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An integrated Monte Carlo tissue optics simulation engine with Zemax OpticStudio for complete instrumentation development

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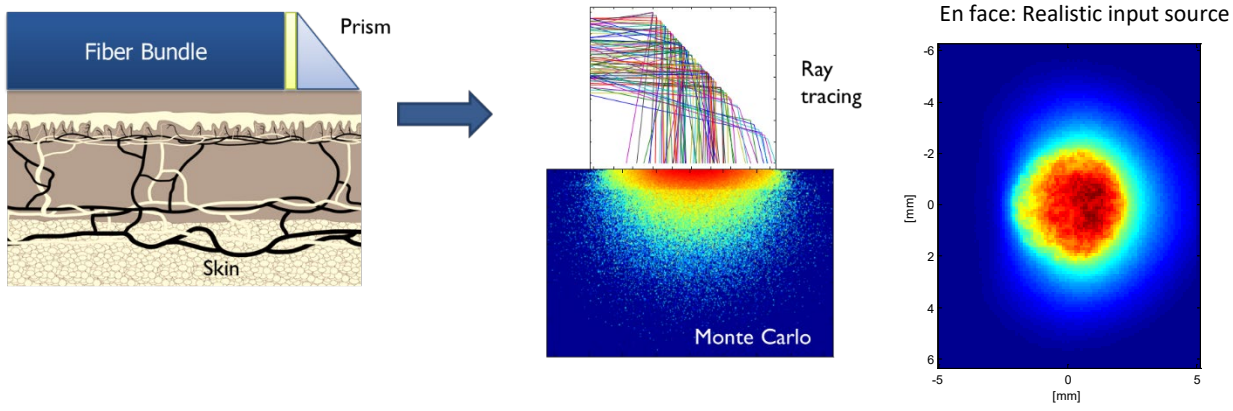
Abstract

Design and optimization of biophotonic devices requires modeling of light propagation in both the tissue and instrument. Monte Carlo simulations are typically used to model the propagation in tissue [1], while geometric ray tracing software such as Zemax OpticStudio is used to model the propagation in the instrument. Typically, these modeling tools are used separately and therefore many of the key benefits of modeling, such as accurate photon budgets, off-angle light effects, device-tissue alignment effects, and device performance over a range of conditions, are missed. Further, many Monte Carlo simulation engines do not have the capability to model realistic source distributions and geometries. Triple Ring Technologies' solution, MCI, is a versatile GPU-accelerated Monte Carlo simulation platform that is integrated with OpticStudio via the ZOS-API to enable complete source→ tissue → detector optical modeling. Our approach is presented and illustrated with two case studies that demonstrate the benefits of an integrated solution.



Triple Ring's MCI platform models complex, real-world light-tissue interaction and does not rely on cylindrical symmetry assumptions or approximations

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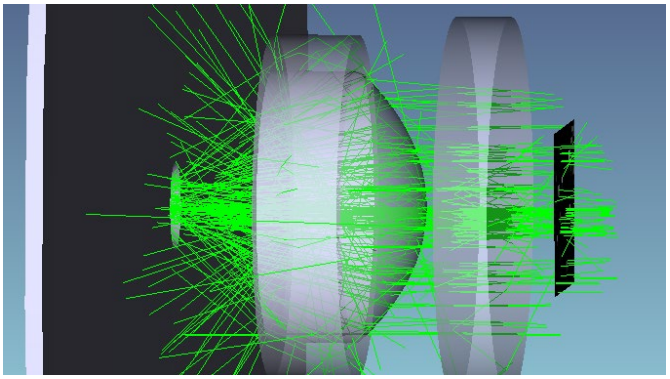
1. Introduction

The field of tissue optics necessitates coping with high optical scattering, whereas traditional optical methods deal with ballistic photons. Information gathered by light propagation through diffuse media can be extremely useful. For example, the use of tissue optics is best known in health and wellness applications such as medical grade pulse oximeters and consumer electronic devices for heart rate and fitness (e.g. Fitbit, Apple watch). There are a wealth of applications in the medical setting that improve quality of care such as fluorescence-guided surgery, diffuse optical imaging, and optical biopsy, among others.

Wearables are often designed ad hoc, with countless design-test cycles in lieu of effective modeling

Due to the complex nature of photon transport in tissue, evaluation and design of instrumentation based on tissue optics require robust simulation capability. Although Monte Carlo methods provide accurate representations of light scattering through tissue, a very large number of photons need to be propagated in order to overcome Poisson noise in the simulation. In addition, tissue optics applications have a highly multi-dimensional design space. Variables such as skin layer thickness, melanin concentration, hydration, and blood volume require multiple simulations to be run for a given instrument configuration; every permutation of properties generally requires its own run, as the interplay between different factors can be highly nonlinear. This leads to long simulation times slowing down the instrument optimization process. To address this issue, Triple Ring Technologies (TRT) has developed Monte Carlo Integrated (MCI), a specialized GPU accelerated program optimized for high speed simulations in diffuse media.

Many elements of an optical system, such as light engines, excitation optics and detection optics are more readily simulated using traditional geometric ray tracing methods. Optical design, such as that done with the well-established Zemax OpticStudio, is performed using numerical ray tracing in which optical elements interact with rays one by one either sequentially or non-sequentially. Models include elements such as lenses, prisms, and mirrors, along with source and detection elements. In these simulations, ray events are not dominated by scattering and can be accurately modeled with many fewer rays.



OpticStudio excels in traditional optical design using components such as lenses, mirrors, and diffractive optical elements. The software package is CPU-based and utilizes sequential processing during ray traces.

Microscopes, camera systems, and other lens based imaging devices are ideal candidates for design optimization with this approach. These simulations are best suited to design optical instrumentation which doesn't interact with a tissue layer.

When designing a tissue-optics-based instrument, the simulation of both the optical elements used in the device and the tissue in which the signal will propagate are necessary. It is critical to consider the entire photon chain, which includes the tissue/instrument interface.

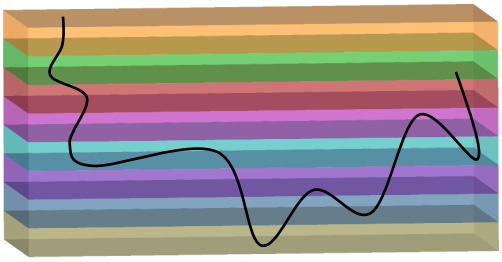
Triple Ring Technologies has formed a method to combine specialized tissue simulation models with Zemax OpticStudio, to offer the best of both worlds. We illustrate our approach with two case studies: a pulse oximetry sensor and a device to perform fluorescence guided surgery.

2. Methods

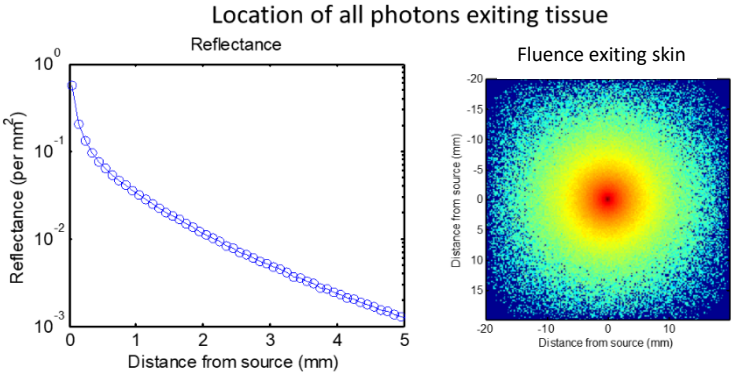
2.1 MCI: TRT's GPU Accelerated Monte Carlo Modeling

To facilitate rapid simulation of photon propagation in tissue, TRT created MCI – a GPU-enabled simulation engine, which is optimized for ray tracing through tissue. Its simulation results have been validated against experimental data and other GPU-based modeling approaches. As a fully featured tissue optics simulation, MCI supports a robust 8 layer skin model, modeling fluorescence in tissue, absorption parallelization, and built-in data analysis such as the calculation of diffuse reflectance curves.

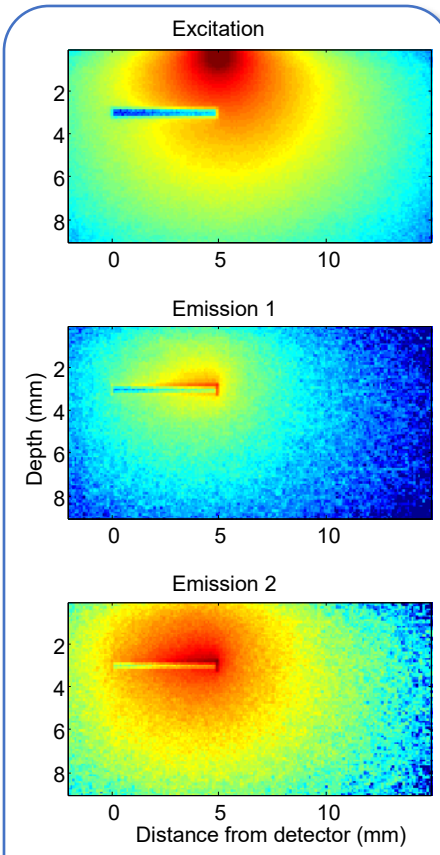
1. Airgap
2. Stratum Corneum
3. Living Epidermis
4. Papillary Dermis
5. Superficial Plexus
6. Reticular Dermis
7. Cutaneous Plexus
8. Subcutaneous Fat



An eight layer tissue model used in MCI, shown here with equivalent thicknesses for illustration purposes. The black line represents a path traveled by a single photon.



Diffuse reflectance curve produced from exiting fluence in MCI.



Example of implanted fluorescence sensor with multiple fluorophores. Excitation light absorption (top panel) and emission at two different wavelengths (middle and bottom panel).

The table below illustrates the speed improvements possible when modeling photon propagation in a complex 8-layer skin model. As compared to Monte Carlo simulations run using a non-parallelized, CPU-based technique, MCI is able to achieve orders of magnitude improvement in required simulation time. In addition, the ability to interface with OpticStudio allows complete system simulation for tissue optics instrumentation.

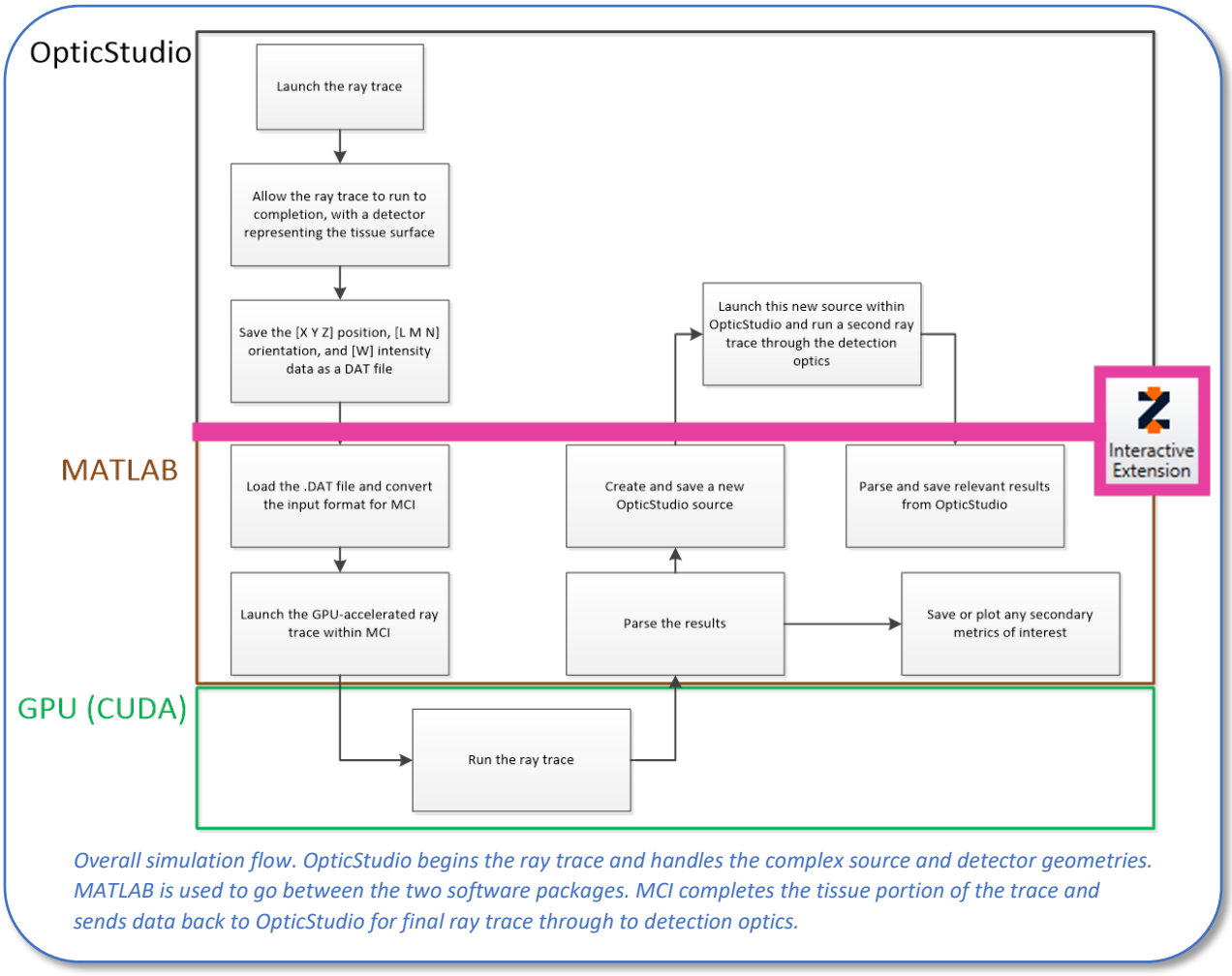
	Simulation Time (seconds)		Speed-up
Number of Rays	**CPU-based MC**	**MCI**	
10^5	13	0.3	43x
10^6	182	1	182x
10^7	1565	8	196x

Results from a simple tissue model simulation with varying amounts of rays traced. When using more than 10^6 rays, GPU-accelerated models benefit from a more than 100X speed increase. System parameters: Win10 64bit, 32GB RAM, Intel Core i7-6700 4GHz CPU, GeForce GTX 1080.

2.2 The Best of Both Worlds: Combining MCI with OpticStudio

In this technique, to take advantage of the rapid diffuse ray tracing offered by MCI while still retaining the complex geometric ray tracing in OpticStudio for instrument modeling, ray traces are broken down into 'time outside of tissue' and 'time within tissue'. Portions of the ray trace that deal with geometrically-complex sources and detection optics outside of the tissue are handled by OpticStudio. When the rays propagate into tissue, MCI takes over. This allows each of the programs to operate in the regime where they work best. The entire workflow occurs seamlessly and automatically without human intervention, leveraging the ZOS-API capabilities in OpticStudio. The overall simulation flow is as follows (see figure on next page):

1. A source-side ray trace launches in OpticStudio. The information (position, orientation, etc.) of rays which reach a detector representing the tissue surface are saved
2. MATLAB loads this saved ray file, converts it to an MCI source, and runs a GPU-accelerated ray trace to model propagation through the tissue
3. The information from rays which reach the tissue surface is saved
4. The output ray from MCI are launched back into the OpticStudio environment
5. Information from both the MCI and OpticStudio traces are saved by MATLAB



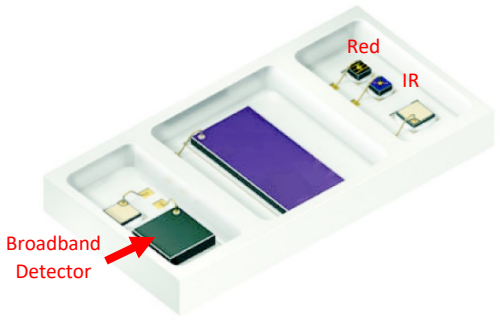
Overall simulation flow. OpticStudio begins the ray trace and handles the complex source and detector geometries. MATLAB is used to go between the two software packages. MCI completes the tissue portion of the trace and sends data back to OpticStudio for final ray trace through to detection optics.

3. Case Studies

To illustrate how our integration of MCI and OpticStudio can be applied to design problems, we present two case studies. In the first, we evaluate an modified version of an off-the-shelf pulse oximetry sensor. Using the combination of MCI and OpticStudio, we simulate the expected signals and variation due to melanin concentration in skin at different wavelengths and source-detector separations. In the second example, we estimate the SNR and loss in image quality when imaging fluorescent blood vessels under a layer of tissue.

3.1 Pulse Oximeter Design Evaluation

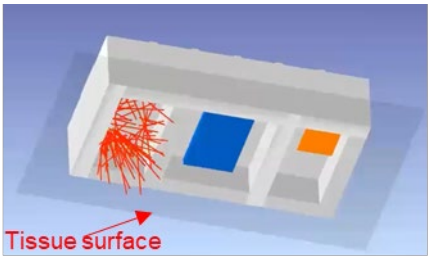
Pulse oximeters are commonly used to make a noninvasive measurement of the blood oxygenation level of a patient. The device functions while in contact with the tissue surface. Light from each LED within the source aperture is detected at a sensor some distance away as it exits the tissue. The signal returned from each LED carries information about the blood oxygenation level. A modified version of an off-the-shelf commercial sensor (OSRAM BIOFY®, SFH 7072) contains two LEDs, and a detector separated by walls.

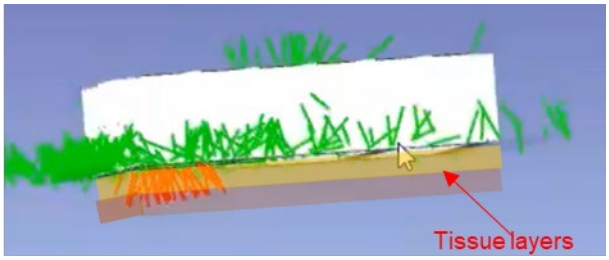


Off-the-shelf oximeter sensor (OSRAM BIOFY®, SFH 7072), which has been modified for this exercise.

A complete model of the device can be captured by using OpticStudio and MCI. In OpticStudio, the device geometry, detector, light source illumination, baffles, and spacing is simulated. To optimize this device, a critical factor is the ideal selection of source-detector separation. These parameters affect depth of penetration, returned signal strength, and skin-type dependence of the output signal. The tissue is simulated in MCI with an eight-layer model with anatomically appropriate thicknesses and optical properties for a range of skin tones and blood volumes.

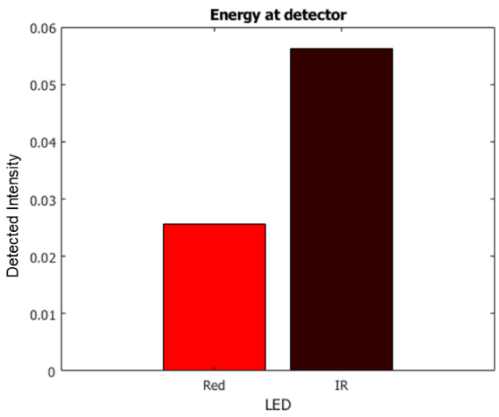
A ray trace is performed using 10^6 rays for each LED. The path begins at the source LEDs in OpticStudio, travels to the tissue surface where MCI continues through the tissue, and then back on the outside of the tissue to the detector which is handled by OpticStudio once again. The end result is the intensity of each LED on the detector as light travels from the device through the tissue and back.



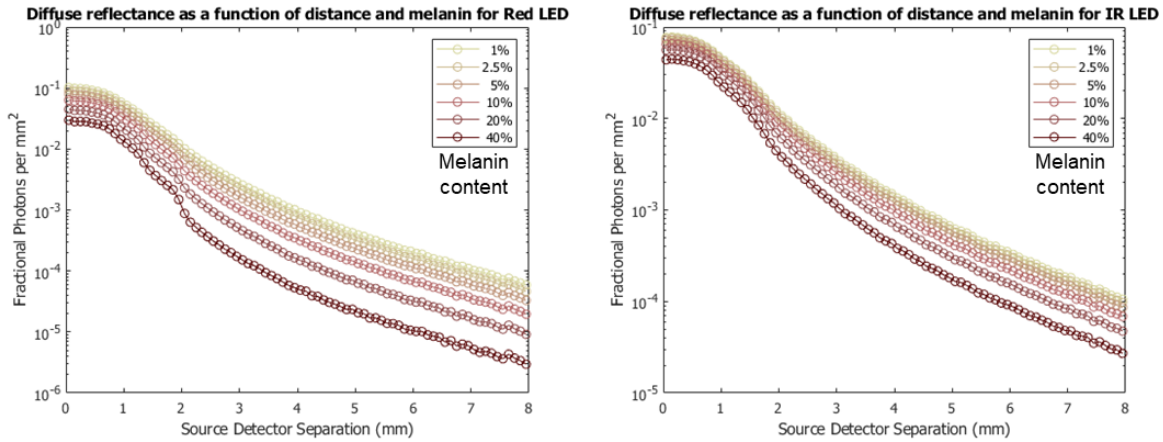


(Left) Geometrical model in OpticStudio. The red lines indicate rays traced from both LEDs, the Orange square represents the sensor. The transparent rectangle is the tissue interface.
(Right) After running the full ray trace, rays propagated through tissue by MCI are returned to the surface to be detected by the sensor in OpticStudio (return rays shown in green).

Once the trace is complete, additional analyses are completed automatically within MCI. For example, diffuse reflectance curves can be generated, providing the relative signal (per input photon) as a function of the source-detector separation. This allows for design optimization. A newly selected source-detector distance informs the geometry that can be modified in OpticStudio and the simulation re-run to obtain precise values. Importantly, MCI provides signals as a function of both source-detector distance and of a set of pre-programmed tissue absorption values that account for melanin and blood volume changes.



Result of full ray trace. Energy at the detector is observed after propagation through tissue.



Diffuse reflectance curves generated in MCI after a complete integrated run with OpticStudio. Signal as a function of source detector separation for multiple absorption values can help guide geometric design.

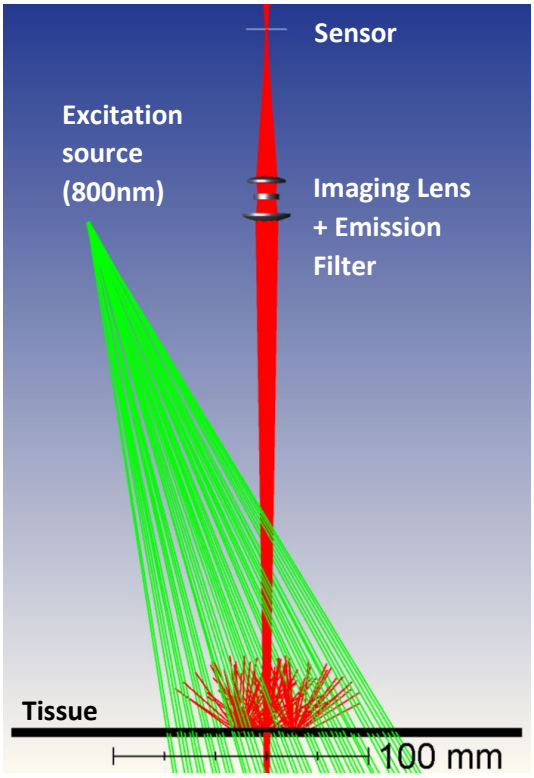
In the example above, diffuse reflectance curves are plotted as a function of changing melanin concentration. Similar curves can be plotted for changes in tissue blood volume. This information is available in a single run of the MCI←→OpticStudio simulation because of the unique way the simulation engine is structured. During each trace, MCI tracks the total path length of each ray within each different type of tissue. The average paths followed by any ray are a function of the scattering, anisotropy, and indices of refractions, but not of the absorption. Therefore the final weight of each ray can be re-calculated for any different assumption of absorption coefficient, owing to differences in melanin levels, blood volume, etc, without the need to re-run the simulation for each case. The end result is a parallelization of both the ray traces (decreasing simulation time per run) and the absorption assumptions (reducing the dimensionality of the design space).

3.2 Fluorescence guided surgery

Fluorescence imaging is a key technology underlying many medical procedures. Indocyanine green (ICG) is a fluorescent dye frequently used in clinical applications [3]. Expanded use in surgeries has enabled imaging technology to provide real-time guidance to surgeons [4]. ICG excitation is primarily in the near infrared, and therefore has the advantage of operating within an ‘optical window’ that allows for deep tissue penetration. A typical method is to illuminate the area of interest using the excitation wavelength (750-800 nm) and observe the emitted signal exclusively at longer wavelengths (>800 nm) with the help of optical filters.

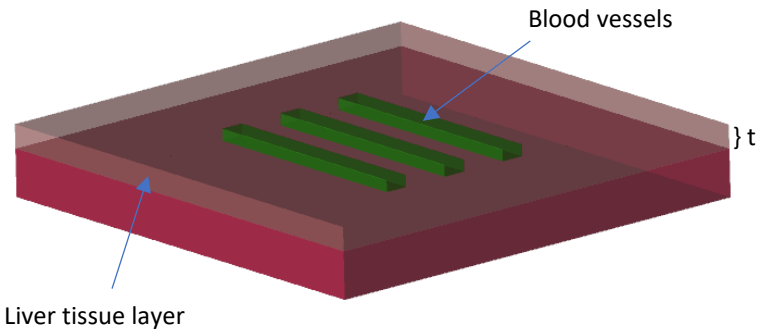
Using a camera to image blood vessels or ducts in-vivo allows helpful anatomical visualization during surgical procedures. For example, during fluorescence-guided cholecystectomy, ICG is injected prior to surgery and concentrates in bile, providing an outline of the gall bladder and bile ducts [5]. The image quality of the fluorescent region is determined by a combination of the imaging optics, sensor, and tissue properties, and should be optimized to suit the use case. Thus, having an accurate model of the camera system and photon transport through tissue provides a rapid path to optimization.

In the following example, such an imaging system with a fiber-based excitation source is modeled. The excitation source is the output from a 0.2 NA, 1 mm diameter fiber, aimed at the target tissue at an angle of 20° (wavelength 800nm). The imaging system consists of a Cooke triplet lens (f = 50mm, f/2, FOV = +/-20°), emission filter, and detector (8x8 mm). A two layer tissue model is used, composed of a top layer of diffuse media, and a lower layer that in addition to absorption and scattering, fluoresces due to the presence of ICG. The top tissue layer (with thickness of 0.1 mm – 2 mm, depending on the simulation) has absorption and scattering coefficients corresponding to liver tissue [1,6], while the lower layer represents a mixture of ICG and blood. The tissue model is placed at a 200 mm working distance from the imaging lens, a technique mimicking use in open surgical environments. A 100 mM ICG concentration is assumed in the blood layer, again corresponding to the commonly used values in fluorescence-guided surgery procedures. To assess image quality, the fluorescent vessels are modeled as three rectangular volumes representing vessels.



OpticStudio provides the modeling capability for complex source and detection components. A commercial off the shelf lens and fiber coupled excitation source (green) can be pulled into the model for optimization with MCI tissue simulation output (red).

In this combined model, OpticStudio simulates the propagation of light from the source to the tissue, providing an accurate distribution of input photons to MCI. MCI then simulates and provides an accurate representation of excitation and fluorescence occurring within tissue layers and feeds the information back into OpticStudio, which propagates the photons from the tissue surface to the camera sensor.



Tissue model used in MCI. Two layers representing liver with embedded blood vessels. The top layer thickness, t, is varied from 0.1mm-2mm in the simulation

Using this combined model, images of the underlying fluorescence expected in the blood vessels can be simulated as a function of the top layer thickness, t, and the image blur can be estimated. The number of photons received by the camera sensor is also measured and provides an absolute irradiance. A photon budget can be constructed from the data to benchmark the optical system, with which SNR for a given camera system (imaging lens + sensor) can be estimated.

Simulated image of vessels as a function of top layer thickness t

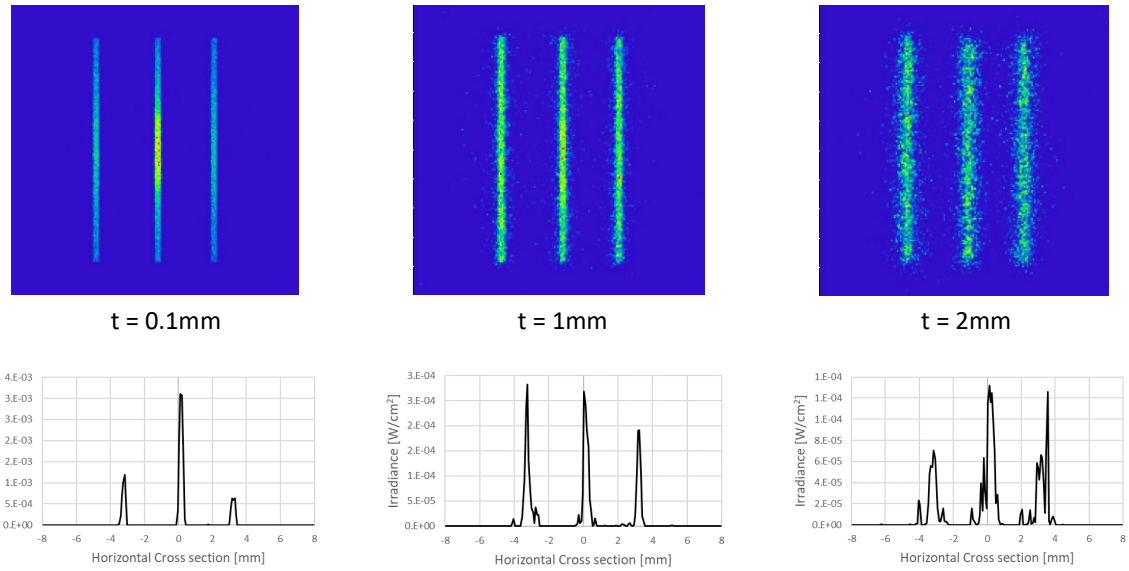


Image blurring as a function of tissue thickness, t. As the fluorescing blood vessels are embedded deeper under the top tissue layer, the image begins to blur and the contrast may be directly calculated. The irradiance measured at the camera sensor plane is plotted below as a horizontal cross section.

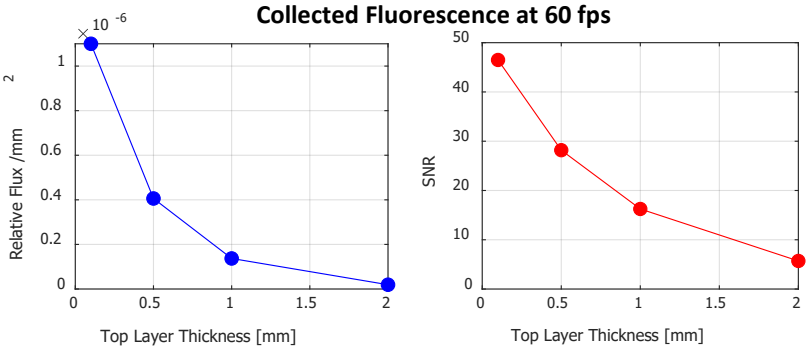
Consider a 1/2.9" class sensor as described in the table below. Assuming 1 mW emitted by the excitation fiber, and a 64mm^2 image sensor operating at 60fps, the relative flux/mm^2 drops off rapidly as a function of tissue depth. The SNR can be estimated from the quantum efficiency of the sensor, read noise of the camera, and photon shot noise. As shown below, the estimated SNR from an image of vessels beneath only 0.1 mm of tissue is 46. However, when the top tissue layer thickness is 2 mm, SNR is reduced to 6. Once the model is in place, alternate sensor types, filters, lenses or excitation power can be explored until the desired signal and image quality are achieved. Quantitative feedback regarding photon simulation in both a complex optical system *and* an accurate tissue model is critical for optimum total system design.

Sensor Specifications

Mfr, PN	FLIR Blackfly BFS-PGE-16S2
Pixel Size	3.45 µm
QE, 800 nm	0.25
Read Noise	2.5 e-

Data shown after complete propagation and fluorescence

Collected Fluorescence at 60 fps



4. Summary

Biophotonic devices that utilize light interaction with tissue for diagnostic or therapeutic applications are rapidly proliferating. The success of many of these devices is negatively impacted by the time and cost spent in the build-test phase and uncertainty in roll-out to a larger population where failures not seen during testing are likely.

TRT leverages GPU-accelerated methods to provide a path forward in this design space. Combining two tools, MCI and OpticStudio, provides advantages that cannot be realized by using either approach alone. A complete system model can be achieved, providing the most accurate feedback during system optimization. MCI's unique capability of running multiple tissue absorption values at once further speeds up and streamlines the design process, allowing a large range of physiological parameters to be simulated, including the corner cases.

The ability to design and optimize instruments and system performance in simulation prior to physical assembly provides both a cost advantage and a reduction in risk that may be the difference between failure and success.

Triple Ring Technologies

Triple Ring is a co-development company headquartered in Silicon Valley, with offices in Boston, Toronto, and Copenhagen. We stand side-by-side with innovators and entrepreneurs to solve hard problems, launch breakthrough products, and create new businesses. ISO 13485 certified, we provide expertise in optical, electrical, mechanical and complete system design of products for medical, consumer and industrial markets. For more information about Triple Ring, contact:

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References

1. S. L. Jacques, "Optical properties of biological tissues: a review," *Physics in Medicine and Biology*, **58**(11), R37–R61 (2013).
2. https://www.osram.com/ecat/BIOFY%C2%AE%20SFH%207072/com/en/class_pim_web_catalog_103489/prd_pim_device_2220016/
3. J. T. Alander et al., "A Review of Indocyanine Green Fluorescent Imaging in Surgery", *International Journal of Biomedical Imaging*, **2012,** Article ID 940585 (2012).
4. A. Vahrmeijer et al., "Image-guided cancer surgery using near-infrared fluorescence," *Nature Reviews Clinical Oncology*, **10**, 507–518 (2013).
5. L. Boni el al., "Clinical applications of indocyanine green (ICG) enhanced fluorescence in laparoscopic surgery," *Surgical endoscopy*, **29**(7), 2046–2055 (2015).
6. A. D'Souza et al., "Review of fluorescence guided surgery systems: identification of key performance capabilities beyond indocyanine green imaging," *Journal of Biomedical Optics*, **21**(8), 80901 (2016).
7. S. Akter et al. "Evaluation of light scattering and absorption properties of in vivo rat liver using a single-reflectance fiber probe during preischemia, ischemia–reperfusion, and postmortem," *Journal of Biomedical Optics*, **20**(7), 076010 (2015).