DIFFUSE OPTICAL TOMOGRAPHY: THEORETICAL BASIS, ADVANTAGES, AND APPLICATIONS

A PREPRINT

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December 18, 2022

ABSTRACT

Diffuse optical tomography (DOT) is an optical medical imaging method that can assess the structural properties of tissues and their functional characteristics, such as hemoglobin concentration, water content, as well as lipid concentration, via three-dimensional image reconstruction. This paper presents the theoretical basis and working principle of diffuse optical tomography. The paper explains how the optical properties of tissue can be imaged by photon migration techniques based on diffusion theory. The author presents the reasoning for near-infrared (NIR) imaging as the most effective technique in terms of quantitative recovery of spectroscopic optical parameters. This work also listed various advantages, applications, and challenges of DOT. The paper also briefly discusses current progress in near-infrared medical imaging and its future direction.

Keywords Diffuse Optical Tomography · Near-infrared · Inverse problem · Spectroscopy · Medical Imaging · fNIRS

1 What is Diffuse optical tomography

Diffuse optical tomography (DOT) is an optical medical imaging method that can assess the structural properties of tissues and their functional characteristics, such as hemoglobin concentration, water content, as well as lipid concentration, via three-dimensional image reconstructionArridge [1999], Gibson et al. [2005]. DOT is based on the principle that measured near-infrared (NIR) signals are indicative of the optical properties of the underlying biological tissues Arridge [1999], Saikia [2021a]. It is possible to reconstruct optical tomographic images using the spatial distribution of these measured optical signals. The problem of image reconstruction is an inverse problem that can be described as determining the internal spatial distribution of the objective function using the measurements taken at the boundaries of the tissues Arridge and Hebden [1997], Poorna et al. [2021]. There are large attenuation and scattering factors in diffusive waves, which makes this problem ill-posed. In DOT, the tissue is illuminated by NIR light sources, one at a time. Arrays of detectors are used to measure the diffuse light that comes out of the boundary. Next, the localized optical properties of the illuminated tissue are derived and estimated using a model.

As DOT can provide functional images of tissue using the nonionizing NIR light, it has gained a lot of attention in the past decades. DOT is mostly used to image brains and breasts. Measurements at the tissue boundary are critical for estimating the internal distribution of optical properties Arridge [1999], Arridge and Hebden [1997]. NIR interaction with tissue is driven primarily by scattering, so the estimation problem, or the inverse problem, isn't linear, ill-posed, and underdetermined Arridge [1999]. A computationally intensive model is needed to solve an inverse problem. Calculated optical properties of tissue are matched iteratively with experimental data using models in a least-squares sense Arridge [1999]. Because these computational models run repeatedly, obtaining real-time optical images is a big challenge Arridge [1999], Gibson et al. [2005].

DOT comes with its most obvious advantage, which is the possibility of spectroscopic delineation of tissue chromophores and the concomitant ability for early diagnosis of malignancy on the basis of the functional information that spectroscopy

provides Saikia and Kanhirodan [2019a]. The disadvantages are caused by the turbid nature of the tissue through which light is modeled to diffuse. The diffusion process with a finite length scale associated with it imposes a limitation on the spatial resolution achievable in DOT images. More importantly, the penetration of light into the human body or organ is rather limited, which limits the application of DOT only to soft-tissue organs such as the breast, prostate, muscles, and neonatal head. One of the reasons for choosing NIR light is to maximize penetration because, in the range of 600 - 900 nm, optical absorption in tissue is relatively small Saikia [2021b]. It's not as spatially detailed as other imaging methods, like magnetic resonance imaging or X-ray CT, but DOT lets us see a lot of physiological parameters that we wouldn't be able to see otherwise, like hemodynamics and other functional processes that happen every few microseconds. In spite of the earlier mentioned disadvantages, spectroscopy-based prediction of such useful functional parameters as total hemoglobin concentration, oxygen partial pressure, etc., has made DOT imaging the subject of intense research leading to the development of either stand-alone NIR clinical imagers or MRI-assisted DOT imagers. Furthermore, at a relatively low cost, DOT can be implemented in small and portable instrumentation.

1.1 Application of DOT

DOT has various applications and here are some of them:

- **Breast cancer imaging:** X-ray mammography can detect breast cancer. To improve the assessment and characterization of breast tumors, a wide range of other techniques such as ultrasound, Electrical Impedance Tomography (EIT), and Magnetic Resonance Imaging (MRI) are being used. Positron Emission Tomography (PET) and MRI are becoming more popular because they provide fundamentally different information than traditional structural pictures. It gives us direct access to physiological data like metabolism, blood flow, blood volume, and oxygen saturation. Tumor angiogenesis alters these parameters, which are also used to track a tumor's response to therapy. These functional parameters can be imaged by DOT. Because tumors are more vascularized than surrounding tissue, they absorb light differently. Through spectroscopic variation in μ_a, the relative concentration of oxygenated hemoglobin can be determined, and thus the oxygen demand-supply ratio can be determined. Furthermore, it can be used to differentiate tumors from background tissue, malignant tumors from non-malignant tumors, and tumors with varying levels of activity (degrees of malignancy).
- **Brain function imaging:** A DOT assessment of brain function complements positron emission tomography (PET), functional MRI (fMRI), electroencephalogram (EEG), and magnetoencephalography (MEG). PET images changes in metabolic activity but has a low temporal and spatial resolution. fMRI provide high spatial and temporal resolution images of blood flow and deoxy-hemoglobin concentration, but cannot measure oxy-hemoglobin concentration simultaneously. EEG and MEG monitor neural activity with much higher temporal resolution (100 to 1 kHz), but localizing electrical and magnetic sources is difficult and spatial resolution is poor compared with fMRI. While its spatial resolution is inferior to that of fMRI, the DOT, when used in combination with fMRI, can simultaneously measure oxy- and deoxyhemoglobin concentrations and blood volume. Combining optical imaging with fMRI and EEG/MEG is expected to result in a whole that is more useful than any of the parts alone.
- **Stroke:** It may be possible to detect ischemic strokes and hemorrhagic strokes more quickly and accurately using DOT, which is essential before applying neuroprotective drugs as it can effectively treat stroke patients in case of ischemic strokes, but can lead to fatality in case of hemorrhagic strokes. It is also possible to monitor the progression of a stroke as well as its response to treatment using DOT at the bedside.
- **Monitoring Brain Trauma and Surgical Intervention:** Detecting a brain hemorrhage early can greatly improve a patient's recovery and long-term effects if the hemorrhage occurs due to trauma or subsequent surgery. Current screening methods include cognitive testing and invasive monitoring (e.g., intracranial pressure gauges). A continuous DOT monitor at the bedside could provide real-time information on bleeding location and size, which is an advantage over these techniques. Collateral damage can also be minimized through monitoring during brain surgery. The use of an EEG during surgery can successfully monitor interference with critical functions, but the placement of electrodes is a time-consuming and painful process. There is also the option of using an fMRI, but a special operating room with an expensive magnet is required for this. An inexpensive alternative could be the DOT with an optical surface imaging technique.

2 Theoretical Basis of Diffuse Optical Tomography

In the past two decades, diffusion theory has been increasingly used to study radiative transfer, particularly in laser diagnosis. The optical properties of tissue can be monitored by photon migration techniques based on diffusion theory Chance et al. [1988a]. To detect objects embedded within tissue phantoms, photon-density waves have been used as solutions to the diffusion equation that exhibit strong damping Knüttel et al. [1993], Boas et al. [1994]. The laser

light must be transported through optical fibers placed on the tissue surface in order for these laser techniques to be noninvasive. As a result, tissue boundaries are inevitable. Diffusion theory must take this boundary into account if optical properties are to be measured without errors of more than 50%. As medical imaging research with diffuse light moves away from high spatial resolution, it is now focused more on functional imaging. Despite the fact that diffuse optical imaging cannot compete with anatomical imaging methods (such as x-radiography, ultrasound, and magnetic resonance imaging), it offers several distinct advantages when it comes to sensitivity to functional changes, safety, cost, and convenience. Through the use of diffuse optical spectroscopy in the near-infrared, it is possible to uncover physiological information noninvasively that cannot be obtained otherwise.

When studying spectroscopic optical parameters of highly scattering media such as tissue, NIR imaging is the most effective technique in terms of quantitative recovery of spectroscopic optical parameters. In the field of photon migration, the biggest advance has been the recognition and general acceptance of light diffusion as a mechanism for transporting light over long distances. By using this model, it is possible to quantify the scattering of tissue and absorption of tissue and to accurately incorporate boundaries, such as air-tissue interfaces, into the theory of transport Patterson et al. [1989, 1991]. Diffusion approximation allows detailed, quantitative investigations of average concentrations of molecular species in highly scattering media due to the separation of scattering and absorption Chance et al. [1988b], Duncan et al. [1993], Ferrari et al. [1992, 1989], Sevick et al. [1991], Svaasand et al. [1993].

2.1 Photon Diffusion Equation

A diffusion equation well describes the propagation of light through highly scattering tissue, according to Patterson's experiment in 1988 Patterson et al. [1989]. A comparison could be drawn between the theory of light diffusion in tissues and the theory of heat diffusion and neutron diffusion. In order to fit their measurements to the diffusion solution, researchers had to incorporate the diffusion solution. Experimental measurements were performed using a pulsed laser source and a time-resolved laser source. Researchers later realized that amplitude-modulated light sources could be used to measure the amplitude and phase of diffusing photon density waves in the frequency domain Tromberg et al. [1993]. It is possible to solve the Helmholtz equation with simple spherical wave solutions when light energy density oscillates for amplitude-modulated sources in homogeneous media. In biological tissue, the waves are composed of random walking photons with a random walk step of approximately 1 mm. However, macroscopically, they form a damped scalar wave of photon density with a wavelength of about 10 cm. A diffusing photon density wave (DPDW) is referred to as this wave. As a result of wave analysis, we are able to draw analogies from electromagnetic radiation, which provides us with useful insights and ease of computation. In contrast to time-resolved imaging, frequency domain measurements are less expensive and more stable, and pulsed illumination data in the form of the temporal point spread function (TPSF) can be viewed as frequency domain data with multiple frequencies at the same time. Fishkin. et al. Tromberg et al. [1993] and Patterson et al. Patterson et al. [1991] developed analytic solutions in the frequency domain and performed some of the first frequency domain measurements to non-invasively recover optical properties. The properties of DPDW s have been verified in both biological models Fishkin et al. [1991] and human breast studies O'Leary et al. [1995].

3 Difficulties in DOT Imaging

DOT is a nonlinear and ill-posed inverse problem. DOT presents some challenges for the following reasons:

- The scattering nature of photons traveling through tissue makes DOT an attractive tool for the noninvasive imaging of diseases. The strong scattering of light by biological tissue leads to poor depth localization in DOT due to the attenuation of detection sensitivity exponentially with depth.
- The tissue is a turbid medium with strong scattering. Light travels through the tissue in a complicated zigzag path. As a result, strength attenuated rapidly, and the propagation is inherently 3-D. this renders the relation between the output photon density and the optical properties dependent on stochastically defined paths.
- In the frequency domain imaging, although the amplitude modulation is of hundreds of Mega Hertz, the wavelength of the DPWD (Diffuse Photon Density wave), which is owing to the intensity modulated illumination, is of the order of a few centimeters, much longer than the typical size of inhomogeneities. This is the fundamental reason for poor resolution in images from DOT.
- When one illuminates the turbid object with a short pulse, the ballistic photons are very few, or none. If ballistic photons are of sufficient strength reconstruction from such photons can give better-resolved images.
- The background properties being not known in advance leads to difficulties in measuring and interpreting measurements for inverse reconstructions.

- Modeling noise is difficult as the sources of noise include both thermal noise in the amplifiers and shot noise due to the quantum nature of the sources.
- Absorption/scattering coefficients and field amplitude and phase are nonlinearly related. Due to these considerations, either a linearized approximation like Born or Rytov must be used or a nonlinear forward model must be used to reduce the numerical burden.
- Depending on the geometry and physical conditions, light may propagate in greatly different ways, for example through highly scattering brain tissue that is surrounded by slightly scattering cerebrospinal fluid (CSF). To deal with such inclusions the DE is inadequate as a model for light transport. One should rely on the RTE, which also takes into account the angles of scattering.
- The optical properties of tissue are characterized by two parameters. Simultaneous reconstruction of both parameters complicates and may induce cross-talk between the images.
- Ill-posedness may also arise from the fact that very small changes in optical parameters can give rise to large changes in measurement or vice versa. Thus inverse solutions must take care to see that the effect of noise, which gives rise to large swings in reconstruction, is properly accounted for.
- In addition, one might estimate the absorption or scattering coefficient at many locations in space, several orders of magnitude more than the number of measurements. This is an ill-posed problem. This also becomes another source of non-uniqueness of solutions.

3.1 Progress and Future Directions

Diffuse optical tomography (DOT) is based on measurement of Near-infrared (NIR) light at multiple locations on the tissue surface, transmitted or reflected from the deep tissue to probe the optical properties of the tissues. It requires source-detector multiplexing techniques to acquire data and system calibration to remove uncertainty Saikia [2021c]. The computational challenge is in the estimation of internal optical properties of tissue using a few measurements on the tissue boundary Arridge [1999], Arridge and Hebden [1997]. However, there is an algorithm developed for high-speed 3D DOT image reconstruction Saikia et al. [2014a]. This algorithm can also be implemented on multiple GPUs for further speed up the image reconstruction Saikia and Kanhirodan [2014a] and real-time imaging of DOT is an another possibility Saikia et al. [2014b]. Method for scanning a small region of the tissue as an efficient imaging technique was proposed Saikia and Kanhirodan [2014b, 2016]. Another interesting tissue imaging method based on DOT, particularly for the brain, is functional near-infrared spectroscopy (fNIRS). It can be used to measure brain activity, such as mental workload Saikia et al. [2021a]. fNIRS system can be built with few hardware components. The hardware can also be in the form of a patch for brain imaging Abtahi et al. [2016], Saikia and Mankodiya [2018]. In fNIRS technology, the light sources and detectors are generally referred to as optodes Saikia and Mankodiya [2019]. There is a trend for portable fNIRS Saikia et al. [2019a]. New concepts, such as internet-of-things, were also implemented in fNIRS system development Saikia et al. [2018a], Saikia [2021d], Saikia et al. [2018a]. Further, machine learning-based classification of the cognitive status of individuals in real-time is possible Saikia et al. [2021b], Saikia and Brunyé [2021]. Researchers are exploring new applications of fNIRS and fNIRS has great future potential. Usually the DOT hardware for breast imaging is bulky. There is a possibility of using LEDs and photodetectors Saikia et al. [2017] to develop compact DOT systems. Further, DOT can be used as a point-of-care imaging system Saikia et al. [2019a,b]. Some of the systems were designed for teaching purposes Saikia and Kanhirodan [2019b]. While probing tissue the unwanted signal from the superficial layer of the tissue is often added to the signal of interest. These unwanted signals can be removed my measuring them separately and accounting them in the image reconstruction Saikia et al. [2018b].

4 Discussion and Conclusion

It is essential to address both the theoretical, computational, and hardware challenges involved in nurturing the idea of imaging using NIR light into a fully developed NIR imaging system. It is an ill-posed (and nonlinear) problem to recover the optical property distribution inside a large object from noisy boundary measurements of light. When creating direct 3-D images, this is especially critical. From a theoretical perspective, it is difficult to determine the distribution of optical properties in the interior of a large object. This is due to the noisy boundary measurement data obtained on the boundary region. There are several reasons for this, but it is especially prevalent when it comes to the reconstruction of direct 3-D images. A computational-theoretical procedure is used to solve the nonlinear ill-posed problem of recovering a large-dimensional unknown parameter vector by an iterative procedure. Because of ill-posedness, DOT requires regularization to yield proper results. Therefore, there is a need for the development of a robust and accurate 3-D optical tomography reconstruction system. This paper suggests the direction toward implementing the computationally intensive part of the 3-D DOT image reconstruction algorithm on GPU. The GPUs have the potential to provide massively parallel computational power for real-time 3D DOT image reconstruction.

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