Model neurons

Synapses

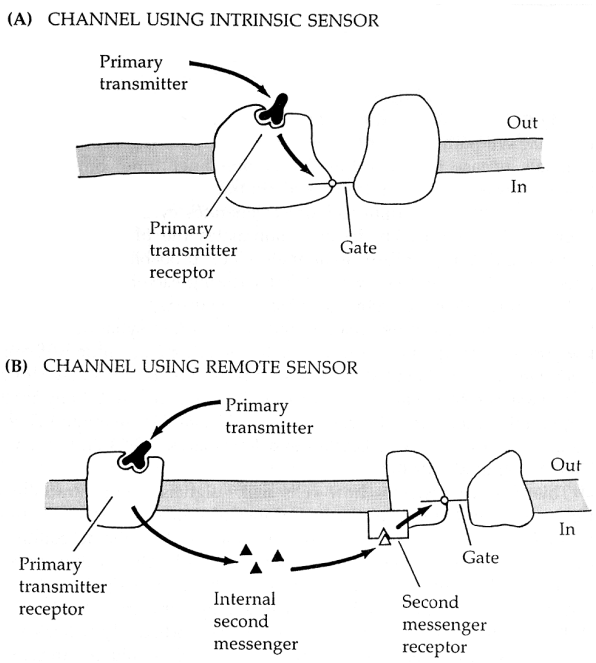
Suggested reading:

Chapter 5.8 in Dayan, P. & Abbott, L., Theoretical Neuroscience, MIT Press, 2001.

Model neurons: Synapse

Contents:

Synapses



The synapse is remarkably complex and involves many simultaneous processes such as the production and degredation of neurotransmitter.

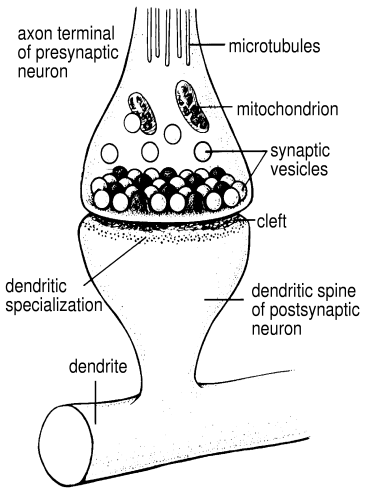
The neurotransmitters directly (A) or indirectly (B) binds to a synaptic channel and activates it.

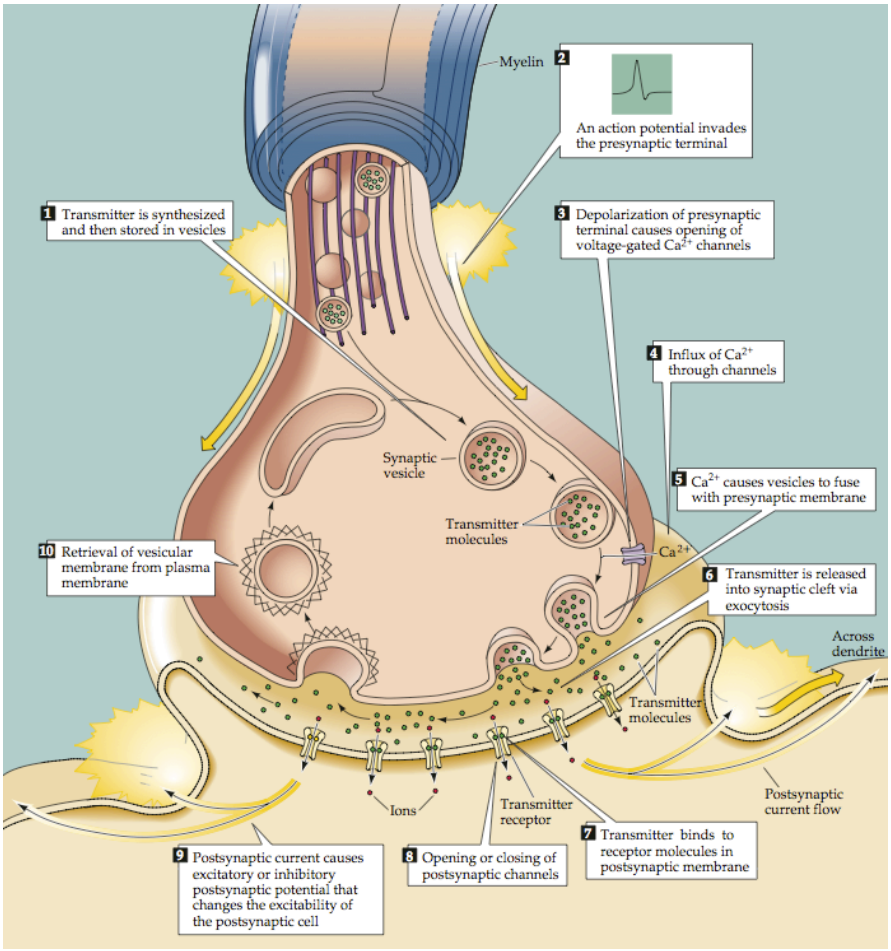
Synaptic conductances

Synaptic transmission begins when an action potential invades the presynaptic terminal and activates voltage dependent Ca^{2+} channels.

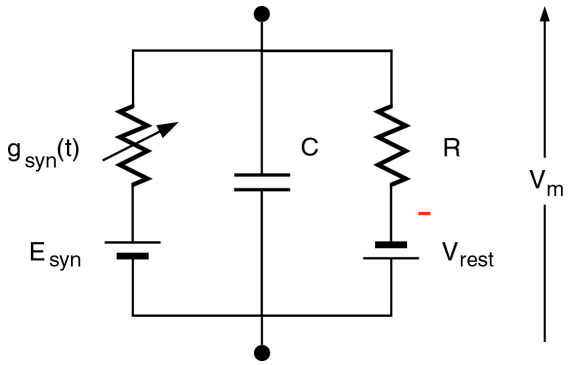
This causes transmitter molecules to enter the cleft and bind to receptors on the postsynaptic neuron.

As a result ion channels open, which modifies the conductance of the postsynaptic neuron





Synaptic input into the RC-circuit

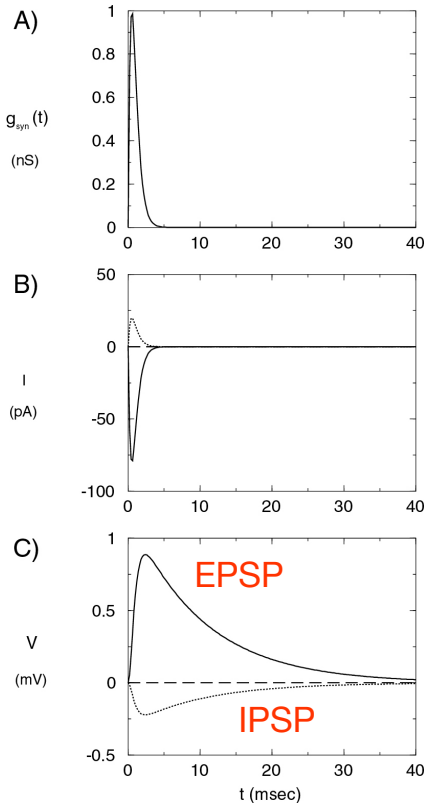


$$I_{syn} = g_{syn}(t)(V_m(t) - E_{syn})$$

$$C\frac{dV_m(t)}{dt} + g_{syn}(t)(V_m(t) - E_{syn}) + \frac{V_m(t) - V_{rest}}{R} = 0$$

$$\tau\frac{dV_m(t)}{dt} = -(1 + Rg_{syn}(t))V_m + Rg_{syn}(t)E_{syn} + V_{rest}$$

Synaptic input into RC-Circuit



$$g_{syn}(t) = const \cdot t \cdot e^{\frac{-t}{t_{peak}}}$$

$$I_{syn} = g_{syn}(t)(V_m(t) - E_{syn})$$

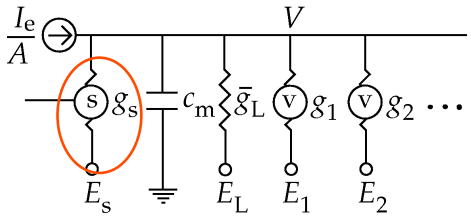
$E_{syn} = 80mV$
$E_{syn} = -20mV$
$E_{syn} = 0mV$

(relative to rest)

$$\tau \frac{dV_m(t)}{dt} = -V_m - RI_{syn}(t)E_{syn} + V_{rest}$$

Synaptic conductances (probabilities)

Synaptic conductance: $g_s = \bar{g}_s P$



P: open channel probability $P = P_s P_{rel}$

P_{rel}: probability of transmitter release
P_s: probability that postsyn. channel opens

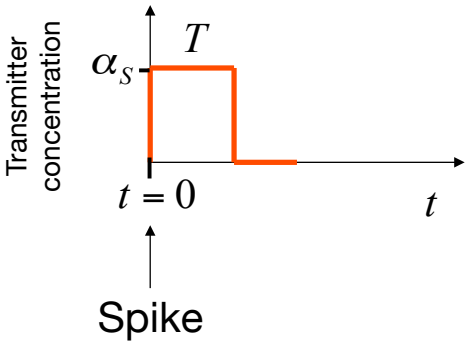
Postsynaptic conductance

$$P_S \underset{\alpha_S}{\overset{\beta_S}{\rightleftarrows}} 1 - P_S \qquad \frac{dP_S}{dt} = \alpha_S(1 - P_S) - \beta_S P_S$$

$\beta_S \approx const.$ closing rate of the channel

α_S opening rate

Simple model of transmitter release:



$t = 0$: $P_S(0)$

$\alpha_S > \beta_S$ ignore β_S during the opening process

This simplification leads us to the following equation

$$\frac{1}{\alpha_S}\frac{dP_S}{dt} = -P_S + 1$$ with the solution $$P_S = \nu_0 e^{-\alpha t} + \nu_1$$

With the boundary conditions above, we obtain:

$$P_S(t) = 1 + (P_S(0) - 1)e^{-\alpha_S t} \quad \text{for} \quad 0 \le t \le T$$

$$P_S(t) = P_S(T)e^{-\beta_S (t-T)} \quad \text{for} \quad t \ge T$$

if there is no synaptic release immediately before the release at t=0

$$P_S(0) = 0$$

$$P_{\max} = P_S(T) = 1 - e^{-\alpha_S T}$$

$$P_S(t) = 1 + (P_S(0) - 1)e^{-\alpha_S t} \quad \text{for} \quad 0 \le t \le T$$

$$P_S(t) = P_S(T)e^{-\beta_S (t-T)} \quad \text{for} \quad t \ge T$$

using

$$P_{\max} = 1 - e^{-\alpha_S T}$$

we can write in the general case

$$P_S(T) = P_S(0) + P_{\max}(1 - P_S(0))$$

Example

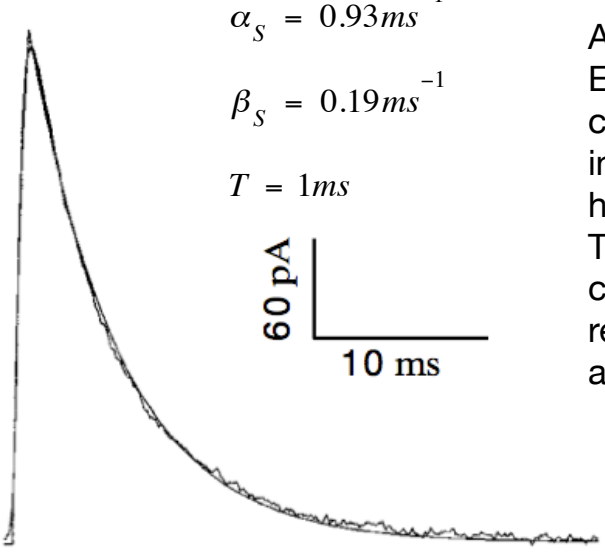
$$P_S(t) = 1 + (P_S(0) - 1)e^{-\alpha_S t} \quad \text{for} \quad 0 \le t \le T$$

$$P_S(t) = P_S(T)e^{-\beta_S (t-T)} \quad \text{for} \quad t \ge T$$

$\alpha_S = 0.93 ms^{-1}$

$\beta_S = 0.19 ms^{-1}$

$T = 1 ms$



A fit of the model 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.

Fast synapse

For a fast synapse the rise of the conductance following a presynaptic action potential can be approximated as instantaneous.
For a single presynaptic action potential occurring at t=0 we can write

$$P_S = P_{\max} e^{-\frac{t}{\tau_S}} \quad \text{with} \quad \tau_S = \frac{1}{\beta_S}$$

A sequence of action potentials at arbitrary times can be modeled with an exponential decay

$$\tau_S \frac{dP_S}{dt} = -P_S$$

and by updating the probability after each action potential with

$$P_S \rightarrow P_S + P_{\max}(1 - P_S)$$

Slow synapse

For an isolated presynaptic action potential occurring at t=0 we can use a difference of two exponentials

(e.g. $GABA_A$ and NMDA)

$$P_S(t) = P_{\max} B \left(e^{-\frac{t}{\tau_1}} - e^{-\frac{t}{\tau_2}} \right)$$

$$\tau_1 > \tau_2$$

$$B = \left(\left(\frac{\tau_2}{\tau_1} \right)^{\tau_{rise}/\tau_1} - \left(\frac{\tau_2}{\tau_1} \right)^{\tau_{rise}/\tau_2} \right)^{-1}$$

$$\tau_{rise} = \frac{\tau_1 \tau_2}{\tau_1 - \tau_2}$$

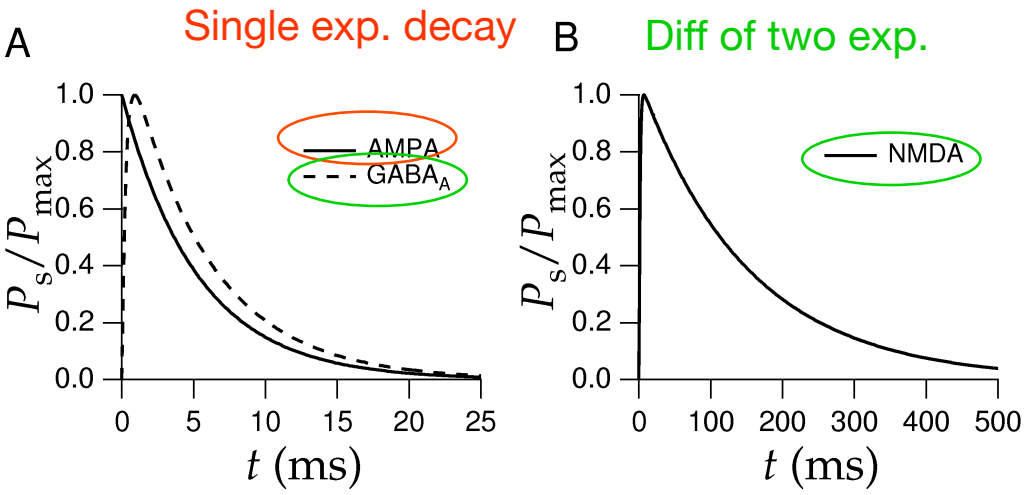
B is a normalization factor and ensures that the peak value is equal to P_{max}

or the alpha function

$$P_S = \frac{P_{\max} t}{\tau_S} e^{1-\frac{t}{\tau_S}}$$

with a peak value at $t = \tau_S$

Examples of synapses



For a fast synapse (AMPA) the rise of the conductance following a presynaptic action potential can be approximated as instantaneous.

Examples of synapses

Glutamate activates two different kinds of receptors:
AMPA and NMDA.

Both receptors lead to an excitation of the membrane.

- AMPA is fast
- NMDA is voltage dependent and slow (20ms rise)

GABA (γ-aminobutyric acid) is the principal inhibitory neurotransmitter.
There are two main receptors for GABA, $GABA_A$ and $GABA_B$.

- $GABA_A$ is responsible for fast inhibition and requires only brief stimuli to produce a response.
- $GABA_B$ involves so-called second messengers.

Examples of synapses: AMPA

Glutamate activates two different kinds of receptors: AMPA and NMDA.

Both receptors lead to an excitation of the membrane.

AMPA:

$$i_{AMPA} = \bar{g}_{AMPA} P_S(t)(V - E_{AMPA})$$

$$\frac{dP_S}{dt} = \alpha_S(1 - P_S) - \beta_S P_S$$

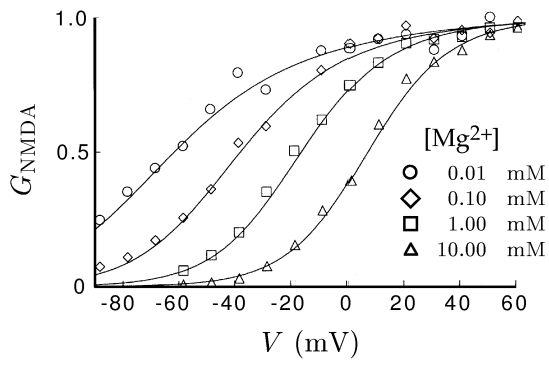
fast

Examples of synapses: NMDA

NMDA: $$i_{NMDA} = \bar{g}_{NMDA} G_{NMDA}(V) P_S(t)(V - E_{NMDA})$$

$$\frac{dP_S}{dt} = \alpha_S(1 - P_S) - \beta_S P_S$$

Slow (20ms rise)



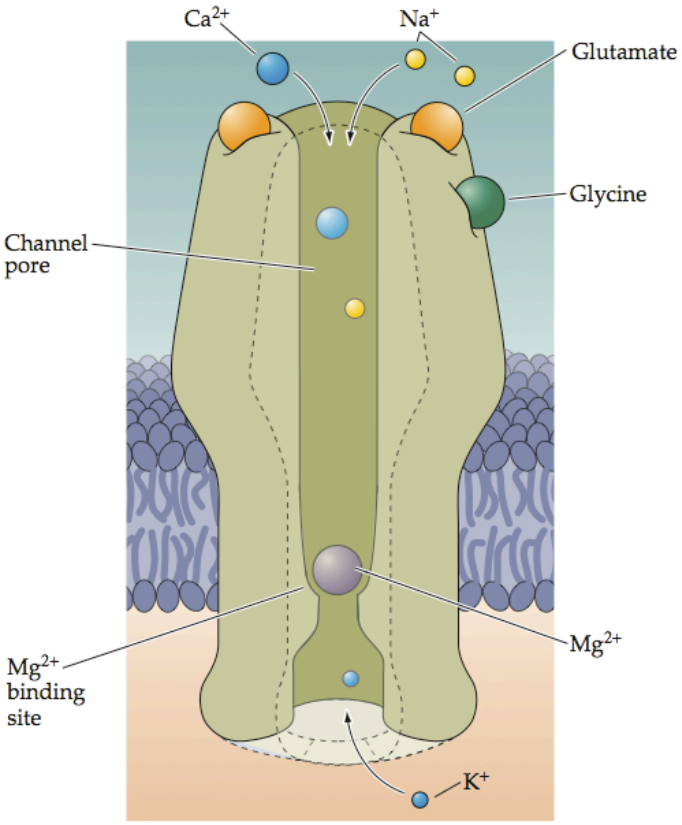
Dependence of the NMDA conductance on the membrane potential V and the extracellular Mg^{2+} concentration.

Physiological correlate of the Hebb learning rule since both, the presynaptic and postsynaptic cell have to be active.

The voltage dependence is mediated by magnesium ions which normally block NDMA receptors. The postsynaptic cell must be sufficiently depolarized to knock out the blocking ions.

$$G_{NMDA} = \left(1 + \frac{[Mg^{2+}]}{3.57\ \text{mM}} \exp(-V/16.13\ \text{mV})\right)^{-1}$$

Examples of synapses: NMDA



NMDA receptors contain binding sites for glutamate and the co-activator glycine, as well as an Mg^{2+} binding site in the pore of the channel. At hyperpolarized potentials, the electrical driving force on Mg^{2+} drives this ion into the pore of the receptor and blocks it.

Examples of synapses: $GABA_A$

GABA (γ-aminobutyric acid) is the principal inhibitory neurotransmitter.
There are two main receptors for GABA, $GABA_A$ and $GABA_B$.

$GABA_A$

$GABA_A$ is responsible for fast inhibtion and require only brief stimuli to produce a response.

$$i_{GABA_A} = \bar{g}_{GABA_A} P_S(t)(V - E_{GABA_A})$$

$$\frac{dP_S}{dt} = \alpha_S(1 - P_S) - \beta_S P_S$$

Examples of synapses: $GABA_B$

$GABA_B$ is a much more complex receptor. It involves so-called second messengers. $GABA_B$ responses occur when the GABA binds to another compound (G-potein) which in turn binds to a Potassim channel and opens it up. It takes 4 activated G-proteins to open the channel.

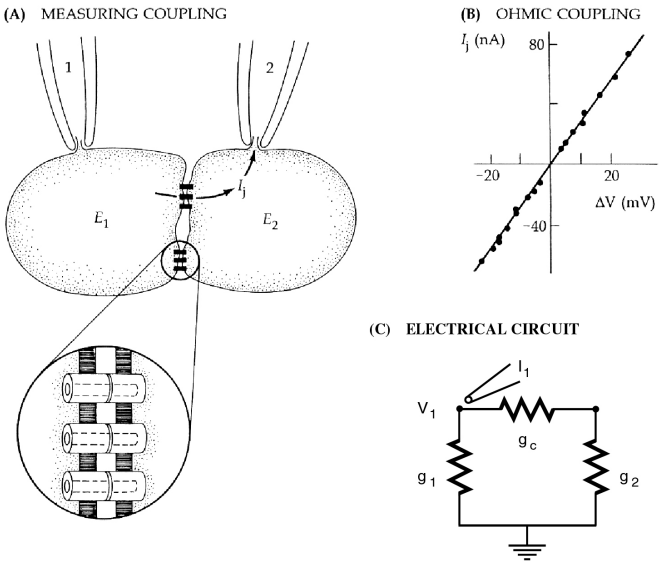
$$i_{GABA_B} = \bar{g}_{GABA_B} \frac{P_S^{\,4}}{P_S^{\,4} + K_d}(V - E_K)$$

$$\frac{dP_S}{dt} = K_3 P_r - K_4 P_S$$

$$\frac{dP_r}{dt} = \alpha_S (1 - P_r) - \beta_r P_r$$

Examples of synapses: Gap junctions

Gap junctions are not chemical synapses but electrical in nature. The produce a current proportional to the difference between pre-and postsynaptic potential. No transmitter or action potential is involved. Many non-neural cells, e.g. muscle, glia, are coupled in this manner.



$$i_{gap} = g_C (V_{post} - V_{pre})$$

Probability of transmitter release

Synaptic conductance: $g_s = \bar{g}_s P$

P: open channel probability $P = P_s P_{rel}$

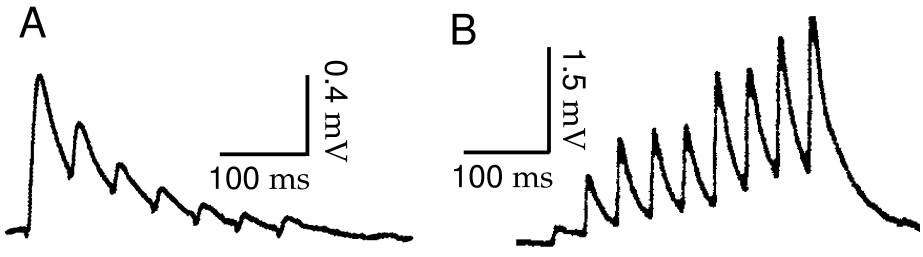
P_{rel}: probability of transmitter release
P_s: probability that postsyn. channel opens

The probability of transmitter release and the magnitude of the resulting conductance change in the postsynaptic neuron can depend on the history of activity at a synapse.

- The effects of activity on synaptic conductances are termed short- and long-term.
- Short-term plasticity refers to a number of phenomena that affect the probability that a presynaptic action potential opens postsynaptic channels.
- Long-term plasticity involves structural changes which are extremely persistent (learning).

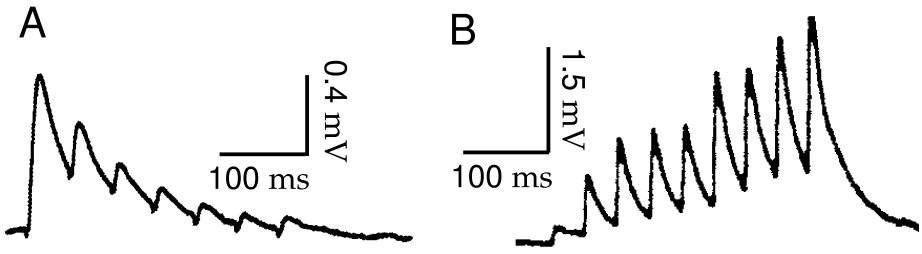
Probability of transmitter release

The probability of transmitter release can be used to model synaptic depression (A) and facilitation (B) of excitatory intercortical synapses



A) Depression of an excitatory synapse between two layer 5 pyramidal cells recorded in a slice of rat somatosensory cortex. Spikes were evoked by current injection into the presynaptic neuron and postsynaptic currents were recorded with a second electrode. B) Facilitation of an excitatory synapse from a pyramidal neuron to an inhibitory interneuron in layer 2/3 of rat somatosensory cortex. (A from Markram and Tsodyks, 1996; B from Markram et al., 1998.)

Probability of transmitter release and short-term plasticity



Depression (D) and facilitation (F) of excitatory intercortical synapses

$$\tau_P \frac{dP_{rel}}{dt} = P_0 - P_{rel}$$

Update after each spike:

$$P_{rel} \rightarrow P_{rel} + f_F(1 - P_{rel})$$

$$P_{rel} \rightarrow f_D P_{rel}$$

Threshold

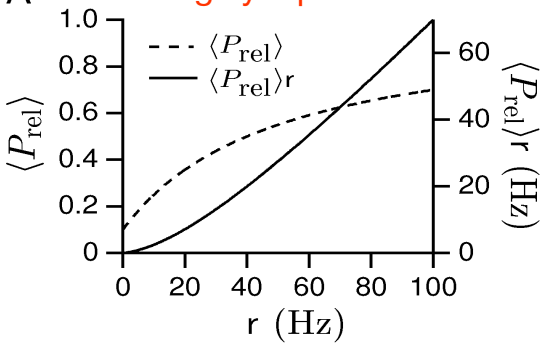
with P_0 the release probability after a long period of silence

Probability of transmitter release and short-term plasticity

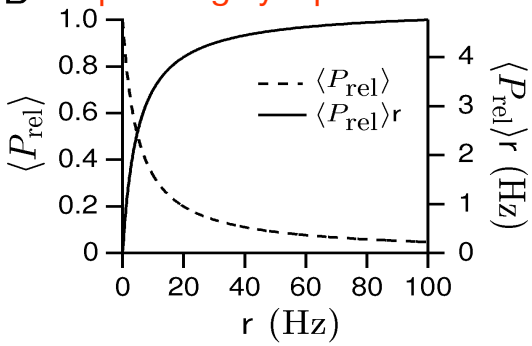
Average steady-state release probability for a presynaptic Poisson spike-train (Dayan & Abbott, p. 187):

$$\langle P_{rel} \rangle = \frac{P_0 + f_F r \tau_p}{1 + f_F r \tau_p} \qquad \langle P_{rel} \rangle = \frac{P_0}{1 + (1 - f_D) r \tau_p}$$

A Facilitating synapse

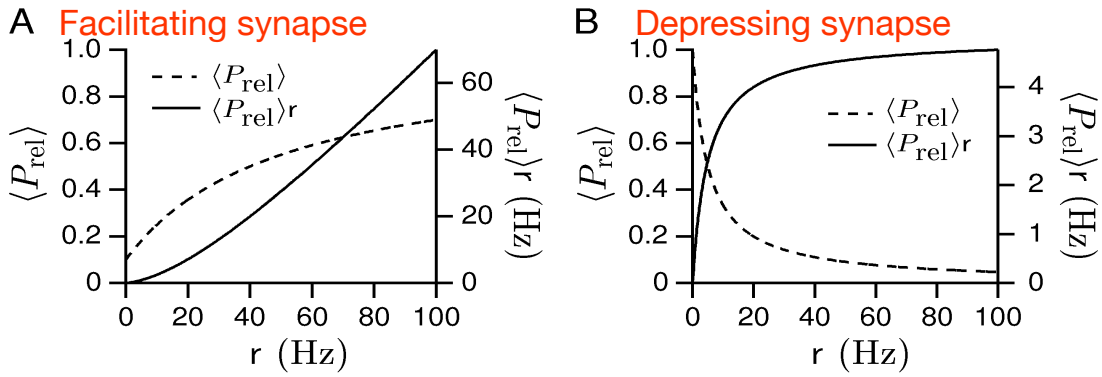


B Depressing synapse



$r\langle P_{rel} \rangle$: Synaptic transmission

Probability of transmitter release and short-term plasticity



In facilitating synapses, isolated spikes in low-frequency trains are transmitted with lower probability than spikes occurring within high-frequency bursts.

Synapses that depress do not convey information about the values of constant high, presynaptic firing rates to their postsynaptic targets.