Short-Term Synaptic Plasticity and Its Role in Cerebellar Information Processing

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Introduction

The cerebellum is an evolutionarily conserved brain structure that plays roles in sensorimotor processing, motor coordination, and cognition. **Short-term synaptic plasticity (STP) brings dynamics to the cerebellar cortical circuit by changing synaptic weights during transmission, enriching cerebellar information processing in many aspects.**

1.1

Short-Term Synaptic Plasticity

- STP is an activity dependent change in synaptic strength.
- STP efficiency quantified by paired-pulse ratio of two post-synaptic current amplitude (Fig. 1):
  $PPR = \frac{R_2}{R_1}$
    - PPR>1: short-term facilitation (STF)
    - PPR<1: short-term depression (STD)
- Cellular mechanism determined by analyzing changes in synaptic transmission parameters: releasing probability P, number of releasing vesicles N, and quantal size Q.
- STP can be pre- or post-synaptic that relates to vesicle release/replenishment rate (pre-) and receptor saturation/desensitization (post-).

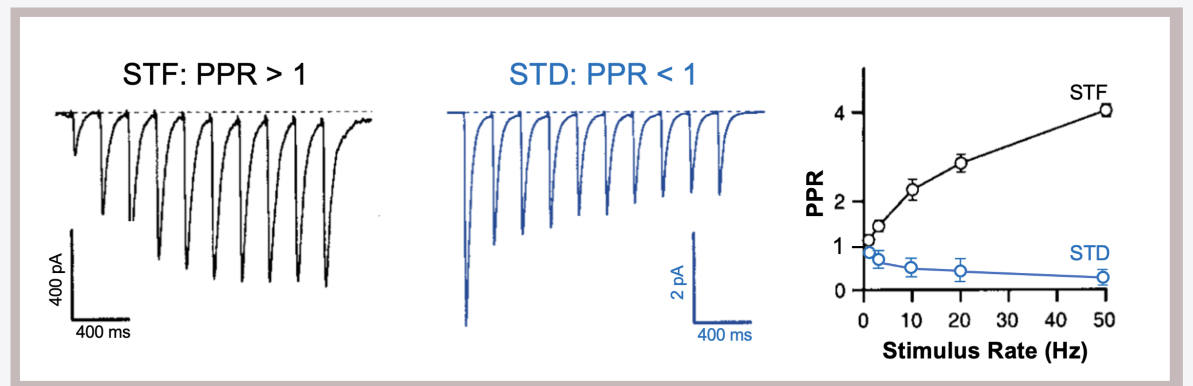

Fig. 1: PPR distinguishes STF and STD. Examples of a facilitating (black) and a depressing (blue) post-synaptic current responses to a train of stimuli. Right panel respective shows PPR for different input frequencies. Adapted from Dittman et al. (2000).

1.2

Cerebellar Cortical Circuitry

- Mossy fibres (MFs) and climbing fibres (CFs) are two major inputs to cerebellar cortex. Processed via the cortical circuit, signals then project from Purkinje cells (PCs) to deep cerebellar nuclei (DCN).
- STP exists in various cerebellar cortical synapses.

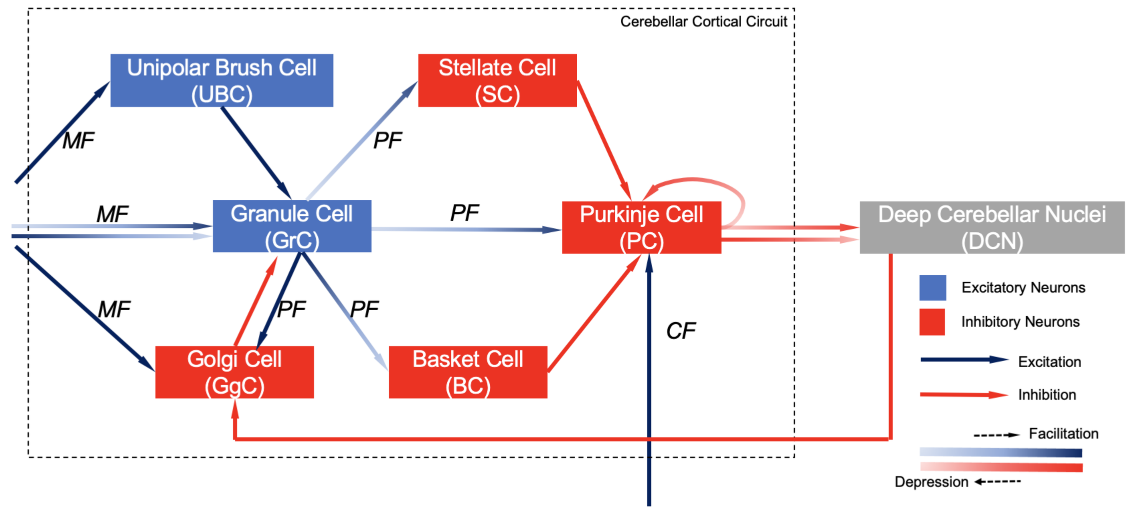

Fig. 2: Simplified connectivity diagram of cerebellar cortical circuit with STP.

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STP at a Single Synapse

- STF maintains high-fidelity synaptic transmission especially at high frequency (Fig. 3).
- STD captures relative input changes (Fig. 4) and modulate neuronal gain control.

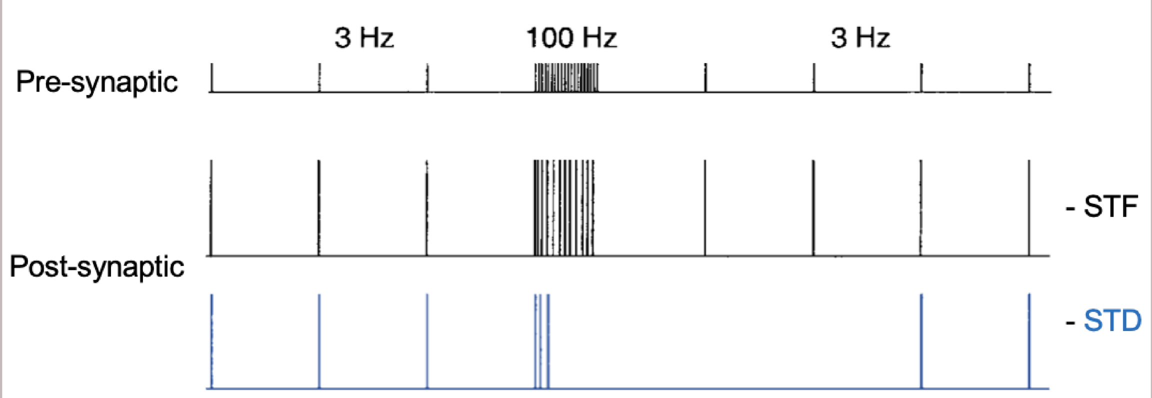

Fig. 3: STF maintaining high-frequency signal transmission. Examples of pre- and post-synaptic spikes during low– and high-frequency transmission, with STF (black) or STD (blue). Adapted from Dittman et al. (2000).

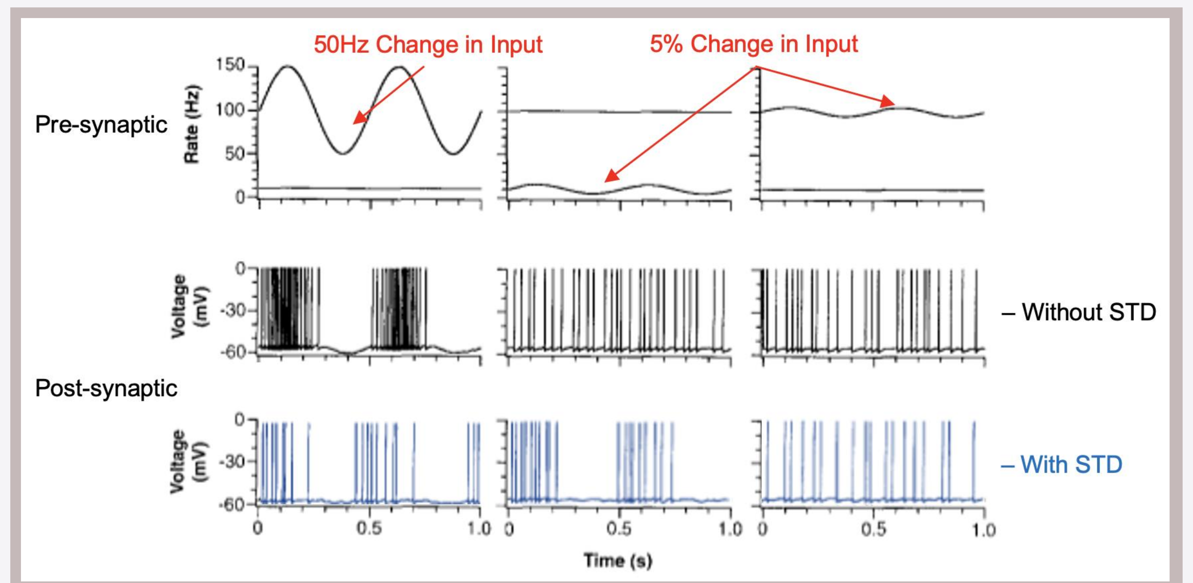

Fig. 4: STD captures relative change of low-frequency input. A large absolute change in high-frequency input (left) can be detected by synapse with/without STD. A 5% relative change in low-frequency input (middle) can be detected in STD synapses only. 5% relative change in high-frequency input (right) cannot be detected by both synapses. Adapted from Abbott et al. (1997).

3

STP in Multi-Synaptic Network

- STP-incorporated neural network can generate a population code for a spectrum of intervals.
- STP in MF-GrC synapse contributes to the temporal properties of GrC output pattern (Fig. 5).
    - Pattern separation: GrC generate distinct output to distinguish similar MF inputs.
- STP in MF-GrC synapse, GrC-SC synapse and GrC-BC synapse can scale the temporal onset of PCs spiking (Fig. 6).
    - Conditioned learning at PC.

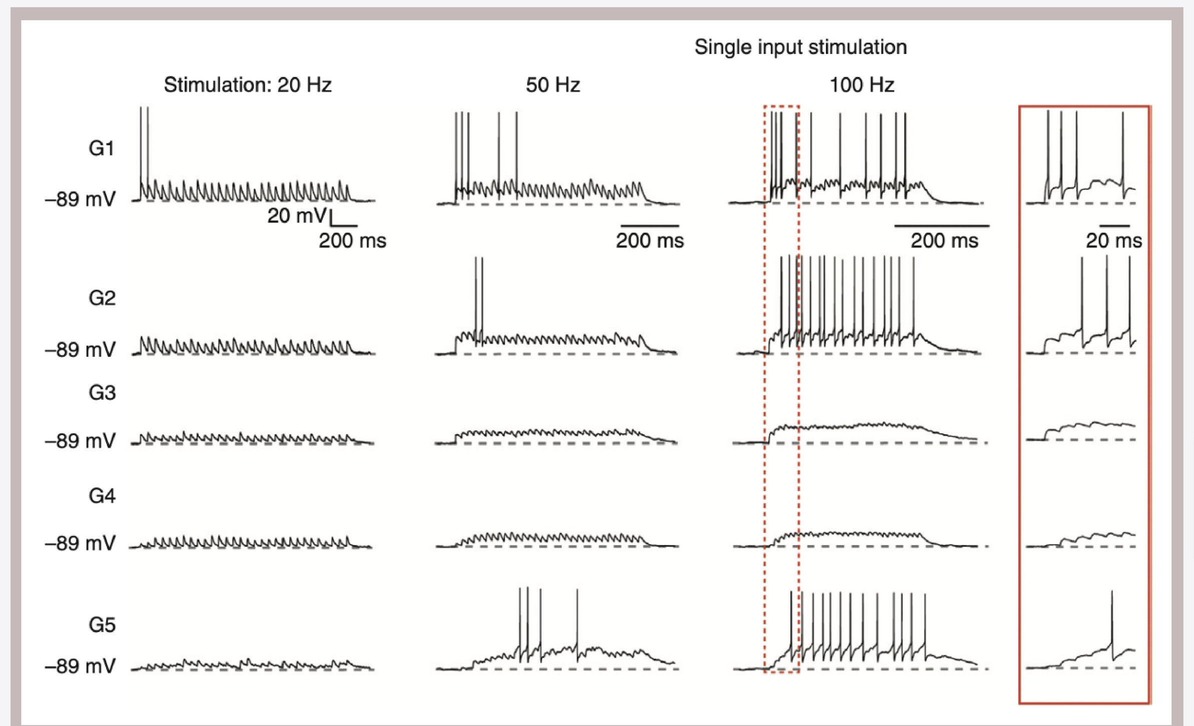

Fig. 5: STP at MF-GrC synapses contributes to pattern separation. Examples of GrC voltage response to inputs from each different MF types (G1-G5) at 20, 50, and 100 Hz frequency. Boxed region displays different GrC first-spike latencies relative to stimulation onset for input at 100 Hz. Adapted from Chabrol et al. (2015).

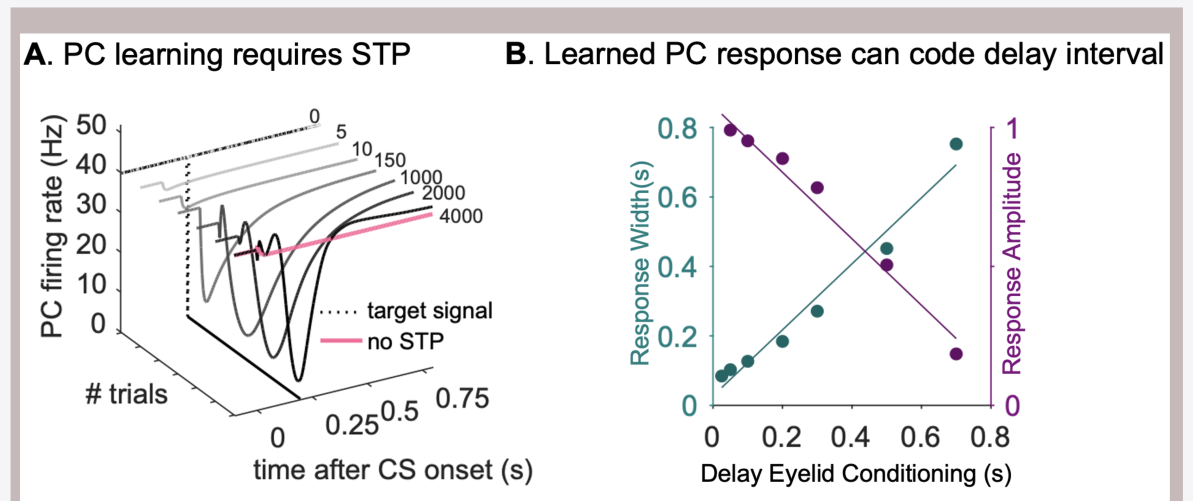

Fig. 6: STP at MF-GrC synapses allow the learning of PC response in eyelid conditioning. Simulated PC response in STP-embedded Cerebellar Cortex Model (CCM_{STP}) learn the timed delay of the stimulus. Width and amplitude of PC learned response relate linearly to the delay interval time. Adapted from: Barri et al. (2022).

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Cerebellar STP for Higher Level Function

- STP enhances temporal pattern coding to predict sensory input from self-generated command (Fig. 7).
- STP may contributes to temporal coding that relates to timing perception and language processing.
- STP may contribute to GrCs' high-dimensional coding that resembles cogtnitive processing.

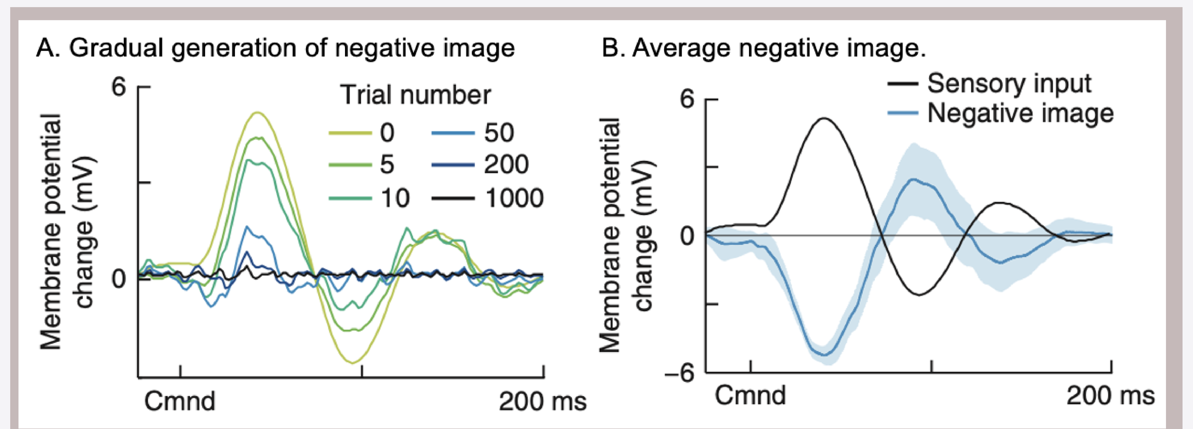

Fig. 7: STP at electric fish GrC-MGC synapses strengthen negative image generation to cancel sensory input from self-generated signals. Adapted from Kennedy et al. (2014).

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Discussion

- STP at cerebellar synapses contributes to the temporal dynamics of information processing by assigning specific temporal properties to cerebellar synaptic responses, serving basis for GrC pattern separation, GrC gain control, and PC learning etc.
- Possible improvements in experimental techniques such as synaptic manipulation, neural data recording methods, and behavioral tasks design.
- Possible improvements in theoretical modelling that consider more types of cerebellar pathways and STP, as well as the stochasticity in vesicle release.
- Distinguish whether the dynamics of STP is indispensable for the mentioned functions in signal processing, or if STP merely acts as a modulator to maintain their robustness.

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