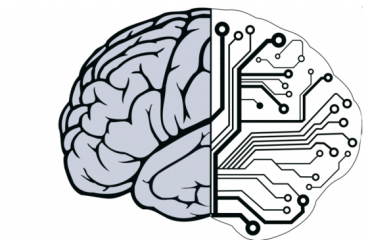
"Though this be madness, yet there is method in't."
Shakespeare: Hamlet: Act 2 Scene 2

Dynamic Abstract Neural Computing with Electronic Simulation (DANCES) Version *0.0.17*

The true physics, physiology, computing & information science behind neuronal operation



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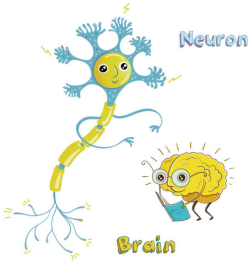

Version *0.0.17*

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Foreword

"The Human Brain Project should lay the technical foundation for a new model of ICT-based brain research, driving *integration between data and knowledge from different disciplines*, and catalysing a community effort to achieve a *new understanding of the brain*, new treatments for brain disease and *new brain-like computing technologies*."

— the Human Brain Project, summarised its goal @2012

"*We stand on the verge of a great journey into the unknown—the interior terrain of thinking, feeling, perceiving, learning, deciding, and acting to achieve our goals—that is the special province of the human brain . . . No single researcher or discovery will solve the brain's mysteries.*"

— from the preamble to "BRAIN 2025: A Scientific Vision" [12] @2015

Understanding the dynamic brain The ***dynamic*** operation of individual neurons, their connections, higher-level organizations, connections, the brain with its information processing capability, and finally, the mind with its conscience and behavior, are still among the big mysteries of science: *at which point the non-living matter becomes a living one*, and at which point *a living matter becomes intelligent* and conscious; whether and how all this stuff can be handled by science. We really need a new understanding. We do not understand, among others, that "the construction [of living matter] is different from anything we have yet tested in the physical laboratory". Moreover, that "it is working in a manner that cannot be reduced to the **ordinary** laws of physics" [13]. We attempted to test and describe living matter, including the brain, with methods based on the ordinary laws of science, which we concluded for non-living matter. Those ***static*** methods did not consider its "special construction"; furthermore, do not need (and, as a consequence, do not have) "laws of motion" in the sense as science does. There is no independent 'life science', only science. Based on the the same 'first principles' but by using different abstractions and approximations for living and non-living matter and having the appropriate relations between them. Without aligning the knowledge elements along the first principles, the "integration between data and knowledge from different disciplines", lacks "integration". "More Is Different" [14]. We arrived at the boundaries of classical science fields and are moving now through terra incognita.

Figure 1: The difficulty of many-disciplinary research on the example of describing the elephant. (a 2,500 years-old Chinese silk painting)

The "great journey into the unknown" [12] must begin earlier and at a much lower level: revisiting the fundamental phenomena, disciplines, laws, interactions, abstractions, omissions, and testing methods of science. We understand that "*the fundamental task of the nervous system is to* ***communicate and process information***". The goal was set decades ago: '*The ultimate aim of computational neuroscience is to explain* ***how electrical and chemical signals are used*** *in the brain to* ***represent and process information***' [15]. However, that research must build on top of classical science, be reinterpreted for living matter, and have a correctly understood physiology.

Many-disciplinarity We need a consistent model that comprises all relevant interactions (and only those!) and aligns with the notions of the related scientific fields. "We make no apologies for making these excursions into other fields, because the separation of fields, as we have emphasised, is merely a human convenience, and an unnatural thing. *Nature is not interested in our separations, and many of the interesting phenomena bridge the gaps between fields.*" (Richard P. Feynman) Different science disciplines consider different details relevant; see Fig. 1. Despite the efforts of the project leader, no picture can be derived about the *elephant*, although *the details of the elephant* are accurate.

Zigzag reading When describing principles of neural computing, for the same reasons, we follow von Neumann's method when describing principles of technical computing [16]. "The ideal procedure would be, to take up the specific parts in some definite order, to treat each one of them exhaustively, and go on to the next one only after the predecessor is completely disposed of. However, this seems hardly feasible. The desirable features of the various parts, and the

decisions based on them, emerge only after a somewhat zigzagging discussion. It is, therefore, necessary to take up one part first, pass after an incomplete discussion to a second part, return after an equally incomplete discussion of the latter with the combined results to the first part, extend the discussion of the first part without yet concluding it, then possibly go on to a third part, etc. Furthermore, these discussions of specific parts will be mixed with discussions of general principles, of the elements to be used, etc." In our case, this zigzag way of reading is made more accessible by using hyperlinks in the document.

Abstract discussion Nature uses an infinite variety of implementing neurons. However, in the CNS they can cooperate with each other. 'Despite the extraordinary diversity and complexity of neuronal morphology and synaptic connectivity, *the nervous systems adopts* ***a number of basic principles*** for all neurons and synapses' [4]. We base our holistic discussion on those general basic principles and create an 'abstract physical neuron', skipping the 'implementation details' nature uses. We need different abstractions and approximations for describing biological processes. However, an abstraction is usable in practice only when paired with a generalization: the more abstract the assumption, the more general and widely applicable the concept or conclusion. *By abstractions, we can reduce the unbelievably detailed world into manageable pieces, and by abstraction, we can learn anything general.* We must show which approximations are oversimplifications and which phenomena are misunderstood, measured, or interpreted in the wrong approach. Abstraction is, in fact, everywhere, including inside each of us. It is a core element of cognition.

Physics Their slowness and complexity require explicitly considering the *time-aware handling* of processes, including the ones of biological and technical computing. Essentially, we make the first steps in section **??** towards answering E. Schrödinger's question: "How can *the events in space and time* which take place within *the spatial boundary* of a living organism be accounted for by physics and chemistry?" [13] (notice the need *of using events and describing the spatiotemporal behavior (in other words: implementing them by slow currents in a finite volume)* implied in the question; three items which our text targets). *No presently available theoretical description and simulator can perform that task.* We show that when considering the correct physics, the finite size of neuronal membranes, and the finite speed of ion currents, we can solve the mystery that the combination of non-living materials shows signs of life at an appropriate combination of their values.

Mathematics We can only admire von Neumann's genial prediction that "the language of the brain, not the language of mathematics" [17], given that most of the cited experimental evidence was unavailable at his age. Similarly, one can also agree with von Neumann [16] and Sejnowski [18] that "whatever the system [of the brain] is, it cannot fail to differ from what we consciously and explicitly consider mathematics"; adding that *maybe the appropriate mathematical*

methods are not yet invented. Our procedure still meets the requirement given by Feynman: [19] "an *effective procedure* is a set of rules telling you, moment by moment, what to do to achieve a particular end; it is an algorithm." Furthermore, it considers that "timing of spike matters" giving way to interpreting Hebb's learning rule [20, 21]. We formulate problems, provide their numerical solutions, and open the way for mathematics to provide analytical solutions. Not surprisingly, the need for applying new approximations for the extraordinary laws for describing living matter needs slightly different (in this sense: extraordinary) of deriving the mathematical formulation describing them. We emphasize again that the first principles are the same, but the different "construction" of the living matter needs different approximations and results is different, 'extraordinary', laws.

Electricity Electronics and brain research were born at the same time, developed together, and fertilized each other. Sometimes, the too-tight parallels led to discrepancies, from assuming identical propagation speeds of diffusion and moving electrons in the free-electron cloud to using equivalent circuits, or misunderstanding the essence of spiking for electronically implemented circuits. Those wrong parallels hide the need for introducing electrodiffusion instead of net electrical and diffusion processes, that life is governed by finite-speed ("slow") currents and that finite-size (distributed) biological objects cannot be directly and accurately mapped to point-like (ideal) electrical components. We need to connect the atomic electricity to the macroscopic one; furthermore, in biology, concentration changes evoke potential changes and create large potential gradients (and vice versa). Those internal gradients start dynamical electrical *ion* currents in biological tissues.

Physiology Physiology, which serves as the "implementation base" for neural computing, needs a revolution and replacing "classical physiology" with "modern physiology" by introducing a new paradigm. Our point of view is new and unusual; it conflicts, on many points, with the commonly accepted opinions of the respective science disciplines. The facts and observations are the same, but their interpretation may be different due to the underlying 'extraordinary' laws of physics. *Neural processes* happen at well-observable speeds which *need a dynamic description instead of an ad-hoc description of state jumps. We introduce for life sciences their laws of motion (in the sense of Newton, Hamilton, and Schrödinger), (based on the time derivatives of the static entities)*, furthermore, *the needed dynamically created component which can implement the needed dynamic processes*. Considering them solves the mystery of how a biological neural network can react at a speed about two orders of magnitude higher than it could be expected based on its static behavior (the time difference between adjacent spikes) and, in general, how life science builds on top of science. We defy that "the emergence of life cannot be predicted by the laws of physics" [22], furthermore, that the existence of life is against the laws of thermodynamics. However, we confirm that for describing the life by physics we need to derive 'extraordi-

nary' laws.

Neuroscience The worst inheritances of neuroscience are the static view from anatomy and classical physiology; omitting to revisite periodically the primary hypotheses in light of new research results; applying the abstractions of the classical science (single speed, isolated, pair-wise, instant interactions in a homogeneous and isotropic infinite medium) to biological materials without revisiting their validity. Moreover, the tradition of applying ad-hoc mathematical formulas without correct physical processes in the background (actually creating an alternative nature) instead of understanding the basics of the underlying processes. To start with, we introduce *science-based abstract dynamics* (by introducing the needed laws of motion), as opposed to the *empirical cell-biology's static* description of neuronal operation. We agree that "the basic structural units of the nervous system are individual neurons" [4], but we are also aware of that neurons "are linked together by dynamically changing constellations of synaptic weights" and "cell assemblies are best understood in light of their output product" [23, 24] so we also model multiple neurons.

Computing "The brain computes! This is accepted as a truism by the majority of neuroscientists." [11] However, even after many years and grandiose projects, "Yet for the most part, we still do not understand the brain's underlying computational logic" [12]. To understand how "computation is done", we generalize computing [25], in close cooperation with communication [26], for biology. We understand that "a piecemeal approach will not yield the major jumps in understanding for which the BRAIN Initiative was designed" [27]. We synthesize the available knowledge with a fresh eye and intend to make a leap in understanding neural computing, scrutinizing our knowledge pieces one by one for credibility, relation to other pieces, other disciplines, finding contradictions and their resolutions, *defying fallacies*. We show how elementary neuronal operation is carried out, why biological computing is by orders of magnitude more effective than the technical one, how the biological implementation enables learning, how and why do the features of the two computing systems differ.

Information Although we experience that the brain processes an enormous amount of information, furthermore, we know impressive details about how the brain uses it to react appropriately to stimuli from its environment, we still do not know the details and the underlying general principles how neuronal networks represent, process, and store the information they use. What makes the case worse, is, that, due to the lack of knowledge of the abstract way of neuron operation, the so-called "neural information science" uses a wrong mathematical background. We understand how neurons represent and process information [24]. We introduce the appropriate interpretation of information for biology.

Intelligence Scrutinizing time awareness of biological computing and learning discovers that they have practically only their name in common with the technical ones. As a consequence, "biological brains are more efficient learners than modern ML algorithms due to extra 'prior structure'" [28]. Furthermore, "it is also possible that non-biological hardware and computational paradigms may permit yet other varieties of machine intelligence we have not yet conceived" [28, 19]. We start to conceive them.

Simulator The site is not exclusively about theory: we also give a programmed implementation of the ideas we describe. Our simulator has a direct science base instead of ad-hoc mathematical formulas; and the only one which is able to reproduce the true biological time course of neurons, from the first principles of science, without arbitrary ad-hoc assumptions and limited variability formulas. Our methods enable discussing the major aspects of phenomena of the natural operation of neurons to analyze the effects of invasive electricity-related investigation methods on neuroscience. We offer demos, class implementations, performance benchmarks, and test cases to demonstrate simulating capabilities. We intend to develop full-value educational, demonstration, and research tools.

Forbidden science Hodgkin and Huxley in 1952 [10] advanced neurophysiology by contributing a long series of *observations* on neuronal operation. However, as they warned, many of the *mechanisms* must be fixed or replaced: "must emphasize that the interpretation given is unlikely to provide a correct picture of the membrane". We honor their outstanding work and want to supplement and enhance their interpretations and hypotheses instead of defying them. However, their work became the "Holy Bible" of physiology. The editors 'do not believe' (see Fig. 2) if science advanced in the past seven decades and they censor publishing new ideas in scientific journals. Likely, they did not know that science must "have no respect whatsoever for authority; forget who said it and instead look what he starts with, where he ends up, and ask yourself, 'Is it reasonable?' ... If we suppress all discussion, all criticism, proclaiming 'This is the answer, my friends; man is saved!' we will doom humanity for a long time to the chains of authority, confined to the limits of our present imagination." (Richard P. Feynman)

The editors' comments on the manuscript "The Physics Behind the Hodgkin-Huxley Empirical Description of the Neuron", submitted to "Physics of Life Reviews". Oct 11, 2024. Rejected without reading. PLREV-D-24-00173

"The physics behind the Hodgkin-Huxley model of the neuron is certainly within the scope of PLRev. This model has been extensively studied since it was proposed in 1952 and its proponents won the Nobel Prize in 1963. So it is a challenge to say something original and relevant about this model in 2024. Since the author has no previous publications on the topic, *the Editorial Board does not believe* that the review will have any impact on this very well-established research topic."

Figure 2: "Believing" in science (in the age of Galillei).

Warning: Please consider that this development is a one-man undertaking. Moreover, it shall develop theory, evaluate published experiments, implement software, test it, and document it. Pre-developed code fragments, science publications, and docs exist, so they develop relatively quickly but need time to be consistently put together. Please come back later and see if something is new (see the date and the version).

Quick Start

As the Human Brain Project formulated, to enter a new level, "a new understanding of the brain" is needed. It is also correct that "integration between data and knowledge from different disciplines, and catalysing a community effort" is requested. It really needs several disciplines, openness and deep knowledge of the related disciplines from the researchers, furthermore also *some knowledge about the bridges to the other disciplines*, as Feynman expressed. Furthermore, *finding the extraordinary laws of physics*, including *developing the needed mathematical handling*, as Schrödinger expected. And after that, *a community effort along the principles of the new theoretical understanding* for validating the new understanding is needed, and revisiting the interpretation of the results of former observations in light of the "new understanding". The present content was written in the spirit of Feynman that we must "have no respect whatsoever for authority; forget who said it and instead look what he starts with, where he ends up, and ask yourself, 'Is it reasonable?'". Reading it, needs the same attitude. It needs a lot of patience; the more patience and effort the more the reader knows about the subject in the "old understanding". The "new understanding", the "extraordinary laws" of physics, spiced with newly developed mathematics, is not easy, not quick and not effortless; furthermore, it requires a well-controlled thinking, much above the level "this way we used to interpret the things and reply to this question for decades". Our discussion is a much more faithful description of neurons' operation than the old one.

The miserable fact is that the "old understanding" is wrong in several aspects. Among others

- physiology has a statical view. Experimentally, clamping and patching (by using feedback) introduce foreign currents into the cell, stop its native operation and enable deriving conclusions from that artificial, statical, operating mode for the native, dynamical, operating mode. Theoretically, statical *states* are assumed and the experienced dynamicity (*processes*) is accounted for as perturbation. The *voltage gradient*, instead of currents, controls the neuronal oscillator's operation; a fact that is known from the well-established theory of electricity, but neglected in physiology.

- the static view does not need (furthermore, does not enable to find) the laws of motion (in the sense of laws of Newton, Schrödinger, Hamilton)

- laws of classical physics developed for infinite, homogeneous, structureless medium, where the interactions have the same speed, are applied to finite, inhomogeneous, structured living matter, where *the interactions have enormously different speeds*
- neglected that neurons' potential changes are the results of electrochemical (electrodiffusional), instead of net electrical, processes
- the biological matter's conduction mechanism differs from the one in metals (leading to assuming the conduction speed of free electrons in ionic solutions for ions; a wrong interpretation of conductance; wrong discussion of the electric operation of cells based on false analogies with classic electric circuits)
- the Coulomb repulsion between ions is neglected (excludes understanding that 1/ ionic currents are present on the surface of the membrane and in the axons 2/ how signals propagate in the absence of external electrical voltage 3/ slow currents and finite sizes are responsible for the timing relations of the cells)
- introduced false electrical equivalent circuits (excludes understanding that 1/ the voltage is location- and time-dependent during AP creation 2/ the communication network has a heavily time-dependent operation 3/ the neuronal signal processing and computation works with temporal arguments and results)
- in the neuronal oscillator, a wrong oscillator type is in use; the vital component AIS, discovered and understood two decades ago, is not yet integrated into neuronal operation (leading to ad-hoc introducing of a non-existent rectifying current)

Consequently, what followed, was wrong. Including the computational principles, just because the wrong model.

You may have arrived with different backgrounds and interests. Consequently, you may have different spots of interest and path through this material. The site is about neuron-based computing, which, for today, may mean very different topics. The primary goal is to deal with biologically implemented neurons' operation (they are created 'as is'; maybe not entirely understood, but attempting to discover it) and also artificially manufactured neurons which attempt to imitate the biological ones, grasping one or more of their true features; furthermore, their networks, operations, features and fallacies. A further goal is to understand the features of their larger assemblies, how they implement advanced computations.

Physiology, with its static view, relys on biophysics, which applies the existing ('ordinary') laws of classic physics in an inadequate way, and the classic physics derived its laws for 'another construction'; that is, the biological matter also needs different mathematical formalism. All this is derived here, in a disciplinary way, needing zigzag reading. As emphasized many times, we confine our

discussion to some abstract disciplinary level, with pointers to the special topics. We interpret known phsiological evidence on top of the correct 'extraordinary' laws of physics, and derive the needed mathematical handling separately but in parallel with that physics. The physiological conclusions should be understood even if you do not understand the details of the underlying physics and that underlying mathematics. If you understand *why* the extraordinary physical laws for living matter are more or less different from the ordinary ones for non-living matter, you may leave the details for your expert colleagues. The mathematical handling also involves the fundamental principles of using the abstractions and approximations of constructing laws for physics and needs a thorough knowledge of both fields. Anyhow, you will need to know that the college level of physics is usually not sufficient to understand the deepness of the material and you will need to re-read the notions; the more you know it (and especially the more false biophysics you learned) the more carefully. A half-understanding of the physical base hinders your learning as well as development of brain science.

0.1 Segmented electrolytes

When ions are contained in a closed volume, they ions exist in a state of thermal and electrical equilibrium. In the absence of external influences or a separating membrane, both gradients are balanced and are at zero. In this scenario, the 'carrier' - the ion - can be influenced by two different types of interactions, each represented by a distinct abstraction in these processes.

We discover that segmented solutions, especially if the segments have largely different concentrations, produce very thin but important layers, which, by using 'Maxwell-demon'-like objects, produce phenomena known as 'signs of life' in biology. Given that, in many cases, inappropriate physical principles, notions, and methods are used in measuring and modeling neurons, we need to discuss the true physics (maybe better to say: the correct approximations) behind biological phenomena.

0.1.1 Electrolytes

In physiology, the electrolyte solutions do not surely satisfy the conditions we use for notions of electricity in physics, see section **??**. The number of charged objects (the ion concentration) may change in time, and a chemical driving force may also move the objects independently from the electrical field. When measuring only the macroscopic electric parameters voltage and current (measuring current believing we measure directly conductance; in addition, measuring it in a wrong way; for the details see section **??**), *we attribute the injected charge carriers' low propagation speed to the medium* when describing the phenomenon that "the conductance changes" in the function of the voltage [48]. (We know that the macroscopical speed of current changes with the clamping speed, see Eq.(**??**), that might change the time difference between the non-matching value pairs, leading to the illusion that the conductance changes.) The measurement

must be fixed: the tacit assumptions about notions of electricity must be fulfilled.

Conductance is a "steady-state" notion; see its definition in section **??** and in section A.3.12 in [4]: "the input impedance measured *after the voltage has reached a steady state* following a step change in injected current is defined as input resistance", or "the input resistance ... obtained by dividing the *steady-state* voltage change by the current using it" [11]. *Using quickly changing (alternating) currents, either sinusoidal or random for measuring conductance, measures some ill-defined current.*

Physiologists are "resetting the clock", instead of explicitly admitting that the current speed is finite. The conductance (per definitionem) does not change; only the (maybe: foreign) charge carriers may need time to deliver the current: *we calculate the conductance from non-matching value pairs* (or not-steady state). Wording that biological systems show "non-ohmic behavior" means that they are not metals (they have a charge transfr mechanism differing from the "free electron cloud"): we abstracted the notion of conductance for conductors. Physics describes biological operations perfectly; although, it may use 'non-ordinary' laws. Electric operations are also ohmic in biology, but one has to use the correct (time-aware, i.e., considering the speed of the charged carrier) interaction speed. *Using the Newtonian 'instant interaction' as the speed of charged ions or the macroscopic speed of their current is a catastrophic hypothesis and contradicts all our phenomena.*

The ohmic behavior means that voltage and current relate to each other, as we learned in college, only when the electrostatic interaction speed is very high (in the mathematical/physical description, the interaction is instant); furthermore, free charge carriers are present in the volume. In biological systems, it is not necessarily the case: the macroscopic speed of ionic current conveying electrostatic interaction is very low, and so they may follow the electrical field propagation apparently with a time shift (if they are improperly distributed, as was explicitly noticed [10]). However, as Fig. **??** displays, when measuring the secondary entities (instead of a ternary one), everything comes to the right: the voltage and current change using the same time course. One should *measure* the voltage instead of *assuming* the potential appears immediately, even without charge carriers. Furthermore, one should not introduce a foreign voltage into a system (by measuring its conductance) when studying the electrical features of that system.

Another problem to solve when measuring chemical electrolytes using electronic devices is their interfacing. At some point, the ionic charge must be converted to electrons (there and back), which usually happens in electrolyte electrodes. Interfacing the analyzed electrolytic wire and metallic wire in the measurement circuit introduces problems, not only the contact potentials but also a time delay. These electrodes need to carry the ions to some distance, and that process is outside of the time scale of the primary measured process. The effect is noticed but not explained [10]: "the steady state relation between sodium current and voltage could be calculated for this system and was found to agree reasonably with the observed curve at 0.2 msec after the onset of a

sudden depolarization." Moreover, given that *the speed of ions depends on the depolarizing voltage (see Eq. (??)), this time gap also depends on the depolarizing voltage*: the higher the voltage, the shorter the time gap, demonstrated in their Fig. 3. As we demonstrate in Figure **??**, this effect may lead to conclusions opposite to the real ones.

When thermal or electrical invasion happens, the ion's distribution changes. (Above we assumed an infinitely large volume. Limiting the volume's size means an asymmetry for the ions in the volume and brings to light unexpected phenomena.) We must also discuss another fallacy that the structured biological objects behave as the metals do under the effect of electrical forces. To derive an abstraction similar to the ones as sciences derive their Laws, we assumed that the ions are tiny charged heavy balls, and they attempt to have a uniformly distributed concentration and potential in the considered space segment. We discuss the cases when an external electrical invasion happens in one segment, when an external chemical invasion happens in one segment, the case when a physical surface mechanically separates the ions in two neighboring segments with different features, when the two separated segments are not symmetrical due to 'Maxwell-demon'-like transmit gates (semipermeable membrane); and when a physical effect concerts the operation of the demons.

The cellular electrodiffusion phenomena are very complex, and it is not a simple task to choose which physical/chemical effects can be omitted so that their omission does not prevent us from explaining physiological phenomena. We discuss mainly the commonly used fundamental omission that the speed of ionic movement cannot play a role in describing neuronal operation.

0.1.2 One segment

Electrodiffusion experience shows that reaching a steady state is a temporal *process*, and even the spatial and temporal development of the voltage/concentration gradient can be measured as individual processes. It is also evident from experiments that diffusion is a fast *process* and that the propagation of the electrostatic field is unimaginably fast (but must be process, too). In other words, we have two enormously different interaction speeds. Eq. (**??**) provides only position derivatives.

Potential in infinite segment

Suppose we have az ion with charge q in an infinite segment with charge density σ. In a volume element at distance r with thickness dr seen by the charge in element of solid angle $d\Omega$, according to Coulomb The electric potential at the position of the charge due to that volume element is

$$V_E = \frac{q}{4 * \pi * \epsilon_0} \frac{\sigma * (r^2 * d\Omega * dr)}{r^2} \tag{1}$$

$$\vec{F} = \frac{q}{4 * \pi * \epsilon_0} \frac{\sigma * (r^2 * d\Omega * dr)}{r^2} = \frac{q * \sigma * d\Omega * dr}{4 * \pi * \epsilon_0} \tag{2}$$

The corresponding potential contribution is $dV = \vec{F} * \vec{r}$, so the resulting potential must be integrated to distance and solid angle

$$V_E = \int_0^{4*\pi} d\Omega \int_0^{+\infty} dr \ \frac{q * \sigma * d\Omega * dr}{4 * \pi * r * \epsilon_0} \tag{3}$$

The integral for the solid angle is simplified to multiplying by $4 * \pi$, so

$$V_E = \int_0^{+\infty} dr \ \frac{q * \sigma * dr}{\epsilon_0} \tag{4}$$

Electrical invasion

By introducing time derivatives by Eqs. (**??**) and (**??**), we can derive further terms that describe the relation between concentration and potential for the case when the first time derivative of the position coordinate is not zero. (Here, we explicitly parallel with the Lorentz transformation in the special theory of relativity: the presence of a speed-dependent term changed the essential behavior of the basic notions of mass, time, force, and so on.) In principle, we could introduce a $\frac{d}{dt}$ term as $\frac{d}{dx}\frac{dx}{dt}$ where $\frac{dx}{dt} = v$ (v is the interaction speed of the respective interaction). The practical difficulty is that the diffusion speed is smaller by several orders of magnitude than that of the EM interaction, see Eq. (**??**). However, what truly sets electrodiffusion apart is the absence of a direct equivalent of the Maxwell-equations. In this unique field, the chemical concentration and the electrical field generate each other at different pace, presenting a fascinating departure from traditional ('ordinary') physics.

In classical physics, the EM interaction is instant, so the time derivatives of the electrical and magnetical fields can change simultaneously. In the approximation we use, we consider the EM speed infinitely high – in the spirit of 'classical physics' – and we consider the finite speed of ions using physical approximations, which are simplified representations of the actual physical processes. In our mathematical model, *the electrical field gradient acts instantly on the charge, but the effect of the concentration gradient reaches its position with some delay.*

Chemical invasion

One of the worst consequences of using 'equivalent circuits' to describe the electrical operation of neurons is believing that the currents in the biological circuit do not change the concentration, and through the concentration, also the potential; see also section **??**. The 'equivalent circuits', of course, use a constant potential (they follow the abstraction used in the theory of electricity, although the 'ideal batteries' also may produce their voltage using chemical processes). This wrong abstraction results in numerous misunderstandings, among others, introducing ideas such as parallel oscillator equivalent of neuron, input resistance, delayed rectifier current, resting current, and time- or voltage-dependent conductance. Furthermore, we cannot interpret, among others, *how neuronal*

electricity works in lack of external potential; *how slow currents operate neuron's infrastructure*, *how and why action potential is generated*. Deriving the time course of the Nernst-Planck potential opens the way to a quantitative understanding of neurophysical electrical processes, including their time course.

Another wrong consequence is that the two secondary abstractions 'potential', and 'current', became independent from the primary abstraction 'charge' and each other. Our equations and the underlying discussion point to the fact that *the potential and the current cannot be separated from the charge*. No 'delayed rectifying current' and 'voltage- (or time-) dependent conductance' exist. Those notions originate from the wrong interpretation of measured data derived from mismatching measured electrical data pairs and the misconception that biological structures and materials must behave like metals.

0.1.3 Two segments

We can separate the volume into two segments by a thin isolating membrane. The membrane is thin; we assume the separating membrane is transparent for the electrical interaction (the electrical field affects the ions in the other segment on the other side of the membrane) but not for their masses (mechanically separates the segments).

We prepare a tiny electrolyte volume filled with a solution containing ions such as Na^+, K^+ and Ca^+, we separate its volume with a semipermeable membrane (bilayer of lipid molecules) having capped ion channels inserted into its material. The ionic concentrations are largely different in its two segments and the ion channels have their cap on the side of segment with lower concentration. Our construction looks like a 'duck'.

Infinitely thin membrane

When we separate the volume by an *infinitely thin* membrane, we actually do not affect the electrical and thermal distributions in the now separated segments. Given that the electrical potential of the ions can have its effect through the separating membrane and the thermodynamic collisions with the membrane are elastic, nothing changes. Although the exchange of ions between the segments will not be possible any more, no change is induced and the equation remains the same.

For the discussion below, we assume that a two-dimensional surface separates the volume and we discuss the gradient along a line, perpendicular to that plane surface. Actually, we discuss a one-dimensional distribution. Due to the presence of fellow charges, an ion with charge q at distance x from one of the surfaces experiences the sum of the forces of all charges, i.e.,

$$F_{pot} = q * \int_0^{+\infty} \frac{dV}{dx}(x) \tag{5}$$

force from one direction, which is counterbalanced by a similar force from the neighbors on the other side.

Finite width membrane

Now let us separate the volume into two segments by a membrane with a finite thickness d, see Figure 3. The membrane is a perfect isolator, i.e., no charge carriers exist between its two surfaces. In this way we separate the two segments by distance 1 (we measure distance in units of the thickness d when deriving the mathematical dependence, but use physical units in the figure), the first force is unchanged while second force reduces. In this way the net force at position x becomes

$$F_m = q * \int_0^{+\infty} \left(\frac{dV}{dx}(x) - \frac{dV}{dx}(x+1) \right) \tag{6}$$

Given that the potential is composed from those of the neighboring individual ions of form $\frac{1}{x^2}$, we assume that

$$F_m = q * \left(\int_0^{-\infty} \frac{V}{x} dx - \int_0^{+\infty} \frac{V}{x+1} dx \right) = -ln(x)\Big|_0^{\infty} + ln(x+1)\Big|_0^{\infty} \tag{7}$$

We use the approximation that $\ln(\infty) \approx \ln(1+\infty)$ and we arrive at that the

$$F_m(x) \propto ln\left(\frac{x}{x+1} \right) \tag{8}$$

As it is well known from the theory of electricity, separating charges creates an extra potential gradient and potential which are proportional with the potential and the concentration. That is, we need to assume that the extra potential along our line is described by a function of form

$$\frac{dV}{dx}(x) \propto F_{bulk}\left(ln(\frac{x}{x+d}) \right) \tag{9}$$

Although from thermodynamical point of view the segments are isolated, the extra potential gradient invokes an extra concentration gradient change according to Eq.(**??**). Integrating by parts (using that $\int udv = uv - \int vdu$) we arrive at that the potential is

$$V(x) = ln\left(\frac{x}{x+d} \right) x - ln(|x+d|) + C \tag{10}$$

or in a different form

$$V(x) = V_o * ln\left(\frac{x}{|x+d| * (x+d)} \right) + C \tag{11}$$

Figure 3 shows the membrane's extra potential gradient in function of the distance from the membrane's surface for three different bulk potentials (i.e., different concentrations). Here, we use physical length units (instead of the abstract distances used during the derivation) and an arbitrary voltage gradient scale. Suppose we assume the estimation given in [1] that in the case of resting potential, the scale of the gradient that accelerates the ions across the ion

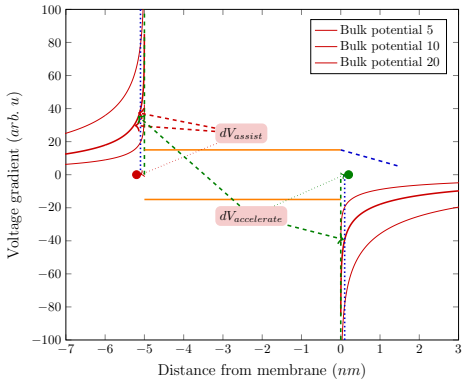

Figure 3: The neuronal membrane's extra *potential gradient* in the function of the distance from the membrane's surface and the bulk potential. The thickness of the atomic layers proximal to membrane's surfaces are also shown.

channel is calibrated approximately as kV/cm. Recall that we are still speaking about the resting state and only about the extra gradient evoked by the finite-width membrane. We are at the boundaries of the macroscopic and microscopic worlds. We derived our integrand from the picture of discrete charges but integrated it into the picture of continuous charge distribution, so we have an empirical factor between them. We assume an atomic layer (a skin) on the surface. However, the layer itself can also be modeled as having just a few ions under their mutual repulsion on the surface or a few atomic layers on top of each other, depending on the concentration and voltage in the bulk on the two sides. (The diagram line is valid in the plane crossing the membrane and the ion channel.)

We assumed that the membrane's width is 5 nm. An ion channel is depicted in the middle of the figure with a diameter of about 1.5 nm. Furthermore, we assume that the ion's size and, correspondingly, the thickness of the atomic layer in the electrolyte on the surface of the membrane is about 0.1 nm. For comparison, recall that the size of the tip of the clamp pipette is in the range of $1,000$ nm and the size of the soma in the range of $10,000$ nm.

The figure shows three different bulk concentrations, so one can estimate (using non-matching diagram lines) what happens if the concentrations change between the two segments (although their interaction slightly complicates the process). The bulk concentration naturally changes the potential, so a difference in the potentials can be measured. However, this may be the voltage between the bulks, one bulk and one layer, or two layers. When measuring potential in the segments using such a pipette and touching the membrane one actually may measure some average potential which contains only a tiny proportion from

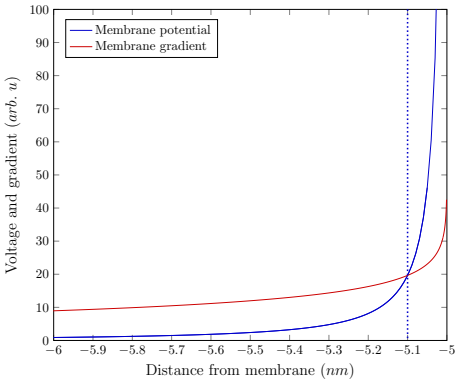

Figure 4: The extra membrane potential gradient see Eq.(9) and extra potential Eq.(10) in the function of the distance from the membrane's surface. Also shown the assumed thickness of the 'atomic ion layer' . For illustration, a simple capped ion channel in the membrane's wall is also displayed, but its effect on the potential is not accounted for.

the layer, so the mentioned extra potential gradient cannot be measured by that method. Anyhow, the ion currents flow between the two layers under the potential, which can drastically differ from the bulk potential. Derived values, such as the GHK potential, should be rethought.

Our results align with the observation (see caption of 11.22 in [1]: "A small flow of ions carries sufficient charge to cause a large change in the membrane potential. The ions that give rise to the membrane potential lie in a thin ($<$ 1 nm) surface layer close to the membrane.

Simple invasion

Separating a volume into two segments has no initial effects: the *bulk* concentration and potential remain the same on the two sides of the membrane. However, the finite thickness will result in a lack of balance near the surfaces of the membrane. Changing the bulk concentration or potential in one of the segments creates a corresponding gradient across the separating membrane (and also evokes new bulk parameters in the resting state). In the layers proximal to the membrane, the ions will experience an extra force. The *concentration and potential, inseparably and having the same time course*, will change across the two sides of the membrane just because of the gap in physical features the membrane represents, as we discussed above. (Notice, however, that while increasing the concentration in one segment means having an unlimited possibility of increasing bulk potential, decreasing it may be limited by the reduced number of charge carriers.)

The electrical repulsion/attraction across the membrane will form two layers on the two surfaces: an ion-rich layer on the high-concentration side and an ion-poor layer on the low-concentration side. Here, refer to Fig.(3). We do not clone the figure, although the bulk parameters differ. The ions in the other segment do not counterbalance the repulsion force at the membrane, so the values of the local potential in the proximal layer near the membrane in the segment with the higher concentration will be above the one in the bulk of the segment and of course, the potential will also be higher. Similarly, the repulsion of the ions in the opposite layer will create an ion-poor layer on the low-concentration segment in the proximal layer near the membrane, with a changed thickness in the skin. However, the values of the local concentration and potential remain the same in the bulk of the respective layer.

The result is a condenser-plate effect: two layers are formed on the isolator's two sides where the charges' repulsion does not counterbalance the repulsion in the bulk of the corresponding segment. Fig. 4 displays how the function shapes of the potential and its gradient change in the function of the distance from the membrane. Here, we assume that no ion channels are in the excellently isolating wall (ion channels would mean a current drain and, therefore, a voltage drop). However, the smaller repulsion acts as a kind of attraction: it prevents ions in the layers on the two sides from diffusing into/from the bulk without a current drain in the layer for an extended period. This steady state results from the interplay of the concentration and the potential described by Eq. (**??**). The gradients change gradually within the segments and step-like across the membrane. Recall our remark above on the limitations of the thickness of the layers in proximity to the membrane, which also enforces limitations on the potential in the layer. No current can flow through the membrane; there is no leaking current.

We also need to notice the difference in the local gradients in the function of distance from the membrane's surface. If something changes, a dV_{assist} gradient appears between the layers and will rearrange concentration and voltage in the segment. Notice that this gradient is by orders of magnitudes smaller than the gradient $dV_{accelerate}$ which accelerates the ions in the proximity of the channel entrance (see the red ball in front of the entrance of the ion channel). According to the Stokes formula (see Eq. (**??**)), the corresponding speeds also differ by orders of magnitudes, enabling us to distinguish *potential-assisted* and *potential-accelerated* speeds, and correspondingly, speak about *'slow' and 'fast' currents* that the ions represent at a macroscopic level. For this study, we assume the diffusion, potential-assisted and potential-accelerated speeds, in m/s to be 10^{-4}, 10^{-1}(also inside neurons [2]), 10^{+3}, respectively (used only to estimate the order of magnitude of some respective operating times). When staging, we assume the greater of the mixing speeds as 'infinitely large' and omit the time that the process needs, while discussing how the slower process proceeds.

0.1.4 Membranes & layers

Membranes, and especially the semipermeable ones, are fundamental pieces in many places, from biological objects to industrial filters. They operate on the border of microscopic and macroscopic worlds, combine movements having speeds differing by several orders of magnitude, separate non-living and living matters and combine electrical and thermodynamical interactions. We show that a fragile skin near the surface of biological membranes is responsible for the biological electrodiffusion processes.

We might imagine this layer's importance and operation in line with the Earth's atmosphere. Its features drastically deviate from the features of the bulks on its two sides. It is separated by a sharp contour on one side and an ill-defined border on the other; its volume is far from homogeneous. Gravity keeps it in place, and it is at rest. However, sometimes, for some periods, also other (thermodynamical and electrical) forces evoke inside it and lead to transient changes, moving huge masses with high-speeds inside it. Its thickness and mass are negligible compared to those of the bulks on their two sides, and we can describe the bulks without considering their density, mass, size, etc. Still, this thin layer is responsible for the weather; its transient processes define the visibility from both sides (define propagation of electromagnetical fields), and it can protect us from EM radiations. It can temporarily absorb products of slow processes (water evaporation) and deliver masses of high density (much above its density, such as water, sand, etc.) to continental distances, creating the illusion that it stores that matter. Minor changes (natural ones, such as a slight difference in air temperature, and artificial ones, such as injecting condensation nuclei in clouds) can result in enormous changes. Even we can imagine volcanic eruptions as semipermeable gates for material with apparently random operation and distribution of the injected material. To describe those complex and continuous phenomena at least approximately, we must separate them into stages. We can describe the stages approximately using omissions, approximations, and abstractions, usually considering only one dominant phenomenon. The described phenomena are interrelated in a very complex way and depend on different parameters. To some point, we can describe that thin layer using a static picture and provide an empirical description of its processes, even though we can give some limited-validity mathematical descriptions for those stages. However, we understand that for describing the time course of the transition (contrasting with step-like stage changes) between those well-defined stages of the atmosphere, we need a *dynamic description* to discover the *laws of motion* governing the processes.

Similar is the case with the neuronal membranes and the neuronal operation. Now, we are at the point where their decades-old static description is insufficient. We need to derive the corresponding laws of motion to describe the neuron's dynamic behavior. We need a meticulous and unusual analysis to derive them. In a neuron, in the abstraction science uses, we put together only an ionic solution, a semipermeable membrane, and currents that reach and leave them. As experienced, at some combination of their parameters, qualitatively

different phenomena happen, which, in the abstraction biology uses, are called signs of life. Given that the approximations, the derived abstractions, and the mathematical formalisms describing them are different for the two cases, *it looks like we have two different, only loosely bound worlds.* We realize we have arrived at the boundary of non-living and living matters, and we must go back to the *first principles of science.* However, by using our approach, we may defy that "the emergence of life cannot be predicted by the laws of physics" [22].

0.1.5 Demon in the membrane

We can build 'Maxwell-demon'-like objects into the separating membrane: gated ion channels, see Fig. (3). In this section we show that our model quacks like a duck.

The ion channels operate as demons (from the point of view of the segments and the observer). Some power opens them, they autonomously transfer ions in a *potential-accelerated* operating mode, and then that power puts the cap back on the top of the channel. Although the channels can stochastically open, close, and re-open, they transmit more or less well defined charge quanta. Even the channels can recognize the ions' chemical nature and transmit only a selected ion type. The channels are passive during those processes, although the enormous voltage gradient can rearrange their structure and change their behavior through that. The demons also concert their actions using the layer containing charges as a communication medium; their population maintains a well defined macroscopic current across the membrane. Our construction swims like a 'duck'.

Voltage sensing

"Voltage sensing by ion channels is the key event enabling the generation and propagation of electrical activity in excitable cells."[76] How voltage gating of channels works is still a mystery; one of the worst consequences that Hodgkin and Huxley separated the potential from ions and their current. It is not easy to investigate it experimentally: "the structural basis of voltage gating is uncertain because the resting state exists only at deeply negative membrane potentials" [77]. Usually, a "sliding helix" (structural) model is assumed.

Under certain conditions, an ion channel can be opened in only one direction and only for a limited period, and this way the membrane becomes semipermeable. We imagine an ion channel as a simple hole (a cylinder) between the high and low-concentration segments with a cap on its top (on the side of the low-concentration segment). Until the cap is removed/lifted (the channel gets open), practically nothing changes. At the points where the ion channels are located, the ions can go somewhat closer to the other segment (the local concentration and potential may get somewhat higher on the high-concentration side, with the corresponding changes on the other side of the cap), but they cannot penetrate the membrane. Unlike the original Maxwell demon, our demon does not have information in advance about which particle should be transmitted: it

is passive in selecting the particle. It only keeps one way closed for part of the time, and the voltage performs selecting the ions.

We can easily interpret why our voltage-controlled ion channel model gets opened and closed due to purely electrostatic reasons. It works as the two-plate simple nano-scale electrometer (of type quadrant, Lindermann, Hoffman, and Wulf) similar to the ones used to measure the small electrical potential between charged elements (e.g., plates or fine quartz fibers). Given that the membrane and the cap in their resting state are isolators, no electrical repulsion is evoked between them and the adhesion sticks them firmly to each other, representing a permanent force. The van der Waals force is inversely proportional to the squared distance between the dipoles in the cap and the membrane, respectively, and is linearly proportional to the perimeter of the channel.

However, when a slow ion current flows into the surface layer in the proximity of the cap, charges appear in the layer proximal to the membrane; the membrane and the cap get covered by a very thin electrical skin. The charge on the cap is proportional to the surface of the cap and similarly inversely proportional to the squared distance between the cap and the membrane. A local voltage gradient is generated by the local gradient of the slow ion current (see below), and the force acting on the cap is proportional to the product of the voltage gradient and the area of the cap. Given that the cap is slightly elevated, the repulsion force may have a component in the direction of lifting the cap. Since the van der Waals force is of fixed size, the electrical repulsion exceeds it at a critical voltage gradient value and the channel opens. The cap is connected to the membrane only at one point, so it cannot fly away and also cannot close again until the charge on the surface is present. The gate remains open as long as the local charge distribution enables it. In the absense of charge the cap makes a random movement and the short-distance van der Waals force may eventually fix the cap again to the membrane, this way closing the channel. The voltage sensing electrometer opens the channel and the lack of charge on the surface enables to close it, but the closing is not immediate. The fluctuation of the voltage gradient due to the gradient of the slow current in the layer in the proximity of the membrane near the ion channel's exit opens, closes, and re-opens the channel in an apparently stochastic way (actually, as the repulsion of charges due to the fluctuating current on the cap and the membrane regulates), as observed.

When one cap is removed, the rushed-in ions in the proximity of the channel's exit suddenly increase the local potential (produce fast transient changes [40]) proximal to the spot centered at the exit in the layer on the membrane's surface. The surface outside the spot remains at a lower potential, so the ions in the layer start moving toward other channel exits, delivering potential to those channel exits. Given that they are voltage-controlled, they get open, and the process continues in an avalanche-like way [37]. The avalanche, as explained, needs a sufficiently large voltage gradient; which can be triggered by several synaptic inputs if they sum up appropriately. Alternatively, a single spike with sufficiently steep front slope [36] can be sufficient; providing a simple way of synchronization.

Passing through the ion channel

The operation of the ion channel, alone, cannot explain that the channel closes after a given number of ions passed the channel; that number is not (entirely) random. Actually, the membrane's surface layers regulate the number of ions.

The segments are no longer mechanically separated when the cap is removed. The charged ions are enabled to rush into the lower concentration segment. They experience an enormous accelerating gradient: "an electrical potential difference about $50-100\ mV$ ... exists across a plasma membrane only about $5\ nm$ thick, so that the resulting voltage gradient is about $100,000\ V/cm$" [1]. That enormous gradient, comparable to that of electrostratic particle accelerators, "snorts" the ions from the high-concentration side into the low-concentration side and causes a process "like a flee hopping in a breeze". Consequently, "transport efficiency of ion channels is 10^5 times greater than the fastest rate of transport mediated by any known carrier protein" [1]. Recall that, in physics, the *drift speed*, the *electrical repulsion-assisted speed,* and the *electrical potential-accelerated speed* of ions differ by several orders of magnitude (for visibility, the ratio of the gradients in Fig. 3 is not proportional).

The snorted ions "hop" into the layer. In the beginning, with their *voltage-accelerated* speed, it could take less than $\frac{5*10^{-9}m}{10^3 m/s}\ s$ to pass the channel (simulation [78] uses a *psec* representative time interval), in the end, they may slow down to the *voltage-assisted* level as the potential gradually decreases (which is still $\frac{5*10^{-9}m}{10^{-1}m/s}\ s$), so we can omit that time when calculating the charged layer formation. Due to the enormous speed difference between the *accelerated* and *assisted* speeds, the passage is practically instant. The accelerating field through the hole across the layers persists, although it decreases. On the high-concentration segment, only the ions in the layer in the immediate proximity of the entrance can feel the accelerating potential and move with the potential-accelerated speed. The after-diffusion with the *potential-assisted* speed from the next neighboring layer in the high potential segment is by orders of magnitude slower than the passage through the hole with the *potential-accelerated* speed. Depending on the process parameters, the local potential can rise above the high-concentration segment's potential for a short period due to the accelerated current's 'ram pressure' (or 'impact pressure'). Due to their electrical repulsion, the ions induce a similar change on the opposite segment.

The accelerating potential gradually (but quickly) disappears when the particle exits the ion channel (see the green ion in the figure), and the ion arrives at the bulk potential. It practically stops: it can continue only with its *potential-assisted* (later with *drift*) *speed, which is several orders of magnitude lower.* However, the rest of the ions are still accelerated through the channel, and somewhat later, they also land in the formerly low-concentration layer, further increasing its potential and concentration. The passed-through ions increase the local potential in the layer in the low-concentration segment and decrease the local potential in the layer in the high-concentration segment. Given that the after-diffusion speeds in the layers are limited, "as ion concentrations are

increased, the flux of ions through a channel increases proportionally but then levels off (saturates) at a maximum rate" [1].

Here the efect of the finite resources explicitly appears. As we discuss in sections **??** and **??**, about 10^3 ions are transferred per channel. These ions are snorted from one layer in the high-concentration segment into another layer in the low-concentration layer. The driving force gradually decreases because ions leave the first layer and they appear in the second mentioned layer. The potential-assisted speed to replace the leaving ions into the first segment from the bulk as well as diffusing out from the second segment without appropriate driving forces is by orders of magnitude slower, so we can approximate the process that a gradually decreasing accelerating force drives the ions. The process leads to a special reversal of concentrations and potentials. In a very short period, in the layer on the formerly low-concentration side a very thin high-potential layer is formed that prevents further ions from entering the formerly high-concentration layer: the process of transferring ions through the channel closes the door behind the needed amount of ions. Now the gradient diminished and the van der Waals force can close the channel again.

The commonly used picture about the operation of ion channels [79] is definitely wrong.

- the potential generated across the membrane is entirely neglected
- the ions have no driving force to approach the arbor
- the considered van der Waaals force is too weak to be noticed by the ions (the 'cation-attractive negative ends' of the Alpha helices are too far)
- the assumed force by the 'cation-attractive negative ends' destabilize the ion path: as the deviation from the central path increases, so increases the deviating driving force
- even if the weak van der Waaals force would work for a sigle ion, the next ion would be rejected by the strong Coulomb-force due to the first ion

Delivering current across the membrane

The passage is too quick to affect the bulk (see also the discussion in section **??**), given that the ions can only use a *potential-assisted* speed to reach distant places in both segments. Again, the charge and mass conservation works: the ions pass suddenly from the high-concentration side to the low-concentration side, only from one layer to another. The mentioned *layers on the two sides will actively initiate and terminate the ion transfer through the ion channels, but the ions can only pass through an open channel.* One layer saturates, and the other empties. After a while, *the source of ions will be exhausted. Those layers' existence suggests revisiting the idea of describing neuronal operation by two single potentials of the bulks on the two sides of the membrane.*

Following their arrival, the driving force perpendicular to the membrane's voltage disappears, and the ions form a thin "hot spot" in the layer. The electric

repulsion acts in parallel with the membrane's surface and leads to distributing the ions (decreasing the gradient by distributing the charge locally) around the channel's exit. The ions saturate the layer on the membrane's surface with a time constant between ($\frac{10^{-8}m}{10^{-1}m/s}$ s) at the beginning and ($\frac{10^{-8}m}{10^{-4}m/s}$ s) at the end of their arrival period (we assumed 10 nm average distance between ion channel exits on the membrane). We shall take the longer time, so that we can expect a time constant for the saturation current around the ion channel's exit in the order of 0.1 ms. When charging up the membrane in an avalanche-like way, the ions must pass on average a distance of about 0.05 mm from its center to its farthest point, so we expect a 0.5 ms ($\frac{5*10^{-5}m}{10^{-1}m/s}$ s) time until the membrane's slow current charges up the membrane to its maximum potential. The created charge must flow out from the farthest point in the neuron membrane of size 0.1 mm in time of order at or below 1 ms ($\frac{10^{-4}m}{10^{-1}m/s}$ s); see the length of the $\frac{dV}{dt}$ pulse measured at the beginning of the AIS [8], see Fig. **??**, which time is prolonged up to 10 ms by the neuronal RC circuit; the ions are slow when the voltage on the AIS is low, see Eq. (**??**). Assuming those distances and speeds, including the *potential-assisted* speed of the slow current, we are on a time scale matching the available observations.

Ion selectivity

Maybe the mechanism of channel passing can also contribute to explaining ion selectivity. "The normal selectivity cannot be explained by pore size, because Na^+ is smaller than K^+ [1]". The two ions have the same charge, but K^+ is nearly 70% heavier than Na^+, a definite disadvantage when accelerated by a vast electrical gradient. When the layer on the arrival side gets saturated, its potential reaches the potential of the bulk on the high concentration side (this is necessary to decelerate the accelerated ions), and so the channel gets closed (the accelerating potential disappears for a short period until the ions from the layer flow away toward the drain or they diffuse toward the bulk). We assume that the ions continuously accelerate, then decelerate, due to the potential gradient (which we assume to be constant for a moment). When Na^+ ions stopped after passing the channel and built up a repulsive layer proximal to the channel's exit, the K^+ ions passed only about 60% of the channel's length. The Na^+ ions, which started from the departure layer with a handicap of 2 *to* 3 nm, will arrive earlier than the K^+ ions from the 0.1 nm thick charged layer proximal to the channel's entrance. That is, this handicap results in a strong enrichment of Na^+ ions. For the detailed calculations see section **??**.

Given the potential reverses, the late ions are decelerated and then accelerated in the reverse direction (recall that the layer they started from is still empty and attractive), they simply go back to the departure side. The ions also repulse each other while being accelerated (the accelerating gradient acts on a distance of 5 nm while the ions may approach each other to a distance of 0.1 nm, so the mutual repulsion can be significant). In this way, the heavier ions help their competitors and vice versa. (The different ions can also connect to differ-

ent, heavy-weight components of the solution, drastically changing the picture.) The result is that only the lighter ions can pass the channel from an ion mixture when the cup is suddenly removed. The passage is super-fast; it is in the *psec* region (with a *voltage-accelerated* speed compared to the *voltage-assisted* speed of after-loading ions from the next layer), and the created potential quickly decays by diffusion.

The commonly used picture about the operation of selectivity filters is surely wrong. The assumed mechanical operation operation of the pores is simply too slow: the assument structural change needs 10^{-8} s and the ions passage time is about 10^{-11} s (furthermore, it must be repeated about 10^3 times per passage). If a wrong ion is catched, it must be transported back to its departure side, through the right ions (against their repulsion), and the right ions must retry. Neither for moving forward nor backward an appropriate driving force is present.

0.1.6 Outward current

Ion channels, in many forms, are used to transfer ionic current quickly.

From the components we described, we can compose a "physical neuron"

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