# Cerebellar motor learning; from behavioral studies to system biology model of LTD

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The cerebellar internal model theory postulates that the cerebellar cortex acquires many internal models of controlled objects, dynamical processes in the external world, and even other one's brain dependent on long-term depression (LTD) of Purkinje cells. A specific version of this theory, the feedback-error-learning model postulates that the climbing fiber inputs to Purkinje cells carry the feedback motor command, which could be regarded as an approximation to the error signal for motor commands and can supervise learning of inverse dynamics models. Many experimental supports were obtained from the ventral paraflocculus of the cerebellum during monkey control of ocular following responses. For arm movements under multiple force fields, firings of many Purkinje cells correlate with dynamics [1]. fMRI studies mapped forward and inverse models of manipulated objects and tools in the cerebellar cortex.

One specific prediction of the feedback-error-learning model is that the climbing fiber inputs should be of low firing rates but should convey high-frequency information. Accordingly, Takahashi, Funabiki, and Hirano recently found that mGluR delta 2 knockout mice with high climbing-fiber firing rates exhibit delayed optokinetic eye movements. A network model of inferior olive nucleus reproduces rhythmic and synchronized firings for strong electrical coupling, but demonstrates chaotic and desynchronized firings for intermediate coupling, which is advantageous for information transmission with low firing rates of climbing fibers [2]. This prediction was also recently supported from unit recording data.

Kinetic models of LTD [3, 4] suggest a cascade of excitable and bistable dynamical processes, which may resolve plasticity-stability dilemma at single spine level. That is, even a single pulse of climbing fiber input combined with an early train of several parallel fiber pulses can induce $Ca^{2+}$ induced $Ca^{2+}$ release via IP3 receptors on ER. The MAPK positive feedback loop leaky integrates resulting large $Ca^{2+}$ elevation and if it crosses the threshold then the state moves to the depressed equilibrium. These models explain diverse LTD experiments and clearly demonstrate that LTD is a supervised learning rule, and not anti-Hebbian as erroneously characterized. The MAPK positive feedback loop model [3] was recently supported by a $Ca^{2+}$ photo-uncaging and imaging experiment [5] that suggests LTD all-or-none character.

**References**

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