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Computational methods for a mathematical model of propagation of nerve impulses in myelinated axons

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ABSTRACT

This paper is concerned with the approximate solution of a nonlinear mixed type functional differential equation (MTFDE) arising from nerve conduction theory. The equation considered describes conduction in a myelinated nerve axon. We search for a monotone solution of the equation defined in the whole real axis, which tends to given values at $\pm\infty$. We introduce new numerical methods for the solution of the equation, analyse their performance, and present and discuss the results of the numerical simulations.

1. Introduction

In 1952, A. Hodgkin and A. Huxley [11] introduced a mathematical model that describes the excitation and flow of electrical current through the surface of a giant nerve fibre from a squid. This model (usually known as the HH-model) consists of a system of four ordinary differential equations with four unknowns (the state variables V, m, h, n), of which V is the membrane potential difference and the remainder are conductance variables. An extensive mathematical analysis of this model has been carried out by R. FitzHugh [8,9]. In order to explain the main features of the HH-model, R. FitzHugh reduced it to a system of two ODES, still conserving the main properties of the original system. The reduced system, which he called the Bonhoeffer–Van der Pol (BVP) model, has the form:

$$\begin{cases} \dfrac{dx}{dt} = c\left(y + x - x^3/3 + z\right) \\ \dfrac{dy}{dt} = -(x - \alpha + \beta y)/c, \end{cases} \tag{1}$$

where z is a known function (the so-called stimulus intensity, which corresponds to membrane current in the HH-model); α, β, c are constants satisfying

$$1 - \frac{2\beta}{3} < \alpha < 1, \quad 0 < \beta < 1, \; \beta < c^2. \tag{2}$$

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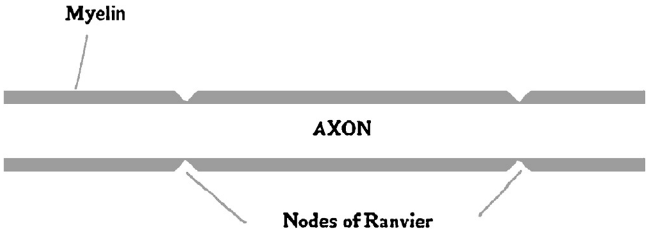

Fig. 1. Structure of a myelinated axon.

In the case $\alpha = \beta = z = 0$, system (1) reduces to the well-known Van der Pol equation. R. FitzHugh used phase space and stability theory to investigate the qualitative behaviour of system (1).

Comparing system (1) with the original HH-model, FitzHugh concluded that the HH variables V and m together behave like x, while h and n behave like y. He also says that "the coordinates x and y are not to be identified physically, except to say that x shares the properties of both membrane potential and excitability, while y is responsible for accommodation and refractoriness".

The study of nerve excitation and conduction has been continued by Nagumo and his co-authors [17], who made an active phase transmission line, using tunnel diodes, and simulated an animal nerve axon. These authors started by simulating electronically the behaviour of the HH and the FitzHugh models in the case of the "space clamp", that is, when the excitation of a nerve axon is spatially uniform. Then, in order to consider propagation of excitation, they considered x as a function of two variables s, t where s is the space variable. Following Hodgkin and Huxley, they assumed that the current intensity z in the first equation of the system (1) can be replaced by

$$z(t) = \frac{1}{r}\frac{\partial^2 x}{\partial s^2},$$

where r is a constant (depending from the axoplasmical resistance and membrane capacitance). In this case, from the system (1) one obtains the following system of partial differential equations:

$$\begin{cases} \dfrac{1}{r}\dfrac{\partial^2 x}{\partial s^2} = \dfrac{1}{c}\dfrac{\partial x}{\partial t} - y - \left(x - x^3/3\right) \\ c\dfrac{\partial y}{\partial t} + \beta y = \alpha - x, \end{cases} \tag{3}$$

which are usually known as the FitzHugh–Nagumo equations.

In all the above-mentioned models of nerve excitation and propagation of electronic impulses, nerves are considered as electric cables, through which electric current flows. This is the case for the squid nerve, studied by Hodgkin and Huxley, but in other animals (like frogs, for example) nerve axons have a different structure. The nerve membrane is insulated by a substance called myelin (see Fig. 1). According to Bell [3], "myelination of an axon allows it to conduct neuroelectric signals by exciting only a small portion of membrane exposed to the extracellular medium at the nodes of Ranvier. This permits transmission at greatly reduced energy expenditure and higher speeds than comparably sized unmyelinated axons". In models of myelinated axons, the following hypothesis is assumed: the myelin has such high resistance and low capacitance that it completely insulates the membrane (pure saltatory condition).

Under this hypothesis the nodes of Ranvier can be represented as active point sources of electric current. Moreover, basic transmission is accomplished by sufficiently stimulating a node so that its transmembrane potential reaches a certain threshold level. Then local ionic currents are generated which excite the neighbouring node enough to achieve the threshold potential. As a consequence, new local currents are generated at the neighbouring node and the process propagates across the nerve axon, giving the effect of excitation jumping from node to node.

As remarked by R. FitzHugh in [9], this case requires that the active membrane equations be solved at far fewer points along the fibre than does the case of a continuous axon. In the paper FitzHugh suggests that in the case of myelinated axons the HH equations are used to represent the membrane current only at the nodes. At other nerve points, nerve conduction is modelled just by an equation of the form:

$$C\frac{\partial V}{\partial t} = \frac{\partial^2 V}{\partial x^2} - \frac{V}{r}, \tag{4}$$

where V is the membrane potential, C and r are constants.

This model yields a large system of equations: four ODEs at each node of Ranvier and the PDE (4). However, only the PDE (4) has to be solved in the whole axon, which makes the case of the myelinated axon more suitable for computation. This was remarked on by R. FitzHugh in 1962, when the potential computational possibilities were quite different from nowadays.