TD 1 – Models of Neurons I

1 Mathematical tools for Differential Equations

1.1 Analytical solutions of linear first order differential equations

Methods

At least two methods can be employed to find solutions of simple differential equations.

Method of the "Separation of variables"

This method can be applied when the equation can be written under the form :

$$\frac{\mathrm{d}y}{\mathrm{d}t} = h(t)g(y)$$

with h and g two continuous functions.

Note : It is assumed here that both h and $\frac{1}{g}$ are integrable on an interval $[0, T]$ and g does not cancel. Otherwise, singular solutions and different intervals have to be distinguished.

In this case, it is possible to gather the variables y on one side on the equality and the variables t on the other side, which provides an equation between two differentials :

$$\frac{1}{g(y)}\,\mathrm{d}y = h(t)\,\mathrm{d}t$$

Then, it is possible to integrate both sides from the initial point to the end point on the time interval :

$$\forall t \in [0, T],\ \int_{y_0}^{y(t)} \frac{1}{g(y)}\,\mathrm{d}y = \int_0^t h(t)\,\mathrm{d}t$$
$$G(y(t)) - G(y_0) = H(t) - H(0)$$

with G a primitive of $\frac{1}{g}$ and H a primitive of h

The final solution can be expressed by the reciprocal :

$$\forall t \in [0, T],\ y(t) = G^{-1}(H(t) - H(0) + G(y_0))$$

Method of "Decomposition"

This method can be applied for **linear** differential equations, i.e. of the form :

$$\frac{\mathrm{d}y}{\mathrm{d}t} = a(t)y(t) + b(t)$$

with a and b two continuous functions.

The idea is to decompose the problem in two steps :

- Finding one *particular* solution y_p which verifies the differential equation.
- Solving the differential equation for the function $y_h = y - y_p$, which is a *homogeneous equation* (i.e. without and additional term $b(t)$). Indeed :
$\frac{y_h}{\mathrm{d}t} = \frac{y}{\mathrm{d}t} - \frac{y_p}{\mathrm{d}t} = (a(t)y(t) + b(t)) - (a(t)y_p(t) + b(t)) = a(t)(y(t) - y_p(t)) = a(t)y_h(t)$

Note : In some cases, the particular solution is evident and can be determined directly (especially when a and b are constant functions). However, in other cases, it may be easier to start by determining the homogeneous solution, and then to use another technique for the particular solution (see below).

① Solution of the homogeneous equation

The solution y_h of the homogeneous equation verifies :

$$\frac{\mathrm{d}y_h}{\mathrm{d}t} = a(t)y_h(t)$$

It can be solved by the methods of the separation of the variables :

$$\begin{aligned} \int_{y_h(0)}^{y_h(t)} \frac{\mathrm{d}y_h}{y_h} &= \int_0^t a(t)\,\mathrm{d}t \\ \ln(|y_h|) &= A(t) + C & \text{with } C \in \mathbb{R} \text{ and } A \text{ a primitive of } a \\ y_h(t) &= \lambda e^{A(t)} & \text{with } \lambda \in \mathbb{R} \end{aligned}$$

Note : For the integration, it is assumed that the solution y_h has a constant sign and does not cancel, which is indeed verified once the exponential solution is found. The constants of integration are expressed through C and λ because they can be determined at the end of the process, when the general solution is expressed, to match the initial condition.

② Particular solution : Method of the "variation of the constant"

The idea is to look for a particular solution under the form $y_p(t) = \lambda(t)e^{A(t)}$ (which is possible without loss of generality), because the exponential has properties of differenciation adapted to linear differential equations (see below).

Now, the unknown becomes the differentiable function $t \mapsto \lambda(t)$. The latter can be identified by differentiating this formula on the one hand (product rule), and reinjecting inside the differential equation on the other hand :

$$\begin{cases} \dfrac{\mathrm{d}y_p}{\mathrm{d}t} = \cancel{\lambda(t)a(t)e^{A(t)}} + \dfrac{\mathrm{d}\lambda}{\mathrm{d}t}e^{A(t)} \\ \dfrac{\mathrm{d}y_p}{\mathrm{d}t} = \cancel{a(t)\left(\lambda(t)e^{A(t)}\right)} + b(t) \end{cases} \implies \frac{\mathrm{d}\lambda}{\mathrm{d}t}e^{A(t)} = b(t) \implies \lambda(t) = \int_0^t b(s)e^{-A(t)}\,\mathrm{d}s$$

Therefore, the particular solution is expressed as :

$$y_p(t) = e^{A(t)} \int_0^t b(s)e^{-A(s)}\,\mathrm{d}s$$

③ General solution

The general solution y is the sum of the particular and the homogeneous solutions. The remaining free constant λ can now be set depending on the initial condition, which gives :

$$y(t) = y_p(t) + y_h(t) = e^{A(t)}\left(y_0 + \int_0^t b(s)e^{-A(s)}\,\mathrm{d}s\right)$$

① *Independent term only* : $\dfrac{\mathrm{d}y}{\mathrm{d}t} = \dfrac{1}{\tau}c(t)$.

Method 1 : Directly exhibiting a solution.

The solution $y(t)$ should be a function whose derivative at any time point is the function $\frac{1}{\tau}c(t)$. Any *primitive* of this function verifies this property, and all those primitives differ only by a constant.
In particular, the primitive which cancels at the initial time $t = 0$ can be obtained by integrating up to time t :

$$t \mapsto \int_0^t \frac{1}{\tau}c(t)\,\mathrm{d}t$$

The only primitive which additionally satisfies the initial condition $y(0) = y_0$ is obtained by adding this constant :

$$y(t) = y_0 + \frac{1}{\tau}\int_0^t c(t)\,\mathrm{d}t$$

Method 2 : Separation of variables.

The equation rewrites $\mathrm{d}y = \dfrac{1}{\tau}c(t)\,\mathrm{d}t$. Integrating leads directly to the solution :

$$\int_{y_0}^{y(t)} \mathrm{d}y = \int_0^t \frac{1}{\tau}c(t)\,\mathrm{d}t \implies y(t) - y_0 = \frac{1}{\tau}\int_0^t c(t)\,\mathrm{d}t$$

② *No independent term* : $\frac{\mathrm{d}y}{\mathrm{d}t} = -\frac{1}{\tau}y(t)$.

Method 1 : Directly exhibiting a solution.

The solution $y(t)$ should be a function which is proportional to its derivative at any time point. The exponential function is known be *equal* to its derivative, therefore a solution can be looked for under the form of a *multiple* of the exponential whose time parameter is rescaled by $-\frac{1}{\tau}$:

$$t \mapsto \lambda e^{-\frac{t}{\tau}},\ \lambda \in \mathbb{R}$$

Its derivative is indeed equal to itself :

$$t \mapsto \lambda \left(-\frac{1}{\tau}\right) e^{-\frac{t}{\tau}} = -\frac{1}{\tau}\lambda e^{-\frac{t}{\tau}}$$

To further verify the initial condition, the constant λ should be set such as $y(0) = y_0$, which imposes :

$$\lambda e^0 = y_0 \implies \lambda = y_0$$

Method 2 : Separation of variables.

The differential equation rewrites : $\frac{\mathrm{d}y}{y(t)} = -\frac{1}{\tau}\mathrm{d}t$.

Integrating both sides leads to :

$$\int_{y_0}^{y(t)} \frac{1}{y}\,\mathrm{d}y = -\frac{1}{\tau}\int_0^t \mathrm{d}t \implies \ln\left(\frac{y(t)}{y_0}\right) = -\frac{1}{\tau}t$$

Exponentiating to express the solution $y(t)$ leads to :

$$\frac{y(t)}{y_0} = e^{-\frac{t}{\tau}} \implies y(t) = y_0 e^{-\frac{t}{\tau}}$$

Conclusion Both methods lead to the unique solution $\boxed{y(t) = y_0 e^{-\frac{t}{\tau}}}$

③ *Constant independent term* : $\frac{\mathrm{d}y}{\mathrm{d}t} = -\frac{1}{\tau}\left(y(t) - c_0\right)$

Method 1 : Separation of variables.

The differential equation rewrites $\frac{\mathrm{d}y}{y(t) - c_0} = -\frac{1}{\tau}\mathrm{d}t$.

It can be integrated by linear change of variable ($z(t) = y(t) - c_0$) :

$$\int_{y_0}^{y(t)} \frac{1}{y - c_0}\,\mathrm{d}y = -\frac{1}{\tau}\int_0^t \mathrm{d}t \implies \ln\left(\frac{y(t) - c_0}{y_0 - c_0}\right) = -\frac{1}{\tau}t \implies y(t) = c_0 + (y_0 - c_0)e^{-\frac{t}{\tau}}$$

Method 2 : Decomposition.

Here, the particular solution and the homogeneous solution can be interpreted with a physical meaning.

- *Particular solution* $y_p(t)$

This can be looked for under the form of a *constant*, which constitutes an *equilibrium* of the system.

Such a constant solution does not evolve in time by definition :

$$\frac{\mathrm{d}y_p}{\mathrm{d}t} = 0 \implies -y_p(t) + c_0 = 0 \implies y_p(t) = c_0$$

- *Homogeneous equation* $y_h(t)$

As the latter is the *difference* between the general solution and the equilibrium, it can e interpreted as the *transient dynamics* by which the system converges towards the equilibrium.

As expected, the dynamics of the difference $y_h(t) = y(t) - y_p(t) = y(t) - c_0$ verify the homogeneous equation and can be solved directly :

$$\frac{\mathrm{d}(y(t) - c_0)}{\mathrm{d}t} = \frac{\mathrm{d}y(t)}{\mathrm{d}t} = -\frac{1}{\tau}\left(y(t) - c_0\right)$$
$$(y(t) - c_0) = (y(t) - c_0)(0) \times e^{-\frac{t}{\tau}} = (y_0 - c_0) \times e^{-\frac{t}{\tau}}$$

- *General solution* : $y(t) = c_0 + (y_0 - c_0)e^{-\frac{t}{\tau}}$.

Conclusion Both methods lead to the unique solution $\boxed{y(t) = c_0 + (y_0 - c_0)e^{-\frac{t}{\tau}}}$.

4 *Arbitrary independent term* : $\dfrac{\mathrm{d}y}{\mathrm{d}t} = -\dfrac{1}{\tau}\,(y(t) - c(t))$

Methods : Decomposition and "Variation of the constant".

- *Homogeneous equation*

The associated homogeneous equation $\dfrac{\mathrm{d}y_h}{\mathrm{d}t} = -\dfrac{1}{\tau}y_h(t)$ is verified by functions of the form $y_h(t) = \lambda e^{-\frac{t}{\tau}}$ with $\lambda \in \mathbb{R}$.

- *Particular solution*

A particular solution can be looked for under the form $y_p(t) = \lambda(t)e^{-\frac{t}{\tau}}$, with $t \mapsto \lambda(t)$ a differentiable function to be determined (without loss of generality). It is identified by :

$$\begin{cases} \dfrac{\mathrm{d}y_p}{\mathrm{d}t} = \lambda'(t)e^{-\frac{t}{\tau}} - \cancel{\dfrac{1}{\tau}\lambda(t)e^{-\frac{t}{\tau}}} \text{ (product rule)} \\ \dfrac{\mathrm{d}y_p}{\mathrm{d}t} = -\dfrac{1}{\tau}\,(y_p(t) - c(t)) = -\cancel{\dfrac{1}{\tau}\lambda(t)e^{-\frac{t}{\tau}}} + \dfrac{1}{\tau}c(t) \end{cases} \implies \lambda'(t)e^{-\frac{t}{\tau}} = \frac{1}{\tau}c(t) \implies \lambda(t) = \frac{1}{\tau}\int_0^t e^{\frac{s}{\tau}}c(s)\,\mathrm{d}s + \alpha$$

with $\alpha \in \mathbb{R}$ a constant.

- *General solution*

The sum of both solutions gives : $y(t) = e^{-\frac{t}{\tau}}\left[\dfrac{1}{\tau}\displaystyle\int_0^t e^{\frac{s}{\tau}}c(s)\,\mathrm{d}s + \alpha\right]$.

To satisfy the initial condition, the constant must verify $1 \times (0 + \alpha) = y_0 \implies \alpha = y_0$.

Conclusion The unique solution is $\boxed{y(t) = e^{-\frac{t}{\tau}}\left[y_0 + \dfrac{1}{\tau}\displaystyle\int_0^t e^{\frac{s}{\tau}}c(s)\,\mathrm{d}s\right]}$.

1.2 Numerical approximation with Euler Method

5 *Taylor expansion*

The value of a function g in the neighboring of a point t can be expressed by its Taylor expansion, provided the function g is infinitely differentiable :

$$g(t + \Delta) = g(t) + \sum_{n=0}^{\infty} \frac{g^{(n)}(t)}{n!}\Delta^n \quad \text{with } g^{(n)} \text{ the } n^{\text{th}} \text{ derivative of } g$$

Truncating at the first order :

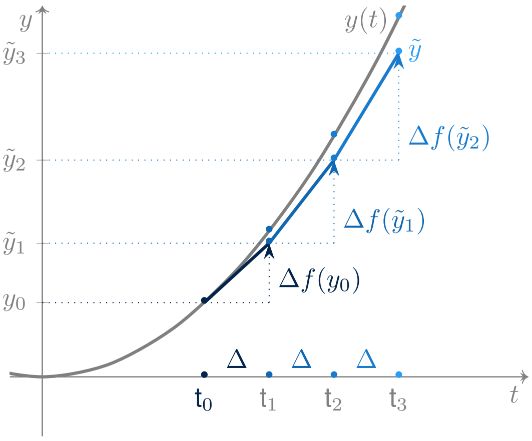
$$g(t + \Delta) = g(t) + g'(t)\,\Delta + \mathcal{O}(\Delta^2)$$

Applying this formula to the problem of numerical approximation :

$$y(t_{k+1}) = y(t_k + \Delta) \approx y(t_k) + \Delta f(t_k, y(t_k))$$

Therefore, Euler's method builds up an approximation by adding an increment proportional to the tangent at a given point (replacing the exact values by their approximations) :

$$\boxed{\tilde{y}_{k+1} \approx \tilde{y}_k + \Delta f(t_k, \tilde{y}_k)}$$



6 **num** *Implementation of the algorithm*

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7 *Analytical solution*

The solution is $y(t) = y_0 e^{-kt}$ (question 2), which tends towards 0 when times grows (as $k > 0$).

8 *Recurrence*

The approximated solution is obtained from the previous time step by (question 5) :

$$\tilde{y}_{n+1} = y_n - k y_n \Delta = y_n(1 - k\Delta)$$

By an immediate recurrence (geometric sequence) : $\tilde{y}_n = y_0(1 - k\Delta)^n$.

This sequence tends to 0 if and only if $|1 - k\Delta| < 1$, i.e. $-1 < 1 - k\Delta < 1$, which is satisfied provided $\boxed{\Delta < \frac{2}{k}}$.

> **First order method**
>
> The error inherent to Euler's method can be estimated more precisely.
> Pushing the Taylor expansion one order further :
>
> $$y(t + \Delta) = y(t) + y'(t)\Delta + \frac{1}{2}y''(t)\Delta^2 + \mathcal{O}(\Delta^3)$$
>
> Therefore, the error made by the Euler scheme at each step is of the order $\epsilon = \Delta^2$. At time t, the approximation requires about t/Δ steps, such that the cumulative effect of the errors is expected to be of order $\frac{t}{\Delta} \times \Delta^2 = t\Delta$.

9 **num** *Failures of Euler's method*

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With $k = 10$, the numerical approximation is stable for $\Delta \in [0; 1/5]$.
Otherwise, oscillations and divergence can be observed.

2 Models of Point Neurons

2.1 Leaky Neuron

10 *Link between current and charges*

The current $I(t)$ is the instantaneous variation of charges :

$$I(t) = \frac{\mathrm{d}Q}{\mathrm{d}t}$$

11 *Differential equation for the membrane potential*

⚠ The description of the electrical properties of the neuron reveals that the variation of the membrane potential at any time point is dependent on itself. Therefore, its behavior should be expressed by a *differential equation* ($\frac{\mathrm{d}V_m}{\mathrm{d}t} = ...$) rather than by a direct expression ($V_m = ...$).

The membrane potential is related to the instantaneous charge of the membrane by : $V_m = \frac{1}{C_m} Q$.

Deriving this expression gives $\frac{\mathrm{d}V_m}{\mathrm{d}t} = \frac{1}{C_m}\frac{\mathrm{d}Q}{\mathrm{d}t} = I$ (question 10).

Replacing I by its expression yields :

$$\boxed{C_m \frac{\mathrm{d}V_m}{\mathrm{d}t} = -g_l(V_m - E_l)}$$

12 *Solution of the membrane potential's dynamics*

The equation rewrites : $\frac{C_m}{g_l}\frac{\mathrm{d}V_m}{\mathrm{d}t} = -V_m + E_l$.

A characteristic time constant of the system can be defined as $\boxed{\tau_m = \frac{C_m}{g_l}}$. It has a dimension of time (to comply with the equation homogeneity).

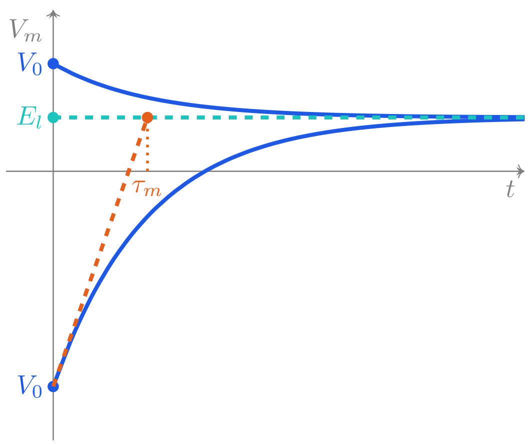
Thus, the membrane potential relaxes exponentially from an initial condition V_0 to its equilibrium E_l (question 3) :

$$\boxed{V_m(t) = E_l + (V_0 - E_l)\, e^{-\frac{t}{\tau_m}}}$$

The time constant represents the time at which the membrane potential has relaxed to $\approx 36\%$ from its deviation from the equilibrium : $t = \tau_m \implies e^{-\frac{t}{\tau_m}} = e^{-1} \approx 0.36$. Alternatively, it can be seen as the time at which the tangent at the initial point crosses the abscisses : $\frac{\mathrm{d}V_m}{\mathrm{d}t}(t=0) = -\frac{V_0 - E_l}{\tau_m}$.

13 *Distinct behaviors*

- $V_0 < E_l \implies V_m$ grows towards E_l.
- $V_0 > E_l \implies V_m$ decreases towards E_l.
- $V_0 = E_l \implies V_m$ is fixed.



2.2 Leaky Integrate-and-Fire model (LIF)

14 *Threshold current*
With the additional current I_{app}, the membrane potential dynamics still follows the same behavior, but with a modified equilibrium. Indeed :

$$0 = -g_l(V_m(t) - E_l) + I_{app} \implies V_m(t) = V_\infty = E_l + \frac{I_{app}}{g_l}$$

Thus, the additional input current switches the equilibrium from E_l to $\boxed{V_\infty = E_l + \frac{I_{app}}{g_l}}$.

Starting from the reset potential, the membrane potential still evolves as :

$$V_m(t) = V_\infty + (V_0 - V_\infty)\, e^{-\frac{t}{\tau_m}}$$

A spike can be emitted only if the membrane potential can reach the threshold V_{th}, which depends on the position of the equilibrium relative to the threshold. The spiking condition therefore is :

$$V_\infty > V_{th} \implies E_l + \frac{I_{app}}{g_l} > V_{th}$$

The threshold current required for this condition to be met is :

$$\boxed{I_{th} = g_l(V_{th} - E_l)}$$

Numerical application : With the parameters given in the table, $I_{th} = 200\ pA$.

15 *Graphical representation of the behaviors*

With the reset mechanism, the membrane potential evolves periodically from the reset potential to the spiking threshold.

16 **num** *Simulation with the reset mechanism*
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17 *Firing rate as a function of current*

The inter-spike-interval T_{ISI} is the duration between two consecutive spikes (which is indeed regular, as shown by the previous questions). It also corresponds to the time required to reach the threshold from the reset potential :

$$V_m(T_{ISI}) = V_{th} \implies V_\infty + (V_r - V_\infty)\, e^{-\frac{T_{ISI}}{\tau_m}} = V_{th} \implies \exp\left(-\frac{T_{ISI}}{\tau_m}\right) = \frac{V_\infty - V_{th}}{V_\infty - V_r}$$

Solutions exist for $V_\infty > V_{th}$, which ensures a positive quotient (by assumption $V_{th} > V_r$, which implies $V_\infty > V_{th}$).
Note : This requirement corresponds to the condition for spiking found at question 14 : it means that the equilibrium is above the threshold, such that the neuron is in a spiking regime, and an inter-spike interval can indeed be defined.

In this case, $V_r < V_{th} < V_\infty$, and the period T_{ISI} is well defined :

$$\boxed{T_{ISI} = \tau_m \ln\left(\frac{V_\infty - V_r}{V_\infty - V_{th}}\right) = \tau_m \ln\left(\frac{E_l + \frac{I_{app}}{g_l} - V_r}{E_l + \frac{I_{app}}{g_l} - V_{th}}\right)}$$

Note : The sign is indeed positive, because quotient is above 1 (according to the distances $V_\infty - V_r > V_\infty - V_{th} > 0$) and thus the logarithm is positive.

The firing rate can be defined as the inverse of the inter-spike interval :

$$f = \frac{1}{T_{ISI}}$$

(18) *Study the function $f(I)$*

Note : It is easier to reason on the formula of T_{ISI} which includes V_∞ instead of I_{app}. This is easy since V_∞ is only linearly dependant on I_{app} (question (14)).

- Domain of validity : solutions exist for $V_\infty > V_{th} \implies I_{app} > I_{th}$ (question (14)).
- Limits of extreme values of the input current :
  - $I_{app} \to +\infty \implies V_\infty \to +\infty \implies \dfrac{V_\infty - V_r}{V_\infty - V_{th}} = \dfrac{1 - \frac{V_r}{V_\infty}}{1 - \frac{V_{th}}{V_\infty}} \to 1 \implies T_{ISI} \to 0 \implies f \to +\infty$
  - $I_{app} \to I_{th}^+ \implies V_\infty \to V_{th} \implies \dfrac{V_\infty - V_r}{V_\infty - V_{th}} \to +\infty \implies T_{ISI} \to +\infty \implies f \to 0$
- Asymptotic behavior for $I_{app} \to +\infty$:

An equivalent of the quotient can be obtained by a limited development of logarithms :

$$T_{ISI} = \tau_m \ln\left(\frac{1 - \frac{V_r}{V_\infty}}{1 - \frac{V_{th}}{V_\infty}}\right) = \tau_m \left(\ln\left(1 - \tfrac{V_r}{V_\infty}\right) - \ln\left(1 - \tfrac{V_{th}}{V_\infty}\right)\right) \sim \tau_m \left(-\tfrac{V_r}{V_\infty} + \tfrac{V_{th}}{V_\infty}\right) = \tau_m \frac{V_{th} - V_r}{V_\infty}$$

Therefore, the firing rate is asymptotically linear in I_{app} : $f \sim \dfrac{1}{\tau_m} \dfrac{V_\infty}{V_{th} - V_r} = \dfrac{1}{\tau_m} \dfrac{E_l + \frac{I_{app}}{g_l}}{V_{th} - V_r}$.

- Slope at the threshold current :

By the chain rule for derivatives : $\dfrac{\mathrm{d}f}{\mathrm{d}I_{app}} = \dfrac{\mathrm{d}f}{\mathrm{d}T_{ISI}} \dfrac{\mathrm{d}T_{ISI}}{\mathrm{d}R} \dfrac{\mathrm{d}R}{\mathrm{d}V_\infty} \dfrac{\mathrm{d}V_\infty}{\mathrm{d}I_{app}}$, with $R = \dfrac{V_\infty - V_r}{V_\infty - V_{th}}$ the quotient.

  - $\dfrac{\mathrm{d}f}{\mathrm{d}T_{ISI}} = -\dfrac{1}{T_{ISI}^2} = -\dfrac{1}{\left[\tau_m \ln\left(\frac{V_\infty - V_r}{V_\infty - V_{th}}\right)\right]^2}$
  - $\dfrac{\mathrm{d}T_{ISI}}{\mathrm{d}R} = \tau_m \dfrac{1}{R} = \tau_m \dfrac{V_\infty - V_{th}}{V_\infty - V_r}$
  - $\dfrac{\mathrm{d}R}{\mathrm{d}V_\infty} = \dfrac{1 \times (V_\infty - V_{th}) - 1 \times (V_\infty - V_r)}{(V_\infty - V_{th})^2} = \dfrac{V_r - V_{th}}{(V_\infty - V_{th})^2}$
  - $\dfrac{\mathrm{d}V_\infty}{\mathrm{d}I_{app}} = \dfrac{1}{g_l}$

Altogether :

$$\frac{\mathrm{d}f}{\mathrm{d}I_{app}} = -\frac{1}{\tau_m^2 g_l} \frac{1}{\left[\ln\left(\frac{V_\infty - V_r}{V_\infty - V_{th}}\right)\right]^2} \frac{V_\infty - V_{th}}{V_\infty - V_r} \frac{V_r - V_{th}}{(V_\infty - V_{th})^2} = -\frac{1}{\tau_m^2 g_l} \frac{1}{\left[\ln\left(\frac{V_\infty - V_r}{V_\infty - V_{th}}\right)\right]^2} \frac{1}{V_\infty - V_{th}} \frac{V_r - V_{th}}{V_\infty - V_r}$$

Finding the limit when $I_{app} \to I_{th}$ is equivalent to find the limit when $V_\infty \to V_{th}$.

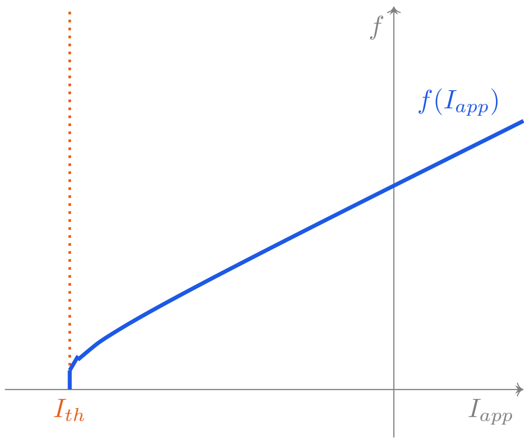
Introducing $(V_\infty - V_r)$ at numerator and denominator allows to get the form $\dfrac{z}{\ln(z)^2}$:

$$\frac{\mathrm{d}f}{\mathrm{d}I_{app}} = -\frac{1}{\tau_m^2 g_l} \frac{1}{\left[\ln\left(\frac{V_\infty - V_r}{V_\infty - V_{th}}\right)\right]^2} \frac{1}{V_\infty - V_{th}} \frac{V_r - V_{th}}{V_\infty - V_r} \times \frac{(V_\infty - V_r)}{(V_\infty - V_r)} = -\frac{1}{\tau_m^2 g_l} \frac{\frac{V_\infty - V_r}{V_\infty - V_{th}}}{\left[\ln\left(\frac{V_\infty - V_r}{V_\infty - V_{th}}\right)\right]^2} \frac{V_r - V_{th}}{(V_\infty - V_r)^2}$$

  - The middle term tends to $+\infty$, because $z = \dfrac{V_\infty - V_r}{V_\infty - V_{th}} \xrightarrow[V_\infty \to V_{th}]{} +\infty$ and $\dfrac{z}{\ln(z)^2} \xrightarrow[z \to +\infty]{} +\infty$.
  - The last term tends to 1 when $V_\infty \to V_{th}$.

Conclusion : The slope of the f-I curve is vertical when the current tends to its threshold value.

(19) *f-I curve*

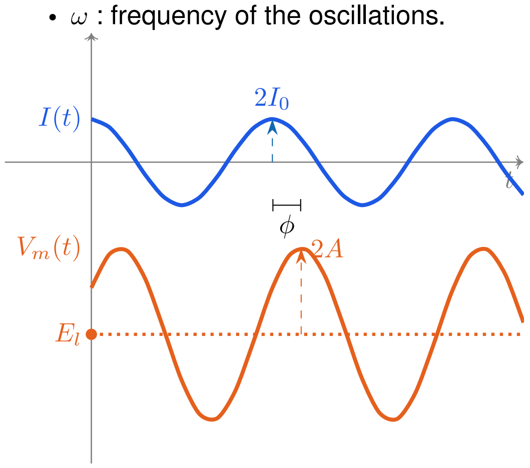


According to this model, the firing rate is not bounded when the input current increases ($\lim_{I \to \infty} f = +\infty$), which is not biologically plausible. In real neurons, spikes are not points in time but last for a few milliseconds, and they moreover induce a refractory period during which the neuron is prevented to spike immediately afterwards.

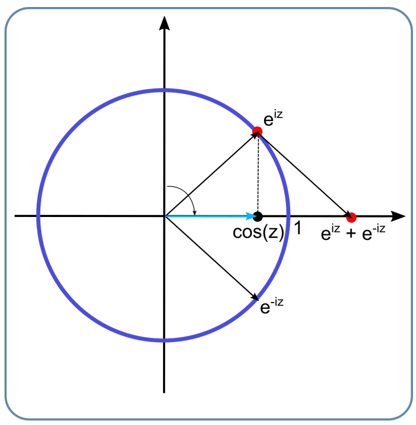
2.3 Response to an oscillating input current

(20) *Oscillatory functions*
Interpretation of the parameters :

- $2I_0$ and $2A$: amplitudes of the oscillations.
- ϕ : phase shift (or time delay) of the response of V_m to the input I_{app}.
- ω : frequency of the oscillations.



(21) *Expressions with complex numbers*



The cosinus can be expressed of two manners : $\cos(\theta) = \dfrac{e^{i\theta} + e^{-i\theta}}{2} = \Re(e^{i\theta})$.
With this formalism :
$I(t) = I_0(e^{i\omega t} + e^{-i\omega t})$
$V_m(t) = E_l + A(e^{i(\omega t + \phi)} + e^{-i(\omega t+\phi)})$.

(22) The expressions found in question (21) can be plugged into the differential equation :
$C_m \dfrac{\mathrm{d}V_m}{\mathrm{d}t} = -g_l(V_m(t) - E_l) + I_{app}(t)$
$C_m A \left(i\omega e^{i(\omega t+\phi)} - i\omega e^{-i(\omega t+\phi)}\right) = -g_l(\left[\cancel{E_l} + A(e^{i(\omega t+\phi)} + e^{-i(\omega t+\phi)})\right] - \cancel{E_l}) + I_0(e^{i\omega t} + e^{-i\omega t})$
Factorizing by the independent functions $t \mapsto e^{i\omega t}$ and $t \mapsto e^{-i\omega t}$:
$(C_m A i\omega e^{i\phi} + g_l A e^{i\phi} - I_0)e^{i\omega t} + (-C_m A i\omega e^{-i\phi} + g_l A e^{i\phi} - I_0)e^{-i\omega t} = 0$

$(Ae^{i\phi}(C_m i\omega + g_l) - I_0)e^{i\omega t} + (Ae^{-i\phi}(-C_m i\omega + g_l) - I_0)e^{-i\omega t} = 0$
Multiplying by $e^{-i\omega t}$:
$(Ae^{i\phi}(C_m i\omega + g_l) - I_0) \times 1 + (Ae^{-i\phi}(-C_m i\omega + g_l) - I_0)e^{-2i\omega t} = 0$
For this equation to hold for all times t, both terms should cancel. For instance $t = \frac{\pi}{4\omega} \implies e^{-2i\omega t} = e^{-i\frac{\pi}{2}} = -i$, which imposes in particular for the first term : $Ae^{i\phi}(C_m i\omega + g_l) - I_0 = 0$.
Simplifying leads to :

$$\boxed{A\exp(i\phi) = \frac{I_0}{g_l + iC_m\omega}}$$

Note : Using the real part expression of the cosinus, the same reasoning could have been carried out by taking a complex oscillating current $I_{app}(t) = I_0 \cdot e^{i\omega t}$ (which has no physical meaning) and then focusing on the real part of the equations.

23 *Amplitude and Phase of the response*
Any complex number z can be written either in a Cartesian representation $z = x + iy$ or polar representation $z = |z|\, e^{i\phi_z}$. From Cartesian to polar coordinates, its module and phase are given by :

$$|z| = \sqrt{x^2 + y^2} \qquad \phi_z = \arctan(y/x) + 1_{\{x<0\}} \cdot \mathrm{sgn}(y) \cdot \pi$$

Applied to the complex number $A\exp(i\phi)$, A corresponds to the amplitude and ϕ to the phase. On the other hand, the expression found above can be rewritten so that imaginary parts appear only at the numerator :

$$\frac{I_0}{g_l + iC_m\omega} \times \frac{g_l - iC_m\omega}{g_l - iC_m\omega} = \frac{I_0}{g_l^2 + C_m^2\omega^2} \cdot (g_l - i\,C_m\omega)$$

By identification :

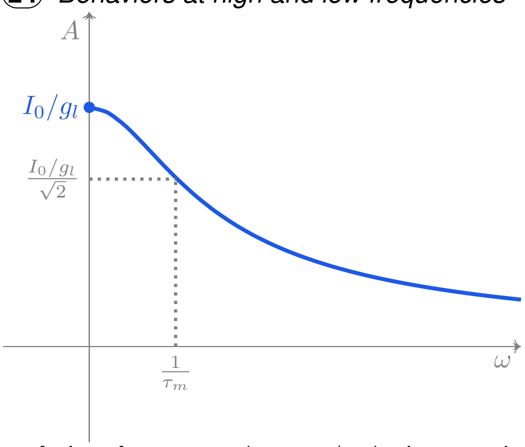
$$A = \frac{I_0}{g_l^2 + C_m^2\omega^2} \times \sqrt{g_l^2 + (C_m\omega)^2} = \frac{I_0}{g_l\sqrt{1 + \left(\frac{C_m}{g_l}\right)^2 \omega^2}} \qquad \phi = \arctan\left(-\frac{C_m\omega}{g_l}\right) = -\arctan\left(\frac{C_m}{g_l}\omega\right)$$

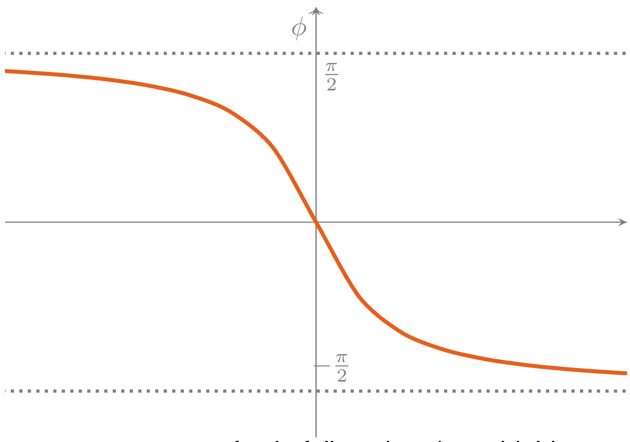
Introducing the characteristic time constant $\tau_m = \frac{C_m}{g_l}$:

$$A = \frac{I_0/g_l}{\sqrt{1 + \tau_m^2\omega^2}} \qquad \phi = -\arctan(\tau_m\omega)$$

Note : Identical results can be obtained by cancelling the factor in front of the exponential instead of the constant one.
$-C_m Ai\omega e^{-i\phi} + g_l Ae^{i\phi} - I_0 = 0 \implies A\exp(-i\phi) = \dfrac{I_0}{g_l - iC_m\omega} = \dfrac{I_0}{g_l^2 + C_m^2\omega^2}(g_l + iC_m\omega)$
This complex number is just the symmetric of the one above relative to the x-axis, which is consistent with the negative sign in the exponential.

24 *Behaviors at high and low frequencies*





• At low frequency ($\omega \ll 1/\tau_m$), the membrane response can perfectly follow the sinusoidal input since the phase tends to 0, and in this case the amplitude tends to its maximum $A = I_0/g_l$.
For small oscillation frequencies ω, the phase can be approximated $\arctan(\tau_m\omega) \approx \tau_m\omega$ such that :

$$V_m(t) \approx E_l + 2I_0/g_l \cos(\omega(t - \tau_m))$$

Thus, the difference in phase just corresponds to the time for the membrane to relax (with the characteristic time scale τ_m).

• At high frequency ($\omega \gg 1/\tau_m$), the input current oscillates too quickly for the membrane to have the time to integrate the signal (which requires an time scale of order τ_m). In that case, the amplitude cannot develop and remains close to 0, while the phase to $-\pi/2$.
For small oscillation frequencies ω, the amplitude becomes equivalent to $A \sim \frac{I_0/g_l}{\sqrt{\tau_m^2 \omega^2}} = \frac{I_0/g_l}{\tau_m \omega} = \frac{I_0}{C_m \omega}$, such that :

$$V_m(t) \approx E_l + 2\frac{I_0}{C_m\omega} \cos\left(\omega t - \pi/2\right)$$

• Conclusion : The membrane acts as such as a first-order low-pass filter. No resonance phenonmenon is observed (as there is no peak in the frequency) as can be seen with higher order integrators.