Introduction to neural dynamics

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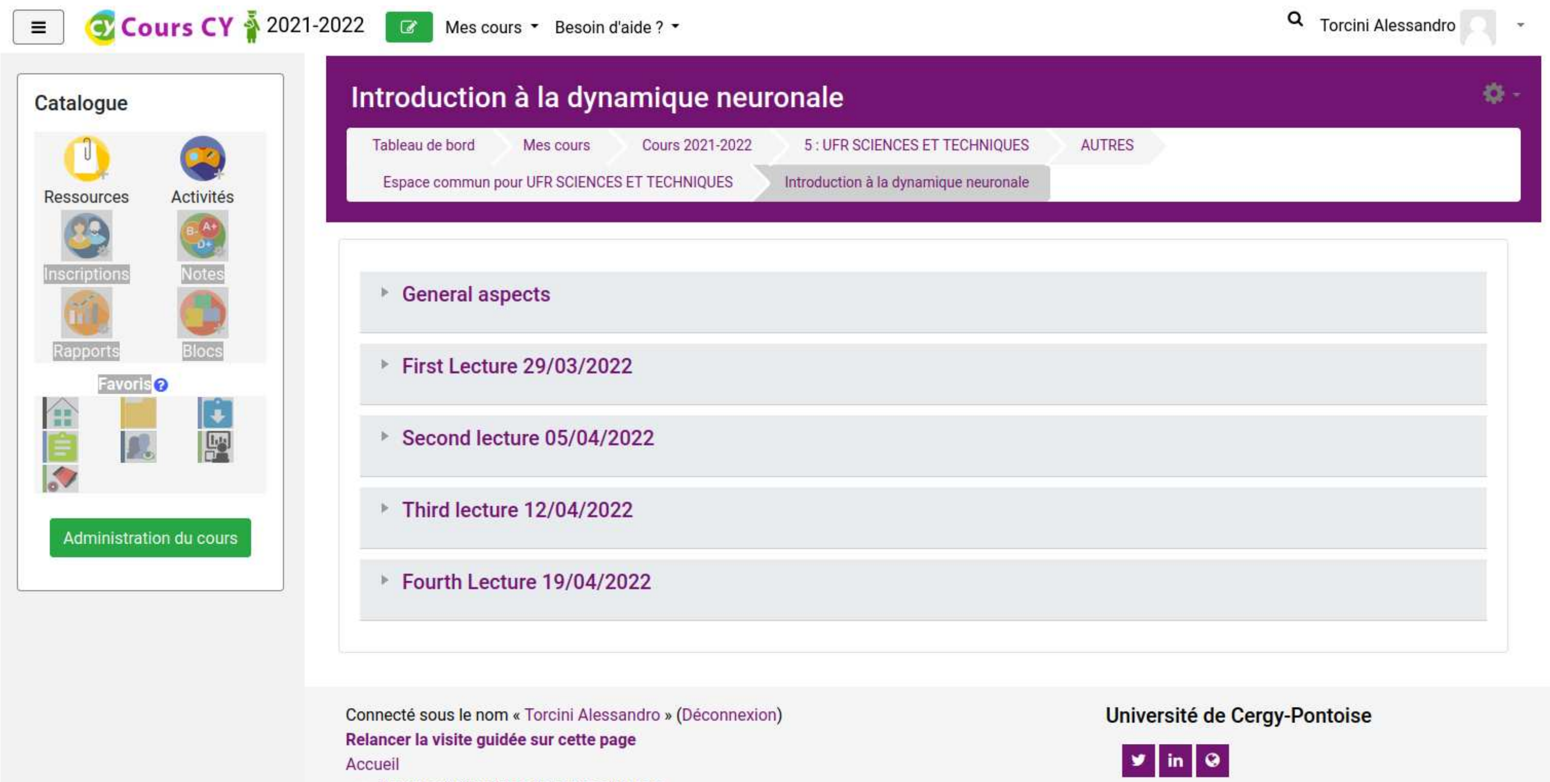
Material of the course

All the material will be uploaded to the ENT - CY Cergy Paris Université web page , where all of you will be registered soon.



Summary

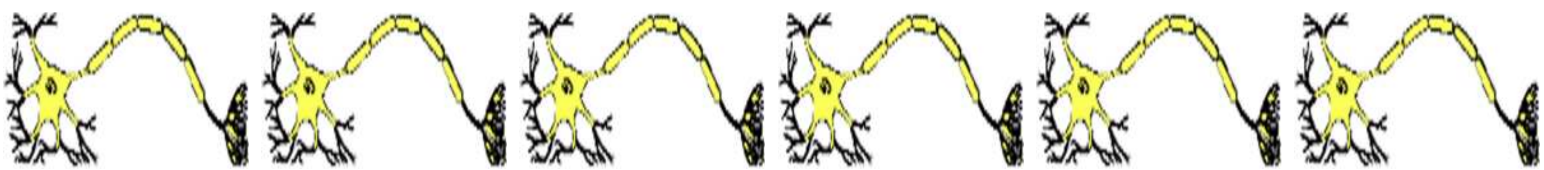
- Neurons in Brief
- Leaky Integrate-and-Fire Model
- Non-linear Integrate-and-Fire Models
  - The exponential integrate-and-fire model
  - The quadratic integrate-and-fire model

Neurons in Brief

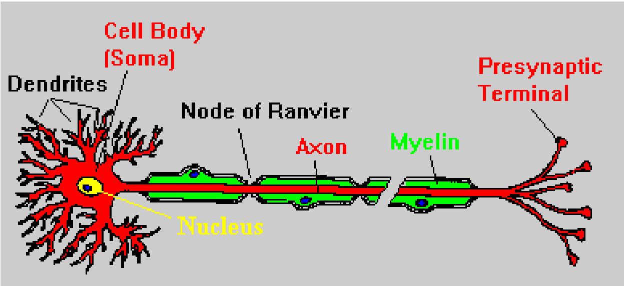
Cells of the nervous system, called neurons, are specialized in transporting and elaborating "messages" (information).

These functions are performed via the transmission of electric signals, associated to ionic currents, through the membrane of the neuronal cells

- The human brain contains 100 billions neurons
- One mm^3 of cerebral cortex contains 100.000 neurons .
- Neurons can have different forms and dimensions: the smallest have diameters of 4 μm, while the largest can have axons of 1 or 2 meters



Neuron Morphology

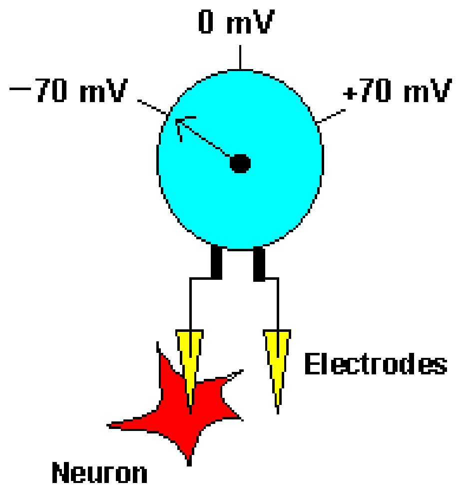


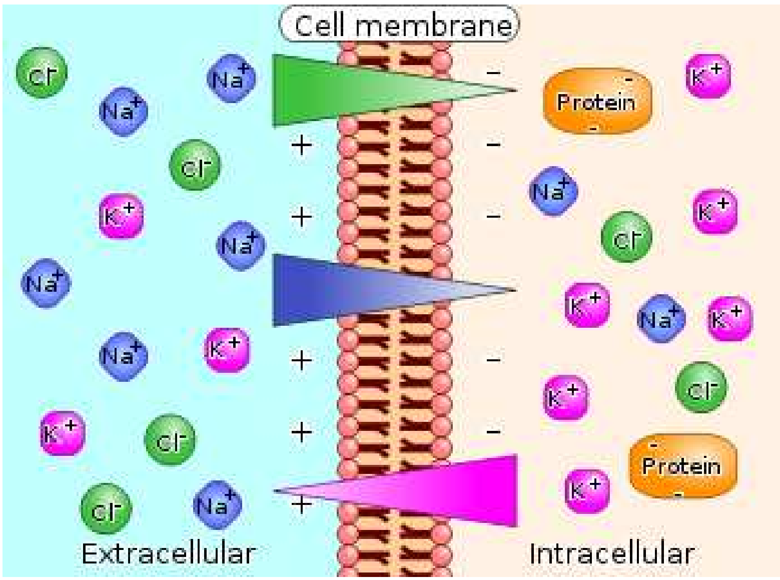
Despite their enourmous variety, neurons have some common morphological aspect:

- The soma is a compact almost sperical structure (diamter $\simeq$ 70 μm) it is the unity deputed to information elaboration (CPU)
- The dendrites collect information from other neurons and bring it to the soma, they are ramified nearby the cell body (lenght up to 1 mm) (Input)
- The axons bring information to other neurons, normally there is only 1 axon for cell, they can be as long as 1 meter (Output)
- The Synapses are the junctions among two neurons. these are the structures transmitting information from one nervous cell to the other. There are two types of synapses: chemical and electrical (gap junction), the most common among the vertebrates is the chemical one. The synapses can be inhibitory as well as excitatory. (explain)

Membrane Potential

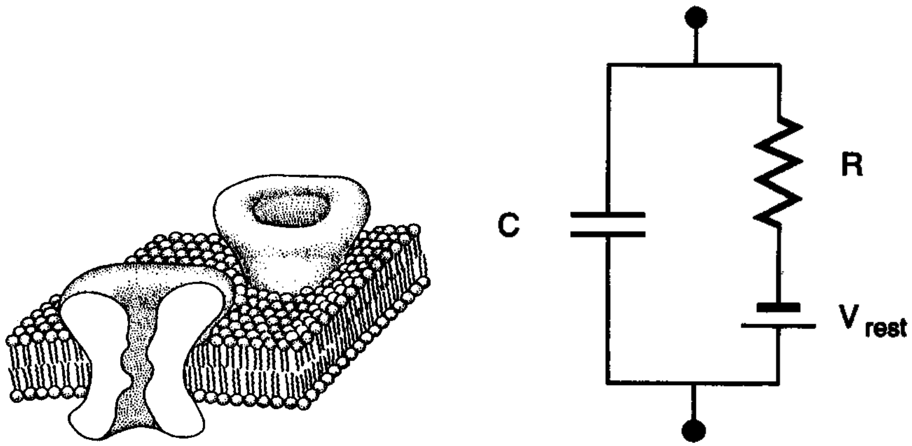
- The membrane potential V_m measures the electrical potential difference between interior and exterior of the neuron.
- The neuron at rest has $V_{rest} \simeq$ -60 mV / -75 mV





The neuron is an dynamical equilibrium state the neuronal signals are electrical signals.

Membrane as an Electric Circuit

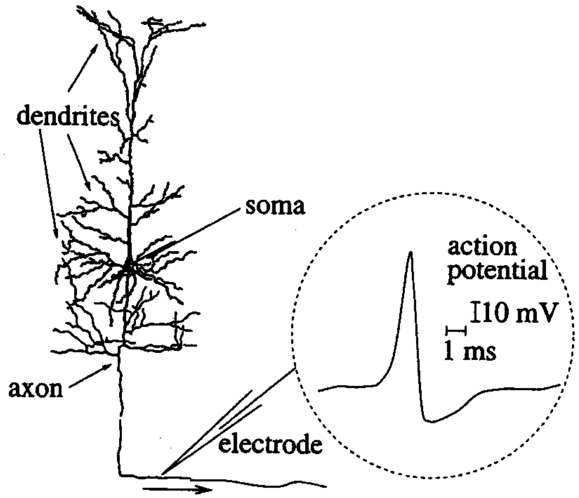


The neural membrane can be seen as an electric circuit with passive characteristics

- the membrane separates positive and negative charges, it acts as a capacitance
  $C_m \simeq 1\mu F/cm^2 \rightarrow 4x10^{11}$ monovalent ions/cm^2
- the ionic channels have specific membrane resistance/conductance :
  Leakage Resistance $R_m \simeq 10^3 \Omega \cdot cm^2$
  Leakage Conductance $G_m = 1/R_m \simeq mS/cm^2$
- V_{rest} can be seen as a voltage generator
- the membrane is also active , e.g. the ionic pumps , and highly nonlinear (some conductance depends on V_m)

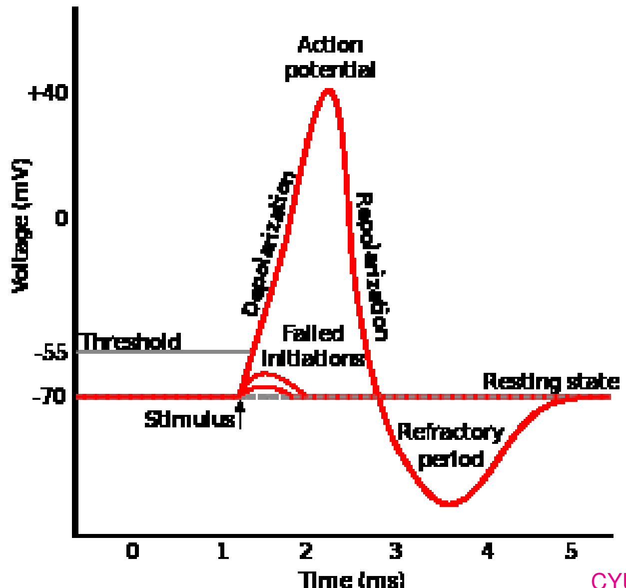
Action Potential

The elementary unit of information transmitted in neural circuits is the Action Potential (AP)



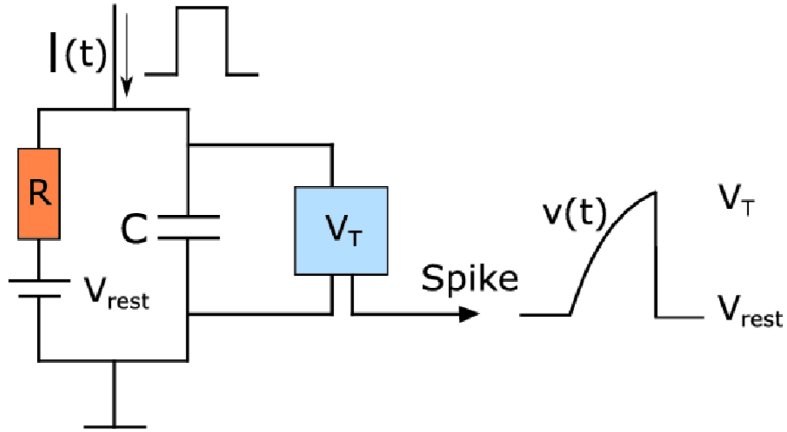
- The neuronal signal is given by the temporal and spatial variation of V_m.
- The action potentials (APs) are electrical impulses delivered when a (depolarizing) stimulus leads V_m above a threshold $\Theta \sim -55$ mV

- The AP lasts 1-2 ms and it has an amplitude of 100-120 mV
- Refractory Period: it is a phase of 10 ms (corresponding to membrane hyperpolarization) occuring after the AP emission
- The AP travels along the axon and it is transmitted to the other neurons.



Leaky integrate-and-fire neuron

A very simple model of neuron has been derived by the following electrical schematization of the membrane.



The current $I(t)$ charges the RC circuit, the potential difference $v(t)$ across the capacitance C is compared with a threshold value $V_T \equiv \Theta$, is $v(t)$ becomes larger than the theshold it is resetted to a value v_r that is the equilibrium membrane potential value. From the Kirchhoff's law for the currents one gets

$$I(t) = C\frac{dv}{dt} + \frac{v(t)-v_r}{R}$$

Leaky integrate-and-fire (LIF) neuron

By introducing the membrane time constant $\tau = RC$, which corresponds to the leaky integrator time constant one finally gets

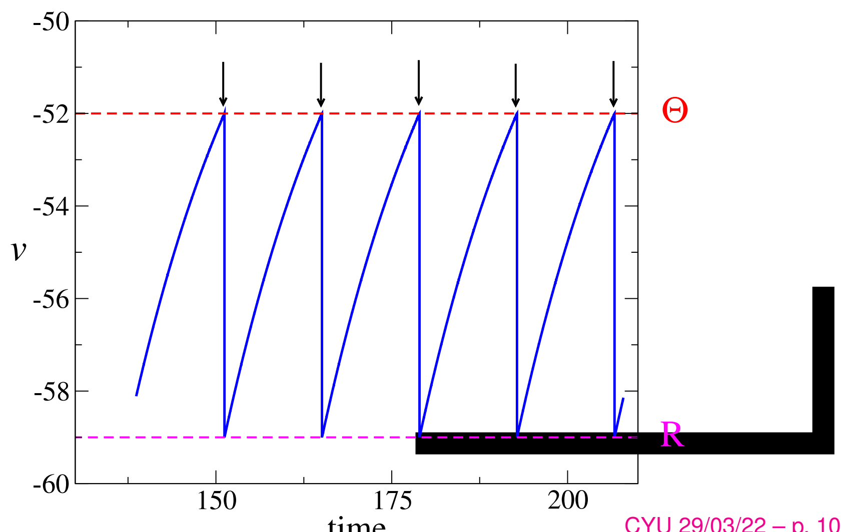
$$\tau \dot{v}(t) = -v(t) + v_{\mathrm{r}} + RI(t)$$

with $\tau \simeq 10 - 20$ ms depending on the considered neuron. This time is quite long with respect to the action potential duration which is around 1 ms.
If $I = const$ and the membrane potential at time $t = 0$ has a value $v(0)$ the evolution is given by

$$v(t) = v(0)\mathrm{e}^{-t/\tau} + (RI + v_{\mathrm{r}})(1 - \mathrm{e}^{-t/\tau}) \qquad v(t \to \infty) = RI + v_{\mathrm{r}}$$

Blackboard

- If $RI + v_r > \Theta$ Repetitive Firing (Oscillator)
- If $RI + v_r < \Theta$ Silent Neuron (Fixed point)



LIF neuron

Periodic Behaviour

- If $RI + v_r > \Theta$ Repetitive Firing (Oscillator)
- At $t = 0$ the neuron has been resetted to $V(0) = v_r$
- After one period $t = T$ the neuron is at threshold $V(T) = \Theta$

Since the solution is

$$v(t) = v(0)\mathrm{e}^{-t/\tau} + (RI + v_\mathrm{r})(1 - \mathrm{e}^{-t/\tau})$$

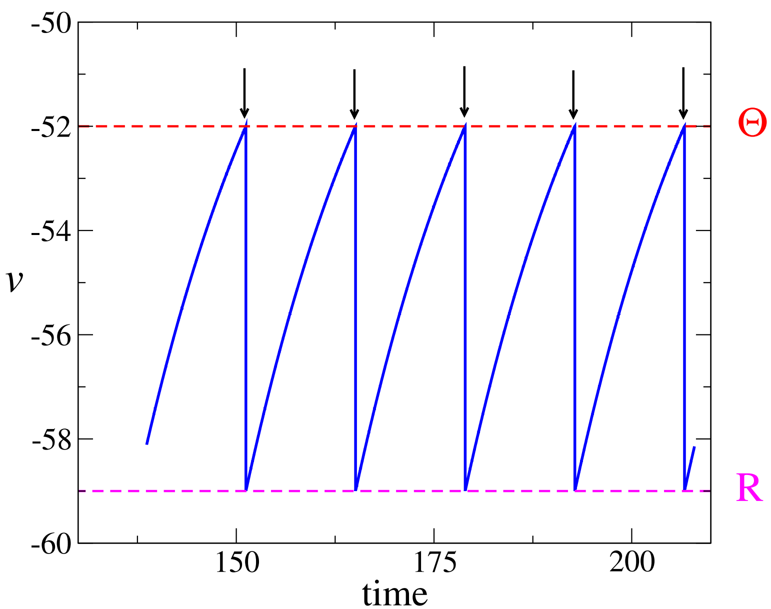
the period T is given by

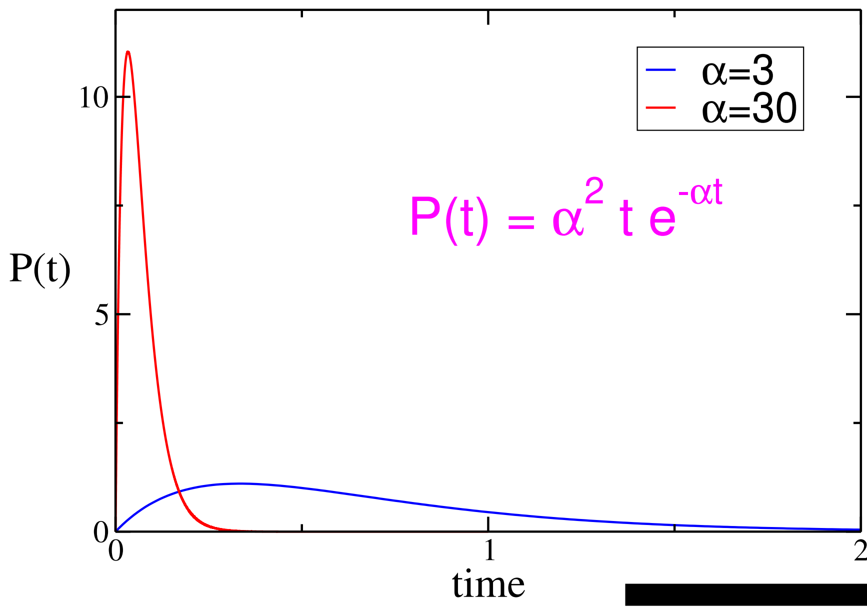
$$T = \tau \ln \frac{RI}{\Theta - v_r - RI}$$

LIF neuron

Formal Spike

- In networks: at the threshold a formal spike $P(t)$ is sent to the other neurons
- the simplest spike form is a Dirac delta $P(t) = \delta(t)$ spike
  $\delta(t) = 0$ for $t \neq 0$ and $\int_{-\infty}^{+\infty} \delta(t)dt = 1$
- The spike train emitted by a neuron can be written as $S(t) = \sum_f P(t - t^{(f)})$ where the spikes have been emitted at the times $\{t^{(f)}\}$
- The firing rate of a neuron is $r = \frac{1}{\Delta t} \int_t^{t+\Delta t} S(x)dx = \frac{N_s}{\Delta t}$ i.e. the number of spikes emitted for unit of time

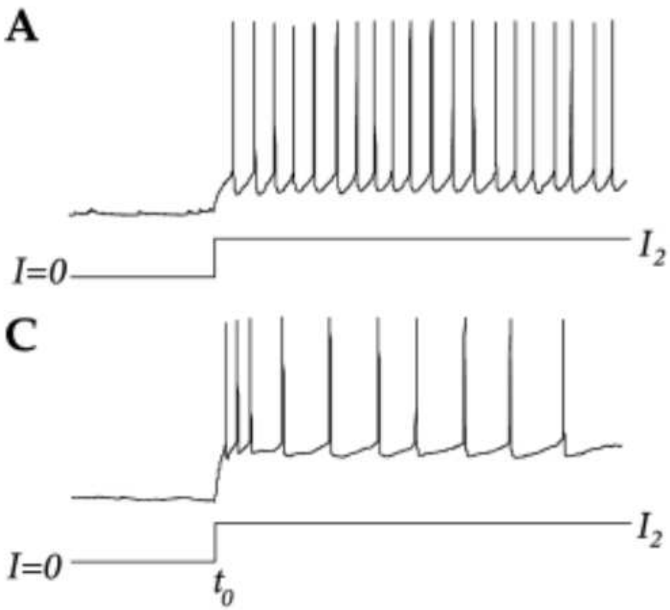




LIF neuron

Limitations of the LIF model

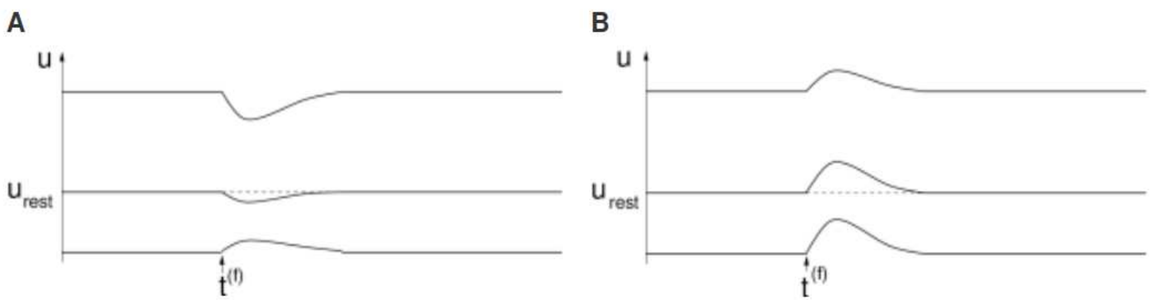
- after the emission of a spike the membrane potential is resetted to a value v_r: all the memory of the past emitted spikes is lost
  - Regularly spiking neurons show adaptation of the interspike intervals (ISI) between 2 successive spikes: not reproduced by LIF
  - Fast spiking inhibitory neurons do not show adaptation: well reproduced by LIF model



LIF neuron

Limitations of the LIF model

- the input is integrated linearly, indipendently of the value of the membrane potential v;
  - When the action potential reaches a synapse it is transformed ia a post-synaptic current (PSc) applied to the neuron .
  - The $PSC \propto (v - E_{syn})$, therefore it depends on the state of the neuron,
  - E_{syn} is called reversal potential, because if $v > E_{syn}$ ($v < E_{syn}$) the PSC is positive (negative);



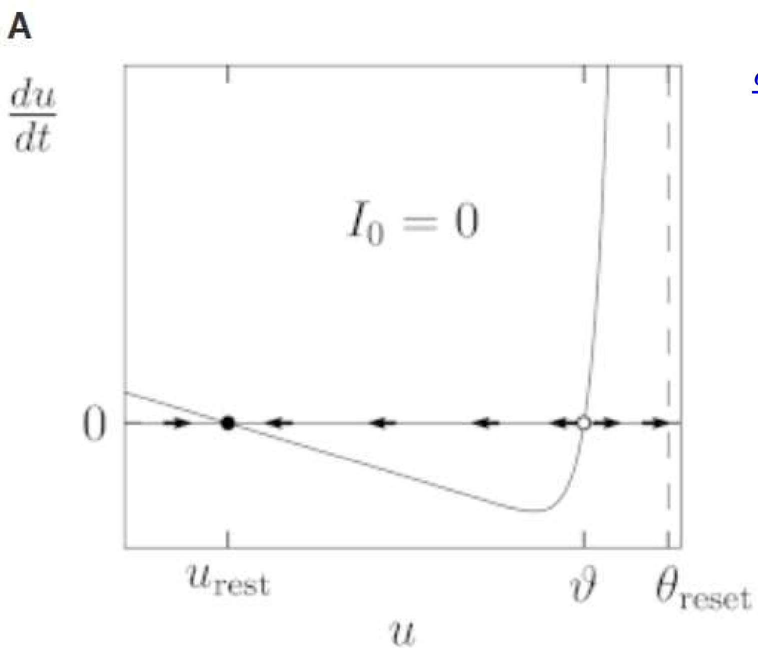
- Inhibitory neurons $E_{syn} \simeq v_r$
- Excitatory neurons $E_{syn} >> v_r$

Nonlinear Integrate-and-Fire Neuron

A generalization of the LIF model can be written as

$$\tau \frac{du}{dt} = f(u) + RI$$

- when u overcomes a threshold θ_{reset} at time $t^{(f)}$ the neuron emits a formal spike
- then u enters in a refractory period of duration Δ_{abs}
- at time $t + \delta_{abs}$ the value of u is resetted to $u = u_r$

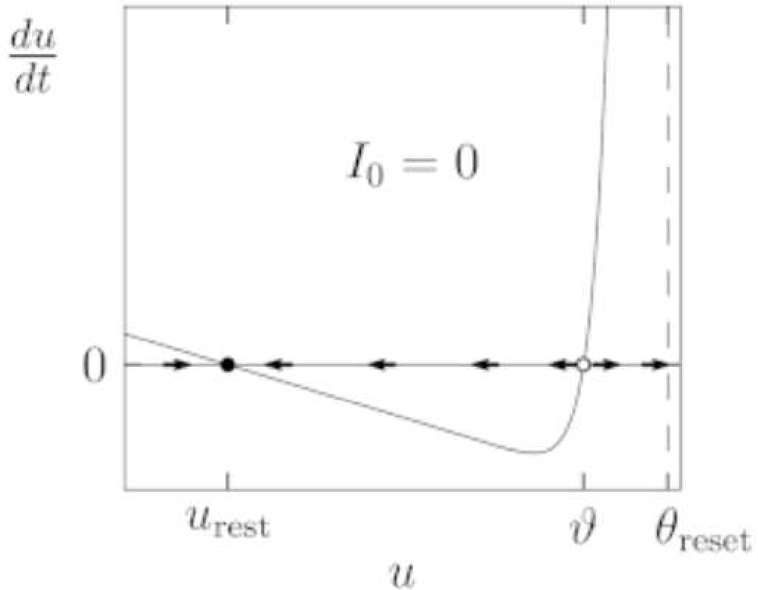


$\frac{du}{dt} = f(u)$ for $I = 0$

- if $\dot{u} = \frac{du}{dt} > 0$ the membrane potential increases
- if $\dot{u} = \frac{du}{dt} < 0$ the membrane potential decreases
- if $\dot{u} = 0$ the membrane potential remains constant (fixed point)

Stability of the fixed points

A



$\frac{du}{dt} = f(u) = 0$ for $I = 0$ define the fixed points

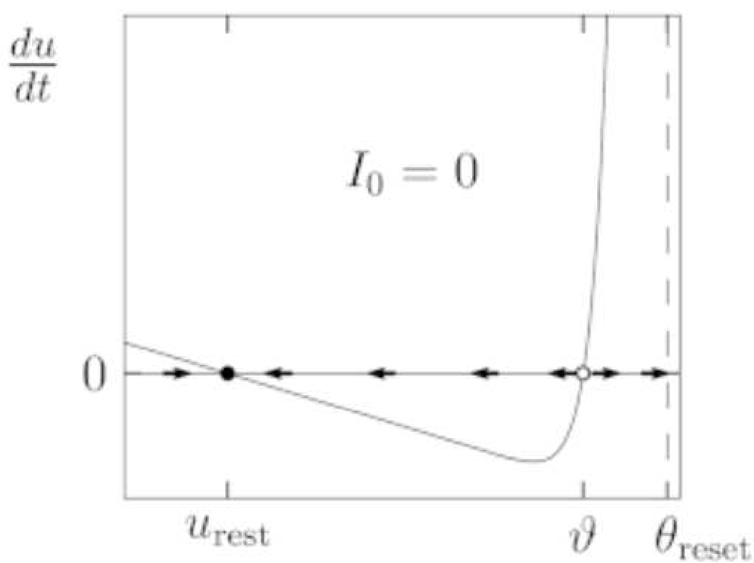
- $u = u_{rest}$ stable fixed point
- $u = \vartheta$ unstable (repulsive) fixed point

Suppose u_0 is a fixed point $f(u_0) = 0$ I want to measure its stability

- I perturb the state $u_0 + x(t_0)$ and look if the perturbation $x(t)$ decays or grows in time
- Therefore $\frac{dx}{dt} = f(u_0 + x(t)) \simeq f(u_0) + \frac{df}{du}|_{u_0} x(t) = \lambda x(t)$ since $f(u_0) = 0$
- $x(t) = x(t_0)\mathrm{e}^{\lambda t}$ if $\lambda = \frac{df}{du}|_{u_0} > 0$ ($\lambda < 0$) the fixed point is unstable (stable)

NIF dynamics

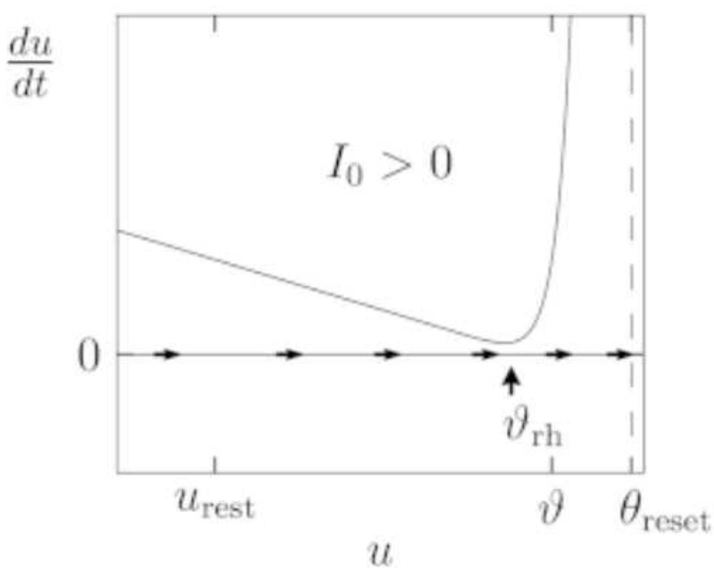
A



$I = 0$

- If $u < \vartheta$ then $u \to u_0$ silent dynamics
- If $u > \vartheta$ then $u \to \theta_{reset}$ the neuron fires

B



$I = I_0 > 0$

- If $I_0 > I_c$ no more fixed points (I_c rheobase current)
- $\dot{u} > 0$ then u grows towards θ_{reset}, the neuron fires and u is resetted to $u = u_r$
- The process restart and the neuron fires periodically

Exponential Integrate-and-Fire (EIF) neuron

The membrane potential evolution is given by

$$\tau \frac{du}{dt} = (u_{rest} - u) + \Delta_T e^{\frac{u-\vartheta_{rh}}{\Delta_T}} + RI$$

with $\Delta_T >> (u_{rest} - \vartheta_{rh})$.

For $I = 0$ we have that $u \simeq u_{rest}$ is a stable fixed point, while

$u = \vartheta = u_{rest} + \Delta_T e^{\frac{\vartheta-\vartheta_{rh}}{\Delta_T}}$ is an unstable one

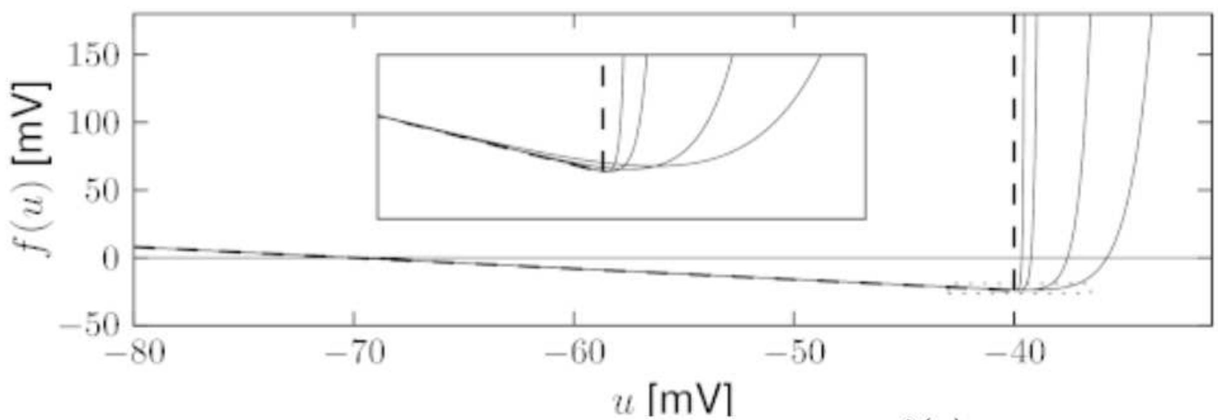


Fig. 5.3: Exponential and leaky integrate-and-fire model. The function $f(u)$ is plotted for different choices of the 'sharpness' of the threshold ($\Delta_T = 1,\ 0.5,\ 0.25,\ 0.05$ mV) In the limit $\Delta_T \to 0$ the exponential integrate-and-fire model becomes equivalent to a leaky integrate-and-fire model (dashed line). The inset shows a zoom onto the threshold region (dotted box).

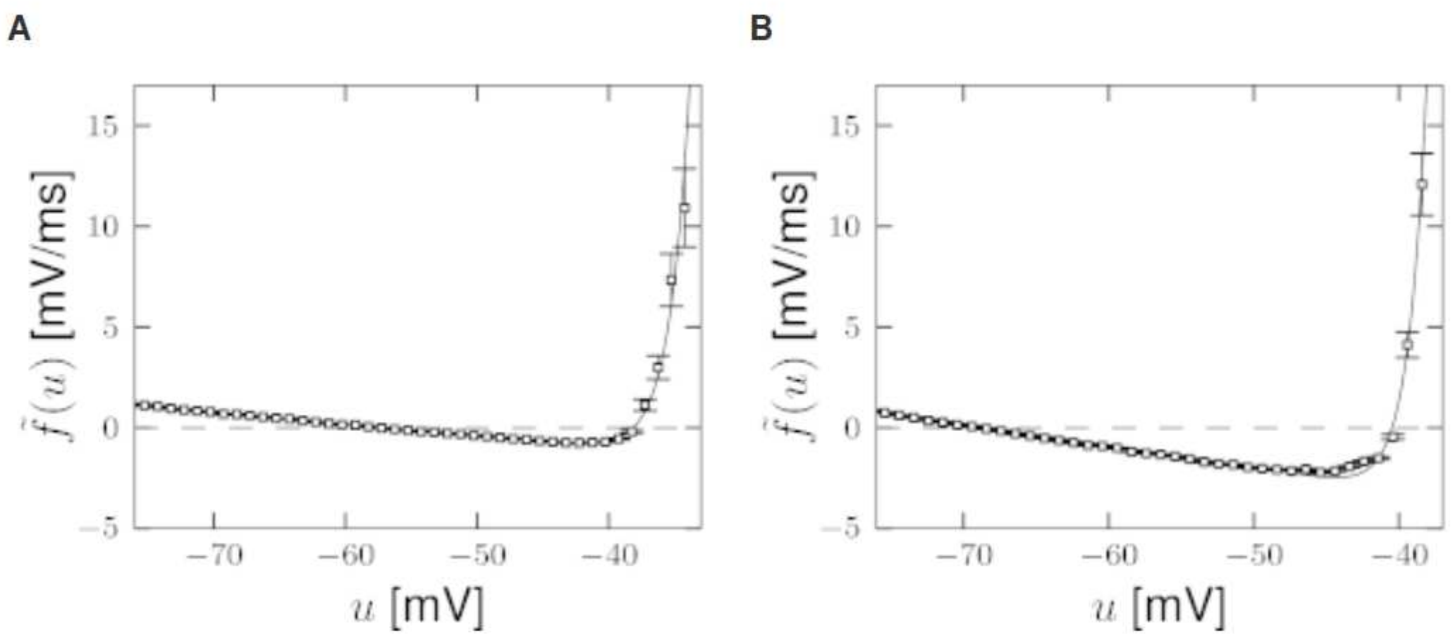
EIF neuron

Frome the experimental data we can measure

$$\tilde{f}(u) = \frac{f(u)}{\tau} = \frac{I(t)}{C} - \frac{du}{dt}$$

where $C = \tau/R$ is the membrane capacitance.

A time-dependent current $I(t)$ is injected in the soma of the neuron, while the membrane potential $u(t)$ is measured and from this its derivative du/dt can be obtained, averaging over many different trials one gets $\tilde{f}(u) = \langle \frac{I(t)}{C} - \frac{du}{dt} \rangle$ which can be well fitted with the EIF Model for excitatory (cortical pyramidal cells) and inhibitory neurons



Quadratic Integrate-and-Fire (QIF) neuron

The evolution of the quadratic integrate-and-fire neuron can be written as

$$\tau \frac{du}{dt} = (u - u_{rest})(u - \vartheta) + RI$$

For $I = 0$ and $\vartheta > u_{rest}$ the QIF has 2 fixed points:

- u_{rest} which is stable and ϑ which is unstable
- for $u > \vartheta$ the membrane potential grows and reach the threshold $u_{reset} = +\infty$ the neuron spikes and it is resetted at $u_r = -\infty$

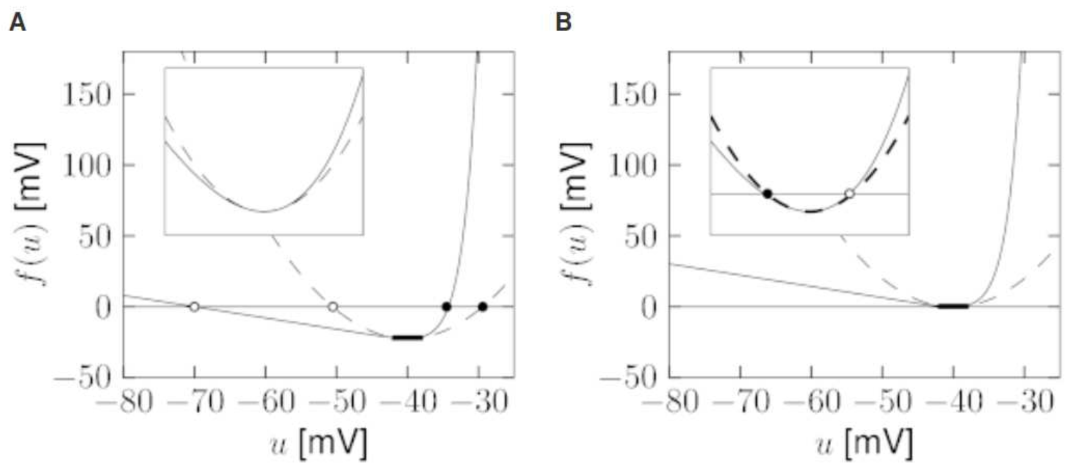
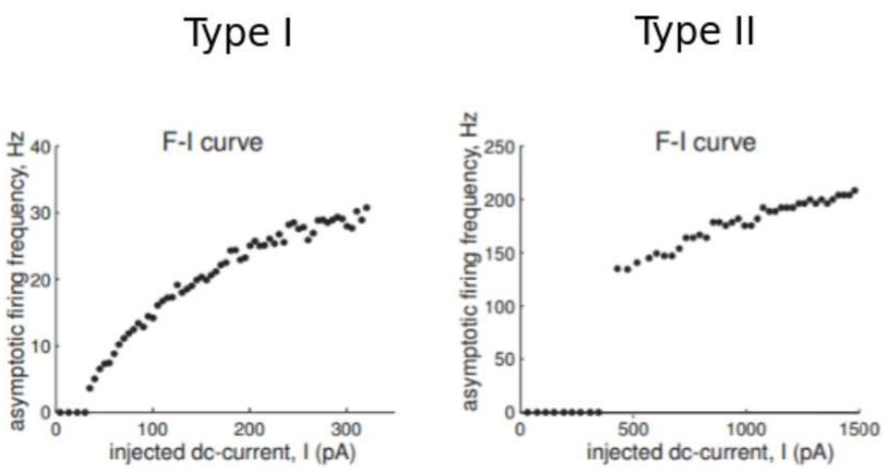


Fig. 5.8: Quadratic Integrate-and-Fire Model. **A**. The quadratic integrate-and-fire model (dashed line), compared to an exponential integrate-and-fire model (solid line). **B**. The quadratic integrate-and-fire model can be seen as an approximation of an exponential integrate-and-fire model (or any other type I model) depolarized to a state close to repetitive firing. In A and B, the value $f(u)$ and curvature $d^2 f/du^2$ are matched at $u = \vartheta_{rh}$. Note that the rise in the quadratic model is slower in the super-threshold regime $u > \vartheta_{rh}$.

QIF neuron

- For $I \simeq I_c$ the stable and unstable fixed point merge together in such a case the QIF neuron approximates very well the EIF model for $u_c \leq u \leq \vartheta$.
- More generally, any type I neuron model close to the bifurcation point can be approximated by a quadratic integrate-and-fire model - and this is why it is sometimes called the ‘canonical’ type I model

Type I and I neurons



- Type I: action potentials can be emitted with arbitrarily small frequency, based on the intensity of the applied current.
- Type II: action potentials can only be emitted with a frequency above a certain value and this frequency is relatively insensitive to the intensity of the applied current.

Type I and II neurons

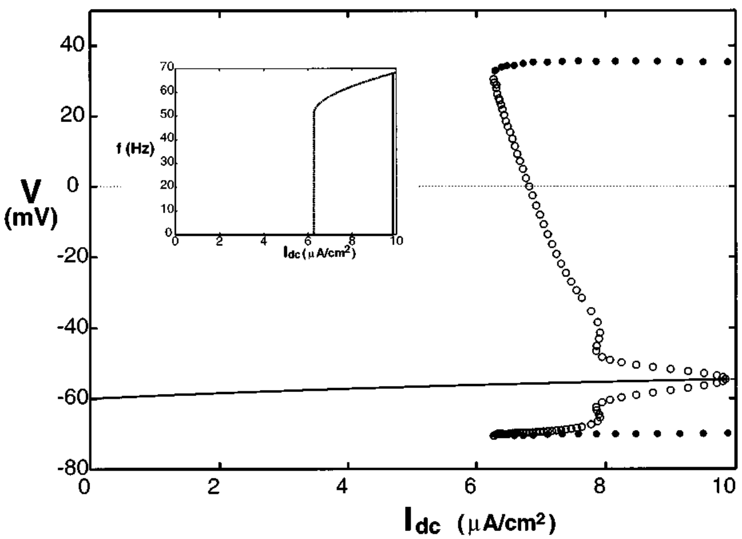
The emergence of repetitive firing from the silent regime in neurons of Type I and II is characterized by different bifurcations:

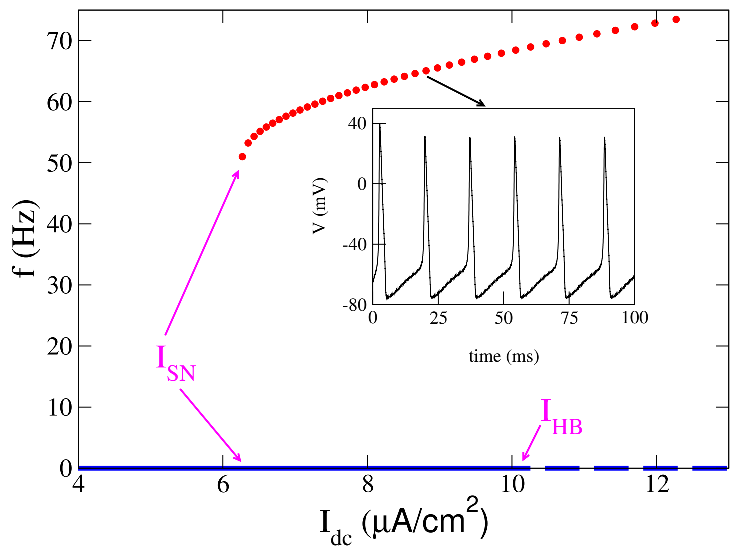
- Type I: Saddle-Node bifurcation ona Invariant Circle (SNIC);
- Type II: Hopf bifurcation super- or sub-critical ones.

- The Hodgkin-Huxley model is a Type II neuron, sinc eit exhibits a sub-critical Hopf bifurcation for the emergence of tonic firing
- The QIF model is a Type I neuron

Phase diagram HH model - Type II

Constant Synaptic Current $I_{syn} = I_{dc}$

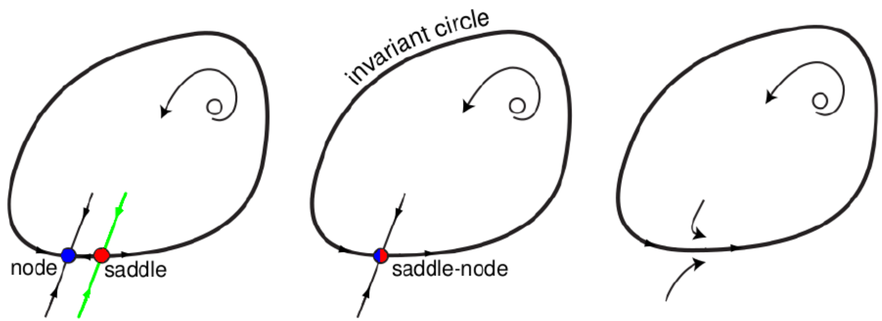




- $I < I_{SN}$ Silent Neuron
- $I_{HB} < I < I_{SN}$ Bistability
- $I > I_{HB}$ Tonic Firing

- Subcritical Hopf bifurcation at $I_{HB} \simeq 9.78 \mu A/cm^2$
- Saddle-node bifurcation of limit cycles at $I_{SN} \simeq 6.27 \mu A/cm^2$

SNIC bifurcation



The SNIC bifurcation in two dimensions is characterized by

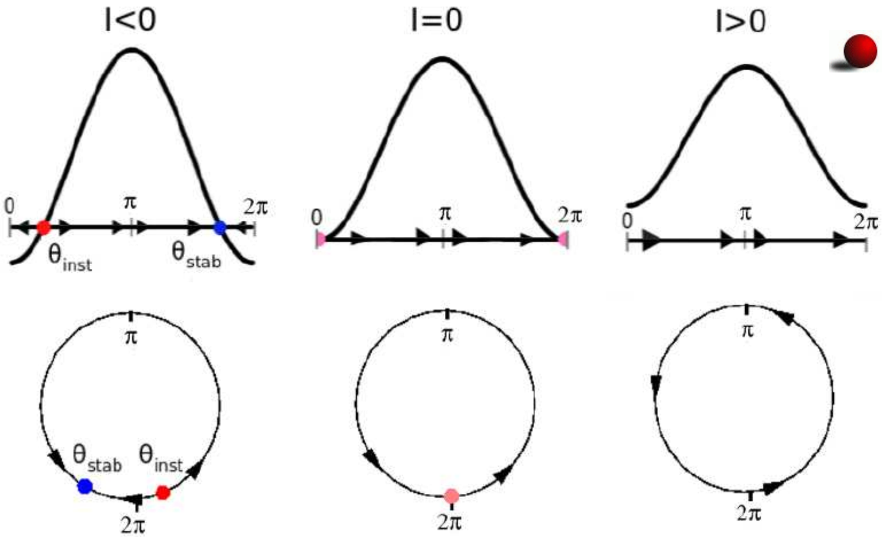
- $I < I_c$ Coexistence of three fixed points : stable node; unstable saddle-point and unstable focus (white):
  - the stable variety of the saddle point divides the trajectories that converges rapidly to the stable node and the ones that makes a large excursion around the focus before reaching the node (action potential);
  - $I = I_c$ sddle and node merges and the period of the action potential becomes infinite (firing with zero frequency);
  - $I > I_c$ Saddle and node disappear and we have a limit cycle of finite period (repetitive firing)

Θ-neuron

The dynamics in proximity of the onset of oscillations for a Type neuron is described by a universal one-dimensional model the θ-neuron:

$$\dot{\theta} = [1 - \cos(\theta)] + [1 + \cos(\theta(t))]I \qquad \theta \in [0, 2\pi]$$

the angle θ is the analogous of the membrane potential.



- I < 0: two fixed points one stable and one unstable.
  - $\theta < \theta_{inst}$ the solution converges towards $\theta stab$
  - $\theta > \theta_{inst}$ the solution makes a complete tour and pass the value $\theta = \pi$ where a spike is emitted, before returing to $\theta stab$
- I=0 : the two fixed point merge
- I>0: no more fixed points, the phase rotates continuously (repetitive firing)

Θ and QIF neuron

The Θ model is stricty related to the QIF, they can be mapped one in the other by the transformation:

$$V = \tan\left(\frac{\theta}{2}\right) \qquad V \in]-\infty, +\infty[$$

Please demonstrate it ...

blackboard

$$\dot{V} = V^2 + I \qquad V \in]-\infty, +\infty[$$

For $I > 0$ periodic motion with period T

- variable separations $\frac{dV}{V^2+I} = dt$
- the period T is the time to go from rest $V = -\infty$ to threshold $V = +\infty$
- $T = \int_{\infty}^{\infty} \frac{dV}{V^2+I} = \frac{1}{\sqrt{I}} \left[\arctan(\frac{V}{\sqrt{I}})\right]_{-\infty}^{\infty}$
- $$T = \frac{\pi}{\sqrt{I}}$$