The mammalian neocortex is a complex brain structure involved in higher brain functions such as sensation, perception, learning and memory. In addition to its macroscopic organization into specialized areas that are responsible for different sensory and motor functions, it is divided into vertical columns and horizontal layers on the microscopic level. On a cellular level the cortex is composed of mostly excitatory neurons and a minority of diverse inhibitory neurons. These inhibitory neurons play important roles in various cortical functions such as adaptation, plasticity, preventing runaway excitation and shaping the tuning of cells. This work focuses on de-coupling the local excitatory inputs on inhibitory neurons in the mouse barrel cortex while maintaining subcortical inputs in order to find if the latter can drive spikes in inhibitory cells. Using different approaches, local excitatory neurons were transduced with inhibitory opsins (archaerhodopsin and halorhodopsin). Subsequently, the firing in inhibitory neurons in response to tactile stimuli was compared to their response to tactile stimuli while the local population of excitatory neurons was silenced optogenetically. Hence, using this approach it is possible to isolate feedforward inhibition (i.e. local inhibitory neurons being directly driven by incoming thalamic excitation) from the naturally occurring mixture of feedforward and feedback inhibition (i.e. local inhibitory neurons being driven by local excitatory neurons, which in turn are driven by the thalamic inputs).

It was observed that archaerhodopsin has a cytotoxic effect in transduced excitatory neurons as well as in inhibitory neurons. This cytotoxicity caused considerable neuronal damage. However, changing to halorhodopsin showed no apparent damage; therefore the experiments were continued with this type of inhibitory opsin. Using intracellular recording it was found that presumable excitatory neurons transduced with halorhodopsin were reliably hyperpolarized by laser illumination of the cortex while this effect was not present in inhibitory neurons. Dependent on the promoter (CamKIIα) used for opsin expression, the silencing of excitatory neurons occurred in a layer-specific manner. Interestingly, even though not directly hyperpolarized by cortical illumination, the firing of inhibitory neurons was affected in a similar way as the firing of excitatory neurons: while inhibitory neurons in layer 2/3 and layer 5 showed strong reduction in firing, inhibitory neurons in layer 4 were less affected by the laser. These finding are in agreement with the low percentage of CamKIIα expressing (pyramidal) cells in layer 4. Even though this data comes from few neurons and more experiments need to be conducted to confirm these results, the data suggests that the firing of inhibitory neurons in response to tactile stimuli relies strongly on the surrounding local excitatory network rather than purely on the thalamic inputs.