TD 3 – Synapses & Dendrites

1   Short term depression and facilitation (STD, STP)
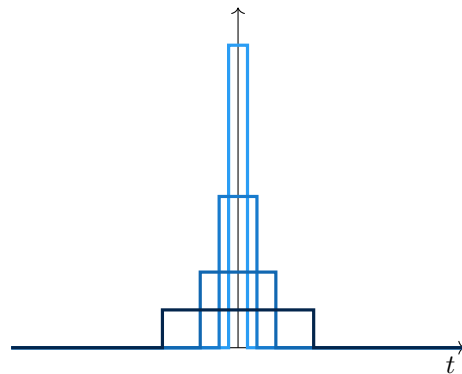
1.1   Dynamics of the vesicular pool

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 $\delta(t)$ which equals 1 only at the time of a 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 :

$\delta = \lim\limits_{\mathrm{d}t \to 0} \phi : t \mapsto \left\{ \begin{array}{ll} \frac{1}{\mathrm{d}t} & \text{if } t \in \left[-\frac{\mathrm{d}t}{2}, \frac{\mathrm{d}t}{2}\right] \\ 0 & \text{otherwise} \end{array} \right.$

② *Kinetic equations*

- Recovery pool

During an time interval $\mathrm{d}t$, the amount of vesicles in the recovery pool varies by a quantity $\mathrm{d}R$, which is the sum of two flows (contributions) proportional to $\mathrm{d}t$:

- 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 : $+I(t) \times \dfrac{\mathrm{d}t}{\tau_r}$

- lif a spike occurs during $\mathrm{d}t$, other vesicles *leave* the recovery pool by becoming effective.
  Note : At most one spike is assumed to occur during $\mathrm{d}t$, as this time interval tends to 0.
  It leads to a negative flow : $-p(t)R(t)\delta(t)\,\mathrm{d}t$.

By dividing by $\mathrm{d}t$:

$$\mathrm{d}R = I(t)\frac{\mathrm{d}t}{\tau_r} - p(t)R(t)\delta(t)\,\mathrm{d}t \implies \frac{\mathrm{d}R}{\mathrm{d}t} = \frac{I(t)}{\tau_r} - p(t)R(t)\delta(t)$$

- Effective pool

During an time interval $\mathrm{d}t$, the amount of vesicles in the effective pool varies by a quantity $\mathrm{d}E$, which is the sum of two flows proportional to $\mathrm{d}t$:

- If a spike occurs during $\mathrm{d}t$, additional vesicles from the recovery pool *enter* the effective pool.
  It leads to a positive flow (which is the opposite of the negative flow of the recovery pool) : $+p(t)R(t)\delta(t)\,\mathrm{d}t$.

- 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 : $-E(t) \times \dfrac{\mathrm{d}t}{\tau_i}$.

By dividing by $\mathrm{d}t$:

$$\mathrm{d}E = -E(t)\frac{\mathrm{d}t}{\tau_i} + p(t)R(t)\delta(t)\,\mathrm{d}t \implies \frac{\mathrm{d}E}{\mathrm{d}t} = -\frac{E(t)}{\tau_i} + p(t)R(t)\delta(t)$$

- Inactivation pool

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

$$\frac{\mathrm{d}I}{\mathrm{d}t} = -\frac{I(t)}{\tau_r} + \frac{E(t)}{\tau_i}$$

To sum up :

$$\begin{cases} \dfrac{\mathrm{d}R}{\mathrm{d}t} = \dfrac{I(t)}{\tau_r} - p(t)R(t)\delta(t) \\ \dfrac{\mathrm{d}E}{\mathrm{d}t} = -\dfrac{E(t)}{\tau_i} + p(t)R(t)\delta(t) \\ \dfrac{\mathrm{d}I}{\mathrm{d}t} = -\dfrac{I(t)}{\tau_r} + \dfrac{E(t)}{\tau_i} \end{cases}$$

Rewriting with relevant variables

The variables of the resource pool are not independent, 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 (which determines the signal transmitted in the synapse) and the recovery pool, so that the inactivation variable I can be eliminated : $I(t) = 1 - R(t) - E(t)$.

⬛ Conclusion ⬛ The kinetic equations become :

$$\begin{cases} \dfrac{\mathrm{d}R}{\mathrm{d}t} = \dfrac{1 - R(t) - E(t)}{\tau_r} - p(t)R(t)\delta(t) \\ \dfrac{\mathrm{d}E}{\mathrm{d}t} = -\dfrac{E(t)}{\tau_i} + p(t)R(t)\delta(t) \\ \dfrac{\mathrm{d}I}{\mathrm{d}t} = -\dfrac{1 - R(t) - E(t)}{\tau_r} + \dfrac{E(t)}{\tau_i} \end{cases}$$

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, which constitute a *coupled system* :

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

- 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 $E(t)$:

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

This equation is a *first order linear differential equation with a time varying coefficient*. It can be solved through the methods of *decomposition* and *variation of constants* ▷[*TD1*].

▤ Homogeneous equation.

The homogeneous equation is $\dfrac{\mathrm{d}R_h}{\mathrm{d}t} = -\dfrac{R_h(t)}{\tau_r}$, whose solution is of the form $R_h(t) = \lambda e^{-t/\tau_r}$, with $\lambda \in \mathbb{R}$.

▤ Particular solution.

A particular solution can be looked for under the form $R_p(t) = \lambda(t)e^{-t/\tau_r}$, where $\lambda(t)$ becomes the unknown function. In this case, the dynamical equation implies a simplification :

$$R'(t) = \begin{cases} \lambda'(t)e^{-t/\tau_r} - \cancel{\lambda(t)\dfrac{1}{\tau_r}e^{-t/\tau_r}} \text{ (by deriving)} \\[2mm] \cancel{\dfrac{\lambda(t)e^{-t/\tau_r}}{\tau_r}} + \dfrac{1 - E_0 e^{-t/\tau_i}}{\tau_r} \text{ (by inserting in the equation)} \end{cases}$$

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

$$\begin{aligned} \lambda'(t) &= \frac{1}{\tau_r}(1 - E_0 e^{-t/\tau_i})e^{t/\tau_r} = \frac{1}{\tau_r}(e^{t/\tau_r} - E_0 e^{-t/\tau}) \quad \text{with the introduction of a new time constant } \tau = \frac{\tau_r \tau_i}{\tau_r - \tau_i} \\[2mm] \lambda(t) &= \frac{1}{\tau_r}\left(\int_0^t e^{s/\tau_r}\,\mathrm{d}s - E_0 \int_0^t e^{-s/\tau}\,\mathrm{d}s \right) + C \qquad \text{with } C \text{ a constant of integration} \\[2mm] &= \frac{1}{\tau_r}\left(\tau_r(e^{t/\tau_r} - 1) - E_0 \tau(e^{-t/\tau} - 1) \right) + C \\[2mm] &= e^{t/\tau_r} - 1 - \underbrace{\frac{\tau}{\tau_r}}_{\frac{\tau_i}{\tau_r - \tau_i}} E_0(e^{-t/\tau} - 1) + C \end{aligned}$$

Thus, the particular solution expresses as a sum of exponentials :

$$\begin{aligned} R_p(t) &= \lambda(t)e^{-t/\tau_r} \\[2mm] &= \left(e^{t/\tau_r} - 1 - \frac{\tau_i}{\tau_r - \tau_i} E_0(e^{-t/\tau} - 1) + C \right)e^{-t/\tau_r} \\[2mm] &= 1 - (1-C)e^{-t/\tau_r} - \frac{\tau_i}{\tau_r - \tau_i} E_0 \left(e^{-t\left(\frac{1}{\tau} + \frac{1}{\tau_r}\right)} - e^{-t/\tau_r} \right) \quad \text{with } \frac{1}{\tau} + \frac{1}{\tau_r} = \frac{1}{\tau_i} \\[2mm] &= 1 - e^{-t/\tau_r} \underbrace{\left(1 - C - \frac{\tau_i}{\tau_r - \tau_i} E_0 \right)}_{\text{new constant } C'} - \frac{\tau_i}{\tau_r - \tau_i} \underbrace{E_0 e^{-t/\tau_i}}_{E(t)} \end{aligned}$$

⊜ Final solution.

The final solution is the sum of the homogeneous and the particular solutions. The homogeneous solution only adds an exponential term $\lambda e^{-t/\tau_r}$.
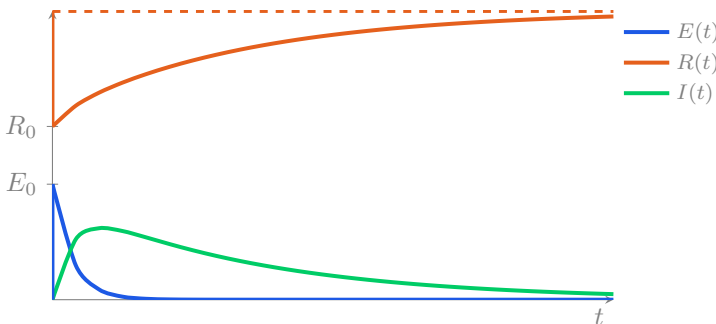
$$R(t) = R_h(t) + R_p(t)$$

The constant λ can be factorized with the constant C' in a new constant C''. The latter is determined by the initial condition :

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

Conclusion

$$\begin{cases} E(t) = E_0 e^{-t/\tau_i} \\[2mm] R(t) = 1 - e^{-t/\tau_r}\left(1 - R_0 - \dfrac{\tau_i}{\tau_r - \tau_i} E_0 \right) - \dfrac{\tau_i}{\tau_r - \tau_i} E_0 e^{-t/\tau_i} \\[2mm] I(t) = 1 - E(t) - R(t) \end{cases}$$

④ *Time constants*

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

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

1.2 Depressive synapse – Rate & Temporal coding

⑤ *Recurrent relation*

The currents produced by the nth 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 :

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

The value of the recovery variable at the time of the second spike $R(t_n + T)$ can be determined from the 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) :

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

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

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

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

1.2.1 Rate coding

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 :

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

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 $I_\infty(r)$.

- In relative terms (i.e. relative to the maximum possible value of the post-synaptic current), by studying its effects on the function $\frac{I_\infty(r)}{A_{SE}U}$.

Both cases require to compute the derivatives of the asymptotic current relative to the release probability U (comprised in [0,1]), for a fixed frequency r (i.e. a fixed inter-spike interval T).

- In absolute terms :

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

$$\frac{\mathrm{d}I_\infty}{\mathrm{d}U} = \frac{\overbrace{A_{SE}(1 - e^{-T/\tau_r})}^{u'(U)}\overbrace{\left(1 - (1-U)e^{-T/\tau_r}\right)}^{v(U)} - \overbrace{A_{SE}U(1 - e^{-T/\tau_r})}^{u(U)}\overbrace{Ue^{-T/\tau_r}}^{v'(U)}}{\left(1 - (1-U)e^{-T/\tau_r}\right)^2}$$

The sign of the derivative is that of the numerator :

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

The sign is that of the second degree polynom :

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

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 polynom 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 $\frac{\mathrm{d}I_\infty}{\mathrm{d}U}$ has a constant positive sign.

$\boxed{\text{Conclusion}}$ This positive effect on *absolute* coding means that an overall higher response (curernt) is elicited in the post-synaptic neuron. However, the limit of the derivative tends to 0 for high frequencies ($T \to 0$), 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 :

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

$$\frac{\mathrm{d}I_\infty/A_{SE}U}{\mathrm{d}U} = \frac{\overbrace{0}^{u'(U)} - \overbrace{(1 - e^{-T/\tau_r})}^{u(U)}\overbrace{Ue^{-T/\tau_r}}^{v'(U)}}{\left(1 - (1-U)e^{-T/\tau_r}\right)^2} \leq 0$$

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*, i.e. increasing frequencies decreases the response faster relative to the maximum responsen.
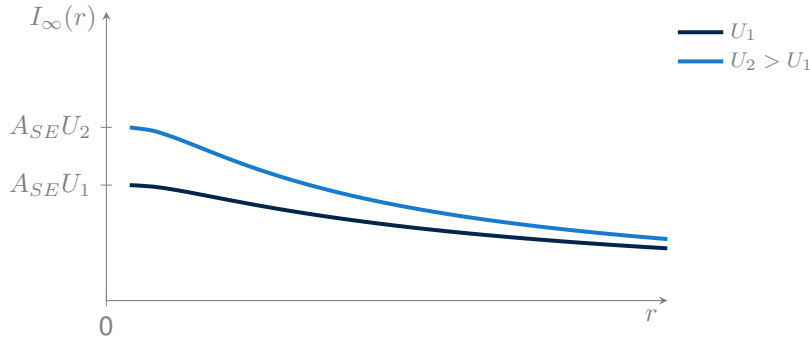
1.2.2 Temporal coding

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.

1.3 Facilitative synapse – Three coding regimes

⑫ *Dynamics of the release probability*

● Differential equation :

The probability of release reflects the fraction of calcium ions in the synapse that are mobilized for vesicular fusion. Similarly to the dynamics of vesicular pools, its evolution depends on two factors :
  • In absence of spiking stimulation, the probability of release $p(t)$ *decays* to the baseline probability U with a time constant τ_p. This leads to a contribution whose sign depends on the position of p relative to its baseline U : $(U - p)\dfrac{dt}{\tau_p}$.

- When a spike occurs, it extends the pool of mobilized calcium ions p by an amount proportional to U and to the calcium stock which is not mobilized yet. This leads to a positive contribution : $\delta(t)U(1-p)\,\mathrm{d}t$.

Thus, the dynamics of the release probability can thus be modeled by the following linear differential equation :

$$\frac{\mathrm{d}p}{\mathrm{d}t} = \frac{U-p}{\tau_p} + \delta(t)U(1-p)$$

- Evolution between two successive spikes :

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

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

When two spikes arrive in the pre-synaptic terminal separated by an interval T, the release probability at the moment of the second spike corresponds to $p_{n+1} = p(T)$, while the initial release probability $p(0)$ can be expressed as a function of p_n.

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

Replacing in the differential equation leads to the following dynamics :

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

⑬ *Stationary values*

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

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

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

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

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

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 :

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

$$p_\infty \xrightarrow[r\to+\infty\ T\to 0]{} \frac{U}{\cancel{1} - (\cancel{1} - U)\times 1} = 1$$

- Stationary current :

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

$$I_\infty \xrightarrow[r\to+\infty\ T\to 0]{} \frac{\cancel{A_{SE}}\ \overbrace{\cancel{p_\infty}}^{1}\cancel{(1 - 1)}}{1 - (1 - \underbrace{p_\infty}_{1})\times 1} = 0$$

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

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

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

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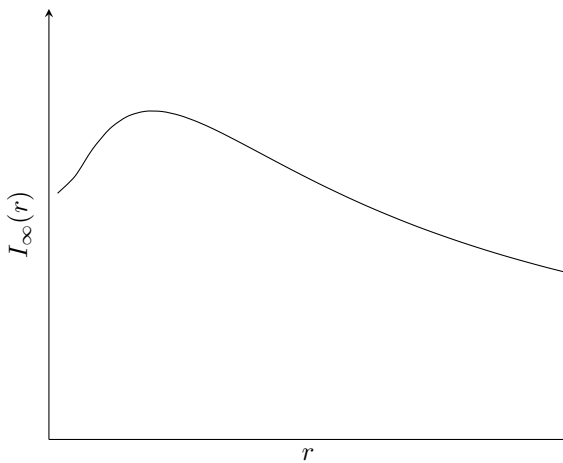
Gray curve : $p_\infty(T) = \dfrac{U}{1 - (1 - U)e^{-T/\tau_p}}$

Black curve : $I_\infty(T) = \dfrac{A_{SE}\, p_\infty(T)(1 - e^{-T/\tau_r})}{1 - (1 - p_\infty(T))e^{-T/\tau_r}}$
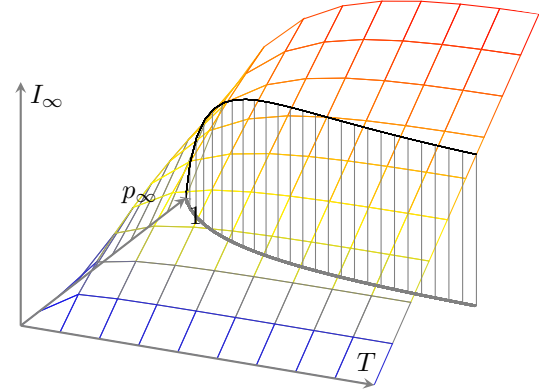
(16) *Consequences for rate coding*

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).

(17) *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, U defines whether a synapse is most efficient in rate coding or temporal coding, and if it is more depressive (low values) of facilitative (high values).

Several biological examples :
- Climbing fibre synapses a 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.

2   Spike-timing-dependent plasticity (STDP)

2.1   Regular pre-synaptic spikes train

⑱ *Synaptic modification induced by a spike train*

- Modification for one pair of spikes :

For $\Delta T > 0$:
- First, each pre-synaptic spike is followed by a post-synaptic spike ΔT later :
  $$t_{\text{post},j} - t_{\text{pre},i} = \Delta T > 0 \implies \Delta w = A^+ e^{-\Delta T/\tau^+}$$
- Then, the post-synaptic spike is followed by a pre-synaptic spike $T - \Delta T$ later :
  $$t_{\text{post},j} - t_{\text{pre},i} = -(t_{\text{pre},i} - t_{\text{post},j}) = -(T - \Delta T) < 0 \implies \Delta w = -A^- e^{(-T+\Delta T)/\tau^-}$$

For $\Delta T < 0$: the same reasoning applies by inverting ΔT and $T - \Delta T$.
- First, each pre-synaptic spike is followed by a post-synaptic spike $T - \Delta T$ later :
  $$t_{\text{post},j} - t_{\text{pre},i} = T - \Delta T > 0 \implies \Delta w = A^+ e^{-(T-\Delta T)/\tau^+}$$
- Then, the post-synaptic spike is followed by a pre-synaptic spike ΔT later :
  $$t_{\text{post},j} - t_{\text{pre},i} = -(t_{\text{pre},i} - t_{\text{post},j}) = -\Delta T < 0 \implies \Delta w = -A^- e^{\Delta T/\tau^-}$$

- Total synaptic modification after n pre and postsynaptic spikes :

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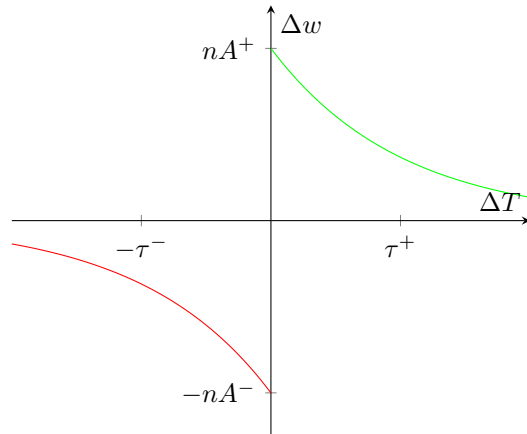
$\boxed{\text{For } \Delta T < 0}$ $\Delta w = n(A^+ e^{-(T-\Delta T)/\tau^+} - A^- e^{\Delta T/\tau^-})$.

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

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

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

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

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

If $T \ll \tau^+, \tau^-$ then also $\Delta T \ll \tau^+, \tau^-$.
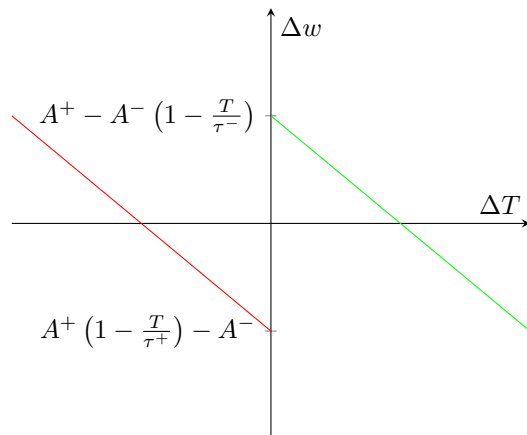
Under this assumption, the arguments of all the exponential terms tend to 0. The expression simplify with a limited development : $\exp(x) \approx 1 + x$.

$\boxed{\text{For } \Delta T > 0}$

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

$\boxed{\text{For } \Delta T < 0}$

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

2.2 Stochastic pre-synaptic 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 $t + \delta t$ ($\delta t \to 0$) 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 $\delta t \to 0$ leads to the probability density of inter-spike intervals :

$$p_{ISI}(t)\,\cancel{\delta t} = e^{-Rt}\ R\,\cancel{\delta t}\ \underbrace{e^{-R\delta t}}_{\to 1}$$

$$p_{ISI}(t) = Re^{-Rt}$$

(22) *Expected total synaptic modification*

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 $\mathbb{E}(\Delta w^-)$:

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

The expectancy is carried out over the ISI distribution :

$$
\begin{aligned}
\mathbb{E}(W) &= n\left(\int_0^\infty \underbrace{A^+ e^{-t/\tau^+}}_{f(t),\text{ pre - post}} p(t)dt - \int_0^\infty \underbrace{A^- e^{-t/\tau^-}}_{f(t),\text{ post - pre}} p(t)dt\right)\\[2mm]
&= n\left(A^+ \int e^{-t/\tau^+} \underbrace{Re^{-Rt}}_{p(t)}dt - A^- \int e^{-t/\tau^-} \underbrace{Re^{-Rt}}_{p(t)}dt\right)\\[2mm]
&= nR\left(A^+ \int e^{-t(R+1/\tau^+)}dt - A^- \int e^{-t(R+1/\tau^-)}dt\right)\\[2mm]
&= nR\left(A^+ \left[-\frac{e^{-t(R+1/\tau^+)}}{R+1/\tau^+}\right]_0^\infty - A^- \left[-\frac{e^{-t(R+1/\tau^-)}}{R+1/\tau^-}\right]_0^\infty\right)\\[2mm]
&= nR\left(A^+ \frac{1}{R+1/\tau^+} - A^- \frac{1}{R+1/\tau^-}\right)\\[2mm]
&= n\left(A^+ \frac{R\tau^+}{1+R\tau^+} - A^- \frac{R\tau^-}{1+R\tau^-}\right)
\end{aligned}
$$

(23) *Equivalents in high and low frequency regimes*

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

For $R \to \infty$, $\mathbb{E}(W) \to n(A^+ - A^-)$.

㉔ *Conditions on parameters for matching the BCM learning rule*

For W to be negative at low frequencies, parameters should be such that :

$$nR(A^+\tau^+ - A^-\tau^-) < 0 \quad \text{i.e.} \quad A^+\tau^+ < A^-\tau^- \quad \text{i.e.} \quad \frac{A^+}{A^-} < \frac{\tau^-}{\tau^+}$$

For W to be positive at high frequencies, parameters should be such that :

$$n(A^+ - A^-) > 0 \quad \text{i.e.} \quad A^+ > A^- \quad \text{i.e.} \quad 1 < \frac{A^+}{A^-}$$

$\boxed{\text{Conclusion}}$ Both conditions are summarized in the following relation :

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

㉕ *Frequency at which learning inverses*

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

$$\frac{A^+\tau^+}{1 + R\tau^+} = \frac{A^-\tau^-}{1 + R\tau^-} \quad \Rightarrow \quad A^+\tau^+(1 + R\tau^-) = A^-\tau^-(1 + R\tau^+)$$

$$\Rightarrow \quad A^+\tau^+ - A^-\tau^- + R(A^+\tau^+\tau^- - A^-\tau^-\tau^+) = 0$$

$$\Rightarrow \quad R_0 = \frac{A^-\tau^- - A^+\tau^+}{\tau^+\tau^-(A^+ - A^-)}$$

㉖ *Slope at 0 and shape of the function $\mathbb{E}(W)(\Delta T)$*

For comparing with the results of the previous part (regular pre-synaptic spiking), the synaptic modification $\mathbb{E}(W)$ can be plotted as a function of the average inter-spike interval $\Delta T = 1/R$, with $1 < \frac{A^+}{A^-} < \frac{\tau^-}{\tau^+}$.
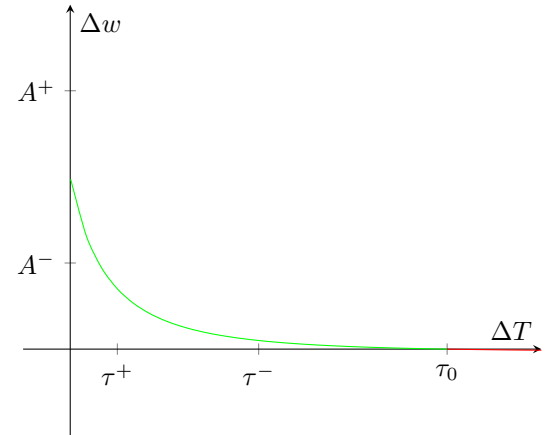
$$\mathbb{E}(W)(\Delta T) = n\left(\frac{A^+\tau^+}{\Delta T + \tau^+} - \frac{A^-\tau^-}{\Delta T + \tau^-}\right)$$

The equivalents ㉓ become :

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

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

The function cancels at $\tau_0 = \dfrac{1}{R_0} = \dfrac{\frac{1}{A^-} - \frac{1}{A^+}}{\frac{1}{A^+\tau^+} - \frac{1}{A^-\tau^-}}$

3   Receptors kinetics & Post-synaptic current

3.1   Comparing alpha functions and Markov kinetics

㉗ *Dynamical equations for the variables O and D*

- Open state

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

The sum of all contributions leads to :
$$dO = r_1[L]C\,dt - r_2 O\,dt - r_3 O\,dt \implies \frac{dO}{dt} = -(r_2 + r_3)O + r_1[L]C$$

- Close state (same reasoning)

$$dC = -r_1[L]C\,dt + r_2 O\,dt + r_4 D\,dt \implies \frac{dC}{dt} = -r_1[L]C + r_2 O + r_4 D$$

- Desensitized state (same reasoning)

$$dC = r_3 O\,dt - r_4 D\,dt \implies \frac{dD}{dt} = r_3 O - r_4 D$$

- 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 $C = 1 - O - D$.

$$\begin{cases} \dfrac{dO}{dt} &= -(r_2 + r_3)O + r_1[L](1 - O - D) = -\underbrace{(r_2 + r_3 + r_1[L])}_{R}O - r_1[L]D + r_1[L] \\ \dfrac{dD}{dt} &= r_3 O - r_4 D \end{cases}$$

> In the next questions, the following notation is used : $R = r_2 + r_3 + r_1[L]$.
>
> The system rewrites :
> $$\begin{cases} \dfrac{dO}{dt} &= -RO - r_1[L]D + r_1[L] \\ \dfrac{dD}{dt} &= r_3 O - r_4 D \end{cases}$$

💡 Solving multidimensional linear differential systems with constant coefficients

The goal is to solve a differential system of the form :

$$\begin{cases} \dfrac{dx}{dt} = ax + by + A \\ \dfrac{dy}{dt} = cx + dy + B \end{cases} \quad \text{with } a, b, c, d, A, B \in \mathbb{R}$$

i.e. to express the time-varying functions :

$$\begin{cases} x(t) = f(t) \\ y(t) = g(t) \end{cases}$$

Note : This method focuses on a 2D system for simplicity, but it extends directly to higher dimensional systems.

☰ Method of "Decomposition"

The idea is to decompose the problem in two steps :

- Finding the *equilibrium* of the system (x_∞, y_∞), which provides a *particular* (constant) solution.

- Solving the differential system for the change of variables which correspond to the *difference to the equilibrium* $(x - x_\infty, y - y_\infty)$, and which verifies a *homogeneous system* (i.e. without and additional terms A and B).

- Expressing the *final solution* as the sum of the *particular* solution and the *homogeneous* solution, and determining the remaining free constants with the initial conditions.

⚠ This method is valid under two conditions : the differential system is **linear** and the coefficients are **constant**.

Note : The method consists in generalizing the approach used for uni-dimensional linear differential systems of the form :

$$\frac{\mathrm{d}x}{\mathrm{d}t} = ax(t) + A \text{ with } a, A \in \mathbb{R}$$

① Equilibrium

The equilibrium of the system is found by cancelling the derivatives :

$$\begin{cases} \dfrac{\mathrm{d}x}{\mathrm{d}t} = 0 \\ \dfrac{\mathrm{d}y}{\mathrm{d}t} = 0 \end{cases} \implies \begin{cases} ax_\infty + by_\infty = -A \\ cx_\infty + dy_\infty = -B \end{cases}$$

This system of equations of unknown (x_∞, y_∞) can be solved by usual method, such as Gaussian Elimination.

Assuming that the coefficients are such that $d \neq 0$ and that a single solution exists :

- Express y_∞ as a function of x_∞ (with the second equation for instance) and substitute it in the other equation :

$$\begin{cases} ax_\infty + by_\infty = -A \\ y_\infty = \dfrac{-B - cx_\infty}{d} \end{cases} \implies \begin{cases} ax_\infty + b\dfrac{-B - cx_\infty}{d} = -A \\ y_\infty = \dfrac{-B - cx_\infty}{d} \end{cases}$$

- Solve for x_∞ :

$$\begin{cases} \left(a - \dfrac{bc}{d}\right)x_\infty = -A\dfrac{bB}{d} \\ y_\infty = \dfrac{-B - cx_\infty}{d} \end{cases} \implies \begin{cases} (ad - bc)\, x_\infty = -dA + bB \\ y_\infty = \dfrac{-B - cx_\infty}{d} \end{cases} \implies \begin{cases} x_\infty = \dfrac{-dA + bB}{ad - bc} \\ y_\infty = \dfrac{-B - cx_\infty}{d} \end{cases}$$

- Solve for y_∞ :

$$\begin{cases} x_\infty = \dfrac{-dA + bB}{ad - bc} \\ y_\infty = -\dfrac{1}{d}\left(B + c\dfrac{-dA + bB}{ad - bc}\right) \end{cases} \implies \begin{cases} x_\infty = \dfrac{-dA + bB}{ad - bc} \\ y_\infty = -\dfrac{1}{d}\dfrac{B(ad - bc) + c(-dA + bB)}{ad - bc} = -\dfrac{1}{d}\dfrac{B(ad - \cancel{bc} + \cancel{cb}) + -cdA)}{ad - bc} \end{cases} \implies$$

$$\begin{cases} x_\infty = \dfrac{-dA + bB}{ad - bc} \\ y_\infty = -\dfrac{1}{\cancel{d}}\dfrac{a\cancel{d}B + -c\cancel{d}A}{ad - bc} \end{cases} \implies \begin{cases} x_\infty = \dfrac{-dA + bB}{ad - bc} \\ y_\infty = \dfrac{cA - aB}{ad - bc} \end{cases}$$

② Homogeneous system

The system defined by the variables $\begin{cases} x_h(t) = x - x_\infty \\ y_h(t) = y - y_\infty \end{cases}$ verifies a *homogeneous* differential system. Indeed :

$$\begin{cases} \dfrac{\mathrm{d}x_h}{\mathrm{d}t} = \dfrac{\mathrm{d}(x - x_\infty)}{\mathrm{d}t} = \dfrac{\mathrm{d}x}{\mathrm{d}t} = ax + by + A \\ \dfrac{\mathrm{d}y_h}{\mathrm{d}t} = \dfrac{\mathrm{d}(y - y_\infty)}{\mathrm{d}t} = \dfrac{\mathrm{d}y}{\mathrm{d}t} = cx + dy + B \end{cases}$$

But this differential system has to be expressed in terms of the *new variables* (x_h, y_h), which requires to substitute $x \to x_h + x_\infty$ and $y \to y_h + y_\infty$. This makes appear the relation which defines the equilibrium, leading to a simplification :

$$\begin{cases} \dfrac{\mathrm{d}x_h}{\mathrm{d}t} = a(x_h + x_\infty) + b(y_h + y_\infty) + A = ax_h + by_h + \underbrace{ax_\infty + by_\infty + A}_{0} \\[2mm] \dfrac{\mathrm{d}y_h}{\mathrm{d}t} = c(x_h + x_\infty) + d(y_h + y_\infty) + B = cx_h + dy_h + \underbrace{cx_\infty + dy_\infty + B}_{0} \end{cases}$$

Thus the system for those new variables is indeed homogeneous :

$$\begin{cases} \dfrac{\mathrm{d}x_h}{\mathrm{d}t} = ax_h + by_h \\ \dfrac{\mathrm{d}y_h}{\mathrm{d}t} = cx_h + dy_h \end{cases}$$

⊜ Solving a homogeneous linear differential system

Often in analysis, the idea consists in finding an appropriate change of variables, so that the problem expressed in terms of the new variables is easier to solve. Once the problem is solved for the new variables, the solution for the initial variables is expressed straightforward, knowing the transformation.

In the case of homogeneous linear differential systems, the difficulty of the problem comes from the *coupling* between the variables in their differential equations (i.e. the evolution of x depends on both itself and y). The goal is to find a of variables such that the resulting system is *uncoupled* (i.e. the evolution of each new variable only depends on itself) :

$$\begin{cases} \dfrac{\mathrm{d}w}{\mathrm{d}t} = \lambda w \\ \dfrac{\mathrm{d}z}{\mathrm{d}t} = \beta z \end{cases}$$

Such a system can be solved directly, independently for each equation :

$$\begin{cases} w(t) = w_0 e^{\lambda t} \\ z(t) = z_0 e^{\beta t} z \end{cases}$$

The appropriate change of variables $(x_h, y_h) \to (w, z)$ can be looked for under a *linear transformation*, which involves finding coefficients $(k, l, m, n) \in \mathbb{R}^4$ such that :

$$\begin{cases} x_h = kw + lz \\ y_h = mw + nz \end{cases}$$

In that case, the solutions of the homogeneous system express directly as linear combinations of exponentials :

$$\begin{cases} x_h(t) = kw_0 e^{\lambda t} + lz_0 e^{\beta t} \\ y_h(t) = mw_0 e^{\lambda t} + nz_0 e^{\beta t} \end{cases} \iff \begin{cases} x_h(t) = Ke^{\lambda t} + Le^{\beta t} \\ y_h(t) = Me^{\lambda t} + Ne^{\beta t} \end{cases}$$

Now that the shape of the solution is determined, it remains to find the appropriate coefficients :
- The four constants (K, L, M, N) in front of the exponentials.
- The two scaling factors (λ, β) in arguments of the exponentials.

To do so, it is useful to switch to the formalism of *linear algebra*, which is adapted when several variables are involved and when their relationships are linear. In this formalism, the problem expresses :

$$\underbrace{\begin{bmatrix} \frac{\mathrm{d}x_h}{\mathrm{d}t} \\ \frac{\mathrm{d}y_h}{\mathrm{d}t} \end{bmatrix}}_{\mathrm{d}\tilde{\mathbf{X}}} = \underbrace{\begin{bmatrix} a & b \\ c & d \end{bmatrix}}_{\mathbf{A}} \underbrace{\begin{bmatrix} x_h \\ y_h \end{bmatrix}}_{\tilde{\mathbf{X}}} \iff \mathrm{d}\tilde{\mathbf{X}} = \mathbf{A}\tilde{\mathbf{X}}$$

$$\underbrace{\begin{bmatrix} \frac{\mathrm{d}w}{\mathrm{d}t} \\ \frac{\mathrm{d}z}{\mathrm{d}t} \end{bmatrix}}_{\mathrm{d}\tilde{\mathbf{Z}}} = \underbrace{\begin{bmatrix} \lambda & 0 \\ 0 & \beta \end{bmatrix}}_{\mathbf{D}} \underbrace{\begin{bmatrix} w \\ z \end{bmatrix}}_{\tilde{\mathbf{Z}}} \iff \mathrm{d}\tilde{\mathbf{Z}} = \mathbf{D}\tilde{\mathbf{Z}}$$

Moreover, any linear transformation can be represented by a matrix in a certain basis. Therefore, the goal is to find a transformation matrix $\mathbf{T}$ (here in the canonical basis) such that :

$$\begin{bmatrix} x_h \\ y_h \end{bmatrix} = \underbrace{\begin{bmatrix} k & l \\ m & n \end{bmatrix}}_{\mathbf{T}} \begin{bmatrix} w \\ z \end{bmatrix} \iff \tilde{\mathbf{X}} = \mathbf{T}\tilde{\mathbf{Z}}$$

To find this transformation matrix $\mathbf{T}$, it can be noticed that the matrix $\mathbf{D}$ for the target change of variable is *diagonal*. If the matrix $\mathbf{A}$ can be diagonalized, then there exist an invertible matrix $\mathbf{P}$ and a diagonal matrix $\mathbf{\Delta}$ such that :

$$\mathrm{d}\tilde{\mathbf{X}} = \underbrace{\mathbf{P}\mathbf{\Delta}\mathbf{P}^{-1}}_{\mathbf{A}} \tilde{\mathbf{X}}$$

This allows to identify the appropriate linear transformation, by applying the matrix $\mathbf{P}^{-1}$ on both sides :

$$\underbrace{\mathbf{P}^{-1}\mathrm{d}\tilde{\mathbf{X}}}_{\mathrm{d}(\mathbf{P}^{-1}\tilde{\mathbf{X}})} = \underbrace{\mathbf{P}^{-1}\mathbf{P}}_{\mathbf{I_2}}\,\mathbf{\Delta}\mathbf{P}^{-1}\tilde{\mathbf{X}} \iff \mathrm{d}\underbrace{\mathbf{P}^{-1}\tilde{\mathbf{X}}}_{\tilde{\mathbf{Z}}} = \underbrace{\mathbf{\Delta}}_{\mathbf{D}}\underbrace{\mathbf{P}^{-1}\tilde{\mathbf{X}}}_{\tilde{\mathbf{Z}}} \iff \mathrm{d}\tilde{\mathbf{Z}} = \mathbf{D}\tilde{\mathbf{Z}}$$

This shows that :
- The constants (k, l, m, n) are the coefficient of the transformation matrix between $\tilde{\mathbf{Z}}$ and $\tilde{\mathbf{X}}$, i.e. they are contained in $\mathbf{T} = \mathbf{P}^{-1}$. This matrix is the inverse of the matrix of the *eigen vectors* of the matrix $\mathbf{A}$.
- The constants (λ, β) are the *eigen values* of the matrix $\mathbf{A}$.

Note : Determination of the coefficients of (K, L, M, N).
It is not necessary to determine explicitly the eigen vectors for the problem considered here. Indeed, the coefficients (k, l, m, n) are encapsulated in other coefficients (K, L, M, N) (after multiplication with w_0 and z_0), which can be can be determined at the moment to express the general solution of the (full) differential system, with the initial conditions ($t = 0$) and/or the constraint on the equilibrium ($t \to \infty$).

▤ Diagonalization of a matrix

Definitions and interpretation of the eigen values and eigen vectors

The matrices $\mathbf{A}$ and $\mathbf{D}$ can be interpreted as two representations of the same linear transformation ϕ in different bases :
- For $\mathbf{A}$, in the canonical basis $\mathcal{B}_{can} = (\tilde{\mathbf{e_1}}, \tilde{\mathbf{e_2}}) = \left(\begin{bmatrix}1\\0\end{bmatrix}, \begin{bmatrix}0\\1\end{bmatrix}\right)$.
- For $\mathbf{D}$, in the basis of "eigen vectors" $\mathcal{B}_{eig} = (\tilde{\mathbf{V}_1}, \tilde{\mathbf{V}_2})$.

In other words, this means that :

$$\mathbf{A} = \mathrm{Mat}_{\mathcal{B}_{can}}(\phi) = \begin{matrix} \phi(\tilde{\mathbf{e_1}}) & \phi(\tilde{\mathbf{e_2}}) & \\ \begin{bmatrix}a\\b\end{bmatrix} & \begin{bmatrix}c\\d\end{bmatrix} & \begin{matrix}\tilde{\mathbf{e_1}}\\\tilde{\mathbf{e_2}}\end{matrix}\end{matrix} \quad \text{i.e.} \quad \begin{cases}\phi(\tilde{\mathbf{e_1}}) = a\tilde{\mathbf{e_1}} + b\tilde{\mathbf{e_1}}\\ \phi(\tilde{\mathbf{e_2}}) = c\tilde{\mathbf{e_1}} + d\tilde{\mathbf{e_2}}\end{cases}$$

$$\mathbf{D} = \mathrm{Mat}_{\mathcal{B}_{eig}}(\phi) = \begin{matrix} \phi(\tilde{\mathbf{V}_1}) & \phi(\tilde{\mathbf{V}_2}) & \\ \begin{bmatrix}\lambda\\0\end{bmatrix} & \begin{bmatrix}0\\\beta\end{bmatrix} & \begin{matrix}\tilde{\mathbf{V}_1}\\\tilde{\mathbf{V}_2}\end{matrix}\end{matrix} \quad \text{i.e.} \quad \begin{cases}\phi(\tilde{\mathbf{V}_1}) = \lambda\tilde{\mathbf{V}_1}\\ \phi(\tilde{\mathbf{V}_2}) = \beta\tilde{\mathbf{V}_2}\end{cases}$$

Thus, an **eigen vector** of the linear transformation ϕ (or equivalently, any matrix which represents it, such as $\mathbf{A}$) is defined as a (non-null) vector $\tilde{\mathbf{V}}$ on which the effect of the linear transformation is a mere *scaling* :

$$\exists \lambda \in \mathbb{R} \ \mathbf{A}\tilde{\mathbf{V}} = \lambda\tilde{\mathbf{V}}$$

The **eigen value** associated to that eigen vector is the scaling factor λ.

Note : As soon as one eigen vector is defined, all the multiples of this vector also are eigen vectors :
$\forall \alpha \in \mathbb{R}, \ \mathbf{A}(\alpha\tilde{\mathbf{V}}) = \alpha\mathbf{A}\tilde{\mathbf{V}} = \alpha(\lambda\tilde{\mathbf{V}}) = \lambda(\alpha\tilde{\mathbf{V}})$.

The matrices $\mathbf{P}$ and $\mathbf{P}^{-1}$ can be interpreted in terms of **change-of-basis matrices** (also called transition matrices). Indeed, the formula $\mathbf{A} = \mathbf{P}\mathbf{\Delta}\mathbf{P}^{-1}$ correspond to two ways to perform the same transformation ϕ on a given vector $\tilde{\mathbf{X}}$. It means that is equivalent to :
- either apply directly $\mathbf{A}$ on $\tilde{\mathbf{X}}$,
- or express the coordinates of $\tilde{\mathbf{X}}$ in the basis of eigen vectors (through the application of the matrix $\mathbf{P}^{-1}$), then apply the linear transformation ϕ in this basis (through the application of the matrix $\mathbf{D}$), and finally express the coordinates of the resulting vector back in the canonical basis (through the application of the matrix $\mathbf{P}$).

. Therefore :
- The matrix $\mathbf{P}$ is the transition matrix from the canonical basis to the basis of eigen vectors : each column contains the coefficients of one eigen vectors expressed in the canonical basis.
- The matrix $\mathbf{P}^{-1}$, is the inverse transformation, i.e. the transition matrix from the basis of eigen vectors to the canonical basis : each column contains the coefficients of the canonical vectors expressed in the basis of eigen vectors.

Diagonalization process

Usually, it is easier to first determine the eigen values, and then (optionally) the eigen vectors.

To do so requires to come back to the definition of an eigen vector and its associated eigen value :

$$\mathbf{A}\tilde{\mathbf{V}} = \lambda\tilde{\mathbf{V}} \iff \mathbf{A}\tilde{\mathbf{V}} - \lambda\tilde{\mathbf{V}} = \tilde{\mathbf{0}} \iff (\mathbf{A} - \lambda\mathbf{I_2})\tilde{\mathbf{V}} = \tilde{\mathbf{0}} \iff \begin{bmatrix} a - \lambda & b \\ c & d - \lambda \end{bmatrix}\tilde{\mathbf{V}} = \tilde{\mathbf{0}}$$

For this system to have an infinity of solutions (and because $\tilde{\mathbf{V}} \neq \tilde{\mathbf{0}}$), it should be the case that the matrix $(\mathbf{A} - \lambda\mathbf{I_2})$ is *not invertible*. This is the case if the two columns (or rows) are *linearly dependent*, i.e. :

$$\exists \alpha \in \mathbb{R} \ \begin{bmatrix} a - \lambda \\ c \end{bmatrix} = \alpha \begin{bmatrix} b \\ d - \lambda \end{bmatrix} \implies \begin{cases} a - \lambda = \alpha b \\ c = \alpha(d - \lambda) \end{cases} \implies \begin{cases} \alpha = \dfrac{a - \lambda}{b} \\ \alpha = \dfrac{c}{(d - \lambda)} \end{cases} \qquad \begin{array}{l} \text{(assuming } b \neq 0 \text{ and } \lambda \neq d \\ \text{otherwise the final relation still holds)} \end{array}$$

$$\implies \frac{a - \lambda}{b} = \frac{c}{(d - \lambda)} \implies (a - \lambda)(d - \lambda) - bc = 0 \implies \lambda^2 - (a + d)\lambda + (ad - bc) = 0$$

To conclude, the two eigen values λ and β are the roots of the polynomial $P[X] = X^2 - (a + d)X + (ad - bc)$.

③ Final solution of the system

Once the equilirbium (x_∞, y_∞) and the factors α, β have been determined, the final solution expresses as the sum of the equilibrium and the homogeneous solution :

$$\begin{cases} x(t) = x_\infty + Ke^{\lambda t} + Le^{\beta t} \\ y(t) = y_\infty + Me^{\lambda t} + Ne^{\beta t} \end{cases}$$

The remaining parameters (K, L, M, N) are set by four constraints, for instance :

- Initial conditions :
$$\begin{cases} x(0) = x_0 = x_\infty + K \times 1 + L \times 1 \\ y(0) = y_0 = y_\infty + M \times 1 + N \times 1 \end{cases} \implies \begin{cases} x_0 = x_\infty + K + L \\ y_0 = y_\infty + M + N \end{cases}$$

- Hypotheses about the derivatives :
$$\begin{cases} x'(t) = K\lambda e^{\lambda t} + L\beta e^{\beta t} \\ y'(t) = M\lambda e^{\lambda t} + N\beta e^{\beta t} \end{cases}$$

SUMMARY

To solve a linear differential system :

① Find the equilibrium (x_∞, y_∞).

② Find the eigen values of the matrix $\begin{bmatrix} a & b \\ c & d \end{bmatrix}$ by diagonalizing it.

③ Express the final solution as $\begin{cases} x(t) = x_\infty + Ke^{\lambda t} + Le^{\beta t} \\ y(t) = y_\infty + Me^{\lambda t} + Ne^{\beta t} \end{cases}$
and determine the remaining parameters (K, L, M, N).

㉘ *Equilibrium*

The equilibrium (O_∞, D_∞) is obtained by cancelling the derivatives : $\begin{cases} \dfrac{\mathrm{d}O}{\mathrm{d}t} = 0 \\ \dfrac{\mathrm{d}D}{\mathrm{d}t} = 0 \end{cases}$

This system with two unknowns can be solved by replacing the variable D by its expression as a function of O :

$$\begin{cases} -RO - r_1[L]D + r_1[L] = 0 \\ r_3O - r_4D = 0 \end{cases}$$

$$\begin{cases} -RO - r_1[L]\dfrac{r_3}{r_4}O + r_1[L] = 0 \\ D = \dfrac{r_3}{r_4}O \end{cases} \implies \begin{cases} O = \dfrac{r_1[L]}{R + \dfrac{r_1[L]r_3}{r_4}} \\ D = \dfrac{r_3}{r_4}O \end{cases} \implies \begin{cases} O_\infty = \dfrac{r_1[L]r_4}{r_4R + r_1[L]r_3} \\ D_\infty = \dfrac{r_1[L]r_3}{r_4R + r_1[L]r_3} \end{cases}$$

㉙ *Solutions of the differential system*

The system is linear with constant coefficients, therefore 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 :

$$\begin{bmatrix} \frac{dO}{dt} \\ \frac{dD}{dt} \end{bmatrix} = \begin{bmatrix} -R & -r_1[L] \\ r_3 & -r_4 \end{bmatrix} \begin{bmatrix} O \\ D \end{bmatrix}.$$

The solutions are exponential functions whose time constants express with the eigen vectors 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 $\mathbf{MX} = \lambda \mathbf{X} \implies (\mathbf{M} - \lambda \mathbf{I}_d)\mathbf{X} = \mathbf{0}$, 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 :

$$(-R - \lambda)(-r_4 - \lambda) + r_3 r_1[L] = \lambda^2 + (R + r_4)\lambda + (r_4 R + r_3 r_1[L]) = 0.$$

The discriminant of this polynomial is :

$$\Delta = (R + r_4)^2 - 4(r_4 R + r_3 r_1[L]) = R^2 + r_4^2 + 2R r_4 - 4r_4 R - 4r_3 r_1[L] = R^2 + r_4^2 - 2r_4 R - 4r_3 r_1[L] = (R - r_4)^2 - 4r_3 r_1[L].$$

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

$\lambda_{1,2} = \dfrac{-(R + r_4) \pm \sqrt{\Delta}}{2}$, both negative because $\sqrt{\Delta} = \sqrt{(R - r_4)^2 - 4r_3 r_1[L]} < \sqrt{(R - r_4)^2} = |R - r_4| < R + r_4$.

The general solution of the homogeneous system is a sum of both eigen-vectors scaled by exponential functions whose time constants are $\dfrac{1}{\tau_{1,2}} = -\lambda_{1,2}$.

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

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

The constants α_O, β_0 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.

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

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

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

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

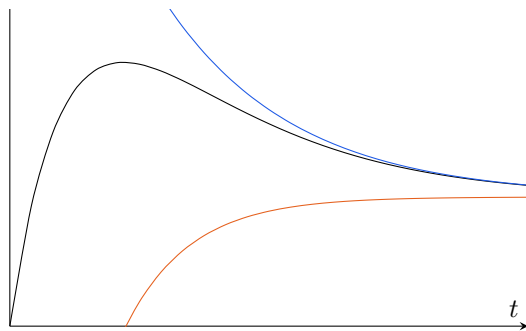$$O(t) = O_\infty + \alpha_O\, e^{-t/\tau_1} + ((O_0 - O_\infty) - \alpha_O)\, e^{-t/\tau_2}$$

(30) *Examples of time courses*

$$\alpha_O > O_0 - O_\infty$$

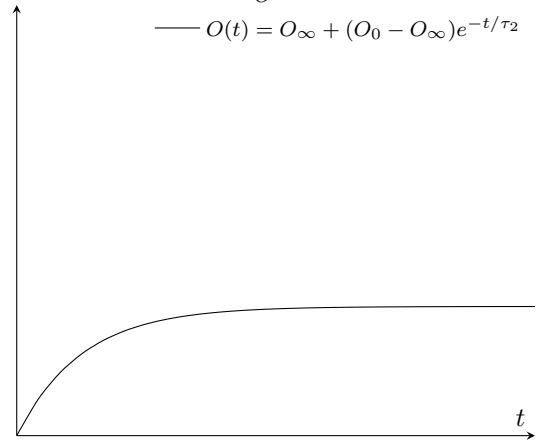—— $O(t) = O_\infty + \alpha_O\, e^{-t/\tau_1} + ((O_0 - O_\infty) - \alpha_O)\, e^{-t/\tau_2}$

—— $O_\infty + \alpha_O\, e^{-t/\tau_1}$

—— $O_\infty + ((O_0 - O_\infty) - \alpha_O)\, e^{-t/\tau_2}$

$$\alpha_O = 0$$

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

3.2　From kinetic models to phenomenological models

3.2.1　Generalities about the Laplace Transform

(31) *Linearity* The Laplace transform is a linear operator because it is an integral, and integration is linear over the space of integrable functions.

(32) *Laplace transform of an exponential function*

$$\mathcal{L}[e^{\lambda t}](s) = \int_0^{+\infty} e^{-st} e^{\lambda t}\,\mathrm{d}t = \int_0^{+\infty} e^{(\lambda - s)t}\,\mathrm{d}t = \left[\frac{e^{(\lambda - s)t}}{\lambda - s}\right]_0^{\infty} = \frac{1}{s - \lambda}$$

(33) *Laplace transform of a Dirac's delta-function*

$$\mathcal{L}\left[\delta(t)\right](s) = \int_0^T e^{-st}\delta(s)\,\mathrm{d}t = e^0 = 1$$

(34) *Laplace transform of the derivative*

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

$$\mathcal{L}[f'(t)](s) = \int_0^T f'(t)e^{-st}\,\mathrm{d}t$$

$$= f(T)e^{-sT} - f(0^+)e^0 + s\int_0^T f(t)e^{-st}\,\mathrm{d}t$$

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

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

3.2.2　Application to the model

(35) *Kinetic equations*

With the same reasoning as in question **(27)** :

$$\frac{\mathrm{d}C}{\mathrm{d}t} = r_2 C^* + r_4 O - r_1[L]C$$

$$\frac{\mathrm{d}C^*}{\mathrm{d}t} = (r_3 - r_2)C^* + r_1[L]C$$

$$\frac{\mathrm{d}O}{\mathrm{d}t} = r_3 C^* - r_4 O$$

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 : $C \approx 1$.

$$\frac{\mathrm{d}C}{\mathrm{d}t} = r_2 C^* + r_4 O - \bar{r}_1 \delta(t)$$

$$\frac{\mathrm{d}C^*}{\mathrm{d}t} = -(r_3 + r_2)C^* + \bar{r}_1 \delta(t)$$

$$\frac{\mathrm{d}O}{\mathrm{d}t} = r_3 C^* - r_4 O$$

(36) *Laplace transform applied on the differential equation*

For the variable C^* :

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

- The left side can be rewritten using the property of the Laplace transform of a derivative (question ㉞) :
  $$\mathcal{L}\left[(C^*)'(t)\right](s) = s\mathcal{L}\left[C^*(t)\right](s)$$
- The right side simplifies by linearity :
  $$\mathcal{L}\left[-(r_3 + r_2)C^* + \overline{r}_1\delta(t)C\right](s) = -(r_3 + r_2)\mathcal{L}\left[C^*\right](s) + \overline{r}_1\mathcal{L}\left[\delta(t)\right](s)$$
- The Laplace transform of a Dirac's delta-function is 1.

Gathering those simplifications leads to :

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

㊲ *Solution for the function $C^*(t)$*

The Laplace transform of the function C^* is :

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

It has the form of the Laplace transform of an exponential function (question ㉜), therefore :

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

㊳ *Solution for the function $O(t)$*

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

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

In order to identify the Laplace transform of $O(t)$, it is more convenient to rewrite the quotient in a sum of fractions whose denominators are linear in s (instead of a product). This can be done trough a partial fraction decomposition ▷[*Method TD2*] :

$$\frac{\alpha}{s + r_4} + \frac{\beta}{s + r_2 + r_3} = \frac{\alpha(s + r_2 + r_3) + \beta(s + r_4)}{(s + r_4)(s + r_2 + r_3)} = \frac{\alpha(s + r_2 + r_3) + \beta(s + r_4)}{(s + r_4)(s + r_2 + r_3)} = \frac{s\overbrace{(\alpha + \beta)}^{0} + \overbrace{(\alpha(r_2 + r_3) + \beta r_4)}^{r_3\overline{r}_1}}{(s + r_4)(s + r_2 + r_3)}$$

$$\begin{cases}\alpha + \beta = 0 \\ \alpha(r_2 + r_3) + \beta r_4 = r_3\overline{r}_1\end{cases} \implies \begin{cases}\beta = -\alpha \\ \alpha(r_2 + r_3 - r_4) = r_3\overline{r}_1\end{cases} \implies \begin{cases}\beta = -\dfrac{r_3\overline{r}_1}{r_2 + r_3 - r_4} \\ \alpha = \dfrac{r_3\overline{r}_1}{r_2 + r_3 - r_4}\end{cases}$$

$$\mathcal{L}\left[O(t)\right](s) = \frac{r_3\overline{r}_1}{r_2 + r_3 - r_4}\left(\frac{1}{s + r_4} - \frac{1}{s + r_2 + r_3}\right)$$

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

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

㊴ *Analogy with the double-exponential model*

The double exponential model has the following shape :

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

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

$$\frac{1}{\tau} = \frac{r_3\overline{r}_1}{r_2 + r_3 - r_4}$$
$$\tau_{slow} = r_4$$
$$\tau_{fast} = r_3 + r_2$$

In terms of receptor kinetics, the time constants imply that $r_4 < r_3 + r_2$. This means in that the speed of closure is inferior to that of opening (in particular).

The double-exponential model can be reduced to the alpha-function model provided that $\tau_{slow} \sim \tau_{fast}$, i.e. $r_4 \sim r_3 + r_2$. This means that the rate at which receptors close is similar to the rate at which bounded receptors either open or close (see the diagramm).

Indeed, in this case :

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

$$= \frac{1}{\tau} e^{-t/\tau_{slow}} \left(1 - e^{\underbrace{-t(1/\tau_{fast} - 1/\tau_{slow})}_{\approx 0}} \right)$$

$$\sim \frac{1}{\tau} e^{-t/\tau_{slow}} \left(\cancel{1} - \left(\cancel{1} - t \left(\frac{1}{\tau_{fast}} - \frac{1}{\tau_{slow}} \right) \right) \right)$$

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

4   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.