# Researches on epi-fluorescence molecular tomography based on depth perturbation and spatially varying regularization

Abstract

論 文 の 内 容 の 要 旨

論文題目　Researches on epi-fluorescence molecular tomography based on depth perturbation and spatially varying regularization
（深度摂動法及び空間変化正則化法に基づく反射式蛍光トモグラフィーに関する研究）

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The main goal of fluorescence molecular tomography (FMT) is to recover the depth, size, and three-dimensional (3D) distribution of fluorophores in tissue from fluorescent signals measured on the tissue surface. FMT commonly works with fluorophore-loaded imaging agents that ideally only accumulate in diseased (or targeted) tissue. Preclinically, it has already been used in drug development. Clinically, it shows great potential in disease diagnosis, tumor staging, surgery margin and other applications. Epi-fluorescence molecular tomography works in epi-illumination geometry, which is clinically more practical than other geometries. Currently, the limitations of epi-fluorescence molecular tomography include but are not limited to inaccuracy in resolving depth, the ill-conditioned nature[1] of the optical inverse problem[2], and high computational cost.

To overcome the above limitations, in this thesis I first proposed a depth perturbation concept for estimating the depth and central location of fluorophore inside tissue: a thin optical phantom with known optical properties is used as a depth perturbator. By superposing the perturbator onto a sample, we deliberately perturb the depth of the fluorophore inside the sample. Fluorescent signals are measured before and after perturbation. According to variations in the measurements, depth information can be obtained.

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[1] The solution is non-unique and vulnerable to measurement noise.

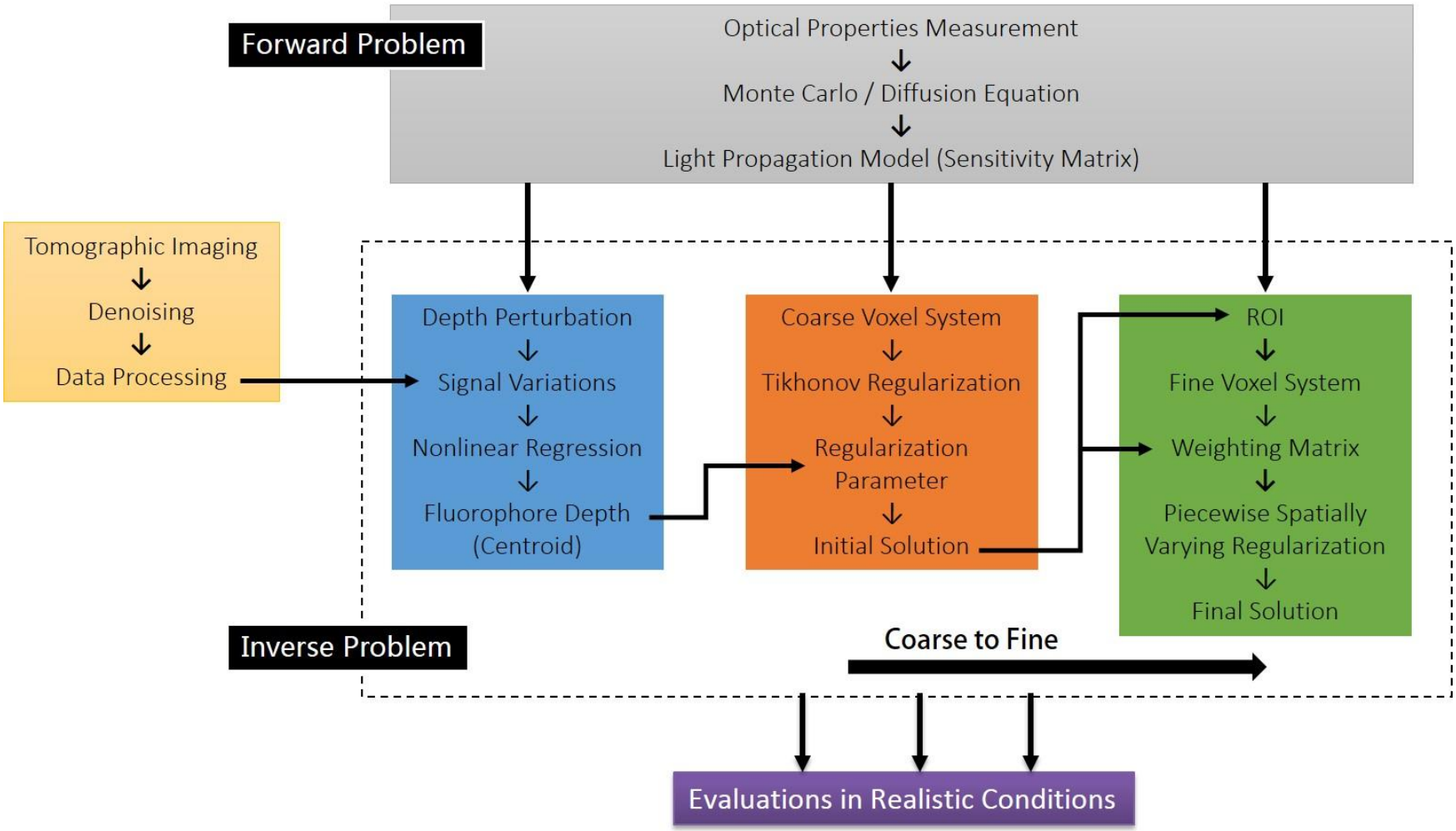
[2] Reconstruction of fluorophore distribution from measured fluorescent signals.

The estimated fluorophore central location was then utilized as a new constraint during the reconstruction of fluorophore 3D distribution to ensure unbiased results. To be more specific, the fluorophore centroid prior was used to determine regularization parameter of Tikhonov regularization. Tikhonov regularization is a common numerical treatment method in solving ill-condition inverse problem. But in most of previous researches, its regularization parameter is decided by manually or empirically.

Third, a piecewise spatially varying regularization method which achieves better estimation accuracy on fluorophore size compared with the conventional reconstruction method was also proposed. In the field of optical inverse problem, spatially varying regularization (SVR) is widely used to compensate reconstruction results in the regions of low detecting sensitivity. By the continuous weighting manner, the profile of fluorescent distribution may be destroyed and local concentration values may be exaggerated too much. Using the piecewise manner proposed by me, the original profile of fluorophore distribution can be kept.

Finally, the coarse to fine strategy was taken to shorten computation time required by the reconstruction. The reconstruction step was divided into at least two steps: coarse step and fine step. In the coarse step, one solves the inverse problem over the whole space but with a large voxel size to obtain a coarse result; in the fine step we set a region of interest (ROI) according to the coarse result, then reconstructing within the ROI and with finner voxels. In each step, we suppress the involved voxel number to realize the fast computation.

Fig.1 shows the framework of these researches.


Forward Problem
Optical Properties Measurement
Monte Carlo / Diffusion Equation
Light Propagation Model (Sensitivity Matrix)
Tomographic Imaging
Denoising
Data Processing
Depth Perturbation
Signal Variations
Nonlinear Regression
Fluorophore Depth (Centroid)
Coarse Voxel System
Tikhonov Regularization
Regularization Parameter
Initial Solution
ROI
Fine Voxel System
Weighting Matrix
Piecewise Spatially Varying Regularization
Final Solution
Inverse Problem
Coarse to Fine
Evaluations in Realistic Conditions

The proposed concepts are verified and evaluated by numerical simulations, phantom experiments, and ex vivo experiments using a custom-built epi-fluorescence tomography system. According to the results of the study, the proposed methods were successful in localizing fluorophore and estimating fluorophore size with relatively short computation time. In addition, potential issues that occur when the proposed methods are applied to biological tissues are discussed and quantitatively evaluated. I expect that the concepts and methods discussed in this thesis will extend the application scope of FMT in the near future.