Local dynamic of ion channels in the neuronal membrane

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Neurons have to integrate information from multiple synaptic contacts and transform this information into an output function. Within a particular synaptic contact, the total number of crucial signalling molecules, like presynaptic calcium channels and postsynaptic transmitter receptors is in the order of a few tens to hundred molecules. Considering the stochastic nature of ion channel gating and the ability of integral proteins to change rapidly their position in a viscose environment as the membrane, the question occurs to which extend such “molecular noise” modulates the input-output relation of a particular neuron or neuronal network.

Within the synapse, transmitter fluctuations, channel kinetics, receptor and channel densities and position of neurotransmitter release are sources of variability. By using single particle tracking (SPT) and electrophysiological methods we have identified that the lateral fluctuations of postsynaptic receptors and their kinetic properties contribute to the variability/plasticity of the synapse. At the presynaptic membrane the number and local arrangement of VDCCs is crucial for the position and probability of transmitter release. Using SPT and photo activated localization microscopy (PALM) we have investigated the surface mobility of α1-(Cav2.1/Cav2.2) and $\alpha 2\delta$-subunits in the presynaptic membrane. Alpha1-subunits are confined in clusters, whereas $\alpha 2\delta$-subunits are only transient confined in synapses or channel clusters. Co-expression of α1- and $\alpha 2\delta$-subunits induces a stronger expression of α1- subunits at the axonal membrane and an isoform dependent alteration in channel densities at the synapse. These suggest that interactions of $\alpha 2\delta$- and α1-subunits are transient, do influence local channel dynamic and density and might modulate presynaptic activity. Simulating the action potential driven opening of stable or mobile calcium channels suggest a significant impact of channel mobility on the evolution of local calcium domains and can be modulated by the interaction with the extracellular located $\alpha 2\delta$-subunits. Hence, local molecular dynamic may be used to fine-tune synaptic transmission and is a mechanism to change synaptic transmission transiently.