Molecular Architecture of Chemical Synapses in the Mammalian Brain

The mammalian brain is an intricately wired network of neuronal cells that is capable of executing complex processing of sensory information to determine organism behavior. Essential for the communication between neurons are chemical synapses, highly organized cell-cell contacts where a propagating pre-synaptic electrical action potential triggers release of neurotransmitter chemicals, which within <1 millisecond bind to opposed cell-surface receptors and evoke a post-synaptic response. Although key in understanding the molecular underpinning of higher-order brain functions, the detailed molecular mechanisms, however, of fast triggered release and of use-dependent regulation of synaptic transmission strength remain unclear.

Our work focuses on unraveling a molecule-specific “atlas” of the synaptic ultra-structure, aimed towards detailing the composition and stoichiometry of the machinery executing fast, Ca^{++}-triggered release and understanding the functional role of the spatial relations between synaptic vesicles, active-zone proteins and voltage-gated Ca^{++} channels.