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ON THE APPLICABILITY OF THE ASHOUR-HANNA NUMERICAL ALGORITHM FOR THE INVESTIGATION OF DIFFUSION-REACTION EQUATIONS

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Abstract

A specific type of nonlinear parabolic partial differential equations (the diffusion-reaction equations) describes the phenomena of wave propagation in excitable media. The application of the method of lines technique reduces the problem to the simultaneous solution of a system of ordinary differential equations on a chosen time interval for each node of the space grid. A novel explicit method for the numerical integration of mildly stiff ordinary differential equations was recently proposed by Ashour and Hanna. Our investigation of the applicability of this method to very stiff ordinary differential equations such as the simplified FitzHugh-Nagumo (FN) equations shows that it is possible to save approximately 60% of computer time, while keeping the desired relative error of the relaxation parameter $\delta\rho < 1\%$. The optimal values of the integration step h and the averaging parameter α are $h = 0.08$, and $\alpha = 0.36$ respectively. The sensitivity of these values to parameter changes of the FN equations shows that FN parameter changes less then 15% do not significantly affect the appearance of spurious oscillations in solution, and therefore the values of h and α may remain unchanged. We conclude that the new Ashour-Hanna method may be successfully used for solving the highly stiff FitzHugh-Nagumo equations.

INTRODUCTION

The class of nonlinear parabolic partial differential equations which are known as diffusion–reaction equations describe the phenomena of wave propagation in excitable media (Tyson and Keener [1]). Excitable media arise in biological systems, chemical processes and in variety of other application areas. The complex character of nonlinearities, the great diversity of the time constants of different variables (which introduces the stiffness of ordinary differential equations (ODE) to which the original problem is reduced), and the necessity to obtain a solution in time and space (often three dimensional) tends to make the solution of these problems excessively time consuming even for modern super computers and massively parallel computer systems. In our previous work (Kogan et.al [2]) we used a special modification of the method of lines which allows one to reduce the overall time of data exchange in a massively parallel computer system. Thus the main component of consumed computer time is the time needed for the numerical integration of the stiff ODE's. Numerical integration algorithms with variable integration step size are not suitable for parallel computations, because the difficulty of synchronizing data exchange between the computing elements. The only alternative is to use the well-known fixed step explicit or implicit methods. The comparison (Victorri et.al [3]) of explicit and implicit methods of numerical integration shows that explicit methods have some advantages in cost per step and required storage in the computer memory. Therefore, most of the computer simulations of wave propagation have been carried out using the explicit Euler first order method or the Runge–Kutta second order method with a comparatively small step size ($h = 0.01$ and $h = 0.02$ respectively). Recently Ashour and Hanna [4] (AH) developed a hybrid method for the solution of moderate and mildly stiff ODE's. This method is based on the average of the Euler and Runge–Kutta 2 solutions at each step of integration. The present investigation was undertaken to determine the possibility of applying the AH method to the solution of highly stiff ODE's such as diffusion-reaction equations. As an example, we consider the simplified FN equations, which approximate the generation of action potential in heart muscle cells (see Kogan et.al.[5]). The AH method is compared to alternative numerical algorithms with respect to: the permissible integration step size by which the amplitude of spurious oscillations in the solution is less than 0.1%, the sensitivity to parameters changes of FN equations, the relative error in relaxation parameter ρ (see Zykov[6]), and the overall time needed for the computation of one cardiac cycle.

THE FITZHUGH-NAGUMO SIMPLIFIED EQUATIONS

The basic FN simplified equations when reduced to dimensionless form [7] are:

$$\frac{\partial E}{\partial t} = \Delta E + F(E) - I + I_{stim} \tag{1}$$

$$\frac{\partial I}{\partial t} = \varepsilon(E)[f(E) - I] \tag{2}$$

E – fast variable (membrane potential displacement between the interior and exterior of the cell)

I – slow variable (generalized outward current)

$\Delta = \partial^2/\partial x^2 + \partial^2/\partial y^2$ – two dimensional Laplacian operator

$F(E)$ – current-voltage characteristic of the fast inward current

$f(E)$ – current-voltage characteristic of slow outward current

$\varepsilon(E)$ – small parameter (inversely proportional to the time constant of the slow outward current)

The initial and boundary conditions used in the simulation are:

$$E(x, y, 0) = I(x, y, 0) = 0; \frac{\partial E}{\partial x} \mid_B = \frac{\partial E}{\partial y} \mid_B = 0 \tag{3}$$

The piece-wise linear approximation of the functions $F(E)$, $f(E)$, and $\varepsilon(E)$ is shown on Fig.1.

The widely used set of parameters is: $G_s = 1$; $G_f = 1$; $G_r = 30$; $E_{th} = 0.16$

$$\varepsilon = \begin{cases} \varepsilon_1 & \text{if } E < 0.01 \text{ and } dI/dt > 0 \\ \varepsilon_2 & \text{if } E \geq 0.01 \text{ and } dI/dt > 0 \\ \varepsilon_3 & \text{if } I > I_{min} \text{ and } dI/dt \leq 0 \\ \varepsilon_4 = k\varepsilon_2 & \text{otherwise,} \end{cases} \tag{4}$$

where ε_4 determines the action potential duration restitution properties (Kogan et.al [5]).

We define an *action potential* as the time course of membrane potential E which is above the threshold potential E_{th}. The action potential is initiated by overtreshold stimulation and formed by the activation and inactivation of inward and outward currents. This mathematical model reflects qualitatively the essential properties of heart muscle cells.

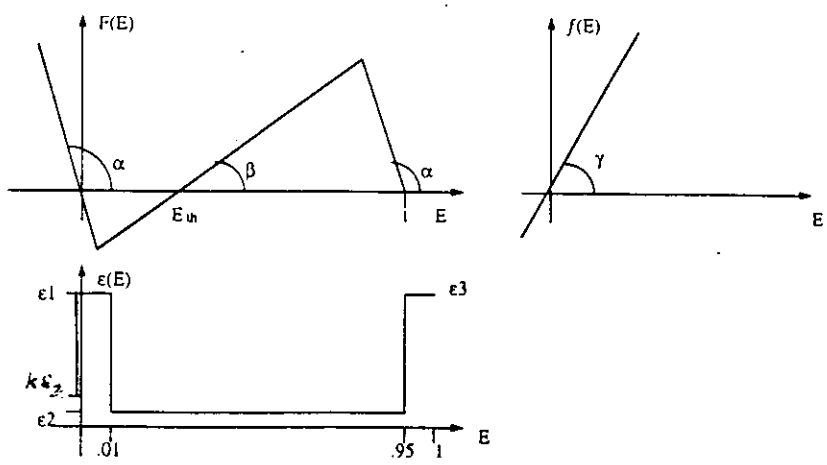

FIG. 1. The piece-wise linear approximation of functions $F(E)$, $f(E)$, and $\varepsilon(E)$. $\tan\alpha = G_r$; $\tan\beta = G_f$; $\tan\gamma = G_s$; E_{th} – the threshold potential.

THE ASHOUR - HANNA METHOD

The classical explicit integration methods (such as Euler and Runge-Kutta) have very limited stability regions. Since the integration step size is restricted mainly by stability rather than by truncation error consideration, these methods tends to become extremely inefficient (Aiken [8]). More efficient implicit methods allowing use of a much larger step size, such as implicit Runge-Kutta and backward differentiation methods, are used to perform the integration for moderately and mildly stiff problems. These methods, however, require more storage and take more computation time per step.

Recently Ashour and Hanna [4] proposed a new simple explicit method for the integration of mildly stiff ODE's. Consider system of ODE's

$$y' = f(t, y) \tag{5}$$

with initial condition

$$y(t_0) = y_0. \tag{6}$$

Using the Ashour-Hanna method, starting from a specified or previously determined $y(t)$ we first

carry out a single step using the first-order explicit Euler method:

$$y_{Euler}(t+h) = y(t) + hf[t, y(t)]. \tag{7}$$

Then we carry out a single step using the second-order explicit Runge-Kutta-Trapezoidal method starting from the $y(t)$:

$$y_{RK2T}(t+h) = y(t) + (h/2) \times \{f[t, y(t)] + f[t+h, y_{Euler}(t+h)]\}. \tag{8}$$

Finally, we average the Euler and RK2T values to obtain the new value as follows:

$$y(t+h) = \alpha y_{Euler}(t+h) + (1-\alpha) y_{RK2T}(t+h) \tag{9}$$

$$= y(t) + (h/2)\{(1+\alpha) f[t, y(t)] + (1-\alpha) f[t+h, y_{Euler}(t+h)]\}, \tag{10}$$

where α is an averaging parameter, $0 < \alpha < 1$. When $\alpha = 0$, the AH algorithm is reduced to the second order RK2T; when $\alpha = 1$, it is reduced to the first-order Euler method. The parameter α is chosen so as to minimize spurious oscillations in the solution and maximize the permissible integration step size.

RESULTS

Analysis of applicability of the AH method is performed using the simplified FN equations (1)–(4) as an example of a highly stiff ODE. The term which describes propagation in equation (1) (the Laplacian, ΔE) was eliminated by making $\Delta E = 0$.

Usually the instability in the numerical computation is defined (Beckett et.al [9]) as appearance in computer solution an undamped oscillations or some other characteristic which the true solution should not have. For our problem it is important that the solution will be aperiodic without any oscillations. Therefore we choose the parameters of AH method α and h so as to eliminate any spurious oscillations of the calculated action potential. That is, a solution is considered suitable only if the derivative of the action potential changes its sign no more than twice during one action potential period. As a reference point, Fig.2a shows an action potential obtained using the Euler method with a very small time step, $h = 0.001$. This curve is considered ideal. Shown in Fig.2b is the action potential obtained using the Euler method with $h = 0.095$. This curve has oscillations and is considered unsuitable following comments from Moore et.al [10].

The region of parameters α and h with the AH method which provides nonoscillatory solution for FN equations with basic parameters is presented in Fig.3. We varied the most important parameters

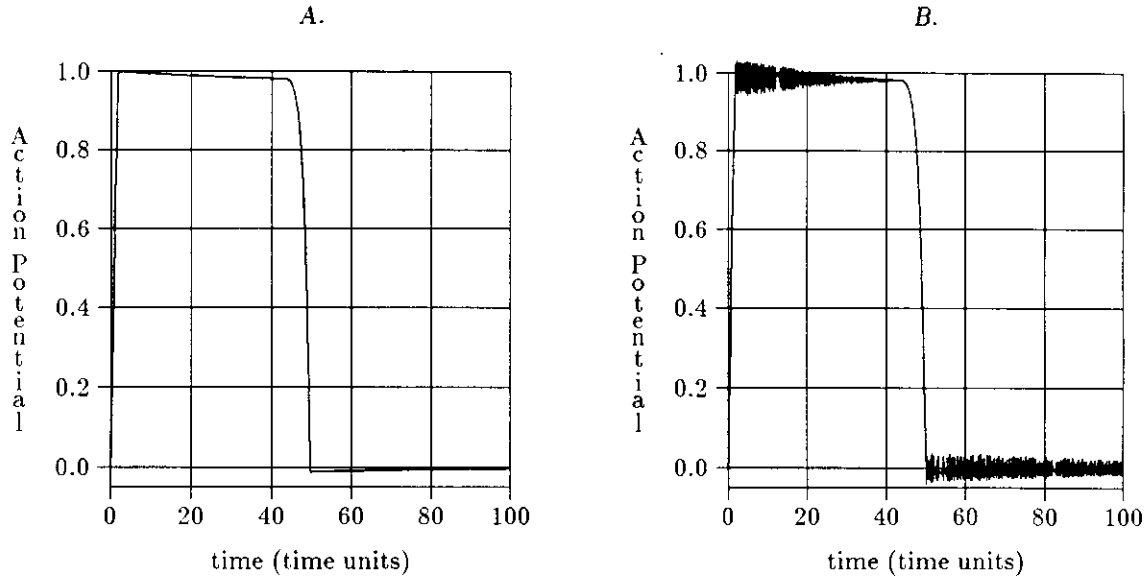

FIG. 2. Action potential generation by Euler method. A. $h = 0.001$, without spurious oscillations. B. $h = 0.095$, with spurious oscillations.

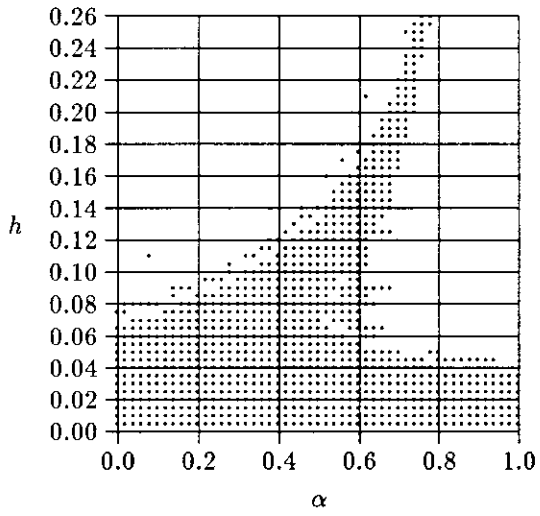

FIG. 3. Nonoscillation region (shown by dots) for AH method. Problem parameters: $G_r = 30.0$, $G_f = 0.7$, $\varepsilon_2 = 0.02$.

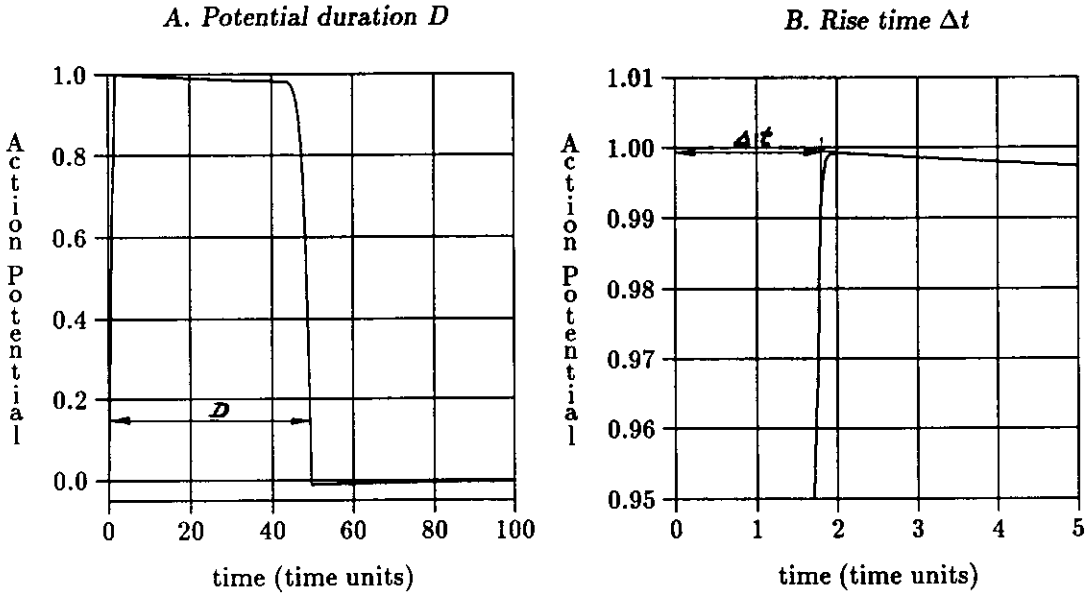

FIG. 4. Determination of relaxation parameter ρ.

of the system, including G_r, G_f and ε_2 by as much as 15% to identify how this region changes. The results are shown in Fig.5-Fig.7. We conclude that problem parameters changes have little influence on spurious oscillations.

To compare the considered methods, we estimate their relative error of the relaxation parameter ρ. This parameter is calculated as the ratio of the action potential duration D at the threshold level, and rise time Δt (Fig.4a). The rise time is determined as shown in Fig.4b, where the action potential is presented in large scale. We compared the ρ obtained in each calculation with ρ obtained by the Euler method with $h = 0.001$. In Table 1 the results are presented for Euler, RK2 and AH methods with the maximum integration time step which provides nonoscillatory solution. One can see from Table 1 that this maximum time step of integration does not provide maximum accuracy and that to get reasonable accuracy for each method it is necessary to decrease the corresponding integration time step. The results of calculation for the maximum integration time step corresponding to solution without spurious oscillations and relative error $\delta\rho < 1\%$ are shown in Table 2.

In Table 2 the times of calculation for each method are also presented. Although the time of calculation of one point of action potential increases from Euler to AH, the overall time of calculation is smaller for AH. This result is due to the larger permissible integration time step which leads to reducing the total number of integration steps for the calculation of an action potential. Since the AH method gives a large permissible value of h for the given permissible relative error $\delta\rho$ and a

Numerical algorithm	Parameters of algorithm		Number of steps	Time of calculation		Error %
	α	h		one point	total	
EUL	-	0.035	2857	1.743-03	4.98	2.45
RK2	-	0.065	1539	3.060-03	4.71	2.84
AH	0.75	0.250	400	4.450-03	1.78	18.59

Table 1. Time of calculation and relative error $\delta\rho$ obtained with maximum time step which provides absence of spurious oscillations.

Numerical algorithm	Parameters of algorithm		Number of steps	Time of calculation		Error %
	α	h		one point	total	
EUL	-	0.010	10000	1.743-03	17.18	0.92
RK2	-	0.018	5556	3.060-03	16.99	0.97
AH	0.36	0.081	1235	4.450-03	5.50	0.93

Table 2. Time of calculation and numerical algorithm parameters for relative error $\delta\rho < 1\%$

shorter time of calculation it can be considered as more efficient.

CONCLUSION

All of the results show that the new AH method can be used not only to obtain the solution of mildly stiff ODE, but also of highly stiff ODE such as the FitzHugh-Nagumo equations. The AH is shown to be more efficient in solving the FN equations than the other explicit methods (Euler, RK2). This method gives the largest region of α and h without spurious oscillations in solution. This does not significantly change with variation in the parameters of the problem. Also, AH provides the required accuracy defined by the parameter ρ. Satisfying the same requirements, this method gives three times faster solution than Euler and RK2.

APPENDIX A. SENSITIVITY OF AH METHOD TO THE VARIATION OF PROBLEM PARAMETERS

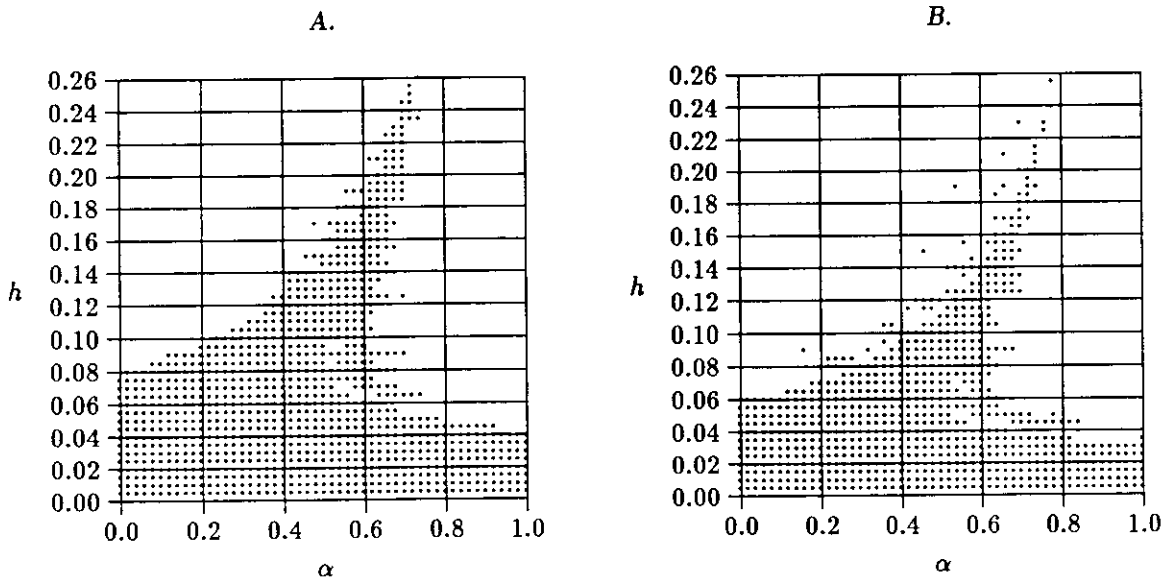

FIG. 5. Nonoscillation region for AH method. A. Problem parameters: $G_r = 24.0$, $G_f = 0.7$, $\varepsilon_2 = 0.02$. B. Problem parameters: $G_r = 36.0$, $G_f = 0.7$, $\varepsilon_2 = 0.02$.

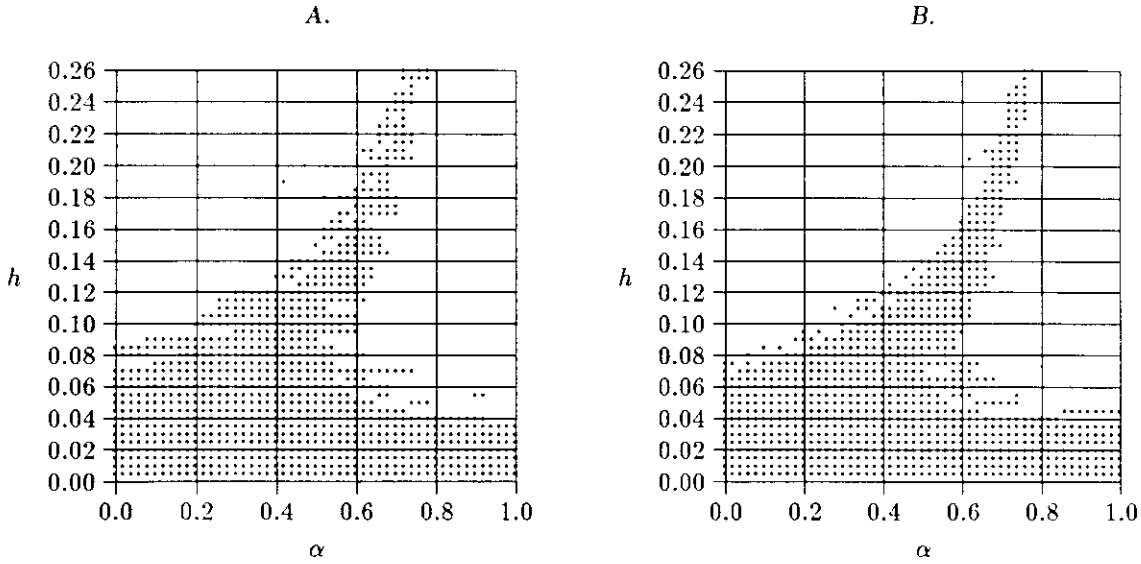

FIG. 6. Nonoscillation region for AH method. A. Problem parameters: $G_r = 30.0$, $G_f = 0.46$, $\varepsilon_2 = 0.02$. B. Problem parameters: $G_r = 30.0$, $G_f = 0.94$, $\varepsilon_2 = 0.02$.

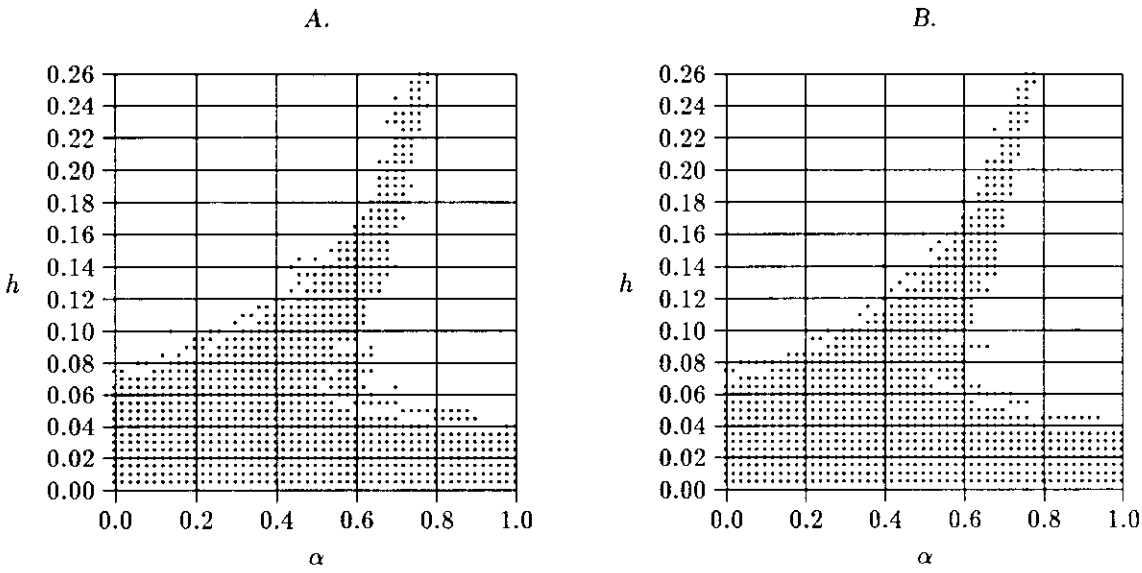

FIG. 7. Nonoscillation region for AH method. A. Problem parameters: $G_r = 30.0$, $G_f = 0.7$, $\varepsilon_2 = 0.012$. B. Problem parameters: $G_r = 30.0$, $G_f = 0.7$, $\varepsilon_2 = 0.028$.

APPENDIX B. PROGRAM FOR AH METHOD

```
/*****************************************************************/
/*  This file contains integration routines.                     */
/*****************************************************************/

#include "heart.h"

/*****************************************************************/
/*  Externs                                                      */
/*****************************************************************/

extern  float delta_t;

extern  float alpha;

extern  float E;
extern  float I;
extern  float SE;
extern  float SI;

extern  float fE();
extern  float fI();


/************************************************/
/* MK implementation of Ashour - Hanna algorithm */
/************************************************/

void ah()
{
float  newE;
```

```
float  newI;
float  newEeul;
float  newIeul;
float  newErk2;
float  newIrk2;


/* First: single step using Euler method */

newEeul = E + delta_t * fE( E, I );
newIeul = I + delta_t * fI( E, I, SE, SI );


/* Second: single step using Runge-Kutta-Trapezoidal */

newErk2 = E + 0.5 * delta_t *
          ( fE( E, I) + fE( newEeul, newIeul ) );
newIrk2 = I + 0.5 * delta_t * ( fI( E, I, SE, SI ) +
          fI( newEeul, newIeul, newEeul-E, newIeul-I ) );


/* Third: average Euler and RK2T to obtain new value */

newE = alpha * newEeul + ( 1 - alpha ) * newErk2;
newI = alpha * newIeul + ( 1 - alpha ) * newIrk2;

SE   = newE - E;
E    = newE;
SI   = newI - I;
I    = newI;
}
```

REFERENCES

[1] J.J. Tyson and J.P. Keener. Singular perturbation theory of traveling waves in excitable media. *Physica D*, 32:327–361, 1988.

[2] B.Y. Kogan, W.J. Karplus, and A.T. Pang. Simulation of nonlinear distributed parameter systems on the connection machine. *Simulation*, 55:271–280, 1990.

[3] B. Victorri, A. Vinet, F.A. Roberge, and J.-P. Drouhard. Numerical integration in the reconstruction of cardiac action potentials using Hodgkin-Huxley-Type models. *Computers and Biomedical Research*, 18:10–23, 1985.

[4] S.S. Ashour and O.T. Hanna. A new very simple explicit method for the integration of mildly stiff ordinary differential equations. *Computers chem. Engng*, 14(3):267–272, 1990.

[5] B.Y. Kogan, W.J. Karplus, B.S. Billett, A.T. Pang, H.S. Karagueuzian, and Khan S.S. The simplified FitzHugh - Nagumo model with action potential duration restitution: Effects on 2-D wave propagation. *Physica D*, 50:327–340, 1991.

[6] V.S. Zykov. *Simulation of Wave Processes in Excitable Media.* Manchester University Press, 1987.

[7] A.M. Pertsov, R.N. Chramov, and A.V. Panfilov. Sharp increase in refractory period induced by oxidation suppression in FitzHugh-Nagumo model. new mechanism of anti-arrythmic drug action. *Biofizika*, 6, 1991 [in Russian].

[8] R.C. Aiken. (ed.). *Stiff computation*, 1985.

[9] R. Beckett and J. Hurt. Numerical calculations and algotithms. pages 215–217, 1967.

[10] J.W. Moore and F. Ramon. On numerical integration of the Hodgkin and Huxley equations for the membrane action potential. *J. theor Biol.*, 45:249–273, 1974.