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One Step Quantitative Fluorescence Photoacoustic Tomography

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Abstract: We propose a one step algorithm to recover the exogenous fluorescent markers concentration from boundary photoacoustic measurements. We numerically validate the proposed scheme in two dimension.

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1. Introduction

The development of tumor increases the blood flow around the diseased tissues and enhances the local absorption co-efficient distribution. For contrast enhancement, fluorescent biomarkers are injected in the tissue, which tag the tumor and using fluorescence optical tomography (FOT), the spatial distribution of biomarkers is reconstructed. But the stability of FOT reconstruction is a major issue. In 2013, Zhao et. Al. proposed to take advantage of photoacoustic tomographic (PAT) reconstruction in order to stabilize FOT reconstructions (fluorescence photoacoustic tomography-fPAT) [1]. In this work we propose an algorithm to recover the fluorophore concentration directly from the boundary PA data. This makes the final reconstruction independent of the quality of intermediate step reconstruction. In section 2 and 3 of this paper, we discuss the forward and inverse problems of one step fPAT. Numerical validations are provided in section 4 and section 5 provides concluding remarks .

2. Forward Problem

Propagation of light in a turbid media is governed by radiative transport equation (RTE) [2], which is an integro-differential equation and solving it is computationally too expensive. For highly scattering media ($\mu_a << \mu_s$), RTE gets reduced to the **diffusion equation**. To model the propagation of excitation light (wavelength λ_x) as well as fluorescence light (wavelength λ_m), in domain $\Omega_d \subset R^d$ (d= 2 or 3) with boundary $\partial\Omega_d$,coupled diffusion equations are used: [3]

$$\begin{aligned} -\nabla\cdot(D_x\nabla\Phi_x)+k_x\Phi_x &= S_x \\ -\nabla\cdot(D_m\nabla\Phi_m)+k_m\Phi_m &= \beta\Phi_x \end{aligned} \qquad \text{in } \Omega_d \tag{1}$$

subjected to the Robin boundary conditions

$$\begin{aligned} \vec{n}\cdot(D_x\nabla\Phi_x)+b_x\Phi_x &= 0 \\ \vec{n}\cdot(D_m\nabla\Phi_m)+b_m\Phi_m &= 0 \end{aligned} \qquad \text{on } \partial\Omega_d \tag{2}$$

The quantities with subscripts x and m correspond to their values at excitation and emission wavelengths respectively. Here
$D_x = \frac{1}{3(\mu_{axi}+\mu_{axf}+\mu'_{sx})}$, $D_m = \frac{1}{3(\mu_{ami}+\mu_{amf}+\mu'_{sm})}$, $k_x = \mu_{axi}+\mu_{axf}$, $k_m = \mu_{ami}+\mu_{amf}$ $\beta = \phi\mu_{axf}$, $b_x = \frac{1-R_x}{2(1+R_x)}$ and $b_m = \frac{1-R_m}{2(1+R_m)}$,

Here ∇ is the gradient operator, $\vec{n}$ is the vector normal to the boundary,
S_x is the source intensity ,$\Phi_{x,m}$ are the excitation/emission fluence, $D_{x,m}$ are Diffusion constants, $k_{x,m}$ are decay co-efficients, (μ_{axi},μ_{ami}) are absorption coefficients due to non-fluorescing chromophore, (μ_{axf},μ_{amf}) are absorption

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coefficients due to exogenous markers, (μ'_{sx}, μ'_{sm}) are reduced scattering coefficients, (all in cm^{-1}), (b_x, b_m) are Robin boundary coefficients and (R_x, R_m) are the reflection coefficients at the excitation and emission wavelengths; β is emission source coefficient, ϕ is fluorescence quantum efficiency, , $i = \sqrt{-1}$. The net absorbed optical fluence at $\vec{r}$ is given by:

$$\mathbb{H}(\vec{r}) = k_x \Phi_x + k_m \Phi_m \tag{3}$$

The absorption of optical energy gives rise to thermoelastic expansion which produces a pressure (photoacoustic) field that propagates through the medium. For excitation by a sufficiently short pulse,we can model the PA propagation as a delta pulse excitation. The propagation of PA waves due to delta pulse excitation in acoustically homogeneous, non absorbing media is governed by photo-acoustic equation [2]:

$$\left(\nabla^2 - \frac{1}{v^2}\frac{\partial^2}{\partial t^2}\right) p(\vec{r},t) = -\frac{p_0(\vec{r})}{v^2}\frac{d\delta(t)}{dt} \qquad \text{in } \Omega_p \tag{4}$$

and the photoacoustic pressure source $p_0(\vec{r})$ is given by:

$$p_0(\vec{r}) = \Gamma(\vec{r})\mathbb{H}(\vec{r}) \tag{5}$$

where $\mathbb{H}(\vec{r})$ is absorbed optical fluence distribution (3), $\Gamma(\vec{r})(= v^2\beta/C_p)$ is the Gruneisen parameter, v is speed of sound, β is volumetric expansion coefficient and C_p is the specific heat at constant pressure. Fourier transform of (4) leads to photo-acoustic equation in frequency domain and using (5), we have

$$(\nabla^2 + k^2) p(\vec{r},k) = ik\frac{v\beta}{C_p}\mathbb{H}(\vec{r}) \tag{6}$$

subjected to absorbing boundary conditions:

$$\vec{n}\cdot\nabla p(\vec{r}) + ikp(\vec{r}) = 0 \qquad \text{on } \partial\Omega_p \tag{7}$$

3. Inverse Problem

The unknown optical parameters in the tissue like medium are $\mu_{axi}, \mu_{ami}\mu'_{sx}, \mu'_{sm}$. The recovery of μ_{axi} and μ'_{sx} can be carried out using quantitative photoacoustic tomography (QPAT) [4] at excitation wavelength, before injecting the markers. Similarly, the recovery of μ_{ami} and μ'_{sm} can be carried out using QPAT at emission wavelength. The exogenous markers, when injected in the tissue, get tagged with the tumor. Now, if we incident of an EM pulse at excitation wavelength (λ_x) internal absorbed fluence and hence the PA source, will have contributions from excitation as well as fluorescence light. The PA signals from this source are acquired on a detector grid and recovering the spatial concentration map i.e. the absorption co-efficient map μ_{axf} of the markers reveals the size and location of tumors inside the medium. In the proposed algorithm, we recover the fluorophore absorption coefficient μ_{axf} directly from the boundary PA data by solving the following Tikhonov regularized least squares problem:

$$\min_{\mu_{axf}\in R^2} \varepsilon(\mu_{axf}) = \sum_{j=1}^{L}\sum_{i=1}^{M} ||p^o_{i,j} - [f(\mu_{axf})]_{i,j}||^2_{L^2(\Omega)} + \lambda^2 ||\mu_{axf}||^2_2 \tag{8}$$

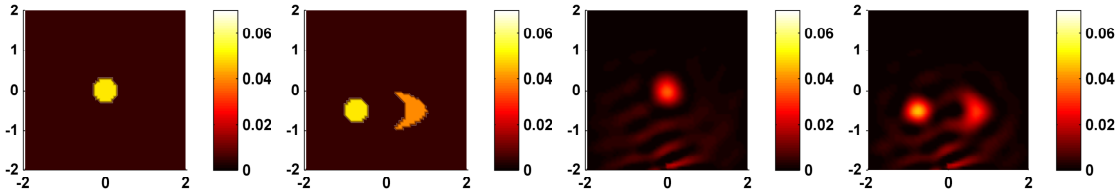
where $p^o_{i,j}$ and $[f(\mu_{axf})]_{i,j}$ are observed and computed photoacoustic measurements at i^{th} detector node and j^{th} frequency and $||.||_2$ denotes the $L^2 - norm$.Updation from the presumed distribution μ_{axf} is done using iterative Newton's method and the update $\triangle\mu_{axf}$ is calculated using Levenberg-Marquardt scheme:

$$\left\{\triangle\mu_{axf}\right\} = (\mathbf{J}^T\mathbf{J} + \lambda^2\mathbf{I})^{-1}\mathbf{J}^T\left\{\mathbf{p}^o - \mathbf{p}^c\right\} \tag{9}$$

4. Numerical Experiments

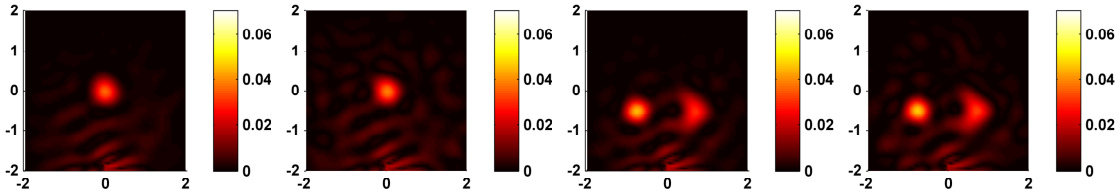
We have considered a 4cm x 4cm domain (4225 nodes and 8192 triangular elements) for FOT modelling and set up the FOT domain in a 7cm x 7cm (12769 nodes and 25088 triangular elements) domain for PAT modelling. The 384 ultrasonic detectors are arranged along a rectangle around the FOT domain uniformly separated by 0.625 mm. The background optical parameters inside the FOT domain were chosen to be homogeneous : $\mu_{axi} = 0.023cm^{-1}, \mu_{ami} =$

$1.257.\mu_{axi}cm^{-1}, \mu'_{sx} = 9.84cm^{-1}, \mu'_{sm} = 0.732\mu'_{sx}cm^{-1}, \phi = 0.016, R_{x,m} = 0.431$. As per the diffusion approximation, the source had been modelled one mean free path $(1/(\mu_{axi} + \mu'_{sx}))$ into the FOT domain from the point of excitation and pressure signal for 100 equidistant frequencies (2.4 kHz to 240 kHz) at 384 detector are modeled.
The reconstruction results (for target-background contrast =10:1) are shown in Figure 1 and 2



(a) (b) (c) (d)

Fig. 1: Original map of μ_{axf} (a)phantom 1 and (b)phantom 2 ; 1 step reconstruction of μ_{axf} (c) phantom 1 and (d) phantom 2.



(a) (b) (c) (d)

Fig. 2: 1-step reconstruction of: phantom 1 with (a)15dB SNR (b)5dB SNR; phantom 2 with(c) 15dB SNR(d) 5dB SNR.

5. Conclusions

We are able to reconstruct the spatial distribution of exogenous fluorophores directly from the boundary photoacoustic measurements in two dimensions without an intermediate step of photoacoustic reconstruction. This idea can be extended to three dimensions as well.

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