Master Thesis Project: Investigating Cortical Plasticity with Patch-Clamp

Keywords: Whole-cell patch-clamp • Synaptic plasticity • Cortical circuits • Mouse electrophysiology • Optogenetics

Project overview

Learning and memory depend on changes in the strength of connections between neurons. In cortical pyramidal neurons, many long-range inputs arrive at apical dendrites, far from the cell body. How these distant signals contribute to synaptic plasticity remains an important open question. Strong dendritic depolarisations, including plateau potentials, may provide a mechanism linking distant synaptic input to neuronal output. Their effects may depend on input timing and inhibitory control by local interneurons.

This thesis is part of our research on single-cell computations in the medial prefrontal cortex (mPFC). In this project you will first develop hands-on expertise in slice electrophysiology and related experimental methods, then pursue one clearly defined subproject depending on technical progress and the status of ongoing experiments.

Scientific question

Under which conditions do long-range inputs to the apical dendrites of mPFC pyramidal neurons undergo lasting changes in synaptic strength? In particular, can plateau-potential-associated activity promote plasticity, and how might input timing or somatostatin (SST) interneuron-mediated inhibition shape that process?

Experimental approach

We will investigate synaptic plasticity in layer 5 pyramidal neurons of the medial prefrontal cortex using whole-cell patch-clamp recordings in acute mouse brain slices. By combining electrophysiology with optogenetic stimulation and pharmacological or chemogenetic manipulations, we aim to understand how long-range inputs and local inhibitory circuits influence synaptic plasticity.

Thesis structure and scope

The primary goal of this Master's thesis is to acquire hands-on experience in experimental neuroscience, with a strong focus on whole-cell patch-clamp electrophysiology.

The project will consist of three stages:

1. **Electrophysiology training:** Learn acute brain-slice preparation, establish stable whole-cell recordings and characterise basic neuronal and synaptic properties.
2. **Surgical training:** Gain experience in animal handling and stereotaxic surgeries under supervision, following the required training and authorisations.
3. **Independent research:** Depending on progress, investigate one specific aspect of synaptic plasticity within the broader research programme.

The exact scope of the experimental subproject will be adapted to the student's progress and the time available.

What we expect

We are looking for a motivated Master's student with a strong interest in experimental neuroscience and a willingness to learn new techniques. As whole-cell patch-clamp is technically demanding, patience, precision and a systematic approach to experimental work are important. Previous experience with electrophysiology is an advantage but not required.

In this project you will be working with laboratory animals. This includes brain-slice preparation and surgical interventions in mice, particularly stereotaxic viral injections. Students should therefore be willing to work with animals and participate in surgical procedures under supervision, following the necessary training and authorisations.

Contact

If you are interested in or have question on the project, please contact Roman under romaboeh@ethz.ch