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

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May 15th 2014, Alghero
Neuroscience

- Experiment
- Measurement
Techniques to study brain function
Temporal and spatial scales

Churchland, Sejnowski 2000
Electric potential in the brain

Mark Hunt

Extracellular potential

Ewa Kublik

http://service.3dbar.org
Electric potential in the brain

Current sources:
CSD (C)

Potential:
LFP (V)

\[ I_1 \]
\[ I_2 \]
\[ I_j \]
Current Source Density

\[ V(\mathbf{r}, t) = \frac{1}{4\pi\sigma} \int \frac{C(\mathbf{r}^\theta, t)}{|\mathbf{r} - \mathbf{r}^\theta|} d^3\mathbf{r}^\theta \]

\[ C = -\sigma \Delta V \]

- \( C \) – current source density
- \( \sigma \) – 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...)

- 100 EPs
- 30s

first session with reinforcement (C1)

- 1-30
- 31-60
- 61-end
- 100 EPs
- 30s

consecutive conditioning sessions (C2, C3...)

- 100 EPs
- 30s
Vibrissa – barrel system of the rat

E. Kublik
Data: evoked potentials

cortex

Cortex

thalamus

Cortex, aroused

thalamus

Cortex, aroused
Data: evoked potentials

cortex

thalamus

Cortex

thalamus

Cortex, aroused

thalamus, aroused
from Varga et al (2002) modified
Experimental setup
Example local field potentials recorded in the rat forebrain
CSD reconstruction methods

• Traditional CSD method
  Pitts, W.H. (1952) *Investigations on synaptic transmission*. In *Cybernetics*

• iCSD (inverse CSD method)
  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

\[ C = -\nabla \cdot [\sigma \nabla V] \]

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

\[ \frac{\partial^2 f}{\partial x^2} \approx \frac{f(x + h) - 2f(x) + f(x - h)}{h^2} \]

- 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

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

\[
V_j = \sum_i \tilde{K}_{ji} a_i
\]

\[
\tilde{a} = (\tilde{K})^{-1} \tilde{V}
\]

- Evaluate potentials on the grid by forward modeling

\[V \text{ at grid points} = F[N \text{ parameters of CSD}]\]

- Invert \( F \)

\[N \text{ parameters of CSD} = F^{-1}[V \text{ at grid points}]\]
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

Interpolated potential

1 electrode
Kernel Current Source Density

CSD in the tissue

Interpolated potential

Reconstructed CSD

1 electrode
Kernel Current Source Density

CSD in the tissue

Interpolated potential

Reconstructed CSD

2 electrodes
Kernel Current Source Density

CSD in the tissue
Interpolated potential
Reconstructed CSD

4 electrodes
Kernel Current Source Density

CSD in the tissue

Interpolated potential

Reconstructed CSD

8 electrodes
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

Interpolated potential

Reconstructed CSD

32 electrodes
ICSD 3D: Experimental setup

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

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iCSD in 3D
Daniel Świejkowski, Ewa Kublik, Andrzej Wróbel

Current Source Density

Interpolated field potential
Interpolated field potential
Difficulties in analyzing LFP

- Electric field propagation (spatial blurring) $\rightarrow$ CSD
- Multiple populations overlapping $\rightarrow$ 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)
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).
Can we trust it?

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Forward modeling
An example:

Traub's model of thalamocortical loop
Forward modeling in Traub's model

Original Traub model

Traub model in 3D

a: nRT
b: TCR
c: layer 6 non-tufted 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)
Example

Simulated network: blue = excitatory, red = inhibitory

Current sources in volumes 50x50x100 μm [150,000 cells]

Current sources smoothed with Gauss kernel of R=100μm

Current sources reconstructed with kCSD from 8x14 electrodes

\[ I_j \]

\[ C(\vec{r}) \]
CSD and LFP from the model
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

Diagram showing cell populations with layer and G and E labels.
ICA components

Individual populations

Pyramids layer 2/3

Pyramids layer 5

Pyramids layer 6
Results

ICA 1 + ICA 4

reconstructed CSD
pyr. layer 2/3

'true' CSD
pyr. layer 2/3

ICA 5

reconstructed CSD
pyr. layer 5

'true' CSD
pyr. layer 5
100 Hz stimulation
100 Hz the whole activity
100 Hz – individual population

Original activity

Best reconstruction

pyr layer II/III

pyr layer V
25 Hz the whole activity
25 Hz – individual population

Original activity

Best reconstruction

pyr layer II/III

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?
  → Repositorie 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  Ewa Kublik  Daniel Świejkowski Potworowski  Jan Andrzej Wróbel  Daniel Wójcik

• Beyond Warsaw:
  • Klas Pettersen  Aas, Norway
  • Gaute Einevoll
  • Beth Tunstall  Manchester, UK
  • John Gigg  Nijmegen Netherlands

• Others:
  • Wit Jakuczun
  • Joanna Tereszczuk
  • Helena Głąbska
  • Chaitanya Chintaluri
  • Mark Hunt
  • Stefan Kasicki

Funding: MNiSW, NCN, MCTN „NAMASEN”, POiG „POWIEW” IBD PAN, ICM UW