This thesis addresses synaptic connectivity and dynamics in rodent and human cortex in both healthy and diseased states. I initially introduce theoretical concepts, relevant to the development of the thesis, and proceed to present results obtained from acute recordings performed in human cortical slices from an information theoretic perspective. The chapters that follow are published papers on spike timing dependent plasticity (STDP) in the human hippocampus, a study on connectivity and synaptic dynamics in the murine model of the Fragile X syndrome and a similar study on the valproic acid model for autism.

Synaptic transmission in the cortex, responsible for coding and transmission of information is dynamic in nature. The postsynaptic responses carry information about the temporal structure of the presynaptic input. Findings on laboratory animals and theoretical studies have extensively characterized the rate of depression which depends on the probability of neurotransmitter release and governs the extent to which rate and temporal structure of firing of action potentials from the presynaptic input is signaled to the postsynaptic population. It is unknown whether short term plasticity also exists in human synapses and if similar rules also hold true for the human brain. Here, we directly tested in human slices cut from neocortex tissue removed for surgical treatment of deeper brain structures in drug-resistant epilepsy patients, whether adult human synapses can modulate responses in a short time scale, we applied and quantified this changes as given by the Tsodyks-Markram model for dynamic synapses. In contrast to values reported on rodent neocortical synapses the time constant for recovery from depression differed significantly (~550ms in rodents and ~140 in humans). This numbers not only show that short term synaptic depression occurs, but also reveals the capacity for higher bandwidth signal processing of the human cortex. Furthermore, by applying temporally varying inputs in individual human principal cells, and tracking its ability to modulate instantaneous firing rates from subthreshold current changes, we demonstrated that single cells are able to receive and follow a barrage of synaptic inputs at a much higher bandwidth than reported in previous studies.

Here, we directly tested whether adult human synapses, at the hippocampus, can change strength in response to millisecond timing of pre- and postsynaptic firing. We find that adult human hippocampal synapses can alter synapse strength in response to both pairing with single spikes or burst activity. In contrast to rodent hippocampal synapses, the sign of plasticity does not sharply switch around 0 millisecond timing. Instead, both positive timing intervals, in which presynaptic firing preceded the postsynaptic action potential, and negative timing intervals, in which postsynaptic firing preceded presynaptic activity down to -80 ms, increase synapse strength (tLTP). Negative timing intervals between -80 to -130 ms induce a lasting reduction of synapse strength (tLTD). Thus, similar to rodent synapses, adult human synapses can show spike-timing-dependent changes in strength.

In chapters 4 and 5 of this thesis, we set out to study connectivity and synaptic properties in two distinct models for autism and mental retardation. Using a similar approach, namely, paired recordings from clusters of layer 5 pyramidal cells, we analyzed connection probability and dynamic properties of synapses in the murine model of the Fragile X syndrome and microcircuit plasticity in the VPA model for autism. In neurodevelopmental disorders of autism and mental retardation, abnormal connectivity is proposed to underlie deficits in attentional and integrating processes. We found short-range hyperconnectivity within neuronal networks accompanied by delayed onset and slower recovery from synaptic depression in medial prefrontal cortex of a mouse model for autism and mental retardation. These impairments in both spatial and temporal parameters of synaptic function may underlie impairments in integration and processing of information in cortical networks.
Finally, using information theory applied to dynamic synapses, and based on the properties measured in our studies, we compare the ability of cortical principal cells, in humans and rodents, in healthy and diseased state, to code and transfer information in the millisecond time scale. This approach is likely to contribute in bridging the gap in the knowledge accumulated in over half-century of rodent electrophysiology and further uncover properties of synapses in the human brain.