How do biological neurons learn?

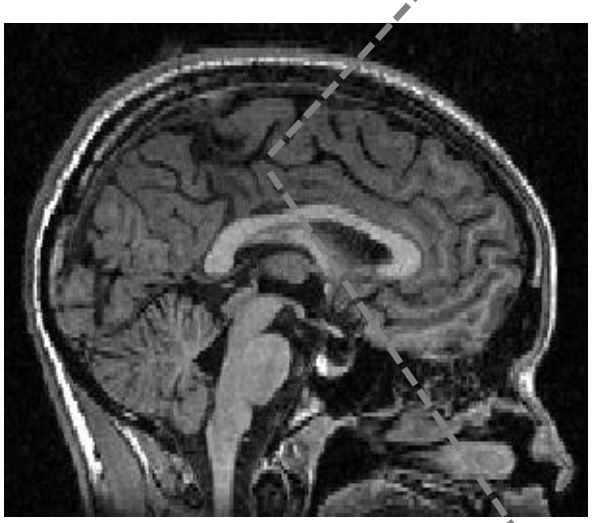
Insights from computational modelling of neurobiological experiments

Lubica Benuskova

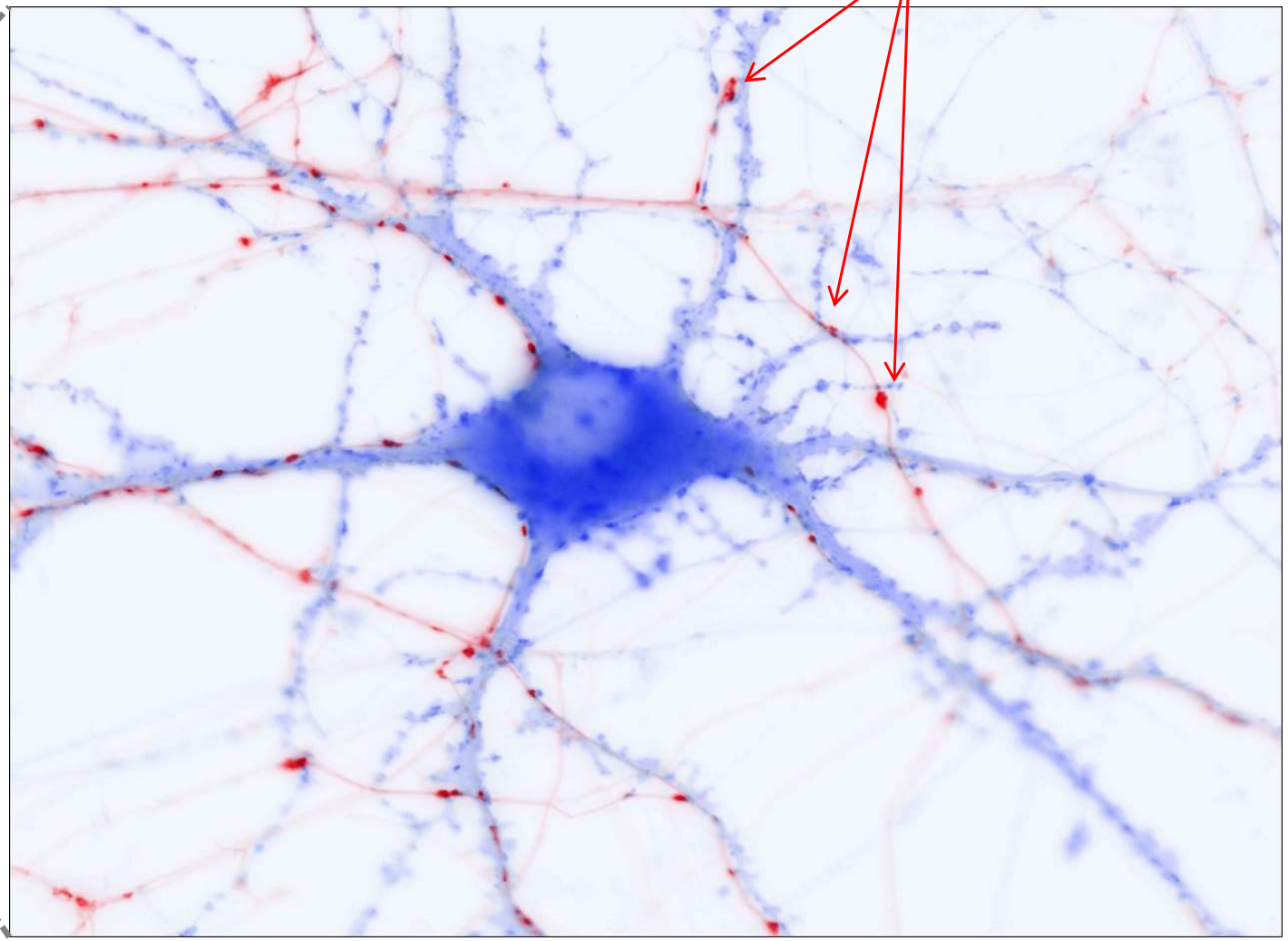
Department of Computer Science

University of Otago, New Zealand

Brain is comprised of networks of neurons connected and communicating via synapses



10^{12} neurons

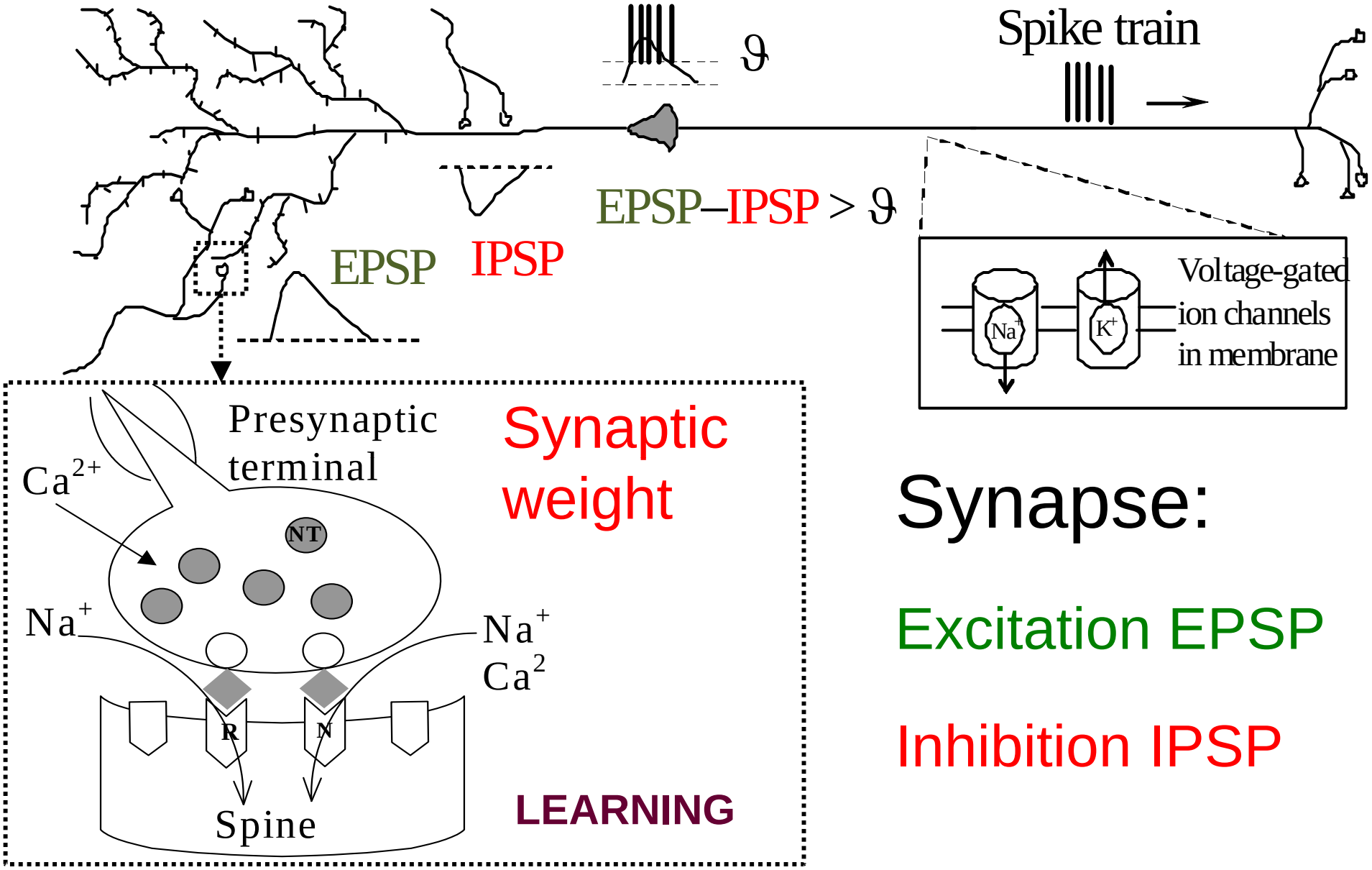


10^{4} synapses

Learning and brain plasticity

- Traditionally: Learning is an acquisition of memories.
- Memory is an organism's ability to store, retain, and subsequently recall information.
- Learning is related to a more general phenomenon, called **brain plasticity**.
- Brain plasticity (neuroplasticity) is a lifelong ability of the brain to reorganize neural circuits based on new experience.

Neuron in action: threshold and spikes

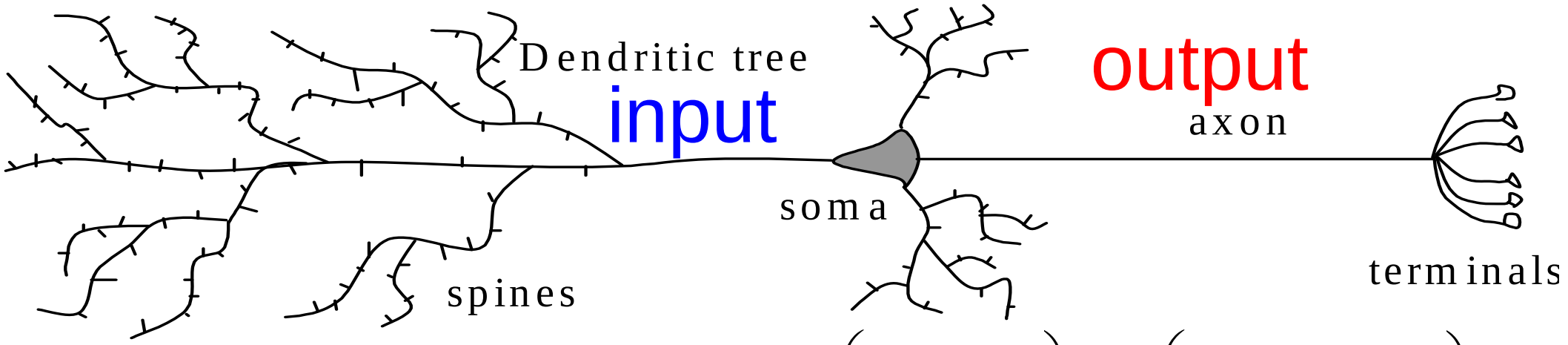


Synapse:

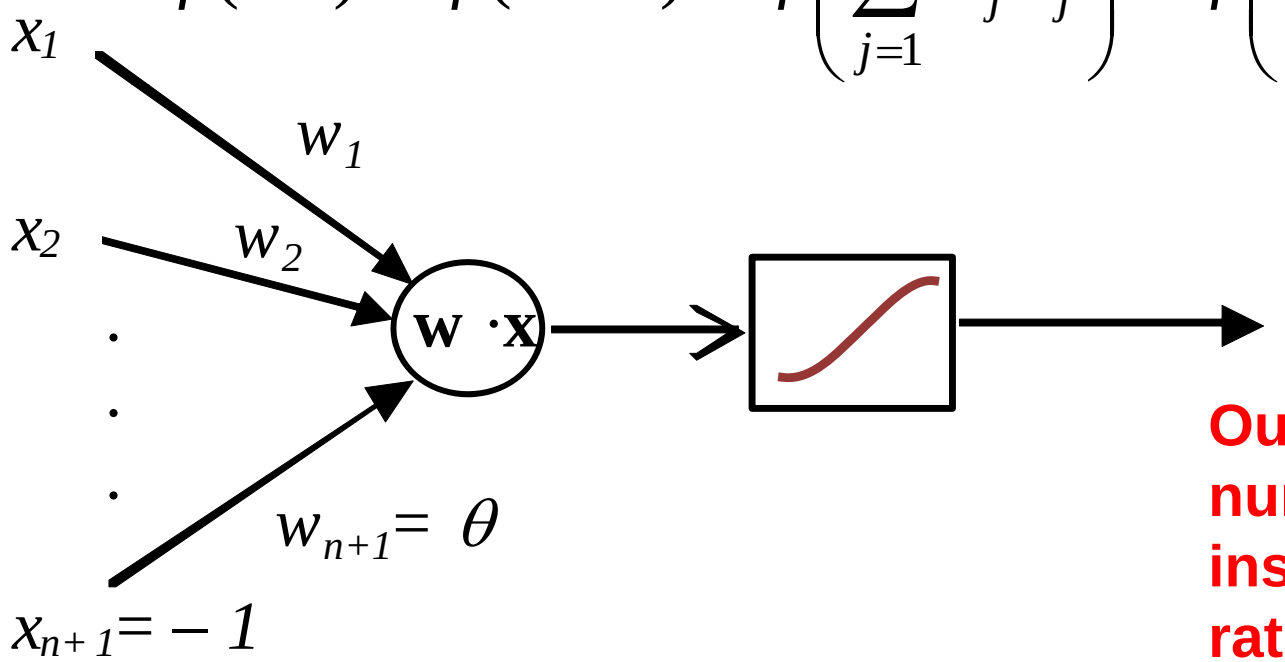
Excitation EPSP

Inhibition IPSP

Neuron rate model schematically and formally



$$o = f(net) = f(\overline{w} \cdot \overline{x}) = f\left(\sum_{j=1}^{n+1} w_j x_j\right) = f\left(\sum_{j=1}^{n} w_j x_j - \theta\right)$$



Input vectors of real numbers (rates of firing)

Output real number = instantaneous rate

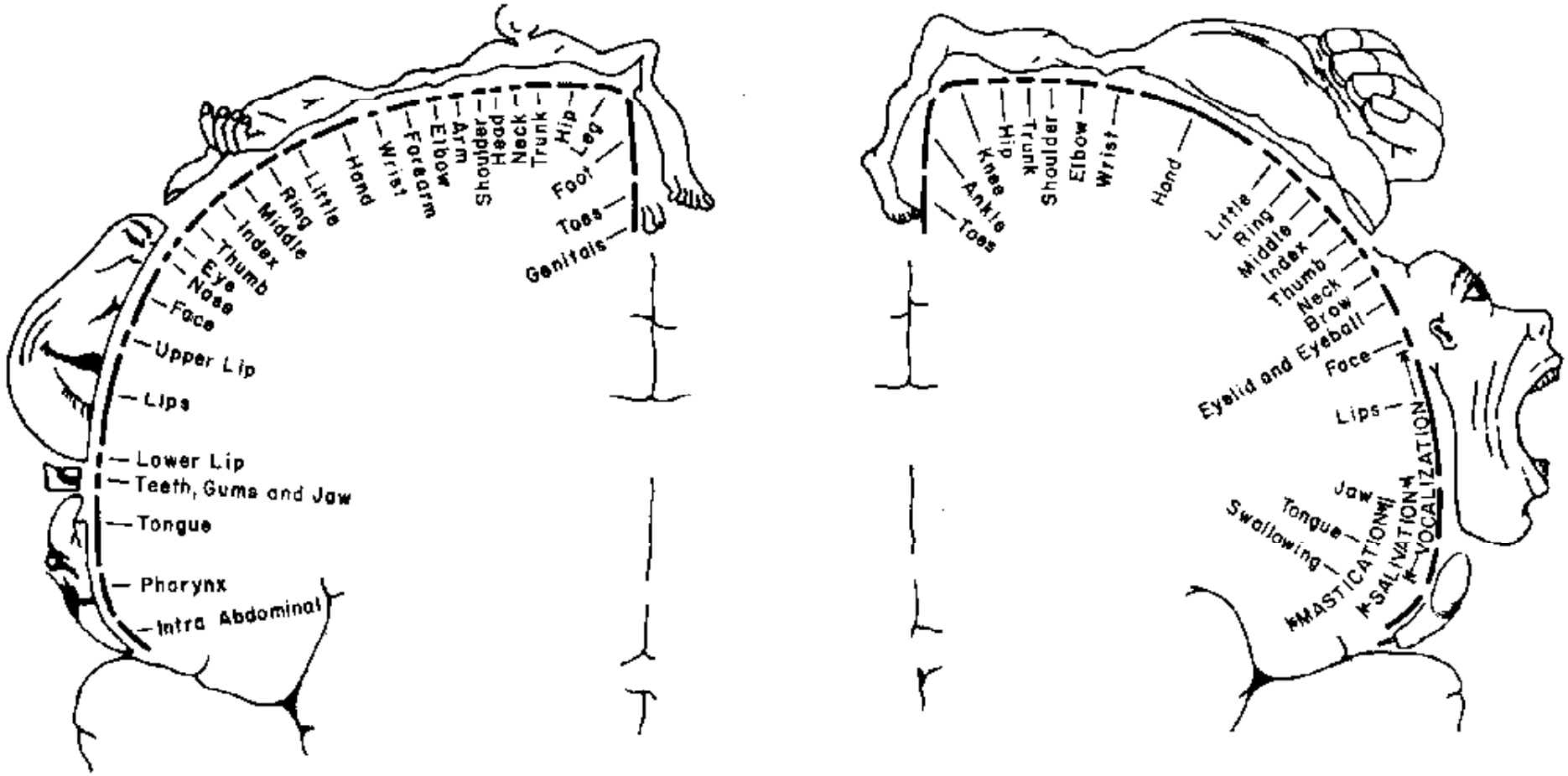
Types of learning in ANN

- **Supervised learning**: ANN weights are adjusted according to the target output (MLP, RBF, RNN)

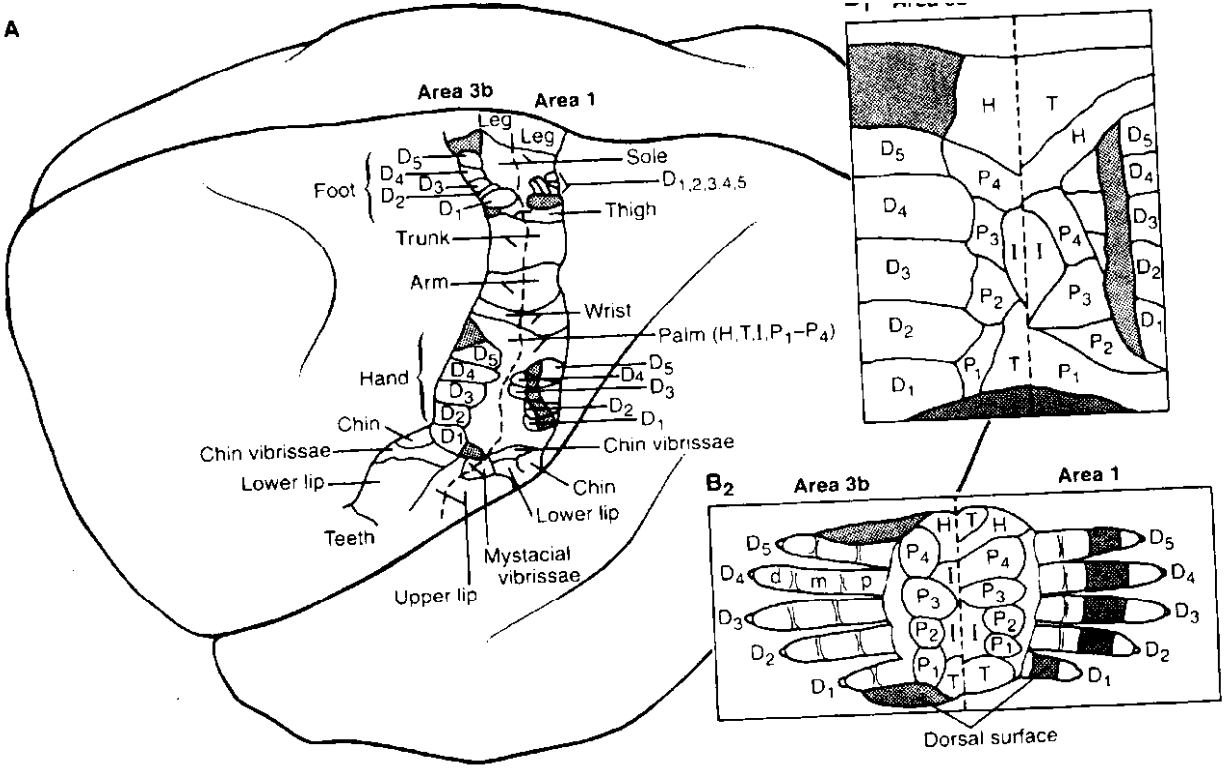
- **Reinforcement learning:** ANN weights are adjusted according to the information about the probability of success (MLP, RBF) – extension of the supervised learning

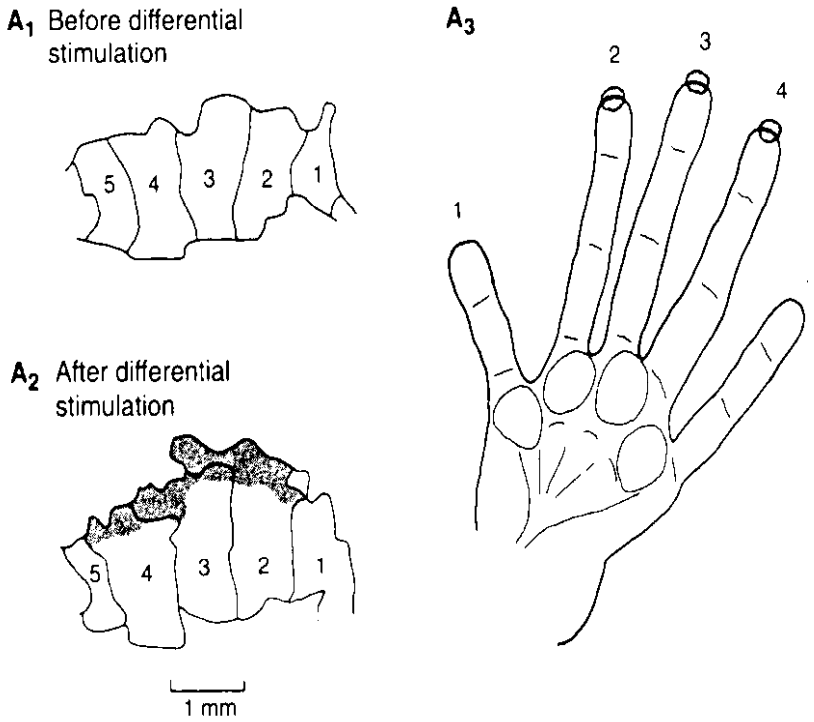
- **Unsupervised learning**: ANN weights are adjusted according to the topology and statistics of the input: THIS SEEMS TO OCCUR IN THE BRAIN !

Somatosensory and motor systems in animals topological mapping from periphery to cortex



Fascinating phenomenon of brain cortex plasticity caused by experience



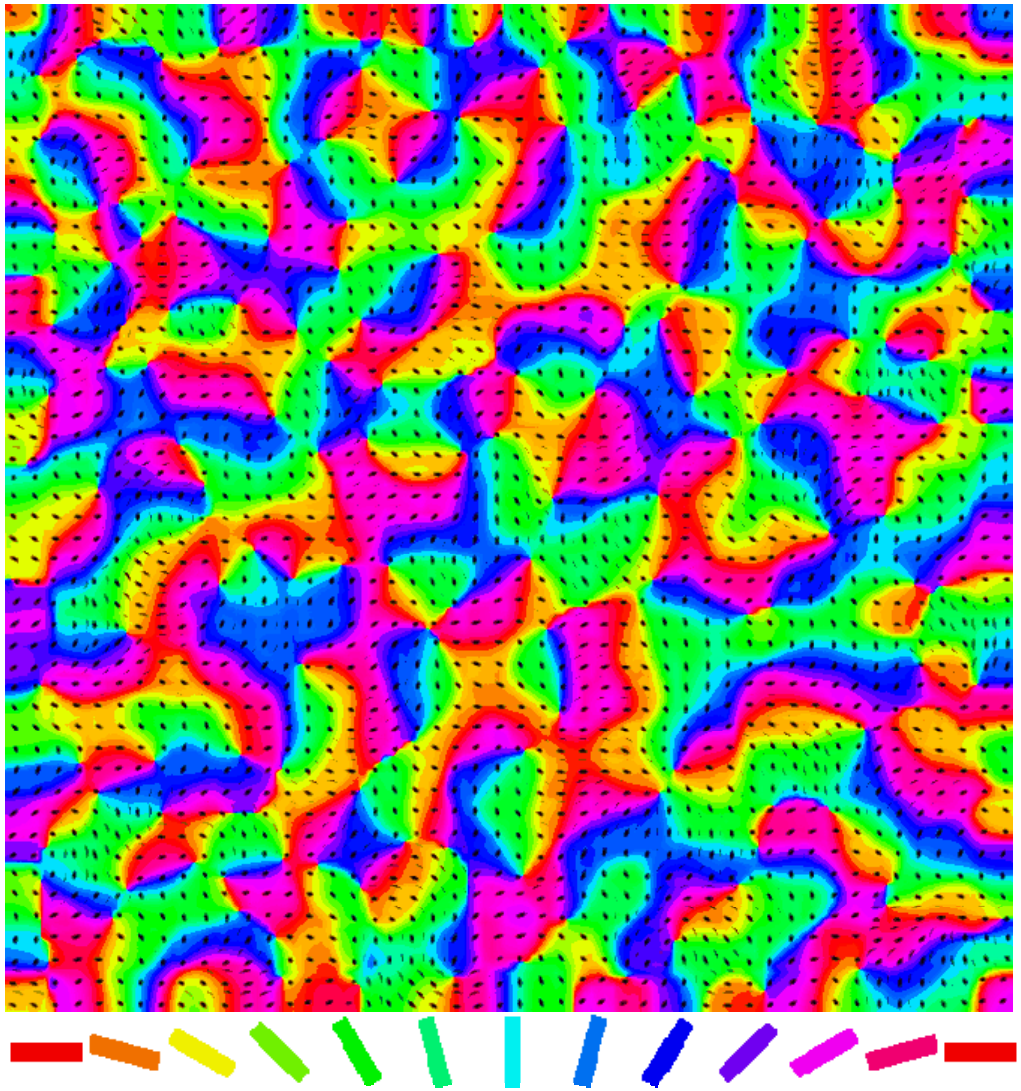


Orderly or topographic representation of somatosensory bodily maps in the cortex

[Merzenich et al]

Use-dependent expansion of representation of more used fingertips

Visual maps of elementary features like orientation of edges and direction of motion

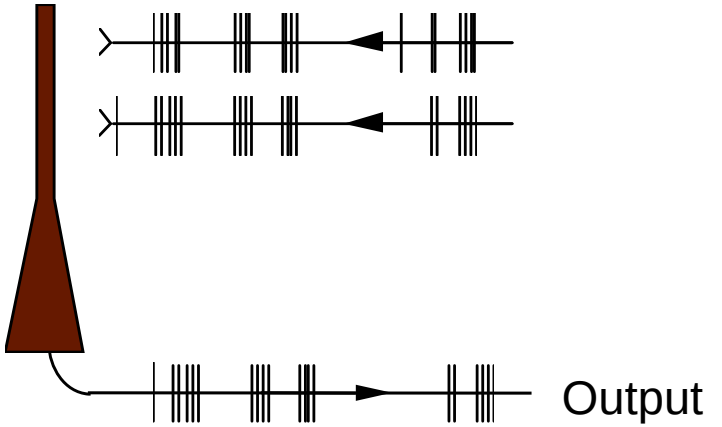


R. Miikkulainen, J.A. Bednar, Y. Choe, J. Sirosh. *Computational Maps in the Visual Cortex*. Springer, Berlin, 2005.

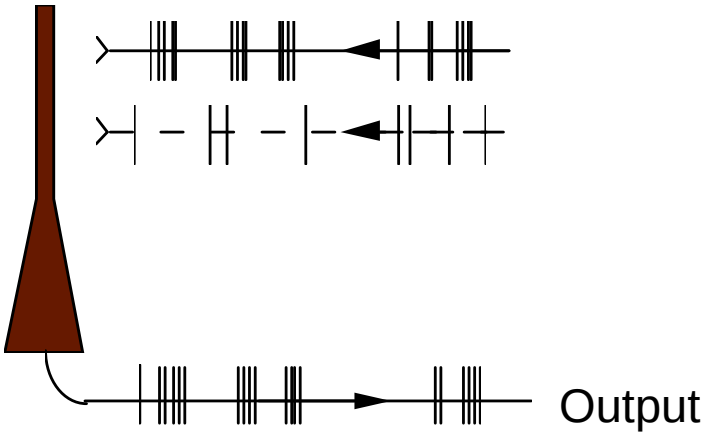
Model based on Self-organizing maps

Hebb rule of synaptic plasticity (1949)

"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."

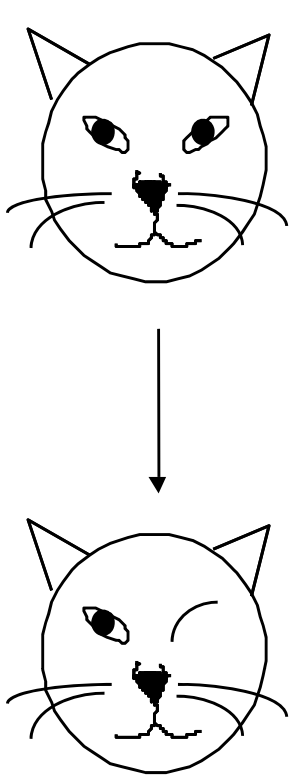


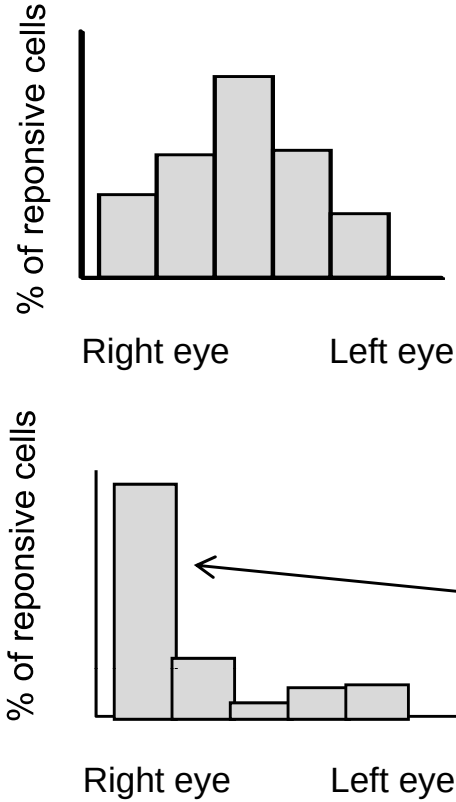
Neurons that fire together wire together.



Neurons that fire out of sync lose their link.

Experimental results in the developing visual cortex



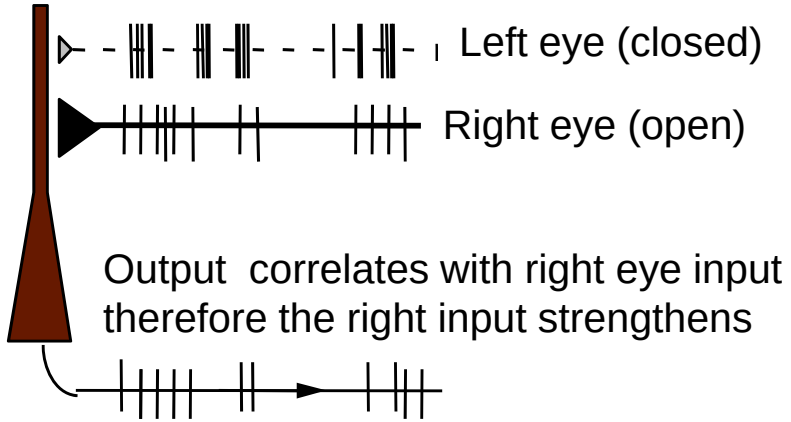


Classical experiments of monocular deprivation

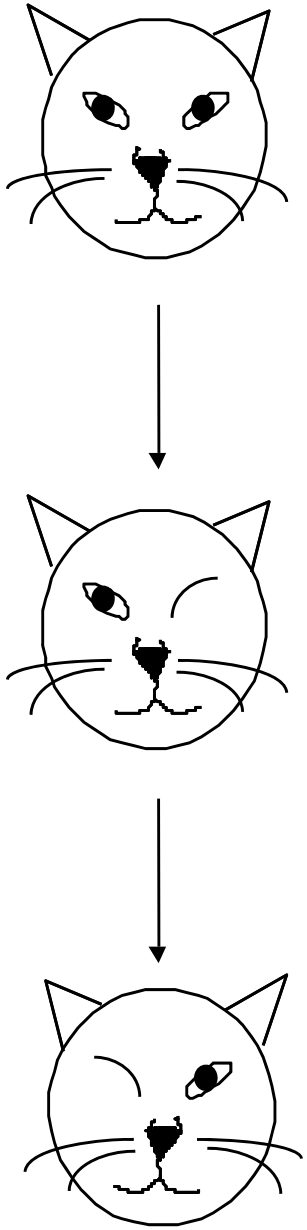
Cells in the visual cortex tend to be binocular and respond to stimulation in both eyes, with different preferences, though.

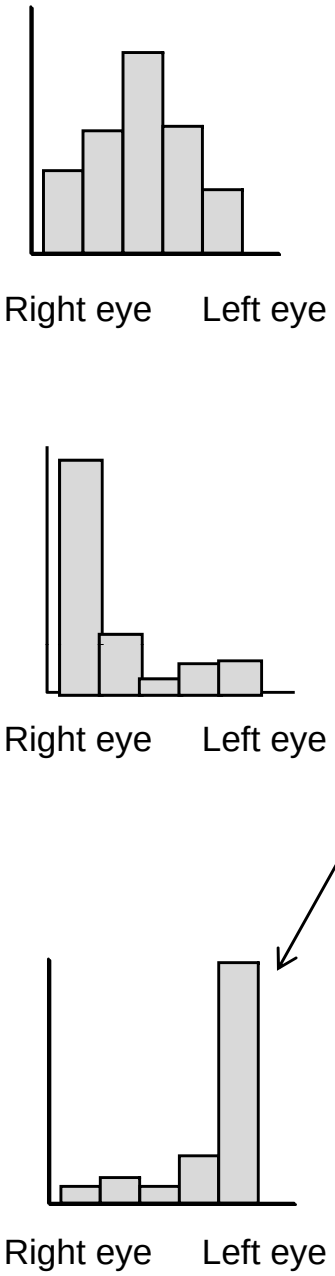
Closing the eye for a brief period causes a shift in the responses towards the non-deprived eye.

This shift in ocular dominance corresponds to Hebbian synaptic plasticity

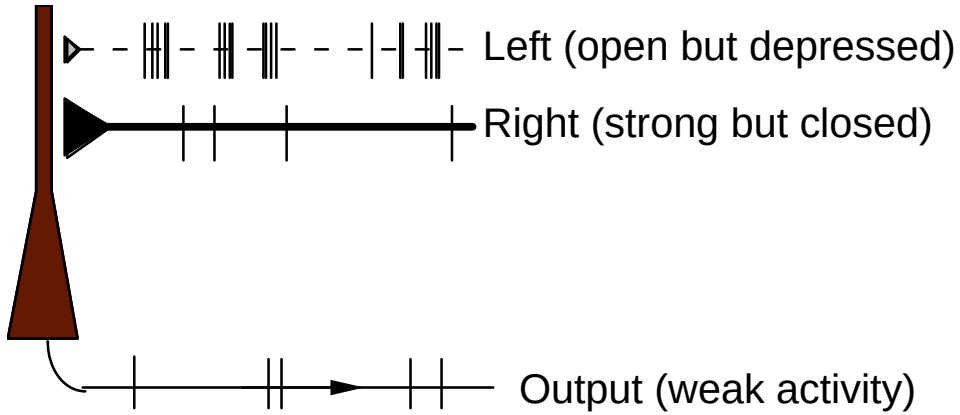


Reverse suture experiments





Can the Hebbian learning explain reverse suture experimental results, when formerly disconnected eye becomes dominant ?

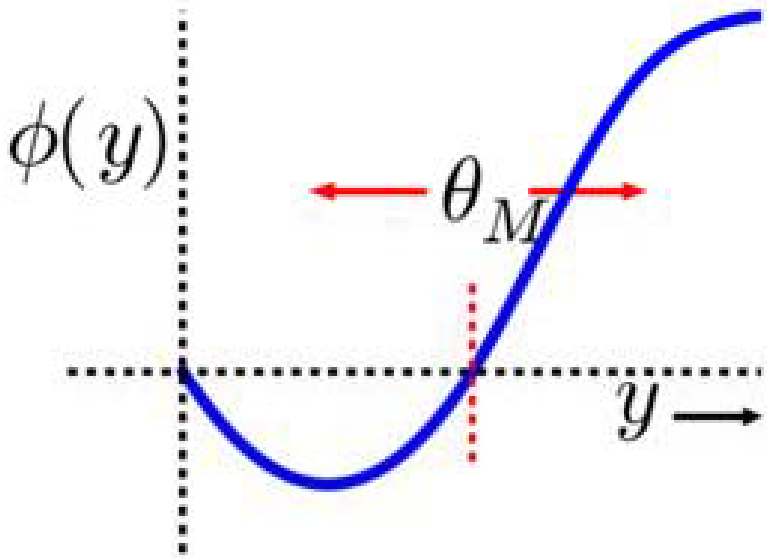


Bienenstock, Cooper, Munro (BCM)

$$y = \sum_j w_j \, x_j$$

$$\frac{dw_j}{dt} = \eta \, x_j \, \phi(y, \theta_M)$$

$$\phi(y, \theta_M) = y(y - \theta_M)$$

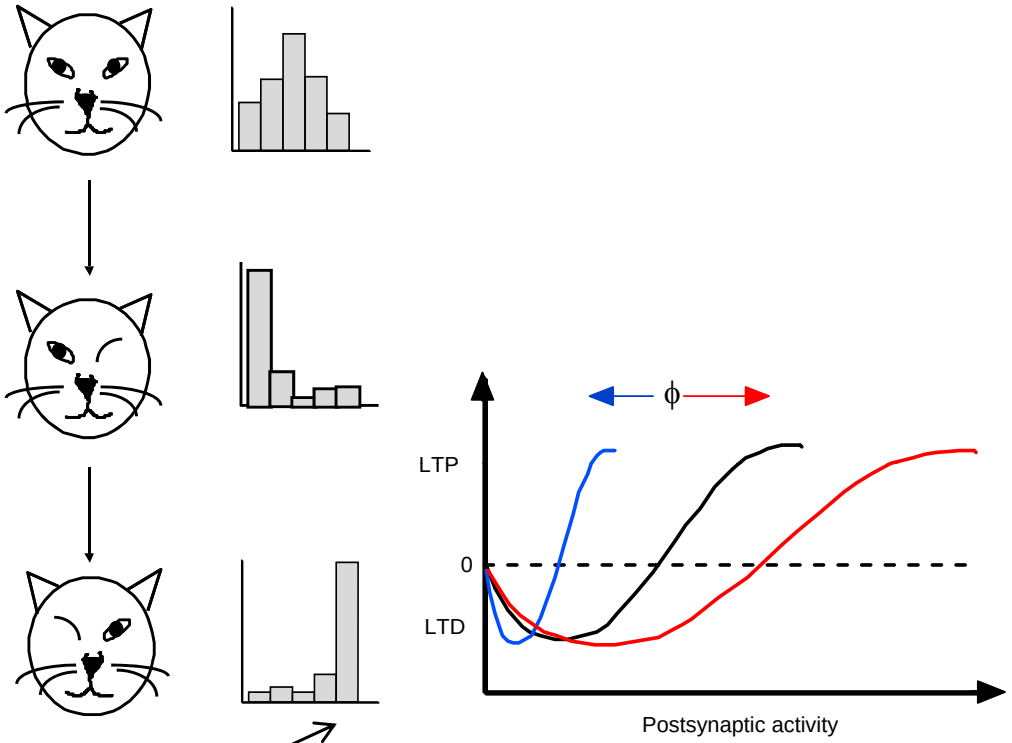


$$\theta_M \propto E\left[y^2\right] = \frac{1}{\tau} \int_{-\infty}^{t} y^2(t') e^{-(t-t')/\tau} dt'$$

METAPLASTICITY: Position of θ_M depends on the neuron's past activity !

Term coined by [Abraham and Bear, TINS, 1996]

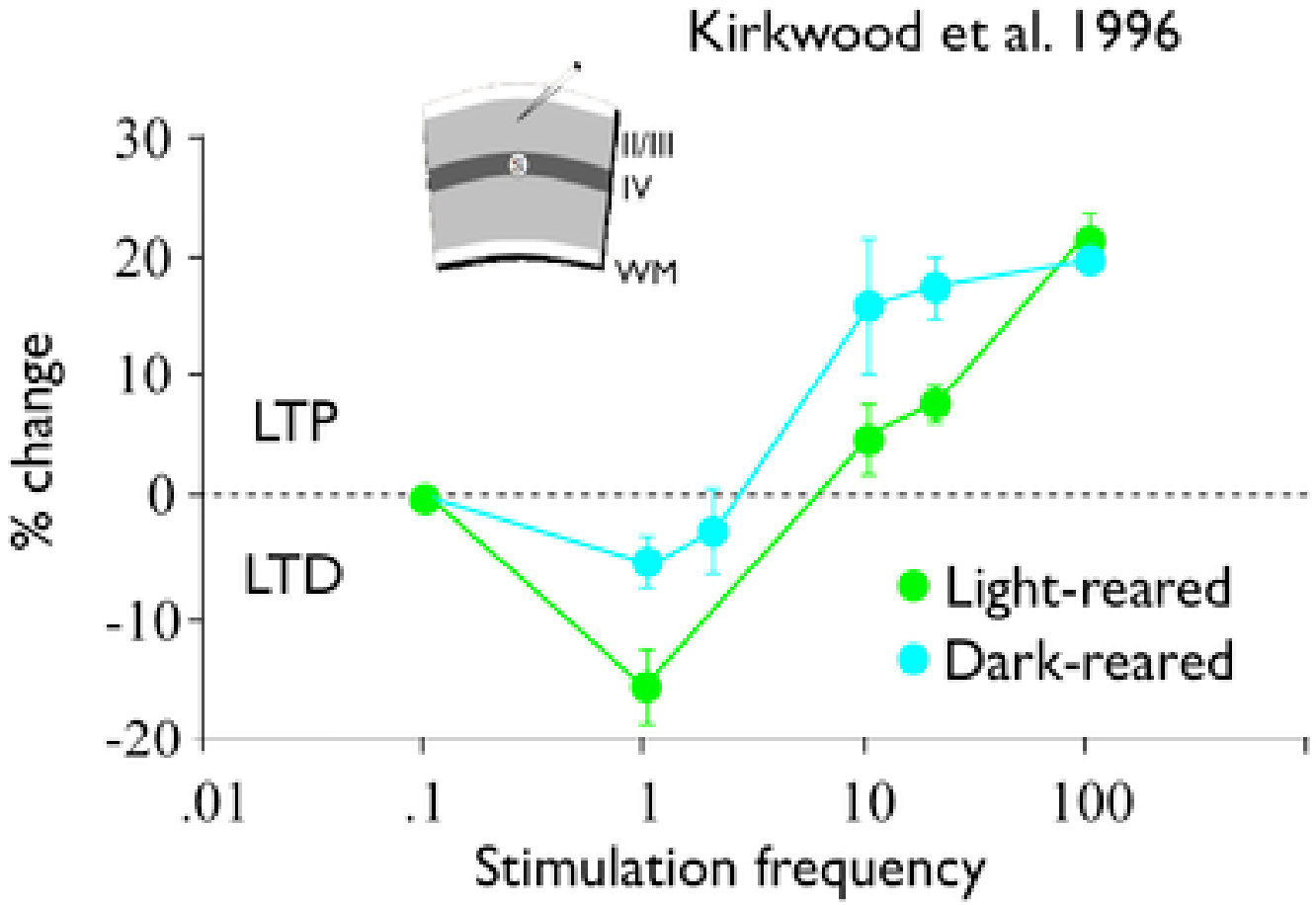
BCM postulated: there is threshold for synaptic potentiation that decreases when postsynaptic activity is low on average and increases when it is high on average



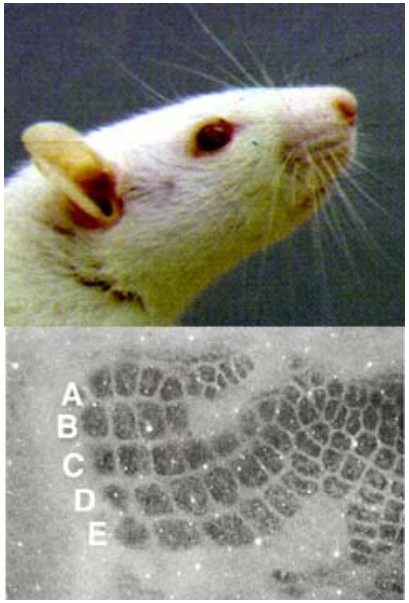
After closing the right eye and opening the left eye, modification function Φ slides to the left, thus allowing weak left eye synapses to strengthen

[Cooper et al, 1982-2004]

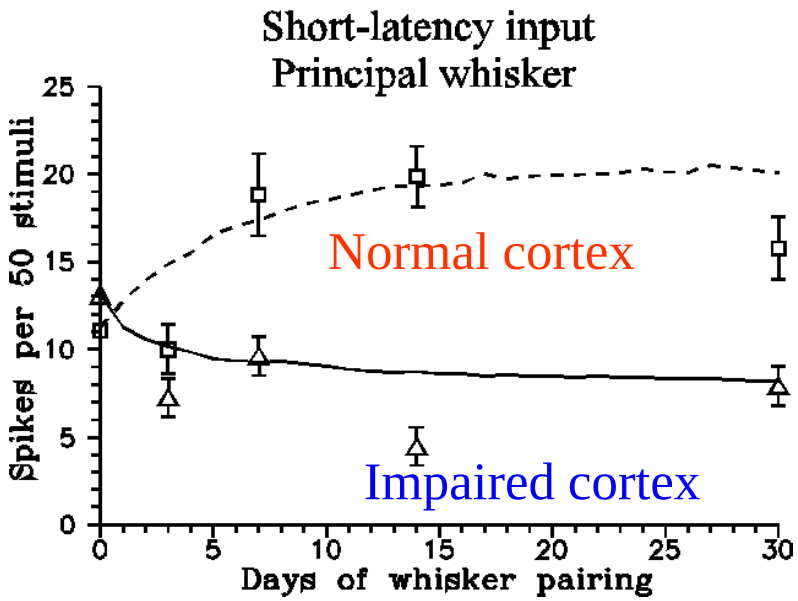
Experimental evidence: It is easier to obtain potentiation in the cortex of dark-reared animals and it is harder to induced synaptic depression in these cortices

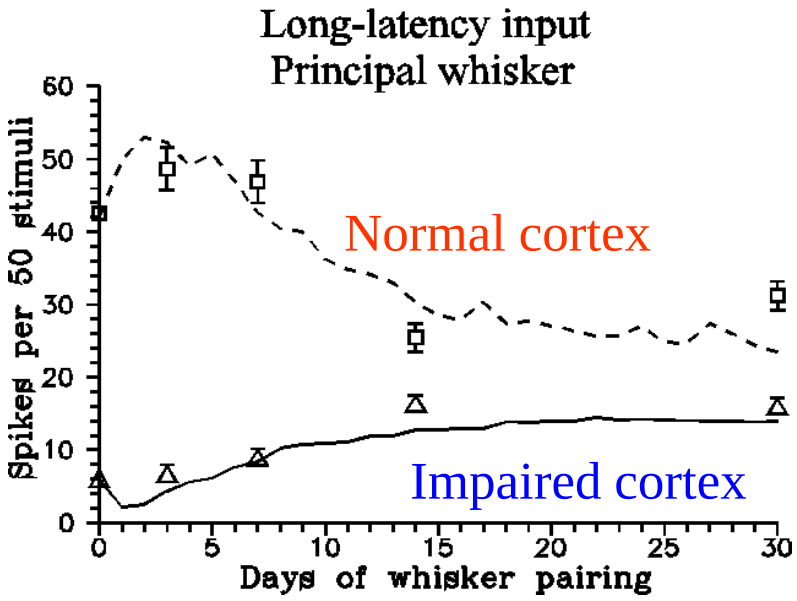


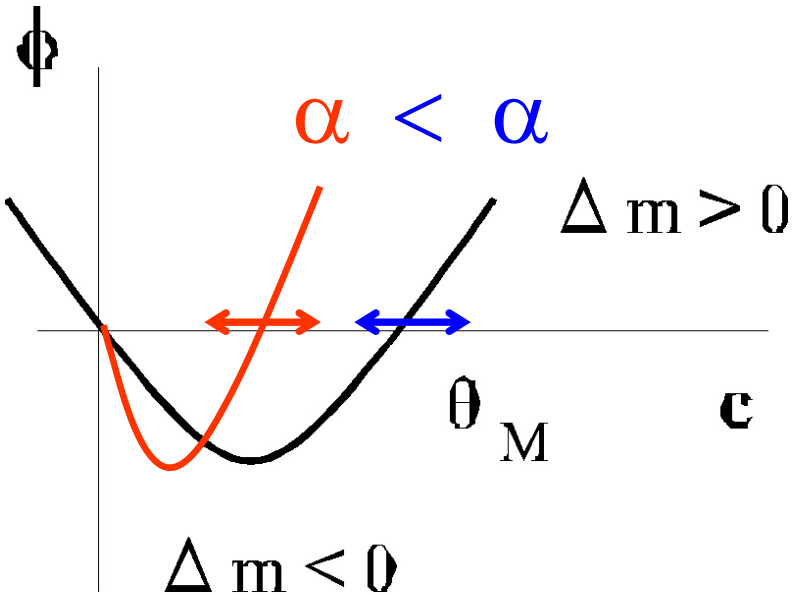
Results for somatosensory cortex of rats



[Benuskova et al., PNAS 1994, 2001]



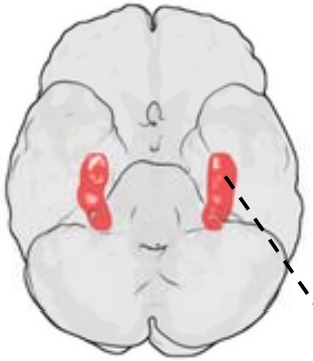


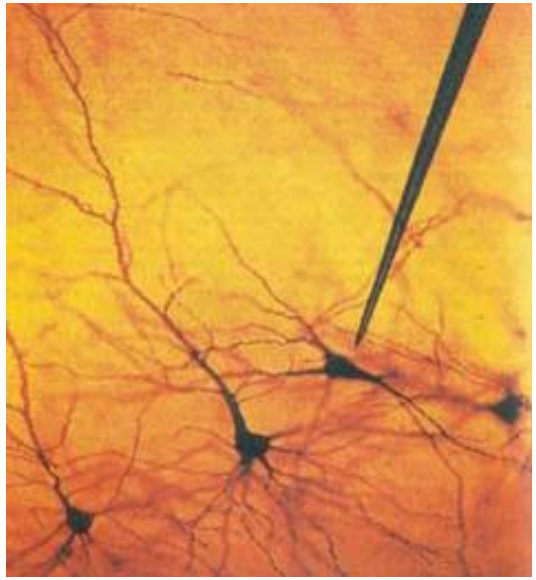


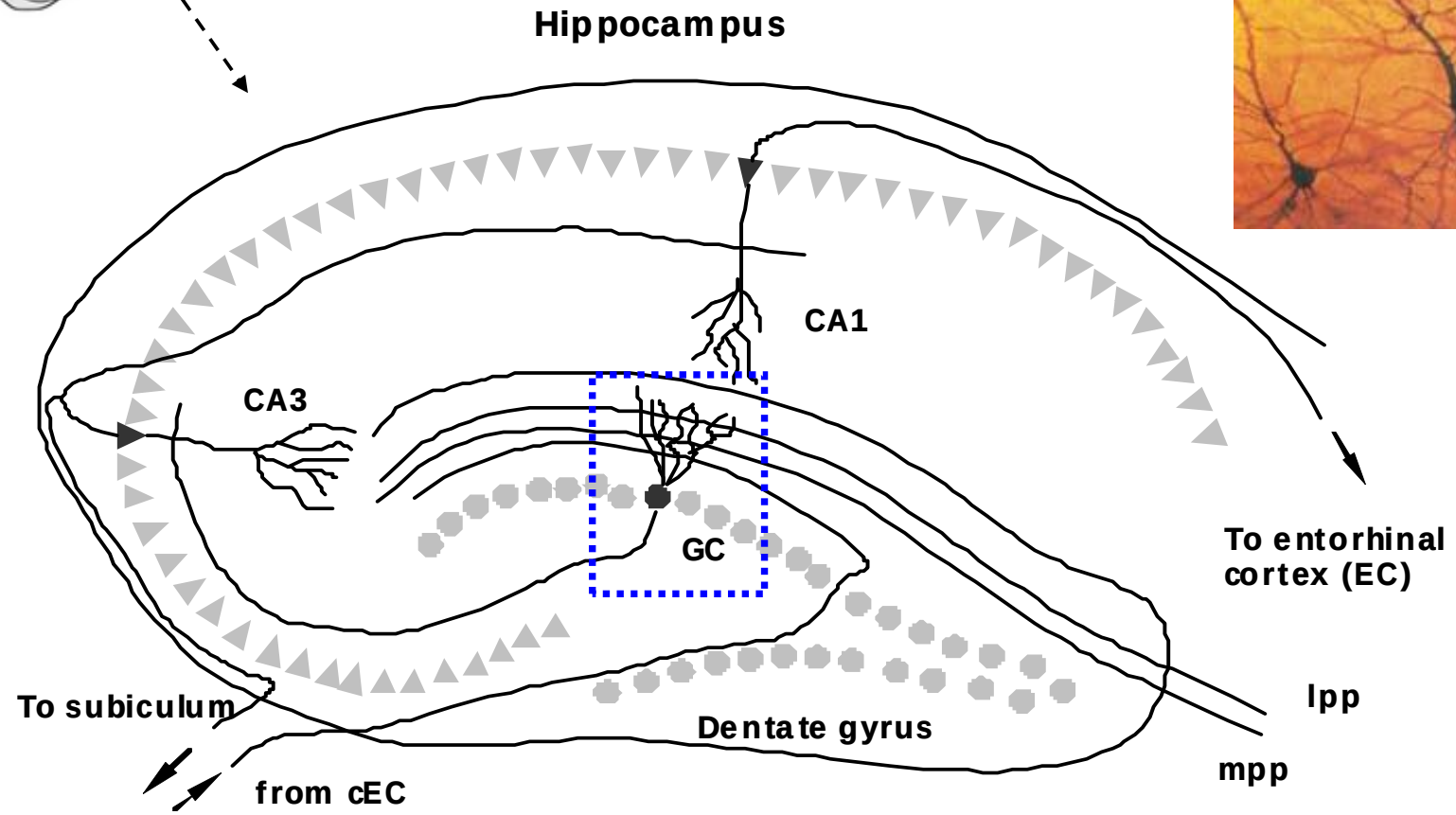
LTP/LTD = long-term potentiation/depression of synaptic efficacy

- LTP/LTD are the gold standard synaptic models for mammalian memory mechanisms for 3 decades;
- LTP/LTD occur in hippocampus and in neocortex, which are brain regions involved in formation of long-term memories;
- LTP/LTD are long-lasting synaptic changes; can last for hours, days even weeks;
- LTP/LTD are synaptic activity-dependent, either in a homo- or heterosynaptic fashion.

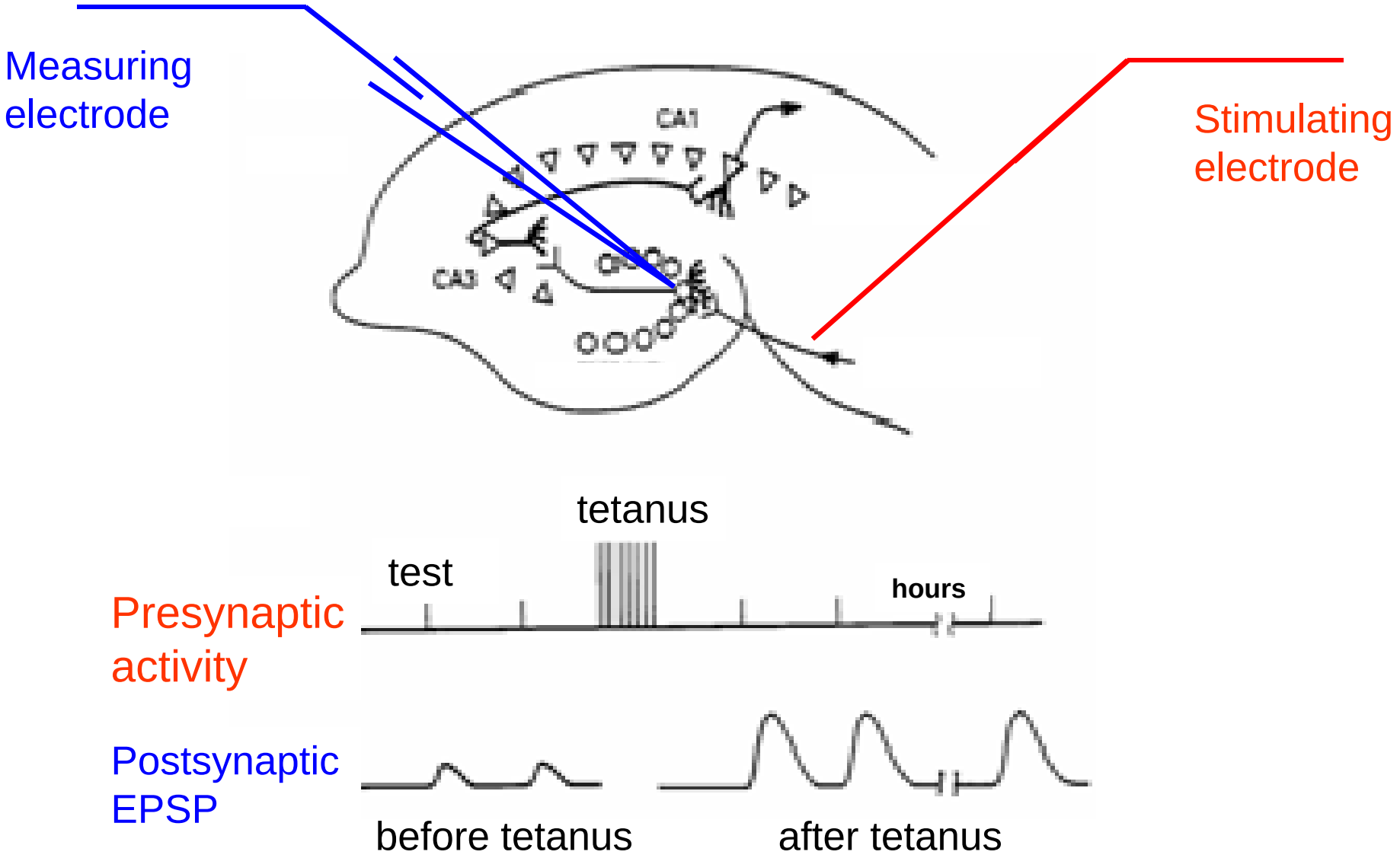
LTP/LTD in hippocampus



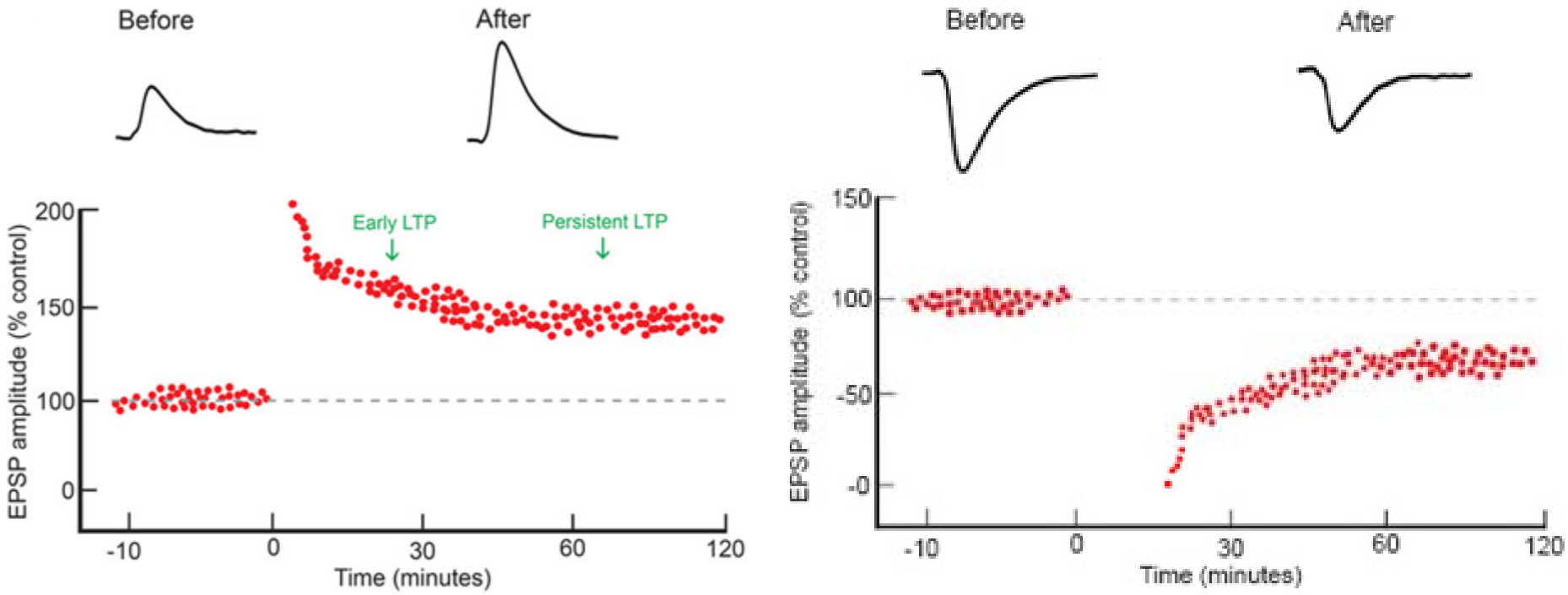




Induction of LTP

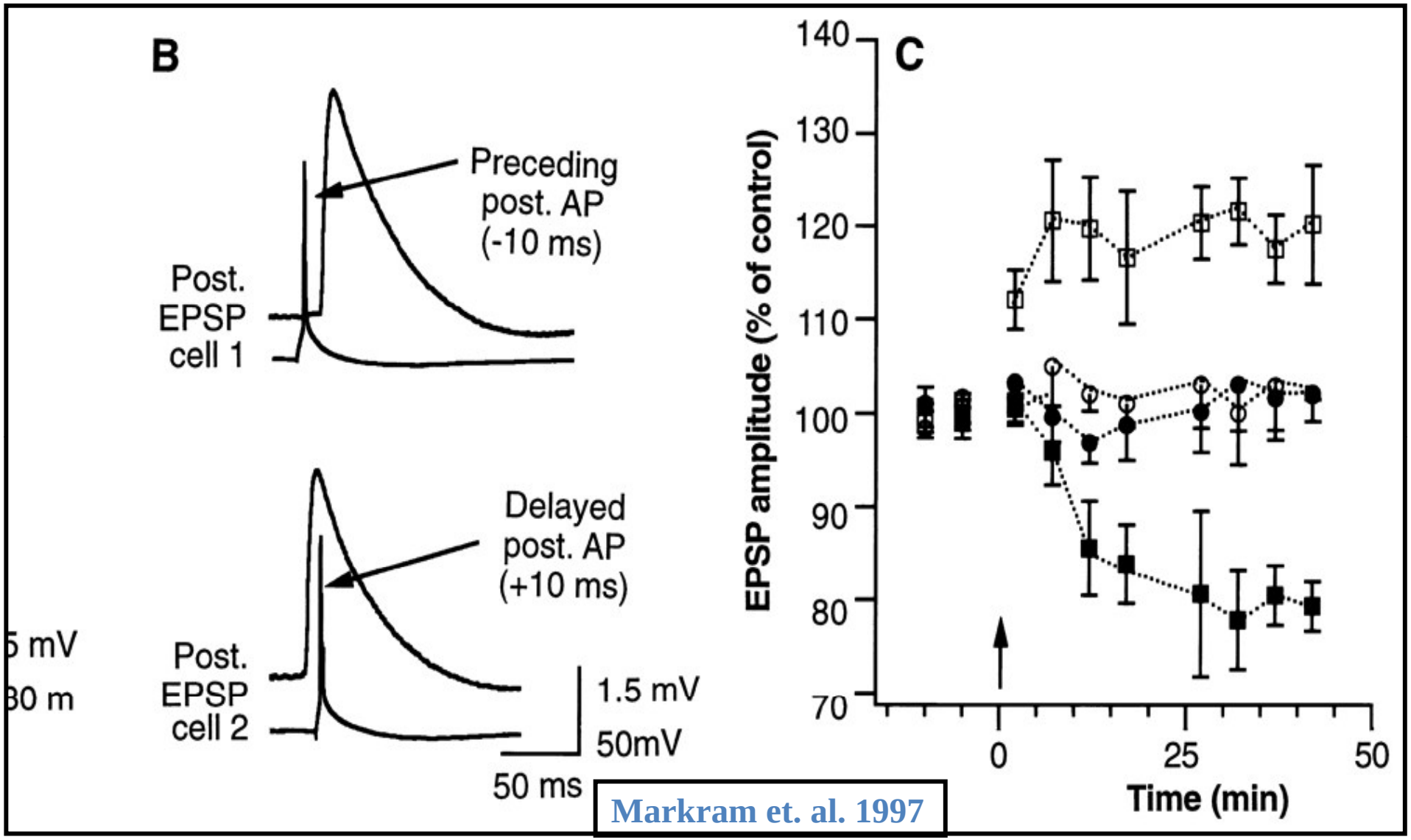


Bidirectional properties of LTP and LTD



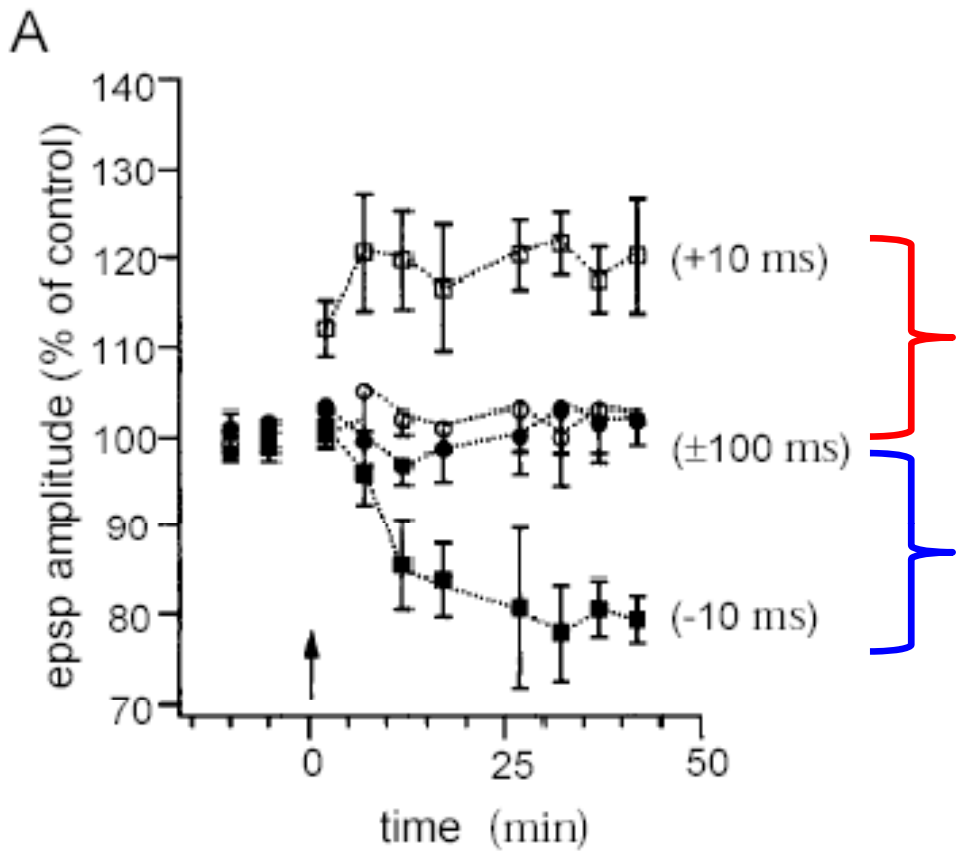
The change is bidirectional, i.e. the same synapse can become potentiated or depressed based on frequency of tetanus: ~ 100 Hz (LTP) ~ 10 Hz (LTD), i.e. there is a **threshold** around 10 Hz

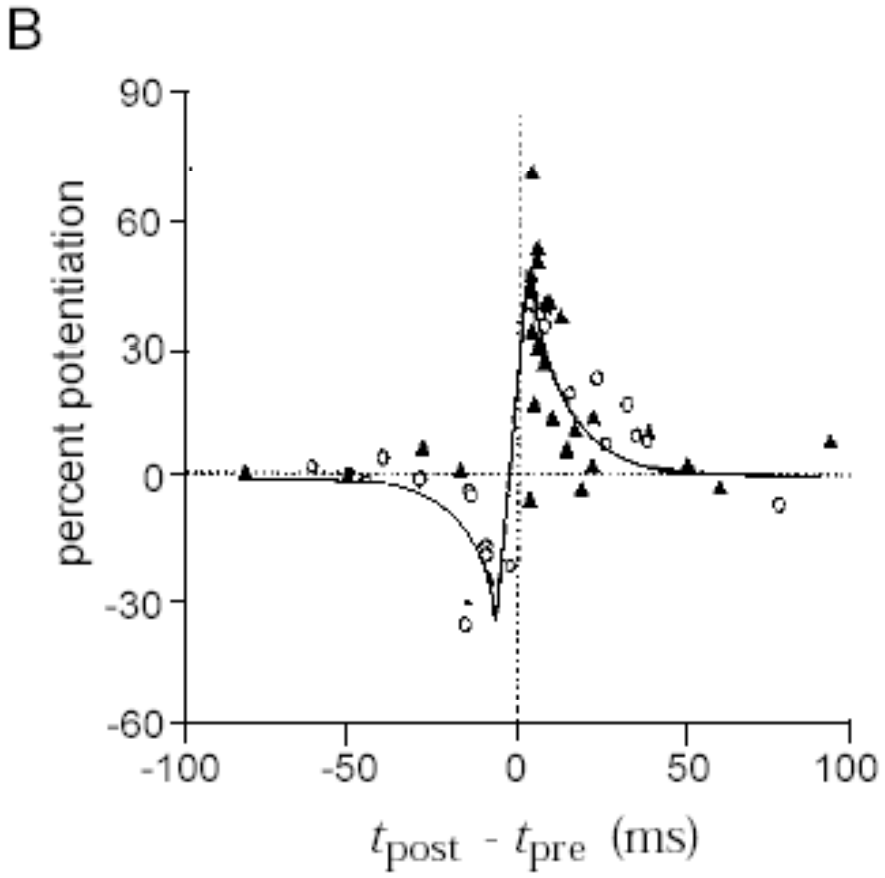
LTP/LTD: spike-timing dependent plasticity



Markram et. al. 1997

Exponential windows of the sign and magnitude of synaptic plasticity





[Dan & Poo, Neuron 2004]

STDP leads to BCM potentiation threshold

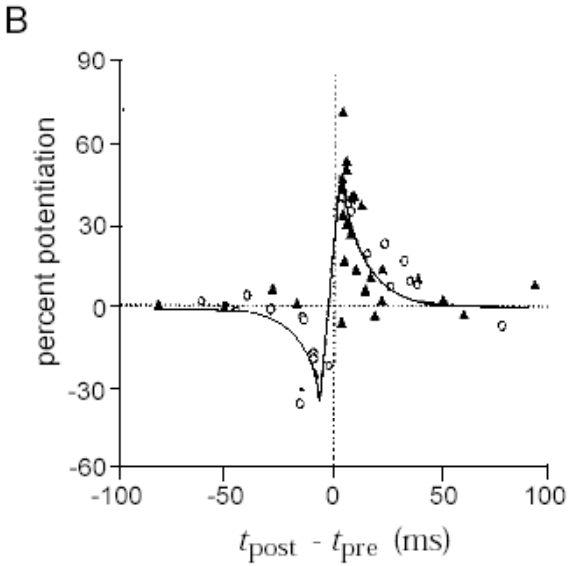
- Izhikevich and Desai (2003) showed STDP leads to BCM for the nearest neighbour STDP, i.e. $w(t+1) = w(t)\,(1 + \Delta w_+ - \Delta w_-)$

$$C(x) = \overbrace{\int_0^\infty A_+\, e^{-t/\tau_+}\, x e^{-xt}\, dt}^{\text{average potentiation}} + \overbrace{\int_{-\infty}^0 A_-\, e^{t/\tau_-}\, x e^{xt}\, dt}^{\text{average depression}}$$

$$= x\left(\frac{A_+}{\tau_+^{-1} + x} + \frac{A_-}{\tau_-^{-1} + x}\right) = 0$$

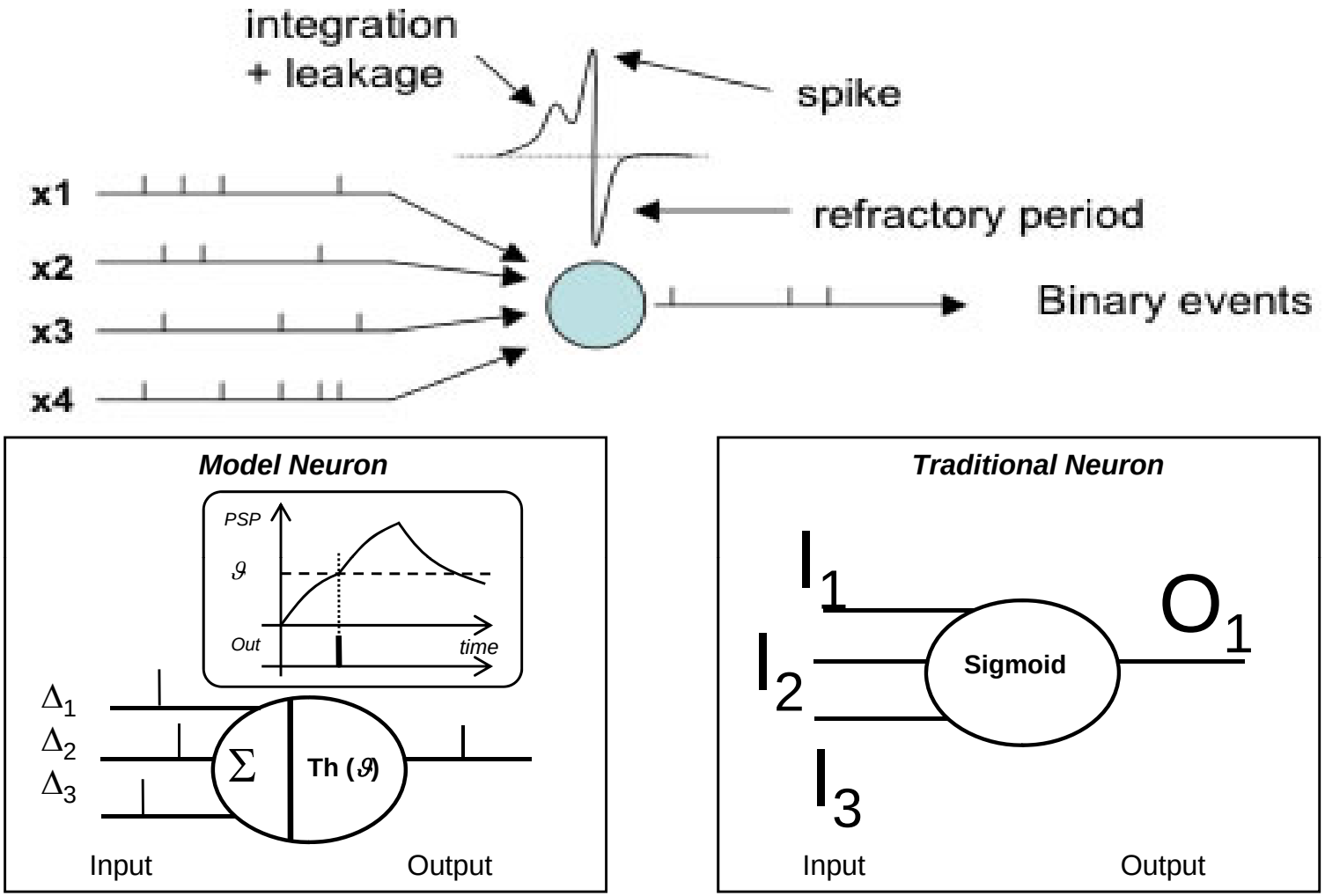
Threshold for potentiation

$$\theta_M = -\frac{A_+/\tau_- + A_-/\tau_+}{A_+ + A_-}$$



Where A's and τ's are **constants**, amplitudes and decays for potentiation and depression windows, respectively

Spiking versus rate neurons



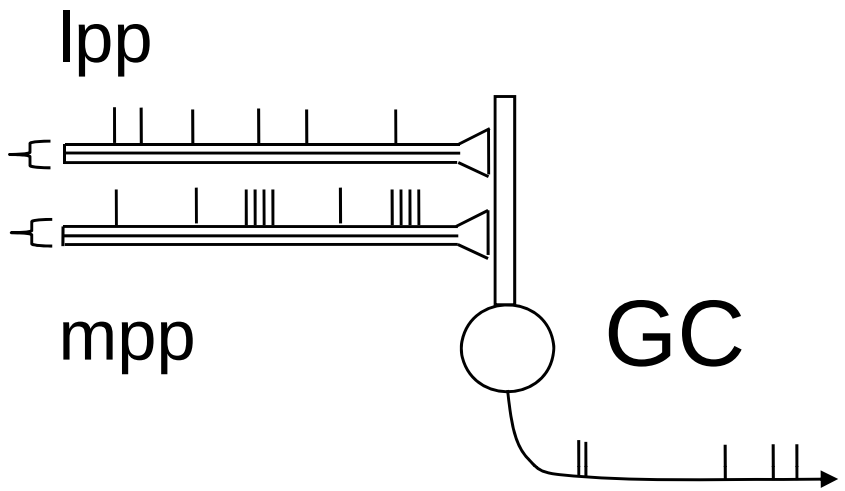
Biological versus traditional neuron models

Izhikevich model – the fast and precise implementation of spiking neuron

$$\dot{v} = 0.04v^2 + 5v + 140 - u + I$$

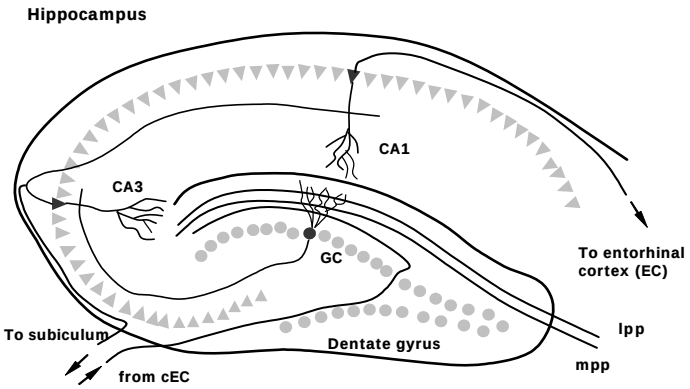
$$\dot{u} = a(bv - u)$$

$$\text{if} \quad v \geq \text{AP}, \quad \text{then} \begin{cases} v \leftarrow c \\ u \leftarrow u + d \end{cases}$$



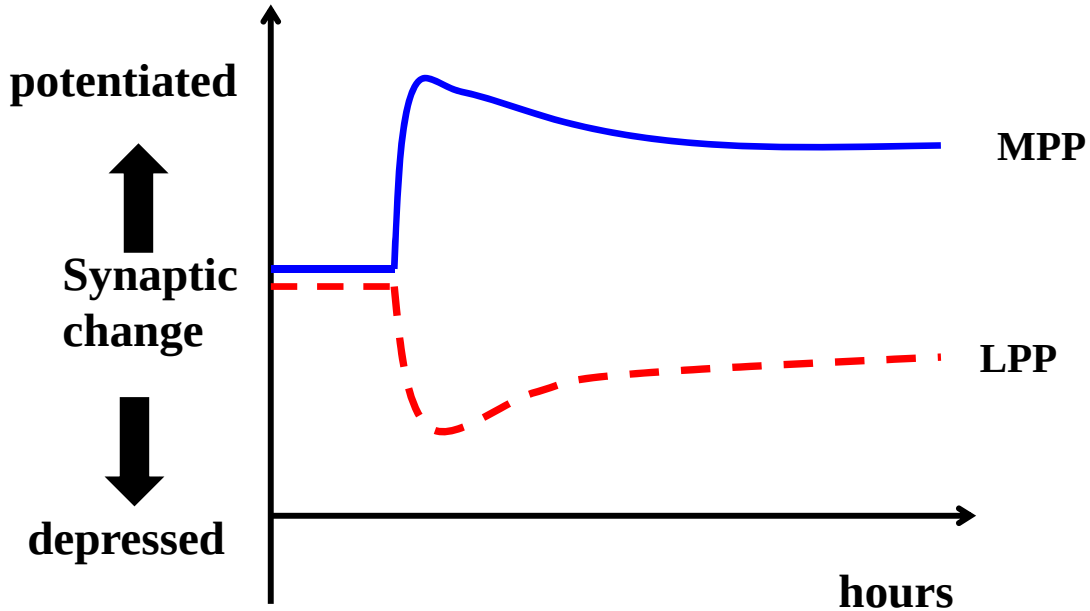
$$I(t) = s_{\text{mpp}}(t)\, w_{\text{mpp}}(t)\, N_{\text{mpp}}(t) + s_{\text{lpp}}(t)\, w_{\text{lpp}}(t)\, N_{\text{lpp}}(t)$$

$$s_{\text{mpp / lpp}} = \begin{cases} 1 & \textit{if there is presynaptic spike} \\ 0 & \textit{otherwise} \end{cases}$$



Data: Tetanus of MPP leads to homosynaptic potentiation of MPP and **hetero**synaptic depression of LPP input upon granule cell (GC)

[Abraham et al, PNAS 2001]



Assumptions of the model

- We take into account the pre- and postsynaptic spontaneous spiking activity, which is correlated and has a theta frequency

- The STDP rule is allowed to dynamically change the sizes of LTP and LTD windows according to the previous mean spike count of the postsynaptic neuron

- We temporarily de-correlate the spiking activity of MPP and LPP pathways during LTP induction

Consequences of assumptions

- De-correlated presynaptic activity leads to lower postsynaptic activity than before tetanus, and thus LTD window shrinks and LTP window expands. This corresponds to lower threshold for homosynaptic LTP.

- MPP presynaptic tetanus is correlated with postsynaptic spikes (due to temporal summation of EPSPs) and thus homosynaptic LTP follows.

- Ongoing spontaneous spiking of LPP is de-correlated with postsynaptic spikes and thus heterosynaptic LTD follows.

Changing windows for LTP / LTD

- Benuskova and Abraham (2007) for the first time introduced moving LTP threshold into the STDP equations through changing LTD/LTP windows according to postsynaptic average activity:

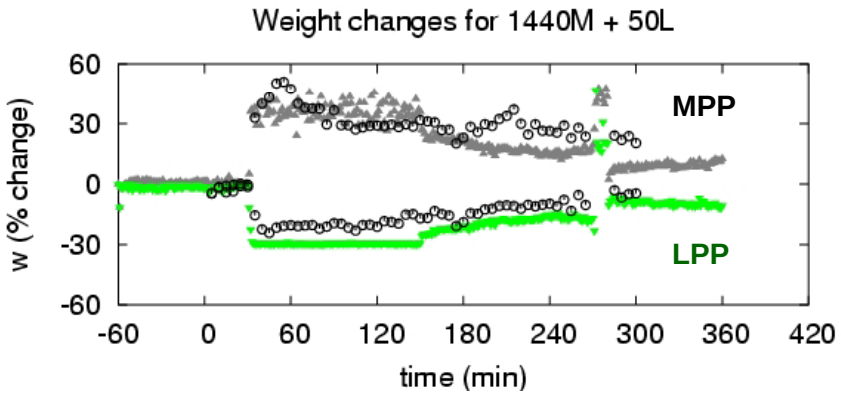
$$\Delta w_+(\Delta t) = A_+ \exp(-\Delta t / \tau_+) \text{ if } \Delta t > 0$$
$$\Delta w\_(\Delta t) = A\_ \exp(\Delta t / \tau\_) \text{ if } \Delta t < 0$$

$$A_+(t) = A_+(0)\,(1 / \langle c(t)\rangle_\tau)$$
$$A\_(t) = A\_(0)\,\langle c(t)\rangle_\tau$$

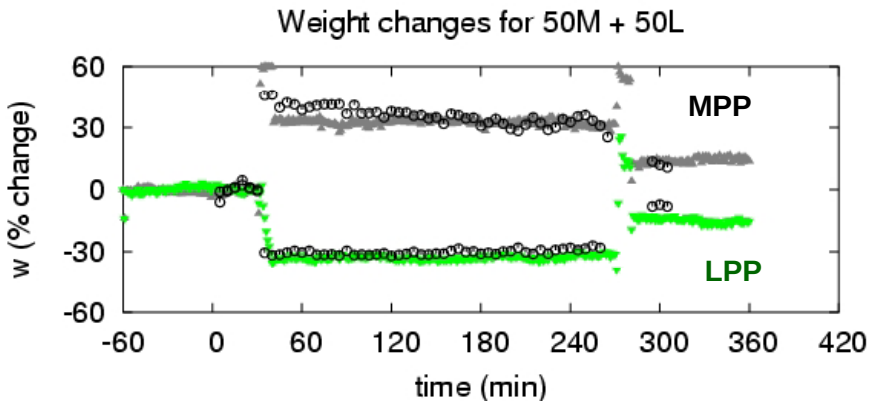
$$\langle c(t)\rangle_\tau = \frac{\alpha}{\tau}\int_{-\infty}^{t} c(t')\exp\left(\frac{-(t-t')}{\tau}\right)dt' \quad \text{where } c(t') = \begin{cases} 1 & \text{if there is a postsynaptic spike} \\ 0 & \text{if there is no postsynaptic spike} \end{cases}$$

Results of STDP with metaplasticity

a



b



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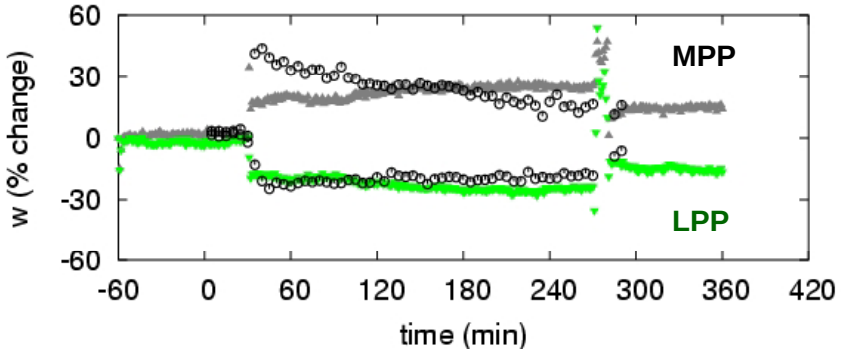

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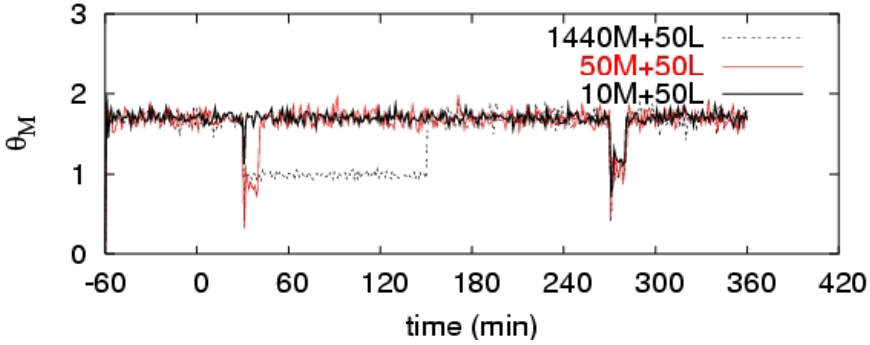
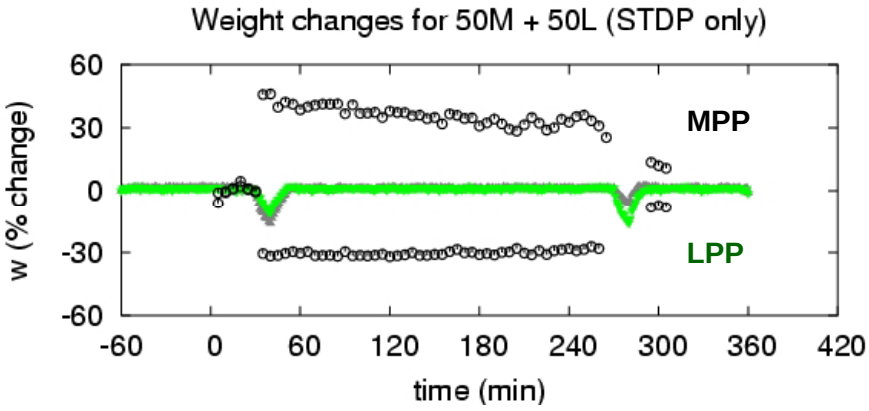


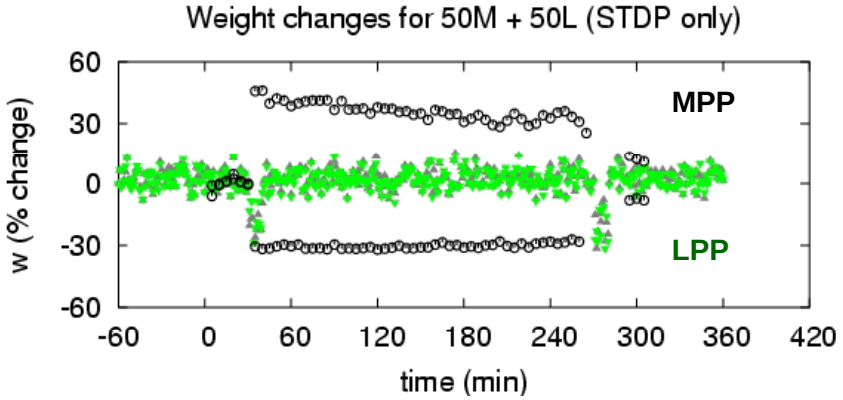
Results of ordinary STDP



Amplitudes and decays for potentiation and depression windows are constant and

$$w(t+1) = w(t)\,(1+\Delta w_+ - \Delta w_-) - \lambda\, w(t)$$

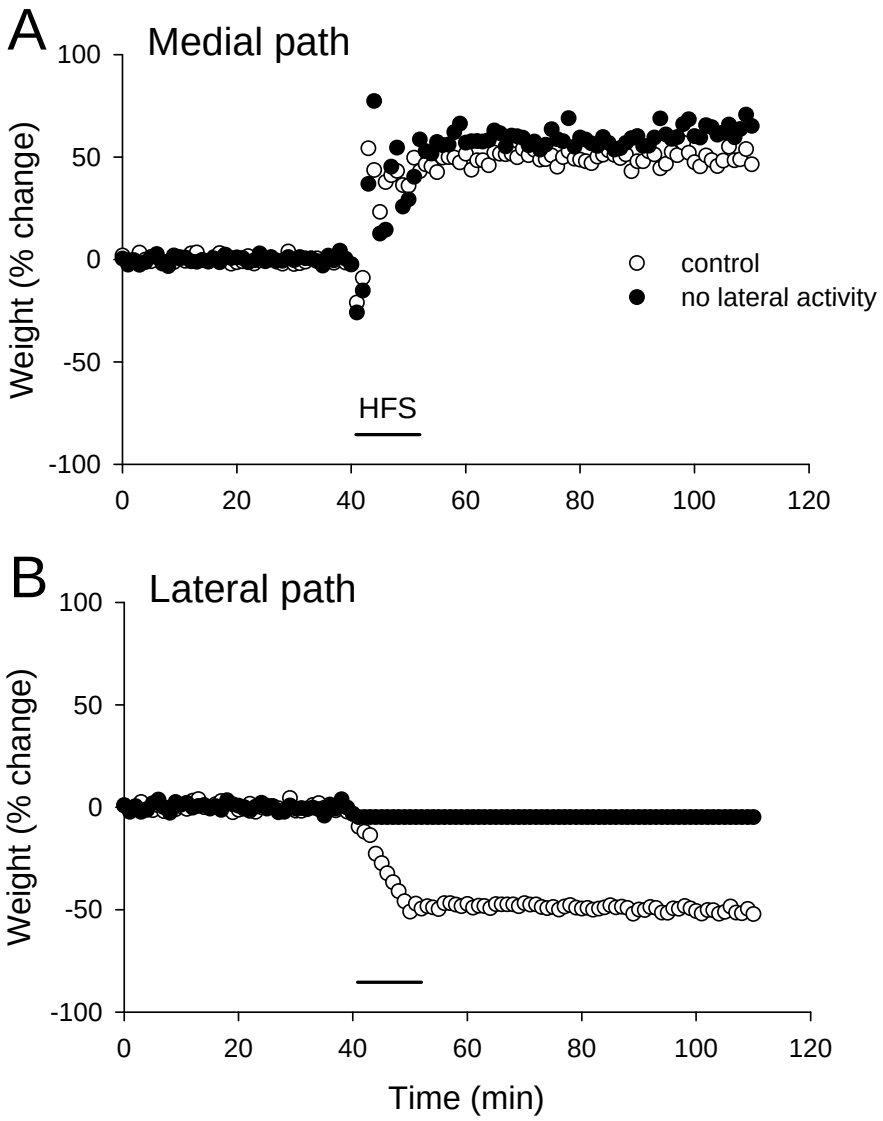
[Song and Abbott, 2000]



$$A_+(t) = \lambda\,(w_{max} - w(t))$$
$$A_-(t) = \lambda\, w(t)$$
$$w(t+1) = w(t)\,(1+\Delta w_+ - \Delta w_-)$$

[Delorme et al., 2001]

Prediction from this model: if the spontaneous activity (noise) is blocked so is the hetero-plasticity

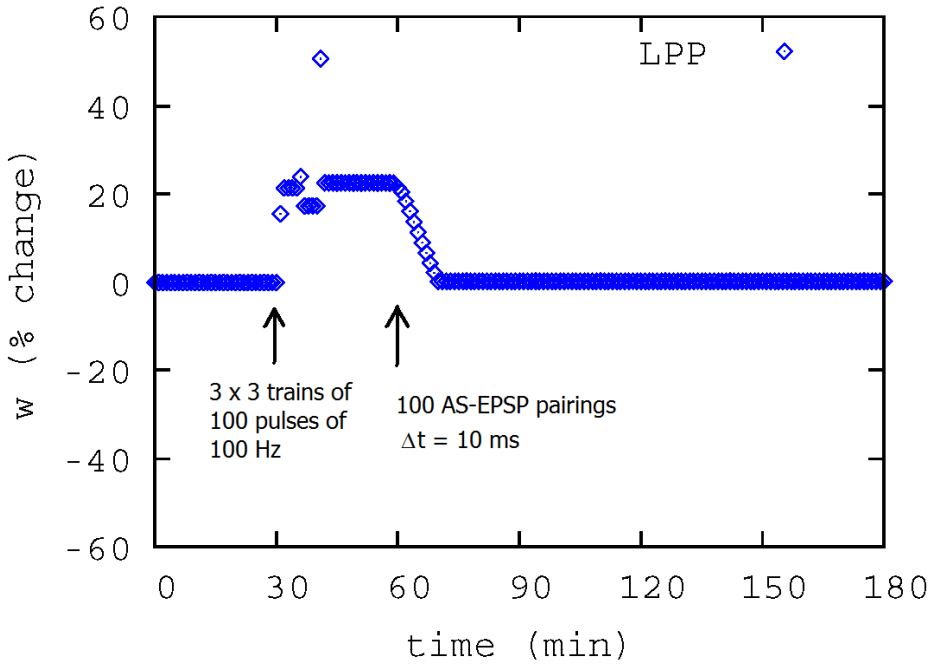


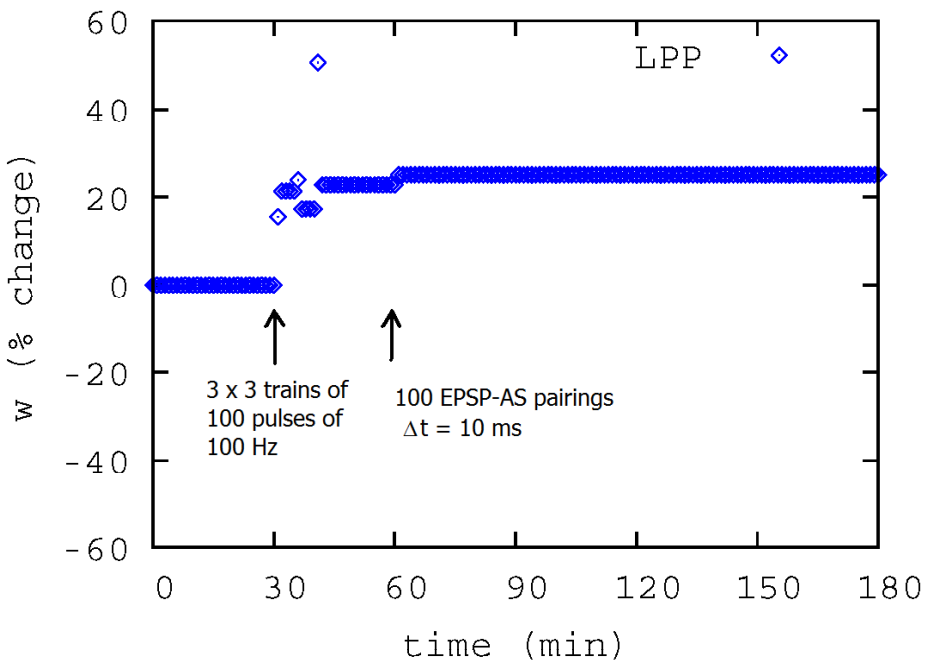
Abraham WC, Logan B, Wolff A, Benuskova L :

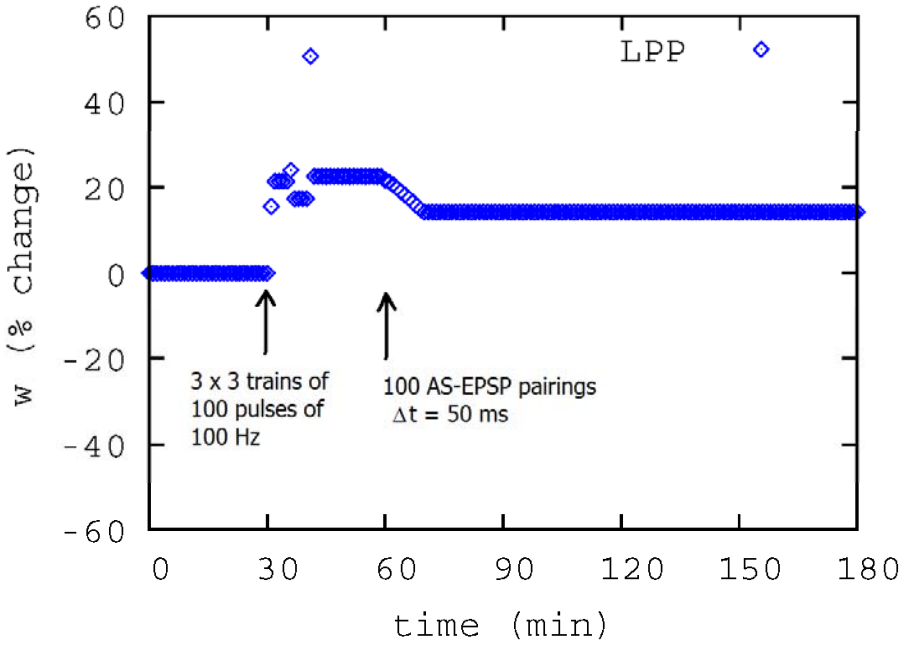
"Heterosynaptic" LTD in the dentate gyrus of anesthetized rat requires homosynaptic activity.

Journal of Neurophysiology, 98: 1048-1051, 2007.

Interplay between frequency and STDP







Simulation of results from Lin et al., J. Eur. Neuroscience, 2006.

Conclusion: towards more general plasticity rule

STDP rule

$\Delta w_+(\Delta t) = A_+ \exp(-\Delta t / \tau_+)$ if $\Delta t > 0$

$\Delta w_-(\Delta t) = A_- \exp(\Delta t / \tau_-)$ if $\Delta t < 0$

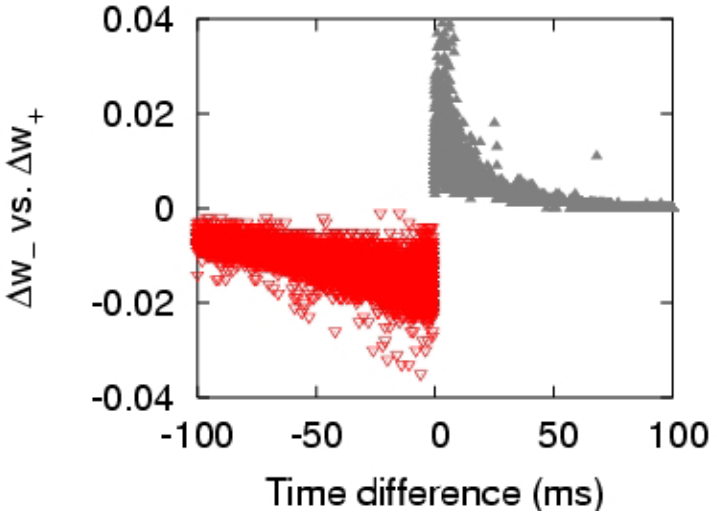
Variable windows

$A_+(t) = A_+(0)\,(1 / \varphi(t)\,\langle c(t)\rangle_\tau)$

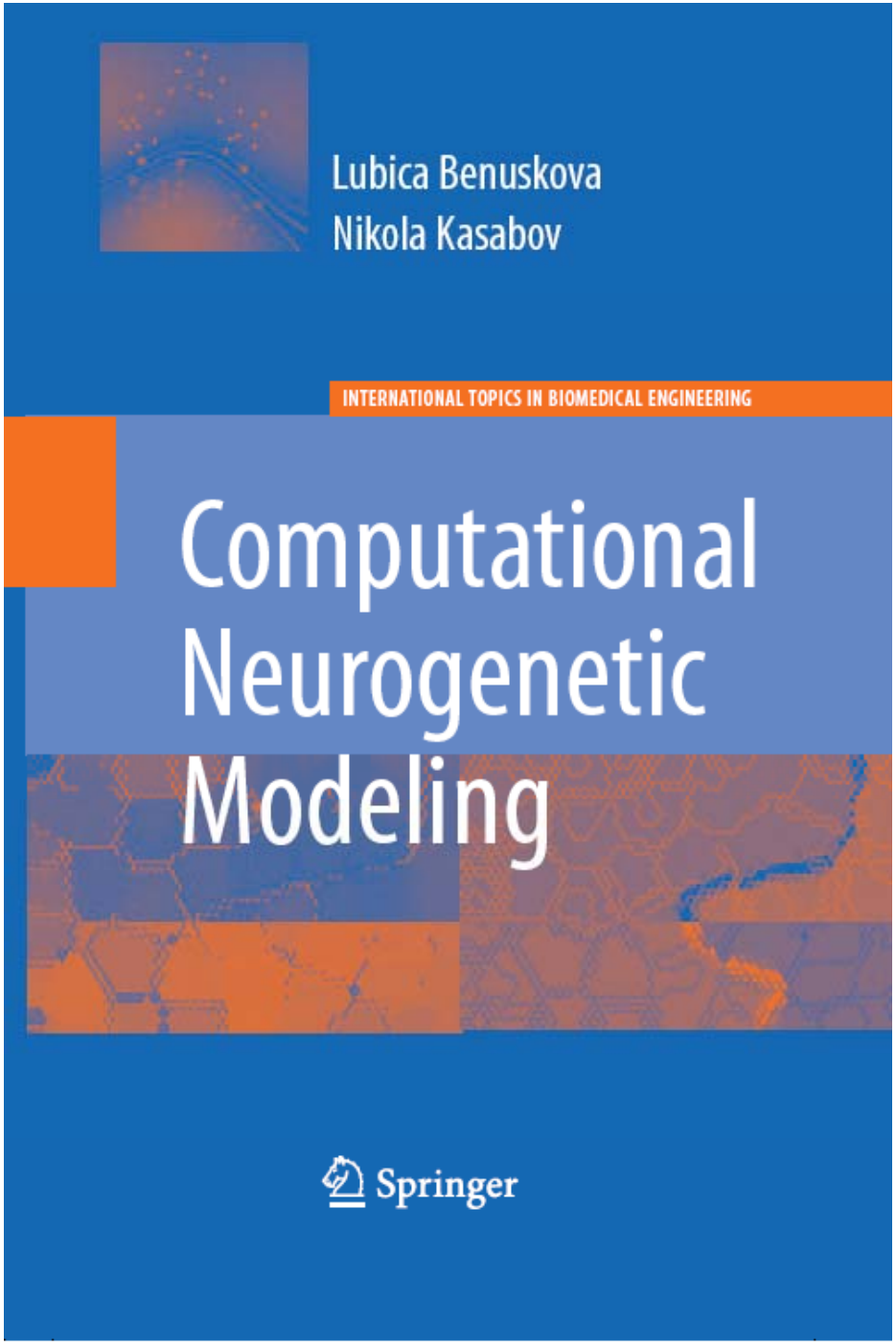
$A_-(t) = A_-(0)\,\varphi(t)\,\langle c(t)\rangle_\tau$

$$\langle c(t)\rangle_\tau = \frac{\alpha}{\tau}\int_{-\infty}^{t} c(t')\exp\left(\frac{-(t-t')}{\tau}\right)dt'$$

$$\varphi(t) = \varphi(\mathrm{X}, \mathrm{Y}, \mathrm{Z}, \ldots, t)$$



Task for future: to find the function φ, which is the function of different biochemical factors X, Y, Z,…., and time.



Benuskova L, Kasabov N
Computational Neurogenetic Modeling.
Springer, New York, 2007