Presynaptic Potentiation and Depression in the Cortex Chair: Kevin Fox Participants: Julie Kauer, Jesper Sjostrom and Kevin Fox.

Recent work on synaptic plasticity has tended to concentrated on post-synaptic mechanisms, including AMPA receptor insertion and changes in spine structure. In this session, we switch attention to the presynaptic side of the synapse and present three examples of presynaptic plasticity mechanisms. **Julie Kauer** will describe the role of TRPV1 receptors in presynaptic LTD mechanisms at hippocampal inhibitory interneurones. Although TRPV1 receptors have classically been defined as ligand-gated, non-selective cation channels that act as heat-, proton- and ligand-activated integrators of nociceptive stimuli in sensory neurons, they have also been identified in various areas of the CNS, including the hippocampus. The data are consistent with a model in which mGluR activation leads to release of 12-(S)-HPETE from interneurons, and that in turn activates TRPV1 channels most likely located on presynaptic terminals where they elicit long-term synaptic depression. Like other forms of synaptic plasticity, TRPV1-mediated LTD may have a role in long-term changes in the physiological and pathological behavior of neural circuits during learning and perhaps epileptic activity. **Jesper Sjostrom** will describe studies on LTP and LTD at synapses between monosynaptically connected neocortical layer-5 pyramidal neurons. Coincident activation of pre- and post-synaptic neurons is detected through presynaptic NMDA receptors that act as autoreceptors for presynaptically released glutamate, while presynaptic CB1 receptors detect postsynaptically released endocannabinoids. The simultaneous activation of these two receptor types is critical for the induction of LTD. In addition, this form of LTD appears to be entirely presynaptically expressed. In contrast, expression of LTP at these synapses is both pre and postsynaptic, although to different degrees at individual monosynaptic connections. The presynaptically expressed component of LTP relies on retrograde nitric oxide signalling and is boosted by CB1 receptor blockade. Our data suggest that high frequency correlated firing at layer-5 synapses simultaneously induces a mixture of presynaptic LTD, presynaptic LTP, and postsynaptic LTP. **Kevin Fox** will describe studies that implicate Nitric oxide and GluR1 in pre- and post-synaptic components (respectively) of LTP in layer II/III neurones in the neocortex. Both mechanisms appear to be involved in experience-dependent neocortical plasticity because they are absent in GluR1/NOS1 double but not single knockouts. While LTP in the cortex requires NOS1, hippocampal LTP involves both NOS1 and NOS3. Evidence will be presented that suggest the nitric oxide component of hippocampal LTP requires somatic spike production in both GluR1 knockouts and wild-type mice and is most readily produced by simple orthodromic theta-frequency stimulation. Given that theta waves and complex spikes occur in the hippocampus naturally during exploration and learning, these processes may also involve a nitric oxide component.