

## MATHEMATICAL MODELLING

MSC 34A08

# MATHEMATICAL MODEL OF NERVE IMPULSE PROPAGATION WITH REGARD TO HEREDITY

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A mathematical model of FitzHugh-Nagumo nerve impulse propagation is proposed. It takes into account the effect of heredity. This hereditary model is described by an integro-differential equation with a power kernel, a function of memory. The algorithm for the numerical solution of this model is implemented in a computer program in Maple symbolic mathematics environment. With the help of this program, calculated curves, oscillograms, and phase trajectories were constructed depending on various values of control parameters.

*Keywords: heredity, FitzHugh-Nagumo model, finite-difference scheme.*

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## Introduction

Development of the theory of hereditary dynamic systems began from the paper of an Italian mathematician, Vito Volterra, [1], where he introduced the term of "heredity" to describe the sequence or memory effect and investigated a hereditary oscillator. Mathematical description of a hereditary oscillator is an integro-differential equation with a kernel which is called the memory function. Further investigations of hereditary dynamic systems were associated with the choice of memory function. Owing to the fact that different mediums can have fractal properties, it is reasonable to choose a power memory function. Then the integro-differential equations can be written as differential equations of fractional orders the theory of which is well developed [2]. In literature, such equations are called fractal ones. They describe the processes with partial memory loss. Fractal dynamic systems were studied the most completely in the monographs [3, 4].

The paper generalizes the FitzHugh-Nagumo dynamic system which was suggested in the paper R. FitzHugh [5] and J. Nagumo [6] to describe a nerve impulse propagation in membrane. A generalized mathematical model contains an equation with fractional derivatives in the sense of Gerasimov-Caputo and is solved by a finite-difference scheme. The main results of the paper are described in the article [7]. In this paper, with the help of computer experiments, we investigated the issues of stability and convergence of the finite-difference scheme realizing the numerical solution of the suggested scheme.

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### Problem statement and solution method

Based on the papers [5], [6], the classic nonlinear dynamic FitzHugh-Nagumo (FHN) system has the following form:

$$\begin{cases} \dot{x}(t) = c \cdot (y(t) - x(t) - \frac{x^3(t)}{3} + z), \\ \dot{y}(t) = -\frac{(x(t) - a + by(t))^3}{c}, \end{cases} \tag{1}$$

where  $a, b, c$  are the constants, satisfying the conditions  $1 - 2b/3 < a < 1, 0 < b < 1, b < c^2$ ,  $x(t)$  is the membrane potential,  $z$  is the stimulus intensity, a constant in the first approximation, which can have the form of a rectangular impulse or delta-function,  $t \in [0, T]$  is the process time,  $T > 0$  is the modeling time.

The dynamic system (1) can be written in the form of one equation

$$\ddot{x}(t) + c\dot{x}(t)(x^2(t) + p) + qx^3(t) - a - bz = 0, \tag{2}$$

where  $p = b/c^2 - 1, q = 1 - b, g = b/3$ . For equation (2) we specify the initial conditions ( $\eta, \varphi - const$ )

$$x(0) = \eta, \dot{x}(0) = \varphi. \tag{3}$$

Problem (2), (3) is the Cauchy problem the solution of which was studied in the paper [5].

In this paper we consider the generalization of Cauchy problem (2) and (3), introduce the heredity into it by the following integro-differential equation:

$$\int_0^t K_1(t - \tau)\ddot{x}(\tau)d\tau - c(x^2(t) + p) \int_0^t K_2(t - \tau)\dot{x}(\tau)d\tau + qx(t) + gx^3(t) - a - bz = 0, \tag{4}$$

where  $K_1(t - \tau)$  and  $K_2(t - \tau)$  are memory functions characterizing the heredity.

**Remark.** We should note that if the memory functions are delta-functions then the heredity is absent in the system. If the memory functions are the Heaviside functions, the system has total memory.

The third variant is of interest. When the memory functions are power functions, for example,

$$K_1(t - \tau) = \frac{(t - \tau)^{1-\alpha}}{\Gamma(2 - \alpha)}, \quad K_2(t - \tau) = \frac{(t - \tau)^{-\beta}}{\Gamma(1 - \beta)}, \quad 1 < \alpha < 2, 0 < \beta < 1, \tag{5}$$

where  $\Gamma(t)$  is the Eulerian gamma-function, than the system has partial "memory loss"[2].

Further, we shall investigate hereditary processes with partial "memory loss". Substitute memory functions (5) into the integro-differential equation (4). In the result we obtain

$$\frac{1}{\Gamma(2 - \alpha)} \int_0^t \frac{\ddot{x}(\tau)d\tau}{(t - \tau)^{\alpha-1}} - \frac{c(x^2(t) + p)}{\Gamma(1 - \beta)} \int_0^t \frac{\dot{x}(\tau)d\tau}{(t - \tau)^\beta} + qx(t) + gx^3(t) - a - bz = 0. \tag{6}$$

We have obtained integro-differential equation of a special form. Memory functions (5) in integro-differential equation (6) can differ from power functions that causes other integro-differential equations. If we turn to the definition of a Gerasimov-Caputo fractional derivative, we come to the equation

$$\partial_{0^+}^\alpha x(\tau) - c(x^2(t) + p)\partial_{0^+}^\beta x(\tau) + qx(t) + gx^3(t) - a - bz = 0, \tag{7}$$

where fractional differential operators are

$$\partial_{0^+}^\alpha x(\tau) = \frac{1}{\Gamma(2 - \alpha)} \int_0^t \frac{\ddot{x}(\tau)d\tau}{(t - \tau)^{\alpha-1}}, \quad \partial_{0^+}^\beta x(\tau) = \frac{1}{\Gamma(1 - \beta)} \int_0^t \frac{\dot{x}(\tau)d\tau}{(t - \tau)^\beta},$$

determined in the sense of Gerasimov-Caputo with fractional orders  $1 < \alpha < 2, 0 < \beta < 1$ .

We can note that in the limiting case, equation (7) transfers into the FHN classical equation (2), thus we can consider equation (2) to be a partial case of equation (7). We should note that equation (7) contains cubic nonlinearity characteristic for Duffing [8] and Van der Pol [9] oscillators.

The FHN integro-differential equation (7) will be called a fractional or a fractal equation and the process describing it is a fractal or a hereditary process.

The Cauchy problem (7) and (3) in the general form does not have an exact solution owing to the fact that the model equation is nonlinear, so numerical methods should be applied for its solution. We use the finite-difference scheme as a numerical method because it can be easily realized in any computer environment.

We consider a uniform grid. To do that, we divide the time interval  $[0, T]$  into  $N$  equal parts. In the result we obtain a uniform grid  $t_j = j\tau$ , where the step is  $\tau = T/N$ ,  $j = 0, \dots, N - 1$ . The required function value is  $x(t_j) = x_j$ , we call it a grid function. Approximation of fractional operators of equation (7) is performed as follows [3, 10]:

$$\begin{aligned} \partial_{0^+}^\alpha x(\tau) &\approx \frac{\tau^{-\alpha}}{\Gamma(3-\alpha)} \cdot \sum_{j=0}^{k-1} a_j \cdot (x_{k-j+1} - 2x_{k-j} + x_{k-j-1}), \quad a_j = (j+1)^{2-\alpha} - j^{2-\alpha}, \\ \partial_{0^+}^\beta x(\tau) &\approx \frac{\tau^{-\beta}}{\Gamma(2-\beta)} \cdot \sum_{j=0}^{k-1} b_j \cdot (x_{k-j+1} - x_{k-j}), \quad b_j = (j+1)^{1-\beta} - j^{1-\beta}. \end{aligned}$$

Substitute these approximations into the model equation (7). Now we come to the following finite-difference scheme:

$$\left\{ \begin{aligned} &x_1 = \varphi + \tau\eta, \quad k = 0, \\ &x_2 = \frac{1}{A + Bc(x_1^2 + p)} ((2A + Bc(x_1^2 + p) - q) \cdot x_1 - x_1^3 g - Ax_0 + a + bz), \quad k = 1, \\ &x_{k+1} = \frac{1}{A + Bc(x_k^2 + p)} ((2A + Bc(x_k^2 + p) - q) \cdot x_k - x_k^3 g - Ax_{k-1} + a + bz - \\ &\quad - Bc(x_k^2 + p) \cdot \sum_{j=1}^{k-1} (b_j(x_{k+1} - x_k)) - A \cdot \sum_{j=1}^{k-1} (a_j(x_{k+1} - 2x_k + x_{k-1}))), \\ &A = \frac{\tau^{-\alpha}}{\Gamma(3-\alpha)}, \quad B = \frac{\tau^{-\beta}}{\Gamma(2-\beta)}, \quad k = 2, \dots, n-1. \end{aligned} \right. \quad (8)$$

**Remark.** We should note that, as a rule, nonlinear dynamic systems are rigid for large values of control parameters that results in the necessity to decrease the sampling rate in the finite-difference scheme. In our case, owing to the boundedness of the parameters  $a, b, c$ , there is no rigidity, thus, we do not need to decrease the rate.

## Modeling results and discussion

The finite-difference scheme (8) was implemented in a software, in symbolic mathematics environment Maple. We consider the application of the finite-difference scheme (8) of the Cauchy problem (2) and (3) numerical solution. The parameter  $a, b, c$  values were taken from the paper [5]. First we consider the case when first the fractional parameter  $\alpha$  and  $\beta$  values change and then the values of the parameter  $z$ . We also study the finite-difference scheme (8) by the method of double calculation on its convergence and show the stability of the initial data and the right part.

**FOREXAMPLE 1.** The control parameters in the Cauchy problem (2) and (3) are  $t \in [0, T], T = 100, N = 2000, \tau = 0.05, a = 0.7, b = 0.8, z = -0.4, c = 3, x(0) = 0.2, \dot{x}(0) = 0.1$  The modeling results are shown in Fig. ??.

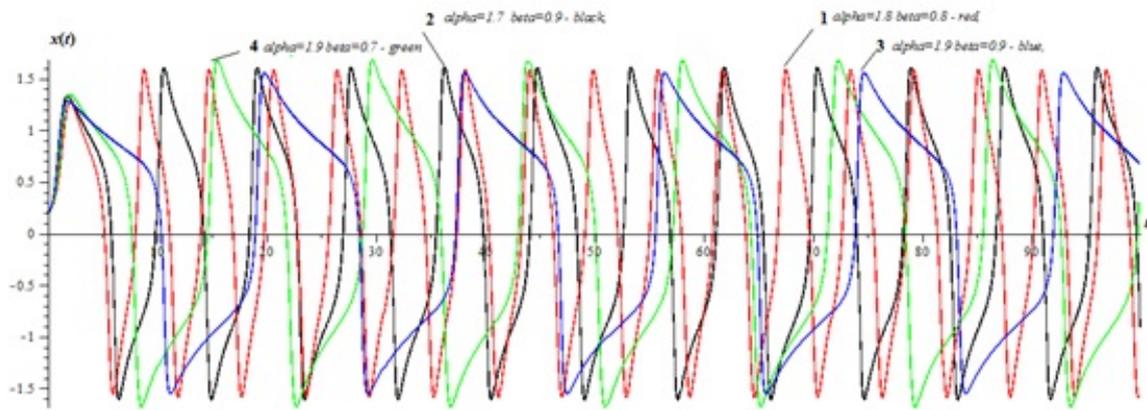


Fig. 1. Oscillograms obtained from the finite-differential scheme (8) for the parameters  $\alpha$  and  $\beta$ : curve 1 -  $\alpha = 1.8, \beta = 0.8$ , curve 2 -  $\alpha = 1.7, \beta = 0.9$ , curve 3 -  $\alpha = 1.9, \beta = 0.9$ , curve 4 -  $\alpha = 1.9, \beta = 0.7$

Fig. 1 illustrates the oscillograms obtained by the scheme (8) for different values of  $\alpha$  and  $\beta$ . The oscillogram 3 is similar in form to the oscillogram from the paper [5]. When the values of  $\alpha$  and  $\beta$  decrease, the oscillogram form changes (oscillation periodicity shifts), however, the oscillation amplitude is constant that corresponds to the limit cycles on the phase plane (Fig. 2).

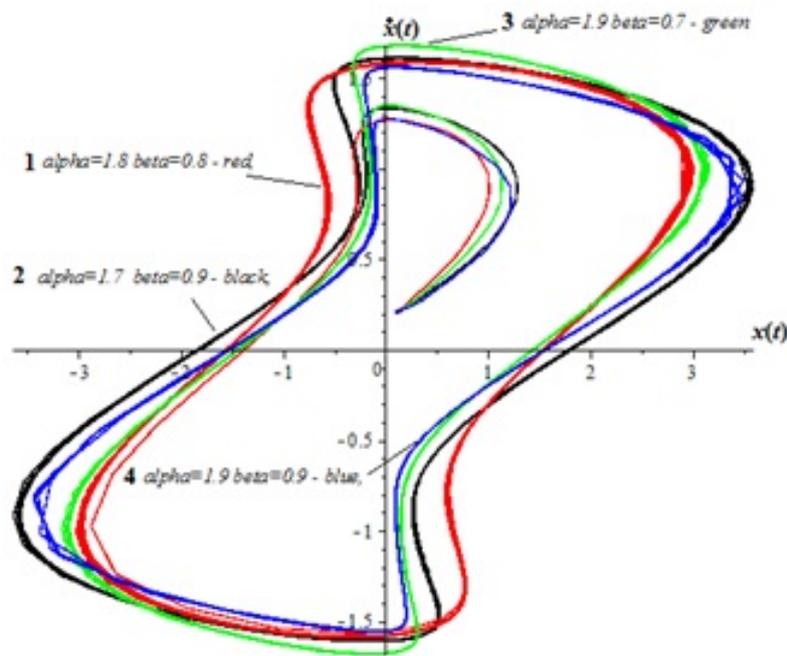


Fig. 2. Phase trajectories

We study the finite-differential scheme (8) on the convergence by the method of double calculation (Runge rule) for different values of the parameters  $\alpha$  and  $\beta$ . Due to the fact that equation (7) approximation has the first order, to calculate the absolute error  $\varepsilon$ , we can apply the following formula:

$$\varepsilon = \max(|x_i - x_{2i}|), i = 1, \dots, N,$$

where  $x_i$  is the numerical solution obtained by the scheme (8) at the step  $\tau$ ,  $x_{2i}$  is a numerical solution obtained by the scheme (8) at the step  $\tau/2$ .

To estimate the designed accuracy we can apply the relation

$$p = \ln(|\varepsilon|) / \ln(\tau/2).$$

The results are shown in Table 1.

Table 7

| <b>Study of scheme (8) for different values of <math>\alpha</math> and <math>\beta</math></b> |        |                |                    |
|---|--------|----------------|--------------------|
| <b><math>\alpha = 1,8</math> and <math>\beta = 0,8</math></b>                                 |        |                |                    |
| N   | $\tau$ | Absolute error | Desined accuracy p |
| 10  | 1/10   | 0.0456         | 1.0307             |
| 20  | 1/20   | 0.0262         | 0.9868             |
| 40  | 1/40   | 0.0141         | 0.9724             |
| 80  | 1/80   | 0.0073         | 0.9688             |
| 160   | 1/160  | 0.0037         | 0.9691             |
| 320   | 1/320  | 0.0019         | 0.9707             |
| <b><math>\alpha = 1.7</math> and <math>\beta = 0.9</math></b>                                 |        |                |                    |
| N   | $\tau$ | Absolute error | Desined accuracy p |
| 10  | 1/10   | 0.0591         | 0.9443             |
| 20  | 1/20   | 0.0324         | 0.9301             |
| 40  | 1/40   | 0.0171         | 0.9286             |
| 80  | 1/80   | 0.0088         | 0.9319             |
| 160   | 1/160  | 0.0045         | 0.9364             |
| 320   | 1/320  | 0.0023         | 0.9397             |
| <b><math>\alpha = 1.9</math> and <math>\beta = 0.9</math></b>                                 |        |                |                    |
| N   | $\tau$ | Absolute error | Desined accuracy p |
| 10  | 1/10   | 0.0436         | 1.0457             |
| 20  | 1/20   | 0.0249         | 1.0003             |
| 40  | 1/40   | 0.0134         | 0.9847             |
| 80  | 1/80   | 0.0069         | 0.9799             |
| 160   | 1/160  | 0.0035         | 0.9790             |
| 320   | 1/320  | 0.0018         | 0.9805             |
| <b><math>\alpha = 1.9</math> and <math>\beta = 0.7</math></b>                                 |        |                |                    |
| N   | $\tau$ | Absolute error | Desined accuracy p |
| 10  | 1/10   | 0.0346         | 1.1221             |
| 20  | 1/20   | 0.0202         | 1.0575             |
| 40  | 1/40   | 0.0108         | 1.0313             |
| 80  | 1/80   | 0.0056         | 1.0196             |
| 160   | 1/160  | 0.0028         | 1.0138             |
| 320   | 1/320  | 0.0014         | 1.0119             |

From Table 1 we can conclude that when the step  $\tau$  decreases, the absolute error  $\varepsilon$  decreases and the designed accuracy order is close to a unit. Such experimental convergence does not guarantee the convergence to the real function of the Cauchy problem (2) and (3) solution. Thus, we need to prove the theorem of convergence.

FOREXAMPLE 2. We consider another case. We fix the values of  $\alpha$  and  $\beta$ , and shall change the values of  $z$  with the following parameter values:  $t \in [0, T], T = 100, N = 2000, \tau = 0.05, a =$

$0.7, b = 0.8, z = -0.4, c = 3, x(0) = 0.2, \dot{x}(0) = 0.1, \alpha = 1.8, \beta = 0.8$  and different values of  $z$ . Fig. ?? illustrates the oscillograms for this case.

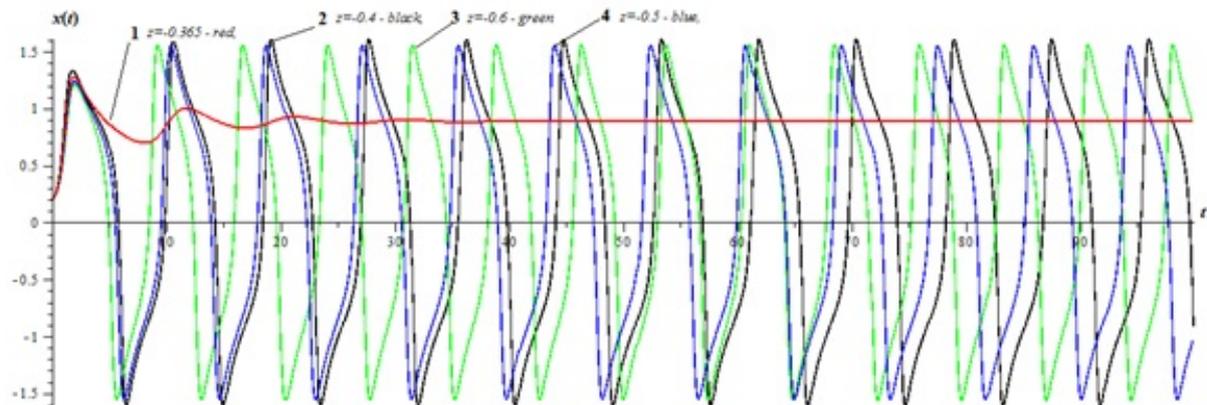


Fig. 3. Oscillograms obtained by the finite-differential scheme (8): curve 1 -  $z = -0.365$ , curve 2 -  $z = -0.4$ , curve 3 -  $z = -0.6$ , curve 4 -  $z = -0.5$

In case  $z = -0.365$  (curve 1) we see that oscillations attenuate and the phase trajectory (Fig. 4) has a curly form. When the parameter  $z$  decreases, oscillograms shift with constant amplitude that provides phase trajectory entrance to the limit cycle (Fig. 4).

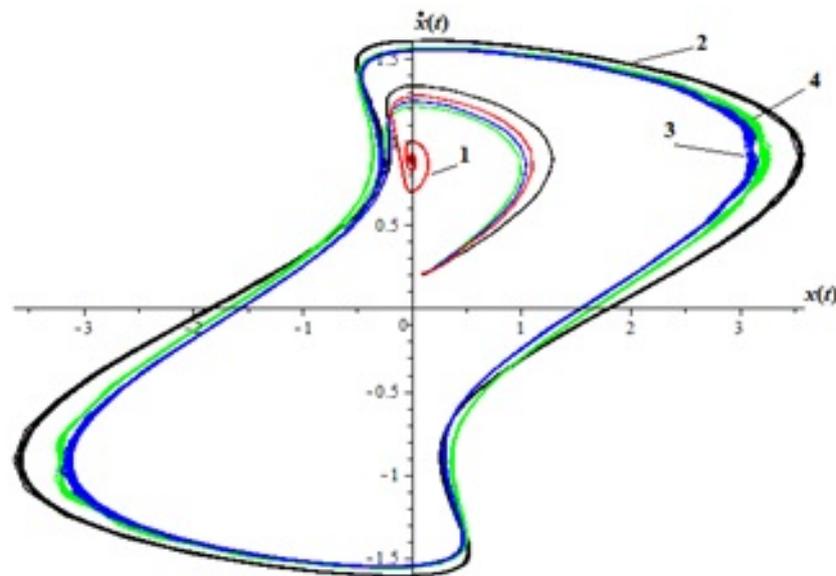


Fig. 4. Phase trajectories: curve 1 -  $z = -0.365$ , curve 2 -  $z = -0.4$ , curve 3 -  $z = -0.6$ , curve 4 -  $z = -0.5$

We study the convergence of the finite-difference scheme (8) depending on parameter  $z$  value. To do that, we apply the method from the previous example. The results are shown in Table 2.

As we see, similar to the previous example, when the step  $\tau$  decreases, the absolute error decreases  $\epsilon$ , and the designed accuracy order tends to a unit.

On an example, we consider the stability of the finite-difference scheme in the initial data and the right part for the following values of the control parameters:  $T = 1, N = 683, c = 3, a_0 = 0.7, z = -0.4, b_0 = 0.8, \alpha = 1.8, \beta = 0.8, x(0) = \dot{x}(0) = 0.2$ . In order to do that, we add a small quantity  $\epsilon = 10^{-5}$  into the initial condition  $x(0)$ , and then to the right part of equation (7).

Table 8

**Study of scheme (8) for different  $z$  values**

| $z = -0,365$ |        |                |                |
|--------------|--------|----------------|----------------|
| N            | $\tau$ | Absolute error | Accuracy order |
| 10           | 1/10   | 0.0482         | 1.0117         |
| 20           | 1/20   | 0.0278         | 0.9710         |
| 40           | 1/40   | 0.0149         | 0.9588         |
| 80           | 1/80   | 0.0077         | 0.9570         |
| 160          | 1/160  | 0.0039         | 0.9587         |
| 320          | 1/320  | 0.0020         | 0.9615         |
| $z = -0,4$   |        |                |                |
| N            | $\tau$ | Absolute error | Accuracy order |
| 10           | 1/10   | 0.0456         | 1.0307         |
| 20           | 1/20   | 0.0262         | 0.9868         |
| 40           | 1/40   | 0.0141         | 0.9724         |
| 80           | 1/80   | 0.0073         | 0.9688         |
| 160          | 1/160  | 0.0037         | 0.9691         |
| 320          | 1/320  | 0.0019         | 0.9707         |
| $z = -0,5$   |        |                |                |
| N            | $\tau$ | Absolute error | Accuracy order |
| 10           | 1/10   | 0.03775        | 1.0938         |
| 20           | 1/20   | 0.02163        | 1.0391         |
| 40           | 1/40   | 0.0116         | 1.0170         |
| 80           | 1/80   | 0.0060         | 1.0074         |
| 160          | 1/160  | 0.0030         | 1.0031         |
| 320          | 1/320  | 0.0015         | 1.0009         |
| $z = -0,6$   |        |                |                |
| N            | $\tau$ | Absolute error | Accuracy order |
| 10           | 1/10   | 0.0295         | 1.1759         |
| 20           | 1/20   | 0.0168         | 1.1067         |
| 40           | 1/40   | 0.0090         | 1.0742         |
| 80           | 1/80   | 0.0046         | 1.0567         |
| 160          | 1/160  | 0.0023         | 1.0462         |
| 320          | 1/320  | 0.0012         | 1.0393         |

Stability in the initial data or the right part is determined by a small change in the solution of the Cauchy problem (2) and (3) by an order of  $\varepsilon$ . In the opposite case, the solution of the Cauchy problem (2) and (3) is unstable. The study results are illustrated in Table 3.

It is clear from Table 3 that there is stability in the initial data and in the right part for this example, as long as the difference  $\delta$  between perturbed and unperturbed solutions has the order of  $\varepsilon$ . Of course, for a more complete picture, we need to prove the theorem on the stability of a finite-difference scheme (8). However, we have shown in the paper that the finite-difference scheme (8) can be applied to solve the Cauchy problem (2) and (3).

Table 9

**Stability in the initial data and the right part for scheme (8)**

| $x(0) + \varepsilon$ |                 |               |              |
|----------------------|-----------------|---------------|--------------|
| $\tau$               | $\varepsilon_0$ | $\varepsilon$ | $\delta$     |
| <b>1/500</b>         | 0.0000100193    | 0.0000100000  | 0.0000000193 |
| <b>1/530</b>         | 0.0000100380    | 0.0000100000  | 0.0000000380 |
| <b>1/600</b>         | 0.0000100543    | 0.0000100000  | 0.0000000543 |
| <b>1/685</b>         | 0.0000100608    | 0.0000100000  | 0.0000000608 |
| <b>1/720</b>         | 0.0000101316    | 0.0000100000  | 0.0000001316 |
| $f + \varepsilon$    |                 |               |              |
| $\tau$               | $\varepsilon_0$ | $\varepsilon$ | $\delta$     |
| <b>1/500</b>         | 0.0000144736    | 0.0000100000  | 0.0000044736 |
| <b>1/530</b>         | 0.0000128115    | 0.0000100000  | 0.0000028115 |
| <b>1/600</b>         | 0.0000122548    | 0.0000100000  | 0.0000022548 |
| <b>1/685</b>         | 0.0000102220    | 0.0000100000  | 0.0000002220 |
| <b>1/720</b>         | 0.0000101831    | 0.0000100000  | 0.0000001831 |

**Conclusions**

In the paper we suggested and studied the hereditary nonlinear FitzHugh-Nagumo oscillator. Based on the theory of finite-difference schemes, we numerically solved the Cauchy problem, plotted oscillograms and phase trajectories. It was shown that the parameters  $\alpha$  and  $\beta$  cause oscillation shift but the amplitude remains constant and the phase trajectory form changes entering the limit cycle. When parameter  $z$  changes, oscillations may attenuate and phase trajectory turns to be a stable focus for a corresponding stationary point.

Introduction of additional control parameters  $\alpha$  and  $\beta$  to model the oscillation regime in a flexible manner, gives additional signal parameterization. Further interest in the study of hereditary FitzHugh-Nagumo oscillator can be the investigation of stationary points on stability similar to the paper [9] as well as further generalization involving functions and [11]. Other direction of the study is associated with qualitative properties of the finite-differential scheme (8), stability and convergence [10].

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