TD 1 – Models of Neurons I

1 Mathematical tools for Differential Equations

1.1 Analytical solutions

① *Independent term only* – Solving $\frac{\mathrm{d}y}{\mathrm{d}t} = \frac{1}{\tau} c(t)$.
Any primitive of this function verifies the differential equation, and all those primitives differ only by a constant. The primitive which cancels at the initial time can be obtained by integrating up to time t : $t \mapsto \int_0^t \frac{1}{\tau} c(t) dt$.
The primitive which satisfies the initial condition is the one which takes the value y_0 at time $t = 0$, which is the constant to add : $y(t) = y_0 + \frac{1}{\tau} \int_0^t c(t) dt$.

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

Method 1 : Directly exhibiting a solution.
The exponential function has the property of being equal to its derivative. Therefore, any function $t \mapsto \lambda e^{-\frac{t}{\tau}},\ \lambda \in \mathbb{R}$ verifies the differential equation, since its derivative is $t \mapsto -\frac{1}{\tau} \lambda e^{-\frac{t}{\tau}}$ with $\lambda \in \mathbb{R}$ a constant.
To further verify the initial condition, the constant λ should be set such as $y(0) = y_0$, i.e. $y_0 = \lambda e^0 = \lambda$.

Method 2 : Separation of variables.
The equation rewrites : $\frac{\mathrm{d}y}{y(t)} = -\frac{1}{\tau} \mathrm{d}t$. Integrating leads to : $\int_0^t \frac{1}{y(t)} \mathrm{d}y = -\frac{1}{\tau} \int_0^t \mathrm{d}t \implies \ln\left(\frac{y(t)}{y_0}\right) = -\frac{1}{\tau} t$.
Exponentiating to express the solution : $\frac{y(t)}{y_0} = e^{-\frac{t}{\tau}} \implies y(t) = y_0 e^{-\frac{t}{\tau}}$.

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

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

Method 1 : Separation of variables.
The equation $\frac{\mathrm{d}y}{y(t) - c_0} = -\frac{1}{\tau} \mathrm{d}t$ can be integrated by linear change of variable ($z(t) = y(t) - c_0$) :
$\ln\left(\frac{y(t) - c_0}{y_0 - c_0}\right) = -\frac{1}{\tau} t \implies y(t) = c_0 + (y_0 - c_0) e^{-\frac{t}{\tau}}$.

Method 2 : Sum of particular solution and homogeneous solution.
This method proceeds in two steps, which can be interpreted by a physical meaning :
① Investigating if there exists a *particular solution* $y_p(t)$ which is *constant*, thereby constituting an *equilibrium* of the system.
Such a constant solution does not evolve in time by definition : $\frac{\mathrm{d}y_p}{\mathrm{d}t} = 0 \implies -y_p(t) + c_0 = 0 \implies y_p(t) = c_0$.
② Finding the *transient dynamics* by which the system converges towards the equilibrium.
This involves finding the dynamics of the difference $y(t) - y_p(t) = y(t) - c_0$, which verifies a differential equation without independent term (as in ②) : $\frac{\mathrm{d}(y(t) - c_0)}{\mathrm{d}t} = \frac{\mathrm{d}y(t)}{\mathrm{d}t} = -\frac{1}{\tau} (y(t) - c_0)$. Therefore, $(y(t) - c_0) = (y(t) - c_0)(0) \times e^{-\frac{t}{\tau}} = (y_0 - c_0) \times e^{-\frac{t}{\tau}}$.
③ Summing both solutions lead to the unique 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* – Solving $\frac{\mathrm{d}y}{\mathrm{d}t} = -\frac{1}{\tau} (y(t) - c(t))$

Method : 'Variation of the constant'.

The associated homogeneous equation $\frac{\mathrm{d}y_h}{\mathrm{d}t} = -\frac{1}{\tau}y_h(t)$ (as in ②) is verified by functions of the form $y_h(t) = \lambda e^{-\frac{t}{\tau}}$ with $\lambda \in \mathbb{R}$. Therefore, an ansatz is to look for the solution of the equation with time-varying independent term under the form $t \mapsto \lambda(t)e^{-\frac{t}{\tau}}$, with $t \mapsto \lambda(t)$ a differentiable function to be determined (without loss of generality).
This form is indeed convenient, since its derivative matches the form of the differential equation :

- On the one hand, $\frac{\mathrm{d}y_p}{\mathrm{d}t} = \lambda'(t)e^{-\frac{t}{\tau}} - \frac{1}{\tau}\lambda(t)e^{-\frac{t}{\tau}} = \lambda'(t)e^{-\frac{t}{\tau}} - \frac{1}{\tau}y_p(t)$, by the product expression of a derivative,
- On the other hand, $\frac{\mathrm{d}y_p}{\mathrm{d}t} = -\frac{1}{\tau}\left(y_p(t) - c(t)\right)$, to satisfy the differential equation.

Equating both expressions leads to a simplification which allows to express the derivative of the function looked for :
$\lambda'(t)e^{-\frac{t}{\tau}} - \cancel{\frac{1}{\tau}y_p}(t) = -\cancel{\frac{1}{\tau}y_p}(t) + \frac{1}{\tau}c(t) \implies \lambda'(t) = \frac{1}{\tau}e^{\frac{t}{\tau}}c(t) \implies \lambda(t) = \frac{1}{\tau}\int_0^t e^{\frac{s}{\tau}}c(s)ds + \alpha$, with $\alpha \in \mathbb{R}$ a constant.

Thus, a solution is given by : $t \mapsto e^{-\frac{t}{\tau}}\left[\frac{1}{\tau}\int_0^t e^{\frac{s}{\tau}}c(s)ds + \alpha\right]$.
To satisfy the initial condition, the constant must verify $1 \times (0 + \alpha) = y_0 \implies \alpha = y_0$.

1.2 Numerical approximation with Euler Method

⑤ *Taylor expansion* The value of a function y in the neighboring of a point t can be expressed by its Taylor expansion, provided the function y is infinitely differentiable :

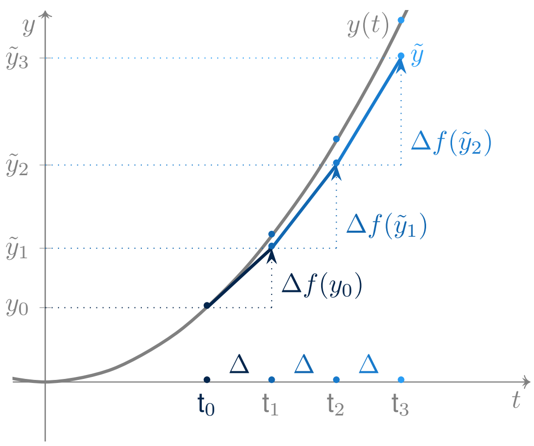
$$y(t + \Delta_t) = y(t) + \sum_{n=0}^{\infty} \frac{y^{(n)}(t)}{n!}\Delta_t^n$$

with $y^{(n)}(t)$ the n^{th} derivative of $y(t)$.
Truncating at the first order :

$$y(t + \Delta_t) = y(t) + y'(t)\,\Delta_t + \mathcal{O}(\Delta_t^2)$$

The Euler method builds up an approximation by adding an increment proportional to the tangent at a given point :

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



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

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

First order method

The error inherent to the Euler's method can be estimated more precisely.
Pushing the Taylor expansion one order further :

$$f(t+\Delta t) = f(t) + f'(t)\Delta x + \frac{1}{2}f''(t)\Delta t^2 + \mathcal{O}(\Delta t^3)$$

Therefore, the error made by the Euler scheme at each step is of the order $\epsilon = \Delta_t^2$. At time t, the approximation requires $\approx t/\Delta_t$ steps, such that the cumulative effect of the errors is expected to be of order $\frac{t}{\Delta_t} \times \Delta_t^2 = t\Delta_t$.

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

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

2 Models of Point Neurons

2.1 Leaky Neuron

10 *Differential equation for the membrane potential*

The membrane potential is related to the instantaneous charge of the membrane by : $V_m = \frac{1}{C_m}Q$, and deriving this expression gives $\frac{\mathrm{d}V_m}{\mathrm{d}t} = \frac{1}{C_m}\frac{\mathrm{d}Q}{\mathrm{d}t} = I$, since the current I is defined as the flow of charges.
Replacing I by its expression yields :

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

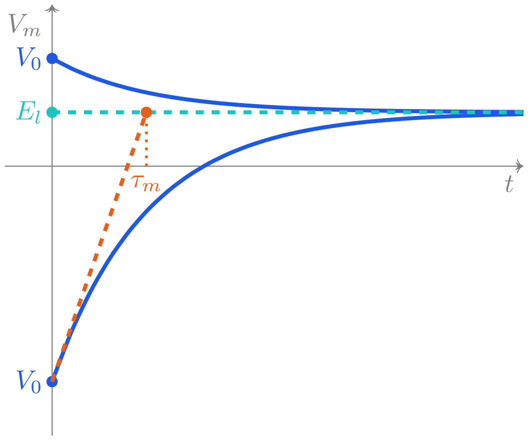
11 *Solution of the membrane potential's dynamics*

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 $\tau_m = \frac{C_m}{g_l}$ (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) :

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

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 : $\frac{\mathrm{d}V_m}{\mathrm{d}t}(t=0) = -\frac{V_0 - E_l}{\tau_m}$



12 *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)

(13) *Threshold current*
The membrane potential dynamics still follows the same differential equation, but with a modified equilibrium, which is switched from E_l to $V_\infty = E_l + \dfrac{I_{app}}{g_l}$ by the additional input current.
Thus, starting from the reset potential, the membrane potential 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 :

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

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

(14) **num** *Simulation with the reset mechanism*
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With the reset mechanism, the membrane potential evolves periodically from the reset potential to the spiking threshold. This allows to define a firing rate as the inverse of the inter-spike interval, that is the time between two consecutive spikes.

(15) *Firing rate as a function of current*
The time T_{ISI} between two spikes 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 $V_\infty > V_{th}$).
In this case :

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

.
The corresponding firing rate is :

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

(16) *Study the function $f(I)$*
- Domain of validity : solutions exist for $V_\infty => V_{th} \implies I_{app} > I_{th}$ (questions (13)).
- Limits of extreme values of the input current :
  - $I_{app} \to +\infty \implies V_\infty \to +\infty \implies \dfrac{V_\infty - V_r}{V_\infty - V_{th}} = \dfrac{1 - \frac{V_r}{V_\infty}}{1 - \frac{V_{th}}{V_\infty}} \to 1 \implies T_{ISI} \to 0 \implies f \to +\infty$
  - $I_{app} \to I_{th}^+ \implies V_\infty \to V_{th} \implies \dfrac{V_\infty - V_r}{V_\infty - V_{th}} \to 0 \implies T_{ISI} \to +\infty \implies f \to 0$
- 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} : $f \sim \dfrac{1}{\tau_m} \dfrac{V_\infty}{V_{th} - V_r}$.
- Slope at the threshold current :

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

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

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

$$= -\frac{1}{\tau_m^2 g_l} \frac{1}{\left[\ln\left(\dfrac{V_\infty - V_r}{V_\infty - V_{th}}\right)(V_\infty - V_{th})\right]^2} \frac{(V_\infty - V_{th})(V_r - V_{th})}{V_\infty - V_r}$$

Finding the limit when $I_{app} \to I_{th}$ is equivalent to find the limit when $V_\infty \to V_{th}$.
Introducing $(V_\infty - V_r)^2$ at numerator and denominator :

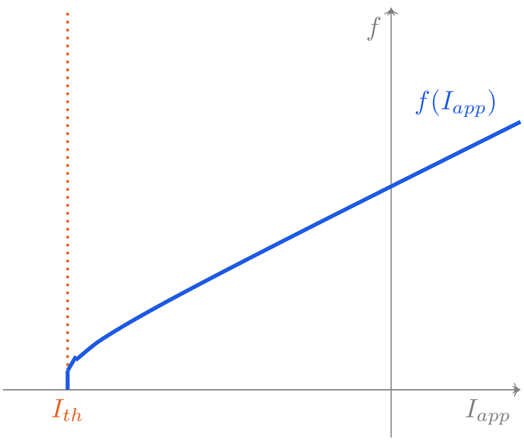
$$= -\frac{1}{\tau_m^2 g_l} \frac{1}{\left[\ln\left(\dfrac{V_\infty - V_r}{V_\infty - V_{th}}\right)(V_\infty - V_{th})\right]^2} \frac{(V_\infty - V_{th})(V_r - V_{th})}{V_\infty - V_r} \times \frac{(V_\infty - V_r)^2}{(V_\infty - V_r)^2}$$

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

- The squared term contains a limit of the form $\dfrac{z}{\ln(z)} \xrightarrow[z \to +\infty]{} 0$ with $z = \dfrac{V_\infty - V_r}{V_\infty - V_{th}} \xrightarrow[V_\infty \to V_{th}]{} +\infty$.
- The middle term tends to a constant when $V_\infty \to V_{th}$.
- The last term rewrites : $\dfrac{V_\infty - V_{th}}{(V_\infty - V_r)^2} = \dfrac{1}{V_\infty} \dfrac{1 - \frac{V_{th}}{V_\infty}}{\left(1 - \frac{V_r}{V_\infty}\right)^2} \xrightarrow[V_\infty \to V_{th}]{} +\infty$.

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

(17) *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.

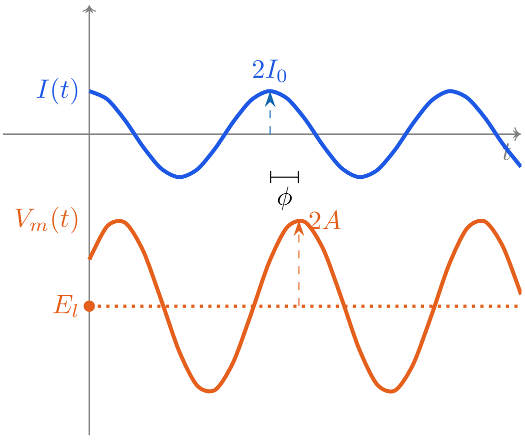
2.3 Response to an oscillating input current

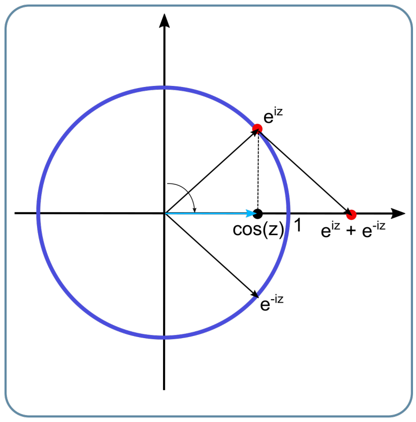
(18) *Oscillatory functions*

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.





(19) *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 :
$I(t) = I_0(e^{i\omega t} + e^{-i\omega t})$
$V_m(t) = E_l + A(e^{i(\omega t+\phi)} + e^{-i(\omega t+\phi)})$.

(20) The expressions found in question (19) can be plugged into the differential equation :
$C_m \dfrac{\mathrm{d}V_m}{\mathrm{d}t} = -g_l(V_m(t) - E_l) + I_{app}(t)$
$C_m A\left(i\omega e^{i(\omega t+\phi)} - i\omega e^{-i(\omega t+\phi)}\right) = -g_l\left(\left[\cancel{E_l} + A(e^{i(\omega t+\phi)} + e^{-i(\omega t+\phi)})\right] - \cancel{E_l}\right) + I_0(e^{i\omega t} + e^{-i\omega t})$
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.

(21) *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 :

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

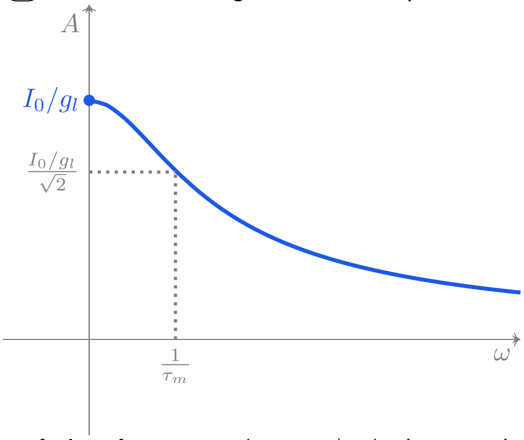
By identification :

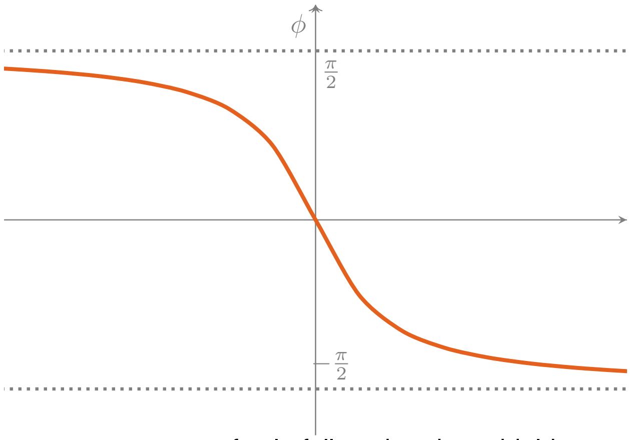
$$A = \frac{I_0}{g_l^2 + C_m^2\omega^2} \times \sqrt{g_l^2 + (C_m\omega)^2} = \frac{I_0}{g_l\sqrt{1 + \left(\frac{C_m}{g_l}\right)^2 \omega^2}} \qquad \phi = \arctan\left(-\frac{C_m\omega}{g_l}\right) = -\arctan\left(\frac{C_m}{g_l}\omega\right)$$

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

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

(22) *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 :

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

• 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.