# Advanced recording techniques
# for studying cellular-level neurophysiology



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*Theses of the Ph.D. Dissertation*

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# 1 Introduction and aims

To reveal the biophysical basis of observable global states of the brain (such as cognitive processes or a particular behaviour) a wide range of different approaches were developed and applied, either based on bottom-up or top-down strategies.

The two leading methods for the bottom-up approach are penetrating electrophysiological recordings via intra- and extracellular probes. The words '*intracellular*' (IC) and '*extracellular*' (EC) refer to the electrode location inside and outside the targeted cells, respectively. While these devices become the workhorses of cellular neurotechnology providing direct access to bioelectrical events generated by single or multiple neurons, their invasiveness limits the applicability for chronic and human usage.

On the other pole of the scale, other top-down imaging (fMRI, PET) and recording (EEG, MEG) methods with the capability of recording multiple regions or even whole-brain activities have been developed in parallel. All of these technologies have the advantage of remaining completely non-invasive and thus becoming applicable even for human clinical applications instead of being mostly restricted to animal-based research. In spite of intensive progresses either in bottom-up and top-down approaches, there is still a significant, uncovered gap in the middle, namely how individual cells can be spatio-temporally coordinated in local networks to form specific cognitive functions [1, 2]. This so called '*mesoscopic*' range is of great interest recently in neurophysiology (and in its corresponding neurotechnology) and thus will be the main focus of this current thesis as well. This mesoscopic range will be investigated by means of extracellular multi-channel probes covering wider area than single-electrode recordings.

In this current thesis work, I focus on *in vitro* brain slice electrophysiology using penetrating EC multi-channel, laminar probes. Cutting the brain into thin slices has allowed access to neurons located deeper in the brain. Brain slice preparations can be used for either imaging or recording neural activities that would be otherwise difficult to reach and detect *in vivo*. Similarly to *in vivo* conditions, it is also possible to observe *in vitro* population responses, such as '*sharp wave ripples*' (SWR) or some other inherent oscillations [3]. Furthermore, an additional advantage of *in vitro* brain slice recordings is the ability to combine different modalities, which would be again, challenging or not feasible *in vivo*. Among others, such combinations are the co-localised and simultaneous IC recording or two-photon (2P) laser scanning microscopy imaging [4, 5, 6].

The main independent topics of the dissertation are the followings:

Chapter '*Theoretical background*' cover the biophysical theory of IC and EC potentials and their relationship as well as will detail the recent technical developments and their limitations. With this knowledge in hand, Chapter '*Materials and methods*' introduces multi-channel silicon probes used throughout the thesis; this same chapter elaborates on the experimental methods and closes with the description of data analysis methods and histological procedures. Once given the theoretical and methodological bases to contextualize this work, Chapter '*Results*' split the results into three independent thesis groups: On Figure 1 a triangle illustrates the relationship
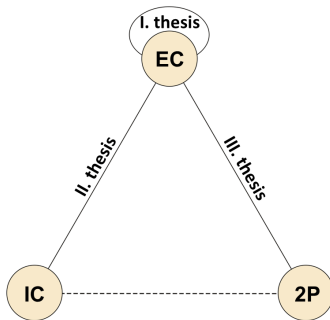


Figure 1: Interconnections between thesis groups (edges) and topics covered (nodes).

of the three theses (edges) and three experimental techniques used (nodes). Although there are small exceptions (such as, occasional IC-2P recordings in II. Thesis group, shown with a dashed line), edges represent the main interactions between recording modalities. I. Thesis group presents the development and testing of a novel, multi-channel silicon probe with protruding contact sites for improved *in vitro* EC recordings and highlights its advantages with a systematic and quantitative comparison against a commercially available, multi-channel surface probe. This chapter will focus only on EC recording without IC patch-clamp and with only one representative 2P figure showing that the spiky probe is compatible with two-photon microscope imaging. II. Thesis group details an approach developed for co-localised and simultaneous IC-EC recording, it describes the resulting '*ground-truth*' dataset, and explores potential further applications of the recorded data in model-based calculations. This thesis does not focus on a thorough evaluation of any data analysis method (such as spike-sorting algorithms or source-localization methods), however, a preliminary application of single-cell level current source density analysis (skCSD) will be presented using

the collected simultaneous data. III. Thesis group starts with the description of the photoelectric artefact generated during the use of combined multi-channel EC recordings and two-photon (2P) laser imaging. Recent strategies to eliminate contaminations of the photoelectric artefact will be discussed together with their limitations. Next I present an experimental protocol for the generation of co-localised and simultaneous EC and 2P measurements either with or without laser artefact. The protocol allows for the investigation of photoelectric artefacts but also for providing control data for validation. Using these combined recordings, a developed specific filtering algorithm will be presented to mitigate the photoelectric effect on recorded extracellular signals. Chapter '*Conclusions and outlook*' closes the dissertation by listing the novel scientific contributions of this thesis work with related publications and giving an outlook for future perspectives and for the application of the results.

## 2   Materials and methods

Intracellular electrochemical activity of neurons inevitably generates extracellular changes due to transmembrane currents. Currents that are moving between inside and outside of the neuron during its activity can be only indirectly measured extracellularly by their influence on the electrical field. The EC electrode picks these changes up and relays them to an amplifier where they can be measured in respect to a reference. EC potential elicited by transmembrane currents varies dynamically in time and space as numerous currents may be superimposed at a given location in the EC medium [1, 7, 8]. Thus, EC potential contains all the summed signals of multiple synaptic inputs and spiking outputs as well as different local and further (volume conducted) activities in the region where the EC electrode is located [9, 8]. Some of the biophysical principles of EC potential generation are long known. However, there are still many theoretical and experimental open questions that limit the interpretation of EC potential to understand its function.

From the a large variety of devices developed for multi-channel EC recordings I use the following squeezed list of features throughout the experiments:

- acute rodent

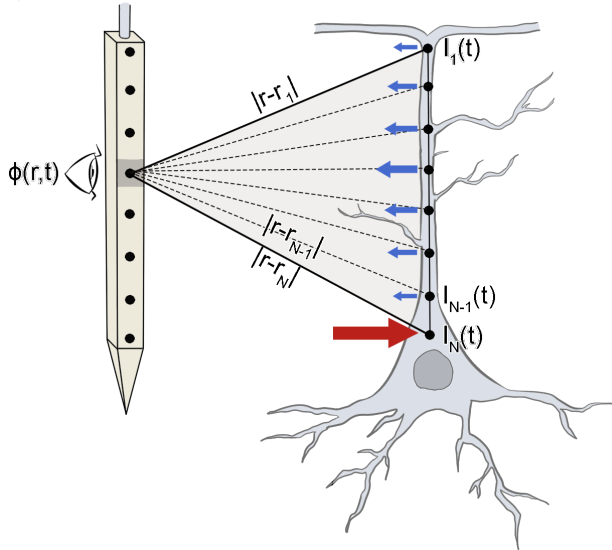- *in vitro* brain slice

- laminar (1D) contact sites

**Figure 2:** Illustration for the theoretical background of extracellular (EC) recordings. EC potential $\Phi(r, t)$ measured at the recording site is generated by the weighted linear sum of net transmembrane currents $I(t)$ based on the compartmental cell-electrode distances ($r$).

- silicon or steel shank

- penetrating or surface

- polytrodes (16-32 channels)

Recordings were carried out with three different multi-channel microelectrodes that met the above criteria. Recording protocols for all the three Thesis groups were performed on the same experimental set-up using very similar tool-kits with minor changes.

Acute horizontal hippocampal slices were prepared from adult Wistar rats (between 200-350 g, gender balanced, in total #30 successful experiments at the date of thesis submission). In addition to Wistar rats, Thy1-GCaMP6 transgenic mice were also used for population imaging under two-photon (2P) microscopy. Animals were bread and reared in the Research Centre of Natural Sciences, Hungarian Academy of Sciences. Animals were supplied with food and water *ad libidum* and were kept on a 12-12 hour light-dark cycle. All of the protocols followed the guidelines

of the Hungarian Act of Animal Care and Experimentation (1998; XXVIII, section 243/1998.). The Animal Care and Experimentation Committee of the Hungarian Academy of Sciences, and the Animal Health and Food Control Station have approved the experimental design (license number: PEI/001/2290-11/2015). Efforts were made to minimize animal suffering and to reduce the number of animals used.

Before the experiment, the animals were deeply anaesthetized with isoflurane (min. 0.2 ml/100 g), quickly decapitated and their brains were immediately removed and dipped into cold (2–3 °C), oxygenated (95% $O_2$, 5% $CO_2$) cutting solution. The cutting solution contained the following composition (in mM): 250 Sucrose, 26 $NaHCO_3$, 10 D-Glucose, 1 $KCl$, 1 $CaCl_2$ and 10 $MgCl_2$. 500 μm-thick horizontal slices were cut by a vibratome (VT1200s; Leica, Nussloch, Germany) from both hemispheres containing the whole hippocampal formation. Slices were kept in a standard '*artificial cerebrospinal fluid*' (aCSF) solution at room temperature (20–22 °C) for at least 1 h before use. The recordings were performed with a standard recording aCSF containing (in mM): 124 $NaCl$, 26 $NaHCO_3$, 10 D-Glucose, 4 $KCl$, 2 $CaCl_2$ and 2 $MgCl_2$. The whole recording system was build under a two-
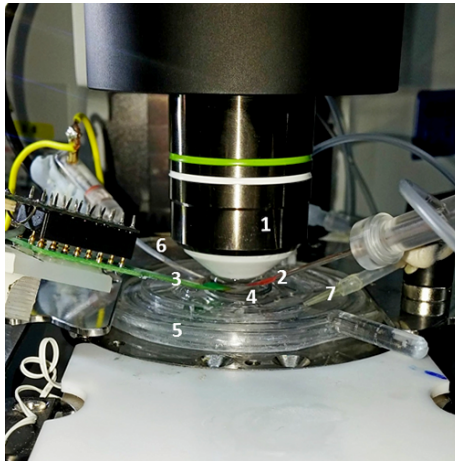


**Figure 3:** Close-up view of the simultaneous IC-EC recordings under the objective of the 2P microscope. Labels are the following: Olympus 20x objective of the 2P microscope (1), patch-clamp pipette filled with IC solution (2), EC multi-channel probe (NeuroNexus comb probe shown here) with its connector (3), brain slice and holder ring (4), dual-perfusion chamber (5), reference electrode pellet (6), outlet of aCSF perfusion (7).

photon laser scanning microscope set-up developed by the Femtonics company (Femtonics Ltd., Budapest, Hungary) from a transformed Olympus BX61 upright microscope, which has a NIR bright-field camera mode and a 2P fluorescent mode as well. Both the stage and two other lateral micromanipulators were controlled by motorised wheels of the Luigs-Neumann (LN) controller system (Luigs&Neumann Feinmechanik und Elektrotechnik GmbH, Ratingen, Germany). We can have a close-up view of the set-up on Figure 3.

The patch-clamp system (Axon Instruments, USA) consists of several subunits. During the recording, the signal was first transferred to Multi-Clamp 700B amplifier, that maximizes signal-to-noise ratio and enables whole-cell voltage-clamp and current clamp recordings, then feed to the computer through Digidata 1550B A/D converter. MultiClamp Commander software was used to operate the glass pipette and set various parameters and compensations. pClamp10 software consists of Clampex visualization software, which is suitable for acquiring digitized data, Ramp-test was also performed on this platform, and Clampfit analysis software, which provides a wide variety of tools for statistics, transforms and different layout designs for intracellular data. Extracellular signals from multi-channel silicon probes were transmitted to the Intan RHD2000 Evaluation system (Intan Technologies, USA), its task is to acquire, pre-amplify and digitize the raw data. It consists of a 32-channel pre-amplifier chip (RHD2132), a RHD2000 FPGA interface board, which is an open-source hardware with up to 128 channels for bio-potential recordings and thin, flexible interface cables for connections. Intan RHD2000 software transfers data to the screen, operates the amplifiers and sampling frequency can be set here. The wideband signals (from 0.1 Hz up to 7 kHz) were recorded with 20 kHz sampling rate.

# 3   Summary of novel scientific results with related publication

## I. Thesis group: Development and testing of a novel, multi-channel spiky probe for extracellular recordings

*I.a. I have designed a novel multi-channel, laminar in vitro silicon probe with protruding, 'spiky' contact sites for improved brain slice recordings. I have optically verified the fabricated arrowhead shape, protruding contact sites under scanning electron microscopy. Moreover, I have characterised the electrochemical impedance magnitudes and phase angles as well as the noise level of the spiky probe in physiological saline solution.*

The spiky probe comprises a single silicon shank carrying 32 protruding $Pt/Ir/IrO_x$ contact sites with three possible spacing layouts of 25 µm, 50 µm and 100 µm. With the help of the optimally angled shank, I have shown that the spiky probes are compatible with large in vitro, water-immersion objectives used typically in two-photon microscopy imaging.
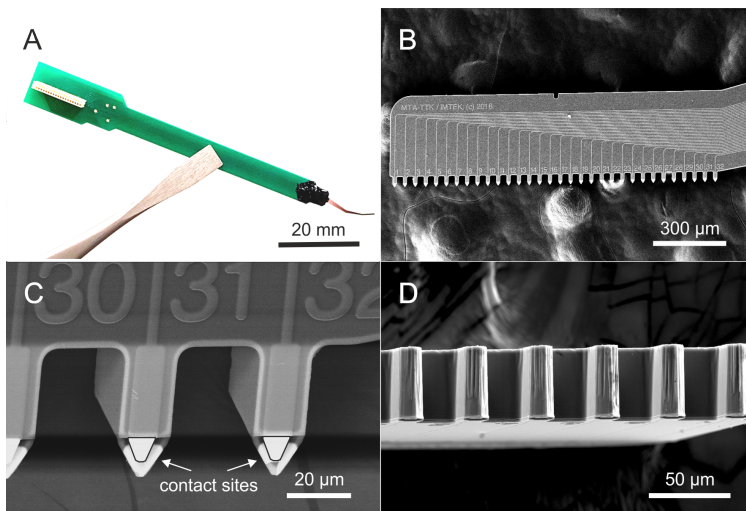


**Figure 4:** Optical photograph (A) and scanning electron microscopy (SEM) images of the spiky probe (B-D). Please note the arrowhead-shape, protruding contact sites.

The high-density spiky probe (with inter-contact distance of 25 µm) used in the comparative test showed an average impedance magnitude of 1.27 ± 0.1 MΩ at 1 kHz across all contact sites with an average phase angle of -70 ± 5°. In addition, I have tested the robustness and re-usability of spiky contact sites. Impedance changes were investigated after an extensive usage (7 experiments with 17 separate insertions, in total) by repeating the impedance test after the last experiment. The average impedance magnitude of all contact sites was slightly increased after the last experiment to 1.5 ± 0.1 MΩ. The impedance phase angles did not change significantly (-69 ± 5° after extensive testing).
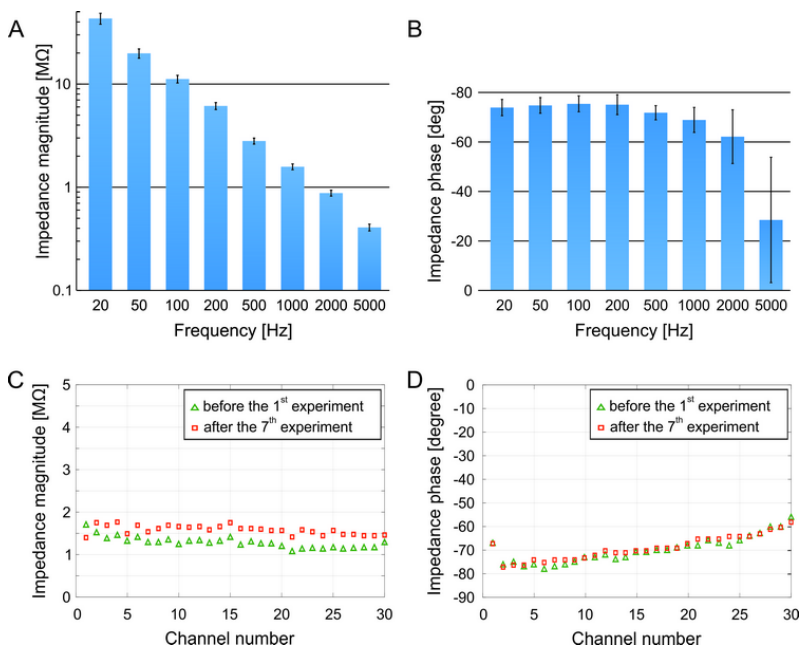


**Figure 5:** Results for impedance spectroscopy (A-B). Please note the monotonically decreasing magnitudes and phase angle values and the small standard deviations across channels. Stability and re-usability of spiky contact sites (C-D).

I have also measured the root mean square noise levels for the 32 contact sites. In the spike band (500 – 5000 Hz) noise level was 4.63 ± 0.51 $\mu V_{rms}$. Placing the probe onto the brain slice elevated measured noise levels by 10 - 20%.

*I.b. With the aid of protruding contact sites I have proven quanti-*
*tatively that the spiky probe provides higher neuronal yield and higher*
*signal amplitude compared to a commercial surface probe. Moreover, I*
*have also shown that the high-density spiky probe is suitable for separat-*
*ing single unit clusters into putative cell types based on a spatio-temporal*
*analysis of their extracellular waveforms oversampled by multiple adja-*
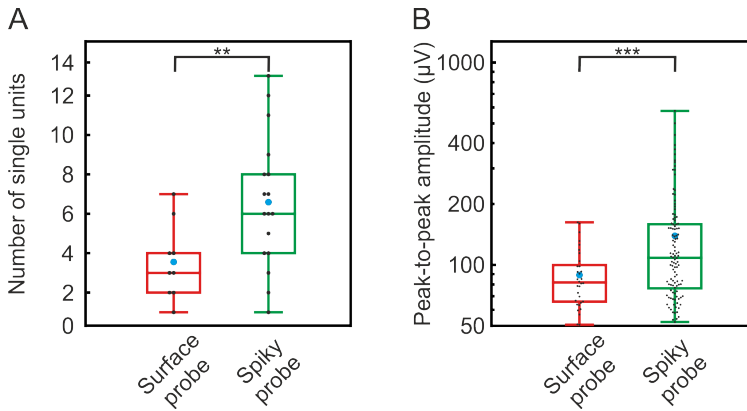*cent contact sites.*



**Figure 6:** Quantitative comparison of recording performances. Box plots showing the distribution of the number of well-separated SUA clusters (A) and the distribution of the peak-to-peak amplitude of spike wave-forms (B) for the high-density spiky probe and the hockey-stick surface probe. ** $p = 0.0078$; *** $p = 0.0000049$; Welch's t-test

The high-density spiky probe (with inter-contact distance of 25 μm) was compared to a commercially available, laminar surface probe called 'hockey-stick' (in vitro U-type probe, Plexon Inc., Texas, USA). The average single unit yield was 6.6 for spiky probe per position and 3.6 for the hockey-stick surface probe. The average signal amplitude was 139.2 ± 96.4 μV in the case of spiky probe and 89.08 ± 30.2 μV for the hockey-stick probe. The maximal measured signal amplitude was only 162.32 μV for the hockey-stick probe, while the spiky probe had a maximal amplitude of 576.79 μV. Consistent with prior studies, larger average spike amplitudes may correspond to closer cells, since extracellular spikes are decreased and flattened over distance [7, 3, 9, 1].
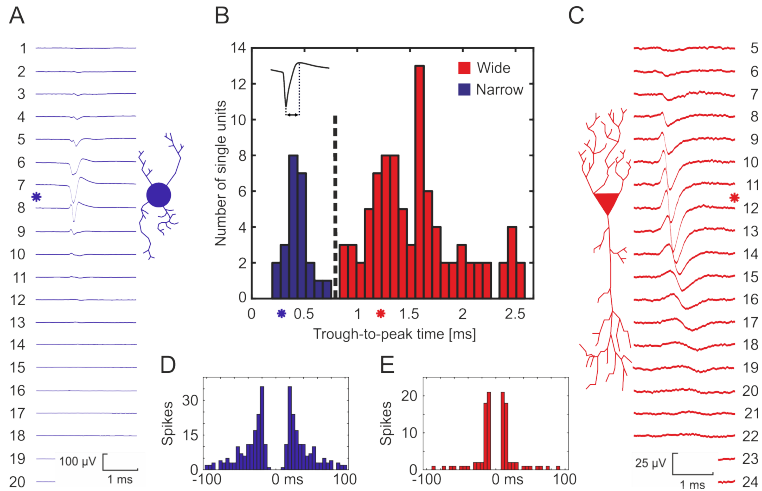
**Figure 7:** Clustering results of a putative interneuron (A,D) and pyramidal cell (C,E) based on their recorded extracellular waveforms. Bimodal distribution of trough-to-peak times of all recorded SUA waveforms (B).

Using the close-packed contact sites of the high-density spiky probe (with 25 μm inter-contact distances) I have illustrated how this probe can spatio-temporally oversample single unit spikes. I have investigated further parameters in the case of two representative single units, namely trough-to-peak time, presence of the initial capacitive peak, features in the autocorrelogram and spatial spread. I clustered the two representative units into putative cell types using these extended, multi-channel level criteria.

Publication related to the I. Thesis group: *[II]*.

## II. Thesis group: Co-localised, simultaneous intra- and laminar extracellular recordings with corresponding morphology: generation of a ground-truth dataset

*II.a. I have created a novel measurement method providing ground-truth data for multi-channel electrophysiology, in vitro. Using this co-localised and simultaneous experimental protocol, both intra- and extracellular data can be acquired reliably from targeted neurons. I have also provided structural information for the ground-truth electrophysiological data by the reconstruction of the full 3D neuronal morphology and corresponding cell-electrode distances in the tissue. From these recordings I have constructed and released an online, open-source library of the recorded cells together with all the physiological and morphological information listed throughout the thesis. The library and the corresponding tabular guide serves as an ever-expanding, constantly updated ground-truth data collection.*
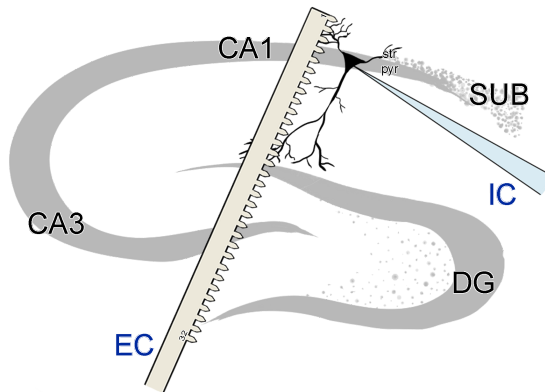


**Figure 8:** Schematics of the intra- and extracellular recording arrangements in the hippocampal CA1 pyramidal region.

I have described the steps developed for the recording of co-localised and simultaneous intra- and extracellular signals with sub-millisecond accuracy. Extracellular recordings were complemented with a whole-cell patch-clamp recording in the closest vicinity of the silicon probe. Since these *in vitro* experiments were designed under a two-photon microscope system, proper visual monitoring both for the electrode and for cell positions could

13

be achieved. Inclusion criteria for a successful simultaneous measurement were the following three conditions:

- I expected detection of at least 100 spike times for each 3-minute recording session to assure reasonable spike count in every data file (1).

- Holding current injected for maintaining stable spiking had to remain constant throughout each recording session and within a physiological range, ideally below 300 pA (2).

- After pre-processing, spikes of the patch-clamped cell should be detectable on at least one extracellular channel in the spike-triggered average form (3).

Additionally, I have also performed a Ramp-test in the beginning of each whole-cell patch-clamp recording to characterise putative cell types and to determine various useful intracellular parameters of the patched cell.
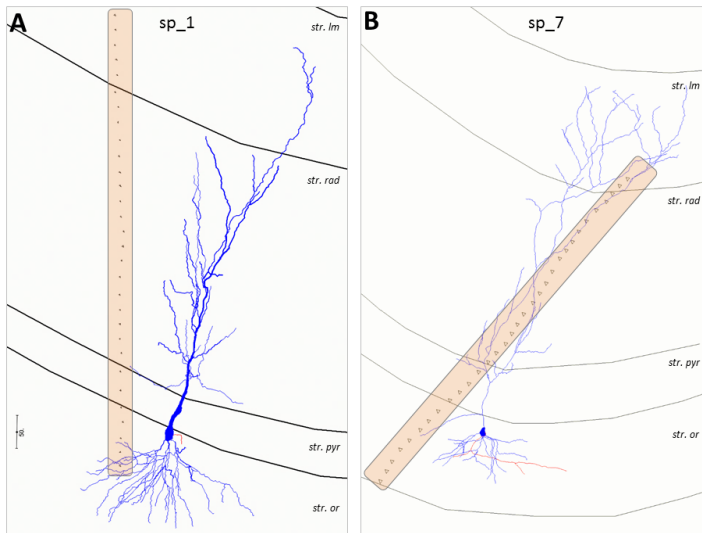


Figure 9: 2-D snapshots of two complete 3-D reconstructions of the complete neuronal morphologies and corresponding EC probe traces.

In addition to electrophysiology, concurrent two-photon imaging was included in the experimental protocol to take full advantage of the available multi-modal set-up. The field-of-view of the two-photon z-stack projection was set to cover both the track of the silicon probe and main cellular compartments (soma, apical trunk region, proximal apical and basal dendrites). Depth levels (z- dimension) typically ranged from -200 µm to 0 µm, (which is the surface of the slices). The resolution of the z-stack (or the step between stacks) was 2-3 µm, which was enough to capture small dendritic processes along the 3D morphology. In the end of the experimental protocol, patch pipette was carefully withdrawn, slice was removed from the dual perfusion chamber and fixated in paraformaldehyde solution for *post-hoc* histological reconstruction. Patch-clamped cells were passively filled with fluorescent markers (Alexa594 and Fluo-4) and with histological tracer molecule (Neurobiotin) via diffusion of the intracellular solution. In cases where all histological steps (fixation, reslicing, and the precipitation of Neurobiotin) were successful, neurons were chosen to be digitally reconstructed in 3D by the Neurolucida system. With the help of 3D reconstructions, Euclidean cell-electrode distances between contact sites and sub-cellular compartments could be calculated properly.

At the time of submission, a total of #16 neurons were successfully recorded from #12 animals by using the simultaneous and co-localised protocol introduced here in Thesis II.a. This library building is currently in progress and to be updated whenever a new successful, candidate data becomes available.

**II.b. With the aid of my acquired simultaneous electrophysiology dataset, a novel single-cell source localisation method called skCSD (developed in a collaborative study) was firstly tested and validated on real experimental data with reconstructed neuronal morphology.**

Having all these structural data together with simultaneous electro-physiology made possible to support model-based single-cell calculations with real experimental validation. This was the first time in literature, when researchers were able to compute single-cell level current source densities (or the transmembrane sources of the extracellularly measured potentials) along a detailed, real neuronal morphology. The observed spatio-temporal dynamics was in accordance with previously estimated patterns, namely that somatic currents mostly dominate the process of spike generation and they are balanced by corresponding counter currents along the proximal
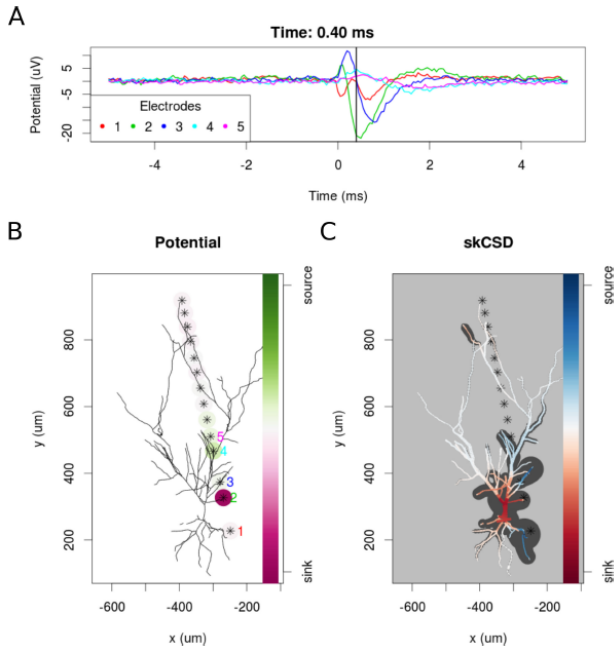
15

**Figure 10:** skCSD reconstruction of spike-triggered average for a CA1 pyramidal cell. Time course of the EC potentials for 5 selected channels (A). 2-D projection of the cell and silicon probe positions with overlaid EC potential dynamics (B). Reconstruction of current source densities based on the measured EC potentials and modelled cellular morphology (C).

dendritic tree. This example demonstrated the feasibility of the skCSD method on recorded experimental data and may help in planning further experiments (as an iterative '*experiment-data analysis cycle*'), aiming to reveal the spatial distribution and temporal dynamics of the synaptic input currents which evoke the firing of a neuron.

Publication related to the II. Thesis group: *[I]*.

# III. Thesis group: Combination of multi-channel extracellular recordings and two-photon laser scanning microscopy imaging for the experimental characterisation of photoelectric artefacts

*III.a. I have designed and carried out experiments for acquiring both laser artefact-free and laser contaminated data in one experimental session. My generated dataset is suitable for the characterisation of the generated photoelectric artefact and for the comprehensive evaluation of any artefact suppression algorithm.*
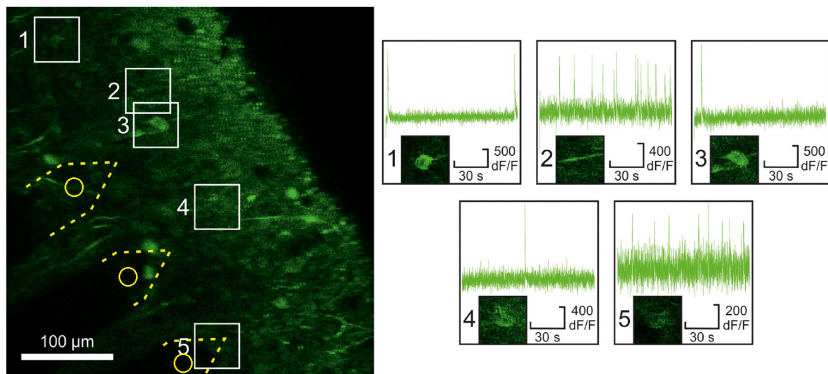


Figure 11: Imaging the close vicinity of the implanted silicon probe in a combined EC-2P recording. Imaging reveals both activities of somas and dendtrites (examples are shown on the left) in the same FoV of EC contact sites (highlighted by yellow circles).

Firstly, I have proved experimentally, that the generated photoelectric artefact is not identical with a simple scanner noise and it has a varying nature across multiple contact sites. Moreover, I have carried simultaneous two-photon imaging and extracellular silicon probe recordings in the same field-of-view. Two-photon excitation was set to be sufficient for detecting reliable transgenic $Ca_{2+}$ signals without causing damage on the metal-based extracellular probe. With the aid of this experiment, multi-cellular $Ca_{2+}$ signals and co-localised extracellularly detected units become comparable.
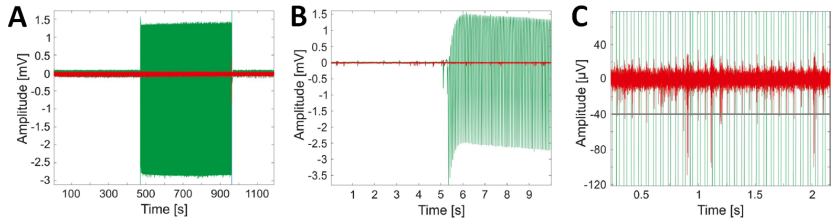
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**Figure 12:** Filtered signal (red) is overlaid on the original (unfiltered, green) data. It is visible that the laser generated photoelectric artefact was significantly reduced and SUAs emerged from the background noise.

*III.b. I have shown that single unit clusters can be detectable even under contaminated signal conditions, as well as clustered spikes before-, under- and after laser scanning remained tractable based on their signal amplitudes, waveforms and autocorrelograms.*

Spike sorted single unit activities remained tractable before and after the laser scanning period after applying an iterative artefact filtering process (which algorithm was developed in collaboration with other colleagues). However, I also pointed out that in a few cases photoelectric artefact (due to laser scanning) may have some effects on the dynamics of scanned cells (e.g. indirect excitation mediated by photoelectric currents).

Publication related to the III. Thesis group: *[III]*.

# 4   Application of results and future perspectives

All the three experimental problems I have addressed throughout the dissertation are very application oriented, even if their current stages of realisation are different.

Firstly, I have presented and tested penetrating a silicon-based multichannel spiky probe. While the current shank design proved a significant improvement for *in vitro* recordings, it is certainly not designed for long-term recordings. Future developments may enable such devices to be further designed in both chronic and acute *in vivo* applications via smaller modifications. Another possible future application would be the investigation of different tissue samples using the same probes, e.g. post-operative human *in vitro* tissue samples. Dimensions of the spiky probes are variable in a wide range, and the longest spiky version (equipped with the largest inter-contact distances of 100 μm) would cover a sufficiently large area to be applicable for human neocortical slices and for multi-layered structures.

Regarding the second Thesis group, multiple potential collaborators indicated their interest in using my dataset containing co-localised and simultaneous intra- and extracellular recordings with corresponding morphology. However, as I have mentioned before, some of the intracellularly patch-clamped cells were not visible immediately on the raw extracellular signal, thus they prevented the application of blind spike sorting on the extracellular single unit activities. In these cases, the calculation of spike triggered averages was the only way for comparing intra- and extracellular signals. As a possible continuation of this study, my goal will be to get even closer to the cells with the silicon probes by further optimizing the measurement set-up and process and as a consequence, to record more cells with sortable spike amplitudes. I will also focus on recording more interneurons to expand the usability of the ground-truth dataset. The simultaneous experimental protocol can also be applied on different regions, such as neocortex or human post-operative slices.

The first collaborative application of the dataset has already occurred within the framework of the theses. We have shown how the series of extracellular recordings in combination with neuronal morphology can be used to estimate current source densities located on the cell contributing to the recorded extracellular potential. Unlike simple somatic patch-clamp recordings, here we are able to obtain intracellular information along the whole cellular morphology, not just at a single point. This new approach may move the field a bit forward by opening a new experimental window into information processing by single cells allowing for their global monitoring, which

was not possible previously. It will be equally important from the theoretical side, as theoretical paradigms are informed by what we are able to extract from available measurements. Since it is now feasible experimentally to obtain the relevant data with the aid of my developed protocol, I believe that the data proposed here may find its uses in future works to constrain the biophysical models of the neuron membrane, as well as guide new discoveries by giving a coherent view of the global synaptic bombardment within a targeted neuron.

Lastly, I have proposed an experimental solution for the investigation and elimination of photoelectric artefacts in co-localised two-photon imaging and extracellular silicon probe recordings. This study showed that it is possible to get insight into the extracellular activity even under two-photon laser scanning. However, I have found putative modulations in spiking behaviour caused by the photoelectric artefact which were undesirable consequences of simultaneous scanning. Further investigations are to be performed to resolve the indirect stimulation effect of laser generated artefacts. Regarding the application of the filtering algorithm, it would be beneficial to develop an automated and more robust software which is independent of the type of silicon probe used and can be applied to other layouts or different channel counts. The greatest challenge would be to search for correlations and causal roles between co-localised fluorescently active (or 'blinking') cells and extracellularly detected single unit spikes. Similarly to the second Thesis group, the application of simultaneous, multi-modal measurements may give rise to novel findings in designing improved neural interfaces.

# 5  Author's publications related to the theses

*Peer-reviewed journal publications*

I. D. Cserpán, <u>D. Meszéna</u>, L. Wittner, K. Tóth, I. Ulbert, Z. Somogyvári and D. Wójcik. Revealing the distribution of transmembrane currents along the dendritic tree of a neuron with known morphology from extracellular recordings. ***eLIFE***, 6:e29384, 2017. (IF: 7.73, Q1/D1) DOI: 10.7554/eLife.29384

II. <u>D. Meszéna</u>, B. P Kerekes, I. Pál, G. Orbán, R. Fiáth, T. Holzhammer, P. Ruther, I. Ulbert and G. Márton. A silicon-based spiky probe providing improved cell accessibility for in vitro brain slice recordings. ***SENSORS & ACTUATORS B – CHEM***, 297C, 126649, 2019. (IF: 6.39, Q1/D1) DOI: 10.1016/j.snb.2019.126649

III. G. Orbán, <u>D. Meszéna</u>, K. R. Tasnády, I. Ulbert and G. Márton. Method for spike detection from microelectrode array recordings contaminated by artifacts of simultaneous two-photon imaging. ***PLOS ONE***, 14(8): e0221510, 2019. (IF: 2.78, Q1) DOI: 10.1371/journal.pone.0221510

# Other publications of the author

*Preprints and works in progress*

- R. Fiáth, <u>D. Meszéna</u>, M. Boda, P. Barthó, P. Ruther and I. Ulbert. Recording site placement on planar silicon-based probes affects neural signal quality: edge sites enhance acute recording performance. ***SCIENTIFIC REPORTS***, 2020. (IF: 4.01, Q1/D1) (*Under review*) (Preprint on ***BioRxiv***) DOI: 10.1101/2020.06.01.127308

- G. Dimitriadis, J. P. Neto, A. Aarts, [. . . ] G. Marton, <u>D. Meszéna</u>, S. Mitra, [. . . ] B. Raducanu, P. Ruther, T. Schroeder, W. Singer, P. Tiesinga, I. Ulbert, S. Wang, M. Welkenhuysen, A. R Kampff. Why not record from every channel with a CMOS scanning probe? ***PNAS***, 2020. (IF: 9.58, Q1/D1) (*Under review*) (Preprint on ***BioRxiv***) DOI: 10.1101/275818

- T. Marek, G. Orbán, <u>D. Meszéna</u>, G. Márton, I. Ulbert, G. Mészáros and Zs. Keresztes. Optimization Aspects of Electrodeposition of Photoluminescent Conductive Polymer Layer onto Neural Microelectrode Arrays. **MATERIALS CHEMISTRY AND PHYSICS**, 2020. (IF: 2.78, Q2) (*Under review*)

*Peer-reviewed journal publications*

- G. Márton, E. Z. Tóth, L. Wittner, R. Fiáth, D.Pinke, G. Orbán, <u>D. Meszéna</u>, I. Pál, E. L. Győri, Z. Bereczki, Á. Kandrács, K. T. Hofer, A. Pongrácz, I. Ulbert and K. Tóth. The neural tissue around SU-8 implants: a quantitative *in vivo* biocompatibility study. **MATERIALS SCIENCE** & **ENGINEERING C**, 112C, 110870, 2020. (IF: 4.96, Q1/D1) DOI: 10.1016/j.snb.2019.126649

- A. Zátonyi, G. Orbán, R. Modi, G. Márton, <u>D. Meszéna</u>, I. Ulbert, A. Pongrácz, M. Ecker, W. E. Voit, A. Joshi-Imre, and Z. Fekete. A softening laminar electrode for recording single unit activity from the rat hippocampus. **SCIENTIFIC REPORTS**, vol. 9, no. 1, p. 2321, 2019. (IF: 4.12, Q1/D1) DOI: 10.1038/s41598-019-39835-6

*Patent*

- I. Ulbert, G. Márton, <u>D. Meszéna</u>, B.P. Kerekes, G. Orbán, K.R. Tasnády, D. Pinke. A design of an ionic conductance-based multielectrode system for mitigating photoelectric artefacts. Hungarian Patent Application (pending), *Registration number: 45B01FEF1C, File number: P 17 00527, Date: 15th December 2017.*

*Selected talks and posters*

- <u>D. Meszéna</u>, G. Orbán, K. R. Tasnády, I. Ulbert and G. Márton. Towards co-localised microelectrode array recordings and two-photon microscopy. *HunDoc 2020*, Szeged, Hungary, 2020. (Invited talk)

- Z. Somogyvári, <u>D. Meszéna</u>, D. Cserpán, L. Wittner and I. Ulbert. Spatiotemporal membrane potential and resistive current reconstruction from parallel multielectrode array and intracellular measurements in single neurons. $10^{th}$ *IBRO World Congress of Neuroscience*, Daegu, Korea, 2019. (Poster)

- R. Fiáth, <u>D. Meszéna</u>, Mihály Boda and I. Ulbert. Impact of the recording site location on the recording performance of silicon probes in acute experiments. *FENS Regional Meeting*, Belgrade, Serbia, 2019. (Poster)

- E. Z. Tóth, <u>D. Meszéna</u>, A Dublecz, D.Pálfi, K. Tóth, L. Erőss, A. Bagó, D. Fabó, I. Ulbert and L. Wittner. Back-propagating action potentials in human neocortical pyramidal cells and interneurons: A preliminary study. *Gordon Research Conference: Dendrites*, Ventura, CA, US, 2019. (Poster)

- <u>D. Meszéna</u>, I. Pál, B. P. Kerekes, G. Marton, K. Tóth, L. Wittner, Z. Somogyvári and I Ulbert. Simultaneous intra- and linear extracellular recordings with corresponding morphology: towards a ground-truth data for multichannel electrodes. *SfN Neuroscience 2018*, San Diego, CA, US 2018. (Poster)

- K. Tóth, E. Z. Tóth, L. Wittner, R. Fiáth, <u>D. Meszéna</u>, I. Pál, E. L. Győri, D. Pinke, Z. Bereczki, G. Orbán, A. Pongrácz, I. Ulbert and G. Márton. Biocompatibility of the SU-8 in the central nervous system. *SfN Neuroscience 2018*, San Diego, CA, US 2018. (Poster)

- G. Orbán, T. Marek, <u>D. Meszéna</u>, B. P. Kerekes, K. R. Tasnády, I. Ulbert, G. Mészáros, Zs. Keresztes, G. Márton. Fluorescent conductive polymer coating on implanted microelectrodes for visualization under two-photon microscopes. $11^{th}$ *FENS Forum of Neuroscience*, Berlin, Germany, 2018. (Poster)

- <u>D. Meszéna</u>, B. P. Kerekes, I. Pál, T. Holzhammer, P. Ruther, I. Ulbert and G. Márton. A novel, silicon-based spiky probe providing improved cell accessibility for in vitro brain slice recordings. *Gordon Research Conference: Neuro-electronic Interfaces*, Galveston, Texas, US, 2018. (Poster)

- D. Cserpán, <u>D. Meszéna</u>, L. Wittner, K. Tóth, I. Ulbert, Z. Somogyvári and D. Wójcik. Revealing the Distribution of Transmembrane Currents along the Dendritic Tree of a Neuron with Known Morphology from Extracellular Recordings. $2^{nd}$ *Nencki Symposium*, Warsaw, Poland, 2017. (Poster)

- I Pál, KT. Hofer, B. P. Kerekes, K. Tóth, B. Rózsa, <u>D. Meszéna</u> and I. Ulbert. Modulation of interictal-like and spontaneous population activity by microsurgical intervention in rat brain slices, $10^{th}$ *Forum of Neuroscience*, Copenhagen, Denmark, 2016. (Poster)

- <u>D. Meszéna</u> and I. Ulbert. Simultaneously recorded multimodal signals in the hippocampal CA1 region, in vitro. *EMBO Practical Course in Advanced Optical Microscopy*, Marine Biological Association, Plymouth, United Kingdom, 2016. (Poster)

- <u>D. Meszéna</u>, E. Lakatos, G. Szederkényi. Sensitivity analysis and parameter estimation of a human blood glucose regulatory system model. In.: Proceedings of the $11^{th}$ *International Workshop on Computational Systems Biology*, TISCP 64, pp. 28, Lisbon, Portugal, 2014. (Talk)

- E. Lakatos, <u>D. Meszéna</u>, G. Szederkényi. Identifiability analysis and improved parameter estimation of a human blood glucose control system model. ***LECTURE NOTES IN COMPUTER SCIENCE***, A. Gupta and T.A. Henzinger (Eds.): CMSB 2013, LNBI 8130 Springer, pp. 248-249, 2013. (Talk) (IF: 1.12, Q2), DOI: 10.1007/978-3-642-40708-6

- L. Négyessy, J. Minich, <u>D. Meszéna</u>, A. Buzás, B. Jákli, M. Bányai, E. Procyk, P. Barone, F. Bazsó. From Neuronal Communication to the Flow of Information in the Cerebral Cortex. 11$^{th}$ *Digital Speech and Image Processing*, Kovacica, Serbia, 2012. (Talk)

### *In Annual Proceedings of the PPCU FITB Doctoral School*

- <u>D. Meszéna</u>. Towards a better understanding of intra- and extracellular neural signals and their relationships. *in PhD Proceedings Annual Issues of the Doctoral School, Faculty of Information Technology and Bionics, Pázmány Péter Catholic University* – 2017. G. Prószéky, P. Szolgay Eds. Budapest: Pázmány University ePress, 2017, pp 27–27.

- <u>D. Meszéna</u>. Targeted simultaneous recordings on rat hippocampal CA1 cells, in vitro. *in PhD Proceedings Annual Issues of the Doctoral School, Faculty of Information Technology and Bionics, Pázmány Péter Catholic University* – 2016. G. Prószéky, P. Szolgay Eds. Budapest: Pázmány University ePress, 2016, pp 69–71.

- <u>D. Meszéna</u>. Using two-photon imaging combined with simultaneous recordings to validate CSD analysis. *in PhD Proceedings Annual Issues of the Doctoral School, Faculty of Information Technology and Bionics, Pázmány Péter Catholic University* – 2015. G. Prószéky, P. Szolgay Eds. Budapest: Pázmány University ePress, 2015, pp 81–84.

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