A fast solver for an inverse problem arising in bioluminescence tomography

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Abstract

Bioluminescence tomography (BLT) is a new method in biomedical imaging, with a promising potential in monitoring non-invasively physiological and pathological processes *in vivo* at the cellular and molecular levels. The goal of BLT is to quantitatively reconstruct a three dimensional bioluminescent source distribution within a small animal from two dimensional optical signals on the surface of the animal body. Mathematically, BLT is an under-determined inverse source problem and is severely ill-posed, making its numerical treatments very challenging. In this paper, we provide a new Tikhonov regularization framework for the BLT problem. Compared with the existing reconstruction methods about BLT, our new method uses an energy functional defined over the whole problem domain for measuring the data fitting, associated with two related but different boundary value problems. Based on the new formulation, a fast solver is introduced by transforming the proposed optimization model into a system of partial differential equations. Moreover, a finite element method is used to obtain a regularized discrete solution. Finally, numerical results show that the fast solver for BLT is feasible and effective.

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1. Introduction

With the accomplishment of human genome sequence and the coming of post-genome era, it is urgent to explore the mechanism of occurrence and development of various diseases (especially malignant diseases) at the cellular, molecular and gene levels, so that we can detect diseases before the appearance of clinical symptoms and enhance therapeutic

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effect through their early alarm and treatment. Molecular imaging is a rapidly developing biomedical imaging technique for this purpose; see e.g. [7, 28, 32, 36, 38] and references therein. Molecular imaging is broadly based on three technologies: nuclear imaging [4, 13], magnetic resonance imaging (MRI) [16, 42], and optical imaging [34, 35]. As an optical molecular imaging, bioluminescence tomography (BLT) is a recently developed promising modality and attracts more and more attention [9, 14, 15, 20, 39]. The goal of BLT is to quantitatively reconstruct a three dimensional bioluminescent source distribution within a small animal from two dimensional optical signals on the surface of the animal body. Currently, BLT is mainly used to cellular, molecular and gene expression imaging in studies of small animals, especially mice, but the success of this research will facilitate disease studies, drug development and therapeutic intervention [10, 32, 34].

Mathematically, BLT is an under-determined inverse source problem and is severely ill-posed, making its numerical treatments very challenging. Light propagation in biological tissue is governed by the radiative transfer equation (RTE) [27]. However, the RTE is highly dimensional and presents a serious challenge for its accurate numerical simulations given the current level of development in computer software and hardware. Experimental evidence shows that the range of light emission peaks is 460–630 nm for characterized luciferase enzymes ([43]), which is very small compared to the size of a typical object in this context. For this spectral range, scattering dominates for the photons in the tissue, and usually a diffusion approximation of the RTE is employed ([2, 33]).

Let $\Omega \subset \mathbb{R}^d$ be the biological medium with the boundary $\Gamma = \partial\Omega$. Although the dimension $d = 3$ for applications, the method we develop here is valid for any dimension. Without going into detail, the BLT problem based on the diffusion approximation is the determination of a light source function p in the differential equation

$$-\mathrm{div}(D\nabla u) + \mu_a\, u = p\chi_{\Omega_0} \quad \text{in } \Omega \tag{1.1}$$

with the following boundary condition

$$u + 2AD\frac{\partial u}{\partial n} = g^- \qquad \text{on } \Gamma \tag{1.2}$$

from measurement data g on the boundary Γ:

$$g = -D\frac{\partial u}{\partial n} \qquad \text{on } \Gamma. \tag{1.3}$$

Here, $D = [3(\mu_a + \mu')]^{-1}$, μ_a and μ' are given absorption and reduced scattering coefficients; $\partial/\partial n$ stands for the outward normal derivative; the function g^- is an incoming flux on the boundary Γ, and $A(x) = (1 + R(x))/(1 - R(x))$; $R(x) \approx -1.4399\gamma(x)^{-2} + 0.7099\gamma(x)^{-1} + 0.6681 + 0.0636\gamma(x)$ with $\gamma(x)$ the refractive index of the medium at $x \in \Gamma$. Moreover, Ω_0 is a measurable subset of Ω, called the permissible region, χ_{Ω_0} is the characteristic function of Ω_0, i.e., its value is 1 in Ω_0 and is 0 outside Ω_0.

Based on the diffusion approximation equation (1.1), many theoretical analysis and numerical methods about BLT have been explored, see e.g. [6, 9, 17, 19, 22, 26, 31, 40, 41] and references therein. To improve the accuracy of the reconstructed light source function, multispectral systems are developed ([8, 11, 18, 25]). We refer to [23, 24] for the BLT problem with enhancement of knowledge of the optical properties. In these works, Tikhonov regularization methods are used, with which various a priori information of a light source can be incorporated conveniently, and the BLT problems are transferred into optimization ones.

Conventionally, an L^2-norm functional is used on a part of or the whole boundary Γ to measure the data fitting, and then gradient-type iterative algorithms are adopted to find the minimizers, see [6, 8, 9, 11, 17, 18, 19, 20, 22, 23, 24, 25, 26, 31, 41] and so on. Alternatively, in this work, a Kohn-Vogelius type energy functional is used for our source function reconstruction. In general, Kohn-Vogelius functionals are expected to lead to more robust optimization procedures [1]. In the literature, these functionals have been used for a long time in the electrical impedance tomography [12]. However, to the best of our knowledge, they have not been used in the BLT problem. In this study, we give a new reconstruction framework based on a Kohn-Vogelius type energy functional. Moreover, instead of using usual gradient-type iterative algorithms for the optimal solution, with a priori information about the light source location, a fast solver is given to compute the density of inner light source function. By using our method, the proposed optimization model is transformed into a system of partial differential equations. As a result, issues occurring in iterative methods such as the choice of initial guess, convergence of iteration and stop criterion are avoided, and then the computation efficiency of light source reconstruction is enhanced.

We end this section with a description of the structure for the rest of this work. In section 2, an optimization framework based on an energy functional is established for BLT. Section 3 introduces a fast solver for the proposed optimization problem via adjoint theory in such a way that the BLT problem is transferred into a system of partial differential equations. In section 4, discretization of the system of equations by the finite element method is discussed. Several numerical examples are presented in section 5 to demonstrate the feasibility and efficiency of the proposed method.

2. An optimization framework based on an energy functional

We first introduce notations for function spaces and sets. Assume the boundary Γ is Lipchitz continuous. For a set G (e.g., Ω, Ω_0 or Γ), we denote by $W^{m,s}(G)$ the standard Sobolev spaces with norm $\|\cdot\|_{m,s,G}$, $W^{0,s}(G) = L^s(G)$. Particularly, $H^m(G)$ represents $W^{m,2}(G)$ with corresponding inner product $(\cdot,\cdot)_{m,G}$ and norm $\|\cdot\|_{m,G}$. Let $V = H^1(\Omega)$ and $Q = L^2(\Omega_0)$. Moreover, we assume $D \in L^\infty(\Omega)$ such that $D \geq D_0$ for some positive constant D_0, $\mu_a \in L^\infty(\Omega)$, $\mu_a \geq 0$ and μ_a is positive in a subset of Ω with a positive measure. Also we assume $g^-, g \in L^2(\Gamma)$.

From the Neumann boundary condition (1.2) and the Robin boundary condition (1.3), we derive a Dirichlet boundary condition

$$u = g_1 := g^- + 2\,A\,g \qquad \text{on } \Gamma. \tag{2.1}$$

Note that only two of the three boundary conditions (1.2), (1.3) and (2.1) are independent. Usually, to determine the source function p, we may associate one of the above three boundary conditions (1.2), (1.3) and (2.1) with the differential equation (1.1) to form a boundary value problem (BVP) while choosing one of the remaining boundary conditions for data matching in forming the inverse problem for p. For instance, in [22], (1.1) and (1.3) are used for the boundary value problem while (2.1) for the measurement matching. Then, because of the ill-posedness of the pointwise formulation of BLT, the following regularized problem is studied.

Problem 2.1. *Find $p_\varepsilon \in Q_{ad}$ such that*

$$J_{\varepsilon,\Gamma}(p_\varepsilon) = \inf_{q \in Q_{ad}} J_{\varepsilon,\Gamma}(q),$$

where

$$J_{\varepsilon,\Gamma}(q) = ||u(q) - g_1||^2_{0,\Gamma} + \varepsilon \|q\|^2_{0,\Omega_0}, \ \varepsilon \geq 0 \tag{2.2}$$

with $u(q) \in V$ being the weak solution of BVP (1.1) and (1.3).

Here Q_{ad}, known as a admissible set for source function p, is a closed convex subset of space Q; a common example of Q_{ad} is the set of non-negatively valued functions from Q. Problem 2.1 admits a stable and unique solution ([22]).

In this paper, based on a Kohn-Vogelius type energy functional, we explore a new optimization framework for the BLT reconstruction. For any $q \in Q$, denote by $u_N = u_N(q) \in V$ the weak solution of the Neumann and Robin BVP:

$$\begin{cases} -\mathrm{div}(D\nabla u_N) + \mu_a\, u_N = q\chi_{\Omega_0} & \text{in } \Omega, \\ D\frac{\partial u_N}{\partial n} = -g & \text{on } \Gamma, \end{cases} \tag{2.3}$$

and by $u_R = u_R(q) \in V$ the weak solution of the Robin BVP:

$$\begin{cases} -\mathrm{div}(D\nabla u_R) + \mu_a\, u_R = q\chi_{\Omega_0} & \text{in } \Omega, \\ u_R + 2AD\frac{\partial u_R}{\partial n} = g^- & \text{on } \Gamma. \end{cases} \tag{2.4}$$

The functions u_N and u_R satisfy

$$\int_\Omega (D\,\nabla u_N \cdot \nabla v + \mu_a\, u_N\, v)\, dx = \int_{\Omega_0} q\, v\, dx - \int_\Gamma g\, v\, ds \qquad \forall\, v \in V, \tag{2.5}$$

and

$$\int_\Omega (D\,\nabla u_R \cdot \nabla v + \mu_a\, u_R\, v)\, dx + \int_\Gamma \frac{1}{2\,A} u_R\, v\, ds = \int_{\Omega_0} q\, v\, dx + \int_\Gamma \frac{1}{2\,A} g^-\, v\, ds \qquad \forall\, v \in V, \tag{2.6}$$

respectively. We define the following Kohn-Vogelius type energy functional

$$J_\varepsilon(q) = \frac{1}{2} |||u_N(q) - u_R(q)|||^2_{1,\Omega} + \frac{\varepsilon}{2} \|q\|^2_{0,\Omega_0}, \ \varepsilon \geq 0 \tag{2.7}$$

with

$$|||v|||_{1,\Omega}^2 = \int_\Omega (D|\nabla v|^2 + \mu_a v^2)\, dx.$$

It is not difficult to verify that the objective functional $J_\varepsilon(\cdot)$ is continuous, coercive and strictly convex for $\varepsilon > 0$. Then we study BLT reconstruction through the following optimization approach.

Problem 2.2. *Find $p_\varepsilon \in Q_{ad}$ such that*

$$J_\varepsilon(p_\varepsilon) = \inf_{q \in Q_{ad}} J_\varepsilon(q).$$

Remark 2.3. *In [37], a different objective functional:*

$$J_{\varepsilon,\Omega}(q) = ||u_N(q) - u_R(q)||_{0,\Omega}^2 + \varepsilon \|q\|_{0,\Omega_0}^2, \ \varepsilon \geq 0, \tag{2.8}$$

and it is concluded ([37, Section 4]) that the reconstruction model using (2.8) performs somewhat better than the one using (2.2) in terms of accuracy for a large noise level. In this work, we focus on the resolution of Problem 2.2. We note that using norm $|||\cdot|||_{1,\Omega}$ in (2.7) rather than $||\cdot||_{0,\Omega}$ in (2.8) makes the deduction of adjoint equation (3.5) simpler.

By using arguments similar to those in [22, 37], we can show a well-posedness result about Problem 2.2 as follows.

Proposition 2.4. *For any $\varepsilon > 0$, Problem 2.2 has a unique solution $p_\varepsilon \in Q_{ad}$ which depends continuously on D, μ_a, g^-, g and $\varepsilon > 0$.*

3. A fast solver for the optimization problem

In the literature, iterative procedures are adopted to find a minimizer of an optimization problem like Problem 2.2. As far as the BLT problem is concerned, these iterative methods include modified Newton method together with an active set strategy [9], preconditioned conjugate gradient method [5], the generalized graph cuts reconstruction method [30], and so on. Issues involved in these iterative methods are related to choosing a proper initial guess, verifying convergence of the iteration, giving a stop criterion, etc. In particular, at each iterative step, we need to solve the BVP (2.6), and thus they are often time-consuming.

The aim of this section is to introduce, under some conditions, a fast solver without iteration for a stable BLT reconstruction. Denote by p_ε the unique solution of Problem 2.2, and by $u_N^* \in V$ and $u_R^* \in V$ the solutions of variational problems (2.5) and (2.6) (with q replaced by p_ε). Moreover, let $\tilde{u}_N \in V$ and $\tilde{u}_R \in V$ be the weak solutions of Neumann and Robin BVP problems

$$\begin{cases} -\mathrm{div}(D\nabla \tilde{u}_N) + \mu_a \tilde{u}_N = q\chi_{\Omega_0} & \text{in } \Omega, \\ D\frac{\partial \tilde{u}_N}{\partial n} = 0 & \text{on } \Gamma, \end{cases} \tag{3.1}$$

and

$$\begin{cases} -\mathrm{div}(D\nabla \tilde{u}_R) + \mu_a\, \tilde{u}_R = q\chi_{\Omega_0} & \text{in } \Omega, \\ \tilde{u}_R + 2\,A\,D\frac{\partial \tilde{u}_R}{\partial n} = 0 & \text{on } \Gamma, \end{cases} \tag{3.2}$$

respectively. Then for any $q \in Q$, $t \in \mathbb{R}$, the solutions $u_N(p_\varepsilon + t\,q)$ of (2.5) and $u_R(p_\varepsilon + t\,q)$ of (2.6) (with q replaced by $p_\varepsilon + t\,q$) satisfy $u_N(p_\varepsilon + t\,q) = u_N^* + t\,\tilde{u}_N$ and $u_R(p_\varepsilon + t\,q) = u_R^* + t\,\tilde{u}_R$, and we have

$$\begin{aligned} & J_\varepsilon(p_\varepsilon + t\,q) - J_\varepsilon(p_\varepsilon) \\ &= \frac{1}{2}\int_\Omega \left\{ D|\nabla\left[u_N(p_\varepsilon + t\,q) - u_R(p_\varepsilon + t\,q)\right]|^2 + \mu_a\left[u_N(p_\varepsilon + t\,q) - u_R(p_\varepsilon + t\,q)\right]^2 \right\} dx \\ &\quad - \frac{1}{2}\int_\Omega \left\{ D|\nabla\left[u_N(p_\varepsilon) - u_R(p_\varepsilon)\right]|^2 + \mu_a\left[u_N(p_\varepsilon) - u_R(p_\varepsilon)\right]^2 \right\} dx \\ &\quad + \frac{\varepsilon}{2}\int_{\Omega_0} (p_\varepsilon + t\,q)^2 dx - \frac{\varepsilon}{2}\int_{\Omega_0} p_\varepsilon^2 dx \\ &= t\left\{ \int_\Omega [D\nabla(u_N^* - u_R^*)\cdot\nabla(\tilde{u}_N - \tilde{u}_R) + \mu_a\,(u_N^* - u_R^*)\,(\tilde{u}_N - \tilde{u}_R)]dx + \varepsilon\int_{\Omega_0} p_\varepsilon q\, dx \right\} \\ &\quad + \frac{1}{2}t^2\left\{ \int_\Omega [D|\nabla(\tilde{u}_N - \tilde{u}_R)|^2 + \mu_a(\tilde{u}_N - \tilde{u}_R)^2]dx + \varepsilon\int_{\Omega_0} q^2 dx \right\}. \end{aligned}$$

Therefore, the Gateaux derivative of J_ε at p_ε in the direction $q \in Q$ is

$$\begin{aligned} J_\varepsilon'(p_\varepsilon)\,q &= \lim_{t\to 0}\frac{J_\varepsilon(p_\varepsilon + t\,q) - J_\varepsilon(p_\varepsilon)}{t} \\ &= \int_\Omega [D\nabla(u_N^* - u_R^*)\cdot\nabla(\tilde{u}_N - \tilde{u}_R) + \mu_a\,(u_N^* - u_R^*)\,(\tilde{u}_N - \tilde{u}_R)]dx + \varepsilon\int_{\Omega_0} p_\varepsilon q dx. \end{aligned} \tag{3.3}$$

By using integration by parts together with the definitions (3.1)–(3.2) of $\tilde{u}_N, \tilde{u}_R$, we find from (3.3) that

$$J_\varepsilon'(p_\varepsilon)\,q = \varepsilon\int_{\Omega_0} p_\varepsilon q dx - \int_\Gamma \frac{1}{2\,A}\tilde{u}_R(u_N^* - u_R^*)ds. \tag{3.4}$$

Let $w \in V$ be the unique weak solution of adjoint problem

$$\begin{cases} -\mathrm{div}(D\nabla w) + \mu_a\, w = 0 & \text{in } \Omega, \\ w + 2AD\frac{\partial w}{\partial n} = u_N^* - u_R^* & \text{on } \Gamma. \end{cases} \tag{3.5}$$

We multiply the equation (3.5) by $\tilde{u}_R$, integrate over Ω and integrate by parts twice, and use the definition (3.2) of $\tilde{u}_R$ to get

$$\int_{\Omega_0} wq dx + \int_\Gamma \frac{1}{2\,A}\tilde{u}_R(u_N^* - u_R^*)ds = 0. \tag{3.6}$$

Then, combine (3.4) and (3.6) to get

$$J'_\varepsilon(p_\varepsilon)\,q = \int_{\Omega_0} (w + \varepsilon p_\varepsilon) q dx.$$

Because Q_{ad} is a convex and closed subset of space Q, the following first order necessary and sufficient condition ([3, 29]) of the solution $p_\varepsilon \in Q_{ad}$ of Problem 2.2 holds:

$$J'_\varepsilon(p_\varepsilon)\,(q - p_\varepsilon) \geq 0 \quad \forall\, q \in Q_{ad}$$

or, equivalently,

$$\int_{\Omega_0} (w + \varepsilon p_\varepsilon)\,(q - p_\varepsilon) dx \geq 0 \quad \forall\, q \in Q_{ad},$$

which shows that p_ε is the projection of $-w/\varepsilon$ onto Q_{ad} with respect to the inner product $(\cdot,\cdot)_{0,\Omega_0}$ ([3, Section 5.3]).

In practice, Q_{ad} consists of non-negatively valued functions in Q, and in this case,

$$p_\varepsilon = \max\{-\frac{1}{\varepsilon} w, 0\} \text{ in } \Omega_0.$$

If $-\frac{w}{\varepsilon} \geq 0$, then

$$p_\varepsilon = -\frac{1}{\varepsilon} w \text{ in } \Omega_0.$$

Thus, we consider the following system of boundary value problems:

$$\left\{\begin{array}{ll} -\mathrm{div}(D\nabla u_N^*) + \mu_a\, u_N^* + \frac{1}{\varepsilon} w \chi_{\Omega_0} = 0 & \text{in } \Omega, \\ -\mathrm{div}(D\nabla u_R^*) + \mu_a\, u_R^* + +\frac{1}{\varepsilon} w \chi_{\Omega_0} = 0 & \text{in } \Omega, \\ -\mathrm{div}(D\nabla w) + \mu_a\, w = 0 & \text{in } \Omega, \\ p_\varepsilon = -\frac{1}{\varepsilon} w & \text{in } \Omega_0, \\ D\frac{\partial u_N}{\partial n}^* = -g & \text{on } \Gamma, \\ u_R^* + 2A\, D\frac{\partial u_R}{\partial n}^* = g^- & \text{on } \Gamma, \\ w + 2A\, D\frac{\partial w}{\partial n} = u_N^* - u_R^* & \text{on } \Gamma. \end{array}\right. \tag{3.7}$$

Now we are in a position to introduce a new formulation for the practical BLT reconstruction.

Problem 3.1. *Find* $(u_N^*, u_R^*, w) \in V \times V \times V$ *such that*

$$\left\{\begin{array}{ll} a_1(u_N^*, v) + b_1(w, v) = f_1(v) & \forall\, v \in V, \\ a_2(u_R^*, v) + b_1(w, v) = f_2(v) & \forall\, v \in V, \\ -b_2(u_N^*, v) + b_2(u_R^*, v) + a_2(w, v) = f_3(v) & \forall\, v \in V, \end{array}\right. \tag{3.8}$$

where

$$a_1(u,v) = \int_\Omega (D\nabla u \cdot \nabla v + \mu_a u\, v)\,dx, \quad a_2(u,v) = a_1(u,v) + \int_\Gamma \frac{1}{2\,A} u\, v\, ds,$$
$$b_1(u,v) = \frac{1}{\varepsilon}\int_{\Omega_0} u\, v\, dx, \quad b_2(u,v) = \int_\Gamma \frac{1}{2\,A} u\, v\, ds,$$
$$f_1(v) = -\int_\Gamma g\, v\, ds, \quad f_2(v) = \int_\Gamma \frac{1}{2\,A} g^- \, v\, ds, \quad f_3(v) = 0.$$

Set $p_\varepsilon = -\frac{1}{\varepsilon} w \chi_{\Omega_0}$.

Remark 3.2. *It is well-known that Problem 3.1 is not equivalent to the original regularized reconstruction model Problem 2.2. However, as we shall see in numerical simulations in Section 5, under the assumption that* Q_{ad} *consists of non-negatively valued functions from* Q*, the solution of Problem 2.2 can be computed through Problem 3.1. Compared to Problem 2.2, the framework Problem 3.1 reconstructs light source functions through solving a system of partial differential equations without the need of iteration, and thus can be solved directly, which makes reconstruction more efficient.*

In the next section, we focus on the finite element discretization of the system (3.8).

4. Numerical approximations

In this section, we consider numerical approximations of the system (3.8). For simplicity, assume both $\Omega \subset \mathbb{R}^d$ and $\Omega_0 \subset \Omega$ are polyhedral sets. We note that it is possible to extend the discussion to the case where Ω and Ω_0 are arbitrary bounded open domains. Then the standard conforming FEMs are applied to discretize the system (3.8). Let $\{\mathcal{T}_h\}_h$ be a regular family of triangulations over domain $\overline{\Omega}$ with meshsize $h > 0$. For each triangulation $\mathcal{T}_h$, define the linear finite element space

$$V^h := \{v \in C(\overline{\Omega}),\ v|_T \in \mathcal{P}_1(T)\ \forall\, T \in \mathcal{T}_h\}.$$

Here $\mathcal{P}_k(T)$ denotes the space of all polynomials of degree $\le k$ on T. Moreover, let $\{\mathcal{T}_{0,H}\}_H$ be a regular family of triangulations of $\overline{\Omega}_0$ with meshsize H, and for any triangulation $\mathcal{T}_{0,H}$, define the finite element space for light source

$$Q^H := \{q \in Q \mid q|_T \in \mathcal{P}_0(T)\ \forall\, T \in \mathcal{T}_{0,H}\}.$$

Then an approximation of Problem 3.1 is as follows.

Problem 4.1. *Find* $(u_N^{*,h}, u_R^{*,h}, w^h) \in V^h \times V^h \times V^h$ *such that*

$$\begin{cases} a_1(u_N^{*,h}, v^h) + b_1(w^h, v^h) = f_1(v^h) & \forall\, v^h \in V^h, \\ a_2(u_R^{*,h}, v^h) + b_1(w^h, v^h) = f_2(v^h) & \forall\, v^h \in V^h, \\ -b_2(u_N^{*,h}, v^h) + b_2(u_R^{*,h}, v^h) + a_2(w^h, v^h) = f_3(v^h) & \forall\, v^h \in V^h, \end{cases}$$

and set $p_\varepsilon^{h,H} = -\frac{1}{\varepsilon}\Pi^H w^h \chi_{\Omega_0}$*, where* $\Pi^H : Q \to Q^H$ *is an orthogonal projection operator defined by*

$$(\Pi^H q, q^H)_{0,\Omega_0} = (q, q^H)_{0,\Omega_0} \ \forall\, q \in Q,\, q^H \in Q^H.$$

For a triangulation $\mathcal{T}_h$, let $\varphi_i \in V^h$, $i = 1, 2, \cdots, n$, be the nodal basis functions of V^h associated with the nodes x_i, where n is the nodal number. Then the solutions $(u_N^{*,h}, u_R^{*,h}, w^h) \in V^h \times V^h \times V^h$ can be written as

$$(u_N^{*,h}, u_R^{*,h}, w^h) = \sum_{i=1}^{n} (u_{N,i}^*, u_{R,i}^*, w_i)\, \varphi_i,$$

where $u_{N,i}^* = u_N^{*,h}(x_i)$, $u_{R,i}^* = u_R^{*,h}(x_i)$, $w_i = w_i^h(x_i)$.

Then, Problem 4.1 is reduced a linear system of the form

$$K\, Y = F, \tag{4.1}$$

where $Y = (u_{N,1}^*, u_{N,2}^*, \cdots, u_{N,n}^*, u_{R,1}^*, u_{R,2}^*, \cdots, u_{R,n}^*, w_1, w_2, \cdots, w_n)^T$ and $(\cdot)^T$ is the transposition of $(\cdot)$. The approximation of light source function p is computed by

$$p_\varepsilon^{h,H}\,|_T = -\frac{1}{\varepsilon}\frac{1}{|T|}\sum_{x_l \in T}\int_T w_l \varphi_l dx \quad \forall\, T \in \mathcal{T}_{0,H}. \tag{4.2}$$

We note that if $\mathcal{T}_h$ and $\mathcal{T}_{0,H}$ are consistent (i.e., $\mathcal{T}_{0,H}$ is a restriction of $\mathcal{T}_h$ on Ω_0), then $H = h$ and (4.2) reduces to

$$p_\varepsilon^{h,h}\,|_T = -\frac{1}{3\varepsilon}\sum_{x_l \in T} w_l \quad \forall\, T \in \mathcal{T}_{0,h}.$$

5. Numerical simulation

Our main aim in this study is to provide a practical fast solver mentioned above for the BLT reconstruction. In this section, we report some numerical results to show its feasibility and efficiency. In the following simulations, assume $A = 1$, and $g^- \equiv 0$ which means the reconstruction is implemented in a dark environment. We use a consistent triangle triangulations for $\overline{\Omega}$ and $\overline{\Omega}_0$ with $H = h$, and use linear conforming finite element spaces V^h for state approximation while piecewise constant function space Q^h for source approximation. In addition, for a practical reconstruction, the problem (2.6) is solved by the given finite element method on a rather fine triangulation to construct the measurement g on the boundary Γ. In all simulations, the measurement data g is polluted by 5% Gaussian random noise. The resulting linear algebra system (4.1) is solved by the biconjugate gradient method.

It is known that the regularization parameter ε has an important effect on the accuracy of the reconstructed light source function. In the literature, there are many methods developed for choosing parameters properly, such as the discrepancy principle (DP), L-curve rule and so on. We refer [21] for some comments on the choice of these regularization parameters. In this section, all optimal regularization parameters are chosen approximately by sweeping them from 1 to $1\times10^{-1}, 1\times10^{-2}, 1\times10^{-3}, \cdots$. Moreover, in the subsequent figures, symbol $\lg(\cdot)$ stands for the logarithm based on 10.

5.1. Example 1

In our first example, we consider a problem with a single homogeneous light source. Let the problem domain be a circle centered at origin with radius 10 mm:

$$\overline{\Omega} = \{(x, y) \in \mathbb{R}^2 \mid x^2 + y^2 \leq 100\,\text{mm}^2\},$$

and a circle light source $p = \frac{1}{\pi}$ be embedded into Ω, centered at $(3.975, -1.423)^T$ with radius 1 mm. Assume the absorption and reduced scattering coefficients of the homogeneous medium are $\mu_a = 0.020\,\text{mm}^{-1}$ and $\mu' = 1.0\,\text{mm}^{-1}$ respectively. Then the measurement data g is computed on a mesh with $N = 184865$ nodes and $NE = 368640$ elements. Here and below, N and NE stand for the number of nodes and the number of elements of a triangulation. Figure 1 provides a sketch of a triangulation of Ω of Example 1.

The light source function p is reconstructed for different triangulations and different regularization parameters. The numerical results are reported in Figures 2 and 3. For three different triangulations, the dependence of errors in p computed through $\|p_\varepsilon^{h,h} - p\|_{0,\Omega_0}$ on regularization parameter ε is shown on the left-hand side of Figure 2 while the dependence of residuals $\|u_N^{*,h} - u_R^{*,h}\|_{0,\Omega}$ is plotted on the right-hand side of Figure 2. We observe that for all triangulations, the errors in light source function p first decrease and then increase as ε decreases. The optimal regularization parameter ε is about 1×10^{-2} for triangulation with $N = 198$, $NE = 360$, 5×10^{-4} for triangulation with $N = 755$, $NE = 1440$, and 6×10^{-4} for triangulation with $N = 2949$, $NE = 5760$. Also, we can see from the right-hand side that for a fixed triangulation, the residual $\|u_N^{*,h} - u_R^{*,h}\|_{0,\Omega}$ decreases as ε gets smaller. Moreover, Figure 3 shows the approximate source function $p_\varepsilon^{h,h}$ reconstructed on the meshes with $N = 755$, $NE = 1440$ and $N = 2949$, $NE = 5760$ respectively.

5.2. Example 2

In this experiment, we simulate a problem with a spatially varying light source. We place a light source of power 1.0 pW in two separate circles:

$$p = \begin{cases} \frac{1}{2\pi \ln 2\,[1+(x-3.975)^2+(y-1.423)^2]} & \text{in } \{(x, y) \mid (x - 3.975)^2 + (y - 1.423)^2) \leq 1\}, \\ \frac{1}{2\pi \ln 2\,[1+(x-3.975)^2+(y+1.423)^2]} & \text{in } \{(x, y) \mid (x - 3.975)^2 + (y + 1.423)^2) \leq 1\}. \end{cases}$$

A boundary measurement g is computed by the finite element method on a mesh with 417792 elements and 209441 nodes. Figure 4 sketches a triangulation in this case.

Again the light source function p is reconstructed for different triangulations and different regularization parameters, and numerical results are reported in Figures 5 and 6. The left-hand side and the right-hand side of Figure 5 are the dependence of errors in p on regularization parameter ε and the dependence of residuals $\|u_N^{*,h} - u_R^{*,h}\|_{0,\Omega}$ on ε respectively. Again, for a fixed triangulation, the errors in p first decrease and then increase as ε decreases, while the residual $\|u_N^{*,h} - u_R^{*,h}\|_{0,\Omega}$ decreases as ε gets smaller. The optimal regularization parameter ε is about 2×10^{-3} for triangulation with $N = 222$, $NE = 408$ and 4×10^{-2} for both triangulations with $N = 851$, $NE = 1632$ and $N = 3333$, $NE = 6528$. Moreover, Figure 6 shows the approximate source function $p_\varepsilon^{h,h}$ reconstructed on the meshes with $N = 851$, $NE = 1632$ and $N = 3333$, $NE = 6528$ respectively.

5.3. Example 3

Here we consider a 3D problem with a single homogeneous light source. Let the problem domain be a sphere centered at origin with radius 10 mm:

$$\overline{\Omega} = \{(x, y, z) \in \mathbb{R}^2 \mid x^2 + y^2 + z^2 \le 100\,\text{mm}^2\},$$

and a sphere light source $p = 1$ of power $\frac{4\pi}{3}$ pW be embedded into Ω, centered at $(5, 5, 5)^T$ with radius 1 mm. The absorption and reduced scattering coefficients of the homogeneous medium are the same as those in Examples 1 and 2. The measurement data g is computed from solving (2.6) on a mesh with 213711 elements and 37492 nodes. Figure 7 sketches a triangulation of the 3D domain.

The light source function p is reconstructed again for different triangulations and regularization parameters. The numerical results are reported Figures 8–12. Figure 8 gives the dependence of relative errors in p and the dependence of relative errors in residual on regularization parameter ε. Relative error in light source function p is computed through $\|p_\varepsilon^{h,h} - p\|_{0,\Omega_0}/\|p\|_{0,\Omega_0}$ while relative error in residual is computed through $\|u_N^{*,h} - u_R^{*,h}\|_{0,\Omega}/\|u_N^{*,h}\|_{0,\Omega}$. The reason of using relative errors rather than error themselves is because the norms of $\|p\|_{0,\Omega_0}$ and $\|u_N^{*,h}\|_{0,\Omega}$ are relatively big in this example. Again, similar conclusions to those in Examples 1 and 2 can be drawn from Figure 8. In addition, the optimal regularization parameter ε is about 3×10^{-3} for triangulation with $N = 371$, $NE = 1700$, 7×10^{-4} for triangulations with $N = 788$, $NE = 3841$, 1×10^{-3} for triangulations with $N = 1862$, $NE = 9648$, and 3×10^{-4} for triangulations with $N = 3436$, $NE = 18330$. Moreover, Figures 9–12 gives the approximate source function $p_\varepsilon^{h,h}$ reconstructed on four meshes with $N = 371$, $N = 788$, $N = 1862$ and $N = 3436$, respectively. Each of these figures contain nine subgraphs. The x-coordinate and y-coordinate of each subgraph are index of elements in $\overline{\Omega}_0$ and values of light source function on the corresponding elements. For instance, there are 76 elements in $\overline{\Omega}_0$ for triangulation with $N = 371$, $NE = 1700$ while 208 elements in $\overline{\Omega}_0$ for triangulation with $N = 788$, $NE = 3841$. In each subgraph, black straight line refers to true light source function $p = 1$ while the curve refers to the reconstructed $p_\varepsilon^{h,h}$ for the current mesh and regularization parameter ε, which is given on the top of the subgraph.

5.4. Example 4

In our last example, we consider a problem with inhomogeneous optical parameters. Set the problem domain Ω:

$$\overline{\Omega} = \{(x, y, z) \in \mathbb{R}^2 \mid x^2 + y^2 \le 100\,\text{mm}^2,\ 0 \le z \le 20\,\text{mm}\},$$

and denote by Ω_1 a subdomain of Ω:

$$\overline{\Omega}_1 = \{(x, y, z) \in \mathbb{R}^2 \mid x^2 + y^2 \le 9\,\text{mm}^2,\ 0 \le z \le 20\,\text{mm}\}.$$

Assume the absorption and reduced scattering coefficients are as follows:

$$\mu' = \begin{cases} 1.5\,\text{mm}^{-1} \text{ in } \overline{\Omega}_1, \\ 0.90\,\text{mm}^{-1} \text{ in } \overline{\Omega}/\overline{\Omega}_1, \end{cases} \qquad \mu_a = \begin{cases} 0.040\,\text{mm}^{-1} \text{ in } \overline{\Omega}_1, \\ 0.050\,\text{mm}^{-1} \text{ in } \overline{\Omega}/\overline{\Omega}_1. \end{cases}$$

Two separate homogeneous light sources are assigned into Ω: $p = 1$ in $\overline{\Omega}_{*,1}$ and $p = 5$ in $\overline{\Omega}_{*,2}$, where both $\Omega_{*,1}$ and $\Omega_{*,2}$ are spheres with radius 2 mm, centered at $(-5.5, -5.5, 15.5)^T$ and $(5.5, 5.5, 15.5)^T$, respectively. The measurement data g is computed from solving (2.6) on a mesh with 312077 elements and 54931 nodes. Figure 13 sketches a triangulation of Ω.

The light source function p is reconstructed again for different triangulations and regularization parameters. The numerical results are reported Figures 14–18. Figure 14 shows the dependence of relative errors in p and the dependence of relative errors in residual on regularization parameter ε. The optimal regularization parameter ε is about 6×10^{-2} for triangulation with $N = 784$, $NE = 3711$, 4×10^{-2} for triangulations with $N = 1383$, $NE = 6881$, 3×10^{-2} for triangulations with $N = 2928$, $NE = 15005$, and 2×10^{-2} for triangulations with $N = 5325$, $NE = 28165$. Moreover, Figures 15–18 gives the approximate source function $p_\varepsilon^{h,h}$ reconstructed on four meshes with $N = 784$, $N = 1383$, $N = 2928$ and $N = 5325$, respectively. Different from Example 3, there are two sources in this example. Correspondingly, each subgraph of Figures 15–18 contains two straight lines and two curves, representing true multiple source function p and reconstructed $p_\varepsilon^{h,h}$.

6. Conclusion

Bioluminescence Tomography is a new modality in optical imaging and aims to reconstruct a bioluminescent source distribution in an organism from surface measurements induced by internal bioluminescent sources. Because of the ill-posedness of the BLT, regularization is often adopted for a stable approximate solution. Instead of using the L2-norm on the boundary for data fidelity, in this paper, we use a Kohn-Vogelius type energy functional. The regularized problem is usually solved by an expensive iterative procedure where at each iteration step, one needs to solve the variational problem (2.5). In contrast, here we propose a fast solver which transfers the regularized problem to a system of partial differential equations. As a result, a series of problems in iterative methods such as the choice of initial guess, convergence of iteration and stop criterion are avoided. Numerical examples presented in Section 5 show that the proposed method in this paper produces a satisfactory performance, and is feasible and effective.

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