Diffuse Optical Tomography: A Simulation Based Approach

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Abstract: Diffuse Optical Tomography (DOT) uses Near Infra-red (NIR) light to monitor physiological changes in internal organs. NIR light being less energetic in nature can be used for continuous monitoring of tumor infected biological tissue, neonatal brain and many such applications where high energy radiation can cause severe damage.
The forward problem of DOT, which involves obtaining of the radiance values of light at the boundary of the specimen (with known 'a' and 's' values) after irradiating it with NIR radiation, can be described by the Radiative Transfer Equation used with diffusion approximation.
The inclusions inside the biological specimen for which the equations are being solved, can be fluorescent in nature. There are natural fluorophores in animal bodies also; fluorescent markers are also artificially inserted in animal bodies for monitoring the spatial location and concentration of diseased tissue.
To probe these concepts of the Forward model also demonstrating presence of multiple fluorescent inclusions, COMSOL simulations were carried out.

Keywords: Diffuse Optical Tomography, Fluorescence, Radiative Transfer Equation And Finite Element Method.

1. Introduction

Since biological tissue is a highly turbid media, multiple scattering events and absorption during propagation of light randomizes the direction of the radiation in the biological specimen. There is a window in the EM spectrum (about 650-950nm, Near Infra-red region) where light can penetrate into the tissue due to comparatively less absorption by biological chromophores [1]. These realizations led to the research being directed to Diffuse Optical Tomography (DOT) which uses Near Infra-red (NIR) light to monitor physiological changes in internal organs [2]. I will explain the phenomena of scattering since it governs the behavior of light as it travels in the biological medium.

1.1 Scattering

In this phenomenon, charged particles in a medium are set into oscillatory motion by the electric field of the incident wave, and re-emit light of the same frequency as the primary wave. It occurs at non-resonance frequencies; hence the scattered intensities are relatively weak. It arises due to a relative refractive index mismatch at the boundaries between two such media or structures.[3]
The reduced scattering coefficient is a property of the medium that incorporates the scattering coefficient μ_s and the anisotropy g:

$$\mu_{s'} = \mu_s(1 - g)\ [cm\text{-}1]$$

1.2 Types of Diffuse Optical Tomography

Three common NIR methods have been developed and they differ in the time dependence of the source intensity.

1. Continuous wave (CW)
2. Time-domain photon migration (TDPM)
3. Frequency-domain photon migration (FDPM)

In this paper, Continuous Wave Domain approach is employed hence I will define CW Domain.
In CW Domain, a constant intensity source is used to illuminate the tissue. The intensity of the propagating radiation in the tissue attenuates exponentially with distance from the tissue surface. The light fluence value is detected at various positions on the tissue surface.
The presence of diseased tissue regions may be characterized by wavelength-dependent light-absorption properties or light-scattering properties than their surrounding normal tissues. In the diseased tissue regions, propagating light is further attenuated when compared to the surrounding normal tissues. From the fluence values obtained at the boundary the interior tissue properties are determined.

2. The Forward Problem

The forward problem involves obtaining of the radiance values of the light at the boundary

of the specimen (with known μa and μs values) after irradiating it with NIR radiation. This phenomena of light propagation in the tissue can be described by the Radiative Transfer Equation used with diffusion approximation.[3]

In order to model these phenomena COMSOL Multiphysics is used. Representing this equation in the form of Helmholtz Equation in COMSOL,

$$\nabla(-c\nabla u)+au=f$$

With Parameters,

$$u=\phi$$

$$c=D=\frac{1}{3(\mu_a+\mu_s')}$$

$$a=\mu_a$$

$$f=S$$

The inclusion inside the biological specimen for which the equations are being solved, can be fluorescent in nature. There are natural fluorophores in animal bodies also; fluorescent markers are also artificially inserted in animal bodies for monitoring spatial location and concentration of diseased tissue.[4]

To allow the inclusion of fluorescent heterogeneities inside the biological media, more PDE modes of COMSOL Multiphysics are used. The fluence (represented by 'u' in COMSOL) can then be used as a source term for the subsequent inclusions. To probe these concepts of the Forward model, simulations were carried out. These simulations and the plots obtained form a major part of the report, followed by a series of conclusions drawn from them.

3. Use of COMSOL Multiphysics

3.1 Biological Specimen with a fixed intensity point Source (Continuous Wave Domain)

A point source is present just inside the boundary of the tissue. Meshing is done so as to divide the entire specimen into nodes where the partial differential equation can be solved. Mesh is intensified where the source is present as it is the area of interest. (See figure 1)

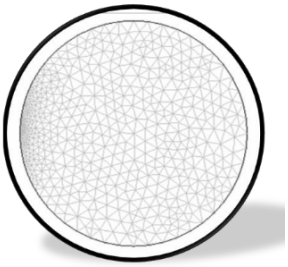

Figure 1

Contour Plot: Depicts the propagation of light waves in the medium by the contours. (See Figure 2)

Contours are closely together in the proximity of the light source and further towards the other side.

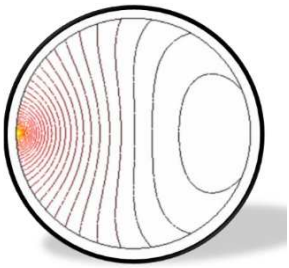

Figure 2

Surface Plot: Point source has a fixed intensity. Fluence values throughout the specimen are found. The values of absorption and reduced scattering coefficients inside the specimen are known.(See figure 3)

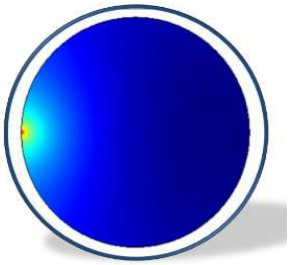

Figure 3

3.2 Biological Specimen with a fixed intensity Point Source (Continuous Wave Domain) and a scattering inclusion.

Meshed Surface: Mesh is intensified around the inclusion to obtain clearer results.(See Figure 4)

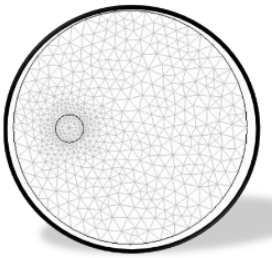

Figure 4

Contour Plot: The wave through which radiation is propagating gets distorted inside the absorbing media. (See figure 5)

Surface Plot: Most of the light gets sucked into the heterogeneity which is absorbing in nature. (See figure 6)

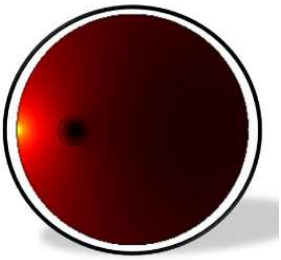

Figure 6

4. Fluorescence in Biological Specimen

Fluorescence is a phenomenon in which light is absorbed by chromophores, the chromophores then return to their ground state by emitting light.

This phenomenon can be used in Medical Imaging to determine the spatial location and concentration of specific cells that are found in case of particular diseases..The fluorescent materials used in this process are known as **fluorescent markers.**

These markers are introduced in the body of animals. In case of a disease, the markers would attach themselves to the molecules that are built up as a result of the particular disease. Hence location of the diseased cells as well as their concentration can be determined.

Examples are, DsRed (a fluorescent protein), Indocyanine green and so on.

Near Infra-red Emitting Fluorophore:

Since we are trying to model a fluorescent heterogeneity in biological medium that emits radiation in Near Infra Red Region, for the purpose of simulation, the properties (absorption and reduced scattering coefficient) of a NIR emitting fluorophore like Indocyanine Green (ICG) will be used.

4.1 Simulation of Fluorescence in COMSOL Multiphysics

To model Fluorescence, we require to solve 2 different equations. Considering the analysis is done in Continuous Wave Domain, a Helmholtz equation can be used to model the propagation of light in the medium.

The first Helmholtz Equation models the excitation phase in the biological medium. Fluence values obtained by solving this equation would act as the source term for fluorescence modelling.

$$\nabla(-D\nabla\phi_{ex}) + \mu_a\phi_{ex} = S$$

The second Helmholtz Equation is used to model fluorescence. Excitation fluence is obtained from the previous model and the subscript 'i' represents the emission wavelength.[4]

We solve for fluence values emitted by the fluorescent heterogeneity.

$$\nabla\left(-D^i\nabla\phi_{em}{}^i\right) + \mu_a{}^i\phi_{em}{}^i = \mu_a{}^{ex}Y^i\phi_{ex}$$

This mathematical model has been used for COMSOL simulation. PDE modes were used to provide the coefficient values.

4.2 Biological Sample with 3 heterogeneities, fluorescent in Nature.

This simulation shows the 3 heterogeneities in the specimen. The meshed output and corresponding results are also depicted.

Meshed structure: a point source is placed on the periphery. There are three inclusions in the medium with the mesh being intensified around them for FEM to produce better results. (See Figure 7)

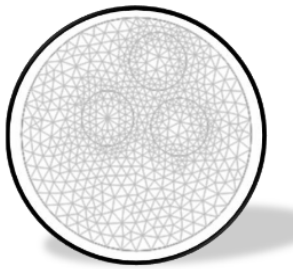

Figure 7

In this simulation, along with fluorescent heterogeneity, there are 2 other heterogeneities with the top one being absorbing in nature. The simulation is carried out in stages. In the next stage, this absorbing heterogeneity undergoes the process of fluorescence (since the current fluorescent heterogeneity is acting as a source of radiation).[5] (See Figure 8)

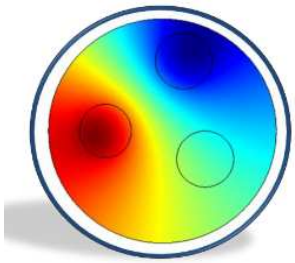

Figure 8

As predicted, the absorbing heterogeneity now is undergoing fluorescence and the 2rd heterogeneity now absorbs light from it. In the next stage, the last heterogeneity will undergo fluorescence. (See Figure 9)

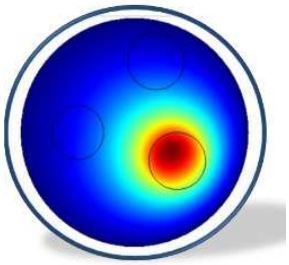

Figure 9

Finally, In the entire simulation, progressively each heterogeneity has acted a source to the next one. Thus the phenomena of fluorescence has passed on from the first to the
third one step by step in each stage. (See Figure 10)

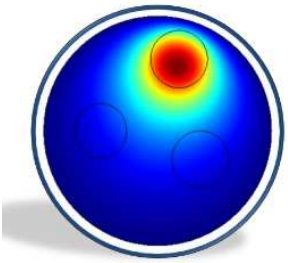

Figure 10

4.3 Florescence Simulation in 3 Dimensions
Meshed Structure: 3 Dimensional specimen with one fluorescent heterogeneity in the center. (See Figure 11)

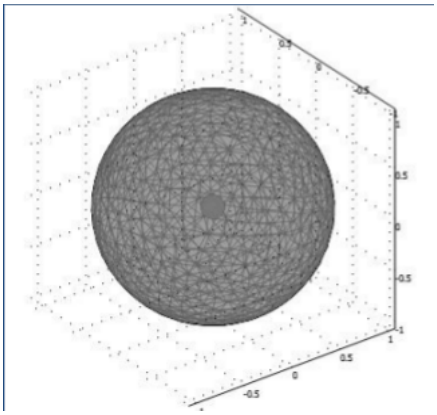

Figure 11

Cut Section view of the fluorescent sphere. (See Figure 12)

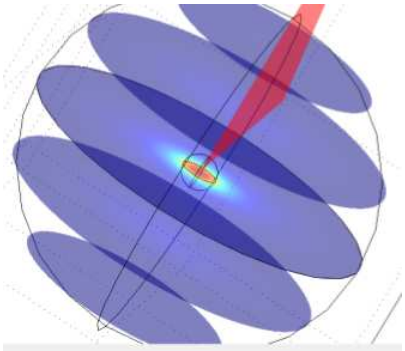

Figure 12

Figure 13 depicts the top View of the sphere (the biological specimen) with the fluorescent heterogeneity exactly in the center. It can be seen that after absorbing radiation, it is emitting light of its own. (See Figure 13)

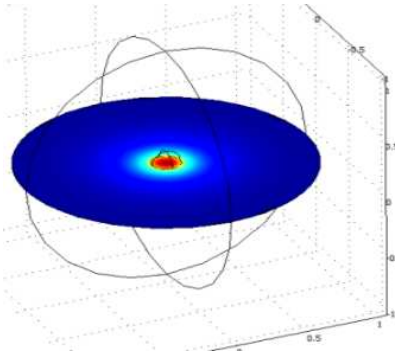

Figure 13

4.4 Three Dimensional Simulation: 2 Heterogeneities

In this simulation, the inclusion at the center of the specimen is acting as the source of radiation while it undergoes fluorescence. The inclusion on the boundary (also fluorescent in nature) absorbs light during this phase. In the next stage of the simulation, it exhibits the phenomenon of florescence. (See Figure 14)

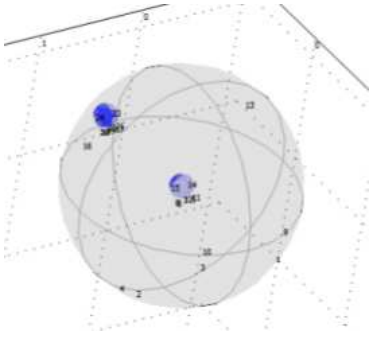

Figure 14

Figure 15 depicts the top View of the fluorescent spherical specimen. The fluorescent inclusion has absorbed radiation from the sphere at the center and is emitting radiation. (See Figure 15)

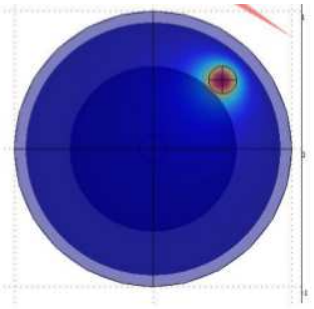

Figure 15

Figure 16 depicts the 3D view with the sphere close to the boundary undergoing fluorescence. (See Figure 16)

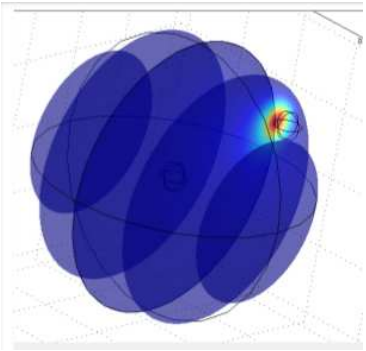

Figure 16

5. Conclusions

To model fluorescent phenomena in biological media, Helmholtz equation was solved using a FEM based approach. For this purpose the model construction was done in COMSOL Multiphysics 3.4. Exploiting its PDE modes, the propagation of electromagnetic wavelength in biological media was simulated. The underlying motive was to model heterogeneity in the specimen that is absorbing in nature. It absorbs a certain wavelength of light and emits the absorbed energy. As expected, this phenomenon could be modeled and the plots obtained depicted that after absorbing the heterogeneity emitted light and had the capability to act as a source embedded within the media. To realize the potential of this finding, more sources were embedded inside the media, and they were also

provided absorbing properties. With this situation when the simulation was carried out again, the plots indicated that the fluorescent heterogeneity does in fact acts as a source and the absorbing heterogeneity absorbs radiation. In the next stages of the simulation, progressively, every heterogeneity is made fluorescent and the previous one acts as a source to it and excites in such a way that it also starts exhibiting fluorescence.

6. References

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7. Acknowledgements

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