# SYNAPTIC COMPUTATION

Participants: Angus Silver, P. Jesper Sjöström, Stephen Williams

## *Pre and Postsynaptic LTP and LTD in Neocortex*

Long-term potentiation (LTP) and depression (LTD) of synaptic connective strength are thought to form the basis for information storage in the brain. Although there is general agreement that such synaptic plasticity is typically induced on the postsynaptic side, the locus of expression of plasticity has been hotly debated. This is understandable, since the mechanisms of plasticity induction and expression have important implications for how information is processed and stored in the brain.

Using quadruple whole-cell recordings to find connected pairs of pyramidal neurons, we investigated LTP and LTD at synapses in neocortical layer 5. Surprisingly, we found that the presynaptic terminal played an active role in the induction of plasticity: Coincident activation of pre and postsynaptic neurons appeared to be detected through a mechanism located in the presynaptic terminal. Here, presynaptic NMDA receptors act as autoreceptors for presynaptically released glutamate, while presynaptic CB1 receptors detect postsynaptically released endocannabinoids. The simultaneous activation of these two receptor types was critical for the induction of LTD. In addition, this form of LTD appeared to be entirely presynaptically expressed.

We also investigated LTP at these synapses. We found that the locus of LTP expression was both pre and postsynaptic, although to varying degrees at individual synaptic connections. The presynaptically expressed component of LTP required transsynaptic nitric oxide signalling. Interestingly, this component of LTP was also boosted by CB1 receptor blockade.

Taken together, these results imply that correlated high-frequency firing at excitatory layer-5 synapses simultaneously induces a mix of presynaptic LTD, presynaptic LTP, and postsynaptic LTP. In conclusion, the presynaptic terminal is not just passively receiving LTP or LTD-inducing signals from the postsynaptic side. Rather, the presynapse is continuously integrating signals from the pre and the postsynaptic side and is also actively participating in coincidence detection in synaptic plasticity.