Neuroplastcicity is one of the most important properties of the nervous system. It is the basis of learning, which allows us to save new information and store it in order to respond adequately to surrounding environment. Understanding the mechanisms of learning is one of the greatest challenges of neurobiology. This project is dedicated to studies of learning related plasticity of the cerebral cortex. It is well recognized that learning alters neuronal circuits to form a memory trace. The changes happen in many sites in the brain, including the sensory cortex.
The project will focus on studying neuronal circuits in the part of the primary somatosensory cortex of mice (the barrel cortex) which is the cortical representation of facial whiskers in rodents. An individual barrel is a cortical cytoarchitectonic structure corresponding to one of the vibrissae located on the contralateral side of the muzzle. The barrel cortex is a widely used experimental model system for investigating cortical structure, function and plasticity. The arrangement of the barrels in the cortex corresponds to the arrangement of whiskers located on the muzzle. It is therefore easy to locate the cortical representation of a particular vibrissa. For example, if the mouse learns that touching a set of vibrissae is linked to appearance of an unpleasant stimulus, barrels representing these vibrissae should be examined for the effects of learning. This learning paradigm (classical conditioning) of the vibrissal system was developed and characterized in my lab. We discovered that it causes a plastic change in the barrel cortex i.e. the cortical representation of vibrissae activated during the training becomes enlarged. This changed cortical representation may be part of neuronal circuit changes associated with formation of the memory trace. We also discovered several changes in the inhibitory neurotransmission GABA system. For example, as a result of learning, GABA level was elevated, the number of inhibitory synapses was increased and, in a subtype of inhibitory neurons, the level of GABA synthesizing enzyme was increased. The aim of this project was to investigate the role of this subtype of inhibitory neurons (besides GABA they contain a peptide, somatostatin) in learning-dependent plasticity of the barrel cortex.

To this end we will use the new chemo-genetic technique DREADDS (designer-receptors-activated by designer-drugs). In this technique artificial receptors are introduced into specific neurons by biotechnological methods. These receptors can be excitatory or inhibitory and can be activated at the moment chosen by the experimenter by intraperitoneal injection of pharmacologically inert metabolite of the drug clozapine. We shall introduce the inhibitory receptors into inhibitory neurons containing somatostatin (SOM) in the cortical barrels of vibrissae activated during the training and undergoing the plastic change as a result of learning.

The role of SOM neurons is to inhibit other inhibitory neurons (disinhibition), which relieves from inhibition the excitatory neurons. My hypothesis is that during our training, application of unpleasant stimulus activates the brain system linked to attention and using acetylcholine as transmitter. Acetylcholine strongly excites SOM neurons. This causes disinhibiton of excitatory neurons, which receive sensory information from the vibrissae touched during the training. As a result of their increased excitation, the sensory signal spreads more in the cortex, inducing the plastic change of cortical representation of vibrissae used in the training. Silencing of SOM neurons should impair this plastic change. To test this hypothesis we shall silence SOM neurons before each of the three training sessions and examine if the plastic change is present after the training. Confirming or disproving our thesis will be an important step in understanding mechanisms of brain plasticity.