Abstraction of dynamics and structure of biological neurons

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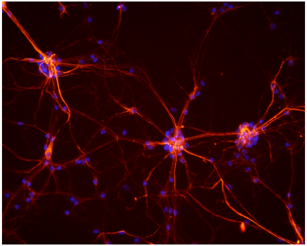
Aims and context

The brain

- 100 billion neurons
- 10 000 connexions per neuron
- Complex network
- Multidisciplinary approach



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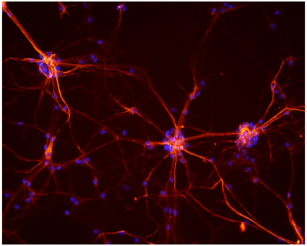


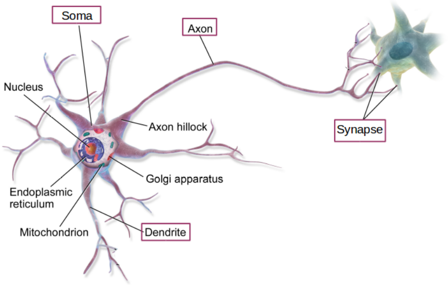
Aims

- Tool to aid understanding, proof of properties
- Questions about structure-function relationship : Influence of geometry and topology ?
- Hybrid modeling at the scale of an individual neuron
- Simplification and biological relevance

Biological neuron and structure

Cell of the nervous system specializing in :

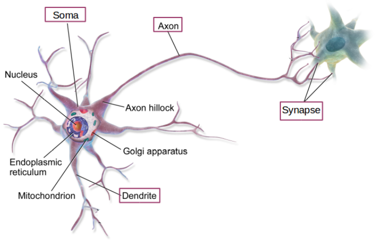
- processing
- transmission of information

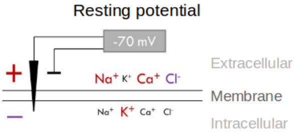


The nerve impulse

Electric pulses

- Resting potential
- Threshold
- Action potential





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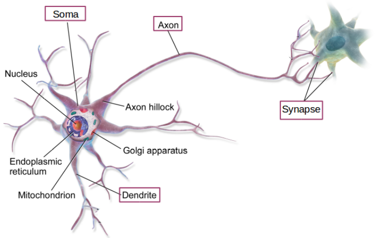
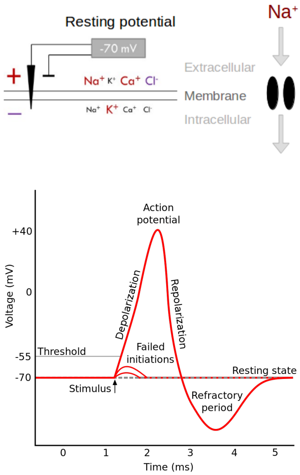
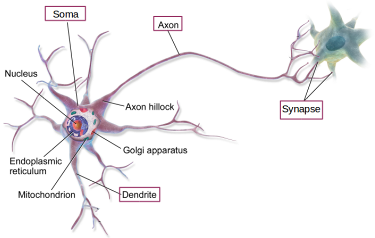
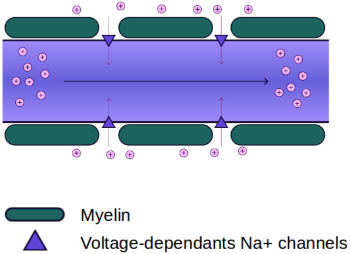




Action potential

Coding in frequencies
Regenerative propagation
Refractory period

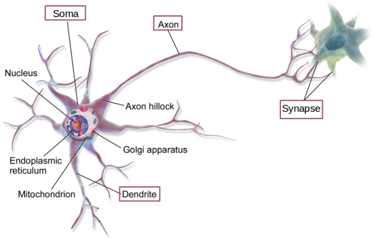


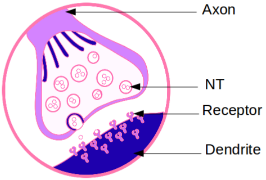


Synapse

Connexion between 2 neurons

- Chemical messenger (NT)
- Post-synaptic potential





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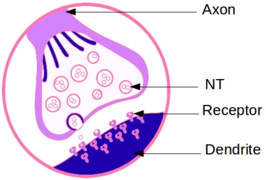
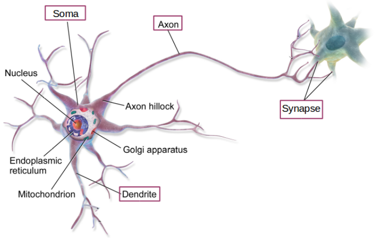
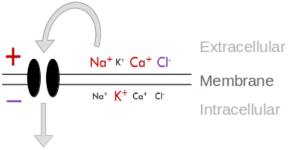


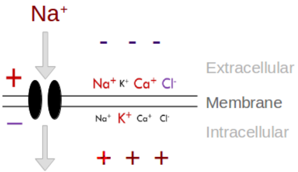




Post-synaptic potential (PSP)

Excitatory synapse (EPSP)

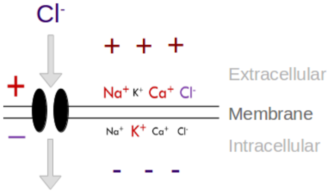
- Positive charges entry
- Depolarisation



Ex : *AMPA* receptor

Inhibitory synapse (IPSP)

- Negative charges entry
- Hyperpolarisation

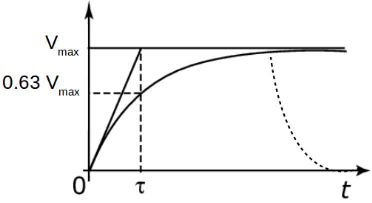


Ex : $GABA_A$ receptor

Excitatory post-synaptic potential (EPSP)

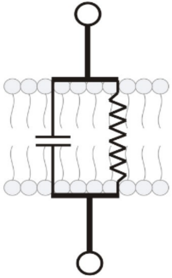
Increase of the potential

- Physics
- Exponential
- Resting potential



RC circuit

- Membrane = capacitor
- Channel = resistor



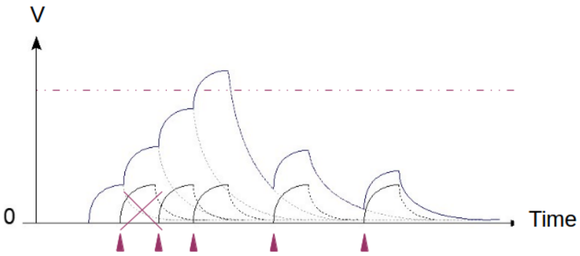
Summation of PPS

Temporal summation

- Only one synapse
- If frequency is high enough

Spatial summation

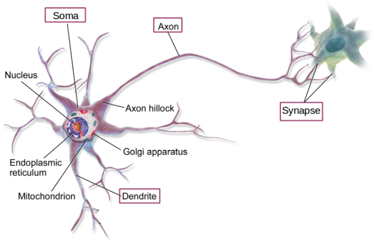
- Multiple synapses
- If synapses are close enough



Dendrites

Decremental propagation

- Cable theory
- Exponential



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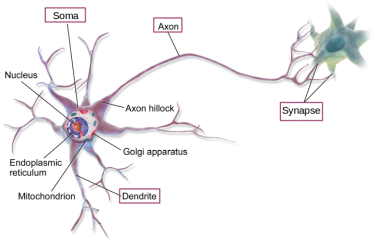
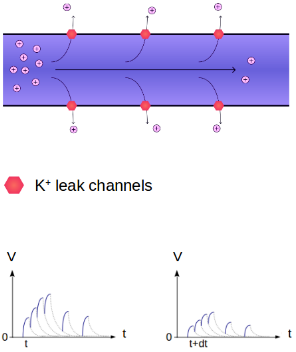
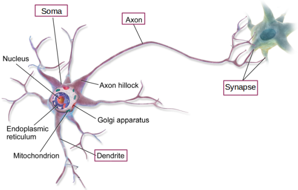




To summarize

The nerve impulse is a sequence of electric pulses which :

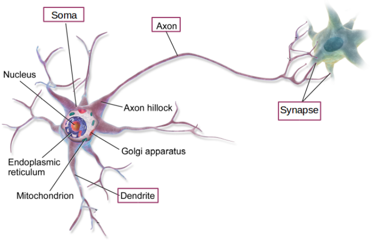
- are received by dendrites (synapses)
- result in an increase of the potential
- are summed
- are propagated along the axon if the potential of the soma is beyond the threshold

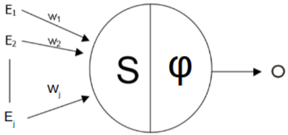


From the biological to the formal neuron

Mc Culloch & Pitts (1943)

- Simple logical calculus
- Artificial intelligence (networks)





1. McCulloch, W. S., Pitts, W., A (1943) Logical Calculus of the Ideas Immanent in Nervous Activity, Bulletin of Mathematical Biophysics, vol. 5, pp. 115-133

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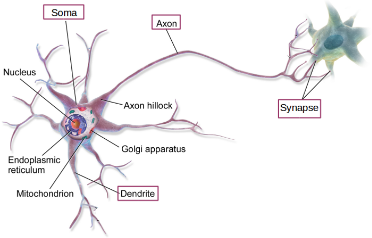
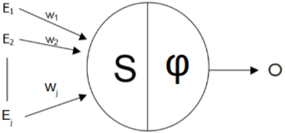




- High level of abstraction
- Biological relevance ?

1. McCulloch, W. S., Pitts, W., A (1943) Logical Calculus of the Ideas Immanent in Nervous Activity, Bulletin of Mathematical Biophysics, vol. 5, pp. 115-133

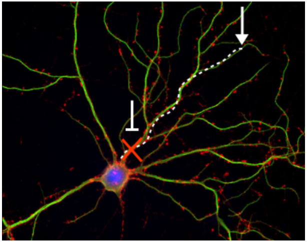
Biological neuron models

Describe and predict biological processes

- Biophysical modeling
- Differential equations
- Very accurate but complex !

A neuron is not punctual !

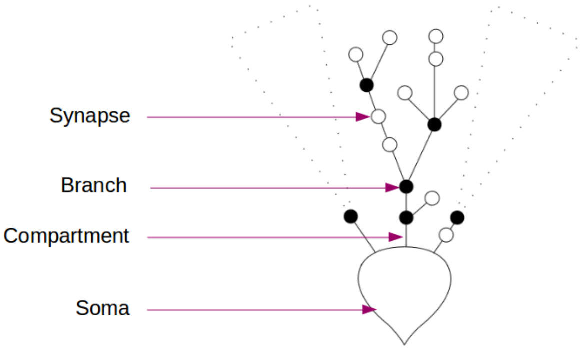
- Delay from synapses to soma
- Attenuation in dendrites
- Variable efficiency of the synapses with location



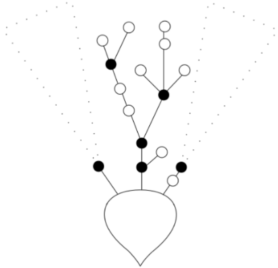
Structure and representation of the model

Oriented system

- Root = soma
- Dendritic trees
- No axon



Function of the model



Merge information

Discrete inputs

- Times for action potentials
- Via synapses
- Modification of the potential (PSP)

Continuous evolution of the potential

- Attenuation in compartments
- Combination at connection points

Discrete output

- Action potential if the threshold is crossed

Synapses

Inputs $\omega : [0, t_0] \to \{0, 1\}$

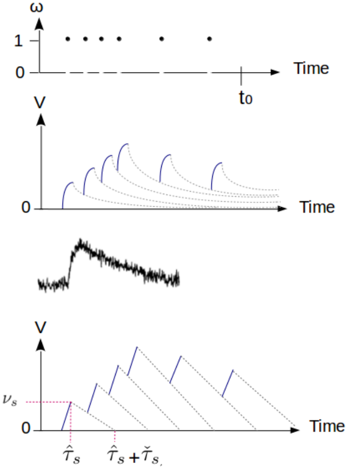
Local variation of the potential V

- Exponential (RC circuit)
- Highly variable (experiments)
- Linear approximation

Definition

A *synapse* is a triplet $s = (\nu, \hat{\tau}_s, \check{\tau}_s)$ where :

- $\nu \in \mathbb{R}^*$
- $\hat{\tau}_s$ and $\check{\tau}_s \in \mathbb{R}^{*+}$



1. Mason, A., Nicoll, A., and Stratford, K. "Synaptic transmission between individual pyramidal neurons of the rat visual cortex in vitro" J. Neurosci. 11 : 72-84 (1991)

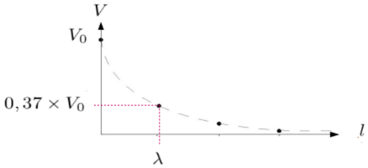
Compartments

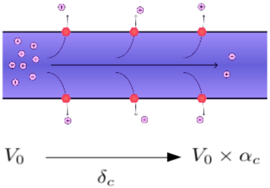
Cable theory :

- $V(l) = V_0 \times e^{-l/\lambda}$
- Space constant : $\lambda = \sqrt{r_m/r_l}$

Attenuation and linearization :

- $\alpha = e^{-l/\lambda}$
- Depends on length and diameter
- $V(l) = V_0 \times \alpha$





Definition

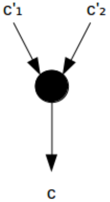
A *compartment* is a doublet $c = (\delta_c, \alpha_c)$ where :

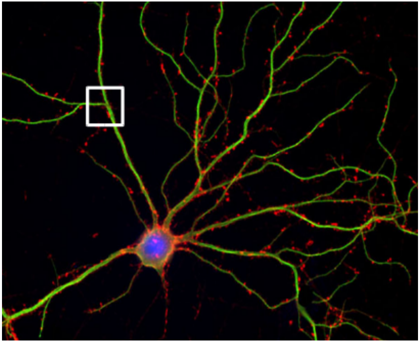
- $\delta_c \in \mathbb{R}^{*+}$
- $\alpha_c \in [0,1]$

Connexion points

Summation of inputs :

$$\left(\sum_{c' \in Pred(c)} V_{c'}(0) \right)$$





Soma

Accumulation

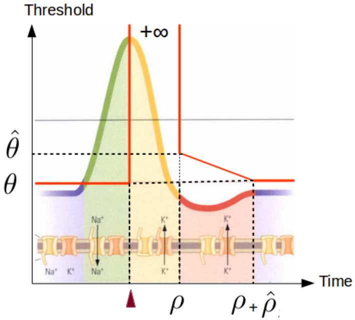
Attenuation

- Constant (γ)

Threshold (θ)

Discrete output (ω) and update

Refractory periods (ρ)

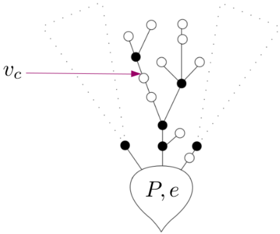


Definition

A *soma* is a tuple $\nabla = (\theta, \hat{\theta}, \rho, \hat{\rho}, \check{\gamma}, \hat{\gamma})$ where :

- $\theta, \hat{\theta}, \rho, \hat{\rho}, \check{\gamma}$ and $\hat{\gamma} \in \mathbb{R}^{*+}$

State of the neuron



Definition

The state of a neuron N is a triplet $\eta = (\mathscr{V}, P, e)$ where :

- $\mathscr{V}$ is a family of segments indexed by the compartments of N, of the form $v_c : [0, \delta_c] \to \mathbb{R}$
- $P \in \mathbb{R}$ is the *soma potential*.
- $e \in \mathbb{R}^+$ is the *time elapsed since the last spike*.

Synapses

We know how a spike influences the potential.

- Summation of the elementary traces.

Definition

Given an ensemble E, a *segment* with values in E in an application $\omega : [0, t] \to E$ where $t \in \mathbb{R}^+$. If $\omega_1 : [0, t_1] \to E$ and $\omega_2 : [0, t_2] \to E$ are two segments such that $\omega_1(t_1) = \omega_2(0)$, then $\omega_1.\omega_2$ is the concatenated segment $\omega_1.\omega_2 : [0, t_1 + t_2] \in E$ such that :

- $(\omega_1.\omega_2)(t) = \omega_1(t)$ si $t \leqslant t_1$
- $(\omega_1.\omega_2)(t) = \omega_2(t - t_1)$ si $t > t_1$

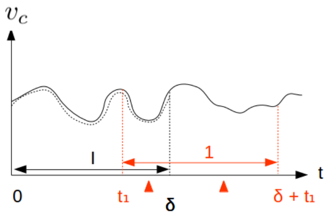
Moreover, if ω_1 and ω_2 are segments of the same length, $\omega_1 + \omega_2 \to E$ is the segment such that $(\omega_1 + \omega_2)(t) = \omega_1(t) + \omega_2(t)$ for all t.

Compartments

Given an initial state η^I with $v_c^I : [0, \delta_c] \to \mathbb{R}$ for each compartment c, we can determine the next state η^1 with $v_c^1 : [t_1, t_1 + \delta_c] \to \mathbb{R}$.

- If $t \leqslant \delta_c$: $v_c(t) = v_c^I(t + t_1)$
- If $\delta_c < t < t_1 + \delta_c$:

$$v_c(t) = \left(\sum_{c' \in Pred(c) \cup \text{Input}(c)} V_{c'}^I(t - \delta_c + t_1) \right) \times \alpha_c$$



Soma

Soma potential is influenced by accumulation and attenuation (constant ?) :

$$P(t) = P(O) + \left(\int_0^t \sum_{c \in \text{input}(\nabla)} V_c(t) \right) + \gamma \cdot t$$

By parts :

$$\int_0^t \sum_{c \in \text{input}(\nabla)} V_c(t) = \frac{A}{2} \cdot t^2 + B \cdot t$$

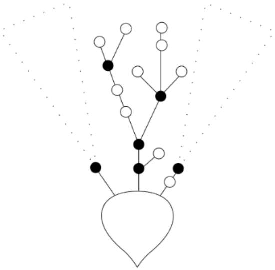
$$P(t) = P(0) + \frac{A}{2} \cdot t^2 + (B + \gamma) \cdot t$$

$$P(t_{i+1}) = P(t_i) + \frac{A}{2} \cdot (t_{i+1} - t_i)^2 + (B + \gamma) \cdot (t_{i+1} - t_i)$$

Conclusion

Work done so far

- Several theoretical difficulties resolved
- First modeling framework
- Collaboration with a local neurobiologist



Perspectives

- Some questions to be answered :
  - Can we find other simplifications ?
  - Can we use only one γ for the return to resting potential ?
  - Is the approximation reasonable for the leak at the soma ?
- The model will be used to validate various biological hypotheses.