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NUMERICAL SOLUTION OF THE INVERSE PROBLEM FOR THE MATHEMATICAL MODEL OF CARDIAC EXCITATION

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We consider the problem of localizing the region of the heart damaged by myocardial infarct. For the two-dimensional modified FitzHugh–Nagumo mathematical model, this inverse problem involves determining the coefficient dependent on spatial variables for a system of partial differential equations in a region with a localized source of cardiac excitation. Additional dynamical measurements of the potential are carried out on the inner boundary of the region representing the section of the heart and its ventricles by a horizontal plane. Potential measurements on the inner boundary correspond to data obtained from ventricular catheters. A numerical method is proposed for the solution of this inverse problem and results of computer experiments are reported.

Keywords: FitzHugh-Nagumo model, inverse problem for the mathematical model of cardiac excitation

Introduction

Mathematical modeling applying computer technologies to investigate the electrophysiology of the heart has become quite popular in cardiology (see, e.g., [1]). In this context, it is important to have methods that solve inverse problems supporting the diagnosis of cardiological issues [6–14].

Widespread mathematical models of the electrophysiology of the heart include the FitzHugh–Nagumo model, the Aliev–Panfilov model, and the bidomain model. These models describe the process of cardiac excitation in terms of transmembrane potential and constitute initial–boundary-value problems for a system of quasilinear partial differential evolution equations [1–5]. Development of noninvasive diagnostic techniques for heart issues involves solving inverse problems that determine the parameters of these mathematical models. Numerical solution methods of some inverse problems for cardiac excitation models have been proposed in [1, 6, 10–13].

In this article, we focus on the modified FitzHugh–Nagumo model to determine the region of heart that has been damaged by myocardial infarct. This inverse problem involves determining the coefficient of a system of partial differential equations that depends on spatial variables. The problem is solved in a two-dimensional region that represents the section of the heart and its ventricles by a horizontal plane. Additional information used to solve the inverse problem is provided by measurements carried out with catheters inserted in one of the ventricles.

A numerical method for solving this inverse problem is proposed and its efficiency is assessed from the reported results of computer experiments. Contrary to publications [1, 11, 12], the mathematical model in the present article includes a localized source, the two-dimensional region matches the real geometry of the heart and its ventricles, and the dynamic measurements of the potential are carried out on the inner, not the outer, boundary of the heart.

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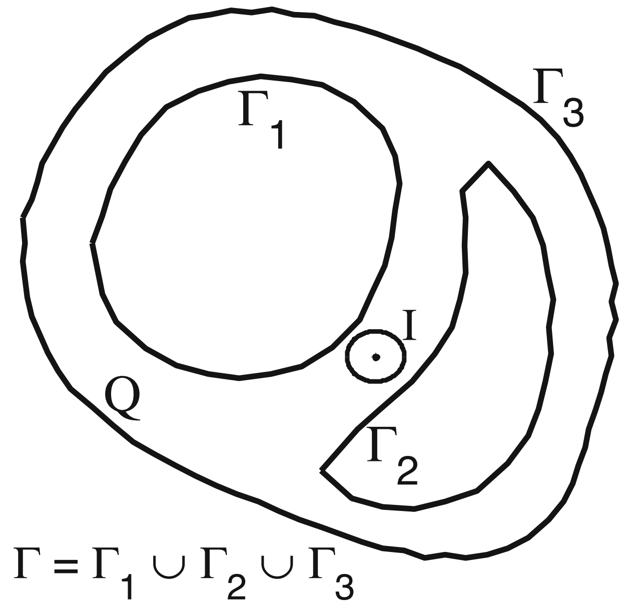

Fig. 1

The Inverse Problem

Consider the modified FitzHugh–Nagumo model describing the propagation of an excitation in the myocardium:

$$u_t = D\Delta u - v(x,y)u(u-\alpha)(u-1) - w(x,y) + g(x,y,t), \quad (x,y) \in Q, \quad t \in (0,T], \tag{1}$$

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

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

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

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

Here $u(x,y,t)$ is the transmembrane potential, the function $w(x,y,t)$ is associated with ion currents, and $g(x,y,t)$ describes the localized source of myocardial excitation; α, β, γ are the reactive coefficients, D is the electrical conductivity (D, α, β, γ are positive constants); Γ is the boundary of the region Q (Fig. 1).

The function $v(x,y)$ models the region of the heart damaged by infarct. This function is such that $v(x,y) \in C^1(Q)$, $v(x,y) \approx 0$ in the region $I \in Q$, and $v(x,y) \approx 1$ in $Q \setminus I$, I is the region of the heart damaged by infarct.

Problem (1)–(5) may be applied to model excitation in a heart damaged by myocardial infarct. In this model, the nonlinear coefficient describing the excitability of the myocardium is $F = v(x,y)u(u-\alpha)(u-1) \approx 0$ in the region I, which corresponds to loss of the heart's ability to respond to excitation in the region I.

We assume that the region I is defined by n parameters $\lambda_1, \ldots, \lambda_n$ and v is a function of these parameters: $v = v(x, y; \lambda_1, \ldots, \lambda_n)$.

Consider the following inverse problems. The coefficients D, α, β, γ are given and the function $v(x, y; \lambda_1, \ldots, \lambda_n)$ is continuous. Find this function given supplementary information about the solution of two problems (1)–(5) corresponding to two different functions $g_i(x, y, t)$. Specifically, given are the functions

$$\psi_i(x, y, t) = u_i(x, y, t), \quad (x, y) \in \Gamma_1, \quad i = 1, 2, \tag{6}$$

where $u_i(x, y, t)$ is the solution of problem (1)–(5) corresponding to the function $g_i(x, y, t)$.

Numerical Solution Method for the Inverse Problem

Consider the numerical solution method for this inverse problem. Assume that, with the function $\bar{v} = v(x, y; \bar{\lambda}_1, \ldots, \bar{\lambda}_n)$ and the localized myocardial excitation source $g_i(x, y, t)$, the direct (forward) problem (1)–(5) has the solution $\bar{\psi}_i(x, y, t)$ on the boundary Γ_1. We assume that the supplementary information $\bar{\psi}_i(x, y, t)$ is given with an error ε, i.e., given is the function $\psi_{i\varepsilon}(x, y, t)$ such that

$$\sum_{i=1}^{2} \int_0^T \int_{\Gamma_1} \left(\psi_{i\varepsilon}(x, y, t) - \bar{\psi}_i(x, y, t)\right)^2 dl dt \le \varepsilon.$$

The residual

$$S(\lambda) = \sum_{i=1}^{2} \int_0^T \int_{\Gamma} \left(u_i(x, y, t; \lambda_1, \ldots, \lambda_n) - \psi_{i\varepsilon}(x, y, t)\right)^2 dl dt$$

is minimized by the gradient method with the stopping rule $S(\lambda) < \varepsilon^2$.

Let us find the gradient of the function $S(\lambda)$. To find the increment δS, define the function $f(u) = u(u - \alpha)(u - 1)$. Denote by λ the parameter vector $\lambda = (\lambda_1, \ldots, \lambda_n)$. Assume that the function $v(x, y; \lambda)$ corresponds to the solution $\{u_i(x, y, t; \lambda), w_i(x, y, t; \lambda)\}$ of problem (1)–(5), and the function $v(x, y; \lambda + \delta\lambda)$ corresponds to the solution $\{u_i(x, y, t; \lambda + \delta\lambda), w_i(x, y, t; \lambda + \delta\lambda)\}$.

Let

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

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

Then

$$f(u_i(x, y, t; \lambda + \delta\lambda)) v(x, y; \lambda + \delta\lambda) - f(u_i(x, y, t; \lambda)) v(x, y; \lambda)$$

$$= f(u_i) \sum_{j=1}^{n} v_{\lambda_j}(x, y; \lambda) \delta\lambda_j + f'_u(u_i) \delta u_i v(x, y; \lambda) + \tilde{R},$$

where $\tilde{R} = O\left((\delta u)^2 + \delta\lambda^2\right)$.

The functions δu_i, δw_i are the solutions of the problem

$$\frac{\partial \delta u_i}{\partial t} = D\Delta \delta u_i - \delta w_i - f(u_i)\sum_{j=1}^{n} v_{\lambda_j}(x,y;\lambda)\delta\lambda_j$$

$$-f'_u(u_i)\delta u_i v(x,y;\lambda) - \tilde{R}, \quad (x,y)\in Q, \quad t\in(0,T], \tag{7}$$

$$\frac{\partial \delta w_i}{\partial t} = \beta\delta u_i - \gamma\delta w_i, \quad (x,y)\in Q, \quad t\in(0,T], \tag{8}$$

$$\frac{\partial \delta u_i}{\partial n}(x,y,t) = 0, \quad (x,y)\in\Gamma, \quad t\in(0,T], \tag{9}$$

$$\delta u_i(x,y,0) = 0, \quad (x,y)\in Q, \tag{10}$$

$$\delta w_i(x,y,0) = 0, \quad (x,y)\in Q. \tag{11}$$

Then the increment of the function $S(\lambda_1,\ldots,\lambda_n)$ equals

$$\delta S = S(\lambda+\delta\lambda) - S(\lambda)$$

$$= \sum_{i=1}^{2}\int_0^T\int_{\Gamma_1}\left(\left(u_i(x,y,t;\lambda+\delta\lambda) - \psi_{i\varepsilon}\right)^2 - \left(u_i(x,y,t;\lambda) - \psi_{i\varepsilon}\right)^2\right)dl\,dt$$

$$= \sum_{i=1}^{2}\int_0^T\int_{\Gamma_1}\left(2(u_i - \psi_{i\varepsilon})\delta u + (\delta u_i)^2\right)dl\,dt.$$

Let us derive an alternative expression for the increment of the function $S(\lambda_1,\ldots,\lambda_n)$. Consider the functions $a_i(x,y,t)$, $b_i(x,y,t)$, which are the solutions of the conjugate initial–boundary-value problems

$$\frac{\partial a_i}{\partial t} = -D\Delta a_i - \beta b_i + a_i f'_u(u_i)v(x,y;\lambda), \quad (x,y)\in Q, \quad t\in[0,T), \tag{12}$$

$$\frac{\partial b_i}{\partial t} = a_i + \gamma b_i, \quad (x,y)\in Q, \quad t\in[0,T), \tag{13}$$

$$D\frac{\partial a_i}{\partial n}(x,y,t) = 2(u_i - \psi_i), \quad (x,y)\in\Gamma_1, \quad t\in[0,T], \tag{14}$$

$$D\frac{\partial a_i}{\partial n}(x,y,t) = 0, \quad (x,y)\in\Gamma\setminus\Gamma_1, \quad t\in[0,T], \tag{15}$$

$$a_i(x, y, \mathrm{T}) = 0, \quad (x, y) \in Q, \tag{16}$$

$$b_i(x, y, \mathrm{T}) = 0 \quad (x, y) \in Q. \tag{17}$$

Since the functions δu_i, δw_i are the solutions of (7)–(11) and a_i, b_i are the solutions of (12)–(17), we obtain

$$I = \sum_{i=1}^{2}\left(\int_0^T\iint_Q\left[a_i\left(\frac{\partial \delta u_i}{\partial t} - D\Delta\delta u_i + \delta w_i + f'_u(u_i)\delta u_i v(x, y; \lambda)\right)\right.\right.$$

$$+ b_i\left(\frac{\partial \delta w_i}{\partial t} - \beta\delta u_i + \gamma\delta w_i\right) + \delta u_i\left(\frac{\partial a_i}{\partial t} + D\Delta a_i + \beta b_i\right.$$

$$\left.\left.\left. - f'_u(u_i)a_i v(x, y; \lambda)\right) + \delta w_i\left(\frac{\partial b_i}{\partial t} - a_i - \gamma b_i\right)\right]dx\,dy\,dt\right)$$

$$= \sum_{i=1}^{2}\int_0^T\iint_Q\left[(a_i\delta u_i + b_i\delta w_i)_t - (Da_i\Delta\delta u_i - D\delta u_i\Delta a_i)\right]dx\,dy\,dt.$$

Applying the Green's formula and the initial and boundary conditions for the functions δu_i, δw_i, a_i, b_i, we obtain

$$I = \sum_{i=1}^{2}\iint_Q(a_i\delta u_i + b_i\delta w_i)\Big|_{t=0}^{t=T}dx\,dy - \int_0^T\int_\Gamma\left(Da_i\frac{\partial \delta u_i}{\partial n} - D\delta u_i\frac{\partial a_i}{\partial n}\right)dldt$$

$$= \sum_{i=1}^{2}\int_0^T\int_{\Gamma_1}2\delta u_i(u_i - \psi_i)\,dl\,dt.$$

On the other hand, this expression equals

$$I = -\sum_{i=1}^{2}\int_0^T\iint_Q a_i\left(f(u_i)\sum_{j=1}^{n}v_{\lambda_j}(x, y; \lambda)\delta\lambda_j + R\right)dxdydt.$$

Then the residual increment equals

$$\delta S = \sum_{i=1}^{2}\left(\int_0^T\iint_Q - a_i\left(f(u_i)\sum_{j=1}^{n}v_{\lambda_j}(x, y; \lambda)\delta\lambda_j + R\right)dx\,dy\,dt + \int_0^T\int_\Gamma(\delta u_i)^2\,dl\,dt\right).$$

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

$$\frac{\partial S}{\partial \lambda_j} = -\sum_{i=1}^{2}\int_0^T\iint_Q a_i f(u_i)v_{\lambda_j}(x, y; \lambda)\,dx\,dy\,dt.$$

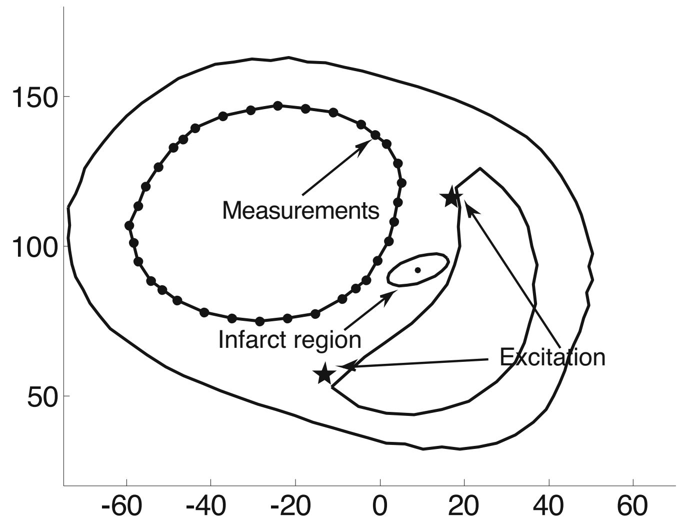

Fig. 2

This gradient is applied to advance from $\left(\lambda_1^m,\ldots,\lambda_{1n}^m\right)$ to $\left(\lambda_1^{m+1},\ldots,\lambda_n^{m+1}\right)$. The iterative process stops as soon as $S(\lambda_1,\ldots,\lambda_n)\le\delta^2$.

The proposed numerical method has been used to find regions I of a special form. Let

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

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

$$r(x,y;\lambda_1,\ldots,\lambda_n)<0,\quad (x,y)\in I \quad \text{and} \quad r(x,y;\lambda_1,\ldots,\lambda_n)>0,\quad (x,y)\in Q\setminus I.$$

We describe computer experiments with functions $r(x,y;\lambda_1,\ldots,\lambda_n)$ corresponding to two types of regions I – a disk and an ellipse.

When I is a disk, $\theta=100$ and $r(x,y,\lambda_1,\lambda_2,\lambda_3)=(x-\lambda_1)^2+(y-\lambda_2)^2-\lambda_3^2$. When I is an ellipse,

$$r(x,y,\lambda_1,\lambda_2,\lambda_3,\lambda_4,\lambda_5)$$

$$=\left(\frac{(x-\lambda_1)\cos(\lambda_5)-(y-\lambda_2)\sin(\lambda_5)}{\lambda_3}\right)^2+\left(\frac{(x-\lambda_1)\sin(\lambda_5)+(y-\lambda_2)\cos(\lambda_5)}{\lambda_4}\right)^2-1.$$

Computer Experiments

Direct problems for the modified FitzHugh–Nagumo model (1)–(5) have been solved in region Q (Fig. 2), which is a section of the heart and its ventricles by a horizontal plane. The solution was obtained by a finite element method as implemented in MatLab. The number of finite triangular elements for the calculations was of the order of $N=600$.

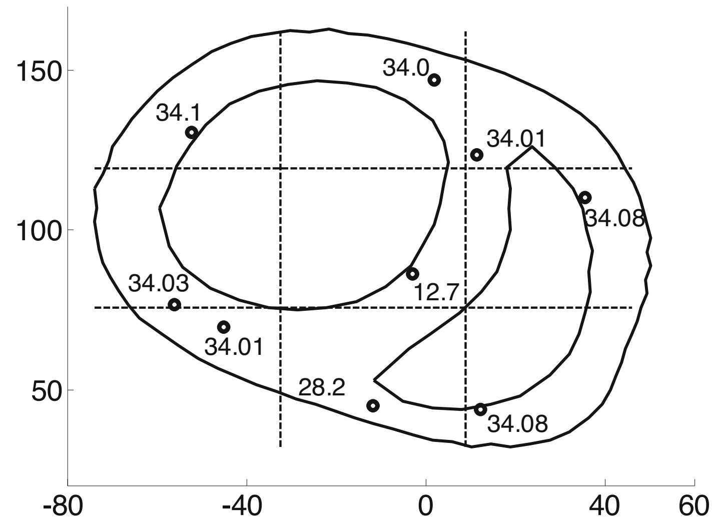

Fig. 3

For the function $g_i(x,y,t)$ modeling the localized excitation source in the heart we took

$$g_i(x,y,t) = e^{-\frac{(t-t_0)^2}{\sigma_1^2}} e^{-\frac{(x-x_i)^2+(y-y_i)^2}{\sigma_2^2}}.$$

The following model parameters were used: $D=1$, $\alpha=0.15$, $\beta=0.005$, $\gamma=0.025$.

Having solved the direct problem, we evaluated the function $\overline{\psi}_i(x,y,t)$ on the inner boundary $(x,y)\in\Gamma_1$, $t\in[0,T]$, injected the experimental error ε, and obtained $\psi_{i\varepsilon}(x,y,t)$ such that

$$\sum_{i=1}^{2}\int_0^T\int_{\Gamma_1}\left(u_i(x,y,t;\lambda_1,\ldots,\lambda_n)-\psi_{i\varepsilon}(x,y,t)\right)^2 dldt \le \varepsilon.$$

In computer experiments, we solved inverse problems reconstructing two types of regions I – a disk defined by three parameters and an ellipse defined by five parameters.

The first approximation of the parameters λ was chosen the same for both the disk and the ellipse. The region Q was partitioned into a certain number of finite elements. The disk was of constant radius and its center was alternately placed at the center of each finite element k, calculating the residual $S_k(\lambda)$. The tuple of parameters λ minimizing the residual $S_k(\lambda)$ was taken as the first approximation λ.

Then the functions $\psi_{i\varepsilon}$ and the tuple λ were applied to solve the inverse problem by the gradient method described above. Figures 3 and 4 present the results of the computer experiments for the region l in the form of a disk.

Figure 3 illustrates the selection of the initial approximation for λ. The values of $S_k(\lambda)$ are shown for various λ_1, λ_2, λ_3. Here (λ_1,λ_2) are the coordinates of the disk center and $\lambda_3=3$ is the disk radius. The end result is the point with the coordinates $\lambda_1=-2.1$, $\lambda_2=87.8$, where $S(\lambda)=12.7$.

Figure 4 shows the reconstructed function

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

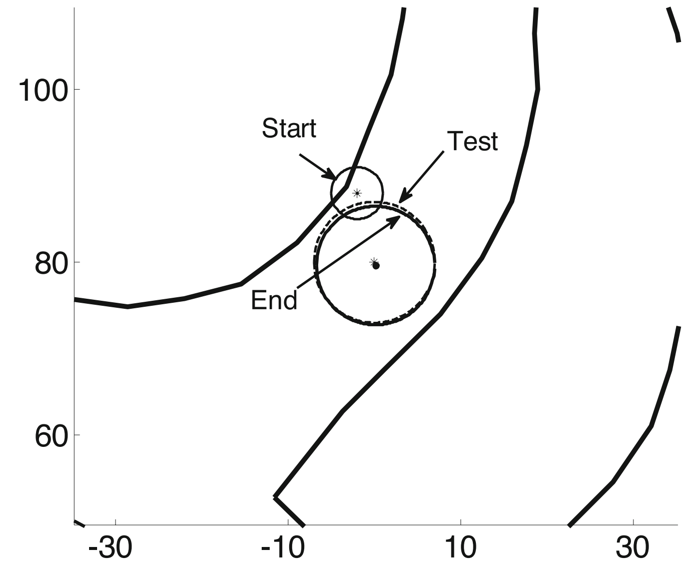

Fig. 4

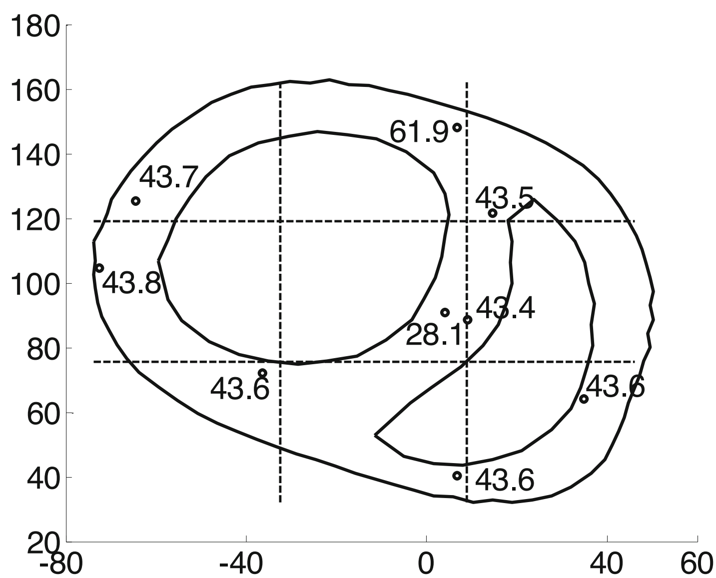

Fig. 5

The broken curve is the test region – the infarct damage – obtained for the tuple $\lambda_1 = 0$, $\lambda_2 = 80$, $\lambda_3 = 7$; the solid curve plots the result for $\lambda_1 = 0.12$, $\lambda_2 = 79.6$, $\lambda_3 = 6.85$. The residual $S(\lambda)$ in this case equals $2.58 \cdot 10^{-7}$.

Figures 5–6 shows the calculated results for a region I in the shape of an ellipse.

Figure 5 demonstrates the choice of the initial approximation for λ. The values of $S_k(\lambda)$ are shown for various tuples λ_1, λ_2, λ_3, λ_4, λ_5. Here (λ_1, λ_2) is the center of symmetry of the ellipse, $\lambda_3 = \lambda_4 = 1$ are the semi-axes, $\lambda_5 = 0$ is the inclination angle. The end result is the point with the coordinates $\lambda_1 = 4.034$, $\lambda_2 = 90.8$, where $S_i(\lambda) = 28.1$.

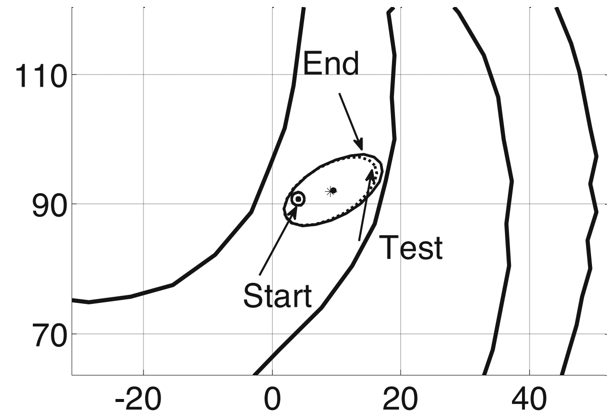

Fig. 6

Figure 6 shows the reconstructed function

$$r(x, y, \lambda_1, \lambda_2, \lambda_3, \lambda_4, \lambda_5)$$

$$= \left(\frac{(x-\lambda_1)\cos(\lambda_5) - (y-\lambda_2)\sin(\lambda_5)}{\lambda_3} \right)^2 + \left(\frac{(x-\lambda_1)\sin(\lambda_5) + \dagger(y-\lambda_2)\cos(\lambda_5)}{\lambda_4} \right)^2 - 1.$$

The broken curve shows the test region – the infarct damage – for the tuple $\lambda_1 = 9$, $\lambda_2 = 92$, $\lambda_3 = 8$, $\lambda_4 = 4$, $\lambda_5 = \frac{\pi}{6}$; the solid curve is the result for $\lambda_1 = 9.47$, $\lambda_2 = 92.17$, $\lambda_3 = 8.5$, $\lambda_4 = 4.08$, $\lambda_5 = 0.52$. The residual $S(\lambda)$ in this case equals $6.34 \cdot 10^{-6}$.

The computational results show that, in our inverse problem, the location and the shape of the infarct-damaged region is reconstructed with adequate accuracy. Note that if only one excitation source is used, the solution is substantially less accurate.

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