Estimation of Single Neuron's Current Source Density Distribution by Using Kernel Methods

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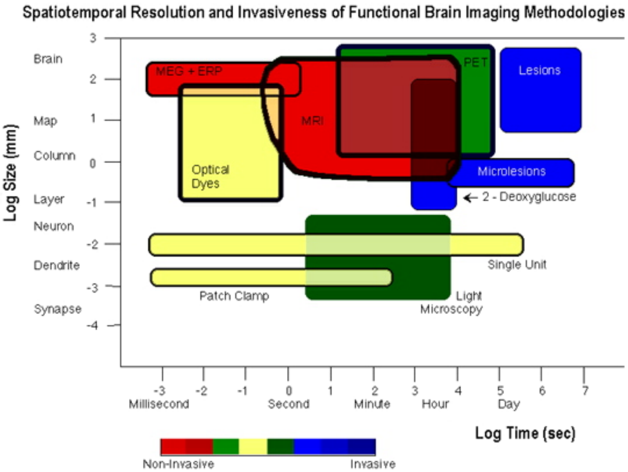
MŰEGYETEM 1782



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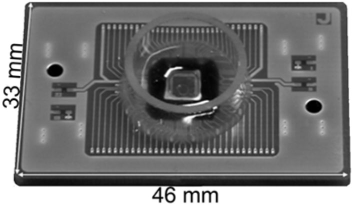
[1]http://www.eahb.org/DeutschEtAl/DeutschEtAlFigure2.jpg

APS-MEA III

Number of Electrodes	4096
Electrode Separation	21 um
Electrode Size	21um x 21um
Active Area	2.67mm x 2.67mm
Static Noise	11 uVrms



- Understanding the neural computational mechanism
- Information about the inputs
- Estimation of the ionchannel distribution

Tools: high density multielectrode arrays

Goal

Method for estimating the current source density distributions of single cells.

[2]

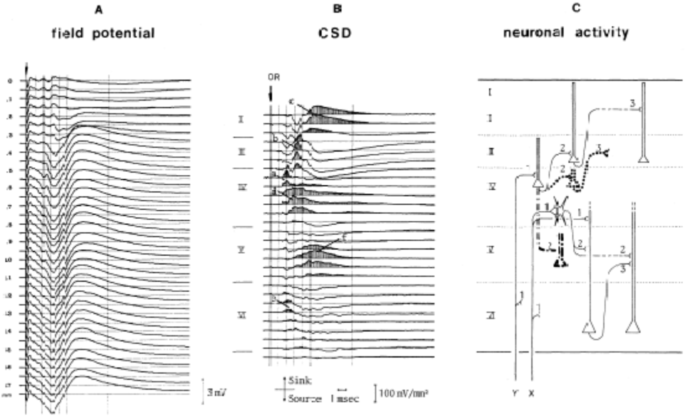
[2] http://www.apsmea.com/product.html

Current Source Density methods

Extracellular potentials $\Rightarrow$ Currents CSD:

$$C(z_j) = -\sigma \frac{\Phi(z_j + h) - 2\Phi(z_j) + \Phi(z_j - h)}{h^2} \tag{1}$$

CSD



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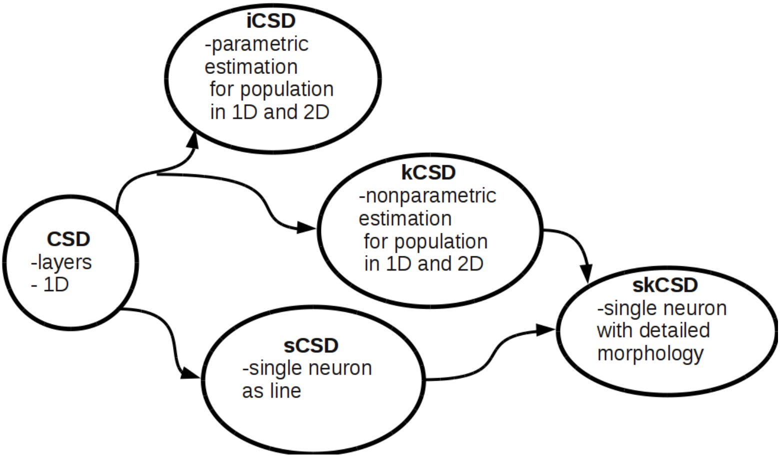
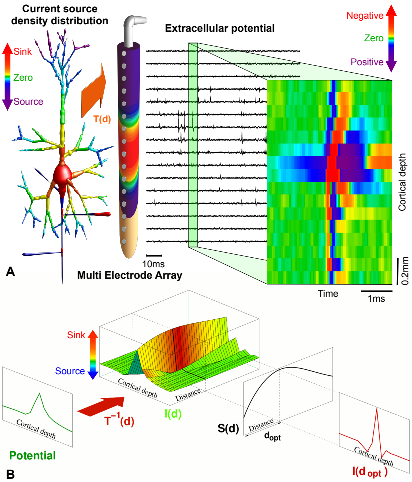
[3] Mitzdorf 1985

CSD family


iCSD
-parametric
estimation
for population
in 1D and 2D
kCSD
-nonparametric
estimation
for population
in 1D and 2D
CSD
-layers
- 1D
skCSD
-single neuron
with detailed
morphology
sCSD
-single neuron
as line

sCSD



[4]

Point-source equation:

$$\Phi_i(r_i) = \frac{1}{4\pi\sigma} \sum_{j=1}^{N} \frac{I_j}{|r_i - r_j|} \quad (2)$$

Matrix formalism:

$$\mathbf{\Phi} = \mathbf{T}\mathbf{I} \quad (3)$$

Inverse solution:

$$\mathbf{I} = \mathbf{T}^{-1}\mathbf{\Phi} \quad (4)$$

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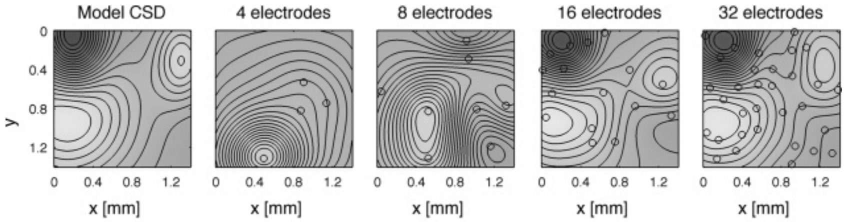
[4] Somogyvari et al 2012

kCSD



- kernel method
- number of current sources $>$ number of electrodes

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[5] Potworowski et al. 2012

skCSD

$\tilde{b}$: source function - the activity of a neural segment

- Gaussian function

$$\tilde{b}_i(t') = e^{-\frac{(t'-t_i)^2}{R^2}} \tag{5}$$

- Cosinus function

$$\tilde{b}_i(t') = \frac{cos(|t'-t_i|)\pi}{R}, \quad \text{if } |t'-t_i| < R \tag{6}$$

Current density at $\mathbf{x}$:

$$C(\mathbf{x}) = \sum_{j=i}^{M} a_j \tilde{b}_j(\mathbf{x}) \tag{7}$$

The extracellular potential generated by the ith source:

$$b_i(x, y, z) = A\tilde{b}_i(t') \tag{8}$$

$$b_i(x, y, z) = \frac{1}{4\pi\sigma} \int \frac{\tilde{b}_i(t')}{\sqrt{(x - x'(t))^2 + (y - y'(t))^2 + (z - z'(t))^2}} dt' \tag{9}$$

$$\Phi(\mathbf{x}) = \sum_{i=1}^{M} a_i b_i(\mathbf{x}) \tag{10}$$

To determine the CSD distribution in arbitrary positions(x), the following kernel functions were introduced:

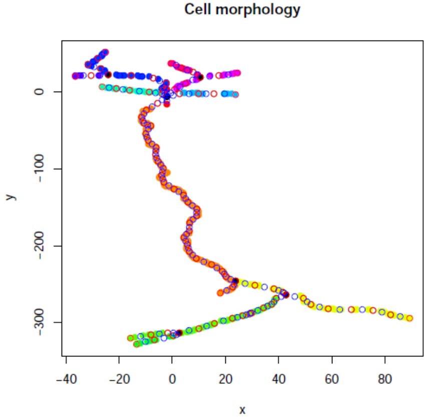
$$K(\mathbf{x}_k, \mathbf{x}_l) = \sum_{i=1}^{M} b_i(\mathbf{x}_k) b_i(\mathbf{x}_l) = B_k^T B_l \tag{11}$$

$$\tilde{K}(\mathbf{x}_k, \mathbf{y}_l) = \sum_{j=1}^{M} b_(\mathbf{x}_k) \tilde{b}_j(\mathbf{y}_l) = B_k^T \tilde{B}_l \tag{12}$$

Using the simulated or measured extracellular potentials (V) and assuming $\tilde{K}$ is invertible the solution for C is straightforward.

$$C(\mathbf{x}) = \tilde{\mathbf{K}}^T(\mathbf{x}) \tilde{\mathbf{K}}^{-1} \mathbf{V} \tag{13}$$

Usually neurons have more, than 1 branch :(



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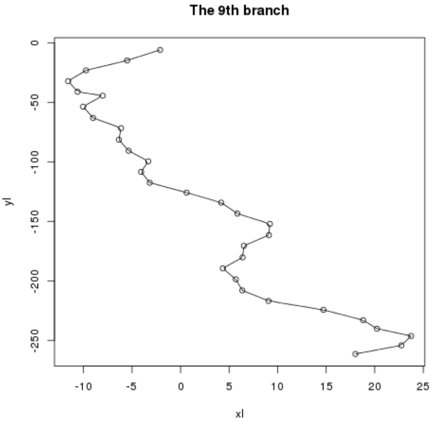
How to handle the branching?

- branches independent
- connect the branches

[6] $http://neuromorpho.org/neuroMorpho/neuron_info.jsp?neuron_name=$ $03a_pyramidal9aFI$ Allman et al 2006

Usually branches are not straight :((



How to handle?

- fit a curve
- position given by parameter t

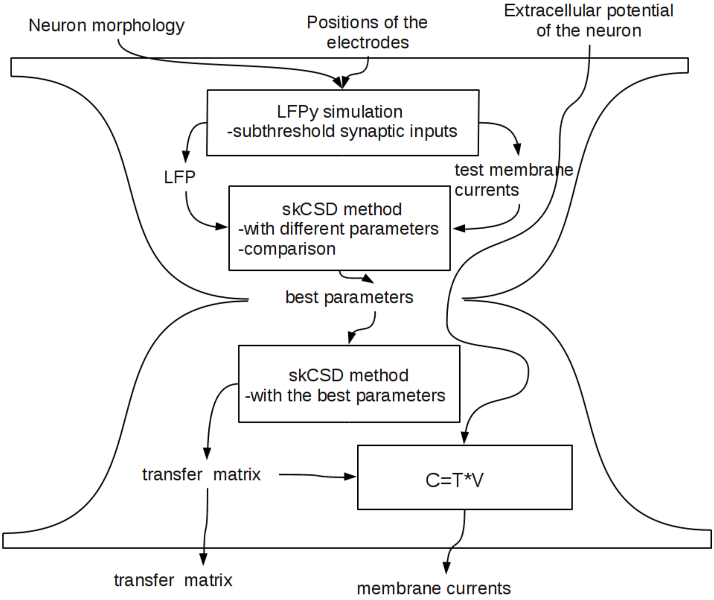
Lots of parameters :(((

Parameters of the method:

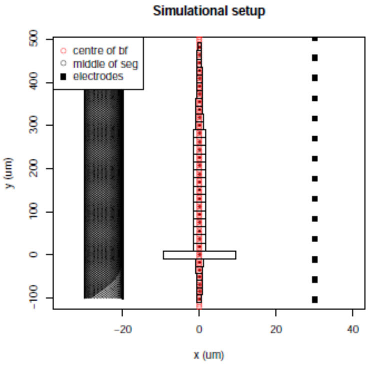
- type of basis function
- number of basis function
- width of basis function

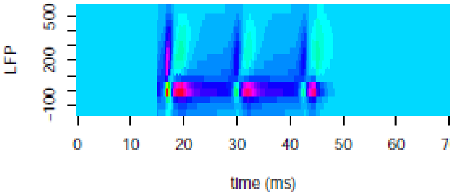
Parameters of the test simulations:

- neuron morphology
- inputs
- cell to electrode distance
- position of the electrode (1D, 2D, 3D)

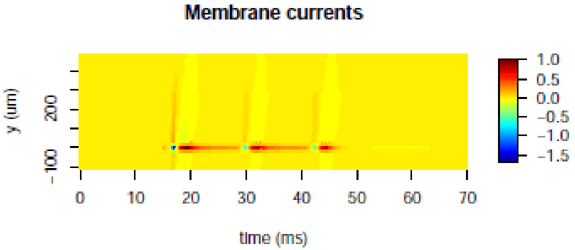

Neuron morphology
Positions of the electrodes
Extracellular potential of the neuron
LFPy simulation
-subthreshold synaptic inputs
LFP
test membrane currents
skCSD method
-with different parameters
-comparison
best parameters
skCSD method
-with the best parameters
transfer matrix
C=T*V
transfer matrix
membrane currents

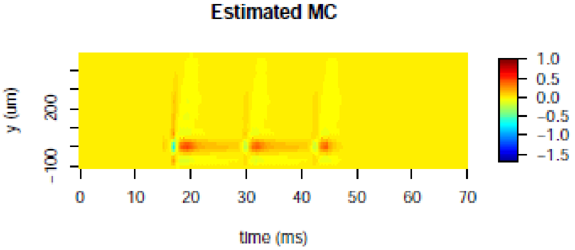
Ballstick neuron



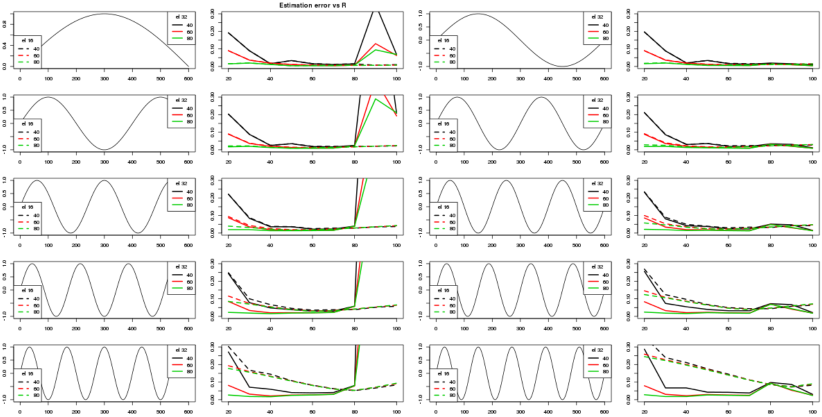


ksCSD for ballstick neuron

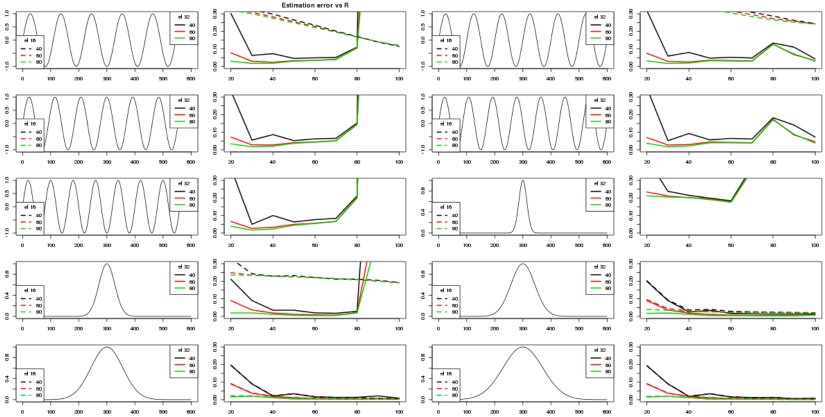




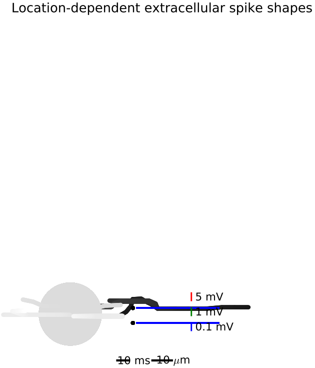
Ballstick neuron

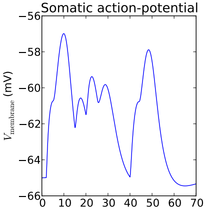


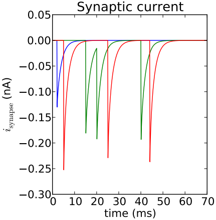
Ballstick neuron

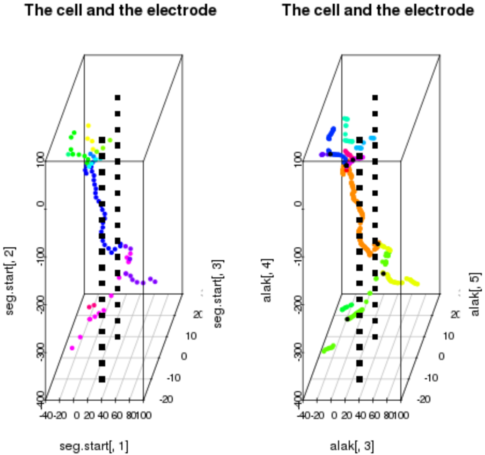


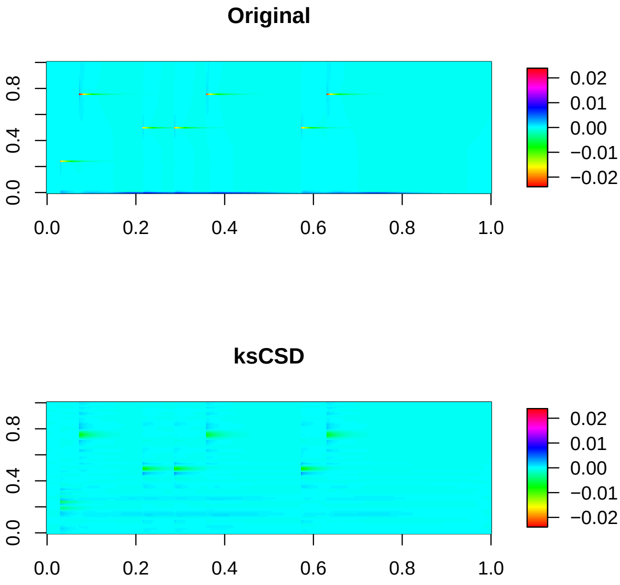
Complex morphology

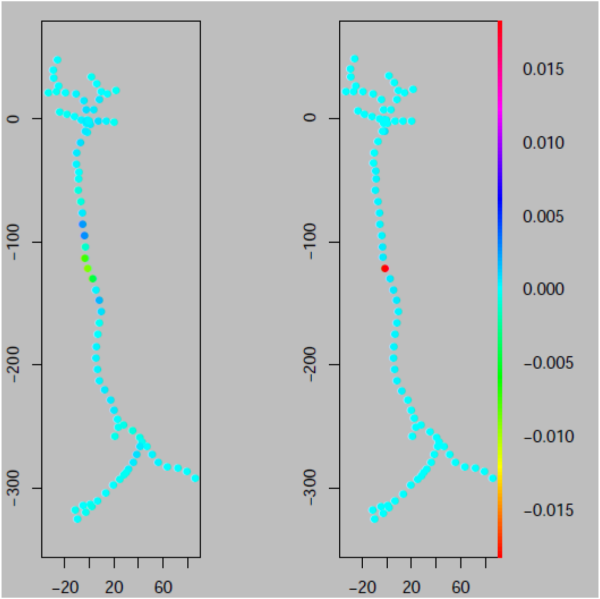







The cell and the electrode
seg.start[, 1]
seg.start[, 2]
seg.start[, 3]
The cell and the electrode
alak[, 3]
alak[, 4]
alak[, 5]


Original
0.0
0.4
0.8
0.0
0.2
0.4
0.6
0.8
1.0
0.02
0.01
0.00
−0.01
−0.02
ksCSD
0.0
0.4
0.8
0.0
0.2
0.4
0.6
0.8
1.0
0.02
0.01
0.00
−0.01
−0.02



0
-100
-200
-300
-20
20
60
0.015
0.010
0.005
0.000
-0.005
-0.010
-0.015

Future plans

- Run more test simulations
- Make the program usable also for others (GUI)
- Test the method on experimental data

Thanks for the attention!

Which is the best set of parameters?

$$e = \frac{\sum_{t,i} |C_{skCSD} - C_o|}{\sum_{t,i} |C_o|} \tag{14}$$