# SYNAPTIC LEARNING BEYOND STDP

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## Introduction

Spike time dependent plasticity (STDP) describes only one aspect of the signalling requirements for learning (long lasting plasticity) at synapses. A fundamental signal for plasticity at excitatory synapses is the time course of the calcium concentration in the postsynaptic spine head. Differential timings of presynaptic and postsynaptic spikes do influence spine calcium concentrations and hence lead to STDP. More generally, spine calcium is the result of ongoing synaptic inputs and local cell excitability, which may or may not involve postsynaptic spiking. Further, plasticity induction is not instantaneous and proceeds over seconds to minutes. Biochemical pathways leading to long term potentiation (LTP) or depression (LTD) are separate and operate with different dynamics. Intense input over tens of milliseconds can initiate LTP, which is then induced over a period of seconds. LTD initiation requires seconds of moderately intense input. So both the intensity and duration of synaptic inputs determines plasticity outcomes.

## Aims

Current experimental data and resultant models of synaptic plasticity based on spine head calcium provide a starting point from which to explore learning in neurons being driven by spatio-temporal patterns of synaptic input that are ultimately the product of animal behaviour. The hypothesis is that LTP enables the remembering of short, intense (important or novel) stimuli, while LTD leads to forgetting of stored patterns that are consistently being recalled out of context (no longer relevant). Recall within context or occasional spontaneous recall are protected from forgetting by being either above or below the threshold for LTD.

## Methods and Results

A detailed computational model of synaptic input onto spines on a reconstructed hippocampal CA1 pyramidal cell is used to explore the hypothesis. An extension of the calcium-based plasticity model of Graupner and Brunel (PNAS 109:3991-3996, 2012) is used to induce synaptic changes on realistic time scales in response to spine head calcium levels.

Results show that synchronously-active groups of synapses undergo LTP or LTD or do not change depending of the number of coactive synapses and their frequency of stimulation. LTD induction requires longer than LTP, such that no change occurs even for many seconds of stimulation that does eventually lead to LTD if sustained for long enough (tens of seconds). Brief, intense stimuli to one group of synapses leads to LTP while coactive synapses on the same cell, receiving less intense activity, undergo LTD at the same time.