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Available Master's Thesis projects at the BIOHYBRID NEUROELECTRONICS (BIONICS) LAB

Project 1:

Smart surface Biofunctionalization for enhancing extracellular neuronal signals to feature intracellular-repertoire on a high-density microelectrode chip

The project explores the application of smart biofunctionalization[1] to provide a novel bio-electronic interface between the high-density microelectrode arrays (HD-MEAs) surface and cell membrane of neuronal networks[2]. The aim is to engineer a large-scale method allowing simultaneous non-invasive, long-term, high spatiotemporal resolution bioelectrical signal detection from several thousands of intracellular-like[3,4] spiking activity of human-derived neurons. This work has a high impact on assessing neuronal network dynamics and connections with a higher throughput capacity than standard electrophysiological methods (i.e., patch-clamp). The goal of a 6-8 month student project is to learn the application of the biofunctionalization method for growing human-derived neurons on HD-MEA devices. Also, recording neuronal intracellular-like signals using planner microelectrodes and simulating a model for a neuron-electrode passive electrical coupling circuit.

Project field:

Neuroscience, bioengineering, microtechnology, surface chemistry, and electrophysiology

Project requirements:

knowledge in neurobiology, extracellular electrophysiology, coding, and simulation.

References

1. Amin, H., Dipalo, M., De Angelis, F. & Berdondini, L. Biofunctionalized 3D nanopillar arrays fostering cell-guidance and promoting synapse stability and neuronal activity in networks. *ACS Appl. Mater. Interfaces* 1–9 (2018) doi:10.1021/acsami.8b00387.

2. Amin, H., Nieus, T., Lonardoni, D., Maccione, A. & Berdondini, L. High-resolution bioelectrical imaging of Aβ-induced network dysfunction on CMOS-MEAs for neurotoxicity and rescue studies. *Sci. Rep.* **7**, 2460 (2017).

3. Spira, M. E. & Hai, A. Multi-electrode array technologies for neuroscience and cardiology. *Nat. Nanotechnol.* **8**, 83–94 (2013).

4. Spira, M. Parallel probing of intracellular neuron potentials. *Nat. Biomed. Eng.* **4**, 146–147 (2020).

Project 2:

Performance of graph-theoretical analysis on large neuronal ensembles for revealing emergent network dynamics

The project exploits the combination of high-resolution network electrophysiological readouts[1] and graph-theoretical analysis[2,3] to construct unique cellular microscale neuronal network features. These graphical features will provide non-invasive microscale composite parameters to understand the biological underpinnings of global and local characteristics of neuronal networks in health and disease. The project will also include data recorded from healthy and a disease model where the extracted graphical features will be provided to a classifier to provide diagnostic parameters for each condition. The goal of a 6-8 month student project is to learn the recording of large-scale neuronal firing activity using high-density microelectrode arrays (HD-MEAs). Then, employing graph-theoretical metrics to automatically extract network functional features as parameters of healthy network performance and disease severity. Finally, implementing a machine learning approach[4] to make competing predictions about how healthy and drug-recovered networks should impact the disease-associated connectional architecture.

Project field:

Neurocomputation, bioengineering, microtechnology, electrophysiology

Project requirements:

Good skills in coding and modeling in Python, basic knowledge in Neurobiology, and neurophysiology/electrophysiology

References

1. Amin, H., Nieus, T., Lonardoni, D., Maccione, A. & Berdondini, L. High-resolution bioelectrical imaging of Aβ-induced network dysfunction on CMOS-MEAs for neurotoxicity and rescue studies. *Sci. Rep.* **7**, 2460 (2017).

2. Bullmore, E. & Sporns, O. Complex brain networks: graph theoretical analysis of structural and functional systems. *Nat Rev Neurosci* **10**, 186–198 (2009).

3. Hu, X., Khanzada, S., Klütsch, D., Calegari, F. & Amin, H. Implementation of biohybrid olfactory bulb on a high-density CMOS-chip to reveal large-scale spatiotemporal circuit information. Biosens. Bioelectron. 198, 113834 (2022).

4. Richards, B. A. *et al.* A deep learning framework for neuroscience. *Nat. Neurosci.* **22**, 1761–1770 (2019).

Project 3:

Investigating neuronal functional consequences of environmental enrichment using high-density biosensors

The project explores the application of large-scale bioelectrical recordings using high-density microelectrode array (HD-MEA) biosensors[1,2] to investigate the impact of environmental stimulation and enrichment[3] on brain functions. The hippocampus in adult brains generates new neurons throughout life with no clear evidence for the primary purpose and how this would impact the information processing of the existing brain network. The aim is to perform bioelectrical imaging based on recording from acute brain slices the extracellular field potentials generated by the superposition of local transmembrane currents passing through multiple neurons. To achieve that, the student will exploit the high spatiotemporal resolution capability of our HD-MEA based monolithic chip combined with wild-type mice exposed to 6 weeks of environmental enrichment[4] (i.e., a large multicompartment mouse housing unit including toys and tunnels that showed to induce the generation of new neurons in the dentate gyrus of the adult hippocampal formation). The project aims to characterize simultaneous large-scale hippocampal processing microcircuits in spanning spatial scales from single neurons up to the entire slice network upon environmental enrichment.

Project field:

Neuroscience, bioengineering, biosensors, adult-neurogenesis, and electrophysiology

Project requirements:

knowledge in neurobiology, extracellular electrophysiology, data analysis, and signal processing.

References

1. Amin, H., Nieus, T., Lonardoni, D., Maccione, A. & Berdondini, L. High-resolution bioelectrical imaging of Aβ-induced network dysfunction on CMOS-MEAs for neurotoxicity and rescue studies. *Sci. Rep.* **7**, 2460 (2017).

2. Hu, X., Khanzada, S., Klütsch, D., Calegari, F. & Amin, H. Implementation of biohybrid olfactory bulb on a high-density CMOS-chip to reveal large-scale spatiotemporal circuit information. Biosens. Bioelectron. 198, 113834 (2022).

3. Givre, S. Kempermann g. why new neurons? possible functions for adult hippocampal neurogenesis. *J. Neurosci.* **23**, 635–638 (2003).

4. Kempermann, G., Kuhn, H. G. & Gage, F. H. More hippocampal neurons in adult mice living in an enriched environment. *Nature* vol. 386 493–495 (1997).

Project 4:

Decoding the rejuvenating hippocampal microcircuit to assess the contribution of adult-neurogenic information processing

The project exploits the combination of high-resolution chip-based technology[1,2] and modulation by opto and chemogenetics appraoches[3] to investigate encoded information by newly generated neurons in a Cdk4/cyclinD1 (4D) mouse model[4] that showed the expansion of the neural stem cell in the developing cortex and adult hippocampus. This unique technology combination will explain how and why new neurons change brain circuitry, activity, and hippocampal network responses and function, causing positive gain on cognitive behaviors. The goal of a 6-8 month student project is to learn the recording of large-scale neuronal firing activity using high-density microelectrode arrays (HD-MEAs). Then, employing opto/-chemogenetic circuit manipulation (i.e., activate and silence only the newborn labeled neurons in the dentate gyrus of the hippocampal formation) and recording the neuronal response from 4096-microelectrode array simultaneously. Finally, analyze the recorded data sets (before and after circuit modulation) to infer the spatiotemporal dynamic changes in the hippocampal circuit in 4D and wild-type mouse models.

Project field:

Neuroscience, bioengineering, biosensors, circuit manipulation (opto-/chemogenetics), electrophysiology

Project requirements:

knowledge in Neurobiology, and neurophysiology/electrophysiology, data analysis, and signal processing

References

1. Amin, H., Nieus, T., Lonardoni, D., Maccione, A. & Berdondini, L. High-resolution bioelectrical imaging of Aβ-induced network dysfunction on CMOS-MEAs for neurotoxicity and rescue studies. *Sci. Rep.* **7**, 2460 (2017).

2. Hu, X., Khanzada, S., Klütsch, D., Calegari, F. & Amin, H. Implementation of biohybrid olfactory bulb on a high-density CMOS-chip to reveal large-scale spatiotemporal circuit information. Biosens. Bioelectron. 198, 113834 (2022).

3. Urban, D. J. & Roth, B. L. DREADDs (Designer Receptors Exclusively Activated by Designer Drugs): Chemogenetic Tools with Therapeutic Utility. *Annu. Rev. Pharmacol. Toxicol.* **55**, 399–417 (2015).

4. Lange, C., Huttner, W. B. & Calegari, F. Cdk4/CyclinD1 Overexpression in Neural Stem Cells Shortens G1, Delays Neurogenesis, and Promotes the Generation and Expansion of Basal Progenitors. *Cell Stem Cell* **5**, 320–331 (2009).