Eur. Phys. J. Special Topics **227**, 2329–2347 (2019)

https://doi.org/10.1140/epjst/e2018-800108-6

THE EUROPEAN
PHYSICAL JOURNAL
SPECIAL TOPICS

Review

Diffusive propagation of nervous signals and their quantum control

Jiří J. Mareš[a], Pavel Hubík, and Václav Špička

Institute of Physics of the Czech Academy of Sciences, Cukrovarnická 10,
162 00 Prague 6, Czech Republic

Received 2 July 2018 / Received in final form 2 August 2018

Abstract. The governing theory of electric signal transfer through nerve fibre, as established by Hodgkin and Huxley in the 1950s, uses for the description of action potential a clever combination of various concepts of electrochemistry and circuit theory; however, this theory neglects some fundamental features of charge transport through any conductor, e.g., the existence of a temporary charged layer on its boundary accompanied by an external electric field. The consequences of this fact are, among others, the introduction of a non-adequate concept of "conduction velocity" and the obscure idea of *saltatory* propagation of action potential in myelinaed nerve fibres. Our approach, based on standard transport theory and, particularly, on the submarine cable model, describes the movement of the front of the action potential as a diffusion process characterized by the diffusion constant D_E. This process is physically realized by the redistribution of ions in the nervous fluid (*axoplasm*), which is controlled by another diffusion constant $D_\Omega \ll D_E$. Since the action bound with the movement of Na^+ and K^+ cations prevailing in the *axoplasm* is comparable with the Planck constant $\hbar$ (i.e. $D_\Omega \to \hbar/2M$, where M is ion mass), signal transfer is actually a quantum process. This fact accounts for the astonishing universality of the transfer of action potential, which is proper to quite different species of animals. As is further shown, the observed diversity in the behaviour of nerve tissues is controlled by the scaling factor $\sqrt{(D_\Omega/D_E)}$, where D_Ω is of a quantum nature and D_E of an essentially geometric one.

1 Introduction

Modern theory of regenerative transmission of electric signals by nerve fibres is based on ideas and models worked out in the early 1950s by Hodgkin and Huxley [1] as well as on the somewhat younger core conductor ("cable") theory of Rall [2]. Now the resulting compound doctrine is used almost exclusively for the modelling and explanation of neuronal processes for both teaching and research purposes [3,4]. Remarkably, this rather complex and essentially deterministic theory is simultaneously a very singular one, differing significantly from the simple physical picture of

---

[a] e-mail: `maresjj@fzu.cz`

the transfer of electric impulses through all other types of conductors. Since we are convinced that there is no serious reason to treat the nervous fibre in a different way than other conductors, we hereby attempt to describe the transfer of electric impulse by nerve fibre alternatively, in terms of a standard physical model. For the sake of simplicity and clarity, in this short paper we address only the transfer of *signal front* in non-relativistic approximation, postponing for further study the discussion of refractory and recovery phases of the signal, which are controlled by operation of voltage-triggered ionic channels [5,6].

There are two physical effects of fundamental significance for the transfer of electricity by conductors; however, they are not often appreciated in literature.

- The first one is the existence of net charges on the surface of current-carrying conductors, the purpose of which is to create a viable path for charge carriers and completely screen the interior of the conductor from external disturbing fields.

- These surface charges simultaneously give rise to a response in the surrounding medium, namely, to the appearance of external electric fields and induced electric currents. In this context, let us mention that this is just the reaction of surrounding tissues which plays a decisive role in most in vivo experiments with nerve excitation.[1] We are convinced that the inclusion of these two important physical phenomena into theoretical considerations may substantially improve the description of the transmission of electric impulses by nerve fibres and can provide better insight into many neurophysiological experiments.

The content of this paper can thus be summarized as follows: Starting with our generalization of Ohm-Kirchhoff's constitutive relation [7] reflecting the existence of surface charges in the conduction process and exploiting a slightly modified theory of submarine cable [8], we will establish an original alternative model for the theoretical description of the transfer of an electric signal through the nerve fibre. Accordingly, the signal transfer has a diffusive character controlled by a couple of largely different diffusion constants, D_E and D_Ω. Based on these findings, we will proceed with the validation of the quantum nature of the diffusion of biogenic cations Na^+ and K^+, the principal agents controlling intracellular and extracellular electrochemical processes in nervous tissue. Finally, we will discuss an important consequence of our model: scaling relations that shed new light on the structural composition and functionality of nerve fibres.

2 Preliminary considerations

Let us begin by recalling basic facts concerning nerve fibre anatomy [9,10] (see Fig. 1). Nerve fibres are classified into two basic groups, namely, in *myelinated* (or *medullated*) and *unmyelinated* nerve fibres, which anatomically differ only by the presence or absence of the myelin covering A typical myelinated nerve fibre consists of an insulating protein tube (*axolemma*) filled with a complex conductive electrolyte (*axoplasm*). A myelin sheath is wrapped around the tube and is interrupted by gaps called

---

[1] Particularly, the experimental observations of these induced currents in extracellular tissue vicinal to the myelinated nerve fibre led to the establishment of very influential *saltatory conduction theory* (e.g. [4]). Accordingly, the conduction velocity of myelinated nerve is appreciably increased because the signal is transferred by the currents flowing through the extracellular domain, which "jump" from one Ranvier node to the next one. This idea originally due to I. Tasaki and T. Takeuchi (1942) and later worked-out by many others, now serves as a standard in contemporary textbooks on neurophysiology.

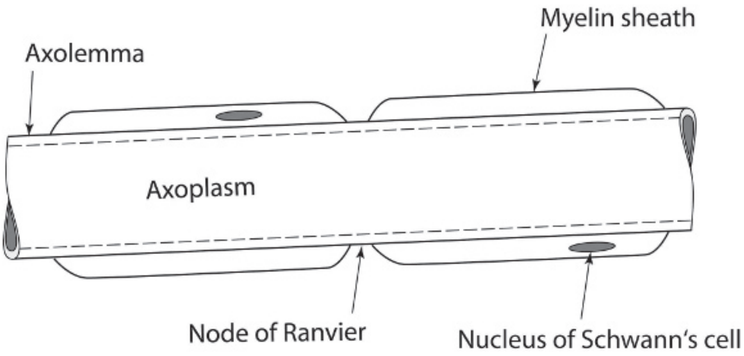

Fig. 1. A schematic view of a myelinated axon, a structure typical for the peripheral nervous system of warm-blooded animals. Myelin, a wax-like lipoprotein substance, originates and is part of the membrane of so-called Schwann's cells.

Ranvier nodes. The entire fibre is immersed in a highly conductive medium consisting of tissue perfused by another electrolyte.

In order to understand the mechanism of the transfer of electric impulses by such a structure, we have to take into account so-called phoronomic conditions from the general theory of electricity. The prominent role among these constrains is played by the *equation of discontinuity.* Accordingly, at every point at the boundary of a leakage-less current-carrying conductor, with the exception of its terminals, there must be

$$i_\nu = 0, \tag{1}$$

where i_ν is a normal component of current density at the surface of the conductor. It can be further shown that condition (1) can be satisfied only if bounded electric charges localized at the surface of the conductor do exist. This very fact, discovered at the beginning of 19th century [11], may be elucidated as follows [12]. If two terminals of a conductor are instantly brought into the contact with the source of electricity, extra net charges of opposite sign appear there. The lines of force of the electric field, which is due to these charges intersect, in general, the surface of the conductor. This obviously prevents the charge carriers from one terminal to reach, along the lines of force, another one and recombine there. Instead, at some point they hit the surface of the conductor and give rise to a surface charge there. This surface charge, however, represents an electric field perpendicular to the surface that deviates the original lines of force into the bulk of the conductor. The process of accumulation of surface charges continues until the inner normal component of the electric field is cancelled and until the bundle of all the lines of force connecting terminals fills up the interior of the conductor. Importantly, just the establishment of this structure, sometimes called a *sphondyloid* ($\sigma\varphi o\nu\delta\upsilon\lambda o\varsigma$, Gk, "backbone") is *sine qua non* for the existence of electric flow from one terminal to another [13,14]. In other words, any conductor is passable for electric current only if net charges and electric fields exist on its surface [15], which are completely decoupling current lines inside the conductor from the external space.

Another relevant question is: How fast do the conductors conduct electricity? This question was the focus of intense interest as long ago as the early 18th century, when the first attempts to determine the speed of electric fluid in a wire were made (see Fig. 2). Nevertheless, it was only Lord Kelvin who, approximately one hundred years later (1855), developed relevant measuring techniques and recognized that the

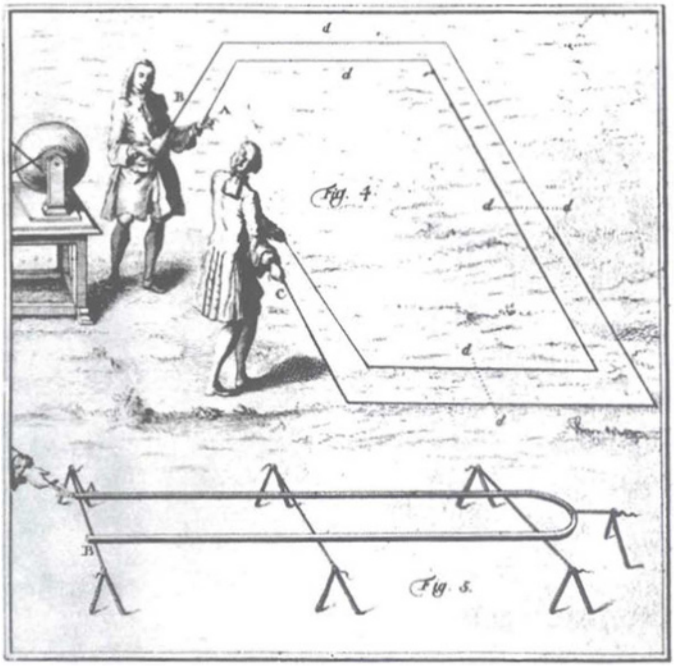

Fig. 2. L.G. Le Monnier's (1746) arrangement for measuring the speed of electric fluid in conductors. A Leyden jar was discharged through the transmission line of actual length of about 1.85 km. The transition time of the signal was then determined from the delay between electric shocks perceived by both experimentalists [16].

progress of electric impulse through the conductor (submarine telegraph cable) is controlled just by the stepwise build-up of surface charges, thus having a character of diffusion [8]. In that case, however, the "*conduction velocity*" (or "apparent speed") of a signal front determined as a ratio of conductor length to the signal transit time, being dependent on the length of the conductor, represents an entity that is unphysical and totally misleading.

Amusingly, this quantity, the "*conduction velocity*", is the central concept of modern neurophysiology [17,18], according to which different types of nerve fibres are classified [19], and it is even used for diagnostic purposes [20]. Moreover, the observed electric response of surrounding conductive tissue to the build-up of a charged layer on the surface of a nerve fibre, inevitably accompanying the transit of electric impulse, was misinterpreted as the essential component of the signal itself (*saltatory conduction*) [4], apparently without awareness of the actual role played by these surface charges in any conduction process.

3 Generalization of Ohm-Kirchhoff's law

For a realistic quantitative description of electric conduction of a nerve fibre and especially for the construction of its consistent physical model, it is essential to discuss first another important issue, namely, the generalized Ohm-Kirchhoff law.

The famous Ohm's law, in fact a constitutive relation controlling linear electric charge transport in many kinds of conductors, including nerve fibres, is probably the most exploited physical relation that has ever been discovered [21]. In differential form, i.e. in terms of the local current density vector i (A/m^2), it reads

$$\mathrm{i} = -\gamma\,\mathrm{grad}K, \tag{2}$$

where γ (S/m) is conductivity and K is the electroscopic force ("*Elektroskopische Kraft*" [22]). In Kirchhoff's interpretation [23], which is accepted in most modern textbooks on electricity, K is identified with the scalar electrostatic potential $\varphi (K \equiv \varphi)$. By applying equation (2) to the steady state current flow, we can formulate the universal law of conservation of electric charge (equation of continuity) as follows:

$$0 = \mathrm{div}\,\mathrm{i} = -\gamma\,\mathrm{div}\,\mathrm{grad}\varphi. \tag{3}$$

For constant conductivity γ, this equation is nothing but the Laplace equation [24] for the distribution of potential φ in a domain containing zero net charge. Astonishingly enough, according to Kirchhoff's interpretation, a current carrying-conductor thus transfers electric charge without net charge in its interior. This fact is compatible only with the two-fluid model of electricity originally elaborated by Weber [25]. According to this model, two streams of opposite charges move relatively in opposite directions in such a way that every volume element within the conductor remains neutral. Examples of such systems are ions in electrolytes, or electrons in lattices consisting of metal cations.

However, as we have already seen above, net charges do exist in current-carrying conductors because they are quite necessary for *sphondyloid* formation. These extra net charges of density ρ (C/m^3), dynamically supplied by the passing current, locally modify the electric potential φ in such a way that condition (1) is satisfied. Formally, this correction to the electroscopic force K, which is due to the temporal capture of extra net charges in the conductor, can be written as

$$K = \varphi + \frac{\rho\lambda^2}{\epsilon\epsilon_0}, \tag{4}$$

where ϵ is relative permittivity of the conductor and where, for the sake of dimensional homogeneity, a factor λ having dimension of length is added. As will be shown later, this parameter has a physical meaning of the electrostatic *screening length* within the conductor. By combining equations (2) and (4), we immediately obtain a formula that we tentatively call *generalized Ohm-Kirchhoff's law* [7], namely

$$\mathrm{i} = -\gamma\,\mathrm{grad}\left(\varphi + \frac{\rho\lambda^2}{\epsilon\epsilon_0}\right). \tag{5}$$

In order to make the physical meaning of the additive correction term in formula (5) clearer, it can be (provided that the conductivity γ is constant and λ is only weakly dependent on ρ) decomposed as follows

$$\mathrm{i} = -\gamma\,\mathrm{grad}\varphi - \frac{\gamma\lambda^2}{\epsilon\epsilon_0}\,\mathrm{grad}\rho. \tag{6}$$

The second term obviously has the form of Fick's first law of diffusion [26] with the diffusion constant given by

$$D_\Omega = \frac{\gamma\lambda^2}{\epsilon\epsilon_0}. \tag{7}$$

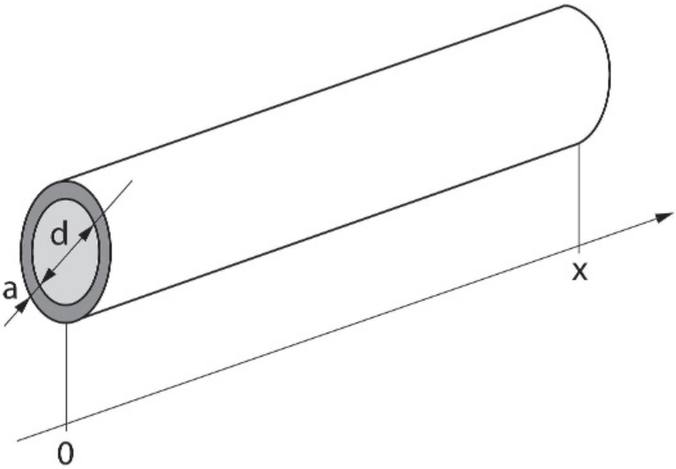

Fig. 3. Schematic view of the submarine cable where d is the diameter of the conductive core, a is the thickness of the insulation, and x the length of the cable segment.

We can thus interpret the second term in (5) as a *diffusion term* controlling the redistribution of net charges throughout the conductor during transient periods.

4 Model of submarine cable

Let us now start the quantitative description of the transmission of electric signal via nerve fibre by analysing anew the original model of submarine telegraph cable [8]. It is a highly apposite model for this purpose because of many close similarities between nerve fibre and submarine cable [2]. Indeed, in both cases we are dealing with an insulating tube (*axolemma* is a perfect insulator because the conductivity γ_A of a pure phospholipid bilayer membrane is as low as $\gamma_A \approx 10^{-13}$ S/m [6]) "stuffed" with a conductor and surrounded by a continuous highly conductive medium (see Fig. 3).

In the past, this suggestive analogy between submarine cable ("core conductor") and nerve fibre has led to many attempts to adapt this model for physiological purposes and treat it mathematically. First, we should mention the imbroglio that developed in the early 1900s between Hermann [27,28] and Hoorweg [29] concerning their attempts to discriminate between the diffusive *pseudowave*-like and wave-like transfer of electric signal through nerves. The core conductor model was very carefully revised again in the 1970s by Rall [2], and since that time his "cable theory" is presented in textbooks side-by-side with the ideas of Hodgkin and Huxley providing thus a somewhat hybridized picture [4,17]. Therefore, in order to avoid confusion, in this paper we are staying in line rather with Kelvin's original cable theory [8], which is physically fairly simple and which, in contrast to Rall's theory, enables one to incorporate quite naturally the diffusion term from generalized Ohm-Kirchhoff's law (5).

Following Lord Kelvin, we then assume that current I is homogeneously distributed within the core of the cable, i.e. that $I \approx iA$, where constant $A = \pi d^2/4$ is its cross section. In such case, we can rewrite Ohm-Kirchhoff's law (2) in a simplified form:

$$I = -\gamma A \frac{\partial K}{\partial x}. \tag{8}$$

Since the rate of build-up of the surface charge on segment $\mathrm{d}x$ of the cable is given by an obvious relation $-c(\partial K/\partial t)\mathrm{d}x$, where c is the capacity per unit length, we may write the balance rate equation for supplied and captured charges in the form

$$-\gamma A\frac{\partial K}{\partial x} = -c\frac{\partial K}{\partial t}\mathrm{d}x. \tag{9}$$

By then making a derivative of this relation with respect to variable x, we immediately obtain

$$\frac{\gamma A}{c}\frac{\partial^2 K}{\partial x^2} = \frac{\partial K}{\partial t}, \tag{10}$$

which is a parabolic equation of Fourier's type [30] with constant factor $\gamma A/c = D_E$. This factor, however, can easily be evaluated considering the well-known relationship for the capacity per unit length of coaxial cable [24] (see Fig. 3), namely,

$$c = \frac{2\pi\epsilon_A\epsilon_0}{\ln(1+2a/d)}, \tag{11}$$

where ϵ_A is the relative permittivity of the insulating tube. The resulting formula then reads:

$$D_E = \frac{\gamma}{8\epsilon_A\epsilon_0}\,d^2\,\ln\left(1+\frac{2a}{d}\right). \tag{12}$$

The formal physical meaning of parameter D_E, which has a dimension of (m^2/s), is the *diffusion constant*[2] controlling the transfer of the front of the electric impulse via the cable.

The elementary solution of equation (10), which corresponds, for example, to the instantaneous injection of electric charge $Q \propto K_0$ into one terminal of the cable, while the second one is kept grounded, takes the form of the following *source integral*

$$K(x,t) = \frac{K_0}{2\sqrt{\pi D_E t}}\exp\left(-\frac{x^2}{4D_E t}\right). \tag{13}$$

Since the times of Fourier [30], a property of this solution has been well known: The time record of function $K(x,t)$ taken in fixed point x has a local maximum which can be interpreted as the passage of the signal front through this point. The mathematical condition for this maximum obviously reads $\partial K/\partial t = 0$, or $\partial^2 K/\partial x^2 = 0$ when taking into account equation (10) and provided that $D_E \neq 0$. These requirements lead to the condition

$$\frac{K_0}{4\sqrt{\pi(D_E t)^3}}\exp\left(-\frac{x^2}{4D_E t}\right)\left(\frac{x^2}{2D_E t}-1\right) = 0, \tag{14}$$

---

[2] The term "diffusion" is traditionally connected with a spontaneous transfer of specific particles through a medium. This concept, however, may also be generalized to other entities such as heat, polarisation state, information, etc. In this paper, we are using the term "diffusion" in both its original and its generalized meaning. Obviously, in all these cases the diffusion constant has the same dimension (m^2/s).

from which an important relation of Einstein-von Smoluchowski's type immediately follows, namely

$$x^2 = 2D_E t. \tag{15}$$

By then making the time derivative of this formula and defining *instant speed of signal front* as $u = \partial x/\partial t$, we obtain the remarkable relationship (cf. [31])

$$xu = D_E. \tag{16}$$

It should be stressed here that the instant speed of signal front u and similarly the apparent speed v (m/s), i.e. "conduction velocity"

$$v = \frac{x}{t} = \frac{2D_E}{x} \tag{17}$$

of the signal, are, according to equations (16) and (17), dependent on x and as such are not good characteristics of specific properties of the cable or nerve fibre. It is thus quite appropriate to mention Lord Kelvin's warning to scholars studying the propagation of electric signals through various conductors [8], namely,

> *"... the retardations of signals are proportional to the squares of the distances, and not to the distances simply; and hence different observers, believing they have found a 'velocity of electric propagation,' may well have obtained widely discrepant results."*

5 Experimental evidence for diffusive character of signal transfer

The straightforward comparison of the formulae given above with actual propagation of electric signal through the nerve fibre is a rather difficult task. This is especially because of the fact that most of the published results are presented just in terms of conduction velocity, while generally there is a lack of rough data and the details of experiments. There are multiple arrangements ranging from rather naïve to very sophisticated; however, the typical one, the in vitro method for measurement of signal transfer, is based on a slightly modified two-point time of flight technique [17,32,33] using miniaturized intracellular electrodes. The sensing electrodes are usually made of very fine glass capillaries filled with a conducting aqueous solution of KCl (salt bridge) and are inserted into a nerve fibre in such a way that the *axolemma* seals itself around the electrode. The reference electrodes used for nerve excitation or biasing are then placed in a surrounding perfused medium. Such an arrangement enables one to determine with high reliability the transit time of the signal and record its shape. Nevertheless, the distance between the sensing electrodes is not chosen intently but purely on practical grounds. Thus, it either depends on the dimensions of the nerve preparation at hand, or on the dimensions of the sample-holder used. For this reason, the data obtained in different laboratories are only hardly comparable, and the results published in compilations concerning various species and nerve types are scattered, revealing no clear systematics [9].

Recently, an alternative and credible technique has appeared that enables one to continuously follow the propagation of the action potential along nerve fibres. This method, known as *action potential microscopy*, makes use of the fluorescence of special molecular protein probes that can be initiated by enhancement of local electric field. The solution of the molecular probe is added to the *axoplasm*, and the nerve fibre is electrically excited in the usual manner. Then, at the point where the action potential peak is localised, a bright fluorescence spot appears. The propagation of this bright

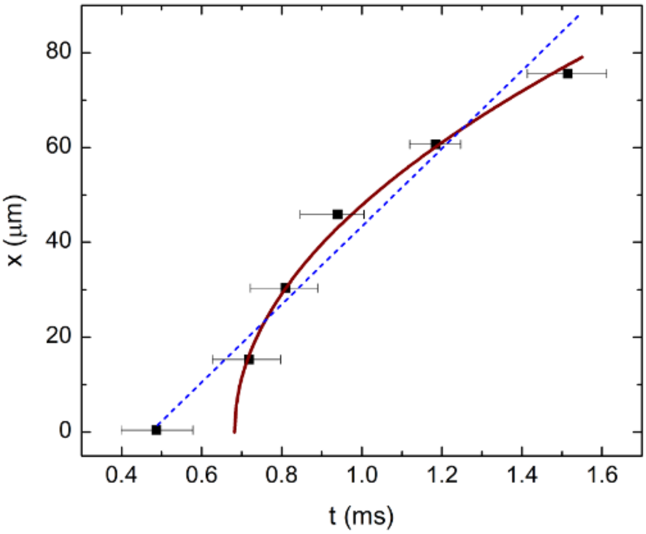

Fig. 4. An example of optical measurement of the propagation of the action potential along the unmyelinated nerve fibre [34]. Comparison of fitting using "conduction velocity law" (blue straight dashed line) and "diffusion square-root law" (red parabola). Latency time ≈0.67 ms corresponds to the delay dictated by Maxwell's relaxation time of the synapsis membrane [5].

spot can be recorded in real time using a convenient optics and digital camera. An example of a result of such an in vitro measurement performed on an unmyelinated axon is depicted in Figure 4 [34]. From this diagram, it can be concluded that the fitting based on the diffusion square-root law, which is equivalent to formula (15), is evidently more successful than that based on the widely used concept of conduction velocity v. This may be also supported by a quantitative argument. Omitting the first point corresponding to the latency phase, during which the bright spot, before starting to move, stays calmly close to the synapsis (nerve terminal, $x \approx 0\,\mu$m), the sums of squared deviations between actual positions of remaining 5 experimental points and curves are 2.9×10^{-2} (ms)^2 for straight line and 2.8×10^{-3} (ms)^2 for parabola, respectively. These facts, directly confirming the diffusive character of the transfer of electrical impulses through nerve fibres, thus simultaneously justifies the applicability of the general theory of electric conduction and, particularly, the applicability of the model of submarine cable to these bio-systems as well.

6 Influence of leakage

There are some as yet neglected differences between the model of an idealized submarine cable and a real nerve fibre. The item worth discussion is the influence of leakage currents, traditionally a significant ingredient of the standard textbook model. Our consideration differs, however, from the standard one and is closer to that of Lord Kelvin [8]. Since the leakage current across the insulation should be directly proportional to the potential difference between its outer and inner surface, we have to add to the right side of equation (10), which expresses the charging-discharging rate balance, an extra correction term, αK, i.e.

$$D_E \frac{\partial^2 K}{\partial x^2} = \frac{\partial K}{\partial t} + \alpha K. \tag{18}$$

In order to clarify the properties of this corrected equation and of the physical meaning of parameter α, instead of K we can introduce a modified potential function κ using a substitution

$$K = \exp(-\alpha t)\kappa. \tag{19}$$

Applying it to equation (18), we immediately obtain for potential κ formally the same equation as (10), namely

$$D_E \frac{\partial^2 \kappa}{\partial x^2} = \frac{\partial \kappa}{\partial t}. \tag{20}$$

The particular solutions of equation (20) are thus of the same form as those of (10) with the proviso that potential K, in comparison with leakage-less solutions, will exponentially decay with Maxwell's relaxation time

$$\alpha^{-1} = \frac{\epsilon_A \epsilon_0}{\gamma_A}, \tag{21}$$

the value of which is proper to the material of the insulating tube. Since the relative permittivity and the conductivity of the *axolemma* are $\epsilon_A \approx 7$, $\gamma_A \approx 10^{-13}$ S/m [6], the decay time, being of the order of hundreds of seconds ($\alpha^{-1} \approx 600$ s), is thus much larger than the signal transit times through the typical unmyelinated and myelinated nerve fibres, which are of the order of milliseconds. Thus, in full agreement with experimental evidence [35,36], the expected signal reduction is quite negligible.

7 Electrostatic screening in electrolytes

As we have already seen above, in Kirchhoff's approach, the presence of domains filled with net charges in a conductor is completely ignored. On the other hand, it was the behaviour of the net charges that proved to be the intrinsic and essential component of charge transport in the conductors. To achieve correct understanding of the effects induced by net charges, we have to answer a crucial question: How and over what distances are electric fields, penetrating into the interior of a conductor, screened? Electrostatic screening requires the presence of a reservoir of movable excess charge carriers, which are apt to compensate external fields by creating a proper new distribution. This extra charge is represented in equation (4) by the diffusion term containing the charge density ρ. In the case of electrolytes (i.e. also in the cases of *axoplasm* and other body tissues), it was shown by Debye and Hückel [37] that the dynamical equilibrium between thermally agitated diffusion of charged particles at temperature T and the opposing external electric field give rise to a charged "atmosphere", where the external field is screened over the distance of length $\sim\lambda$, which is given by

$$\lambda = \sqrt{\frac{\epsilon \epsilon_0 k T}{e \rho_0}}. \tag{22}$$

In this formula, $\epsilon\epsilon_0$ means permittivity of the conductor, k is the Boltzmann constant, ρ_0 is the background charge density, and e the elementary electric charge ($e \approx 1.6 \times 10^{-19}$ C). In terms of ionic molar concentration, $[X^Z]$ (mole/m^3) can be the background charge density evaluated as

$$\rho_0 = ze[X^Z]N_A, \tag{23}$$

where z is the ion valency and N_A is the Avogadro constant, $N_A \approx 6.02 \times 10^{23}$ mole^{-1}. In the derivation of formula (22), it is assumed that the electrolyte is electrically neutral, i.e. that it contains anions and cations of various valency in amounts represented by absolutely the same background charge density $|\rho_0|$ and that the local excess charge is due to local depletion of ions of one polarity. Under these conditions, it can be shown that the parameter λ controls the net charge density $\rho(\nu)$ within the charged atmosphere in the vicinity of the surface of the electrolyte according to the exponential law

$$\rho(\nu) = \rho(0) \exp\left(-\frac{\nu}{\lambda}\right), \tag{24}$$

where ν is the length of the vector normal to the surface element of the electrolyte and $|\rho(0)| \leq |\rho_0|$. Thus, in the immediate vicinity of the inner surface of the conductor there is a thin "skin" made of distributed net charge with a thickness of a few screening lengths λ that screens external electric fields and is also apt to form the current-carrying *sphondyloid*.[3]

8 Quantitative estimates, consistency with experimental data

In order to verify our model and the consistency of the formulae given above, it is necessary to compare the computed quantities with experimental data obtained from a typical real case. For such purposes, we have chosen a cat's peripheral myelinated nerve fibre with inner diameter $d = 1.4 \times 10^{-5}$ m and myelin sheath thickness $a = 2 \times 10^{-6}$ m [39,40]. The mean value of the relative permittivity of the *axolemma* and myelin together is assumed to be $\epsilon_A \approx 2$ (the relative permittivity of the *axolemma* alone is $\approx$7 and its thickness $\approx 6 \times 10^{-9}$ m) [6]. Taking into account the fact that the room temperature electrical conductivity of *axoplasm* is practically the same as that of isotonic saline solution, $\gamma = 1.44$ Sm^{-1} [41,42], we obtain from equation (12) for diffusion constant D_E, controlling electrical signal transfer, value $D_E = 0.50\,\mathrm{m}^2/\mathrm{s}$. Since the experimental results concerning the transfer of electrical impulse by nervous fibre are given mostly in terms of "conduction velocity" (i.e. of apparent speed v), the plausibility of our figure above can be compared only with these rare works involving additional information about the experimental arrangement, particularly the actual length of the studied fibre.[4] For example, for a cat's myelinated peripheral nerve with diameter $d = 1.4 \times 10^{-5}$ m measured over distance $x = 2$ cm, the published result reads $v \approx 60$ m/s [43] (cf. [44] for rabbits); however, using our value of D_E and relationship (17) for apparent speed, we obtain an estimate of $v \approx 50$ m/s, which is fairly near to the value given above. These reconstructed results strongly support our belief that formula (12) for D_E also correctly reflects the quantitative aspects of electric signal transfer through the nerve fibre.

---

[3] Qualitatively the same behaviour takes place in other types of conductors, such as metals, with the proviso that the analytical expression for λ has a different form. For metals, the so-called Thomas-Fermi formula [38] should be used instead of (22), giving for ordinary metal screening length in the sub-Angstrom range.

[4] In this connection we would like to stress the fact that just the introduction of "*conduction velocity*" led in the past to many confusions and insurmountable difficulties, when experimental data obtained in different laboratories were compared.

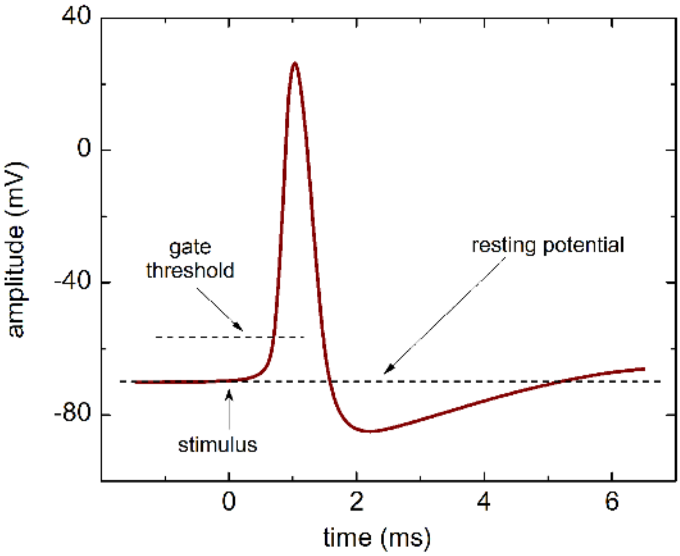

Fig. 5. Standardized shape of electrical impulse spreading through the peripheral nerve fibre of a warm-blooded animal. Gate threshold laying $\approx kT/2e$ (=13.4 mV) above the resting potential prevents the transfer of spurious signals generated by thermal noise. (Adapted according to [45].)

Table 1. Ion composition of *axoplasm* and extracellular fluid.

Ion	Molar concentrations of ions (mole/m^3)	
	In *axoplasm*	In extracellular fluid
Na$^+$	15	150
K$^+$	150	5.5
Miscellaneous$^+$	~0	4.5
Cl$^-$	9	125
Miscellaneous$^-$	156	30

Our model must also be compatible with the electric parameters proper to the action potential impulse (see Fig. 5, [45]), which are determined by the molar concentrations and other electrochemical properties of ions consisting *axoplasm* and extracellular fluid. Molar concentrations of ions in these fluids, which are known to be almost the same for various warm-blooded species, are summarized in Table 1 [45].

It is immediately apparent that both these aqueous solutions are electrically neutral, having the same total amount of anions and cations, Nevertheless, due to their different chemical compositions, in equilibrium there is between these fluids a contact potential difference called the *resting potential*, φ_R, which in the typical mammal (cat's) nerve attains the value ≈ -70 mV (cf. Fig. 5). In direct consequence of this fact, the potential difference φ_R (in cases where the nerve is inactive) induces permanent equilibrium polarisation of the *axolemma* or myelin sheath.

Let us now evaluate some of the parameters related to the electric impulse transfer in the cat's nerve. According to equation (23), monovalent ions ($z = +1$) of sodium (Na$^+$) and potassium (K$^+$) with an overall molar concentration in *axoplasm* of 165 mole/m^3 generate a background charge density of $\rho_0 = 1.59 \times 10^7$ C/m^3. This parameter can be further used to evaluate the screening length λ. For a normal temperature of ~37 °C, i.e. for $T \approx 310$ K and aqueous solutions where $\epsilon \approx 81$, we obtain from equation (22) that $\lambda = 1.1 \times 10^{-9}$ m.

Of interest is also the amount of net charge redistributed during transit of the signal through the nerve fibre. Since the amplitude of the front of the signal is $\Delta\varphi \approx 85$ mV (see Fig. 5), the charge q deposited on the unit length of the fibre can be evaluated by means of relation for specific capacitance (11) i.e. $q = c\,\Delta\varphi$. Corresponding estimates are: $c = 1.56 \times 10^{-9}$ F/m and $q = 1.32 \times 10^{-10}$ C/m . Assuming, moreover, that this net charge is contained within a thin layer ("skin") of thickness $\approx \lambda$ adjacent to the inner surface of the *axolemma*, we can use for excess net charge density ρ the obvious relation $\rho \approx q/\pi\lambda d$. It then follows that $\rho = 2.73 \times 10^4$ C/m^3, which is approximately a thousand times smaller than the background concentration of free charge carriers inside the nerve ($\rho_0 = 1.59 \times 10^7$ C/m^3). From this point of view, the spreading of the electrical impulse through the nerve fibre, represented by the temporary redistribution of space charge in close proximity to the *axolemma*, is an effect characterized as a "small disturbance". Moreover, since the amplitude of the signal is comparable with the absolute value of the resting potential ($\Delta\varphi \approx |\varphi_R|$), the amount of redistributed charge taking part in the formation of the signal ("depolarisation wave") and that which is responsible for equilibrium polarisation of the *axolemma* and myelin sheath must be of the same order of magnitude.

9 Quantum control of nervous signal

As we have already mentioned above, the transfer of information by means of electrical signal is physically realized by redistribution of free charges both inside and outside the nerve fibre. This rather complex process is, according to generalized Ohm-Kirchhoff's law (6), controlled by another diffusion constant, namely D_Ω. Considering the above computed value $\lambda = 1.1 \times 10^{-9}$ m and again using for conductivity value $\gamma = 1.44$ S/m, from equation (7) we then arrive at a final estimate of $D_\Omega = 2.43 \times 10^{-9}$ m^2/s. It is a remarkable fact that the diffusion constant controlling information transfer via nerve fibre, D_E, is about 8 orders of magnitude larger than the diffusion constant D_Ω related to the process providing its physical basis. In order to assess the significance of this very fact, let us evaluate the *mechanical action* [46] associated with diffusion of one sodium cation of mass $M(\mathrm{Na}^+)$ in *axoplasm*. Astonishingly, we obtain the rather low value

$$D_\Omega \times M(\mathrm{Na}^+) = 9.33 \times 10^{-35}\mathrm{Js}, \tag{25}$$

which differs from the tiniest quantum of action, Planck's quantum $\hbar = 1.05 \times 10^{-34}$ Js, by only ~12%.

These purely quantitative facts are, however, of far reaching consequence. According to *Sommerfeld's criterion on mechanical action* [46,47], the diffusion of Na$^+$ cations and, as can easily be proved, also of K$^+$ cations, namely, falls unambiguously into the domain of quantum effects.

Simultaneously, the diffusion constant D_Ω is very near to the quantum diffusion constant D_Q of a particle having mass M, which is defined as [47,48]

$$D_Q = \frac{\hbar}{2M}. \tag{26}$$

For the sodium ion, D_Q attains a value of ~1.37×10^{-9} m^2/s, which is comparable with the corresponding D_Ω.

It is convenient to interpret the above facts in the frame of *stochastic electrodynamics* (SED) [49], a conceptual alternative to quantum mechanics. When the diffusion constant of a particle approaches its theoretically lowest possible value, the so-called Fürth's limit ($D_\Omega \approx D_Q$, [47]), it is assumed that diffusion is not due to collisions with surrounding molecules, which are not very frequent, but rather to interactions with omnipresent *zero-point electromagnetic fluctuations of vacuum* (ZPF) [50]. The characteristic feature of this entity is its ultimately low action $\approx\hbar/2$ per mode, corresponding to the temperature-independent part of black-body radiation. The drop of action of a particle to this extremely low level and the sharing of its action with ZPF give rise to observable effects, which are generally known as quantum behaviour [49]. Based on these robust quantitative arguments, we can thus claim that the redistribution of Na^+ and K^+ ions in nerves and extracellular fluid are controlled by quantum effects, i.e. by collisions with the universal zero-point electromagnetic fluctuations of vacuum.

Interestingly enough, the universality of this quantum constrain puts serious limitations on the biophysical properties of *axoplasm* and extracellular liquid as well. Indeed, their possible variability is controlled generally by two factors, namely, by the chemical composition and by the chemical kinetics. Taking now into account the fact that the chemical composition of the Global Ocean, which is the cradle of all living creatures, determined their common material basis, the further degrees of freedom for their development must depend on the choice of chemical kinetics. However, as was already shown in [47], for the cations Na^+ and K^+ in aqueous solution it is permissible only diffusion-controlled kinetics of Nernst-Brunner type, which is due just to the presence of universal zero point electromagnetic fluctuations. The following conjecture may be thus formulated:

> *The chemical composition of the liquids consisting nervous tissue of all living creatures is derived from the global seawater while the ionic kinetic processes there are controlled by universal zero-point electromagnetic fluctuations of vacuum.*

One of the direct consequences of this conjecture may be the observed universality [51] of the response of nervous tissue of all terrestrial animals to external stimuli. This is, as we believe, an idea with significant epistemological impact.

10 Scaling relations

Finally, we would like to add some considerations concerning so-called *scaling relations* [52]. The significance of these relations lies not in the exact description of signal transmission via nerve fibre but rather in the visualization of the general properties of electrically excitable tissue, which may be of interest in medicine or evolutionary biology, for instance.

As we have seen above, the process of signal transfer is described by two quantities, D_E and D_Ω, explicitly involving universal constants, macroscopic material constants, and geometrical parameters. Of course, by evaluating these two quantities we can account for observed behaviour in any particular case. Nevertheless, being aware of the large structural variability of nervous tissue of different species and, at the same time, of the conspicuous contrast with its almost universal functionality, such a result is not very ambitious. In order to obtain greater insight into these problems, it is helpful to study the influence of various quantities of different nature and origin separately. Inspecting, for example, formula (12) for the diffusion constant D_E, two parts are immediately distinguishable: the purely geometrical part $d^2 \ln(1 + 2a/d)$ and the part depending on the material constants of *axoplasm* and the nervous body. The

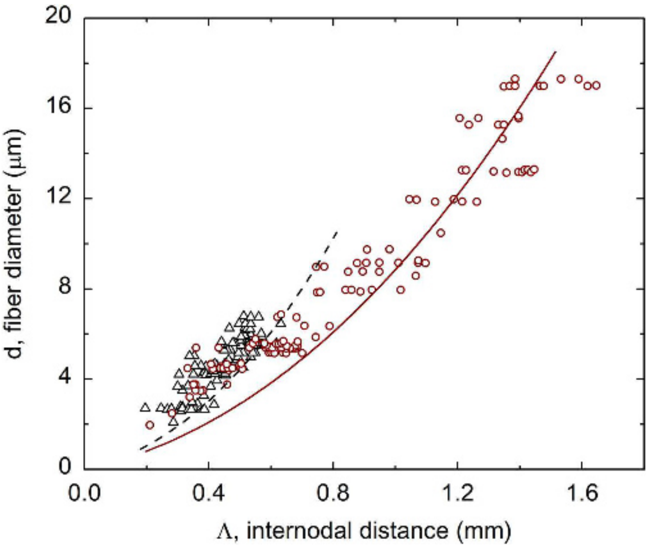

Fig. 6. Correlation between diameters of cat (circles) and kitten (triangles) myelinated nerve fibres and distances between Ranvier nodes. The curves correspond to the scaling relation (27) with $a = 2 \times 10^{-6}$ m (full line) and $a = 1 \times 10^{-6}$ m (dashed line). Data are taken from [43].

geometrical part representing the local properties of building blocks or segments of some larger integral system should scale with certain structural length characteristics Λ belonging to the system as a whole [52]. Since such a relationship must satisfy the general requirements of dimensional homogeneity [53], its simplest expected form is the following one:

$$\Lambda^2 \propto d^2 \ln\left(1 + \frac{2a}{d}\right). \tag{27}$$

Experimentally, this scaling relation for quantity Λ can be applied to the branching of nervous fibres or to the modular structure of Ranvier nodes (cf. also [54]). The latter case can be illustrated by the dependence of distance between Ranvier nodes on fibre diameter in Figure 6 [43]. Both curves in this figure are traced in accordance with scaling relation (27) in such a way that they have the same pre-factor and differ only by parameter a, corresponding to the thickness of the myelin layer. The result is very instructive. While the curve corresponding to parameter $a = 2 \times 10^{-6}$ m (full line) satisfactorily approximates the behaviour of thicker nerves of adult cats, the one with parameter $a = 1 \times 10^{-6}$ m (dashed line) better fits the thinner nerves of either cats or kittens. The significance of these facts is obvious: the evolutionary younger thinner nerve fibres also likely have thinner myelin layers and smaller distances between Ranvier nodes. During growth, these parameters then change proportionally.

The physical meaning of the material-related monomial $(\gamma/8\epsilon_A\epsilon_0)$ in equation (12) is evidently an inverse of Maxwell's relaxation time of the system consisting of *axoplasm* and the surrounding tube. Since the possible range of quantity γ is strongly limited by the condition for osmotic equilibrium between *axoplasm* and extracellular fluid, and ϵ_A ranges from 2 to 8, the possible changes in material properties alone provide only a small amount of room for variability of the nerve tissue.

Valuable scaling relations can also be obtained by direct comparison of the diffusion constants D_E and D_Ω. In close analogy with the construction of the so-called

Péclet's number known from thermal kinetics [55], we can introduce a dimensionless monomial $\sqrt{D_E/D_\Omega}$ as a new variable. Then, using equations (7) and (12), we can write

$$\frac{d}{\lambda} = \sqrt{\frac{8\epsilon_A}{\epsilon \ln(1+2a/d)}}\sqrt{\frac{D_E}{D_\Omega}}. \tag{28}$$

Considering that $a = 2 \times 10^{-6}$ m, $\epsilon_A = 2$ is typical for myelinated nerve and $a = 6 \times 10^{-9}$ m, $\epsilon_A = 7$ is typical for unmyelinated nerve [56], it is possible to estimate the range of the pre-factor in equation (28). It varies, from the tiniest fibres to giant ones, i.e. for diameters $d \in (5 \times 10^{-7}, 5 \times 10^{-4})$ m, from $\sim$0.3 to $\sim$5 for myelinated and from $\sim$5 to $\sim$170 for unmyelinated fibres. Thus, again, we can clearly see that in addition to nerve diameter, nerve myelination is the most effective vehicle for changing the transport properties of a nerve fibre. For any particular class of nerve fibre, however, we obtain from equation (28) the following scaling relation

$$\frac{d}{\lambda} \propto \sqrt{\frac{D_E}{D_\Omega}}. \tag{29}$$

Since the diffusion of electrical signal or spreading of the surface polarisation/depolarisation wave and the diffusion of ions are inevitably synchronous processes, the right side of equation (29) thus represents the ratio of paths diffused during the same time by the signal and ions, respectively (cf. Eq. (15)). As such, scaling relation (29) can be applied to any electrically excitable tissue, particularly, for instance, to the extracellular domain, with the proviso that quantity d is interpreted as its external Hausdorf's measure. Direct application of relation (7) then leads to the essentially macroscopic and quite general scaling relation

$$D_E \propto \frac{\gamma}{\epsilon\epsilon_0} d^2, \tag{30}$$

according to which signal transmission is controlled by inverted Maxwell's relaxation time of the *axoplasm* and nerve cross-section. Despite this, relationship (29) also allows for a microphysical approach. Indeed, since the diffusion constant D_Ω, due to its quantum nature, may be substituted with high precision by D_Q, a universal "quantum" scaling relation for D_E is obtained, namely

$$D_E \propto \frac{\hbar}{M\lambda^2} d^2. \tag{31}$$

The plausibility of both relations (30) and (31) can be tested immediately. Firstly, the pre-factors should be approximately the same, and secondly, both formulae should yield the correct order of magnitude estimates for D_E [53]. Indeed, by evaluating the corresponding pre-factors, we obtain $\gamma/\epsilon\epsilon_0 \approx 2.01 \times 10^9$ s^{-1} and $\hbar/M\lambda^2 \approx 2.26 \times 10^9$ s^{-1}, i.e. values which are very close to each other. Moreover, the direct application of formulae (30) and (31) to the "mean" mammal nerve (e.g. that of a cat) of diameter $d = 1.4 \times 10^{-5}$ m provides estimates $D_E \approx 0.39$ m^2/s and $D_E \approx 0.44$ m^2/s, respectively, which are not too far from those obtained from analytic formula (12). (Let us recall, in this case $D_E \approx 0.50$ m^2/s).

It is also worth mentioning another fact that may be of far-reaching practical significance. It is apparent that the pre-factors in (30) and (31), having a dimension of s^{-1}, can be interpreted as a collision frequency between ions and electromagnetic ZPF background radiation. The frequency band responsible for such an interaction, which according to our estimates above is centred at ~2 GHz, inevitably overlaps with many mobile network communication channels.[5] Of course, the possible consequences of such a remarkable coincidence is very difficult to analyse; nonetheless, their very existence should be taken seriously.

11 Conclusions

We have developed an approach to the transfer of electrical signals via nerve fibres that is alternative to the purely descriptive standard theories of Hodgkin and Huxley [57] and Rall [2]. Our theory, which is based on generalized Ohm-Kirchhoff's law and a modified model of submarine cable, enables one to extend, quite naturally, the description into the microphysical domain. It has been proven that, in contrast to the standard theory, but in agreement with the experimental evidence, the transfer of the signal front has a character of diffusion with diffusion constant D_E.

It has been further shown that this process, actually the forming of a current-carrying *sphondyloid*, is physically realized by diffusion of Na^+ and K^+ cations in *axoplasm* with diffusion constant $D_\Omega \ll D_E$. According to our numerical estimates $D_\Omega \to \hbar/2M$, where M is ion mass and $\hbar$ Planck's constant, we can thus conclude that a signal transfer through nerves is essentially a quantum process. In addition to this, our model also provides useful scaling relations that give deeper insight into general problems concerning electrically excitable tissues.

As for our future plans, we are going to extend our physical model to describe the refractory and recovery phases of nerve excitation and also to improve the understanding of the electrical response of extracellular tissue to nerve signals.

References

1. A.L. Hodgkin, A.F. Huxley, Proc. R. Soc. B: Biol. Sci. **140**, 177 (1952)
2. W. Rall, Core conductor theory and cable properties of neurons, in *The Nervous System, Cellular Biology of Neurons*, edited by E.R. Kandel (Am. Physiol. Soc., Bethesda MD, 1977), Vol. 1, p. 39
3. E.R. Kandel, J.H. Schwartz, T.M. Jessell, S.A. Siegelbaum, A.J. Hudspeth, *Principles of Neural Science* (McGraw Hill Inc., New York, 2013)
4. L.R. Squire, F.E. Bloom, N.C. Spitzer, S. du Lac, A. Ghosh, D. Berg, *Fundamental Neuroscience*, 3rd edn. (Elsevier-Academic Press, Amsterdam, 2008)
5. A.L. Hodgkin, A.F. Huxley, J. Physiol. **117**, 500 (1952)
6. B. Hille, *Ion channels of excitable membranes*, 3rd edn. (Sinauer Associates, Inc., Sunderland, MA, 2001)
7. J.J. Mareš, J. Krištofik, P. Hubík, Physica E **12**, 340 (2002)
8. W. Thomson (Lord Kelvin), Proc. R. Soc. London **7**, 382 (1854–1855)
9. B.M. Koeppen, B.A. Stanton, *Berne and Levy Physiology*, 6th edn. (Mosby-Elsevier, Philadelphia, 2008)
10. E. Babsky, B. Khodorov, G. Kositsky, A. Zubkov, in *Human Physiology* (Mir Publishers, Moscow, 1982), Vol. 2
11. P. Erman, Ann. Phys. **8**, 197 (1801)
12. H. Weber, J. Wellstein, *Encyklopädie der Elementar-Mathematik*, 3. Bd. (B.G. Teubner, Leipzig, 1907)
13. W.G.V. Rosser, Am. J. Phys. **31**, 884 (1963)
14. A.K.T. Assis, J.A. Hernandes, *Elektrischer Strom und Oberflächen-ladungen* (C. Roy Keys Inc., Montreal, 2013)

---

[5] https://www.gsmweb.cz/clanky/freq2.htm

15. O. Jefimenko, Am. J. Phys. **30**, 19 (1962)
16. L.G. Le Monnier, in *Histoire de l'Académie Royale des Sciences, Année 1746* (Imprimerie Royale, Paris, 1751), p. 447
17. A.G. Brown, *Nerve Cells and Nervous Systems: An Introduction to Neuroscience*, 2nd edn. (Springer, London, 2001)
18. I. Tasaki, *Physiology and Electrochemistry of Nerve Fibers* (Academic Press, New York, 1982)
19. H.S. Gasser, Ohio J. Sci. **41**, 145 (1941)
20. C.C. Chernecky, B.J. Berger, *Laboratory Tests and Diagnostic Procedures*, 6th edn. (Saunders, St. Louis, 2013)
21. M.L. Schagrin, Am. J. Phys. **31**, 536 (1963)
22. G.S. Ohm, *Die galvanische Kette, mathematisch bearbeitet* (T.H. Riemann, Berlin, 1827)
23. G. Kirchhoff, Ann. Phys. **154**, 506 (1848)
24. W.R. Smythe, *Static and Dynamic Electricity*, 3rd edn. (McGraw-Hill Co., New York, 1968)
25. W. Weber, Ann. Phys. **232**, 1 (1875)
26. A. Fick, Ann. Phys. **170**, 59 (1855)
27. L. Hermann, Pflueger's Arch. Ges. Physiol. **75**, 574 (1899)
28. L. Hermann, Pflueger's Arch. Ges. Physiol. **109**, 95 (1905)
29. J.L. Hoorweg, Pflueger's Arch. Ges. Physiol. **71**, 128 (1898)
30. J. Fourier, *Théorie analytique de la chaleur* (F. Didot et Fils, Paris, 1822), [English transl.: The Analytical Theory of Heat (Dover Publications, Inc., New York, 2003)]
31. J.B. Jack, D. Noble, R. Tsien, *Electric Current Flow in Excitable Cells* (Oxford University Press, London, 1975)
32. A.L. Hodgkin, A.F. Huxley, Nature **144**, 710 (1939)
33. J.J. Rosenthal, F. Bezanilla, Biol. Bull. **199**, 135 (2000)
34. R. Milo, R. Phillips, *Cell Biology by the Numbers* (Garland Science, New York, 2016)
35. K.S. Cole, *Membranes Ions and Impulses* (University of California Press, Berkeley, 1972)
36. B. Katz, *Nerve, Muscle, and Synapse* (McGraw-Hill, New York, 1966)
37. P. Debye, E. Hückel, Phys. Z. **24**, 185 (1923)
38. C. Kittel, *Introduction to Solid State Physics*, 5th edn. (John Wiley and Sons, Inc., New York, 1976)
39. C.-H. Berthold, I. Nilsson, M. Rydmark, J. Anat. **136**, 483 (1983)
40. S.G. Waxman, J.D. Kocsis, P.K. Stys, *The Axon* (Oxford University Press, New York, 1995)
41. R.A. Robinson, R.H. Stokes, *Electrolyte Solutions*, 2nd revised edn. (Dover Publications, Mineola NY, 2002)
42. K.S. Cole, J. Gen. Physiol. **66**, 133 (1975)
43. J.B. Hursh, Am. J. Physiol. **127**, 131 (1939)
44. F.K. Sanders, D. Whitteridge, J. Physiol. **105**, 152 (1946)
45. R.K. Hobbie, B.J. Roth, *Intermediate Physics for Medicine and Biology*, 4th edn. (Springer, New York, 2007)
46. J.-M. Lévy-Leblond, F. Balibar, *Quantics: Rudiments of Quantum Physics* (North-Holland, Amsterdam, 1990)
47. J.J. Mareš, J. Stávek, J. Šesták, J. Chem. Phys. **121**, 1499 (2004)
48. R. Fürth, Z. Phys. **81**, 143 (1933)
49. L. de la Peña, A.M. Cetto, *The Quantum Dice – An Introduction to Stochastic Electrodynamics* (Kluwer Academic Publishers, Dordrecht, 1996)
50. P.W. Milloni, *The Quantum Vacuum – An Introduction to Quantum Electrodynamics* (Academic Press, Inc., New York, 1994)
51. K. Bogdanov, *Biology in Physics* (Academic Press, San Diego, 2000)
52. B.B. Mandelbrot, *The Fractal Geometry of Nature* (W.H. Freeman and Co., New York, 1983)
53. J. Palacios, *Dimensional Analysis* (MacMillan and Comp., Ltd., London, 1964)
54. W.A.H. Rushton, J. Physiol. **115**, 101 (1951)

55. T.L. Bergman, A.S. Lavine, F.P. Incropera, *Fundamentals of Heat and Mass Transfer*, 7th edn. (John Wiley & Sons, Inc., New York, 2011)
56. D.J. Aidley, *The Physiology of Excitable Cells*, 4th edn. (Cambridge University Press, Cambridge, 1998)
57. A.L. Hodgkin, The Ionic Basis of Nervous Conduction, Nobel Lecture, December 11, 1963