COMS30017
Computational Neuroscience

Week 4: Synapses and Synaptic Plasticity
Video 5: LONG-TERM SYNAPTIC PLASTICITY

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Intended learning outcomes

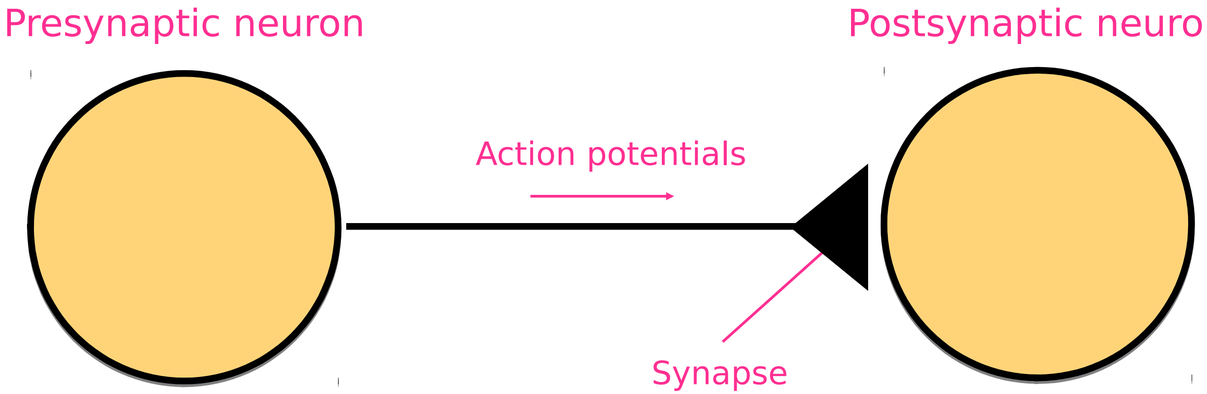
- Recognize a variety of long-term plasticity rules;
- Be able to write an equation for a synaptic plasticity rule;
- Know some properties of common of synaptic plasticity rules;

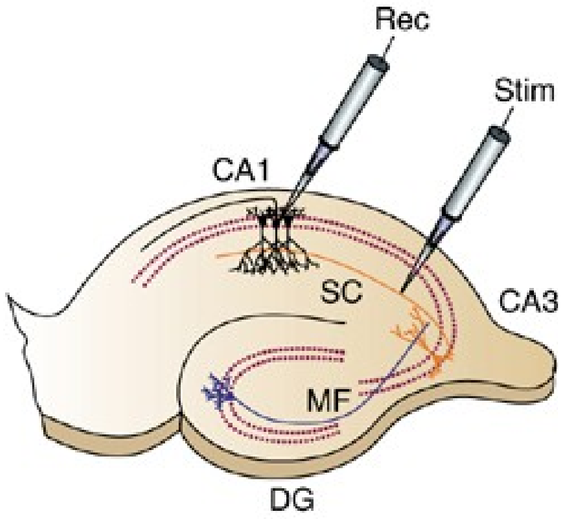
Long-term plasticity

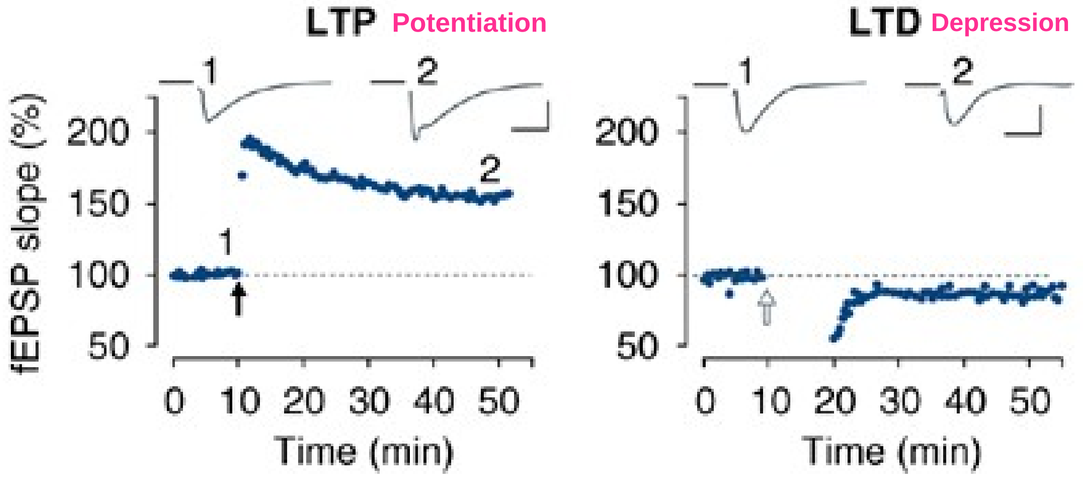
- Long-term synaptic plasticity, in contrast to STP, is thought to mediate long-term memory.
- Much slower timescale than electrical dynamics.
- Long-term synaptic strength increases are called potentiation (LTP), while synaptic strength decreases are called depression (LTD).
- Most synapses can do both.

Long-term synaptic plasticity

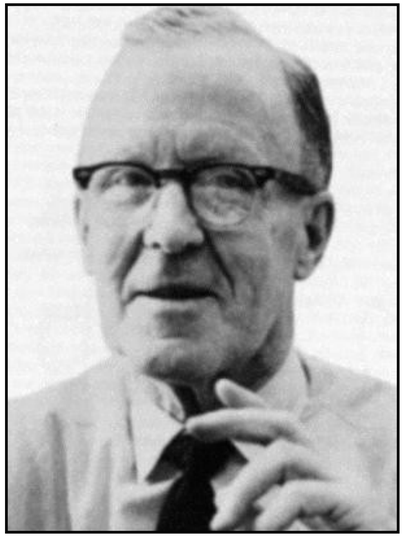
Long-term synaptic plasticity is a (activity-dependent) semi-permanent change in the strength of the connection from one neuron to another.







Hebbian rule



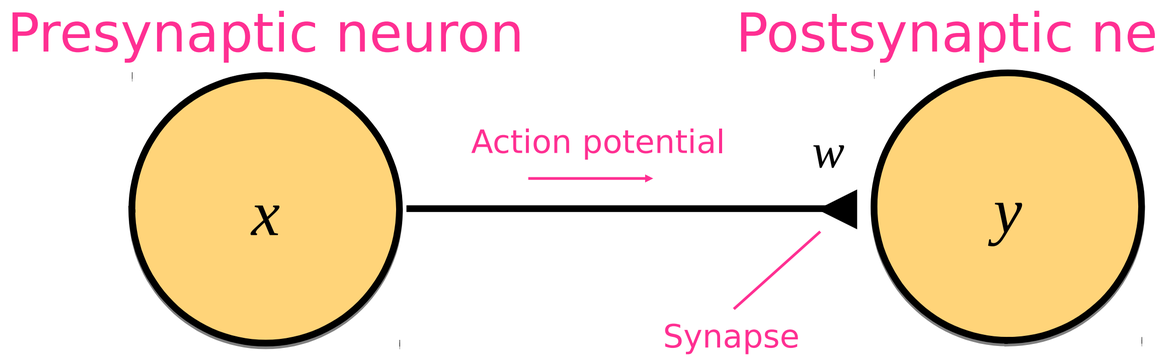
Donald Hebb

“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.”

— Donald Hebb (1949)

a.k.a. “neurons that fire together wire together.”

Rules of synaptic plasticity



$$\Delta w = f(x, y)$$ = ???

$$\Delta w = \eta x y$$

A Hebbian rule:

- Note that dynamics are unstable: w and hence y grow without bound.

BCM rule

- Similar plasticity rule as on earlier slide, but multiplied by a term to allow decreases in synaptic strength, for low levels of postsynaptic activity.

- Their key idea was to add a second rule that let the threshold vary depending on activity:

- This sliding threshold has two effects:
  - It stabilises plasticity and hence activity.
  - It introduces competition between the synapses.

$$\frac{d\mathbf{w}}{dt} = \eta_w \mathbf{x} y (y - \theta_y)$$

$$\frac{d\theta_y}{dt} = \eta_\theta y^2 - \theta_y$$

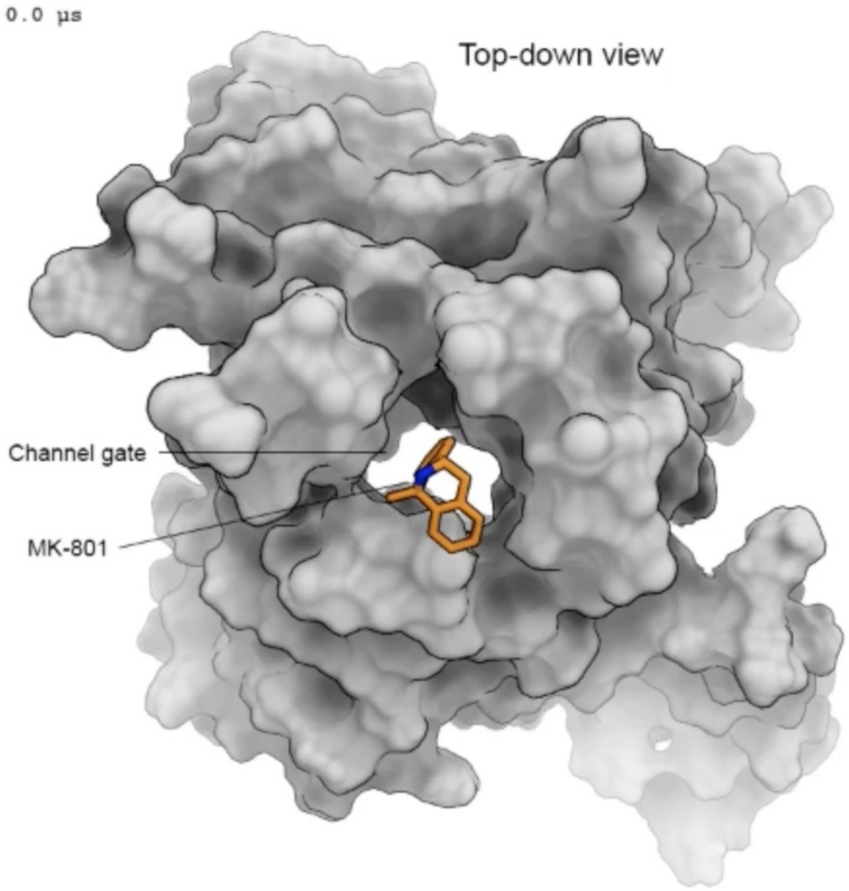
$$\eta_\theta \ll \eta_w$$

Bienenstock, Cooper & Munro, J Neurosci (1982)

NMDA receptors: the synapse’s co-incidence detector

- One of the best-studied brain molecules.
- Ionotropic glutamate receptor passing sodium, potassium and calcium (NMDA is a human-made chemical that selectively activates the receptor).
- Affected by many common drugs (PCP, alcohol, ketamine, nitrous oxide).
- Crucial for many forms of long-term synaptic plasticity, and learning and memory.
- Key co-incidence detection mechanism is that it requires both glutamate binding (presynaptic activity) AND postsynaptic depolarisation to relieve Magnesium block.

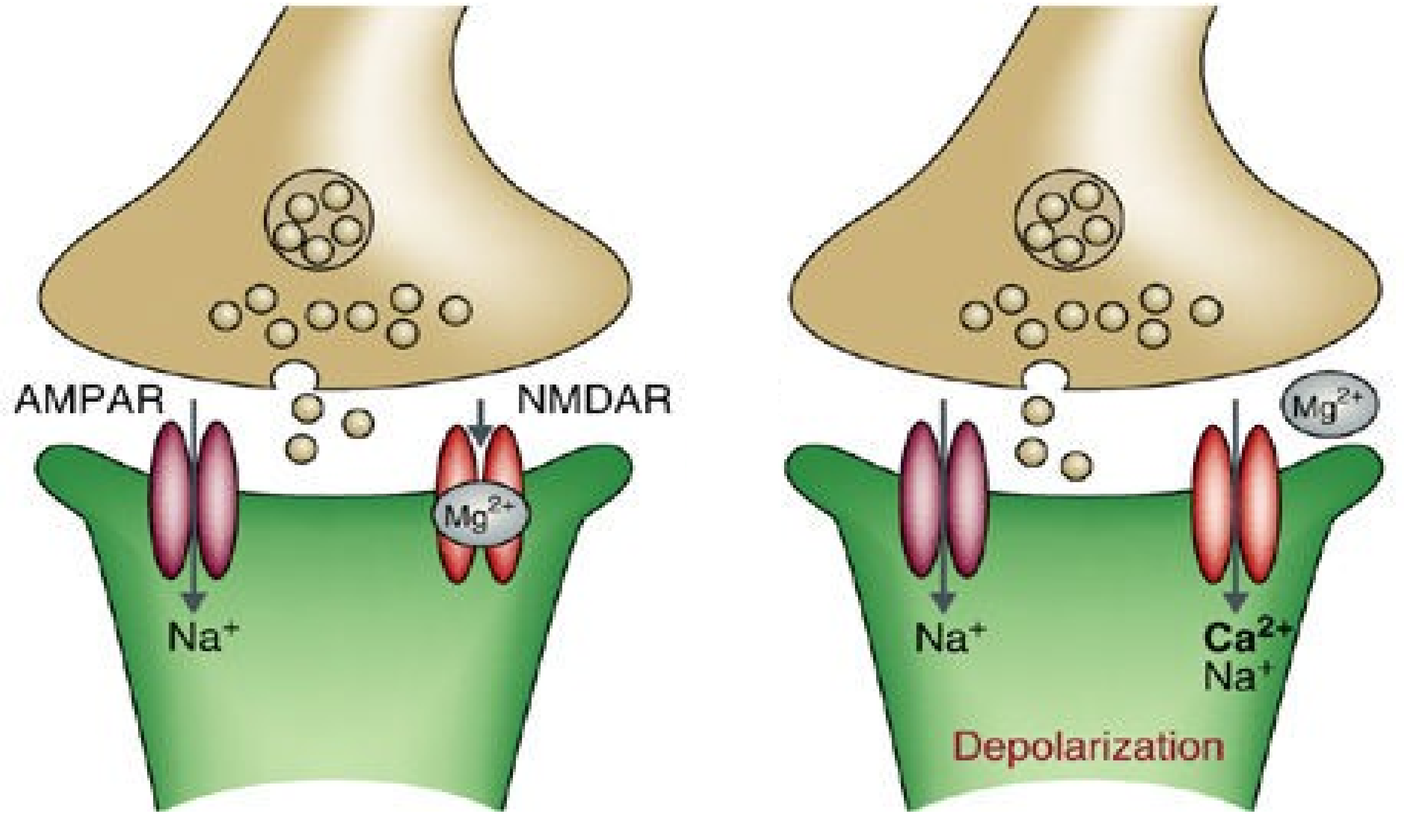
NMDA receptors: the synapse’s co-incidence detector



https://static-content.springer.com/esm/art%3A10.1038%2Fs41586-018-0039-9/MediaObjects/41586_2018_39_MOESM5_ESM.mp4

Song et al, Nature (2018)

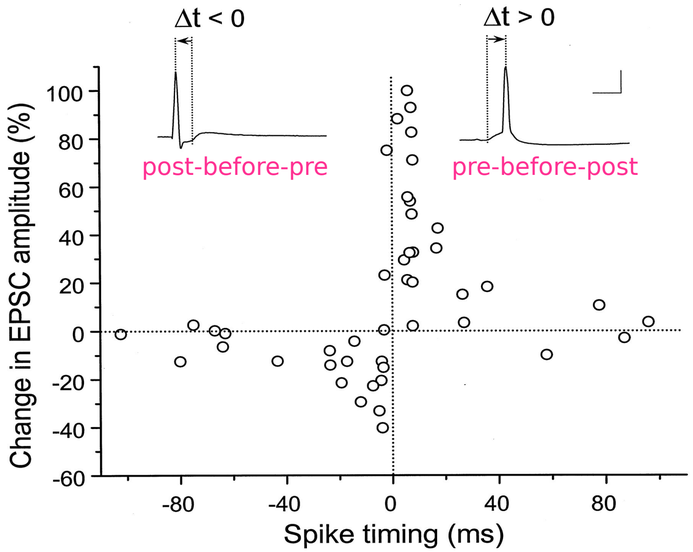
NMDA receptors: the synapse's co-incidence detector



Citri and Malenka, Neuropsychopharmacology (2007)

Spike-timing-dependent plasticity

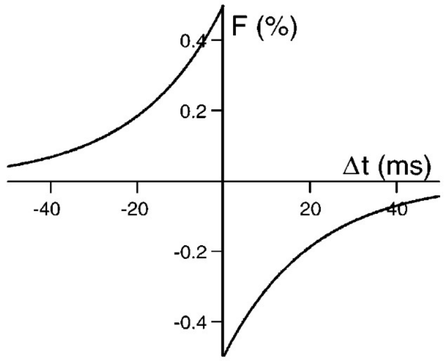
- STDP (discovered in late 1990s) encapsulates the idea of causality implied by Hebb:
  - ➔if presynaptic spike A happened just before postsynaptic spike B, A could have caused B.
  - ➔on the other hand, if presynaptic spike A happened just after postsynaptic spike B, A could not have caused B.
- Classic STDP: Pre-before-post causes LTP, post-before-pre causes LTD.
- STDP's existence implies that synapses can detect millisecond-level differences in spike timing when deciding whether to strengthen or weaken.
- When first discovered it was seen as the possible "atom of plasticity".
- "Things turned out to be just as simple as we first thought"
  — No biologist, ever



Bi & Poo, J Neurosci (1998)

Competitive Hebbian learning via STDP

- A simple computational model of STDP demonstrated that it can induce competition between the inputs.
- The group of synaptic inputs with the strongest correlations ‘wins’.



$$F(\Delta t) = \begin{cases} A_+ \exp(\Delta t/\tau_+) & \text{if } \Delta t < 0 \\ -A_- \exp(-\Delta t/\tau_-) & \text{if } \Delta t \geq 0 \end{cases}$$

Song, Miller & Abbott, Nat Neurosci (2001)

Summary

- LTP exists in many different forms;
- Hebb proposed the idea of correlated activity causing synaptic potentiation;
- Hebbian plasticity has no mechanism of homeostatic control;
- BCM rule was one proposal to address this issue;
- NMDAR works as an AP coincidence detector;
- STDP is a form of Hebbian plasticity based on AP coincidence;

Further reading on synaptic plasticity

- Simple rate-based plasticity models:
  Dayan and Abbott book (2001), chapter 8.
- BCM review:
  Cooper, L.N., and Bear, M.F. (2012). The BCM theory of synapse modification at 30: interaction of theory with experiment. Nat Rev Neurosci 13, 798–810.
- STDP:
  Feldman, D.E. (2012). The spike-timing dependence of plasticity. Neuron 75, 556–571.
- Problems with STDP:
  Lisman, J., and Spruston, N. (2005). Postsynaptic depolarization requirements for LTP and LTD: a critique of spike timing-dependent plasticity. Nat Neurosci 8, 839–841.