

TD 4 – Synapses & Dendrites

1 Synaptic plasticity

1.1 Short term depression and facilitation (STD, STP)

1.1.1 Dynamics of the vesicular pool

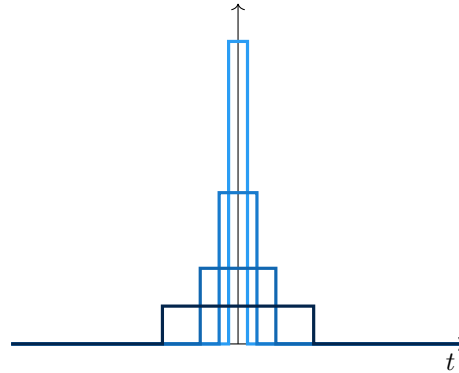
① Amount of vesicles mobilized during a spiking event

The amount of vesicles released by a spike is a fraction of the recovery pool $R(t)$, with a proportionality factor equal to the probability of release $p(t)$. The release event is assumed to be instantaneous, which can be indicated by a Dirac's delta function $\delta(t)$ at the time of the spike :

$$p(t)R(t)\delta(t)$$

More rigorously, the Dirac's delta function δ can be defined as the limit of a family of 'square' functions ϕ of unit integral whose base length tends to 0 :

$$\delta = \lim_{dt \rightarrow 0} \phi : t \mapsto \begin{cases} \frac{1}{dt} & \text{if } t \in \left[-\frac{dt}{2}, \frac{dt}{2}\right] \\ 0 & \text{otherwise} \end{cases}$$



② Kinetic equations

• Recovery pool

During an time interval dt , the amount of vesicles in the recovery pool varies by a quantity dR , which is the sum of two flows (contributions) proportional to dt :

- Additional vesicles *replenish* the recovery pool by recovering from the inactivated pool. It occurs proportionally to the amount of vesicles $I(t)$ in the inactivated pool and with a time constant τ_r .

It leads to positive flow : $+I(t) \times \frac{dt}{\tau_r}$

- Other vesicles can *leave* the recovery pool by becoming effective if a spike occurs during dt (as this time interval tends to 0, at most one spike is assumed to occur).

It leads to a negative flow : $-p(t)R(t)\delta(t) dt$.

By dividing by dt :

$$dR = I(t) \frac{dt}{\tau_r} - p(t)R(t)\delta(t) dt \implies \frac{dR}{dt} = \frac{I(t)}{\tau_r} - p(t)R(t)\delta(t)$$

• Effective pool

During an time interval dt , the amount of vesicles in the recovery pool varies by a quantity dE , which is the sum of two flows proportional to dt :

- Additional vesicles from the recovery pool *enter* the effective pool if a spike occurs during dt . It leads to a positive flow (which is the opposite of the negative flow of the recovery pool) : $+p(t)R(t)\delta(t) dt$.
- The effective pool *empties* when vesicles inactivate spontaneously. It occurs proportionally to the amount of vesicles $E(t)$ in the effective pool, with a time constant τ_i .

It leads to a negative flow : $-E(t) \times \frac{dt}{\tau_i}$.

By dividing by dt :

$$dE = -E(t) \frac{dt}{\tau_i} + p(t)R(t)\delta(t) dt \implies \frac{dE}{dt} = -\frac{E(t)}{\tau_i} + p(t)R(t)\delta(t)$$

- Inactivation pool

By the conservation of the total number of vesicles in the population, the sum of all flows should cancel. Therefore :

$$\frac{dI}{dt} = -\frac{I(t)}{\tau_r} + \frac{E(t)}{\tau_i}$$

To sum up :

$$\begin{cases} \frac{dR}{dt} = \frac{I(t)}{\tau_r} - p(t)R(t)\delta(t) \\ \frac{dE}{dt} = -\frac{E(t)}{\tau_i} + p(t)R(t)\delta(t) \\ \frac{dI}{dt} = -\frac{I(t)}{\tau_r} + \frac{E(t)}{\tau_i} \end{cases}$$

Moreover, the system can be written with only two variables, because the sum of all vesicles in the different pools is constant : $\forall t, R(t) + E(t) + I(t) = 1$. The variables of interest are the effective pool (as it imposes the signal transmitted in the synapse) and the recovery pool, so that the inactivation variable I can be eliminated : $I(t) = 1 - R(t) - E(t)$. Thus, the kinetic equations become :

$$\begin{cases} \frac{dR}{dt} = \frac{1 - R(t) - E(t)}{\tau_r} - p(t)R(t)\delta(t) \\ \frac{dE}{dt} = -\frac{E(t)}{\tau_i} + p(t)R(t)\delta(t) \\ \frac{dI}{dt} = -\frac{1 - R(t) - E(t)}{\tau_r} + \frac{E(t)}{\tau_i} \end{cases}$$

③ Evolution of the pool after a spike

The effect of a spike (delta function) can be modeled by instantaneously incrementing the amount of vesicles in the effective pool, while instantaneously decreasing that in the recovery pool by the same quantity, such that the system is brought to a state (R_0, E_0, I_0) (then, the terms with the delta function can be ignored from the dynamical equations as no more spike occurs).

It is sufficient to determine the evolution of the variables E and R :

$$\begin{aligned} \frac{dR}{dt} &= \frac{1 - R(t) - E(t)}{\tau_r} & R(0) &= R_0 \\ \frac{dE}{dt} &= -\frac{E(t)}{\tau_i} & E(0) &= E_0 \end{aligned}$$

- Solving for the variable E first is immediate :

$$E(t) = E_0 e^{-t/\tau_i}$$

- Solving for the variable R can be done by inserting the expression of $E(t)$:

$$\frac{dR}{dt} = -\frac{R(t)}{\tau_r} + \frac{1 - E(t)}{\tau_r} = -\frac{R(t)}{\tau_r} + \frac{1 - E_0 e^{-t/\tau_i}}{\tau_r}$$

The solution of this form of equation can be looked for under the form $R(t) = \lambda(t)e^{-t/\tau_r} \triangleright$ [TD1 : Method of the variation of constants]. In this case, the dynamical equation implies a simplification :

$$R'(t) \underbrace{=}_{\text{deriving}} \lambda'(t)e^{-t/\tau_r} - \underbrace{\lambda(t)}_{\text{equation}} \frac{1}{\tau_r} e^{-t/\tau_r} = -\frac{\lambda(t)e^{-t/\tau_r}}{\tau_r} + \frac{1 - E_0 e^{-t/\tau_i}}{\tau_r}$$

This enables to solve for the unknown function $\lambda(t)$:

$$\begin{aligned} \lambda'(t) &= \frac{1}{\tau_r} (1 - E_0 e^{-t/\tau_i}) e^{t/\tau_r} = \frac{1}{\tau_r} (e^{t/\tau_r} - E_0 e^{-t/\tau_r}) & \text{with the introduction of a new time constant } \tau = \frac{\tau_r \tau_i}{\tau_r - \tau_i} \\ \lambda(t) &= \frac{1}{\tau_r} \left(\int_0^t e^{s/\tau_r} ds - E_0 \int_0^t e^{-s/\tau_r} ds \right) + C & \text{with } C \text{ a constant of integration} \\ &= \frac{1}{\tau_r} (\tau_r (e^{t/\tau_r} - 1) - E_0 \tau (e^{-t/\tau} - 1)) + C \\ &= e^{t/\tau_r} - 1 - \underbrace{\frac{\tau}{\tau_r}}_{\frac{\tau_i}{\tau_r - \tau_i}} E_0 (e^{-t/\tau} - 1) + C \end{aligned}$$

The solution expresses with a sum of exponentials :

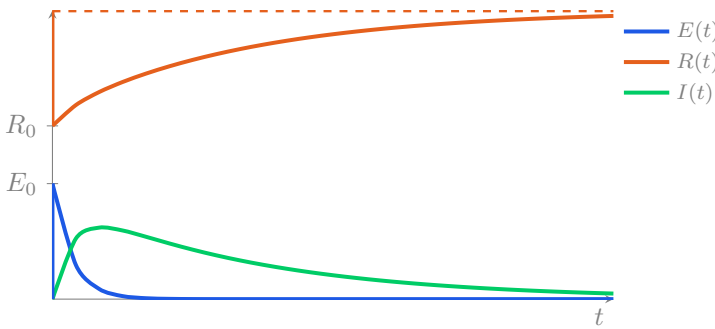
$$\begin{aligned}
 R(t) &= \lambda(t)e^{-t/\tau_r} \\
 &= \left(e^{t/\tau_r} - 1 - \frac{\tau_i}{\tau_r - \tau_i} E_0 (e^{-t/\tau} - 1) + C \right) e^{-t/\tau_r} \\
 &= 1 - (1 - C)e^{-t/\tau_r} - \frac{\tau_i}{\tau_r - \tau_i} E_0 \left(e^{-t(\frac{1}{\tau} + \frac{1}{\tau_r})} - e^{-t/\tau_r} \right) \quad \text{with } \frac{1}{\tau} + \frac{1}{\tau_r} = \frac{1}{\tau_i} \\
 &= 1 - e^{-t/\tau_r} \left(1 - C - \frac{\tau_i}{\tau_r - \tau_i} E_0 \right) - \frac{\tau_i}{\tau_r - \tau_i} \underbrace{E_0 e^{-t/\tau_i}}_{E(t)}
 \end{aligned}$$

The constant C is determined by the initial condition :

$$R(0) = R_0 = 1 - \left(1 - C - \frac{\tau_i}{\tau_r - \tau_i} E_0 \right) - \frac{\tau_i}{\tau_r - \tau_i} E_0 \implies C = R_0$$

Finally :

$$\begin{cases} E(t) = E_0 e^{-t/\tau_i} \\ R(t) = 1 - e^{-t/\tau_r} \left(1 - R_0 - \frac{\tau_i}{\tau_r - \tau_i} E_0 \right) - \frac{\tau_i}{\tau_r - \tau_i} E_0 e^{-t/\tau_i} \\ I(t) = 1 - E(t) - R(t) \end{cases}$$



④ Time constants

The time constants of recovery and inactivation are of different orders : $\tau_r \approx 1 \text{ sec} \gg \tau_i \approx 10^{-3} \text{ sec}$.

Therefore, the dynamics of the effective pool can be considered to be instantaneous and modeled as a Dirac function. The system can thus be fully described by the recovery variable alone. Under this approximation, the dynamics of this variable become :

$$\frac{dR}{dt} = \frac{1 - R(t)}{\tau_r} \implies R(t) = 1 - (1 - R_0)e^{-t/\tau_r}$$

1.1.2 Depressive synapse – Rate & Temporal coding

⑤ Recurrent relation

The currents produced by the n^{th} and $(n+1)^{th}$ spikes are proportional to the effective variable at the respective spiking times, which is itself proportional to the recovery variable by a factor U :

$$\begin{cases} I_{syn,n} = A_{SE} E(t_n) = A_{SE} U R(t_n) \\ I_{syn,n+1} = A_{SE} E(t_{n+1}) = A_{SE} U R(t_{n+1}) = A_{SE} U R(t_n + T) \end{cases}$$

The value of the recovery variable at the time of the second spike $R(t_n + T)$ can be determined from its value just after the first spike $R(t_n^+)$ (question ④) :

$$R(t_n + T) = 1 - (1 - R(t_n^+))e^{-T/\tau_r}$$

Moreover, the value of the recovery variable *after* the first spike $R(t_n^+)$ is decreased relative to its value *before* this spike $R(t_n^-)$ by an amount proportional to itself (fraction used) :

$$R(t_n^+) = R(t_n^-) - U R(t_n^-) = (1 - U) R(t_n^-)$$

The value $R(t_n^-)$ can be expressed using the current at this time : $I_{syn,n} = A_{SE} U R(t_n^-) \implies R(t_n^-) = \frac{I_{syn,n}}{A_{SE} U}$.

Gathering those expressions leads to express the recurrent relation involving the currents :

$$\begin{aligned}
 I_{syn,n+1} &= A_{SE}UR(t_n + T) \\
 &= A_{SE}U \left(1 - (1 - R(t_n^+))e^{-T/\tau_r} \right) \\
 &= A_{SE}U \left(1 - (1 - (1 - U)R(t_n^-))e^{-T/\tau_r} \right) \\
 &= A_{SE}U \left(1 - \left(1 - (1 - U) \frac{I_{syn,n}}{A_{SE}U} \right) e^{-T/\tau_r} \right) \\
 &= A_{SE}U - A_{SE}Ue^{-T/\tau_r} + (1 - U)I_{syn,n}e^{-T/\tau_r} \\
 I_{syn,n+1} &= A_{SE}U(1 - e^{-T/\tau_r}) + I_{syn,n}(1 - U)e^{-T/\tau_r}
 \end{aligned}$$

⑥ Post-synaptic current in the stationary regime

In the stationary regime, all successive spikes are identical : $I_{syn,n+1} = I_{syn,n} = I_\infty$. The post-synaptic current I_∞ in this regime is obtained by using this stationarity condition in the recurrent relation (question ⑤) :

$$I_\infty = A_{SE}U(1 - e^{-T/\tau_r}) + I_\infty(1 - U)e^{-T/\tau_r} \implies I_\infty(T) = \frac{A_{SE}U(1 - e^{-T/\tau_r})}{1 - (1 - U)e^{-T/\tau_r}}$$

⑦ Asymptotic behavior

When the firing rate r tends to ∞ , then the inter-spike interval $T = \frac{1}{r}$ tends to 0. Thus, the behavior of the stationary current can be approximated by a limited development in 0 for the variable T :

$$\begin{aligned}
 I_\infty(T) &= A_{SE}U(1 - e^{-T/\tau_r}) \left(1 - (1 - U)e^{-T/\tau_r} \right)^{-1} \\
 &\underset{T \rightarrow 0}{\sim} A_{SE}U \left(1 - \left(1 - \frac{T}{\tau_r} \right) \right) \left(1 - (1 - U) \left(1 - \frac{T}{\tau_r} \right) \right) \\
 &= \frac{A_{SE}U \frac{T}{\tau_r}}{\underbrace{(1 - U) \frac{T}{\tau_r} + U}_{\rightarrow 0}} \\
 &\underset{T \rightarrow 0}{\sim} \frac{A_{SE}T}{\tau_r} \\
 I_\infty(r) &\underset{r \rightarrow \infty}{\sim} \frac{A_{SE}}{\tau_r} \frac{1}{r}
 \end{aligned}$$

⑧ Limitation for rate coding

The $1/r$ law implies that the transmission of information is impaired when the pre-synaptic neuron fires at a high frequency. Indeed, in the high-frequency regime, variations in the pre-synaptic firing rate will not change much the current received by the post-synaptic neuron, such that the average postsynaptic depolarization will not vary. In other words, the post-synaptic neuron will not be sensitive to variations in the pre-synaptic firing rate.

⑨ Effect of the release probability on rate coding

The influence of the parameter U on the synaptic transfer function can be investigated either in absolute terms, by studying its effects on the function $I_\infty(r)$, or in relative terms, by studying its effects on the function $\frac{I_\infty(r)}{A_{SE}U}$ (as $A_{SE}U$ is the maximum possible value of the post-synaptic current). This can be done by computing the derivatives $\frac{dI_\infty}{dr}$ and $\frac{dI_\infty/A_{SE}U}{dU}$ for a fixed frequency (i.e. a fixed inter-spike interval T).

- In absolute terms :

$$I_{\infty}(U) = \frac{\overbrace{A_{SE}U(1 - e^{-T/\tau_r})}^{u(U)}}{\underbrace{1 - (1 - U)e^{-T/\tau_r}}_{v(U)}}$$

$$\frac{dI_{\infty}}{dU} = \frac{\overbrace{A_{SE}(1 - e^{-T/\tau_r})}^{u'(U)} \underbrace{\left(1 - (1 - U)e^{-T/\tau_r}\right)}_{v(U)} - \overbrace{A_{SE}U(1 - e^{-T/\tau_r})}^{u(U)} \underbrace{Ue^{-T/\tau_r}}_{v'(U)}}{(1 - (1 - U)e^{-T/\tau_r})^2}$$

The sign of the derivative is that of the numerator :

$$\begin{aligned} & A_{SE}(1 - e^{-T/\tau_r}) \left(1 - (1 - U)e^{-T/\tau_r}\right) - A_{SE}U(1 - e^{-T/\tau_r})Ue^{-T/\tau_r} \\ &= A_{SE}(1 - e^{-T/\tau_r}) \left(1 - (1 - U)e^{-T/\tau_r} - U^2e^{-T/\tau_r}\right) \\ &= A_{SE}(1 - e^{-T/\tau_r}) \left((1 - e^{-T/\tau_r}) + Ue^{-T/\tau_r} - U^2e^{-T/\tau_r}\right) \\ &= \underbrace{A_{SE}e^{-T/\tau_r}(1 - e^{-T/\tau_r})}_{\geq 0} \left((e^{T/\tau_r} - 1) + U - U^2\right) \end{aligned}$$

The sign is that of the second degree polynomial :

$$\Delta = 1 + 4(e^{T/\tau_r} - 1) \in [1, +\infty[, \text{ therefore it always admits roots } \lambda_{\pm} = \frac{1 \pm \sqrt{1 + 4(e^{T/\tau_r} - 1)}}{2}.$$

The highest root is always above 1, while the lowest root is always negative :

$$1 + 4 \underbrace{(e^{T/\tau_r} - 1)}_{\geq 0} \geq 1 \implies \begin{cases} 1 + \sqrt{1 + 4(e^{T/\tau_r} - 1)} \geq 1 \\ 1 - \sqrt{1 + 4(e^{T/\tau_r} - 1)} \leq 0 \end{cases}$$

The polynomial has a negative dominant term, therefore it has a positive sign between its roots. As the parameter U is comprised between 0 and 1, this means that the derivative $\frac{dI_{\infty}}{dU}$ has a constant positive sign over the range in which U varies.

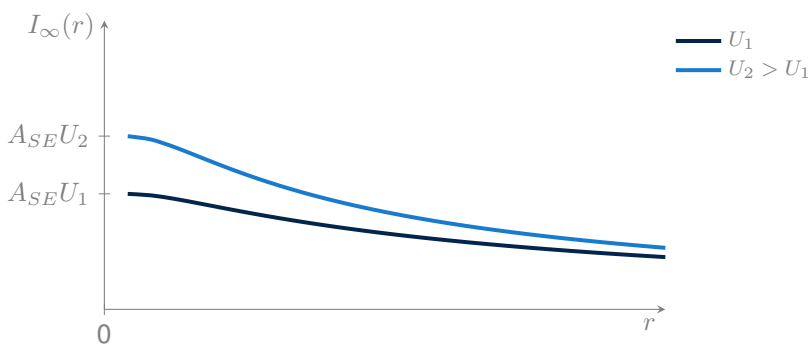
Conclusion : Rate coding is enhanced by increasing the release probability U . However, the limit of the derivative tends to 0 for high frequencies ($T \rightarrow 0$), which entails that the effect of the release probability is most relevant for coding low frequencies. In other words, it will not prevent the loss of information in high frequency coding.

- In relative terms :

$$\frac{I_{\infty}(U)}{A_{SE}U} = \frac{\overbrace{1 - e^{-T/\tau_r}}^{u(U)}}{\underbrace{1 - (1 - U)e^{-T/\tau_r}}_{v(U)}}$$

$$\frac{dI_{\infty}/A_{SE}U}{dU} = \frac{\underbrace{0}_{u'(U)} - \overbrace{(1 - e^{-T/\tau_r})}^{u(U)} \underbrace{Ue^{-T/\tau_r}}_{v'(U)}}{(1 - (1 - U)e^{-T/\tau_r})^2} \leq 0$$

Conclusion : This negative effect of the release probability on *relative* coding means that a synapse which is more prone to release (high value of U) is also *saturated sooner* for increasing frequencies.



⑩ Explicit expression of the post-synaptic current

The recurrence relation ⑤ is that of an arithmetico-geometric sequence. It can be written under the following form :

$$I_{syn,n+1} = \underbrace{A_{SE}U(1 - e^{-T/\tau_r})}_{\alpha} + I_{syn,n} \underbrace{(1 - U)e^{-T/\tau_r}}_{\beta}$$

The asymptotic value I_{∞} (question ⑥) also expresses as follows :

$$I_{\infty} = \alpha + I_{\infty}\beta \implies I_{\infty} = \frac{\alpha}{1 - \beta}$$

The difference between the current at a given step n relative to the asymptotic value follows a geometric sequence :

$$\underbrace{I_{syn,n+1} - I_{\infty}}_{u_{n+1}} = (\alpha - \beta I_{syn,n+1}) - (\alpha - \beta I_{\infty}) = \beta \underbrace{(I_{syn,n} - I_{\infty})}_{u_n}$$

The solution is given by $u_n = u_0\beta^n$, which corresponds to $I_{syn,n} - I_{\infty} = (A_{SE}U - I_{\infty})\beta^n$, because the initial spike elicits the maximum possible current $A_{SE}U$ (no depression).

Conclusion : $I_{syn,n} = I_{\infty} + (A_{SE}U - I_{\infty})\beta^n$ with $\beta = (1 - U)e^{-T/\tau_r}$

⑪ Effect of the release probability on temporal coding

The speed at which the sequence $I_{syn,n}$ converges towards its asymptotic value I_{∞} is determined by the parameter $\beta = (1 - U)e^{-T/\tau_r}$ (which is indeed < 1 for $U < 1$). Higher values of the release probability U lead to lower values of β and thus faster synaptic depression to the stationary current (for a fixed stimulation frequency). Thus, this parameter can be interpreted as setting the time window over which the summation of synchronized inputs is possible.

To conclude on questions ⑨ and ⑪, the release probability has opposite effects on rate and temporal coding. Therefore, it determines the contributions of rate and temporal signals to the postsynaptic response by modulating the relative amplitudes of its transient and stationary components.

1.1.3 Facilitative synapse – Three coding regimes

⑫ Dynamics of the release probability

• Differential equation :

The probability of release $p(t)$ decays to the baseline probability U with a time constant τ_p , and is incremented by an amount U by each spike. It can thus be modeled by a linear differential equation of the following type :

$$\frac{dp}{dt} = \frac{U - p}{\tau_p} + \delta(t)U$$

In absence of spiking event, this equation reduces to $\frac{dp}{dt} = \frac{U - p}{\tau_p}$. It indeed has an equilibrium is $p_{\infty} = U$ and exponential decay, which leads to the following solution \triangleright [TD1] :

$$p(t) = U + (p(0) - U)e^{-\frac{t}{\tau_p}}$$

• Evolution between two successive spikes :

When two spikes arrive in the pre-synaptic terminal separated by an interval T , the release probability at the moment of the second one corresponds to $p_{n+1} = p(T)$, while the initial release probability $p(0)$ can be expressed as a function of p_n . The probability of release reflects the fraction of calcium ions in the synapse that are mobilized for vesicular fusion. The first spike increases the pool of mobilized calcium ions p_n by an amount proportional to U and to the calcium stock which is not mobilized yet :

$$p(0) = p_n + U(1 - p_n) = (1 - U)p_n + U$$

Note : The formula could not be $p(0) = p_n + U$, since it does not ensure that the resulting probability remains in $[0, 1]$ whatever the value of p_n .

Replacing in the differential equation leads to the following dynamics :

$$p_{n+1} = U + \underbrace{((1 - U)p_n + U)}_{p(0)} e^{-\frac{T}{\tau_p}} = p_n e^{-T/\tau_p} + U(1 - p_n e^{-T/\tau_p})$$

⑬ Stationary values

The stationary value of the release probability is obtained by setting $p_\infty = p_n = p_{n+1}$:

$$p_\infty = p_\infty e^{-T/\tau_p} + U(1 - p_\infty e^{-T/\tau_p})$$

$$p_\infty(1 - (1 - U)e^{-T/\tau_p}) = U$$

$$p_\infty(T) = \frac{U}{1 - (1 - U)e^{-T/\tau_p}}$$

$$p_\infty(r) = \frac{U}{1 - (1 - U)e^{-1/r\tau_p}}$$

The stationary value of the current is obtained from equation ⑥, by replacing the constant U by the stationary probability p_∞ :

$$I_\infty(T) = \frac{A_{SE} p_\infty(1 - e^{-T/\tau_r})}{1 - (1 - p_\infty)e^{-T/\tau_r}}$$

$$I_\infty(r) = A_{SE} \frac{p_\infty(1 - e^{-1/r\tau_r})}{1 - (1 - p_\infty)e^{-1/r\tau_r}}$$

⑭ Limits

- Stationary probability :

$$p_\infty \xrightarrow{r \rightarrow 0, T \rightarrow +\infty} \frac{U}{1 - (1 - U) \times 0} = U$$

$$p_\infty \xrightarrow{r \rightarrow +\infty, T \rightarrow 0} \frac{U}{1 - (1 - U) \times 1} = 1$$

- Stationary current :

$$I_\infty \xrightarrow{r \rightarrow 0, T \rightarrow +\infty} \frac{A_{SE} \overbrace{p_\infty}^U (1 - 0)}{1 - (1 - \underbrace{p_\infty}_U) \times 0} = A_{SE}$$

$$I_\infty \xrightarrow{r \rightarrow +\infty, T \rightarrow 0} \frac{A_{SE} \overbrace{p_\infty}^1 (1 - 1)}{1 - (1 - \underbrace{p_\infty}_1) \times 1} = 0$$

- Limits of I_∞ for a fixed frequency when $p_\infty \rightarrow 0, p_\infty \rightarrow +1$:

$$I_\infty \xrightarrow{p_\infty \rightarrow 0} \frac{A_{SE} \times 0 \times (1 - e^{-T/\tau_r})}{1 - (1 - 0)e^{-T/\tau_r}} = 0$$

$$I_\infty \xrightarrow{p_\infty \rightarrow 1} \frac{A_{SE} \times 1 \times (1 - e^{-T/\tau_r})}{1 - (1 - 1)e^{-T/\tau_r}} = A_{SE}$$

⑮ Shape of the transfer function

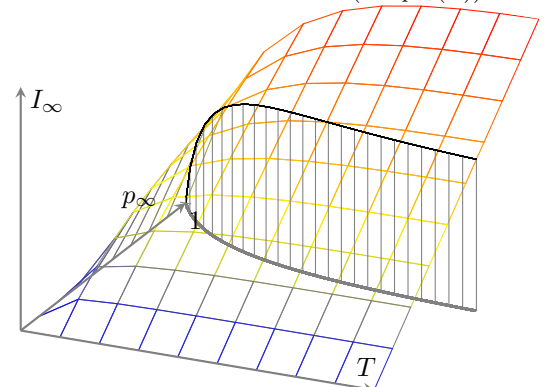
• In a graph of axes (T, p_∞, I_∞) , the surface $I_\infty(T, p_\infty)$ can be found qualitatively from the analysis of the limits (question ⑭). Then, it is possible to plot the curve the $p_\infty(T)$ in the plane (p_∞, I_∞) , and the parametric curve of the stationary synaptic current $I_\infty(T)$.

• The curve $I_\infty(T)$ appears to increase and then decrease while T grows, which suggests the existence of a maximum for a particular period T^* . Equivalently, this means that the transfer function of a facilitative synapse displays a maximum at an intermediate frequency $f^* = \frac{1}{T^*}$.

• The maximum could be found by the method of Lagrange Multipliers or by cancelling the differential of the function (which is an intricate expression of T).

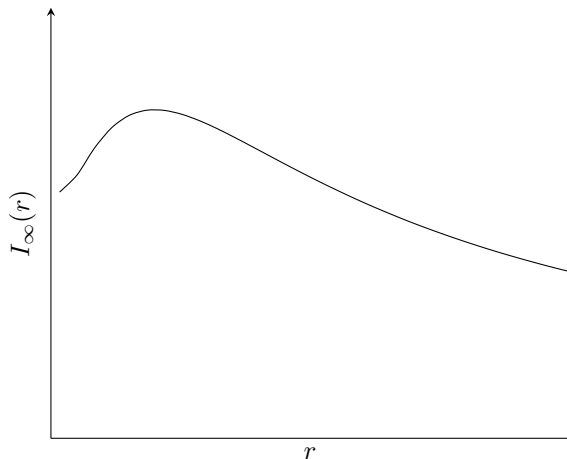
Gray curve : $p_\infty(T) = \frac{U}{1 - (1 - U)e^{-T/\tau_p}}$

Black curve : $I_\infty(T) = \frac{A_{SE} p_\infty(T)(1 - e^{-T/\tau_r})}{1 - (1 - p_\infty(T))e^{-T/\tau_r}}$



⑩ Consequences for rate coding

The existence of a maximum implies that the synapse behaves as a *band-pass filter*.



The shape of the current as a function of the frequency is obtained qualitatively by spanning the function $I_\infty(T)$ in the opposite direction (from high values of T to low values).

⑪ Influence of the baseline release probability on depression and facilitation

The analytical results above about the effects of the parameter U on the synaptic transfer function can be interpreted from a biological perspective. The baseline probability of release can reflect the amount of calcium in the pre-synaptic synapse which is produced by the arrival of a single spike. On the one hand, when this amount is large, the synapse might be expected to enhance temporal coding, because a single spike would elicit a wider vesicular release and a subsequent higher post-synaptic current. On the other hand, it might be expected to impair rate coding for high frequencies, because it would lead to faster vesicular depletion. To sum up, defines whether a synapse is most efficient in rate coding or temporal coding, and if it is more depressive (low values) or facilitative (high values).

Several biological examples :

- Climbing fibre synapses exhibit a high initial probability of release, they act as low-pass filters that are most effective at the onset of presynaptic activity.
- Parallel fibre synapses exhibit a low initial probability of neuro-transmitter release, they behave as high-pass filters that are more effective to sum spikes occurring in sequence.
- Schaffer collateral synapses exhibit an intermediate probability of release, they act as band-pass filters.

Learning might act by increasing or decreasing the probability of release to switch the balance between both regimes.

1.2 Spike-timing-dependent plasticity (STDP)

1.2.1 Regular pre-synaptic spikes train

⑫ Synaptic modification induced by a spike train

For $\Delta T > 0$, each pre-synaptic spike is followed by a post-synaptic spike ΔT later, leading to a modification $\Delta w = A^+ e^{-\Delta T/\tau^+}$. The post-synaptic spike is then followed by a pre-synaptic spike $T - \Delta T$ later, leading to a modification $\Delta w = -A^- e^{-(T-\Delta T)/\tau^-}$.

For $\Delta T < 0$, the same reasoning applies by inverting ΔT and $T - \Delta T$.

The total synaptic modification after n pre and postsynaptic spikes is therefore :

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

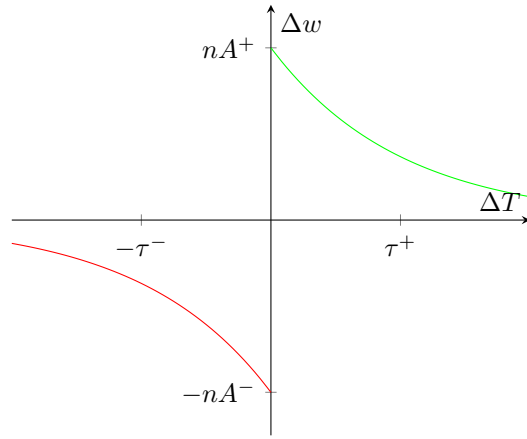
For $\Delta T < 0$, $\Delta w = n(A^+ e^{-(T+\Delta T)/\tau^+} - A^- e^{\Delta T/\tau^-})$.

(19) Synaptic modification with $T \gg \tau^+, \tau^-$

Under this assumption, $\exp(-T/\tau^\pm) \approx 0$, such that the expressions simplify :

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

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



(20) Synaptic modification with $T, \Delta T \ll \tau^+, \tau^-$

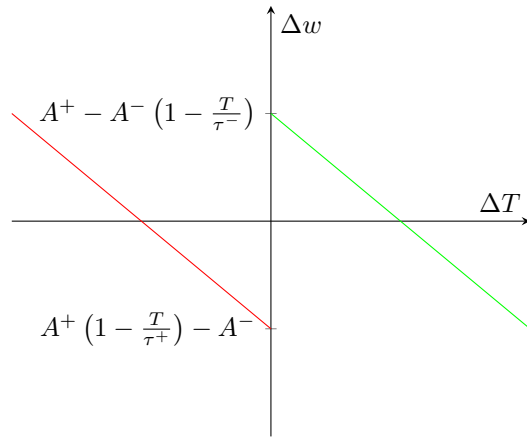
Under this assumption, $\exp(x) \approx 1 + x$, such that the expressions simplify :

For $\Delta T > 0$:

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

For $\Delta T < 0$:

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



1.2.2 Stochastic pre-synaptic spikes train

(21) Distribution of inter-spike intervals

The inter-spike interval is a continuous random variable, thus the probability that an inter-spike intervals lasts between t and $t + \delta t$ ($\delta t \rightarrow 0$) is proportional to the value of the density function $p_{ISI}(t)$:

$$\mathbb{P}(ISI \in [t, t + \delta t]) = p_{ISI}(t) \delta t$$

On the other hand, the probability that an inter-spike interval lasts between t and $t + \delta t$ is the product of the probability that no spike occurs during t and one spike occurs between t and $t + \delta t$ (by independence of the Poisson process on disjoint intervals) :

$$\mathbb{P}(ISI \in [t, t + \delta t]) = \mathbb{P}(0, t) \mathbb{P}(1, \delta t) = \frac{1}{0!} e^{-Rt} \frac{R\delta t}{1!} e^{-R\delta t} = e^{-Rt} R \delta t e^{-R\delta t}$$

Equating both expressions and taking $\delta t \rightarrow 0$ leads to the probability density of inter-spike intervals :

$$\begin{aligned}p_{ISI}(t) \cancel{\delta t} &= e^{-Rt} R \cancel{\delta t} \underbrace{e^{-R\delta t}}_{\rightarrow 1} \\ p_{ISI}(t) &= R e^{-Rt}\end{aligned}$$

(22) Average total synaptic modification

The average synaptic modification after n spikes is proportional to the a single pre-post and post-pre couple of

synaptic modifications. The average is carried out over the ISI distribution :

$$\begin{aligned}
 W &= \mathbb{E} \left(\sum_{i=1}^n \Delta w_i \right) = n \mathbb{E} (\Delta w) \\
 &= n \left(\int_0^\infty \underbrace{A^+ e^{-t/\tau^+}}_{f(t), \text{ pre - post}} p(t) dt - \int_0^\infty \underbrace{A^- e^{-t/\tau^-}}_{f(t), \text{ post - pre}} p(t) dt \right) \\
 &= n \left(A^+ \int e^{-t/\tau^+} \underbrace{R e^{-Rt}}_{p(t)} dt - A^- \int e^{-t/\tau^-} \underbrace{R e^{-Rt}}_{p(t)} dt \right) \\
 &= nR \left(A^+ \int e^{-t(R+1/\tau^+)} dt - A^- \int e^{-t(R+1/\tau^-)} dt \right) \\
 &= nR \left(\frac{A^+}{R+1/\tau^+} - \frac{A^-}{R+1/\tau^-} \right) = n \left(A^+ \frac{R\tau^+}{1+R\tau^+} - A^- \frac{R\tau^-}{1+R\tau^-} \right)
 \end{aligned}$$

②③ Equivalents in high and low frequency regimes

For $R \rightarrow 0$, $W \sim nR(A^+\tau^+ - A^-\tau^-)$.

For $R \rightarrow \infty$, $W \rightarrow n(A^+ - A^-)$.

②④ Conditions on parameters for matching the BCM learning rule

For W to be negative at low frequencies, parameters should be such that $A^+\tau^+ < A^-\tau^-$.

For W to be positive at high frequencies, parameters should be such that $A^+ > A^-$.

For both to hold, the following relation is required :

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

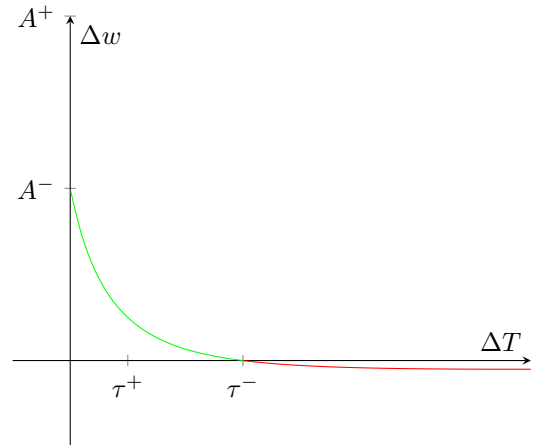
②⑤ Slope at 0 and shape of the function W

For comparing with the above results, the synaptic modification W can be plotted as a function of the average inter-spike interval $\Delta T = 1/R$, with $1 < \frac{A^+}{A^-} < \frac{\tau^-}{\tau^+}$.

$$W(\Delta T) = n \frac{1}{\Delta T} \left(\frac{A^+\tau^+}{1 + \frac{\tau^+}{\Delta T}} - \frac{A^-\tau^-}{1 + \frac{\tau^-}{\Delta T}} \right) = n \left(\frac{A^+\tau^+}{\Delta T + \tau^+} - \frac{A^-\tau^-}{\Delta T + \tau^-} \right)$$

For $\Delta T \rightarrow 0$, $R \rightarrow +\infty$, $W(\Delta T) \rightarrow n(A^+ - A^-)$.

For $\Delta T \rightarrow +\infty$, $R \rightarrow 0$, $W(\Delta T) \sim \frac{nR(A^+\tau^+ - A^-\tau^-)}{\Delta T}$.



②⑥ Frequency at which learning inverts

The sign of the modification W changes for R such that :

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

2 Receptors kinetics & Post-synaptic current

2.1 Comparing alpha functions and Markov kinetics

(27) Dynamical equations for the variables O and D

- During an time interval dt , the amount of receptors in the *open state* varies by a quantity dO , which is the sum of two flows (contributions) proportional to dt :
 - A positive flow from the pool of closed receptors, with a rate $r_1[L]$ (dependent on the neurotransmitter concentration $[L]$).
 - A negative flow from itself towards the closed state, with a rate r_2 .
 - A negative flow from itself towards the deactivated state, with a rate r_3 .

The sum of all contributions leads to :

$$dO = r_1[L]C dt - r_2O dt - r_3O dt \Rightarrow \frac{dO}{dt} = -(r_2 + r_3)O + r_1[L]C$$

- With the same reasoning, the amount of receptors in the *close state* varies by a quantity dC :

$$dC = -r_1[L]C dt + r_2O dt + r_4D dt \Rightarrow \frac{dC}{dt} = -r_1[L]C + r_2O + r_4D$$

- With the same reasoning, the amount of receptors in the *close state* varies by a quantity dD :

$$dD = r_3O dt - r_4D dt \Rightarrow \frac{dD}{dt} = r_3O - r_4D$$

- By the conservation of mass : $\forall t, O(t) + C(t) + D(t) = 1$. Therefore, the system can be reduced to a two-dimensional system, for instance keeping the variables O and D , while $C = 1 - O - D$. The equations re-express as follows :

$$\begin{aligned} \frac{dO}{dt} &= -(r_2 + r_3)O + r_1[L](1 - O - D) = -(r_2 + r_3 + r_1[L])O - r_1[L]D + r_1[L] \\ \frac{dD}{dt} &= r_3O - r_4D \end{aligned}$$

(28) Equilibrium

The equilibrium (O_∞, D_∞) is obtained by cancelling the derivatives :

$$\begin{aligned} \begin{cases} \frac{dO}{dt} = 0 \\ \frac{dD}{dt} = 0 \end{cases} &\Rightarrow \begin{cases} -(r_2 + r_3 + r_1[L])O - r_1[L]D + r_1[L] = 0 \\ r_3O - r_4D = 0 \end{cases} \\ \begin{cases} -(r_2 + r_3 + r_1[L])O - r_1[L]\frac{r_3}{r_4}O + r_1[L] = 0 \\ D = \frac{r_3}{r_4}O \end{cases} &\Rightarrow \begin{cases} O = \frac{r_1[L]}{r_2 + r_3 + r_1[L] + \frac{r_1[L]r_3}{r_4}} \\ D = \frac{r_3}{r_4}O \end{cases} \\ \begin{cases} O_\infty = \frac{r_1[L]r_4}{r_4(r_2 + r_3 + r_1[L]) + r_1[L]r_3} \\ D_\infty = \frac{r_1[L]r_3}{r_4(r_2 + r_3 + r_1[L]) + r_1[L]r_3} \end{cases} & \end{aligned}$$

(29) Solutions

The system is linear, it can be solved by the sum of a particular solution corresponding to the equilibrium (question (28)) and a homogeneous solution. The homogeneous system can be written with the vectorial formalism :

$$\begin{bmatrix} \frac{dO}{dt} \\ \frac{dD}{dt} \end{bmatrix} = \begin{bmatrix} -R & -r_1[L] \\ r_3 & -r_4 \end{bmatrix} \begin{bmatrix} O \\ D \end{bmatrix}, \text{ with } R = (r_2 + r_3 + r_1[L]).$$

The solutions are exponential functions whose time constants express with the eigenvectors and eigen-values of the matrix $\mathbf{M} = \begin{bmatrix} -R & -r_1[L] \\ r_3 & -r_4 \end{bmatrix}$.

Eigenvectors $\mathbf{X} \in \mathbb{C}^2$ associated to an eigenvalue $\lambda \in \mathbb{C}$ are non null vectors such that $\mathbf{M}\mathbf{X} = \lambda\mathbf{X} \Rightarrow (\mathbf{M} - \lambda\mathbf{I}_d)\mathbf{X} = \mathbf{0}$,

which exist for values of λ such that the discriminant of the matrix $\mathbf{M} - \lambda\mathbf{I}_d = \begin{bmatrix} -R - \lambda & -r_1[L] \\ r_3 & -r_4 - \lambda \end{bmatrix}$ cancels :

$$(-R - \lambda)(-r_4 - \lambda) + r_3r_1[L] = \lambda^2 + (R + r_4)\lambda + (r_4R + r_3r_1[L]) = 0.$$

The discriminant of this polynomial is :

$$\Delta = (R + r_4)^2 - 4(r_4R + r_3r_1[L]) = R^2 + r_4^2 + 2Rr_4 - 4r_4R - 4r_3r_1[L] = R^2 + r_4^2 - 2r_4R - 4r_3r_1[L] = (R - r_4)^2 - 4r_3r_1[L].$$

Assuming that the parameters for the rates guarantee that $\Delta > 0$, the eigen-values express as :

$\lambda_{1,2} = \frac{-(R+r_4) \pm \sqrt{\Delta}}{2}$, both negative because $\sqrt{\Delta} = \sqrt{(R-r_4)^2 - 4r_3r_1[L]} < \sqrt{(R-r_4)^2} = |R-r_4| < R+r_4$.
 The general solution of the homogeneous system is a sum of both eigen-vectors scaled by exponential functions whose time constants are $\frac{1}{\tau_{1,2}} = -\lambda_{1,2}$: $\begin{bmatrix} O(t) \\ D(t) \end{bmatrix} = c_1 e^{-t/\tau_1} \mathbf{X}_1 + c_2 e^{-t/\tau_2} \mathbf{X}_2$

Thus, the general solution of the initial system expresses with 4 constants :

$$\begin{aligned} O(t) &= O_\infty + \alpha_O e^{-t/\tau_1} + \beta_O e^{-t/\tau_2} \\ D(t) &= D_\infty + \alpha_D e^{-t/\tau_1} + \beta_D e^{-t/\tau_2} \end{aligned}$$

The constants α_O, β_O can be determined with the initial and equilibrium conditions :

Note : Two equations are needed for two unknowns, so the initial condition $O(0)$ is not sufficient. Additionally, it is possible to use the initial value of the derivative.

$$\begin{aligned} O(0) &= O_\infty + \alpha_O + \beta_O \\ O'(0) &= -(r_2 + r_3 + r_1[L])O_0 - r_1[L]D_0 + r_1[L] = -\frac{\alpha_O}{\tau_1} e^0 - \frac{\beta_O}{\tau_2} e^0 \quad (\text{after deriving the solution}) \\ O'(\infty) &= -(r_2 + r_3 + r_1[L])O_\infty - r_1[L]D_\infty + r_1[L] = 0 \quad (\text{by definition of the equilibrium}) \end{aligned}$$

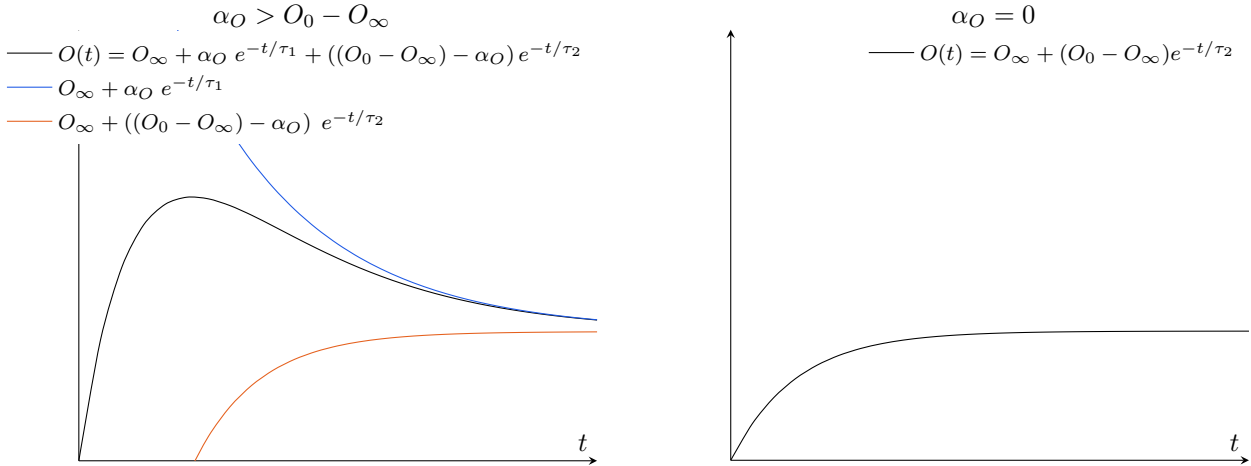
Solving for α_O, β_O can be done by keeping the first equation and subtracting the two last ones, which leads to :

$$\begin{cases} \alpha_O = -\frac{(O_0 - O_\infty)(a + \frac{1}{\tau_2}) + b(D_0 - D_\infty)}{\frac{1}{\tau_2} - \frac{1}{\tau_1}} \\ \beta_O = (O_0 - O_\infty) - \alpha_O \end{cases} \quad \text{with } a = -(r_1[L] + r_2 + r_3) \text{ and } b = r_4 - r_1[L].$$

The function $O(t)$ comes back to :

$$O(t) = O_\infty + \alpha_O e^{-t/\tau_1} + ((O_0 - O_\infty) - \alpha_O) e^{-t/\tau_2}$$

30 Examples of time courses



2.2 From kinetic models to phenomenological models

31 Laplace transform of an exponential function

$$\mathcal{L}[e^{\lambda t}](s) = \int_0^{+\infty} e^{-st} e^{\lambda t} dt = \int_0^{+\infty} e^{(\lambda-s)t} dt = \frac{1}{s-\lambda}$$

32 Laplace transform of the derivative

By integrating by parts from 0 to $T \in \mathbb{R}^+$:

$$\begin{aligned}\mathcal{L}[f'(t)](s) &= \int_0^T f'(t)e^{-st} dt \\ &= f(T)e^{-sT} - f(0^+)e^0 + s \int_0^T f(t)e^{-st} dt\end{aligned}$$

The term $f(T)e^{-sT}$ tends to 0 when $T \rightarrow \infty$, as soon as the function f grows slower than the exponential. Under this assumption :

$$\mathcal{L}[f'(t)](s) = s\mathcal{L}[f(t)](s) - f(0^+)$$

33 Kinetic equations

With the same reasoning as in question 27 :

$$\begin{aligned}\frac{dC}{dt} &= r_2C^* + r_4O - r_1[L]C \\ \frac{dC^*}{dt} &= (r_3 - r_2)C^* + r_1[L]C \\ \frac{dO}{dt} &= r_3C^* - r_4O\end{aligned}$$

Those equations simplify with the following hypotheses :

- The neurotransmitter concentration occurs as an instantaneous pulse : $r_1([L]) = \bar{r}_1\delta(t)$.
- The variable C can be considered constant : $C \approx 1$.

$$\begin{aligned}\frac{dC}{dt} &= r_2C^* + r_4O - \bar{r}_1\delta(t) \\ \frac{dC^*}{dt} &= -(r_3 + r_2)C^* + \bar{r}_1\delta(t) \\ \frac{dO}{dt} &= r_3C^* - r_4O\end{aligned}$$

34 Laplace transform applied on the differential equation

For the variable C^* :

$$\mathcal{L}[(C^*)'(t)](s) = \mathcal{L}[-(r_3 + r_2)C^* + \bar{r}_1\delta(t)](s)$$

- The left side can be rewritten using the property of the Laplace transform of a derivative (question 32) :
 $\mathcal{L}[(C^*)'(t)](s) = s\mathcal{L}[C^*(t)](s)$
- The right side simplifies by linearity (as the Laplace transform is an integral) :
 $\mathcal{L}[-(r_3 + r_2)C^* + \bar{r}_1\delta(t)](s) = -(r_3 + r_2)\mathcal{L}[C^*](s) + \bar{r}_1\mathcal{L}[\delta(t)](s)$
- The Laplace transform of a Dirac's delta-function is :

$$\mathcal{L}[\delta(t)](s) = \int_0^T e^{-st}\delta(s) dt = e^0 = 1$$

Gathering those simplifications leads to :

$$s\mathcal{L}[C^*(t)](s) = -(r_3 + r_2)\mathcal{L}[C^*(t)](s) + \bar{r}_1$$

35 Solution for the function $C^*(t)$

The Laplace transform of the function C^* is :

$$\mathcal{L}[C^*(t)](s) = \frac{\bar{r}_1}{s + (r_3 + r_2)}$$

It has the form of the Laplace transform of an exponential function (question 31), therefore :

$$C^*(t) = \bar{r}_1 e^{-(r_3 + r_2)t}$$

36 Solution for the function $O(t)$

The Laplace transform for the function $O(t)$ expresses as follows :

$$\begin{aligned}\mathcal{L}[O'(t)](s) &= \mathcal{L}[r_3 C^* - r_4 O](s) \\ &= r_3 \mathcal{L}[\bar{r}_1 e^{-(r_3+r_2)t}](s) - r_4 \mathcal{L}[O](s) \\ s\mathcal{L}[O(t)](s) &= r_3 \bar{r}_1 \frac{1}{s + (r_2 + r_3)} - r_4 \mathcal{L}[O](s) \\ \mathcal{L}[O(t)](s) &= \frac{r_3 \bar{r}_1}{(s + r_4)(s + (r_2 + r_3))}\end{aligned}$$

This quotient whose denominator is a product can be rewritten as a sum of two quotients with a simple denominator, using the partial fraction decomposition :

$$\begin{aligned}\frac{\alpha}{s + r_4} + \frac{\beta}{s + r_2 + r_3} &= \frac{\alpha(s + r_2 + r_3) + \beta(s + r_4)}{(s + r_4)(s + r_2 + r_3)} = \frac{\alpha(s + r_2 + r_3) + \beta(s + r_4)}{(s + r_4)(s + r_2 + r_3)} = \frac{s \overbrace{(\alpha + \beta)}^0 + \overbrace{(\alpha(r_2 + r_3) + \beta r_4)}^{r_3 \bar{r}_1}}{(s + r_4)(s + r_2 + r_3)} \\ \begin{cases} \alpha + \beta = 0 \\ \alpha(r_2 + r_3) + \beta r_4 = r_3 \bar{r}_1 \end{cases} &\implies \begin{cases} \beta = -\alpha \\ \alpha(r_2 + r_3 - r_4) = r_3 \bar{r}_1 \end{cases} \implies \begin{cases} \beta = -\frac{r_3 \bar{r}_1}{r_2 + r_3 - r_4} \\ \alpha = \frac{r_3 \bar{r}_1}{r_2 + r_3 - r_4} \end{cases} \\ \mathcal{L}[O(t)](s) &= \frac{r_3 \bar{r}_1}{r_2 + r_3 - r_4} \left(\frac{1}{s + r_4} - \frac{1}{s + r_2 + r_3} \right)\end{aligned}$$

The resulting expression of the Laplace transform has the form of a difference of Laplace transforms of exponential functions. By identification :

$$O(t) = \frac{r_3 \bar{r}_1}{r_2 + r_3 - r_4} (e^{-r_4 t} - e^{-(r_3+r_2)t})$$

③7 Analogy with the double-exponential model

The double exponential model has the following shape :

$$g_{syn}(t) = \frac{1}{\tau} (e^{-t/\tau_{slow}} - e^{-t/\tau_{fast}})$$

with $\tau_{slow} < \tau_{fast}$ By identification, transition rates should be such that :

$$\begin{aligned}\frac{1}{\tau} &= \frac{r_3 \bar{r}_1}{r_2 + r_3 - r_4} \\ \tau_{slow} &= r_4 \\ \tau_{fast} &= r_3 + r_2\end{aligned}$$

In terms of receptor kinetics, the time constants imply that $r_4 < r_3 + r_2$.

The double-exponential model can be reduced to the alpha-function model of the following form :

$$g_{syn}(t) = \frac{1}{\tau} t e^{-t/\tau_{slow}}$$

provided that $\tau_{slow} \sim \tau_{fast}$, i.e. $r_4 \sim r_3 + r_2$. The rate at which receptors close is similar to the rate at which bounded receptors either open or close (see the diagramm).

3 Dendritic processing – From synaptic input to soma integration

This part is not necessary for the exam. If you need corrections, please do not hesitate to send me an email.