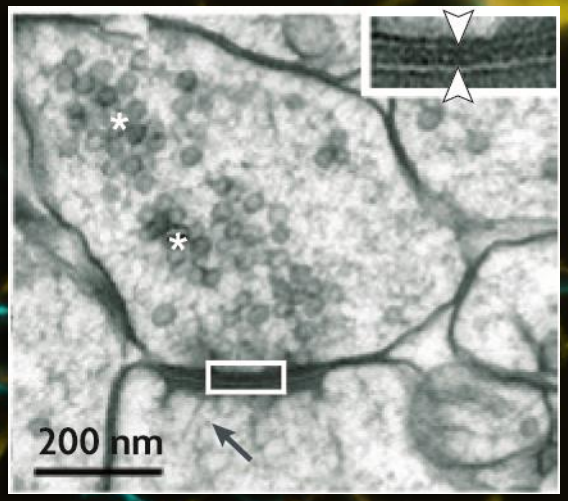
Short-term synaptic plasticity

Synaptic transmission is plastic

- **Synaptic plasticity**: neurons change the way in which they communicate with each others (synaptic strength) in an activity-dependent manner.

- In this way, they keep track of the history of activity (**memory!**)

- Synaptic plasticity can be **functional** and structural.



Synaptic plasticity

1. **Long-term synaptic plasticity** (from minutes to hours, days…a life time)
   a) **Hebbian-type synaptic plasticity** (LTP, LTD) as molecular correlate of memory
   b) **Homeostatic synaptic plasticity**

2. **Short-term synaptic plasticity** (**STP**; from milliseconds to seconds and few minutes)

   Function: **information processing…**

STP can lead to bidirectional changes in synaptic strength

1. **Short-term synaptic depression (STD)**: reduction of synaptic strength for hundreds of milliseconds to seconds

2. **Short-term-synaptic facilitation (STF)**: increase in synaptic strength for hundreds of milliseconds to seconds

3. **Augmentation and post-tetanic potentiation (PTP)**: increase in synaptic strength for tens of seconds to minutes

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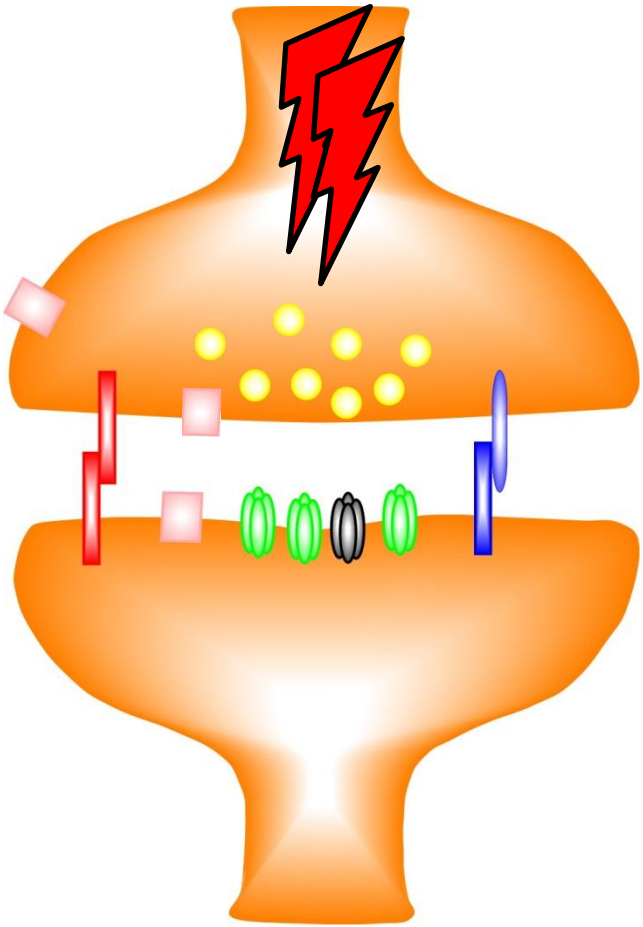
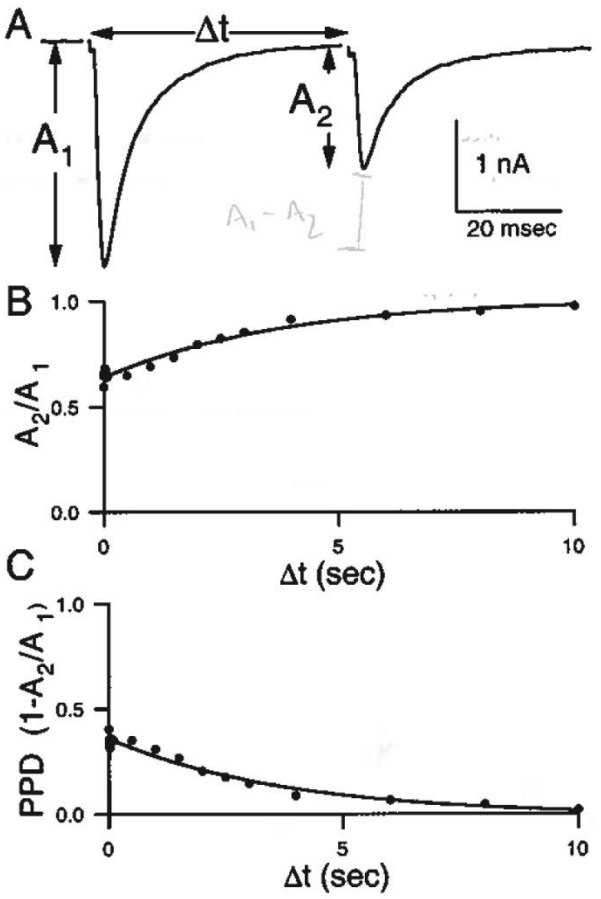
Short-term synaptic depression (STD)

Repeated stimuli delivered at short time intervals lead to a transient decrease in synaptic strength.

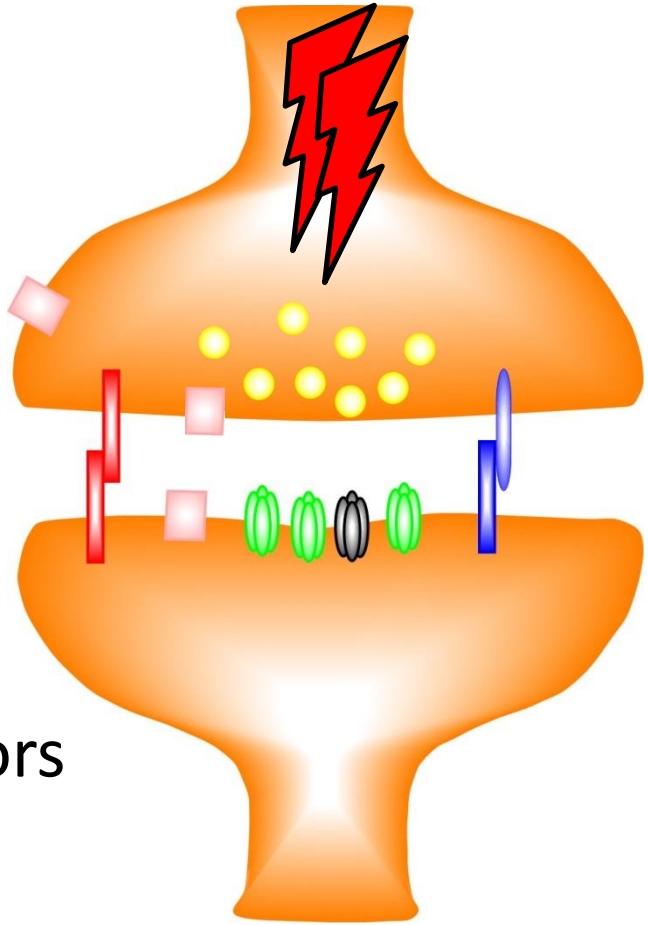




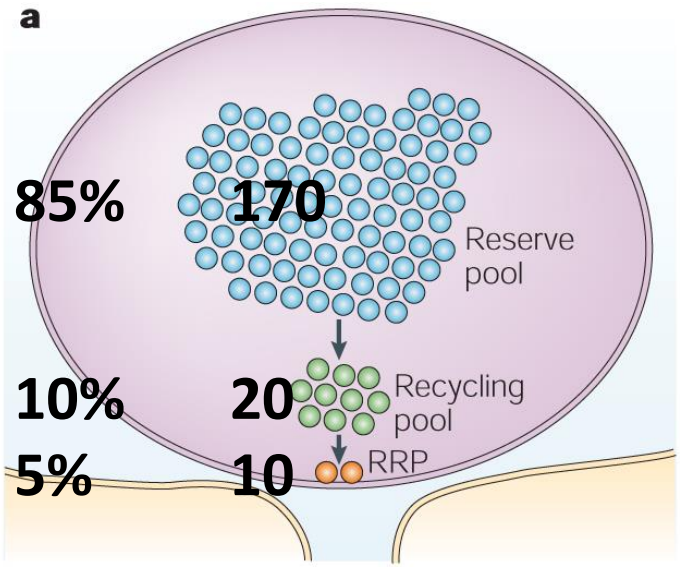
STD can be due to:

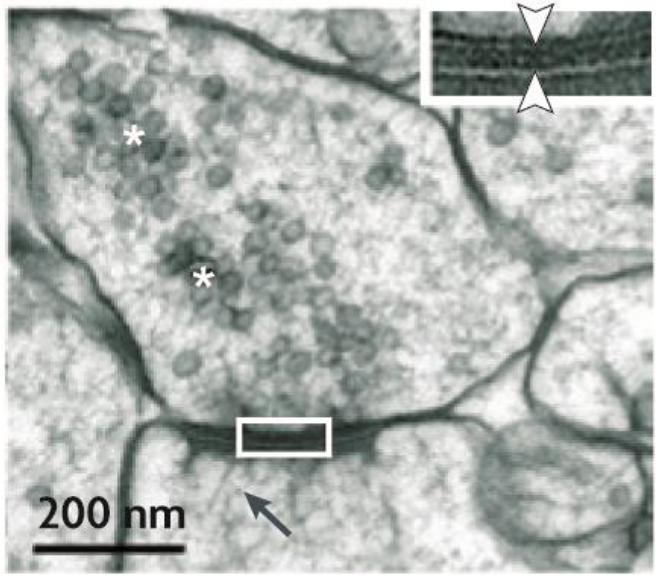
1. <u>Presynaptic mechanims:</u>
   a. Depletion of vesicles ready to be released
   b. Reduction of calcium influx

2. <u>Postsynaptic mechanisms:</u>
   a. Desensitization of postsynaptic receptors
   b. Saturation of postsynaptic receptors



Readily releasable pool (RRP)

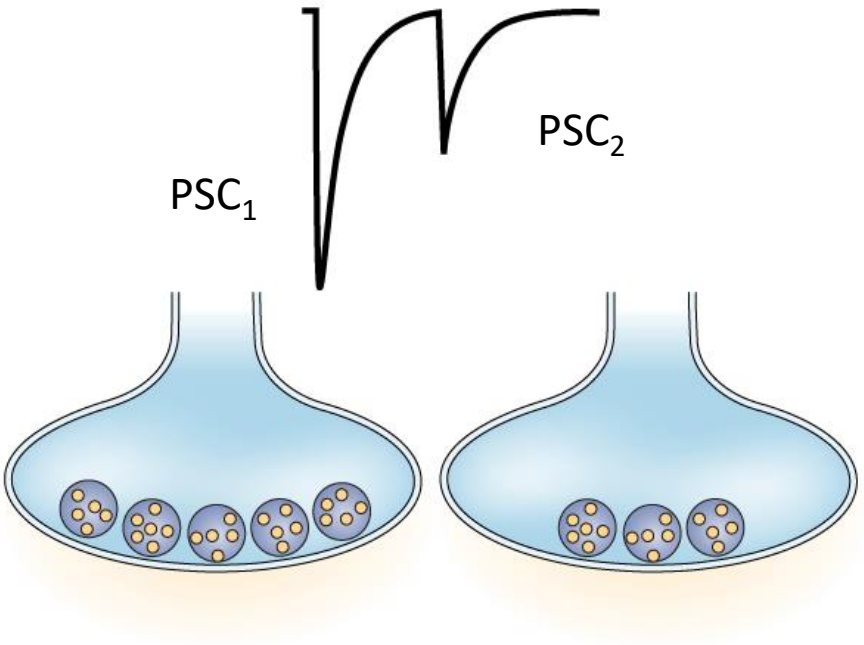




STD due to depletion of the RRP

$$N_{\text{released vesicles with 1 AP}} = RRP * p_v$$

N is limiting factor

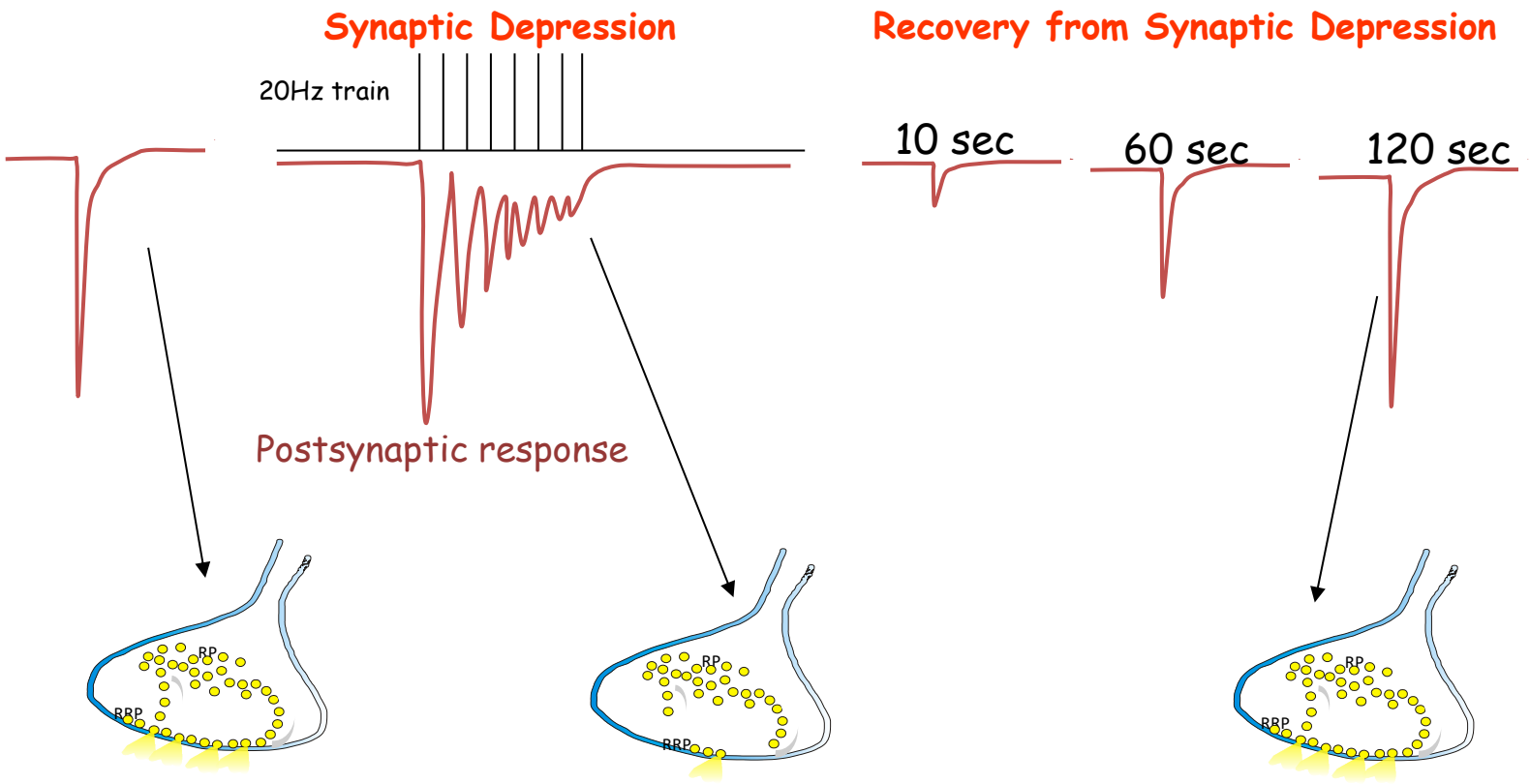


$RRP_1 = 10$
$P_v = 0.8$

$PSC_1 = RRP_1 * P_v = 10 * 0.8 = 8$

$PSC_2 = RRP_2 * P_v = (10-8) * 0.8 = 1.6$

STD due to depletion of the RRP

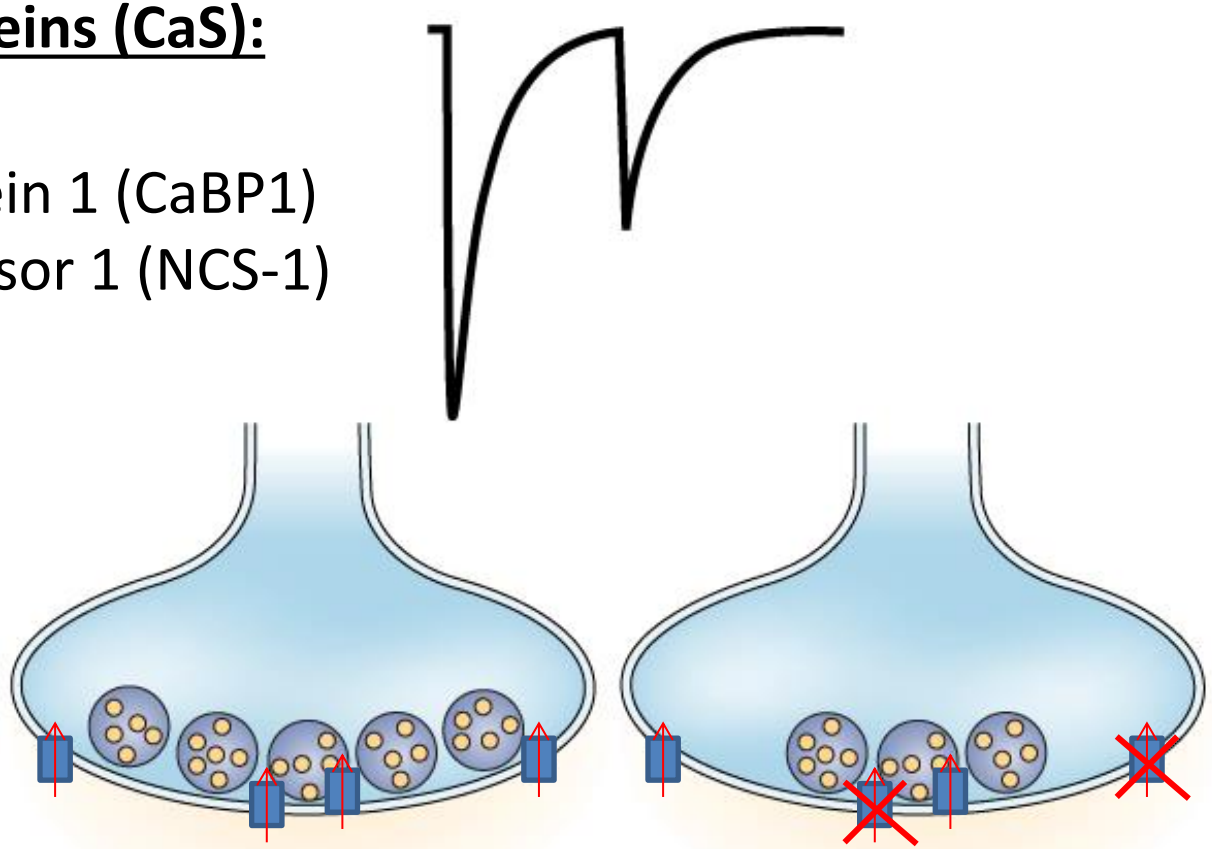


STD due to reduction of calcium influx

Calcium-dependent inactivation of calcium channels due to

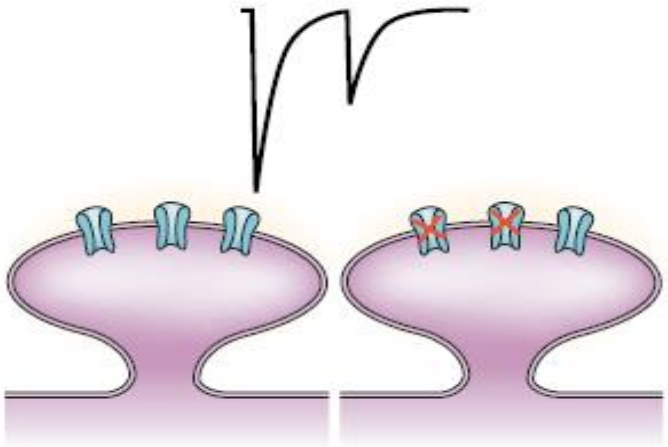
<u>Calcium-sensing proteins (CaS):</u>

Calmodulin (CaM)
Calcium binding protein 1 (CaBP1)
Neuronal calcium sensor 1 (NCS-1)



Deleting the CaM-binding domain on P/Q-type calcium channels prevents their inactivation and reduces synaptic depression!

STD due to desensitization of postsynaptic receptors



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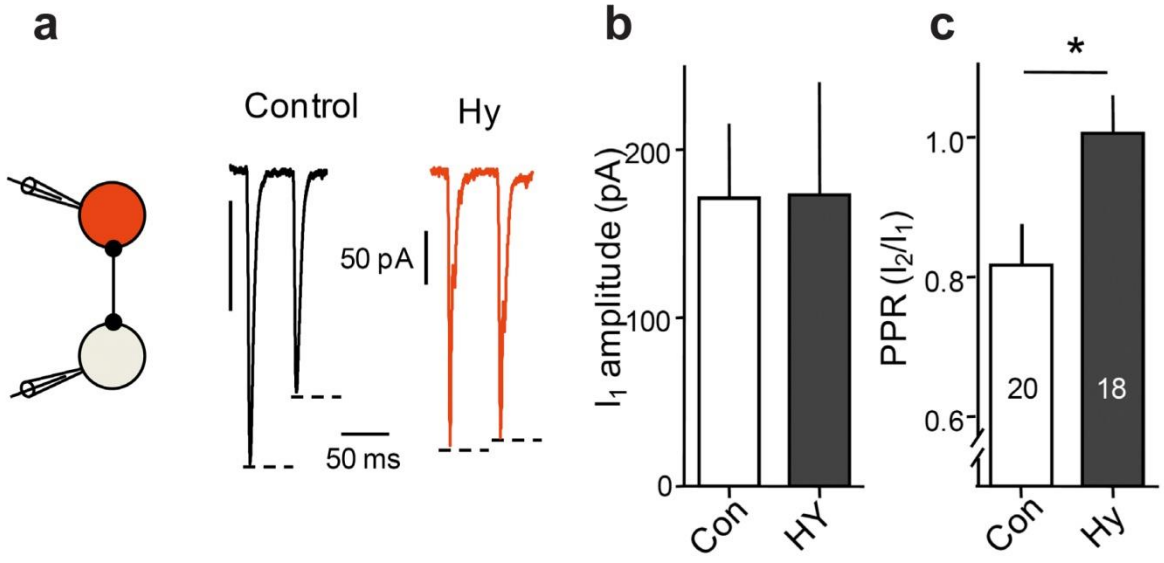
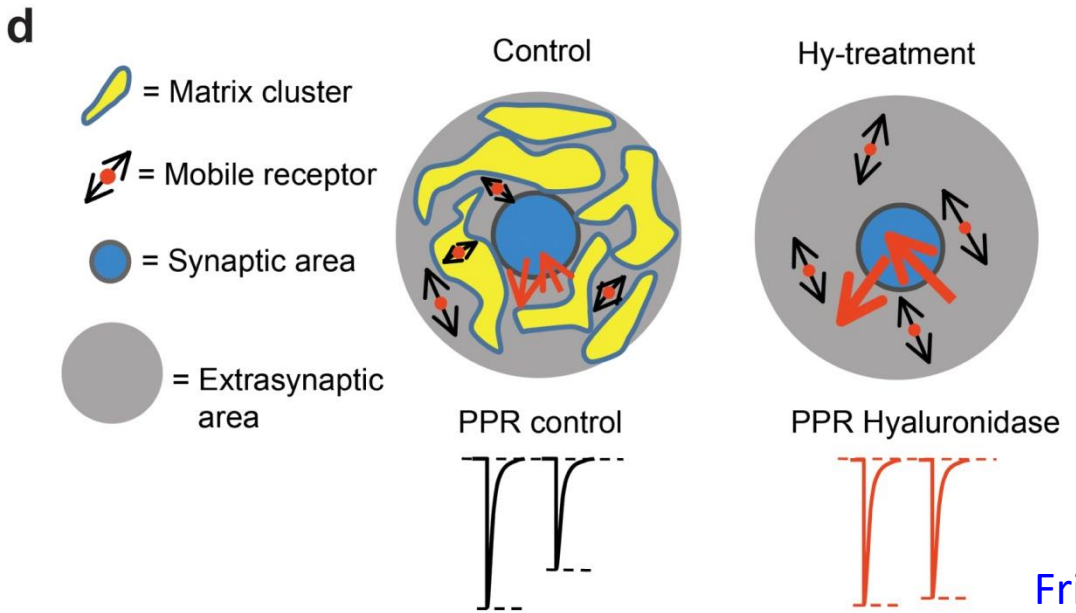


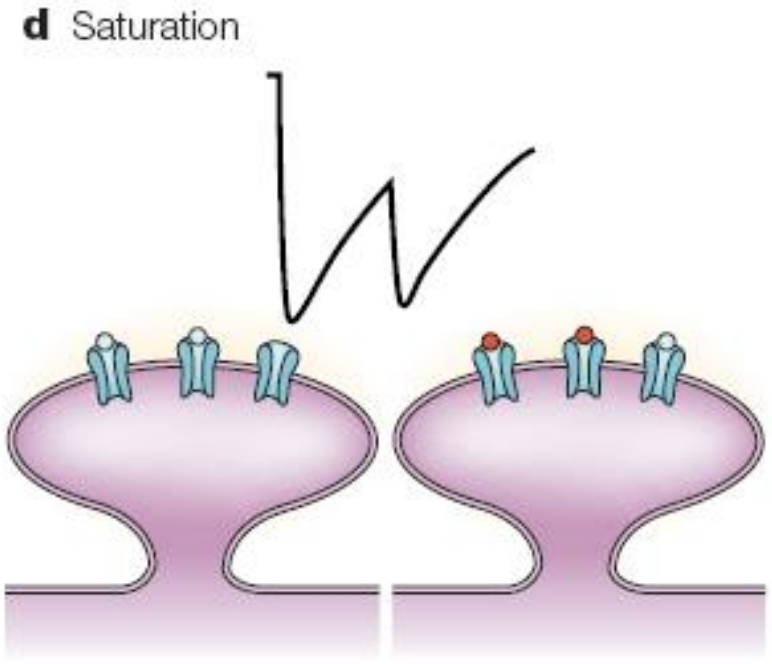


Frischknecht et al., Nat Neurosci, 2009

STD due to saturation of postsynaptic receptors

Receptors with high affinity for transmitter

Some synapses show saturation, some not.



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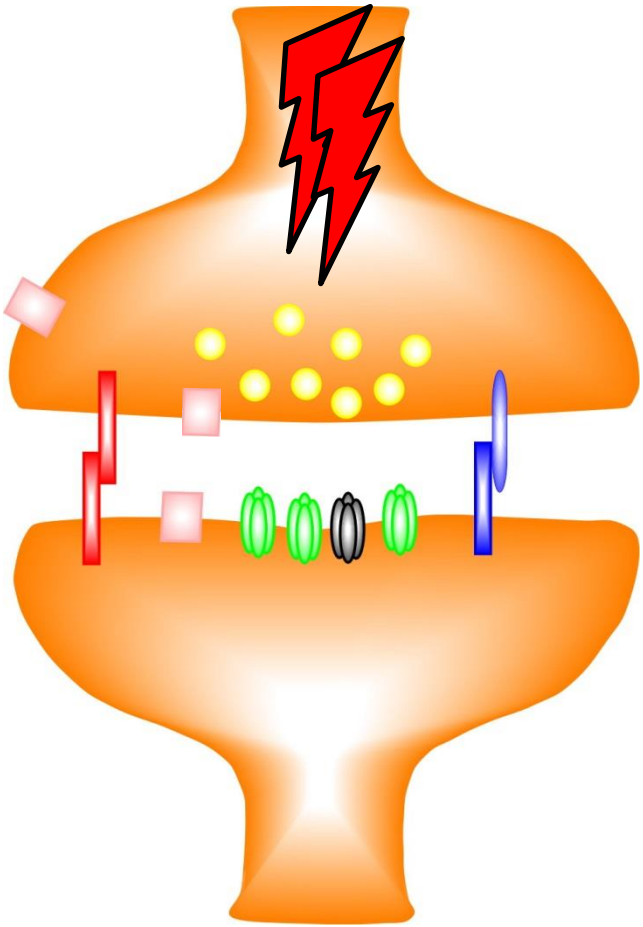
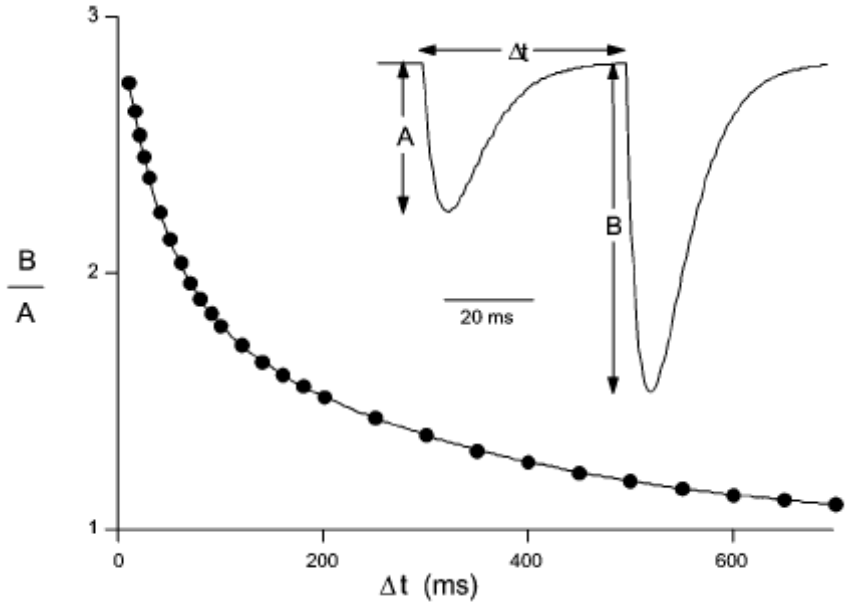
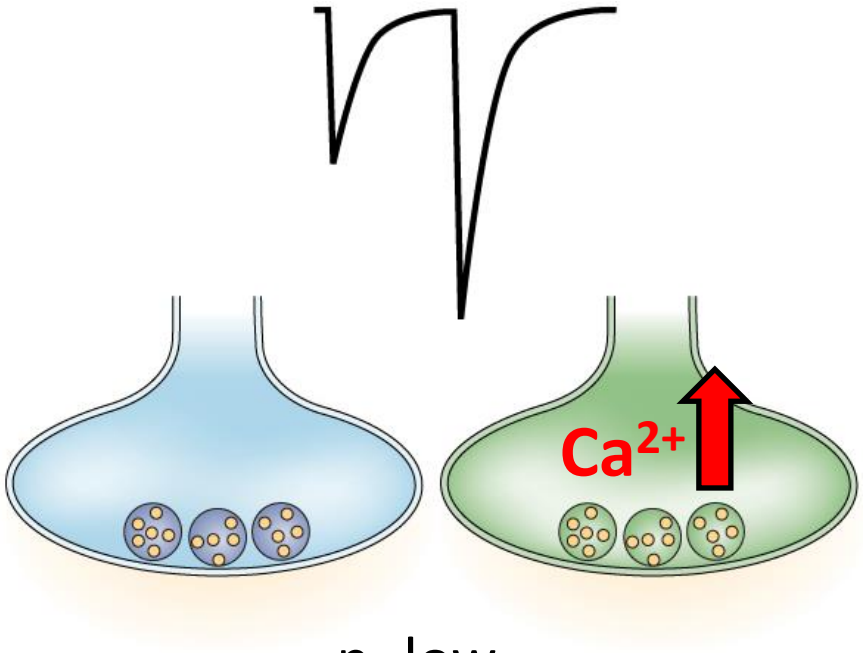
Short-term synaptic facilitation (STF)

Repeated stimuli delivered at short time intervals lead to a transient <u>increase</u> in synaptic strength.





STF is due to the build-up of Ca^{2+} in the presynaptic terminal during synaptic activity



p_v low

Residual Ca^{2+} hypothesis

Power law relationship between Ca^{2+} entry and release

$$EPSC = k*(Ca^{2+}\ influx)^n$$

$$n = 3 – 4$$

which means that doubling Ca^{2+} influx

will increase the synaptic response 8- to 16-fold

1. ‘Original’ residual Ca^{2+} model

(Katz and Miledi, 1968)

Problems:

$[Ca^{2+}]_{out}$ = 1 - 2 mM

$[Ca^{2+}]_{rest}$ = 50 - 100 nM

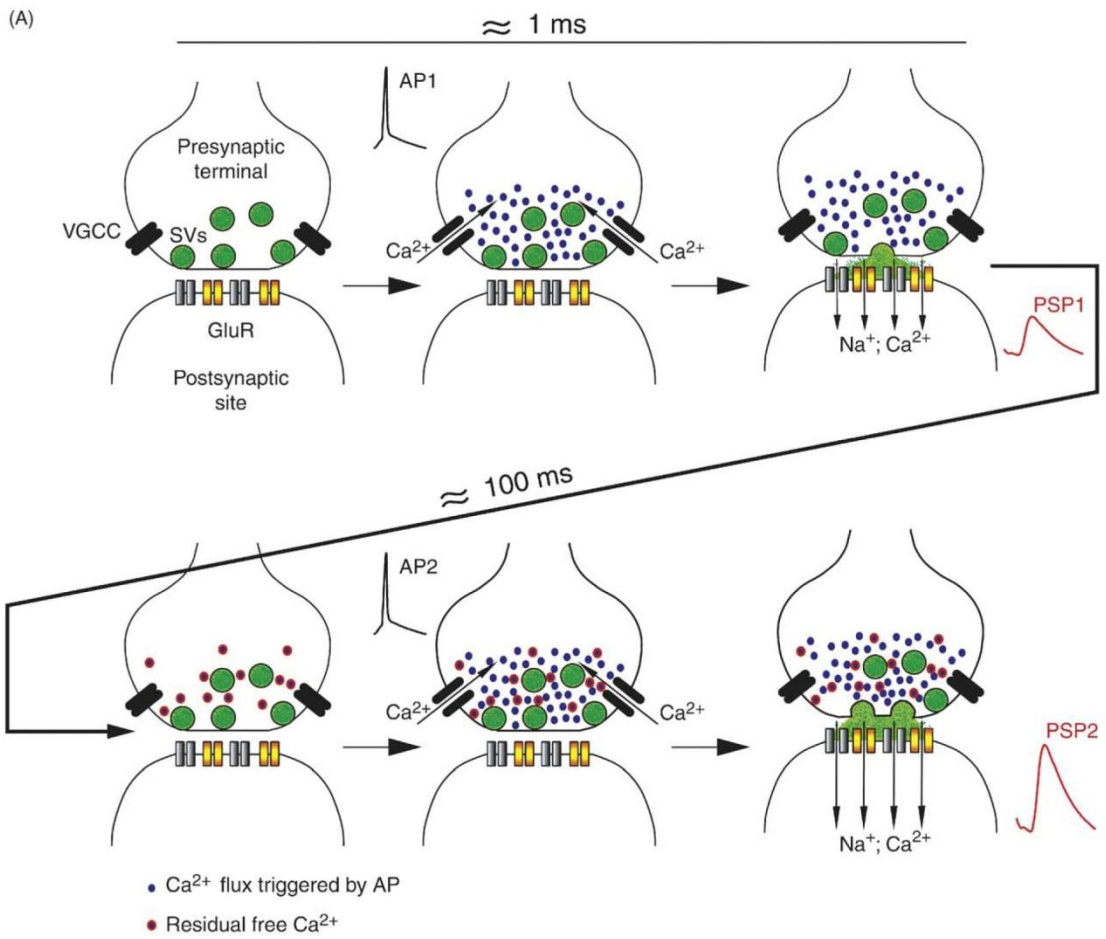
$[Ca^{2+}]_{channel\ mouth}$ ≈ 100 μM

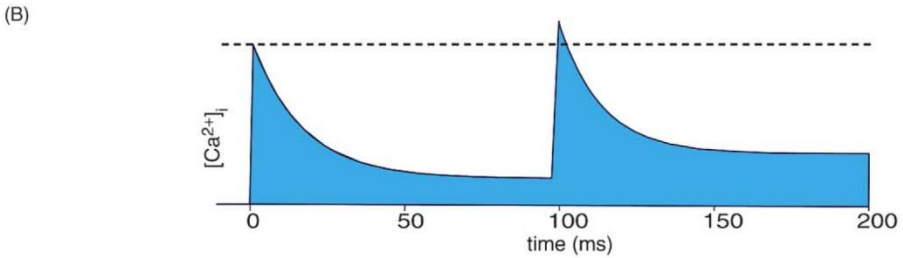
(not at equilibrium)

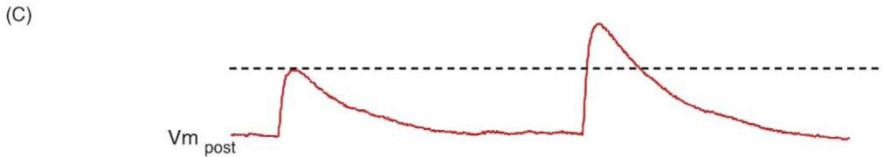
$[Ca^{2+}]_{residual}$ < 1 μM

(Ca^{2+} equilibrates throughout the bouton within 1 msec; residual Ca^{2+} lasting for tens of msec to sec)

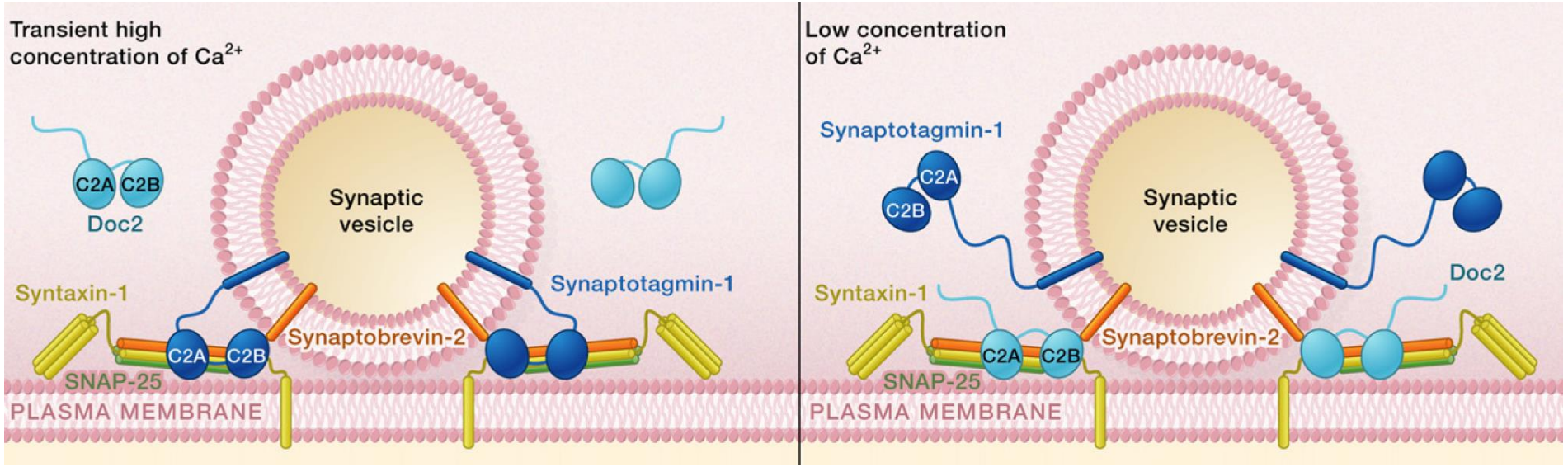
Too little even for the power law!







2. Two sensors model

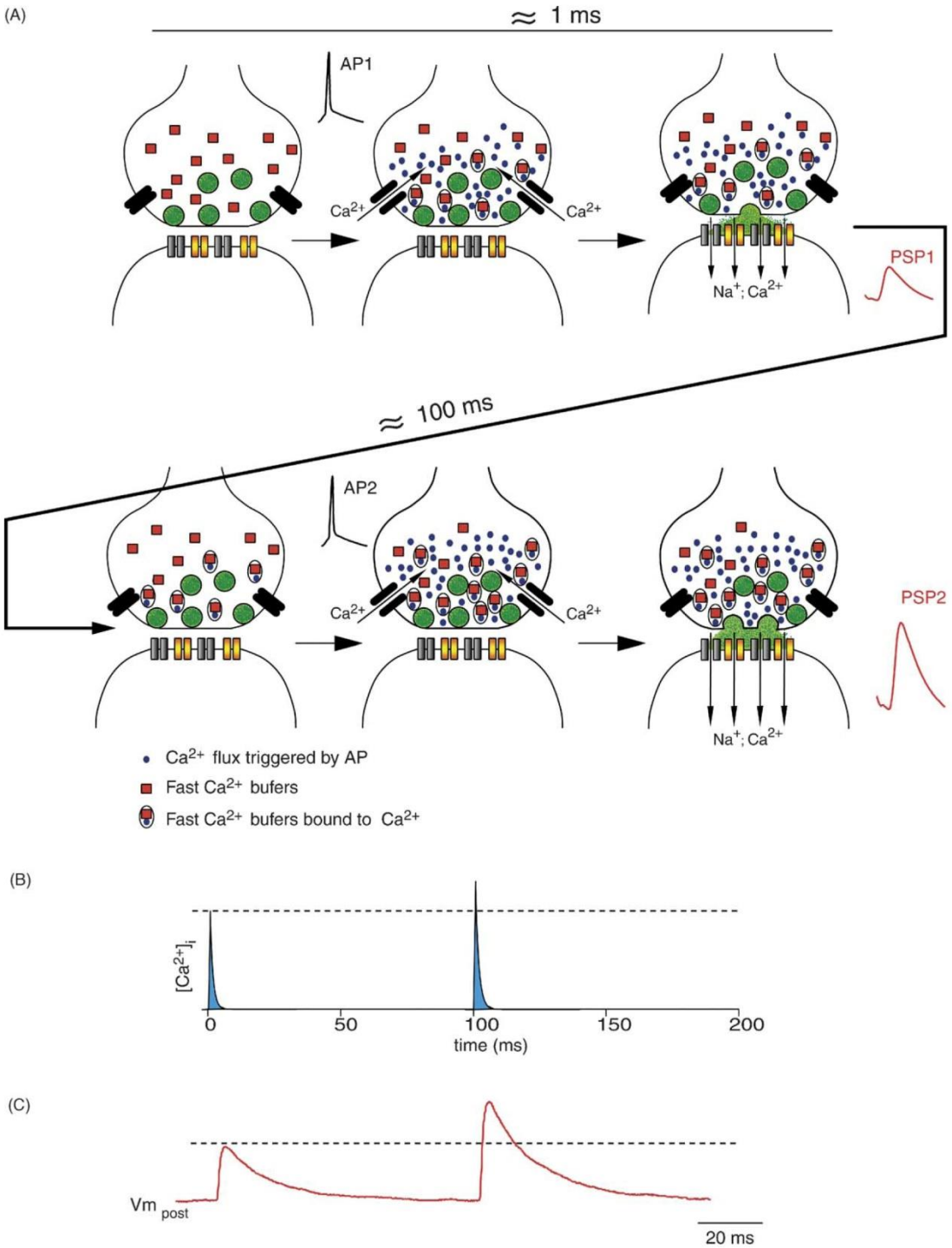


K_d ~ 10 μM

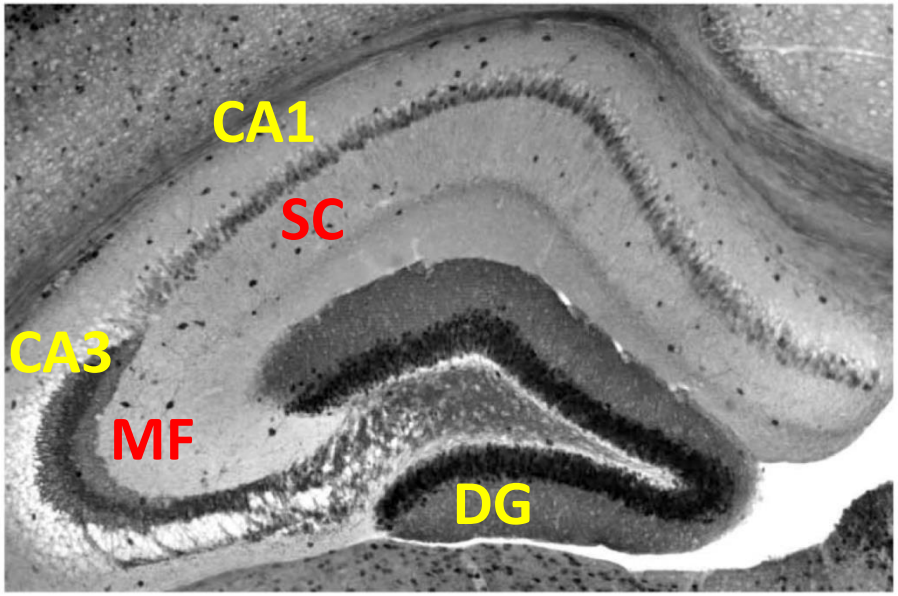
K_d < 1 μM

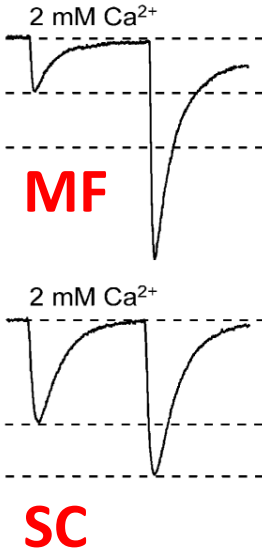
An additional high-affinity Ca^{2+} binding site (**Doc2**) with slow unbinding kinetics could operates cooperatively with the main release sensor (**synaptotagmin**). Ca^{2+} would bind to the additional site during the first AP and remain bound by the time of the second AP, thus increasing the amount of neurotransmitter release in response to the second AP .

3. Partial saturation of fast Ca^{2+} buffers model



The endogenous buffer Calbindin D_{28k} can explain the large facilitation of the Mossy fiber synapses



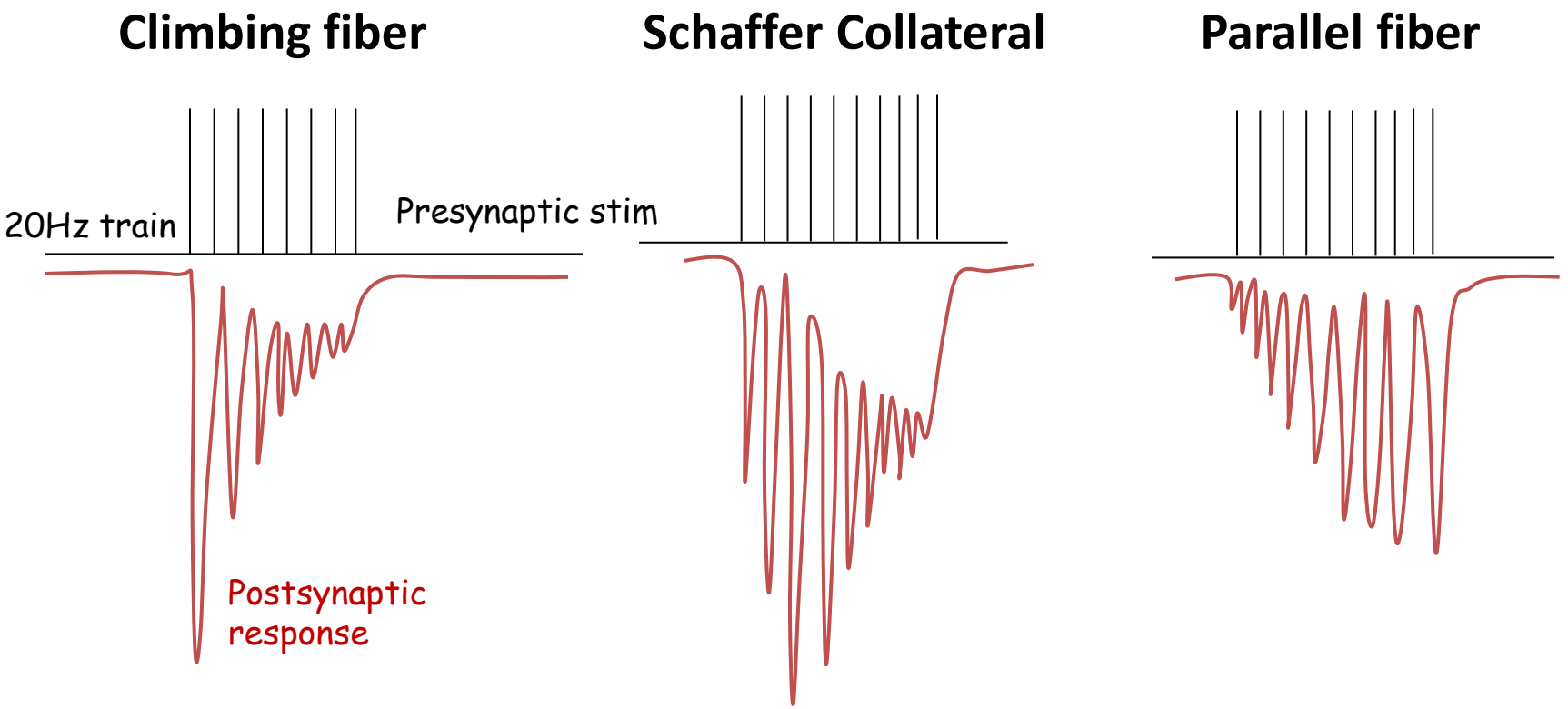


Blatow et al., Neuron 2003

Filtering function of

Short-term synaptic Plasticity (STP)

Different synapses have different STP



Depressing synapse

High P_r

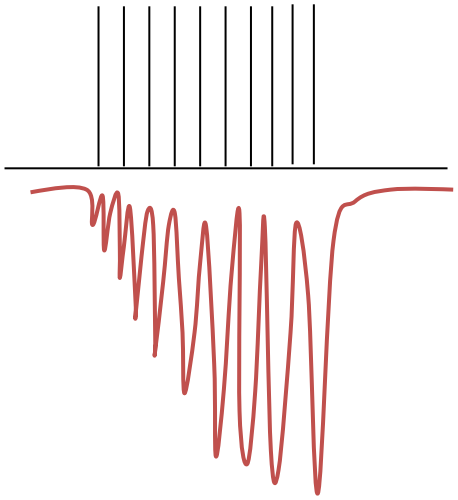
Intermediate synapse

Intermediate P_r

Facilitating synapse

Low P_r

Parallel fiber



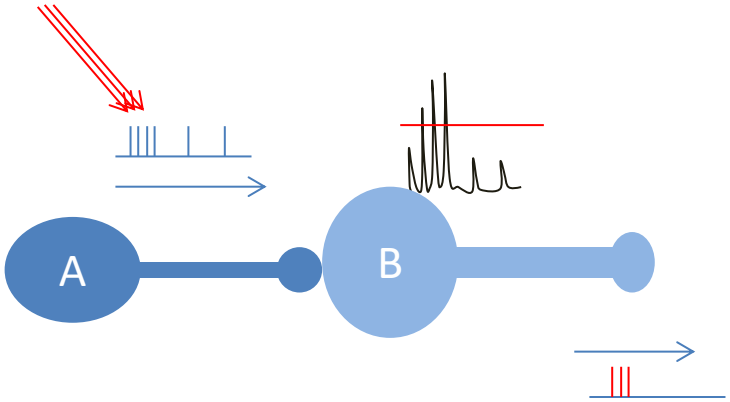
Facilitating synapse

Low P_r

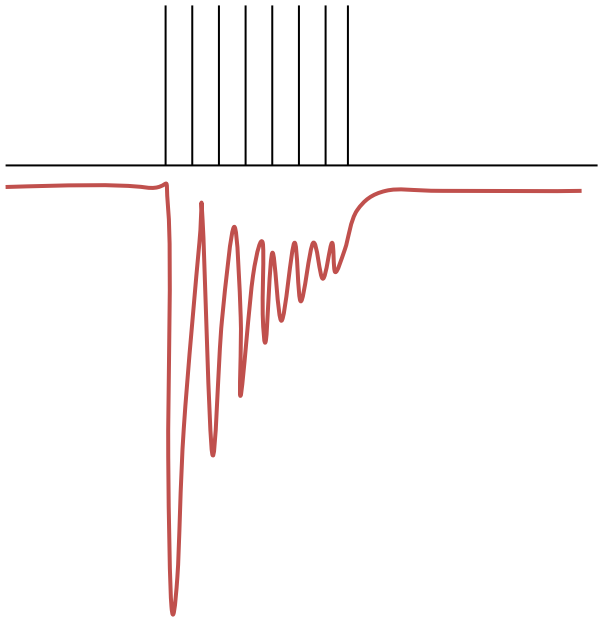
Parallel fiber

Is a **low P_r** synapse

It works as a **high pass filter**



Climbing fiber



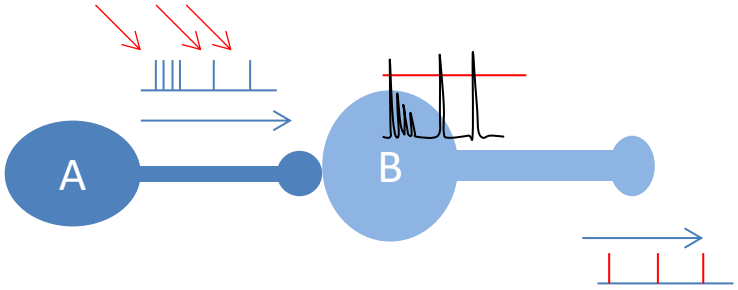
Depressing synapse

High P_r

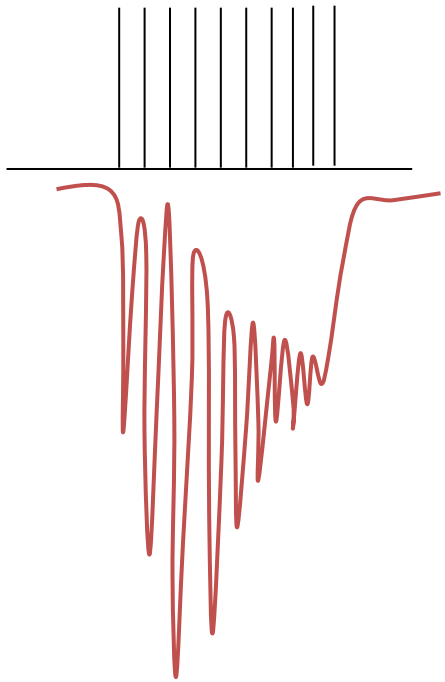
Climbing fiber

Is a **high P_r** synapse

It works as a **low pass filter**



Schaffer Collateral



Intermediate synapse

Intermediate P_r

Schaffer Collateral

Is an **intermediate P_r** synapse

It works as a **band pass filter**