Cerebellar internal model, Purkinje cell LTD as supervised learning rule supported by bioinformatics, and control of learning degree-of-freedom by electrical coupling in inferior Olive nucleus

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Where is ATR located?

Shishi Odoshi (Deer Scaring)

Cerebellar Purkinje-cell Long-Term Depression is controlled by Ca²⁺ in a Single Spine

0-or-1 LTD is like Shishi Odoshi

Understanding the Brain by Creating the Brain

- Robots and computers are much inferior to humans.
- This demonstrates that we do not fully understand brain functions.
- Only if we try to create a brain, we can understand information processing in the brain.
- Creating only a brain does not make sense, and a body and its environment are essential.
Computational Neuroscience

We elucidate information processing of the brain to the extent that artificial machines, either computer programs or robots, can be built to solve the same computational problems that are solved by the brain, essentially in the same principle.

Object Recognition on a Humanoid Robot - Alesh Ude

Based on the capabilities of a humanoid visual system with foveated vision, we developed an object recognition system that integrates visuomotor processes and foveation to achieve reliable recognition. Training is done in interaction with the teacher. Self acquisition of multiple views by reaching, grasping and manipulation, explored also.
Cerebellar Internal Model Theory

- The cerebellum consists of many modules (micro-zones) which perform different input-output transformations.
- Synaptic weights change and different transformations can be learned.
- Supervised learning guided by an error signal
- Different modules acquire internal models of controlled objects, tools, other brains, etc.

Stiffness Measurement by PFM

Hitaki Goni

Mechanical perturbations in 8 directions were given during point-to-point movement and reaction forces were measured. Then stiffness and viscosity were estimated.

Ocular Following Responses and Related Brain Regions

Experiments by Kawano, Shidara, Takemura, Kobayashi et al. (ETL at Tsukuba)

Direction Selectivity of Simple and Complex Spikes

Reconstruction of Firing Frequency for Different Stimulus Speeds and Duration

\[ f(t) = M(t + \delta) + B(t + \delta) + K(t + \delta) + f_{bias} \]

Signaling Networks in Cerebellar LTD

Model of Cerebellar LTD


Ca\(^{2+}\) Dynamics Model for Coherent Understanding of Diverse and Confusing Experimental Data on LTD Time Window

- Cerebellar learning theories require LTD time window where CF is delayed with respect to PF for 100-200 msec.
- Several experimental supports to this prediction
- Strong bundle stimulation to PF alone, uncaging of Ca\(^{2+}\) or IP\(_3\) can induce LTD without PF-CF conjunction or time delay.
- Some experiments even reported CF preceding PF is optimal.
- Serious doubts and criticisms on LTD as a cellular basis of cerebellar supervised learning

Ca\(^{2+}\) Imaging in Purkinje-cell Spines

Temporal Window of Spike Timing Dependent Plasticity of LTD

Formulation of Biochemical Reaction

(1) Binding Reaction

\[
\text{A} + \text{B} \xrightarrow{k_f} \text{AB} \quad \xrightarrow{k_b} \text{A} + \text{B}
\]

\[
d[\text{AB}] / dt = + k_f [\text{A}][\text{B}] - k_b [\text{AB}]
\]

Dissociation Constant, \( K_d = k_b / k_f \): equilibrium point
Time Constant, \( \tau = 1 / (k_f + k_b) \): speed for convergence

Supralinear Ca\(^{2+}\) signal appears when PF is followed by CF

Ca\(^{2+}\) Signaling is determined by Timing of PF and CF Inputs

Block Diagram of Ca\(^{2+}\) Signaling


Formulation of Biochemical Reaction

(2) Enzymatic Reaction (Michaelis-Menten)

\[
\text{E} + \text{S} \xrightarrow{k_1} \text{ES} \xrightarrow{k_{-1}} \text{E} + \text{P}
\]

\[
K_m = \frac{k_{-1} + k_{cat}}{k_1}
\]

E: Enzyme, S: Substrate, P: Product
IP$_3$-dependent Ca$^{2+}$ Dynamics

(i) CF alone does not induce LTD
(ii) PF alone does not induce LTD
(iii) Conjunctive PF-CF induces LTD
(iv) Ca$^{2+}$ uncaging induces LTD
(v) IP$_3$ uncaging induces LTD
(vi) Massive PF stimulus induces LTD

Ca$^{2+}$ Dynamics and LTD Experiments

• Delay in slow PF metabotropic pathway compared with fast CF electrical pathway as a mechanism for timing-detection
• Fast positive feedback loop generates large Ca$^{2+}$ signals.
• Slow negative feedback loop shuts down the Ca$^{2+}$ increase.

Schematic Model of Timing-detection


Un-caging and imaging of Ca$^{2+}$, PF stimulation and Purkinje cell voltage clamp
Keiko Tanaka, George Augustine, Tomokazu Doi et al.
Neuron, 54, 787-800, 2007

• LTD is suggested 0 or 1 at single synapse
• Leaky integration of Ca$^{2+}$ by MAPK positive feedback loop and resulting bistability

Ca$^{2+}$ threshold for LTD induction

Experimental tests of Kuroda et al. positive feedback model
Collaborations with George Augustine and Keiko Tanaka and their colleagues at Duke University under De Schutter HFSP
Experimental confirmation that dynamic Ca$^{2+}$ threshold depends on MAPK positive feedback loop

All or Nothing Nature of Single Synapse LTD

- Each PF-PC synapse on a spine undergoes LTD in all-or-none manner
  - Cooperativity (large Hill coefficients)
  - Constant maximum LTD
  - Reproduction of experimental data by bistable dynamics

Specialization by Learning Algorithms (Doya K, Neural Networks 1999)

Spruston Lecture and Hebbian Rule

Hebbian synaptic plasticity rule … When an axon of cell A is near enough to excite a cell B and repeatedly or persistently takes part in firing it, some growth process or metabolic change takes place in one or both cells such that A’s efficiency, as one of the cells firing B, is increased.

Purkinje-cell LTD is not anti-Hebbian but Supervised

- No backpropagation of somatic action potentials (too much dendritic branching); output does not matter; different from statistical or reinforcement learning rule; not Hebbian (Spruston OCNC Lecture, Stuart et al. 1994, Vetter et al. 2001)
- No functional NMDA receptors in adults
- STDP of 100 msec order
- Supervised learning with the Ca$^{2+}$ error signal carried by decisive climbing fiber