Name: Alan Cham
Project 15: Optical Properties for Bioluminescence Tomography in Mice
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**Contents**



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## I. Technical Summary

### Ia. Background

The Small Animal Radiation Research Platform (SARRP) is a preclinical system for imaging and radiation delivery in small animal models. In cancer research, relevant radiation targets, such as orthotopic tumor models may have low contrast in CT imaging, which is inhibitive for CT-based radiation targeting. The SARRP approaches the quandary by implementation of bioluminescence tomography (BLT) as an alternative imaging method for localization of the target.

BLT is a reconstruction method for the distribution of a light source. Based on 2D bioluminescence image (BLI) projections of surface emittance, as well as on the spatial distribution of optical properties (absorption $\mu_a$ and reduced scattering $\mu_s'$) within the subject, BLT aims to identify the internal distribution of light sources that produces surface intensities matching the observed values. This is achieved by modeling light transport with a diffusion approximation.

The existing home-built SARRP BLT implementation reconstructs using BLI images at four wavelengths 590, 610, 630 and 650 nm, chosen light in this range tends to be less attenuated by biological tissue. A CT image of the mouse subject is segmented and processed to produce a tetrahedral mesh; subsequently each BLI projection is back-projected and mapped to the mesh surface. A set of Green's functions is computed for each pair of internal node and surface emittance, where the Green's function relates the source strength at the internal node. The linearized problem of solving for the source strength at each node is achieved with the use of a regularization term. An iterative region shrinking scheme was used to repeatedly cull out some

fraction of nodes with the weakest source strengths until only one remains. An objective function is evaluated at each iteration and is used as the basis to select the optimal solution for the spatial distribution of light source strength.

**Ib. Problem**

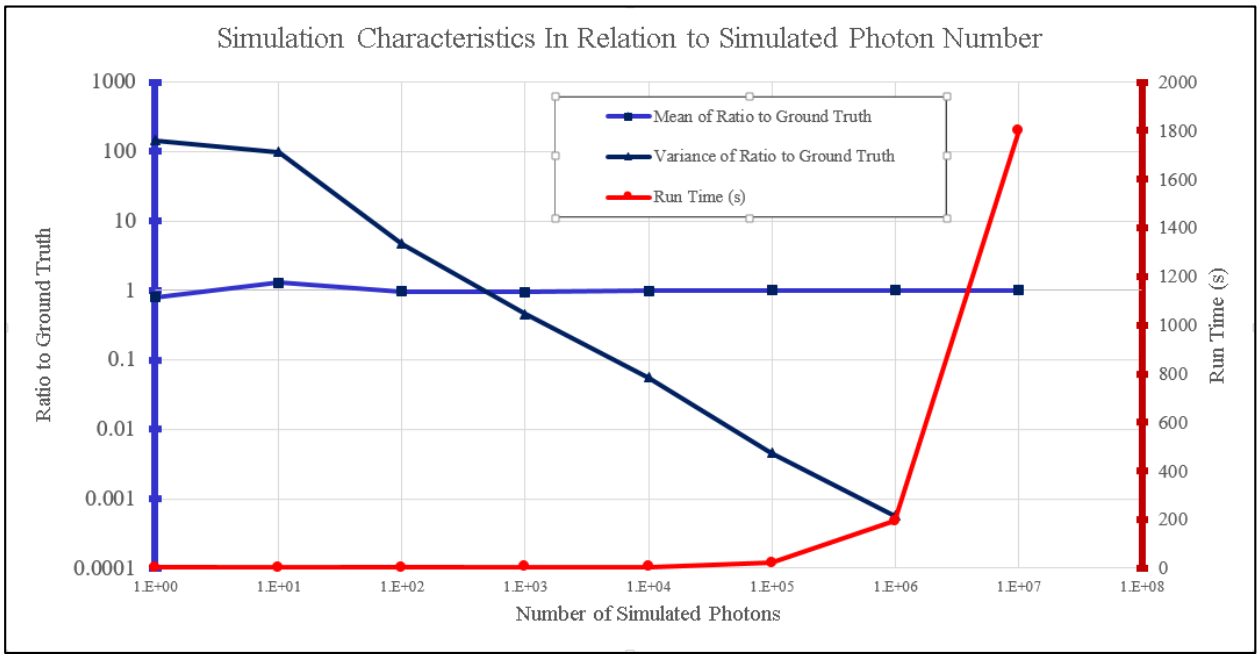
Previous experiments using the SARRP BLT implementation primarily explored localization of targets in regions of mouse that are relatively optically homogeneous (i.e. abdomen). Localization of targets in heterogeneous regions requires segmentation of organs as well as knowledge of optical properties to assign to those regions in reconstruction. However, these optical properties can vary with respect to physiological conditions, measurement method, species, etc. Furthermore, literature values for mouse organ optical properties are relatively sparse and have considerable variation. Nonetheless it is useful to produce a set of reasonable optical properties for potential use as approximations in simulation and reconstruction. Also, it is useful to describe the target (e.g. tumor) localization uncertainty introduced to the SARRP BLT's reconstruction in an optical heterogeneous environment as another initial step toward SARRP BLT-based radiation targeting in relatively optically heterogeneous areas of the mouse.

**Ic. Approach**

In order to select a set of optical properties for use in simulation and reconstruction, reported values of $\mu_a$ and $\mu_s$' were gathered from a sizeable body of literature, without rejecting on the basis of differences in species, experimental method, treatment status, etc. In some cases, optical property values were not provided, but rather parameters were reported, and these could be used to extract expected property values from the corresponding model. Next, some values were rejected if they were far beyond the relevant wavelength range of 590-650 nm. After formatting the data for presentation and reviewing with a mentor, Alexandrakis's empirical model was deemed reasonable for use as source for the optical property values in simulation and reconstruction experiments. The following is a table of the optical properties as calculated based on Alexandrakis's reported parameters.

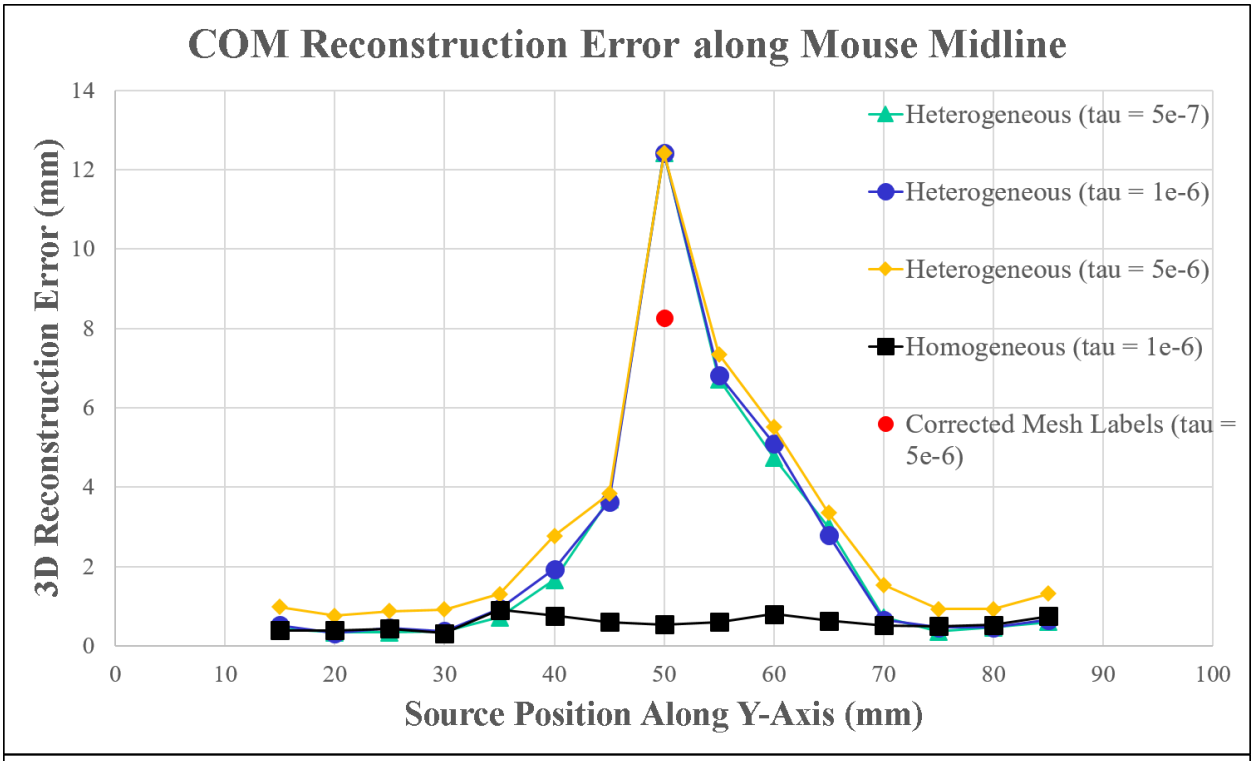
| λ (nm) | | Alexandrakis | | | | | | SARRP Red Journal | |
|---|---|---|---|---|---|---|---|---|---|
| | | Adipose | Heart | Kidney | Liver | Lung | Stomach | Abdomen* | Tumor** |
| 590 | $\mu_a$ ($cm^{-1}$) | 0.431 | 6.65 | 7.45 | 39.90 | 21.08 | 1.29 | 0.431 | 3.8 |
| | $\mu_s$' ($cm^{-1}$) | 12.900 | 11.60 | 27.3 | 7.75 | 23.25 | 16.26 | 15.300 | 9.0 |
| 610 | $\mu_a$ ($cm^{-1}$) | 0.127 | 2.00 | 2.24 | 11.99 | 6.63 | 0.38 | 0.127 | 2.3 |
| | $\mu_s$' ($cm^{-1}$) | 12.700 | 11.00 | 26 | 7.50 | 22.85 | 15.74 | 14.600 | 7.6 |
| 630 | $\mu_a$ ($cm^{-1}$) | 0.069 | 1.08 | 1.21 | 6.45 | 3.59 | 0.21 | 0.069 | 1.9 |
| | $\mu_s$' ($cm^{-1}$) | 12.480 | 10.50 | 24.7 | 7.23 | 22.46 | 15.25 | 14.000 | 6.9 |
| 650 | $\mu_a$ ($cm^{-1}$) | 0.050 | 0.78 | 0.87 | 4.67 | 2.61 | 0.15 | 0.050 | 1.6 |
| | $\mu_s$' ($cm^{-1}$) | 12.270 | 10.10 | 23.6 | 7.00 | 22.09 | 14.80 | 13.500 | 6.6 |

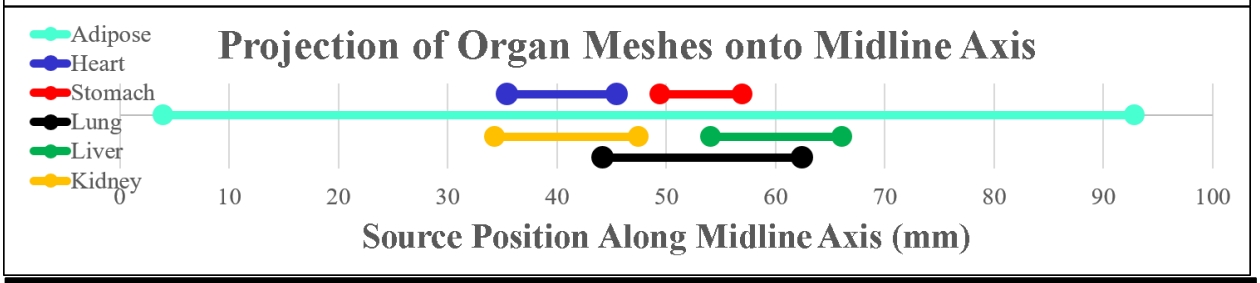
In preparation for conducting simulation experiments in heterogeneous areas of the mouse, a small set of experiments were conducted using the Molecular Optical Simulation Environment (MOSE) software. For simulations experiments to generate surface transmittance maps for reconstruction, a simulated photon count of 1e6 per wavelength was selected, due to considerations for runtime and marginal improvements in convergence. The results from the case with 1e7 results was used as 'ground truth'. Convergence was measured by the mean ratio of transmittance values at each particular node to the observed transmittance in the 'ground truth' case. When the photon count has increased to 1e6, the mean ratio of the transmittance results to the ground truth transmittance results were very near 1, and the ratios had a mean variance less than 0.001.

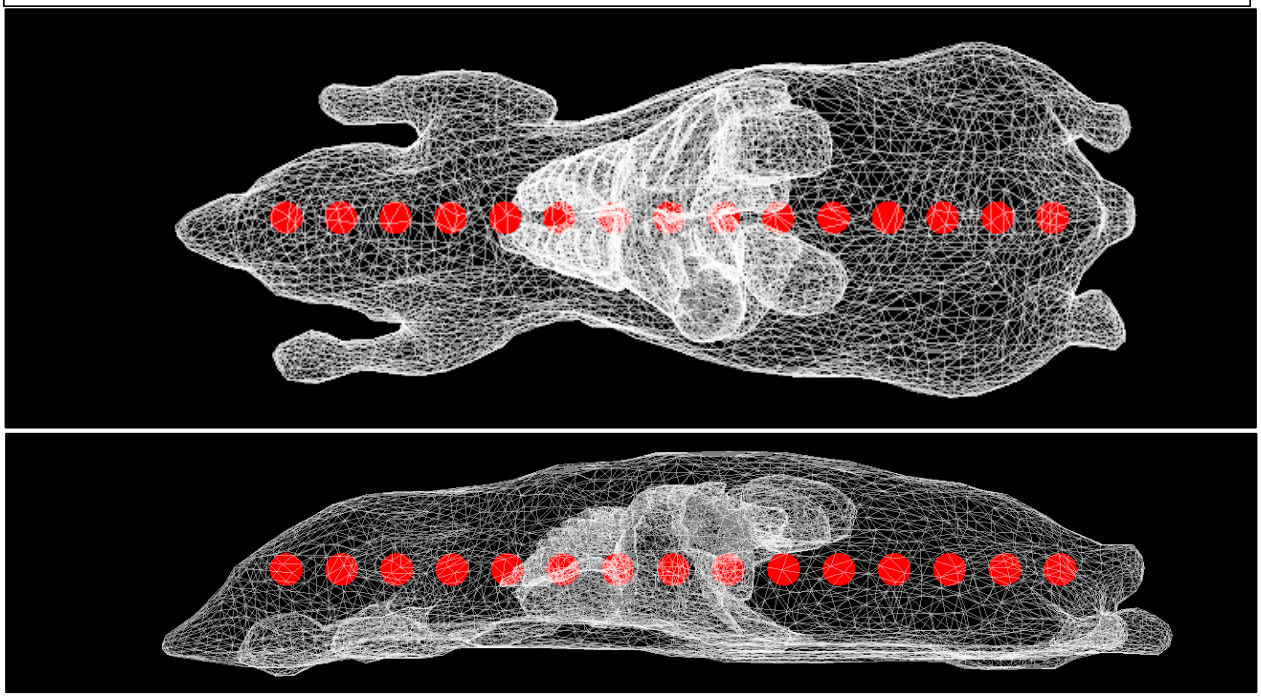



**Id. Results**

A series of forward simulation experiments were conducted using a 3 mm diameter spherical light source translated along the mouse midline axis. Matlab functions were written to adapt the MOSE simulation output results for use in the existing home-built BLT implementation by converting to the Nirfast mesh formats. An older version of the BLT implementation was provided by the mentors, such that it could readily use the Nirfast meshes as input without much modification, and perform reconstruction on those inputs. The following plots show the error between the true source COM and the reconstructed COM based on the forward simulation results.


COM Reconstruction Error along Mouse Midline
3D Reconstruction Error (mm)
Source Position Along Y-Axis (mm)
Heterogeneous (tau = 5e-7)
Heterogeneous (tau = 1e-6)
Heterogeneous (tau = 5e-6)
Homogeneous (tau = 1e-6)
Corrected Mesh Labels (tau = 5e-6)
0
2
4
6
8
10
12
14
0
10
20
30
40
50
60
70
80
90
100


Projection of Organ Meshes onto Midline Axis
Adipose
Heart
Stomach
Lung
Liver
Kidney
Source Position Along Midline Axis (mm)
0
10
20
30
40
50
60
70
80
90
100



**Ie. Significance**

These experiments demonstrated an inherent increase in localization uncertainty, even when provided complete knowledge of optical properties and organ segmentations in simulated condition. This could be a result worthy of additional inquiry, since the peak COM error observed at position y = 50 mm may be an important consideration for feasibility of BLT-based radiation targeting in heterogeneous areas. COM reconstruction errors in homogeneous areas were consistently less than 1 mm, which were corroborated by previous experiments by the mentors using physical implants in mouse abdomens, which also were able to reconstruct target COM with less than 1mm error.

## II. Management Summary

**IIa. Division of Labor**

Because I did not have a student partner, I worked alone under the guidance and support of my mentors.

**IIb. Plans vs Accomplishments**

In the original 'possible projects' descriptions, this project was listed described as entailing determination of organ specific optical properties by (1) working with surgeon placing light source into the organ, (2) building an auto-segmentation tool to segment simple organ structures, (3) performing BLT reconstruction using a set of optical properties from either literature values or analytical formulas. However, the goals were reduced somewhat early on, in light of limitations in time and skillset.

Physical experiments with implanted light sources were replaced by simulation experiments with implanted sources. A set of organ specific properties for six major organs (i.e. heart, lung, liver, kidney, stomach, and adipose) at wavelengths 590-650 nm was satisfactorily chosen. The goal for development of an automatic segmentation tool was cancelled. A workflow for performing BLT reconstruction on forward simulation results was produced as well.

**IIc. Next Steps**

Next steps in this project involve correction of the mesh-labeling error described below. It will involve recreating the previously completed experiments using the same code and workflow but with corrected mesh labels, i.e. organ specific optical properties assigned to the correct region.

**IId. Lessons Learned**

Another prudent lesson was that even published resources should warrant some verification or corroboration before acceptance for use in subsequent projects. In some instances, attempted verification of some calculations for optical properties led to discovery of some discrepancies between the cited calculation method and the resulting values.

One small error with particularly significant effect on the project was the swapping of tissue labels in a tetrahedral mesh provided with MOSE. As a result, optical properties of kidney

were assigned to the lung space, optical properties of lung were assigned to the liver space, and optical properties of liver were assigned to the kidney space.

One of the the lessons emphasized in this project experience was that clarity of presentation may be as important as the actual material being presented. Particularly, because the optical properties results were varied in source and value and relevance, paring the results and attempting to present a concise yet well-documented summary became a significant task.

## III. Technical Appendices

Please refer to the section 'Other Resources and Project Files' in the project wiki for more detailed presentation of results and procedure.

## IV. Project Bibliography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