THEORY, ADVANTAGES, APPLICATIONS AND FUTURE OF DIFFUSE OPTICAL TOMOGRAPHY

A PREPRINT

Connor Peirson
Biomedical Engineering
Drexel University
Philadelphia, PA 19104, USA
connor.peirson@mail.com

ABSTRACT

Diffuse optical tomography (DOT) is a medical imaging procedure using light to measure the geometric and working properties of cells, for instance, oxygen consumption, water content, and fat percentage in the tissue by performing three-dimensional visualization of the tissue. This paper aims to explain the theory behind diffuse optical tomography imaging and how the technology works. The paper explains how photon migration techniques based on diffusion theory can be used to image the optical properties of tissue. There are several reasons why near-infrared (NIR) imaging is the most effective method in terms of recovering optical parameters quantitatively in the near-infrared region. The author discusses the methods in detail. This research also presents various advantages, practical uses, and potential problems that have been related to DOT in this work. There is also a brief discussion of current research developments in medical imaging using near-infrared wavelengths, and what the future holds for that area.

Keywords Inverse problem; Biomedical; Diffuse Optics; Imaging; Tomography; NIRS

1 What is Diffuse optical tomography

Diffuse optical tomography (DOT) is a light-based imaging concept applied in medicine that is capable of imaging the geometrical properties of tissues and their working characteristics, such as the concentration of different components of the tissue Arridge [1999], Gibson et al. [2005]. DOT is based on the principle that measured near-infrared (NIR) signals are signature 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 region of interest optical tissue properties of the radiated 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]. Figure 2 shown an algorithm used for DOT image reconstruction Saikia [2021b]. Because these computational models run repeatedly, obtaining real-time optical images is a big challenge Arridge [1999], Gibson et al. [2005].

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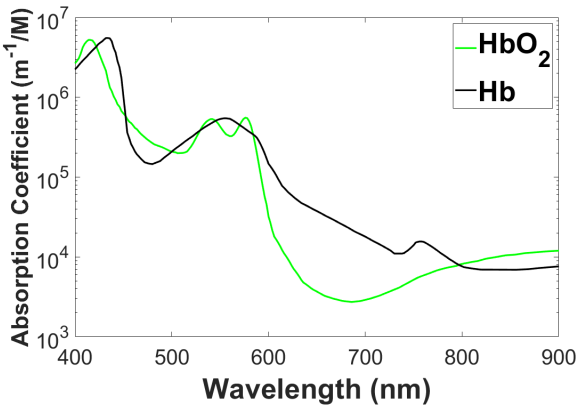

Figure 1: Absorption spectra of HbO_2 and Hb.

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]. The absorption spectra of HbO_2 and Hb is shown in figure 1. 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.

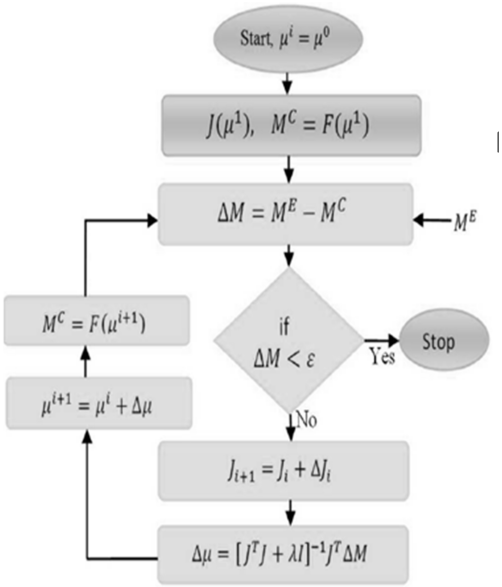

Figure 2: Image reconstruction algorithm.

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 amount of blood, metabolic state, flow of blood, and oxygen level. Tumor angiogenesis alters these tissue characteristics, 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 oxyhemoglobin level simultaneously. EEG as well as MEG can monitor electrical activity of the brain with much higher time resolution (50 to 1 kHz), but pin pointing sources of these electrical and magnetic fields is difficult and resolution in space is not upto as expectation 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 light-based imaging with fMRI and MEG/EEG could provide result in a complete picture 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 and treatment response 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 because of brain injury. Current screening methods include cognitive testing and invasive monitoring (e.g., measurement of cranial pressure). A continuous DOT monitor at the bedside could provide continuous monitoring on bleeding site and spreading, which is an advantage over these techniques. Collateral damage can also be minimized through monitoring during brain surgery. The use of an EEG while performing a surgery could disrupt the critical surgical 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 room with a costly magnet is required for this. An inexpensive alternative could be the DOT that can provide optical imaging on the surface of the body.

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 light interesction of tissue could be monitored by photon transport concept derived from the 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 biomedical research with diffusion 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-ray, ultrasound, and MRI 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-based imaging is the most viable method with respect to the of recovering of spectroscopic tissue light characteristics. In the area of photon as a light migration, the biggest advance was the accepting the light diffusion as a mechanism for transporting light over

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long distances. By using this model, we can quantify the scattering of tissue and absorption of tissue and to precisely include boundarie conditions, for example tissue-air interfaces, with the theory of transport Patterson et al. [1989, 1991]. Diffusion approximation allows detailed, quantitative investigations of mean volume of species in majorly scattering space 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].

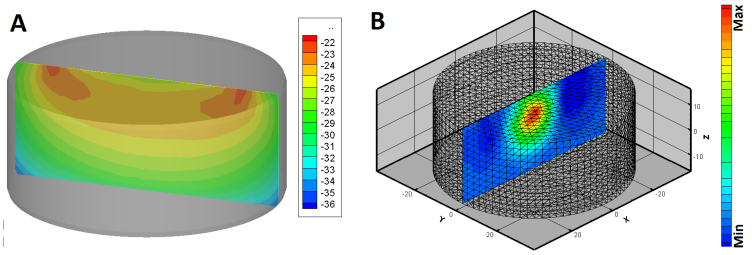

Figure 3: Diffuse optical tomography. (A) sensitivity matrix and (B) Reconstructed image from a phantom having inclusion at the center.

2.1 Photon Diffusion Equation

A diffusion equation well describes the moving of light via strongly scattering tissue, according to Patterson's experiment in 1988 Patterson et al. [1989]. Light from a source to a detector yield a banana-shaped sensitivity as shown in figure 3 (A). A comparison could be drawn between the theory of light diffusion within tissues, the concept 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 conducted 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 formula with simple solution of spherical wave when light energy density oscillates for amplitude-modulated sources in homogeneous media. In biological tissue, the waves are considered as randomly moving photons exhibiting a random moving step of approximately 1 mm. However, macroscopically, they form a damping wave of photon density with 10 cm wavelength. 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 were verified in both bio-models Fishkin et al. [1991] and human breast studies O'Leary et al. [1995].

3 Difficulties in DOT Imaging

Image reconstruction is a non-linear as well as an ill-posed problem. DOT presents few 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 like a turbid property with heavily scattering property. Light travels through the tissue in a complicated zigzag path. As a result, strength attenuated. this renders the relation between the output photon density and the optical properties dependent on stochastically defined paths.
- In the imaging for frequency space, although the amplitude changes during modulation at Mega Hertz, the wavelength of DPWD (Diffuse Photon Density wave), which is owing to the intensity modulated illumination, is of the order of a few cm, much greater 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.

 doi:10.20944/preprints202301.0281.v1

- The background properties being not known in advance leads to difficulties in measuring and interpreting measurements for inverse reconstructions.
- As a result of the quantum nature of noise, modeling it is a challenging task. This is because the sources of noise include both thermal noise in the amplification unit and the noise generated by the shots due to the quantum source nature.
- 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 significantly scattered brain tissue that is covered by slightly scattering cerebrospinal fluid. In order for dealing 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 light interection 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 times of amplitude more than the taken datapoints. 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 taking 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). Figure 4 shown an fNIRS image of the brain. 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

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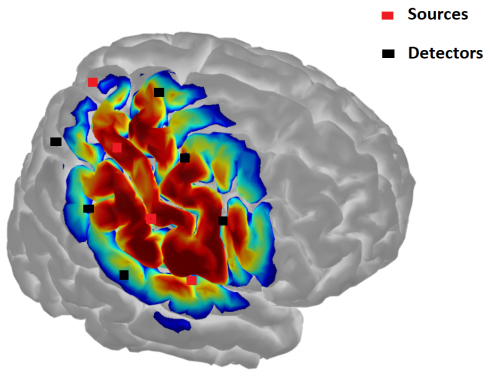

Figure 4: Functional near-infrared spectroscopy (fNIRS).

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 continuous 3D DOT imaging.

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