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Teaching unit: Neurons: biological and physical model of electrical signal transmission

DiFC - University of Palermo

BIOS4YOU
AR 2.0

BIO-INSPIRED STEM TOPICS FOR ENGAGING YOUNG GENERATIONS
THANKS TO THE USE OF AUGMENTED REALITY

Project Number: KA220-BW-23-30-126516

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Contents

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General topic of the learning path	Neuroscience
Specific name of the learning unit	Neurons: biological and physical model of electrical signal transmission
Age of the target users	17-19 years old
Requirements for the learner	Baisc knowledge of Mathematics, Physics, Chemistry, Biology.
Description of the learning unit	Didactic description of the unit It will guide teachers and students through a multidisciplinary teaching/learning path to discover the basics of neuroscience and the contributions of STEM disciplines to current research, AR Tool enhance visualization and engagement
Subject: Parties involved	Biology, Chemistry, Physics, Mathematics, Engineering
Keywords	Neurons, synaptic transmission, electrical signal, neural communication, AR, Assemblr EDU, Scene-based learning, Interactive visualization
Key qualifications, skills and knowledge that can be acquired	• Problem solving, design thinking, reasoning • Conceptual and practical knowledge of Physics, Chemistry, Mathematics, Biology • AR-based skills: 3D spatial visualization, scene-based navigation, digital scientific modeling • Interactive learning through technology integration
Resources and didactic aids used	Web resources, virtual laboratories, research articles, scientific databases, Assemblr EDU

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	platform with PRO library access (anatomical 3D models, molecular representations, Thunder Particle effects), custom PNG navigation buttons
Assessment criteria and evaluation	Different levels of knowledge of the concepts and skills achieved, including AR-based assessment through scene navigation completion, collaborative interpretation of synaptic processes, and demonstration of understanding neural communication principles via interactive 3D model exploration.

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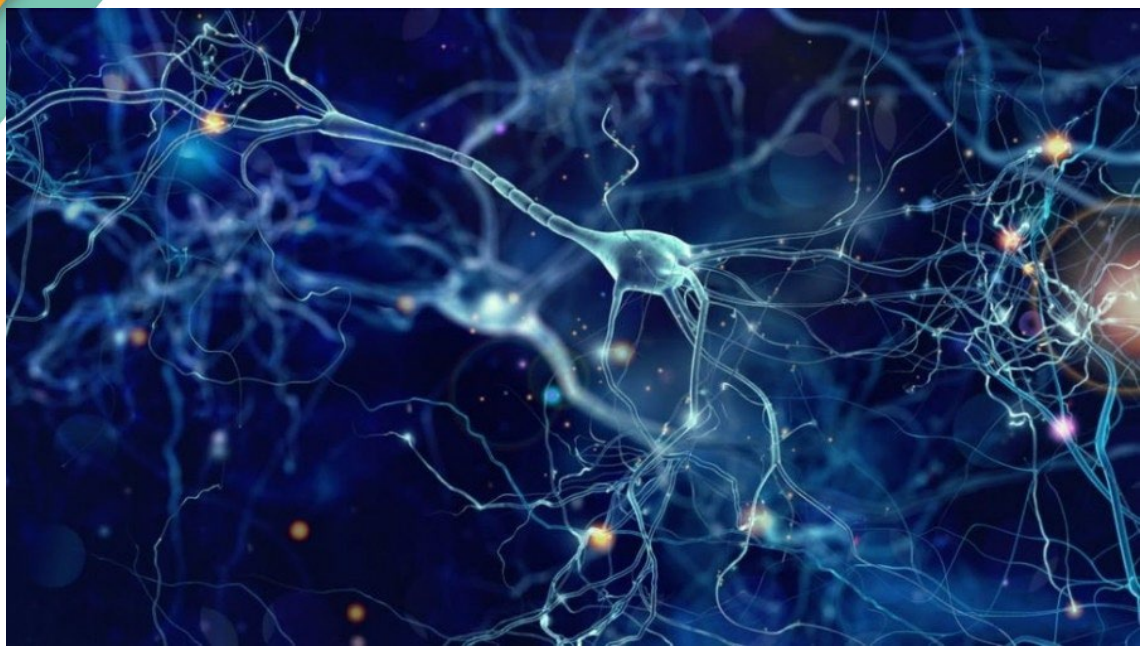
1. Neuroscience

Neurons: biological and physical models of electrical signal transmission



Neuroscience is a group of disciplines, very different from each other, that study the nervous system, i.e. the brain, the spinal cord and the networks of neurons present throughout the body. Over the years, they have acquired the methodologies and research techniques of mathematics, physics, computer science and engineering. Thanks to the fundamental contribution of these disciplines, as well as biology, chemistry and physiology, it is possible to develop models of functioning capable of explaining the behaviour of biological systems such as the brain.
Nobel laureate Eric Kandel writes: "The task of neuroscience is to explain the behaviour in terms of brain activity. How can the brain direct its millions of individual nerve cells to produce behaviour, and how can these cells be influenced by the environment? The last frontier of the science of mind, its ultimate challenge, is to understand the biological basis of consciousness, and the mental processes through which we perceive, act, learn, and remember."

The human brain is a wonderful but very complex system. The functional units of the nervous system, neurons, communicate with each other through electrical signals that propagate even over long distances and release chemicals, called neurotransmitters.
The aim of the study is to stimulate interest in a topic that lends itself well to a multidisciplinary approach in the field of STEM through the discovery of the basics of neuroscience and to increase curiosity towards a topic whose research is frontier research and has important implications for well-being and health.

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Exploring synaptic transmission and neural communication can be greatly enhanced through the use of augmented reality (AR) tools and resources. The implementation of AR technology in neuroscience education facilitates deeper understanding of complex neurobiological processes.

Augmented Synapse: Travel Inside the Brain - Assemblr EDU Implementation

This AR experience guides students through sequential scenes that demonstrate complete synaptic transmission processes. Beginning with an anatomical overview of the human nervous system, students progress to detailed examination of individual neurons and synaptic communication. Using Assemblr EDU's PRO library, the experience employs anatomically accurate MotorNeuron and SensoryNeuron models, molecular representations of neurotransmitters, and Thunder Particle effects to visualize electrical impulses. Students navigate through dedicated scenes showing impulse initiation, neurotransmitter release, and signal reception, accompanied by scientific data including voltage measurements and transmission speeds.

Educational Benefits of AR in Neuroscience

Augmented Reality superimposes virtual elements onto the real world, creating an interactive learning environment. In neuroscience education, AR enhances understanding of invisible biological processes by providing three-dimensional visualizations and step-by-step exploration. The scene-based navigation approach allows students to observe abstract concepts like electrical impulse propagation and chemical signal transmission in concrete, visual terms. This methodology bridges theoretical knowledge with observable phenomena, supporting interdisciplinary connections between biology, physics, and technology while maintaining scientific accuracy in the representation of synaptic processes.

2. Explore Module

"Docking" phase

1) Journey Inside Our Brain – YouTube
http://www.youtube.com/watch?app=desktop&v=IrXuyxDt5jo

Brainstorming activities in the classroom

Guiding phrase: All the activities we perform and all the emotions we feel depend on the transmission of the nerve signal between neurons. How can organic matter collect, analyse and transmit information with very high precision and speed? Our well-being is based on the proper functioning of every element of the neuronal network. What technologies can be used to intervene if something is not going right?

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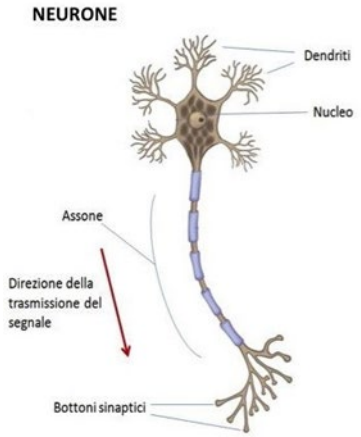
Neurons

What is the structure of the neuron?

The human brain contains about 100 billion cells, neurons, specialized in the transmission of nerve signals, mainly of an electrical nature. A neuron is made up of several parts, with specific functions: a cell body (or soma), containing the nucleus, dendrites and axon. The nerve signal, coming from other neurons or from the receptor organs is collected and transmitted to the nucleus through the dendrites, short and branched extensions of the nucleus. Inside the cell body, the signal is processed and transmitted to the axon, which is a very long extension with the task of carrying the electrical signal to other cells. Separating the inside of the neuron from the external interstitial fluid is the cytoplasmic membrane. Axons are sometimes enveloped for most of their length by a thick insulating material, the myelin sheath. In its final part, the axon branches into a variable number of endings, the synaptic buttons, where the electrical signal is converted into a chemical signal, through a neurotransmitter.



Source image: Online Medicine

What happens when a neuron is not stimulated? What physicochemical characteristics allow us to describe the behaviour of the neuron?

Neurons have a difference in electrical potential between the inside and outside of the cytoplasmic membrane, mainly due to a different concentration of sodium Na+ and potassium K+ ions on the two sides of the membrane. When the neuron is at rest, i.e. it does not transmit signals, this potential difference, called resting potential, has values between -60 mV and -80 mV. The cytoplasmic membrane has ion channels and pumps that open and close in response to certain stimuli, regulating the passage of ions and consequently changing the electrical potential.

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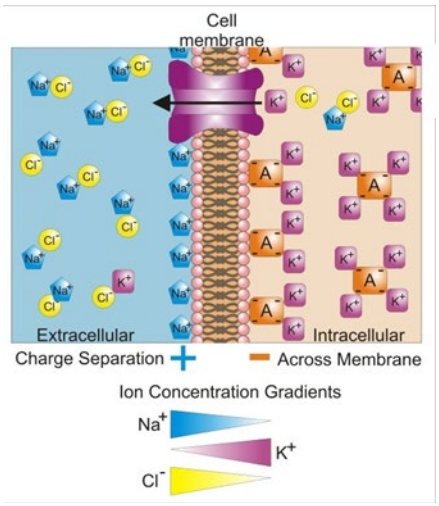

The inside of the cell is rich in K+ ions and negative ions bound to organic macromolecules, while the outside of the cell is rich in Na+ and Cl- ions. The concentration of Na+ ions and K+ ions is regulated by three membrane proteins called ion channels or pumps:
- sodium channels;
- potassium channels
- the sodium-potassium pump.
The neuron's membrane has many potassium channels: these channels push K+ ions from inside the membrane to the outside, although in this way they increase negativity inside the cell. On the other hand, negative ions inside the cell cannot diffuse outside because they are too large to cross the membrane.

Sodium channels are few and tend to diffuse sodium ions inwards.
The sodium-potassium pump acts against the natural direction of ion flow, pushing Na+ out and K+ inside the cell. When at rest, the membrane is practically impermeable to the ingress of Na+ ions.

Let's think about it together: Neurons are the oldest cells in the body: they are unable to duplicate themselves and in the event of lesions that lead to their death, those around them are unable to replace them. As the years go by, the functionality of the Nervous System becomes less effective: research is therefore interested in finding new methods to enhance the brain's ability to produce new neurons (neurogenesis) to improve learning and memory. What can you do to keep your neurons healthy? How can you keep your mind trained?

The genesis of the nerve stimulus

How do neurons communicate?
All signals from the outside are picked up by the dendrites and transferred to the nucleus. If a stimulus arrives at the nucleus of a neuron that can modify the resting potential up to a threshold value (about -50 mV), an action potential or nerve impulse is generated that propagates along the axon.
The genesis of the action potential is linked to the exchange of ions through some voltage-gated channels of sodium Na+ and potassium K+. Sodium channels open first, when the potential reaches the threshold

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value, pushing ions inside the cell that is negative and rapidly depolarizing the membrane. The flow of sodium ions inside the membrane causes a polarity reversal: inside the membrane there is now an excess of positive charge, and outside a lack of positive charge. In this way, the membrane depolarizes, until it assumes a potential of +50mV, the maximum value of the action potential.

The depolarisation condition, however, lasts from 1 to 2 milliseconds. After this Over time, the voltage-gated sodium channels close and the voltage-gated potassium channels open. The latter open more slowly and remain open longer: the K+ ions flow to the outside of the membrane which begins to repolarize, bringing the potential back to a negative value. The flow of K+ persists generating a phase of hyperpolarization and the potential becomes more negative than the resting potential. Finally, all voltage-gated channels close and the activity of the sodium-potassium pump resumes, which restores the resting potential of the plasma membrane. The amplitude (about + 50 mV) and the duration (about 2 milliseconds) of the action potential are fixed, i.e. they do not depend on the amount of excitation.

How does the action potential propagate along the axon?

The electrical signal that propagates through the neuron and is then transmitted to subsequent neurons performs the following sequence of extremely rapid events:

- the electrical stimulus processed by the nucleus causes the opening of voltage-gated sodium channels in a segment near the nucleus; When the threshold value is reached, the first action potential is generated.
- depolarization propagates along the axon causing the channels to open
voltage-gated sodium found in adjacent membrane zones; consequently, a second action potential is generated, which in turn will generate a third and so on.
- At the same time, in the area that had depolarized first, voltage-gated potassium channels opened, bringing the membrane back to the resting potential.
- potentials propagate only in one direction because, after closing, voltage-gated sodium channels undergo a refractory period during which they do not
can open again.

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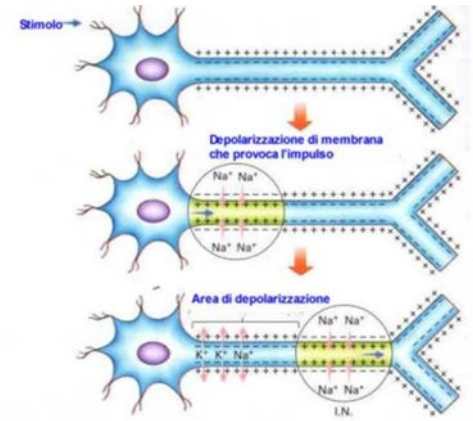
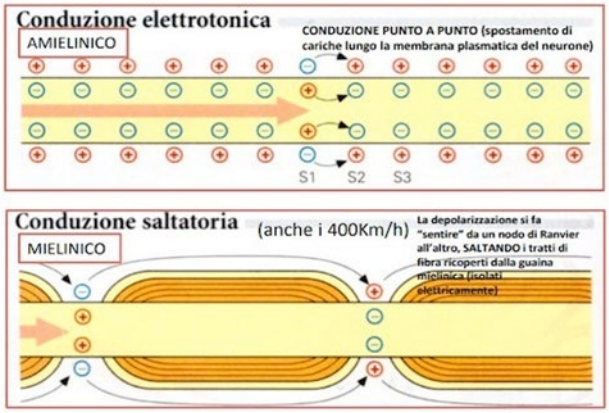


Propagation of action potential along an unmyelinated axon: video at: Propagation of action potential in an unmyelinated axon - Animated medical physiology - YouTube
https:// www.youtube.com/watch?v=RNdvrkolW0M&t=7s

What role does the myelin sheath play?

Nerve fibres coated with myelin sheath are more waterproof, as the sheath acts as an electrical insulator: consequently, the depolarization and propagation of the action potential occurs only in the sections where it is not present, called Ranvier's nodes. The nerve signal "jumps" from one node to the next with a higher speed than unmyelinated fibres.



Let's think about it together: The transmission of the electrical signal in a neuron first and to other neurons later, is fast and precise. The speed of transmission and the accuracy of information are decisive factors in carrying out all human activities correctly. When something in this wonderful mechanism jams or stops, causing a neurological disease, the impact on the quality of life of affected individuals is devastating. Research on the operating principles of signal transmission

neuronal stimulation is the basis of the most advanced neuro-technologies, which exploit electrical stimulation as a therapy. Have you ever heard of electrodes being applied to paralyzed patients who have walked again?

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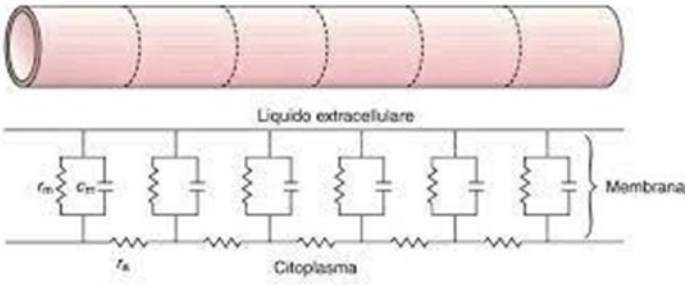
The physical model of signal propagation in a neuron

What physical model can explain the principle of operation of a neuron?

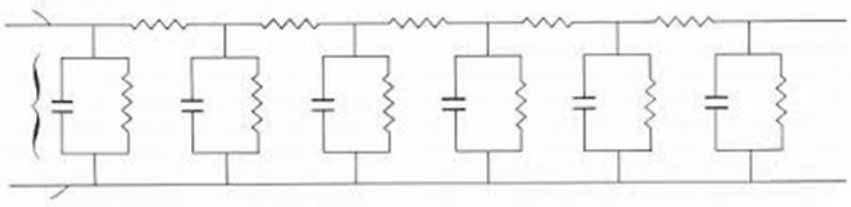
For a quick refresher on capacitance and capacitors: Capacitors and capacitance of a capacitor (youmath.it)
For a quick refresher on resistance and resistors: Resistors, electrical resistance and electrical resistivity (youmath.it)

The axon is similar to a coaxial cable. The inner part of the axon is the central conducting core of the cable.



Its strength is high, mainly due to its small cross-section. To describe the electrical properties of the cytoplasm, the resistance per unit length ri is introduced.
The external part of the axon is also a conductor, but the external section is much larger than the internal one and therefore the resistance offered by the interstitial fluid is negligible compared to the internal one.
The insulating membrane constitutes a capacitor, since the inside and outside of the axon behave like two conducting plates, storing charges of opposite signs. In parallel with the capacitor, a resistance must be considered, which considers the flow of ions through the membrane itself. To schematize the electrical behaviour of the membrane, two quantities are introduced, the capacitance per unit length cm and the conductivity per unit length of the membrane σμ (φρομ ωηιχη ωε ωιλλ δεριϖε the resistance of the membrane per meter rm).

The axon can then be schematized by a circuit consisting of a succession of meshes with resistors and capacitors.



The stimulus potential will depend on the time and location along the axon. In fact, it is characterized by two parameters: the time constant τ and the space constant λ. The mathematical model of the circuit allows us to derive the trend of the potential both as a function of time and as a function of position. In the first case we will have:

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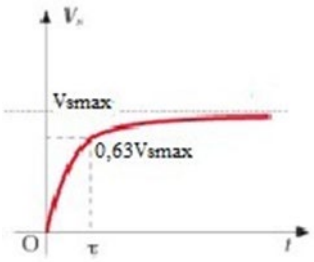


$$V_s(t) = V_{smax}(1 - e^{-\frac{t}{\tau}})$$

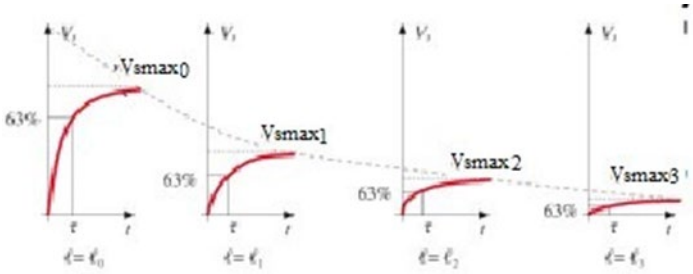
where Vsmax is the maximum value reached by the potential and τ =rmcm.

The time constant τ (on the order of ms) is the time interval it takes for the stimulus potential to reach 63% of its maximum value: it is a measure of how fast the neuron responds.

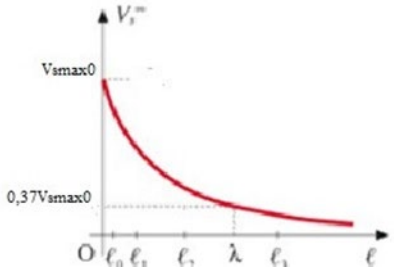
As we move away from the point where it is generated, the stimulus potential decays with distance due to the combined effects of the ri and rm resistances.
The stimulus potential tends to decrease according to the law:

$$V_{smax}(x) = V_{smax0}e^{-\frac{x}{\lambda}}$$

where Vsmax0 is the stimulus potential at the site of origin and λ is the space constant.



The space constant λ (of the order of mm) is the distance at which the initial potential difference decays to 37% of its maximum value.



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It is a measure of how far the current can flow down the axon before dissipating due to leakage currents. So after traveling a distance of λ, the signal has reduced to about 1/3 and after 2 λ it is about 1/7 of the original signal and can no longer trigger the action potential. In reality, the stimuli travel considerably longer distances, of the order of a couple of meters, due to the intervention of other mechanisms that we are not considering. Mathematically, the space constant is described as:

$$\lambda = \sqrt{\frac{r_m}{r_i}}$$

The main factor influencing the internal resistance ri is the radius of the axon: axons of large diameter have a lower resistance to longitudinal current flows and, therefore, a lower axial resistance; consequently, they will have a greater constant of space. In fact, λ increases with the square root of the radius of the axon ra.

$$\lambda \propto \sqrt{r_a}$$

What does the speed of propagation of the nerve impulse depend on?
The knowledge of the two constants allows us to find the speed of propagation of the electrical signal along an axon:

$$v = \frac{\lambda}{\tau}$$

and therefore, to deduce that

$$v \propto \sqrt{r_a}$$

relationship that agrees with the experimental results.

Let's reflect together: The term model is a representation sometimes a simplification of a phenomenon capable of explaining how it works. Using a physical model to interpret and understand a biological phenomenon answers to the need highlighted by several neuroscience scholars of
remove barriers between different disciplines, taking full advantage of
the resources and techniques of different disciplinary fields. Have you thought about using your knowledge in fields other than your own?

Advanced Level

Analysis of the model from a mathematical point of view

Let's consider the first elementary circuit with which we can schematize the axon.
To determine the trend of the potential and currents we use Kirchooff's laws:

$$Vsmax = V_{r_i} + V_C$$

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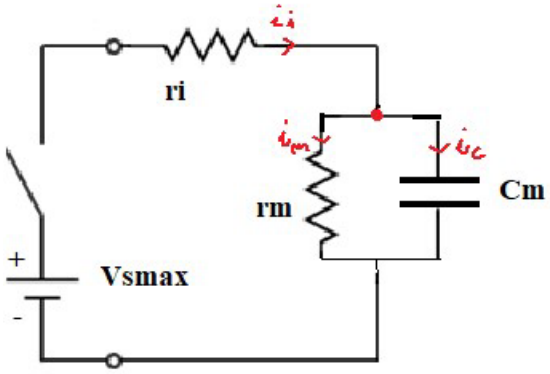
and

$$i_i = i_c + i_m$$



where Vsmax is the potential across the RC circuit that we imagine as the d.d.p of a generator, Vri is the ddp across the internal resistance of the axon and Vc is the d.d.p ai Condenser C ends. By im we also indicate the current through the membrane.
We derive ic and express everything as a function of the potentials:

$$i_m = \frac{Vc}{r_m}, \qquad i_i = \frac{Vsmax - Vc}{r_i}, \qquad i_c = i_i - i_m$$

so what

$$i_c = \frac{Vsmax - Vc}{r_i} - \frac{Vc}{r_m}$$

Since the following relation holds for a capacitor:

$$Vc = \frac{q}{c_m}$$

we will have

$$i_c = \frac{Vsmax}{r_i} - \frac{q}{r_i c_m} - \frac{q}{r_m c_m}$$

Deriving the previous expression with respect to time, we obtain:

$$\frac{di_c}{dt} = -\left(\frac{1}{r_i} + \frac{1}{r_m}\right)\frac{i_c}{c_m}$$

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which is a linear differential equation with separable variables whose solution is obtained by integrating:

$$\int \frac{di_c}{i_c} = -\left(\frac{1}{r_i} + \frac{1}{r_m}\right)\frac{1}{c_m}\int dt$$

$$i_c(t) = Ae^{-\frac{t}{\tau}}$$

The time constant τ is

$$\tau = \frac{r_i r_m c_m}{r_i + r_m}$$

The constant A is determined by the initial conditions of the circuit.

For

t=0 $i_c(0) = A = i_i(0) = \frac{Vsmax}{r_i}$

and then

$$i_c(t) = \frac{Vsmax}{r_i}e^{-\frac{t}{\tau}}$$

Usually rm ~ 104 Ω/m and ri ~ 1010 Ωμ and rm can be neglected compared to ri, which allows to simplify τ:

$$\tau = \frac{r_i r_m c_m}{r_i + r_m} \sim r_m c_m$$

We then find the other currents as a function of time:

$$i_m(t) = \frac{Vc}{r_m} = \int \frac{i_c(t)}{r_m c_m}dt$$

The solution is:

$$i_m(t) = \frac{Vsmax}{r_i + r_m}\left(1 - e^{-\frac{t}{\tau}}\right)$$

In the end

$$i_i(t) = i_c(t) + i_m(t) = \frac{Vsmax}{r_i + r_m}\left(1 + \frac{r_m}{r_i}e^{-\frac{t}{\tau}}\right)$$

For t=0 all the current passes through the resistor ri and goes to charge the capacitor cm. No current circulates through rm, im(0) = 0, in accordance with the fact that it is in parallel with cm and has no d.d.p. at its ends.

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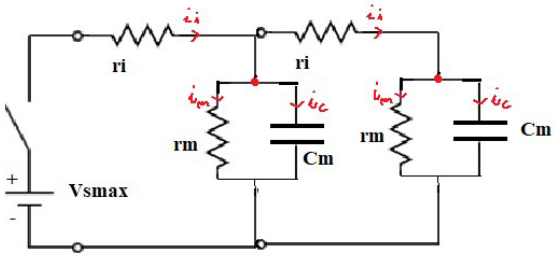
For long times, (t→∞) the capacitor is charged and no longer circulates current through the branch i.e. ic(∞) = 0, while all the current passes through the internal and membrane resistance:

$$i_i(\infty) = i_m(\infty) = \frac{Vsmax}{r_i + r_m}$$

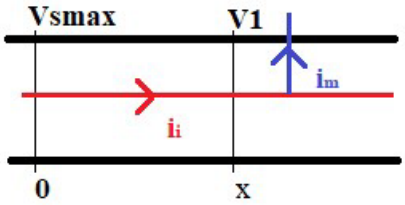
The expressions found analytically for currents justify a result that we had previously introduced, namely the stimulus potential:

$$V_s(t) = V_{smax}(1 - e^{-\frac{t}{\tau}})$$

To simulate the axon, we consider other similar circuits connected to the first. For this second circuit, the potential or f.e.m. is no longer Vsmax but the potential present to the heads of the parallel



$$V_c = i_m r_m = \frac{Vsmax\, r_m}{r_i + r_m} \sim \frac{r_m}{r_i} Vsmax$$



The stimulus potential decreases along the axon.
Let us consider the stimulus potential Vsmax at the point x=0. Its propagation depends on the current flowing within axon II, which in turn depends (according to Ohm's first law) on the variation of potential along the axon:

$$i_i(x) = -\frac{1}{r_i}\frac{dVs}{dx}$$

The minus sign depends on the fact that the current flows from points to higher potentials points with lower potentials, then in the opposite direction to the gradient of Vs. The internal current decreases because the charges flow out of the membrane via the current im:

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$$\frac{di_i}{dx} = -i_m = -\frac{Vs}{r_m}$$

Substituting we get the following second-order differential equation:

$$Vs = -r_m \frac{di_i}{dx} = \frac{r_m}{r_i} \frac{d^2Vs}{dx^2}$$

The solution is:

$$Vs(x) = Vsmaxe^{-\frac{x}{\lambda}}$$

with

$$\lambda = \sqrt{\frac{r_m}{r_i}}$$

as we had previously introduced.

Flipped Learning:

Read the proposed article. Focus especially on the study of nerve signals and electrophysiology techniques described in the article. He then completes the study by analysing which fields of research, according to the article, are most effective for the study of neuronal circuits

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Articoli AIRInforma - Quando membrane, proteine e sali creano elettricità
AIRInforma: Il portale di divulgazione di AIRIcerca - http://informa.airicerca.org - Pubblicato il 14-12-2015

AIRInforma

Quando membrane, proteine e sali creano elettricità.

di Elia Magrinelli
Editor: Olivia Candini
Revisori Esperti: Annalisa Zuccotti, Giorgio Grasselli
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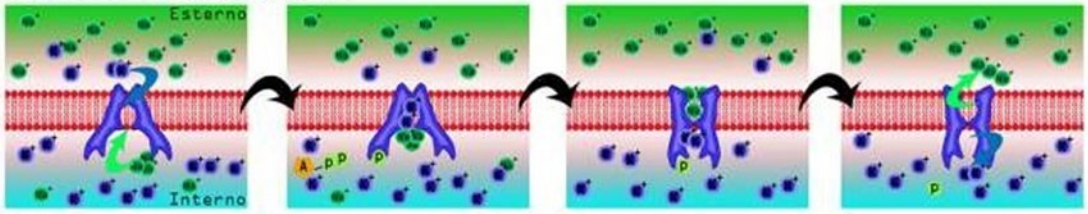
Permalink: http://informa.airicerca.org/2015/12/14/quando-membrane-proteine-e-sali-creano-elettricita

doi: 10.13140/RG.2.2.12876.72328



We comment on the study of nerve signals proposed in the article:

Most common electrophysiology techniques:

- The Patch Clamp technique
- The inside-out and outside-out technique
- extracellular recording

Particularly effective alliances with electrophysiology:
pharmacology
genetic engineering, optogenetics

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3. Operation Module

Basic Level

Test your knowledge

Activity:
Knowledge test
Multiple-choice question tests

1) A neuron consists of:
• Dendrites, nucleus, axon, synaptic buttons
• Dendrites and axon
• nucleus and axon
• Dendrites, nucleus, axon, myelin sheath

2) Which of the following statements regarding action potential is incorrect?
• corresponds to a hyperpolarisation
• is triggered only in response to a stimulus
• starts only if a certain threshold is exceeded
• causes polarity reversal

3) The propagation process is triggered by:
• the presence of voltage-gated channels for Na+
• the existence of a particular refractory period
• the repeated recurrence of the triggering stimulus
• the existence of potential even in the sections at rest

4) The resting potential is due to the presence of:
• Na+ ions outside the cell and K+ inside the cell
• Na+ ions inside the cell and K+ outside the cell
• Na+ ions inside the cell and Cl- outside the cell
• K+ ions outside the cell and Cl- ions inside the cell

5) Which of the following statements about the cable model is incorrect?
• The axon can be schematized by a circuit containing two resistors and a capacitance in series
• The axon can be schematized by a succession of meshes with resistors and capacitors
• The inner part of the axon has a very high resistance

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• The membrane itself forms a capacitor in parallel with a resistor

6) Short answer: What value does resting potential have?

7) Open Answer: How does the action potential propagate along the axon?

8) Open Answer: How does the stimulus potential vary at a certain point as a function of time? Provide a qualitative description

9) Match each question with the correct answer:
• What measures the space constant?
• What does the time constant measure?
• What does the space constant depend on?
• What does the time constant depend on?

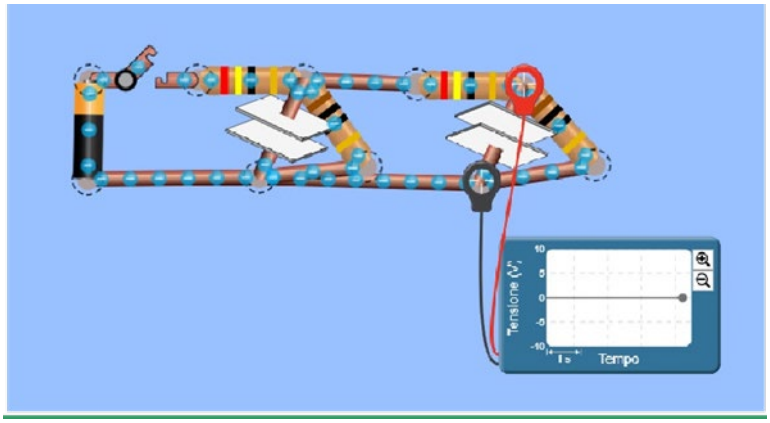
10) Short answer: What does the speed of nerve impulse propagation in unmyelinated neurons depend on according to the cable model?

PhEt simulation: neuron

https://phet.colorado.edu/sims/html/neuron/latest/neuron_it.html
Activity:
• link to the worksheet in English: Neuron - Biology | Neurons | Cells - Interactive Simulations of PhET (colorado.edu)
• It explores the behavior of a neuron in the presence of an action potential.

PhEt Simulation: Circuit Construction Kit-Virtual Lab

Circuit Building Kit: Virtual Lab (colorado.edu)



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Activity:

• link to the operational sheet in English: Circuit Construction Kit: Virtual Laboratory - RLC Circuit | AC Circuits | Kirchoff's Law - Interactive Simulations of PhET (colorado.edu)

• Build a circuit that simulates the behaviour of the cable model of the neuron. Highlight the potential trend across the capacitors and see if it agrees with what you have studied

Advanced Level

Try it yourself:

Indicatively, and with a certain margin of approximation that takes into account the variability of the different types of axons and the various animal structures, an axon has a radius of the order of μμ, an internal resistance per unit of length ri ~ 1010 Ω/m and a transmembrane resistance per unit of length rm ~ 104 Ω/m. The thickness of the membrane is about 10-8 m and the relative dielectric constant of about 3.

1. Choose a capacitor model and its capacitance and estimate with this data the order of magnitude of the capacitance per unit axon length; (one capacity per meter cm ~ 5·10 cm-8 F/m)
2. Verifies that the approximations used in the exploratory part are legitimate and calculates the time and space constant;
3. It then estimates the propagation speed of the electrical signal and compares the results obtained with the experimental data;
4. Why is the propagation rate different from the experimental results? How can we improve the model to obtain propagation speeds closer to the real ones?

4. Extra in-depth material

Web-based resources:

Brochure-NEUROSCIENCE-Battaglini (units.it): Information and dissemination manual on neuroscience by the BRAIN centre in Trieste

https://www2.units.it/brain/Manuali/Scienza%20del%20Cervello-web.pdf: A popular handbook on neuroscience: interesting references to research frontiers and links to other sites

https://userswww.pd.infn.it/~soramel/FisicaMedicina/Altro/CircuitiRC.pdf: Presentation of RC circuits and application of these circuits in medical physics.

5. References

D. Sadava et al : Biologia.blu PLUS. The human body, Zanichelli

G. Bellini et al : Physics for medicine, Piccin

Walker J: PHYSICS: Theoretical models and problem solving, 3 Linx

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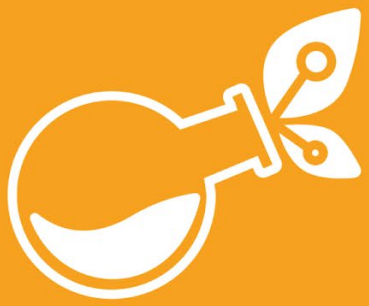

BIOS4YOU AR 2.0

BIO-INSPIRED STEM TOPICS FOR ENGAGING YOUNG GENERATIONS
THANKS TO THE USE OF AUGMENTED REALITY

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