



The Abdus Salam  
International Centre for Theoretical Physics



Minischool and Workshop on Multiple Time Scale in the  
Dynamics of the Nervous System  
16 to 29 June 2008, ICTP, Trieste, Italy

**NOTES FOR TALK ON**

**"LEARNING RULES IN THE HIPPOCAMPUS AND CEREBELLUM"**

**by Prof. Samuel WANG**

**Department of Molecular Biology and Princeton Neuroscience Institute, Princeton  
University, Princeton, New Jersey 08544, USA.**

**Order-dependent coincidence detection in cerebellar Purkinje neurons at the  
inositol trisphosphate receptor.  
Sarkisov DV, Wang SS.**

Editor: J Neurosci. 2008 Jan 2;28(1):133-42.  
Comment in: J Neurosci. 2008 Apr 23;28(17):4293-4.

Associative long-term depression (LTD) at cerebellar parallel fiber-Purkinje cell synapses is sensitive to the temporal order in which the parallel fiber is coactivated with the climbing fiber input, but how order sensitivity is achieved is unknown. Here we show that the cerebellar inositol-1,4,5-trisphosphate (IP3) receptor, whose activation is required for LTD induction, is sensitive in situ to the order of presentation of its coagonists, IP3 and cytoplasmic calcium. By focally photolyzing a novel caged IP3 compound in dendritic spines, we find that pairing IP3 with climbing fiber-mediated calcium entry leads to a large calcium release transient if the climbing fiber is activated up to 100 ms before or up to 500 ms after IP3 uncaging. This asymmetric timing window for coactivation follows the kinetics of calcium removal and IP3 unbinding from the receptor and is not limited by IP3 metabolism. IP3 receptor binding thus acts as an eligibility trace that can drive temporal order-dependent calcium release and LTD induction in Purkinje cells and event order-dependent sensory plasticity in the whole animal.