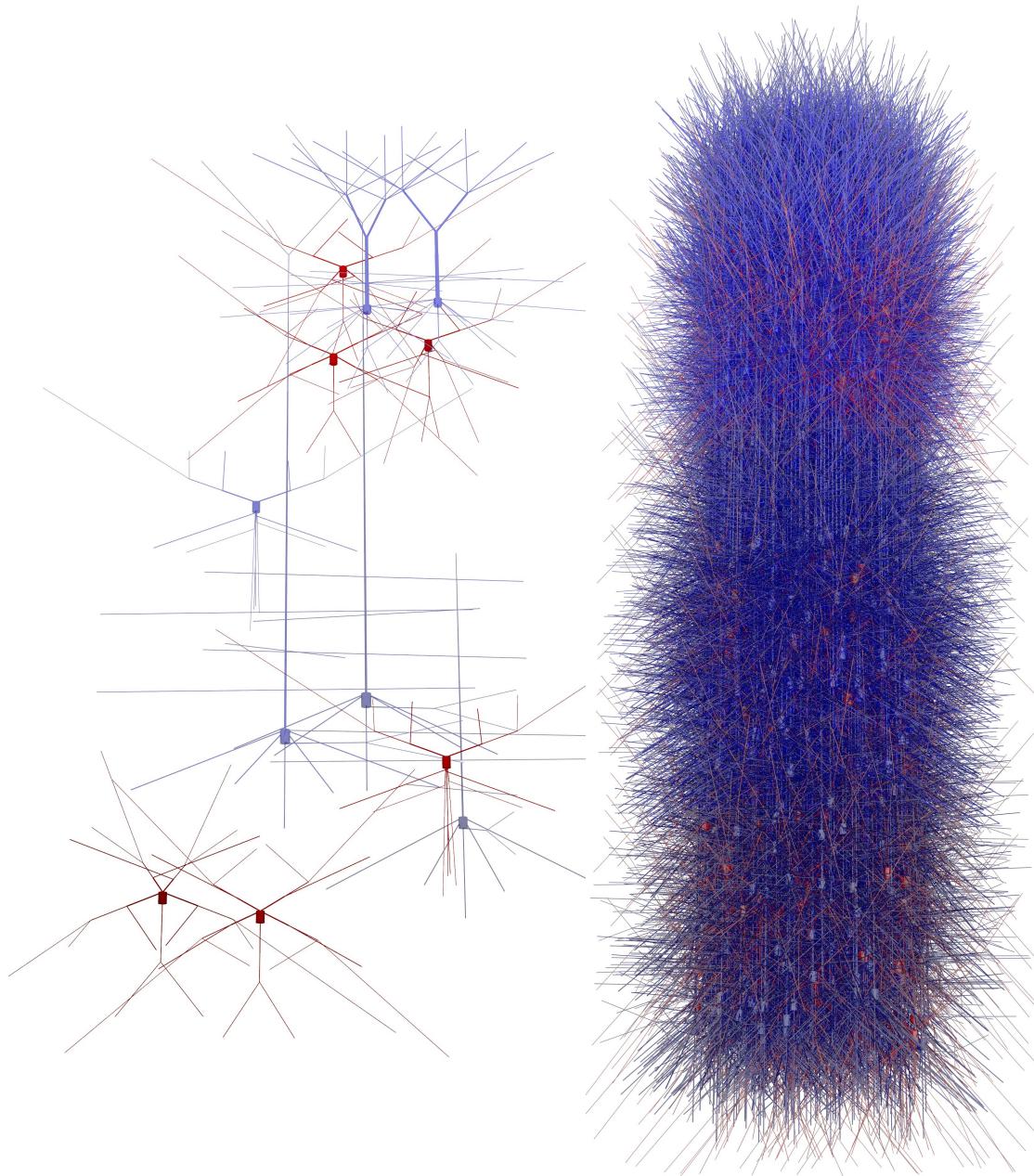
Original Traub model

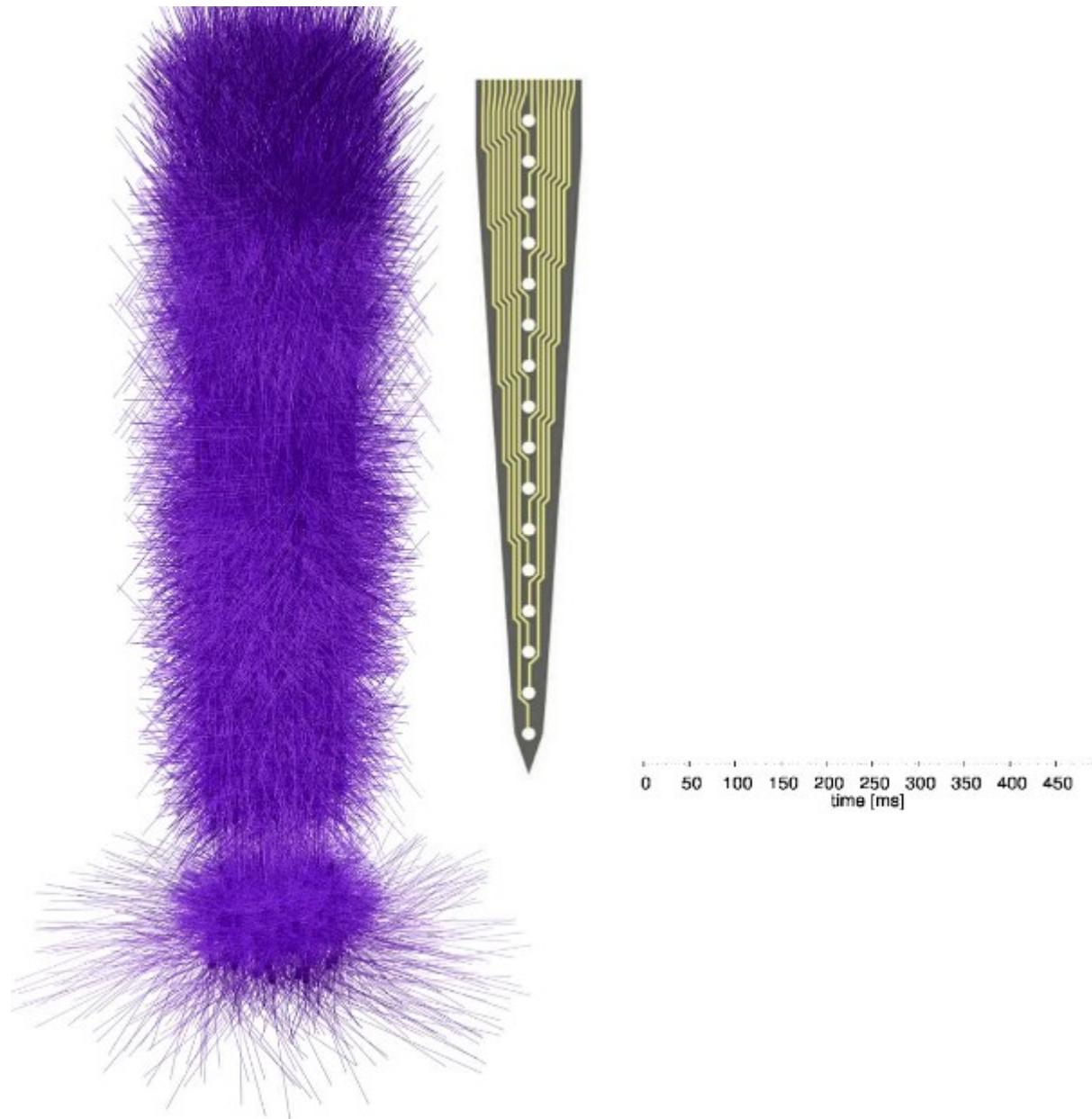


- a: nRT
- b: TCR
- c: layer 6 nontufted pyr. (RS)
- d: deep interneurons (FS, LTS)
- e: layer 5 tufted pyr. (IB, RS)
- f: layer 4 spiny stellate
- g: layer 2/3 pyr. (RS, FRB)
- h: superficial interneurons (FS, LTS)



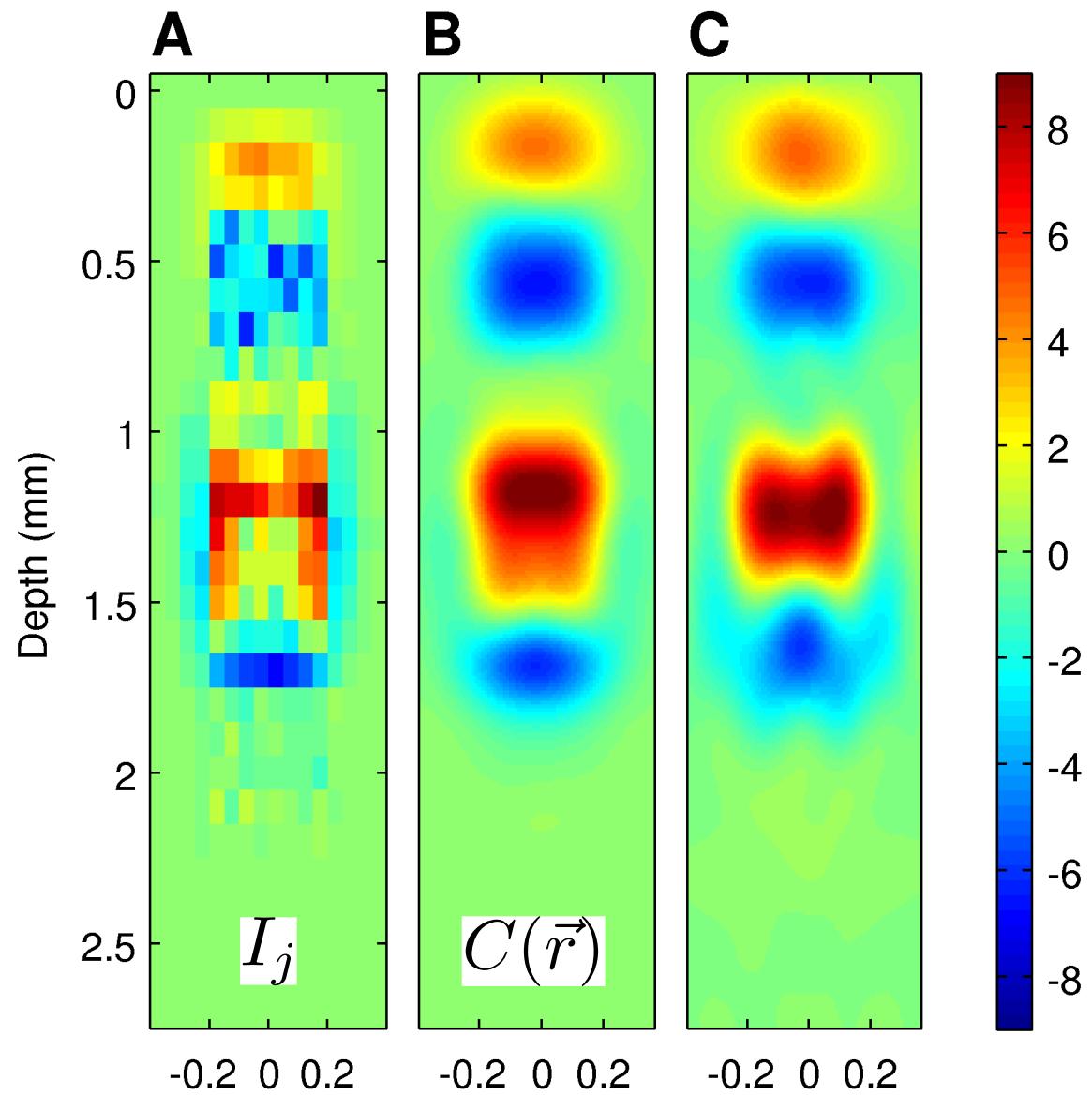
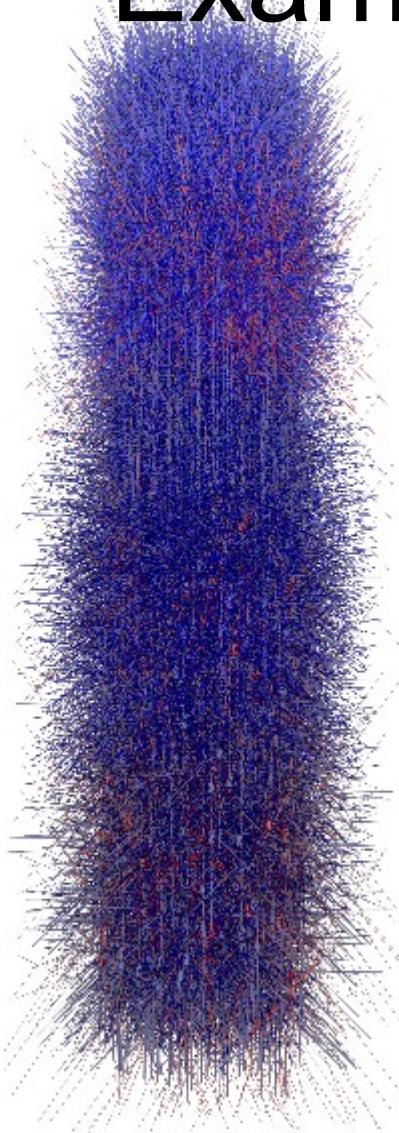
Traub model in 3D





Helena Głąbska, Piotr Majka – pr. Neuroinformatyki
Traub et al., . J Neurophysiol 2005, 93:2194-2232

Example



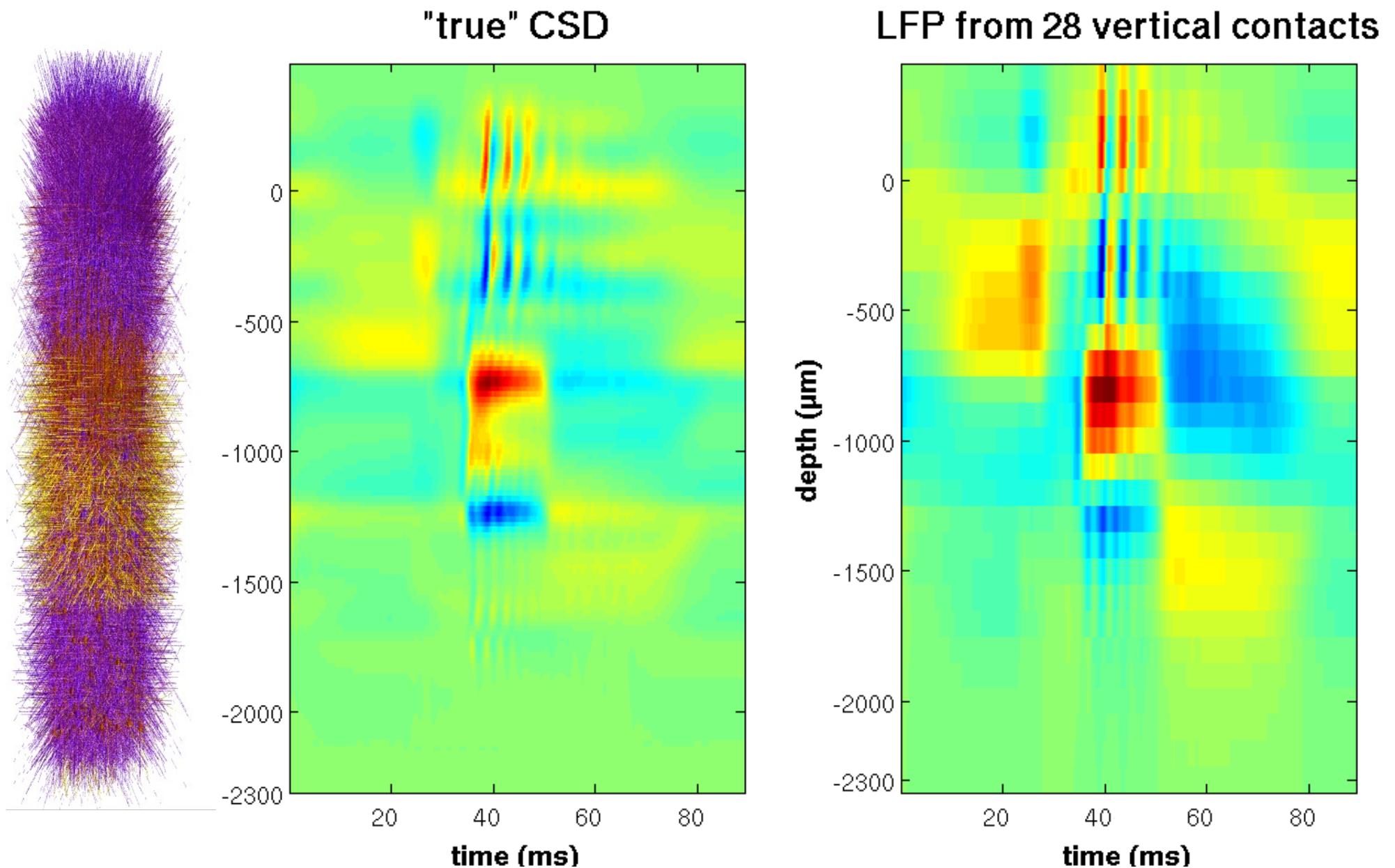
Simulated network
blue: excitatory
red: inhibitory

Current sources
in volumes
50x50x100 um
[150 000 cells]

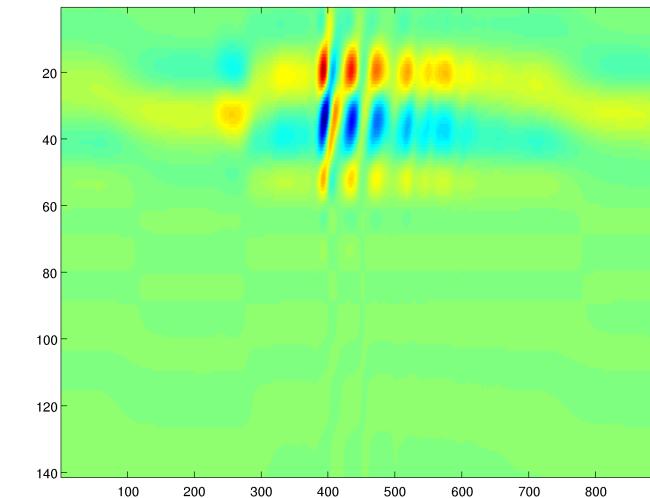
$x^{(mm)}$
Current sources
smoothed with
Gauss kernel of
R=100um

Current sources
reconstructed
with kCSD from
8x14 electrodes

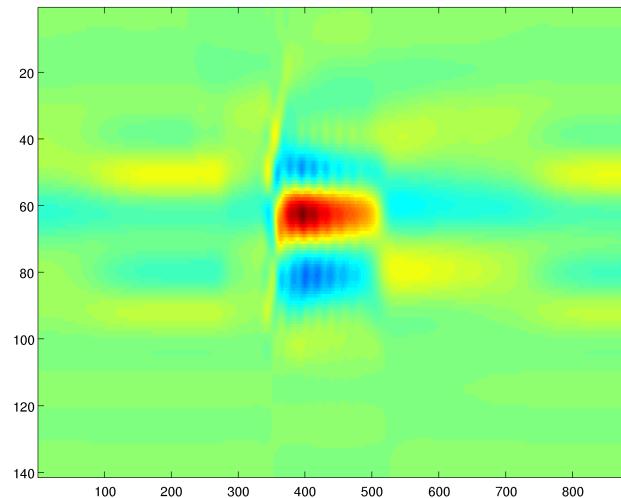
CSD and LFP from the model



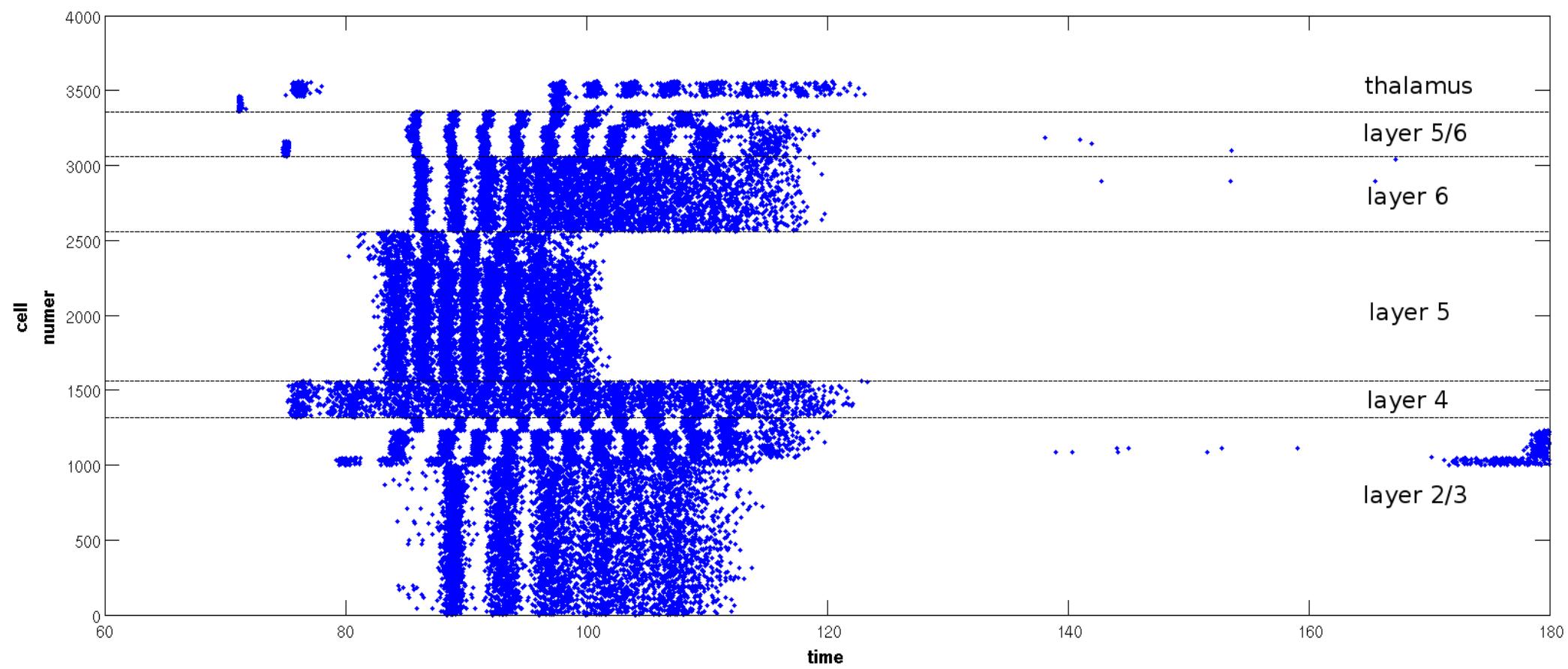
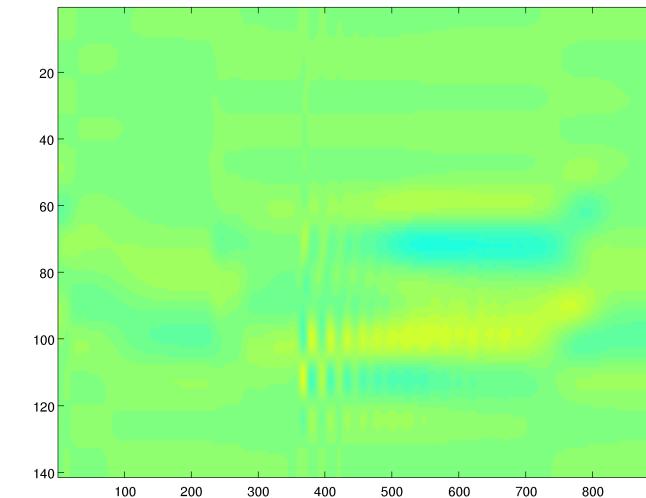
Pyramids layer 2/3



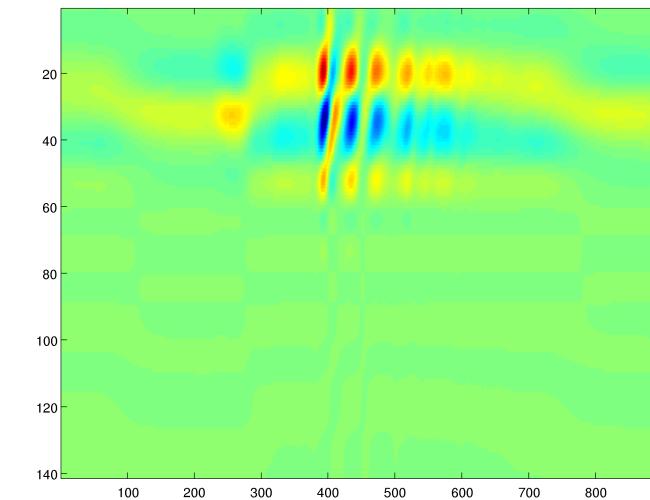
Pyramids layer 5



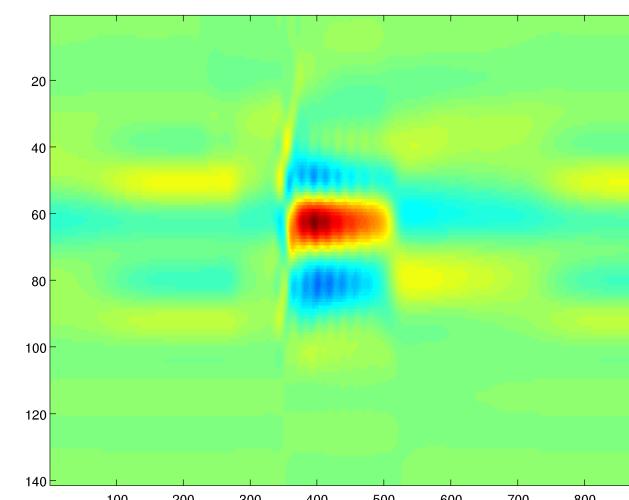
Pyramids layer 6



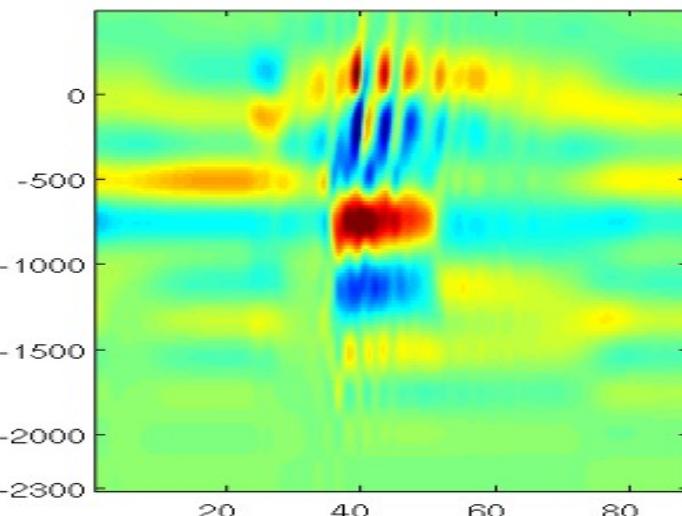
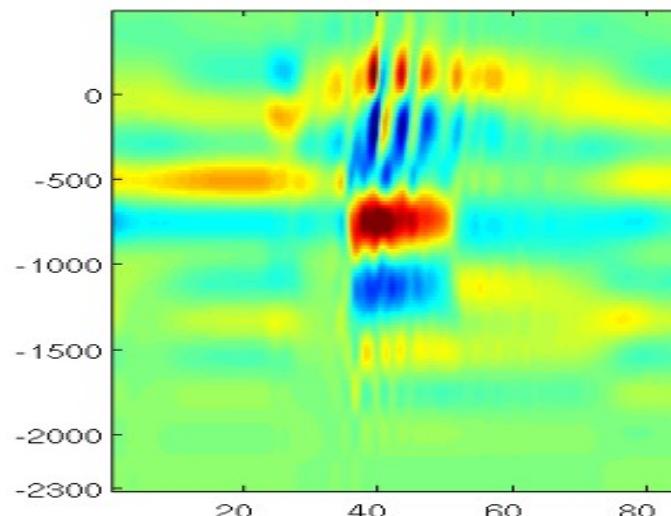
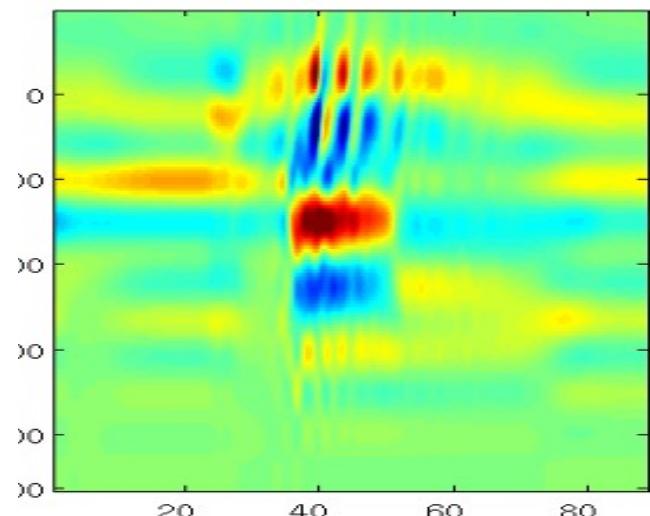
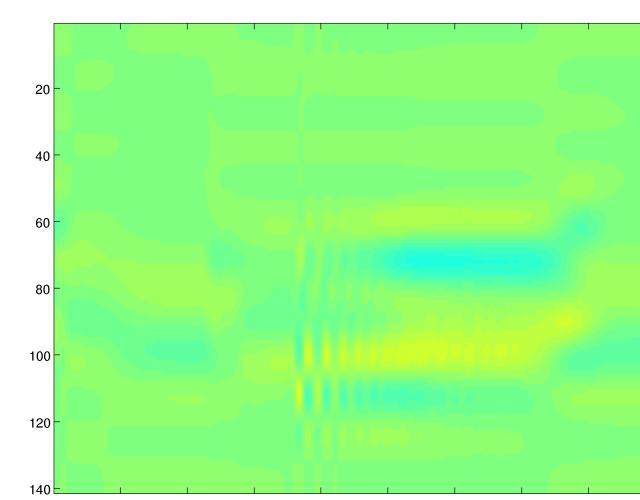
Pyramids layer 2/3



Pyramids layer 5



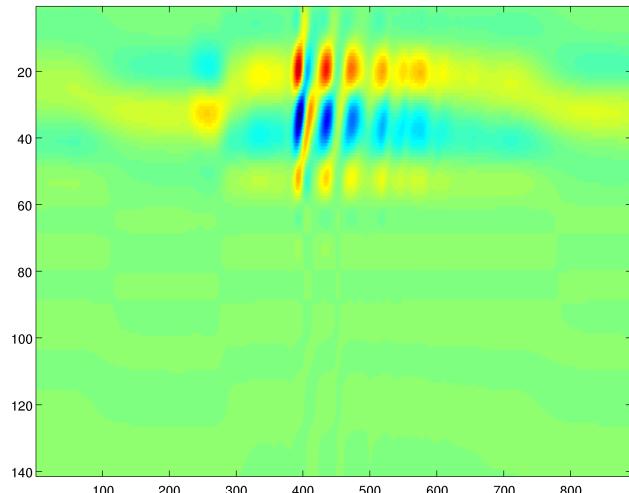
Pyramids layer 6



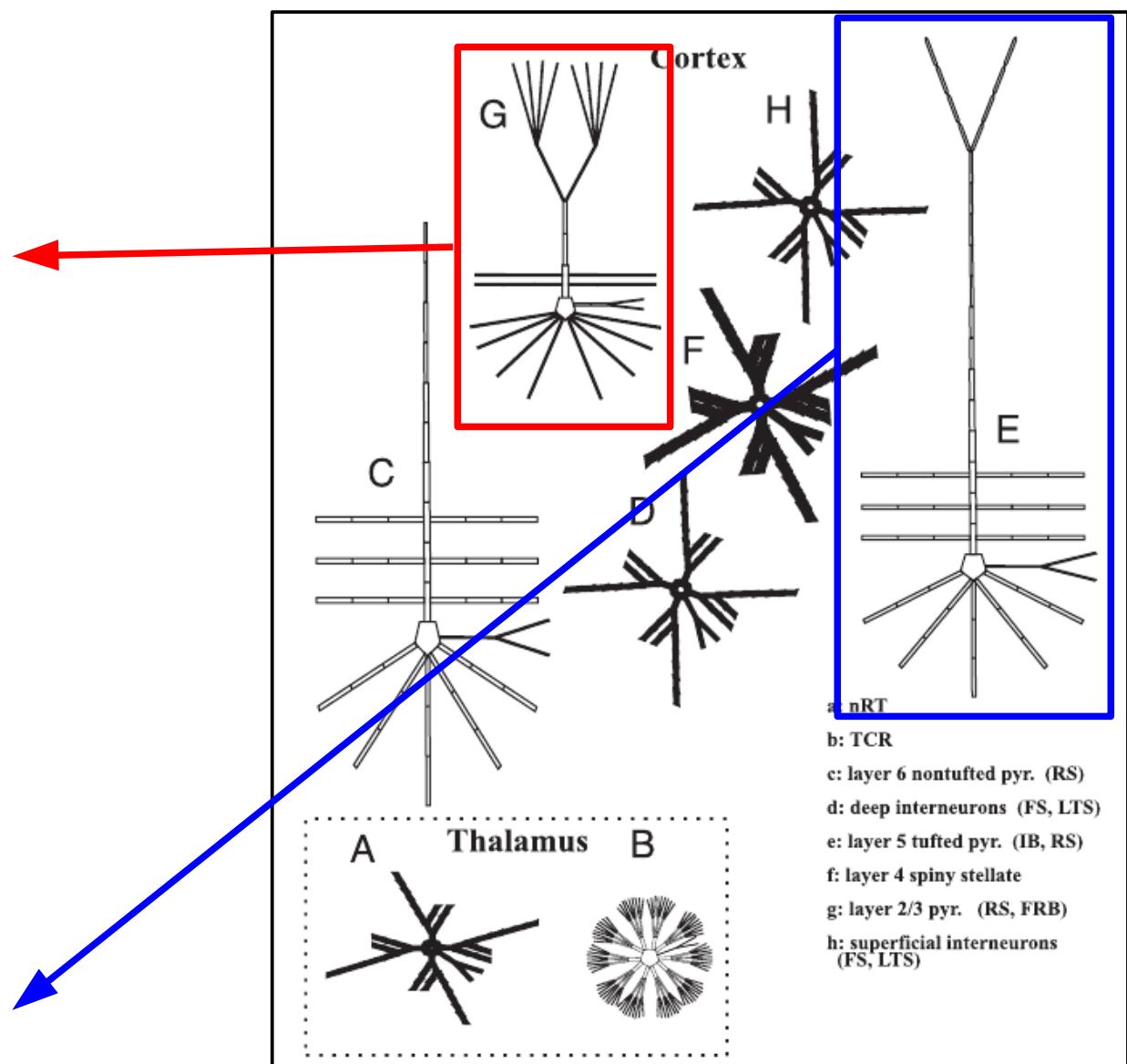
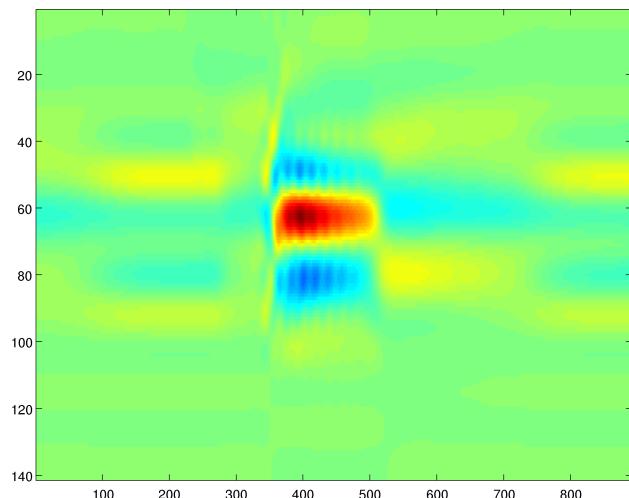
Complete CSD

Model – cell populations

Population 1
Layer 2/3 – G

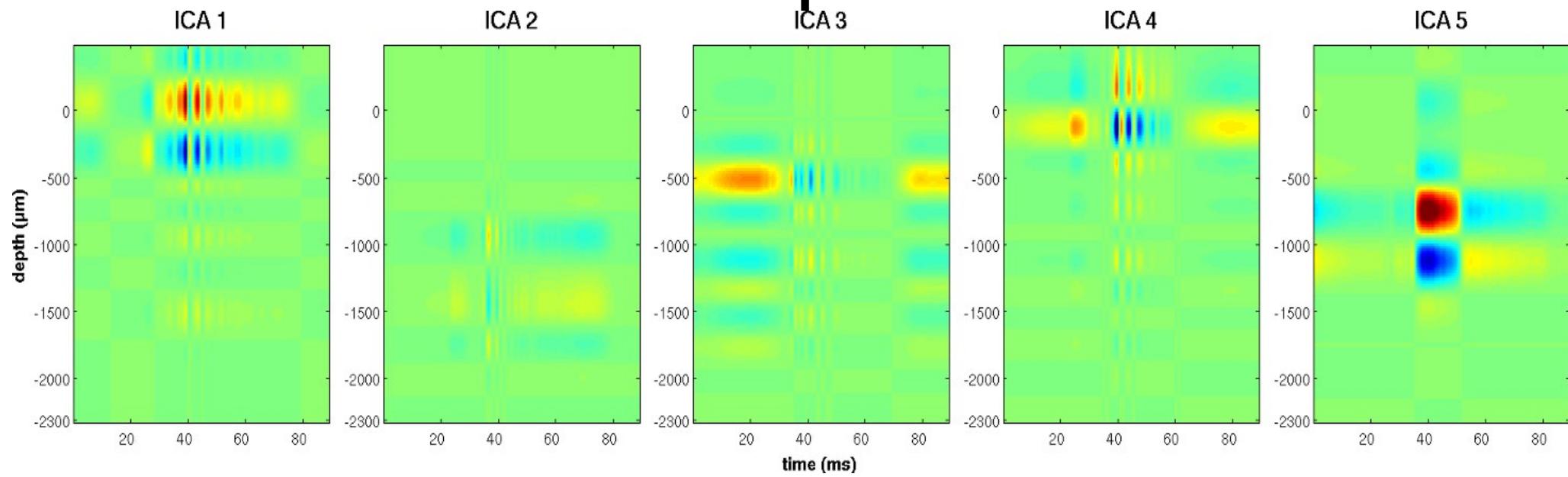


Population 9
Layer 5 – E



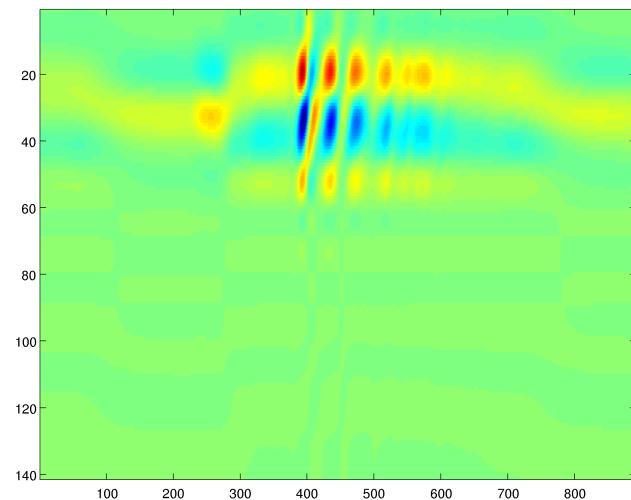
- a: nRT
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- f: layer 4 spiny stellate
- g: layer 2/3 pyr. (RS, FRB)
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ICA components

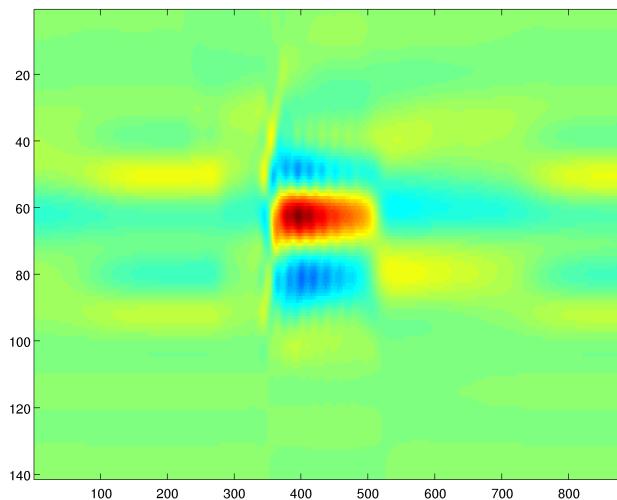


Individual populations

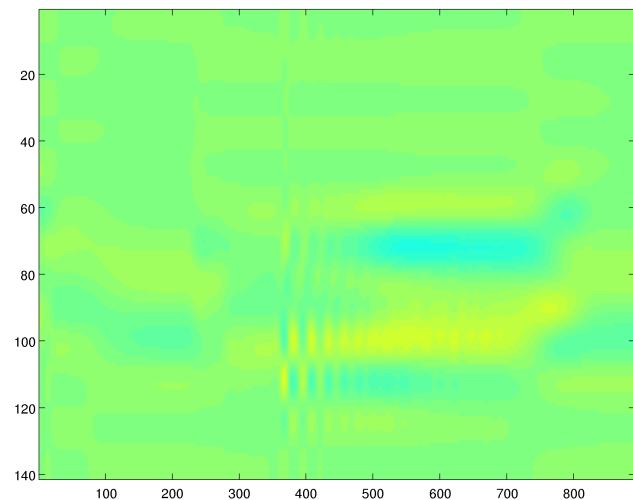
Pyramids layer 2/3



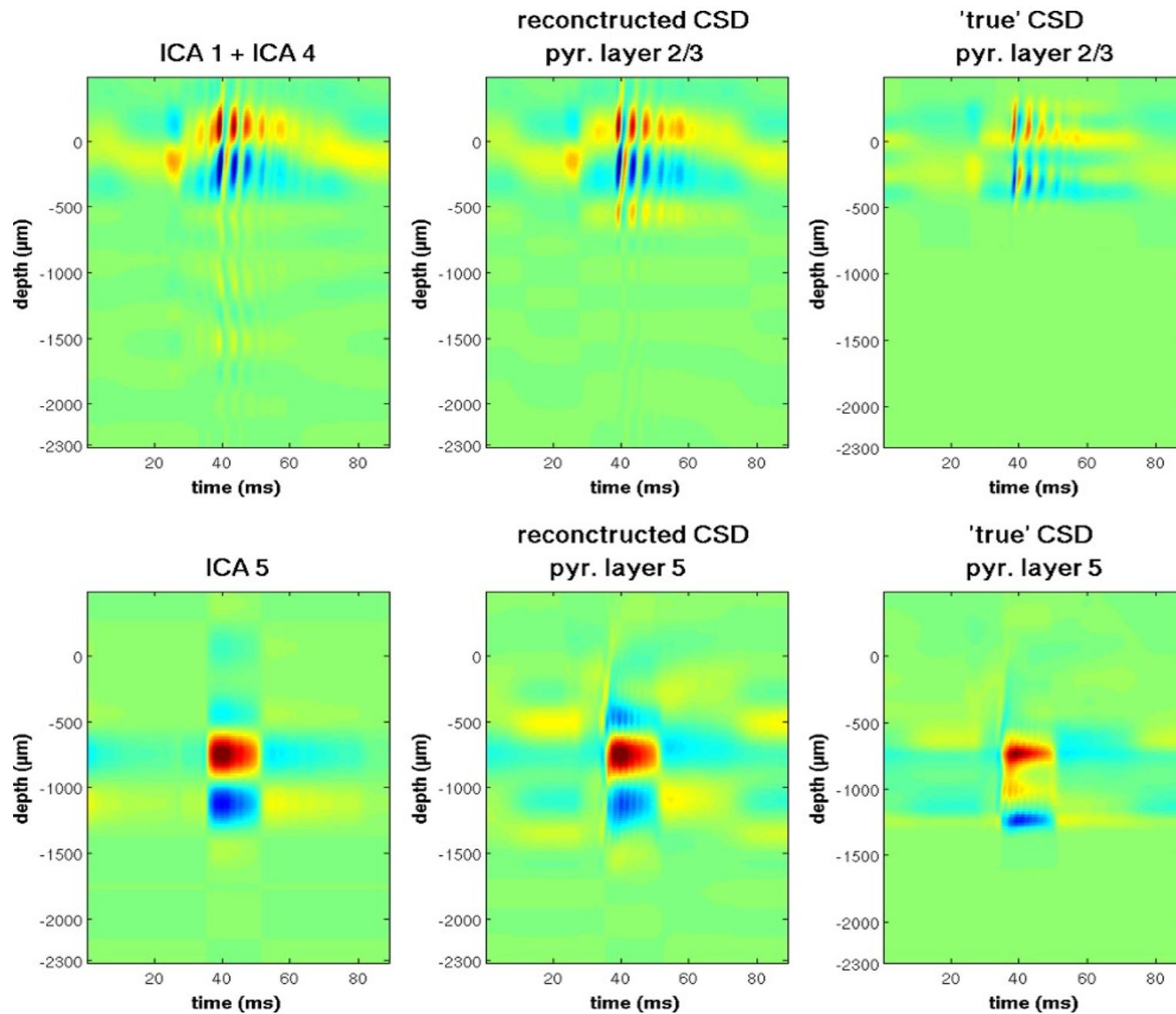
Pyramids layer 5



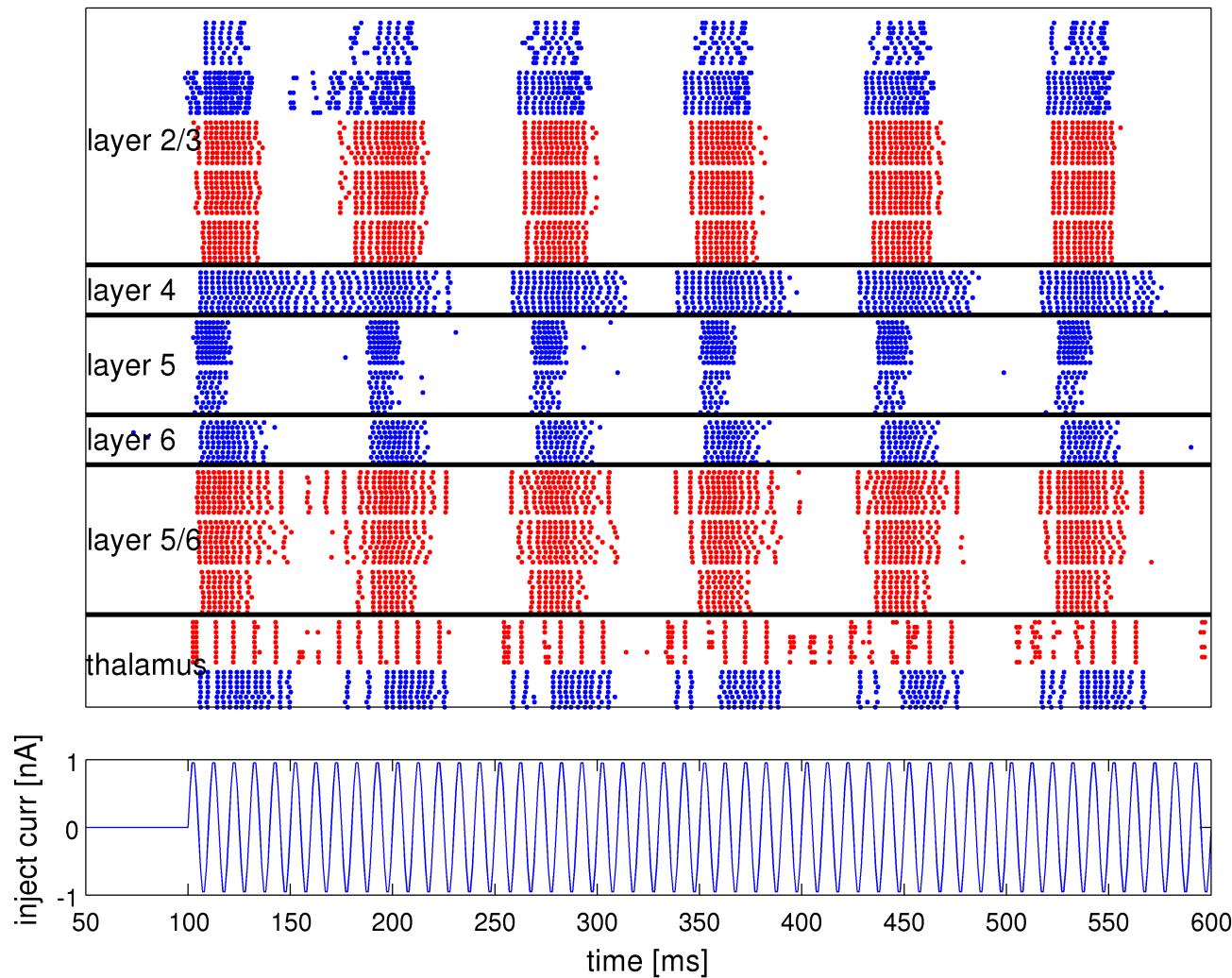
Pyramids layer 6



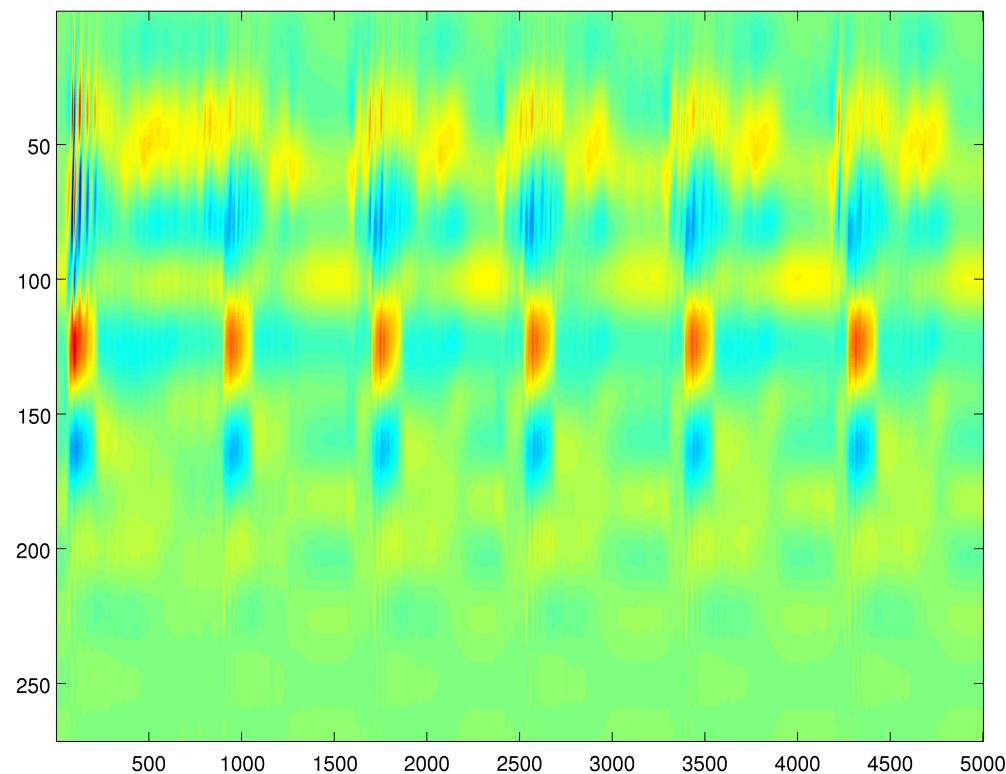
Results



100 Hz stimulation



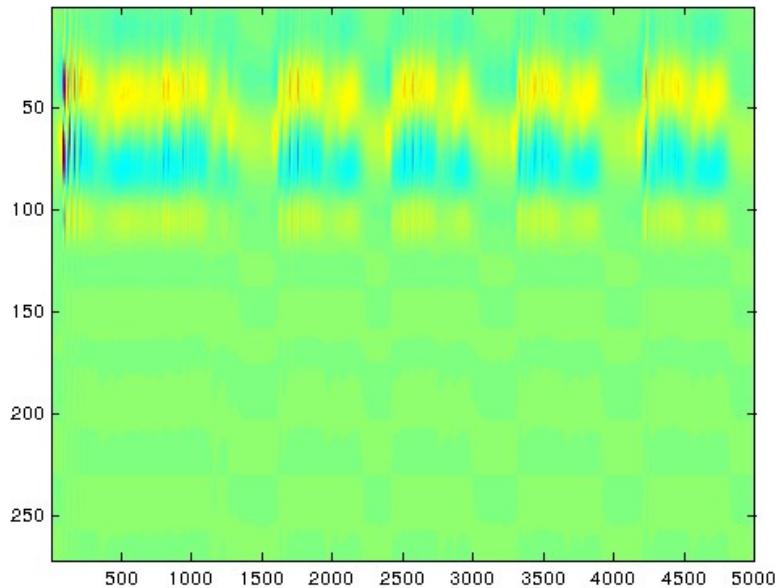
100 Hz the whole activity



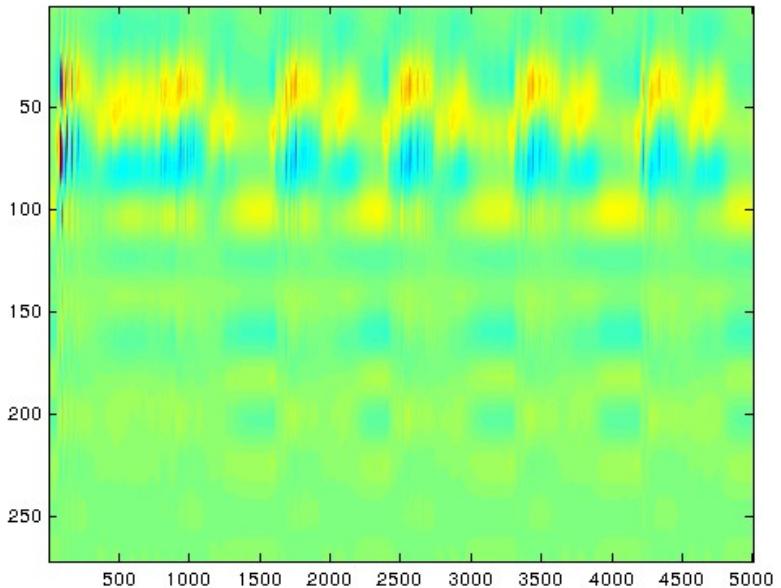
100 Hz – individual population

pyr layer II/III

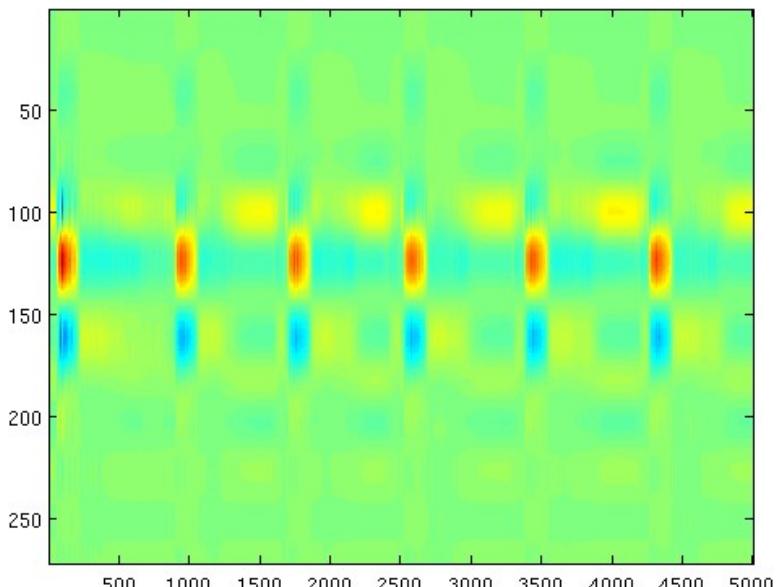
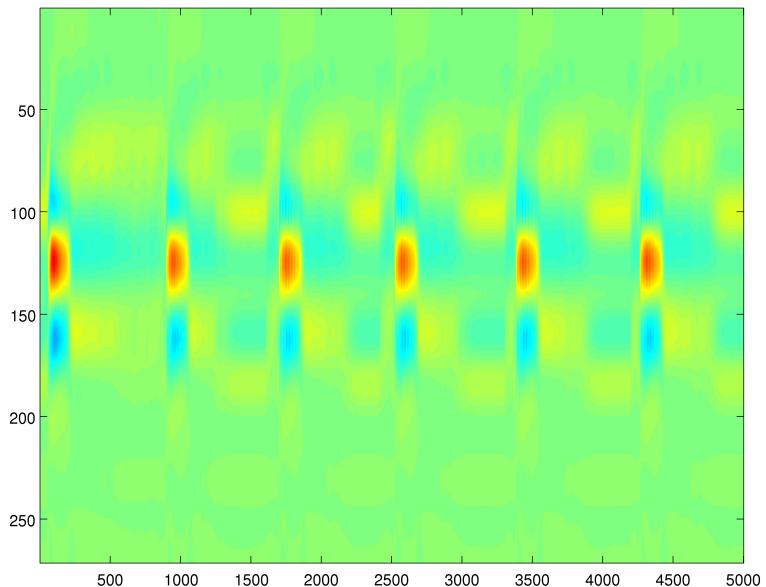
Original activity



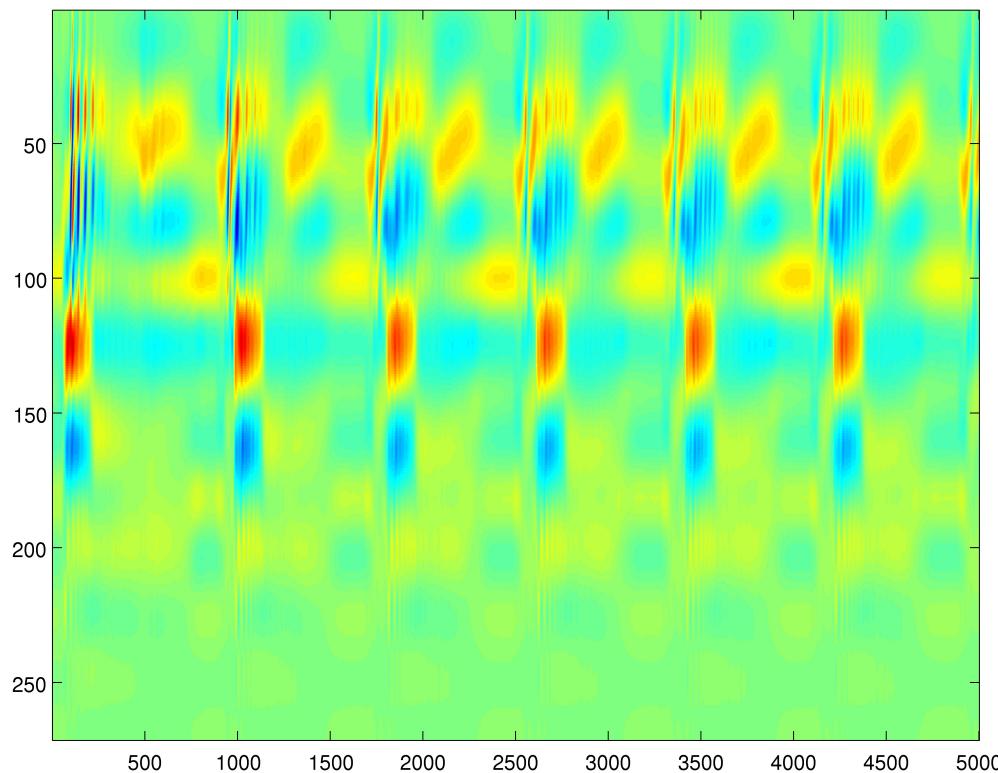
Best reconstruction



pyr layer V



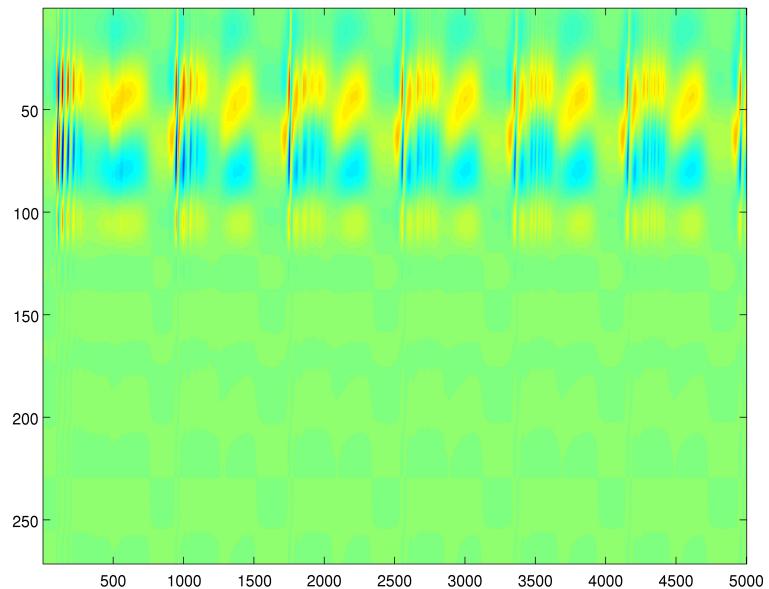
25 Hz the whole activity



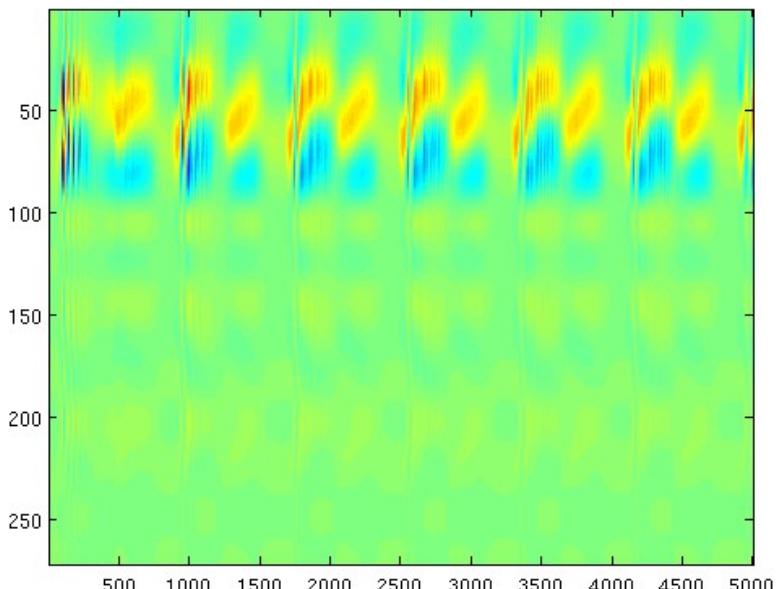
25 Hz – individual population

pyr layer II/III

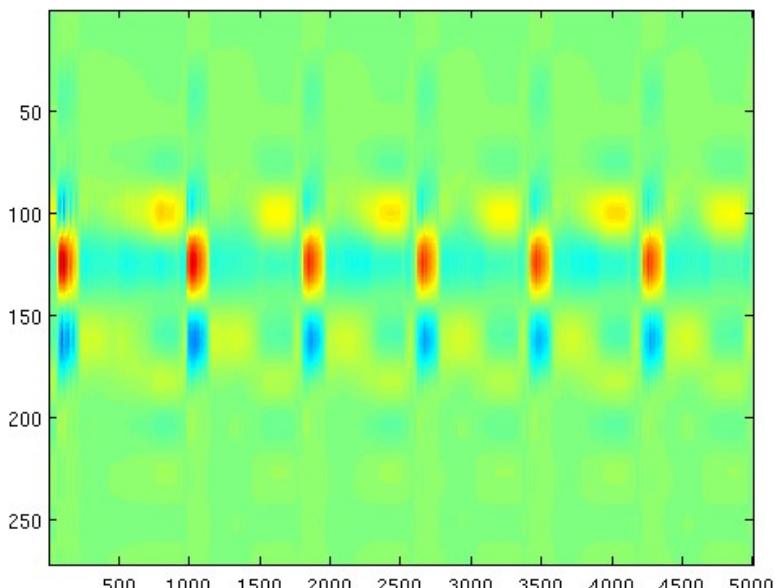
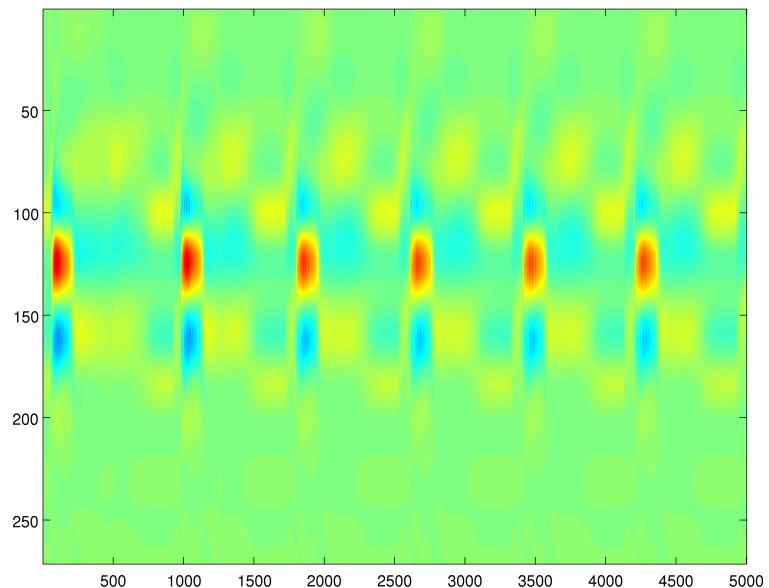
Original activity



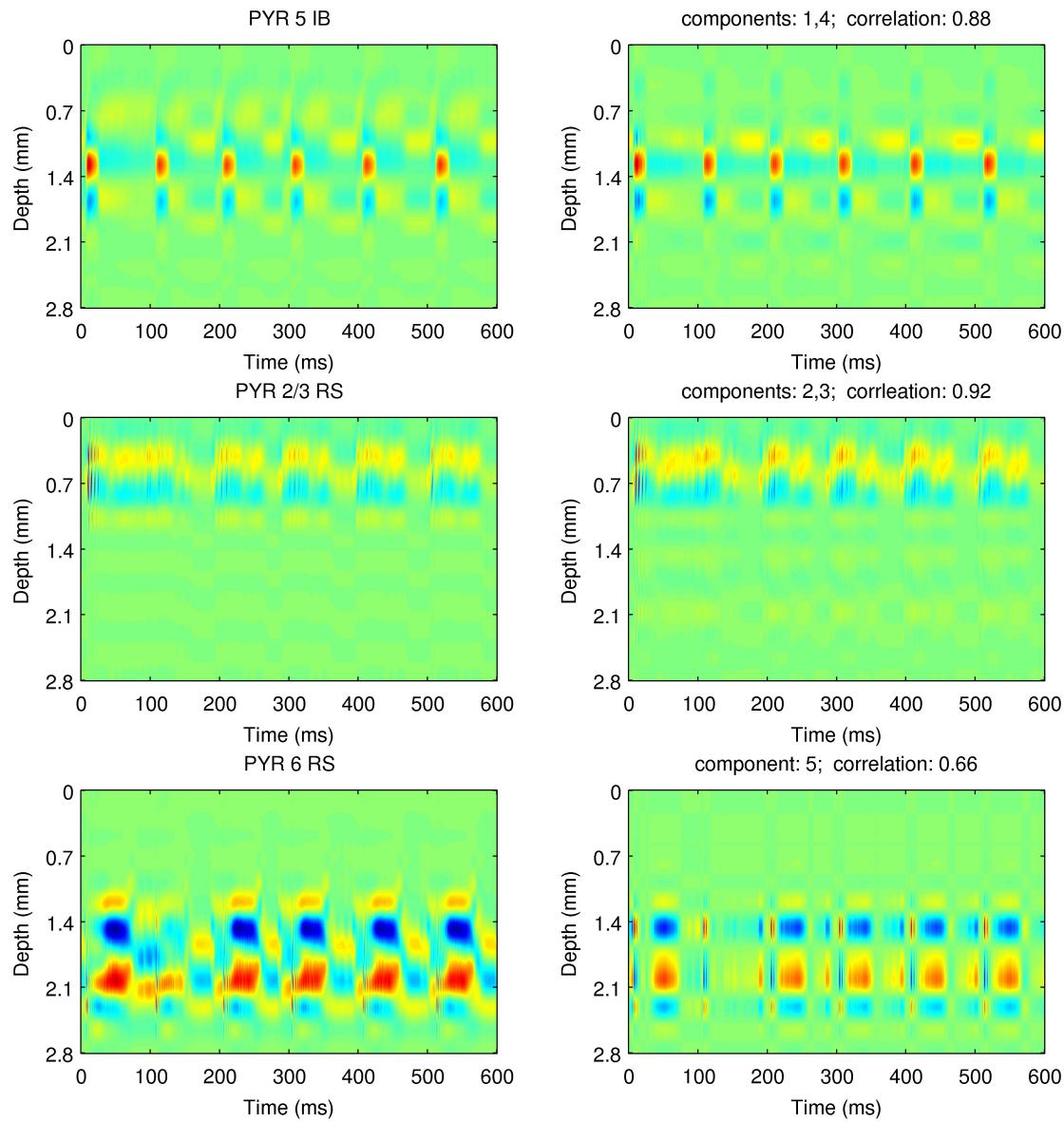
Best reconstruction



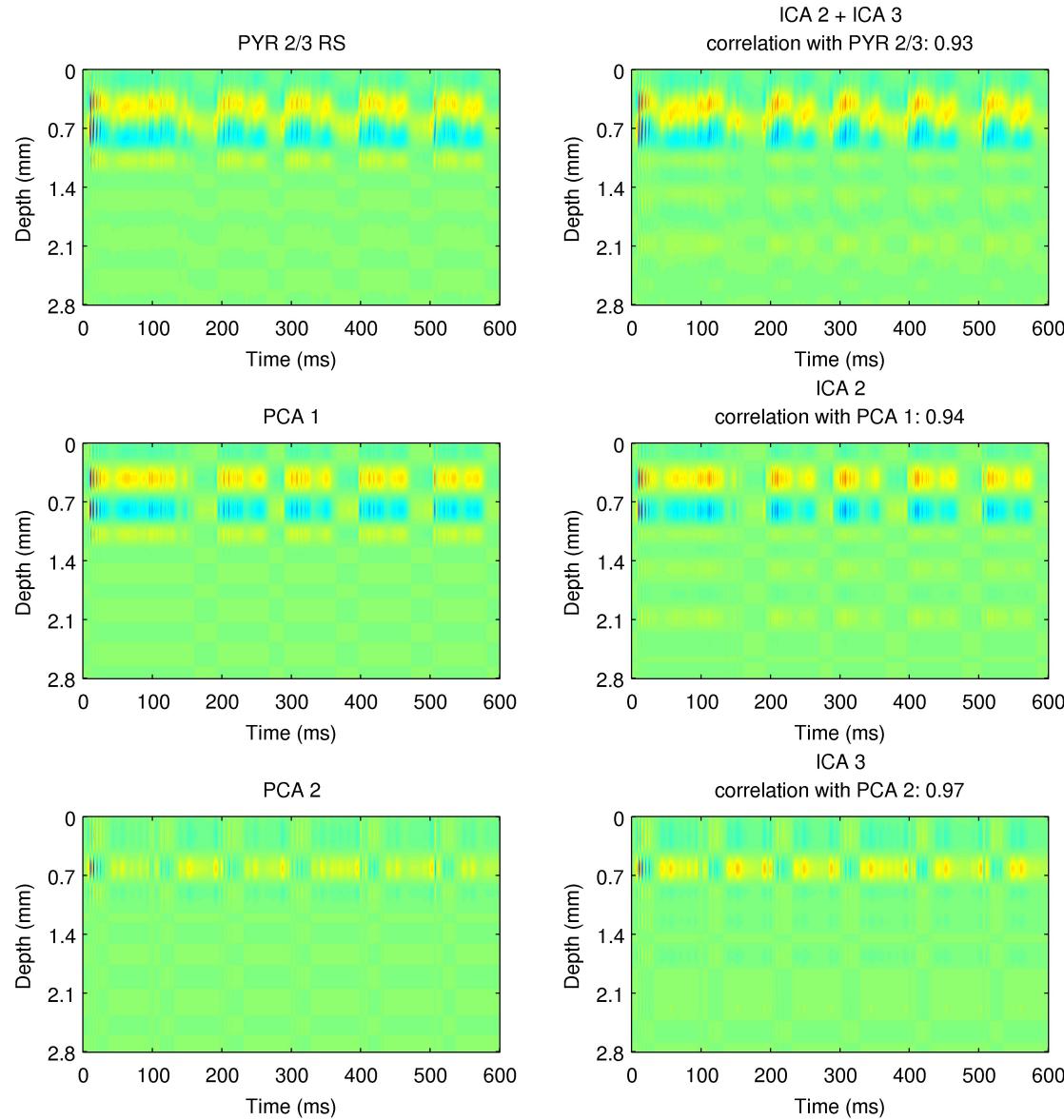
pyr layer V



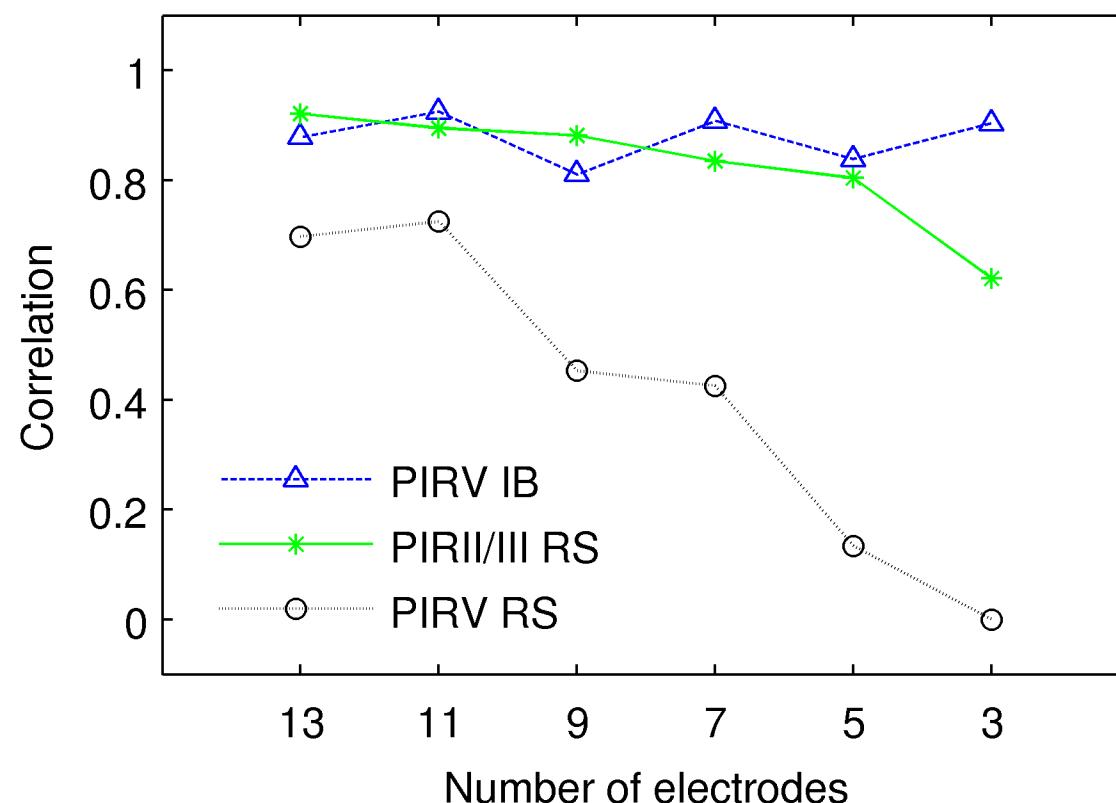
The best we can do?



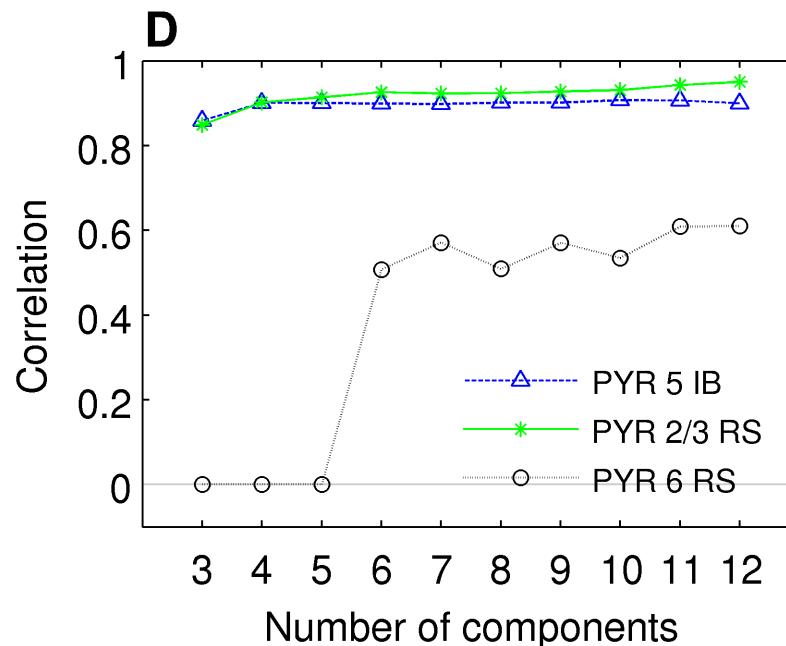
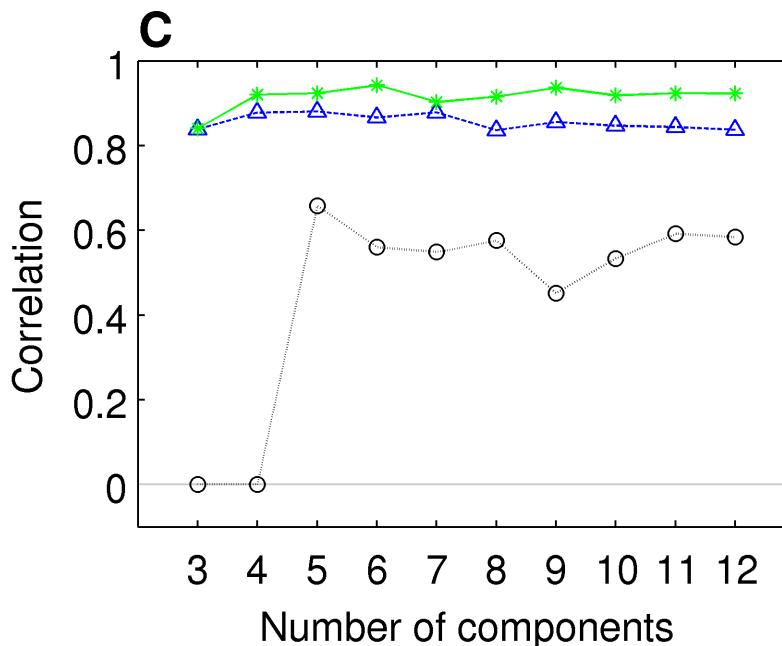
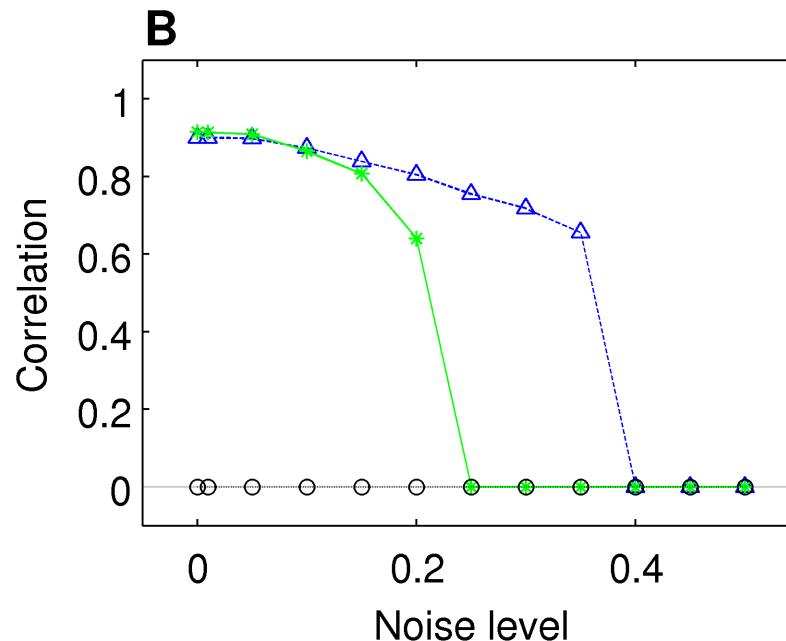
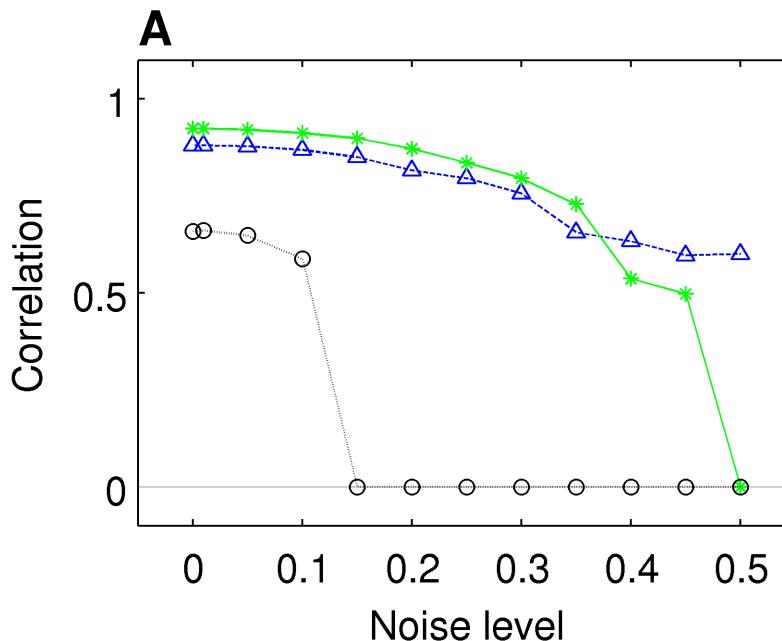
ICA from CSD = PCA from a population



How many electrodes we need?



What about noise?



What if somebody else wants to test another method of LFP analysis?

Data publication

- Running complex models is time consuming
- Tweaking models to run is time consuming
- Different environments may give different results: problems with reproducibility even given the code

Solution

Data publication

Solution

- How?
 - Neuroscience Data Format (NSDF)
 - Chaitanya
 - Storage?
 - Repository needed

Summary

- Traub's model: wrong, but gives useful insights
- We need realistic models to validate methods of data analysis, before application

Thanks for your attention



Szymon
Łęski

- Beyond Warsaw:
 - **Klas Pettersen**
 - **Gaute Einevoll**
 - **Beth Tunstall**
 - **John Gigg**
 - **Dirk Schubert**



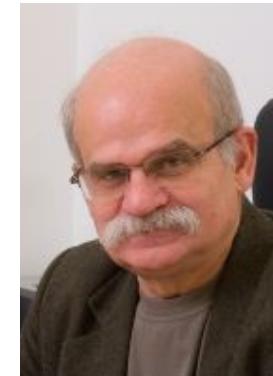
Ewa
Kublik



Daniel
Świejkowski



Jan
Potworowski



Andrzej
Wróbel



Daniel
Wójcik

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- **Wit Jakuczun**
- **Joanna Tereszczuk**
- **Helena Głabska**
- **Chaitanya Chintaluri**
- **Mark Hunt**
- **Stefan Kasicki**

Aas, Norway

Manchester, UK

Nijmegen
Netherlands



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IBD PAN, ICM UW