

# Abstract

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Non-ionizing nature, low-cost, and portability for bedside measurements have always attracted research towards continuous-wave diffuse optical tomography (CW-DOT). However, numerical stability is still an issue primarily due to the non-linear, ill-posed inverse problem, even with the most state-of-art reconstruction schemes. A non-recursive linear model in the literature estimated the photon paths using a linear relationship and produced fast and usable images without any inverse transforms. For such methods stability is not an issue, but the linear approximations have resulted in distortions in the reconstruction.

The objective of this research work is to circumvent the above adversities and develop a generalized curved-beam method using a non-linear Rosenbrock's banana function. The NIR light is reported to follow a banana-shaped path in the tissue between a source-detector pair. Thus, the fitting of a non-linear function to each source-detector channel approximates the average photon path as curved one unlike the linear model along with the depth penetration of each photon channel. This helped in detecting inclusions up to depths of (4-6) cm and allows to perform deep-body imaging with reduced distortion compared to linear reconstruction model, demonstrated here as a proof-of-principle. The estimation of photon path has enabled the use of modified Beer-Lambert law (MBLL) in a proposed differential form assuming each channel as a local region having different absorption coefficient. This differential form leads to the reduction of partial volume effect associated with MBLL and the cross-talk problem of DOT. Now, the calculated absorption coefficient ( $\mu_a$ ) is assigned along the curved photon path for image reconstruction. The essence of this method is that the non-linear function serves as the basis for image reconstruction without solving the inverse problem thereby reducing the computational burden to a great extent with no prior information on perturbation, unlike the iterative methods. The technique is extended to three-dimensional (3D) volumetric reconstructions from two-dimensional (2D) slices, to have tomographic imaging in its true sense. In 3D imaging, 2D image slices are reconstructed by taking measurements at three different depths covering the entire depth of the phantom. These 2D slices are stacked together followed by interpolation to form the 3D  $\mu_a$  image of the phantoms. A simulation study in COMSOL Multiphysics showed that the photon propagation is same in all the three planes. So, for the 3D imaging, the 3D banana function is not considered that would have led to simultaneous measurements at different depths of the phantom and considerably increase the data collection time. TOAST++ numerical simulations, wax-phantom experiments with different geometries and inclusion with optical contrast and *in vivo* finger joint imaging have validated this method with satisfactory results. This method is further compared with the state-of-art Greedy algorithms like compressive sampling matching pursuit (CoSaMP) and the sub-space augmented multiple signal classification (SA-MUSIC) with encouraging results. A promising dual-wavelength CW-DOT system is developed for functional imaging of finger joints to extract the physiological parameters directly. The advantage of this in-house system is that there is no need for baseline measurement. The reconstructed transverse cross-sectional images of the distal interphalangeal (DIP) and proximal interphalangeal (PIP) joints of left index finger of the same male volunteer showed good consistency and the optical contrast between the joint cavities filled with synovial fluid and bones is also in good agreement with results reported in the literature. The physiologically significant parameters like concentrations of oxy-hemoglobin ( $[HbO_2]$ ), deoxy-hemoglobin ( $[Hb]$ ), total hemoglobin concentrations ( $[HbT]$ ), and oxygen saturation ( $StO_2$ ) are calculated and are comparable to the already reported results. The reconstructed images of  $[HbO_2]$  and  $[Hb]$  showed that the maximum value of  $[HbO_2]$  0.65 mM is approximately five times higher than that of  $[Hb]$  value of 0.14 mM. This is in accordance already reported results of healthy finger joints. The proposed reconstruction method with the in-house DOT system is also applied to some real-life applications other than biomedical imaging like dispersion of ink drop and the internal quality assessment of optically translucent fruit like apple. This reconstruction technique holds great promise in DOT applications that require absolute quantification of tissue optical properties, in functional imaging of finger joints, and in dynamic imaging for direct measurement of chromophore concentrations without any baseline measurement.

Finally, the combination of the proposed reconstruction algorithm along with the CW-DOT system could provide simpler, efficient DOT instrumentation that can lead to easier clinical translation. The investigations in the thesis are related to general issues of CW-DOT and these findings and conclusions should be relevant to the biomedical optics community.

**Keywords:** Diffuse optical tomography, Rosenbrock's banana function, back-projection, functional imaging, dynamic imaging, fruit quality assessment.

