Preprocession and Interpretation of Multielectrode Array Recordings

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Brain Imaging Technics

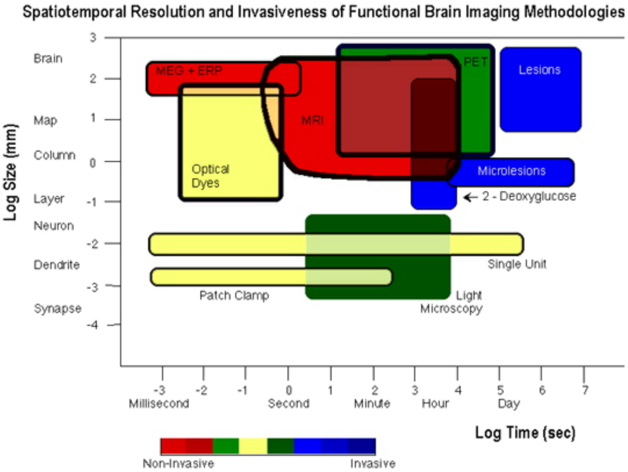


Figure : Spatial and temporal resolution of brain imaging technincs

Multielectrode Probes

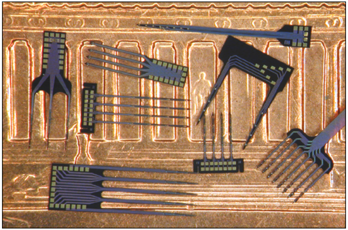


Figure : Several different probe designs shown on the back of a U.S. penny.

Advantages of MEA Recordings:

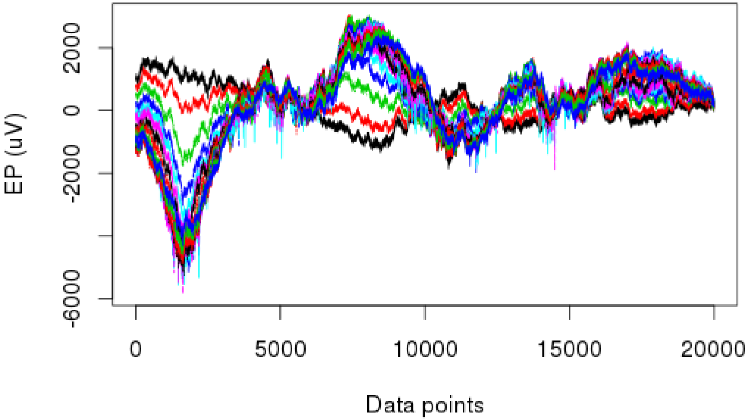
- high temporal ans spatial resolution - big data in vivo, in vitro and behaving animals
- structures deep in the brain also observable
- affordable (?)

Disadvantages of MEA Recordings:

- big data
- interpretation

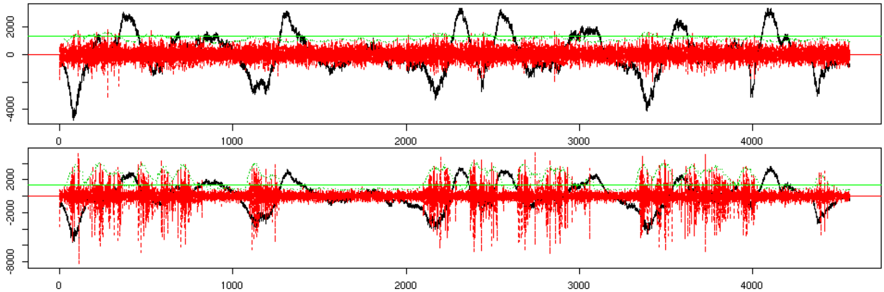
MEA Recordings

20 kHz, 3 linear shanks (2 in neocortex, 1 in thalamus)
100 and 50 μm interelectrode distance

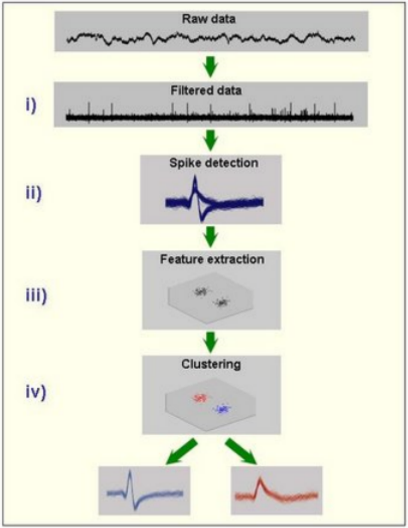


Population activity

- population oscillations: delta, theta, alfa, beta, gamma
- up and down state detection - depolarization of cell membrane - anything different in the input of the thalamical cells?



Single unit



- firing statistics
- correlation, causality
- spike triggered average

Goal

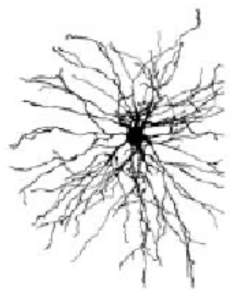
Goal

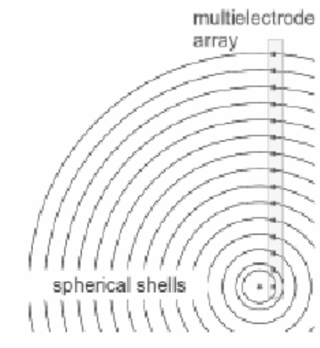
Developement of a new method for the estimation of current source densitiy distribution of single neurons given the morphology and the extracellular potential

- assumptions about the morphology (spherical symmetry)
- exact morphology known

The task: solution of the Poisson equation under various assumptions regarding the morphology

Spherical CSD





Assumptions:

- The cell has an "onion-structured" morphology
- azimuthal symmetry

Potential calculation for spherical shell with exterior recording site

Relationship between CSD distribution, C, the EC potential, V, in a homogeneous electrolytic volume conductor with conductivity σ_e is given via Maxwell's equations by Poisson's equation:

$$\Delta V(\mathbf{r}, t) = -\frac{C(\mathbf{r}, t)}{\sigma_e} \tag{1}$$

- Forward problem: solving for potential distribution $V(\mathbf{r}, t)$ given the CSD distribution $C(\mathbf{r}, t)$
- Inverse problem: solving for $C(\mathbf{r}, t)$ given $V(\mathbf{r}, t)$.
- Solution of forward problem at recording site $\mathbf{r}$ for point-source at $\mathbf{r}'$ is the electric potential field of a monopole:

$$= \frac{1}{4\pi\sigma_e} \frac{C(\mathbf{r}')}{|\mathbf{r} - \mathbf{r}'|} \tag{2}$$

Assume charge distribution of thalamic cells is spherical in nature, i.e. charges are distributed on concentric spherical shells. Converting to spherical coordinates yields:

$$= \frac{1}{4\pi\sigma_e} \int_D \frac{C(\mathbf{r}')}{\sqrt{r^2 + r'^2 - 2rr'\cos\gamma}} r'^2 \sin\theta' r' \theta' \phi' \qquad (3)$$

where γ is the angle between $\mathbf{r}$ and $\mathbf{r}'$.

Assume charge distribution of thalamic cells is spherical in nature, i.e. charges are distributed on concentric spherical shells. Converting to spherical coordinates yields:

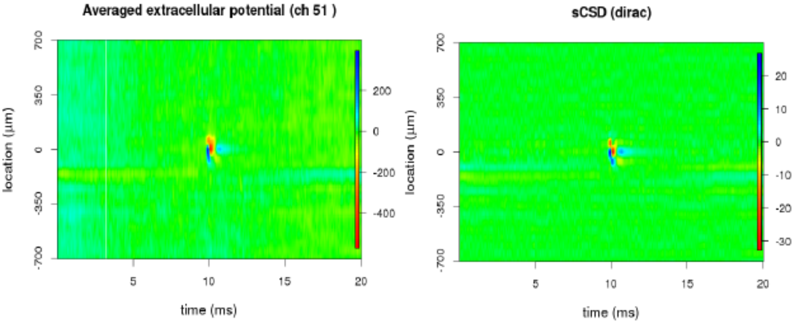
$$= \frac{1}{4\pi\sigma_e} \int_D \frac{C(\mathbf{r}')}{\sqrt{r^2 + r'^2 - 2rr'\cos\gamma}} r'^2 \sin\theta' r'\theta'\phi' \qquad (3)$$

where γ is the angle between $\mathbf{r}$ and $\mathbf{r}'$.
Note: $1/\sqrt{1 - 2xt + t^2} = \sum_{\ell=0}^{\infty} P_\ell(x)t^\ell$. Thus,

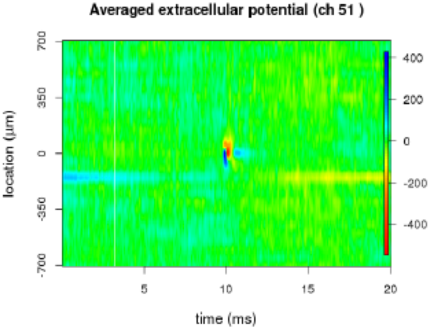
$$\frac{1}{\sqrt{r^2 + r'^2 - 2rr'\cos\gamma}} = \frac{1}{r\sqrt{1 + (r'/r)^2 - 2(r'/r)\cos\gamma}} = \frac{1}{r}\sum_{\ell=0}^{\infty} P_\ell(\cos\gamma)(\frac{r'}{r})^\ell.$$

Legendre polynomial expansion in (3) yields:

$$= \frac{1}{4\pi\sigma_e} \int_D C(\mathbf{r}'){r'}^2 \sin\theta' \sum_{\ell=0}^{\infty} P_\ell(\cos\gamma)\frac{r'^\ell}{r^{\ell+1}} r'\theta'\phi' \qquad (4)$$



Averaged extracellular potential (ch 51)
location (µm)
700
350
0
-350
-700
200
0
-200
-400
5
10
15
20
time (ms)
sCSD (dirac)
location (µm)
700
350
0
-350
-700
20
10
0
-10
-20
-30
5
10
15
20
time (ms)


Averaged extracellular potential (ch 51)
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700
350
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-350
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5
10
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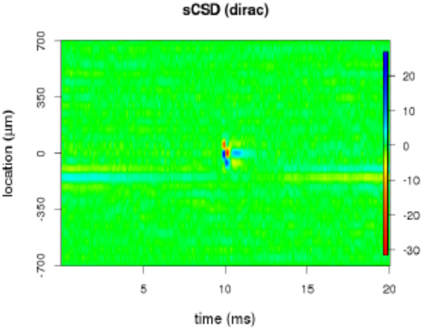
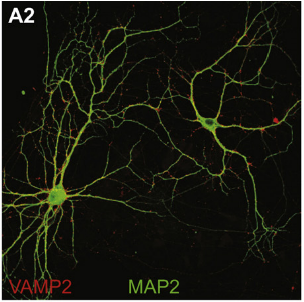
time (ms)
400
200
0
-200
-400


sCSD (dirac)
location (µm)
700
350
0
-350
-700
5
10
15
20
time (ms)
20
10
0
-10
-20
-30

kernel spike CSD



2

- morphology of the cell known
- dense electrode array

[2] Sabine K. Schmitz et al 2010.

The kernel single cell CSD

The CSD distribution at point $\mathbf{x}$:

$$C(\mathbf{x}) = \sum_{j=i}^{M} a_j \tilde{b}_j(\mathbf{x}) \tag{5}$$

$\tilde{b}$ basis functions, a_j multiplication constant
The curves in the 3D space can be parametrized with variable t.

$$\begin{aligned} x &= f_x(t) \\ y &= f_y(t) \\ z &= f_z(t) \end{aligned} \tag{6}$$

$$\tilde{b}_i(t') = e^{-\frac{(t'-t_i)^2}{R^2}} \tag{7}$$

[3]

[3] Potworowski et al 2012

b_i generated potential by $\tilde{b}_i$:

$$b_i(x,y,z) = \frac{1}{4\pi\sigma}\int \frac{\tilde{b}_i(t')}{\sqrt{(x-x'(t))^2+(y-y'(t))^2+(z-z'(t))^2}}dt' \tag{8}$$

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

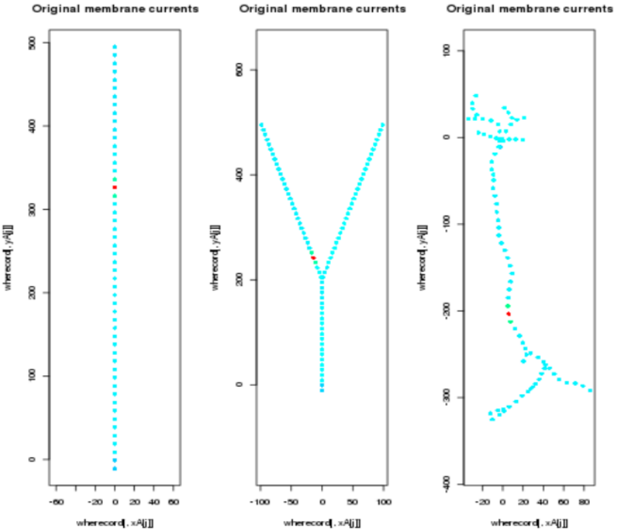
$$K(\mathbf{x}_k,\mathbf{x}_l) = \sum_{i=1}^{M} b_i(\mathbf{x}_k)b_i(\mathbf{x}_l) \tag{9}$$

$$\tilde{K}(\mathbf{x}_k,\mathbf{y}_l) = \sum_{j=1}^{M} b_j(\mathbf{x}_k)\tilde{b}_j(\mathbf{y}_l) \tag{10}$$

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

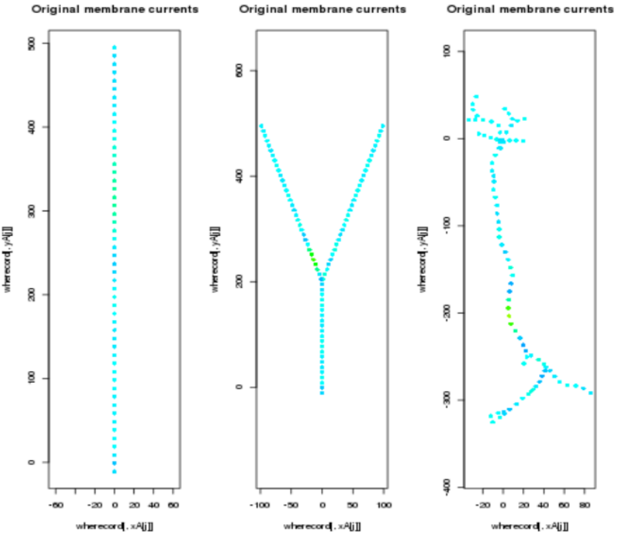
$$C(\mathbf{x}) = \tilde{\mathbf{K}}^T(\mathbf{x})\tilde{\mathbf{K}}^{-1}\mathbf{V} \tag{11}$$

Validation



Original membrane currents
Original membrane currents
Original membrane currents
wherecord[, yA[j]]
wherecord[, xA[j]]

Validation


Original membrane currents
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wherecord[, yA[j]]
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wherecord[, xA[j]]
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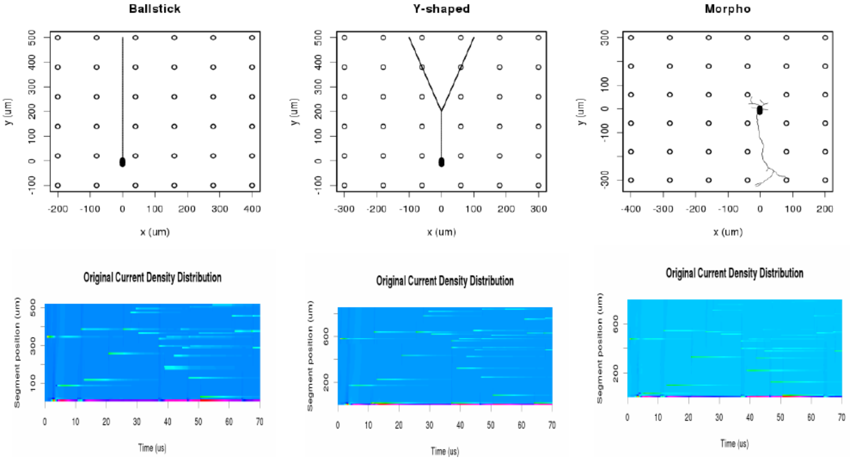
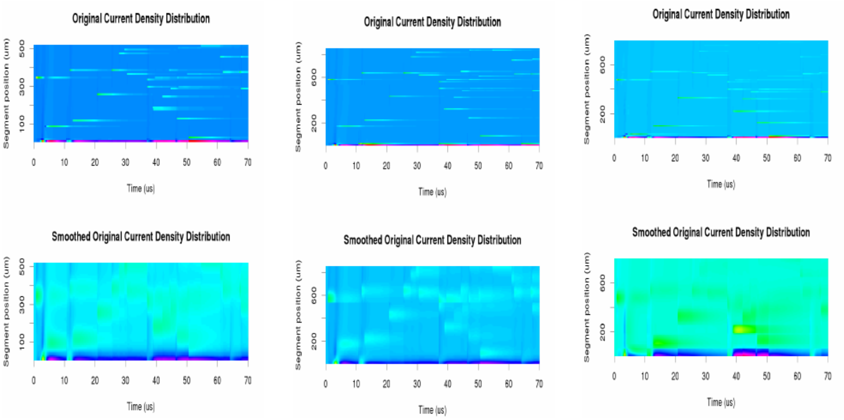
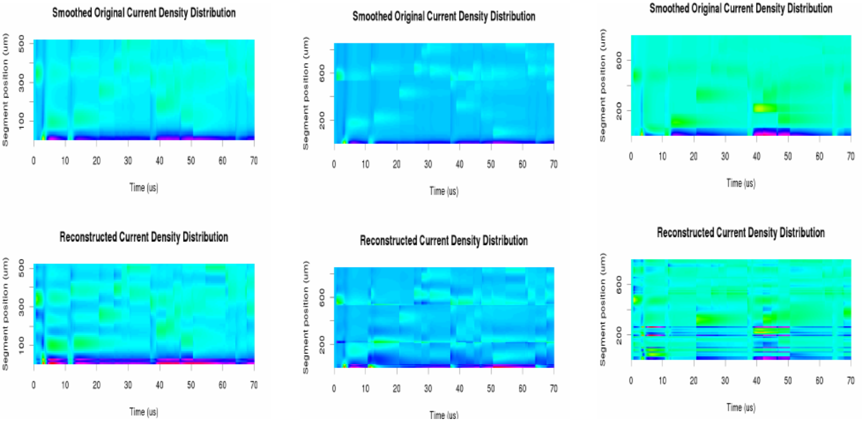
Validation


Ballstick
Y-shaped
Morpho
y (um)
x (um)
Original Current Density Distribution
Segment position (um)
Time (us)

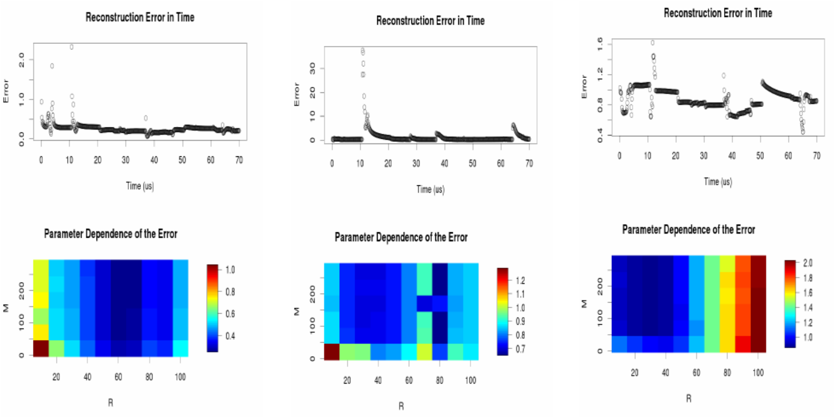
Validation


Original Current Density Distribution
Segment position (um)
Time (us)
0 10 20 30 40 50 60 70
100 300 500
Original Current Density Distribution
Segment position (um)
Time (us)
0 10 20 30 40 50 60 70
200 600
Original Current Density Distribution
Segment position (um)
Time (us)
0 10 20 30 40 50 60 70
200 600
Smoothed Original Current Density Distribution
Segment position (um)
Time (us)
0 10 20 30 40 50 60 70
100 300 500
Smoothed Original Current Density Distribution
Segment position (um)
Time (us)
0 10 20 30 40 50 60 70
200 600
Smoothed Original Current Density Distribution
Segment position (um)
Time (us)
0 10 20 30 40 50 60 70
200 600

Validation


Smoothed Original Current Density Distribution
Segment position (um)
100
300
500
0
10
20
30
40
50
60
70
Time (us)
Smoothed Original Current Density Distribution
Segment position (um)
200
600
Time (us)
Smoothed Original Current Density Distribution
Segment position (um)
200
600
Time (us)
Reconstructed Current Density Distribution
Segment position (um)
100
300
500
Time (us)
Reconstructed Current Density Distribution
Segment position (um)
200
600
Time (us)
Reconstructed Current Density Distribution
Segment position (um)
200
600
Time (us)

Validation


Reconstruction Error in Time
Error
Time (us)
Reconstruction Error in Time
Error
Time (us)
Reconstruction Error in Time
Error
Time (us)
Parameter Dependence of the Error
M
R
Parameter Dependence of the Error
M
R
Parameter Dependence of the Error
M
R

Results

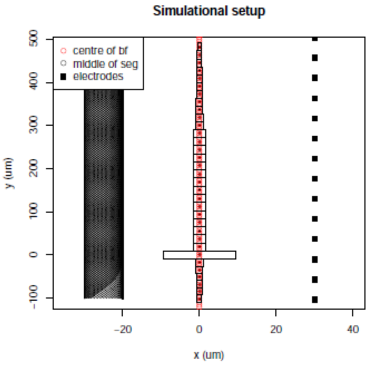
- Algorithm to detect up and down states
- Spherical CSD
  theory
  propagation of membrane potential- back and forth
  different events during up and down states
- kernel spikeCSD theory
  simulated data
  waiting for real data to try on

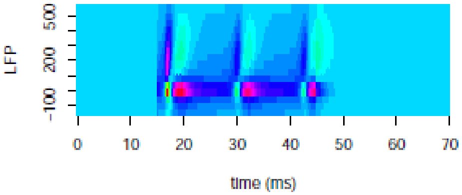
Aknowledgement

I am indebted first of all to Zoltán Somogyvári and Gábor Horváth, to József Lálics and to my many colleagues from the Complex Systems and Computational Neuroscience Group at Wigner Research Center and at BME MIT who supported me, furthermore to Daniel Wójcik who gave me the the opportunity to work in his Laboratory of Neuroinformatics at Nencki Institute.

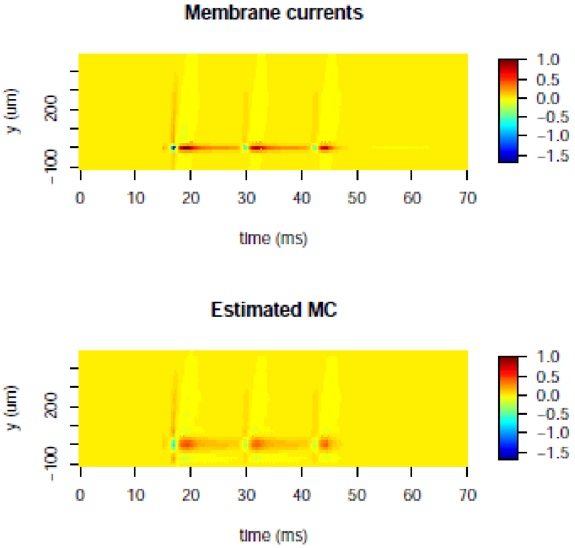
Thanks for the attention!

Ballstick neuron





ksCSD for ballstick neuron



Some other morphologies

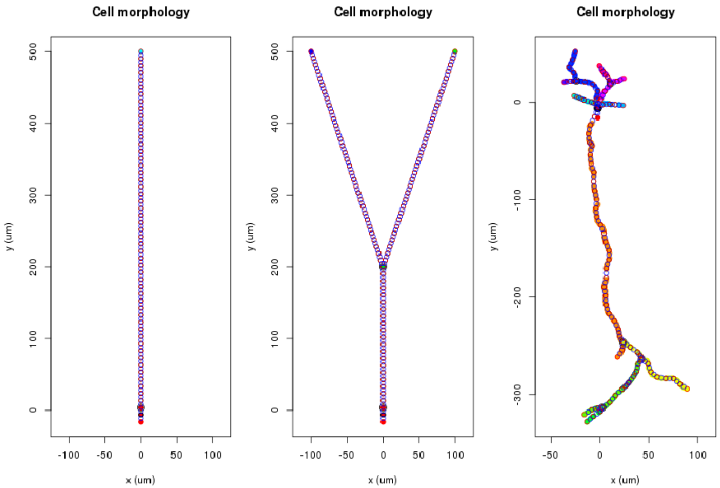


Figure : The ksCSD method was tested for 3 different morphologies: ballstick, Y-shaped and branching.

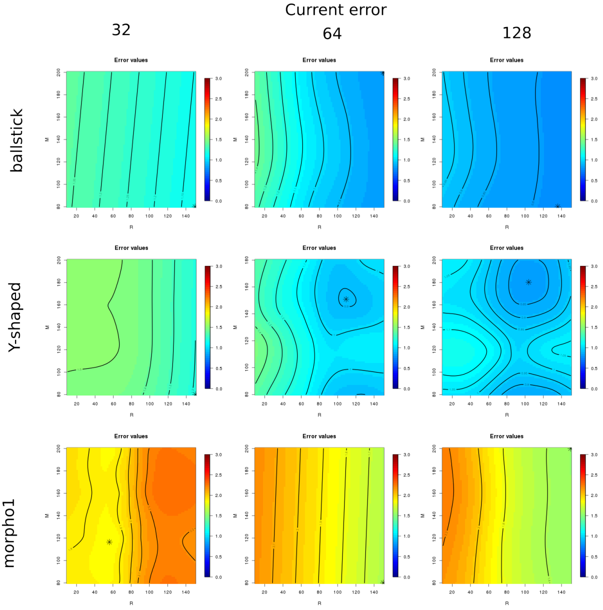


Figure : Colour map of the error of the ksCSD method.

Summary

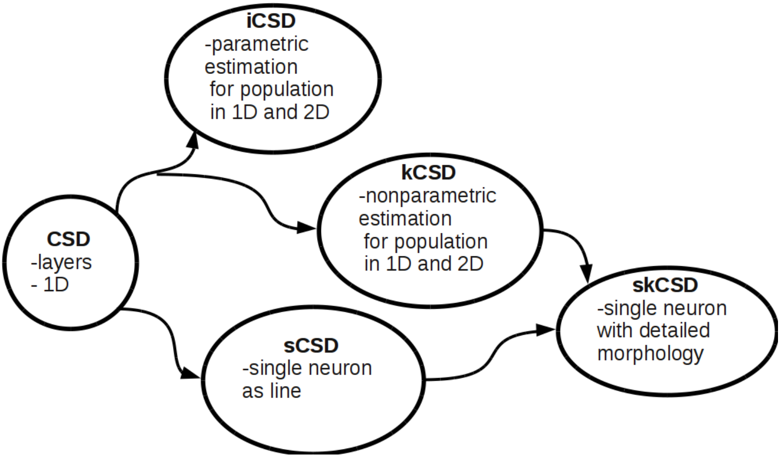
- A novel method for calculating the CSD distributions of single cells given the morphology.
- More simulation needed - huge parameter space
- Next step: testing the method on experimental data

Aknowledgement

I am indebted first of all to Zoltán Somogyvári and Gábor Horváth, to my many colleagues from the Complex Systems and Computational Neuroscience Group at Wigner Research Center and at BME MIT who supported me, furthermore to Daniel Wójcik who gave me the the opportunity to work in his Laboratory of Neuroinformatics at Nencki Institute.

Thank you for your attention!

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

skCSD

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

- Gaussian function

$$\tilde{b}_i(t') = e^{-\frac{(t'-t_i)^2}{R^2}} \tag{12}$$

- Cosinus function

$$\tilde{b}_i(t') = \frac{cos(|t'-t_i|)\pi}{R}, \quad \text{if } |t'-t_i| < R \tag{13}$$

Current density at $\mathbf{x}$:

$$C(\mathbf{x}) = \sum_{j=i}^{M} a_j \tilde{b}_j(\mathbf{x}) \tag{14}$$

The extracellular potential generated by the ith source:

$$b_i(x, y, z) = A\tilde{b}_i(t') \tag{15}$$

$$b_i(x, y, z) = \frac{1}{4\pi\sigma} \int \frac{\tilde{b}_i(t')}{\sqrt{(x - x'(t))^2 + (y - y'(t))^2 + (z - z'(t))^2}} dt' \tag{16}$$

$$\Phi(\mathbf{x}) = \sum_{i=1}^{M} a_i b_i(\mathbf{x}) \tag{17}$$

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

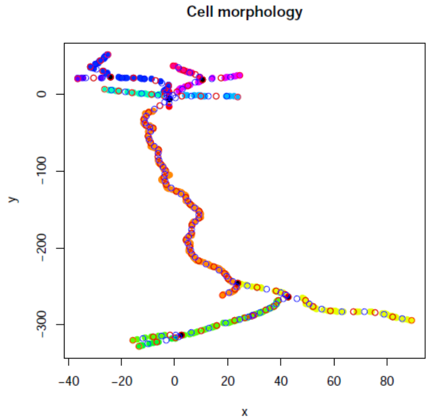
$$K(\mathbf{x}_k, \mathbf{x}_l) = \sum_{i=1}^{M} b_i(\mathbf{x}_k) b_i(\mathbf{x}_l) = B_k^T B_l \tag{18}$$

$$\tilde{K}(\mathbf{x}_k, \mathbf{y}_l) = \sum_{j=1}^{M} b_(\mathbf{x}_k) \tilde{b}_j(\mathbf{y}_l) = B_k^T \tilde{B}_l \tag{19}$$

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

$$C(\mathbf{x}) = \tilde{\mathbf{K}}^T(\mathbf{x}) \tilde{\mathbf{K}}^{-1} \mathbf{V} \tag{20}$$

Usually neurons have more, than 1 branch :(



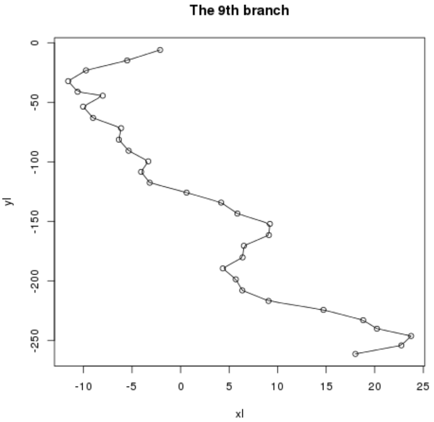
[4]

How to handle the branching?

- branches independent
- connect the branches

[4] $http://neuromorpho.org/neuroMorpho/neuron_{i}nfo.jsp?neuron_{n}ame = 03a_{p}yramidal9aFI$ Allman et al 2006

Usually branches are not straight :((



How to handle?

- fit a curve
- position given by parameter t

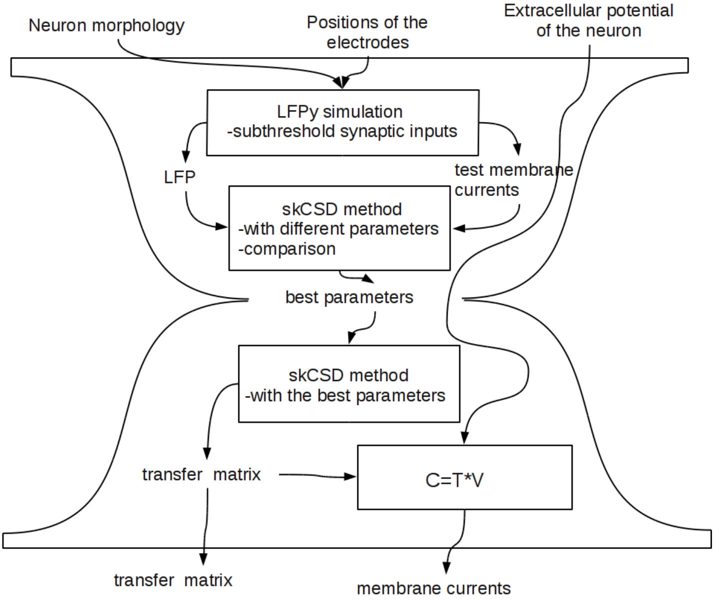
Lots of parameters :(((

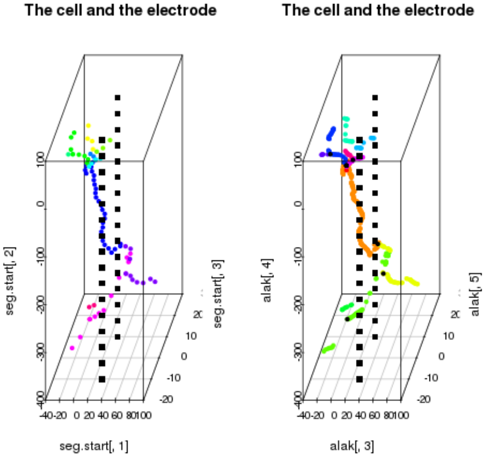
Parameters of the method:

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

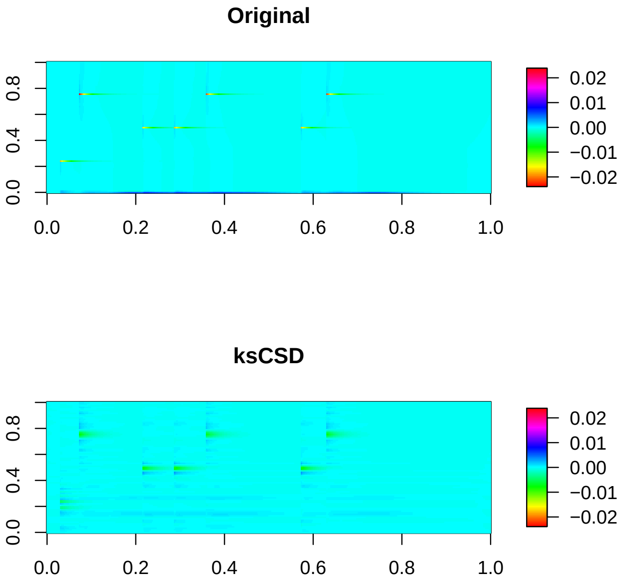
Parameters of the test simulations:

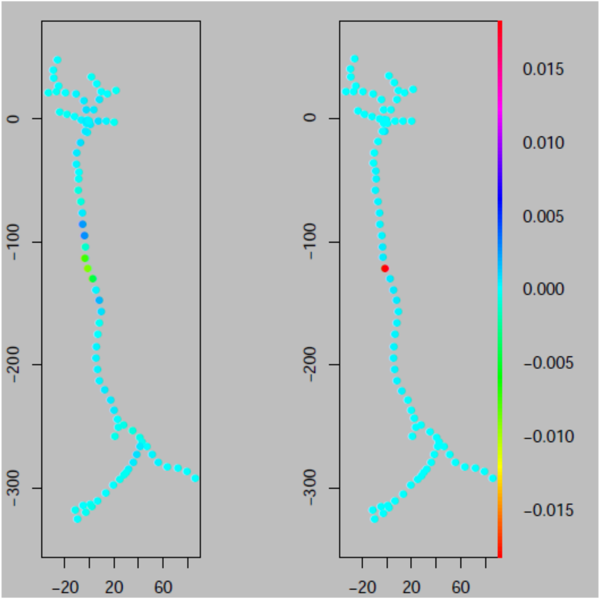
- neuron morphology
- inputs
- cell to electrode distance
- position of the electrode (1D, 2D, 3D)


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


The cell and the electrode
seg.start[, 1]
seg.start[, 2]
seg.start[, 3]
-40-20 0 20 40 60 80100
100
0
-100
-200
-300
-400
20
10
0
-10
-20
The cell and the electrode
alak[, 3]
alak[, 4]
alak[, 5]
-40-20 0 20 40 60 80100
100
0
-100
-200
-300
-400
20
10
0
-10
-20

we want this method what we have: morphology, electrode in N points how to connect these? there is a relationship between the currents and potentials, but its not straightforward


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?

$$e = \frac{\sum_{t,i} |C_{skCSD} - C_o|}{\sum_{t,i} |C_o|} \tag{21}$$