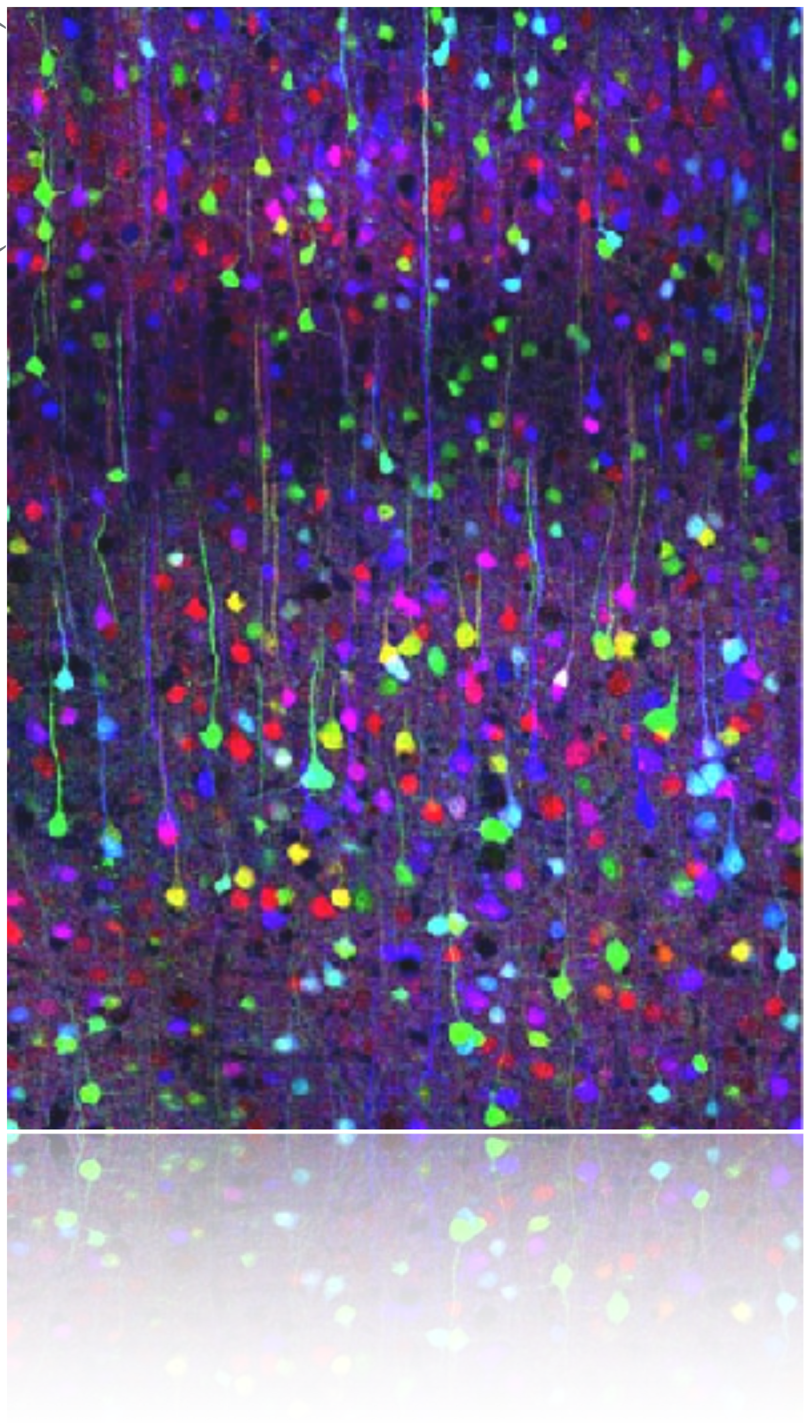
Computational Neuroscience 2018/2019

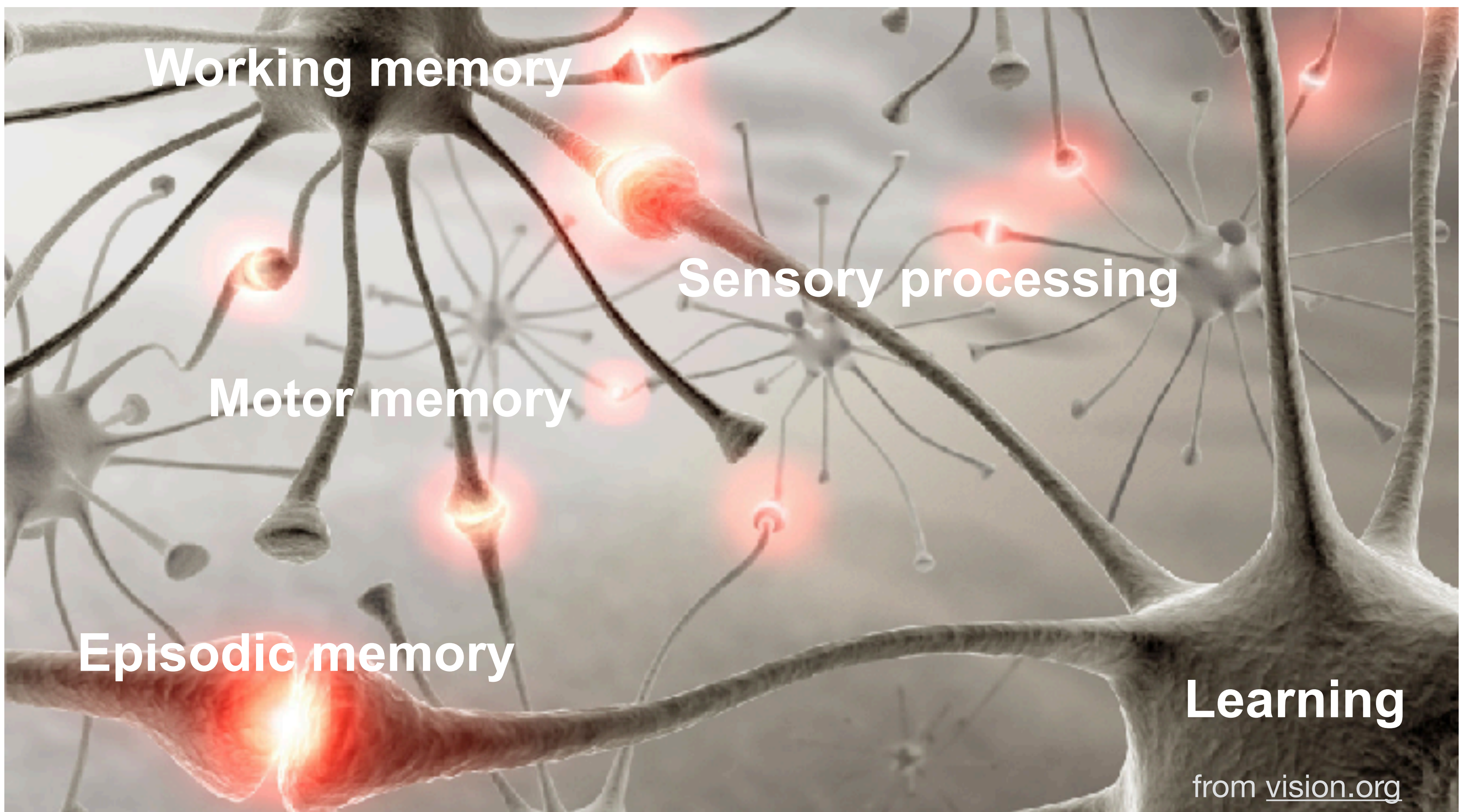
University of BRISTOL

Brainbow (Litchman Lab)

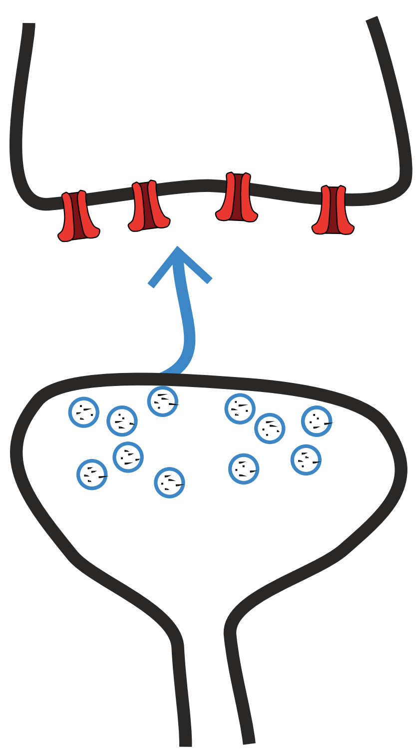


Lecture 17
Synaptic plasticity:
Long-term synaptic plasticity

Synaptic plasticity
underlies memory and learning



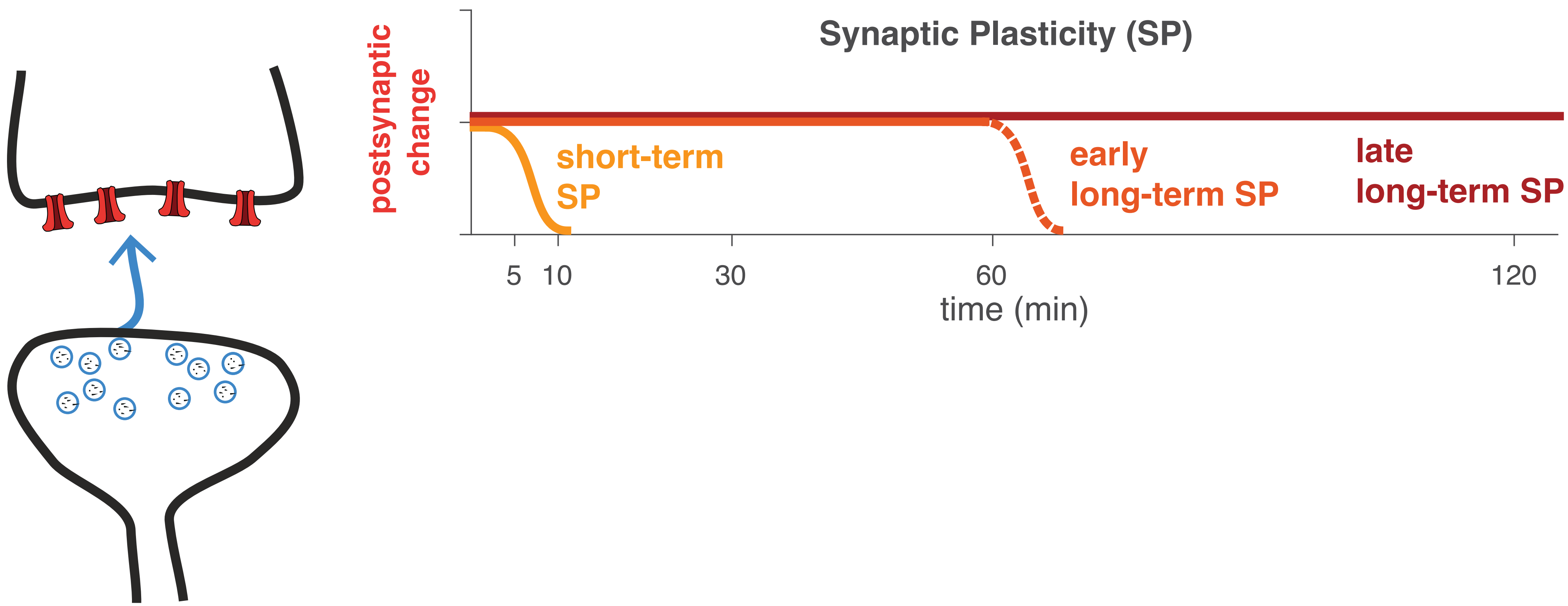
Synaptic plasticity



Synaptic plasticity: Multiple timescales and locations

Synapses can change **postsynaptically**

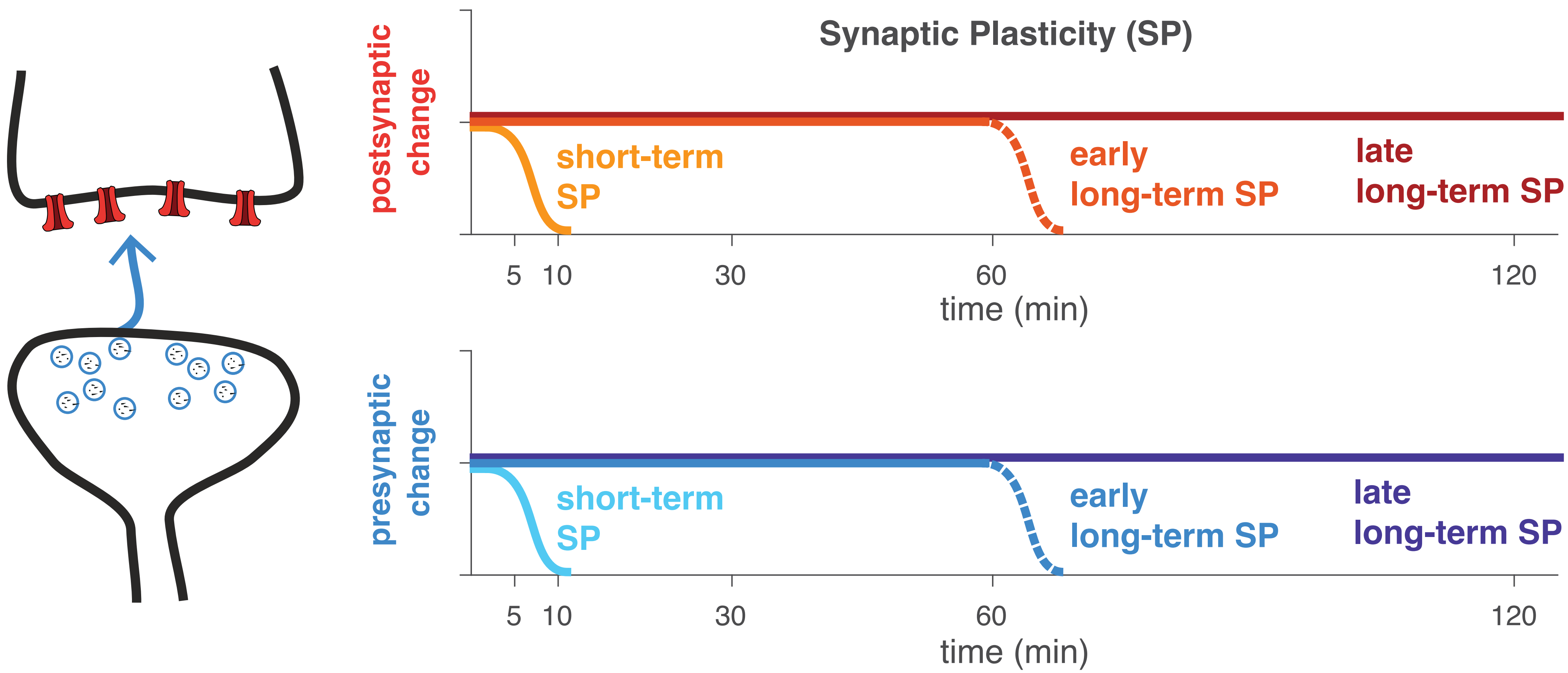
(from a few seconds (**short-term**) to tens of minutes, hours (**long-term**) or even days/years!):



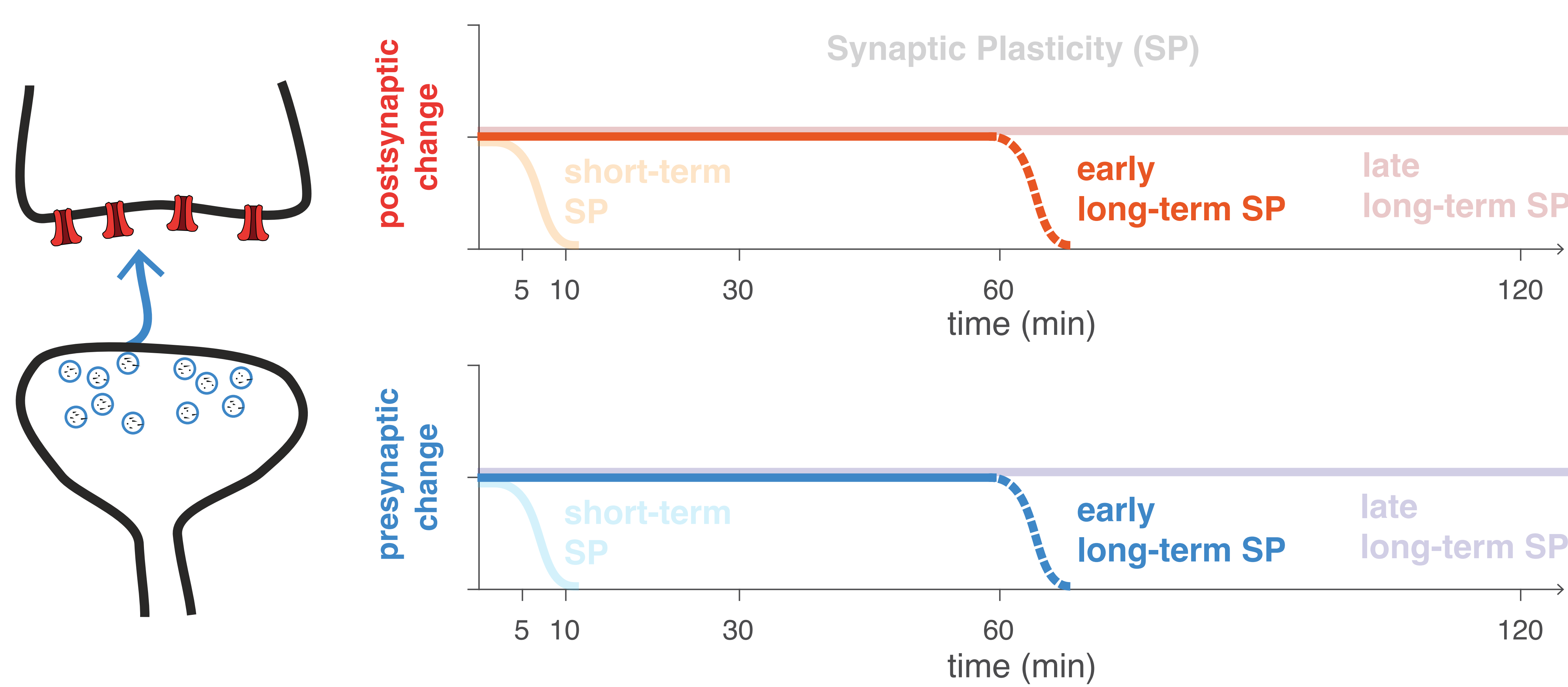
Synaptic plasticity: Multiple timescales and locations

But they can also change **presynaptically**

(from a few seconds (**short-term**) to tens of minutes, hours (**long-term**) or even days/years!):



Today's focus:
Pre- and postsynaptic long-term plasticity



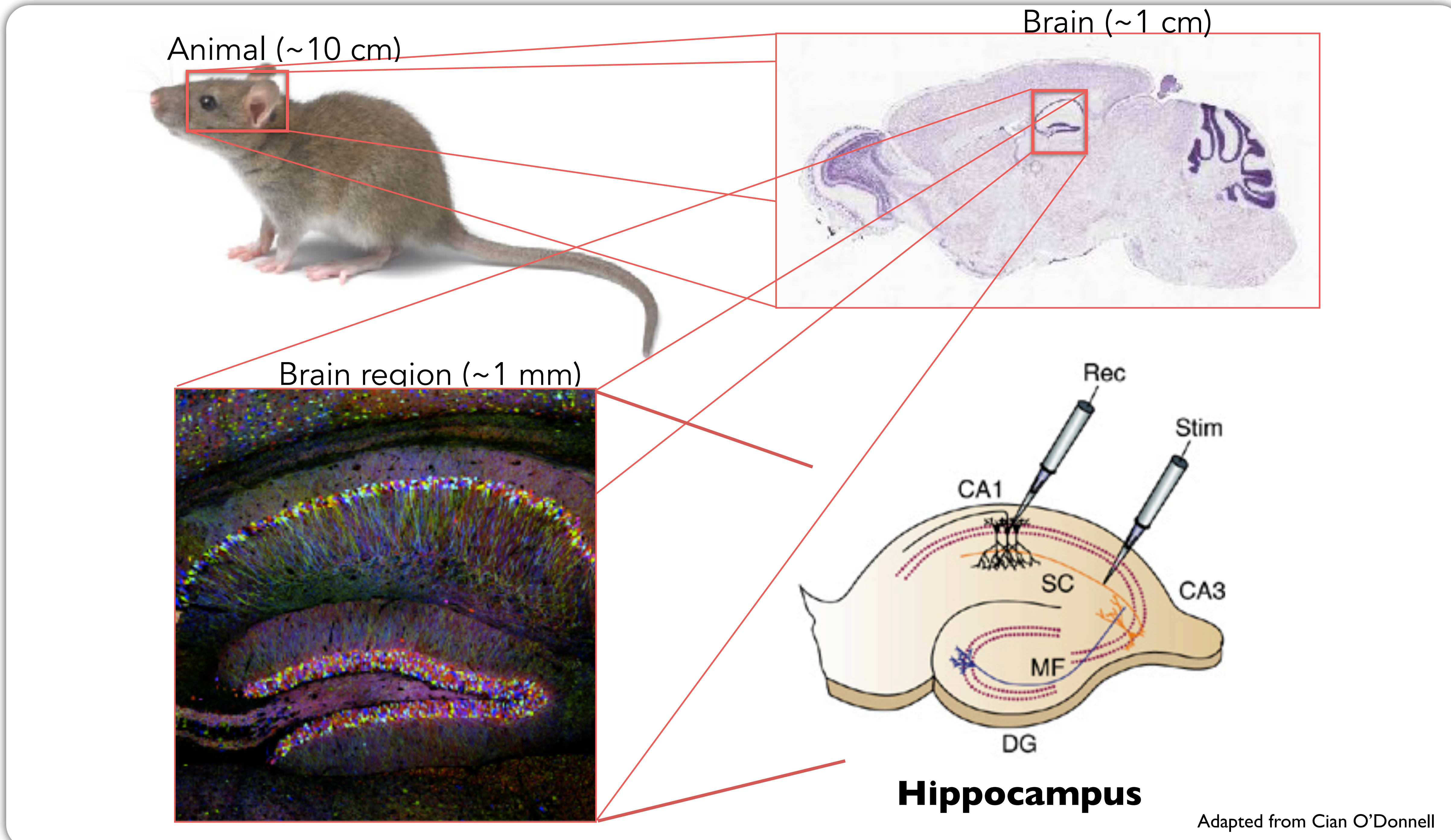
Outline:

a crash course on long-term synaptic plasticity

Long-term synaptic plasticity (LTSP)

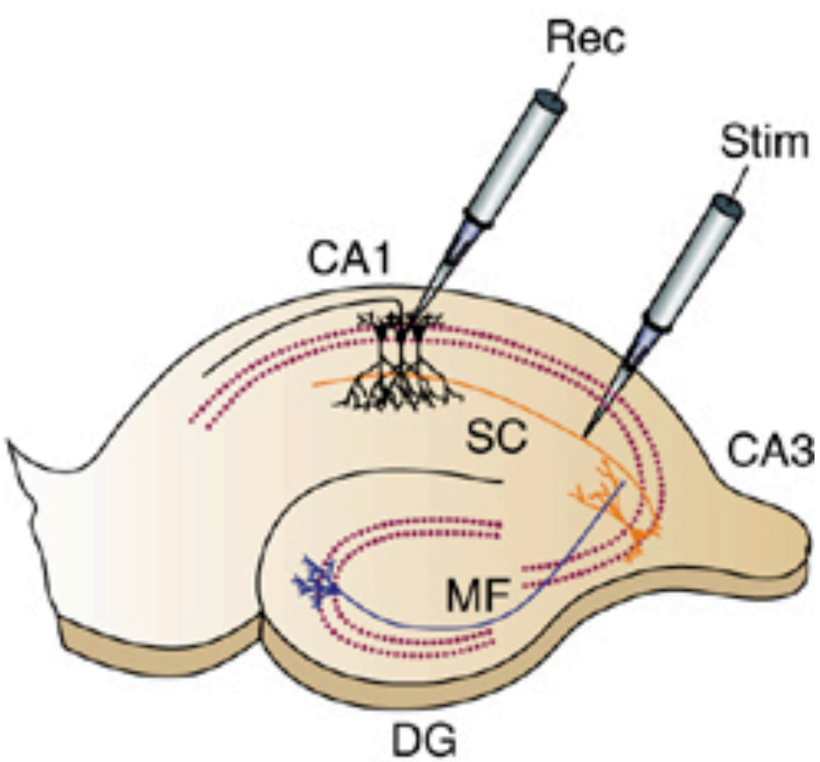
1. **Classical long-term synaptic plasticity experiments and models:**
   1.1. **First experiments**
   1.2. **Hebbian learning**
   1.3. **Stability issues**
   1.4. **Oja learning**
2. **More recent observations and learning rules:**
   2.1. **Timing dependence (STDP)**
   2.2. **Location dependence (Pre/post expression)**
   2.3. **Synaptic theory of memory savings**
   2.4. **Inhibitory plasticity as a controller of network dynamics**

Zooming in on Hippocampus

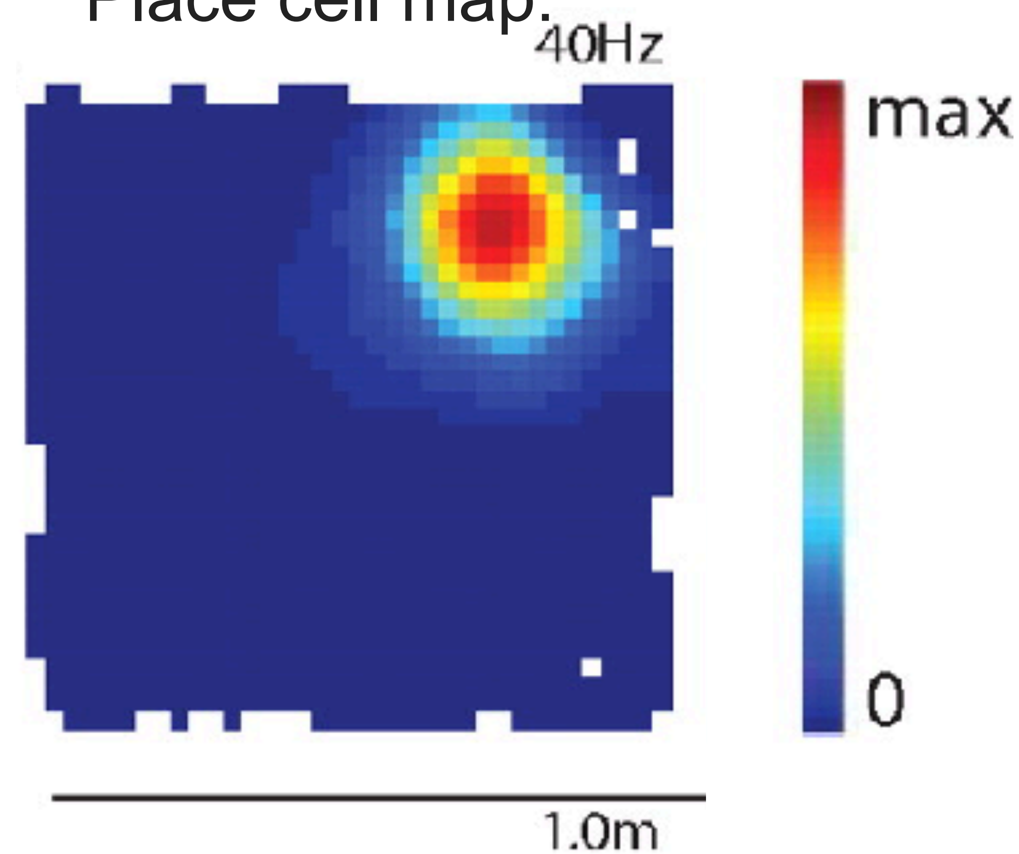


Hippocampus is involved in memory/learning

The hippocampus is a brain region known to be involved in memory consolidation, in particular spatial memories (e.g. where did I last saw you?). It is the classical region for studies of learning/memory and synaptic plasticity.

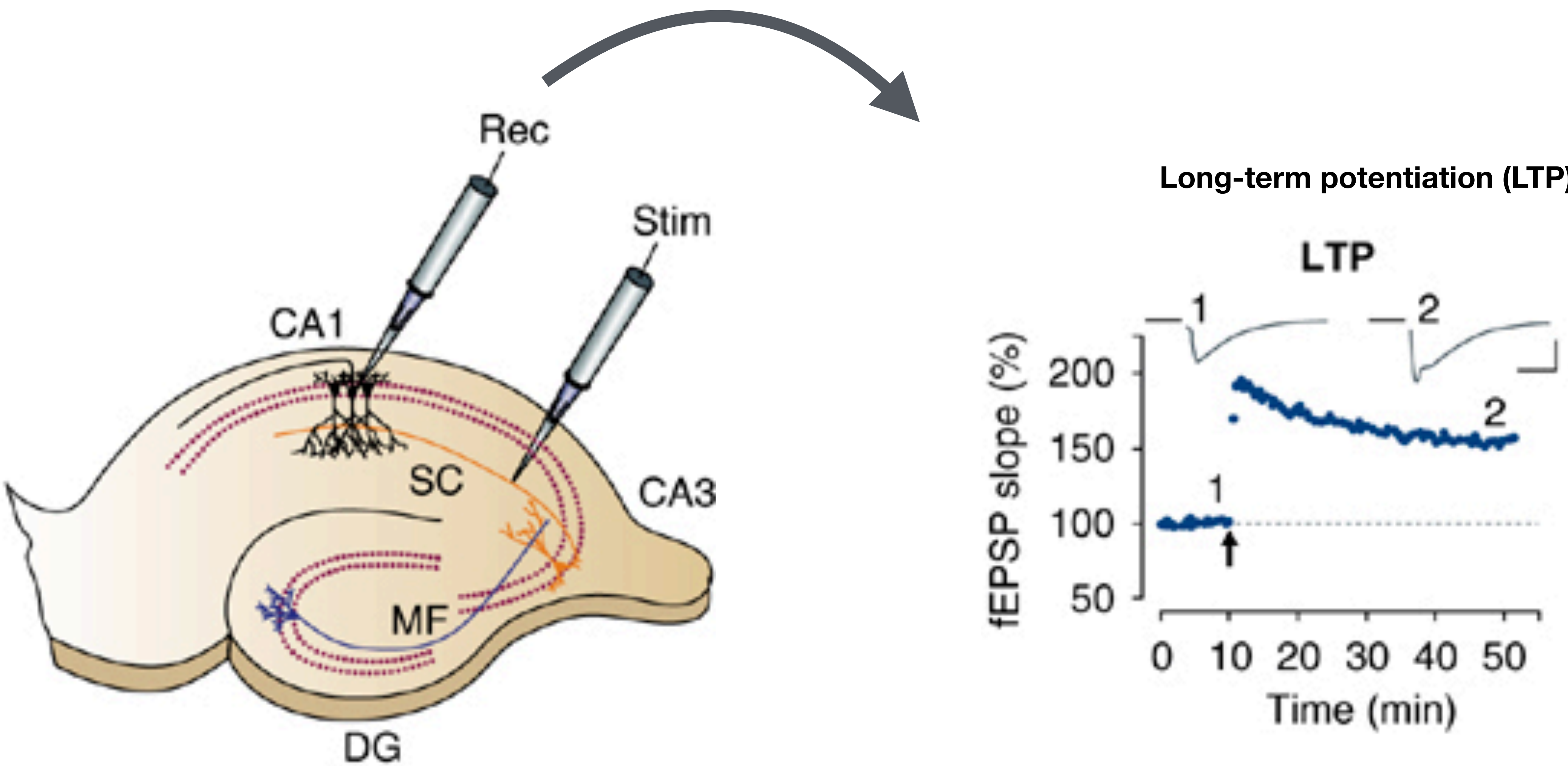


Place cell map:



Bird and Burgess, Nature Reviews Neurosci (2008)

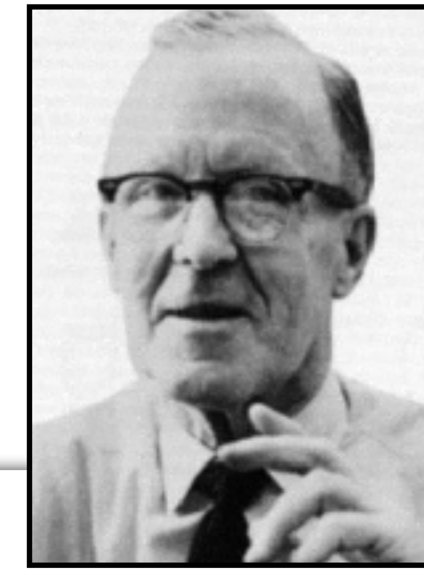
Long-term plasticity has a mechanism for memory in the hippocampus?



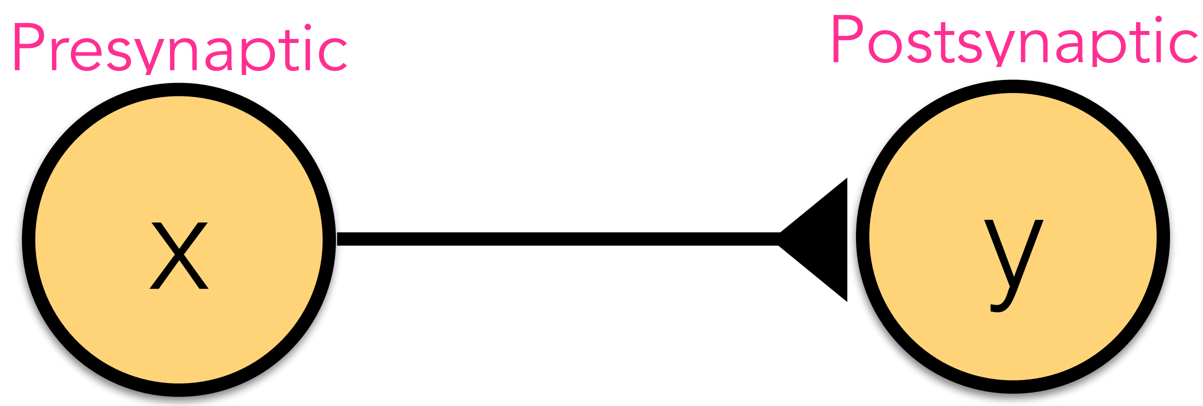
1: Before LTP induction (rec)
Induction (arrow)**: High frequency stimulation** (stim)
2: After LTP induction (rec)

Bliss and Lomo (1973)

Hebbian plasticity



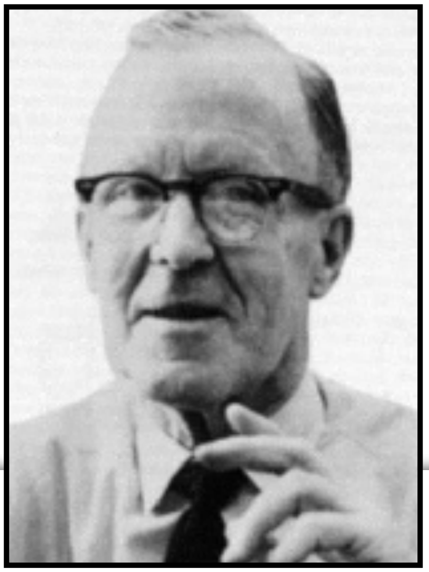
Donald Hebb



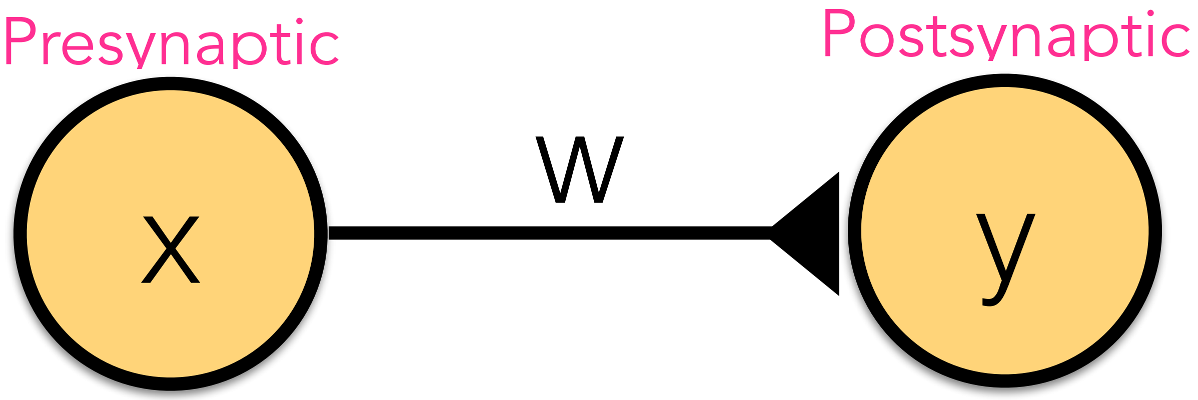
"When an *axon of cell X* is near enough to *excite a cell Y* and repeatedly or persistently takes part in firing it, some growth process or metabolic change takes place in one or both cells such that X's efficiency, as one of the cells firing Y, is increased."
— Donald Hebb (1949)

"**Neurons that fire together wire together**!" by Carla J. Shatz

Hebbian plasticity



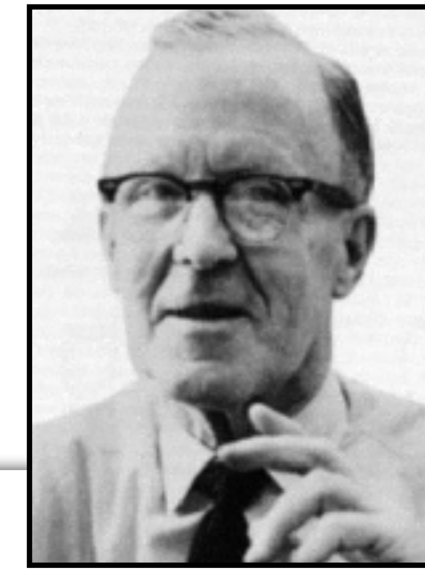
Donald Hebb



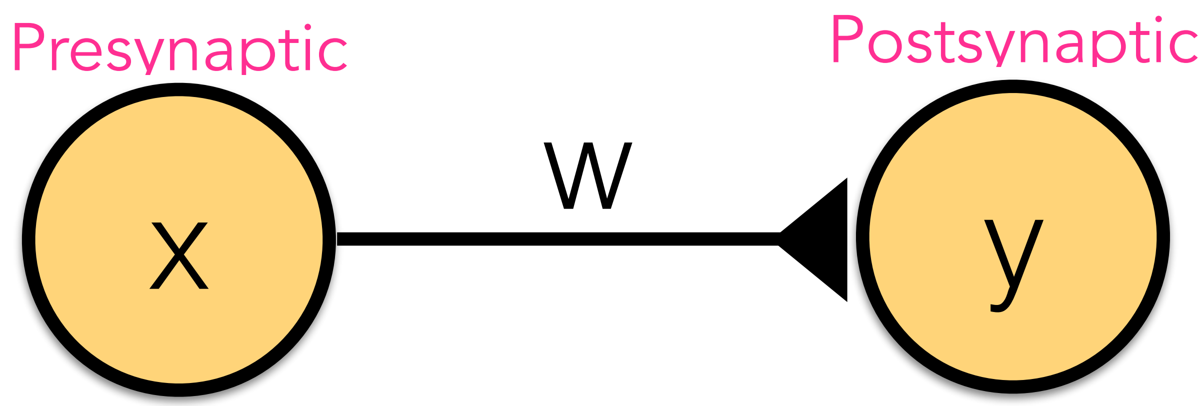
- *Synaptic plasticity can be formulated as a change in W (ΔW), which is a function of pre- and postsynaptic activity/rate (x and y, respectively):*

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

Hebbian plasticity



Donald Hebb



- *Synaptic plasticity can be formulated as a change in W (ΔW), which is a function of pre- and postsynaptic activity/rate (x and y, respectively):*

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

The simplest Hebbian learning rule!

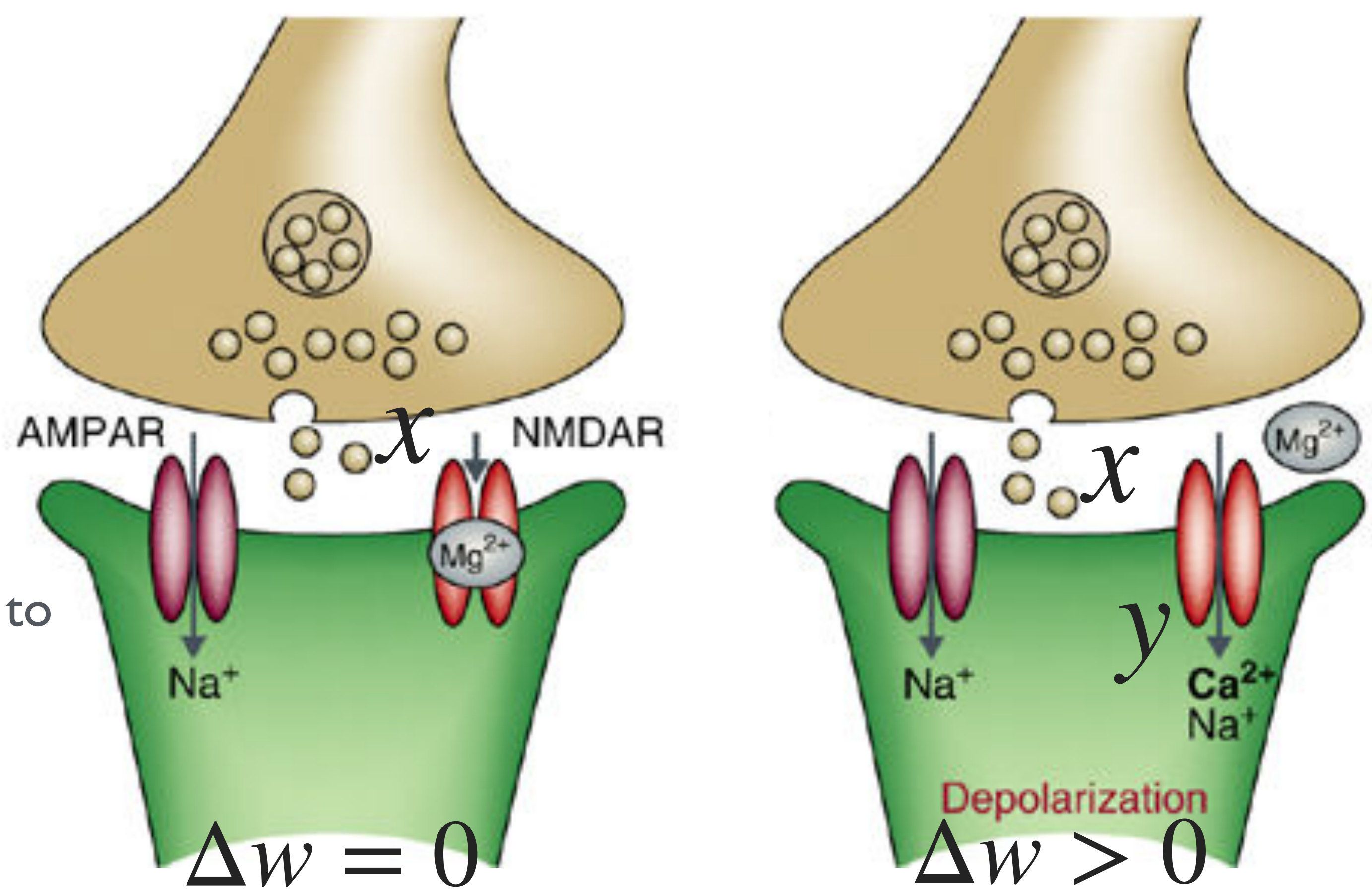
η : learning rate

How is Hebbian plasticity implemented?

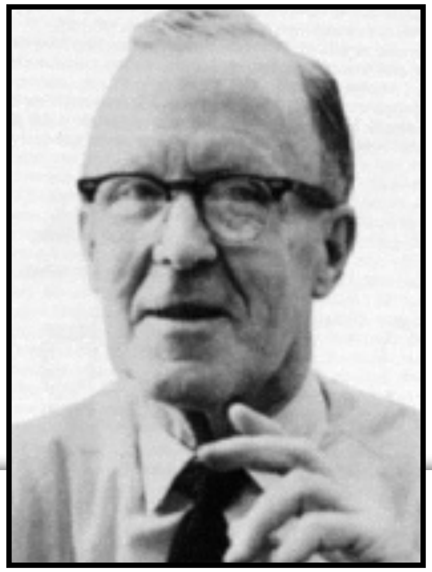
$$\Delta w = f(x, y) = \eta x y$$

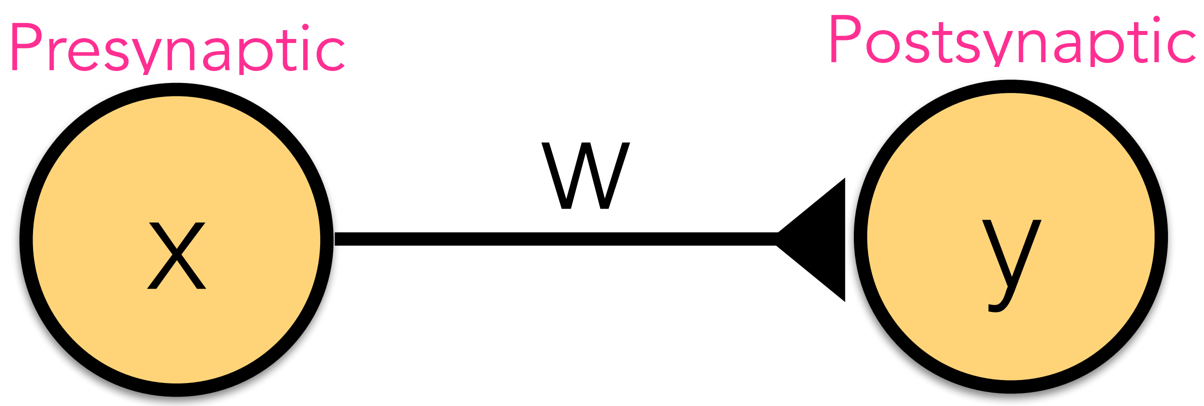
NMDA receptors as coincidence detectors (of pre and postsynaptic activity): **they need glutamate (*x*) and postsynaptic depolarisation (y) to release the magnesium block (Mg^{2+}):**

AMPA activation leads to postsynaptic activity:



Hebbian plasticity


Donald Hebb

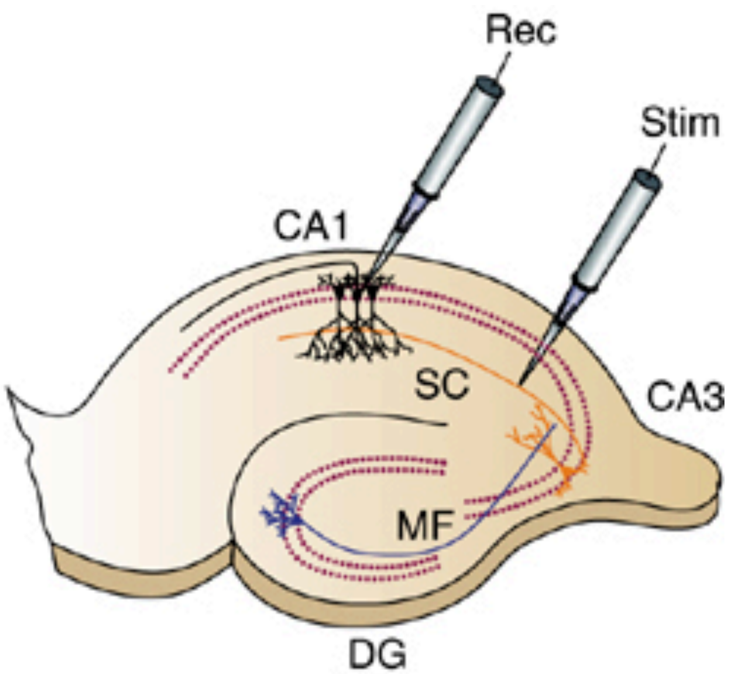


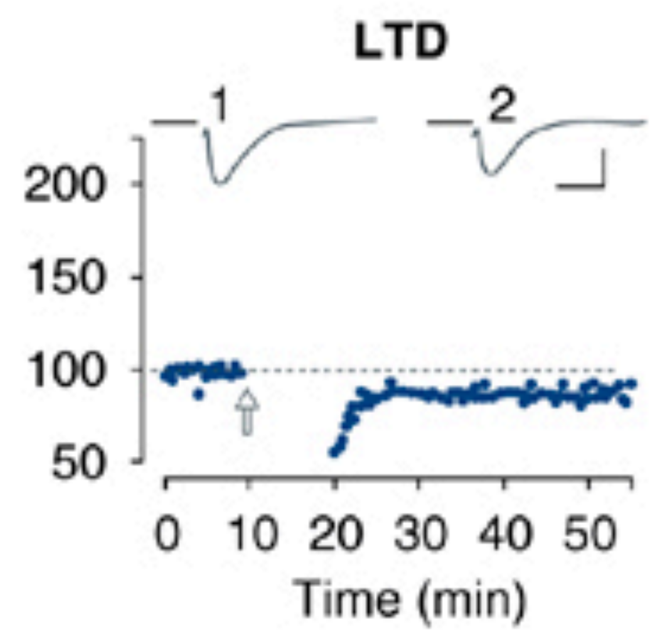
- *Note that because neuronal activities are either zero or positive the change in the weights are either positive or zero, which can lead to unstable weights (i.e. too strong weights)!*

$$\eta x y \geq 0$$

This is unstable, as both w and in turn y grow without bonds!

Long-term synaptic depression
(LTD)





- Using a different protocol long-term depression (LTD) in the synaptic weight can be induced! This can help to make the previous learning rule less unstable.

$$\Delta w = \eta(xy - y)$$

But there is still a tendency for more LTP and LTD!

How to get stable+useful learning ?

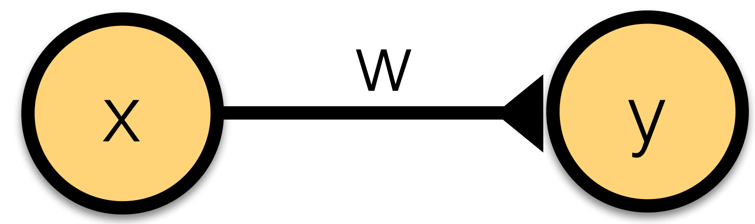
- **Synaptic scaling/normalization**: The sum over all the incoming synaptic weights is kept constant [Miller and MacKay, Neural Computation (1994) and Turrigiano, Cell (2008)]

- **Error-correcting learning rules**: Learning rules such as the perception learning rule are designed to specifically minimise some error function, which helps painting the weights within reasonable bounds.

- **Use short-term depression** [see previous lecture]

- **Learning rules with stability properties:** BCM learning rule [Bienenstock, Cooper & Munro, J Neurosci (1982)], **Oja learning rule** [we are going to discuss this one]

Oja learning rule



Now we explicitly use vector notation

(***w*** and ***x*** are a vector of weights and inputs):

$$y = \mathbf{w}^T \mathbf{x}$$

Oja learning rule:

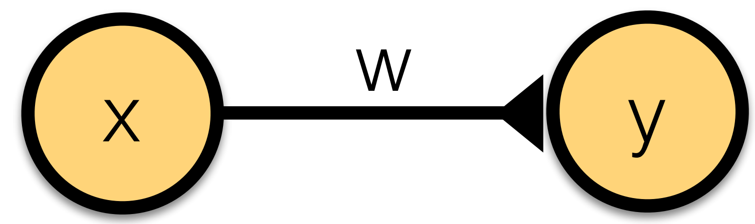
$$\Delta \mathbf{w} = \eta(\mathbf{x}y - y^2 \mathbf{w})$$

Note: decay (LTD) component is now quadratic on *y* (i.e. stronger).

Oja, Scholarpedia 2008

Oja learning rule:
studying its convergence

$$\Delta \mathbf{w} = \eta(\mathbf{x}y - y^2\mathbf{w})$$



note that:

$$y = \mathbf{w}^T\mathbf{x} = \mathbf{x}^T\mathbf{w}$$

y can be expanded giving:

$$\Delta \mathbf{w} = \eta(\mathbf{x}\mathbf{x}^T\mathbf{w} - \mathbf{w}^T\mathbf{x}\mathbf{x}^T\mathbf{w}\mathbf{w})$$

$$\Delta \mathbf{w} = \eta(\mathbf{C}\mathbf{w} - \mathbf{w}^T\mathbf{C}\mathbf{w}\mathbf{w})$$

To look at convergence we set the Δw to 0:

$$0 = \eta(\mathbf{C}\mathbf{w} - \mathbf{w}^T\mathbf{C}\mathbf{w}\mathbf{w})$$

with:

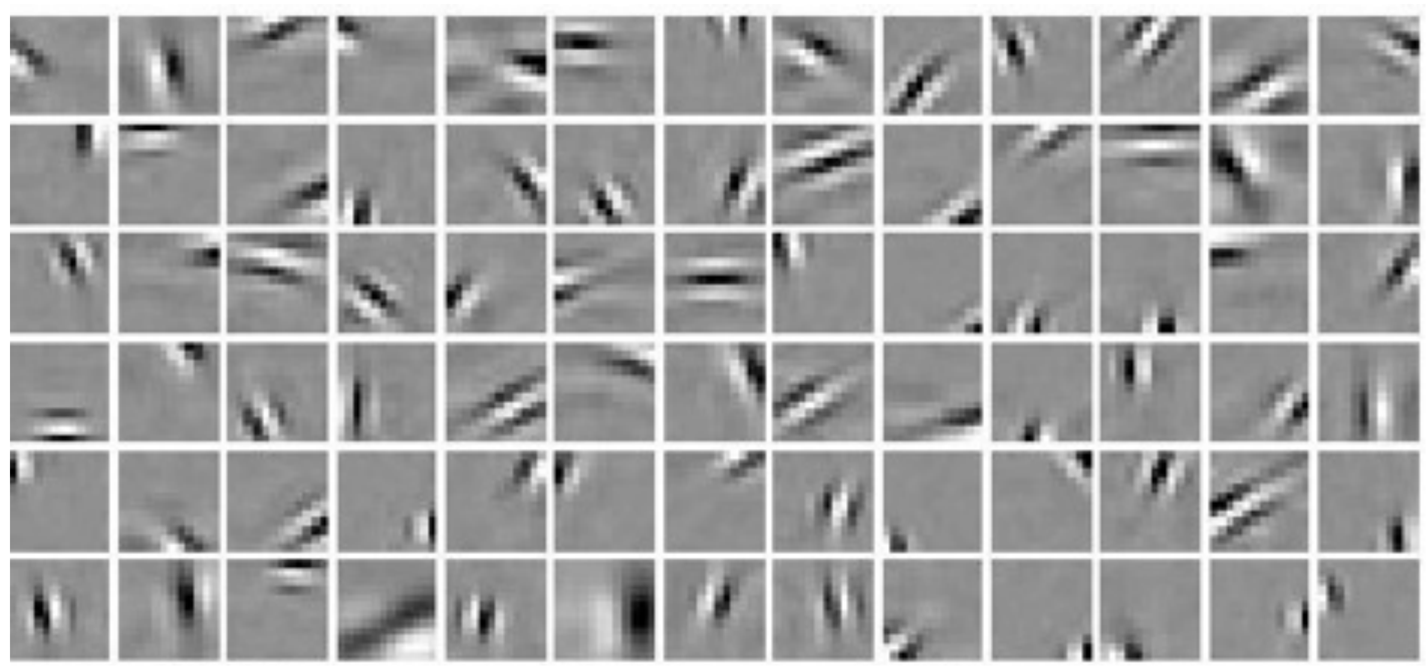
$$\mathbf{C} = \mathbf{x}\mathbf{x}^T$$

It extracts the covariance matrix of the inputs, and its **first principal component** (as in principal component analysis).

Oja, Scholarpedia 2008

Learning receptive fields

A modified Oja learning rule can perform independent component analysis (ICA). Algorithms that perform ICA-like computations give realistic receptive fields (similar to the ones found in the visual cortex), for example:



Sparse coding used to develop similar receptive fields (Olshausen and Field, Nature (1996)).

Hyvärinen and Oja, 1998

Summary: long-term plasticity (part 1)

1. Long-term plasticity was discovered in Hippocampus
2. Hebbian plasticity: Neurons that fire together wire together
3. Basic Hebbian learning rules are unstable
4. Multiple strategies to solve this stability issues
5. Oja learning rule extracts the first principal component

Questions?

Animal learning is impressive!

https://youtu.be/UB_37encRCI

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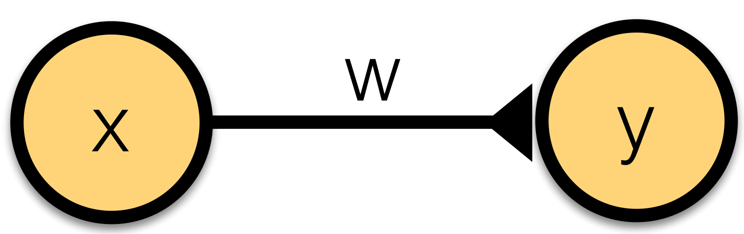
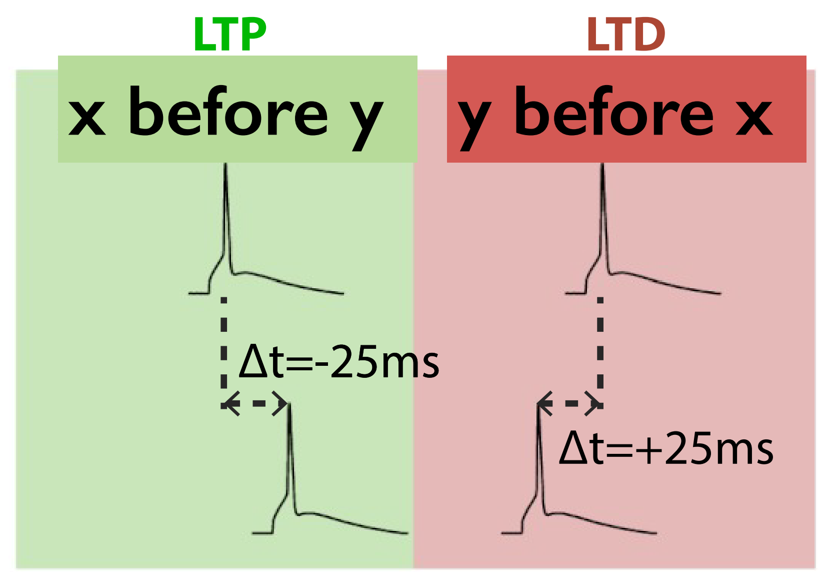
Long-term synaptic plasticity depends on timing





Δt = time of presynaptic spike - time of postsynaptic spike

An extension to Hebbs postulate!

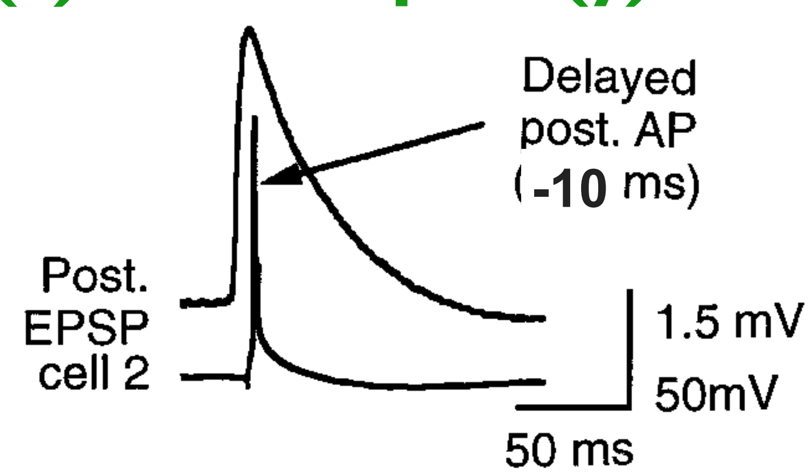
For example:

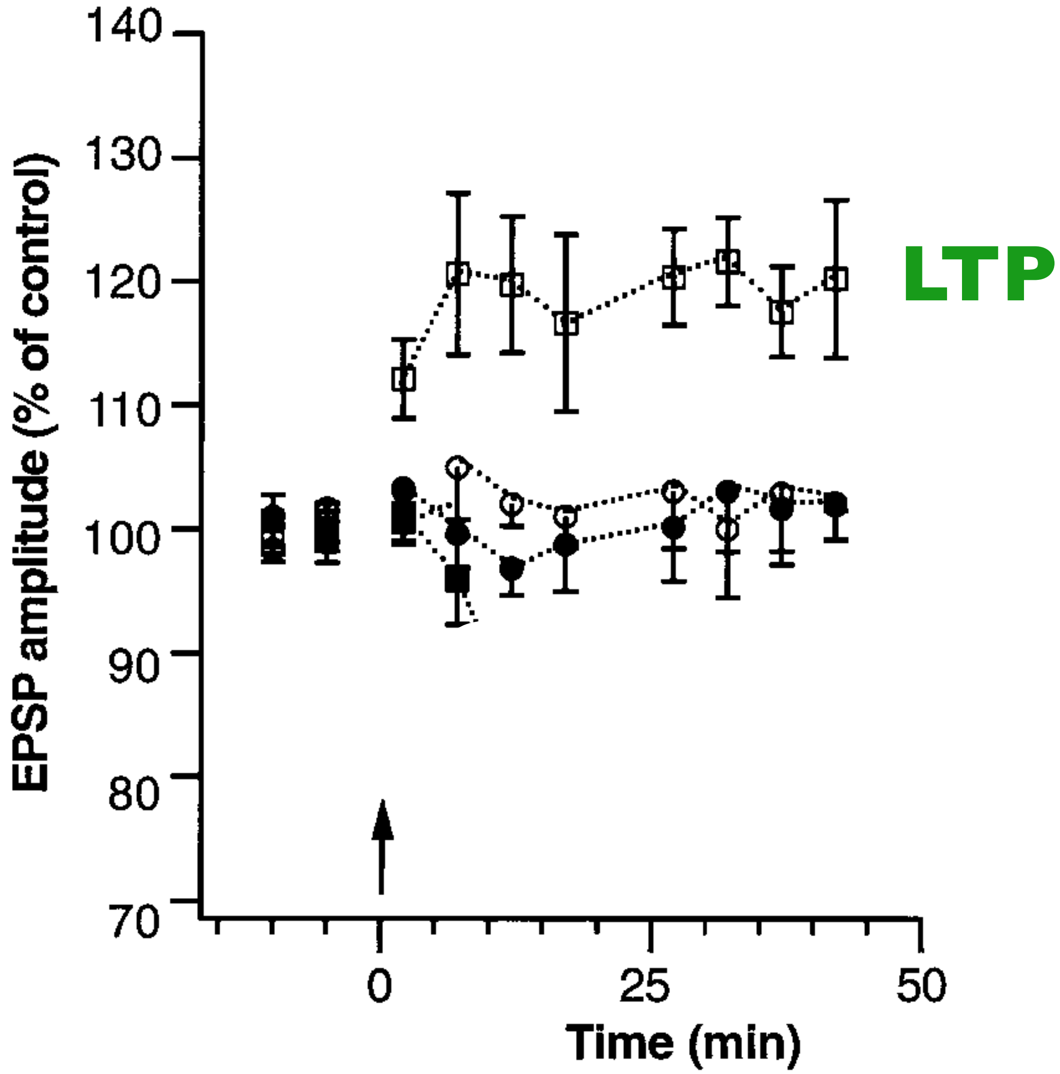
$$\Delta t = \text{time}_x - \text{time}_y = 2\text{ms} - 12\text{ms} = -10\text{ms (LTP case)}$$

Markram et al. 1997 Science
Caporale and Dan 2008 Annu. Rev. Neurosci.

Spike-timing dependent plasticity

pre (x)—10ms—post (y)



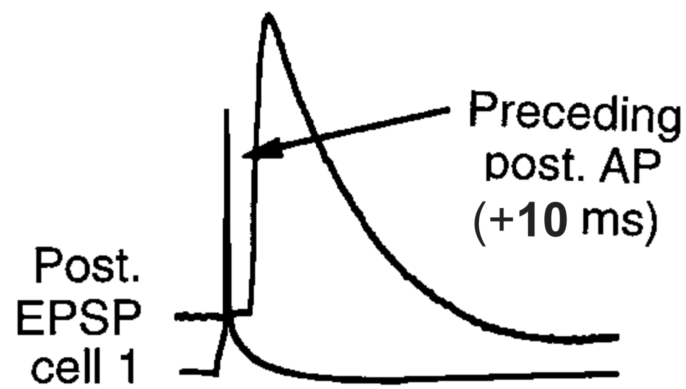


Protocol: 5 spikes, 10 to 15 times every 4s

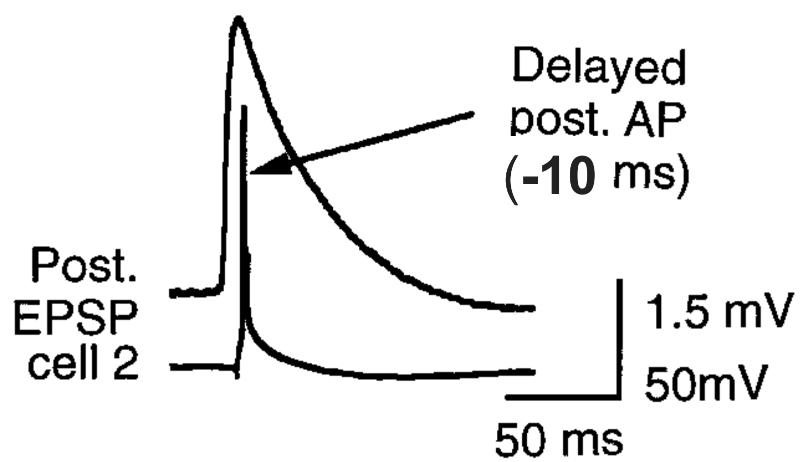
Markram et al. 1997 Science
Caporale and Dan 2008 Annu. Rev. Neurosci.

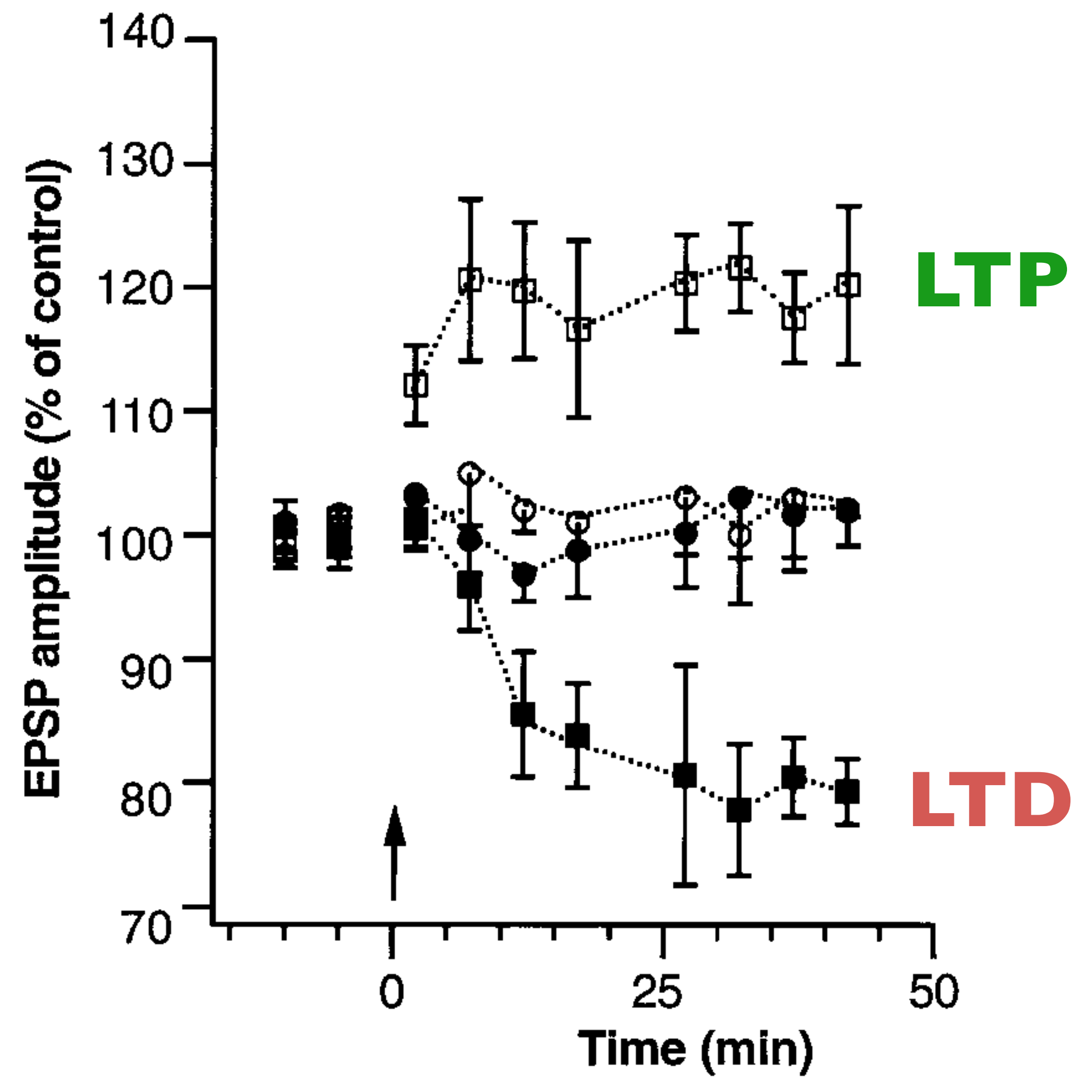
Spike-timing dependent plasticity

post (y)—10ms—pre (x)



pre (x)—10ms—post (y)





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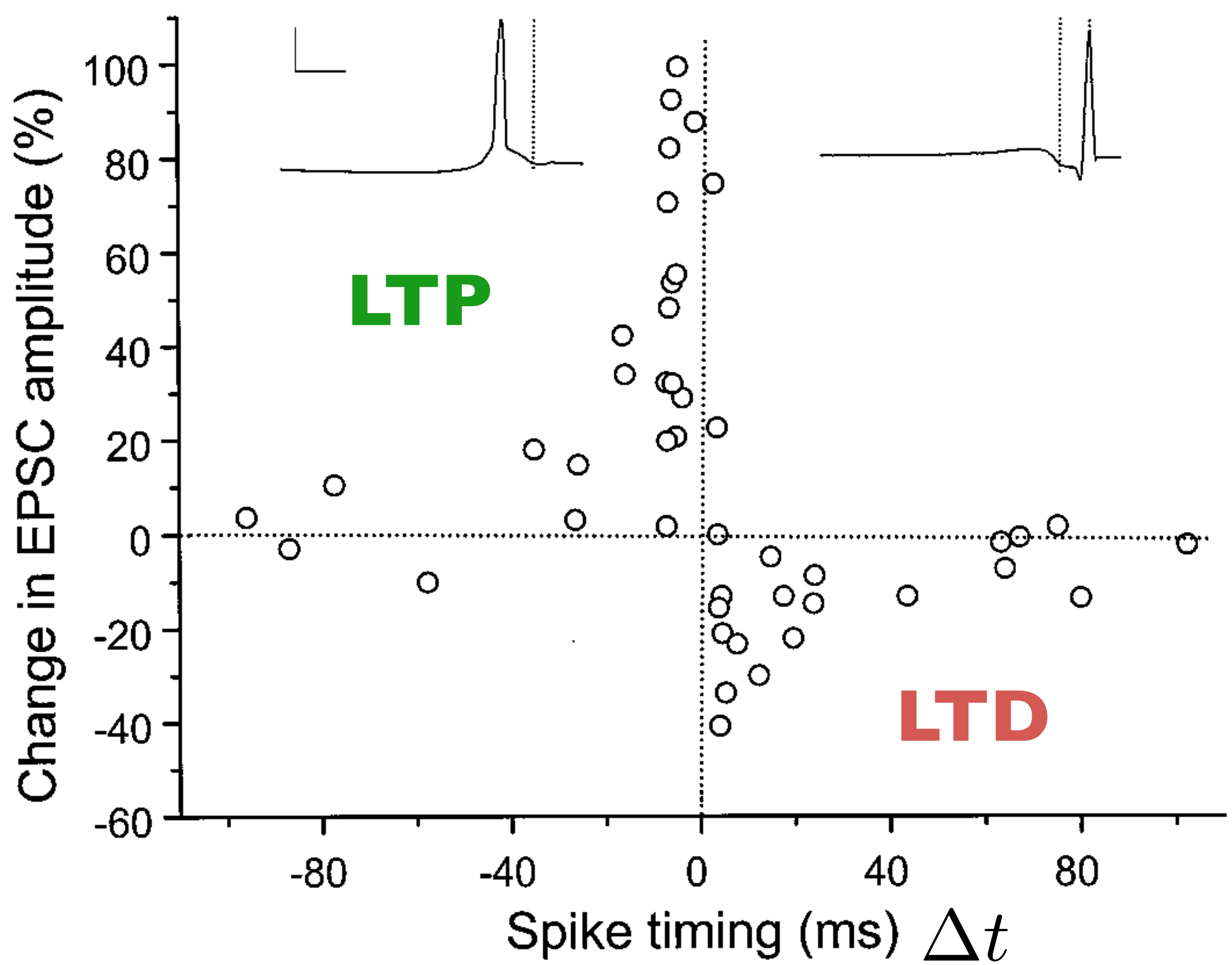
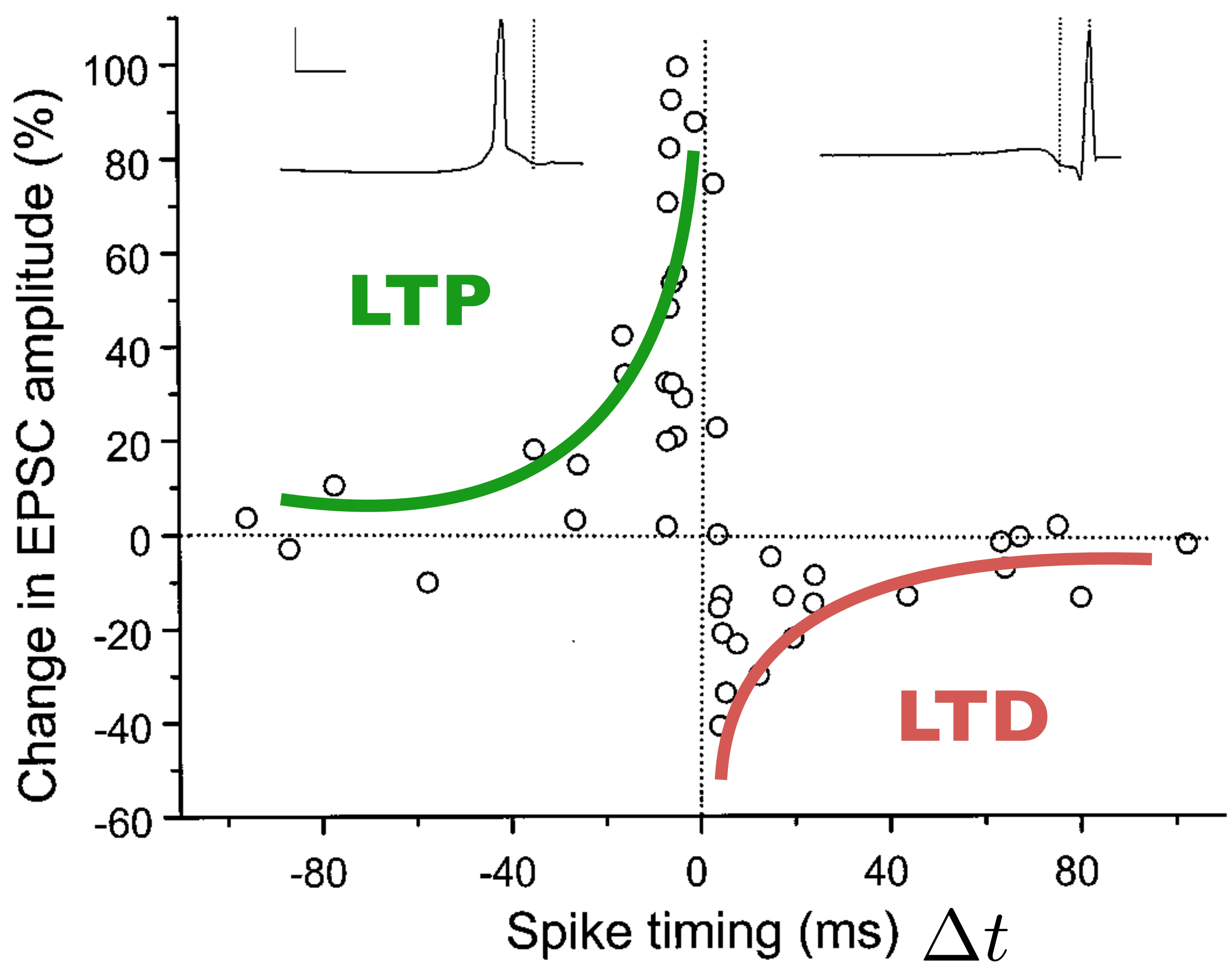


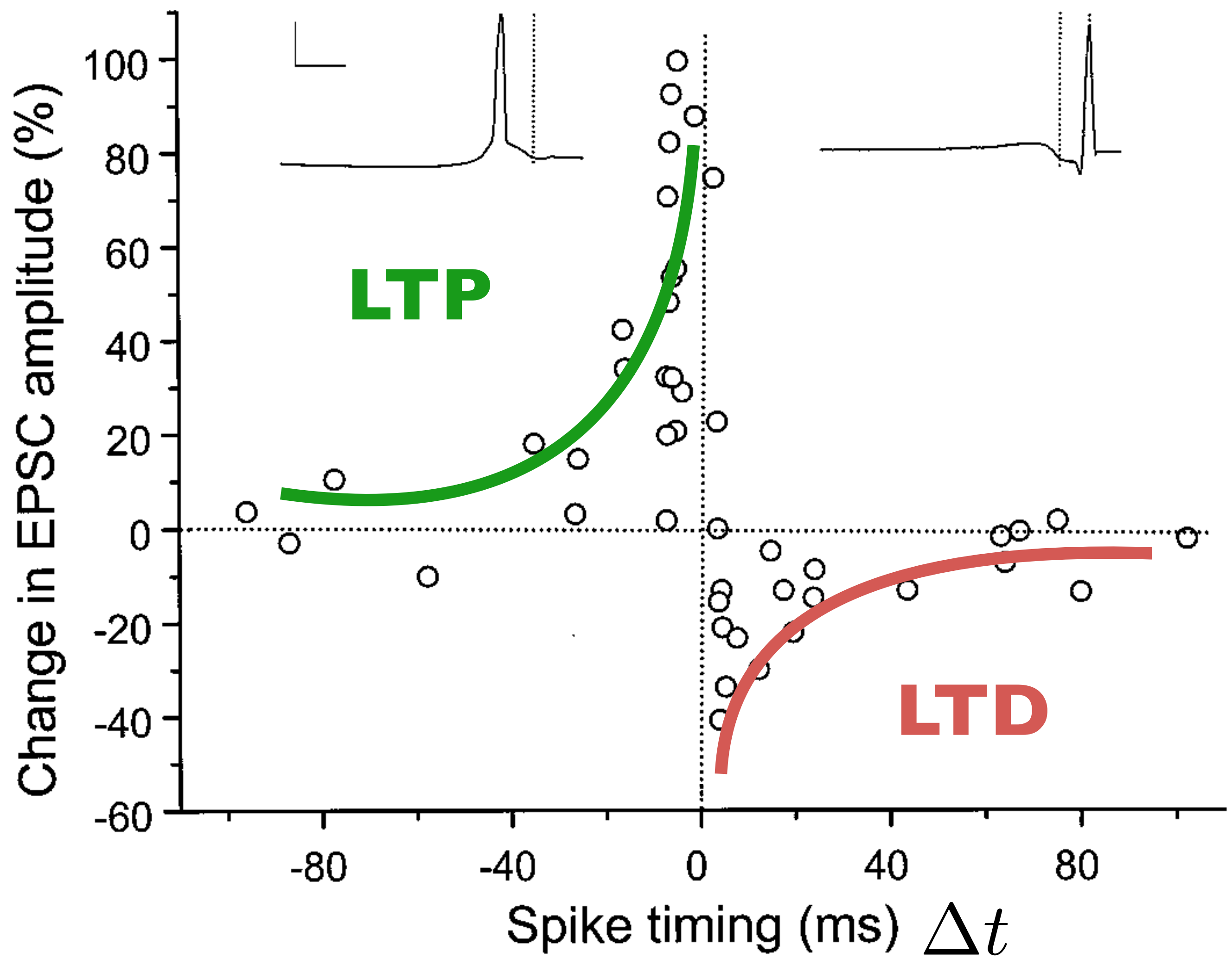
Bi and Poo 1998 JNeurosci

Spike-timing dependent plasticity



Bi and Poo 1998 JNeurosci

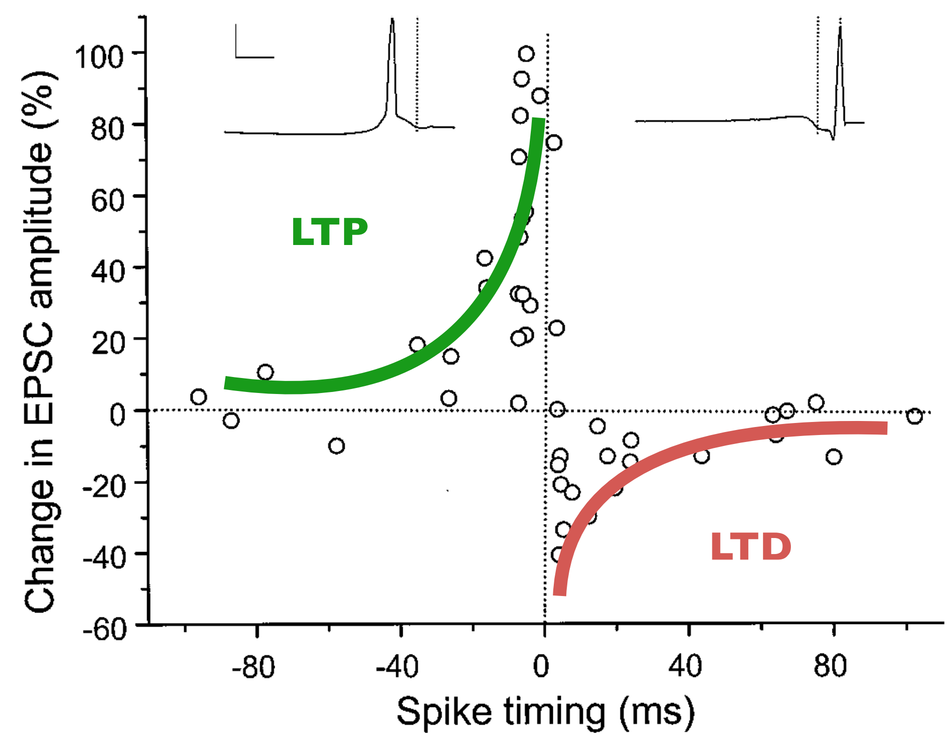
Spike-timing dependent plasticity



Bi and Poo 1998 JNeurosci

This curves can be modelled as simple exponentials!

Spike-timing dependent plasticity



Δt

If $\Delta t \leq 0$:

$$\Delta W = A_{\mathrm{LTP}} \exp(\frac{\Delta t}{\tau_{\mathrm{LTP}}})$$

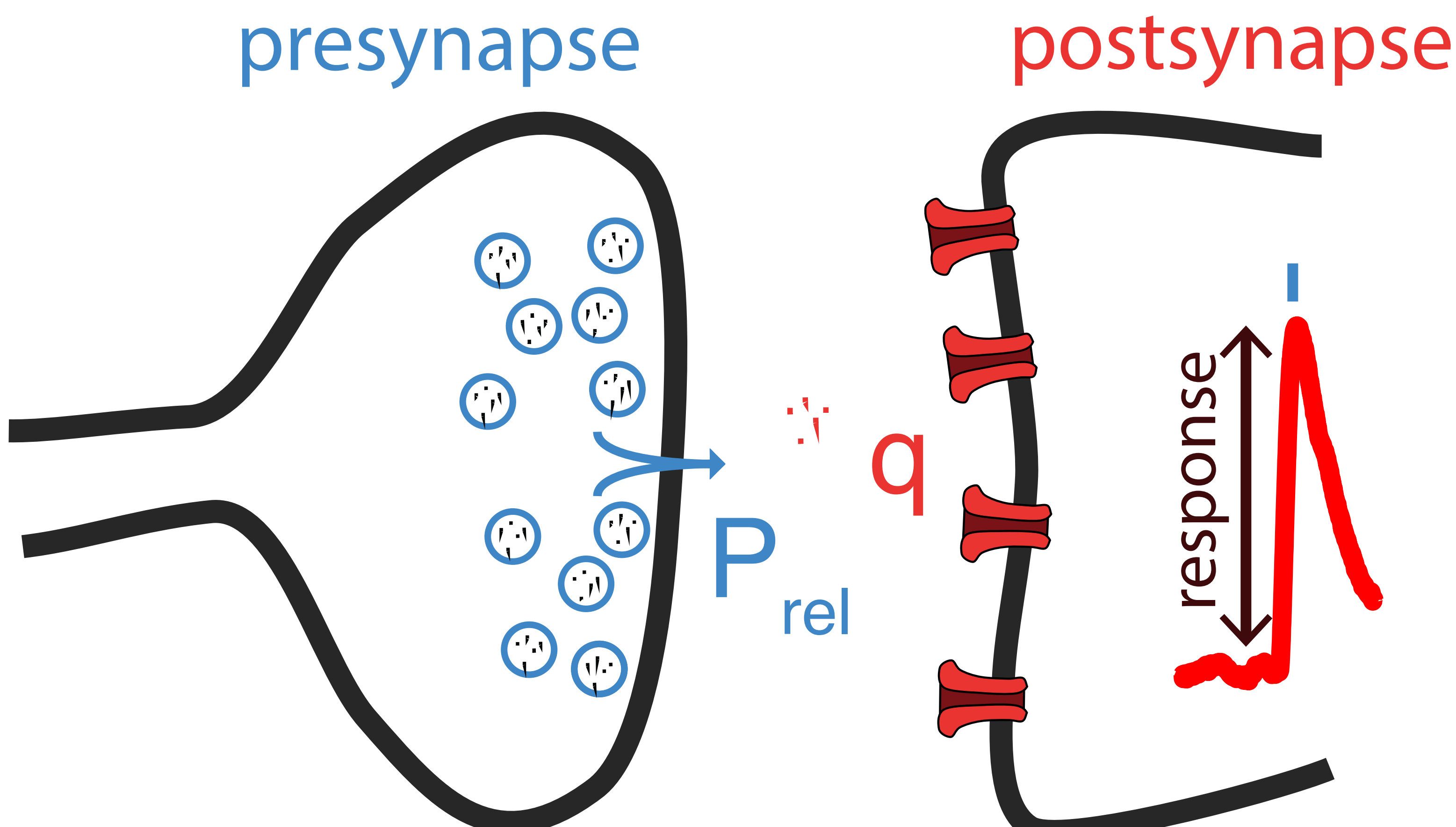
If $\Delta t > 0$:

$$\Delta W = -A_{\mathrm{LTD}} \exp(-\frac{\Delta t}{\tau_{\mathrm{LTD}}})$$

Sjöström and Gerstner, Scholarpedia 2010

Long-term synaptic plasticity is also location specific

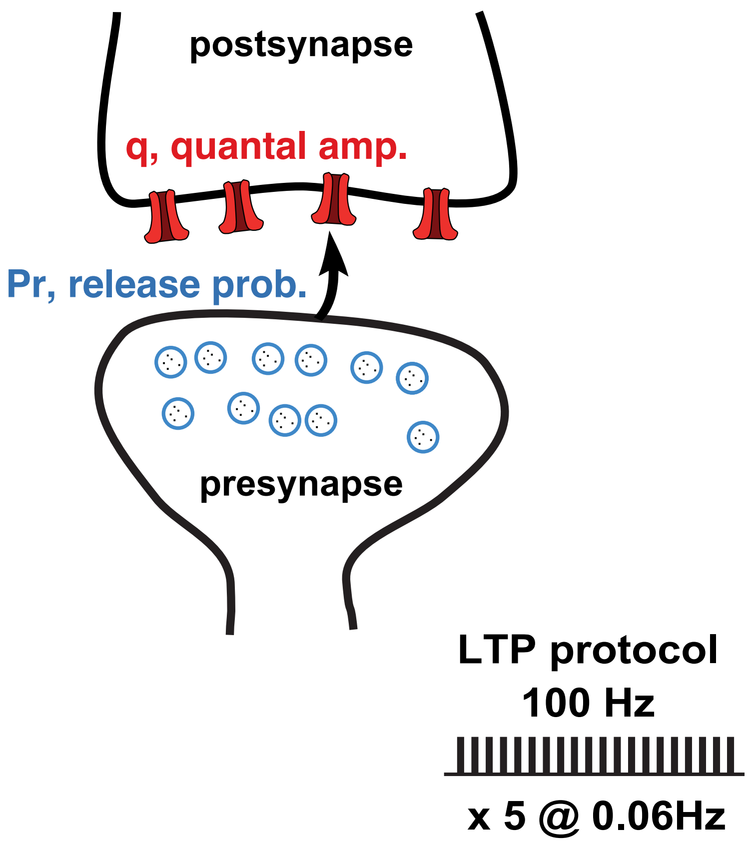
Recall from previous lectures that the weight has at least two components:



$$\text{response} \sim w = P_{\text{rel}}\, q$$

Long-term synaptic plasticity is also location specific

Both P_{rel} and q can change during long-term plasticity!



Larkman et al. Nature (1992)

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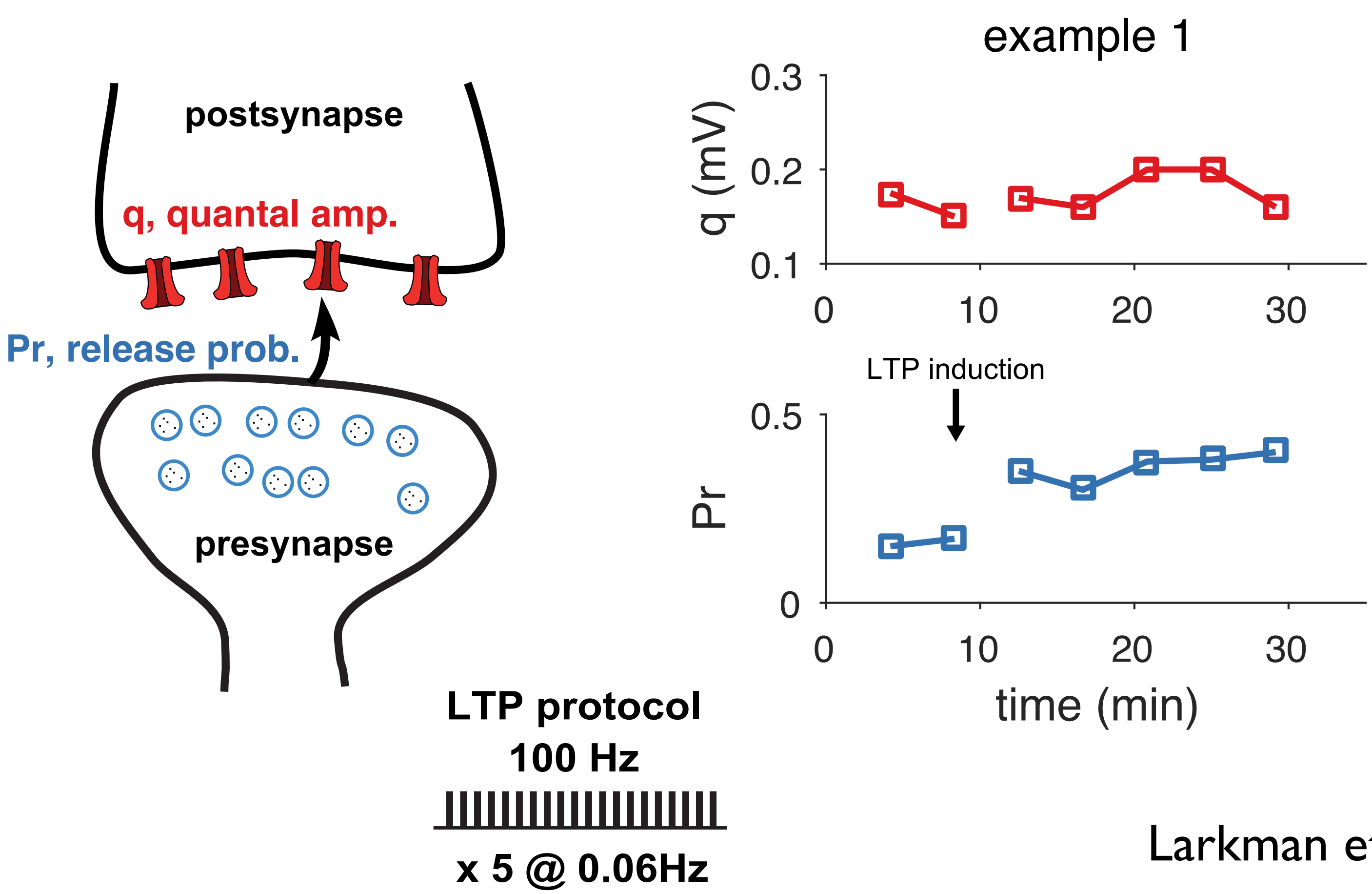

Larkman et al. Nature (1992)

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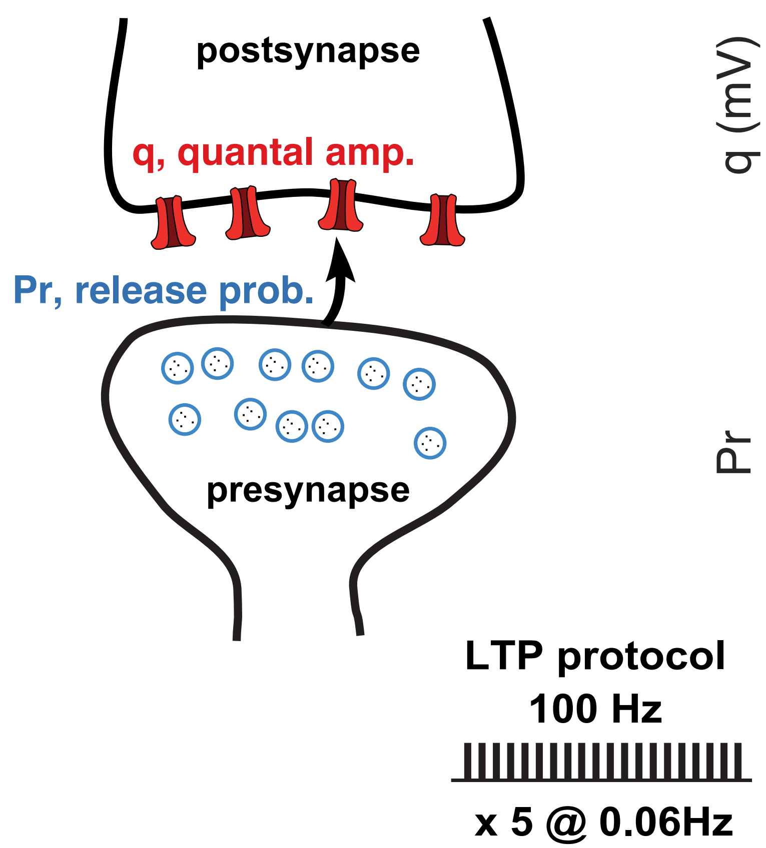
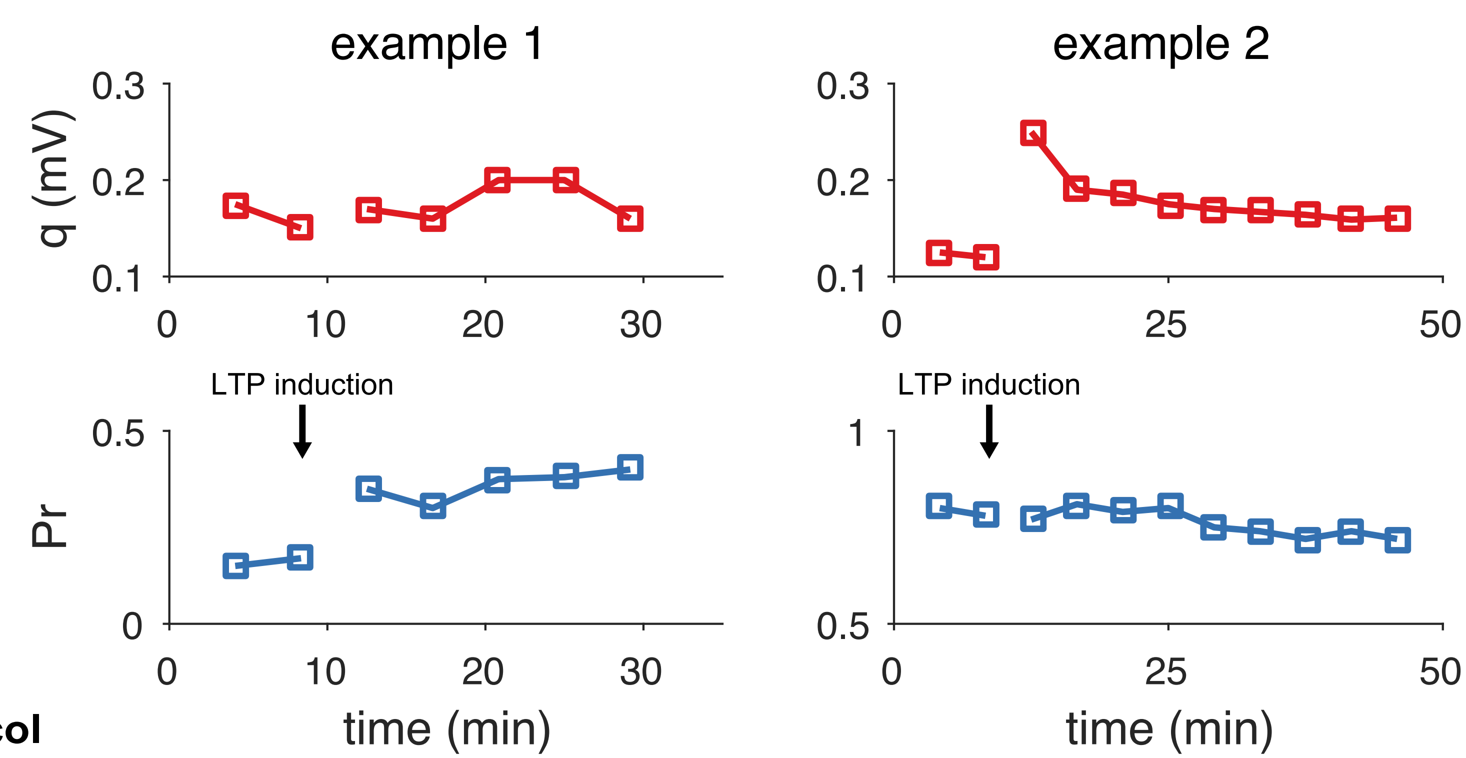


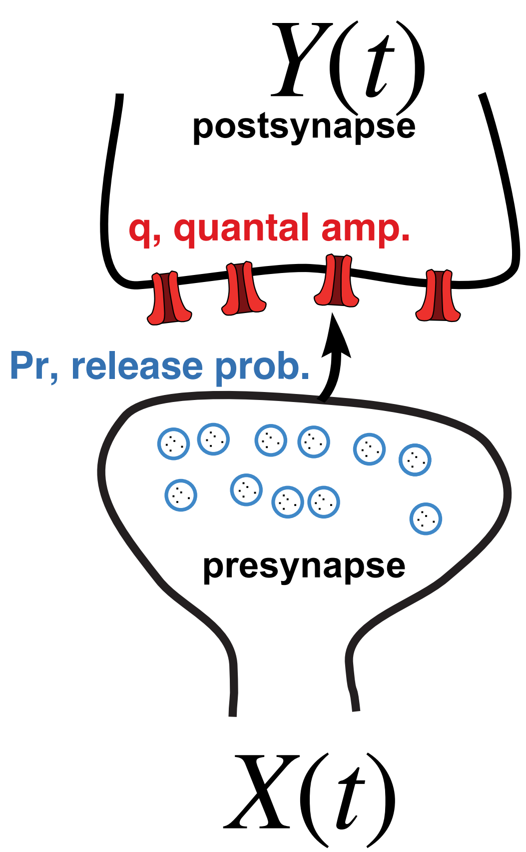


Larkman et al. Nature (1992)

See recent reviews:
Costa et al. Phil. Trans. R. Soc. B (2017);
Llera-Montero et al. CONB (2019)

A unified pre and postsynaptic learning rule

An unified model of pre- and postsynaptic plasticity:



$$\Delta q \sim \underbrace{Y(t)x_+}_{\text{Hebbian}_{\text{postsynaptic}}}$$

$$\Delta P_r \sim \underbrace{X(t)(-y_- + y_+)}_{\text{Hebbian}_{\text{presynaptic}}}$$

X(t) and *Y(t)* represent pre- and postsynaptic spike trains, and *y*, *x* represent traces of previous pre- and postsynaptic activity. This learning rule captures a wide range of experimental data.

Costa et al. 2015 eLife

Memory savings

Hermann Ebbinghaus

"… concept of "**memory savings**" put forward more than 100 years ago by **Hermann Ebbinghaus** (1880), who experimentally demonstrated the everyday experience that **relearning** is **easier/quicker** than **learning**."

Hubener and Bonhoeffer. Neuron 2010

A synaptic plasticity theory of memory savings

Presynaptic long-term plasticity is more dynamic (with both LTP and LTD):

$$\Delta q \sim \underbrace{Y(t)x_+}_{\text{Hebbian}_{\text{postsynaptic}}}$$

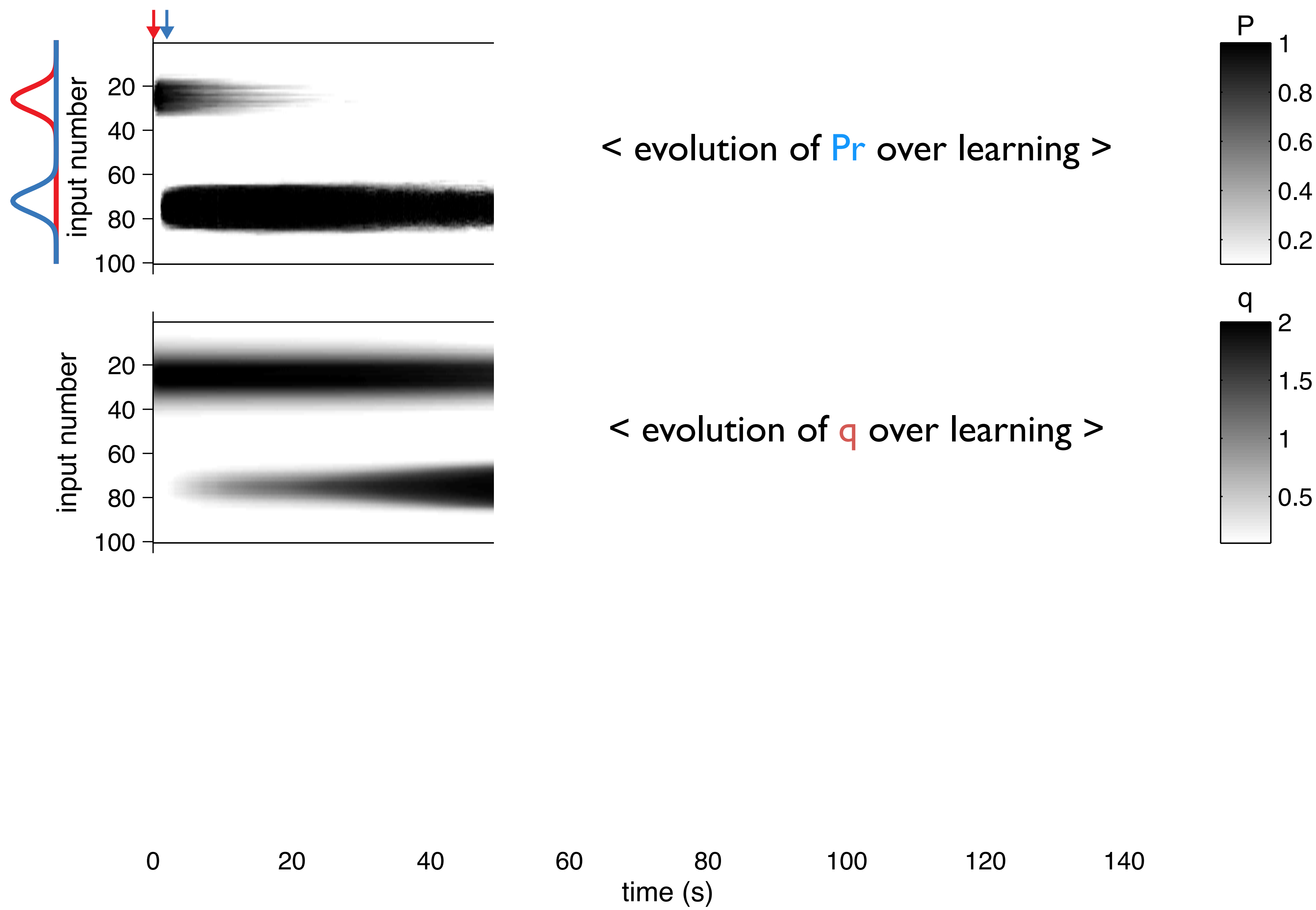
$$\Delta P_r \sim \underbrace{X(t)(-y_- + y_+)}_{\text{Hebbian}_{\text{presynaptic}}}$$

This means that the presynapse can forget (via LTD) while the postsynapse keeps a memory of previous 'experiences' (as it doesn't have LTD).

Costa et al. 2015 eLife

A synaptic plasticity theory of memory savings

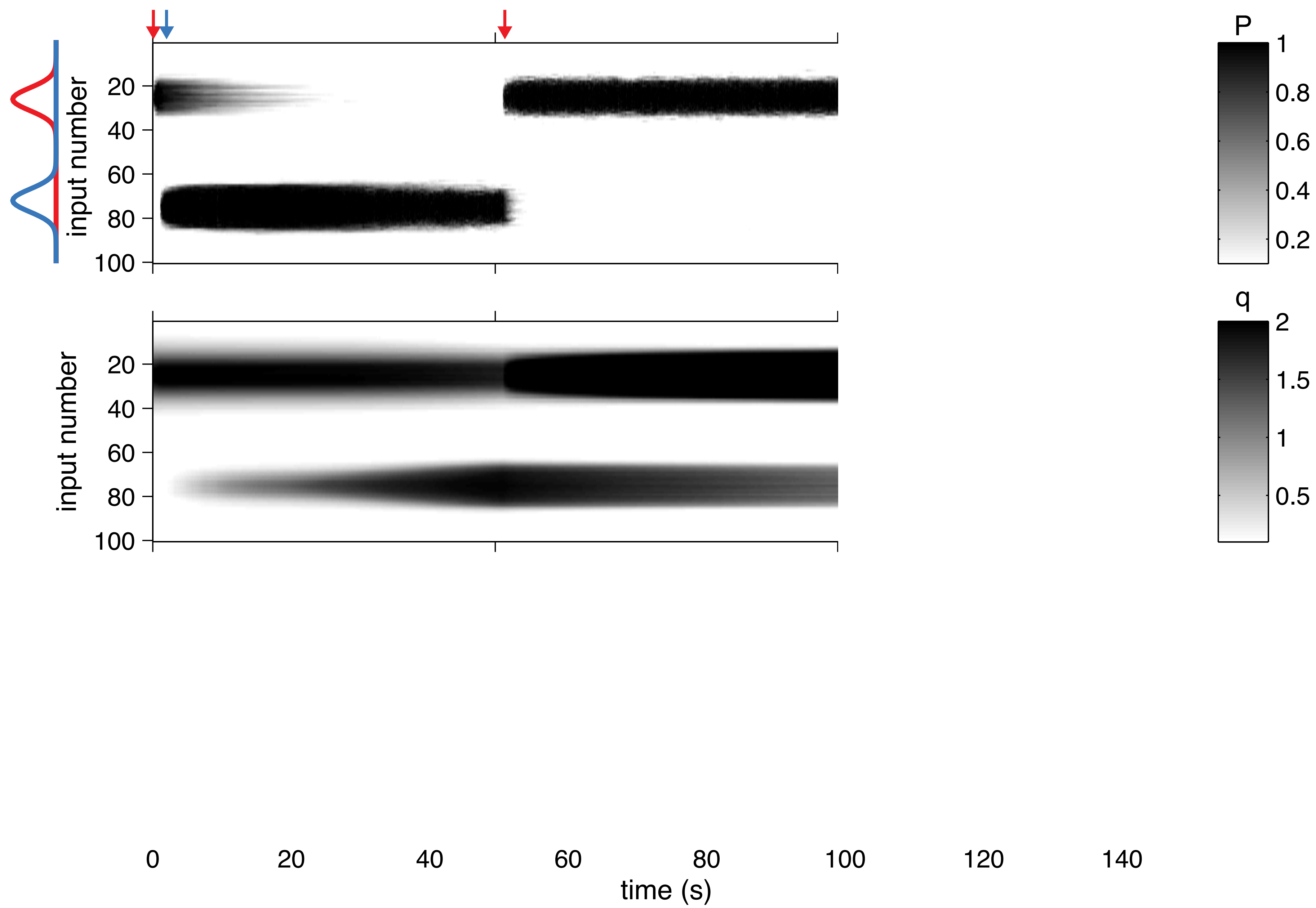
1. A simple example of a feedforward network that receives two sets of inputs (blue and red gaussians):



Costa et al. 2015 eLife

A synaptic plasticity theory of memory savings

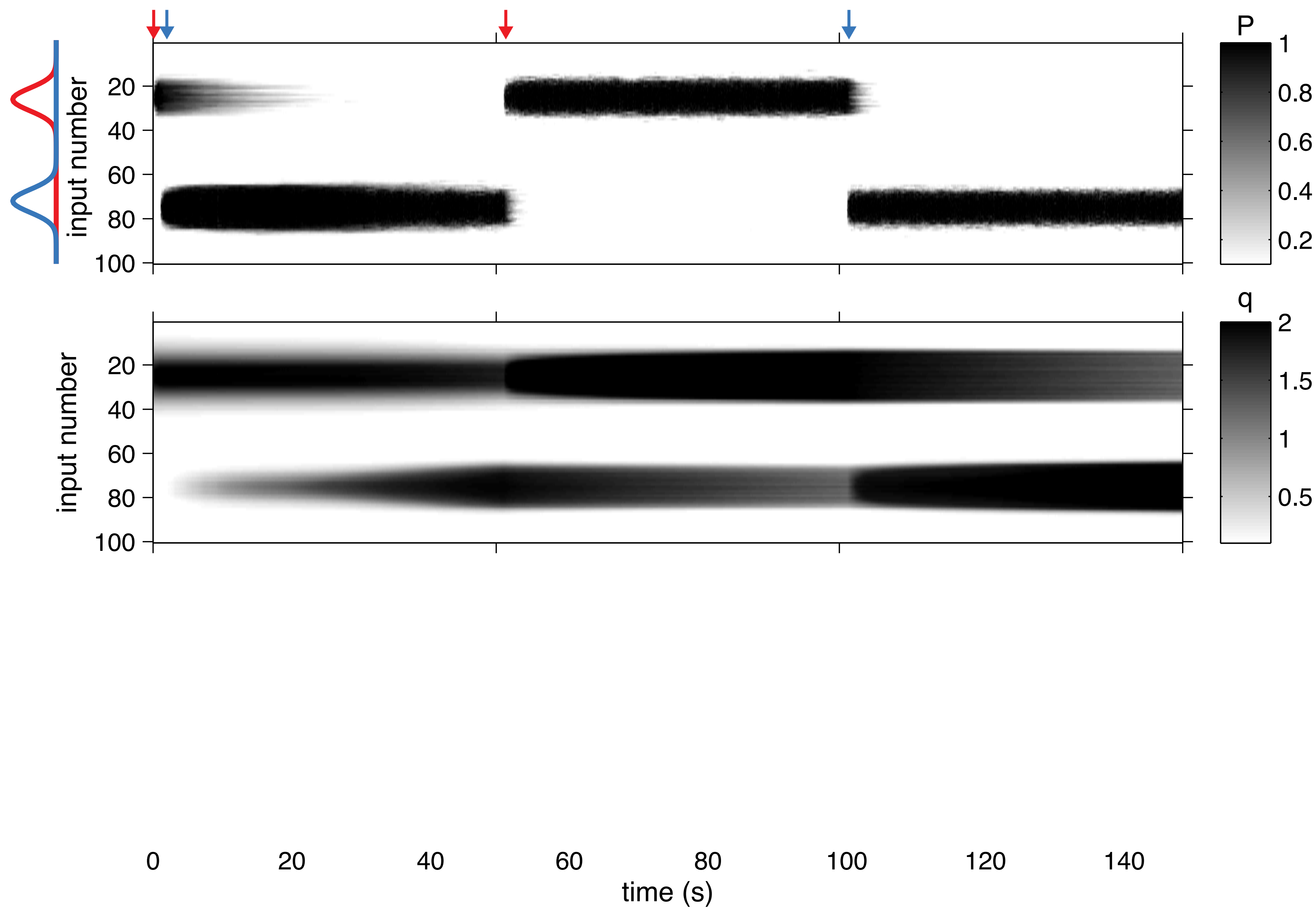
2. Arrows on top indicate which input is presented, note that P quickly forgets the new input (blue).



Costa et al. 2015 eLife

A synaptic plasticity theory of memory savings

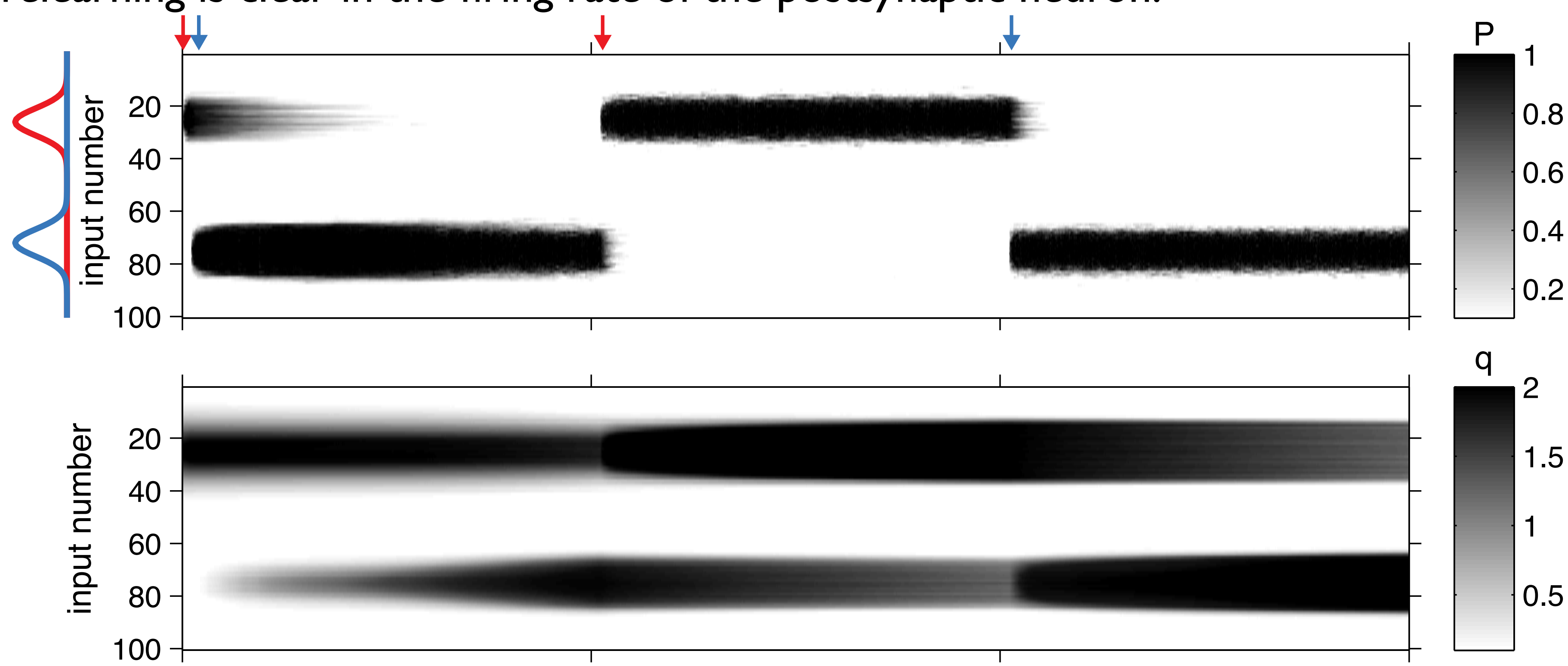
3. While q remembers the new input (blue), which means that relearning should be quicker.



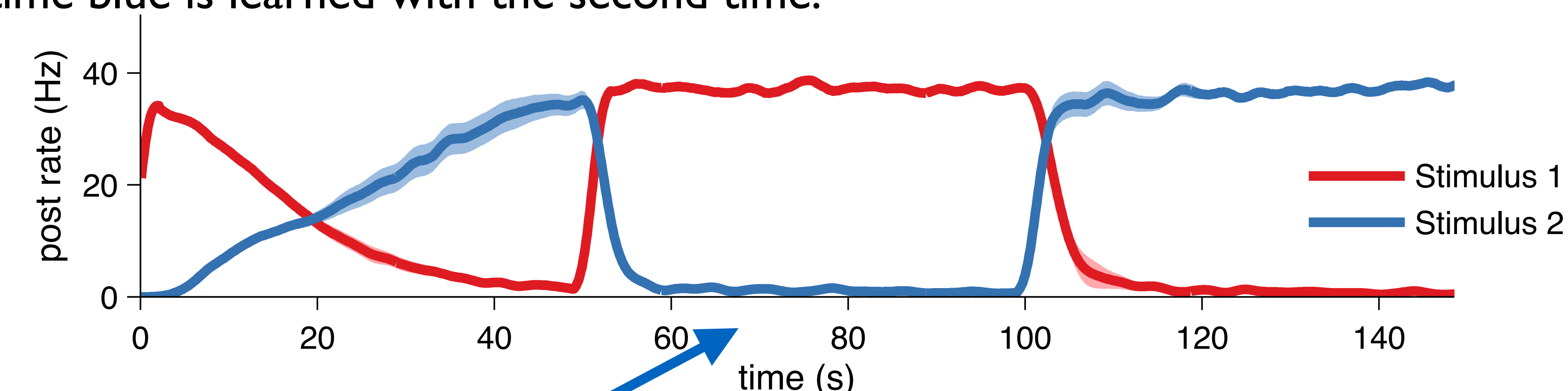
Costa et al. 2015 eLife

A synaptic plasticity theory of memory savings

4. This quick relearning is clear in the firing rate of the postsynaptic neuron.



Compare first time blue is learned with the second time:

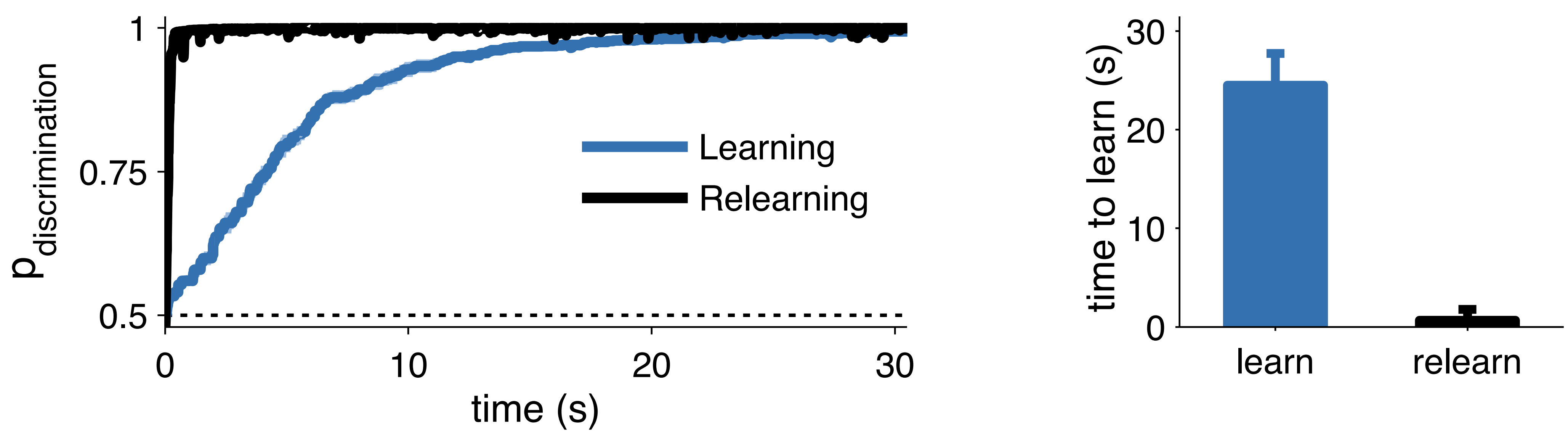


Note that the neuron effectively forgot the blue experience!

Costa et al. 2015 eLife

A synaptic plasticity theory of memory savings

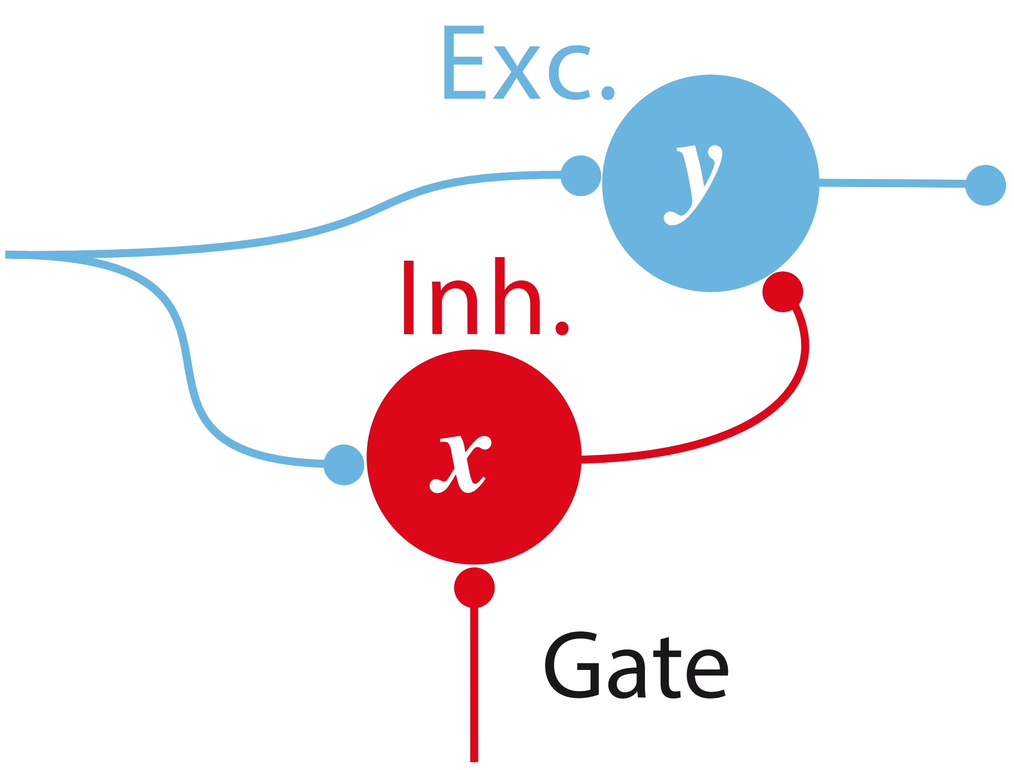
The ability of the postsynaptic neuron to discriminate the input is much quicker during the second learning phase - this is a form of memory savings!



Costa et al. 2015 eLife

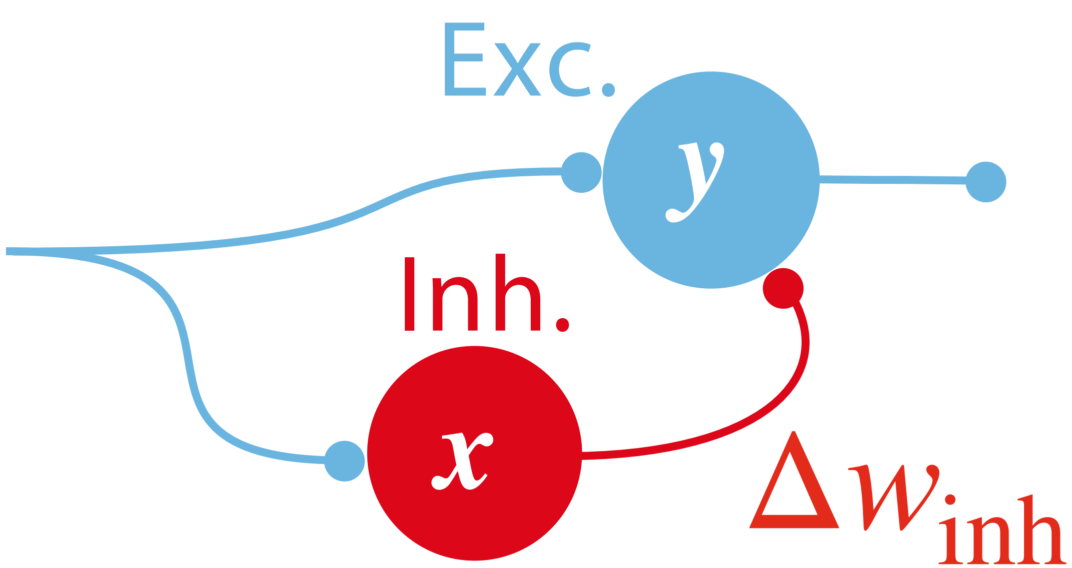
Inhibitory long-term synaptic plasticity

Inhibition is key to maintain the brain in a healthy state. So if excitation changes inhibition should quickly follow!



Hennequin et al. review (2017)

Inhibitory long-term synaptic plasticity



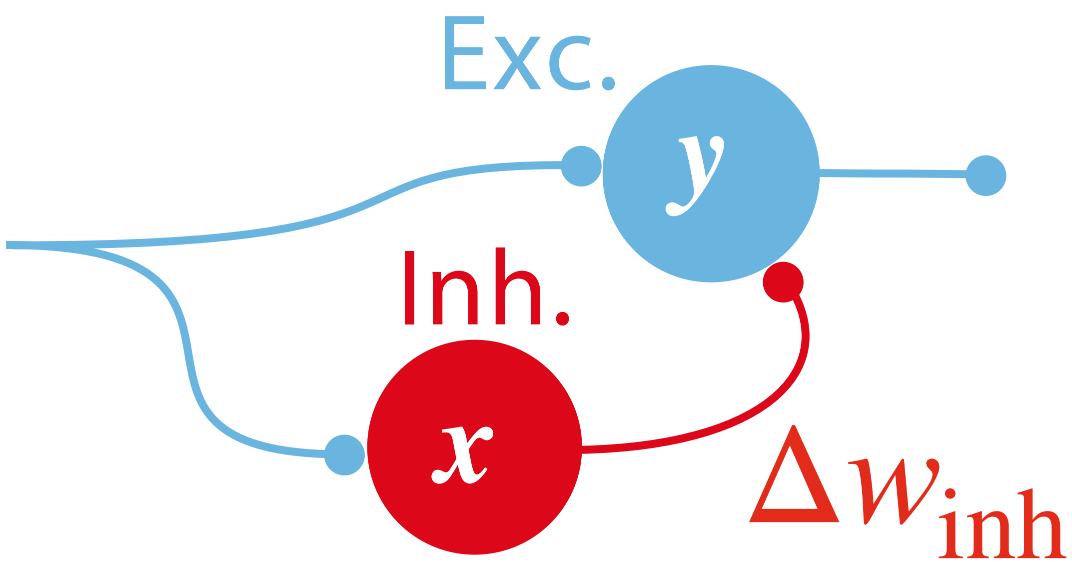
Inhibitory learning rule:

$$\Delta w_{\text{inh}} = \eta x(y - r_0)$$

target rate

Vogels et al. Science (2011)

Inhibitory long-term synaptic plasticity



Inhibitory learning rule:

$$\Delta w_{\text{inh}} = \eta x(y - r_0)$$

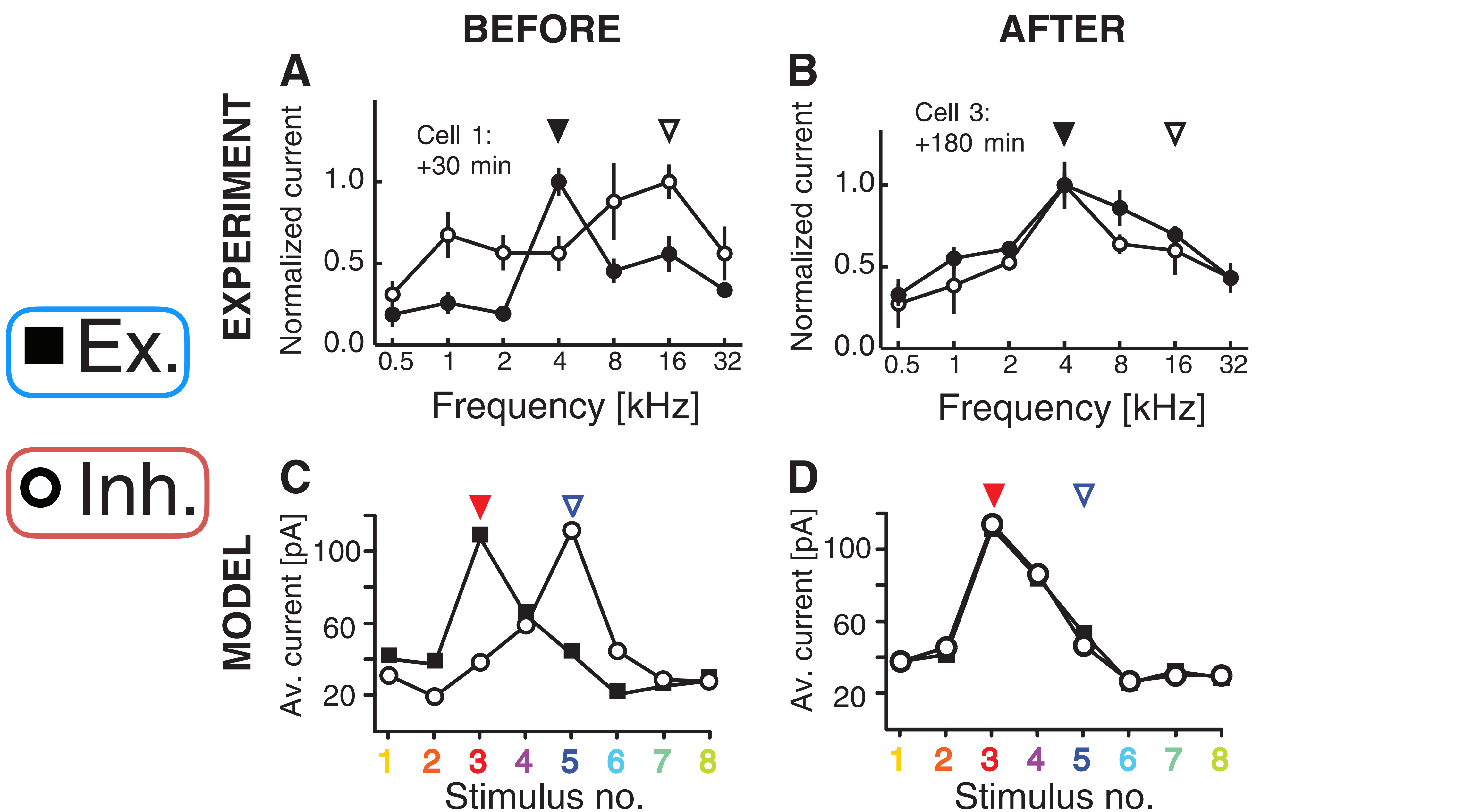
$$0 = \eta x(y - r_0)$$

$$y = r_0$$

postsynaptic neuron, *y* = target rate (*r_0*)

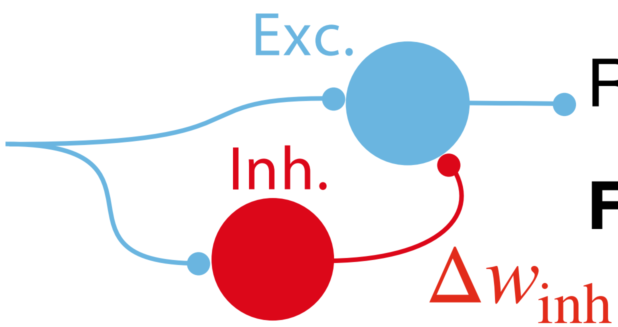
Vogels et al. Science (2011)

Inhibitory plasticity balances receptive fields



Vogels et al. Science (2011)

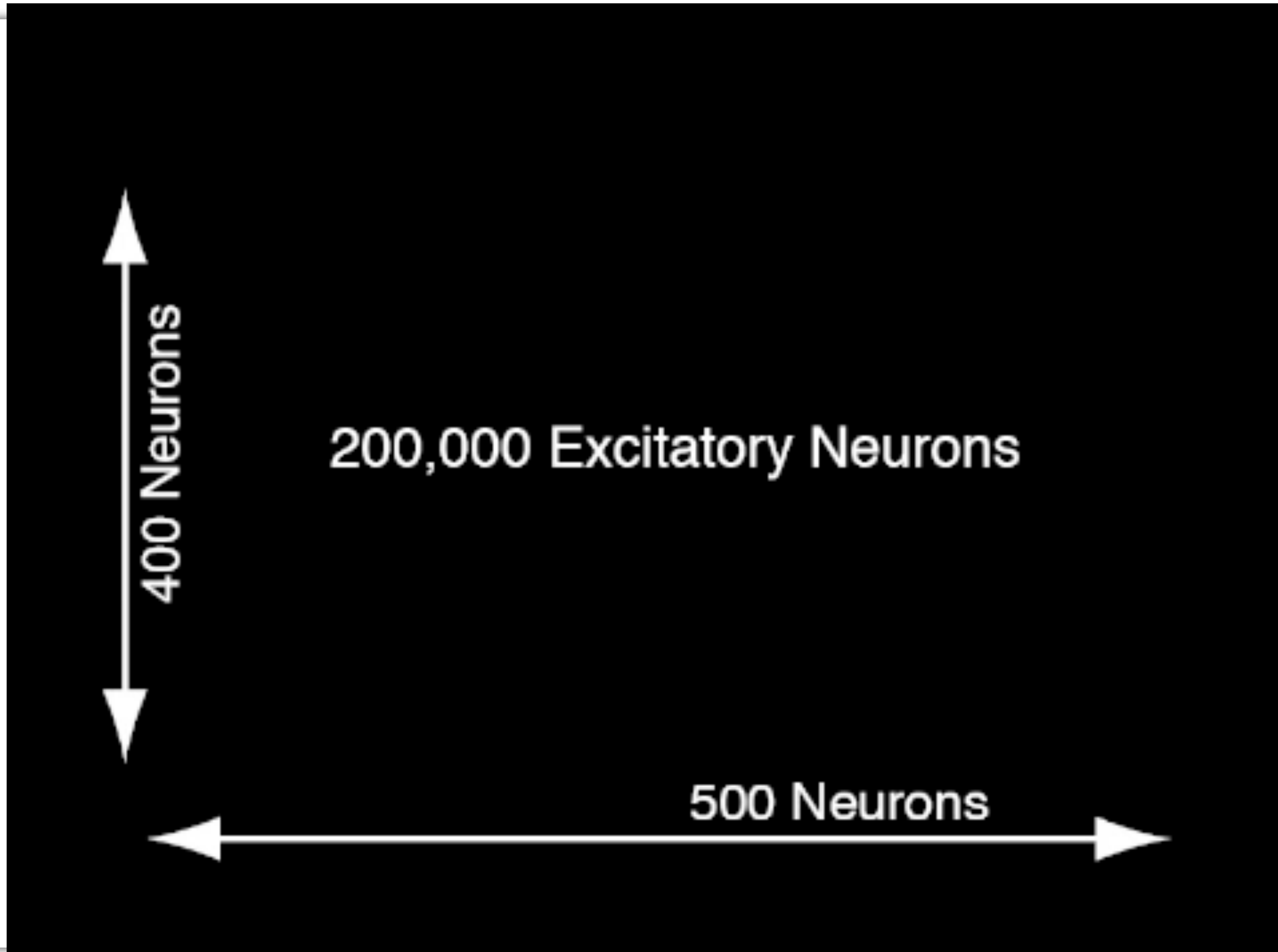
Inhibitory balance in a recurrent neural network



Recurrent network: 200 000 exc. neurons + ~40 000 inh. neurons

Features: keeps activity under control (homeostasis) and memories hidden

Vogels et al. Science (2011)



Summary: time, location and inhibition (part 2)

1. Long-term plasticity also depends on timing: spike-timing-dependent plasticity

2. ..and location: pre and postsynaptic expression

3. This dual expression suggest a synaptic mechanism for memory savings

4. Inhibitory synaptic plasticity can control network activity

References

Text books:

General biology: Wikipedia/Principles of neuroscience [neuroscience bible]

Computational Neuroscience: Neuronal Dynamics by Gerstner, Kistler, Naud and Paninski

Computational Neuroscience: Principles of Computational Modelling in Neuroscience by Sterratt, Gillies, Graham and Willshaw

[Scholarpedia is a good free source of reviews on computational neuroscience, see references in the slides]

And the papers referred to during the lecture.

Questions?