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THEORETICAL NEUROSCIENCE

TD2: MODELS OF NEURONS II

All TD materials will be made available at https://github.com/helene-todd/TheoNeuro2425.

Previously, we studied the most basic model for firing neurons: the LIF. In this tutorial, we will extend the LIF model to include post-synaptic refractoriness and firing rate adaptation, while also underlying its limits. We then introduce a more realistic model that can account for a larger repertoire of neural behaviours, the quadratic integrate-and-fire (QIF). Unlike the LIF, this model is described by a nonlinear ODE: we will give tools for understanding the dynamics of such systems without the need of explicitly solving the ODE.

1 Extending leaky integrate-and-fire

1.1 Refractory Period

Additional rules can be added to account for other observed features of real spikes, also called action potentials. One of the observed features is a refractory period; immediately after a spike the neuron cannot produce another spike for a short period of time called the refractory period. The refractory period can be included in models of neurons in a number of ways.

One way is forced voltage clamp: the voltage is fixed at its reset value following a spike for the duration of the refractory period τ_{ref}.

1. What is the maximal firing rate f with this method ?

> The maximal firing rate f is obtained when the neuron fires immediately after the refractory period, therefore
> $$\max f = \frac{1}{\tau_{ref}}.$$

Other ways of incorporating the refractory period include adding a refractory conductance (adding a large conductance g_k at spike time to produce an outward hyperpolarising current) and raising the threshold (rising the threshold value after a spike, so that the neuron is less prone to spiking).

1.2 Firing Rate Adaptation

A well-known property of neurons is adaptation. For instance, driven by an injected current, a decrease in time of the firing rate of a neuron to a steady-state value can be observed.

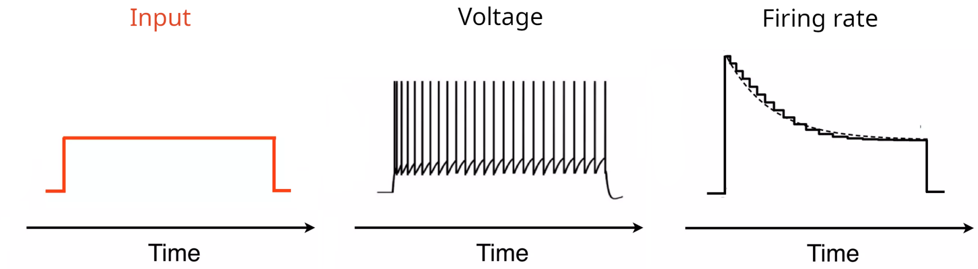


Figure 1: Example of firing rate adaptation in response to injecting a step current.

We are going to model this phenomenon by considering the effect of ion channels which open whenever a neuron fires a spike and let in negative current, such that

$$\tau_m \frac{dV(t)}{dt} = -V(t) - W(t) + I, \tag{1}$$

where, after each spike occurring at V_{th}, W is increased by W_R and V is reset to 0. Between spikes, W decays back to zero with time constant τ_w

$$\tau_w \frac{dW(t)}{dt} = -W(t). \tag{2}$$

1.2.1 Neglecting decay

We make a first approximation that W is **constant** between spikes. A constant current $I_{syn} > V_{th}$ is injected into the neuron.

2. Discuss qualitatively what happens after the first spike.

> After the first spike, W increases by W_R. The equilibrium $V^* = I_{syn} - W$ is shifted to $V^* = I_{syn} - (W + W_R)$, making it closer to V_{th}.

3. At which value W does the model stop spiking? Show that the total number of spikes emitted is roughly $(I_{syn} - V_{th})/W_R$.

> After several spikes, the steady-state may end up below V_{th}, in which case the neuron stops spiking. This happens for
>
> $$I_{syn} - W < V_{th} \Leftrightarrow W > I_{syn} - V_{th}.$$
>
> Starting from $W = 0, W = kW_R$ after k spikes, thus the limit is reached for
>
> $$k > \frac{I_{syn} - V_{th}}{W_R}.$$

4. Compute the duration of an inter-spike interval (ISI) as a function of W in that interval.

> In an interval, W is constant and equation (1) is a first-order linear equation. The solution to the ODE is (see previous tutorial)
>
> $$V(t) = (-W + I)(e^{t/\tau_m} - 1)e^{-t/\tau_m}, \text{ taking } t_0 = 0 \text{ and } V_0 = 0.$$

> Then we can compute the ISI interval T
>
> $$\begin{aligned} V(T) = V_{th} &\Leftrightarrow (-We^{T/\tau_m} + W + Ie^{T/\tau_m} - I)e^{-T/\tau_m} = V_{th} \\ &\Leftrightarrow e^{-T/\tau_m}(W - I) - W + I = V_{th} \\ &\Leftrightarrow e^{-T/\tau_m} = \frac{I - W - V_{th}}{I - W} \\ &\Leftrightarrow T = \tau_m \log\left(\frac{I - W}{I - W - V_{th}}\right). \end{aligned}$$

1.2.2 Taking decay into account

It is no longer possible to ignore the decay W if the ISI becomes comparable to the time constant of the decay τ_w.

5. Can you explain why? Is it possible for the neuron to stop spiking?

> In that case the decay of W during the interval becomes significant and W cannot be considered constant anymore. This necessarily happens at some point because as we have seen previously, the neuron necessarily stops spiking if W is considered constant (corresponding to an infinite ISI); this approximation cannot hold all along.

We therefore consider that the system has reached its equilibrium firing rate and fires spikes with a period T.

6. Compute the time course of W between two successive spikes, assuming that immediately after the first two spikes $W(t = 0) = W_0$.

> Solving equation (2), we get
> $$W(t) = W_0 e^{-t/\tau_w}.$$

7. Show that W_0 is given by
$$W_0 = \frac{W_R}{1 - \exp(-T/\tau_w)}. \tag{3}$$

> At equilibrium, W decays from W_0 until a spike is emitted at $t = T$. W_R is added to W and the stationary condition is
>
> $$W(t = T^-) + W_R = W_0.$$
>
> Having $W(t = T^-) = W_0 e^{-T/\tau_w}$, we find the desired result.

8. **Bonus:** we assume that $T \ll \tau_w$, such that W can be approximated by its average value during the whole inter-spike interval. Show that the period of spike emission is given by
$$T = \tau_m \log\left(\frac{I - W_R\tau_w/T}{I - W_R\tau_w/T - V_{th}}\right). \tag{4}$$

If $T \ll \tau_w$ then W does not vary much - we can therefore approximate it by its average value

$$\langle W \rangle_{ISI} = \frac{1}{T}\int_0^T W(t)dt = \frac{1}{T}\int_0^T W_0 e^{-t/\tau_w} dt = \frac{\tau_w}{T} W_0 (1 - e^{-T/\tau_w}) = \frac{\tau_w}{T} W_R.$$

Using question (4), we therefore have

$$T = \tau_m \log\left(\frac{I - \langle W \rangle_{ISI}}{I - \langle W \rangle_{ISI} - V_{th}}\right) = \tau_m \log\left(\frac{I - W_R \tau_w / T}{I - W_R \tau_w / T - V_{th}}\right).$$

9. **Bonus:** show that, as the injected current increases, the neuron firing rate $r(I)$ behaves as

$$r(I) \sim aI, \tag{5}$$

with $a = (\tau_w W_R + \tau_m V_{th})^{-1}$. How does this compare to an integrate-and-fire neuron without firing rate adaptation?

T can be rewritten as

$$T = -\tau_m \log\left(1 - \frac{V_{th}}{I - W_R \tau_w / T}\right).$$

Using the Taylor expansion, we have that for a high current I,

$$T \approx \frac{\tau_m V_{th}}{I - W_R \tau_w / T} \;\Leftrightarrow\; TI \approx \tau_m V_{th} + \tau_w W_R.$$

Therefore

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

Without firing rate adaptation, i.e. setting $W_R = 0$ in the previous calculations (one could also do all the calculations again), we have

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

Adaptation corresponds to the reduction of the firing rate by a term proportional to the gain W_R of the inhibitory current times its decay constant τ_w . The higher the gain and the larger the decay constant, the stronger adaptation is, effectively reducing the firing rate.

2 Quadratic integrate-and-fire (QIF) neurons

Linear models cannot reproduce all the behaviours of biological neurons. We propose to study a nonlinear model of neurons and show how it can display a richer repertoire of behaviours.

The model we consider is the quadratic integrate-and-fire (QIF) model

$$\frac{dV(t)}{dt} = V(t)^2 + b, \text{ if } V > V_{th} \text{ then } V = V_{reset}, \tag{6}$$

with b that can be a function of time (e.g. a varying current), but we consider it constant for the time being.

2.1 Case $b > 0$.

10. Describe the behaviour of the system in this case.

> We have that $V(t)^2 + b > 0$, therefore the system is oscillating.

11. **Bonus:** show that the solution to equation (6) is

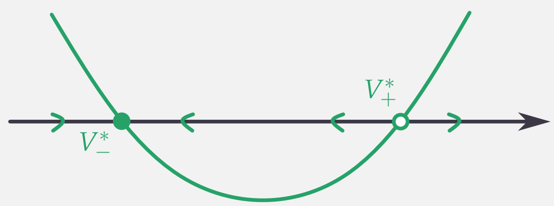
$$V(t) = \sqrt{b}\tan\left(\sqrt{b}(t+t_0)\right), \text{ with } t_0 = \frac{1}{\sqrt{b}}\arctan\left(\frac{V_0}{\sqrt{b}}\right). \tag{7}$$

and compute the period of the oscillations.

> Usually, nonlinear ODEs cannot be solved explicitly. However, for equation (6), using the separation of variables method yields an explicit solution
>
> $$\frac{dV(t)}{dt} = V(t)^2 + b \Leftrightarrow \frac{dV(t)}{V(t)^2+b} = dt,$$
>
> integrating both sides we have
>
> $$\int_{V(0)=V_0}^{V(t)} \frac{1}{V^2+b}dV = \int_{t=0}^{t} 1ds \Leftrightarrow \frac{1}{b}\int_{V_0}^{V(t)} \frac{1}{(V/\sqrt{b})^2+1}dV = t.$$
>
> Using the change of variables $y = \dfrac{V}{\sqrt{b}} \Rightarrow \dfrac{dy}{dV} = \dfrac{1}{\sqrt{b}}$
>
> $$\begin{aligned}\frac{1}{b}\int_{V_0}^{V(t)} \frac{1}{(V/\sqrt{b})^2+1}dV &= \frac{1}{\sqrt{b}}\int_{y(0)=V_{reset}/\sqrt{b}}^{y(t)=V(t)/\sqrt{b}} \frac{1}{y^2+1}dy = \frac{1}{\sqrt{b}}\Big[\arctan(y)\Big]_{y(0)=V_0/\sqrt{b}}^{y(t)=V(t)/\sqrt{b}} \\ &= \frac{1}{\sqrt{b}}\left(\arctan\left(V(t)/\sqrt{b}\right) - \arctan\left(V_0/\sqrt{b}\right)\right).\end{aligned}$$
>
> Therefore, we have
>
> $$t = \frac{1}{\sqrt{b}}\left(\arctan\left(V(t)/\sqrt{b}\right) - \arctan\left(V_0/\sqrt{b}\right)\right) \Leftrightarrow V(t) = \sqrt{b}\tan\left(\sqrt{b}(t+t_0)\right),$$
>
> with
>
> $$t_0 = \frac{1}{\sqrt{b}}\arctan\left(\frac{V_0}{\sqrt{b}}\right).$$
>
> Setting the initial condition $V_0 = V_{reset}$, the period T of an oscillation is given by
>
> $$\begin{aligned}T &= \frac{1}{\sqrt{b}}\left(\arctan\left(V(T)/\sqrt{b}\right) - \arctan\left(V_0/\sqrt{b}\right)\right) \\ &= \frac{1}{\sqrt{b}}\arctan\left(\frac{V_{th}-V_{reset}}{\sqrt{b}+V_{th}V_{reset}/\sqrt{b}}\right) < \frac{\pi}{2\sqrt{b}}.\end{aligned}$$

2.2 Case $b < 0$.

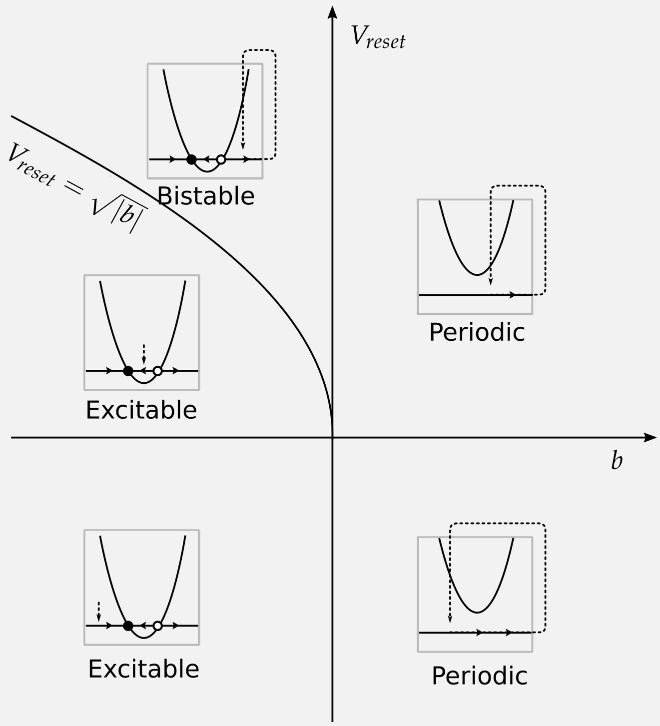
12. Find the steady-states (equilibria) of the system in this case.

> Finding the equilibria of the system means finding when equation (6) is equal to zero
>
> $$\frac{dV}{dt} = V^2 + b = 0 \Leftrightarrow V^*_{\pm} = \pm\sqrt{-b} = \pm\sqrt{|b|}.$$
>
> The stability is determined by looking at the sign of the derivative of equation (6) with respect to V evaluated at its equilibria $V^*_{\pm}$. Denoting $f(V) := V^2 + b$, we have
>
> $$f'(V) = \frac{df(V)}{dV} = 2V,$$
>
> and therefore
>
> $$f'(V^*_-) = -2\sqrt{|b|} < 0 : \text{the equilibrium } V^*_- = -\sqrt{|b|} \text{ is stable,}$$
> $$f'(V^*_+) = 2\sqrt{|b|} > 0 : \text{the equilibrium } V^*_+ = \sqrt{|b|} \text{ is unstable.}$$
>
> Another way of understanding and representing the equilibria of the system as well as their stability is summarised in the figure below.
>
> 
>
>
> The green line represents dV/dt, and its intersections with 0 give us the equilibria $V^*_{\pm}$ of the system. Furthermore, let $V \in [V^*_-, V^*_+]$; since dV/dt is negative in this interval, V will decrease towards V^*_-. Conversely, let $V \in]-\infty, V^*_-]$ (resp. $V \in [V^*_+, \infty[$); since dV/dt is positive in this interval, V will increase towards V^*_+ (resp. ∞).

13. Depending on V_{reset} and $b < 0$, describe the three different behaviours of the system.

> Three different behaviours can occur depending on the value of V_{reset} relatively to the unstable equilibrium V^*_+
>
> – $V_{reset} < \sqrt{|b|}$: after a reset, the system decays back to the stable fixed point V^*_-. However, a sufficiently high perturbation can drive it above the unstable point and make it emit a single spike. The system is excitable.
>
> – $V_{reset} = \sqrt{|b|}$: after a reset, the system lies on the unstable point V^*_+. A small perturbation can either drive it to spiking or to the stable fixed point V^*_-.
>
> – $V_{reset} > \sqrt{|b|}$: after a reset, the system displays periodic oscillations as in the case $b > 0$. 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.

The following figure (called a bifurcation diagram) summarises all the behaviours of the system we have studied above (cases $b > 0$ and $b < 0$).



14. **Bonus:** considering that $V_{reset} > \sqrt{|b|}$, show that the solution to equation (6) is

$$V(t) = \sqrt{|b|}\,\frac{1+\exp\left(2\sqrt{|b|}(t+t_0)\right)}{1-\exp\left(2\sqrt{|b|}(t+t_0)\right)}, \text{ with } t_0 = \frac{1}{2\sqrt{|b|}}\log\left(\frac{V_0-\sqrt{|b|}}{V_0+\sqrt{|b|}}\right). \tag{8}$$

and compute the period of the oscillations.

Using again the separation of variables method, we have

$$\int_{V(0)=V_0}^{V(t)} \frac{1}{V^2-|b|}dV = \int_{t=0}^{t} 1ds.$$

We apply a partial fraction decomposition to obtain

$$\frac{1}{V^2-|b|} = \frac{1}{(V-\sqrt{|b|})(V+\sqrt{|b|})} = \frac{1}{2\sqrt{|b|}(V-\sqrt{|b|})} - \frac{1}{2\sqrt{|b|}(V+\sqrt{|b|})}.$$

We have

$$\begin{aligned}
\int_{V_0}^{V(t)} \frac{1}{V^2-|b|}dV &= \int_{V_0}^{V(t)} \frac{1}{2\sqrt{|b|}(V-\sqrt{|b|})} - \frac{1}{2\sqrt{|b|}(V+\sqrt{|b|})}dV \\
&= \frac{1}{2\sqrt{|b|}}\int_{V_0}^{V(t)} \frac{1}{V-\sqrt{|b|}} - \frac{1}{V+\sqrt{|b|}}dV \\
&= \frac{1}{2\sqrt{|b|}}\left[\log\left(V-\sqrt{|b|}\right) - \log\left(V+\sqrt{|b|}\right)\right]_{V_0}^{V(t)}
\end{aligned}$$

$$= \frac{1}{2\sqrt{|b|}} \left[\log\left(\frac{V - \sqrt{|b|}}{V + \sqrt{|b|}} \right) \right]_{V_0}^{V(t)}$$
$$= \frac{1}{2\sqrt{|b|}} \left(\log\left(\frac{V(t) - \sqrt{|b|}}{V(t) + \sqrt{|b|}} \right) - \log\left(\frac{V_0 - \sqrt{|b|}}{V_0 + \sqrt{|b|}} \right) \right).$$

Therefore, we have

$$t = \frac{1}{2\sqrt{|b|}} \left(\log\left(\frac{V(t) - \sqrt{|b|}}{V(t) + \sqrt{|b|}} \right) - \log\left(\frac{V_0 - \sqrt{|b|}}{V_0 + \sqrt{|b|}} \right) \right)$$
$$\Leftrightarrow \frac{V(t) - \sqrt{|b|}}{V(t) + \sqrt{|b|}} = \exp\left(2\sqrt{|b|}t + \log\left(\frac{V_0 - \sqrt{|b|}}{V_0 + \sqrt{|b|}} \right) \right)$$
$$\Leftrightarrow V(t) = \sqrt{|b|} \frac{1 + \exp\left(2\sqrt{|b|}(t + t_0)\right)}{1 - \exp\left(2\sqrt{|b|}(t + t_0)\right)},$$

with

$$t_0 = \frac{1}{2\sqrt{|b|}} \log\left(\frac{V_0 - \sqrt{|b|}}{V_0 + \sqrt{|b|}} \right).$$

Setting the initial condition $V_0 = V_{reset}$, the period T of an oscillation is given by

$$T = \frac{1}{2\sqrt{|b|}} \left(\log\left(\frac{V_{th} - \sqrt{|b|}}{V_{th} + \sqrt{|b|}} \right) - \log\left(\frac{V_{reset} - \sqrt{|b|}}{V_{reset} + \sqrt{|b|}} \right) \right).$$

3 Bonus: Theta neurons

The theta model is described by the following ODE

$$\frac{d\theta(t)}{dt} = 1 - \cos\theta(t) + (1 + \cos\theta(t))I(t). \tag{9}$$

We consider that a spike is emitted when θ reaches the value π.

15. Show that for $I > 0$, there is no equilibrium. Conclude that the trajectories are periodic orbits with regular spiking.

We have that

$$I > 0 \Rightarrow -1 + I > -1 \Rightarrow (\cos\theta)(-1 + I) > -1$$
$$\Rightarrow (\cos\theta)(-1 + I) + 1 + I > -1 + 1 + I > 0.$$

Therefore, $d\theta/dt$ is always strictly positive, meaning there is no equilibrium and the system oscillates.

16. Show that for $I < 0$, there are two equilibria for the system, one stable and one unstable.

> Let $I < 0$. Then
>
> $$\frac{d\theta}{dt} = 1 - \cos\theta + (1 + \cos\theta)I = 0 \Leftrightarrow \cos\theta = \frac{1+I}{1-I},$$
>
> which has two distinct solutions because $\cos(\theta) = \cos(-\theta)$. Let $\theta_*^{\pm}$ denote these two equilibria and $f(\theta) := 1 - \cos\theta + (1 + \cos\theta)I$. Then
>
> $$f'(\theta) = (\sin\theta)(1 - I), \text{ with } 1 - I > 0,$$
>
> meaning the stability of $\theta_*^{\pm}$ is determined by the sign of $\sin\theta_*^{\pm}$. Since $\theta_*^{-} = -\theta_*^{+}$ and $\sin(-\theta) = -\sin(\theta)$, we necessarily have that one equilibria is stable and the other unstable.

17. Show that this model is equivalent to the QIF model.

> We have seen that the dynamics of the theta model are the same as those of the QIF model. We can explicitly show that both models are equivalent: indeed, the change of variables $V = \tan\theta$ transforms the QIF model into the theta model.