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INVERSE PARAMETER IDENTIFICATION IN A NONLINEAR HEMODYNAMIC MODEL OF THROMBUS FORMATION

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Abstract. In this paper a nonlinear inverse problem in hemodynamics associated with thrombus formation in blood flow is studied. The inverse problem is formulated as the identification of an unknown constant diffusion coefficient in a two-dimensional diffusion equation from final-time observations. The diffusion coefficient is reconstructed by minimizing a normalized least-squares objective functional using a gradient descent algorithm. The direct model describes blood flow in a planar vessel and incorporates a fibrin formation mechanism on the vessel wall. The governing diffusion equation is solved numerically by an alternating direction implicit (ADI) scheme, which provides unconditional stability for the two-dimensional problem. To reduce the computational complexity, the gradient of the objective functional with respect to the unknown coefficient is evaluated numerically via a central finite-difference approximation, thereby avoiding the construction of an adjoint problem. Numerical experiments with synthetically generated data demonstrate stable convergence of the iterative process and accurate recovery of the diffusion coefficient for a wide range of initial guesses and step-size parameters. The results confirm the robustness, simplicity, and computational efficiency of the proposed gradient-based reconstruction approach for hemodynamic inverse problems.

Keywords: nonlinear inverse problem; diffusion coefficient identification; thrombosis; gradient descent.

INTRODUCTION

One of the central challenges in modern applied mathematics and computational medicine is the development of methods for the quantitative analysis of biophysical processes associated with pathological conditions. Among these processes is thrombosis - a multifactorial biochemical phenomenon that gives rise to fibrin clot formation in blood vessels. Despite an exponential growth in research focused on thrombus formation and significant progress in the field of blood coagulation, this process has not yet been fully elucidated and remains an active area of investigation. This reflects the increasing role of computational modeling in the study of thrombosis and hemostasis. Studies in this field cover a broad range of scales-from the molecular level to large-scale continuum models-and involve components such as fibrinogen [1], erythrocytes, platelets, hemoglobin, and fibrin [2, 3, 4]. A comprehensive review of discrete particle methods used for blood flow modeling was presented in [5, 6, 7, 8, 9]. The most detailed models of thrombus formation are based on the hydrodynamic equations governing blood flow, complemented by additional equations that describe thrombosis-related processes [10, 11, 12, 13].

The results obtained for the phenomenological model demonstrate that the dynamics of blood coagulation and thrombus formation arise from the interaction of two coupled concentration waves - an activator and an inhibitor [14, 15, 16]. In [17], the dynamics of blood coagulation, dependent on space and time, were modeled using differential approximation methods by numerically solving the corresponding differential equations.

A variety of experimental methods are used to predict the development of stenosis in blood vessels. However, numerical methods are of the greatest interest for calculating hemodynamic parameters in the region of thrombus formation. The development of mathematical models is the principal approach to analyzing real hemodynamic problems, due to the inherent complexity of biological systems. Since their behavior depends nonlinearly on a large number of factors, analytical solution methods have a very limited range of applicability. Numerical methods enable the calculation of key hemodynamic characteristics of blood flow and the prediction of stenosis progression.

From a practical standpoint, the development of efficient numerical algorithms for such problems can be employed in blood coagulation monitoring systems, biomedical simulators, and personalized diagnostic tasks.

Inverse problems in hydrodynamics, gas dynamics, and hemodynamics constitute a relatively new field of mathematical physics. Such problems frequently arise in mechanics, engineering, hydrodynamics, and hemodynamics when attempting to determine the properties of a medium in which various physicochemical processes occur, based on observations of these processes within a measurable region. The study of inverse problems involving the reconstruction of the right-hand side in the Stokes equations is presented in [18], which also provides a review of research conducted in this field. Research contributions in this area are predominantly theoretical.

Inverse problems for partial differential equations have been extensively studied in mathematical physics, particularly in the context of heat and diffusion processes. The theoretical foundations of inverse and ill-posed problems, including issues of uniqueness, stability, and numerical reconstruction, are presented in the classical monographs [19, 20, 21, 22, 23]. Variational and optimal-control approaches to parameter identification were further developed in [24]. In recent years, considerable attention has been devoted to inverse coefficient problems for parabolic equations. In particular, simultaneous identification of thermal conductivity and radiative coefficients in the heat equation was investigated in [25], while the recovery of multiple space-dependent coefficients was studied in [26]. Theoretical aspects of uniqueness and stability for parabolic inverse problems have been widely analyzed using Carleman estimates, as discussed in [27]. A related diffusion-coefficient identification problem for the heat equation was recently considered in [28]. Alongside coefficient identification, inverse source problems for diffusion and advectiondiffusion equations have also been actively investigated. For example, a boundary-measurement-based reconstruction method for an advectiondiffusion model was developed in [29], demonstrating the effectiveness of numerical approaches for recovering unknown source terms. In addition to diffusion-type applications, numerical techniques for inverse problems have been successfully applied in other areas of mathematical physics. In particular, computational methods for the inverse problem of magnetotelluric sounding were developed in [30], illustrating the broad applicability of iterative reconstruction approaches. Despite the significant advances in inverse coefficient and source problems for heat and diffusion models, the application of gradient-based identification techniques to hemodynamic models of thrombus formation remains relatively unexplored. This gap motivates the development of computationally efficient reconstruction algorithms tailored to diffusion processes in blood flow modeling.

In the present work, the unknown diffusion coefficient is reconstructed by minimizing a normalized least-squares objective functional using a gradient descent method with numerically approximated gradients. This approach avoids the construction of an adjoint problem and provides a computationally simple and robust identification procedure.

Inverse Problem Statement

In the inverse problem considered below, the objective is to identify parameters governing the fibrin dynamics based on observations of the fibrin concentration ψ. In the present study, this task is formulated as the identification of an unknown constant diffusion coefficient in the two-dimensional diffusion equation. The corresponding state equation is given by

$$\frac{\partial \psi}{\partial t} = D\Delta\psi + \theta(x,y,t), \quad (x,y) \in \Omega,\ 0 < t \le T \tag{1}$$

where $D > 0$ is an unknown constant diffusion coefficient to be identified, $\theta(x,y,t)$ is a known activator source term obtained from the direct biochemical model [12, 13, 14, 15, 16, 17], and

$$\Omega = [0,7] \times [0,1] \subset \mathbb{R}^2, \qquad 0 < t \le T,$$

denotes the computational spatial domain and time interval considered in the present study.

The direct hemodynamic and biochemical model together with its numerical solution procedure has been investigated previously in [31]. In the present study, this model is employed mainly for generating synthetic observational data, while the primary focus is placed on the inverse reconstruction of the diffusion coefficient.

The problem is supplemented with the initial condition

$$\psi(x,y,0) = \psi_0(x,y) \tag{2}$$

and homogeneous Neumann boundary conditions

$$\frac{\partial \psi}{\partial n} = 0, \quad \text{on } \partial\Omega \tag{3}$$

It is assumed that at the final time $t = T$ the observation data are available over the spatial domain Ω in the form

$$\psi^{\text{obs}}(x,y) = \psi(x,y,T) \tag{4}$$

In the numerical experiments, the observation data are generated synthetically from the numerical solution of the direct problem [18, 31].

To solve the inverse problem defined by (1)-(4), the unknown diffusion coefficient is estimated by minimizing the following least-squares objective functional:

$$J(D) = \frac{1}{2}\left\| \psi(\cdot,\cdot,T;D) - \psi^{\text{obs}} \right\|^2_{L^2(\Omega)} \tag{5}$$

Here, $\psi(\cdot,\cdot,T;D)$ denotes the solution of the direct diffusion problem at the final time corresponding to the diffusion coefficient D, while ψ^{obs} represents the observational data. Minimization of the functional $J(D)$ provides an estimate of the unknown constant diffusion coefficient. This functional measures the discrepancy between the simulated and observed states at the final time.

Since the direct problem is solved numerically on a finite-difference grid, the functional is evaluated in discrete normalized form:

$$J(D) = \frac{\sum_{i,j} \left(\psi^N_{i,j}(D) - \psi^{\text{obs}}_{i,j} \right)^2}{\sum_{i,j} \left(\psi^{\text{obs}}_{i,j} \right)^2 + \varepsilon}, \tag{6}$$

here, $\varepsilon > 0$ denotes a small stabilization parameter introduced to prevent division by zero and ensure numerical stability of the normalized functional. The normalization makes the functional dimensionless and improves numerical stability. The inverse problem is formulated as the following minimization problem:

$$D^* = \arg\min_{D>0} J(D) \tag{7}$$

The numerical minimization procedure is described in the next section.

Numerical Solution of the Inverse Problem

To solve the inverse problem defined above, a gradient-based iterative procedure is employed. The unknown constant diffusion coefficient is identified by minimizing the objective functional that measures the discrepancy between the simulated and observed states at the final time.

At each iteration of the reconstruction algorithm, the diffusion equation for fibrin concentration is solved numerically for the current approximation of the diffusion coefficient D_n. Since this auxiliary direct problem does not admit a closed-form solution in the general case, it is discretized using an alternating direction implicit (ADI) finite-difference scheme [32]. The ADI discretization provides computational efficiency for the repeated solution of the direct problem arising within the iterative reconstruction procedure.

The employed ADI scheme possesses consistency, unconditional stability, and convergence properties for the considered linear diffusion equation. For sufficiently smooth solutions, the scheme achieves second-order accuracy in both space and time, with truncation error

$$O(\Delta t^2 + \Delta x^2 + \Delta y^2).$$

The minimization of the objective functional is performed by a gradient descent method. Because the unknown parameter is scalar, the gradient of the functional with respect to the diffusion coefficient is evaluated numerically using the central finite-difference approximation, which avoids the construction of the adjoint problem and simplifies the overall implementation.

At iteration n, the gradient is computed as

$$g_n \approx \frac{J(D_n + \delta_n) - J(D_n - \delta_n)}{2\delta_n} \tag{8}$$

The perturbation parameter used in the finite-difference approximation of the gradient is chosen as

$$\delta_n = \delta_0 \max(1, |D_n|), \qquad \delta_0 \ll 1,$$

where δ_0 is a small positive constant controlling the perturbation magnitude.

The diffusion coefficient is updated using the gradient descent scheme

$$D_{n+1} = D_n - \eta_n g_n \tag{9}$$

where the step size is chosen in decreasing form [28]

$$\eta_n = \frac{\eta_0}{(1+n)^{\mu}}, \qquad 0 < \mu < 1 \tag{10}$$

Here, $\eta_0 > 0$ denotes the initial step size, while the parameter $0 < \mu < 1$ controls the decay rate of the iteration step. The influence of different values of μ on the convergence behavior and reconstruction accuracy is investigated in the numerical experiments. The decreasing step-size strategy improves the stability of the iterative process and reduces oscillatory behavior at later iterations.

The proposed method generates a sequence $\{D_n\}$ that decreases the objective functional in a neighborhood of the minimum, provided that the initial step size η_0 is chosen sufficiently small. For the scalar parameter case considered in the present work, the finite-difference approximation of the gradient provides sufficient accuracy while preserving a relatively simple computational implementation.

RECONSTRUCTION ALGORITHM

The main steps of the proposed gradient-based reconstruction procedure are summarized below.

Given: measured final-time data $\psi^{\text{obs}}(x_i, y_j)$, known source field $\theta(x_i, y_j, t_k)$, initial guess $D_0 > 0$, parameters $\eta_0 > 0$, $\mu \in (0,1)$, tolerances ε_D, ε_J, and maximum number of iterations $N_{\max}$.

Step 1. Initialization.
Set $n = 0$ and choose the initial approximation D_0.

Step 2. Compute the numerical solution.
Solve equations (1)-(3) using the ADI scheme with coefficient D_n and compute the numerical solution at the final time $\psi_{i,j}^N(D_n)$.

Step 3. Evaluate the functional.
Compute $J(D_n)$ from (6).

Step 4. Compute the gradient.
Evaluate g_n using (8).

Step 5. Compute the step size.
Evaluate η_n from (10).

Step 6. Update the coefficient.
Update the diffusion coefficient according to

$$D_{n+1} = D_n - \eta_n g_n.$$

Step 7. Check stopping criteria.
Stop if at least one of the following conditions holds:

$$|D_{n+1} - D_n| < \varepsilon_D, \quad J(D_n) < \varepsilon_J, \quad n \geq N_{\max}.$$

Otherwise, set $n \leftarrow n+1$ and return to Step 2.

ANALYSIS OF THE RESULTS

In this section, we present and analyze the results of numerical experiments performed to validate the proposed gradient-based reconstruction algorithm. The main objective is to assess the accuracy, stability, and convergence behavior of the method for identifying the constant diffusion coefficient. In all experiments, the observation data are generated synthetically by solving the direct diffusion problem with a known coefficient. The reconstructed values are then compared with the exact coefficient in order to evaluate the performance of the proposed approach.

Particular attention is paid to the influence of the initial guess D_0 and the step-size parameter μ on the convergence of the iterative process. The parameter μ controls the rate of decrease of the gradient-descent step size and therefore affects both the convergence speed and the stability of the method.

The spatial domain

$$\Omega = [0,7] \times [0,1]$$

is discretized using a uniform finite-difference mesh with

$$N_x = 200, \qquad N_y = 100,$$

while the time interval $[0,T]$ is divided into uniform time steps with

$$\Delta t = 0.0001.$$

At each iteration of the reconstruction procedure, the auxiliary diffusion equation corresponding to the current approximation of the diffusion coefficient is solved numerically using the alternating direction implicit (ADI) finite-difference scheme. Different initial approximations D_0 are considered in order to investigate the robustness and convergence behavior of the proposed reconstruction method. The gradient descent parameters η_0 and μ are selected empirically to ensure stable convergence. The iterative process is terminated once at least one of the stopping criteria introduced in the previous section is fulfilled. In the following experiments, the exact diffusion coefficient is set to $D_{\text{exact}} = 0.5$, and the initial step-size parameter is chosen as $\eta_0 = 0.05$. The dashed horizontal line indicates the exact value of the diffusion coefficient. The results demonstrate stable convergence of the proposed gradient-based method for a wide range of initial guesses. Figure 1 illustrates the evolution of the reconstructed diffusion coefficient for various initial deviations and different values of the parameter μ. In all tested cases, the iterative process converges toward the exact diffusion coefficient, demonstrating robustness of the proposed gradient-based approach.

The results clearly show that smaller values of μ lead to faster convergence, whereas larger values produce a smoother but slower approach to the exact solution. Moreover, stable reconstruction is observed even for relatively large initial deviations (up to $\pm 50\%$), indicating low sensitivity of the method to the initial approximation. This property is particularly important for practical inverse problems where accurate initial guesses are often unavailable.

The parameter μ governs the rate of decrease of the gradient-descent step size and therefore affects both the convergence speed and the stability of the iterative process. By varying these parameters, we assess the robustness of the proposed reconstruction algorithm with respect to initialization and step-size scheduling.

Conclusions

In this work, an inverse problem of identifying a constant diffusion coefficient in a two-dimensional diffusion equation describing fibrin formation has been investigated. The reconstruction approach is based on the minimization of a least-squares objective functional using a gradient descent method. To simplify the implementation, the gradient of the functional with respect to the unknown coefficient is evaluated numerically via a central finite-difference approximation, thereby avoiding the construction of an adjoint problem.

The direct diffusion problem governing the evolution of fibrin concentration is solved using an alternating direction implicit finite-difference scheme, providing unconditional stability and computational efficiency. A decreasing step-size strategy is employed in the gradient descent iterations, where the parameter μ controls the rate of step-size reduction.

Numerical experiments with synthetically generated data demonstrate stable and accurate reconstruction of the diffusion coefficient. The re-

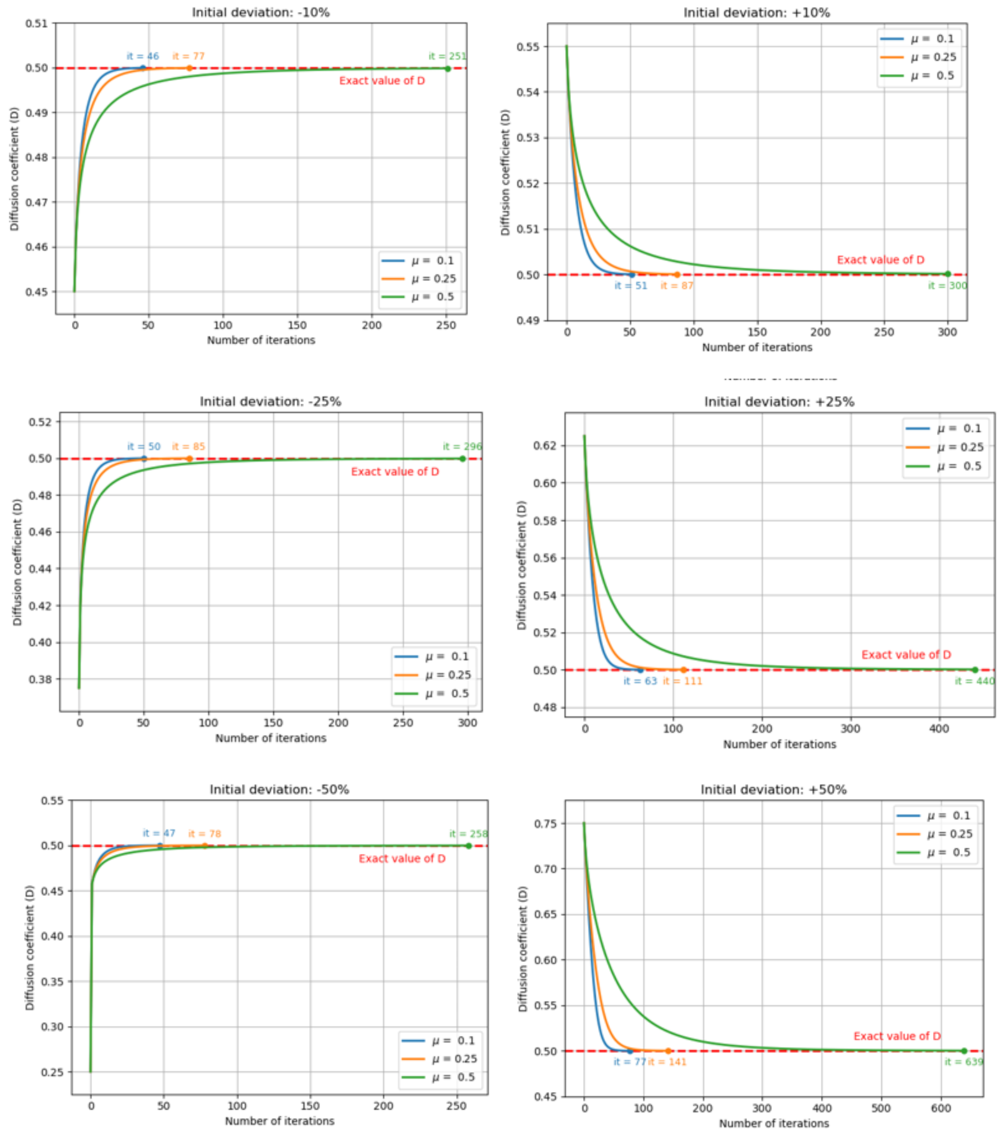

Figure 1 - Convergence of the reconstructed diffusion coefficient for different initial deviations and values of the step-size parameter μ.

sults indicate that the proposed method is robust with respect to the initial approximation and that the parameter μ has a significant influence on the convergence behavior: smaller values accelerate convergence, whereas larger values ensure a smoother iterative evolution.

Overall, the proposed gradient-based reconstruction algorithm provides a simple and effective tool for identifying diffusion parameters in mathematical models of fibrin formation. The approach is straightforward to implement and does not require adjoint problem formulation.

The present study is limited to the reconstruction of a constant diffusion coefficient using synthetically generated observation data within a simplified diffusion model of fibrin transport. The proposed approach is primarily applicable to diffusion-dominated hemodynamic models with sufficiently smooth solutions and low-dimensional parameter spaces. For more complex settings involving spatially varying coefficients, strongly heterogeneous media, or experimentally measured noisy data, additional regularization techniques and more advanced optimization procedures may be required.

Future work will focus on extending the proposed reconstruction framework to spatially varying diffusion coefficients $D(x,y)$, incorporating noisy observational data, and investigating inverse source identification problems within the same hemodynamic setting. Additional research directions include the development of adaptive step-size strategies and the application of the proposed approach to more detailed and physiologically realistic models of thrombus formation.

Author Contributions: The main idea of the inverse problem formulation for the hemodynamic model was proposed by S.D. Maussumbekova. The formulation of the direct problem and its numerical solution were developed by A.O. Beketaeva and S.D. Maussumbekova. The mathematical formulation and solution of the inverse problem were carried out by M.N. Kulbay. The development of the numerical algorithm and software implementation were performed by D.Zh. Orynbekova. All authors participated in the analysis and discussion of the obtained results and contributed to the preparation of the manuscript. All authors have read and agreed to the published version of the manuscript.

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