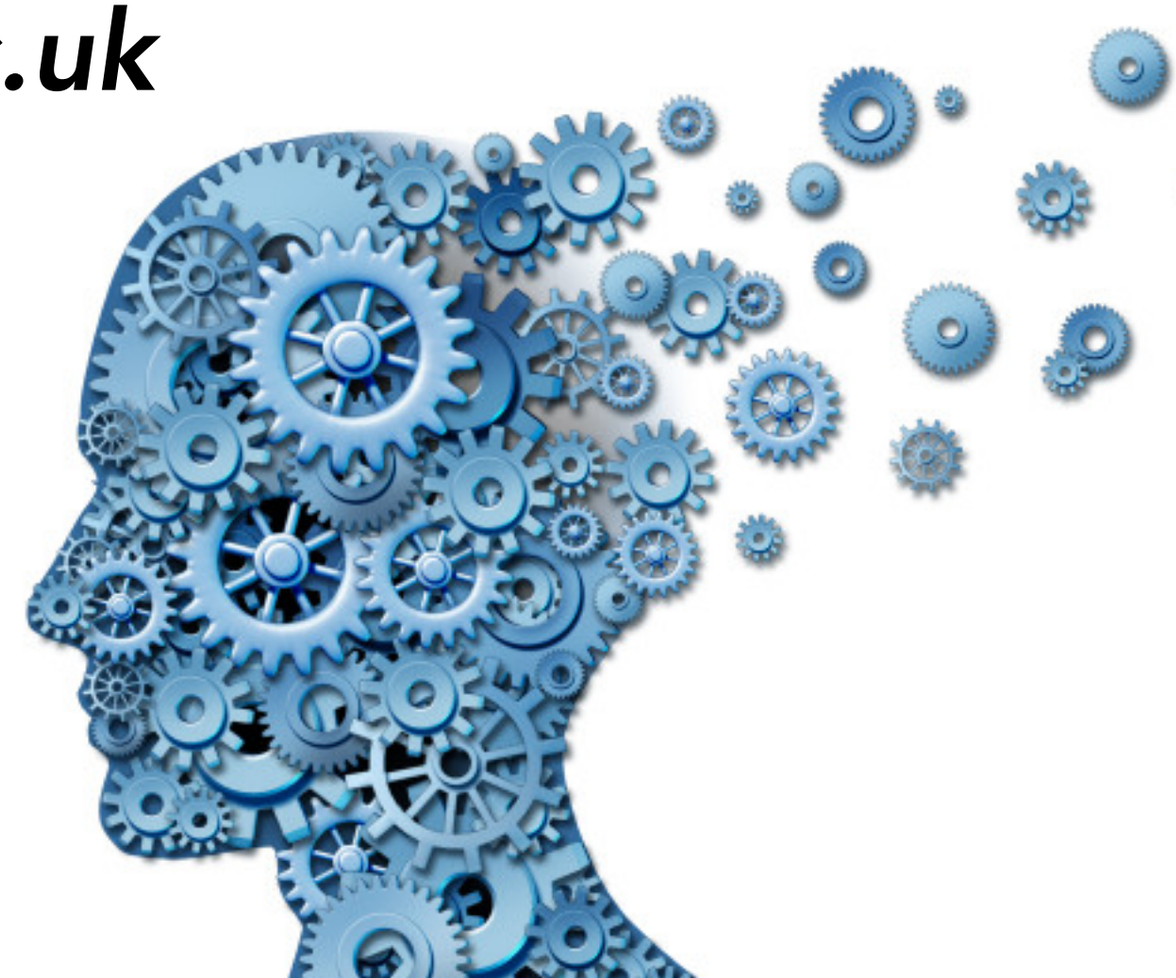
COMS30127: Computational Neuroscience

Synapses, synaptic plasticity, and STDP (i, j)

Dr. Cian O'Donnell

cian.odonnell@bristol.ac.uk



What we will cover today

Synapses

- What is a synapse?
- How do synapses work?
- How can we computationally model synapses?

Synaptic plasticity

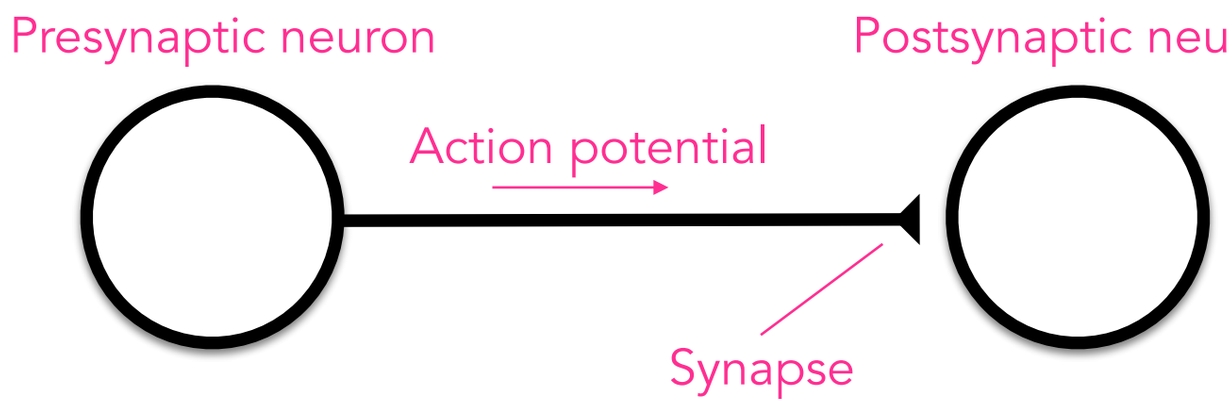
- Short vs long-term synaptic plasticity.
- Classic rate-based models of plasticity.
- Spike-timing dependent plasticity.

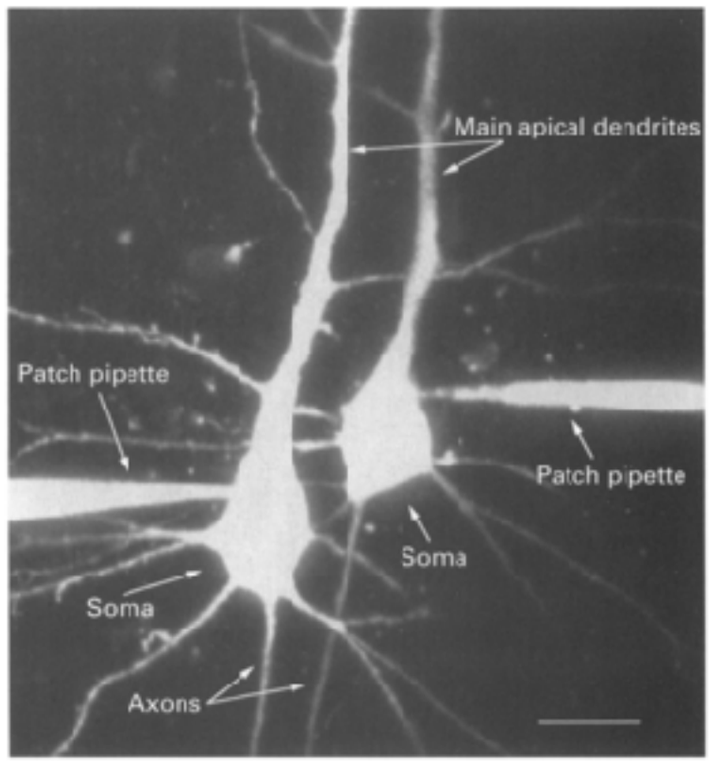
What is a synapse?

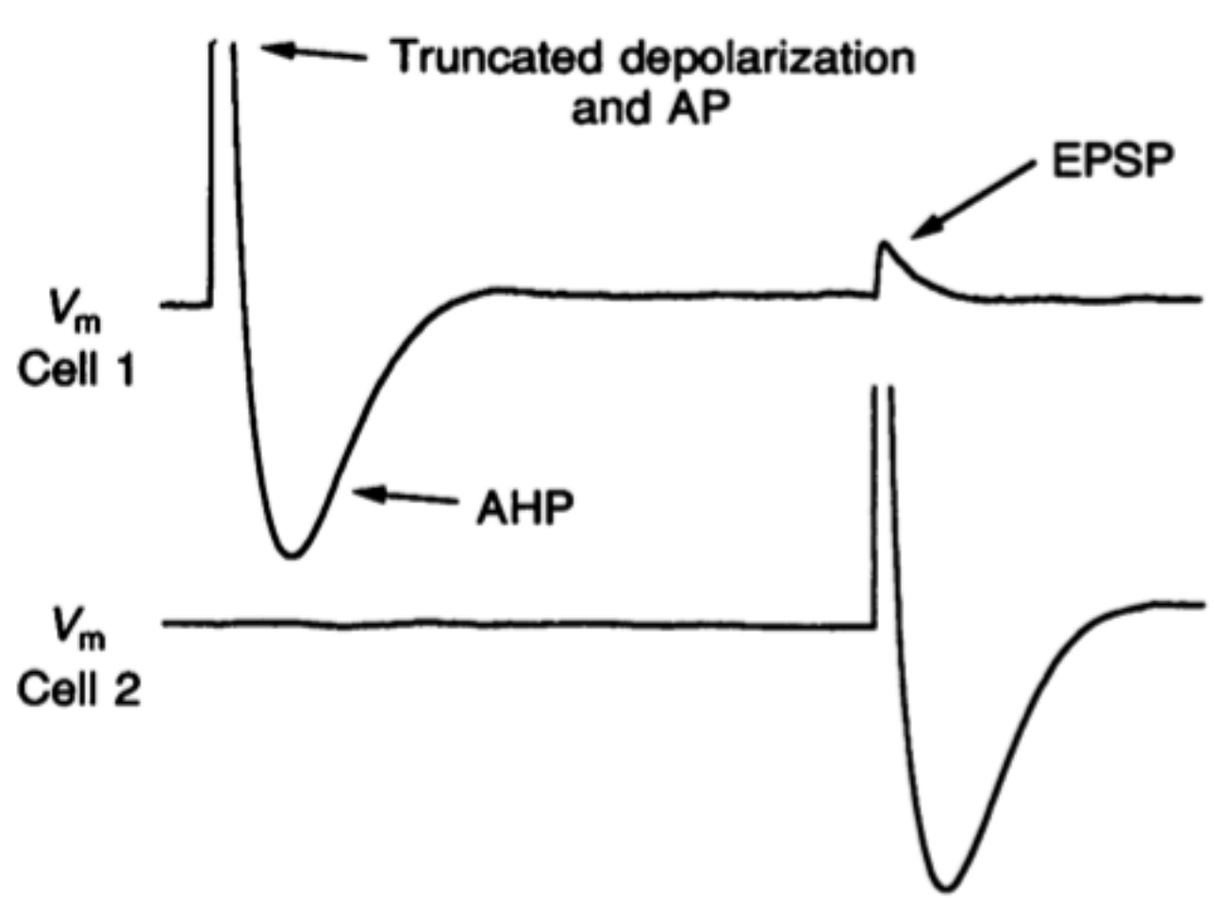
- Synapses are the connections between neurons.
- They convert the action potential from one neuron's axon into a 'post-synaptic-potential' in the dendrite of another neuron.
- Although both a synapse's input and output signals are electrical, the most common type of synapse converts the signal into chemical form at an intermediate stage.
- There are also purely electrical synapses (called 'gap junctions') but in this course we will focus on chemical synapses.
- From a functional point of view, synapses are interesting for two reasons:
  1. they are nonlinear, so can perform computations.
  2. they are plastic, so can store information (memories).

↳ So essentially a bit like art. neur. nets.

What is a synapse?



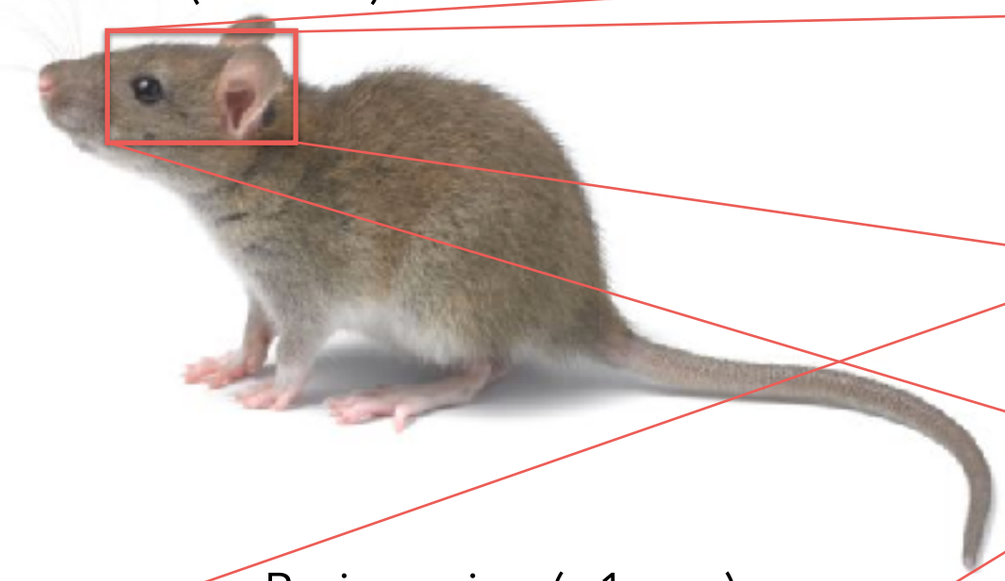




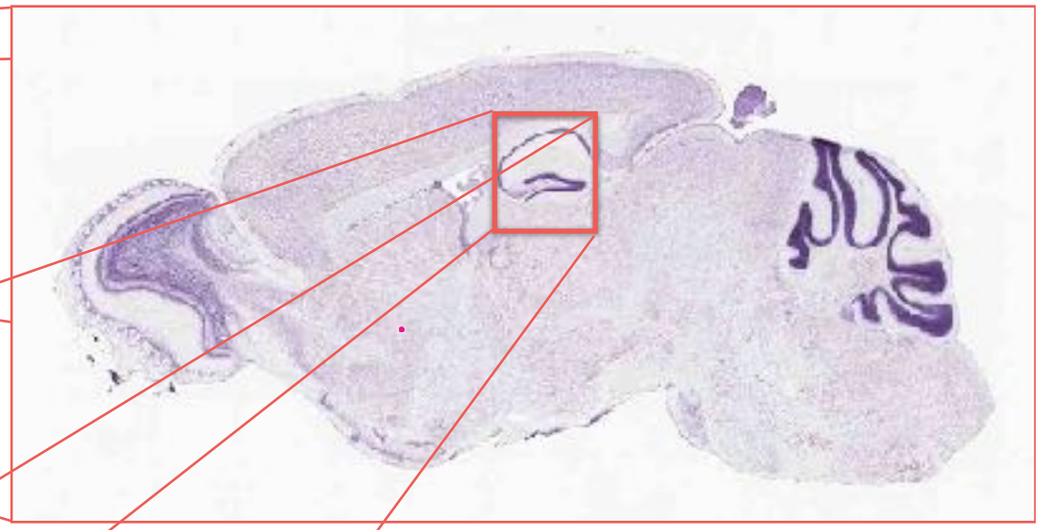
Markram et al, *J Physiol* (1997)

Zooming in on synapses

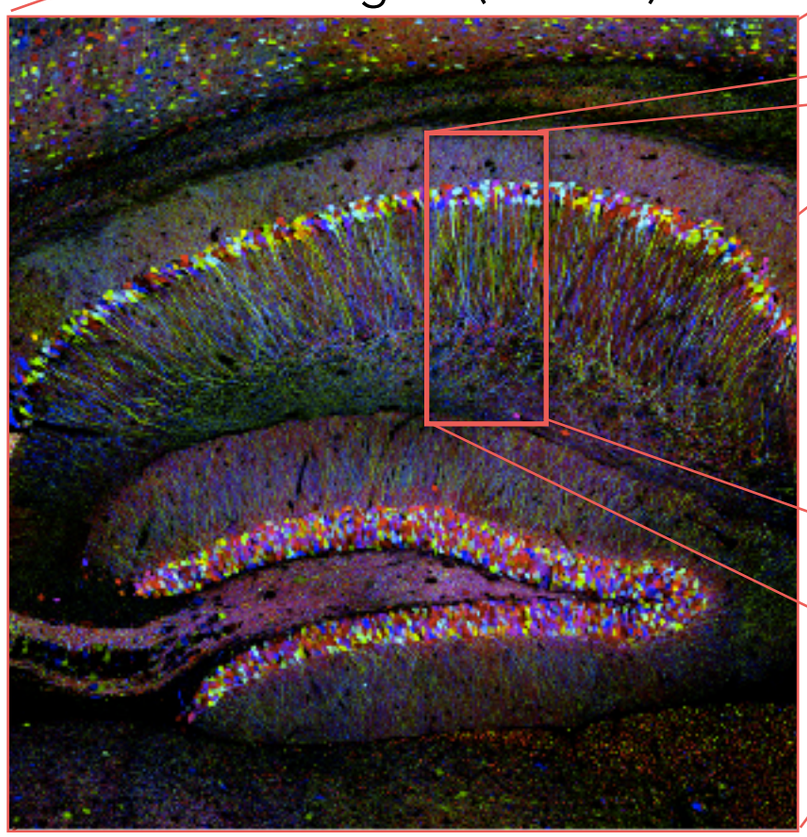
Animal (~10 cm)



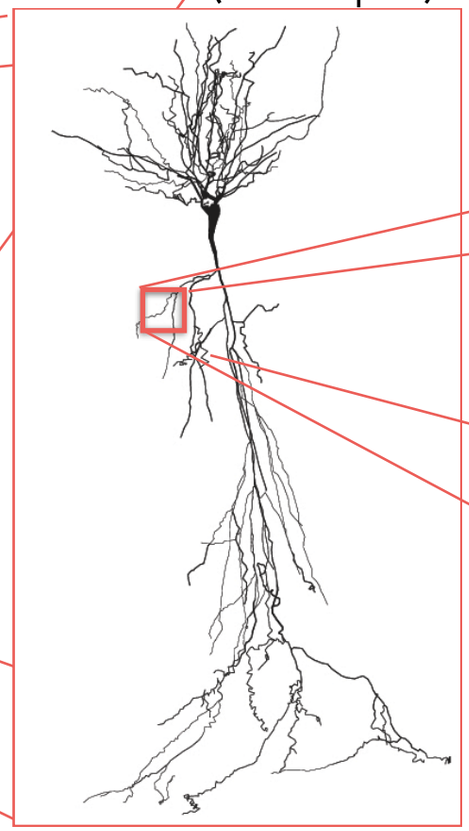
Brain (~1 cm)



Brain region (~1 mm)



Neuron (~100 µm)



Synapses (~1 µm)

How do synapses work?

Axon
(presynaptic action potential)

Chemical signalling

Dendrite
(postsynaptic potential)

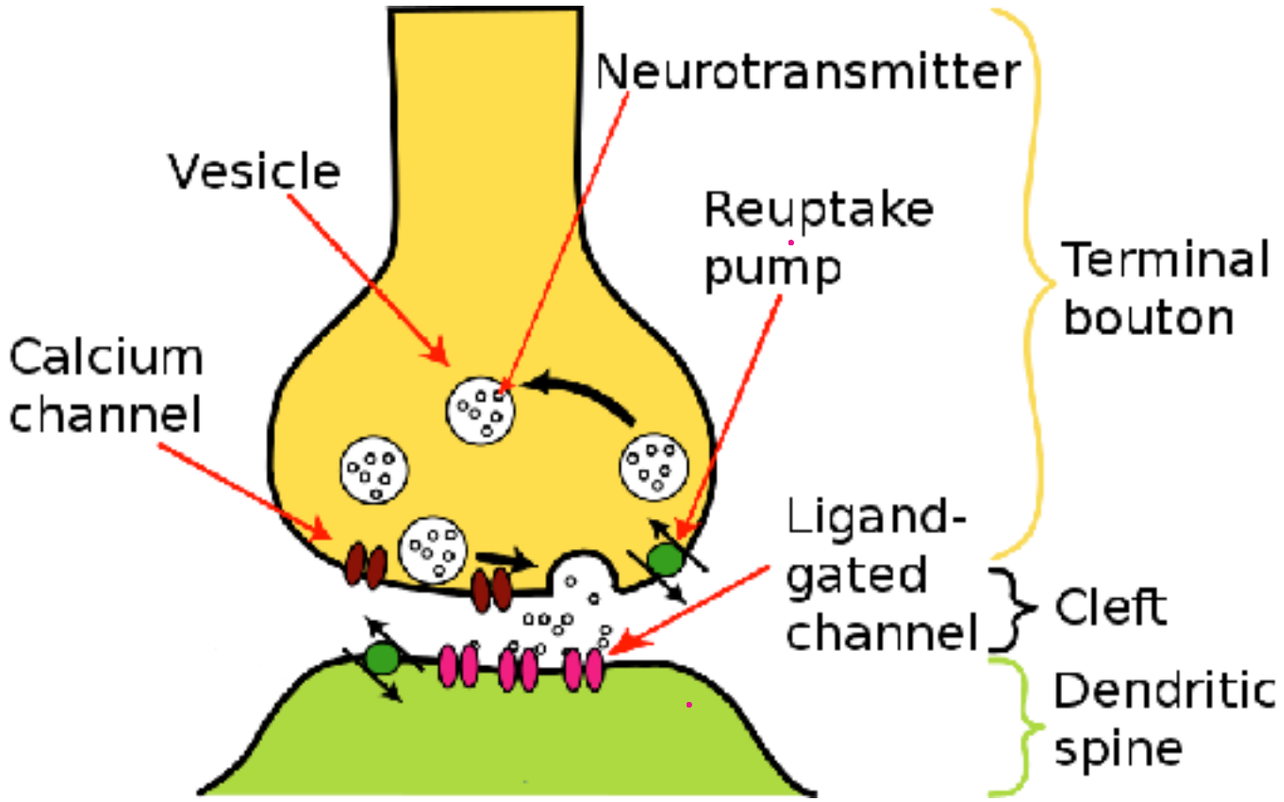
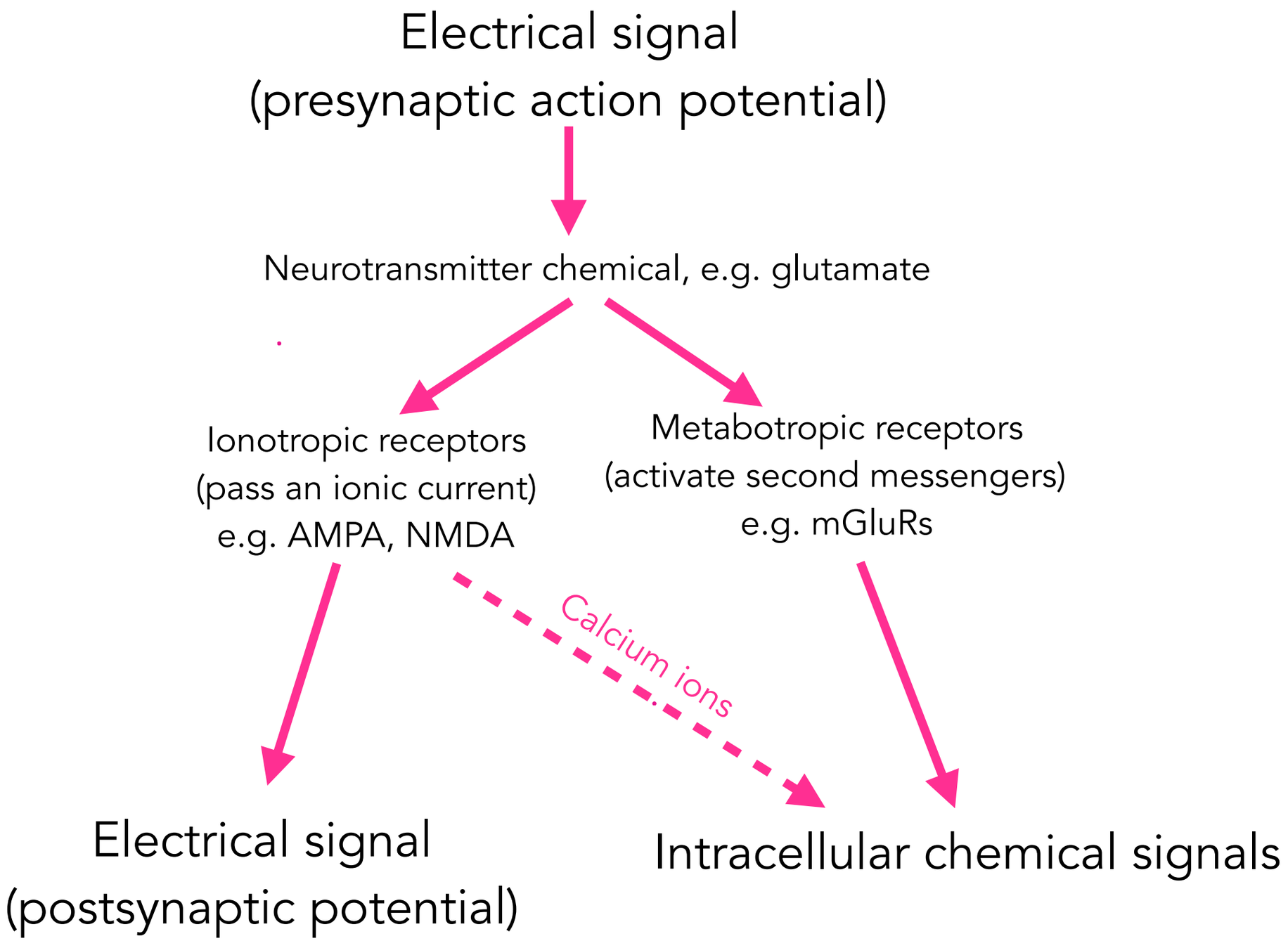


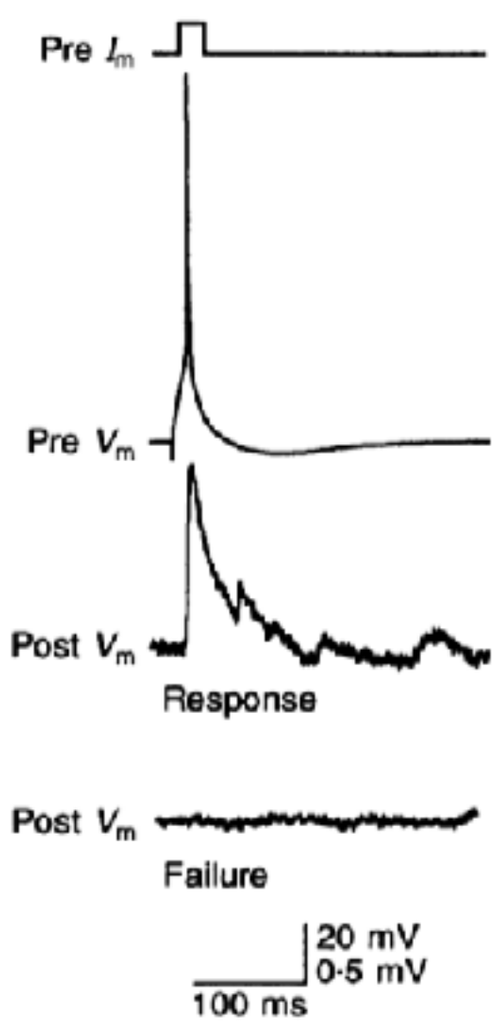
Image from Wikipedia (modified by C Houghton)

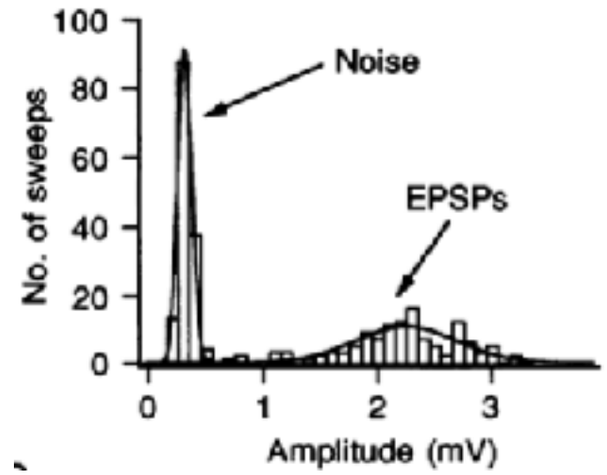
How do synapses work? (elaborated)

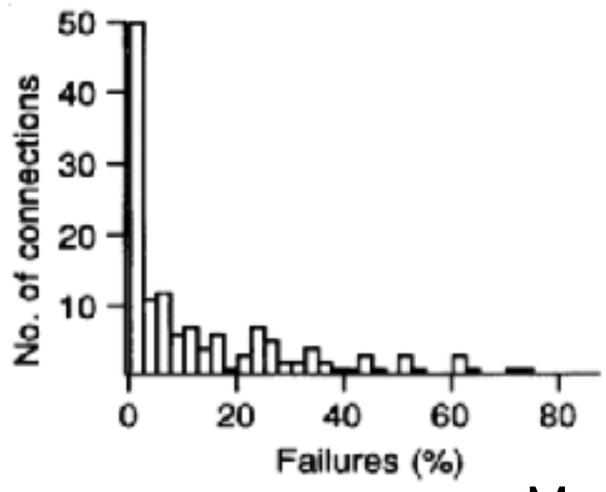


Synapses are probabilistic

- When an action potential arrives at a synapse, it may or may not lead to release of neurotransmitter.
- The 'release probability' *p* is often quantified experimentally, $0<p<1$.

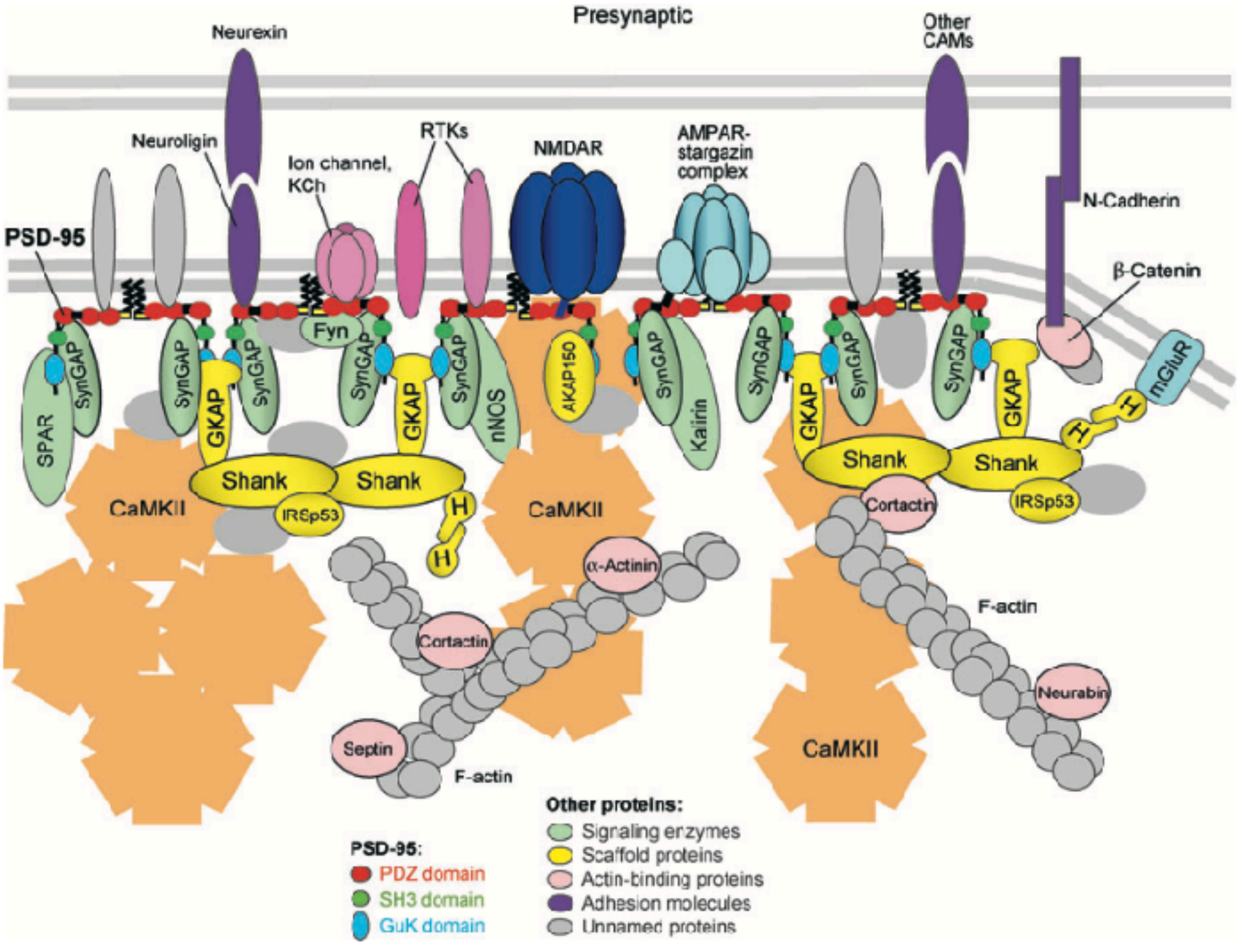






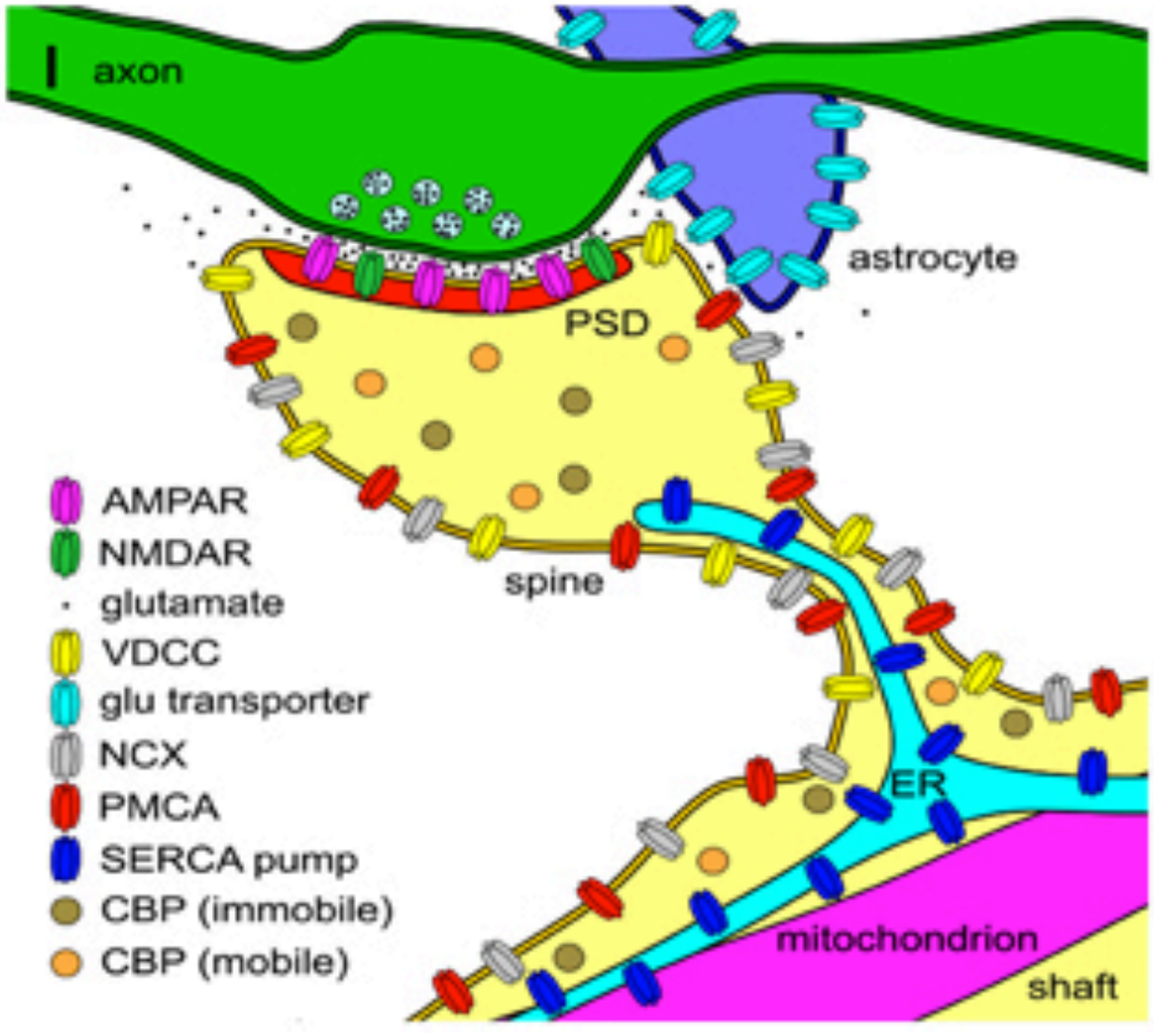
Markram et al, *J Physiol* (1997)

Synapses are complex

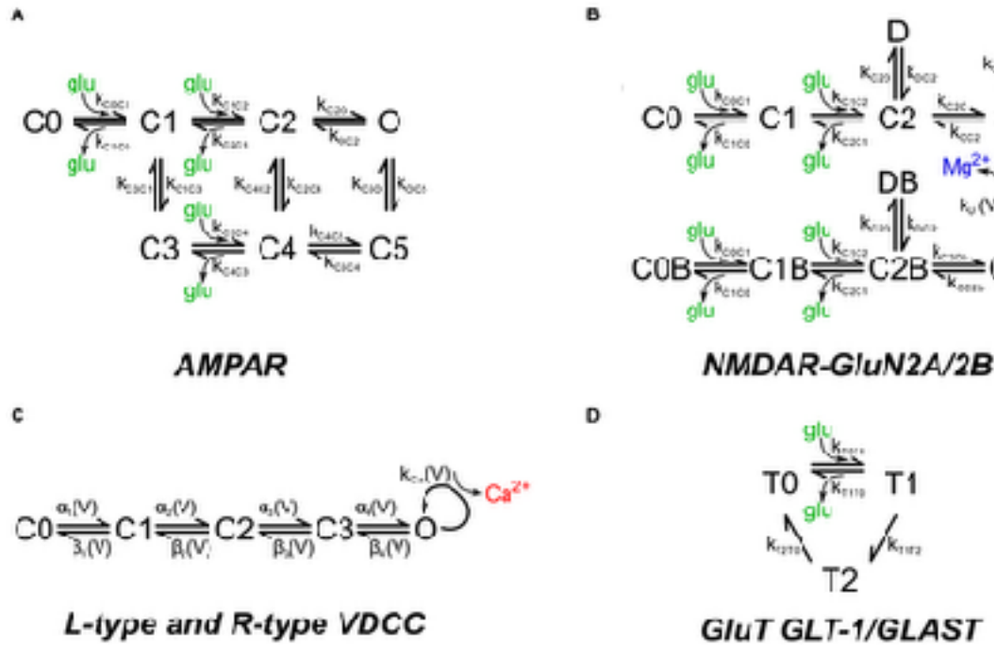


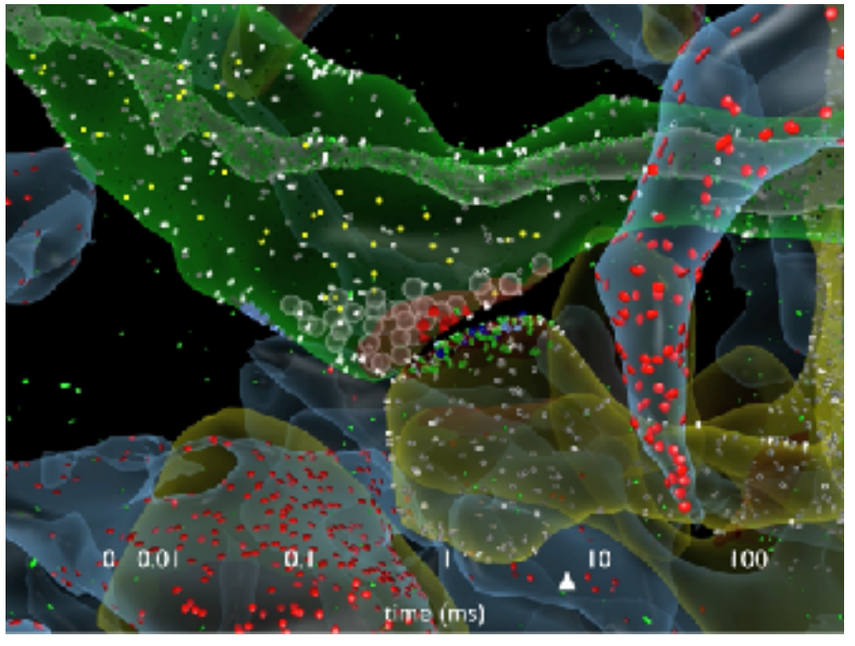
Sheng & Hoogenraad, *Annu Rev Neurosci* (2007)

MCell simulation of synaptic release



Bartol et al, *Frontiers Syn Neuro* (2015)





Video courtesy of Tom Bartol (Salk Institute, California)

How can we computationally model a synapse?

- We could simulate the dynamics of each molecule involved in the signalling process (like the MCell simulation).
- But since that is (very) computationally expensive, we might instead go for a reduced mass-action chemical-kinetics model.
- However for many purposes that is still too expensive and parameter heavy, so instead we use even simpler phenomenological models that black-box the synapse as a simple input-output system.

Simple synapse models

The most common way to phenomenologically model a synapse is as a time-dependent conductor in series with a battery.

$$I_s(t) = \bar{g}_s s(t)(E_s - V)$$

The value of E_s determines whether the synapse is excitatory or inhibitory:

for excitatory synapses E_s usually = 0 mV

for inhibitory synapses E_s usually = V_{rest}

But how should we model $s(t)$?

Simple synapse models

Single exponential

$$s(t) \rightarrow s(t) + 1$$

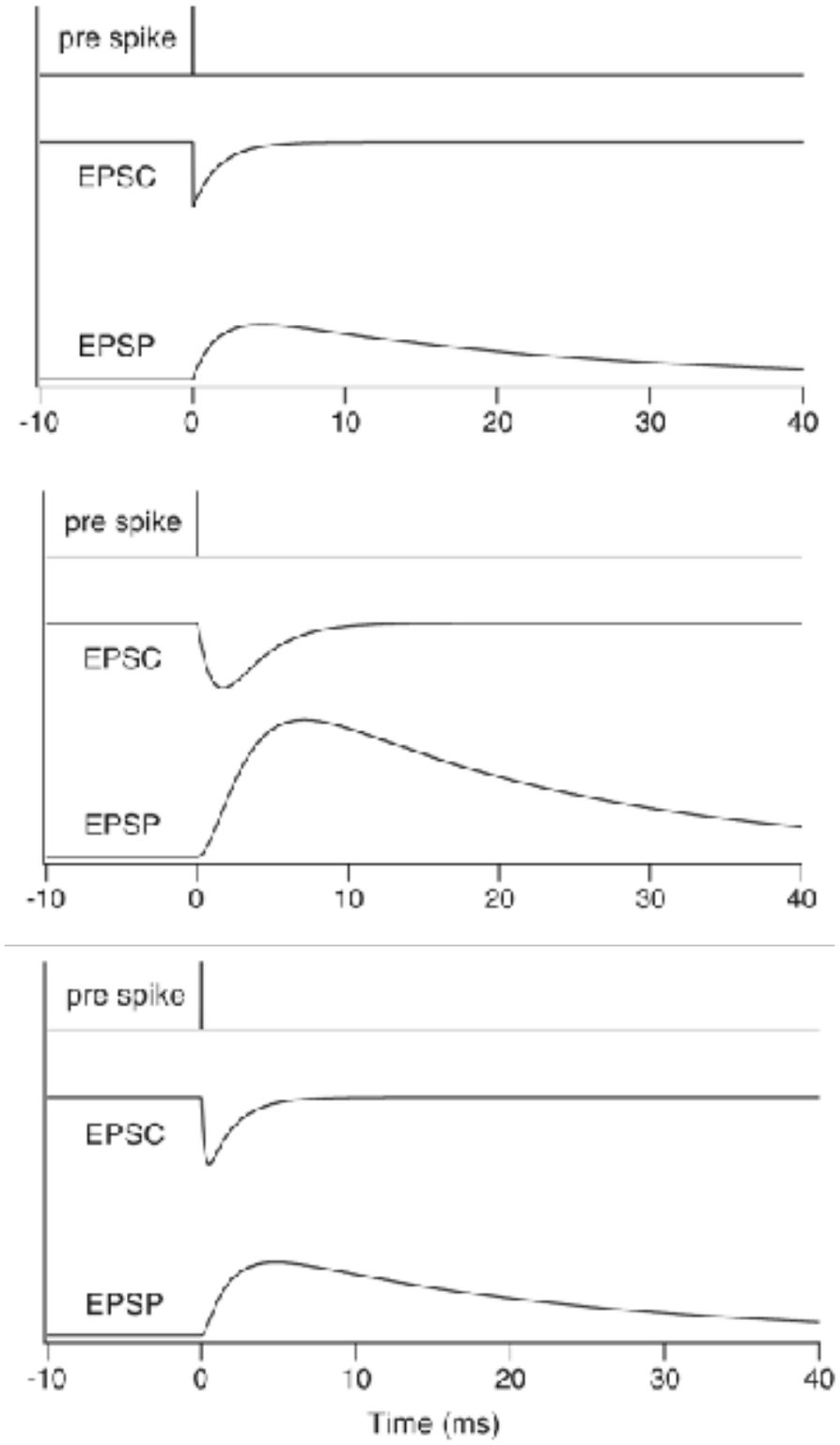
$$s(t) = e^{-t/\tau_s}$$

Alpha function

$$s(t) = te^{-t/\tau_s}$$

Difference of two exponentials

$$s(t) = e^{-t/\tau_{decay}} - e^{-t/\tau_{rise}}$$



Figures from Roth & van Rossum
http://homepages.inf.ed.ac.uk/mvanross/reprints/roth_mvr_chap.pdf

Summary on synapses

- Synapses are the connections between neurons.
- The convert the pre-synaptic action potential to a (excitatory or inhibitory) post-synaptic potential via a chemical intermediate stage.
- They are highly stochastic (noisy).
- They are also complicated molecular machines.
- We can model them at multiple levels of granularity, as appropriate for the task at hand.

Synaptic plasticity

Synaptic plasticity

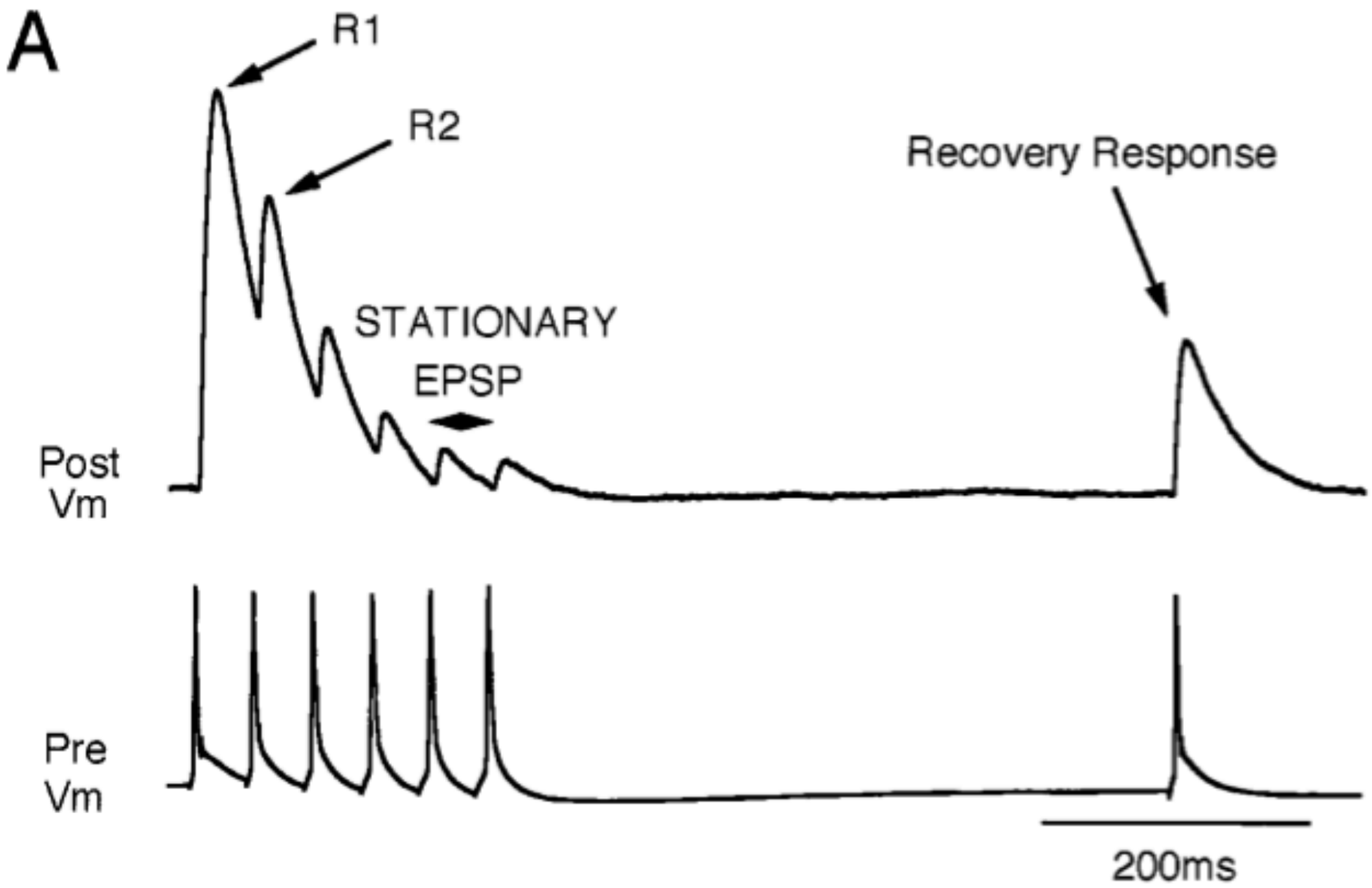
- The magnitude of a synapse's electrical response to an action potential can change depending on the activity history of the synapse (known as plasticity).

- These changes can be short-lasting (ms—s) or long-lasting (hours—years).

- Short-term synaptic plasticity is thought to be involved in fast cognitive processing.
  - Similar timescale to electrical dynamics.
  - Some synapses facilitate (increase their strength with use) while others depress (decrease their strength with use).
  - Most synapses fall into one category or the other.

- Long-term synaptic plasticity, in contrast, 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.

Short-term plasticity

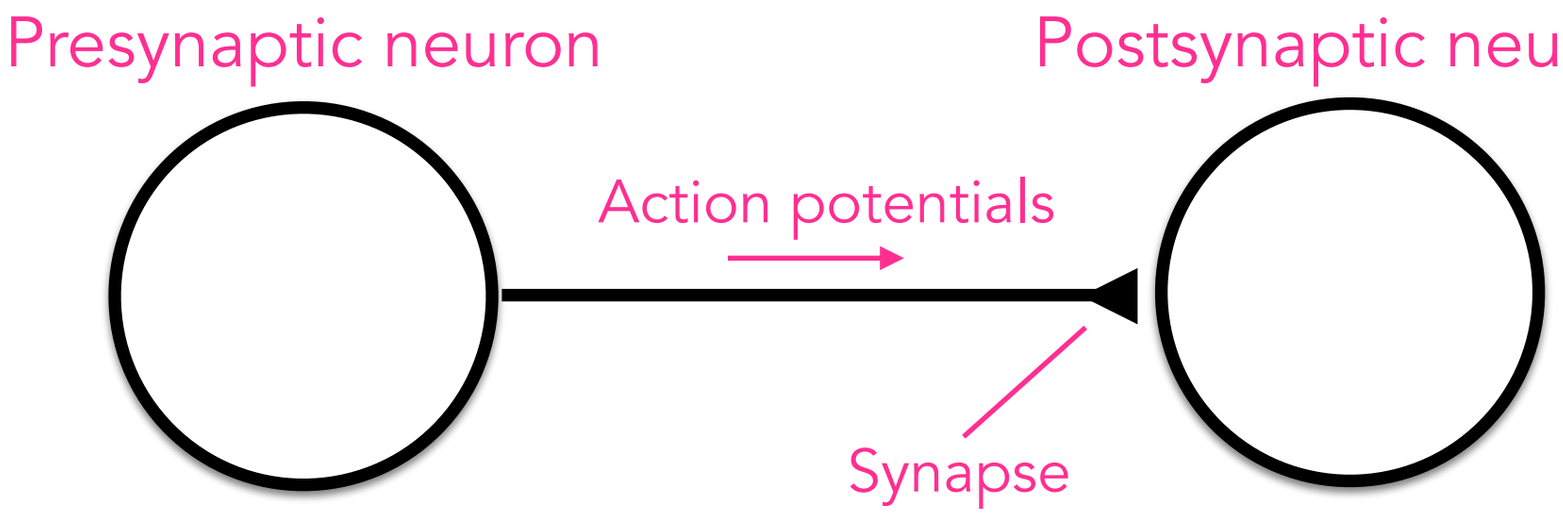


Short-term synaptic depression due to a use-dependent decrease in release probability.

Tsodyks & Markram, *PNAS* (1997)

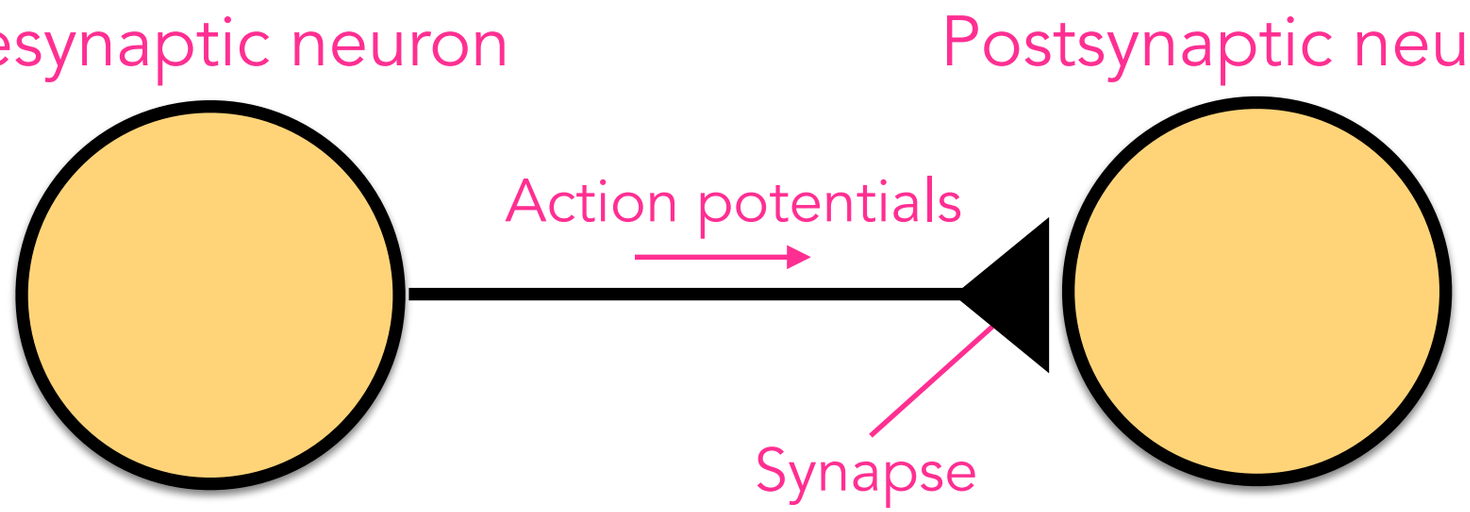
Long-term plasticity

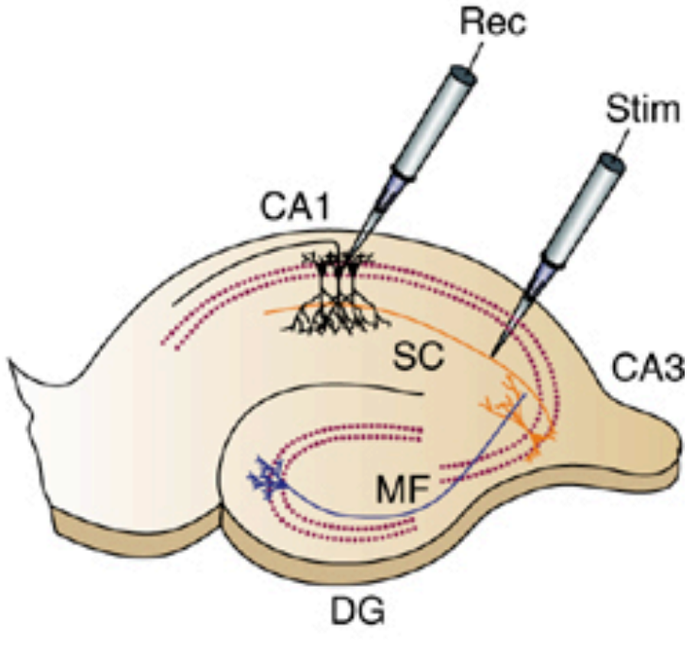
Long-term synaptic plasticity

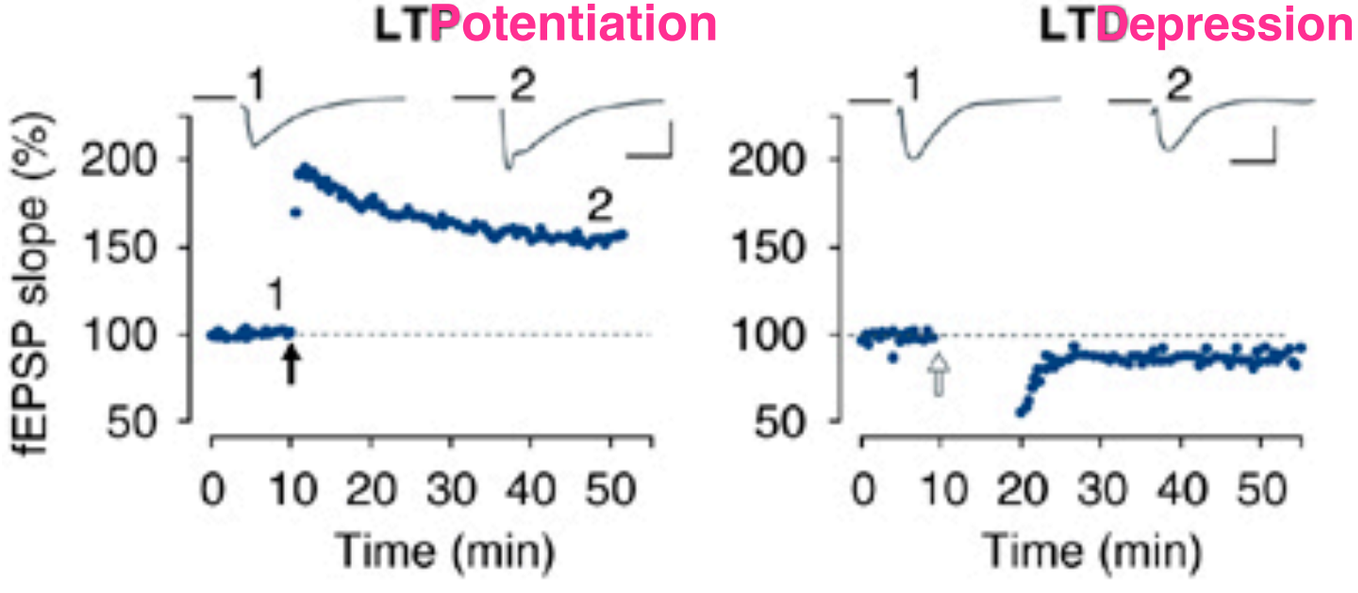


Long-term synaptic plasticity

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







Learning and memory via synaptic plasticity

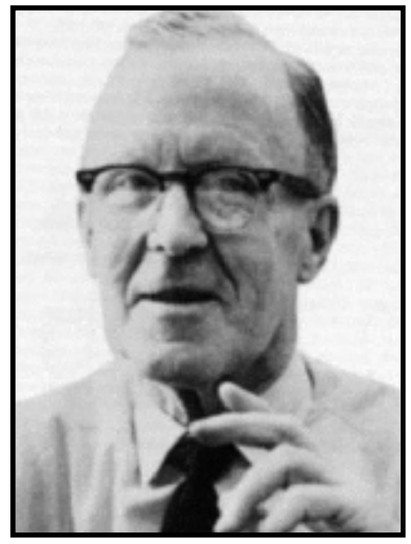
- Synaptic plasticity is generally believed to be the primary basis of long-term memory in the brain.

- Other neural components are also plastic (intrinsic excitability, neural morphology, etc), but their role in learning and memory is poorly understood. We will not cover them in this unit.

- Synapses increase or decrease their strength according to certain ‘rules of plasticity’.

- Linked to learning and memory in the following way:
  - Neural activity during learning triggers synaptic strength changes.
  - Synaptic strength changes alters the propensity for neurons to fire.
  - Next time the same neural circuit receives an input, it responds in a different fashion than it otherwise would have. **That’s memory.**

Hebbian plasticity



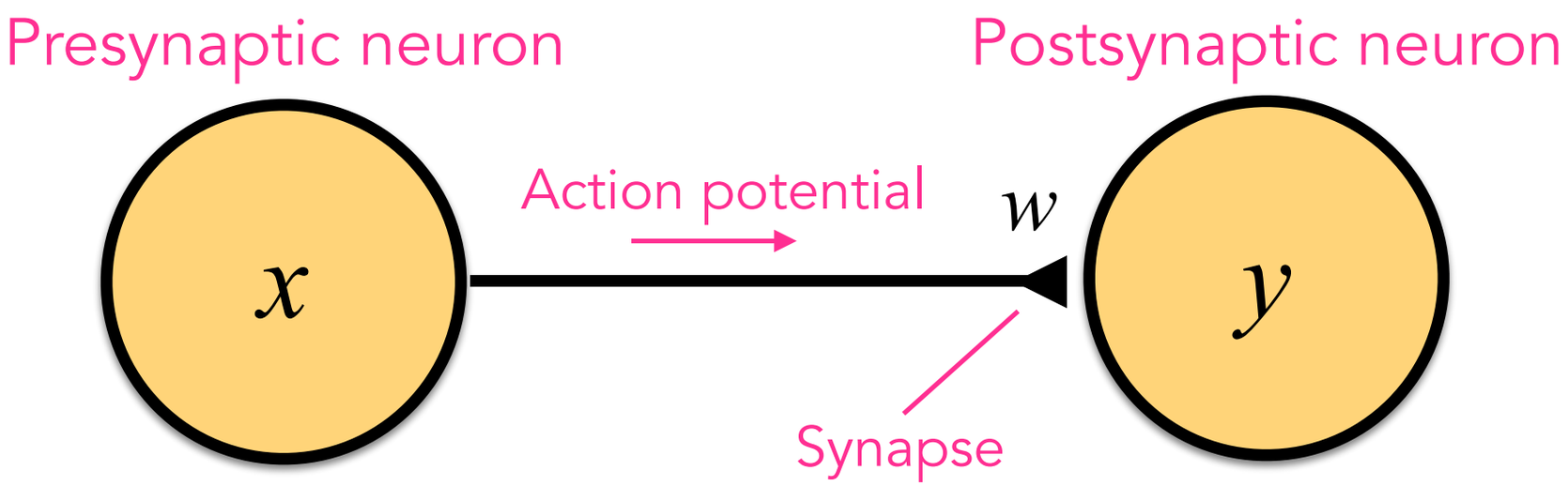
Donald Hebb

"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



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

A Hebbian rule: $\Delta w = \eta x y$

- Can explain Pavlov's dogs!
- Note that dynamics are unstable: $\boldsymbol{w}$ 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.

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

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

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

$$\eta_\theta \gg \eta_w$$

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

Bienenstock, Cooper & Munro, *J Neurosci* (1982)

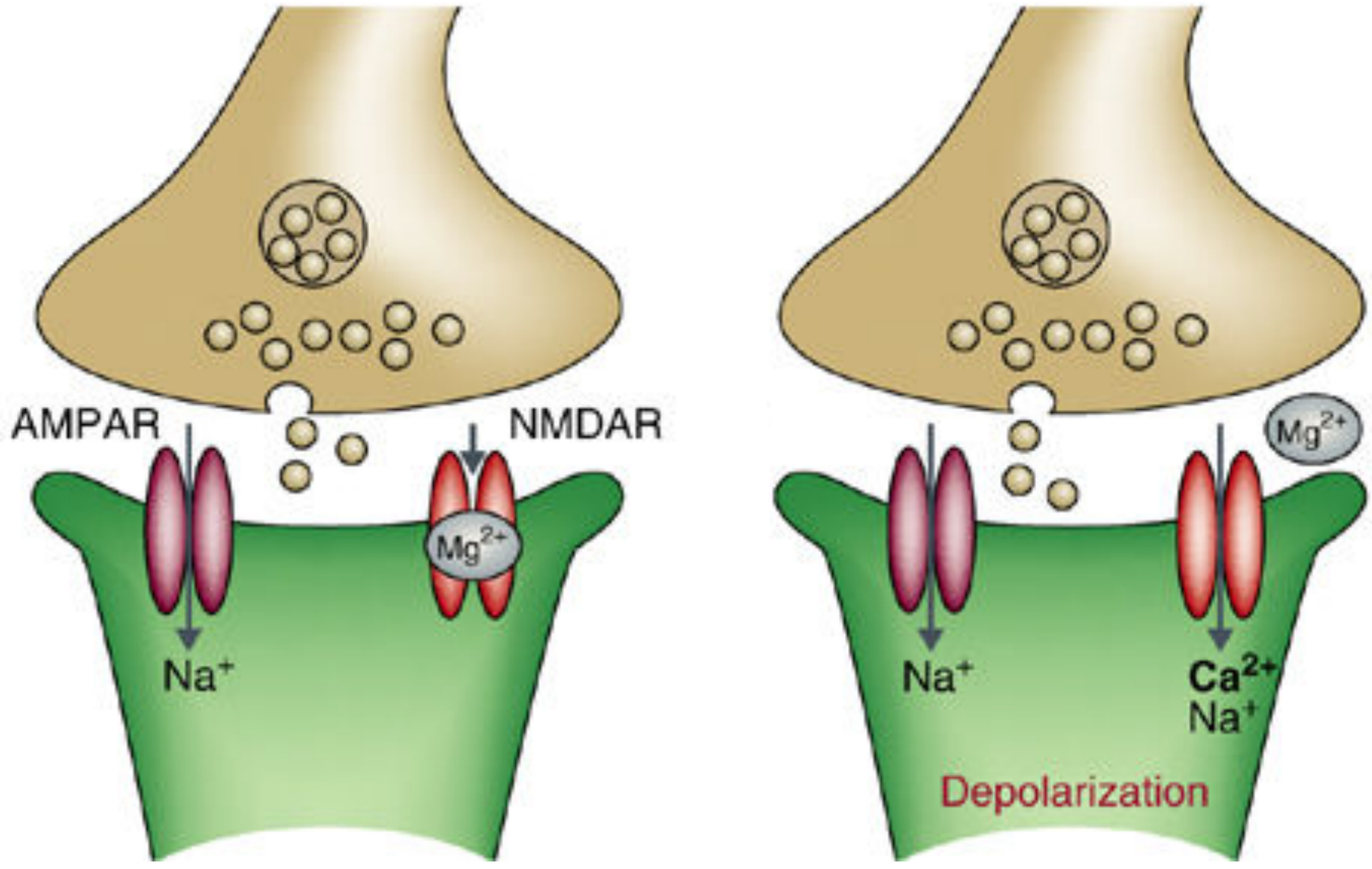
NMDA receptors

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

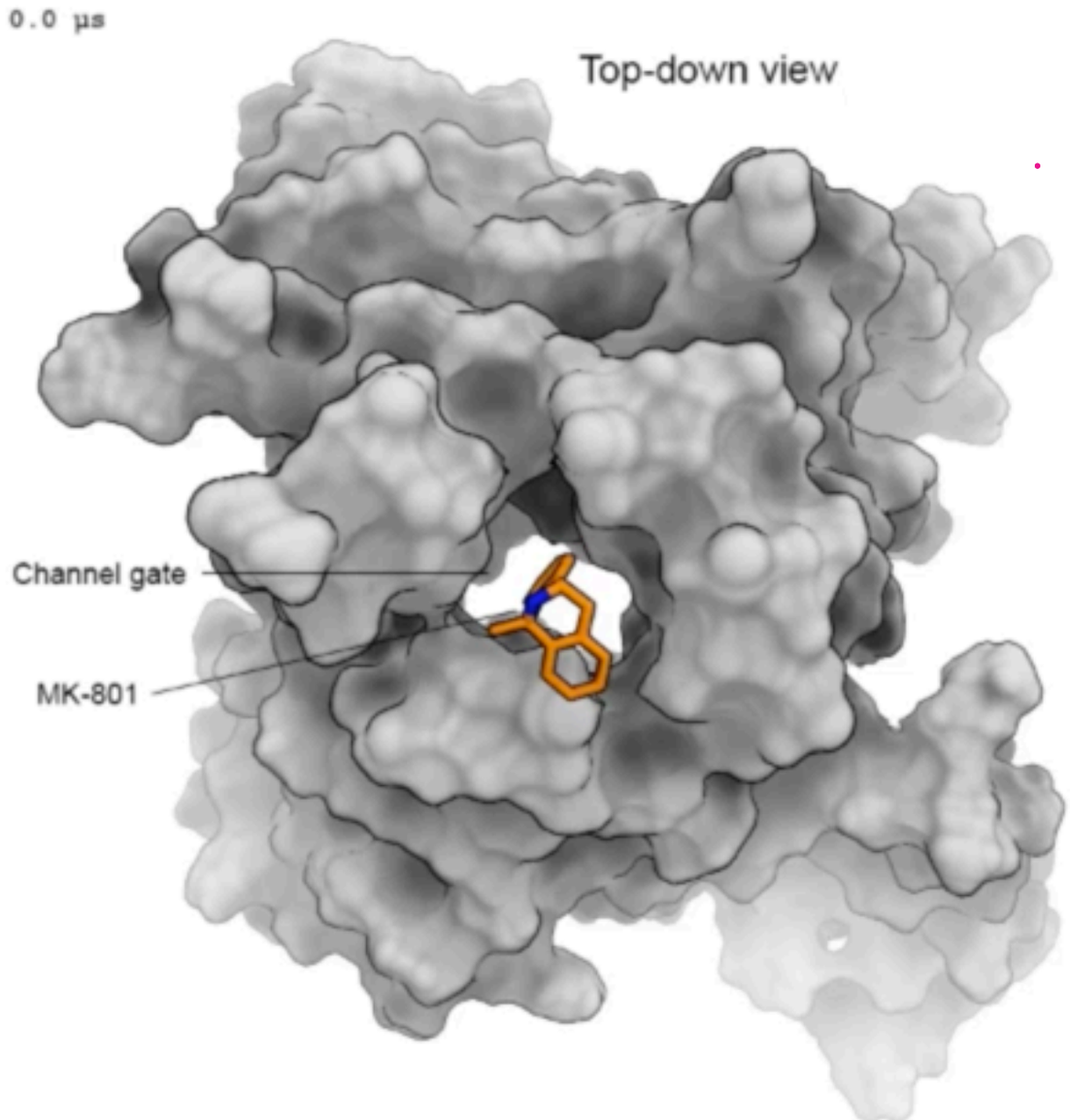
the synapse's co-incidence detector



Citri and Malenka, *Neuropsychopharmacology* (2007)

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)

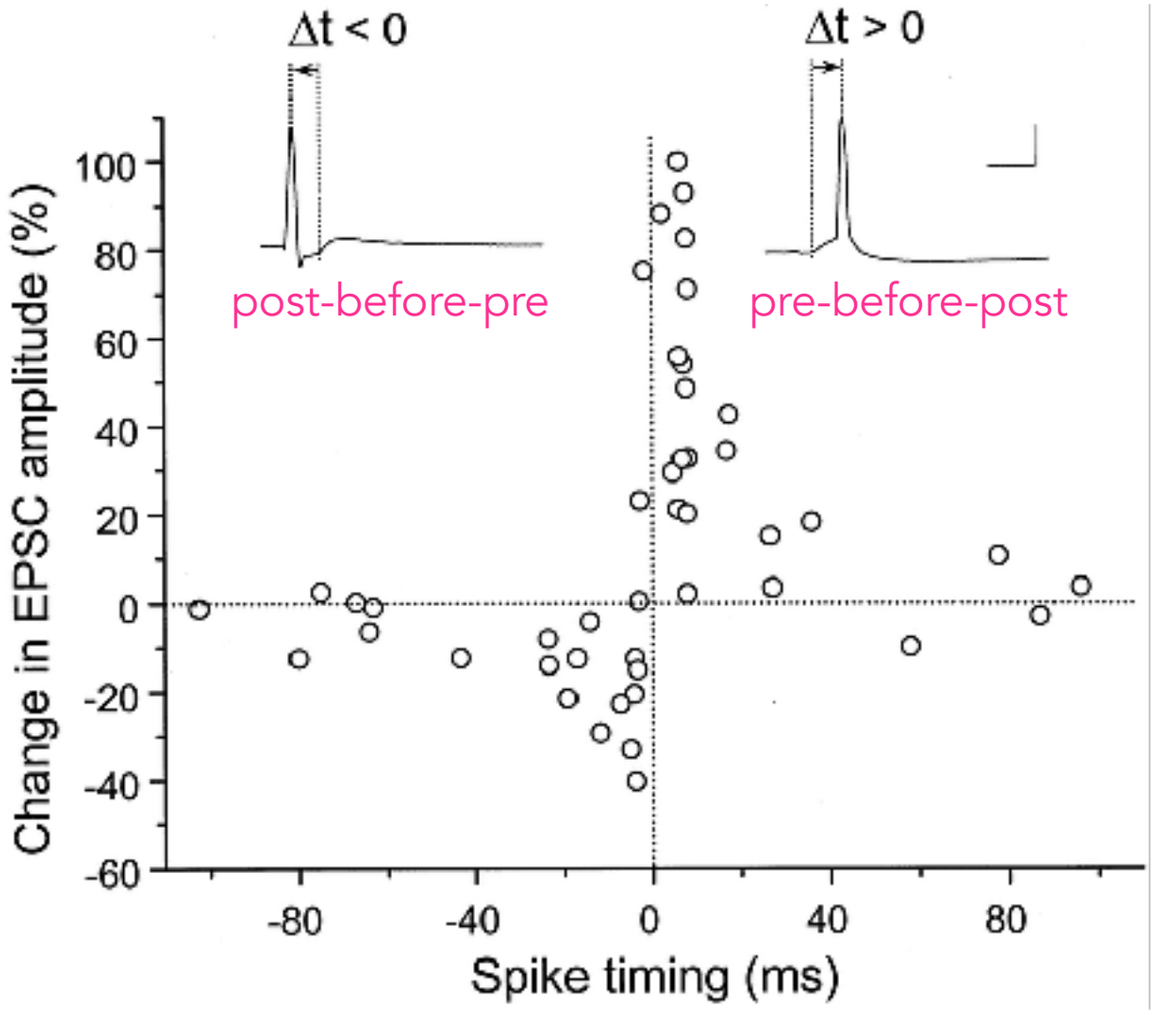
Spike-timing-dependent plasticity

- 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.

- 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".

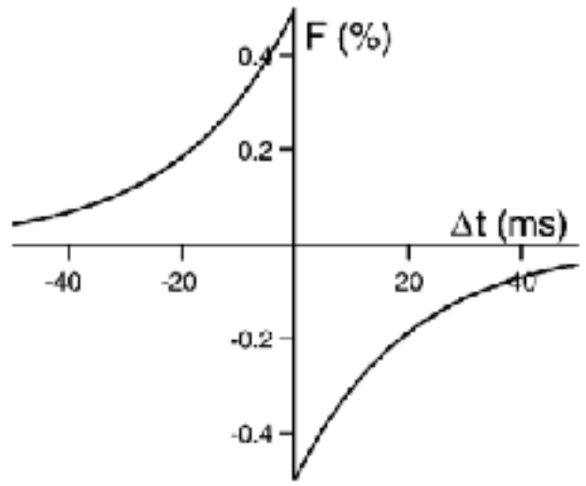
- "Things turned out to be just as simple as we first thought"
  — *No biologist, ever*



Bi & Poo, *J Neurosci* (1998)

Competitive Hebbian learning via STDP

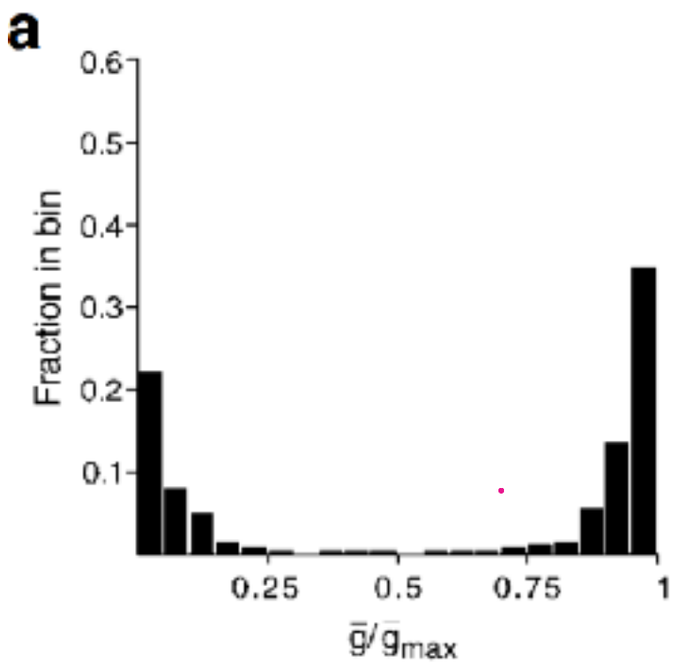
- A simple computational model of STDP demonstrated that it can induce competition between the inputs.



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

- The group of synaptic inputs with the strongest correlations 'wins'.

- However, synaptic weight dynamics in this model are unstable, and must be artificially capped.
  The resulting weight distribution is bimodal.



Song, Miller & Abbott, *Nat Neurosci* (2001)

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.

End