AI applications in Biophysics and Neuroscience

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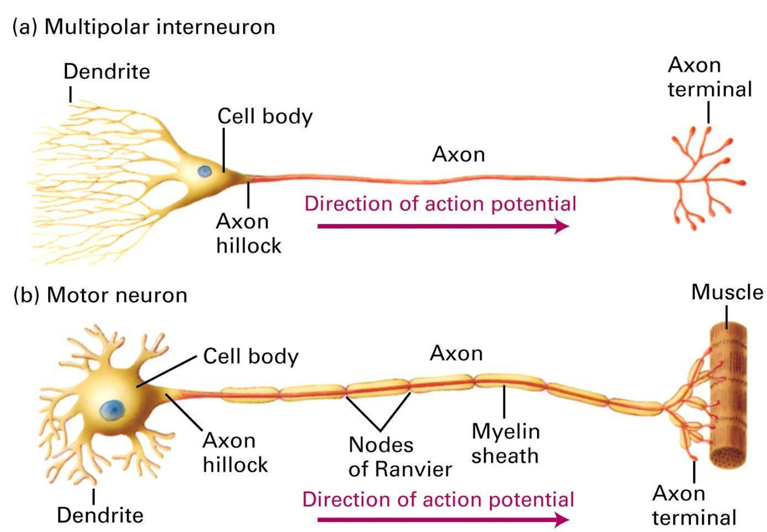
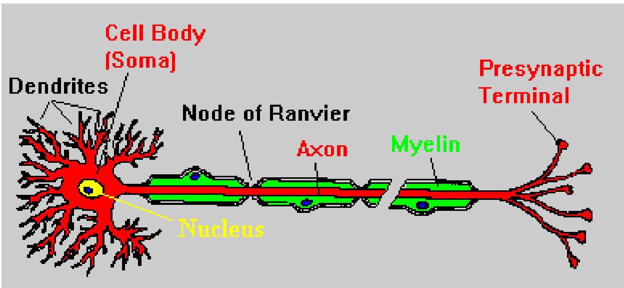
Neurons in Bref

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

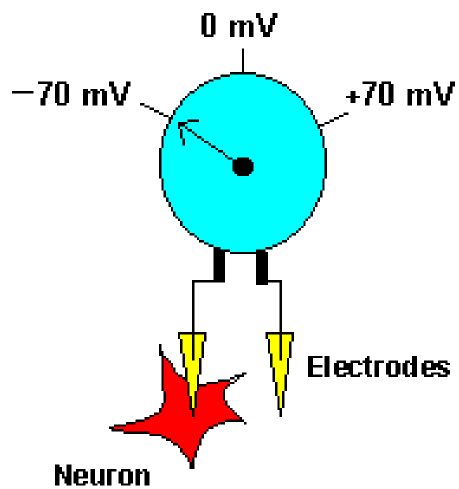


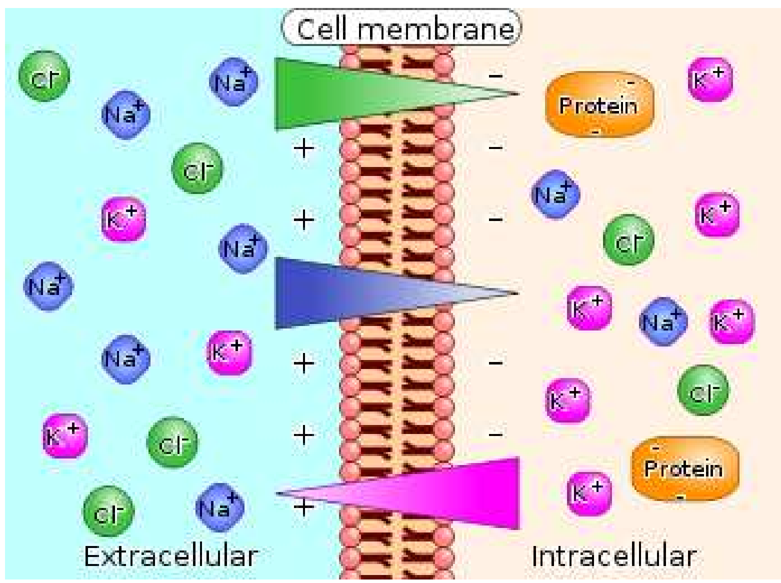
Despite their enourmous variety, neurons have some common morphological aspect:

- The soma is a compact almost spherical structure (diameter $\simeq$ 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 each 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

Membrane Potential

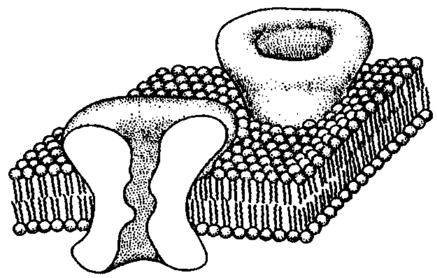
- The membrane potential V_m measures the electrical potential difference between interior and exterior of the neuron.
- The neuron at rest has $V_{rest} \simeq$ -60 mV / -75 mV

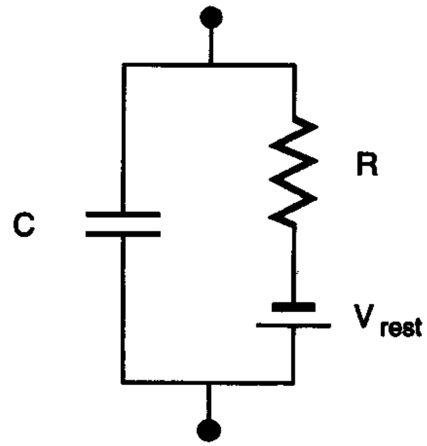




The neuron is in a dynamical equilibrium state the neuronal signals are electrical signals.

Membrane as an Electric Circuit



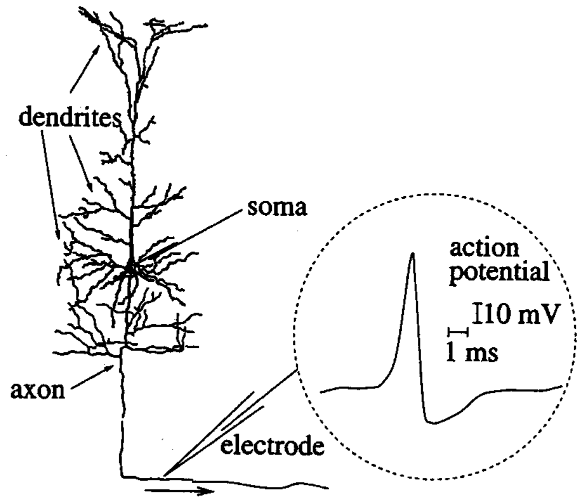


The neural membrane can be seen as an electric circuit with passive characteristics

- the membrane separates positive and negative charges, it acts as a capacitance
  $\boxed{C_m \simeq 1\mu F/cm^2 \rightarrow 4x10^{11} \text{ monovalent ions/cm}^2}$
- the ionic channels have specific membrane resistance/conductance :
  Leakage Resistance $\boxed{R_m \simeq 10^3 \Omega \cdot cm^2}$
  Leakage Conductance $\boxed{G_m = 1/R_m \simeq mS/cm^2}$
- 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)

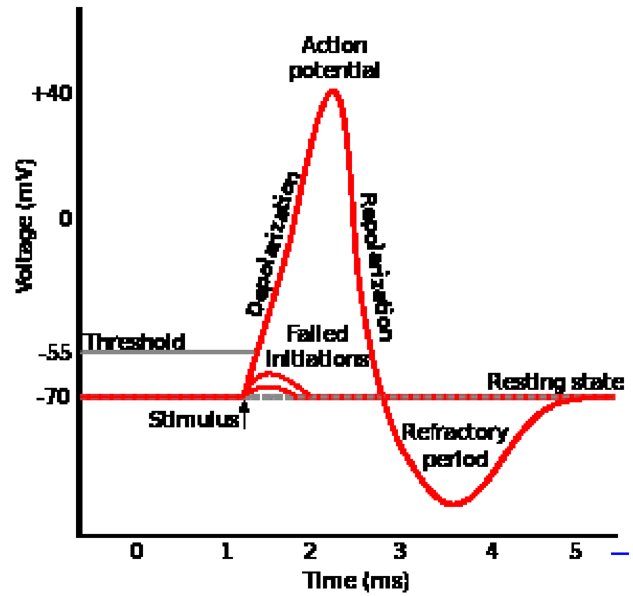
Action Potential

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



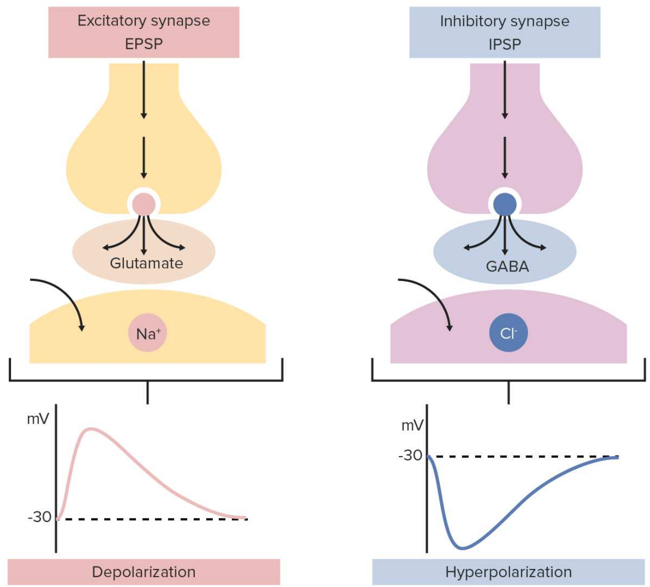
- The neuronal signal is given by the temporal and spatial variation of the membrane potential V_m.
- The action potentials (APs) are electrical impulses delivered when a (depolarizing) stimulus leads V_m above a certain threshold $\Theta \sim -55$ mV

- 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.



Synapses

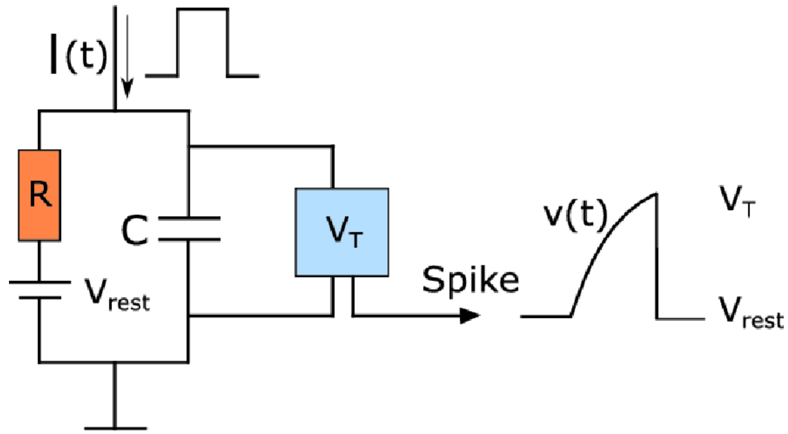
The junction between two neurons is called a synapse. The synapse allows a neuron to pass an electrical or chemical signal to another neuron. The neuron that sends the signal to another neuron is called the pre-synaptic neuron, while the neuron that receives the signal is called the post-synaptic neuron. The molecules that mediate the interaction are called neurotransmitters.



Dale’s principle : a neurotransmitter released at one axon terminal of a neuron can be presumed to be released at other axon terminals of the same neuron. A neuron can be identified as excitatory or inhibitory in an univoque manner, it cannot be at the same time excitatory and inhibitory

Leaky integrate-and-fire (LIF) neuron

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



From the Kirchhoff's law for the currents one gets

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

The current $I(t)$ charges the RC circuit, the potential difference $v(t)$ across the capacitance C is compared with a threshold value $V_T \equiv \Theta$: if $v(t)$ becomes larger than the theshold it is reset to a value $v_{rest} = v_r$ that is the equilibrium value of the membrane potential.

Leaky integrate-and-fire neuron

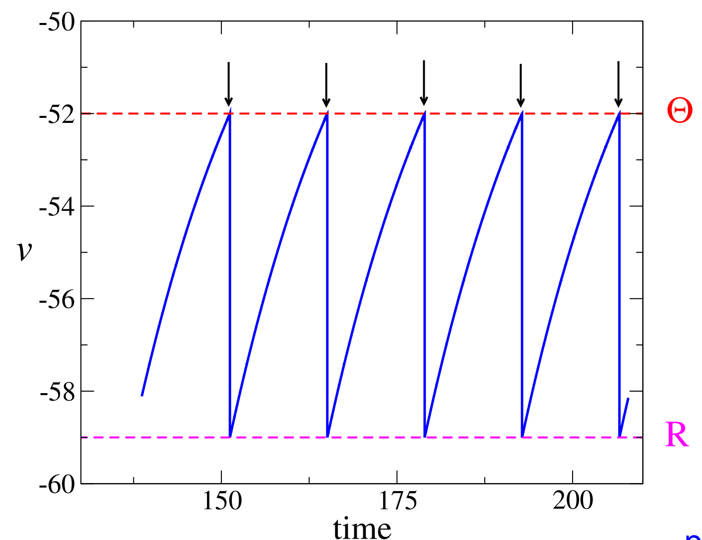
By introducing the membrane time constant $\tau = RC$ one gets:

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

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 $v(t=0) = v(0)$ the membrane potential evolution is given by

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

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



LIF neuron

Periodic Behaviour

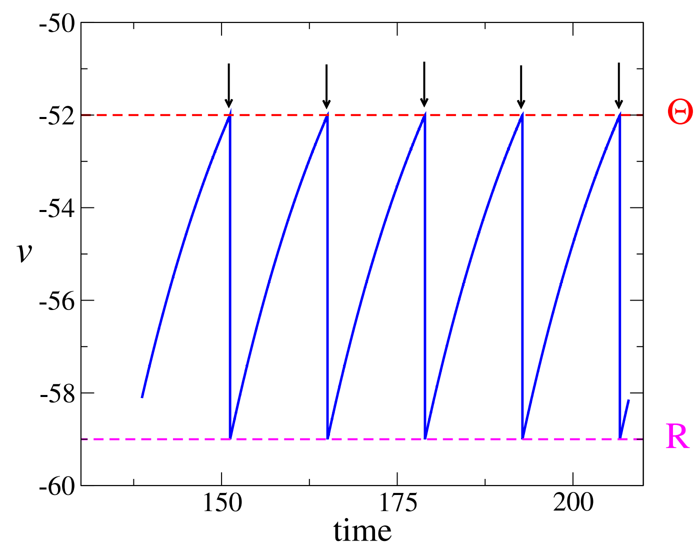
- If $RI + v_r > \Theta$ Repetitive Firing (Oscillator)
- At $t = 0$ the neuron has been resetted to $V(0) = v_r$
- After one period $t = T$ the neuron is at threshold $V(T) = \Theta$

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

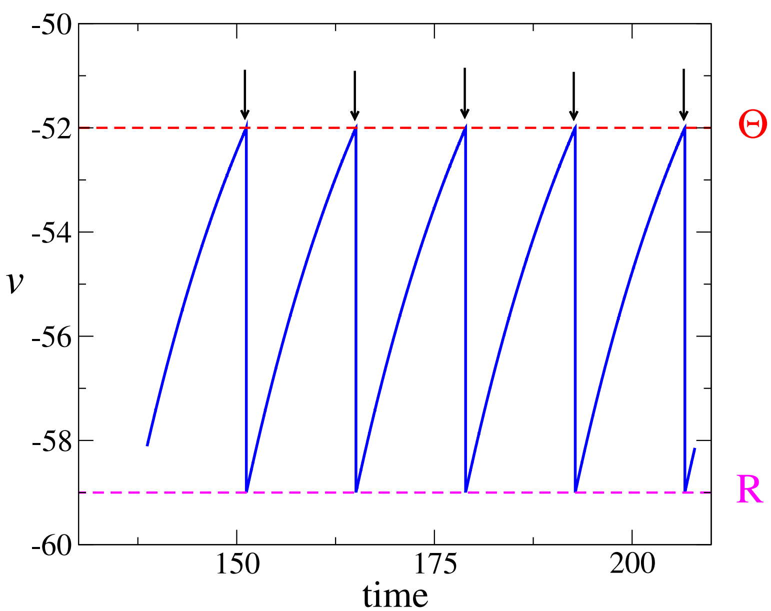
$$T = \tau \ln \frac{RI}{v_r + RI - \Theta}$$

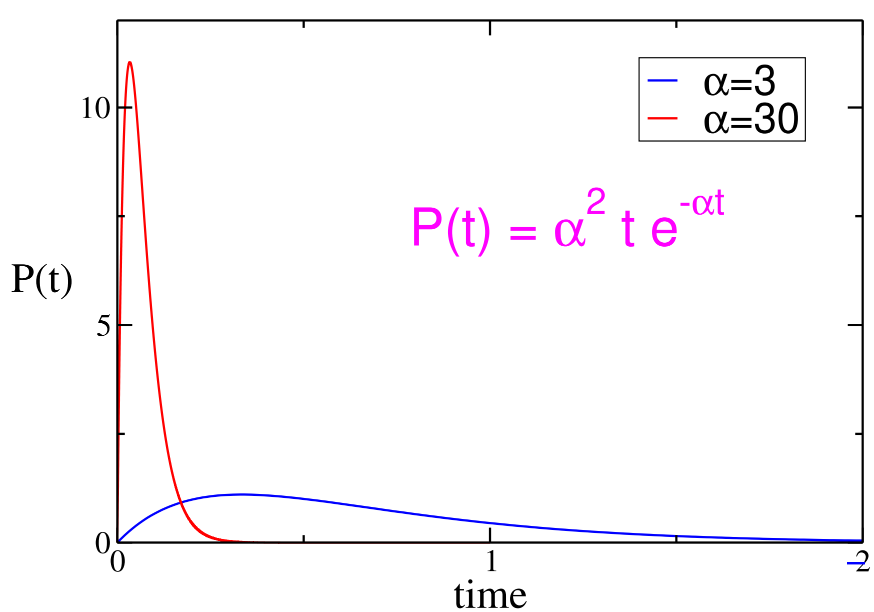


LIF neuron

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





Spiking Neural Network

$$\dot{v}_i(t) = a - v_i(t) + gE_i(t) \qquad E_i(t) = \frac{1}{N} \sum_{n|t_n<t} J_{j(n),i}\theta(t-t_n)p(t-t_n)$$

- $a > 0$ suprathreshold input current
- g coupling strength of the excitatory (inhibitory) interaction with the neural field $E_i(t)$
- $p(t)$ pulse received by the connected neurons
- $J_{j(n),i}$ connectivity matrix (between the emitting $j(n)$ and the receiving i neuron)
- $\theta(x)$ Heavyside function

Learning in neural networks involves the modification of the connectivity of neurons.

- supervised learning with gradient descent and spike backpropagation
- **(un)supervised learning with local learning rule at the synapse (e.g. spike-time-dependent plasticity)**
- reinforcement learning with reward/error signal using reward modulated plasticity

Spiking Neural Network

- Supervised learning of a task is generally cast as an optimization problem in very high dimensions

Given a population of N (artificial) neurons connected through S synaptic connections J_{ij} , one looks for the minimum of the cost (loss) function $U(\{J_{ij}\})$ expressing the mismatch between the target and actual computation carried out by the network: U can be gradually reduced through gradient descent along the gradient of the cost

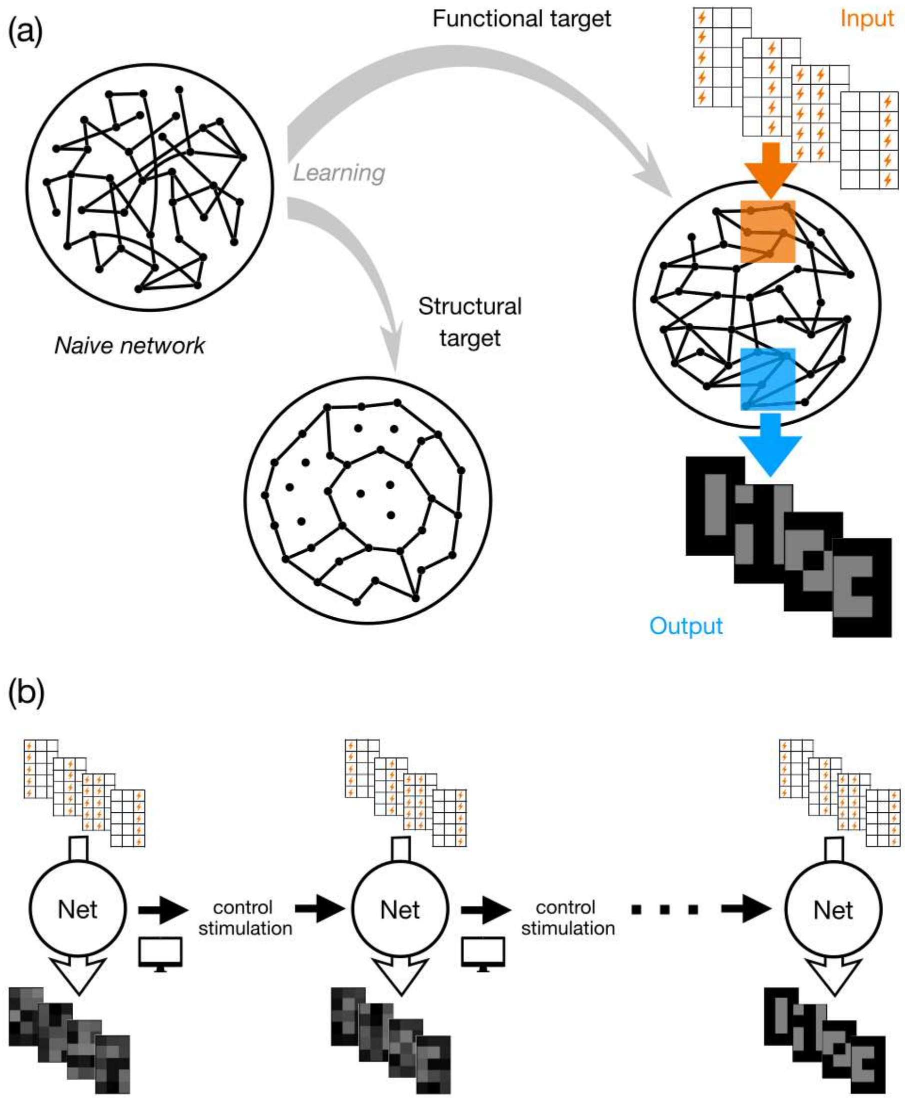
- Hebbian like plasticity rule

The changes in the connections J_{ij} are functions of the firing rates r_i of the neurons. As the number N of neurons is generally much smaller than the number N^2 of synaptic interactions, the plastic changes J_{ij} are highly interdependent, and cannot be individually tuned to match the gradient components $\frac{\partial U}{\partial J_{ij}}$

- Training through the application of adequate control stimulations neuron- and time-dependent (obtained by solving a sequence of optimization problems)

[Borra, Cocco, Monasson, PRX LIFE 2, 043014 (2024)]

Computational targets for plastic neural networks



Multiple cycles of stimulations and recordings of the network population.

At the beginning of each cycle, the responses of the network to a few short probing stimulations are recorded, and used to infer the connectivity of the network. Based on this estimate of the connectivity, we plan a control stimulation pattern, which is subsequently applied to the neurons. Under this control, plastic changes to the connections take place and enhance the network performance in achieving the desired computation. **The procedure is iterated until the computational target is reached.**

Model

$r_i(t)$ firing rate, $f_i(t)$ time-dependent control stimulation on neuron i, Φ input-to-rate transfer function (sigmoidal function), $\eta(\epsilon_j) = \eta(E), \eta(I)$ neuron type

$$\tau_n \frac{dr_i(t)}{dt} = -r_i(t) + \Phi\left(\sum_j J_{ij} r_i(t) + f_i(t)\right)$$

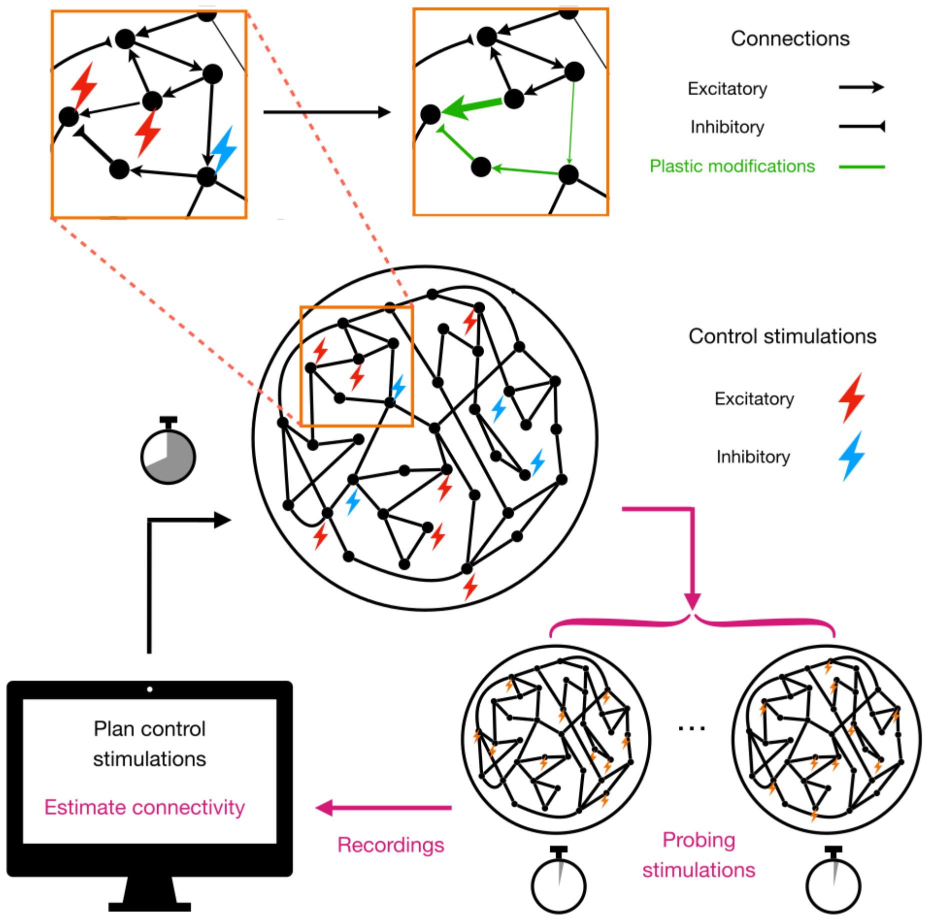
$$\tau_s \frac{dJ_{ij}(t)}{dt} = \eta(\epsilon_j)\left[r_i(t) - \theta(\epsilon_j)\right] r_j + homeostatic \quad feedback$$

Hebbian rule: the weight between two neurons increases if the two neurons activate simultaneously, and reduces if they activate separately. Train the neural network connectivity J to meet some target

- Structural J^{target}: $U_{task}(J) = \sum_{i,j} w_{\epsilon_i,\epsilon_j}[J_{ij} - J^{target}]^2$
- Functional: the target the computation carried out by the network $U_{task}(J) = \sum_{\mu=1}^{n_{pairs}} \sum_{i\in out}[r_i(J, f^\mu) - r_i^\mu]^2$

where $r_i(J, f^\mu)$ stationary solution of the rate equation, f^μ input stimulation, n_{pairs} set of input/output mappings, network= input, processing, and output (“out”)

Training Loop

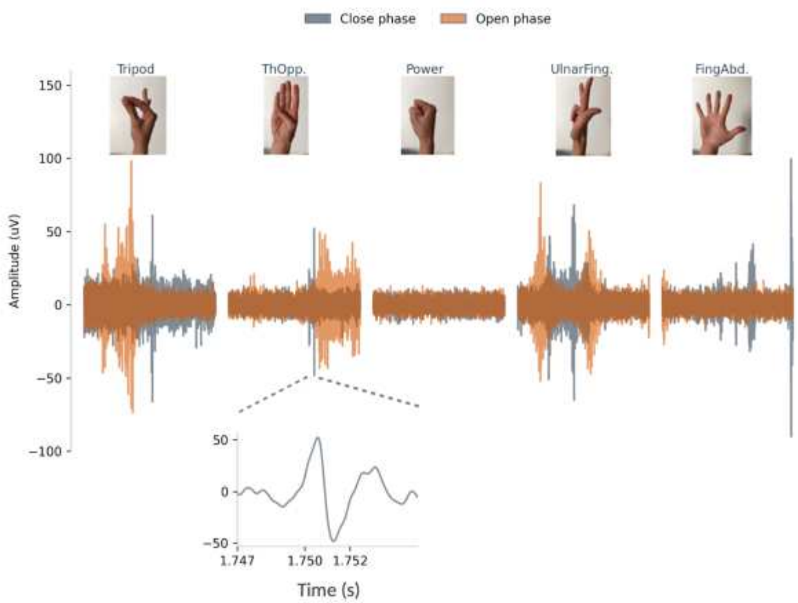


- Estimation of the current connectivity, J_k , through fast probing of the responses of the network to random stimuli.
- Calculation of the optimal control to be applied, f_k^* , to shift the network connectivity state towards the desired target.
- Application of this control during the period Δt, leading to a reorganization of the network through its intrinsic plasticity mechanisms.

The learning process stops when the value of the loss U_k is considered small enough

Nerve-level Neural Interfaces

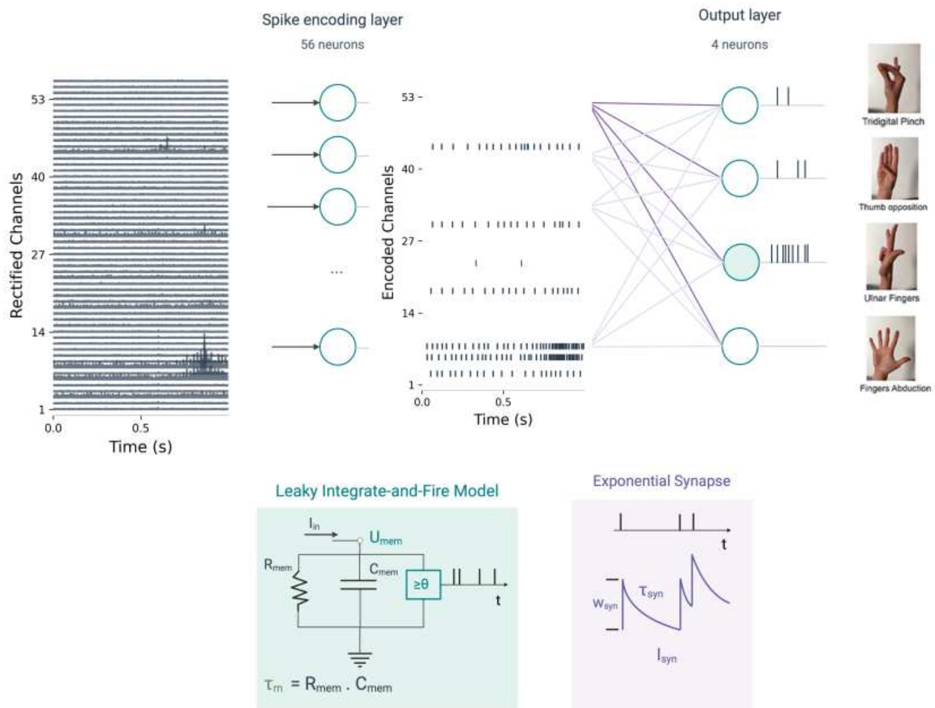
- Transverse Intrafascicular Multichannel Electrodes (TIMEs): single strip with platinum electrode sites that is threaded transversely through the nerves
- Nerve stimulation with TIMEs allowes for object discrimination and modulation of grasping forces
- Motor commands are decoded in real-time from five surface peripheral nerves (electroneurographic ENG) electrodes placed on the amputee's residual muscles
- Each filtered ENG channel is first converted into a sequence of events or spike trains before being presented to the SNN



Filtered ENG signal recorded from a channel of the ulnar electrode [Baracat et al (2024). Decoding gestures from intraneural recordings of a transradial amputee using event-based processing. TechRxiv]

Network Architecture

Spiking neural network computational model for pre-processing and decoding motor commands from TIMEs



- Neurons in the first layer encode the rectified ENG (each neuron corresponding to one channel) into spike trains which are transmitted to the output layer.
- Four neurons in the output layer are trained to predict the correct gesture. Gesture identity is encoded within the firing rates of the input channels, with distinct rates associated with each gestur.

Computational Neuroscience Lab

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via Madonna del Piano 10,
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- Thomas Kreuz (analysis of electrophysiological recordings, neuronal population coding)
- Alessandro Torcini, Antonio Politi (modelling and simulation of neuronal networks using simple models, analysis of multi-scale models of brain function)

Ongoing project: learning algorithm capable of achieving image and text classification accuracy in a realistic network of neural mass models.
In collaboration with Raffaele Marino (UniFi)

https://www.firenze-neuro.org/

EBRAINS

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