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NUMERICAL SOLUTION METHOD FOR THE INVERSE PROBLEM OF THE MODIFIED FITZHUGH–NAGUMO MODEL

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The article considers a modified FitzHugh–Nagumo model that may be applied to model processes associated with myocardial infarct analysis. The inverse problem for this model involves finding the coefficient of a system of partial differential equations dependent on the spatial variables and the solution from supplementary observations of the solution on the boundary. This inverse problem may be interpreted as determining the shape and the location of the region of the heart damaged by myocardial infarct. A numerical method is proposed for the solution of the inverse problem and some computer experiments illustrating its implementation are reported.

Keywords: FitzHugh–Nagumo mathematical model, inverse problem, numerical methods.

Introduction

Mathematical modeling methods are actively applied in cardiology, in particular for the analysis of heart excitation processes. The propagation of electromagnetic excitation in the heart is described by initial boundary-value problems for systems of evolutionary quasi-linear partial differential equations in two- or three-dimensional spatial geometry. The best known mathematical models describing the excitation of electric potentials in the cardiac muscle or the nerve system include the FitzHugh–Nagumo model [1, 2] and the Aliev–Panfilov model [3]. Inverse problems and their numerical solution methods play an important role in the development of mathematical diagnosis techniques in cardiology. Inverse problems for mathematical models of cardiac excitation have been considered in [4–6].

In this article we focus on the modified FitzHugh–Nagumo mathematical model that can be used to model processes associated with myocardial infarct analysis. The inverse problem for this model involves determining the coefficient of a system of partial differential equations dependent on spatial variables from supplementary observations of the solution on the boundary. This inverse problem may be interpreted as determining the shape and the location of the region of the heart that has been damaged by myocardial infarct. A numerical method is proposed for the solution of the inverse problem and computer experiments illustrating its implementation are reported.

The Inverse Problem

Consider the FitzHugh–Nagumo mathematical model [1, 2]

$$u_t = D\Delta u - u(u-\alpha)(u-1) - w, \qquad (x, y) \in G, \quad t \in (0, T],$$

$$w_t = \beta u - \gamma w, \qquad (x, y) \in G, \quad t \in (0, T],$$

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$$\frac{\partial u}{\partial n}(x, y, t) = 0, \qquad (x, y) \in \Gamma, \quad t \in (0, T],$$

$$u(x, y, 0) = \varphi(x, y), \qquad (x, y) \in G,$$

$$w(x, y, 0) = 0, \qquad (x, y) \in G.$$

Here the function $u(x, y, t)$ is the transmembrane potential, the function $w(x, y, t)$ is the slow restoring variable associated with ion currents, $\varphi(x, y)$ is the initial potential perturbation, D is the electrical conductivity, α, β, γ are reactive coefficients (D, α, β, and γ are positive constants), G is a bounded region with the boundary Γ. This model is used to describe the propagation of an electromagnetic excitation in the myocardium, assuming homogeneity of the tissue characteristics responsible for current conduction and excitation of the medium.

Let us consider a modification of the FitzHugh–Nagumo model. Let $\chi(x, y) \in \mathbb{C}^1(G)$ be such that it takes values close to zero over most of the region $H \subset G$, and values close to 1 over most of the region $G \setminus \bar{H}$. In other words, the main changes of the function $\chi(x, y)$ occur near the boundary of the region H. The modified FitzHugh–Nagumo model has the form

$$u_t = D\Delta u - \chi(x, y)u(u - \alpha)(u - 1) - w, \qquad (x, y) \in G, \quad t \in (0, T], \tag{1}$$

$$w_t = \beta u - \gamma w, \qquad (x, y) \in G, \quad t \in (0, T], \tag{2}$$

$$\frac{\partial u}{\partial n}(x, y, t) = 0, \qquad (x, y) \in \Gamma, \quad t \in (0, T], \tag{3}$$

$$u(x, y, 0) = \varphi(x, y), \quad (x, y) \in G, \tag{4}$$

$$w(x, y, 0) = 0, \quad (x, y) \in G. \tag{5}$$

In the original FitzHugh–Nagumo model the nonlinear source $u(u - \alpha)(u - 1)$ determines the excitability of the medium. In the modified FitzHugh–Nagumo model the nonlinear source $\chi(x, y)u(u - \alpha)(u - 1)$ characterizes a medium capable of being excited in the region $G \setminus \bar{H}$ and incapable of being excited in the region H. Thus the mathematical model (1)–(5) may be applied to describe excitation processes in a heart where the region H has been damaged by myocardial infract. Such an approach for a different excitation model has been considered in [5].

We assume that the boundary of the region H is specified by n parameters $\lambda_1 \ldots \lambda_n$. Define the function $\chi(x, y; \lambda_1, \ldots, \lambda_n)$ as

$$\chi(x, y; \lambda_1, \ldots, \lambda_n) = \frac{1}{2} + \frac{1}{\pi}\arctan\left(\theta^2 g(x, y; \lambda_1, \ldots, \lambda_n)\right)$$

where $g(x, y; \lambda_1, \dots, \lambda_n)$ is a known function taking the values

$$g(x, y; \lambda_1, \dots, \lambda_n) < 0, \quad (x, y) \in H \quad \text{and} \quad g(x, y; \lambda_1, \dots, \lambda_n) > 0, \quad (x, y) \in G \setminus \bar{H},$$

θ is a given constant.

We can now state the inverse problem for the modified model (1)–(5). Assume that the function $g(x, y; \lambda_1, \dots, \lambda_n)$ defining the boundary of the region H is unknown. It is required to determine the boundary of the region H given the solutions of problem (1)–(5)

$$u_i(x, y, t) = \psi_i(x, y, t), \qquad (x, y) \in \Gamma, \quad t \in [0, T], \quad i = 1, \dots, k,$$

on the set $\Gamma \times [0, T]$, corresponding to different initial conditions $u_i(x, y, 0) = \varphi_i(x, y)$. The coefficients D, α, β, γ, θ and the functions $\varphi_i(x, y)$, $(x, y) \in G$, $i = 1, \dots, k$, are known.

Numerical Solution of the Inverse Problem

Let us consider a numerical method for solving the inverse problem. Let $u_i(x, y, t; \bar{\lambda}_1, \dots, \bar{\lambda}_n)$, $i = 1, \dots, k$, be the solutions of problem (1)–(5) corresponding to the initial conditions $\varphi_i(x, y)$, $i = 1, \dots, k$, and $\bar{\chi} = \chi(x, y; \bar{\lambda}_1, \dots, \bar{\lambda}_n)$. Denote by $\bar{\psi}_i(x, y, t)$, $i = 1, \dots, k$, the values of $u_i(x, y, t; \bar{\lambda}_1, \dots, \bar{\lambda}_n)$ for $(x, y, t) \in \Gamma \times [0, T]$. We assume that the functions $\bar{\psi}_i(x, y, t)$, $i = 1, \dots, k$, are unknown, and instead we have the functions $\psi_{\delta i}(x, y, t)$, $i = 1, \dots, k$, such that

$$\sum_{i=1}^{k} \int_0^T \int_\Gamma \left(\psi_{\delta i}(x, y, t) - \bar{\psi}_i(x, y, t)\right)^2 dl dt < \delta^2.$$

As an approximate solution of the inverse problem we take the parameter values $\lambda_1 \dots \lambda_n$, such that

$$\sum_{i=1}^{k} \int_0^T \int_\Gamma (u_i(x, y, t; \lambda_1, \dots, \lambda_n) - \psi_{\delta i}(x, y, t))^2 dl dt < \delta^2.$$

Solution of the inverse problem thus reduces to minimizing the function

$$\Phi(\lambda_1, \dots, \lambda_n) = \sum_{i=1}^{k} \int_0^T \int_\Gamma \left(u_i(x, y, t; \lambda_1, \dots, \lambda_n) - \psi_{\delta i}(x, y, t)\right)^2 dl dt.$$

We minimize $\Phi(\lambda_1, \dots, \lambda_n)$ by the gradient descent method.

Let us determine the gradient of the function $\Phi(\lambda_1, \dots, \lambda_n)$. To this end find its increment $\delta\Phi$. Define $f(u) = u(u - \alpha)(u - 1)$. Denote by λ the parameter vector $\lambda = (\lambda_1, \dots, \lambda_n)$, and by $\delta\lambda = (\delta\lambda_1, \dots, \delta\lambda_n)$ its increment. Assume that the function $\chi(x, y; \lambda)$ corresponds to the solution $\{u(x, y, t; \lambda), w(x, y, t; \lambda)\}$ of problem (1)–(5) and the function $\chi(x, y; \lambda + \delta\lambda)$ to the solution $\{u(x, y, t; \lambda + \delta\lambda),$

$w(x, y, t; \lambda + \delta\lambda)\}$. Denote

$$p_i(x, y, t; \lambda, \delta\lambda) = u_i(x, y, t; \lambda + \delta\lambda) - u_i(x, y, t; \lambda),$$

$$q_i(x, y, t; \lambda, \delta\lambda) = w_i(x, y, t; \lambda + \delta\lambda) - w_i(x, y, t; \lambda).$$

Note that

$$f(u_i + p_i)\,\chi(x, y; \lambda + \delta\lambda) - f(u_i)\,\chi(x, y; \lambda) = f(u_i)\sum_{j=1}^{n} \frac{\partial \chi}{\partial \lambda_j}\delta\lambda_j + f_u'(u_i)\,p_i\chi(x, y; \lambda) + \tilde{R}_i,$$

where $\tilde{R}_i = O(p_i^2 + \delta\lambda^2)$.

Using this formula, we find that the functions p, q are solutions of the problem

$$\frac{\partial p_i}{\partial t} = D\Delta p_i - q_i - f(u_i)\sum_{j=1}^{n} \frac{\partial \chi}{\partial \lambda_j}\delta\lambda_j - f_u'(u_i)\,p_i\chi(x, y; \lambda) - \tilde{R}_i, \quad (x, y) \in G, \quad t \in (0, T], \tag{6}$$

$$\frac{\partial q_i}{\partial t} = \beta p_i - \gamma q_i, \quad (x, y) \in G, \quad t \in (0, T], \tag{7}$$

$$\frac{\partial p_i}{\partial n}(x, y, t) = 0, \quad (x, y) \in \Gamma, \quad t \in (0, T], \tag{8}$$

$$p_i(x, y, 0) = 0, \quad (x, y) \in G, \tag{9}$$

$$q_i(x, y, 0) = 0, \quad (x, y) \in G. \tag{10}$$

Consider the increment of the function $\Phi(\lambda_1, \ldots, \lambda_n)$:

$$\delta\Phi = \Phi(\lambda + \delta\lambda) - \Phi(\lambda) = \sum_{i=1}^{k}\int_0^T\!\!\int_\Gamma \left((u_i + p_i - \psi_{\delta i})^2 - (u_i - \psi_{\delta i})^2\right) dl\,dt$$

$$= \sum_{i=1}^{k}\int_0^T\!\!\int_\Gamma (2(u_i - \psi_{\delta i})\,p_i + p_i^2)\,dl\,dt.$$

Let us derive a different form for the increment of $\Phi(\lambda_1, \ldots, \lambda_n)$. Consider the functions $a_i(x, y, t)$, $b_i(x, y, t)$, which are solutions of the conjugate initial boundary-value problems

$$\frac{\partial a_i}{\partial t} = -D\Delta a_i - \beta b_i + f_u'(u_i)\,a_i\chi(x, y; \lambda), \quad (x, y) \in G, \quad t \in [0, T), \tag{11}$$

$$\frac{\partial b_i}{\partial t} = a_i + \gamma b_i, \qquad (x, y) \in G, \quad t \in [0, T), \tag{12}$$

$$D\frac{\partial a_i}{\partial n}(x, y, t) = 2(u_i - \psi_i), \qquad (x, y) \in \Gamma, \quad t \in [0, T], \tag{13}$$

$$a_i(x, y, \mathrm{T}) = 0, \quad (x, y) \in G, \tag{14}$$

$$b_i(x, y, \mathrm{T}) = 0, \quad (x, y) \in G. \tag{15}$$

Since the functions $\{p_i, q_i\}$ are solutions of (6)–(10) and $\{a_i, b_i\}$ are solutions of (11)–(15), we obtain

$$I = \sum_{i=1}^{k}\int_0^T\iint_G \left[a_i\left(\frac{\partial p_i}{\partial t} - D\Delta p_i + q_i + f_u^{'}(u_i)p_i\chi(x, y; \lambda)\right) + b_i\left(\frac{\partial q_i}{\partial t} - \beta p_i + \gamma q_i\right)\right.$$

$$\left. - p_i\left(\frac{\partial a_i}{\partial t} + D\Delta a_i + \beta b_i - f_u'(u_i)a_i\chi(x, y; \lambda)\right) + q_i\left(\frac{\partial b_i}{\partial t} - a_i - \gamma b_i\right)\right] dxdydt$$

$$= \sum_{i=1}^{k}\int_0^T\iint_G \left[(a_i p_i + b_i q_i)_t - (Da_i\Delta p_i - Dp_i\Delta a_i)\right] dxdydt.$$

We transform this expressing using Green's formula and the initial and boundary conditions for the functions $\{p_i, q_i\}$, $\{a_i, b_i\}$,

$$I = \sum_{i=1}^{k}\iint_G (a_i p_i + b_i q_i)\Big|_{t=0}^{t=T} dxdy - \sum_{i=1}^{k}\int_0^T\int_\Gamma \left(Da_i\frac{\partial p_i}{\partial n} - Dp_i\frac{\partial a_i}{\partial n}\right) dldt$$

$$= \sum_{i=1}^{k}\int_0^T\int_\Gamma (p_i 2(u_i - \psi_i))\, dldt.$$

On the other hand, this expression equals

$$I = -\sum_{i=1}^{k}\int_0^T\iint_G a\left(f(u_i)\sum_{j=1}^{n}\frac{\partial\chi}{\partial\lambda_j}\delta\lambda_j + \tilde{R}_i\right) dx\, dy\, dt.$$

Then the discrepancy increment equals

$$\delta\Phi = \sum_{i=1}^{k}\left[\int_0^T\iint_G - a\left(f(u_i)\sum_{j=1}^{n}\frac{\partial\chi}{\partial\lambda_j}\delta\lambda_j + \tilde{R}_i\right) dx\, dy\, dt + \int_0^T\int_\Gamma p_i^2\, dl\, dt\right].$$

Ignoring terms of second order of smallness, we obtain the following expression for the gradient:

$$\frac{\partial \Phi}{\partial \lambda_j} = -\sum_{i=1}^{k} \int_0^T \iint_G af(u_i)\chi_{\lambda_j}(x, y; \lambda)\, dx\, dy\, dt, \quad 1 \le j \le n.$$

This gradient is now used to construct the gradient descent method for the minimization of the function $\Phi(\lambda_1, \dots, \lambda_n)$. The iterative process stops as soon as $\Phi(\lambda_1, \dots, \lambda_n) \le \delta^2$.

As the functions $\varphi_i(x, y)$ we take the localized perturbations $\varphi_i(x, y) = \exp\left\{-\left((x - x_i)^2 + (y - y_i)^2\right)/\sigma^2\right\}$. Consider the choice of the first approximation for the parameters λ and the choice of the initial excitation points for the functions $\varphi_i(x, y; x_i, y_i, \sigma_i)$. Assume that we know the region $\tilde{H}$ that contains the sought H and at the same time its area does not exceed 70 % of the area of G. As the first approximation for the iterative method we take the set of parameters λ such that the region being described lies in $\tilde{H}$ and the points (x_i, y_i) are in $G \setminus \bar{\tilde{H}}$.

Computer Experiments

The numerical method described for the solution of the inverse problem has been applied to determine regions H of special type.

Direct problems for the modified FitzHugh–Nagumo model (1)–(5) have been solved in the region G approximating the heart section (see Figs. 1–4) by the finite element method; the deal.II library[3] has been used to develop the software implementation. An order of 150,000 finite elements were used in our computations. The following parameter values were used in all computer experiments: $D = 1$, $\alpha = 0.15$, $\beta = 0.005$, $\gamma = 0.025$, $\theta = 100$. By solving the direct problem for one or several initial conditions, we evaluated $\bar{\psi}_i(x, y, t)$ on the boundary $(x, y) \in \Gamma$, $t \in [0, T]$; an error was then injected into these functions to obtain $\psi_{\delta i}(x, y, t)$ such that

$$\sum_{i=1}^{k} \int_0^T \int_\Gamma (u_i(x, y, t; \lambda_1, \dots, \lambda_n) - \psi_{\delta i}(x, y, t))^2\, dl dt = \delta^2.$$

Then these functions were applied to solve the inverse problem by the proposed numerical method. In our computer experiments we solved inverse problems reconstructing regions H of two types: a circle parametrized by three parameters and an oval parametrized by five parameters. The computation error was set at a small value

$$\delta = 0.01 \sqrt{\sum_{i=1}^{k} \int_0^T \int_\Gamma \bar{\psi}_i^{\,2}(x, y, t)\, dl\, dt}.$$

When reconstructing a circular region H, we took the function g in the form

$$g(x, y, \lambda_1, \lambda_2, \lambda_3) = (x - \lambda_1)^2 + (y - \lambda_2)^2 - \lambda_3^{\,2}.$$

[3] A Finite Element Differential Equations Analysis Library (http://www.dealii.org/).

The inverse problem was solved utilizing information from the solution of the direct problem. Figure 1 shows the result of one such computer experiment. Here, and in the figures that follow, the crosses mark the points of localization of the initial distribution for the direct problem, the broken curve is the boundary of the sought region H, and the solid curve shows in the left panel the region used as the first approximation and in the right panel the result obtained by solving the inverse problem.

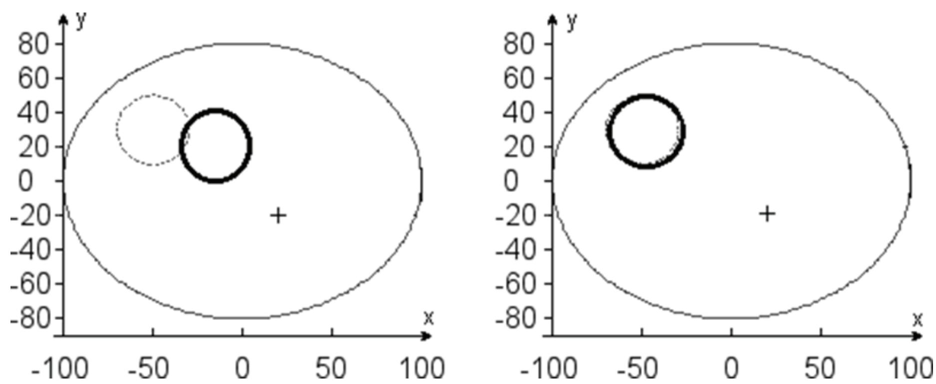

Fig. 1

When reconstructing an oval-shaped region H, the function g was taken in the form

$$g(x,y,\lambda_1,\lambda_2,\lambda_3,\lambda_4,\lambda_5) = \left(((x-\lambda_1)\cos(\lambda_5) - (y-\lambda_2)\sin(\lambda_5))/\lambda_3\right)^2$$

$$+ \left(((x-\lambda_1)*\sin(\lambda_5) + (y-\lambda_2)*\cos(\lambda_5))/\lambda_4\right)^2 - 1 .$$

Computer experiments to find the function χ of this kind were carried out using information about the solution of one and two direct problems. The information from one solution was insufficient to reconstruct the oval region: the outcome was inaccurate, preserving the circle shape of the first approximation (see Fig. 2).

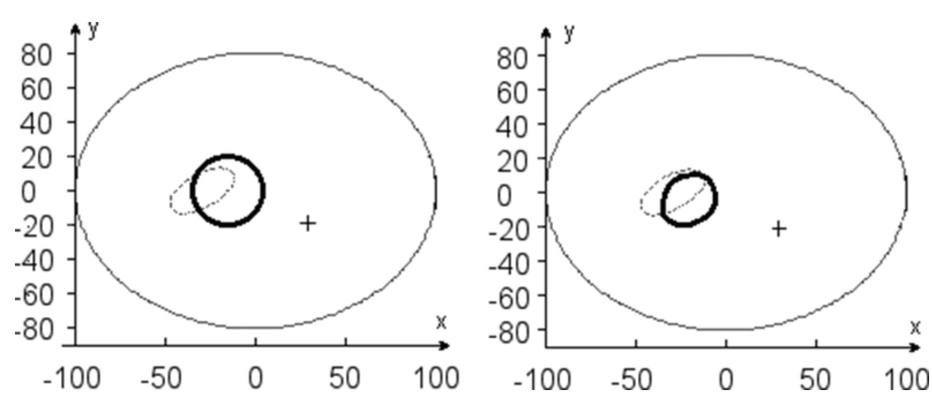

Fig. 2

Computer experiments reconstructing the oval region from two direct-problem solutions have shown that the accuracy of the end result depends on the relative position of the sought region H and the localization points of the initial distribution. High accuracy of the inverse solution is attained if the localization points of the initial distribution are close to different axes of the oval describing the region H (see Fig. 3). If the localization points are near one of the axes, the reconstructed region deviates to a greater extent from the sought region for equal error values δ (see Fig. 4).

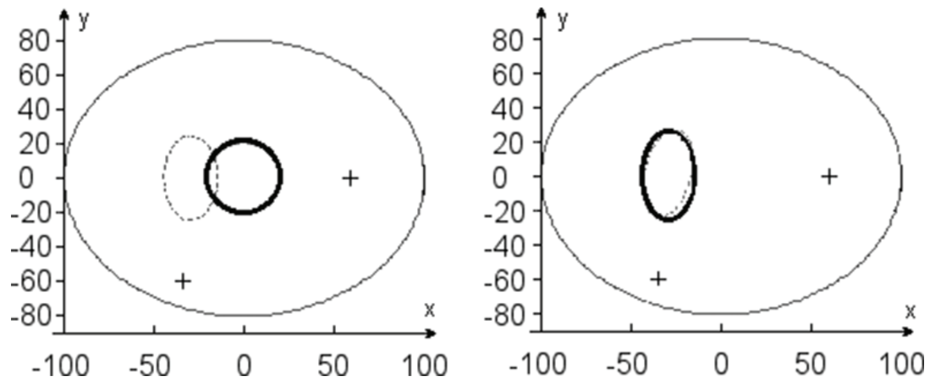

Fig. 3

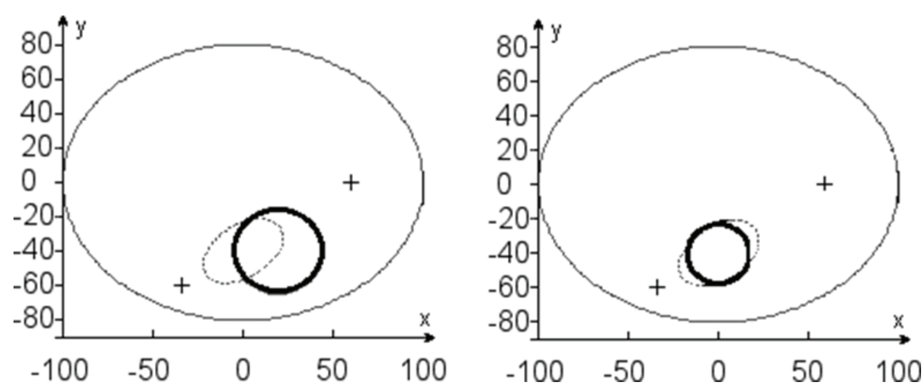

Fig. 4

Our results demonstrate the efficiency of the proposed algorithm for the solution of the inverse problem.

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