Time-resolved perturbation Monte Carlo for 3D optical imaging in small animals

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Abstract—We developed a new optical time-gated forward model based on a perturbation Monte Carlo technique to perform 3D optical imaging in small animals. This new forward model overcomes many limitations encountered with the classical forward model based on the diffusion equation.

I. INTRODUCTION

Optical imaging has been intensively investigated in the last years, since light at visible and near-infrared wavelengths is a non-ionizing, non-invasive probe with numerous applications in medicine [1]. Spatial variations in the optical properties of the interrogated tissue provide non-invasively information on its structure, function and molecular state.

Diffuse Optical Tomography (DOT) is posed as an inverse problem and aims at retrieving the 3D maps of the optical properties from surface measurements. The forward model in DOT is generally based on the diffusion approximation to the Radiative Transfer Equation (RTE) due to the complexity to solve the RTE either analytically or numerically [2, 3]. However the diffusion approximation has known limitations: inadequate in the case of non scattering medium, inaccurate near the boundary within distance that is comparable to transport mean free path and fails in the case of highly absorbing tissues. Such conditions are encountered in the case of pre-clinical applications where the specimens exhibit wide variations in optical properties with void regions (lung, bladder for instances). In such cases it is preferable to cast the forward model with a more robust model.

The perturbation Monte Carlo (pMC) approach [4-6] allows to generate with computational efficiency the forward model without the limitations that are inherent to the diffusion approximation. In this paper, we report the first use of the pMC method for optical time-gated imaging in small animals. An anatomically accurate model of a mouse is employed to generate forward Monte Carlo simulations. By using perturbation Monte Carlo method, three-dimensional time-resolved Jacobians are calculated to solve accurately the inverse problem.

II. METHODS

A. Synthetic model

A 3D mouse atlas created from PET, CT and cryosection slices at University of Southern California is used to generate the synthetic model to perform the MC simulations [7]. Only the skin shape and lungs are extracted in this example (cf. Fig. 1 (a)). We simulated a transmission geometry mimicking the configuration of the non-contact imaging platform that we are currently integrating in our laboratory. We simulated an array of 9 sources placed on the top of the lungs and 25 detectors on the transmission surface as shown in Fig. 1 (b).

Fig. 1 (a) Mouse segmentation of skin and lungs (b) Sources and detectors location. The white lines represent the sources positions; the pink lines represent detectors positions.

B. Time-resolved Monte Carlo

MC model is considered to be equivalent of implementing the RTE. However, MC simulations take large computational times due to the necessity of simulating millions of photons. pMC method provides a computational efficient approach to incorporate MC simulation in the inverse problem. pMC extracts the Jacobian which is the derivative of the measurements (forward model) with respect to the optical parameters reconstructed. Thorough explanation of the photon propagation rules can be obtained in previous work [8, 9].

C. Noise consideration

Optical imaging of thick tissues with time-resolved techniques is a photon starved technique characterized by a Poisson noise. The same statistic applies to the MC simulations. We employ denoising algorithms to the computed Jacobian, by transforming the data into an approximately Gaussian additive signal independent noise through the Anscombe transformation [10]:

\[ b = 2 \sqrt{\frac{a + \frac{3}{8}}{8}}. \]  

where \( a \) is the variable with a Poisson distribution and \( b \) with a Gaussian additive white noise which has zero mean and unity variance.
D. Perturbation Monte Carlo

pMC optical reconstruction is based on a perturbation approach involving the inversion of large Jacobian matrices. This method assumes that the unknown distribution of optical properties is a small perturbation to an estimated distribution. With \( w \) the initial measurement, \( j \) the number of scattering events and \( S \) the path length in the perturbed region, a prediction of the measurement of each photon can be estimated by

\[
\hat{w} = w \left( \frac{\mu_s}{\mu_t} \right)^j \left( \frac{\mu_s}{\mu_t} \right) \exp \left( -\left( \mu_s - \mu_t \right) S \right),
\]

(2)

Where \( \hat{\mu}_s = \mu_s + \delta \mu_s \), \( \hat{\mu}_t = \mu_s + \delta \mu_s \), \( \mu_s = \mu_s + \mu_s \) and \( \mu_t = \mu_s + \mu_s \), with \( \mu_s \) and \( \mu_t \) being the initial guess of the absorption and scattering coefficient. The derivative information \( \partial W / \partial \mu \) of signal summation \( W \) at a detector can be drawn from this analytical expression.

III. RESULTS

The computational efficiency of the proposed approach was tested on a 64 CPU cluster. The impact of gate width, photon packet size, optical parameters probed was evaluated with numerous simulations. We found that 50 time gates with gate width 20ps and for a \( 10^8 \) photon packet was the optimal set for computational efficiency and statistical accuracy for small animal imaging. Figure 2 shows the Jacobian for absorption and scattering at three different time gates using this optimal parameter set. Producing the map of photon path length and number of scattering events needed to generate the Jacobian of figure 2 took in average 5 minutes per source.

IV. DISCUSSION

The main goal of this study was to assess the potential to generate time-gated Jacobian for 3D optical imaging in small animal geometries. Such Jacobian cannot be computed analytically based on the diffusion equation. We demonstrated that pMC is a computationally efficient method to provide accurate sensitivity maps in complex geometries and without the restrictions of the diffusion equation. Moreover, Figure 2 clearly shows the benefit to cast the optical inverse problem within the time-gating framework.

As expected, the Jacobian shape expands as time increases. Photons collected shortly after the pulse experience significantly fewer scattering events and travel around a straight line connecting the source to the detector (snake photons), while the late photons sample much greater volumes.

DOT is by nature an ill-posed, ill-conditioned inverse problem. Thus the 3D estimation of optical parameters suffers from low resolution, partial volume effect and inter-parameter cross-talk. However, time-gating inverse techniques provide additional information since early photons are associated with structural information (scattering) and later photon with functional information (absorption). The quantitative combination of all the time- and spatially dependent data may yield accurate and stable calculations to provide both anatomical and physiological information, which is critical for pre-clinical applications.

REFERENCES