Positive and bounded nonstandard finite difference scheme for the Hodgkin-Huxley equations

A.A. Aderogba¹ and M. Chapwanya *²

¹Department of Mathematics, Obafemi Awolowo University, Ile-Ife, Nigeria ²Department of Mathematics & Applied Mathematics, University of Pretoria, Pretoria 0002, South Africa

Abstract

In this work we consider the Hodgkin Huxley model in the form of a coupled system of one singularly perturbed partial differential equation and three ordinary differential equations. The existence of a small parameter, the nonlinearity and the coupling makes the numerical approximations using explicit finite difference schemes very difficult. In particular, spurious oscillations have been observed to exist. Here we propose the use of nonstandard finite difference to improve on the existing time step restrictions. In addition, we prove that the proposed scheme preserve positivity and is elementary stable. Numerical simulations will be given to support the performance of the proposed scheme.

Keywords: Hodgkin-Huxley equation Non standard finite difference Explicit schemes **AMS Subject Classification:** 65M06; 65M08; 65L12; 97N40

1 Introduction

Response to external impulses is one of the main characteristics of living organisms. This constitutes a series of neuronal activities in the body of the organism which are related to passage of electrical current through an electrical cable. The axon serves as the conductor for impulses from the receptor organ to the brain. A model that has served as the bedrock for the transference of these impulses via the squid giant axon was proposed by Hodgkin and Huxley [13]. Their observation is modeled by a coupled system of a reaction diffusion equation and three ordinary differential equations [17],

$$\epsilon \frac{\partial u}{\partial t} = \mu \frac{\partial^2 u}{\partial x^2} - \left(g_{na}m^3h\left(u - E_{na}\right) + g_kn^4\left(u - E_k\right) + g_l\left(u - E_l\right)\right) + I,$$

$$\frac{dm}{dt} = (1 - m)\alpha_m(u) - m\beta_m(u),$$

$$\frac{dh}{dt} = (1 - h)\alpha_h(u) - h\beta_h(u),$$

$$\frac{dn}{dt} = (1 - n)\alpha_n(u) - n\beta_n(u),$$
(1.1)

*Corresponding author. m.chapwanya@up.ac.za; Tel.: +27 12 420 2837; Fax.: +27 12 420 3893

where u(x,t) is the electrical potential across the cell membrane, E_i , (i = na, k, l) are the equilibrium potentials of the sodium, potassium and leakage currents, $g_m \ge 0$, (i = na, k, l) models membrane conductivities. The parameters m, h, n are gating variables where m, and h control the sodium current while n controls the potassium current. In addition, α_j , $\beta_j \ge 0$, (j = m, h, n) are specified nonnegative functions and given by [16, 17], as follows

$$\alpha_m = \frac{25 - u}{10\left(\exp\left(\frac{25 - u}{10}\right) - 1\right)}, \quad \beta_m = 4\exp\left(-\frac{u}{18}\right), \quad \alpha_h = 0.07\exp\left(-\frac{u}{20}\right),$$

$$\beta_h = \frac{1}{\exp\left(\frac{30 - u}{10}\right) + 1}, \quad \alpha_n = \frac{10 - u}{100\left(\exp\left(\frac{10 - u}{10}\right) - 1\right)}, \quad \beta_n = 0.125\exp\left(-\frac{u}{80}\right).$$
 (1.2)

The mathematical analysis of this system of equations is challenging since it is strongly coupled, nonlinear and it is a four dimensional system. Various authors have considered the reduction of this system of equations to a system of two equations in order to reduce the challenges in its mathematical analysis. Following a series of papers on this subject, the first formal mathematical model was presented in [12]. Later, the same authors performed experiments to support the formulated model in [13]. It is in this work that they observed E_{na} , E_k and E_l can be assumed constants. FitzHugh [9] reduced the system (1.1) to a system of two singularly perturbed differential equations in u and m with h and n held constant. Later, a step by step and mathematically explicit reduction from a four dimensional system to a two dimensional one and finally to a single equation was proposed in [1]. Recently, equation (1.1) has been reduced to a single variable equation when it was approximated by a response kernel expansion in terms of the membrane voltage in [14]. It was generally documented by these authors that based on the assumptions leading to the reduction, some vital information might have been lost.

It is essential, if possible, to study the equation in its original form. The well-posedness, existence and uniqueness of solution of system (1.1) and (1.2) was discussed in [16]. The author in [17] later proposed and analysed a backward Euler scheme for the approximation of the system. The scheme is implicit and follows some iterative processes that needs more computer memory for storage as compared to explicit schemes. Recently, an explicit finite difference scheme that satisfies a maximum principle was designed and analysed in [10]. A major challenge they observed and reported is the emergence of spurious oscillation at some point in time during the integration of one of the gate variables as a result of instability in the scheme that approximates the membrane potential. This is due to the fact that the system (1.1) is singularly perturbed as the model is valid for $\mu, \epsilon \ll 1$. It has also been proposed that the singular perturbation theory is a plausible tool to analyze (1.1) and (1.2). We also highlight the work [6] where the use of an exponential finite difference scheme for (1.1) was investigated. They observed that for standard schemes, stable computations of the rapid rising phase of action potential, forces the time steps to be very small.

In this work we propose the use of nonstandard finite difference (NSFD) method for the numerical solution of system (1.1). The approach, first introduced by Mickens [18], has been shown recently to be dynamically consistent [5] and accurate in approximating systems of differential equations [7] and singularly perturbed differential equations [2, 15]. We will design, apply and compare some nonstandard finite difference schemes for (1.1).

The structure of this work is as follow. Section 2 is devoted to developing and qualitative analysis of nonstandard numerical schemes to approximate the equation. The better performance of the schemes were shown through some numerical experiments in Section 3. We discuss our observation and give some idea on further research in Section 4.

2 Numerical Schemes

In this section we will present preliminaries in the derivation of nonstandard explicit finite difference schemes to approximate the solutions of equations (1.1) and (1.2). Following [10], the model (1.1) can be formulated mathematically as follows. Let $\Omega \subset \mathbb{R}$ be a bounded interval, then we summarise the equations as

$$\epsilon \frac{\partial u}{\partial t} = \mu \frac{\partial^2 u}{\partial x^2} - \sum_{i=1}^q g_i(y_1, \dots, y_p)(u - E_i) + I,$$

$$\frac{\partial y_\ell}{\partial t} = (1 - y_\ell) \alpha_\ell(u) - y_\ell \beta_\ell(u),$$
(2.1)

where $(x,t) \in \Omega \times (0,T)$, E_{\min} are the electric potentials and $\ell = 1, \dots, p$. Without loss of generality, we will take $\mu = \epsilon$, unless otherwise stated. The appropriate initial conditions are $u(x,0) = u_0(x)$ and $y_{\ell}(x,0) = y_{\ell 0}(x)$. Further, by the maximum principle,

$$E_{\min} \le u(x,t) \le E_{\max}, \quad \text{and} \quad 0 \le y_{\ell} \le 1,$$

$$(2.2)$$

whenever $E_i \leq u_0(x) \leq E_{\max}$ and $0 \leq y_{\ell 0}(x) \leq 1$ respectively, where $E_{\min} = \min_{1 \leq i \leq q} E_i$ and $E_{\max} = \max_{1 \leq i \leq q} E_i$. Throughout the paper, a numerical approximation of the unknown variables w(x,t) on a uniform

grid will be written as w_m^n at time $t^n = n\Delta t$ and spatial point $x_m = m\Delta x$, where $m = 0, 1, 2, \dots, M$ and $n = 0, 1, 2, \dots$.

2.1 Temporal models and mathematical preliminaries

Consider an autonomous differential equation

$$\frac{dw}{dt} = f(w,a) \tag{2.3}$$

where a represent any scalar constant, with a finite difference scheme

$$w^{n+1} = F(w^n, \Delta t, a).$$
 (2.4)

Definition 1 ([8]). A difference method is called NSFD method if at least one of the following properties is satisfied,

- In the first order discrete derivative, the denominator Δt is replaced by a (carefully chosen) nonnegative function $\phi(\Delta t)$ satisfying $\phi(\Delta t) = \Delta t + \mathcal{O}[(\Delta t)^2]$, e.g., $\phi(\Delta t) = 1 e^{-\Delta t}$.
- In the expression f, nonlinear terms are approximated in a nonlocal way. E.g., $w^2 \approx w^{n+1}w^n$.

Definition 2 ([18]). An exact difference scheme is one for which the solution to the difference scheme has the same general solution as the associated equation.

Definition 3 ([4]). *The finite difference scheme* (2.4) *is stable with respect to monotone dependence on initial values if*

$$\frac{\partial F}{\partial y}(\Delta t; y) \ge 0, \quad y \in \mathbb{R}, \quad \Delta x > 0.$$

Notice that using Definition 2, if the solution of (2.3) and (2.4) have the same general solution, then scheme (2.4) is an exact scheme. To illustrate the ideas presented in the above definitions we consider the following subequation of (1.1).

$$\epsilon \frac{dw}{dt} = \lambda - \gamma w. \tag{2.5}$$

In particular, equation (2.5) is motivated by observing that all the equations in (1.1) have this structure in their reaction terms. Assuming γ and λ are positive, then (2.5) has exactly one positive equilibrium which is asymptotically stable. Following the procedure highlighted in [18], and references therein, we propose the following exact scheme

$$\epsilon \frac{w^{n+1} - w^n}{\phi(\Delta t)} = \lambda - \gamma w^{n+1}, \qquad (2.6)$$

which can also be written as

$$w^{n+1} = \frac{\lambda \phi(\Delta t) + \epsilon w^n}{\epsilon + \phi(\Delta t)\gamma},$$
(2.7)

where $\phi(\Delta t)$ takes the form

$$\phi(\Delta t) = \frac{\exp((\gamma/\epsilon)\Delta t) - 1}{(\gamma/\epsilon)},$$

and satisfies $\phi(\Delta t) = \Delta t + O([\Delta t]^2)$. As indicated, scheme (2.6) is exact, hence it preserves all the qualitative properties of (2.5). Some properties possessed by any scheme of type (2.6) will be discussed next. In particular, scheme (2.7) clearly preserves the following:

- \mathcal{P}_1 Positivity: given that $w^n > 0$, then $w^{n+1} > 0$.
- \mathcal{P}_2 Boundedness: given that $w^n \in \left(0, \frac{\lambda}{\gamma}\right)$, then $w^{n+1} \in \left(0, \frac{\lambda}{\gamma}\right)$.
- \mathcal{P}_3 Preservation of fixed points.

2.1.1 Discretization of the gating equations

Motivated by the discussion above, we propose the following scheme for equations $(2.1)_2$,

$$\frac{y_{\ell}^{n+1} - y_{\ell}^{n}}{\phi} = (1 - y_{\ell}^{n+1})\alpha_{\ell}(u^{n}) - y_{\ell}^{n+1}\beta_{\ell}(u^{n}).$$
(2.8)

We rewrite scheme (2.8) to get

$$y_{\ell}^{n+1} = F \coloneqq \frac{y_{\ell}^{n} + \phi \alpha_{\ell}(u^{n})}{1 + \phi(\alpha_{\ell}(u^{n}) + \beta_{\ell}(u^{n}))}.$$
(2.9)

Now

$$\frac{\partial F}{\partial y_{\ell}^n} = \frac{1}{1 + \phi(\alpha_{\ell}(u^n) + \beta_{\ell}(u^n))} > 0,$$

since $\alpha_{\ell}(u^n) > 0$ and $\beta_{\ell}(u^n) > 0$. We also notice that if $0 \le y_{\ell}^n \le 1$ then $0 \le y_{\ell}^{n+1} \le 1$, hence the discrete solution is bounded. In particular, (2.8) is topologically dynamically consistent with system (2.5) on the subinterval $[0, \infty)$.

2.1.2 Discretization of the full temporal model

In this section we are interested in

$$\epsilon \frac{\partial u}{\partial t} = -\sum_{i=1}^{q} g_i(y_1, \dots, y_p)(u - E_i) + I,$$

$$\frac{\partial y_\ell}{\partial t} = (1 - y_\ell)\alpha_\ell(u) - y_\ell\beta_\ell(u),$$
(2.10)

Putting together the ideas above, we can present a full difference scheme for the temporal model (2.10), i.e.,

$$\epsilon \frac{u_m^{n+1} - u_m^n}{\phi} = -\sum_{i=1}^q g_i(y_1^n, \dots, y_p^n)(u_m^{n+1} - E_i) + I,$$

$$\frac{y_\ell^{n+1} - y_\ell^n}{\phi} = (1 - y_\ell^{n+1})\alpha_\ell(u^n) - y_\ell^{n+1}\beta_\ell(u^n).$$
(2.11)

Scheme (2.11) preserves the positivity and boundedness of the solutions.

Numerical simulations will be given here to support the properties of system (2.11). For the purpose of comparison, we will also consider the following standard foward Euler scheme.

$$\epsilon \frac{u_m^{n+1} - u_m^n}{\Delta t} = -\sum_{i=1}^q g_i(y_1^n, \dots, y_p^n)(u_m^n - E_i) + I,$$

$$\frac{y_\ell^{n+1} - y_\ell^n}{\Delta t} = (1 - y_\ell^n)\alpha_\ell(u^n) - y_\ell^n\beta_\ell(u^n).$$
(2.12)

Example 1. Solve the temporal model (2.10) subject to initial conditions m(0) = 0.1, h(0) = 0.4, n(0) = 0.4, $\nu(0) = -15$. We choose parameters as follows: $\epsilon = 0.5$ and $\epsilon = 1$, I = 6.9, $(E_{na}, g_{na}) = (115, 120)$, $(E_k, g_k) = (-12, 36)$, $(E_l, g_l) = (10.6, 0.3)$.



Figure 1: Simulations for (2.10) when $\epsilon = 0.5$ with various number of grids showing convergence of the numerical approximation

These simulations show that the proposed scheme, (2.11) is stable independently of the value or relationship between temporal step size and ϵ . The standard scheme breaks down at some points during the simulation because its stability depends on the temporal step size.



Figure 2: Simulations for (2.10) when $\epsilon = 1$ with various number of grids showing convergence of the numerical approximation



(a) Comparison of schemes (2.11) and (2.12). (b) Scheme (2.11) with integration time T = 100. Figure 3: Simulation of the action potential for (2.10) when $\epsilon = 1$ with 200 grid points

2.2 The spatial models

Given that the model under investigation is a reaction diffusion system, a natural example to consider is the following partial differential equation

$$\epsilon \frac{\partial w}{\partial t} = \varepsilon \frac{\partial^2 w}{\partial x^2} + \lambda - \gamma w.$$
(2.13)

In particular, equation (2.13) is a constant coefficient version of equation $(1.1)_1$. The procedure listed in [5] allows us to design a NSFD scheme for equation (2.13) by considering the schemes for its sub equations. The temporal sub equation is given by (2.5), while the spatial sub equation is

$$\frac{d^2w}{dx^2} - \bar{\gamma}w + \bar{\lambda} = 0, \qquad (2.14)$$

where $\bar{\gamma} = \frac{\gamma}{\epsilon}$, $\bar{\lambda} = \frac{\lambda}{\epsilon}$. We, here design scheme for equation (2.14) which is a singularly perturbed ordinary differential equation. We give a brief description on the derivation of a nonstandard



Figure 4: Simulations of the action potential for (2.10) when $\epsilon = 1$ and $\epsilon = 0.5$

scheme for (2.14). Interested readers can consult [3] for a more general and detailed explanation. The homogenous part of equation (2.14) has two linearly independent solutions $\exp(\sqrt{\overline{\gamma}x})$ and $\exp(-\sqrt{\overline{\gamma}x})$ implying that

$$\begin{array}{ccc} w_m & e^{m\sqrt{\gamma}\Delta x} & e^{-m\sqrt{\gamma}\Delta x} \\ w_{m+1} & e^{(m+1)\sqrt{\gamma}\Delta x} & e^{-(m+1)\sqrt{\gamma}\Delta x} \\ w_{m+2} & e^{(m+2)\sqrt{\gamma}\Delta x} & e^{-(m+2)\sqrt{\gamma}\Delta x} \end{array} = 0$$

and with $\bar{\gamma} = \gamma/\varepsilon$, this leads to

$$\varepsilon \frac{w_{m+1} - 2w_m + w_{m-1}}{\psi^2(\Delta x)} - \gamma w_m = 0, \quad \psi(\Delta x) = \frac{2}{\sqrt{\gamma/\varepsilon}} \sinh\left(\frac{\sqrt{\gamma/\varepsilon}}{2}\Delta x\right), \quad (2.15)$$

where $\psi(\Delta x)$ satisfies $\psi(\Delta x) = \Delta x + \mathcal{O}([\Delta x]^2)$. In particular we see that

$$\psi(\Delta x) \approx \Delta x + \frac{\tilde{\gamma}}{4} \frac{\Delta x^3}{3!} + \cdots,$$

making the scheme consistant with the differential equation. Hence the exact scheme for the homogeneous part of equation (2.14) is therefore given as

$$e^{\frac{w_{m+1} - 2w_m + w_{m-1}}{\psi^2(\Delta x)} - \gamma w_m + \lambda} = 0.$$
(2.16)

Combining schemes (2.7) with (2.16), the ideas suggested in [5], we have a scheme for equation (2.13) as follows.

$$\epsilon \frac{w_m^{n+1} - w_m^n}{\phi(\Delta t)} = \epsilon \frac{w_{m+1}^n - 2w_m^n + w_{m-1}^n}{\psi^2(\Delta x)} + \left(\lambda - \gamma w_m^{n+1}\right).$$
(2.17)

2.2.1 Discretization of the electrical potential equation

Taking motivation from the above derivation we propose the following scheme for equation $(2.1)_2$,

$$\epsilon \frac{u_m^{n+1} - u_m^n}{\phi} = \epsilon \frac{u_{m-1}^n - 2u_m^n + u_{m+1}^n}{\psi^2(\Delta x)} - \sum_{i=1}^q g_i(y_1^n, \dots, y_p^n)(u_m^{n+1} - E_i).$$
(2.18)

Assuming $\frac{\phi(\Delta t)}{\psi^2(\Delta x)} = \frac{1}{2}$, scheme (2.18) can be written in the form

$$u_m^{n+1} = G := \frac{\frac{1}{2}(u_{m-1}^n + u_{m+1}^n) + \phi \sum_{i=1}^q g_i(y_1^n, \dots, y_p^n) E_i}{1 + \phi \sum_{i=1}^q g_i(y_1^n, \dots, y_p^n)}.$$
(2.19)

Clearly if $u_m^n \ge 0$, then $u_m^{n+1} \ge 0$. In addition,

$$\frac{\partial G}{\partial u_{m-1}^n} > 0, \quad \text{and} \quad \frac{\partial G}{\partial u_{m+1}^n} > 0$$

since $g_k > 0$. Let $u_m^n \leq E_{\max}$, then

$$u_m^{n+1} \le \frac{E_{\max} + \phi \sum_{i=1}^q g_i(y_1^n, \dots, y_p^n) E_i}{1 + \phi \sum_{i=1}^q g_i(y_1^n, \dots, y_p^n)} \le \frac{E_{\max} + \phi E_{\max} \sum_{i=1}^q g_i(y_1^n, \dots, y_p^n)}{1 + \phi \sum_{i=1}^q g_i(y_1^n, \dots, y_p^n)} = E_{\max}.$$

That is $u_m^{n+1} \leq E_{\max}$. A lower bound is obtained in the same manner so that $u_m^{n+1} \in [E_{\min}, E_{\max}]$. We have the following result.

Theorem 1. For any initial condition $u_m^0 \in [E_{\min}, E_{\max}]$, the discrete solution generated by scheme (2.18) is positive, elementary stable and bounded on $[E_{\min}, E_{\max}]$ provided $\frac{\phi(\Delta t)}{\psi^2(\Delta x)} = \frac{1}{2}$.

2.3 The discretisation of the full model

In this section we propose two schemes for the Hodgkin-Huxley model (2.1). The first scheme follows the ideas above, i.e., combining ideas in scheme (2.8) and (2.18), while the second scheme follows from the work of [10]. That is,

$$\epsilon \frac{u_m^{n+1} - u_m^n}{\phi_n(\Delta t)} = \epsilon \frac{u_{m-1}^n - 2u_m^n + u_{m+1}^n}{\psi_n^2(\Delta x)} - \sum_{i=1}^q g_i(y_1^n, \dots, y_p^n)(u_m^{n+1} - E_i),$$

$$\frac{y_\ell^{n+1} - y_\ell^n}{\phi_n(\Delta t)} = (1 - y_\ell^{n+1})\alpha_\ell(u^n) - y_\ell^{n+1}\beta_\ell(u^n),$$
(2.20)

where

$$\phi_n(\Delta t) = \frac{\exp((\bar{g}^n/\epsilon)\Delta t) - 1}{(\bar{g}^n/\epsilon)}, \quad \psi_n(\Delta x) = \frac{2}{\sqrt{\bar{g}^n/\epsilon}} \sinh\left(\frac{\sqrt{\bar{g}^n/\epsilon}}{2}\Delta x\right),$$

and $\bar{g}^n = \sum_{i=1}^q g_i(y_1^n, \dots, y_p^n)$. The scheme is explicit and for implementation, we use the corresponding versions (2.9) and (2.19) above. The performance of scheme (2.20) can be improved by introducing

the Dufort-Frankel simplification

$$\epsilon(1-\alpha)\frac{\nu_m^{n+1}-\nu_m^n}{\phi_n(\Delta t)} + \epsilon\alpha \frac{\nu_m^{n+1}-\nu_m^{n-1}}{2\phi} = \epsilon \frac{\nu_{m+1}^n - 2\nu_m^{ave} + \nu_{m-1}^n}{\psi_n^2(\Delta x)} - \sum_{i=1}^q g_i(y_1^n, \dots, y_p^n)(u_m^{ave} - E_i), \qquad (2.21)$$
$$\frac{y_\ell^{n+1}-y_\ell^n}{\phi_n(\Delta t)} = (1-y_\ell^{n+1})\alpha_\ell(u^n) - y_\ell^{n+1}\beta_\ell(u^n),$$

where $\nu_m^{ave} = \frac{\nu_m^{n+1} + \nu_m^{n-1}}{2}$ and $0 < \alpha < 1$. ν_m^1 is approximated by the standard Euler scheme. For completeness we state the scheme from [10] as follows

3 Numerical experiments

This section is devoted to the illustration of the performance of the derived scheme for the Hodgkin Huxley model. We will present results for schemes (2.20) and (2.22). The choice of parameters is motivated by the work of [10]. In particular, the values, (E_{\min}, g_m) , of the equilibrium potentials and membrane conductivities used here are $(E_{na}, g_{na}) = (115, 120)$, $(E_k, g_k) = (-12, 36)$, $(E_l, g_l) = (10.6, 0.3)$.

Example 2. Solve the nonlinear equation (1.1) with variable coefficients subject to initial conditions $y_{\ell}(x,0) = \{0.1, 0.4, 0.4\}$, and

$$u(x,0) = \begin{cases} 30, \ x \in [0,0.2] \\ -8.0, \ otherwise \end{cases}$$

and homogeneous Neumann boundary conditions at both ends with $\mu = \frac{5}{396}$, $\epsilon = 1$.

The comparison between the simulations using schemes (2.20) and (2.21) are shown in Figures 5 and 6.

4 Conclusion

The Hodgkin-Huxley equation models excitation due to conduction of impulses through the squid large axon. This, being a biomedical model, needs a reliable approximation technique. Schemes are designed here for both the temporal model and also the spatial-temporal model of the Hodgkin-Huxley equation. The schemes are shown to be dynamically consistent in that they preserve the qualitative properties of the continuous model. In addition to these, several numerical experiment



Figure 5: Comparison of schemes with $\Delta x = 0.05$, $\Delta t = 0.12$, $\mu = 0.0126$, $\epsilon = 1$



Figure 6: Simulation for various values of μ with $\epsilon = 1$ with scheme (2.21)

are performed to show the accuracy and convergence of the proposed schemes and their ability to produce non oscillatory solutions.

The proposed scheme (2.11), for the temporal model was shown to converge consistently to the solution of the Hodgkin-Huxley model (2.10) for $\epsilon = 0.5$ and $\epsilon = 1.0$. As shown in Figure 1 to Figure 4 the standard scheme gives reliable results within some stability boundary as expected for classical schemes while the stability of scheme (2.11) is independent of number of grid points chosen. In addition to these, the oscillations reported by [10] in their simulation is removed by scheme (2.21) both in the simulation of the gating variable and in the potential as shown in Figure 5. Our simulation, shown in Figure 6, reveals that the value of the small parameter does not necessarily affect the convergence of the scheme.

We observe that traveling wave solution will serve as a good standard of comparison of numerical schemes. We are, presently, investigating the existence of traveling wave solution for the Hodgkin-Huxley model (1.1). Another interesting model in neuroscience is the model of defibrillation. It is a strongly nonlinear partial differential equation. The main challenge in its numerical

analysis is the presence of negative concentration in the solution of one of the equations in the system [11]. This abnormality can be eliminated by the ideas proposed here. This will be investigated as part of our on going work.

Acknowledgements

The authors acknowledge the support of South African DST/NRF SARChI Chair on Mathematical Models and Methods in Bioengineering and Biosciences (M3B2). Thanks are also addressed to the anonymous reviewers whose suggestions have contributed to the improvement of the paper.

References

- [1] L. F. Abbott and T. B. Kepler. Model neurons: from hodgkin-huxley to hopfield. In *Statistical mechanics of neural networks*, pages 5–18. Springer, 1990.
- [2] A. A. Aderogba and M. Chapwanya. An explicit nonstandard finite difference scheme for the allen–cahn equation. *Journal of Difference Equations and Applications*, 21(10):875–886, 2015.
- [3] A. A. Aderogba, M. Chapwanya, Djoko J. K., and J. M-S. Lubuma. Coupling finite volume and nonstandard finite difference schemes for a singularly perturbed schrödinger equation. *International Journal of Computer Mathematics*, pages 1–12, 2015.
- [4] R. Anguelov and J. M-S Lubuma. Nonstandard finite difference method by nonlocal approximation. *Mathematics and Computers in simulation*, 61(3):465–475, 2003.
- [5] R. Anguelov, J. M-S Lubuma, and M. Shillor. Topological dynamic consistency of nonstandard finite difference schemes for dynamical systems. *Journal of Difference Equations and Applications*, 17(12):1769–1791, 2011.
- [6] C. Börgers and A. R Nectow. Exponential time differencing for Hodgkin–Huxley-like ODEs. *SIAM Journal on Scientific Computing*, 35(3):B623–B643, 2013.
- [7] M. Chapwanya, J. M-S. Lubuma, and R. E. Mickens. Positivity-preserving nonstandard finite difference schemes for cross-diffusion equations in biosciences. *Computers & Mathematics with Applications*, 68(9):1071–1082, 2014.
- [8] D. T. Dimitrov and H. V. Kojouharov. Positive and elementary stable nonstandard numerical methods with applications to predator–prey models. *Journal of Computational and Applied Mathematics*, 189(1):98–108, 2006.
- [9] R. Fitzhugh. Thresholds and plateaus in the hodgkin-huxley nerve equations. *The Journal of General Physiology*, 43(5):867–896, 1960.
- [10] M. Hanslien, K. H. Karlsen, and A. Tveito. A maximum principle for an explicit finite difference scheme approximating the hodgkin-huxley model. *BIT Numerical Mathematics*, 45(4): 725–741, 2005.

- [11] M. Hanslien, J. Sundnes, and A. Tveito. An unconditionally stable numerical method for the Luo–Rudy 1 model used in simulations of defibrillation. *Mathematical biosciences*, 208(2): 375–392, 2007.
- [12] A. L. Hodgkin and A. F. Huxley. A quantitative description of membrane current and its application to conduction and excitation in nerve. *The Journal of physiology*, 117(4):500, 1952.
- [13] A. L. Hodgkin and A. F. Huxley. A quantitative description of membrane current and its application to conduction and excitation in nerve. *Bulletin of Mathematical Biology*, 52(1-2): 25–71, 1990.
- [14] W. M. Kistler, W. Gerstner, and J. L. van Hemmen. Reduction of the hodgkin-huxley equations to a single-variable threshold model. *Neural Computation*, 9(5):1015–1045, 1997.
- [15] J. M-S. Lubuma and K. C. Patidar. Solving singularly perturbed advection–reaction equations via non-standard finite difference methods. *Mathematical Methods in the Applied Sciences*, 30(14):1627–1637, 2007.
- [16] M. Mascagni. An initial-boundary value problem of physiological significance for equations of nerve conduction. *Communications on Pure and Applied Mathematics*, 42(2):213–227, 1989.
- [17] M. Mascagni. The backward euler method for numerical solution of the hodgkin-huxley equations of nerve conduction. *SIAM Journal on Numerical Analysis*, 27(4):941–962, 1990.
- [18] R. E Mickens. *Nonstandard finite difference models of differential equations*. World Scientific, 1994.