Synaptic Physiology

All brain functions rely upon synapses, which are the sites of communication between neurons. Synapses are complex, each one comprising thousands of different types of macromolecules working in concert. Synapses are organized by adhesive and scaffolding molecules that align presynaptic vesicular release with postsynaptic neurotransmitter receptors, thereby allowing rapid and reliable intercellular communication. Formation of chemical synapses in the nervous system is a highly regulated, multistep process that requires bidirectional flow of information-carrying molecules across the synaptic cleft. Active Zones (AZs) are highly organized presynaptic regions where synaptic vesicles are prepared to fuse with plasma membrane to release neurotransmitters. Most transmitter release at synapses is spatially restricted to AZs, where synaptic vesicle docking, priming, and Ca2+-dependent fusion take place in a temporally highly coordinated manner. During development, synaptic vesicles and AZs evolves towards a more efficient organization allowing rapid and reliable neurotransmitter release in mature synapses. AZ proteins, in addition, may play a fundamental role in regulating the coupling between neurotransmitter release and endocytosis. We study the synaptic spatial and temporal organization of neurotransmitter release and vesicle recycling in nerve terminals of newborn and mature NMJs. We are interested in understanding synapse physiology and how the organization of the synaptic elements is reorganized during the maturation process.For the study of synaptic function and dysfunction we combine molecular, electrophysiological and optical tools and use genetic mouse models. Dynamic optical techniques allow the monitoring of exocytosis and endocytosis in real time. We use synaptopHuorin and synaptophysin-pHlourin transgenic mice with this purpose.