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An Anatomical Method for the Calibration of Diffuse Optical Tomography

Muralidharak K.

Research Scholar, CMJ University, Shillong, Meghalaya

Abstract – Diffuse optical imaging is an emerging modality that uses Near Infrared (NIR) light to reveal structural and functional information of deep biological tissue. It provides contrast mechanisms for molecular, chemical, and anatomical imaging that is not available from other imaging modalities. Diffuse Optical Tomography (DOT) deals with 3D reconstruction of optical properties of tissue given the measurements and a forward model of photon propagation. DOT has inherently low spatial resolution due to diffuse nature of photons. In this work, we focus to improve the spatial resolution and the quantitative accuracy of DOT by using a priori anatomical information specific to unknown image. Such specific a priori information can be obtained from a secondary high-resolution imaging modality such as Magnetic Resonance (MR) or X-ray. Image reconstruction Is formulated within a Bayesian framework to determine the spatial distribution of the absorption coefficients of the medium. A spatially varying a priori probability density function is designed based on the segmented anatomical information. Conjugate gradient method Is utilized to solve the resulting optimization problem. Proposed method is evaluated using simulation and phantom measurements collected with a novel time- resolved optical imaging system. Results demonstrate that the proposed method leads to improved spatial resolution, quantitative accuracy and faster convergence than standard least squares approach.

Diffuse optical tomography (DOT) Ls a sensitive and relatively low cost imaging modality that reconstructs optical properties of a highly scattering medium. However, due to the diffusive nature of light propagation, the problem Ls severely ill-conditioned and highly nonlinear. Even though nonlinear iterative methods have been commonly used, they are computationally expensive especially for three dimensional imaging geometry. Recently, compressed sensing theory has provided a systematic understanding of high resolution reconstruction of sparse objects in many imaging problems: hence, the goal of this paper Ls to extend the theory to the diffuse optical tomography problem. The main contributions of this paper are to formulate the imaging problem as a joint sparse recovery problem in a compressive sensing framework and to propose a novel no iterative and exact inversion algorithm that achieves the l_0 optimality as the rank of measurement increases to the unknown sparsely level. The algorithm Ls based on the recently discovered generalized MUSIC criterion, which exploits the advantages of both compressive sensing and array signal processing. A theoretical criterion for optimizing the imaging geometry is provided, and simulation results confirm that the new algorithm outperforms the existing algorithms and reliably reconstructs the optical in homogeneities when we assume that the optical background is known to a reasonable accuracy.

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INTRODUCTION

Optical diffusion tomography (ODT) is an imaging modality that has potential in applications such as medical imaging, environmental sensing, and non-destructive testing. In this technique, measurements of the light that propagates through a highly scattering medium are used to reconstruct the absorption and/or the scattering properties of the medium as a function of position. In highly scattering media such as tissue, the diffusion approximation to the transport equations is sufficiently accurate and provides a computationally tractable forward model. However, the inverse problem of reconstructing the absorption and/or scattering coefficients from measurements of the scattered light is highly nonlinear. This nonlinear inverse problem can be very computationally expensive, so methods that reduce the computational burden are of critical importance.

Another important issue for practical ODT imaging, which is addressed in this paper, is accurate modeling of the source and detector coupling coefficients. These coupling coefficients determine weights for sources and detectors in a diffusion equation model for the scattering domain. The physical source of the source/detector coupling variability is associated with the optical components

external to the scattering domain, for example, the placement of fibers, the variability in switches, etc. Variations in the coupling coefficients can result in severe, systematic reconstruction distortions. In spite of its practical importance, this issue has received little attention.

Two preprocessing methods have been investigated to correct for source/detector coupling errors before inversion. Jiang *et* al. calibrated coupling coefficients and a boundary coefficient by comparing prior measurements of photon flux density for a homogeneous medium with the corresponding computed values. This scheme has been applied in clinical studies. This method of calibration requires a set of reference measurements from a homogeneous sample, in addition to the measurements used to reconstruct the inhomogeneous image. Iftimia *et* al. proposed a preprocessing scheme that involved minimization of the mean square error between the measurements for the given inhomogeneous phantom and the computed values with an assumed homogeneous medium. However, although this approach does not require prior homogeneous reference measurements, it neglects the influence of an inhomogeneous domain when determining the source and detector weights.

In order to reconstruct the image from a single set of measurements from the domain to be imaged, it is necessary to estimate the coupling coefficients as the image is reconstructed. For example, Boas *et al.* proposed a scheme for estimating individual coupling coefficients as part of the reconstruction process. They simultaneously estimated both absorption and coupling coefficients by formulating a linear system which consisted of the perturbations of the measurements in a Rytov approximation and the logarithms of the source and detector coupling coefficients. No results have been reported for nonlinear reconstruction of both absorption and diffusion images, and the individual coupling coefficients.

THEORY OF DIFFUSION OPTICAL TOMOGRAPHY

The diffusion approximation to the radiative transport equation is the most widely used model to describe the migration of light through biological tissues. The Time-Domain Optical Breast Imaging System described in this dissertation is based on slab geometry. Thus, time-dependant solutions to the diffusion approximation are discussed for the homogeneous infinite slab along with the relative merits of various boundary conditions. The challenge of DOT is that of imaging heterogeneities in the tissue that may be due to functional changes in the tissue indicative of cancer or benign lesions. The homogenous solutions of the diffusion approximation can be used in a perturbation approach to derive approximate analytical solutions to the heterogeneous problem. The linear first born approximation that has been widely used in optical tomography is reviewed. This section closes with a discussion of the inverse problem and image reconstruction techniques.

THE RADIATIVE TRANSFER EQUATION

The most general model for light transport that may be given is the theory of radiative transfer, or photon transport theory, which has been extensively studied in atmospheric physics, and in neutron transport.

The radiative transfer equation, also referred to as the Boltzmann transport equation, is the expression of the balance of energy inside a volume element of the scattering medium. Generally, only elastic scattering is considered, that is a scattering event changes the direction of the photon, not the frequency . This also implies that the absorbed energy is completely lost in the sense that it is converted to kinetic energy manifest as heat. The equation describes the behavior of the specific intensity $I(\mathbf{r}, t, \hat{s})$ with units of $\mathrm{Wm^{-2}sr^{-1}}$, i.e., the energy moving in the direction $\hat{s}$, per unit solid angle, per unit time, and per unit area normal to the $\hat{s}$ direction. The radiative transfer equation can be obtained by considering the total space and time variation of the radiance along a direction $\hat{s}$ in an elementary volume and making this equal to the variation of specific intensity due to scattering and absorption inside the medium. The final equation for the time-dependent case

$$\frac{1}{\upsilon}\frac{\partial}{\partial t}I(\mathbf{r},t,\hat{s})+\hat{s}\cdot\nabla I(\mathbf{r},t,\hat{s})=-\mu_t I(\mathbf{r},t,\hat{s})+\frac{\mu_s}{4\pi}\int_{4\pi} p(\hat{s},\hat{s}')I(\mathbf{r},t,\hat{s})d\hat{s}'+S(\mathbf{r},t,\hat{s})$$

where u is the speed of light inside the diffusing medium defined by $\upsilon = c/n$, where c is the speed of light in vacuum and n is the effective index of the medium, $\mu_t = \mu_s + \mu_a$ is the extinction coefficient where μ_s and μ_a are the scattering and absorption coefficients respectively (the inverse of μ_s and μ_a represent the mean path between two consecutive scattering events and the mean path between two absorption events, respectively), $S(\mathbf{r}, t, \hat{s})$ is the source term representing the spatial and angular distribution of the source in units of $\mathrm{Wm^{-3}sr^{-1}}$, and $p(\hat{s},\hat{s}')$ is the scattering function that defines the probability of a photon moving in the direction s to be scattered into direction $\hat{s}'$.

$$\int_{4\pi} p(\hat{s},\hat{s}')d\hat{s}' = \frac{4\pi\mu_s}{\mu_t} \quad .$$

If the source term is assumed to be a Dirac delta function, the solution represents the Green's function of the problem from which the solution for a generic source can be obtained with convolution integrals. In the time-domain, the Green's function is referred to as the Temporal Point Spread Function (TPSF) having a damped exponential form that is limited by the absorption coefficient. The source term of unit strength is thus represented by

$$S(\mathbf{r},t,\hat{s}) = \delta(\mathbf{r})\delta(\hat{s})\delta(t)$$

If $I(\mathbf{r},t,\hat{s})\big|_{\mu_a=0}$ is a solution of Equation for a non-absorbing medium with the source term described by a Dirac delta function, then

$$I(\mathbf{r},t,\hat{s}) = \exp(-\mu_a vt)\, I(\mathbf{r},t,\hat{s})\big|_{\mu_a=0}$$

is the solution to the same equation when the absorption coefficient (independent of **r)** is μ_a. The validity can be checked by substitution of Equation into Equation with the assumption that the source term is zero except at r = 0, giving

$$\frac{1}{v}\frac{\partial}{\partial t} I_0(\mathbf{r},t,\hat{s}) + \hat{s}\cdot\nabla I_0(\mathbf{r},t,\hat{s}) = -\mu_t I_0(\mathbf{r},t,\hat{s}) + \frac{\mu_t}{4\pi}\int_{4\pi} p(\hat{s},\hat{s}') I_0(\mathbf{r},t,\hat{s})\, d\hat{s}'$$

where the zero subscript has been used to denote the solution for $\mu_a = 0$. Thus, the time-dependent impulse response of a homogeneous medium has two separable parts: one that is determined by the scattering coefficient $[I_0(\mathbf{r},t,\hat{s})]$ and one that is determined by the medium absorption $[\exp(-\mu_a vt)]$. Diffusion theory is derived from transport theory and would therefore be expected to have the same transformation property. This property is made use of in the next section for which the diffusion approximation to the radiative transport equation is introduced.

APPLICATIONS OF OPTICAL TOMOGRAPHY

The following areas have been suggested for application of Optical Tomography.

Monitoring the neonatal brain using OT

Between the third and fifth months of the development, neuronal production in the fetal brain is massive which is apparent in the rapid growth of the cortex. The bi parietal diameter, d (in cm), can be approximated as function of the age, a (in weeks), by the following equation

$$\begin{aligned} d &= 0.3a - 1.65 \qquad (\text{for } 12 < a < 20) \\ d &= 0.21\,a + 0.15 \qquad (\text{for } 20 < a). \end{aligned}$$

Due to the high growth rate, the rate of oxygen consumption in the fetus increases exponentially and doubles about every 40 days, reaching about 15 ml/min for the average-sized fetus at term. A relatively high proportion of the total body oxygen consumption is allocated to the fetal brain. Immaturity of the vascular system leads to a higher risk of haemorrhages especially for the neonate between 26 and 32 weeks of gestation.

One of the primary aims of Optical Tomography is to provide an instrument that can continuously monitor the oxygenation state and can early detect lesions in the baby's brain.

Functional brain imaging using OT

The average neural density in the human brain is about 20,000 neurons per cubic millimeter and reaches a maximum density of 100,000 per cubic millimeter in the visual cortex. In total there are between about 10^{11} and 10^{12} neurons in the entire human nervous system. All neurons have a cell body with cytoplasm that contains many mitochondria that provide the energy required for the cell function. It is in the mitochondria where oxygen is needed for the generation of ATP from ADP in the respiratory cycle.

Although the brain represents only 2% of body weight, it actually utilizes 15% of blood flow (about 700 ml/min) and some 25% of the overall oxygen consumption (about 60 ml/min). While in need, muscles may derive supplemental energy from anaerobic processes, our brains are *absolutely* dependent on continuous supply of well-oxygenated blood.The amount of oxygen delivery to the tissue depends both on the ***blood flow*** and ***blood volume.*** Regional changes in cerebral blood flow (CBF) and cerebral blood volume (CBV) are mainly due to dilation of cerebral vessels in response to an increase in $C0_2$ tension. Changes in local cerebral blood volume and cortical oxygenation are believed to be related with local brain activity and its measurement is one of the application objectives for Optical Tomography.

For functional studies using near-infrared techniques see for example Hoshi and Tamura, or for REM sleep associated brain studies on monkeys Onoe ***et al*** .

Breast cancer detection using OT

Optical detection of cancerous lesions depends on the fact that most cancers show an increased vascularity around the lesion and therefore have a locally increased blood volume that in turn adds to the total attenuation. A prototype system for the optical screening of breast has been build and used for clinical trials at Philips, Netherlands. The system irradiates the breast that is placed inside a conical shaped cup with low power continuous-wave (CW) laser light from a combination of 255 surrounding sources and 255 surrounding detectors.

CONCLUSION

In this thesis, we have developed several different regularization methods for stationary and non-stationary DOT. The classical Tikhonov regularization methods were used instead of the statistical inversion methods, however the connection was kept in mind during the design of the regularization functional. Much work was done on the regularization, but developing the measurement model, or in the statistical framework the likelihood functional, was not done here.

There have been much progress in the approximation error modelling, where errors are taken into account in the likelihood functional. Utilizing these methods more, one could make more realistic models of the errors in the measured signal. Error sources could be from, e.g., the measurement device, the approximatively forward model, the incorrect or truncated shape of the object or the sparse discretization. A more accurate likelihood functional would make the Bayesian framework in DOT more feasible. Over or underestimated noise covariance would lead to too broad or too narrow posterior distribution. However, this does not effect on the value of the MAP estimate, but would make the statistical interpretation incorrect.

The feasibility of the developed regularization methods was shown using measurements from simple phantoms. However, in brain imaging for example, the object has a much more complex structure. Some additional information, such as anatomical information, would improve reconstructions.

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