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MATHEMATICAL MODELLING OF NERVE PULSE TRANSMISSION

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Abstract

In this expository paper some key problems of nerve pulse dynamics are briefly analysed. Instead of the traditional parabolic models, the evolution equation modelling the propagation of a single nerve pulse is used. Such an approach together with the formalism of inner variables permits to bridge the various branches of wave dynamics, especially to distinguish between dissipative and solitonic structures.

Keywords: nerve pulse, evolution equation, nonlinear solitary wave.

1.Introduction

The pulse transmission in nerve fibres is a fascinating physical phenomenon that has already attracted researchers' attention for a long time. Isaac Newton has put the question about '...vibrations of this medium, excited in the brain ...' (see [1], p. 487), being fairly close to the electrodynamics. Contemporary theory of nerve pulse transmission is based on the famous results of HODGKIN and HUXLEY [2] who have explained the role of the ion currents responsible for the stable wave-profile. There are still many questions to be answered and the research in this field is developing fast bearing also in mind the artificial neural networks.

The main structural feature in nerve pulse dynamics in a stable solitary pulse of a characteristical asymmetric profile (*Fig. 1a*). Solitary waves as carriers of energy are well understood in conservative media [3]. Here the situation is different – the medium is highly dissipative but the source terms balance the energy outflux resulting in a solitary wave. The physical background is the following (see also *Fig. 1b*). The nerve pulse (voltage) is transmitted down the axoplasm core of a nerve which is surrounded by a cylindrical membrane. The relative concentration of ions (mainly sodium

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and potassium) create the transmembrane potential. If an electric stimulus is applied to the nerve then the membrane acts in different ways depending on the value of the stimulus. If the stimulus is below a certain threshold value, then the depolarisation process of the membrane is reversible and the equilibrium state returns fast without any pulse propagating. If, however, the stimulus is above this threshold, the inward flow of the sodium ions starts. This process is followed then by an increase in the potassium permeability which causes an outward flow of the potassium ions. Later due to the balance of inward and outward flows the process returns to the equilibrium again but through an undershoot. This all results in an asymmetric solitary wave shown in *Fig. 1* and propagating without changes in its profile, i.e. representing a constant profile solution.

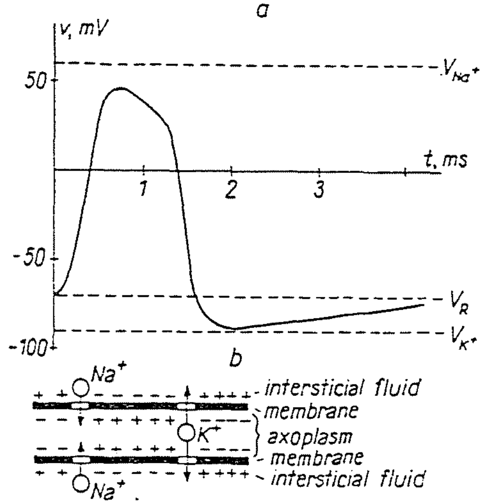

Fig. 1. A schematical nerve pulse: (a) a typical profile; (b) idealised nerve with ion currents. Dashed lines – values of resting potentials

In solid mechanics, the wave processes are fairly well understood [4] and the main point in wave dynamics is the concept of finite velocities – every excitation propagates with a finite velocity determined mainly by the properties of the medium. This physical understanding is reflected in the hyperbolicity of the governing equations in wave dynamics. The real physical models, however, are sometimes so complicated that waves are not necessarily governed by strictly hyperbolic equations since various asymptotic methods have been used for deriving the governing equations from conservation laws. Nevertheless, every mathematical model should be traced back to initial hyperbolic equations as complicated as they could be and every wave motion should be related to finite velocities.

Now the interesting paradox appears – the classical theory of nerve pulse transmission [1,2] is based on the parabolic equations which strictly speaking lead to infinite velocities. However, the situation is more complicated while the governing equations consist of a nonlinear source term responsible for modelling ion current. It is shown then that in this case, the governing equations have a progressive type solution for which the finite velocity exists [1,5]. In this way the paradox is seemingly solved but only theoretically. The constant profile solution corresponds to a separatrix in the phase portrait and, in order to follow it, a physically abnormal accuracy of calculations is needed. In other words, this accuracy is needed for determining the wave velocity that should be given according to COLE [5] with an accuracy of 10^{-18}. Even in this case, some special methods are needed in order to calculate a full profile [6]. This situation leads back to inspecting the governing equations in order to estimate the validities of basic assumptions and to find other possibilities to represent the main features of the process. Such an approach is also quite logical in the general sense because once a certain theory is settled, it is used widely without questioning until some of its shortcomings become vital. Then, taking into account the progress in physical understandings, mathematical methods, etc., the next step can be made, at least to get rid of some shortcomings.

Before presenting some relatively novel ideas in modelling the nerve pulse transmission it must be stressed that nerve pulse is usually classified as a dissipative structure [1], modelled by the parabolic (diffusion-type) system with source terms. These models are widely used in biology and chemistry [7] and the notion of dissipative structures itself belongs to PRIGOGINE [8]. On the other hand, solitonic structures belong to conservative systems [3]. There is an urgent need to make very clear distinction as between the corresponding systems as well as between the solitary waves the origin of which is not always clear from physical observations.

The first idea is to reinspect the basic mathematical models governing the nerve pulse transmission. The usual approach is to start from telegraph equations and neglect the inductance. This means that the hyperbolicity is neglected from the very beginning and the natural result is the parabolic equation which in terms of solid mechanics corresponds to the heat conduction equations with an additional source term. It must be stressed that the conventional theory of nerve pulse transmission was established in the fifties of this century when the knowledge about solitary waves was limited. Note that the concept of solitons was introduced only in 1965 [9] and later the intensive research began including the development of reductive methods in order to construct one-wave equations, i.e. evolution equations [10]. The evolution equations, as a rule, are given in a moving frame that stems from the hyperbolicity of the basic governing system. Quite naturally, the elegant approaches from the soliton theory were not used for parabolic equations derived for nerve pulse dynamics. In 1967, LIEBERSTEIN [11] has used the natural form of telegraph equations in nerve pulse dynamics solving the problem numerically. In the eighties the time was ripe to apply the ideas of solitonic structures in neighbouring areas. The evolution equation for a nerve pulse was derived in 1981 [12] and its various aspects analysed later (see summary in [13]). As a result, a novel second-order evolution equation typical for nerve pulse transmission gives a natural prolongation to the family of known but mainly first-order evolution equations [3].

The quest for possible unification of dissipative and solitonic structures has got recently an important milestone in the framework of continuum mechanics [14]. It has been shown that starting from the Lagrangian formulation and introducing a dissipation potential, it is possible from a common starting point to derive either diffusion-type systems that may exhibit dissipative structures or conservative systems (perturbed by dissipation) which may exhibit solitonic structures.

This extremely interesting facet of nonlinear dynamics is now fast developing. Here, in this paper we present in Section 2 the basic equations in order to demonstrate the various approaches and then, in Section 3 we draw some parallels between the modelling the nerve pulse dynamics and the problems of solid mechanics.

2. Basic Equations

The conventional initial system of an axon is the following [1]:

$$\pi a^2 C_a \frac{\partial v}{\partial t} + \frac{\partial i_a}{\partial x} + 2\pi a\, I = 0, \tag{2.1a}$$

$$\frac{\partial v}{\partial x} + \frac{R}{\pi a^2} i_a = 0, \tag{2.1b}$$

where the notations of [11] are used: v is the potential difference across the membrane, i_a is the axon current per unit length and a is the axon radius. Further, C_a is the axon self-capacitance per unit area per unit length, R is the specific resistance and I is the membrane current density. It is easy to derive a second-order equation in terms of v

$$\frac{\partial^2 v}{\partial x^2} = RC_a \frac{\partial v}{\partial t} + \frac{2}{a} RI, \tag{2.2}$$

which can easily be compared with the heat conduction equation. In many applications corresponding transmission line equivalent circuit is shown to demonstrate the nature of the process, here it is depicted in *Fig. 2* [1].

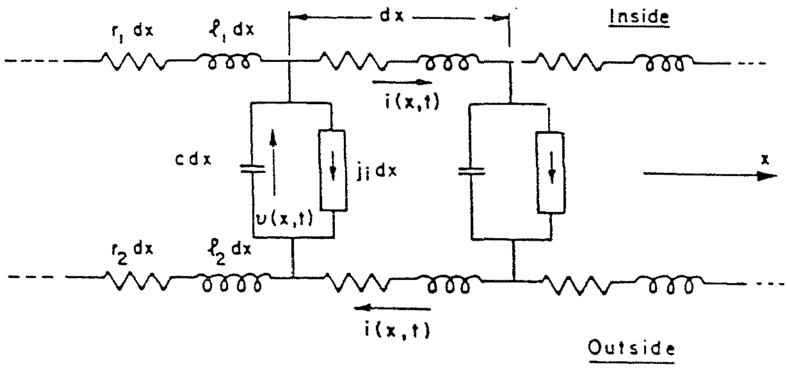

Fig. 2. Transmission line equivalent circuit for a nerve fibre [1]

If the axon specific self-inductance is not neglected then instead of (2.1) we have

$$\pi a^2 C_a \frac{\partial v}{\partial t} + \frac{\partial i_a}{\partial x} + 2\pi a\, I = 0, \tag{2.3a}$$

$$\frac{L}{\pi a^2}\frac{\partial i_a}{\partial t} + \frac{\partial v}{\partial x} + \frac{R}{\pi a^2} i_a = 0 \tag{2.3b}$$

and its second-order equivalent

$$\frac{\partial^2 v}{\partial x^2} - LC_a \frac{\partial^2 v}{\partial t^2} = RC_a \frac{\partial v}{\partial t} + \frac{2}{a} RI + \frac{2}{a} L \frac{\partial I}{\partial t}. \tag{2.4}$$

In both cases, membrane current I as a source term plays an important role affecting also the final velocity of the pulse [14]. For a moving frame, however, the standard wave velocity c_0 (c.f. with sound velocity in solids [9]) can be used. Following the general ideas of reductive methods [10, 16] from the 'two-wave' system (2.3) a 'single-wave' evolution equation

$$c_0 \frac{\partial v}{\partial x} + \frac{1}{2} m_4 v + \frac{1}{2} m_2 I = 0 \tag{2.5}$$

can be derived. Here m_2, m_4 are constants [13] and $v = v(x, \xi)$, $\xi = c_0 t - x$. The membrane current I according to the HODGKIN–HUXLEY model [2] depends upon 3 additional so-called phenomenological variables, but for the basic model only 1 additional variable w is sufficient. This is the FITZ HUGH–NAGUMO [17] model where

$$I = k_1 v + k_3 v^3 + w \tag{2.6}$$

with k_1, k_3 constants. As the additional variable w is not a field variable then there is no inertia related to it [14] but it needs its own governing equation. For dissipative structures the governing equation is usually [1, 2, 17] of relaxation type

$$\frac{\partial w}{\partial t} + c_0 \gamma w = q_0(v + q_1), \tag{2.7}$$

where again γ, q_0, q_1 are constants. Quite often $\gamma = 0$ [17]. Following this line in terms of $z = v + q_1$ equations (2.5), (2.6), (2.7) yield

$$\frac{\partial^2 z}{\partial \xi \partial x} + f(z)\frac{\partial z}{\partial \xi} + g(z) = 0, \tag{2.8a}$$

$$f(z) = b_0 + b_1 z + b_2 z^2, \tag{2.8b}$$

$$g(z) = b_{00} z. \tag{2.8c}$$

Here b_0, b_1, b_2, b_{00} are constants [13]. This is the sought simplest second-order evolution equation for a nerve pulse transmission that must be solved under initial excitation $z(0, \xi)$ and the proper boundary conditions. In case of $\gamma \neq 0$, a first order addition leads to the wave hierarchy. The full analysis of *Eq.* (2.8) and its stationary variant

$$z'' + f(z)z' + \Theta^{-1} g(z) = 0 \tag{2.9}$$

is given in [13]. In (2.9), the following notation is used: $()' = d/d\eta$, $\eta = x + \Theta\xi$. The asymmetric pulse obeying all the main physical features is easily calculated numerically without any convergence problems.

3. Qualitative Analysis

Here we start with some remarks on the stationary form (2.9) of the evolution *Eq.* (2.8). *Eq.* (2.9) as an ODE is of the Liénard type. Its properties depend on the roots of $f(z) = 0$. The physics of the nerve pulse predict the following properties of the roots z_1, z_2:

$$z_1 > 0, \quad z_2 > 0, \quad z_1 \neq z_2. \tag{3.1}$$

In this case the origin is a stable node and we can get a pulse-type solution starting from $z(0) = 0$, $z'(0) \neq 0$. It is easily seen, that the well-known van der Pol equation has

$$z_1 < 0, \quad z_2 > 0 \tag{3.2}$$

and consequently, the origin is an unstable focus, but there exists a stable finite cycle. The van der Pol equation describes relaxation oscillations and starting from the pioneering paper by VAN DER POL [18], it has been used in electronics, biology, mechanics, etc. The map of a Liénard-type equation obeying (2.8b) and (2.8c) contains both cases (3.1) and (3.2) [19]. In some sense the situation can be compared to the case of a linear oscillator with weak and strong damping. In the case of weak damping the motion is still oscillatory (c.f. with the limit cycle) and in the case of strong damping there is no oscillatory character at all (c.f. with the pulse-type solution of (2.9) obeying (3.1)). The coupling of oscillatory and pulse-type ODE's of (2.9)-type can be of interest in heart dynamics.

The next problem is centered around the physical motivation of inner variables. Here we have employed the fact that voltage v is treated as an observable variable and variable w – as an inner variable. From the wave equation for v a first order evolution equation is derived while inner variable w is governed by a kinetic equation. Both equations together form a second-order evolution equation (see (2.8)). A natural question arises – is this approach general and can it be used also for other cases? The answer needs a serious analysis. The general formalism of inner variables is given by MAUGIN [14]. His examples in solid mechanics are related to damage coupled to elasticity or to plasticity. In elasticity, for example, damage is described by a scalar $\mathcal{D}$ satisfying $0 \leq \mathcal{D} \leq 1$ and it measures the decrease in material surface transmitting internal forces together with the isotropy hypothesis. It seems that the general idea, shown in Section 2, could also be applied in this case because of the linear coupling.

Within the framework of inner variables, the notions of thermodynamical forces are naturally involved. Consequently, the concepts of irreversible thermodynamics must be used, particularly also in nerve pulse dynamics. As to the latter problem, only recently attention was paid to the thermodynamical justification of mathematical models widely used in practice [20].

Finally, let us mention the role of the Fischer equation

$$\frac{\partial u}{\partial t} - D\frac{\partial^2 u}{\partial x^2} = f(u), \tag{3.3}$$

where D is the diffusion coefficient and $f(u)$ is a quadratic polynomial [21]. Its first application was in biology (propagation of genes) but later equation (3.3) with special $f(u)$ was also applied in nerve pulse transmission [1,5]. On the other hand, however, this is a heat conduction equation with a source terms processing also the progressive-type solutions. Reflecting the diffuse character of the process, this model could be compared with (2.8), especially on the stationary level (2.9). It is easily concluded that the ODE derived from (3.3) is also of the Liénard type. The similarity of various physical processes gives a ground to serious comparative analysis of dissipative and solitonic structures started in [14]. The modified heat conduction equations [22] may also serve as a test problem for the comparison.

There are two tendencies in classical science that are sometimes working against the progress. First, some understandings in a specific area of science might be 'graven on a stone tablet' [1]. Second, there is a tendency to split up the problems into their smallest components forgetting to put the pieces back together again [8]. However, the universality of basic ideas of Nature gives rise to striking interdisciplinary ideas permitting to avoid these tendencies. Wave motion is one of such rich areas of science, were ideas from comparatively unrelated areas – solid mechanics, biophisics, seismology, acoustics, etc. – can be correlated in a natural way.

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