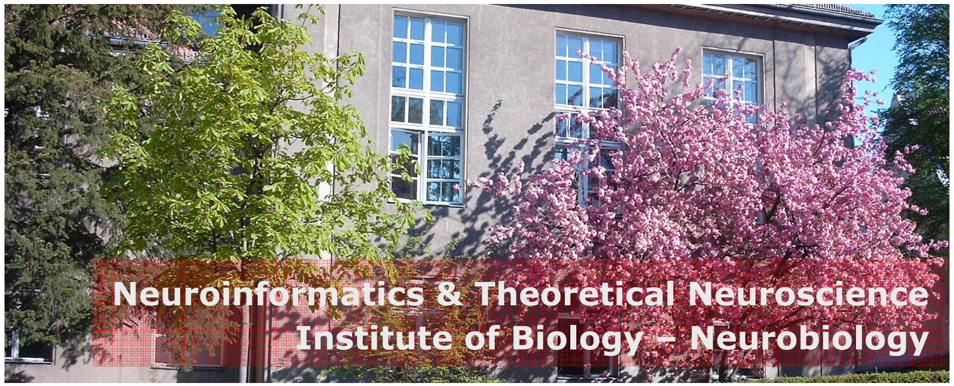
VS : Systemische Physiologie - Animalische Physiologie für Bioinformatiker

Neuronenmodelle III

- **Synaptische Übertragung**
- **Modelle synaptischer Kurz- und Langzeitplastizität**

Martin Nawrot



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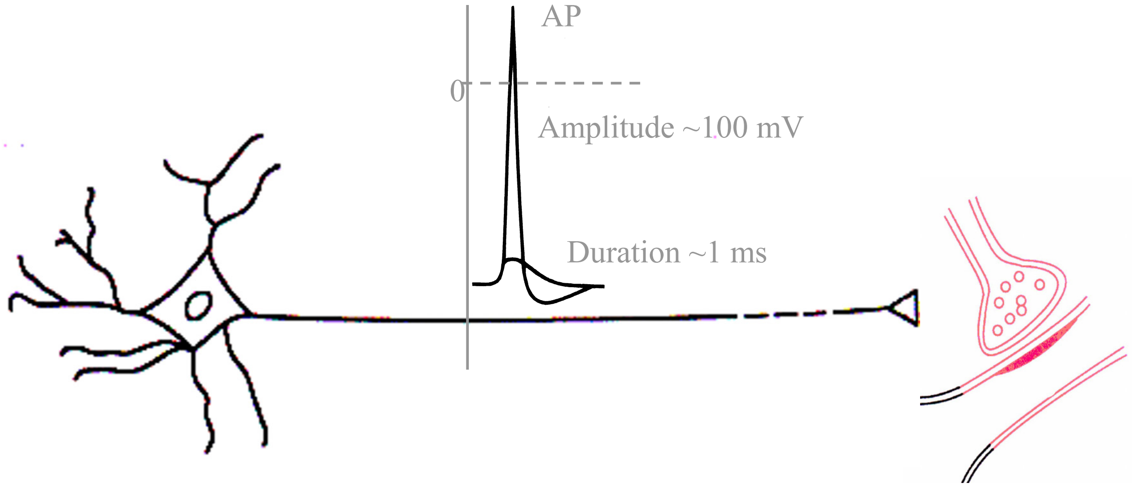
Outline

1. Synaptic transmission
2. *Short*-term synaptic plasticity
3. *Long*-term synaptic plasticity

1 Synaptic Transmission

1 Synaptic Transmission ► Excitatory PostSynaptic Current (EPSC)



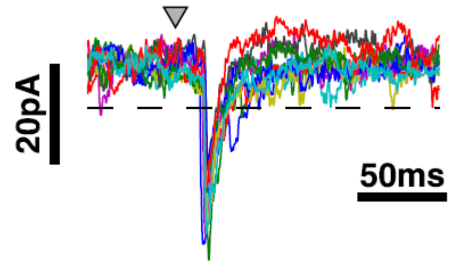
stimulation of
presynaptic excitatory neuron
(e.g. electric or photolysis of Glu)

→

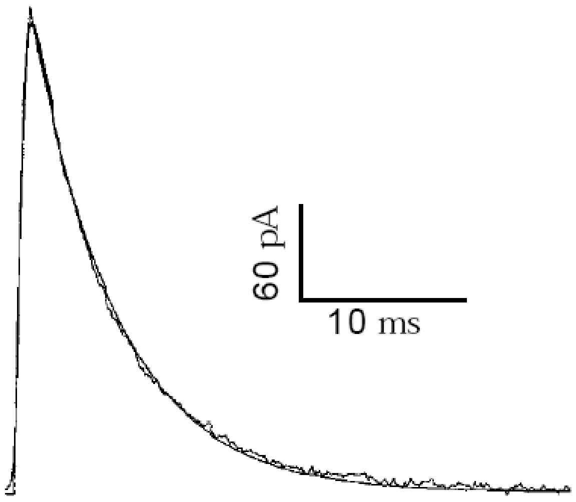
presynaptic
action potential

→

measurement of
excitatory postsynaptic current
(EPSC)



Experimental traces from: Boucsein et al. (2005) J Neurophysiol. 94:2948-58



Simplified model for PSC:

$$I(t) = I_0 \cdot \exp(-t/\tau_s)$$

I_0 : *maximum amplitude*

τ_s : *synaptic time constant*

Figure 5.14: A fit of the model discussed in the text to the average EPSC (excitatory postsynaptic current) recorded from mossy fiber input to a CA3 pyramidal cell in a hippocampal slice preparation. The smooth line is the theoretical curve and the wiggly line is the result of averaging recordings from a number of trials. (Adapted from Destexhe et al., 1994.)

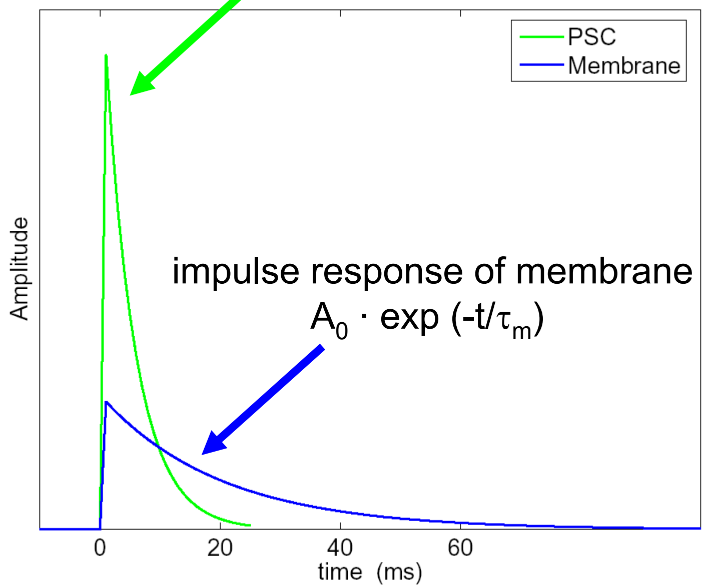
from: Dyan & Abbott (2001)

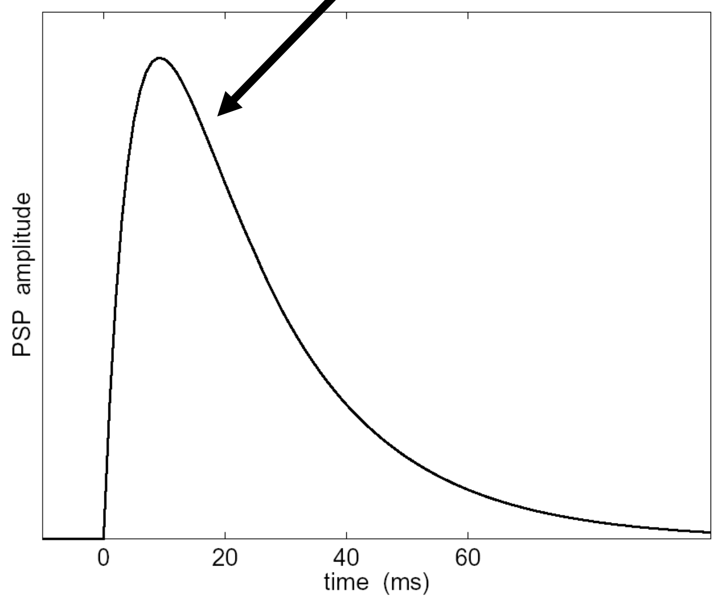
1 Synaptic Transmission ▶ Membrane response (EPSP) to a single EPSC

current input to membrane

$I(t) = I_0 \cdot \exp(-t/\tau_s)$

voltage output to membrane
(excitatory postsynaptic potential, EPSP)





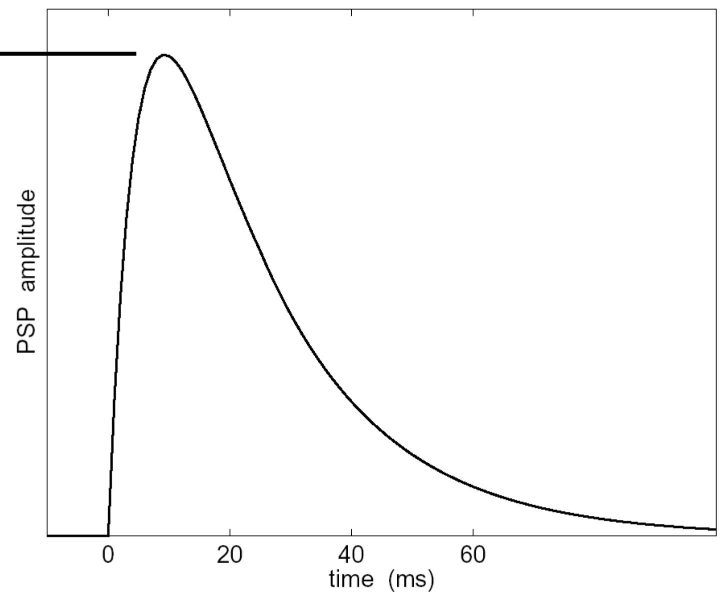
blackboard calculus

convolution of EPSC with membrane impulse response fcn results in postsynaptic potential

$$PSP = PSC_{\text{Synapse}} \otimes IR_{\text{Membrane}}$$

1 Synaptic Transmission ► Membrane response (EPSP) to a single EPSC

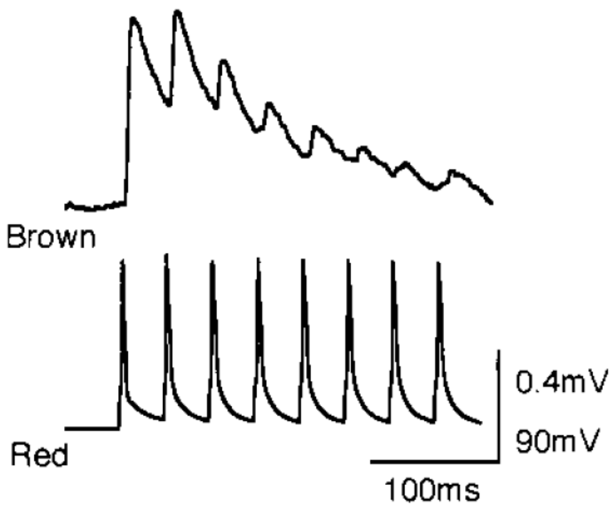
‘synaptic weight’ (*w*)



2 Short-Term Synaptic Plasticity

2 Short term synaptic plasticity ► short term *depression* (STD)

Physiology



► changes induced with only few presynaptic spikes

Experiments: Markram H, Wang Y, and Tsodyks M (1998) PNAS. 95:5323-8

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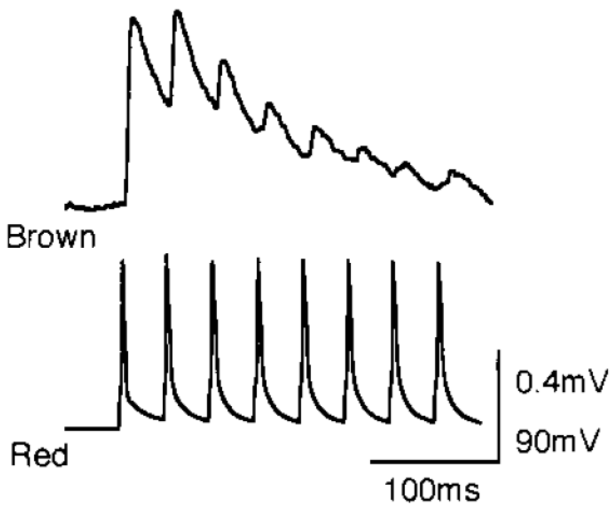
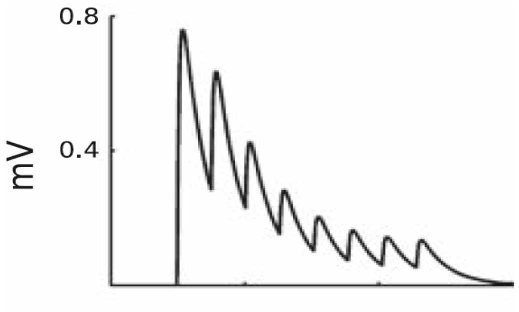


Model

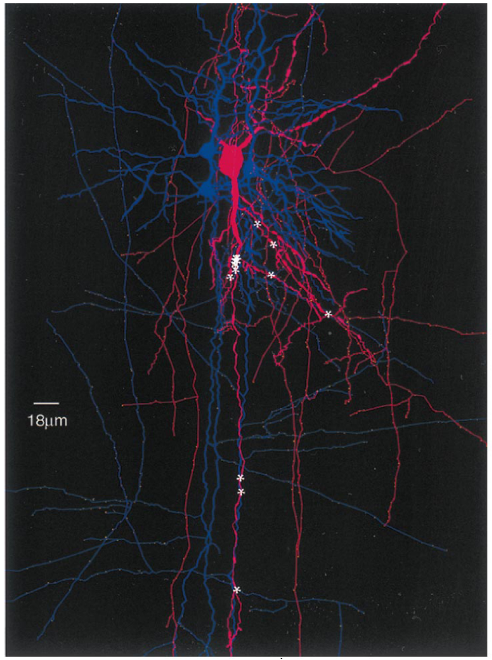


► changes induced with only few presynaptic spikes

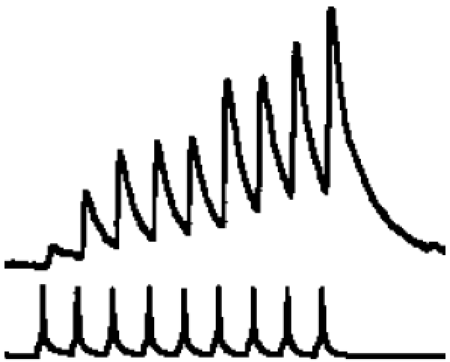
► phenomenological model can describe this behaviour

Experiments: Markram H, Wang Y, and Tsodyks M (1998) PNAS. 95:5323-8
Model Review: Morrison A, Diesmann M, and Gerstner W (2008) Biol Cybern. 98(6):459-78

2 Short term synaptic plasticity ► short term *potentiation* (or *fascilitation*)



Physiology



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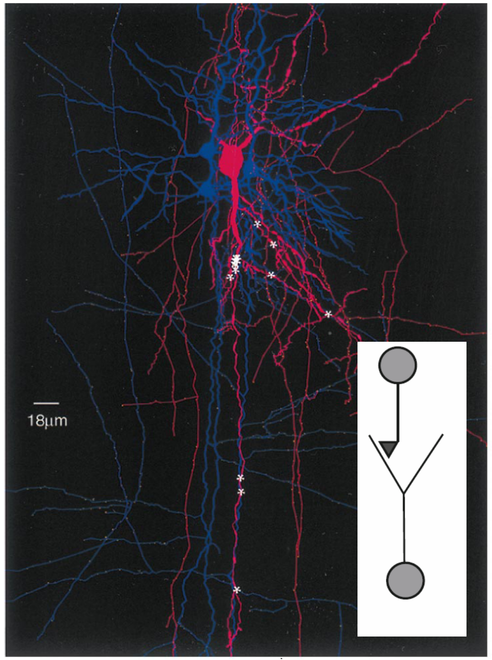
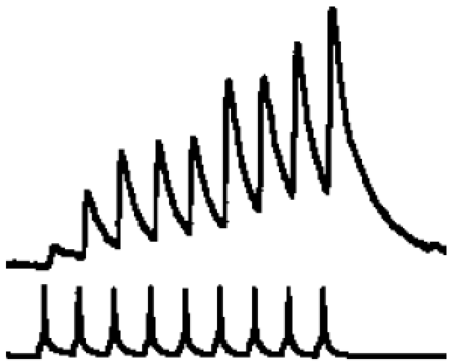


Physiology



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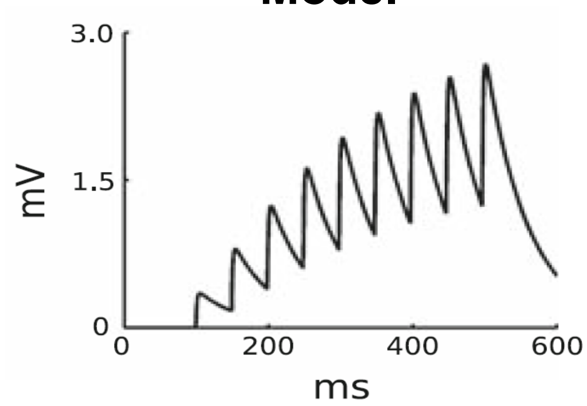

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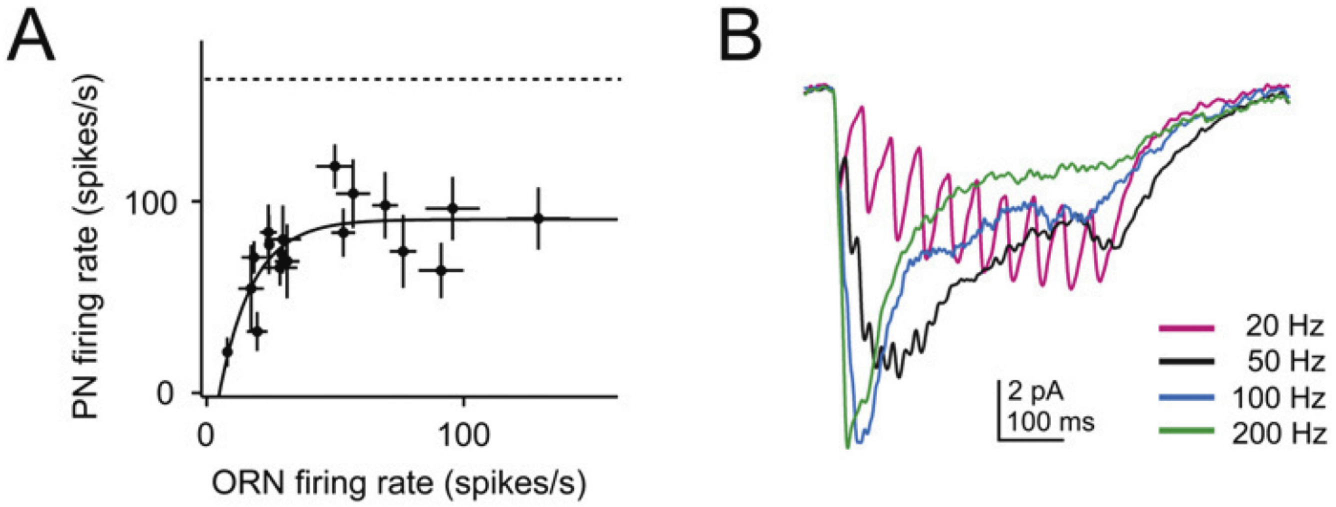
2 Short term synaptic plasticity ► example for functional implication

Olfactory system in the insect

► excitatory synapses between the olfactory receptor neurons (ORNs) and the antennal lobe projection neurons (PNs) exhibit short term depression (STD)



A: stimulation with different odors; B: antennal nerve stimulation

Kazama & Wilson (2008) Neuron 58: 401-413

► STD results in an adaptation of PN input current and output spike frequency with increasing input frequency. Thus, high odor concentration responses saturate at the level of PNs.

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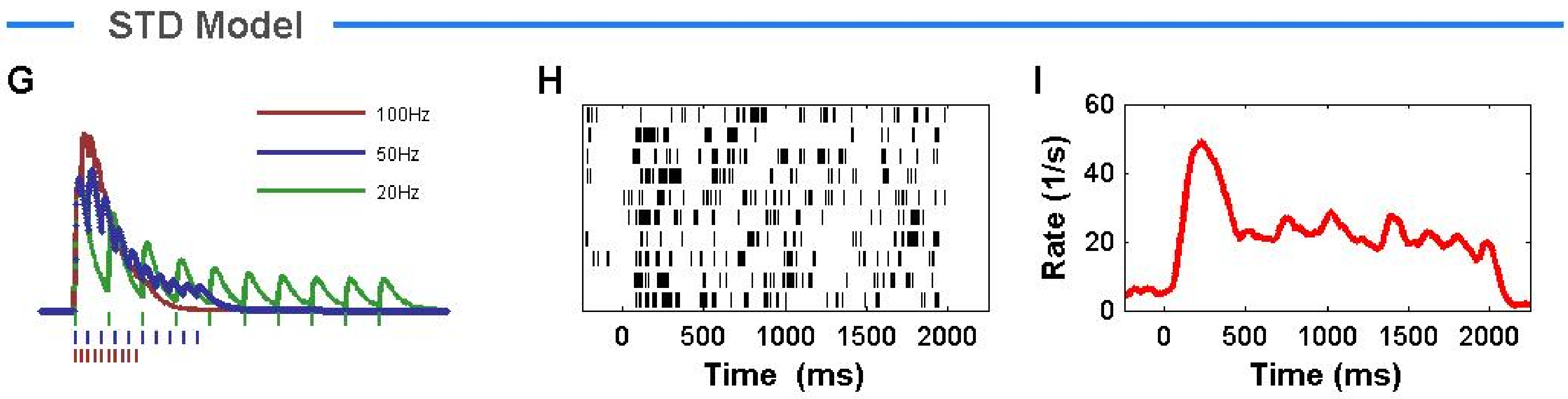


G: synapse model; H: Single PN responses to 2s stimulus; I: phasic-tonic response rate, trial-averaged

Nawrot, Krofczik, Farkhooi, Menzel (2010)

► STD can regulate response dynamics. A constant intensity odor stimulus results in a phasic-tonic PN response following odor onset.

► we distinguish **short term *potentiation*** at facilitating synapses and **short term *depression*** at depressive synapses

► short-term plasticity is induced by repeated presynaptic activation within a very short time, i.e. within tens of milliseconds (Markram et al. 1998; Thomson et al. 1993).

► the induced change does not persist for longer than a few hundred milliseconds (short term); original PSP amplitude is typically recovered within less than 1s.

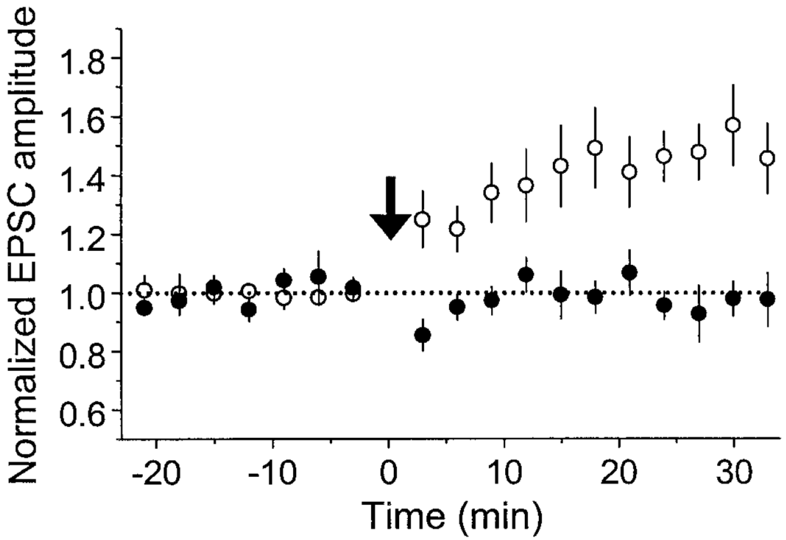
3 Long-Term Synaptic Plasticity

Hebb's postulate

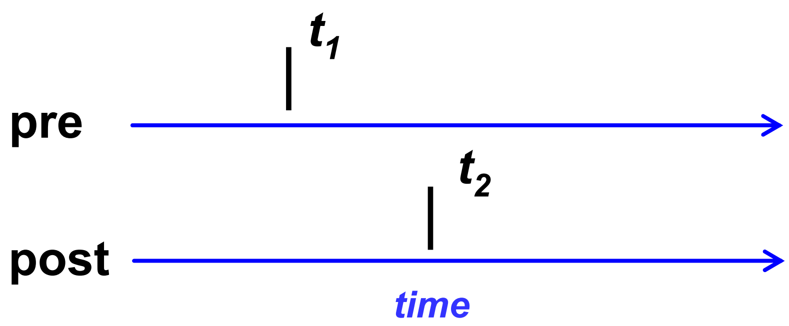
"When an axon of cell A is near enough to excite cell B or repeatedly or persistently takes part in firing it, some growth process or metabolic change takes place in one or both cells such that A's efficiency, as one of the cells firing B, is increased".

Donald O. Hebb (1949)

► synaptic **long term potentiation** is induced by repetitive stimulation with **positively** correlated spike times of post and pre-synaptic neuron



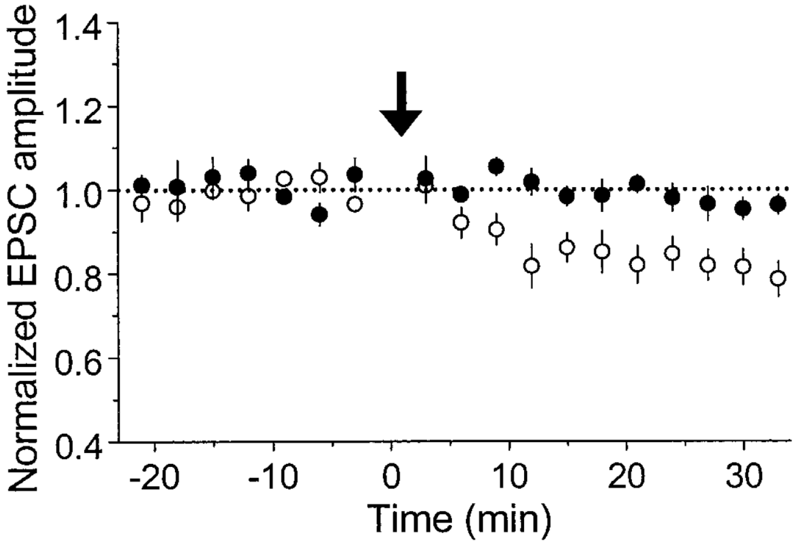
● D-AP-5 (25 mM) - antagonist of NMDA subtype glutamate receptors



$\Delta t = t_2 - t_1 > 0$ **potentiation**

Bi G-q, Poo M-m (1998) J Neurosci 18

► synaptic **long term depression** is induced by repetitive stimulation with **negatively** correlated spike times of post and pre-synaptic neuron



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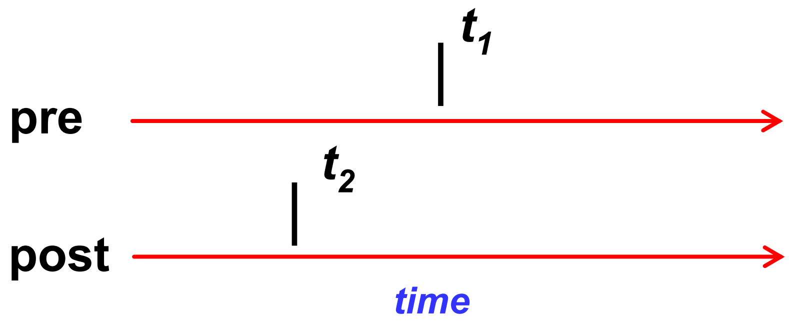
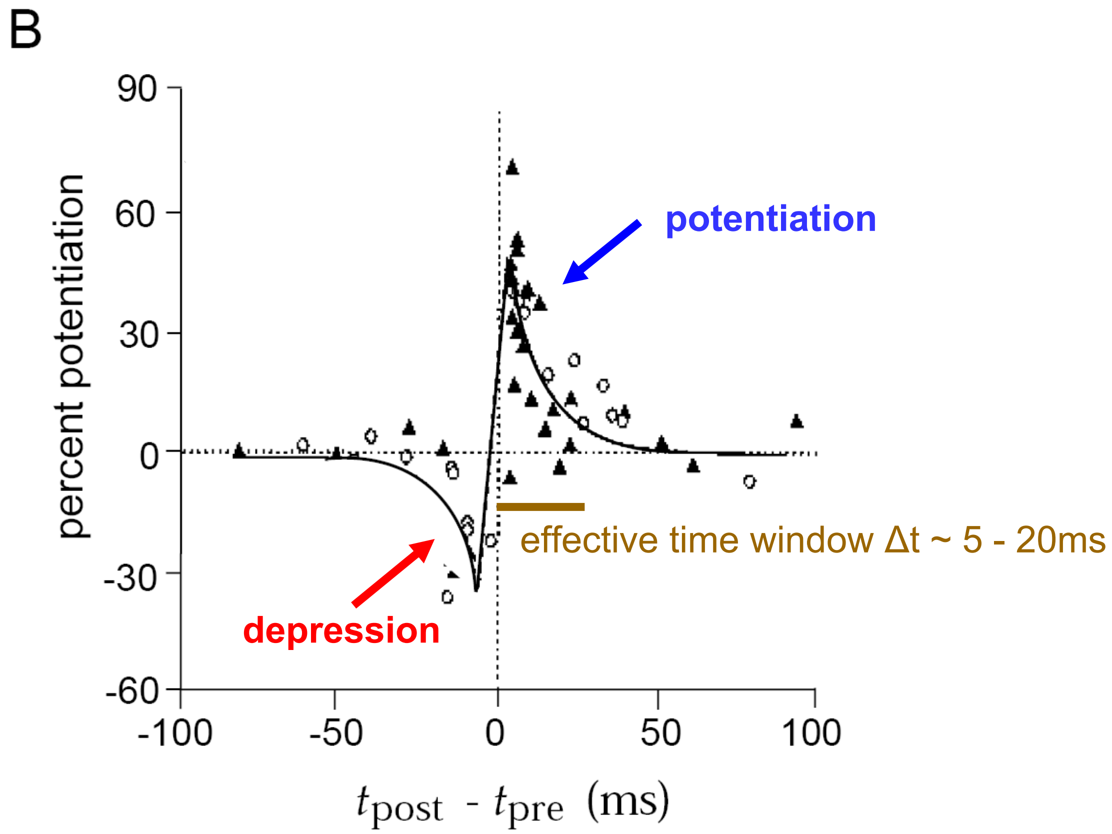


$\Delta t = t_2 - t_1 < 0$ **depression**

Bi G-q, Poo M-m (1998) J Neurosci 18

► the STDP rule describes an time-*asymmetric* learning rule that incorporates the phenomena of potentiation *and* depression



from Dyan & Abbott (2001)

3 Long term plasticity ► STDP ► updating rules

► phenomenological models of synaptic plasticity generally operate with *update rules* which are central to the numeric algorithms

$$\Delta w^{+} = F_{+}(w) \cdot \exp\left(- |\Delta t| / \tau_{+}\right) \qquad \text{if } \Delta t > 0$$

$$\Delta w^{-} = -F_{-}(w) \cdot \exp\left(- |\Delta t| / \tau_{-}\right) \qquad \text{if } \Delta t \leq 0,$$

for review see: Morrison A, Diesmann M, and Gerstner W (2008) Biol Cybern. 98(6):459-78

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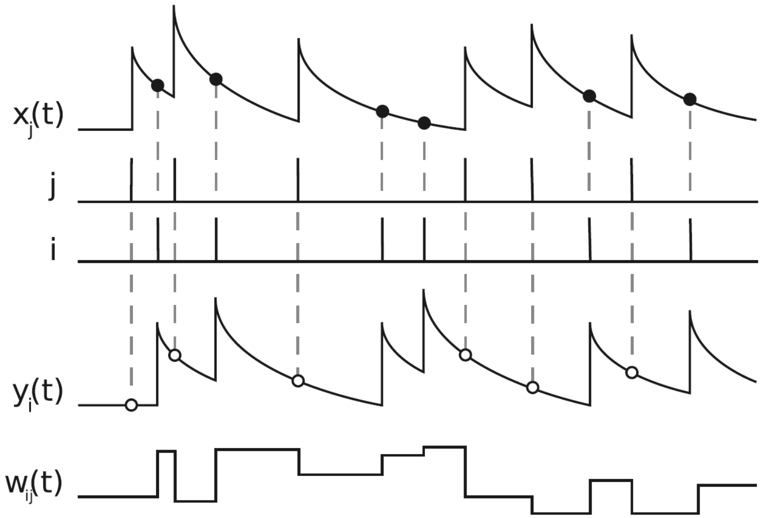

Fig. 3 Implementation of pair-based plasticity by local variables. The spikes of presynaptic neuron j leave a trace $x_j(t)$ and the spikes of the postsynaptic neuron i leave a trace $y_i(t)$. The update of the weight w_{ij} at the moment of a postsynaptic spike is proportional to the momentary value of the trace $x_j(t)$ (*filled circles*). This gives the amount of potentiation due to pre-before-post pairings. Analogously, the update of w_{ij} on the occurrence of a presynaptic spike is proportional to the momentary value of the trace $y_i(t)$ (*unfilled circles*), which gives the amount of depression due to post-before-pre pairings

Morrison A, Diesmann M, and Gerstner W (2008) Biol Cybern. 98(6):459-78

3 Long term plasticity ► Summary

► we distinguish two (phenomenological) types of long term synaptic changes:

- **Long Term Potentiation** (LTP)
- **Long Term Depression** (LTD)

► long-term plastic changes can be induced rapidly within 1s or less (i.e. within a rather short period, similar to the induction of short-term plasticity!)

► the experimentally induced change in synaptic weight are long-lasting (typically for hours or days)

► long term plasticity is thought to be the substance of long term memory (LTM)

► experimental induction protocols and underlying mechanisms are fundamentally different for short-term and long-term plastic changes

We concentrated here on the well-established phenomenon of *spike timing dependent plasticity* (STDP) as one prominent form of establishing long-term synaptic modifications

► STDP is a form of *Hebbian learning*

► In STDP changes in the synaptic weight depend on the *temporal relation of action potential firing* in the PRE-synaptic and in the POST-synaptic neuron.

FIN

Reading

Dayan & Abbott (2001) Theoretical Neuroscience: Computational and mathematical Modeling of Neural Systems, MIT Press; chapter 5.8: “The Postsynaptic Conductance”

References

Bi G-q, PooM-m (1998) *Synaptic modifications in cultured hippocampal neurons: Dependence on spike timing, synaptic strength, and postsynaptic cell type*. J Neurosci 18:10464–10472

Boucsein C, Nawrot M, Rotter S, Aertsen A, Heck D (2005) *Controlling synaptic input patterns in vitro by dynamic photo stimulation*. J Neurophysiol. 94:2948-58

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Morrison A, Diesmann M, Gerstner W. (2008) *Phenomenological models of synaptic plasticity based on spike timing.* Biol Cybern. 98(6):459-78

Nawrot MP, Krofczik S, Farkhooi F, Menzel R (2010) Temporal Dynamics of odor processing in the insect antennal lobe. Frontiers in Neuroscience (*submitted*)

Thomson AM, Deuchars J, West DC (1993) *Large, deep layer pyramid-pyramid single axon EPSPs in slices of rat motor cortex display paired pulse and frequency-dependent depression, mediated presynaptically and self-facilitation, mediated postsynaptically.* J Neurophysiol. 1993 Dec;70(6):2354-69.

4 Unsupervised – Supervised - Reward-Based Learning

►for all Hebbian learning rules only variables that are locally available at the synapse can be used to change the synaptic weight (unsupervised)

► teaching signal provides non-local (global) control

► reward-based (reinforcement) learning allows for self-controlled systems

- not covered in WS 09/10