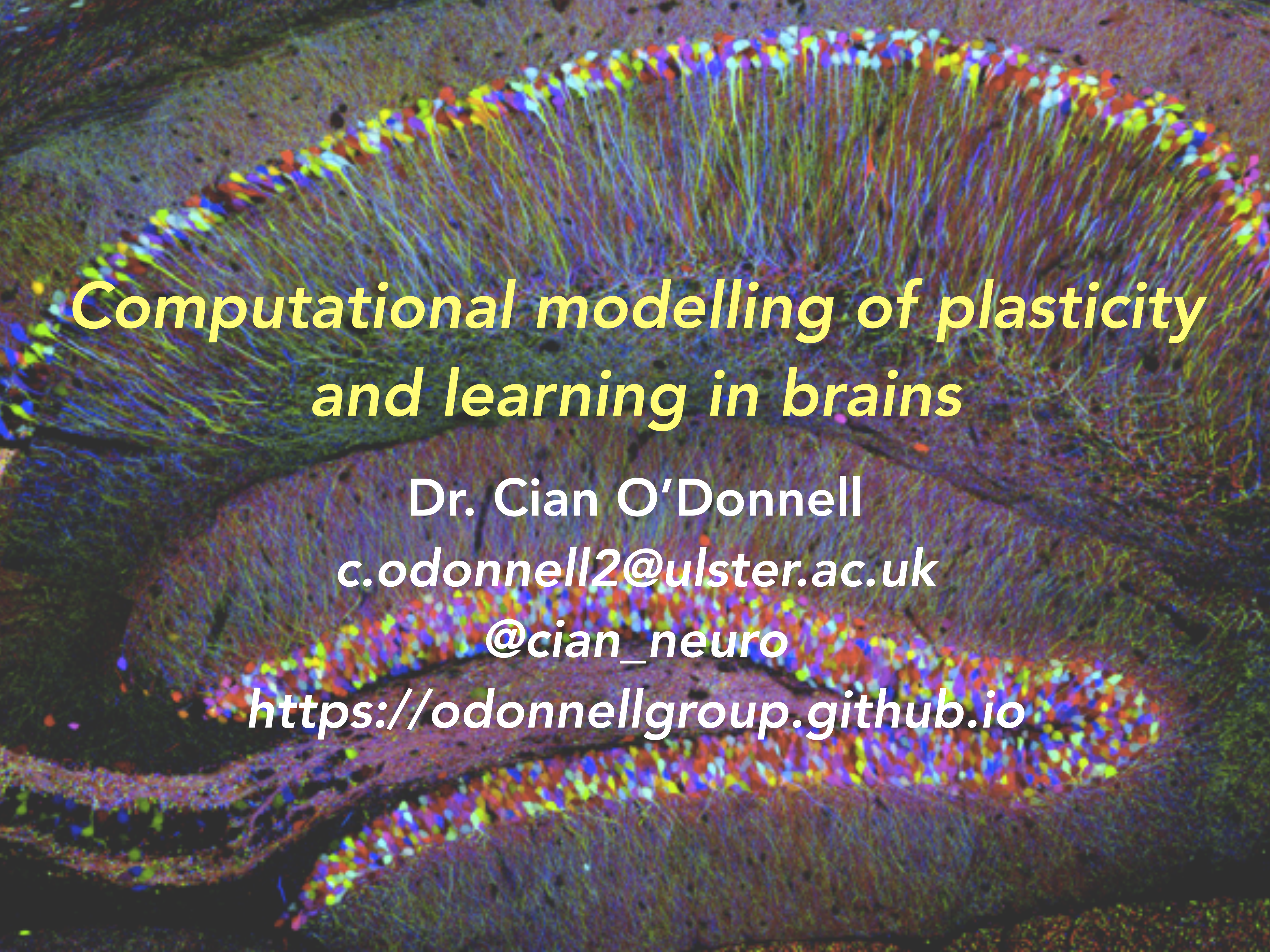

Computational modelling of plasticity and learning in brains

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Why study learning?

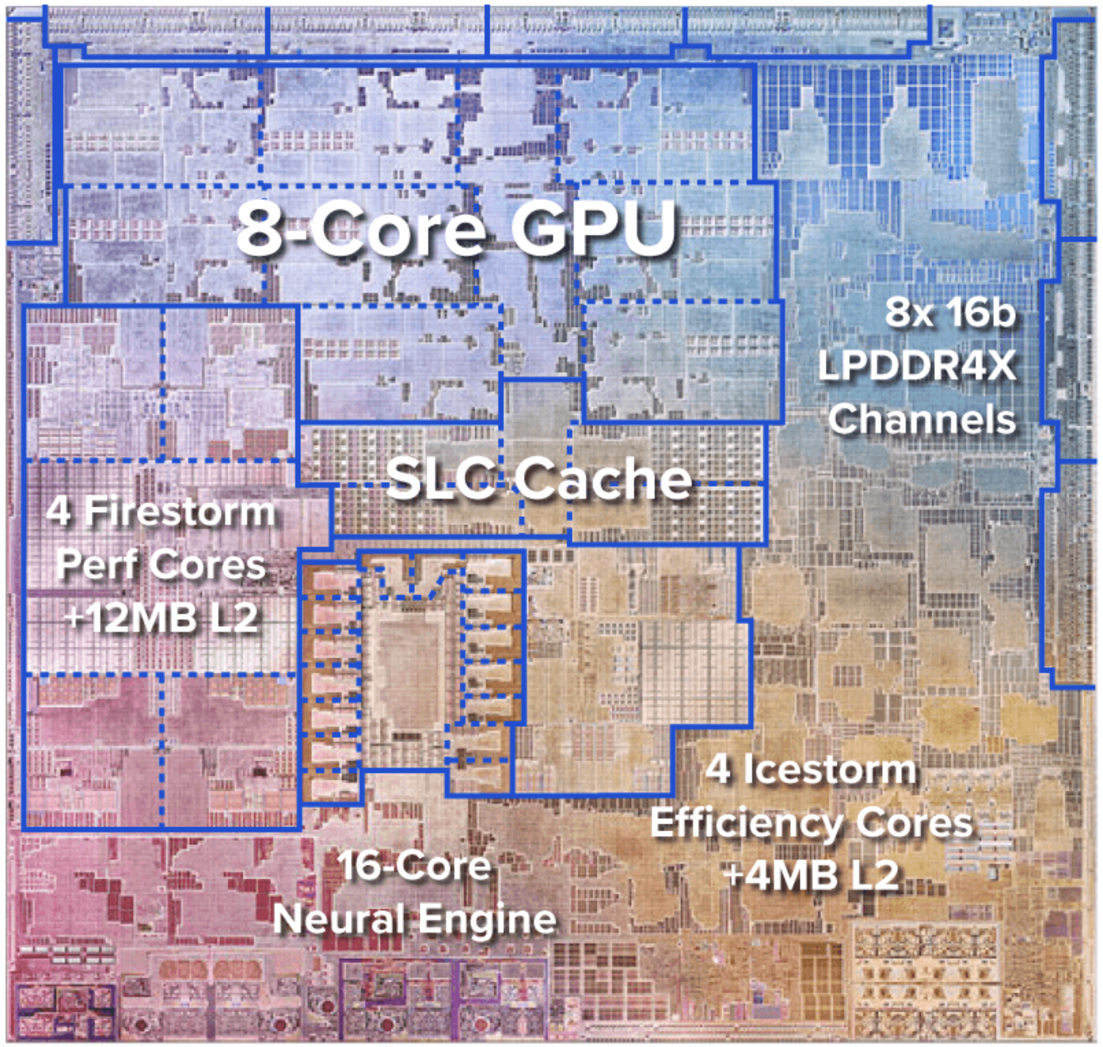
KordingLab 👨‍💻🧠∇🔬📈,🏋️⛷️🏂🛹🧗⛰️☕🦖
@KordingLab

In computational neuroscience can we realistically understand computation (say how we see a hand) or can we at best hope to understand the learning that gives rise to the computation?

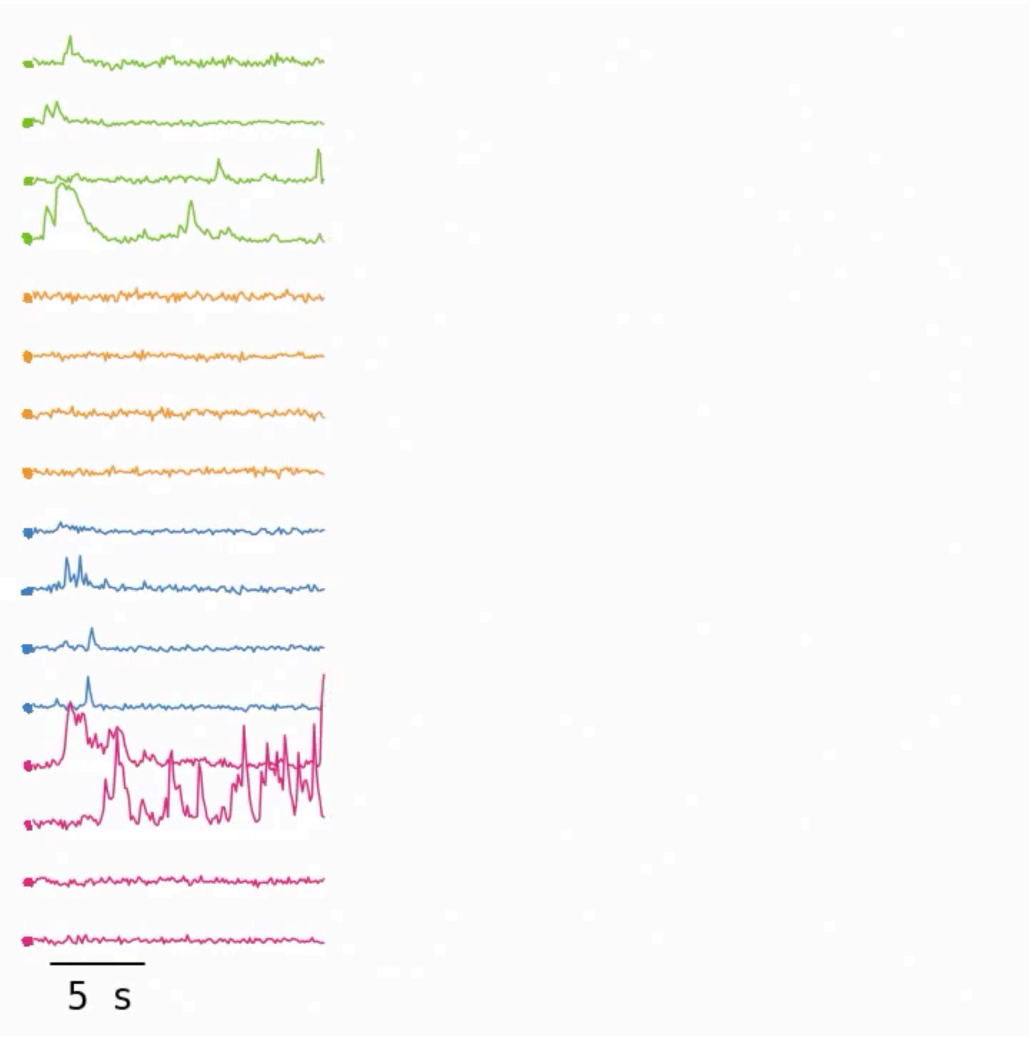
4:30 PM · Oct 14, 2021 · Twitter Web App

15 Retweets **5** Quote Tweets **130** Likes

Why study learning?



Apple M1 chip



Sonifriew et al, eLife (2016)

Why study learning?

My totally subjective answer:

- Explaining what every single neuron is doing and how they contribute to computations *may be impossible*.

- But we may *hope* to someday write down (understand) the rules of brain learning.

What we will cover

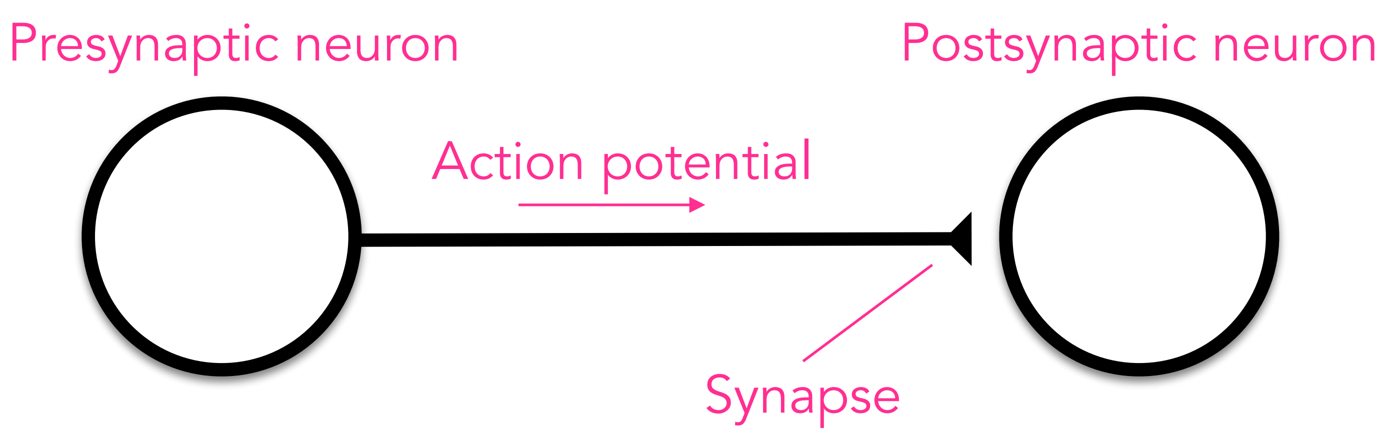
1. **Synapses**
   - What is a synapse?
   - How do synapses work?
2. **Synaptic plasticity**
   - Classic rate-based models of plasticity, Hebbian learning.
   - Spike-timing dependent plasticity.
3. **Associative memories and attractor networks**
   - The hippocampus
   - Hopfield networks
4. **Links to artificial neural networks**
   - The backpropagation rule
   - Mapping deep learning to neurobiology

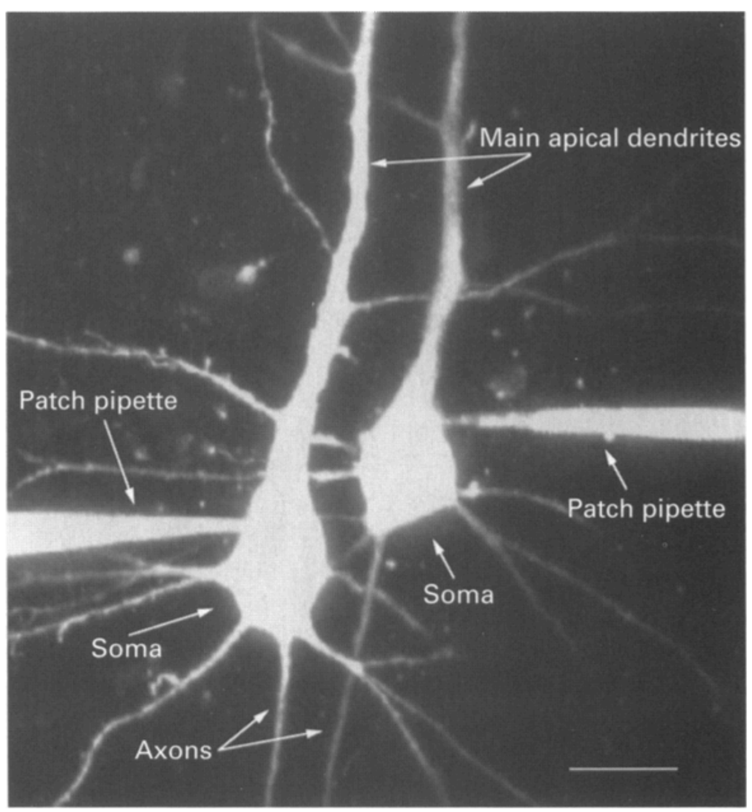
1. Synapses

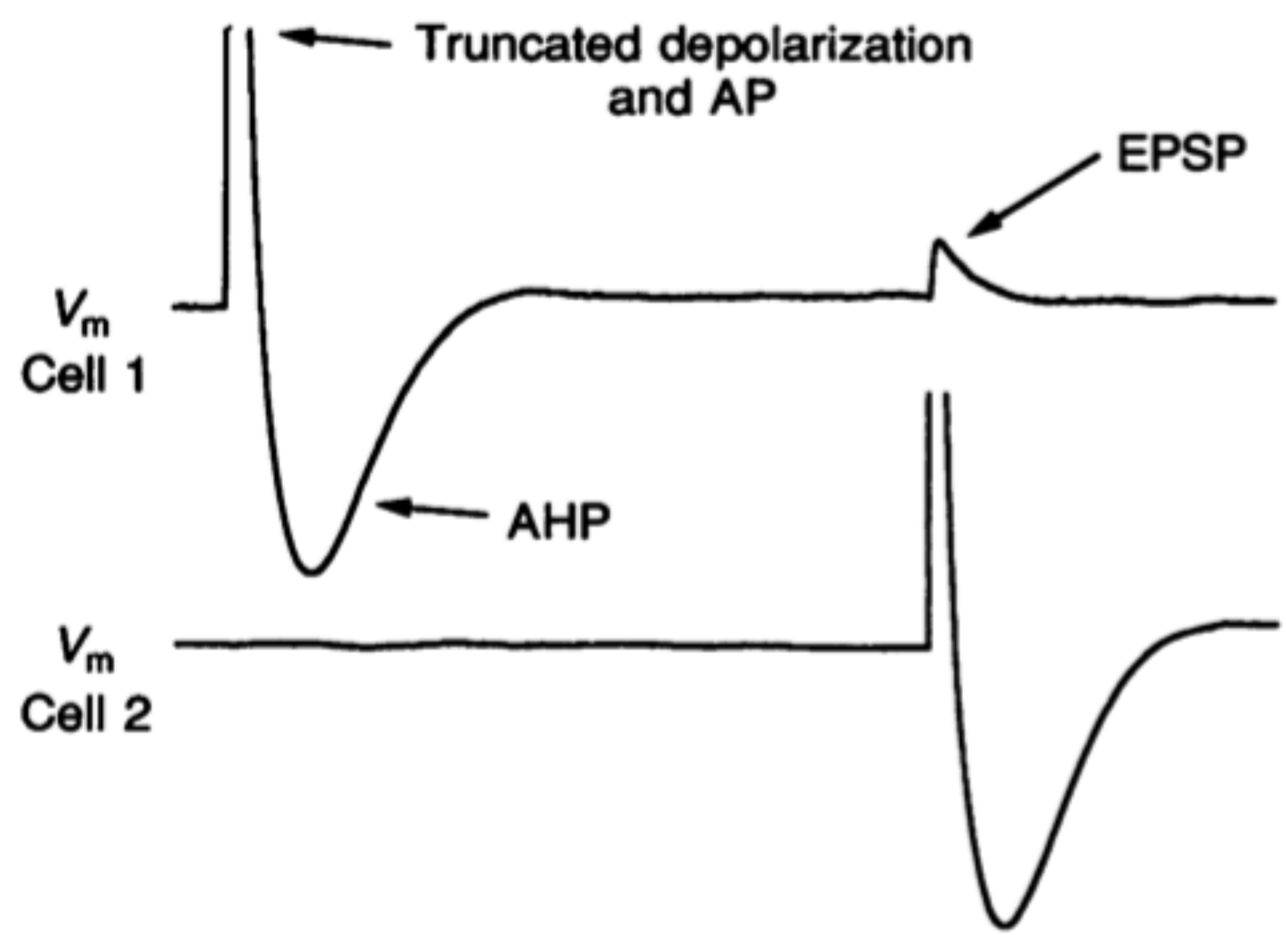
What is a synapse?

- 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.
- From a computational 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).

What is a synapse?

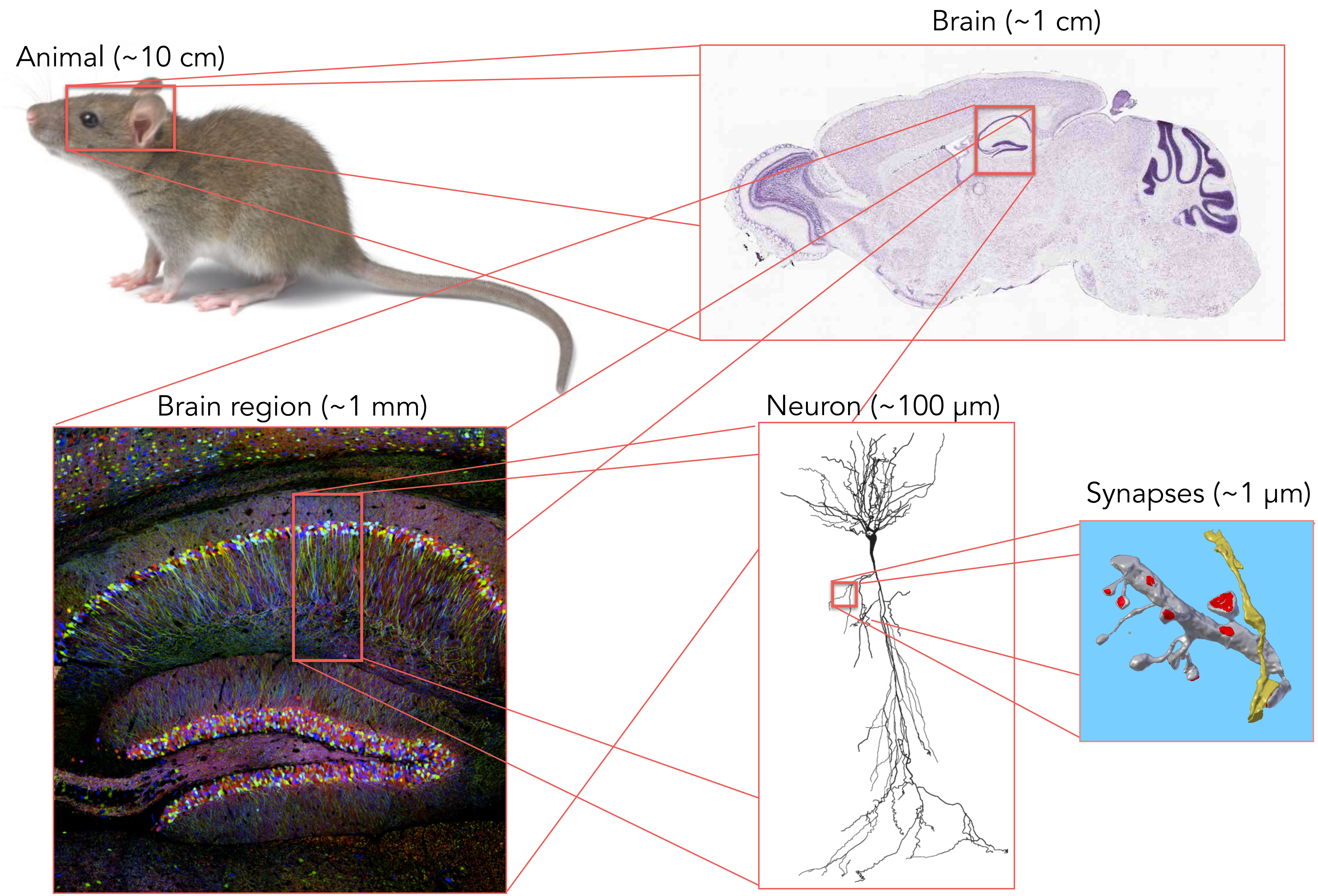






Markram et al, *J Physiol* (1997)

Zooming in on synapses



How do synapses work?

Axon
(presynaptic action potential)

Chemical
signalling

Dendrite
(postsynaptic potential)

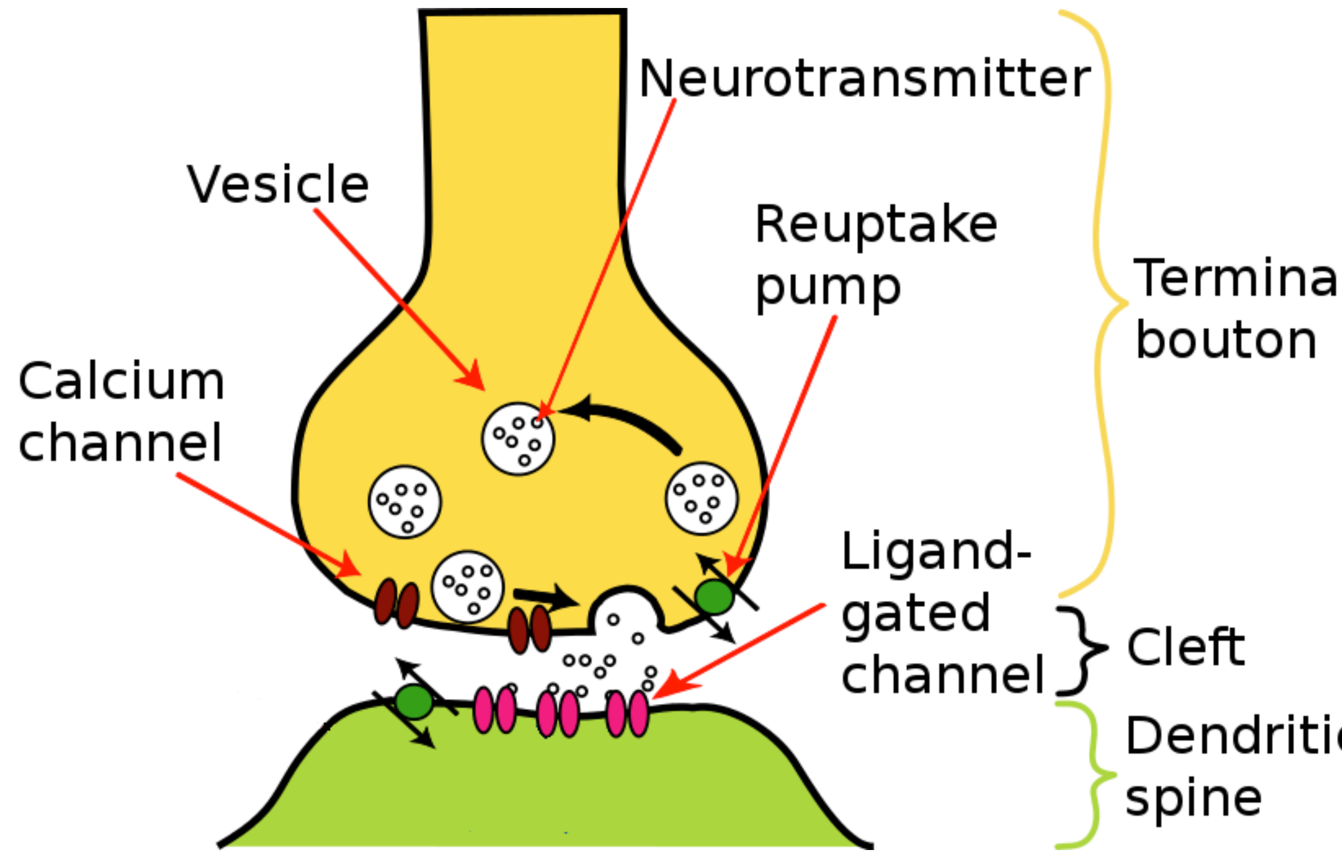
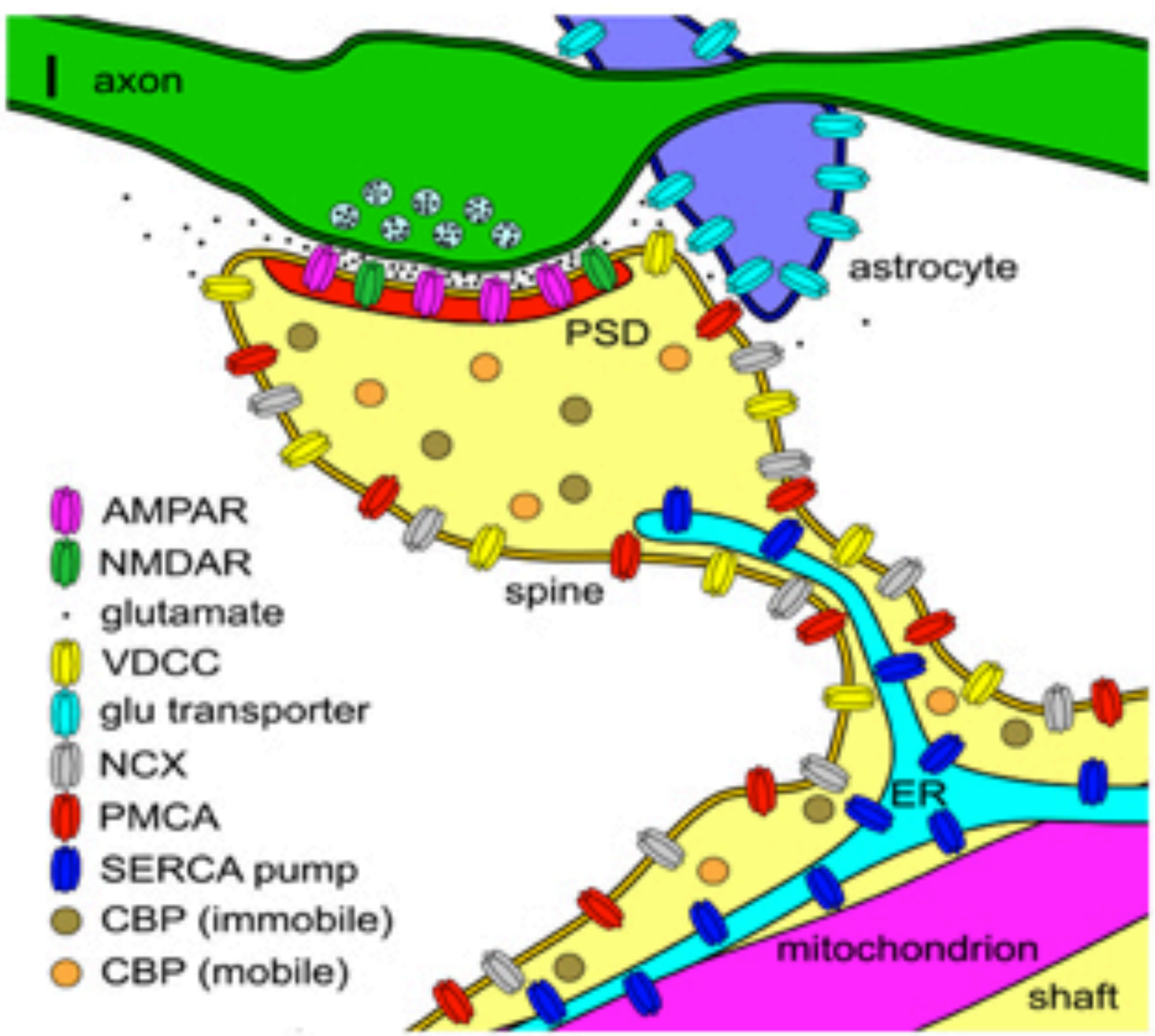
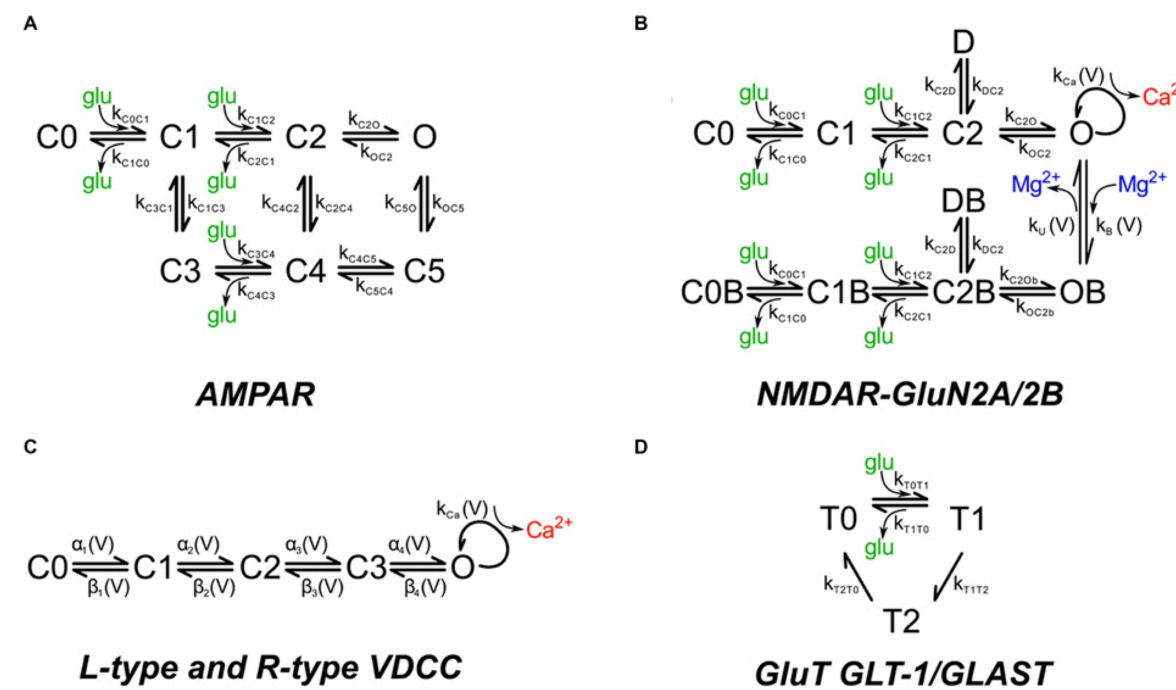


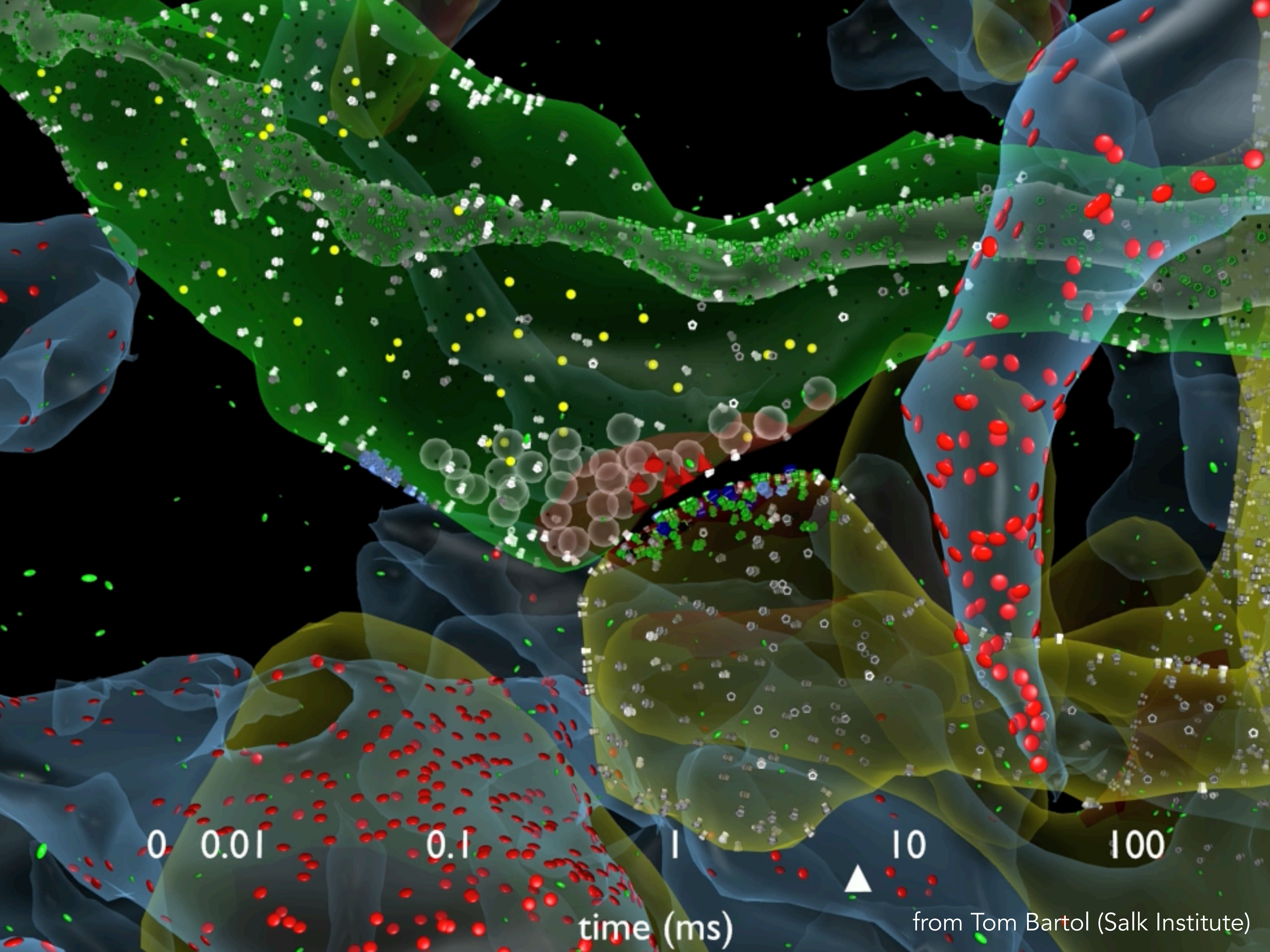
Image from Wikipedia (modified by C Houghton)

MCell simulation of synaptic release



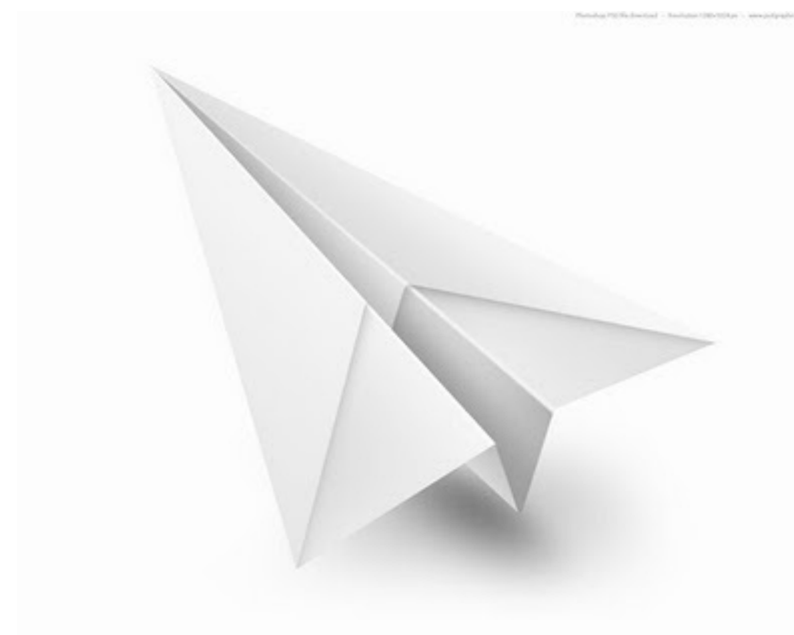
Bartol et al, *Frontiers Syn Neuro* (2015)




0
0.01
0.1
1
10
100
time (ms)
from Tom Bartol (Salk Institute)

How detailed should a model be?

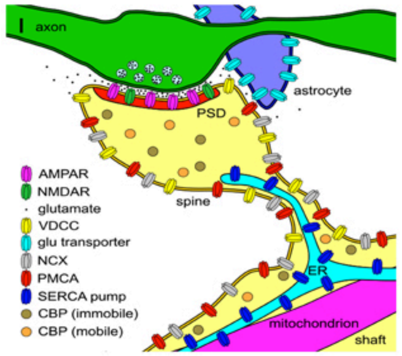
Details vs realism



c.f. Brette, *PLoS Comput Biol*, 2015

Models

Abstract ⟷ Realistic



Abstract models		**Realistic models**
Simple	vs	Detailed
Hard to relate to biology	vs	Contains stuff you could measure
Few parameters	vs	Lots of parameters
Fast simulation	vs	Slow simulation
Mathematical analysis	vs	Intractable
Generic	vs	Specific

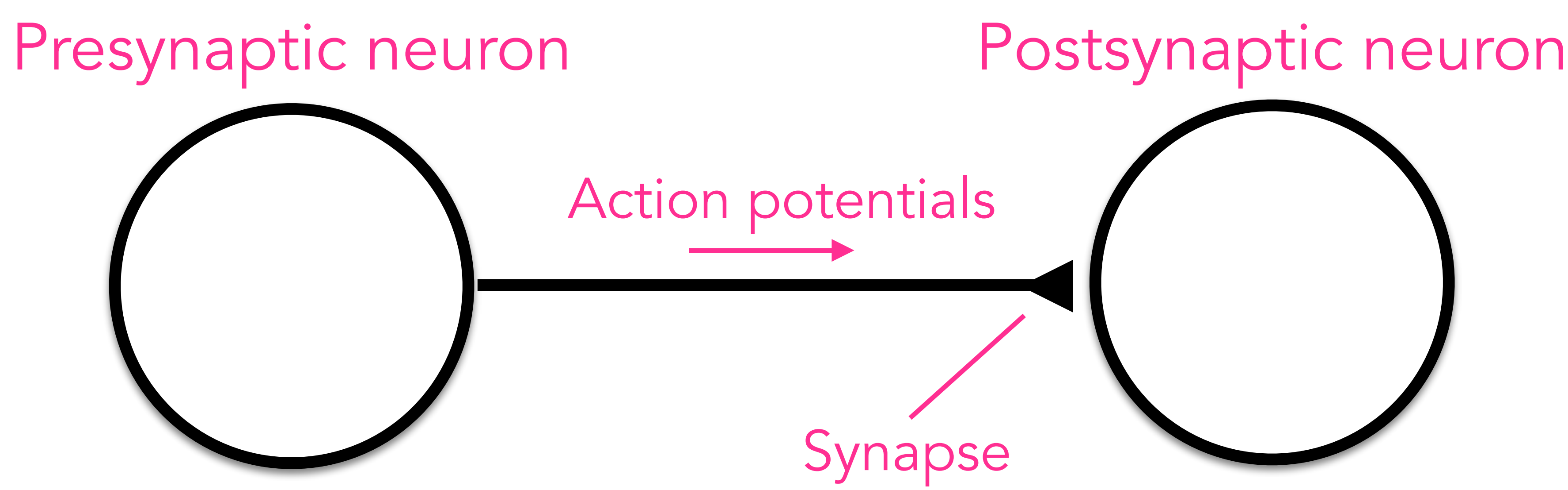
Summary on synapses

- 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 complicated molecular machines.
- We can model them at multiple levels of granularity, as appropriate for the task at hand.

2. 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.



Long-term synaptic plasticity

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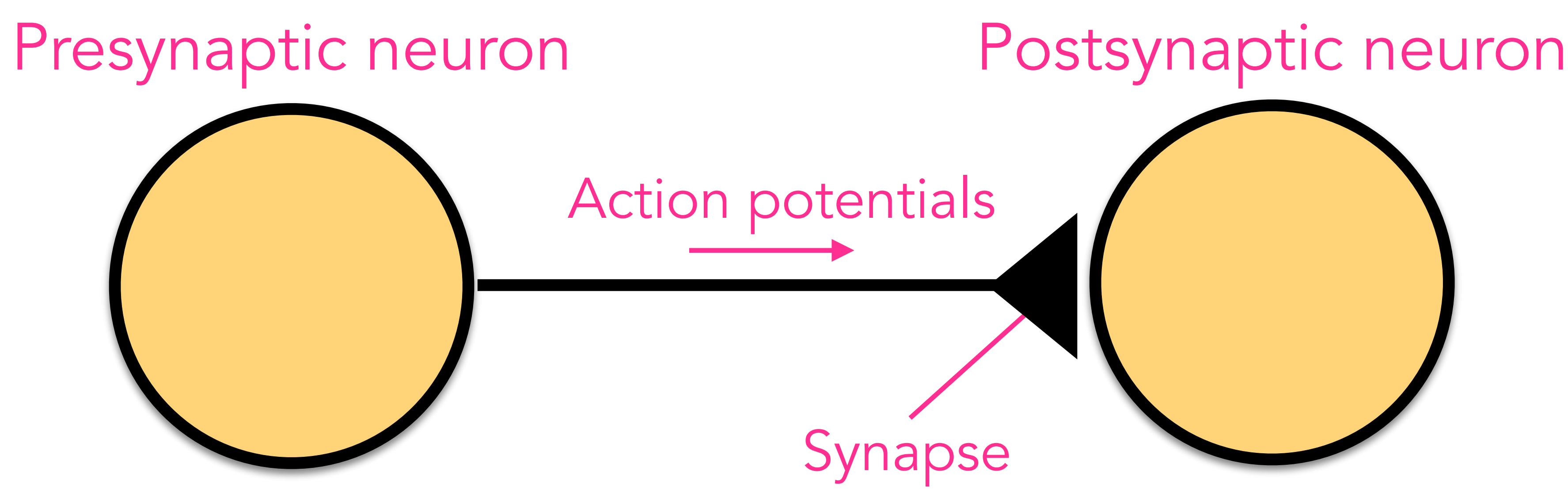
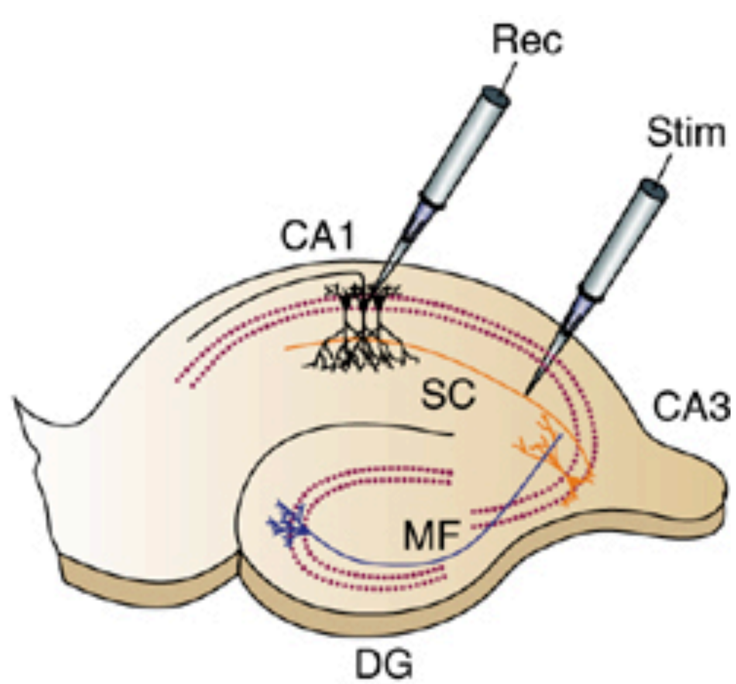
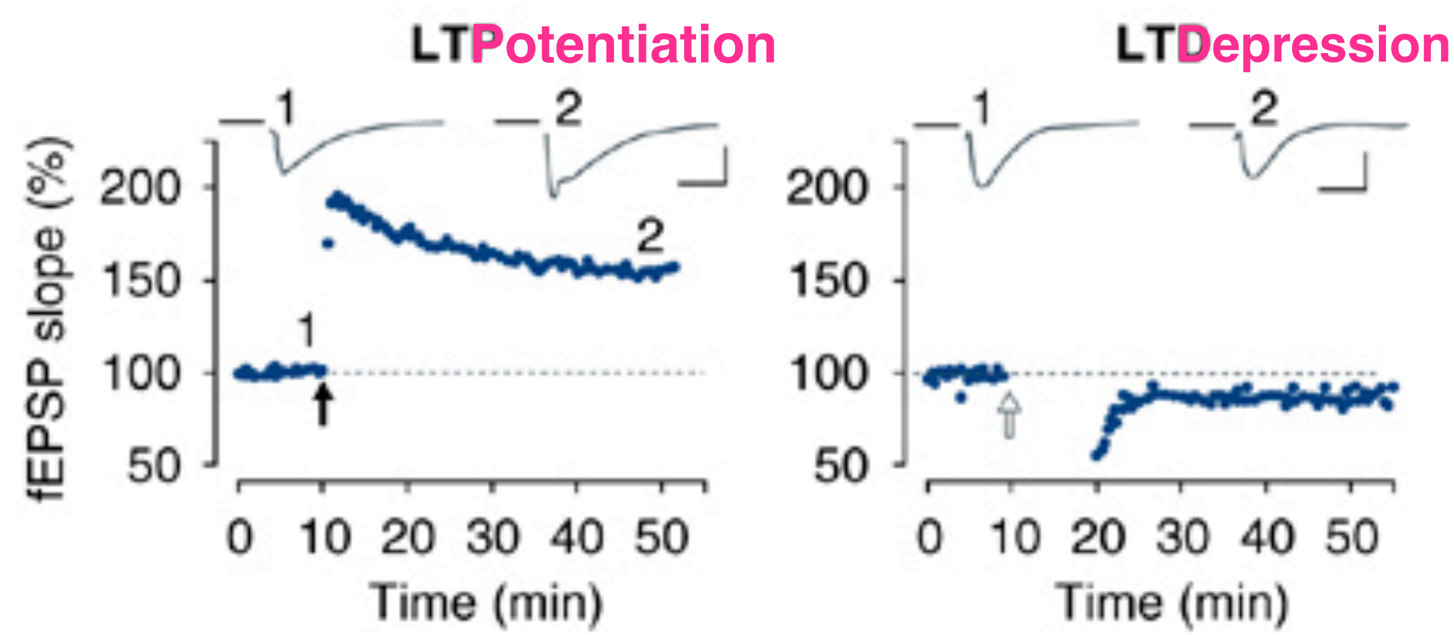






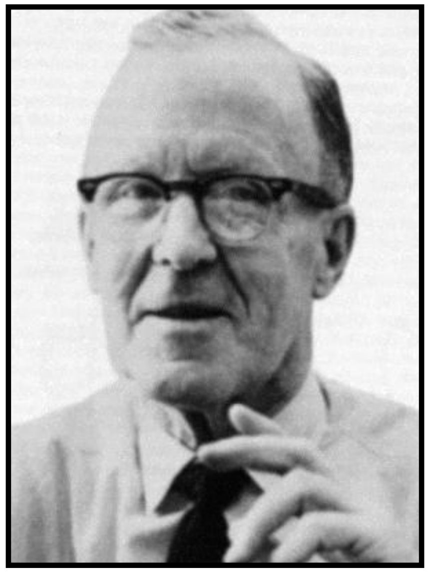
Learning and memory via synaptic plasticity

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

- 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

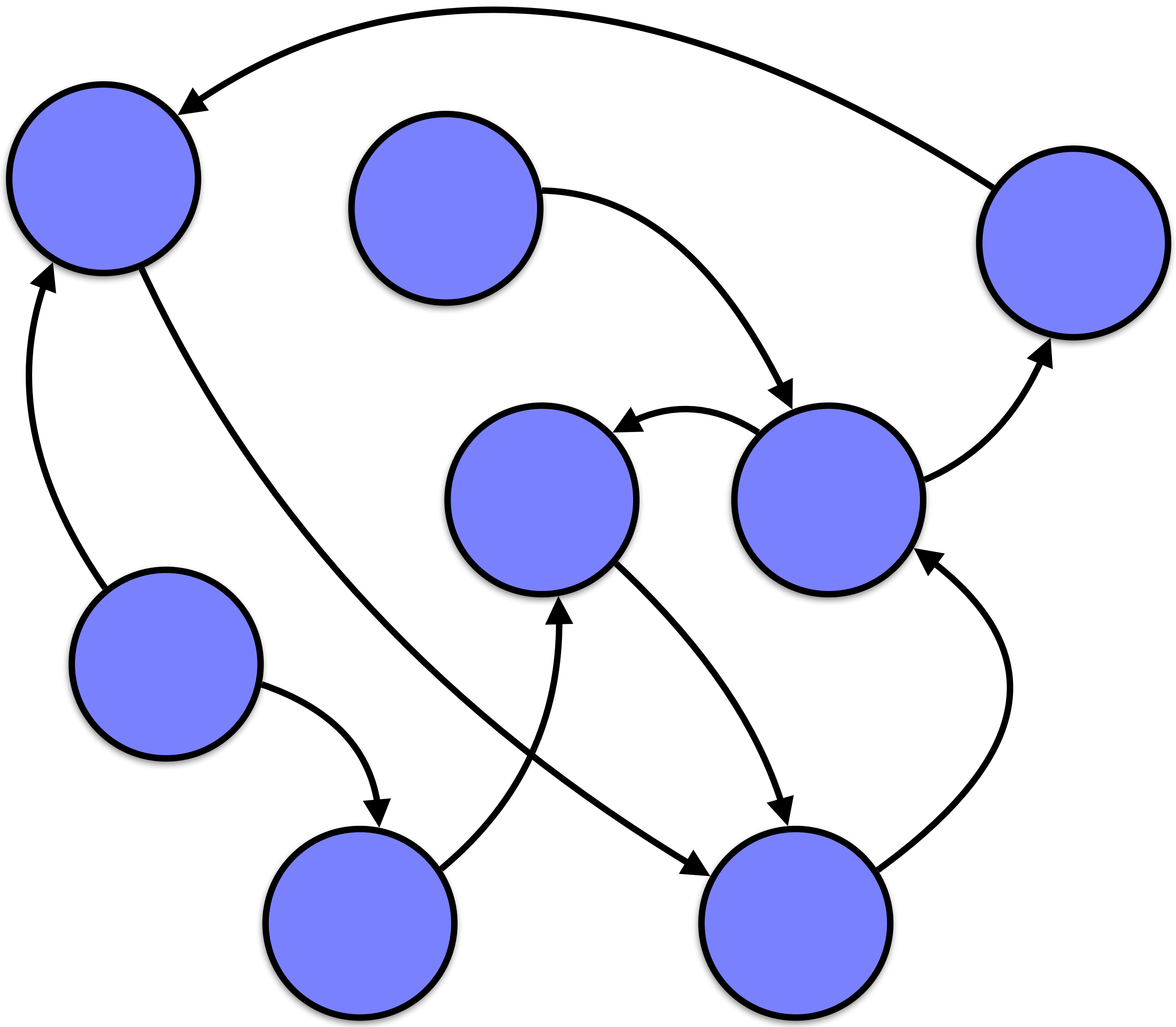


Donald Hebb

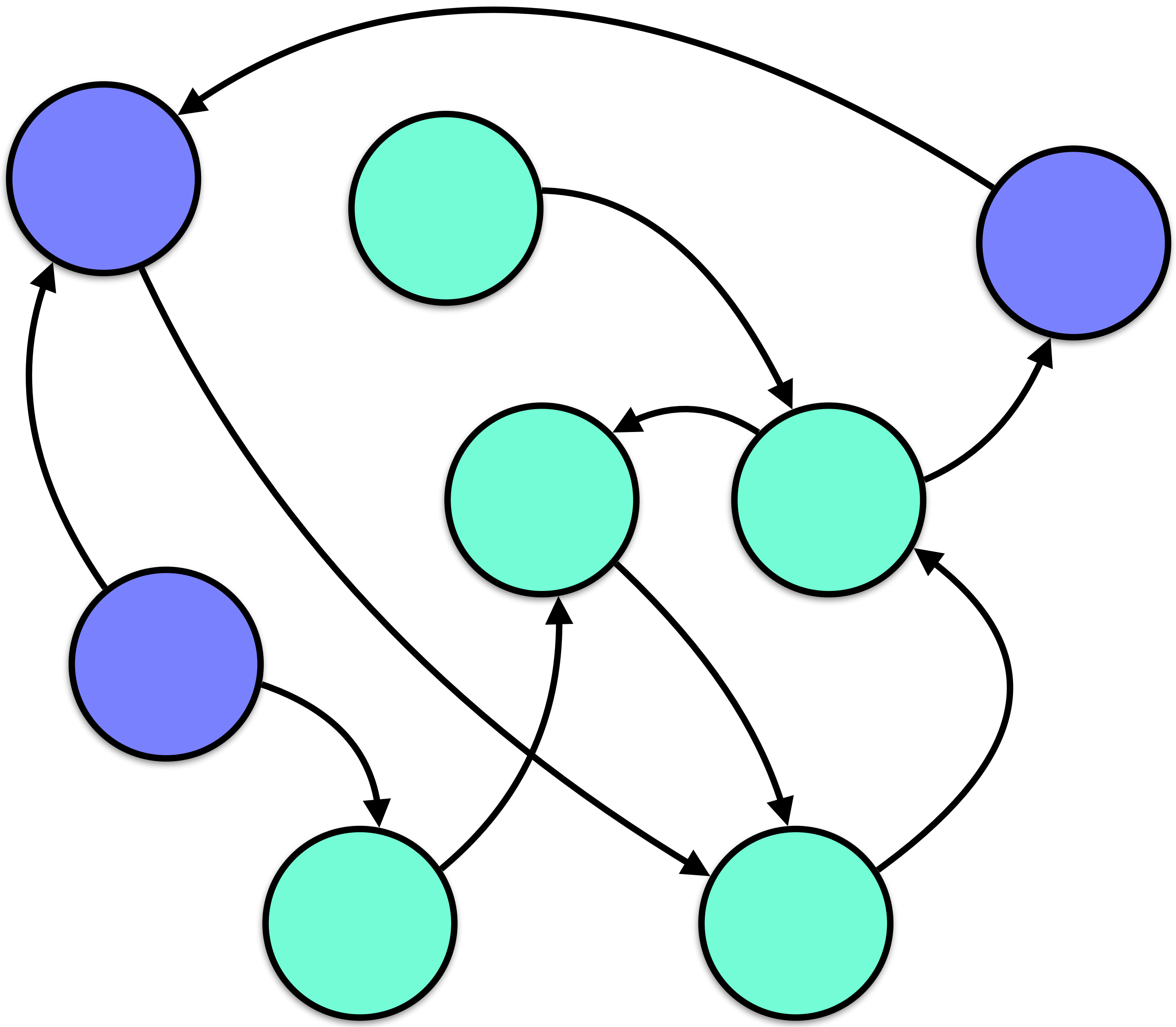
"When an axon of cell A is near enough to excite a cell B and repeatedly or persistently takes part in firing it, some growth process or metabolic change takes place in one or both cells such that A's efficiency, as one of the cells firing B, is increased."
— Donald Hebb (1949)

a.k.a. "neurons that fire together wire together."

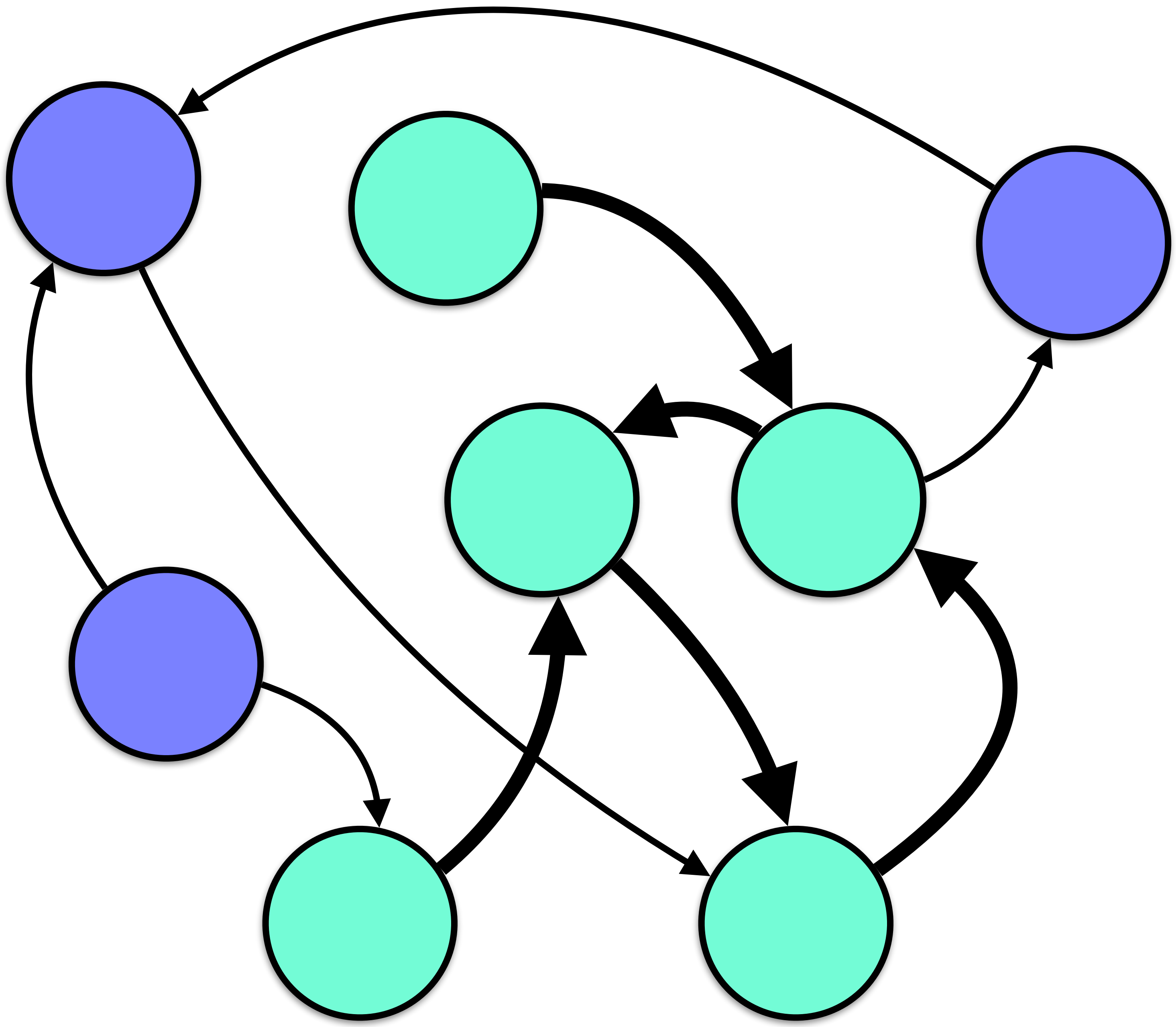
Hebbian plasticity



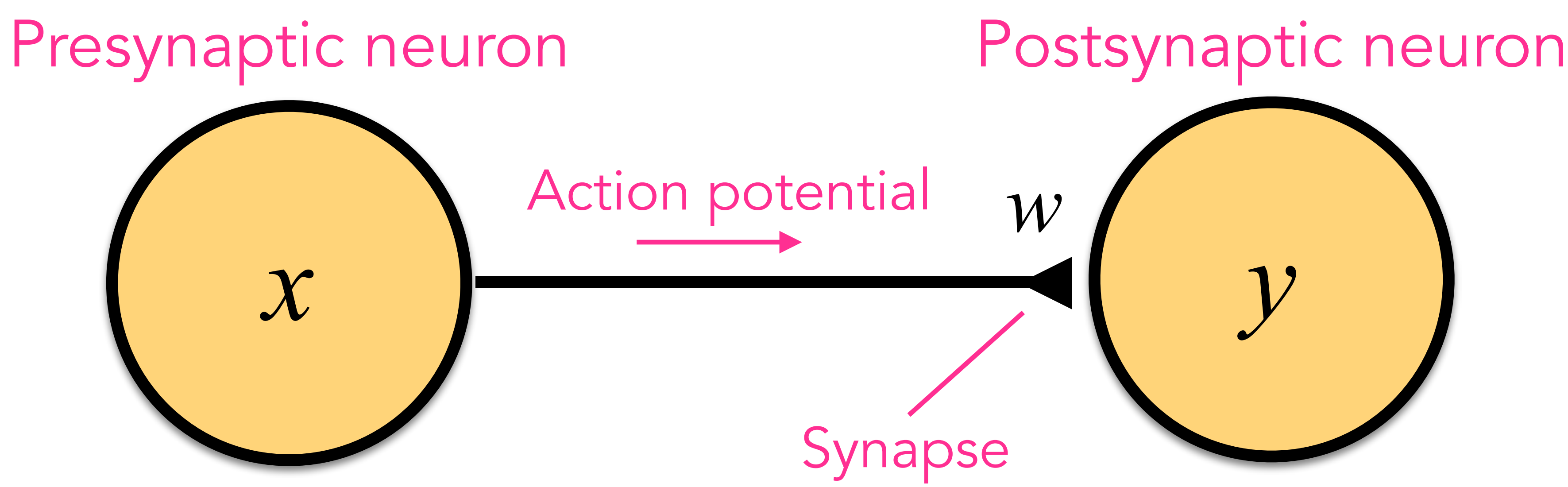
Hebbian plasticity



Hebbian plasticity



Hebbian plasticity



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

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

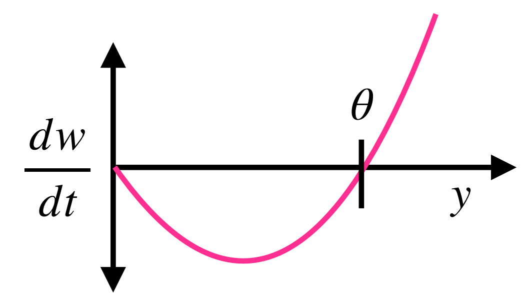
Note that dynamics are unstable: $\boldsymbol{w}$ and therefor y grow without bound.

How to stabilise plasticity?

Idea 1: BCM (Bienenstock, Cooper & Munro, 1982)

Modify the basic Hebbian rule by including a postsynaptic threshold for plasticity:

$$\frac{dw}{dt} = \eta_w x y (y - \theta)$$



The key idea for stability is that the threshold is also plastic:

$$\frac{d\theta}{dt} = \eta_\theta (y^2 - \theta_\infty)$$

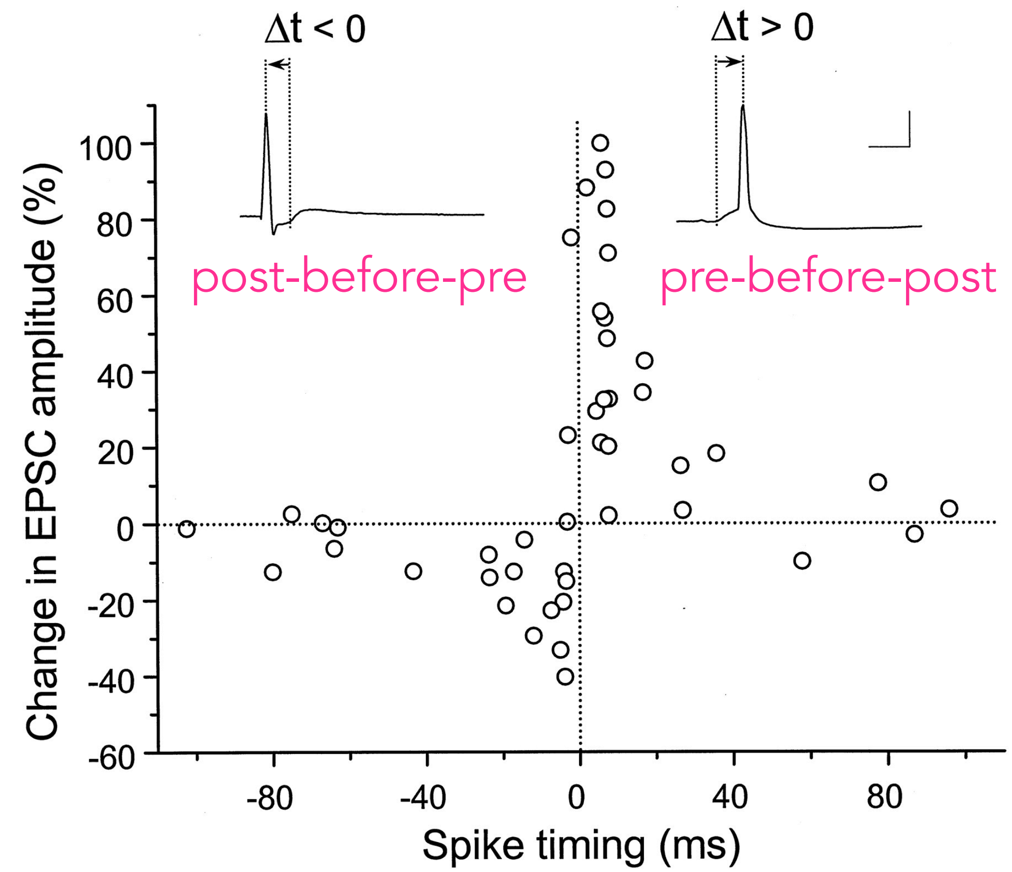
Idea 2: Homeostatic plasticity/synaptic scaling (Turrigiano et al, 1998)

Make the weights scale multiplicatively on a slow timescale, to keep postsynaptic activity at some target level:

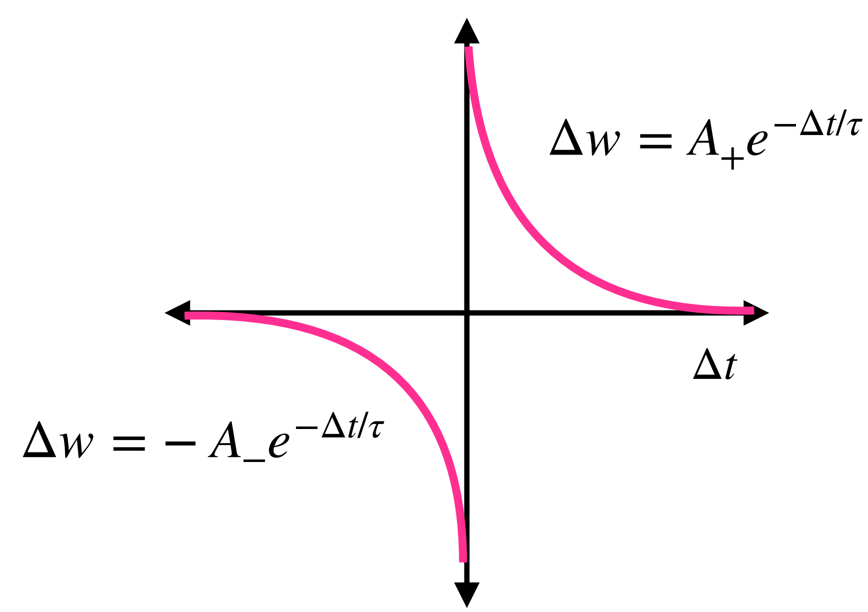
$$\frac{dw}{dt} = \eta_{ss} w (y_{target} - y)$$

Spike-timing-dependent plasticity

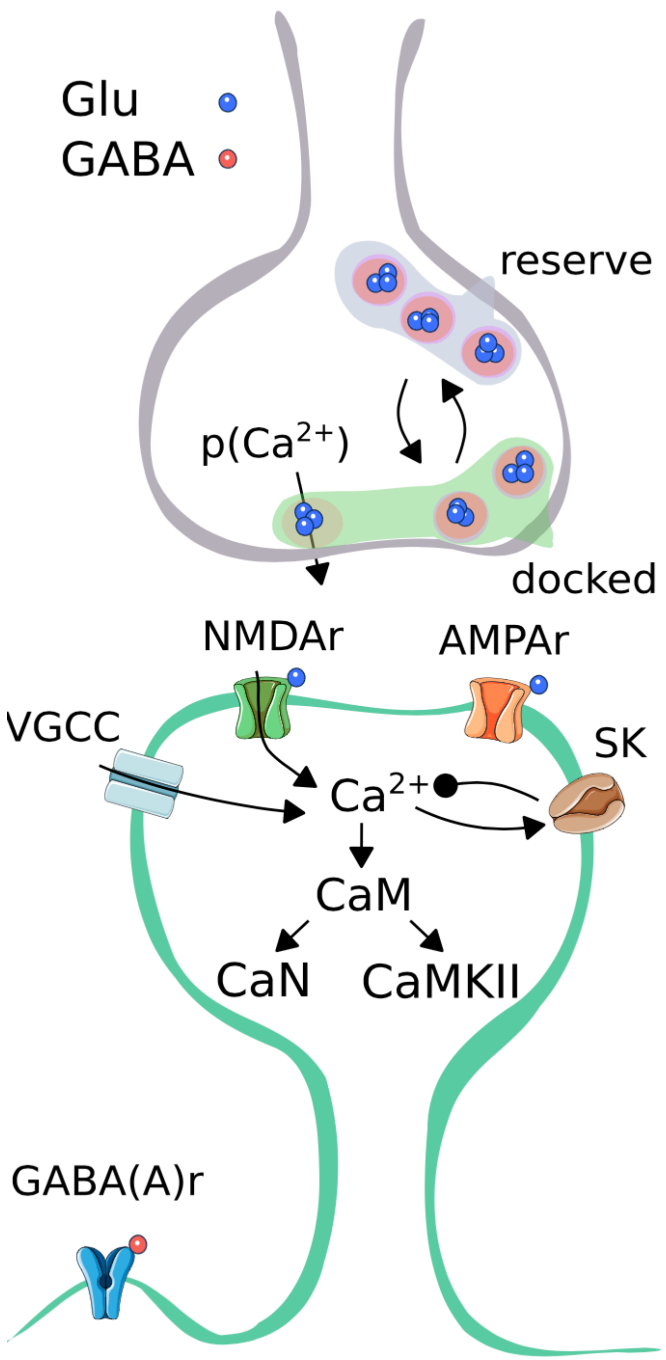
- STDP (discovered in late 1990s) encapsulates the idea of causality implied by Hebb:
  - if presynaptic spike A happened just *before* postsynaptic spike B, A *could have caused* B.
  - on the other hand, if presynaptic spike A happened just *after* postsynaptic spike B, A *could not have caused* B.
- 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*

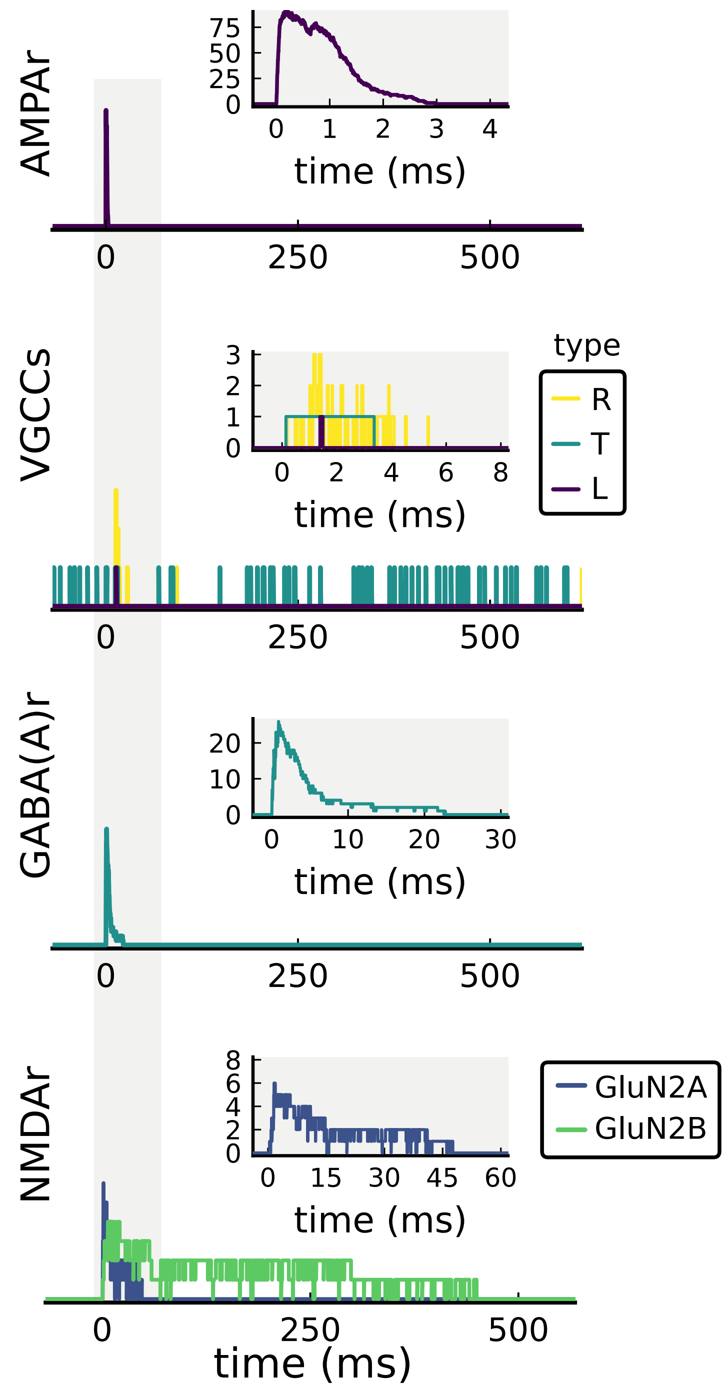


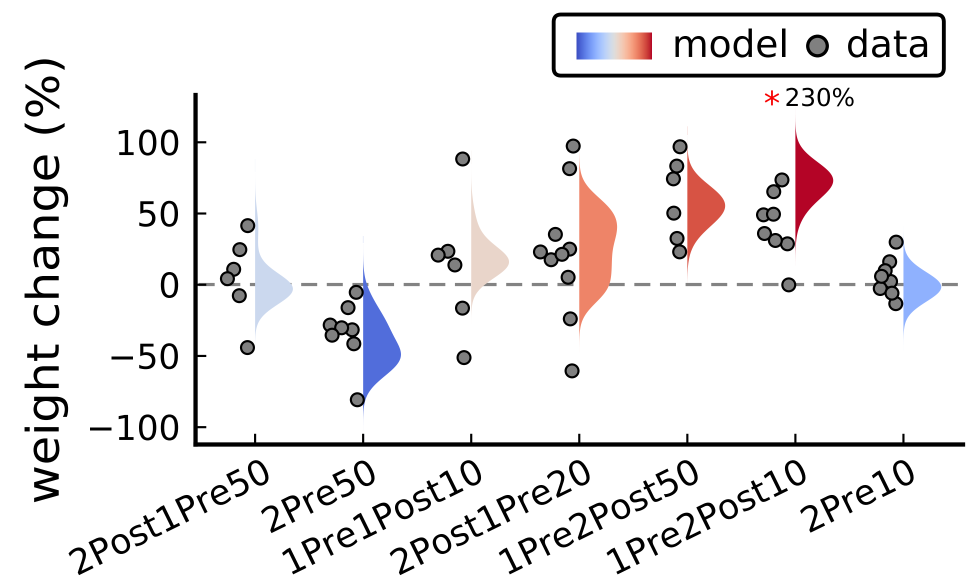
Bi & Poo, *J Neurosci* (1998)



Adding more biology



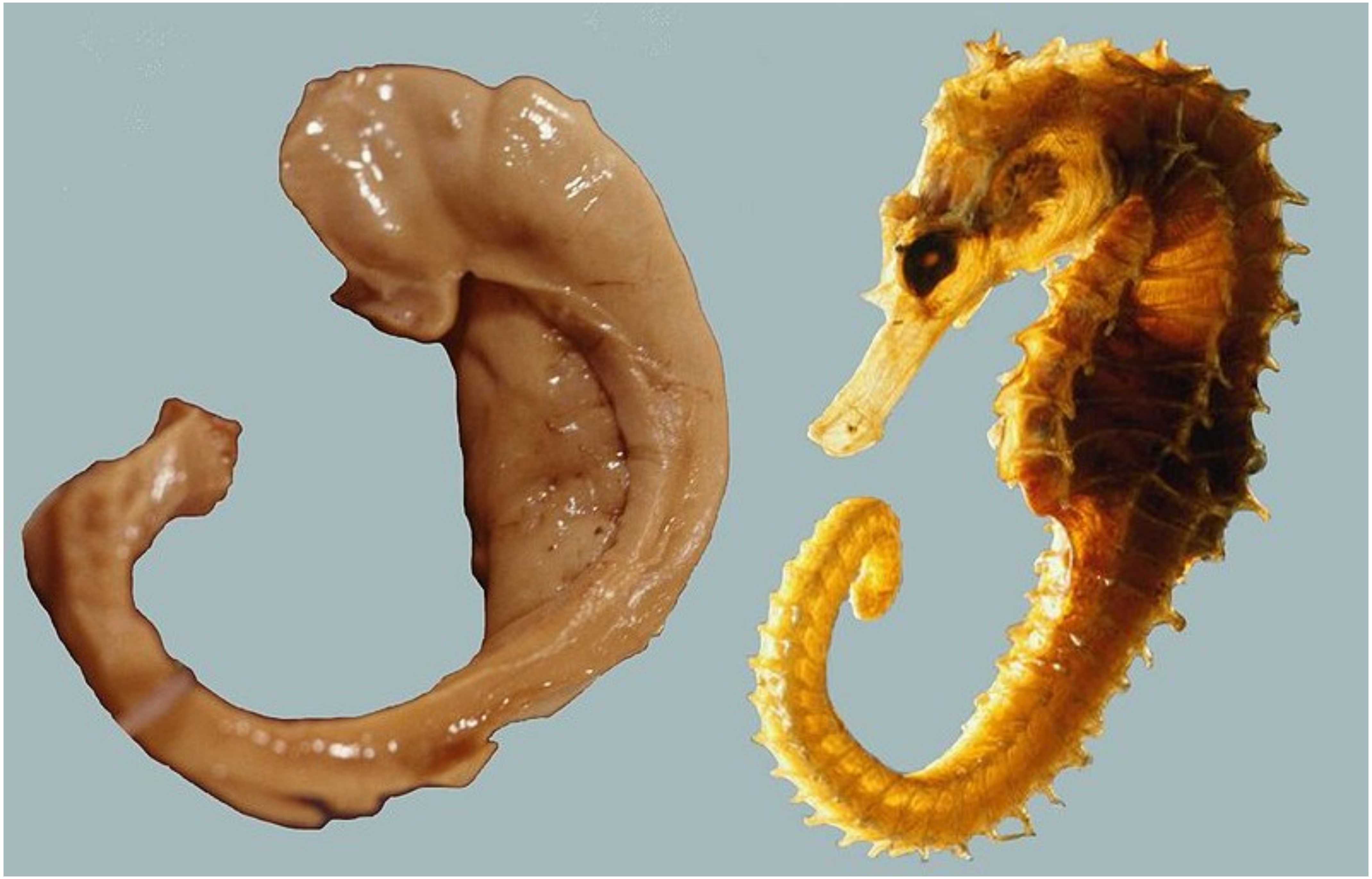




Rodrigues, Tigaret, Marie, O'Donnell, Veltz, *eLife* (2023)

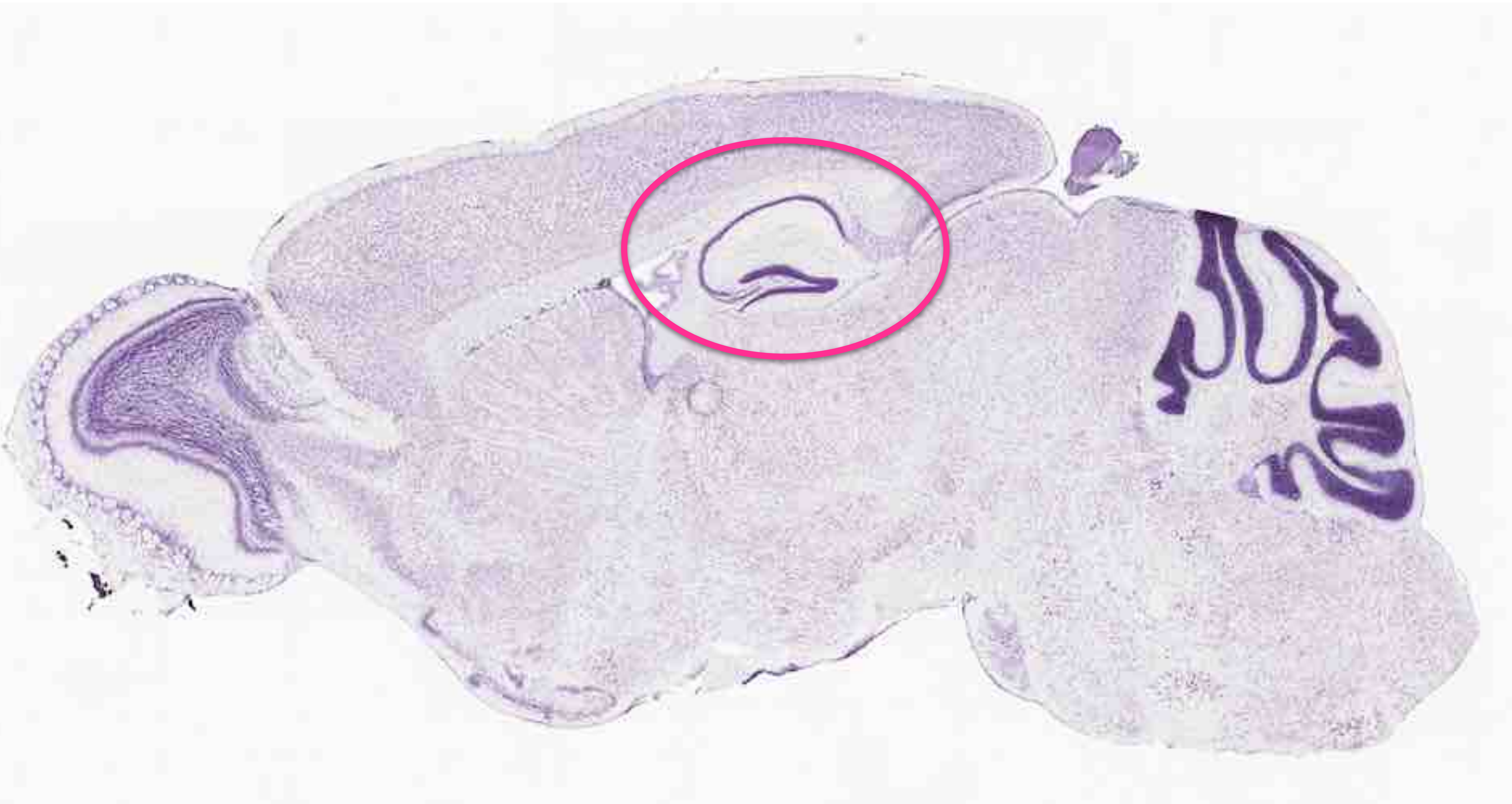
3. Attractor networks

Hippocampus, from the greek words for “horse" and “sea-monster”



https://en.wikipedia.org/wiki/Hippocampus#/media/File:Hippocampus_and_seahorse_cropped.JPG

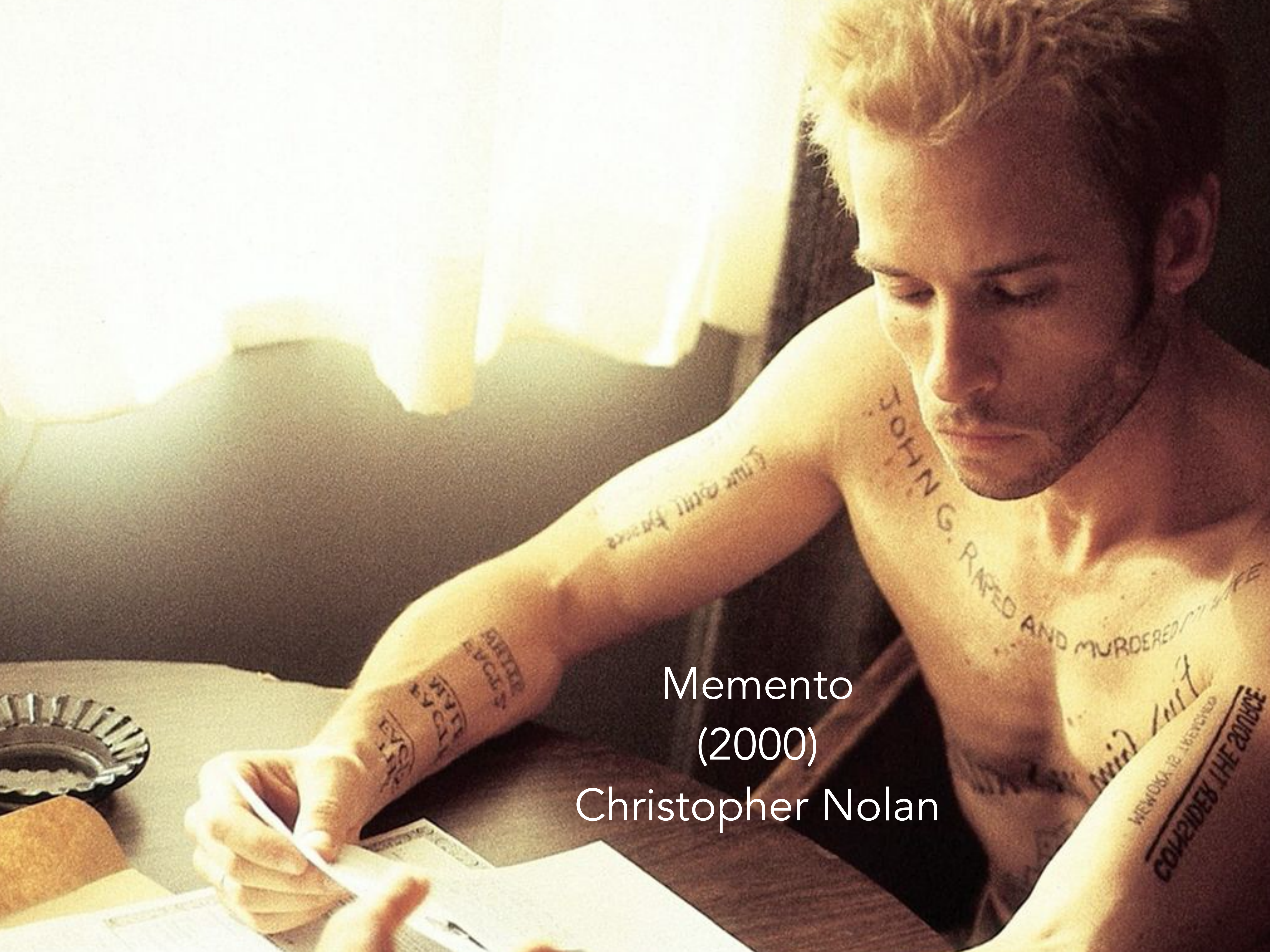
Anatomy of the hippocampus



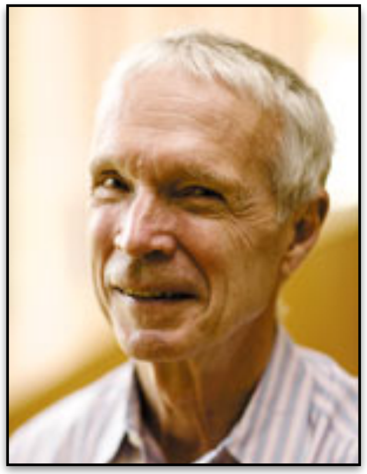
https://mouse.brain-map.org

Hippocampus and memory

- Patient HM (who had his hippocampus surgically removed) could not form new long-term memories, and also had time-limited retrograde amnesia.
- The hippocampus is specifically needed for encoding new episodic memories, but is not necessary for other memories (e.g. procedural).
- Memory encoding requires synaptic plasticity in the hippocampus.


JOHN G. RAPED AND MURDERED
Memento
(2000)
Christopher Nolan

Hopfield networks



John Hopfield

- A basic model of associative memory recall, as in the CA3 region of the hippocampus.
- A Hopfield network is a recurrent network of "neurons" with synaptic connections set so to store memories as attractors.
- Proposed by John Hopfield in 1982.
- The network state evolves dynamically, typically toward some "attractor" state.
- A simple Hebb-like synaptic plasticity rule can imprint attractors in the network weights.
- Incredibly influential model in the history of computational neuroscience (attracted a bunch of physicists to the field).

Hopfield networks

- Network state evolves as:

$$\text{if } \sum_{j \neq i}^{N} [w_{ij} x_j(t) - \theta] > 0 \qquad \text{then } x_i \rightarrow +1$$

$$\text{otherwise } x_i \rightarrow -1$$

- There are two common flavours: synchronous or asynchronous updates.

- The weights follow a Hebbian-like rule:

$$w_{ij} = \frac{1}{N_{patterns}} \sum_{a}^{N_{patterns}} x_i^a x_j^a$$

- Usually the weights are symmetric: $w_{ij} = w_{ji}$
  and the connectivity is all-to-all.

- The network dynamics evolve to minimise an "energy":

$$E = -\frac{1}{2} \sum_{ij} w_{ij} x_i x_j$$

Hopfield network dynamics

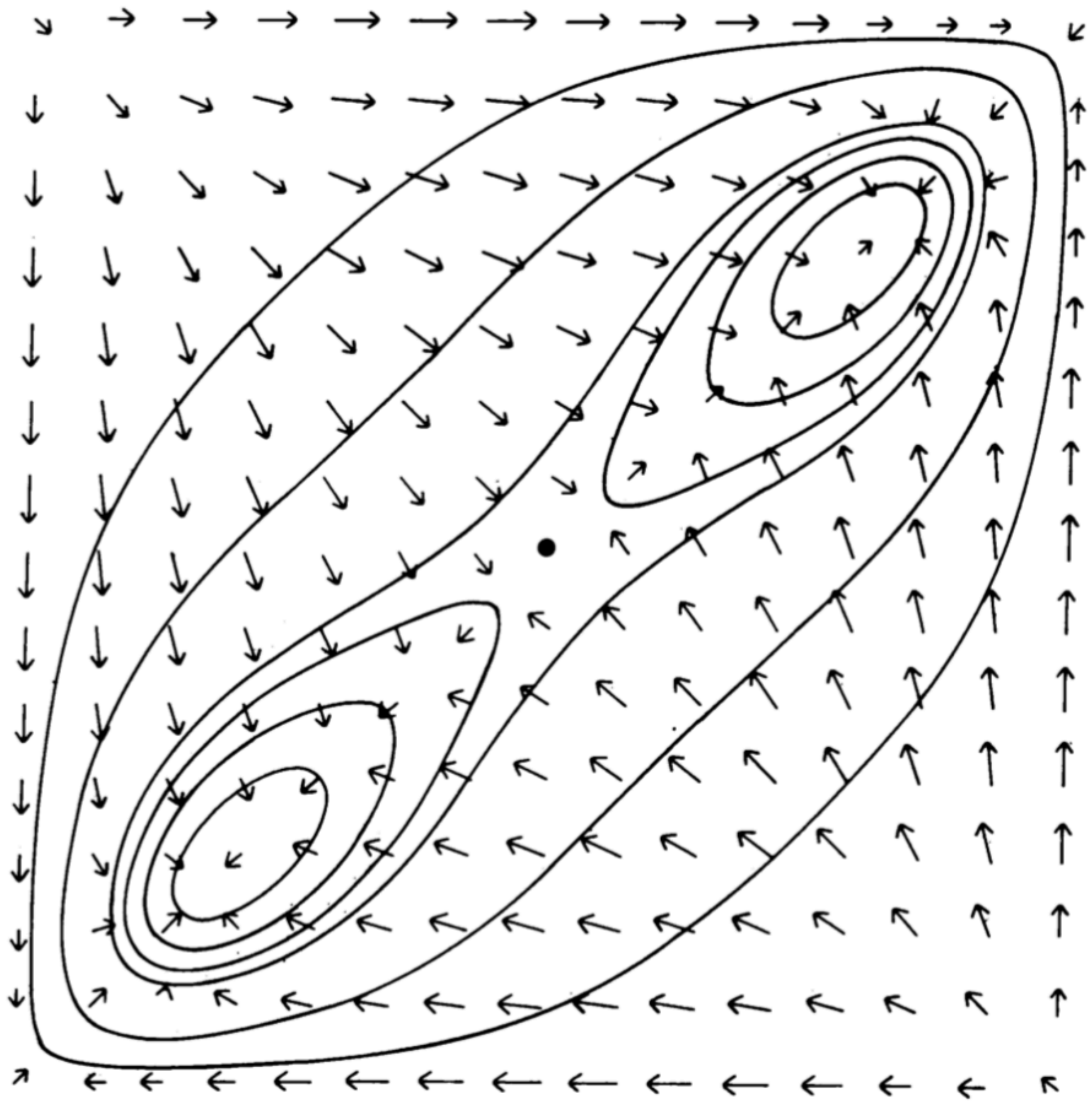


FIG. 3. An energy contour map for a two-neuron, two-stable-state system. The ordinate and abscissa are the outputs of the two neurons. Stable states are located near the lower left and upper right corners, and unstable extrema at the other two corners. The arrows show the motion of the state from Eq. 5. This motion is not in general perpendicular to the energy contours. The system parameters are $T_{12} = T_{21} = 1$, $\lambda = 1.4$, and $g(u) = (2/\pi)\tan^{-1}(\pi\lambda u/2)$. Energy contours are 0.449, 0.156, 0.017, −0.003, −0.023, and −0.041.

Hopfield, *PNAS* 1984

- Each of local minima in the energy landscape is known as an "attractor".
- The network can do pattern completion: retrieving the full pattern from a partial cue.
- The capacity of the network, or maximum number of attractors, is ~$0.14N$.

Content-addressable memory in Hopfield networks

Hertz, Krogh & Palmer, *Introduction to the Theory of Neural Computation* (1991)

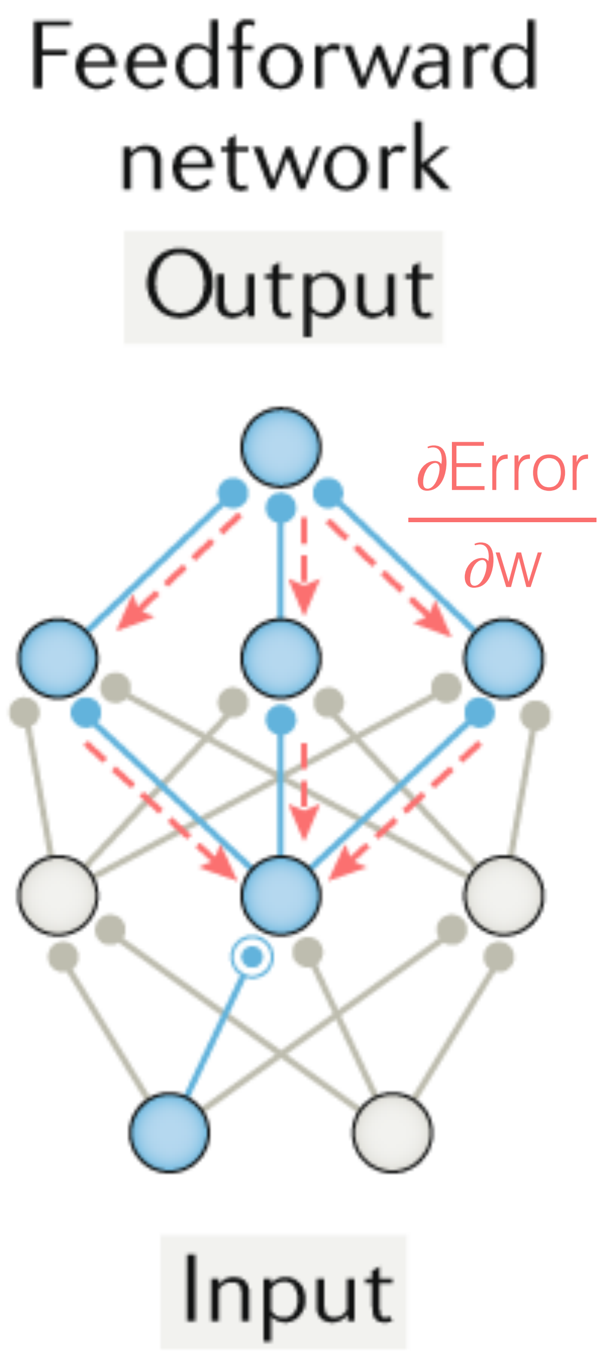
4. Links between learning in biological and artificial neural networks

The back-propagation learning rule

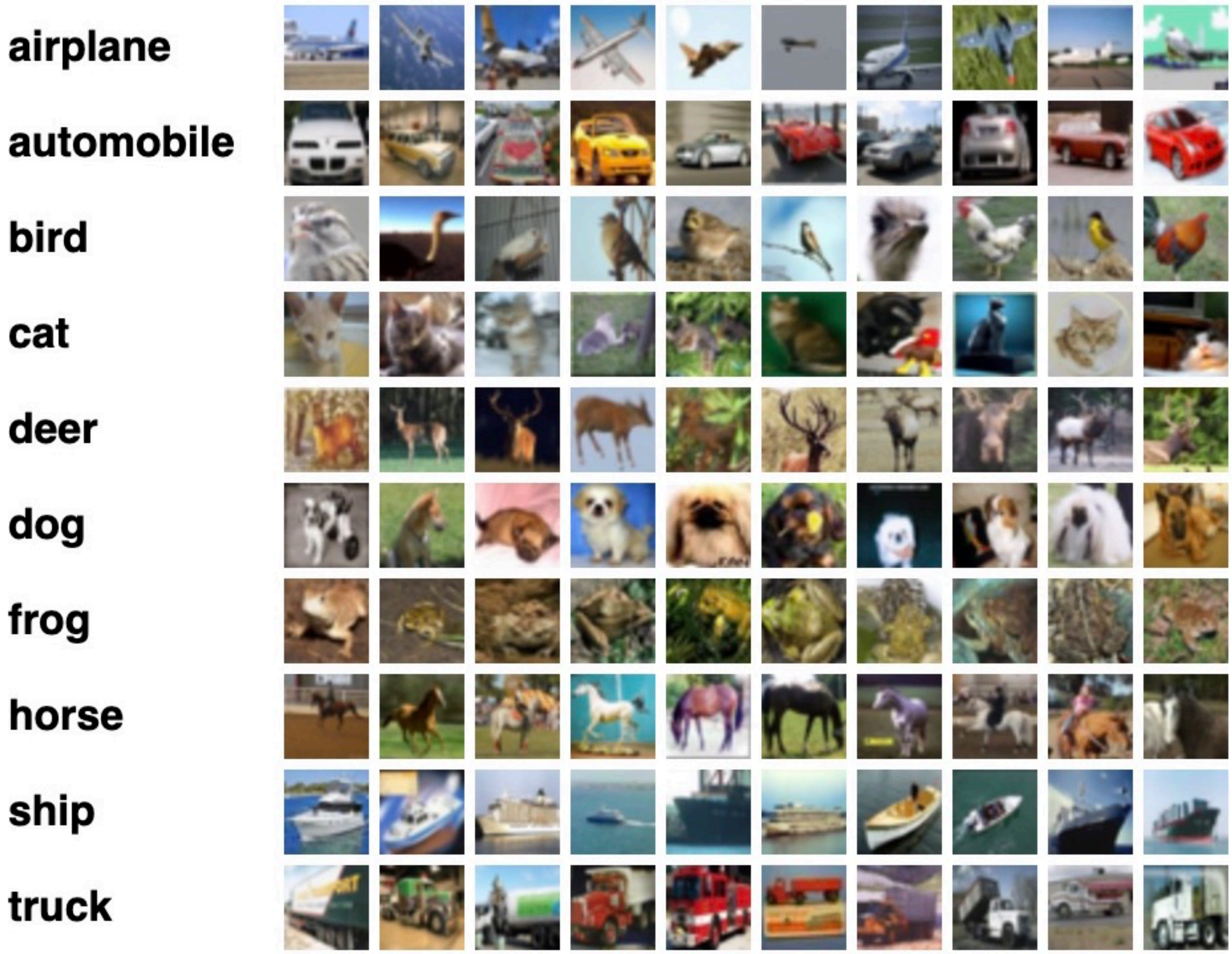
- Unlike Hebb's rule, in machine learning artificial neural networks are trained via *supervised* learning: performance errors are fed back into the system to adjust connection weights, so reducing future errors.

- The main method for doing this is called back-propagation (basically the calculus chain rule).

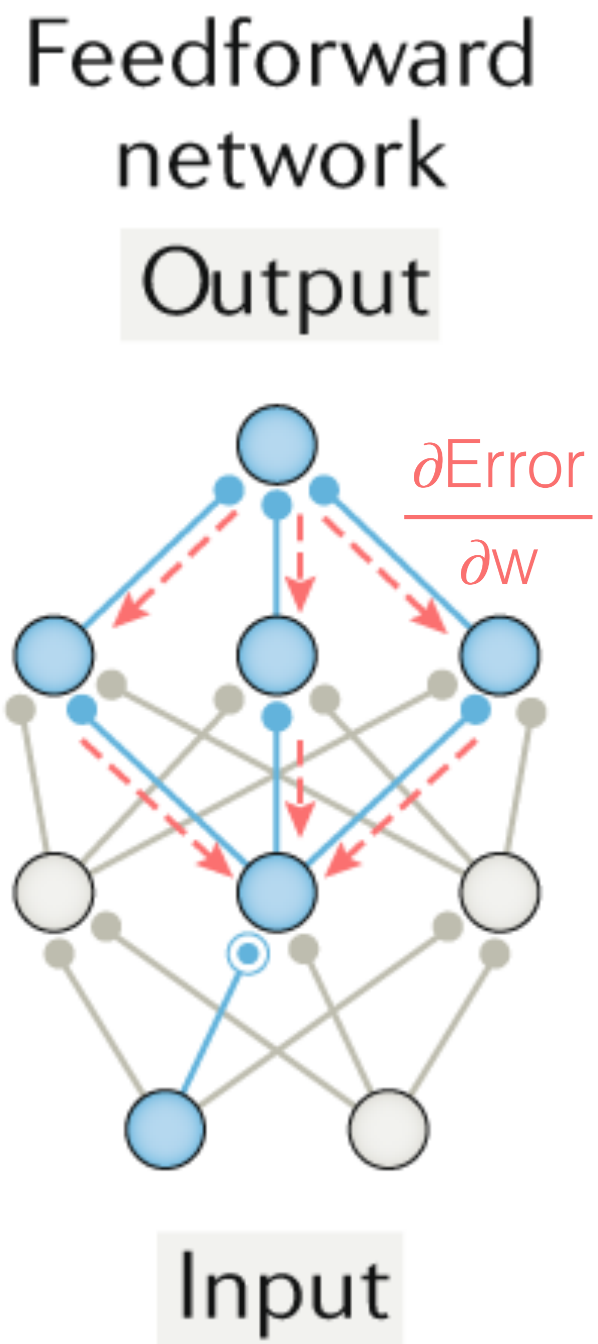
The back-propagation learning rule



Deep learning is everywhere



Issues with backprop as a model of brain learning



- Plasticity rules at each synapse needs non-local information.
- Requires symmetry in backwards and forwards weights.
- Error signals need to contain sign information (+/- error).
- Feedforward and feedback 'passes' need to be separated in time.

Example ideas for biologically plausible backprop

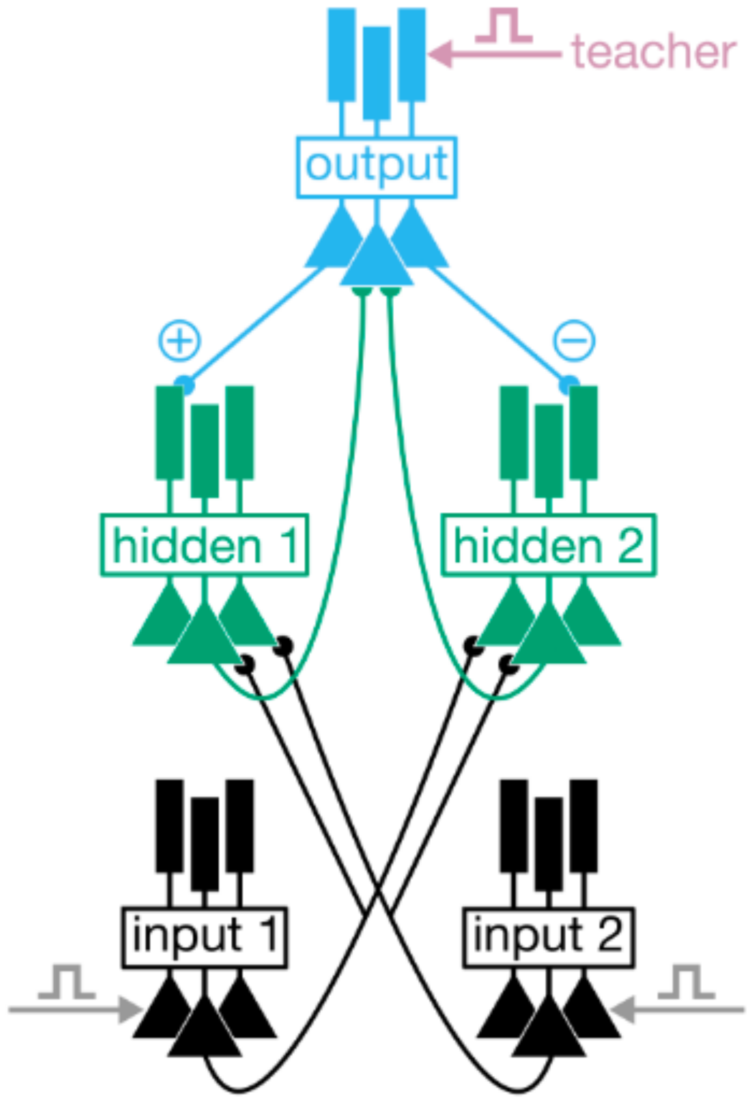
Feedback alignment *even by random feedback*.

"B pushes the network in roughly the same direction as backprop would"

$$\mathbf{e}^T W B \mathbf{e} > 0$$

Lillicrap et al, *Nature Comms* (2016)

Feedback signals to distal dendrites, driving bursts that gate plasticity.



Payeur et al, *Nature Neurosci* (2021)

Deep learning and brains summary

- Backpropagation of error gradients is a ubiquitous algorithm for learning in artificial neural networks.
- But the basic version in not biologically realistic.
- Current research is trying to dream up biologically plausible alternatives that approximate backprop.
- However the idea that the brain even learns by supervised gradient descent is controversial! Maybe *unsupervised* or *reinforcement learning* rules are all it takes.

Overall session summary

1. What synapses and plasticity are and how we think they underly brain learning.

2. Classic plasticity rules: Hebb, STDP.

3. The hippocampus as a Hopfield attractor network.

4. Does the brain do deep learning?? Maybe.

Thanks