TD 2 – Models of neurons II Generalized Integrate-and-Fire models

1 Generalized Integrate-and-Fire models (1 variable)

Method – Dynamical systems analysis for a one-dimensional system

The **dynamical systems analysis** aims to predict the **qualitative properties** of a dynamical system, even when its differential equations cannot be solved analytically.

Specifically, a basic study consists in identifying :

- **Fixed points** of the system and their stability,
- **Bifurcations** of the system, i.e. transitions in "regimes" (behaviors that the system could adopt) induced by variations in the parameters, in particular depending on its initial conditions.

This approach can be applied to one-dimensional systems defined by a differential equation of the form :

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

Phase portrait

A phase portrait is a **graph** which displays the function F as a function of the variable y.
It helps to get insights about how the system evolves in each possible state (because its derivative depends on itself through the function F).

Fixed points

Fixed points correspond to **equilibria** (steady-states), i.e. states in which the system does not evolve anymore. Thus, a fixed point y^* verifies :

$$\frac{\mathrm{d}y}{\mathrm{d}t}(y^*) = 0$$

- Computationally, fixed points are the solutions of the equation $F(y) = 0$.
- Graphically, in the phase portrait, fixed points occur at the intersections of the function $F(y)$ with the horizontal axis.

Stability

Stability characterizes how the system reacts when it is perturbed around one of its fixed point, i.e. whether it tends to go back to the equilibrium or to move away from it.

- Graphically, stability at a given fixed point is indicated by the slope of the $F(y)$ at this fixed point.
  - If the slope is negative, then $\frac{\mathrm{d}y}{\mathrm{d}t}$ is positive *below* the fixed point and negative *above* the fixed point. Thus, a small deviation *below* the fixed point will lead the system to go up, bringing it *closer* to the fixed point, and conversely a small deviation *above* the fixed point will lead the system to go down, again *closer* to the fixed point. Consequently, departures from the fixed point will be *dampened* and the system will go back to its equilibrium.
  - If the slope is positive, then signs reverse compared to the previous case. Thus, a small deviation *below* the fixed point will lead the system to go down, *farther* away to the fixed point, and conversely for a small deviation *above* the fixed point. Thus, departures from the fixed point will be *amplified* and the system will diverge from its equilibrium.
- Computationally, those results can be proved by approximating the function $y \mapsto \frac{\mathrm{d}y}{\mathrm{d}t}(y) = F(y)$ at a point near the fixed point y^*, i.e. at a value $y^* + \delta y$, where δy reflects a small perturbation. At the first order :

$$\frac{\mathrm{d}y}{\mathrm{d}t}(y^* + \delta y) = F(y^* + \delta y) = \cancelto{0}{F(y^*)} + F'(y^*)\, \delta y + o(\delta y)$$

The cancellation of $F(y^*)$ stems from the property of the fixed point itself.
This equation shows that the sign of the time derivative at a value $y^* + \delta y$ is determined by the *sign of* F' at the fixed point.

- If $F'(y^*) > 0$, then $\frac{\mathrm{d}y}{\mathrm{d}t}(y^* + \delta y)$ has the same sign than δy : the system is driven in the same direction than the perturbation, which leads to its amplification away from the equilibrium.
- If $F'(y^*) < 0$, then $\frac{\mathrm{d}y}{\mathrm{d}t}(y^* + \delta y)$ is of the opposite sign than δy : the system is driven in the opposite direction than the perturbation, which leads to its dampening towards the equilibrium.

⚠Note : The derivative F' is relative to the variable y (i.e. $\frac{\mathrm{d}}{\mathrm{d}y}$), it should not be confused with the *time derivative* (i.e. $\frac{\mathrm{d}}{\mathrm{d}t}$). In a way, it can be written : $F' = \frac{\mathrm{d}}{\mathrm{d}y}\left(\frac{\mathrm{d}y}{\mathrm{d}t}\right)$.

Bifurcations

A bifurcation is a qualitative change in the system's behavior produced by varying parameters.

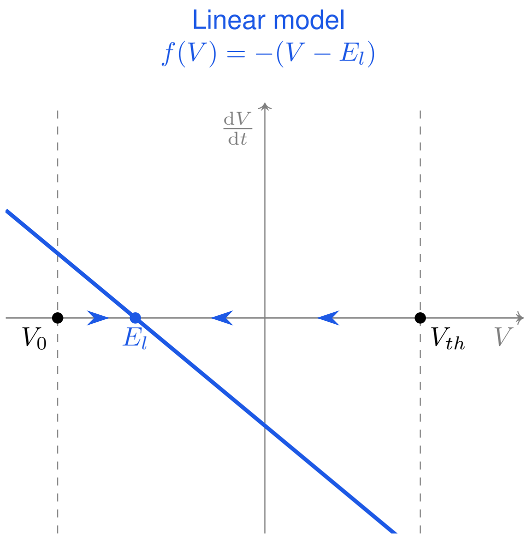
One goal of the bifurcation analysis is to divide the parameter space into regions of *topologically equivalent* systems. Two dynamical systems are considered equivalent when it is possible to establish a mapping between their respective trajectories, preserving the direction of time. In particular, such equivalent systems exhibit the same number of fixed points with the same stability.

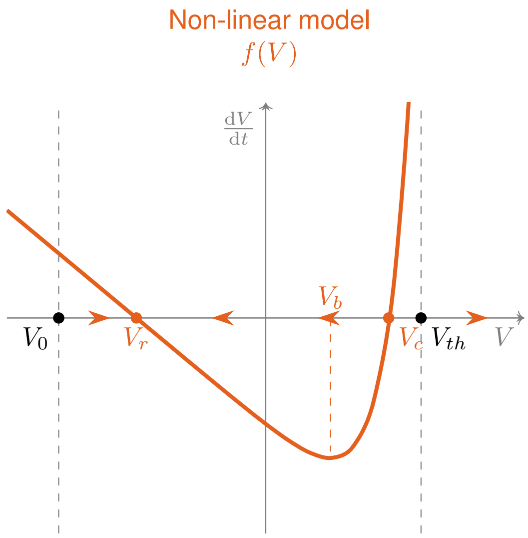
A bifurcation occurs when the equivalence is broken between systems for a critical set of parameters. For instance, the perturbations of one parameter may cause the disappearance of one fixed point, or the conversion of one stable fixed point to an unstable one.

The bifurcation can be visualised in a **bifurcation diagram**, where the axes correspond to the range of variation of the selected parameters (parameter space). Different classes of topologically equivalent systems are identified by distinct areas in the diagram, and the lines delimiting those areas represent the bifurcations at critical parameter values.

1.1 General properties of non-linear models

① *Phase portrait*
Drawing the phase portraits requires to sketch the functions $f(V)$ of those systems as a function of the variable V (assuming $RI = 0$). This function is a straight line for the linear model, and a U-shaped curve for the non-linear model.





② *Fixed points and Stability*

- Linear model – There is a single fixed point at E_l, which is stable because the slope of the function is negative.
- Non-linear model – There are two fixed points at V_r and V_c, respectively stable and unstable.

The state V_r can be interpreted as a *resting state* while the value V_c plays the role of a *critical* potential above which a spike is initiated. Indeed, for any initial condition $V < V_c$, the membrane potential tends to the potential V_r. For $V > V_c$, the membrane potential increases until the threshold V_{th} is reached, which triggers a spike.

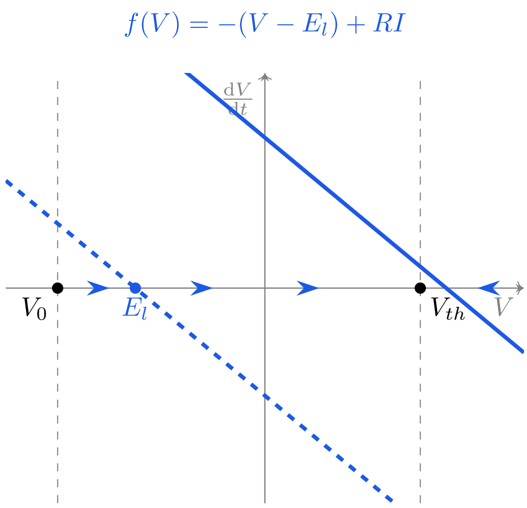
⚠Note : V_c is different from the threshold V_{th} for spike emission itself.

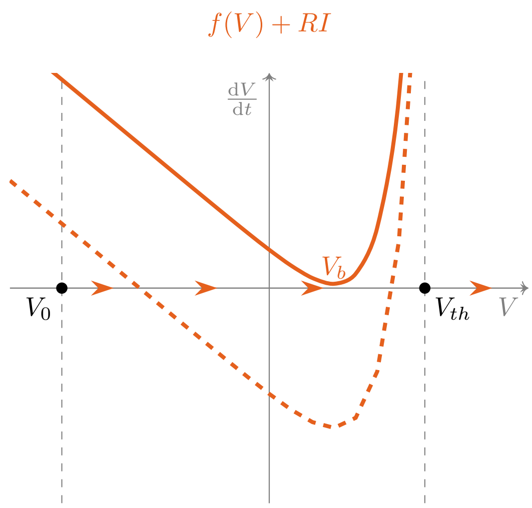
③ *Bifurcations*

Increasing the input current adds an offset RI (constant relative to the variable V) in the expression of the differential equation, which slides the curve F along the vertical axis.

• Linear model – Increasing the input current brings the fixed point closer to the threshold V_{th}, until it crosses it. In this regime, the neuron now fires regularly : because the fixed point is attractive, the membrane potential evolves from V_0 up to reaching V_{th}, then is reset, and reproduces the same trajectory again.

• Non-linear model – Increasing the input current produces a *saddle-node bifurcation* : it brings both fixed points closer to each other, until they fuse at the minimum V_b of the function f. At this stage, the single fixed point is a named *saddle*, because it is attractive at the left and repulsive at the right. Then, keeping increasing the current removes any intersection with the horizontal axis and thus any fixed point. In this regime, the membrane potential fires regularly : it constantly evolves towards the threshold and is reset periodically.





④ *Pulse and Step currents*

Pulse and step current are integrated on different time scales :

- A pulse input current is *strong* and *transient*. In the phase portrait, its effect is to drive a *quasi-instantaneous* upshot of the membrane potential (provided it is sufficiently strong), during a sharp sliding up and down of the derivative curve. When the derivative curve has returned back to its initial state ($I = 0$), the membrane potential has been *perturbed above its initial equilibrium*, and slowly decays towards it.
- A step current is *moderate* and maintained for a *longer period*. In the phase portrait, its effect is to *shift* the derivative curve in a higher position, which allows the membrane potential to adopt a new behavior consistent with this new dynamical equation.

▷[*See question ⑥ for time courses.*]

⑤ *Threshold and Rheobase potentials*

• Linear model – The condition for spiking is similar for both pulse and step currents : it is necessary that the membrane potential is driven to (or above) V_{th}.

- A pulse current should perturb the membrane potential above V_{th} quasi instantaneously.
- A step current should attract the membrane potential towards V_{th} over a longer time scale, by imposing a new equilibrium above V_{th}.

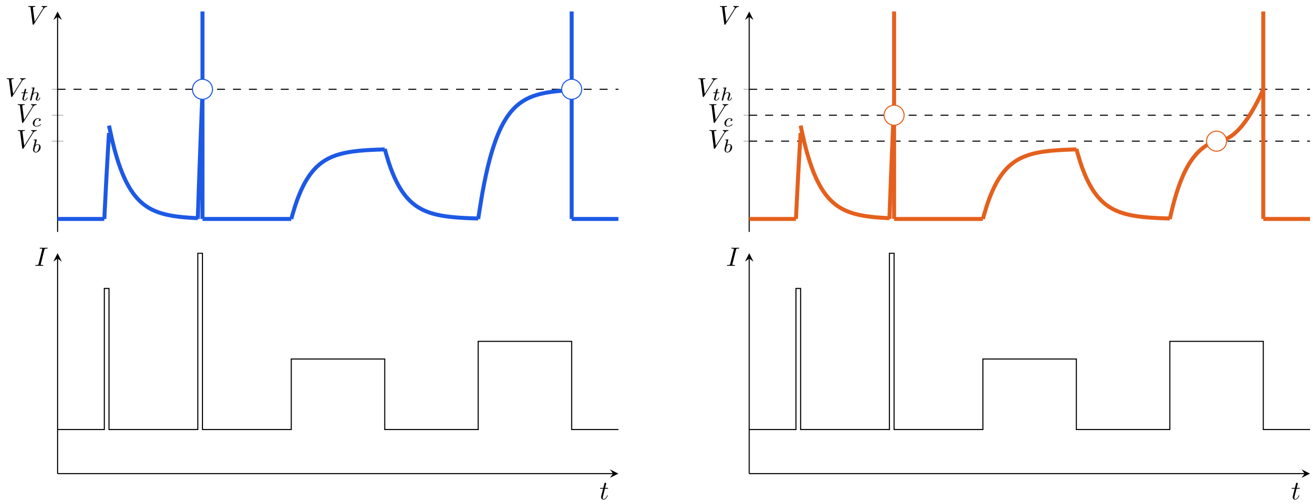
• Non-linear model – The condition for spiking differs for a pulse current and a step current.

- A pulse current should perturb the membrane potential above the V_c. Then the potential is forced to increase up to V_{th} even if the transient current has ceased, because V_c is an *unstable* fixed point in the absence of input ($I = 0$). However, setting the membrane potential below V_c leads to a decay towards V_r.
- A step current should attract the membrane potential above the 'rheobase' potential V_b. Indeed, as soon as the derivative curve is maintained sufficiently high, the system spontaneously evolves towards V_b, crosses it, and then it is forced to increase up to reaching V_{th}. However, if the curve is not sufficiently high, then the system remains trapped at a stable equilibrium below V_b, and thus is prevented from reaching V_{th}.

⑥ *Response time courses*

The following plots illustrate the responses of both models to sub-threshold and supra-threshold pulse and step currents, as predicted by question ⑤.

Note : When the membrane potential does not cross the threshold potential V_{th} for spike emission, it decays exponentially with its time course τ_m. Conversely, when it reaches the threshold potential V_{th} and emits a spike, then it is instantaneously reset at the baseline potential.



1.2 Quadratic Integrate-and-Fire

⑦ *Interpretation of the parameters*

The equation is that of a parabola, which has two crossing points with the abscissa : V_- and V_+, with $V_- < V_+$. Thus, those parameters correspond to the stable and unstable fixed points respectively : $V_- = V_r$ and $V_+ = V_c$.

⑧ *Normal form*

Both equations $\frac{\mathrm{d}V}{\mathrm{d}t} = a(V - V_+)(V - V_-)$ (factorized form) and $\frac{\mathrm{d}V}{\mathrm{d}t} = c(b - b_n) + a(V - V_n)^2$ (canonical form) are the expressions of the same parabola.

The extremum is reached at V_n in the canonical form, which is the middle point between both roots V_- and V_+ in the factorized form :

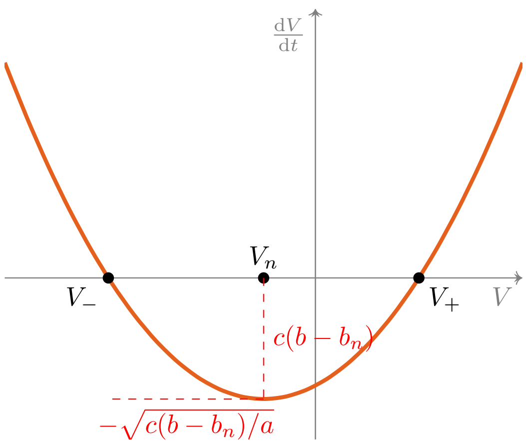
$$V_n = \frac{V_+ + V_-}{2}$$

The roots can also be expressed from the canonical form :

$$c(b-b_n) + a(V-V_n)^2 = 0 \implies V - V_n = \pm\sqrt{\frac{c(b_n-b)}{a}} \implies$$

$$V_- = V_n - \sqrt{\frac{c(b_n-b)}{a}} \text{ and } V_+ = V_n + \sqrt{\frac{c(b_n-b)}{a}}$$

provided $c(b_n - b) > 0$.



Change of variable

The goal is to find a change of variable $v = \phi(V)$ such that the following equations are equivalent :

$$\frac{\mathrm{d}V}{\mathrm{d}t} = c(b - b_n) + a(V - V_n)^2 \quad (1)$$

$$\frac{\mathrm{d}v}{\mathrm{d}t} = \beta + v^2 \quad (2)$$

This change of variable can be looked for under a linear form $v = \alpha(V - V_n)$, with α a normalization constant to be determined.

Change of variable for equivalent differential equations

The goal is to show the equivalence between two differential equations

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

under a change of variable $z = \phi(y)$.

Method 1 : Through the variable z

The idea is to express the derivative of the variable z as a function of the variable y in two manners :

① Replace the variable z by the change of variable in the expression of its derivative : $\frac{\mathrm{d}z}{\mathrm{d}t} = g(z) = g(\phi(y))$.

② Derive the composed function $\frac{\mathrm{d}z}{\mathrm{d}t} = \frac{\mathrm{d}\phi(y)}{\mathrm{d}t} = \frac{\mathrm{d}\phi}{\mathrm{d}y}\frac{\mathrm{d}y}{\mathrm{d}t} = \phi'(y)f(y)$.

③ Show that both expressions are equal, i.e. : $\phi'(y)f(y) = g(\phi(y))$.

Method 2 : Through the variable y

The idea is to express the derivative of the variable y as a function of the variable y itself using the formula of z :

① Derive the composed function $\frac{\mathrm{d}y}{\mathrm{d}t} = \frac{\mathrm{d}y}{\mathrm{d}z}\frac{\mathrm{d}z}{\mathrm{d}t} = \frac{1}{\frac{\mathrm{d}y}{\mathrm{d}z}}g(z) = \frac{1}{\phi'(y)}g(\phi(y))$.

② Reorganize the terms to show that is is equal to the other expression : $\frac{\mathrm{d}y}{\mathrm{d}t} = f(y))$.

Note : Both methods lead to verify the same equality.

Starting from the derivative $\frac{\mathrm{d}v}{\mathrm{d}t}$ (method 1), replacing with the change of variable on the one hand and deriving the change of variable on the other hand leads to :

$$\frac{\mathrm{d}v}{\mathrm{d}t} = \frac{\mathrm{d}\alpha(V-V_n)}{\mathrm{d}t} = \alpha\frac{\mathrm{d}V}{\mathrm{d}t} = \alpha\left(c(b-b_n) + a(V-V_n)^2\right) \qquad = \alpha c(b-b_n) + \alpha a(V-V_n)^2 \tag{3}$$
$$\frac{\mathrm{d}v}{\mathrm{d}t} = \beta + v^2 = \beta + (\alpha(V-V_n))^2 \qquad = \beta + \alpha^2(V-V_n)^2 \tag{4}$$

By identification, it suffices that : $\begin{cases}\alpha a = \alpha^2 \implies \alpha = a \\ \beta = ac(b-b_n)\end{cases}$ to ensure the equivalence.

9 *Qualitative behaviors*

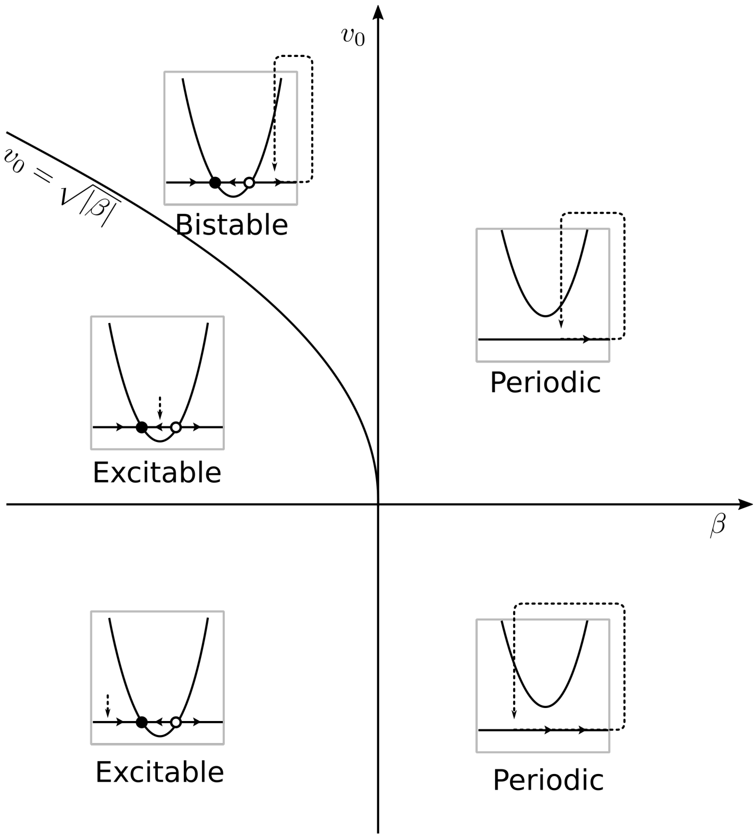
• If $\beta > 0$, then the derivative of V is always strictly positive, thus the system displays periodic oscillations between v_0 and v_{th}.

• If $\beta < 0$, then the derivative is a parabola with two zero-crossing points : $v_\pm = \pm\sqrt{|\beta|}$. The lower is a stable fixed point and the upper is an unstable fixed point. Indeed, this is indicated by computing the slope of the function f at those values :

$$f'(v) = 2v \implies \begin{cases} f'(v_-) = -2\sqrt{|\beta|} < 0 & \text{stable fixed point} \\ f'(v_+) = 2\sqrt{|\beta|} > 0 & \text{unstable fixed point}\end{cases}$$

Three possible behaviors can be observed depending on the position of v_0 relative to the unstable fixed point :

- $v_0 < \sqrt{|\beta|}$ After a reset, the system decays back to the stable fixed point. However, a sufficiently high perturbation can drive it above the unstable point and make it emit a single spike.
  The system is *excitable*.
- $v_0 = \sqrt{|\beta|}$ After a reset, the system lies on the unstable point. A small perturbation can either drive it to spiking or to the stable fixed point.
- $v_0 > \sqrt{|\beta|}$ After a reset, the system displays periodic oscillations as in the case $\beta > 0$. However, a strong (inhibitory) perturbation could set it on the stable fixed point, where it would require a strong (excitatory) perturbation to restart oscillatory spiking.
  The system is *bistable*.



(10) *Bifurcation diagram*

Lines correspond to changes of behaviors :

- A bifurcation occurs at $\beta = 0$ regardless of the value of v_0 which gives a straight vertical line.
- Another bifurcation occurs in the domain $\beta < 0$ for $v_0 = \sqrt{-\beta}$, thus the shape of the bifurcation curve is a square root.

Inserts show the phase portrait parabola depending on β. On the horizontal axis v are spotted the possible fixed points, as well as v_0 (point of the with arrow), whereas v_{th} is at the left border of the insert.

(11) *Quantitative behaviors*

The evolution of the system from a value v_0 during a time t and the period of oscillation T can be computed by integrating the differential equation. The period T of oscillations is the time required to reach v_{th} starting from v_0.

$\boxed{\beta > 0}$ The differential equation can be integrated directly, by the method of the "separation of variables" :

$$\frac{\mathrm{d}v}{\beta + v^2} = \mathrm{d}t \quad \Longrightarrow \quad \int_{v_0}^{v(t)} \frac{\mathrm{d}v}{\beta + v^2} = t \quad \Longrightarrow \quad \frac{1}{\beta} \int_{v_0}^{v(t)} \frac{\mathrm{d}v}{1 + \left(v/\sqrt{\beta}\right)^2} = t$$

With the change of variable $y = v/\sqrt{\beta}$:

$$\begin{cases} v = v_0 \implies y = v_0/\sqrt{\beta} \\ v = v(t) \implies y = v(t)/\sqrt{\beta} \end{cases} \quad \text{and } \mathrm{d}v = \sqrt{\beta}\,\mathrm{d}y$$

$$t = \frac{1}{\sqrt{\beta}} \int_{v_0/\sqrt{\beta}}^{v(t)/\sqrt{\beta}} \frac{\mathrm{d}y}{1 + y^2} = \frac{1}{\sqrt{\beta}} \left[\arctan\left(v(t)/\sqrt{\beta}\right) - \arctan\left(v_0/\sqrt{\beta}\right)\right] = \frac{1}{\sqrt{\beta}} \arctan\left(\frac{v_0 - v(t)}{\sqrt{\beta} + v_0 v(t)/\sqrt{\beta}}\right)$$

The last line results from the identity $\arctan(x) - \arctan(y) = \arctan\left(\frac{x-y}{1+xy}\right)$.

- Evolution of the variable v (obtained by inverting the middle expression) :

$$v(t) = \sqrt{\beta}\ \tan\left(\sqrt{\beta}\ (t + t_0)\right) \text{ with } t_0 = \frac{1}{\sqrt{\beta}} \arctan\left(v_0/\sqrt{\beta}\right)$$

- Period of oscillations (obtained by replacing $t \to T$ and $v(t) \to v_{th}$) :

$$T = \frac{1}{\sqrt{\beta}} \arctan\left(\frac{v_0 - v_{th}}{\sqrt{\beta} + v_0 v_{th}/\sqrt{\beta}}\right) < \frac{\pi}{2\sqrt{\beta}}$$

$\boxed{\beta < 0}$ The differential equation can be integrated after a partial fraction decomposition :

The goal is to decompose the quotient (whose primitive is unknown), in a sum of two fractions whose denominators are linear (whose primitives are logarithms). The denominator can be factorized thanks to a remarkable identity :

$$\frac{1}{v^2 + \beta} = \frac{1}{v^2 - |\beta|} = \frac{1}{(v + \sqrt{|\beta|})(v - \sqrt{|\beta|})}$$

Then, this quotient can be decomposed in a sum of quotients of the form :
$\dfrac{1}{(v+\sqrt{|\beta|})(v-\sqrt{|\beta|})} = \dfrac{\alpha}{v+\sqrt{|\beta|}} + \dfrac{\gamma}{v-\sqrt{|\beta|}}$
The unknowns α and γ can be determined by identification :

$$\frac{\alpha}{v+\sqrt{|\beta|}} + \frac{\gamma}{v-\sqrt{|\beta|}} = \frac{\alpha(v-\sqrt{|\beta|})+\gamma(v+\sqrt{|\beta|})}{(v+\sqrt{|\beta|})(v-\sqrt{|\beta|})} = \frac{v\,\overbrace{(\alpha+\gamma)}^{0}+\overbrace{\sqrt{|\beta|}(\gamma-\alpha)}^{1}}{(v+\sqrt{|\beta|})(v-\sqrt{|\beta|})}$$

$$\begin{cases} \alpha+\gamma = 0 \implies \gamma = -\alpha \\ \sqrt{|\beta|}(\gamma-\alpha) = 1 \implies 2\gamma\sqrt{|\beta|} = 1 \implies \gamma = \dfrac{1}{2\sqrt{|\beta|}} \end{cases}$$

Therefore :

$$t = \int_{v_0}^{v(t)} \frac{\mathrm{d}v}{v^2-|\beta|} = \int_{v_0}^{v(t)} \frac{1}{2\sqrt{|\beta|}}\left(\frac{\mathrm{d}v}{v-\sqrt{|\beta|}} - \frac{\mathrm{d}v}{v-\sqrt{|\beta|}}\right) = \frac{1}{2\sqrt{|\beta|}}\left[\ln\left(\frac{v(t)-\sqrt{|\beta|}}{v(t)+\sqrt{|\beta|}}\right) - \ln\left(\frac{v_0-\sqrt{|b|}}{v_0+\sqrt{|\beta|}}\right)\right]$$

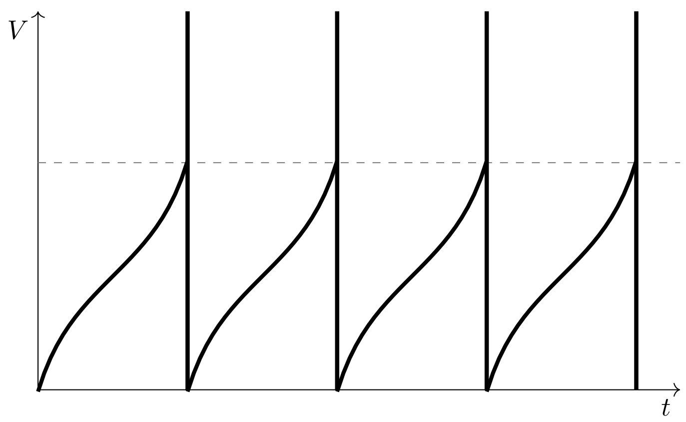
- Evolution of the variable v :

$$v(t) = \sqrt{|\beta|}\,\frac{1+\exp\left(2\sqrt{|\beta|}(t+t_0)\right)}{1-\exp\left(2\sqrt{|\beta|}(t+t_0)\right)} \text{ with } t_0 = \frac{1}{2\sqrt{|\beta|}}\ln\left(\frac{v_0-\sqrt{|\beta|}}{v_0+\sqrt{|\beta|}}\right)$$

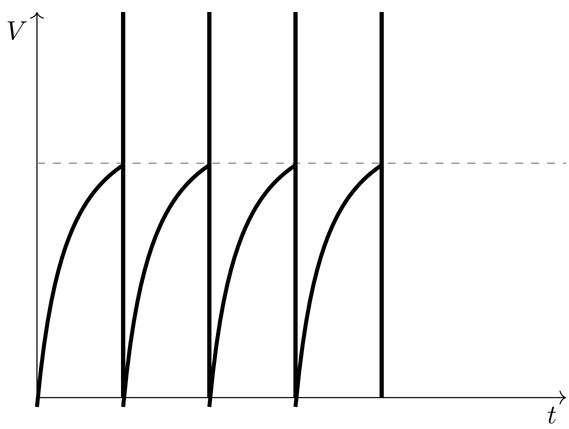
. • Period of oscillations :

$$T = \frac{1}{2\sqrt{|\beta|}}\ln\left(\frac{(v_{th}-\sqrt{|\beta|})(v_0+\sqrt{|\beta|})}{(v_{th}+\sqrt{|\beta|})(v_0-\sqrt{|b|})}\right)$$

$\beta > 0$



$\beta < 0$



1.3 Theta model

12 *Qualitative equivalence*

The fixed points can be determined by canceling the derivative (provided $I \neq 1$) :

$$1-\cos(\theta)+[1+\cos(\theta)]\,I = 0 \implies \cos(\theta)(I-1)+(I+1) = 0 \implies \cos(\theta) = \frac{I+1}{I-1} = \frac{I-1+1+1}{I-1} = 1+\frac{2}{I-1}$$

This equation admits solutions for $1+\dfrac{2}{I-1} \in [-1,1]$ (range of the cosinus). Two cases can be distinguished :

- For $I > 0$:

The expression $1+\dfrac{2}{I-1}$ is minored by 1 (since the fraction is positive). Thus, there is no fixed point in this case.
The derivative is always positive : $1-\cos(\theta)+\underbrace{[1+\cos(\theta)]}_{\geq 0}I \geq 1-\cos(\theta) \geq 0$. Thus, the system increases periodically from θ_0 to θ_{th}.

- For $I < 0$:

The inequality $-1 \leq 1 + \dfrac{2}{I-1} \leq 1$ is fulfilled for $-1 \leq \dfrac{1}{I-1} \leq 0 \implies -(I-1) \geq 1 \implies I < 0$.

Thus, for any negative value of I, there are two fixed points θ_+ and $\theta_- = -\theta_+$ modulo 2π, which verify $\theta_- = -\theta_+$ (see the trigonometric circle). Those two fixed points fuse when $I = -1$ (since $\cos(\theta) = 0$ in this case).

Stability is obtained by examining the derivative with respects to θ at each fixed point :

$$\frac{\mathrm{d}\left(\frac{\mathrm{d}\theta}{\mathrm{d}t}\right)}{\mathrm{d}\theta} = \frac{\mathrm{d}}{\mathrm{d}\theta}\left(1 - \cos(\theta) + [1 + \cos(\theta)]\, I\right) = -\sin(\theta)(I-1)$$

The sign of this derivative is imposed by $\sin(\theta)$ because $-(I-1)$ is always positive for $I < 0$.

The positive fixed point θ_+ has a positive sinus and thus is stable, whereas the negative fixed point θ_- has a negative sinus and thus is unstable.

Conclusion Overall, the system behaves similarly as the Quadratic Integrate-and-Fire model.

13 *Quantitative equivalence*

The goal is to prove the equivalence between the following differential equations :

$$\frac{d\theta}{dt} = 1 - \cos(\theta(t)) + [1 + \cos(\theta(t))]I \tag{5}$$

$$\frac{dv}{dt} = v^2 + \beta \tag{6}$$

Change of variable : $v = \tan(\theta)$

Starting from the derivative $\frac{d\theta}{dt}$ (method 2), and applying the chain rule :

$$\frac{\mathrm{d}\theta}{\mathrm{d}t} = \frac{\mathrm{d}\theta}{\mathrm{d}v}\frac{\mathrm{d}v}{\mathrm{d}t}$$

$$\begin{cases} \dfrac{\mathrm{d}v}{\mathrm{d}t} = \tan^2(\theta) + \beta = \dfrac{\sin^2(\theta)}{\cos^2(\theta)} + \beta \\ \dfrac{\mathrm{d}\theta}{\mathrm{d}v} = \dfrac{1}{\frac{\mathrm{d}v}{\mathrm{d}\theta}} = \dfrac{1}{\frac{1}{\cos^2(\theta)}} = \cos^2(\theta) \end{cases} \implies \frac{\mathrm{d}\theta}{\mathrm{d}t} = \cos^2(\theta)\left(\frac{\sin^2(\theta)}{\cos^2(\theta)} + \beta\right) = \sin^2(\theta) + \beta\cos^2(\theta)$$

The squared cosine and sine can be replaced by their linear expressions (equation (9)), which gives :

$$\frac{d\theta}{dt} = \sin^2(\theta) + \beta\cos^2(\theta) = \frac{1-\cos(2\theta)}{2} + \beta\frac{1+\cos(2\theta)}{2} \implies \frac{\mathrm{d}2\theta}{\mathrm{d}t} = (1 - \cos(2\theta)) + \beta(1 + \cos(2\theta))$$

Reorganizing with a new change of variable $\widehat{\theta} = 2\theta$ and with $\beta = I$, the differential equation is that of the theta model :

$$\frac{\mathrm{d}\widehat{\theta}}{\mathrm{d}t} = (1 - \cos(\widehat{\theta})) + (1 + \cos(\widehat{\theta}))I$$

Note : Method 1 also works, by expressing $\cos(\theta) = 2\cos(\theta/2)$ *and by using the relations* $\tan(\theta) = 1 + \tan^2(\theta)$, $\tan(\theta) = \frac{\sin(\theta)}{\cos(\theta)}$ *and* $\cos^2(\theta) + \sin^2(\theta) = 1$.

Method – Linearizing powers of trigonometric functions

The squared sine and cosine can be linearized thanks to trigonometric relations, which can be obtained through complex exponentials :

$$(e^{i\theta})^2 = (\cos(\theta) + i\sin(\theta))^2 = \cos^2(\theta) - \sin^2(\theta) + i2\cos(\theta)\sin(\theta) \tag{7}$$

$$(e^{i\theta})^2 = e^{i2\theta} = \cos(2\theta) + i\sin(2\theta)) \tag{8}$$

Equating the real parts provides $\cos(2\theta) = \cos^2(\theta) - \sin^2(\theta) = \cos^2(\theta) - (1 - \cos^2(\theta)) = 2\cos^2(\theta) - 1$
Thus the squared cosine and sine express as follow :

$$\cos^2(\theta) = \frac{1 + \cos(2\theta)}{2} \tag{9}$$

$$\sin^2(\theta) = 1 - \cos^2(\theta) = \frac{1 - \cos(2\theta)}{2} \tag{10}$$

(14) *Response to a slow wave current*

The slow wave input current takes both negative and positive values.

- When $\alpha t \in [0, \pi]$, the input $I(t)$ is strictly positive and therefore the variable θ makes multiple passes through the threshold π, resulting in multiple spikes (bursting).
- When $\alpha t \approx 0$ or $\alpha t \approx \pi$, the theta neuron spikes at relatively a low frequency.
- When $\alpha t \approx \pi/2$ the theta neuron spikes with high frequency.
- When $\alpha t \in [\pi, 2\pi]$, the theta neuron no longer bursts, since the inter-spike interval is infinite, and θ can no longer pass through the threshold π.

1.4 Exponential Integrate-and-Fire

(15) *Condition over the parameters for the existence of a fixed point*

The function $\frac{\mathrm{d}V}{\mathrm{d}t}$ admits a minimum, which is reached for $V = \mathcal{V}$. Indeed :

$$\frac{\mathrm{d}\left(\frac{\mathrm{d}V}{\mathrm{d}t}\right)}{\mathrm{d}V} = -1 + \Delta_T \frac{1}{\Delta_T} \exp\left(\frac{V - \mathcal{V}}{\Delta_T}\right) = 0 \implies \exp\left(\frac{V - \mathcal{V}}{\Delta_T}\right) = 1 \implies V = \mathcal{V}$$

For the existence of a fixed point, the function $\dfrac{\mathrm{d}V}{\mathrm{d}t}$ should cancel at least once, therefore it requires that $\mathcal{V} \leq 0$. As this condition on this parameter is necessary and sufficient to ensure the existence of fixed point, it explains why it is called a "critical potential".

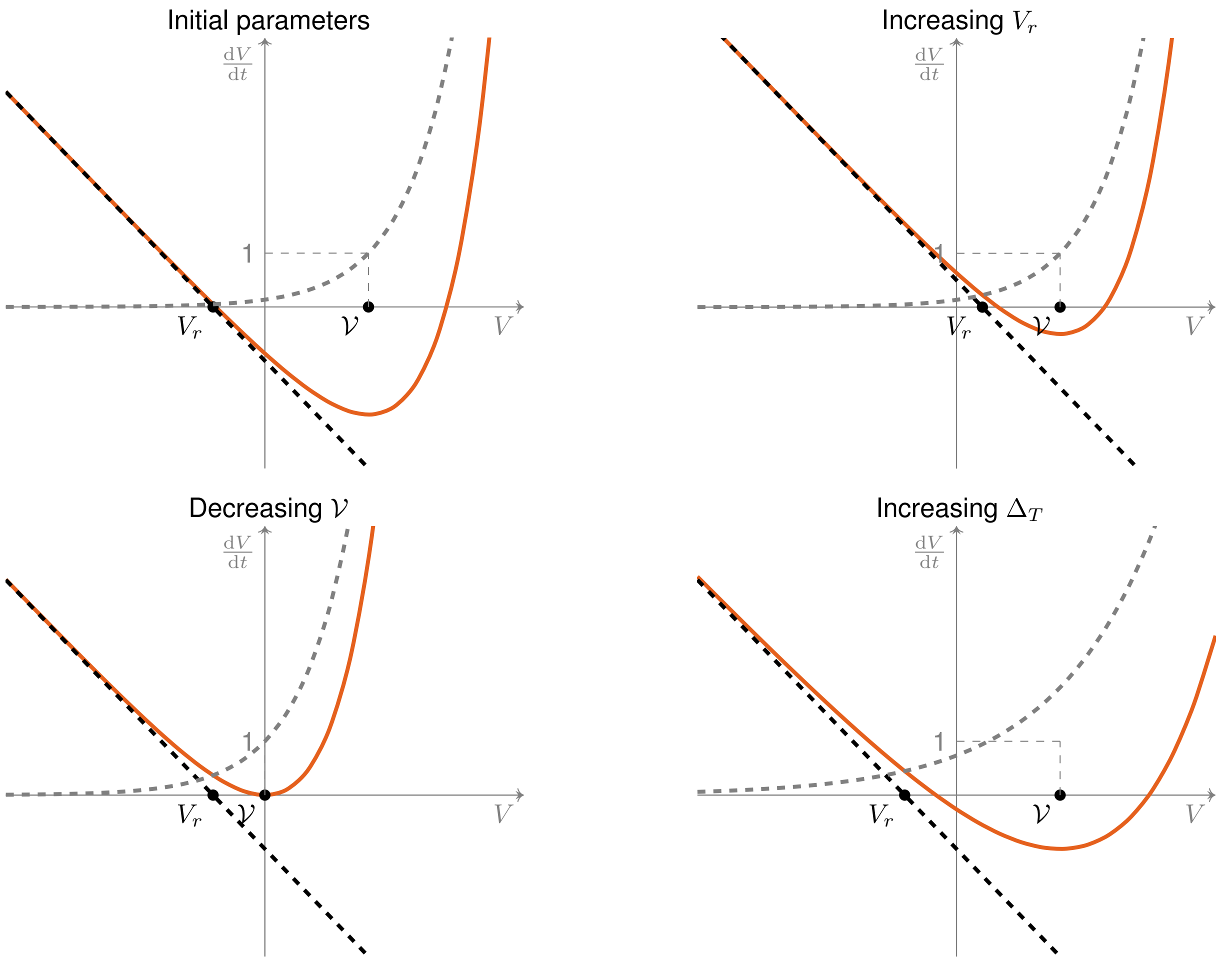
Fixed point near V_r

Fixed points are characterized by the cancellation of the derivative. At the value V_r, the linear term cancels, while the hypotheses on the parameters imply that the exponential term is negligible : $\mathcal{V} \gg V_r + \Delta_T \implies V_r - \mathcal{V} \ll -\Delta_T$:

$$-(V_r - V_r) + \Delta_T \exp\left(\underbrace{\frac{V_r - \mathcal{V}}{\Delta_T}}_{\ll -1}\right) = 0 + \Delta_T\, o(1) \approx 0$$

(16) *Influence of the parameters*

- The parameter $\mathcal{V}$ determines the location of the minimum of the function f. It conditions the existence of equilibria.
- The parameter V_r is the zero-crossing point of the *linear term*. It influences position of the equilibria (if they exist) : by sliding up the function f, the both crossing points of f go closer or farther from the minimum of the function.
- The parameter Δ_T rescales the exponential term, shaping its sharpness. It also modulates the position of the equilibria.



17 *Rescaling of the non-linear function*

The differential equation can be rewritten by moving the function f to the left-hand side and all other terms to the right-hand-side of the equation, and rescaling with the time constant τ :

$$\tilde{f}(V) = \frac{1}{\tau} f(V) = \frac{1}{C_m} I(t) - \frac{\mathrm{d}}{\mathrm{d}t} V(t) \text{ with } C = \frac{\tau}{R}$$

18 *Fitting to data*

Experimental times courses of $V(t)$ and $I(t)$ would contain a set of sample points.

Tracing the exprimental non-linearity thus requires :

- Computing a discrete approximation of the derivative $\frac{\mathrm{d}}{\mathrm{d}t} V(t)$, by substracting successive recorded values and dividing by the sampling time step.
- Plotting the experimental graph $t \mapsto \frac{1}{C_m} I(t) - \frac{\mathrm{d}}{\mathrm{d}t} V(t)$.
- Fitting the obtained graph with a function of the form of the Exponential Integrate-and-Fire model.

2 Adaptive Generalized Integrate-and-Fire (2 variables)

2.1 Adaptive Leaky Integrate-and-Fire model

2.1.1 Neglecting the decay of the adaptation variable

19 *Modification after the first spike*

After the first spike, the adaptation variable w is increased by Δ_w. The equilibrium $V^* = I - w$ is shifted down, from I to $I - \Delta_w$, and thus becomes closer to V_{th}.

20 *Spiking stop*

The neuron stops spiking when the equilibrium is brought *below* V_{th}, which happens for :

$$I - w < V_{th} \implies w > I - V_{th}$$

Number of spikes emitted
Starting from $w = 0$, the adaptation variable reacches a value $w = k\Delta_w$ after k spikes, and crosses the critical value for :

$$k \sim \frac{I - V_{th}}{\Delta_w}$$

21 *Duration of an inter-spike interval*

The period is the time T_{ISI} required to go from $V_0 = 0$ to V_{th}. During an inter-spike interval, the membrane potential evolves according to the classical leaky first-order linear differential equation, with w constant by assumption (see below). The period can be found by integrating this differential equation from $t = 0$ to T_{ISI} and $V_0 = 0$ to V_{th}.

$$\tau_m \frac{\mathrm{d}V}{\mathrm{d}t} = -V - w + I = -(V - (I - w)) \implies \frac{\mathrm{d}V}{V - (I - w)} = -\frac{\mathrm{d}t}{\tau_m} \implies \int_0^{V_{th}} \frac{\mathrm{d}V}{V - (I - w)} = -\int_0^T \frac{\mathrm{d}t}{\tau_m}$$

$$\ln\left(\frac{V_{th} - (I - w)}{-(I - w)}\right) = -\frac{T}{\tau_m} \implies T = \tau_m \ln\left(\frac{I - w}{I - w - V_{th}}\right)$$

This expression is valid for $w > I - V_{th}$, which is once again the condition for spiking found at question 20.
Note : Signs are correct as the equilibrium is above the threshold : $I - w > V_{th} > V_0 = 0$*, consequently* $I - w > I - w - V_{th}$*, which implies that the quotient is above 1 and the logarithm is positive.*

2.1.2 Taking decay into account

22 *Condition for valid approximation*

The decay of the variable w becomes significant when the inter-spike interval becomes comparable to the time constant of the decay τ_w, such that w cannot be considered constant anymore.
This necessarily happens because the inter-spike-interval becomes progressively longer as w is incremented after each spike. Indeed, the analysis above shows that the neuron may stop spiking, which would correspond to an infinite inter-spike interval.

23 *Time course of w between two successive spikes*

Between two spikes, the evolution of the variable w follows a classical linear differential equation without independent term (δ functions cancel as no spike is emitted during this period).

$$\tau_w \frac{\mathrm{d}w}{\mathrm{d}t} = -w \implies w(t) = w_0 \cdot e^{-\frac{t}{\tau_w}}$$

24 *Relation between w_0 and Δ_w*

The stationarity of the firing rate imposes that the variable w also evolves periodically. The adapatation variable starts from w_0 just after a spike, and decays until the next spike is emitted at $t = T$. Applying the expression of its evolution during an inter-spike interval (question 23) leads to its new value at the end of the period (just before the next spike) :

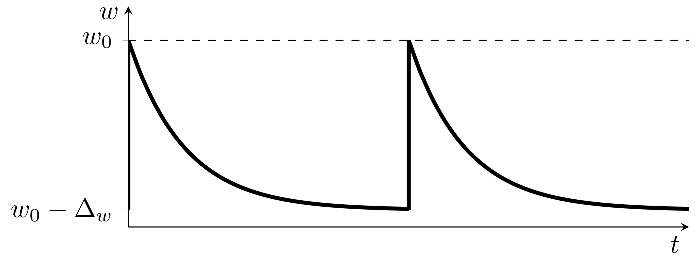
$$w(t = T^-) = w_0 \cdot e^{-\frac{T}{\tau_w}}$$

After the next spike, w is incremented by Δ_w again, which has to reset it at w_0 by stationarity :

$$w(t = T^-) + \Delta_w = w_0 \implies w(t = T^-) = w_0 - \Delta_w$$

Equating both expressions yields :

$$w_0 - \Delta_w = w_0 \cdot e^{-\frac{T}{\tau_w}} \implies w_0 = \frac{\Delta_w}{1 - e^{-T/\tau_w}}$$



25 *Period of spike emission*

The average value of the variable w over an inter-spike interval is obtained by integrating its expression over the interval ('summing' its values on each infinitely small time step $\mathrm{d}t$) and dividing by the length of the time interval :

$$\langle w \rangle_{ISI} = \frac{1}{T} \int_0^T w(t)\,\mathrm{d}t = \frac{w_0}{T} \int_0^T e^{-t/\tau_w}\,\mathrm{d}t = \frac{\tau_w}{T} \cdot w_0 (1 - e^{-t/\tau_w})$$

Using the relation found at question 24 :

$$\langle w \rangle_{ISI} = \frac{\tau_w}{T}\,\Delta_w$$

With this expression for w in the formula from question(21), the duration of the inter-spike interval rewrites :

$$T = \tau_m \ln\left(\frac{I - \langle w \rangle_{ISI}}{I - \langle w \rangle_{ISI} - V_{th}}\right) = \tau_m \ln\left(\frac{I - \frac{\tau_w}{T}\Delta_w}{I - \frac{\tau_w}{T}\Delta_w - V_{th}}\right)$$

26 *Asymptotic behavior of the firing rate*

The goal is to show that the firing rate is equivalent to a multiple of the input current when the latter increases to ∞ :

$$r(I) = \frac{1}{T} \underset{I \to \infty}{\sim} \lambda I, \text{ with } \lambda \in \mathbb{R}\backslash\{0\}$$

To determine the constant λ (and to check that this hypothetical equivalent above is correct), it is useful to replace the expression of T in the implicit formula and to use equivalents when $I \to \infty$:

$$\frac{1}{\lambda I} \sim -\tau_m \ln\left(1 - \frac{V_{th}}{I - \tau_w \Delta_w I}\right) = -\tau_m \ln\left(1 - \frac{V_{th}}{I(1 - \tau_w \Delta_w)}\right)$$

The quotient in the logarithm tends to 0 when $I \to \infty$, which leads to use the limited development at the first order of the form $\ln(1 + h) = h + o(h)$ with $h \to 0$.

$$\frac{1}{\lambda \cancel{I}} \sim \tau_m \frac{V_{th}}{\cancel{I}(1 - \tau_w \Delta_w \lambda)}$$

The simplification of I validates the hypothesis of the equivalent of the order $\frac{1}{I}$. (Note : It would not have been the case for other hypothetical equivalents, such as $\frac{1}{T} \underset{I \to \infty}{\sim} \lambda$ or $\frac{1}{T} \underset{I \to \infty}{\sim} \lambda I^2$ for instance).

From now on, the value of λ can be set :

$$\frac{1}{\lambda} = \frac{\tau_m V_{th}}{1 - \tau_w \Delta_w \lambda} \implies \frac{1}{\lambda}(1 - \tau_w \Delta_w \lambda) = \tau_m V_{th} \implies \frac{1}{\lambda} = \tau_m V_{th} + \tau_w \Delta_w \implies \lambda = \frac{1}{\tau_m V_{th} + \tau_w \Delta_w}$$

Conclusion The linear asymptotic behavior of the firing rate as a function of I is given by :

$$\boxed{r(I) = \frac{1}{T} \sim \frac{I}{\tau_m V_{th} + \tau_w \Delta_w}}$$

27 *Comparison with the integrate-and-fire model without adaptation*

Without firing rate adaptation, the parameter Δ_w can be set to 0 in the previous developments :

$$r(I) \sim \frac{I}{\tau_m V_{th}}$$

Thus, adaptation reduces of the firing rate by adding a term in the denominator, proportional to the gain Δ_w and the decay constant τ_w of the inhibitory current. This seems biologically plausible : a more intense the inhibitory current which persists longer results in a stronger the reduction in the neuronal activity.

2.2 Adaptive Exponential Integrate-and-Fire

Method – Phase plane analysis for a two-dimensional system

The dynamical system analysis described previously for a one-dimensional system can be extended to predict the behavior of *couples variables*. A two-dimensional system is defined by two differential equations of the form :

$$\frac{\mathrm{d}x}{\mathrm{d}t} = F(x, y)$$
$$\frac{\mathrm{d}y}{\mathrm{d}t} = G(x, y)$$

Phase diagram

With a two-dimensional system, *two time derivative functions* have to be represented simultaneously, and both are functions of *two variables*. Therefore, the appropriate graph has two axes corresponding to *both variables* x and y (instead of one axis for one variable and one axis for its time derivative function).

In this graph, each point stands for one possible state of the system (i.e. a couple of values (x, y)).

The time derivatives can be represented by a *vector field*, indicating in each possible state the direction of the system's evolution. The projections of each vector along the axes of both variables reflect the magnitude and the sign of their respective derivatives. In summary, each vector collects both time derivatives in a given state (x, y) and is anchored at this state.

$$\vec{v}(x, y) = \begin{pmatrix} \frac{\mathrm{d}x}{\mathrm{d}t}(x, y) \\ \frac{\mathrm{d}y}{\mathrm{d}t}(x, y) \end{pmatrix}$$

Nullclines and Fixed points

The *nullclines* of the system are the two curves along which one derivative cancels. The nullcline for the variable x (resp. y) is defined by the set of points (x, y) where $F(x, y) = 0$ (resp. $G(x, y) = 0$).

In the diagram, the nullclines can be plotted because each equation of the differential system leads to a relation between the variables y and x :

$$\begin{cases} F(x, y) = 0 \implies y = f(x) \\ G(x, y) = 0 \implies y = g(x) \end{cases}$$

Fixed points correspond to states at which both derivatives cancel. Therefore, they are spotted by the *intersections* between the two nullclines.

Vector field of the system and Trajectories

Each area delimited by the nullclines corresponds to one type of behavior, because the time derivatives hold a *constant sign*. The signs of the derivatives in each area can be determined by solving separately the inequalities $F(x, y) > 0$ or $G(x, y) > 0$.

The possible trajectories of the system in the states' space can be visualised by following the vectors. *Along the nullclines*, the vectors of the time derivatives are parallel to the axes, as one of the derivative cancels.

(28) *Phase plane diagram*

- Nullclines

With the system defining the Adaptive Exponential Integrate-and-Fire model, the nullclines are given by :

$$\begin{cases} \dfrac{\mathrm{d}V}{\mathrm{d}t} &= 0 \\ \dfrac{\mathrm{d}w}{\mathrm{d}t} &= 0 \end{cases} \implies \begin{cases} Rw &= -(V - V_r) + \Delta_T \exp\left(\dfrac{V - \mathcal{V}}{\Delta_T}\right) + RI \\ w &= a(V - V_r) \end{cases} \tag{11}$$

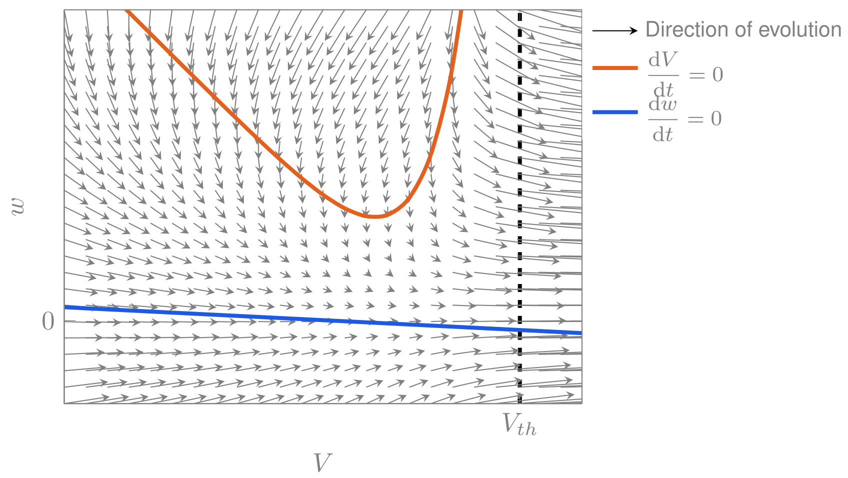
The w-nullcline is a linear function of slope a, while the V-nullcline has a shape similar to the non-linear function of the Exponential Integrate-and-Fire model, shifted upwards by an input RI.

- Vector field

$$\begin{cases} \dfrac{\mathrm{d}V}{\mathrm{d}t} &> 0 \\ \dfrac{\mathrm{d}w}{\mathrm{d}t} &> 0 \end{cases} \implies \begin{cases} -(V - V_r) + \Delta_T \exp\left(\dfrac{V - \mathcal{V}}{\Delta_T}\right) - Rw + RI &> 0 \\ a(V - V_r) - w &> 0 \end{cases} \tag{12}$$

$$\implies \begin{cases} Rw &< -(V - V_r) + \Delta_T \exp\left(\dfrac{V - \mathcal{V}}{\Delta_T}\right) + RI \\ w &< a(V - V_r) \end{cases} \tag{13}$$

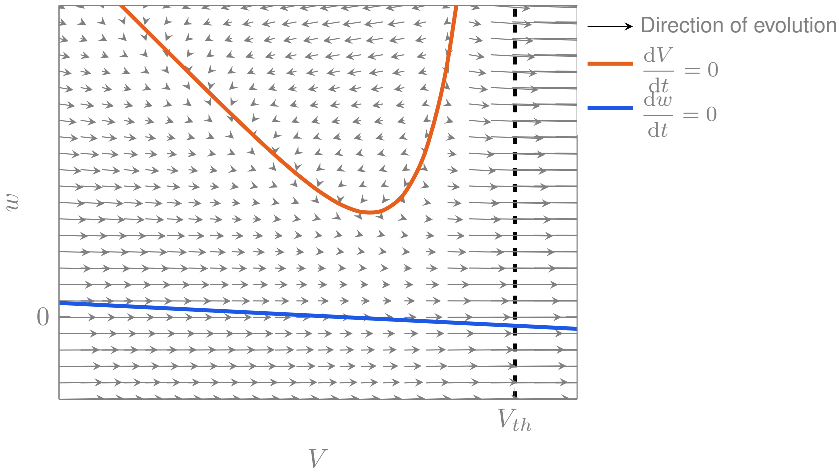
Along the V-nullcline, the vector field is parallel to the w-axis (because $\frac{\mathrm{d}V}{\mathrm{d}t} = 0$) and oriented towards *lower* values of V (because w is *above* its own w-nullcline, such that $\frac{\mathrm{d}w}{\mathrm{d}t} < 0$ according to the second inequality (12)).
Along the w-nullcline, the vector field is parallel to the V-axis (because $\frac{\mathrm{d}w}{\mathrm{d}t} = 0$) and oriented towards *higher* values of V.



(29) *Separation of time scales*

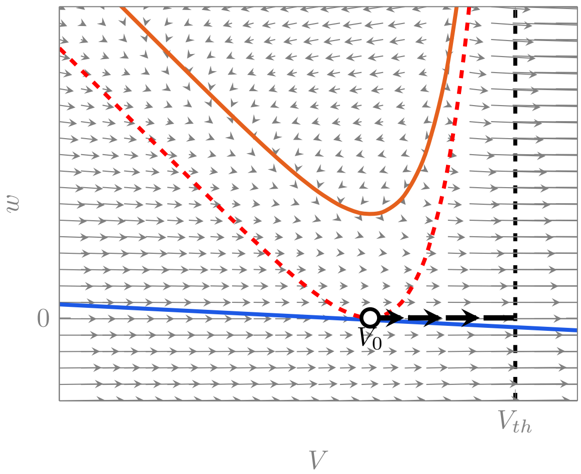
The assumption of the separation of time scales $\tau_m \ll \tau_w$ entails that the adaptation variable reacts much slower than the membrane potential. As a first approximation, the variable w can be considered to remain near constant when V evolves. In the phase diagram, this translates by roughly horizontal trajectories (i.e. evolution along the variable V), except in the surround of the V-nullcline (where the derivative of V cancels, by definition).

In particular, all trajectories which start at a value w below the trough of the V-nullcline stay horizontal and pass unperturbed below the V-nullcline ▷[*see question (31).*]



30 *Initial point and trajectory*

Initially, the membrane potential is in its resting state V_r (stable fixed point before any current is injected, according to question 15) and the adaptive variable is inactive ($w_0 = 0$). As soon as current is applied, the resting state is no more a fixed point, thus the membrane potential increases. According to the separation of timescales (question 29), the trajectory is roughly a straight line up to reaching the threshold V_{th}, which produces a first spike.

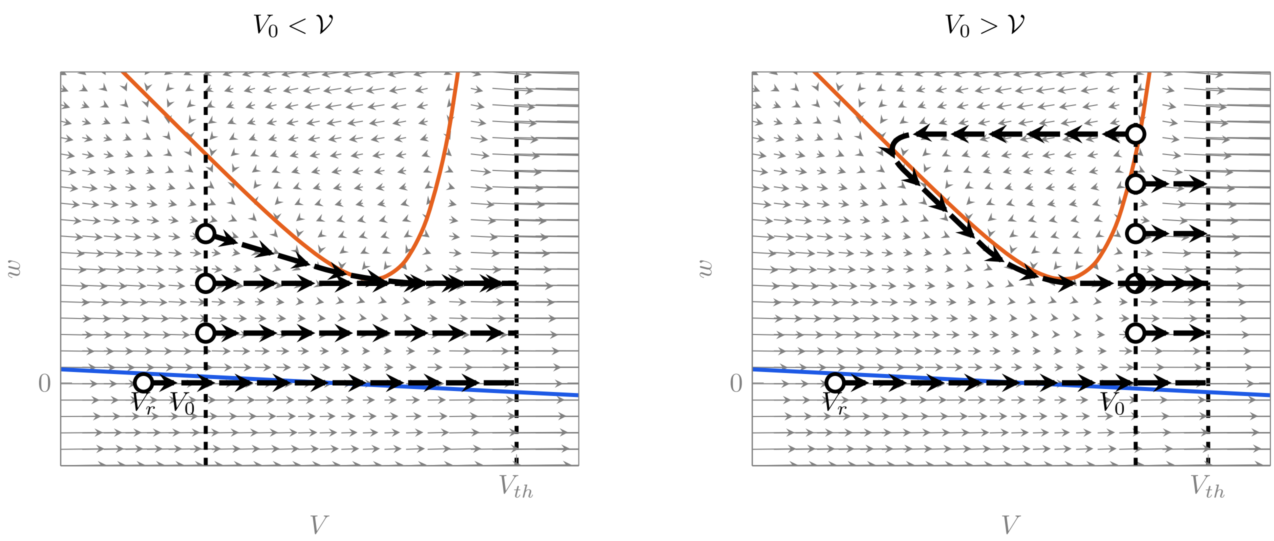


31 *Multiple trajectories and resets*

After each spike, the adaptation variable w is incremented by an amount Δ_w, which slides the reset point w_0 along the vertical axis of abscissa V_0.

- In the case $V_0 < \mathcal{V}$, successive trajectories tend to evolve horizontally, converge at the extremum of the V-nullcline, and reach V_{th}. This process ends up in a stationary behavior where trajectories all reach the same point (V_{th}, w^*) and are all reset at the same point $(V_0, w^* + \Delta_w)$.

- In the case $V_0 > \mathcal{V}$, there is one moment at which a trajectory starts above the V-nullcline, in the most rightwards part of the inner area in which $\frac{dV}{dt} < 0$. Therefore, it makes an excursion towards lower values, until it comes closer to the other branch of the V-nullcline. Here, V evolves slower, and the decay of the variable w becomes the most significant. The trajectory thus crosses the V-nullcline and keeps evolving along it, until it goes beyond the extremum of the V-nullcline, and ends up in a straight line up to the threshold V_{th}. This process can repeat again.



(32) *Firing patterns*

- In the case $V_0 < \mathcal{V}$, the membrane potential reaches a steady, regular firing activity, which gives rise to a *tonic firing pattern*.

- In the case $V_0 < \mathcal{V}$, the membrane potential alternates between two kinds of behaviors : periods of regular firing (emission of several spikes in close temporal succession) are interrupted by longer periods without spike (during the excursion of the variable V). This gives rise to a *bursting firing pattern*.