
THEORETICAL NEUROSCIENCE

TD5: SYNAPSES & DENDRITES

All TD materials will be made available at <https://github.com/helene-todd/TheoNeuro2425>.

In previous tutorials, we have developed models of point neurons responding to injection of currents. Biologically, these currents correspond to synaptic inputs from other neurons, making the synapse a key element of the communication between neurons. Importantly, synapses are thought to be the substrate of learning, as the modulation of their strength, or plasticity, modifies the interaction between neurons. Plasticity can obey different rules depending on the structure of synapses. In this tutorial, we propose to model two phenomena related to plasticity at the level of the synapse: short-term plasticity (through STD and STF) and long-term plasticity (through STDP).

Note: we will use slightly different notations than those introduced in the lesson; A_{SE} instead of A , U_{SE} instead of U , U_{SE}^1 instead of u , τ_{facil} instead of τ_F and τ_{rec} instead of τ_D .

1 Short term plasticity (STP)

Short-term plasticity refers to the activity-dependent variation of synaptic efficacy on short time scales (milliseconds to seconds). Two main types of plasticity can coexist in the same synapse: facilitation (enhancement of synaptic efficacy with past activity and depression (reduction of synaptic efficacy with past activity).

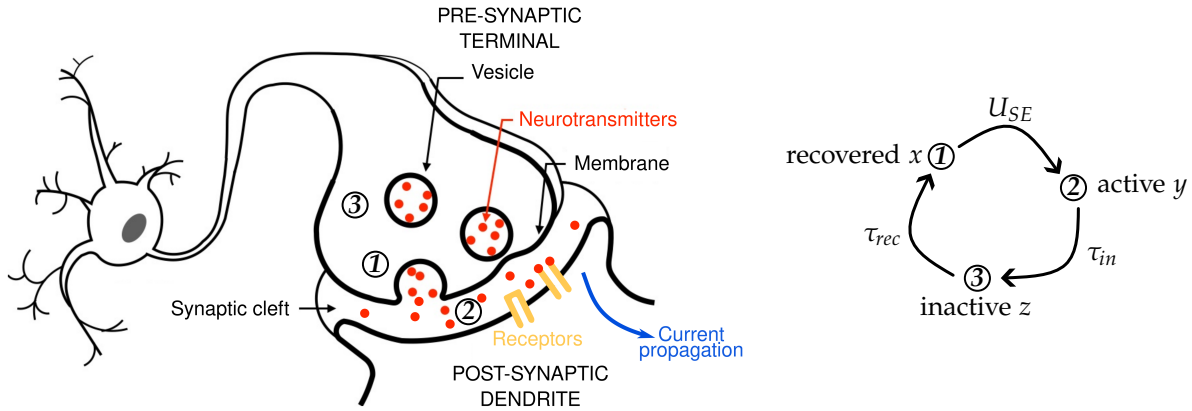
1.1 Vesicular pool dynamics

In this model, it is assumed that a synapse is characterised by a finite amount of resources (i.e. vesicles). Each vesicle is either in the recovered, active or inactive state. To model this, we denote the variables x, y and z as the fractions of resources in the recovered, active and inactive states respectively, such that $x + y + z = 1$.

- The variable U_{SE} stands for the release probability, which corresponds to the fraction of vesicles from the recovered pool released by a single spike arriving at the pre-synaptic axon terminal.
- Those vesicles immediately become active, and then quickly inactivate with a time constant τ_{in} (of the order of a few milliseconds).
- The pool of available resources is replenished by the recovery of inactivated vesicles with a time constant τ_{rec} (of the order of 1 sec).

On the post-synaptic side, the net input current is assumed to be directly proportional to the fraction of resources in the active state $y(t)$ by a factor A_{SE} (absolute synaptic efficacy)

$$I_{syn}(t) = A_{SE}y(t). \quad (1)$$



1.1.1 Short term depression (STD)

The short term depression (STD) effect is captured through the the fraction of resources available after synaptic vesicle depletion, i.e. the fraction of resources in the recovered state x .

1. Write down the equations governing the time evolution of variables x, y and z .

Let us begin with the equation of the recovered pool x . During a small time interval dt in which there is a spike, the probability of release is U_{SE} , therefore the amount of vesicles released is $U_{SE}x(t_{sp})\delta(t - t_{sp})$, where t_{sp} is the time at which the spike occurs and $\delta(t)$ the Dirac delta function. The amount of vesicles replenished during a time interval dt is z/τ_{rec} . Therefore, the equation for the recovered pool x is

$$\begin{aligned} x(t + dt) &= x(t) + dt \frac{z}{\tau_{rec}} - dt U_{SE}x(t)\delta(t - t_{sp}) \\ \Rightarrow \frac{dx(t)}{dt} &= \frac{z(t)}{\tau_{rec}} - U_{SE}x(t)\delta(t - t_{sp}). \end{aligned}$$

The amount of U_{SE} available synaptic resources get used up and end up in the pool of active vesicles y . Furthermore, active vesicles become inactive with a time constant τ_{in} , leading to the equation for the active pool y

$$\frac{dy(t)}{dt} = -\frac{y(t)}{\tau_{in}} + U_{SE}x(t)\delta(t - t_{sp}).$$

The inactivation of the previously active vesicles y goes in the pool of inactive vesicles z , and inactive vesicles recover with time constant τ_{rec} , leading to the equation for the inactive pool z

$$\frac{dz(t)}{dt} = \frac{y(t)}{\tau_{in}} - \frac{z(t)}{\tau_{rec}}.$$

One can observe that these equations form a closed loop ($\dot{x} + \dot{y} + \dot{z} = 0$) since there is preservation of the amount of total resources.

1.1.2 Short term facilitation (STF)

The short term facilitation (STF) effect is captured by the parameter U_{SE} , representing the fraction of available resources ready for use (i.e. the release probability).

The parameter U_{SE} is not fixed, but rather increases by a certain amount at each pre-synaptic spike. Between spikes, U_{SE} decays back to 0 with time constant τ_{facil} . The running value of U_{SE} will be referred to as U_{SE}^1 . The following differential equation describes this dynamic

$$\frac{dU_{SE}^1(t)}{dt} = -\frac{U_{SE}^1(t)}{\tau_{facil}} + U_{SE}(1 - U_{SE}^1(t))\delta(t - t_{sp}). \quad (2)$$

2. The above equation can be transformed into an iterative expression for the value U_{SE} upon the arrival of the n th spike. Let t_{sp}^+ and t_{sp}^- denote the times right before and after a spike t_{sp} . Determine the iterative expression that results from equation (2).

We begin by looking at what happens right before a spike : at time t_{sp}^- , we have that for all $t < t_{sp}^-$, $\delta(t - t_{sp}) = 0$, therefore equation (2) simply becomes

$$\frac{dU_{SE}^1(t)}{dt} = -\frac{U_{SE}^1(t)}{\tau_{facil}}.$$

The solution to this first-order linear ODE is

$$U_{SE}^1(t) = U_{SE}^1(0)e^{-t/\tau_{facil}}.$$

We will denote $U_{SE}^{1(n)}$ the value at of U_{SE}^1 at the n -th spike. We therefore have

$$U_{SE}^{1(n+1)}(t_{sp}^-) = U_{SE}^{1(n)}e^{-\delta t/\tau_{facil}},$$

where δt is the time interval between the previous spike and t_{sp} (i.e. between the n th and the $(n + 1)$ th spikes).

At time t_{sp}^+ , a spike has just occurred; using the previous equality, we can now determine what happens right after a spike, yielding the iterative expression

$$\begin{aligned} U_{SE}^{1(n+1)}(t_{sp}^+) &= U_{SE}^{1(n)}e^{-\delta t/\tau_{facil}} + U_{SE} \left(1 - U_{SE}^{1(n+1)}(t_{sp}^-)\right) \\ \Leftrightarrow U_{SE}^{1(n+1)}(t_{sp}^+) &= U_{SE}^{1(n)}e^{-\delta t/\tau_{facil}} + U_{SE} \left(1 - U_{SE}^{1(n)}e^{-\delta t/\tau_{facil}}\right) \\ \Leftrightarrow U_{SE}^{1(n+1)}(t_{sp}^+) &= U_{SE}^{1(n)}(1 - U_{SE})e^{-\delta t/\tau_{facil}} + U_{SE}. \end{aligned}$$

3. Suppose the pre-synaptic neuron emits a regular spiking train at a frequency $\delta t = 1/r$. Determine the steady-state solution of U_{SE}^1 at the time of a spike.

We determine the steady-state solution by solving $U_{SE}^{1(n+1)} = U_{SE}^{1(n)} = U_{SE}^1$. Using the previous question, we get

$$U_{SE}^1 = U_{SE}^1(1 - U_{SE})e^{-1/r\tau_{facil}} + U_{SE}$$

$$\Leftrightarrow U_{SE}^1 \left(1 - (1 - U_{SE})e^{-1/r\tau_{facil}} \right) = U_{SE}$$

$$\Leftrightarrow U_{SE}^1 = \frac{U_{SE}}{1 - (1 - U_{SE})e^{-1/r\tau_{facil}}}.$$

We have seen that this model captures both depressing and facilitating synaptic mechanisms. In what follows, we will consider only a depressing synapse - this is done by setting U_{SE}^1 as a constant equal to U_{SE} .

1.2 A focus on STD

We now suppose that the synapse receives irregular spikes: this is captured in the model by replacing $\delta(t - t_{sp})$ by $\lambda(t)$, where $\lambda(t)$ is the rate of a Poisson process. Furthermore, we suppose that $\tau_{in} \ll \tau_{rec}$, i.e. the dynamics of the active pool can be considered to be instantaneous.

4. Write down the new equations governing the time evolution of the variable x .

Since the resources get inactivated right away, the effect of y on the dynamics of x is negligible - therefore, we have $z = 1 - x$. Our previous equation for x now becomes

$$\frac{dx(t)}{dt} = \frac{1 - x}{\tau_{rec}} - U_{SE}x(t)\lambda(t).$$

We now also consider the system at a slow time scale ($\gg \tau_{in}$).

5. Give the new expression of y and deduce a relationship between the post-synaptic current I_{syn} and the variable x .

Since we consider a timescale much slower than τ_{in} , we have that $dy(t)/dt = 0$. The equation for y therefore takes the more simple form

$$y(t) = \lambda(t)\tau_{in}U_{SE}x(t).$$

Recalling equation (1), we therefore have

$$I_{syn}(t) = A_{SE}\lambda(t)\tau_{in}U_{SE}x(t).$$

We suppose the input firing rate is constant $\lambda(t) = \lambda$

6. What is the time course of x and I_{syn} ?

Solving the ODE with initial condition $x(t = 0) = x_0$ from question 4. yields

$$x(t) = \frac{1}{1 + \tau_{rec}U_{SE}\lambda} + \left(x_0 - \frac{1}{1 + \tau_{rec}U_{SE}\lambda} \right) e^{-\left(\frac{1}{\tau_{rec}} + U_{SE}\lambda\right)t},$$

Using the expression of I_{syn} given in question 5., we have

$$I_{syn}(t) = A_{SE}\lambda\tau_{in}U_{SE} \left(\frac{1}{1 + \tau_{rec}U_{SE}\lambda} + \left(x_0 - \frac{1}{1 + \tau_{rec}U_{SE}\lambda} \right) e^{-\left(\frac{1}{\tau_{rec}} + U_{SE}\lambda\right)t} \right).$$

7. What are the values x^* and I_{syn}^* at equilibrium? Contrast this to the case without STD.

Taking the limit $t \rightarrow \infty$, we find

$$x^* = \frac{1}{1 + \tau_{rec} U_{SE} \lambda} \text{ and } I_{syn}^* = \frac{A_{SE} \lambda \tau_{in} U_{SE}}{1 + \tau_{rec} U_{SE} \lambda}.$$

Without STD, $\tau_{rec} = 0$ such that $x^* = 1$ and $I_{syn}^* = A_{SE} \lambda \tau_{in} U_{SE}$.

8. **Bonus:** give the limits of x^* and I_{syn}^* for $\lambda \rightarrow 0$ and $\lambda \rightarrow \infty$.

- For $\lambda \rightarrow 0$: $x^* \rightarrow 1$ and $I_{syn}^* \rightarrow 0$.
- For $\lambda \rightarrow \infty$: $x^* \sim 1/(\tau_{rec} \lambda U_{SE})$ and $I_{syn}^* \rightarrow A_{SE} \tau_{in} / \tau_{rec}$.

The post-synaptic neuron then integrates this current according to

$$\tau_m \frac{dV(t)}{dt} = -V(t) + RI(t)$$

and emits a spike whenever the voltage reaches the threshold V_{th} .

9. **Bonus:** show that there is a critical threshold θ such that, whatever the input firing rate, the neuron eventually stops spiking.

The maximum voltage that can be reached at equilibrium is $RI_{syn}^* < RA_{SE} \tau_{in} / \tau_{rec}$, therefore for $V_{th} > \theta = RA_{SE} \tau_{in} / \tau_{rec}$, whatever the input firing rate, the neuron stops spiking.

2 Long term plasticity (LTP)

Spike-timing-dependent plasticity (STDP) is a class of long term modulation of synaptic efficacy, which depends on both pre-synaptic and post-synaptic mechanisms. In this sense, this is an associative process, which reinforces or weakens synaptic strengths between neurons based on their relative spike timings. This biological mechanism can be considered as an implementation of the Hebbian learning rule for adjusting the strength of connections between neurons. This computational rule has been proposed as a proxy for causality.

We consider a synapse connecting two neurons. The pre-synaptic neuron emits a train of n_{pre} pre-synaptic spikes $(t_{pre,1}, t_{pre,2}, \dots, t_{pre,n_{pre}})$, while the post-synaptic neuron emits a train of n_{post} post-synaptic spikes $(t_{post,1}, t_{post,2}, \dots, t_{post,n_{post}})$.

The synaptic weight w is modified according to the following rule: each pair of nearest-neighbour spikes $(t_{pre,i}, t_{post,j})$ induces a modification $\Delta w = f(t_{post,j} - t_{pre,i})$, with

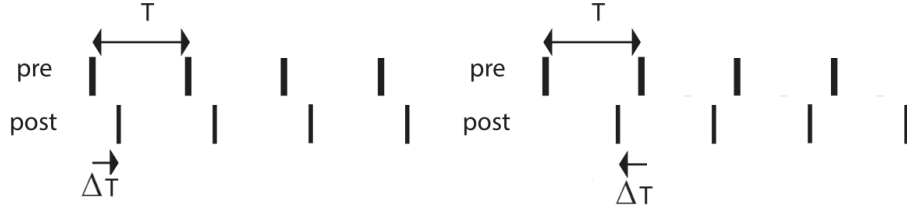
$$f(s) = \begin{cases} A^+ e^{-s/\tau^+} & \text{if } s \geq 0, \\ -A^- e^{s/\tau^-} & \text{if } s < 0, \end{cases} \quad (3)$$

where A^+, A^-, τ^+ and τ^- are positive real parameters. Pairs of spikes are considered nearest-neighbour if and only if there is no other (pre-synaptic or post-synaptic) spike in the interval

between the two spikes $]t_{pre,i}, t_{post,j}[$ (or $]t_{post,j}, t_{pre,i}[$). The synaptic modification is the sum of all modifications induced by the individual nearest-neighbour pairs.

2.1 Regular pre-synaptic train

Both neurons fire n spikes periodically with a frequency $F = 1/T$ (where T is the inter-spike interval), with a fixed interval ΔT between the spikes, $\Delta T = t_{post,i} - t_{pre,i}$ for all $i = 1, \dots, n$.



10. Compute the total synaptic modification W induced by these spike trains for ΔT in $[-T/2, T/2]$.

We have two cases to consider: either $\Delta T > 0$, either $\Delta T < 0$. The modification for one pair of spikes is as follows.

For $\Delta T > 0$:

- First, each pre-synaptic spike is followed by a post-synaptic spike ΔT later

$$t_{post,j} - t_{pre,i} = \Delta T > 0 \Rightarrow \Delta w = A^+ e^{-\Delta T / \tau^+}.$$

- Then, the post-synaptic spike is followed by a pre-synaptic spike $T - \Delta T$ later

$$t_{post,j} - t_{pre,i} = -(t_{pre,i} - t_{post,j}) = -(T - \Delta T) < 0 \Rightarrow \Delta w = -A^- e^{-(T - \Delta T) / \tau^-}.$$

For $\Delta T < 0$, the reasoning is strictly equivalent to considering $\Delta T > 0$ by simply interchanging the terms ΔT and $T - \Delta T$ in the previous equalities such that:

- First, each pre-synaptic spike is followed by a post-synaptic spike $T - \Delta T$ later

$$t_{post,j} - t_{pre,i} = T - \Delta T > 0 \Rightarrow \Delta w = A^+ e^{-(T - \Delta T) / \tau^+}.$$

- Then, the post-synaptic spike is followed by a pre-synaptic spike ΔT later

$$t_{post,j} - t_{pre,i} = -(t_{pre,i} - t_{post,j}) = -\Delta T < 0 \Rightarrow \Delta w = -A^- e^{\Delta T / \tau^-}.$$

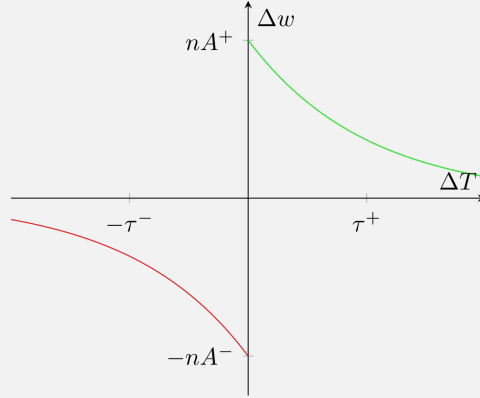
The total synaptic modification after n pre and post-synaptic spikes is as follows.

- For $\Delta T > 0$: $\Delta w = n(A^+ e^{-\Delta T / \tau^+} - A^- e^{-(T - \Delta T) / \tau^-})$.
- For $\Delta T < 0$: $\Delta w = n(A^+ e^{-(T - \Delta T) / \tau^+} - A^- e^{\Delta T / \tau^-})$.

11. Compute the synaptic modification W when the inter-spike interval T is much longer than the widths of the STDP windows τ^+ and τ^- , for both $\Delta T > 0$ and $\Delta T < 0$. Sketch how W depends on ΔT .

Under this assumption, $e^{-T/\tau^\pm} \approx 0$ such that the expressions are simplified.

- For $\Delta T > 0$: $\Delta w \approx nA^+e^{-\Delta T/\tau^+}$.
- For $\Delta T < 0$: $\Delta w \approx -nA^-e^{\Delta T/\tau^-}$.



12. Compute the synaptic modification when the inter-spike interval T is much shorter than the widths of the STDP windows. Sketch again the dependence of W on ΔT .

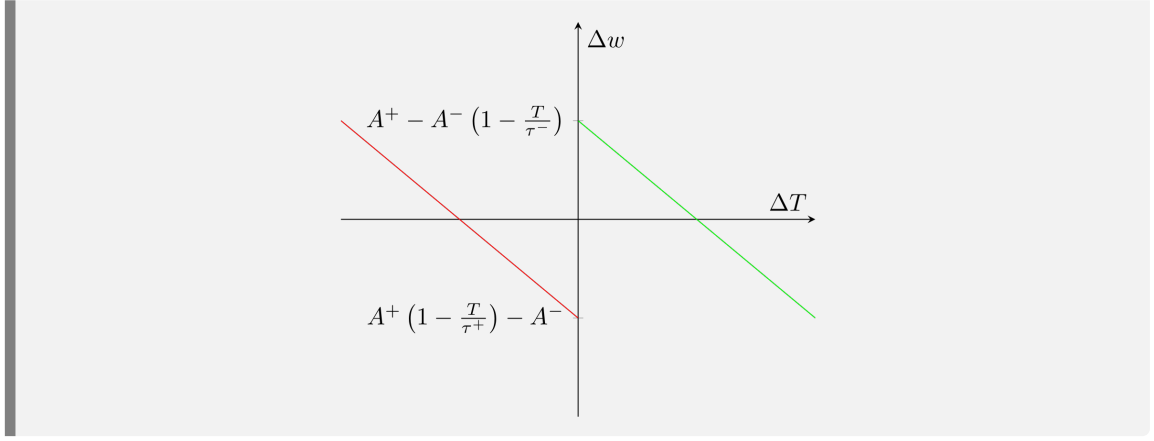
If $T \ll \tau^+, \tau^-$ then we also have that $\Delta T \ll \tau^+, \tau^-$. Under this assumption, the arguments of all the exponential terms tend to zero: we can therefore use the Taylor series expansion $e^x \approx 1 + x$.

- For $\Delta T > 0$:

$$\begin{aligned}\Delta w &\approx n \left(A^+ (1 - \Delta T / \tau^+) - A^- (1 + (-T + \Delta T) / \tau^-) \right) \\ &= n \left(A^+ - A^- \left(1 - \frac{T}{\tau^-} \right) - \Delta T \left(\frac{A^+}{\tau^+} + \frac{A^-}{\tau^-} \right) \right).\end{aligned}$$

- For $\Delta T < 0$:

$$\begin{aligned}\Delta w &\approx n \left(A^+ (1 - (T + \Delta T) / \tau^+) - A^- (1 + \Delta T / \tau^-) \right) \\ &= n \left(A^+ \left(1 - \frac{T}{\tau^+} \right) - A^- - \Delta T \left(\frac{A^+}{\tau^+} + \frac{A^-}{\tau^-} \right) \right).\end{aligned}$$



2.2 Stochastic pre-synaptic train

We now consider spikes produced randomly. For the sake of simplification, spikes still alternate between pre-synaptic and post-synaptic neurons, but the duration between successive spikes is stochastic. In total, $2n$ spikes are generated, n per neuron. Spikes are produced following a Poisson process of mean frequency $R = 1/T$ and assigned to each neuron in alternation.

13. Recalling that the probability density of inter-spike intervals is given by $p_{ISI}(t) = Re^{-Rt}$, what is the average total synaptic modification W at the end of the spike trains, as a function of n, R, A^+, A^-, τ^+ and τ^- ?

Reminder: let X be a continuous random variable. For any function $f : \mathbb{R} \rightarrow \mathbb{R}$,

$$\mathbb{E}(f(X)) \stackrel{\text{def}}{=} \int_{\mathbb{R}} f(x) p_X(x) dx,$$

where p_X is the probability density function of X .

The expected synaptic modification after n spikes $\mathbb{E}(W)$ is the expectancy of a sum of $2n$ modifications Δw_i , because the spike train is composed of $2n$ inter-spikes intervals. By linearity of the expectancy,

$$\mathbb{E}(W) = \mathbb{E} \left(\sum_{i=1}^{2n} \Delta w_i \right) = \sum_{i=1}^{2n} \mathbb{E}(\Delta w_i).$$

Because of the hypothesis of alternation between the spikes of each neuron, those Δw_i are divided in two categories which follow their own probability law : n positive modifications (for intervals in which the pre-synaptic spike precedes the post-synaptic spike) and n negative modifications (for intervals in which the post-synaptic spike precedes the pre-synaptic spike).

Thus, the expectancy is proportional to the a single pre-post and post-pre couple of synaptic modifications $\mathbb{E}(\Delta w^+)$ and $\mathbb{E}(\Delta w^-)$ such that

$$\mathbb{E}(W) = n\mathbb{E}(\Delta w^+) + n\mathbb{E}(\Delta w^-) = n (\mathbb{E}(\Delta w^+) + \mathbb{E}(\Delta w^-)).$$

The expectancy is carried out over the *ISI* distribution (since $\Delta w^\pm = f(ISI)$)

$$\begin{aligned}
\mathbb{E}(W) &= n \left(\int_0^\infty A^+ e^{-t/\tau^+} p(t) dt - \int_0^\infty A^- e^{-t/\tau^-} p(t) dt \right) \\
&= n \left(A^+ \int_0^\infty e^{-t/\tau^+} R e^{-Rt} dt - A^- \int_0^\infty e^{-t/\tau^-} R e^{-Rt} dt \right) \\
&= nR \left(A^+ \int_0^\infty e^{-t(R+1/\tau^+)} dt - A^- \int_0^\infty e^{-t(R+1/\tau^-)} dt \right) \\
&= nR \left(A^+ \left[-\frac{e^{-t(R+1/\tau^+)}}{R+1/\tau^+} \right]_0^\infty - A^- \left[-\frac{e^{-t(R+1/\tau^-)}}{R+1/\tau^-} \right]_0^\infty \right) \\
&= nR \left(A^+ \frac{1}{R+1/\tau^+} - A^- \frac{1}{R+1/\tau^-} \right) = n \left(A^+ \frac{R\tau^+}{1+R\tau^+} - A^- \frac{R\tau^-}{1+R\tau^-} \right).
\end{aligned}$$

14. What are the limits of W in the low ($R \rightarrow 0$) and high ($R \rightarrow \infty$) frequency limits?

- For $R \rightarrow 0$, $\mathbb{E}(W) \sim nR(A^+\tau^+ - A^-\tau^-)$.
- For $R \rightarrow \infty$, $\mathbb{E}(W) \rightarrow n(A^+ - A^-)$.

15. In the BCM learning rule, the synaptic modification is negative at low frequencies, and positive at high frequencies. Determine the conditions on the parameters for implementing this rule.

For W to be negative at low frequencies, we need

$$nR(A^+\tau^+ - A^-\tau^-) < 0 \Leftrightarrow A^+\tau^+ < A^-\tau^- \Leftrightarrow \frac{A^+}{A^-} < \frac{\tau^-}{\tau^+}.$$

For W to be positive at high frequencies, we need

$$n(A^+ - A^-) > 0 \Leftrightarrow A^+ > A^- \Leftrightarrow 1 < \frac{A^+}{A^-}.$$

For both conditions to hold, we therefore need

$$1 < \frac{A^+}{A^-} < \frac{\tau^-}{\tau^+}.$$

16. Determine the frequency R_0 at which the total synaptic modification changes sign.

The sign of the modification $\mathbb{E}(W)$ changes for R_0 such that

$$\begin{aligned}
\frac{A^+\tau^+}{1+R\tau^+} &= \frac{A^-\tau^-}{1+R\tau^-} \Rightarrow A^+\tau^+(1+R\tau^-) = A^-\tau^-(1+R\tau^+) \\
&\Rightarrow A^+\tau^+ - A^-\tau^- + R(A^+\tau^+\tau^- - A^-\tau^-\tau^+) = 0 \\
&\Rightarrow R_0 = \frac{A^-\tau^- - A^+\tau^+}{\tau^+\tau^-(A^+ - A^-)}.
\end{aligned}$$