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ORIGINAL PAPER

On mathematical modelling of solitary pulses in cylindrical biomembranes

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Abstract The propagation of action potentials in nerve fibres is usually described by models based on the ionic hypotheses. However, this hypothesis does not provide explanation of other experimentally verified phenomena like the swelling of fibres and heat production during the nerve pulse propagation. Heimburg and Jackson (Proc Natl Acad Sci USA 102(28):9790–9795, 2005, Biophys Rev Lett 2:57–78, 2007) have proposed a model describing the swelling of fibres like a mechanical wave related to changes of longitudinal compressibility of the cylindrical membrane. In this paper, the possible dispersive effects in such microstructured cylinders are analysed from the viewpoint of solid mechanics, particularly using the information from the analysis of the well-known rod models. A more general governing equation is proposed which satisfies the conditions imposed by the physics of wave processes. The numerical simulations demonstrate the influence of nonlinearities, the role of various dispersion terms and the formation and propagation of solitary waves along the wall together with the corresponding transverse displacement. It is conjectured that due to the coupling effects between longitudinal and transverse displacements of a cylinder, the transverse displacement (i.e. swelling) is related to the derivative of the longitudinal displacement. In this way, the correspondence between theoretical and experimental (Tasaki in Physiol Chem Phys Med NMR 20:251–268, 1988) results can be described.

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1 Introduction

The Hodgkin–Huxley (HH) model is a widely known description for a nerve pulse propagation (Hodgkin and Huxley 1952). This model is based on the electric circuit analogue in which ionic currents through the cylindrical membrane are taken into account. The changes in the relative concentration of sodium and potassium ions in the axoplasm core of a nerve create the transmembrane (action) potential carried along the nerve fibre. There are several voltage and time dependences which enter to the governing equation of a parabolic (diffusive) type with a source term. The HH model is actually based on the telegraph equations where the inductivity is neglected. Such a model is able to describe several important and experimentally checked properties, such as a typical asymmetric pulse with an overshoot, the existence of a threshold for an excitation for triggering the pulse (the all-or-none phenomenon), the refraction length and the annihilation of pulses at the head-on collision. The model proposed by Nagumo et al. (1962) is a simpler one based on only one ionic current and is called nowadays the FitzHugh–Nagumo (FHN) model. Lieberstein (1967) has used the full hyperbolic telegraph equations for describing the nerve pulse propagation and Engelbrecht (1981) has derived an evolution equation (one-wave equation) on the same basis. If the simplified ion current following the FHN model is used, then the evolution equation can be easily analysed and its stationary form belongs to the class of Liénard equations (Engelbrecht 1981). This evolution equation is also able to describe an asymmetric pulse, the all-or-none phenomenon and the refractoriness.

However, there are several phenomena which are not described by models mentioned above. Namely, it has been shown experimentally by Iwasa et al. (1980) and Tasaki (1988); Tasaki et al. (1989), etc. that the propagation of an action potential is accompanied by the movement of the nerve surface which is a cylindrical biomembrane. This means that there is also a mechanical wave accompanying the nerve pulse. In addition, it is found that temperature and heat have an important role during the propagation process of an action potential (Heimburg and Jackson 2005, see also the references therein). None of these phenomena can be described by models based on a purely electrical description of conductors.

In order to overcome this difficulty, Heimburg and Jackson (2005, 2007) and Andersen et al. (2009) have proposed a model for describing the propagation of mechanical wave in a cylindrical biomembrane which could also be a model for the nerve pulse. Biomembranes are made of ordered lipids (Andersen et al. 2009) and it is difficult to apply the conventional approaches known in mechanics of continua for deriving the governing equations for waves in such structures. In physical terms, the compression of such a biomembrane will change its density, resulting in the transfer from its liquid state to a gel state. This process is also associated with the release of heat. So an action potential in a nerve fibre causes a local compression of the biomembrane which, as said above, means the transfer from one state to another. And vice versa, it is shown (Andersen et al. 2009) that the local cooling of a nerve causes a local transition from a liquid state to a gel state and therefore will induce an action potential. Consequently, two processes, electrical and mechanical ones are coupled as shown already by Gross et al. (1983). The model of Heimburg and Jackson (2005, 2007) is written in terms of the density change in the membrane under the influence of the action potential and takes nonlinearity and dispersion into account. The similarity to a rod model is noted and most of the coefficients of the governing equation are determined by thermodynamical considerations (see Heimburg and Jackson 2005). However, the direct coupling between an action potential and the corresponding density wave is not described in terms of mathematical models.

In this paper, we examine the Heimburg–Jackson (HJ) model from a viewpoint of dispersion analysis known from mechanics and compare the results with well-known rod models. The HJ model is actually an extended wave equation like those derived for waves in microstructured solids (Berezovski et al. 2013). It is important not only to find steady solutions to such equations but also to solve initial and/or boundary value problems in order to understand the process of emergence of steady solutions. This is the main topic of this paper. The numerical solutions of the modified nonlinear governing equation of HJ permit to analyse the shape and velocities of solitary pulses and establish the mechanism of their distortion.

2 Brief overview of mathematical models of nerve pulses

The models of pulse propagation as an action potential are based on telegraph equations neglecting the inductance. The celebrated Hodgkin–Huxley model is actually a reaction–diffusion equation

$$\frac{\partial^2 v}{\partial x^2} = RC_a \frac{\partial v}{\partial t} + \frac{2}{a} RI, \tag{1}$$

where v is the potential difference across the membrane and a is the axon radius. The constants are: C_a is the axon self-capacitance per unit area per unite length, R is the specific resistance and I is the ion current density. In this model, the ion current $j_i = 2\pi a I$ is determined in terms of three phenomenological variables: n, m and h. These variables govern: n—the potassium conductance (turning on); m, h—the sodium conductance (turning on and turning off, respectively). The ion current expression according to Hodgkin and Huxley (1952) is

$$j_i = g_K n^4 (v - V_K) + g_{Na} m^3 h (v - N_{Na}) + g_L (v - V_L), \tag{2}$$

where g_K, g_{Na} and g_L are potassium, sodium and leakage conductances, respectively, and V_K, V_{Na} and V_L are corresponding equilibrium potentials. For variables n, m and h, Hodgkin and Huxley (1952) proposed to use the kinetic equations.

FitzHugh (1961) and Nagumo et al. (1962) have proposed a simpler model with only one phenomenological variable. Then, the final governing equation is

$$\frac{\partial^3 v}{\partial t \partial x^2} = \frac{\partial^2 v}{\partial t^2} + \mu \left(1 - v - \varepsilon v^2\right) \frac{\partial v}{\partial t} + v \tag{3}$$

with constants μ and ε.

Based on the full telegraph equations (Lieberstein 1967), it is possible to derive an evolution equation for a nerve pulse. Using the simplified variant of Nagumo et al. (1962) for the ion current, the evolution equation in a moving frame $\xi = c_0 t - x$ is obtained in the following form (Engelbrecht 1981, 1991)

$$\frac{\partial^2 z}{\partial \xi \partial x} + f(z) \frac{\partial z}{\partial \xi} + g(z) = 0, \tag{4}$$

where $z = v + q_1$, $f(z) = b_0 + b_1 z + b_2 z^2$, $g(z) = b_3 z$ and q_1 is the reference level; b_0, b_1, b_2, b_3 are the constants. The moving frame includes the velocity c_0 determined from the telegraph equation, but the final velocity of the pulse is dictated by the ion current. Like HH and FHN models, the evolution equation is also able to reflect the main properties of the action potential (Engelbrecht 1991).

The propagating action potential cannot describe all the dynamical effects in nerve fibres. Experiments by Iwasa et al. (1980); Tasaki (1988), etc. have clearly demonstrated the swelling of the biomembrane and the accompanying heat. Swelling is related to the mechanical wave and Heimburg and Jackson (2005, 2007) have proposed a mathematical model governing such a wave motion. Their model is based on the wave equation in terms of density change $\Delta\rho^A = u$. Two essential assumptions are made. The starting point is a wave equation which actually is the balance of momentum

$$\frac{\partial^2 u}{\partial t^2} = \frac{\partial}{\partial x}\left(c^2 \frac{\partial u}{\partial x}\right). \tag{5}$$

The first assumption relates velocity c with the compressibility of the circular biomembrane which is made of lipids. It is assumed that

$$c^2 = c_0^2 + pu + qu^2, \tag{6}$$

where c_0 is the velocity of the small amplitude sound and p and q are constants determined from experiments. The second assumption is to add a higher-order term $-h\partial^4 u/\partial x^4$ responsible for dispersion. The governing equation reads then

$$\frac{\partial^2 u}{\partial t^2} = \frac{\partial}{\partial x}\left[\left(c_0^2 + pu + qu^2\right)\frac{\partial u}{\partial x}\right] - h\frac{\partial^4 u}{\partial x^4}. \tag{7}$$

Here, h is an ad hoc constant. Further, this equation is called the Heimburg–Jackson (HJ) model.

Heimburg and Jackson (2005) have demonstrated that a solitary wave solution to Eq. (7) exists and have found such an analytic solution (see Heimburg and Jackson (2007)). This solution has the width of about 10 cm. They also gave later a possible physical explanation to the constant h (Mosgaard et al. 2012).

Equation (7) is of the Boussinesq-type (Christov et al. 2007) grasping the following effects: (i) bi-directionality of waves; (ii) nonlinearity (of any order), (iii) dispersion (of any order, modelled by space and time derivatives of the fourth order at least). There are many Boussinesq-type equations used in solid mechanics (Christov et al. 2007; Engelbrecht et al. 2011; Berezovski et al. 2013), and further in our analysis, we rely upon these results.

3 Dispersion analysis

For dispersion analysis, we assume a solution to the linearised version of Eq. (7) in the form of a harmonic wave

$$u(x,t) = \hat{u}\exp[i(kx - \omega t)], \tag{8}$$

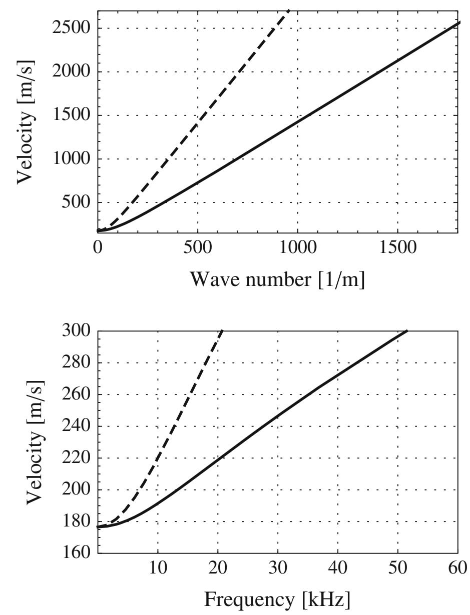

Fig. 1 Phase (*solid lines*) and group (*dashed lines*) velocity curves against the wave number (*top*) and the frequency (*bottom*) for $h = 2\mathrm{m}^4/\mathrm{s}^2$ and $c_0 = 176.6$ m/s

where k and ω are the wave number and the angular frequency, respectively. The dispersion relation then is (Heimburg and Jackson 2005)

$$\omega^2 = k^2(c_0^2 + hk^2) \tag{9}$$

with the following expressions for the phase ($c_{ph} = \omega/k$) and the group velocity ($c_{gr} = \partial\omega/\partial k$)

$$c_{ph} = \sqrt{c_0^2 + hk^2}, \quad c_{gr} = \frac{c_0^2 + 2hk^2}{\sqrt{c_0^2 + hk^2}}, \tag{10}$$

which are plotted in Fig. 1 with the same parameters as in Heimburg and Jackson (2005).

It is easy to see from Eq. (10) and in Fig. 1 that although dispersion relation (9) meets the requirement of anomalous dispersion (Heimburg and Jackson 2005) (i.e. higher frequencies result in higher velocities), the velocity is unbounded when the wave number k or the frequency ω approach the infinity. This does not only conflict with physical considerations but also with Fig. 2 in Heimburg and Jackson (2005) where it can be seen that the parameters defining the velocity remain finite.

The infinite velocity of high-frequency harmonics is physically not plausible. One should also take into account that pulses, in general, contain wide variety of harmonics, and the infinite velocity of high frequencies can cause problems in causality. Moreover, it has been shown that the existence of only the fourth-order spacial derivatives can lead to instabilities in wave propagation (see Maugin 1999, for example).

The dispersion relation (9) can be modified by considering a similarity between the nerve fibre and the rods. Although the material properties of biomembrane close to transition are quite different to that of rods, the dispersion is modelled by linear terms and taking inspiration from the physically well-motivated one-dimensional rod models seems to be justified.

As far as modelling wave propagation in rods is a rather complex problem, then there are number of approximations (Abramson et al. 1958; Achenbach 1973; Erofeyev et al. 2002; Graff 1975). Two assumptions are used when deriving a approximate model of wave propagation in rods—the Navier–Bernoulli hypothesis that is the assumption that the plane cross sections remain planar and normal to the rod axis and the Rayleigh–Love correction which assumes that the transverse displacement w along the radial axis r is related to the longitudinal strain as in statics

$$w = -\nu r \frac{\partial u}{\partial x}, \tag{11}$$

where ν is the Poisson coefficient. Making use of these two assumptions, we arrive to the Rayleigh–Love model (Abramson et al. 1958)

$$u_{tt} - c_R^2 u_{xx} - \nu^2 r_{gp}^2 u_{xxtt} = 0 \tag{12}$$

with the following dispersion relation:

$$\omega = \frac{c_R k}{\sqrt{1 + \nu^2 r_{gp}^2 k^2}}. \tag{13}$$

Here, r_{gp} is the polar radius of gyration, $c_R^2 = E/\rho$ is the velocity of the long waves, where E is the Young modulus and ρ is the density. In case of a physical rod, this model leads to normal dispersion ($c_{gr} < c_{ph}$). Anomalous dispersion can be achieved if the Poisson ratio is allowed to be negative. However, this results in complex velocity when $k > (\nu r_{gp})^{-1}$ which is physically not sound.

More general model can be achieved when the effect of shear deformation is accounted for as it is in case of the Bishop's model (Erofeyev et al. 2002)

$$u_{tt} - c_R^2 u_{xx} - \nu^2 r_{gp}^2 (u_{tt} - c_\tau^2 u_{xx})_{xx} = 0, \tag{14}$$

with the following dispersion relation:

$$\omega = k\sqrt{\frac{c_R^2 + c_\tau^2 \nu^2 r_{gp}^2 k^2}{1 + \nu^2 r_{gp}^2 k^2}}, \tag{15}$$

where $c_\tau^2 = \mu/\rho$ is the shear wave velocity and μ is the Lamé parameter.

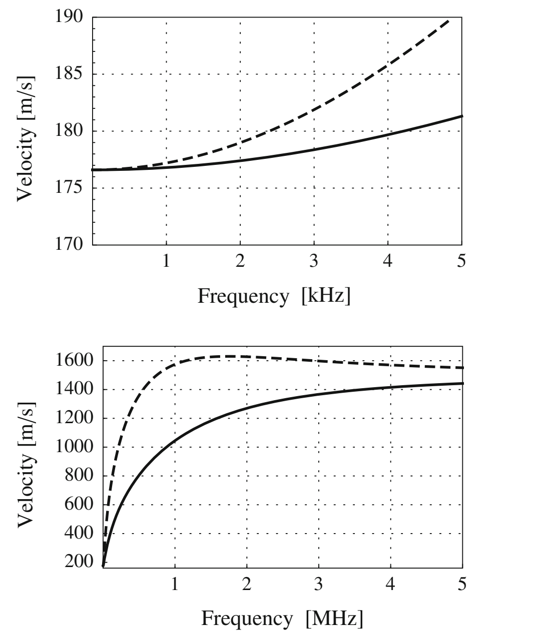

Fig. 2 Phase (*solid lines*) and group (*dashed lines*) velocity curves agains frequency (*top panel* up to 5 kHz and *bottom panel* up to 5 MHz) for $h_2 = 10^{-6}$ m^2, $h_1 = 2.25$ m^4/s^2 and $c_R = 176.6$ m/s

Following Porubov (Porubov 2003), we can rewrite (14) in the following form

$$u_{tt} - c_R^2 u_{xx} + h_1 u_{xxxx} - h_2 u_{ttxx} = 0, \tag{16}$$

with the following dispersion relation:

$$\omega = k\sqrt{\frac{c_R^2 + h_1 k^2}{1 + h_2 k^2}}. \tag{17}$$

Note that in (Porubov 2003) $h_1 = \alpha_4$ and $h_2 = \alpha_3$ where $\alpha_3 = 0.5\nu(\nu - 1)R^2$ and $\alpha_4 = -0.5\nu c_R^2 R^2$ with R as the radius of the rod.

In case of positive ν normal dispersion follows. If the parameters h_1 and h_2 are treated as arbitrary ad hoc parameters, then anomalous dispersion relation follows if $h_2 < h_1$. Moreover, the velocity is bounded and approaches the value $c_1 = (h_1/h_2)^{-1/2}$ as the wavelength approaches infinity (see Fig. 2). The parameters in Fig. 2 are adjusted so that the velocity of the 5 MHz wave would have the same value as given by Heimburg (1998). The exact value of this upper bound can be determined from the experiments and can be adjusted by choosing the appropriate value for the ratio h_1/h_2. The slope of the dispersion curve can be adjusted by changing the parameter h_2. In our example, the parameter h_2 is taken equal to 10^{-6} m^2 in order to achieve relatively small changes in case of low frequencies as it is the case in Heimburg and Jackson (2005) (see Fig. 2 top panel). Also note that the parameter h_1

is similar to the parameter h in Eq. (7) and is approximately in the same order as it is in Heimburg and Jackson (2005).

The meaning of the parameter h_2 can be explained by considering Eqs. (12) and (14) where the fourth-order mixed derivative is responsible for inertial effects. A similar parameter, only for the microinertia, is also present in the Mindlin-type microstructure model [see Eq. (16) in Peets et al. (2008) for example]. Lipids in biomembranes also represent a certain microstructure, and therefore, the parameter h_2 can be related to the inertia of the lipids. This opens also the way to find the value of h_2 from experiments. Moreover, the parameter h_1, which is related to the elasticity of the biomembrane, can be expressed as $c_1^2 h_2$, thus relating parameters h_1 and h_2 to the microstructure of the biomembrane.

Based on these arguments, we propose the modified [cf. Eq. (7)] governing equation:

$$\frac{\partial^2 u}{\partial t^2} = (c_0^2 + pu + qu^2)\frac{\partial^2 u}{\partial x^2} + (p + 2qu)\left(\frac{\partial u}{\partial x}\right)^2 - h_1\frac{\partial^4 u}{\partial x^4} + h_2\frac{\partial^4 u}{\partial x^2 \partial t^2} \quad (18)$$

where $h_1 = h$ and h_2 is a new constant. As far as the value of h was proposed (Heimburg and Jackson 2005) without special physical considerations, we propose here to use $h_2 = 10^{-6}\,\mathrm{m}^2$ in order to get a physically more plausible dispersion relation like Eq. (17). With these values of h_1 and h_2, phase and group velocities are shown in Fig. 2.

For the following analysis, we go into dimensionless form:

$$\frac{\partial^2 U}{\partial T^2} = \left(1 + PU + QU^2\right)\frac{\partial^2 U}{\partial X^2} + (P + 2QU) \times \left(\frac{\partial U}{\partial X}\right)^2 - H_1\frac{\partial^4 U}{\partial X^4} + H_2\frac{\partial^4 U}{\partial X^2 \partial T^2} \quad (19)$$

with $X = x/l$, $T = c_0 t/l$, $U = u/\rho_0$ and $P = p\rho_0/c_0^2$, $Q = q\rho_0^2/c_0^2$, $H_1 = h/(c_0^2 l^2)$; l is a certain length (see later).

The higher-order terms in Eq. (19) could be interpreted as a wave operator

$$L_4 = H_2\frac{\partial^2}{\partial X^2}\left(\frac{\partial^2 U}{\partial T^2} - \frac{H_1}{H_2}\frac{\partial^2 U}{\partial X^2}\right) \quad (20)$$

which is characteristic to hierarchy of waves (Berezovski et al. 2013).

Equation (19) is solved under the pulse-type initial condition which is interpreted as a forcing from the propagating action potential.

4 Numerical simulation

4.1 Numerical scheme

For the numerical integration, the Discrete Fourier Transform (DFT)-based pseudospectral method (PSM) is used. For applying the PSM, the equation needs to be in a specific form with only time derivatives on the right-hand side of the equation and only spatial derivatives on the left-hand side of the equation which is clearly not the case with Eq. (19) which has a mixed partial derivative present.

A new variable is introduced following Salupere (2009)

$$\Phi = U - H_2\frac{\partial^2 U}{\partial X^2}, \quad (21)$$

and the variable U and its spatial derivatives are expressed in terms of the variable Φ as

$$U = \mathrm{F}^{-1}\left[\frac{\mathrm{F}(\Phi)}{1 + H_2 k^2}\right], \qquad \frac{\partial^m U}{\partial X^m} = \mathrm{F}^{-1}\left[\frac{(\mathrm{i}k)^m \mathrm{F}(\Phi)}{1 + H_2 k^2}\right], \quad (22)$$

where F^{-1} denotes inverse Fourier transform and F the Fourier transform. Equation (19) is rewritten in terms of the variable Φ as

$$\Phi_{TT} = \left(1 + PU + QU^2\right)\frac{\partial^2 U}{\partial X^2} + (P + 2QU)\left(\frac{\partial U}{\partial X}\right)^2 - H_1\frac{\partial^4 U}{\partial X^4}. \quad (23)$$

Equation (23) can be solved with the use of the PSM after reducing it to a system of two first-order differential equations (see Salupere 2009, for details).

4.2 Material and numerical parameters

The material parameters are taken similar to Heimburg and Jackson (2005) i.e.

$$c_0 = 176.6\ \mathrm{m/s}; \quad p = -16.6\, c_0^2/\rho_0^A; \quad q = 79.5\, c_0^2/(\rho_0^A)^2; \quad h_1 = 2.25\ \mathrm{m}^4/\mathrm{s}^2; \quad h_2 = 10^{-6}\,\mathrm{m}^2; \quad \rho_0 = 4.107 \cdot 10^{-3}\ \mathrm{g/m}^2; \quad (24)$$

which correspond roughly to unilamellar DPPC vesicles at $T = 45\,^\circ\mathrm{C}$ and the value of l used for the transforming into dimensionless form is 10^{-3} m. The parameter h_2 is not present in the Heimburg and Jackson (2005) and is chosen so that the limiting speed for the high frequencies (at 5 MHz) will be 1,500 m/s as indicated by Heimburg (1998). The initial condition is a sech^2-type (bell shaped) pulse with zero initial speed ($U_0(x) = A_0 \cdot \mathrm{sech}^2(B_0 \cdot x)$). The relevant parameters for the numerical scheme and initial condition are $n = 1{,}024$ (the number of grid points), $B_0 = 1/128$ (the width parameter of the $sech^2$-type initial pulse) and $A_0 = 2$ (the amplitude of the initial pulse). The governing equations are solved and results presented in the dimensionless form.

It should be noted that the numerical experiments were also performed with the second set of material parameters presented in Heimburg and Jackson (2005) corresponding roughly to lung surfactant data at bulk temperature of $T = 37\,°\mathrm{C}$. The results from the second parameter set are very similar to the one from the first set.

4.3 Numerical results

In all cases, the leading terms of governing equations are of the second order. Consequently, the original pulse splits into two identical pulses both having the half of the initial amplitude and propagating in opposite directions.

In the case of the original HJ model (7) in the dimensionless form, the single dispersive term U_{XXXX} is overwhelmingly dominant and destroys the propagating single waveprofile even over very short propagation distances. This situation is similar to the linearised Korteweg–de Vries equation where the dominant dispersion leads to a wave described by an Airy function (Ablowitz 2011).

Let us start with few words about dispersion in the physically motivated model (19). If $H_1 = H_2$; then, we have 'dispersionless case' as the phase (c_{ph}) and group (c_{gr}) speeds are equal. If these parameters are different, then we have either anomalous or normal dispersion.

As modelled for the original Bishop model (14), the physically correct dispersion type should be normal ($c_{ph} > c_{gr}$), here, however, we need to get anomalous dispersion type ($c_{ph} < c_{gr}$) as this would be in agreement with observations from physical experiments (Heimburg and Jackson 2005) for the mechanical nerve impulse so the relationship of the dispersion-related coefficients is changed to the opposite compared with the original Bishop model (14).

In Fig. 3 example, solutions are presented at a certain distance X at time T. Here, $X = n\Delta x$ where Δx is the grid step size. The linear case is the one where nonlinearity-related parameters p and q are taken to be zero. The 'wave equation' case is where all additional terms (p, q, h_1 and h_2) in the Eq. (19) are taken to be zero and the '$H_2 = 1$' case is where all parameters are at their designated values. In the dimensionless form, the $H_1 = 72.14$ corresponds to the $h_1 = 2.25\,\mathrm{m^4 s^{-2}}$ and parameter $H_2 = 1$ corresponds to the $h_2 = 10^{-6}\,\mathrm{m}^2$. In the bottom panel, in Fig. 3, one can see demonstration of the normal dispersion case ($H_2 = 100$) which means that on the dispersion curve the initial speed for the long waves is $c_0 = 176.6\,\mathrm{m\ s^{-1}}$ and the limiting speed for the short waves is smaller than c_0 at 150 $\mathrm{m\ s^{-1}}$. The main visible difference is that in the case of anomalous dispersion the oscillatory tail emerges in 'front' of the propagating pulse, but in the case of normal dispersion 'behind' the propagating

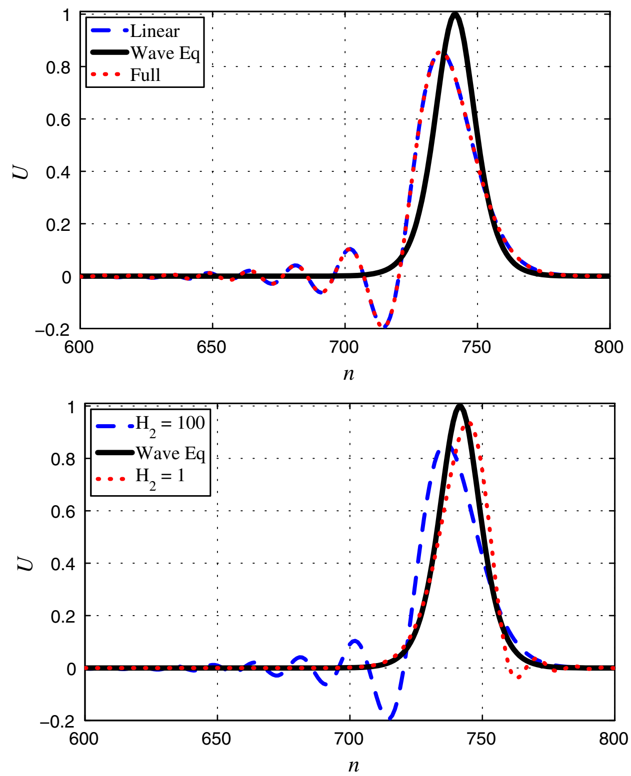

Fig. 3 Waveprofiles at $T = 9{,}999$ ($t = 56.7\,\mathrm{ms}$). The waveprofiles propagate from the *right* to *left*. *Top*—nonlinear versus linear at $H_2 = 1$. *Bottom*—nonlinear anomalous dispersion ($H_2 = 1$) versus normal dispersion ($H_2 = 100$) case

pulse (where 'front' is defined as the direction of propagation for the pulse). It should be noted that parameters H_1 and H_2 have very similar but opposite effect on the solutions. For example, if H_2 is increased by a small amount (≈10 %) over the dispersionless case (where $H_1 = H_2$), the effect is almost the same when parameter H_1 is reduced by the same amount. What is also worth of noting is that the solution is very sensitive towards small changes in the dispersion-related parameters. On the other hand, the effect of nonlinearity seems to be negligible compared with the magnitude of the dispersion-related effects as 'Linear' and 'Full' solutions are identical and overlapping in Fig. 3 top panel even after long evolution (≈ 56.7 ms in real time). It seems that although the parameter $h = h_1$ is related to compressibility of the membrane (Mosgaard et al. 2012), the role and values of h_1 and h_2 need more explanation. Note that the existence of small amplitude waves has been shown also for the HJ model by (Lautrup et al. 2011). Here, these waves are directly related to the dispersion type.

In order to investigate the role and significance of nonlinearity in Eq. (19), two approaches are used: (i) investigation of long-term evolution of the solution at chosen material parameter values; (ii) increasing the nonlinear terms relevance significantly by multiplying relevant terms in governing equation by a large number (10^5). At this stage, these values are hypothetical but needed for obtaining numerical results in course of realistic time (in milliseconds). Three sets of material parameters are considered: (a) the basic wave equation ($P = Q = H_1 = H_2 = 0$), (b) the nonlinear wave equation without dispersive terms ($H_1 = H_2 = 0$) and (c) the full governing equation (19) with increased nonlinearity.

The dispersion-related parameters are taken so that even with dispersive terms present we will have dispersionless case. The parameter h_1 is kept as it is at $2.25\,\mathrm{m^2 s^{-2}}$ while parameter h_2 is taken as $7.214 \cdot 10^{-5}\,\mathrm{m}^2$ so that $H_1 = H_2$. That means that the speed for the long waves is the same as the speed for the short waves.

Over long-term evolution of solutions ($t \approx 350\,\mathrm{ms}$ in physical time or $T = 60{,}000$), the difference between wave equations (a) and (b) is negligible (maximum amplitude difference between solutions is of the order of 10^{-5} with no significant phase differences). For the long-term evolution, the case (c) with increased nonlinearity is not considered as such a strong nonlinearity destroys the numerical scheme before reaching that far.

In the case (c), the relevance of the nonlinear term is increased by changing the constants P and Q by multiplying them with 10^5 in order to get visible changes in solution.

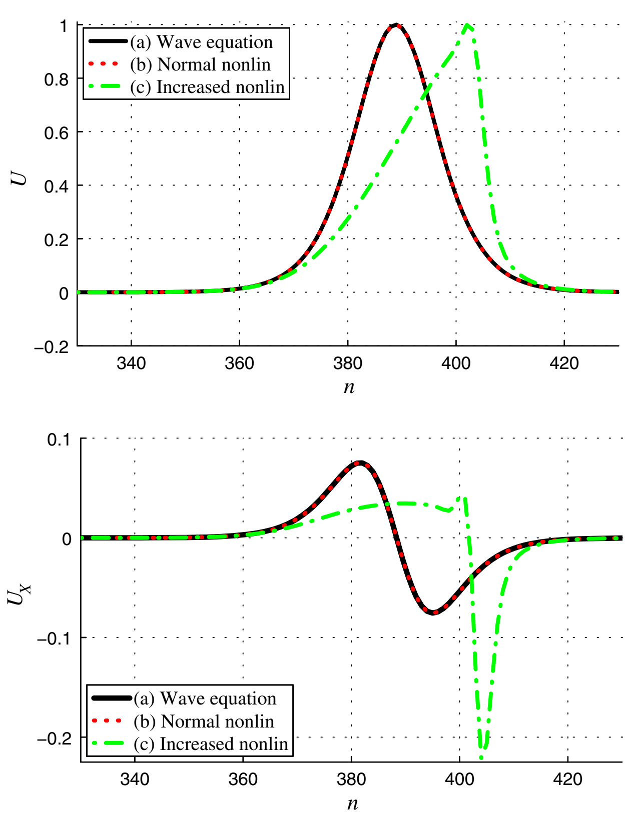

Fig. 4 Waveprofiles at $T = 1{,}563$ (*top*) and corresponding spatial derivatives (*bottom*). The waveprofiles propagate from the *right* to *left*

It turns out that the wave profile gets asymmetric as higher amplitudes seem to be propagating slower than the low amplitudes (see Fig. 4). This can be explained by the influence of the term PU. Taking $P < 0$ as in HJ model, the deformation of the pulse is backwards to the propagation direction (Fig. 4, top panel). In addition, here, $|P| > |Q|$ that means the larger the U the smaller the speed.

It is interesting to note that usually in Boussinesq-type equations the nonlinear terms present are dependent on U_X (Christov et al. 2007) not just on plain U like it is the case here. The emergence of waveprofile asymmetry is a somewhat unexpected phenomenon as usually the nonlinear effects increase the amplitude of the solution. It is clear that the values of coefficients in governing equations need further analysis.

5 Discussion

Many experiments have shown that the action potential propagating in a nerve fibre is accompanied by geometrical changes, i.e. changes of dimensions of a fibre (Iwasa et al. 1980; Tasaki 1988; Tasaki et al. 1989). These effects are described also in Heimburg and Jackson (2005, 2007). The mechanical wave, called also swelling (Iwasa et al. 1980; Tasaki 1988), is of the asymmetrical type characterised by a positive and negative phases (see Fig. 1 in Tasaki 1988). For mammalian nerve terminals, however, the negative phase (dip) is not so clearly evident (Kim et al. 2007).

The mathematical model proposed by Heimburg and Jackson (2005, 2007) is an important step in order to explain the propagation of a mechanical wave. The governing wave equation (7) proposed by them involves both nonlinear and dispersive terms and belongs to the class of Boussinesq equations (Christov et al. 2007).

Here, we analyse the HJ model from the viewpoint of wave mechanics. The starting point is the excitation of a mechanical wave. All the studies concerning mechanical phenomena in nerve fibres agree that these are excited by action potentials and propagate in phase with them (Tasaki 1988). The mechanism of the electromechanical transduction could be based either on electrostrictive or piezoelectric effects (Gross et al. 1983). In the first case, the excited strain is proportional to the square of the field, the second case—directly proportional. As fas as the action potential is an asymmetric pulse with an overshoot, it is clear that the influence of the overshoot is smaller for the electrostrictive mechanism. We solved the governing equations for a pulse-type initial excitation that can be taken as a good approximation to the real situation.

The governing equation (7) and the modified variant (19) are solved numerically by using the pseudospectral method (Salupere 2009) under an initial pulse-type excitation. The aim is to understand the influence of nonlinearity/nonlinearities and dispersive effects for the formation of a mechanical wave in a fibre.

The nonlinearity in HJ equation (7) is based on the changes of compressibility in the fibre wall (Heimburg and Jackson 2005). This is motivated by the special structure of the fibre made of lipids and proteins. The nonlinearity is of the type $F(u)$ where u denotes the density changes $\Delta\rho^A$ in the fibre wall. The wave operator $L(u)$ takes then the form

$$L(u) = u_{tt} - c_0^2(1 + F(u))u_{xx}. \tag{25}$$

Note that in mechanics of solids the operator is usually in the form

$$L(u) = u_{tt} - c_0^2(1 + G(u_x))u_{xx}. \tag{26}$$

The model (25) deserves full attention in the analysis provided it is typical for complicated biosystems.

The numerical simulation has shown that the nonlinear effects with values suggested in the HJ model are not visible at time typical for nerve pulse propagation and only at large time may affect the profile. Typically to the operator (25), the nonlinear effects increase the derivative u_x backwards.

Another important physical effects to be analysed is dispersion. The ad hoc dispersive term u_{xxxx} (Heimburg and Jackson 2005) leads to unbounded velocities in higher frequencies. Although the propagating wave is probably confined to lower frequencies, from a viewpoint of wave dynamics, such limits should be avoided. That is why a more realistic dispersion mechanism is proposed (Eq. (18)) motivated by the analysis of rod models (Abramson et al. 1958; Erofeyev et al. 2002, etc.). In this case, the group (c_{gr}) and phase (c_{ph}) velocities are bounded (Fig. 2) which is physically rational. The numerical simulation shows that this model with terms u_{xxxx} and u_{ttxx} satisfies the conditions for anomalous dispersion ($c_{ph} < c_{gr}$) and is close to physical experiments. A real challenge is to link the coefficients h_1 and h_2 to the real physical situation based on structural inhomogeneities of lipids. In general terms, dispersion effects in biomembranes should be related to the structural characteristics of lipids like it is done for microstructured materials. These studies are in progress.

It must be stressed that the compression along the propagation direction is not directly related to the swelling which means displacements in the transverse direction (measured by Tasaki 1988). Following the ideas from the rod models where Rayleigh–Love correction is introduced [expression (11)], we propose to use the same idea. It means that after the longitudinal wave profile is obtained (Figs. 3 and 4a), the transverse displacement is related to its derivative (Fig. 4b). The similarity to the experiments is obvious—see Fig. 1 in Tasaki (1988). Whether the longitudinal and transverse displacements in the cylindrical membrane are linked by the Poisson coefficient (expression (11)) or not, is an open question.

To sum up, the governing equation (18) proposed in this study is physically consistent (involving bounding velocity) from the viewpoint of wave dynamics, the possibility to model anomalous dispersion corresponds to observations by Heimburg and Jackson (2005) and the swelling of the biomembrane is properly coupled with the density pulse.

Some remarks should still be added. In this paper, we avoided the notion of soliton while in mathematical physics soliton is attributed to a solitary wave which interacts elastically with other solitons. The situation is different for nerve pulse because in the interaction process they annihilate each other (Hodgkin and Huxley 1952).

We also note that we did not analyse here the possible thermodynamical conditions for a nerve pulse propagation. This analysis is in progress based on the theory of internal variables. The general ideas were already described in Maugin and Engelbrecht (1994) and Engelbrecht (1997) where the dissipation potentials for known HH and FHN models were introduced. However, such an analysis must be cast into the framework of experiments (Tasaki 1988; Tasaki et al. 1989; Andersen et al. 2009).

Without any doubt, the structure of nonlinearities [$f(u)u_{xx}$-type] in the HJ model (7) and its modified version (18) opens a wide area for future studies in soliton dynamics. As stressed by Eisenberg (2007), the quest in nerve pulse dynamics also goes on.

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