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

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

1.1 General properties of non-linear models

Method – Dynamical systems analysis for a one-dimensional system

The goal of dynamical systems analysis is to predict the qualitative properties of a one-dimensional system, even when its differential equations cannot be solved analytically. Specifically, a basic investigation of the system's behavior involves finding its fixed points (equilibria), their stability, identifying the different dynamical regimes that the system could adopt according to its initial conditions, and the bifurcations of the system, i.e. transitions in behaviors induced by variations in the parameters (detailed below). This analysis can be carried out graphically and/or with more rigorous computations.

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

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

The appearance of the variable y itself in the function F entails that the dynamics of the system depends on its own state at any time point, thus the goal is to predict how the system evolves in each possible state.

Phase portrait

A phase portrait is a graph which displays the function F as a function of the variable y.

Fixed points

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

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

Computationally, finding fixed points requires to solve the equation $F(y) = 0$ with unknown y.

Graphically, 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 is given by the slope of the time derivative curve at the 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 evolve to *higher* states, bringing it *closer* to the fixed point, and conversely a small deviation *above* the fixed point will lead the system to evolve to *lower* states, 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 between both sides of the fixed point compared to the previous case. Thus, a small deviation *below* the fixed point will lead the system to evolve to even *lower* states, *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.

More rigorously, 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 $y^* + \delta y$ which reflects a small perturbation (with δy small). At the first order :

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

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 the latters' 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 the latter's dampening towards the equilibrium.

⚠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 : $F' = \frac{\mathrm{d}}{\mathrm{d}y}\left(\frac{\mathrm{d}F}{\mathrm{d}t}\right)$.

Bifurcations

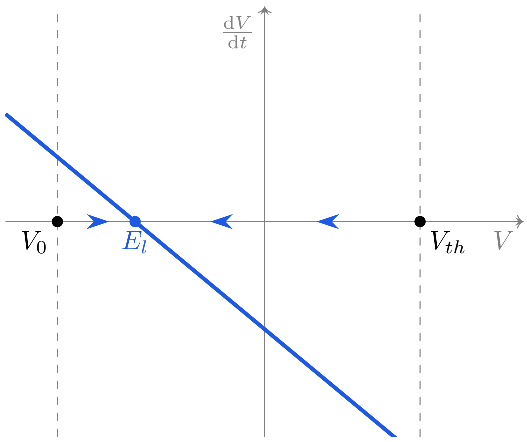
A bifurcation is a qualitative change in the system's dynamics produced by varying parameters. One goal of the bifurcation analysis is to divide the parameter space into regions of *topologically equivalent* systems. Dynamical systems are considered equivalent when it is possible to establish a mapping 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.

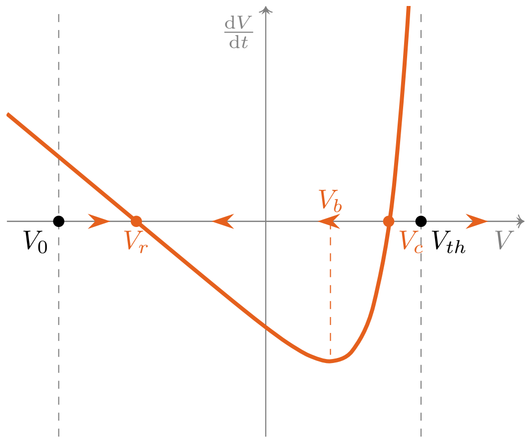
A bifurcation occurs when the equivalence is broken between systems beyond a critical set of parameters. For instance, the perturbations of one parameter may cause the disappearance of one fixed point, or the conversion of one stable fixed point to an unstable one.

In a *bifurcation diagram*, the axes correspond to selected parameters which can be continuously varied, producing a 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 *Phase portrait*

Drawing the phase portraits requires to sketch the functions $f(V)$ of those systems as a function of the variable V (assuming $RI = 0$) : 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 a negative constant.

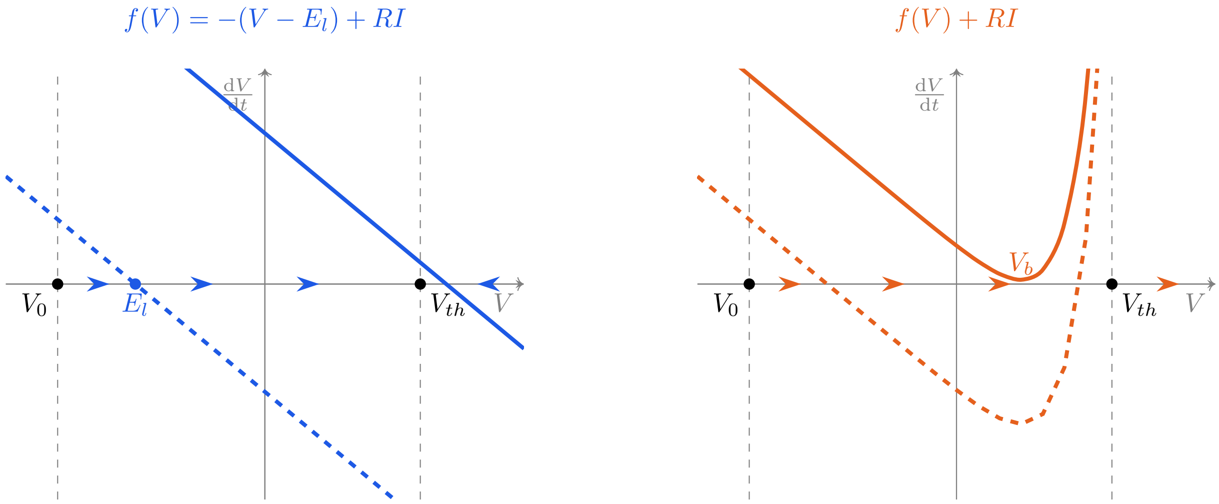
• Non-linear model – There are two fixed points at V_r and V_c, respectively stable and unstable.
The state V_r can be interpreted as a *resting state*, while the value V_c plays the role of a *critical* potential above which a spike will be initiated. Indeed, for any initial condition $V < V_c$, the membrane potential necessarily tends to the potential V_r. For $V > V_c$, the membrane potential increases so that the threshold V_{th} can be reached and a spike is triggered (however, V_c is not the same as the threshold V_{th} for spike emission itself).

③ *Bifurcation*

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 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 case, 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. Thus the neuron fires regularly.

• Non-linear model – Increasing the input current 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 *saddle*, because it is attractive at the left and repulsive at the right. The fusion of two fixed points in a single saddle fixed point is named a *saddle-node bifurcation*. Keeping increasing the current removes any intersection with the horizontal axis and thus any fixed point. The membrane potential 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 available *transiently*, it is integrated fast and drives a *quasi-instantaneous* upshot of the membrane potential (provided it is sufficiently strong). In the phase portrait, its effect is to *set the membrane potential to a higher value quasi-immediately*, during a transient and sharp sliding up of the derivative curve. The derivative curve immediately returns back to its initial state (at which $I = 0$) because the applied current does not persist. However, the membrane potential is let *perturbed above its initial equilibrium*, as it does not follow as fast as the current switch. Therefore, it slowly decays towards its initial equilibrium.

- A step current is *moderate* and available for a *longer period*, which lets time for the membrane potential to integrate it. In the phase portrait, its effect is to *maintain* the derivative curve in a slided 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 – For the emission of a spike, it is necessary that the membrane potential is driven at (or above) V_{th}, for both pulse and step currents.

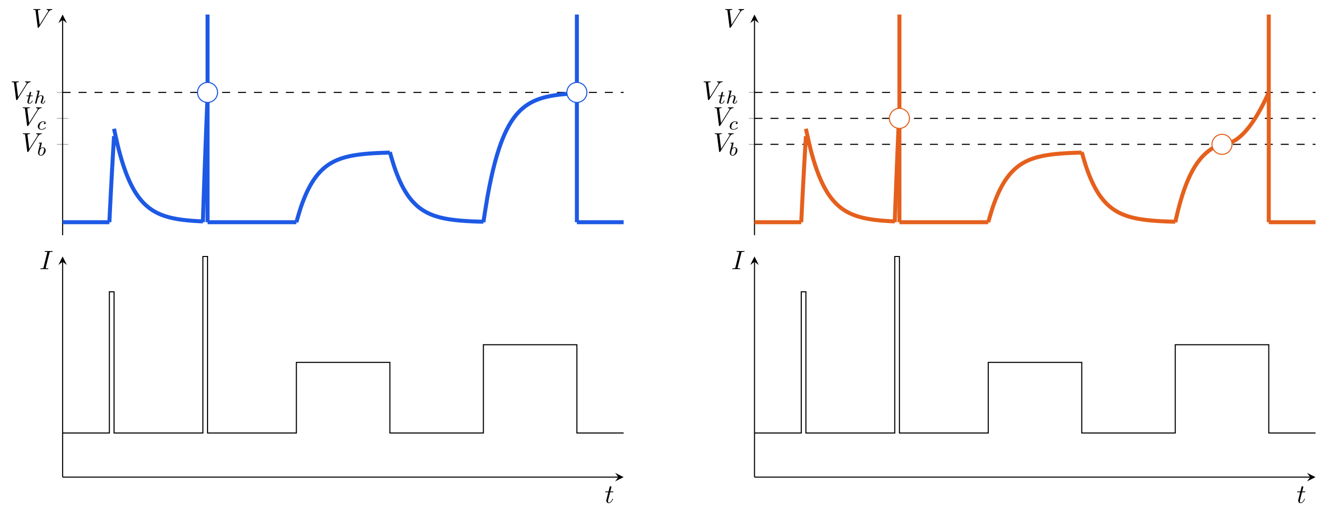
- A pulse current can set the membrane potential at V_{th} quasi instantaneously (while the theoretical equilibrium implied by this strong current is never reached).
- A step current can attract the membrane potential towards V_{th} over a longer time scale, by imposing and maintaining a new equilibrium above V_{th}.

• Non-linear model – For the emission of a spike, conditions differ for a pulse current and a step current.

- In response to a pulse current, it is necessary to set the membrane potential above the unstable fixed point V_c. Then the potential is forced to increase up to reaching V_{th}, even if the transient current has ceased, because this fixed point is unstable in the absence of input ($I = 0$). However, setting the membrane potential below V_c leads to a decay towards V_r.
- In response to a step current, it is necessary to drive the membrane potential above the 'rheobase' potential V_b. Indeed, as the derivative curve is maintained in an upper state by the persistant current, the state V_b is a saddle point. The system spontaneously evolves towards V_b, and if it crosses it, then it is forced to increase up to reaching V_{th}. However, if the curve is not sufficiently slided upwards, 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 crosses the potential threshold V_{th} for spike emission, it decays exponentially with its time course τ_m. Converselty, when it reach the potential threshold V_{th} and emits a spike, it is instantaneously reset at the baseline potential.



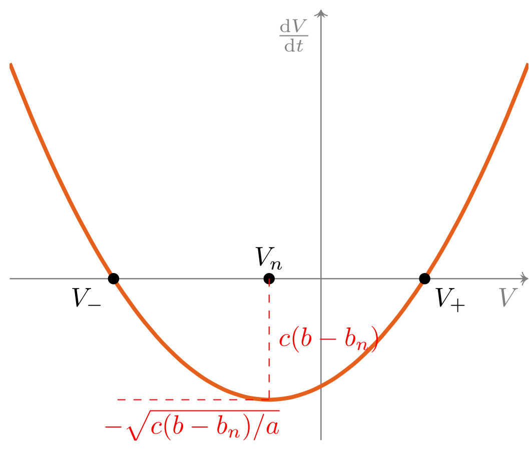
1.2 Quadratic Integrate-and-Fire

⑦ *Interpretation of the parameters*
For $I = 0$, those parameters correspond to the stable and unstable fixed points respectively : $V_- = V_r$ and $V_+ = V_c$.

⑧ *Normal form*
Both equations $\frac{\mathrm{d}V}{\mathrm{d}t} = c(b - b_n) + a(V - V_n)^2$ (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 according to 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 are also given in the canonical form by $c(b - b_n) + a(V - V_n)^2 = 0$, hence (provided $\frac{c(b_n - b)}{a} > 0$) :
$V_- = V_n - \sqrt{\frac{c(b_n-b)}{a}}$ and $V_+ = V_n + \sqrt{\frac{c(b_n-b)}{a}}$.



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

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

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 for the equations to be equivalent.

Change of variable for equivalent differential equations

Several methods are available 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 $z = \phi(y)$.

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, and to equate those two formulas :

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 Identify both expressions.

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 expressions of z, and to find back the desired expression :

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 desired expression of $\frac{\mathrm{d}y}{\mathrm{d}t}$.

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, $\alpha a(V-V_n)^2 = \alpha^2(V-V_n)^2$, thus it suffices to set $\alpha = a$ to ensure equivalence. In this case :

$\beta = ac(b-b_n)$ and $v = a(V-V_n)$ such that $\frac{\mathrm{d}v}{\mathrm{d}t} = \beta + v^2$

9 *Qualitative behaviors*

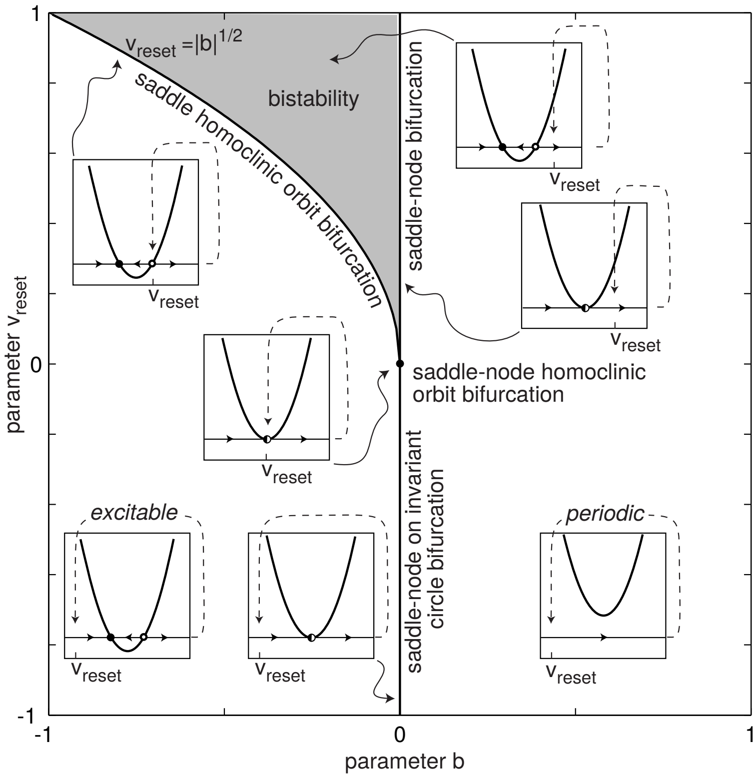
• If $\beta > 0$, then the derivative of V is always strictly positive, thus the system displays periodic oscillations between v_0 and v_{th}.

• 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.

Insets show the phase portrait parabola depending on β. On the horizontal axis v are spotted the possible fixed points, as well as v_0 and v_{th}. Reproduction from Izhikevich, Dynamical Systems in Neuroscience.

(11) *Quantitative behaviors*

The period T of oscillations is the time required to reach v_{th} starting from v_0, which can be computed by integrating the differential equation.

- For $\beta > 0$, it can be integrated directly, with the change of variable $y = v/\sqrt{\beta}$:

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

$$T = \frac{1}{\sqrt{\beta}}\int_{v_0/\sqrt{\beta}}^{v_{th}/\sqrt{\beta}} \frac{\mathrm{d}y}{1+y^2} = \frac{1}{\sqrt{\beta}}\left[\arctan\left(v_{th}/\sqrt{\beta}\right) - \arctan\left(v_0/\sqrt{\beta}\right)\right] = \frac{1}{\sqrt{\beta}}\arctan\left(\frac{v_0 - v_{th}}{\sqrt{\beta} + v_0 v_{th}/\sqrt{\beta}}\right) < \frac{\pi}{2\sqrt{\beta}}$$

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

The evolution of the variable v from a value v_0 during a time t is obtained by inverting the expression (the middle one for instance) and replacing $T \to t$ and $v_{th} \to v(t)$:

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

- For $\beta > 0$, the differential equation can be integrated through a partial fraction decomposition :

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

The evolution of the variable v is :

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

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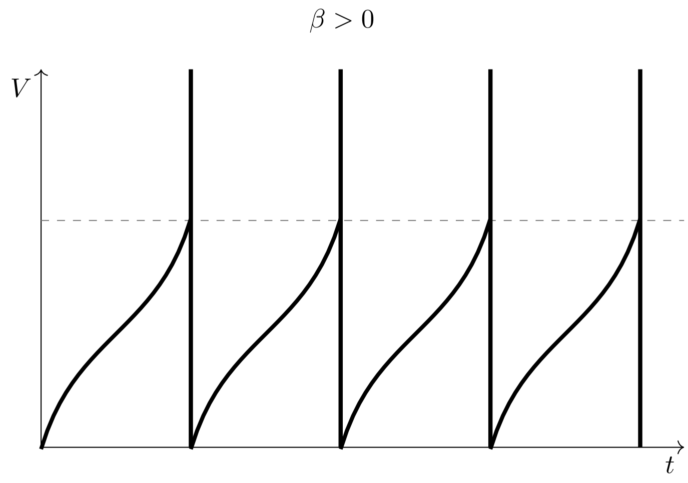
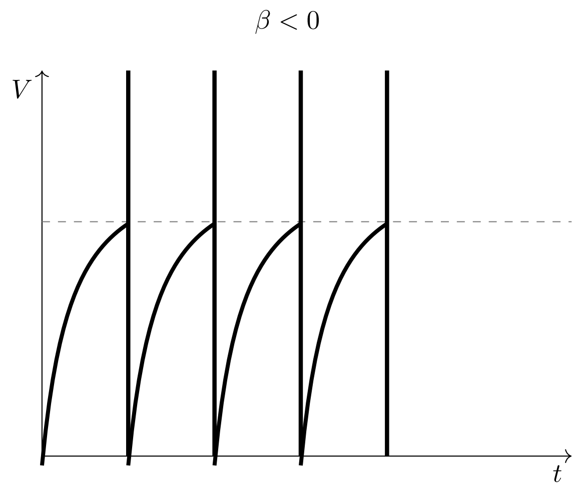




1.3 Theta model

(12) *Qualitative equivalence*
Canceling the derivative allows to solve for the fixed points (provided $I \neq 1$) :

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

This equation admits solutions for $\frac{I+1}{I-1} \in [-1, 1]$ (as it equals a cosinus), which is the case for $I < 0$. Indeed :

- For $I > 1$, the quotient $\frac{I+1}{I-1} = \frac{I-1+1+1}{I-1} = 1 + 2\frac{1}{I-1}$ is majored by 1.
- For $I < 1$ the inequality $-1 \leq 1 + 2\frac{1}{I-1} \leq 1$ is fulfilled for $-(I-1) > 1 \implies I < 0$.

• For $I > 0$, 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 $I < 0$, there are two fixed points θ_+ and $\theta_- = -\theta_+$ (symmetric in the trigonometric circle relative to the x-axis), which fuse when $I = -1$ (since $\cos(\theta) = 0$ in this case).
Stability is obtained by examining the derivative with respects to θ :

$$\frac{\mathrm{d}}{\mathrm{d}\theta}\left(\frac{\mathrm{d}\theta}{\mathrm{d}t}\right) = -\sin(\theta)(I-1)$$

This is of the sign of $\sin(\theta)$ because $-1 \times (I-1) < 0$ for $I < 0$. The two fixed points verify $\theta_- = -\theta_+$, the positive one has a positive sinus and the negative has a negative sinus, thus θ_- is stable and θ_+ 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 :

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

Both derivatives are given by :

- $\dfrac{\mathrm{d}v}{\mathrm{d}t} = \tan^2(\theta) + \beta$

- $\dfrac{\mathrm{d}\theta}{\mathrm{d}v} = \dfrac{1}{\frac{\mathrm{d}v}{\mathrm{d}\theta}} = \dfrac{1}{\frac{1}{\cos^2(\theta)}} = \cos^2(\theta)$

Hence : $\dfrac{\mathrm{d}\theta}{\mathrm{d}t} = \cos^2(\theta)\left(\dfrac{\sin^2(\theta)}{\cos^2(\theta)} + \beta\right) = \sin^2(\theta) + \beta\cos^2(\theta)$

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

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

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 an 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 *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 : $\mathcal{V} \gg V_r + \Delta_T \implies V_r - \mathcal{V} \ll -\Delta_T$:

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

16 *Influence of the parameters*

- The parameter V_r is the zero-crossing point of the linear term, which sets the lower equilibrium, but it also influences the upper one (by sliding the minimum of the function f).
- The parameter $\mathcal{V}$ slides the *exponential term* along the x-axis (it is the point where the argument of the exponential

cancels, thus where the exponential equals 1). Consequently, it slides the *function* f along the linear branch, which mainly displaces the upper fixed point (the latter can even disappear).

• The parameter Δ_T rescales the exponential term, shaping its sharpness. It mainly modulates the right-hand branch of the function f, where the exponential is prevalent, but cannot make fixed points disappear.

(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 is shifted down, from I to $I - w$, 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. The period can be found by integrating this differential equation from $t = 0$ to T_{ISI} and $V_0 = 0$ to V_{th}. *In the following expression, the equilibrium $I - w$ is isolated for better understanding.*

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

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

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) :

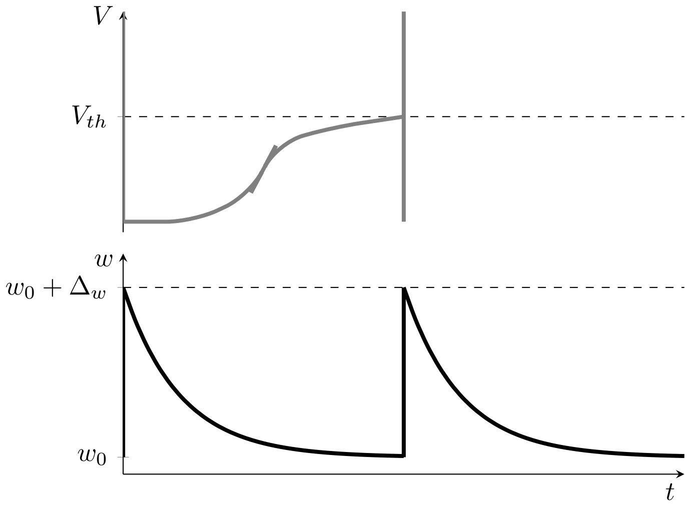
$$w(t = T^-) = w_0 \cdot e^{-\frac{T}{\tau_w}}$$

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) :

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

(26) *Asymptotic behavior of the firing rate*

Method – Asymptotic development of the logarithm of a quotient

The goal is to express the logarithm under the form $\ln(1+h)$ with $h \to 0$, in order to use a limited development at the first order : $\ln(1+h) = h + o(h)$. When the logarithm contains a quotient, the first step is thus to decompose the quotient itself in $1+h$ by using a limited development of a fraction.

- By factorizing by the dominant part in the numerator and in the denominator, with $D_1 \gg N_1$ and $D_2 \gg N_2$:

$$\frac{D_1 + N_1}{D_2 + N_2} = \frac{D_1\left(1 + \frac{N_1}{D_1}\right)}{D_2\left(1 + \frac{N_2}{D_2}\right)} = \frac{D_1}{D_2}\left(1 + \frac{N_1}{D_1}\right)\frac{1}{\left(1 + \frac{N_2}{D_2}\right)} = \frac{D_1}{D_2}\left(1 + \frac{N_1}{D_1}\right)\left(1 - \frac{N_2}{D_2} + o\left(\frac{N_2}{D_2}\right)\right)$$

Often, $D_1 = D_2 = D$, leading to $\left(1 + \frac{N_1}{D}\right)\left(1 - \frac{N_2}{D} + o\left(\frac{N_2}{D}\right)\right) \approx 1 + \frac{N_1 - N_2}{D} + \frac{N_1 N_2}{D^2} \approx 1 + \frac{N_1 - N_2}{D}$ at the first order, because $\frac{N_1 N_2}{D^2} = o\left(\frac{N_1}{D}\right)$.

- Alternatively, the quotient can be decomposed more directly by introducing the missing term N_2 at the numerator in order to simplify :

$$\frac{D + N_1}{D + N_2} = \frac{D + N_2 - N_2 + N_1}{D - N_2} = 1 + \frac{N_1 - N_2}{D + N_1} \approx 1 + \frac{N_1 - N_2}{D}$$

- Even more simply, if $N_1 = 0$, the limited development of an inverse can be used directly :

$$\frac{D}{D + N_2} = \left(\frac{D + N_2}{D}\right)^{-1} = \left(1 + \frac{N_2}{D}\right)^{-1} \approx 1 - \frac{N_2}{D}$$ (which gives back the expression above by setting $N_1 = 0$).

Taking $w = \langle w \rangle_{ISI} = \frac{\tau_w}{T}$ (question 25) and $I \to \infty$, the duration of the inter-spike interval rewrites :

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

With $I \to \infty$, the term $\dfrac{\tau_w}{T} \Delta_w$ cannot be neglected compared to I (as $T \xrightarrow[I \to \infty]{} 0$), thus the only negligible term is V_{th}. The quotient rewrites thanks to the limited development of an inverse :

$$T \approx \tau_m \ln \left(1 - \frac{V_{th}}{I - \frac{\tau_w}{T} \Delta_w} \right) \approx \tau_m \frac{V_{th}}{I - \frac{\tau_w}{T} \Delta_w} \implies TI \approx \tau_m V_{th} + \tau_w \Delta_w \implies T \approx \frac{\tau_m V_{th} + \tau_w \Delta_w}{I}$$

This gives a linear asymptotic behavior for the firing rate as a function of I :

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

27 *Comparison with the integrate-and-fire model without adaptation*
Without firing rate adaptation, computations can be done from scratch, or alternatively 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 – Dynamical system analysis for a two-dimensional system

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

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

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 evolution of the system. The projections of each vector along both variables' axes reflect the magnitude and the sign of their respective derivatives. 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. $G(x, y) = 0$).

Each equation leads to a relation between the variables y and x, which can be expressed as a function $y = g(x)$ (or alternatively $x = f(y)$). This allows to plot the shape of the nullclines in the diagram.

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 $G(x, y) > 0$. Signs can be represented by horizontal and vertical vectors in each area, oriented in the direction of evolution of the corresponding variables.

Then, summing the horizontal and vertical vectors in each area provides insights about the direction of the evolution of the system as a whole in the states space. *Along the nullclines*, the vectors of the time derivatives are parallel to the axes, as one of the derivative cancels.

This representation helps to visualise the possible trajectories by following the vectors.

28 *Phase plane diagram*

- Nullclines

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

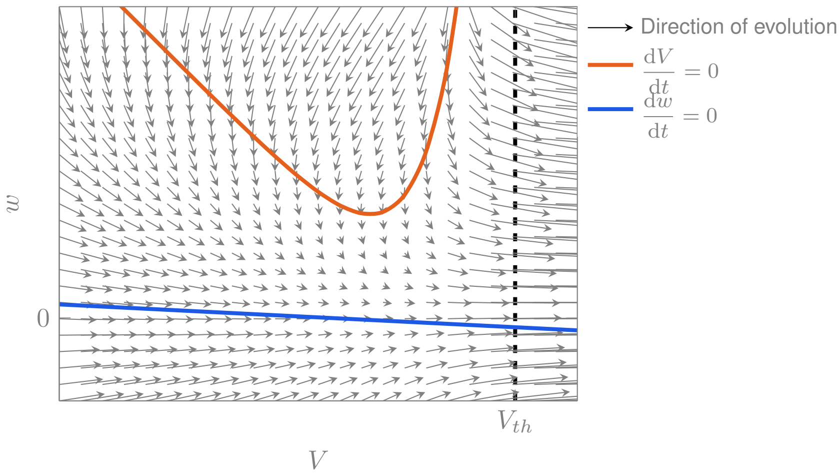
$$\begin{cases} \dfrac{\mathrm{d}V}{\mathrm{d}t} &= 0 \\ \dfrac{\mathrm{d}w}{\mathrm{d}t} &= 0 \end{cases} \implies \begin{cases} Rw &= -(V - V_r) + \Delta_T \exp\left(\dfrac{V - \mathcal{V}}{\Delta_T}\right) + RI \\ w &= a(V - V_r) \end{cases} \tag{11}$$

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

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

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 (because w is *below* the V-nullcline, such that $\frac{\mathrm{d}V}{\mathrm{d}t} > 0$, according to the first inequality (12)).
Along the V-nullcline, the vector field is parallel to the w-axis (where $\frac{\mathrm{d}V}{\mathrm{d}t} = 0$) 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)).



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 in most of the areas (i.e. evolution along the variable V), unless 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 the adjustment of the vector field at question 31.*]

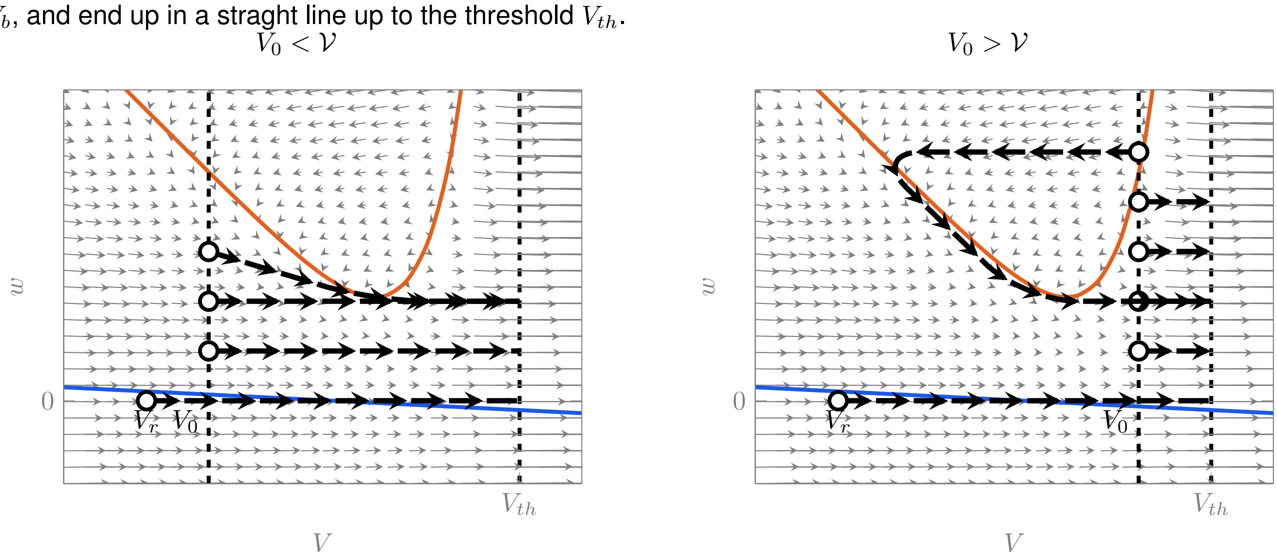
30 *Initial point and trajectory*

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 system 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} of the 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 along the vertical axis of abscissa V_0.

• In the case $V_0 < \mathcal{V}$, successive trajectories tend to reach a stationary behavior, in which they follow the V-nullcline, converge at the extremum of the V nullcline at V_b, and end up at the same point when they reach V_{th}.

• 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 $\frac{\mathrm{d}V}{\mathrm{d}t} < 0$. 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 at V_b, and end up in a straght line up to the threshold V_{th}.



(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*.