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affiliée à l'Université de Montréal

**Experimentally and numerically validated Monte Carlo simulator for optical
coherence tomography**

KHALIUN ERDENEDALAI

Institut de génie biomédical

Mémoire présenté en vue de l'obtention du diplôme de *Maîtrise ès sciences appliquées*
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Ce mémoire intitulé :

**Experimentally and numerically validated Monte Carlo simulator for optical
coherence tomography**

présenté par **Khaliun ERDENEDALAI**

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DEDICATION

This thesis is dedicated to my role model:

Dr. Ing. Purevsuren Tsoozol.

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RÉSUMÉ

La tomographie par cohérence optique (OCT) est une technique d'imagerie non invasive de plus en plus populaire dans de nombreuses applications biomédicales. Il est possible de visualiser les structures tissulaires avec une précision de quelques millimètres et une résolution en profondeur d'environ 10 microns. En OCT, le problème inverse consiste à déduire la structure interne ou les caractéristiques d'un échantillon en analysant les signaux OCT acquis à partir de celui-ci. La résolution de ce problème inverse fournit des informations significatives, facilite l'analyse quantitative et améliore la compréhension et l'utilisation de cette technologie d'imagerie dans divers domaines de la médecine et de la recherche. Cela faciliterait l'interprétation des images OCT pour diagnostiquer les maladies, suivre l'évolution des traitements et guider les procédures chirurgicales. L'une des façons de résoudre ce problème est d'utiliser la technique de l'apprentissage automatique, qui nécessite à la fois des données et une représentation précise de différents objets. La simulation numérique est l'un des moyens possibles de capturer des images OCT.

La simulation de Monte Carlo (MC) est la méthode établie pour étudier l'interaction lumière-tissu dans les tissus biologiques, et elle peut être utilisée pour étudier des techniques d'imagerie comme l'OCT. Toutefois, certaines modifications sont nécessaires pour répondre aux exigences spécifiques de l'OCT et atteindre une grande précision de simulation. Étant donné que l'OCT repose sur la détection de photons rétrodiffusés par le tissu, il devient essentiel d'incorporer un schéma de détection de paquets de photons dans la simulation. En outre, pour modéliser avec précision la propagation de la lumière dans le système d'imagerie, il est crucial de tenir compte du comportement réel de la lumière. De nombreux photons simulés peuvent ne pas contribuer au signal OCT détecté à l'aide d'un moteur MC standard en raison de la décroissance exponentielle de l'intensité lumineuse avec la profondeur. Ce phénomène a un impact significatif sur le temps de calcul. Il existe donc un besoin pressant de méthodes permettant d'améliorer le temps de calcul et de générer efficacement des images OCT tout en maintenant la précision.

Nous présentons ici MCOCT, un simulateur Monte Carlo open-source qui a été validé expérimentalement et numériquement. Son objectif est de simuler précisément la propagation de la lumière dans un milieu trouble pour la tomographie par cohérence optique dans le domaine de Fourier (FD-OCT). MCOCT incorpore un système d'illumination et de détection aux propriétés identiques en termes d'ouverture numérique, de géométrie et d'emplacements

spatiaux. Au cours de la simulation, la distance parcourue par les photons est suivie afin d’extraire leur phase, essentielle pour reconstruire le signal OCT. Cela implique de prendre en compte les interférences à plusieurs longueurs d’onde, imitant ainsi le contrôle de la cohérence, crucial pour l’OCT. Pour obtenir une focalisation du faisceau plus réaliste, le simulateur prend en compte la forme et la profondeur de focalisation du faisceau d’illumination. Pour ce faire, les photons sont propagés le long d’une trajectoire courbe basée sur l’optique gaussienne. En tenant compte à la fois de la nature particulière et ondulatoire des photons, MCOCT atteint un haut niveau de précision. Pour optimiser le temps de simulation, la méthode validée de *importance sampling* est employée, ce qui améliore l’efficacité du simulateur.

Nous avons procédé à une validation numérique et expérimentale du simulateur. Lors de la validation numérique, nous avons comparé le taux de fluence avec un autre simulateur établi et avons trouvé une correspondance très satisfaisante, en particulier au niveau du point focal. Pour la validation expérimentale, nous avons utilisé différentes ouvertures numériques et testé le simulateur sur des fantômes monocouches et bicouches en polydiméthylsiloxane imitant les tissus *in vitro*. En comparant les signaux OCT simulés avec ceux obtenus expérimentalement sur des fantômes aux propriétés optiques différentes, nous avons observé une progression remarquablement similaire et convaincante des signaux pour les deux longueurs focales. À notre connaissance, il s’agit du premier simulateur MC open-source disponible pour le FD-OCT. Nous sommes convaincus que l’accès à un simulateur validé de ce type serait très bénéfique pour la communauté de l’OCT.

ABSTRACT

Optical coherence tomography (OCT) is a non-invasive imaging technique that is gaining popularity in numerous biomedical applications. It allows for the visualization of tissue structures within a few millimeters of depth and provides a depth resolution of approximately 10 microns. In OCT, the inverse problem refers to the task of reconstructing the internal structure or properties of a sample based on the measured OCT signals obtained from it. Solving this inverse problem enables the extraction of meaningful information, facilitates quantitative analysis, and enhances our comprehension and utilization of this imaging technique across different medical and research fields. This would assist in the interpretation of OCT images to diagnose diseases, monitor treatment progress, and guide surgical procedures. One approach to tackle this is through the utilization of machine learning, which requires both data and the accurate representation of various objects and one way to acquire OCT images is through numerical simulations.

Monte Carlo (MC) simulation for light propagation in biological tissue is the gold standard for investigating light-tissue interaction, which can be used to study imaging procedures, such as OCT. To address the specific requirements of OCT and ensure simulation accuracy, some modifications need to be implemented. Since OCT relies on detecting backscattered photons from the tissue, it becomes necessary to incorporate a photon packet detection scheme. Additionally, to accurately simulate light propagation within the imaging system, the actual behavior of light must be taken into account. Furthermore, using a standard MC engine, most simulated photons will not contribute to the detected OCT signal due to the exponential decay of light intensity with depth, while having a significant impact on computation time. Therefore, methods to improve the computation time are needed to efficiently generate OCT images.

We introduce here an experimentally and numerically validated, open-source Monte Carlo simulator (MCOCT) designed to accurately simulate light propagation in a turbid medium in Fourier-domain OCT (FD-OCT). In MCOCT, an illumination and detection system with identical properties of numerical aperture, geometry, and spatial locations is implemented. Throughout the simulation, the traveled distance of the photons is tracked to extract their phase for reconstructing the OCT signal. Thereby, the interference at multiple wavelengths is used, thus mimicking coherence gating which is an essential part of OCT. The shape of an illumination beam and its depth of focus are considered to mimic a more realistic beam

focusing and are implemented by propagating the photons along a curved trajectory based on Gaussian optics. This method takes into account both the particle as well as the wave nature of photons, making it highly accurate. To improve simulation time, the validated method of importance sampling was utilized.

We initially validated the simulator numerically by comparing the fluence rate with another established simulator and observed a highly satisfying match, especially at the focus. The experimental validation was performed with varying numerical apertures on several one-layer and one bi-layer polydimethylsiloxane tissue-mimicking phantoms in vitro. Comparing the simulated OCT signals to the experimentally obtained ones, for all phantoms of different optical properties, the progression of the signals was very similar and convincing for both focal lengths. To the best of our knowledge, this is the first open-source available MC simulator for FD-OCT and we believe that the OCT community would benefit from having access to a validated simulator of this kind.

TABLE OF CONTENTS

DEDICATION	iii
ACKNOWLEDGEMENTS	iv
RÉSUMÉ	v
ABSTRACT	vii
TABLE OF CONTENTS	ix
LIST OF TABLES	xii
LIST OF FIGURES	xiii
LIST OF SYMBOLS AND ACRONYMS	xv
LIST OF APPENDICES	xvi
CHAPTER 1 INTRODUCTION	1
1.1 Research objective	1
1.2 Thesis outline	2
CHAPTER 2 LITERATURE REVIEW	3
2.1 Optical coherence tomography	3
2.1.1 Working principle	3
2.1.2 Technical realizations	5
2.1.3 Resolution of SS-OCT	7
2.1.4 OCT signal construction	8
2.2 Beam characteristics	10
2.2.1 Beam propagation	10
2.2.2 Beam source	12
2.3 Modeling light-tissue interaction	12
2.3.1 Beer-Lambert Equation	12
2.3.2 Fresnel equation	13
2.3.3 Radiative Transfer Equation	14
2.4 Monte Carlo Simulation	15

2.4.1	Standard Monte Carlo algorithm	15
2.4.2	Modifications	17
2.4.3	OCT simulators	22
2.5	Optical Phantoms	24
2.5.1	Phantom materials	24
2.5.2	Phantom characterization	25
CHAPTER 3	INITIAL WORK	26
3.1	Validation of OCT signal reconstruction algorithm	26
3.2	Validation of Gaussian beam	28
3.3	Effect of importance sampling	30
3.4	Optical phantom fabrication	31
3.5	Determining the anisotropy coefficient	32
CHAPTER 4	ARTICLE 1 : MCOCT: AN EXPERIMENTALLY AND NUMER- ICALLY VALIDATED, OPEN-SOURCE MONTE CARLO SIMULATOR FOR OPTICAL COHERENCE TOMOGRAPHY	34
4.1	Introduction	35
4.2	Methods	37
4.2.1	Monte Carlo photon propagation	37
4.2.2	OCT signal simulation	37
4.2.3	OCT signal reconstruction	41
4.2.4	Tissue-mimicking optical phantoms	43
4.2.5	MCOCT simulations for comparison with MCX simulations	45
4.2.6	MCOCT simulations for comparison with OCT imaging in phantoms	46
4.3	Results	46
4.4	Discussion	49
4.5	Conclusion	53
4.6	Appendix	53
CHAPTER 5	ADDITIONAL FINDINGS	55
5.1	Additional phantoms	55
5.2	Effect of different beams	56
CHAPTER 6	GENERAL DISCUSSION	58
6.1	Modifications to standard MC	58
6.2	Possible modifications to MCOCT code	59

6.3	Phantoms	60
CHAPTER 7 CONCLUSION		62
7.1	Summary of Works	62
7.2	Limitations	62
7.3	Future Research	63
REFERENCES		65
APPENDICES		73

LIST OF TABLES

Table 2.1	Variables used in Figure 2.6	22
Table 3.1	Computation time and quantity of launched and detected photons with and without importance sampling. IS refers to simulations with importance sampling and HG to those using only the HG function.	30
Table 4.1	Concentrations of the scattering (titanium dioxide) and absorbing (ni-grosine) agents of the phantoms.	44
Table 4.2	Optical properties of the phantoms characterized by spectrophotometry.	44
Table 4.3	Position of focus z_f [mm] below the phantom surface for each focal lens f	45
Table 4.4	Computation time and quantity of launched and detected photons for MCOCT simulations presented in Figure 4.6 and Figure 4.7.	48
Table 4.5	Variables used for Figures 4.1, 4.2, 4.3, and 4.4	54

LIST OF FIGURES

Figure 2.1	OCT image and signal of a finger pad in vivo.	4
Figure 2.2	Schematic of an SS-OCT system.	6
Figure 2.3	Parameters used to describe the Gaussian beam propagation.	11
Figure 2.4	The law of refraction.	14
Figure 2.5	Flowchart describing the standard Monte Carlo algorithm.	16
Figure 2.6	Importance sampling method to increase the probability of photon detection.	21
Figure 3.1	Example of the FD-OCT signal at the different stages of reconstruction	27
Figure 3.2	Simulated OCT B-Scan.	27
Figure 3.3	Photon propagation using Gaussian beam.	28
Figure 3.4	Optical fluence rates ϕ comparison using a Gaussian beam in the simulator between (a) $n = 1$ and (b) $n = 1.5$. Comparison of fluence rates with the simulator (red) <i>vs.</i> the mathematical model (blue) along x (b) and along z (c).	29
Figure 3.5	MCOCT generated A-line from 10^9 launched photon packets using importance sampling and averaged over 500 detection probes.	31
Figure 3.6	Images of optical phantoms	32
Figure 3.7	Single scattering model (blue) <i>vs.</i> Normalized OCT A-line (red) to estimate anisotropy g	33
Figure 4.1	Description of the geometry and parameters used to simulate the Gaussian focusing beam. The dashed lines show the trajectory in a crossing propagation. Variables are described in Table 4.5 of the Appendix.	38
Figure 4.2	Flowchart describing the scattering process of the simulator. Variables are described in Table 4.5 of the Appendix.	41
Figure 4.3	MCOCT Flowchart	42
Figure 4.4	OCT signal reconstruction. Variables are described in Table 4.5 of the Appendix.	43
Figure 4.5	Optical fluence rates Φ [$\text{W}/\text{cm}^2/\text{W}_{\text{incident}}$] comparison between (a) MCOCT and (b) MCX simulated with the same optical properties. (c) Comparison of optical fluence rates along x at $z = 1.5$ mm and $y = 0$ mm generated by MCOCT (red) and MCX (blue). (d) Comparison of optical fluence rates along z at $x = 0$ mm and $y = 0$ mm simulated with MCOCT (red) and MCX (blue).	47

Figure 4.6	Experimentally obtained (red) <i>vs.</i> simulated (blue) OCT A-lines using an imaging lens of $f = 30$ mm of (a) Phantom #1 (b) Phantom #2 (c) Phantom #3 and (d) Phantom #4.	48
Figure 4.7	Experimentally obtained (red) <i>vs.</i> simulated (blue) OCT A-lines using an imaging lens of $f = 75$ mm of (a) Phantom #1 (b) Phantom #2 (c) Phantom #3 and (d) Phantom #4.	49
Figure 5.1	Experimentally obtained (red) <i>vs.</i> simulated (blue) OCT A-lines using an imaging lens of f of phantom #5	55
Figure 5.2	OCT images of phantom #6	56
Figure 5.3	Experimentally obtained (red) <i>vs.</i> simulated using a Gaussian beam (blue) <i>vs.</i> geometric focused (orange) <i>vs.</i> pencil (green) beam OCT A-lines using an imaging lens of with the focal length f of phantom 1.	57
Figure A.1	Poster presented at the Gordon Research Seminar and Conference.	73
Figure B.1	Poster presented at the Optica Biophotonics Congress: Optics in the Life Science.	74

LIST OF SYMBOLS AND ACRONYMS

CPU	Central processing unit
CUDA	Compute Unified Device Architecture
FD-OCT	Fourier-domain optical coherence tomography
GPU	Graphics processing unit
HG	Henry-Greenstein
IAD	Inverse adding-doubling
MC	Monte Carlo
MCEO-OCT	Monte Carlo simulation for tissue layers with embedded objects for OCT
MCML	Monte Carlo multi-layered
MCX	Monte Carlo eXtreme
MMC	Mesh-based Monte Carlo
NA	Numerical aperture
NIR	Near-infrared
OCT	Optical coherence tomography
OCT-MPS	OCT massively parallel simulator
OFDI	Optical frequency domain imaging
PDMS	Polydimethylsiloxane
RTE	Radiative transfer equation
SD-OCT	Spectral-domain optical coherence tomography
SNR	Signal to noise ratio
SS-OCT	Swept-source optical coherence tomography
TIM-OS	Tetrahedron-based inhomogeneous Monte Carlo optical simulator
TD-OCT	Time-domain optical coherence tomography

LIST OF APPENDICES

Appendix A	GRS/GRC poster	73
Appendix B	Optica poster	74

CHAPTER 1 INTRODUCTION

Optical coherence tomography (OCT) is a high-resolution, non-invasive imaging technique gaining popularity in medical and biological applications. It relies on the detection of backscattered photons from the sample medium. As light penetrates deeper into the tissue, its intensity diminishes exponentially, resulting in weak and distorted OCT signals from deeper regions. Addressing the inverse problem in the future necessitates an extensive dataset of OCT images. These can be obtained experimentally with an actual OCT system or with computer simulation. Monte Carlo (MC) methods can be used for simulating light propagation in tissue, that can be adapted for OCT. For that, modifications need to be implemented to accommodate the particular requirements of OCT. Furthermore, the classic MC algorithm requires long simulation times since only a tiny fraction of the simulated photons participate in the OCT signal due to the high anisotropy of biological tissue. Optimization of the current models by changing computation methods presents opportunities to expedite OCT image formation. We propose an open-source simulator named MCOCT, designed specifically for Fourier-domain OCT. This simulator allows for the generation of OCT signals from tissue with known optical properties. We conducted numerical and experimental validations to demonstrate the accuracy of MCOCT.

1.1 Research objective

The research objective is to develop a simulator capable of accurately creating FD-OCT images. This can be further divided into the following sub-objectives (SO):

- SO 1: Add functions to existing code to increase computational efficiency.
- SO 2: Add FD-OCT specific relevant features, such as a photon detection system and Gaussian beam focusing.
- SO 3: Develop an OCT post-processing algorithm to recreate OCT signals from simulator output.
- SO 4: Create and characterize tissue-mimicking phantoms.
- SO 5: Validate the simulator numerically with other existing simulators and experimentally using these phantoms.

1.2 Thesis outline

In this master's thesis, we study the steps that led to the development of MCOCT, our open-source Monte Carlo (MC) simulator for FD-OCT. In the first step, a literature review in Chapter 2 introduces the underlying principles of optical coherence tomography (OCT). Various approaches to simulate light-tissue interaction are explained, pointing out the need for an MC-based simulator is necessary. In parallel, the standard MC algorithm and modifications that were proposed throughout the years are presented. Since our goal is simulating OCT signals, the necessary modification to accommodate the particular requirements of FD-OCT are described. Finally, we will briefly present optical phantoms as these are used as the decisive validation of MCOCT.

In Chapter 3, the simulations and experiments leading to the article will be presented. It can be seen as the validation results of each sub-objective SO 1 to SO 4 as these paved the way to get our final results.

Chapter 4 is the core of the thesis in the form of a scientific paper. There, we go into the details of the theory and methodology used. The final validation results of the simulator using one-layered and bi-layered phantoms are presented.

Chapter 5 is dedicated to presenting additional findings throughout the work. These include presenting optical phantoms that were not included in the article. We also compare not only the developed curved beam propagation results to the experimental phantom OCT A-lines but also use a pencil beam as well as a geometric-focused beam to show the effect of our method.

Finally, a general discussion in Chapter 6 and conclusion in Chapter 7 review the key elements and suggest avenues to explore based on the results obtained.

CHAPTER 2 LITERATURE REVIEW

This chapter describes the necessary theoretical aspects for the comprehension of the presented thesis. It introduces optical coherence tomography (OCT) and the characteristics of the illumination/collection geometry typically used in an OCT system. Furthermore, different approaches to modeling light-tissue interaction are described with an in-depth review of the Monte Carlo method. Finally, we provide an overview of optical phantoms, including their key properties and fabrication methodology. It provides the underlying theory related to our presented method of the article in the next Section 4.

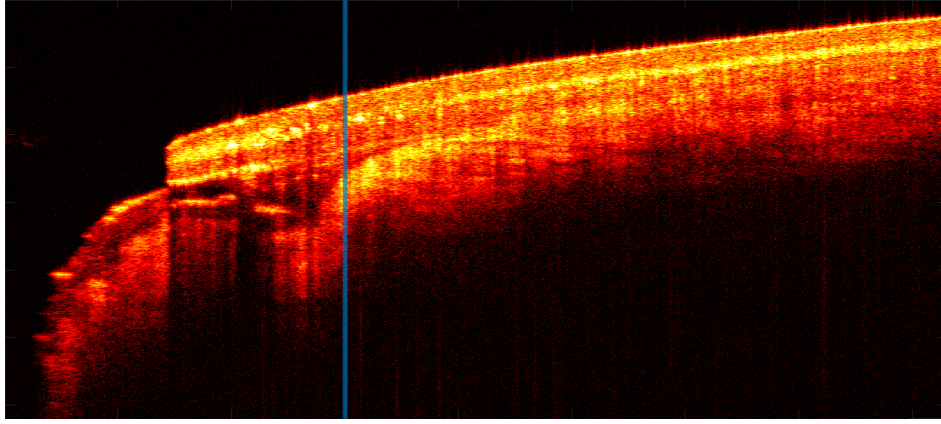
2.1 Optical coherence tomography

Optical coherence tomography is an imaging technique that employs a broadband light source with low temporal coherence to reconstruct high-resolution, depth-resolved reflectivity maps of scattering media, such as biological tissues [1]. OCT typically provides information on tissue morphology over a depth of 1-2 mm, limited by the attenuation of light by the tissue. The central wavelength employed for OCT imaging is chosen depending on the tissue under examination and the desired light penetration. Typically, to achieve deeper penetration in scattering mediums a wavelength around 1310 nm is used [2,3]. OCT initially found its first medical application in ophthalmology, specifically in the examination of retinal layers in the human eye [4]. Its utility has extended beyond ophthalmology and is now gaining popularity in various other medical fields, such as cardiology, dermatology, and laryngology [5–8]. In ophthalmology, OCT is now a standard tool for diagnosing and monitoring retinal diseases. In dermatology, it is a promising diagnostic tool for the detection of skin diseases and assists in the evaluation of treatment effects and skin functions [7]. Furthermore, it has emerged as a valuable imaging technique in laryngology for detailed visualization of the vocal folds, providing valuable insights into their structure and possible lesions [8].

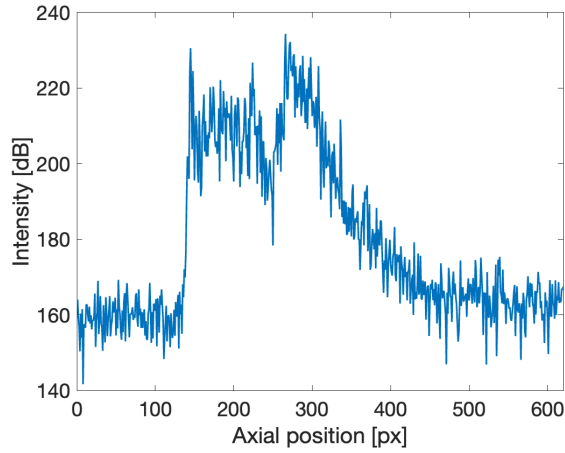
2.1.1 Working principle

OCT works on the principle of a Michelson interferometer, where the light source emits a coherent beam divided by a splitter into two arms of the interferometer, namely a reference and a sample arm. In the reference arm, the beam is cast onto a mirror and reflected back, whereas in the sample arm light gets backscattered from the tissue. These reflected beams interfere with each other upon combination at the beamsplitter in a constructive or

destructive manner depending on the difference of optical path through these two arms. This interference signal is used to obtain a reflectance profile of the tissue at distinct probed depths. This 1D measurement along the axial or z -direction through a laser scan at a single position is called an A-line. By scanning the laser along one lateral dimension, a 2D cross-sectional image is created, which is called a B-scan. Scanning along the other lateral dimension using an additional scanner while acquiring B-scan allows for 3D imaging also referred to as a C-scan [1,2]. Fig. 2.1 shows a B-Scan of an in-vivo finger pad as seen in OCT imaging with the underlying A-line at the lateral (x) position marked with by blue line.



(a) OCT B-Scan



(b) OCT A-line

Figure 2.1 OCT image and signal of a finger pad in vivo.

2.1.2 Technical realizations

There are two varying approaches to measuring the signal intensity at the detector resulting in two different OCT methods, namely time-domain OCT (TD-OCT) and Fourier-domain OCT (FD-OCT) [1, 9]. They differ in their practical implementations resulting in their key performance differences regarding sensitivity, the resulting signal-to-noise ratio (SNR), and the consequent speed, which are explained later in this chapter. Their difference in implementation need to be considered when simulating OCT signals.

TD-OCT

In TD-OCT, signal intensity is measured as a function of the position of the reference mirror, which is scanned across a distance equal to the desired imaging range. Here, light from a broadband source is split and sent into the reference and the sample arm, where it is reflected by a mirror and scatterer, respectively. Low-coherence light can only interfere over a very short distance, which is referred to as the coherence length of the source. This means, that the two reflected beams interfere when the reference mirror position matches approximately that of the scatterer in the sample, i.e., the path length difference is within the coherence length, also known as coherence gating. This path length difference creates a temporal delay in the reflected light, wherefore it is possible to obtain the reflectivity of a sample as a function of the depth. In the case of multiple scatterers, each one produces an interference pattern with a peak at the position that matches that of the moving reference arm. The amplitude of the signal modulation at the detector is related to the reflectivity of the scatterer present. The axial displacement of the mirror continuously collects the reflectivity profile of the sample, i.e., A-lines [1, 2]. The acquisition rate of TD-OCT is therefore constrained by the physical movement of the reference mirror.

FD-OCT

In FD-OCT, the interference signal is measured spectrally, i.e. as a function of wavenumber while the reference mirror stays stationary. The position of the scatterers can be defined relative to the position of the mirror, wherefore the interference spectrum contains the depth information of the sample. FD-OCT can be implemented in two different ways: spectral domain OCT (SD-OCT) and swept-source OCT (SS-OCT), also referred to as optical frequency domain imaging (OFDI) [9–11].

The optical setup of SD-OCT includes a broad bandwidth source for illumination, a fixed reference arm, and a spectrometer for wavelength separation and detection. The spectrometer consists of a dispersive element, such as a diffraction grating, that separates spatially the different spectral components as a function of the wavenumber k which are then detected by a linear detector array, such as a CCD camera [12].

In SS-OCT, spectral separation occurs at illumination, as opposed to detection, by using a swept-source laser that changes linearly its illumination frequency in time. The sweep covers the required broad bandwidth by generating the spectrum in narrow successive frequency steps. Here, the reference arm is also fixed, and the detection system requires a single photodetector since the acquisition is done for different wavelengths as a function of time [11,12].

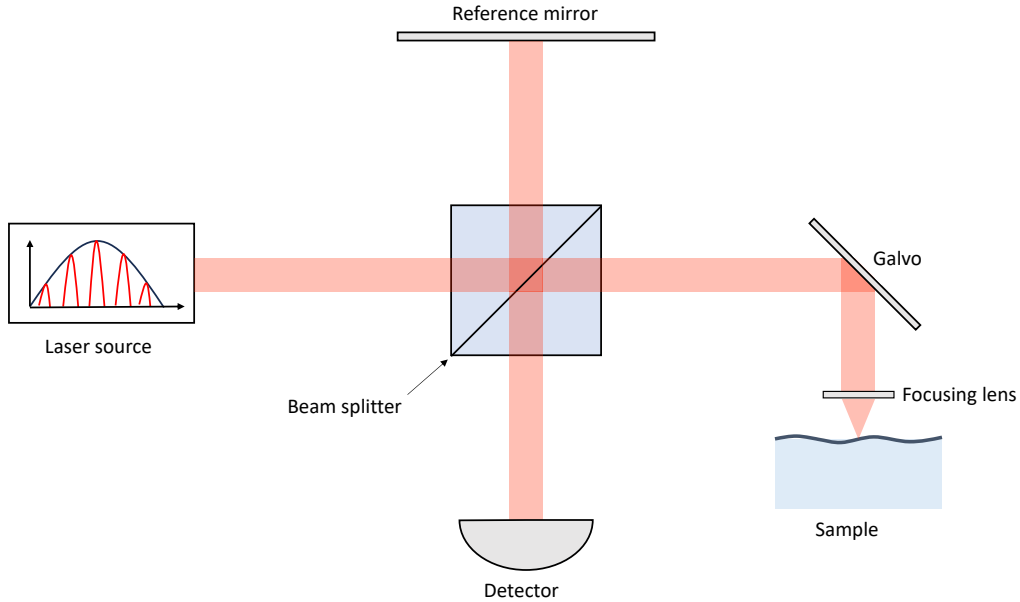


Figure 2.2 Schematic of an SS-OCT system.

FD-OCT offers improved sensitivity over TD-OCT due to the use of high-speed spectrometers and advanced signal processing techniques, which have been investigated theoretically and experimentally in different FD-OCT configurations [13–15]. It is also less susceptible to motion artifacts since it requires fewer moving parts and captures the entire depth profile simultaneously. SNR refers to the ratio of the strength of the signal of interest to the level of noise present in the OCT measurement. A higher SNR indicates a stronger and clearer signal compared to the noise, resulting in better image quality and more accurate measurements.

The increased sensitivity enables the detection of weaker signals, minimizing the impact of noise and leading to a better SNR in an FD-OCT system. Here, all depth profiles are acquired in parallel rather than sequentially enabling a faster acquisition speed and allowing for the capture of more A-lines per second. This increased data acquisition rate allows for more averaging of signals, which helps reduce the impact of noise and improves the SNR [16].

2.1.3 Resolution of SS-OCT

Axial resolution

The axial resolution δz of an OCT system is determined by the used source as axial sectioning is achieved through coherence gating. It depends on the central wavelength λ_0 , the spectral width of the source $\Delta\lambda$, and the refractive index of the medium n and is characterized as [11]:

$$\delta z = \frac{2 \cdot \ln(2)}{\pi} \frac{\lambda_0^2}{n \cdot \Delta\lambda}. \quad (2.1)$$

The depth range in the Fourier-domain z_{max} is limited by the wavelength spacing between pixels of the spectrometer $\delta\lambda$ and given by:

$$z_{max} = \frac{\lambda_0^2}{4n \cdot \delta\lambda}, \quad (2.2)$$

with $\delta\lambda = \Delta\lambda/N$, where N corresponds to the number of wavelength steps [11].

Lateral resolution

Lateral resolution δx is defined by the focusing parameters of the OCT system and is therefore completely independent of its axial resolution. The lateral resolution is equal to the beam width at the focal point. Assuming the input beam is Gaussian, this is given by:

$$\delta x = \frac{4\lambda_0 f}{\pi D}, \quad (2.3)$$

with f as the focal length of the used focusing lens and D as the beam width of the incident beam on the lens [12].

2.1.4 OCT signal construction

OCT is based on the principle of a Michelson interferometer, where the starting point is an incident polychromatic plane wave which can be described mathematically as [2, 3, 12]:

$$E_i = s(\omega, k)e^{i(kz - \omega t)}, \quad (2.4)$$

with $s(k)$ as the amplitude of the electrical field of the initial power spectrum, k as the wavenumber, and ω as the angular frequency. The beamsplitter splits the beam into two arms and the electric field from the reference arm can be described as:

$$E_R = \frac{s(\omega, k)}{2} r_R e^{i(2kz_R - \omega t)}, \quad (2.5)$$

where r_R refers to the reflectivity of the reference mirror and z_R describes the distance between the beamsplitter and the mirror. The factor 2 arises from the round-trip light propagation in the arm. The sample is characterized by the sum of the backscattered waves from the different depths $z_{S,j}$ with their corresponding reflectivity $r_{S,j}$. The electric field from the sample arm is therefore:

$$E_S = \frac{s(\omega, k)}{2} \sum_j r_{S,j} e^{i(2kz_{S,j} - \omega t)}. \quad (2.6)$$

The electrical field incident on the detector can then be expressed as the sum of these two fields from each interferometer arm as:

$$E_{det} = E_R + E_S. \quad (2.7)$$

At the photodetector, the incident light is converted into photocurrent and the detected short-time-averaged light intensity can be described as:

$$I_{det} = \langle |E_{det}|^2 \rangle. \quad (2.8)$$

Substituting Equations 2.5 and 2.6 into Equation 2.8 yields the entire expression of the intensity of the signal measured at the detector $I_{int}(k)$:

$$\begin{aligned}
I_{int}(k) = & \frac{S(k)}{4} \cdot \left[R_R + \sum_j R_{S,j} \right] \text{ (DC)} \\
& + \frac{S(k)}{2} \cdot \left[\sum_j \sqrt{R_R R_{S,j}} \cos 2k(z_{S,j} - z_R) \right] \text{ (Cross-correlation)} \\
& + \frac{S(k)}{4} \cdot \left[\sum_{j \neq k} \sqrt{R_{S,j} R_{S,k}} \cos 2k(z_{S,j} - z_{S,k}) \right] \text{ (Auto-correlation)},
\end{aligned} \tag{2.9}$$

where $S(k) = \langle |s(k, \omega)|^2 \rangle$ is the power spectral density, $R_R = |r_R|^2$ and $R_{S,j} = |r_{S,j}|^2$ describe the intensity reflectivity coefficients, and δz_j is the position of each reflector in the tissue. This consists of a DC component, which depends on $S(k)$ and the reflectances, thereby carrying no depth information, wherefore it can be removed. This is done through background removal and/or balanced detection, as is the case in SS-OCT. Another part is the auto-correlation term resulting from interference between different scatterers in the sample arm. Since the reflectivity of the reference mirror is typically much bigger than that of biological tissue ($R_R \gg R_{S,j}$), this term is also negligible. The valuable part for OCT is the cross-correlation component, which contains depth information about each reflector in the tissue. This part accounts for the interference between the reference and sample fields and generates depth-resolved profiles and structural information. Neglecting the auto-correlation and the DC-terms, the intensity at the detector can be described as:

$$I_{int}(k) = \frac{S(k)}{2} \cdot \left[\sum_j \sqrt{R_R R_{S,j}} \cos(2kz_j) \right], \tag{2.10}$$

with z_j referring to the path length difference $z_{S,j} - z_R$. As the signal is a function of the wavenumber, a depth profile can be obtained by a Fourier transformation of the spectrally resolved interference signal as the spatial space and wavenumber space build a Fourier pair [2, 3, 12]:

$$I(k) \xleftrightarrow{\mathcal{F}} I(z). \tag{2.11}$$

Applying this to Eq. 2.10 leads to:

$$\begin{aligned}
I_{int}(z) &= \mathcal{F}\{I_{int}(k)\} \\
&= \frac{1}{2} \mathcal{F}\{S(k)\} * \mathcal{F}\left\{\sum_j \sqrt{R_R R_{S,j}} \cos(2kz_j)\right\} \\
&= \frac{1}{4} \sum_j \sqrt{R_R R_{S,j}} [\gamma(2z_j) + \gamma(-2z_j)],
\end{aligned} \tag{2.12}$$

with the coherence envelope $\gamma(z_j)$ as the inverse Fourier transform of the normalized spectrum $S(k)$ [2,3,12,17]. As can be seen, the Fourier transform of the real-valued signal $I_{int}(k)$ has an ambiguity between positive and negative frequencies, leading to a symmetry to the zero-delay plane. From the spectral interferogram, it is not possible to distinguish if a reflector is before or after the reference plane. The duplicated information is also referred to as the mirror artifact and is usually not used [2,3,12]. The algorithm used for generating OCT A-lines from the simulator outputs is based on Equations 2.5-2.12 and described in the article in Section 4.

2.2 Beam characteristics

Gaussian beams are typically used to model the illumination beam from lasers or light propagation through lenses and optical systems, as in an OCT setup [3,18]. When modeling light-tissue interactions, the illumination beam is often described as a pencil beam for simplicity, though the actual behavior of light propagation in imaging systems needs to be considered to ensure accuracy [19,20].

2.2.1 Beam propagation

Figure 2.3 illustrates the propagation of such Gaussian beams. Here, D describes the initial beam diameter at the imaging lens of focal length f . In the direction of light propagation, Gaussian beams converge and diverge from the position of minimal beam diameter, the beam waist w_0 . The beam waist w_0 is defined as:

$$w_0 = \frac{2\lambda f}{\pi D}. \tag{2.13}$$

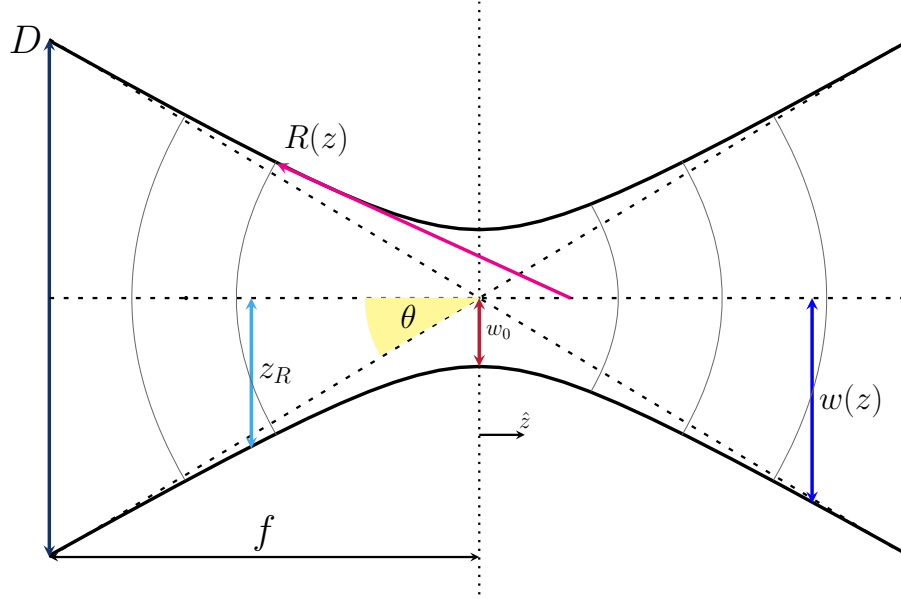


Figure 2.3 Parameters used to describe the Gaussian beam propagation.

The Rayleigh length z_R determines the range in the z direction over which the beam propagates without diverging significantly and defined as:

$$z_R = \frac{\pi w_0^2}{\lambda}. \quad (2.14)$$

With these, the beam radius along the z -axis can be described as:

$$w(z) = w_0 \sqrt{1 + \left(\frac{z}{z_R}\right)^2}, \quad (2.15)$$

where $z = 0$ corresponds to the beam waist position. The radius of curvature $R(z)$ of the wavefronts progresses according to:

$$R(z) = z \left(1 + \left(\frac{z_R}{z}\right)^2 \right). \quad (2.16)$$

For z values much larger than z_R , the beam radius evolves in a nearly linear fashion, and the beam divergence is given by the beam divergence angle θ as:

$$\theta = \frac{\lambda}{\pi w_0}. \quad (2.17)$$

The divergence of the beam far from the waist increases with a smaller beam waist and longer wavelength.

2.2.2 Beam source

The illumination beam of an OCT system is usually assumed to have a Gaussian profile [3,18]. It is defined in the perpendicular plane to the direction of light propagation and centered on the line of maximum beam intensity following an ideal Gaussian distribution. The amplitude of the complex electric field is given as a function of $r = \sqrt{x^2 + y^2}$ as:

$$E(r, z) = E_0 \frac{w_0}{w(z)} \exp \left[-\frac{r^2}{w(z)^2} \right] \exp \left[i \left(kz + k \frac{r^2}{2R(z)} - \xi(z) \right) \right], \quad (2.18)$$

with $\xi(z) = \arctan(z/z_0)$ referring to the Gouy phase shift. The corresponding intensity distribution at any given plane perpendicular to the direction of light propagation is a scaled version of a Gaussian distribution centered on the propagation axis and can be described as:

$$I(r, z) = I_0 \frac{w_0}{w(z)} \exp \left[-\frac{2r^2}{w(z)^2} \right]. \quad (2.19)$$

2.3 Modeling light-tissue interaction

Modeling light-tissue interaction is essential in simulating how an OCT signal is generated. For that, tissue can be parameterized in many ways, such as by the scattering and absorption cross-sections or the distribution of scatterer sizes when considering a sample with multiple types of particles in them [21]. Here, we use the approach of characterizing the tissue with its optical coefficients, i.e., the scattering coefficient μ_s , the absorption coefficient μ_a , the refractive index n , and the anisotropy coefficient g [19]. There exist a variety of ways of modeling the interactions of photons with matter as they propagate through biological tissue, which are presented in the following section.

2.3.1 Beer-Lambert Equation

The probability of absorption and scattering is described by the wavelength-dependent coefficients μ_a and μ_s and increases exponentially with the distance traveled in the tissue. The simplest method to model this light-tissue interaction is given by the Beer-Lambert equation as:

$$I(d) = I_0 \cdot e^{-\mu_t \cdot d}. \quad (2.20)$$

Here, $I(d)$ is the intensity of transmitted light, d denotes the ballistic path length in the scattering medium, $\mu_t = \mu_a + \mu_s$ represents the attenuation coefficient, and I_0 the initial intensity of the incident light [3,22]. In OCT, the signal amplitude in a homogeneous turbid medium can be modelled as a single exponential decay function as given by Beer's law [23–25]. Then, the signal intensity is given by:

$$I(z) = I_0 \cdot e^{-2\mu_t \cdot z}, \quad (2.21)$$

with the factor of 2 to account for the round-trip attenuation of the photon due to the backscattering and $z = 0$ referring to the sample interface. This also referred to as the single scattering model and works under the assumption that the detected backscattered light underwent only one scattering event in the sample. Furthermore, absorption, noise, and additional scattering interactions with the sample are neglected.

2.3.2 Fresnel equation

When photons encounter any interface where there is a change of refractive index, for example, light traveling through air incident on biological tissue, a part of the photons is reflected and a part is transmitted (refracted) at the surface [2,3]. The proportions of reflected and transmitted light are described with Fresnel coefficients. The Fresnel formulas are a function of the angle of incidence, the polarization of the incident light, and the two indices of refraction of each medium. The ratios of reflected and transmitted light are given by the reflectance R and the transmittance T . The transmitted part of the light beam is refracted at the boundary surface according to Snell's law:

$$\frac{\sin \theta_i}{\sin \theta_t} = \frac{n_2}{n_1}. \quad (2.22)$$

Figure 2.4 shows the principle of Snell's law, also referred to as the law of refraction. The fraction of light reflected $R(\theta_i)$ can then be calculated as the average of the reflectances for the two orthogonal polarization directions of the incident light and described as:

$$R(\theta_i) = \frac{1}{2} \left[\frac{\sin^2(\theta_i - \theta_t)}{\sin^2(\theta_i + \theta_t)} + \frac{\tan^2(\theta_i - \theta_t)}{\tan^2(\theta_i + \theta_t)} \right]. \quad (2.23)$$

The total fraction of light reflected and transmitted must total to 1 due to energy conservation, which gives a transmittance $T(\theta_i)$ of:

$$T(\theta_i) = 1 - R(\theta_i). \quad (2.24)$$

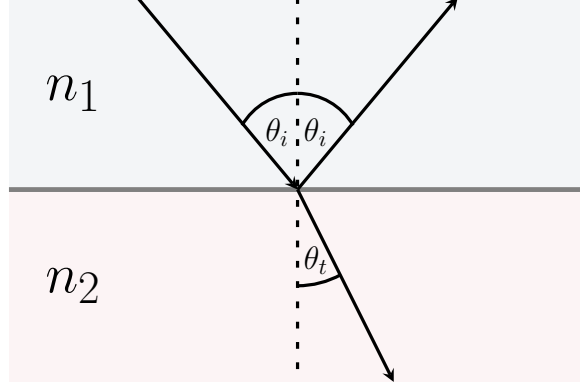


Figure 2.4 The law of refraction.

The photons then can undergo events of scattering and absorption after their reflection or transmittance [2].

2.3.3 Radiative Transfer Equation

In inhomogeneous media, such as biological tissue, the radiative transfer equation (RTE) has been established as an accurate method for analytically modeling photon transport [2, 3]. The RTE describes the transport of radiant energy (light) through a medium accounting for processes like absorption, emission, and scattering. It provides a mathematical framework to model the variation of this power as light interacts with the medium. The RTE is an integro-differential equation consisting of four contributions and the variation can be expressed as:

$$\begin{aligned}
 \frac{dL(\vec{r}, \hat{s}, t)}{dt} \frac{1}{v} &= \pm \hat{s} \cdot \nabla L(\vec{r}, \hat{s}, t) && \text{(Beam convergence/divergence)} \\
 &- \mu_t L(\vec{r}, \hat{s}, t) && \text{(Photon extinction)} \\
 &+ \mu_s \int_{4\pi} L(\vec{r}, \hat{s}', t) \phi(\hat{s}' \cdot \hat{s}) d\Omega' && \text{(Gains from scattering)} \\
 &+ S(\vec{r}, \hat{s}, t) && \text{(Source).}
 \end{aligned} \tag{2.25}$$

The first part accounts for the contribution from the beam and is positive for divergence and negative for convergence. Photons can be absorbed along their path or scattered out of the volume resulting in a loss of radiant power through extinction, which leads to the second part of the equation. Also, photons can be scattered from other locations into the volume, leading to a gain of power which is mathematically expressed in the third term. The last term, source term, represents the contributions within the medium from external sources of radiation, such as the tip of an optical fiber for example. In order to compute the attenuation coefficient of tissue μ_t , one needs to solve this equation, which is difficult

since it has six independent variables, namely x, y, z, θ, ϕ and t . Exact analytical solutions of the RTE are currently only known for simple scenarios, such as no scattering. In more complex cases, numerical methods must be employed to obtain solutions. A known approach to numerically solving the RTE is using the Monte Carlo method [2, 3].

2.4 Monte Carlo Simulation

Monte Carlo simulations of photon transport can be used to predict photon behavior in a scattering medium and will be explained in more detail in this Chapter.

2.4.1 Standard Monte Carlo algorithm

Monte Carlo simulation of light transport in multilayered media (MCML) was the first simulator based on the Monte Carlo method and was introduced by Wang et al. in 1995 [20]. Here, the simulation geometry is represented as a multilayered structure defined by the number of layers, the thickness, and the optical properties of each layer which is the most common and simple approach. Figure 2.5 shows the algorithm used in a standard Monte Carlo simulation simplified from [20].

A simulation starts with the launch of a photon packet at a position (x, y, z) into a medium that is defined by the following parameters: index of refraction n , absorption coefficient μ_a , scattering coefficient μ_s , and anisotropy coefficient g . Thereby, each photon packet has an initial weight equal to unity, i.e., $W = 1$, that represents the packet intensity and decreases due to absorption events. After launching, the photon packet travels a free path to its first site of interaction, i.e., absorption or scattering events. Thereby, this propagating distance s is determined by:

$$s_1 = \frac{\ln(\xi)}{\mu_a + \mu_s}, \quad (2.26)$$

with ξ as a random generated number in the range between $[0, 1]$ using the inverse transform sampling method [2, 20]. The propagation direction is given by (μ_x, μ_y, μ_z) and used to propagate the photon packet over the distance s_1 . In a typical simulator, the photon packets are launched at the tissue surface with an initial propagation direction, generally orthogonal into the sample, i.e., $(\mu_x, \mu_y, \mu_z) = (0, 0, 1)$. At the site of an absorption interaction, W gets updated according to $W \leftarrow W - \Delta W$, where $\Delta W = W \cdot (1 - \exp(-\mu_a \cdot s_1))$. When the fluence is tracked, the absorbed weight is added to the fluence map to account for the deposition of energy as $F(x, y, z) = F(x, y, z) + \Delta W$. In the case of a scattering interaction, the diffusion direction is to be calculated from the azimuthal angle ϕ and the deflection angle θ_s . ϕ is uniformly distributed in the range $[0, 2\pi]$ by $\phi = 2\pi\xi$, whereas θ_s depends on the

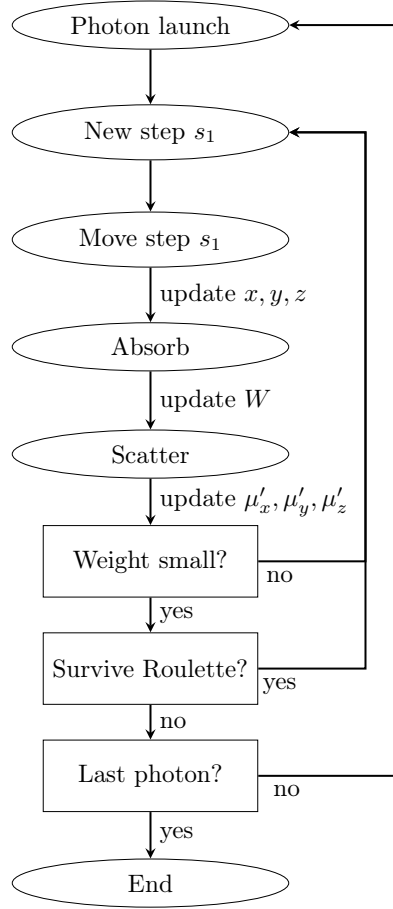


Figure 2.5 Flowchart describing the standard Monte Carlo algorithm.

optical properties of the scattering medium and is modeled by the Henyey-Greenstein (HG) probability density function f_{HG} [26]:

$$f_{HG}(\cos \theta_s) = \frac{1 - g^2}{2(1 + g^2 - 2g \cos \theta_s)^{\frac{3}{2}}}. \quad (2.27)$$

Using the inverse transform sampling method, one can compute θ_s , the angle between the photon packet propagation direction prior to the scattering (μ_x, μ_y, μ_z) and after the scattering (μ'_x, μ'_y, μ'_z) from the distribution as:

$$\cos \theta = \begin{cases} \frac{1}{2g} \left\{ 1 + g^2 - \left[\frac{1-g^2}{1-g+2g\xi} \right]^2 \right\} & \text{if } g > 0 \\ 2\xi - 1 & \text{if } g = 0 \end{cases} \quad (2.28)$$

When W is below a predetermined critical threshold, a termination process is initialized. During this roulette process, the photon packet is associated with a probability to continue to be simulated, otherwise, the sequence is terminated for this particular photon packet, and W is zeroed. The simulation ends upon the launch of all photon packets. This was described and validated in the MCML engine where an ensemble of photon packets are launched as a pencil beam, perpendicular to the surface medium into a multilayered medium with a simulation geometry that is cylindrically symmetric around the z -axis [20].

2.4.2 Modifications

MCML forms the foundation of a variety of other simulators that have been developed in the past years. Typical modifications are defining the simulation geometry in other ways, optimizing the code to enhance computational efficiency, and changing the interaction of the photon with the medium to accommodate the simulated optical imaging techniques.

Modeling simulation medium

The layered structured geometry has been used to simulate the effect of the cerebrospinal fluid increase on diffuse reflected photons, where the brain was modeled as five parallel layers [27]. Another organ, which is often modeled with a layered structure is the skin. Here, the skin was represented as a seven-layered medium in order to study the effectiveness of optical clearing agents to enhance light penetration in the tissue [28].

The first efforts to model more complex media were made by Pfefer et al., where the tissue geometry was represented as a 3D matrix of voxels, where each voxel is assigned to the corresponding optical properties and photon packets are tracked from voxel to voxel [29]. This geometry has been used to simulate light propagation in various biological media, such as skin or the human brain [29,30]. The 3D voxel system was also implemented with the standard MC algorithm and is available as *mcxyz* and is the base of our developed simulator [31]. This approach is more flexible than the layered model since each voxel can be assigned with different optical properties, though it is difficult to incorporate precise boundary information. In order to achieve higher accuracy, for example to model regions with curved boundaries, a finer voxel system is needed, which leads to more memory needed and extensive computation.

Mesh-based geometry was proposed to model irregular-shaped media with higher accuracy, where the mesh elements are assigned the optical properties of the medium, similar to the voxel system. One proposed method was modeling the surface of homogeneous regions inside

turbid media by a triangular surface mesh [32,33]. This can be used to achieve high accuracy between domains, however, it cannot model media with continuously varying optical properties in the lateral direction. Furthermore, determining the ray-surface intersection leads to a high computational cost for this method. To overcome this limitation, tetrahedron-based mesh MC was proposed [34,35]. As tetrahedrons are convex volumes, by using this geometry, one can model domains with smooth, curved boundaries, continuously varying random media, and meshes with complex types accurately and efficiently. Known MC simulators exploiting this geometry model are TIM-OS, MMC, and OCT-MPS [34–36].

Light illumination in MC

In a traditional MC approach, a simple point source light illumination is used, which is unrealistic since most light sources emit Gaussian beams, which are described in detail in Section 2.2. The most known way of modeling the focusing is the so-called *geometric-focus* method [37]. Here, the initial transverse photon position is computed according to the Gaussian intensity distribution as described in Section 2.2.2 and the photon packet is then propagated towards the geometrical focus of the beam, as illustrated by the dashed lines in Figure 2.3. This method is also implemented in our simulator and can be chosen upon simulation start. Another approach is the so-called *spot-focus* method [37]. The initial photon position is sampled as in the geometric-focus approach, though the photon packets are then propagated toward a random position within an area in the focal plane of the beam.

Convolution was also proposed for MC simulation of finite beam light propagation [38]. Simulation results of an infinitely narrow photon beam are convoluted with a finite-size input beam of a Gaussian shape. Here, the system is assumed to be linear and shift invariant, as is it the case for OCT imaging of a simple planar layered medium. In these methods, all launched photon packets are focused towards a point in the medium, thereby ignoring the diffraction of photons and not considering the wave nature of photons. Since the beam focus plays an important role in OCT signal intensity and resolution, the performance of the MC technique to simulate OCT signals may be improved by considering this.

In order to overcome this limitation, two different approaches of focusing the photon packets during their launch towards a diffraction-limited focal spot were proposed [39–41]. One is exploiting a hyperboloid of one sheet, a double-ruled surface that can be described by straight lines and is given by [42]:

$$\frac{x^2}{a^2} + \frac{y^2}{b^2} - \frac{z^2}{c^2} = 1, \quad (2.29)$$

with a, b, c as numerical constants that affect how much the hyperboloid stretches in the x, y, z -directions. From Eq. 2.15, one can rewrite the beam radius along the z -axis $w(z)$ in the form of a hyperboloid of one sheet using $w(z)^2 = r^2 = x^2 + y^2$ as:

$$\frac{x^2 + y^2}{w_0^2} - \frac{z^2}{z_R^2} = 1. \quad (2.30)$$

These straight lines can then be used for photon packet propagation and ensure beam focusing at a spot with the radius w_0 . This approach was added as an additional feature to the Monte Carlo eXtreme (MCX) simulator in October 2021 and constitutes the numerical validation of our simulator [41, 43, 44]. In the second approach, photon packets are propagated along the curved trajectories predicted by Gaussian optics as described in Section 2.2.1 [39, 40]. This method for simulating focusing geometries was adopted in an MC simulator considering a more general setup of focusing lens distance and the refractive index of the medium [45]. In both cases, the trajectories are approximated by solving the equation of motion after each time step. This is similar to the Gaussian beam focusing method that we developed in our simulator. In our simulator, the photon packet propagates along the curved trajectory with a predefined step size s_{min} , ensuring accuracy and eliminating the necessity to solve an equation of motion. This used method is described in more detail in Chapter 4.

Photon detection in MC

In order to use the MC method for simulating imaging techniques that depend on detecting the photons, detection setups were incorporated in MC modeling [46]. The used fiber optic probes can be divided in two groups: the same fiber is used for illumination and detection or separate fibers are used. For simulating OCT imaging, the first option is commonly used [36, 45–47]. The simulated fibers are associated with a fiber radius, an acceptance angle, and a distance to the fiber center of the neighboring fiber. In order to detect a photon packet, it needs to be exiting within the area defined by the radius of the detecting fiber and the exiting direction of the photon packet needs to be within the acceptance angle of the detecting fiber [46]. When multiple source/detector pairs are simulated, it is to verify if the photon packet is getting detected at the same position of its source [36]. In our work, we employed an optical illumination and detection configuration by using the same fiber probe and varied its lateral position to simulate multiple OCT A-lines.

Acceleration of the MC simulation

The stochastic nature of MC simulations makes it computationally quite intensive to achieve results with desirable accuracy. Furthermore, the standard MC code is written in ANSI standard C and runs on a single-threaded central processing unit (CPU), making such simulation time-consuming since only one photon packet can be launched and tracked at a time. One proposed method to accelerate the speed and improve computational efficiency is parallel computing the propagation by using a graphics processing unit (GPU) [48]. The most known GPU-based MC simulator for simulating photon transport in 3D media is MCX, which utilizes a 3D volumetric voxel system [41, 43, 44]. For MC codes, which run on a CPU, one proposed method to reduce computation time is the method of importance sampling, which is used in our simulator and explained more in detail in the following Section 2.4.2.

Importance Sampling

Importance sampling is a probabilistic method that can be used to accelerate a Monte Carlo simulation by biasing certain random events, thereby increasing the probability of events of interest and computational efficiency. Most biological tissue has an anisotropy of close to 1 at the clinically applied wavelength of OCT, making the photon packets more prone to scatter in a forward direction. Thus, imaging techniques that rely on backscattered photons, like OCT, detect scarcely any of the emitted photons causing photon detection to become a rare event. To increase this probability of detecting backscattered photon packets, the method of importance sampling can be applied to the MC algorithm. Lima et al. applied this method combined with photon splitting for simulating TD-OCT signals [49, 50]. In this method, an updated biased scattering function f_B based on the HG probability density function f_{HG} was introduced:

$$f_B(\cos \theta_B) = \left(1 - \frac{1-a}{\sqrt{a^2+1}}\right)^{-1} \frac{a(1-a)}{(1+a^2-2a \cos \theta_B)^{3/2}} \quad (2.31)$$

with a as the bias coefficient ranging between 0 and 1. The biased scattering angle $\cos \theta_B$ is computed using the function:

$$\cos \theta_{B,i} = \frac{1}{2a} \left\{ a^2 + 1 - \left[\xi_i + \left(\frac{1}{1-a} - \frac{1}{\sqrt{a^2+1}} \right) + \frac{1}{\sqrt{a^2+1}} \right]^{-2} \right\}, \quad (2.32)$$

with ξ_i as a generated random number in the range $[0,1]$. Using this function, the photon packet propagation direction after a scattering event $\hat{v}$ is biased towards the detector position, i.e. the collecting fiber system, if the photon packet direction was away from the probe, i.e., $\mu_z > 0$, as illustrated in Figure 2.6 (a). This creates a bias, which is corrected by introducing

a corresponding likelihood ratio L that is tracked with each scattering event as

$$L(\cos \theta_B) = \frac{f_{HG}(\cos \theta_s)}{f_B(\cos \theta_B)}, \quad (2.33)$$

expressing the probability of observing the biased scattering angle in an unbiased simulation. Additional scattering events can be applied once the photon packet undergoes a first biased scattering event. These can be unbiased or biased, wherefore for each scattering, a corresponding probability value of p and $1 - p$ are exploited respectively, which leads to the following likelihood function for additional scattering:

$$L(\cos \theta_B) = \frac{f_{HG}(\cos \theta_s)}{p * f_B(\cos \theta_B) + (1 - p) * f_{HG}(\cos \theta_s)}. \quad (2.34)$$

Forward-scattered photon packets can contribute toward the OCT signal by undergoing additional backscattering events. To consider this, the method of photon splitting was additionally applied [49]. In order to track forward scattered photons, photon packets are split at each scattering event into two halves, each half according to f_B and f_{HG} , respectively. To ensure no systematic statistical bias, each half is assigned a respective likelihood ratio. The half backscattered according to f_B is assigned the likelihood ratio L as previously described and the forward propagating split photon packet is assigned the complement likelihood ratio $L' = 1 - L$. Figure 2.6 (b) shows the different scattering and propagation directions of the photon halves after their split. The total likelihood of a photon is the product of all its assigned likelihood values from the scattering events it underwent to compensate for the weight of the photon packet. The used variables are explained in Table 2.1.

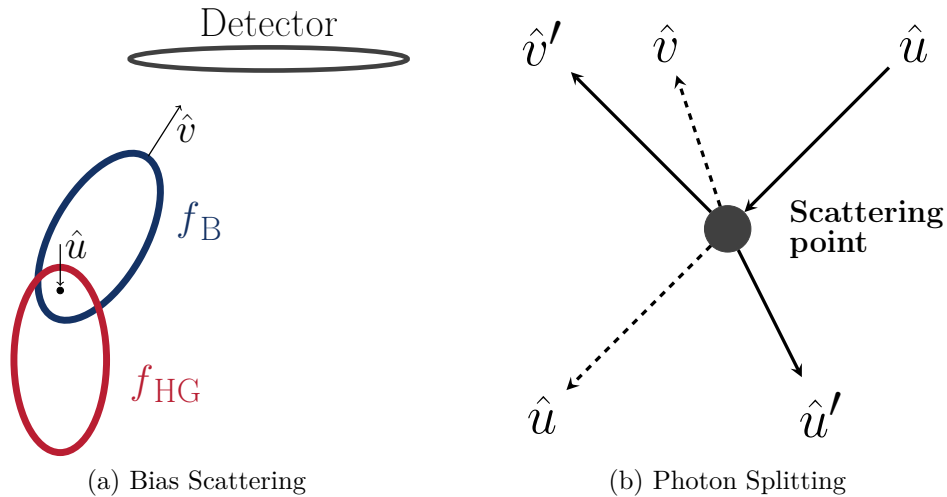


Figure 2.6 Importance sampling method to increase the probability of photon detection.

Table 2.1 Variables used in Figure 2.6

Variables	Description
$\hat{u}$	Previous propagation direction
$\hat{u}'$	Split photon scattered direction
$\hat{v}$	Bias scattering direction
$\hat{v}'$	Photon bias scattered direction

2.4.3 OCT simulators

In the past years, some groups applied the Monte Carlo method to simulate TD-OCT as well as FD-OCT signals, which are presented in this section.

The first Monte Carlo simulator for TD-OCT was based on MCML and developed by Yao and Wang [46]. They introduced a division of the OCT signal into two parts, namely Class I and Class II photons. Class I photons are the photon packets that are backscattered and detected from the target layer of the medium and are the ones that contain the local optical information. Class II photons are backscattered photons from the rest of the medium above the target layer, thereby ensuring that the path-length difference between the detected photon packets and the reference light is within the coherence length of the simulated system. These were assumed to contribute to the noise in the OCT signal as it does not furnish any local information about the target layer. For light illumination and detection, a fiber probe that emits a pencil beam was assumed. Lima et al. introduced a TD-OCT simulator with their importance sampling method based on the one from Yao and Wang [46]. Here, the optical fiber also emitted a pencil beam toward the multilayered medium. The developed method is explained in detail in Section 2.4.2 and reduces the computation time of obtaining Class I and Class II diffuse reflectances by two orders of magnitude. Importance sampling was validated by comparing the diffuse reflectances as a function of the depth to the previous simulator [49, 50]. As these previous simulators are based on MCML and restricted to multilayered media, a 2D TD-OCT simulator was proposed that used a non-planar multilayered model, such as a skin model with its curved shape. The shape of the boundaries and the thickness of the layers in the medium are characterized by mathematical equations rather than by the simulation geometry [51]. In the past years, two MC-based simulators for TD-OCT were published open-source as opposed to the previously described one, namely MCEO-OCT and OCT-MPS [36, 47]. MCEO-OCT is an MC simulator for multi-layered tissue based on MCML and written in C [47]. Objects, such as spheres, cylinders, ellipsoids, and cuboids can be embedded in the tissue structure and improved importance sampling

was incorporated for faster speed. Photon-boundary interaction of these objects was checked by ray-plane equations, eliminating the need for complex mesh-based geometry [52]. As the photons are classified with regard to their path lengths, the simulation needs to be done for each probing/target depth to compute an A-line. The incident light source emits a pencil beam and the simulator was validated by comparing the simulated Class I and II reflectances to previous simulators. OCT-MPS is based on TIM-OS [35] and it is the only TD-OCT simulator that is implemented on GPU [36]. Here, the tissue geometry is represented as a tetrahedron mesh enabling the modeling of arbitrary shapes of the desired accuracy as described in Section 2.4.2. Importance sampling, which was developed by this group, is also included in their algorithm, making this simulator considerably faster than any other. The light source is also assumed to emit a pencil beam and the simulator is validated by comparison of the diffuse reflectance from a multilayered medium to the previous simulators of Lima et al. and Yao and Wang [46, 49].

To the best of our knowledge, two groups applied the MC method to simulate FD-OCT signals, which are both not available open-source. When simulating FD-OCT signals, the detected photon packets do not need to be differentiated based on their maximum depth reached since the difference is at the detector side as described in Section 2.1.2. The first simulator uses a 3D voxel geometry to represent the medium with an incident pencil beam and was developed for image generation of angiographic OCT [53]. It is proposed to model the photon detector as a wavenumber-resolved detector array where each detector corresponds to a wavenumber depending on the simulated wavelength range. This generates depth-resolved fringes, which can be inverse Fourier transformed in order to reconstruct an A-line. The algorithm was first validated by comparing the absorption distribution in a two-layered medium to MCML. Then, the appearance and signal statistics of the simulated image were compared to in vivo acquired angiographic ones. In the other simulator, a layered tissue geometry is used and the incident light beam is assumed to have a Gaussian shape [45]. Their implementation of the Gaussian beam is described in Section 2.4.2. Coherence gating methods as in FD-OCT are then used to generate wavenumber-dependent fringe signals in which the optical photon paths are encoded, as proposed by Hartinger et al. [53]. This simulator was validated by comparing the MC-generated OCT A-lines to an analytical OCT model. It is to note that each simulator has its respective advantages, however, there is not an FD-OCT simulator that considers the illumination beam as a Gaussian beam, allows a more complex tissue geometry, and reconstructs A-lines. Our developed MC simulator for FD-OCT considers these aspects and we included importance sampling for faster computation. Furthermore, the different iterations of MC codes have been validated by comparison to previously vali-

dated simulators or using numerical methods such as RTE. We validated our simulator by comparing the fluence rates to other validated simulators. We furthermore created tissue-mimicking optical phantoms and imaged these with an OCT system to compare the obtained signals to the simulated ones. These results are presented in Section 4.

2.5 Optical Phantoms

Optical phantoms are designed to replicate the optical and structural properties of a range of tissues and are frequently employed in the field of imaging for testing and validating systems and theoretical models. While there are commercially available optical phantoms, there are none that are fully characterized in the near-infrared (NIR) range in which OCT operates [54]. Therefore, it is common for researchers and institutions to fabricate custom phantoms in-house to meet their specific needs.

2.5.1 Phantom materials

Several parameters influence the optical phantom design, such as the phantom matrix material, the scattering and absorbing agents, and the phantom thickness. An optical phantom can be fabricated using a variety of materials for its matrix, such as elastomers, resins, biological components, and gelatinous substances [55]. This component determines primarily the refractive index n of the phantom. Each material possesses its own set of advantages and disadvantages and can be used depending on what is needed. Polydimethylsiloxane (PDMS) is a silicone elastomer that is commonly used for fabricating tissue-simulating phantoms due to several advantageous properties it possesses. These include its processability, durability, flexibility, and the ability to selectively modify its optical, mechanical, and thermal properties [56]. Furthermore, as most biological tissues have a refractive index between 1.35 and 1.52 at the wavelength of 1310 nm, PDMS allows a good representation with its refractive index of around 1.4 [57,58]. The scattering coefficient of the phantom is determined by the scattering agent, which can be inter alia titanium dioxide, barium sulfate, and silica microspheres [59]. The most common choice for the scattering agent when fabricating tissue-mimicking phantoms is titanium dioxide powder due to its wide availability as the main pigment in common white paint [60]. The absorbing agent modifies the absorption coefficient of the phantom. Some widely used absorbing agents are nigrosine and India ink due to their ready availability and inexpensive nature [55,56]. Depending on the mimicked scattering and absorption coefficients, the agents' concentration needs to be adapted. In this work, PDMS was chosen for the matrix, titanium dioxide as the scattering agent, and nigrosine as the absorbing agent.

2.5.2 Phantom characterization

In order to use phantoms, their optical properties, such as absorption and scattering coefficients, anisotropy, and refractive index need to be determined. There are various measuring techniques, such as OCT as well as inverse methods, each of them possessing its advantages and drawbacks [21]. In this work, the inverse adding-doubling (IAD) method was chosen to solve the inverse problem of finding the optical parameters. IAD is a computational technique used in tissue optics to estimate the absorption and scattering coefficients of tissues based on experimental measurements of reflectance and transmittance [61–63]. The IAD method employs an iterative process where initial estimates of the optical properties are refined until the calculated reflectance and transmittance closely match the measured values. The method involves solving a set of nonlinear equations that link the optical properties to the light transport equation. During each iteration, the optical properties are updated based on the mismatch between the calculated and measured reflectance and transmittance. This process continues until a satisfactory match is achieved, indicating that the estimated optical properties accurately represent the tissue’s behavior, in this case, the behavior of the optical phantoms. It accounts for multiple scattering effects by iteratively adding and doubling the layers within the tissue model allowing a more accurate estimation of the scattering and absorption coefficients. As the anisotropy is not known, this method was used to determine the reduced scattering coefficient $\mu'_s = \mu_s \cdot (1 - g)$, instead of the scattering coefficient μ_s [62,63]. The program based on this technique is available open-source and was used in our work [64]. To determine the refractive index of a homogeneous slab, an OCT system can be used employing the so-called optical path length matching technique [65]. By comparing the optical path length of the slab to that of a reference sample with a known refractive index, the refractive index of the slab can be determined. This is achieved by analyzing the interference patterns generated by the backscattered or reflected light from both the slab and the reference sample, providing an accurate measurement of the refractive index. This is our used approach since the phantoms needed to be characterized at the wavelength of OCT imaging for the project.

CHAPTER 3 INITIAL WORK

This chapter is dedicated to the work that led to the findings presented in Chapter 4. We first implemented a detection system for photon packets and developed an algorithm to convert the data of the detected photons into OCT signals and verified the OCT signal reconstruction algorithm using a specular target. Additionally, we incorporated Gaussian beam focusing and compared the flux and intensity distributions to the underlying mathematical model. The impact of the refractive index of the medium was also assessed by the fluence. For faster speed, we introduced the method of importance sampling and checked its impact. Optical phantoms were developed and their optical properties were estimated. Finally, we estimated the anisotropy coefficients of the optical phantoms using the single scattering model.

3.1 Validation of OCT signal reconstruction algorithm

As our goal is to reconstruct OCT signals from the simulator output, we first validated our OCT signal reconstruction algorithm. To do so, we generated simulated OCT images of a simple tissue structure with a homogeneous non-scattering background and a reflector at $z=0.5$ mm in the tissue. The tissue was described as a slab of $1 \times 1 \times 2$ mm³. The optical properties of the tissue were set at $n = 1$ and $\mu_a = 20$ cm⁻¹. An amount of 500 source and detector setups were used to describe the OCT system, thereby mimicking the formation of 500 A-lines, and the photon packets were launched in a pencil beam. As most photons reach the reflector, the total photon pathlength TP of the detected photons is twice the reflector position inside the tissue z_S due to the round-trip. This equals to $TP = 2 \cdot z_S = 1$ mm, which can be observed in Fig. 3.1 (a). The algorithm for reconstructing the OCT signals from the simulator output is described in the article in Section 4 more in detail. Interfering the sample arm signal with the reference arm leads to the interference spectrum as a function of wavelength shown in Fig. 3.1 (b). FD-OCT systems lack the ability to differentiate between a reflector positioned before or after the reference plane in the axial plane. Consequently, when Fourier-transforming the raw signal, two symmetrical peaks emerge on both sides of the zero-delay plane, corresponding to the axial location of the reflector. This is shown in Fig. 3.1 (c). Removing the mirror artifact and averaging over the generated A-lines of all 500 source/detector pairs leads to the OCT A-line as a function of depth as shown in Fig. 3.1 (d). Figure 3.2 shows the reconstructed OCT B-Scan consisting of these 500 A-lines, where we can clearly observe a reflective at the position $z = 0.5$ mm. The algorithm is explained more in detail in the article in Chapter 4.

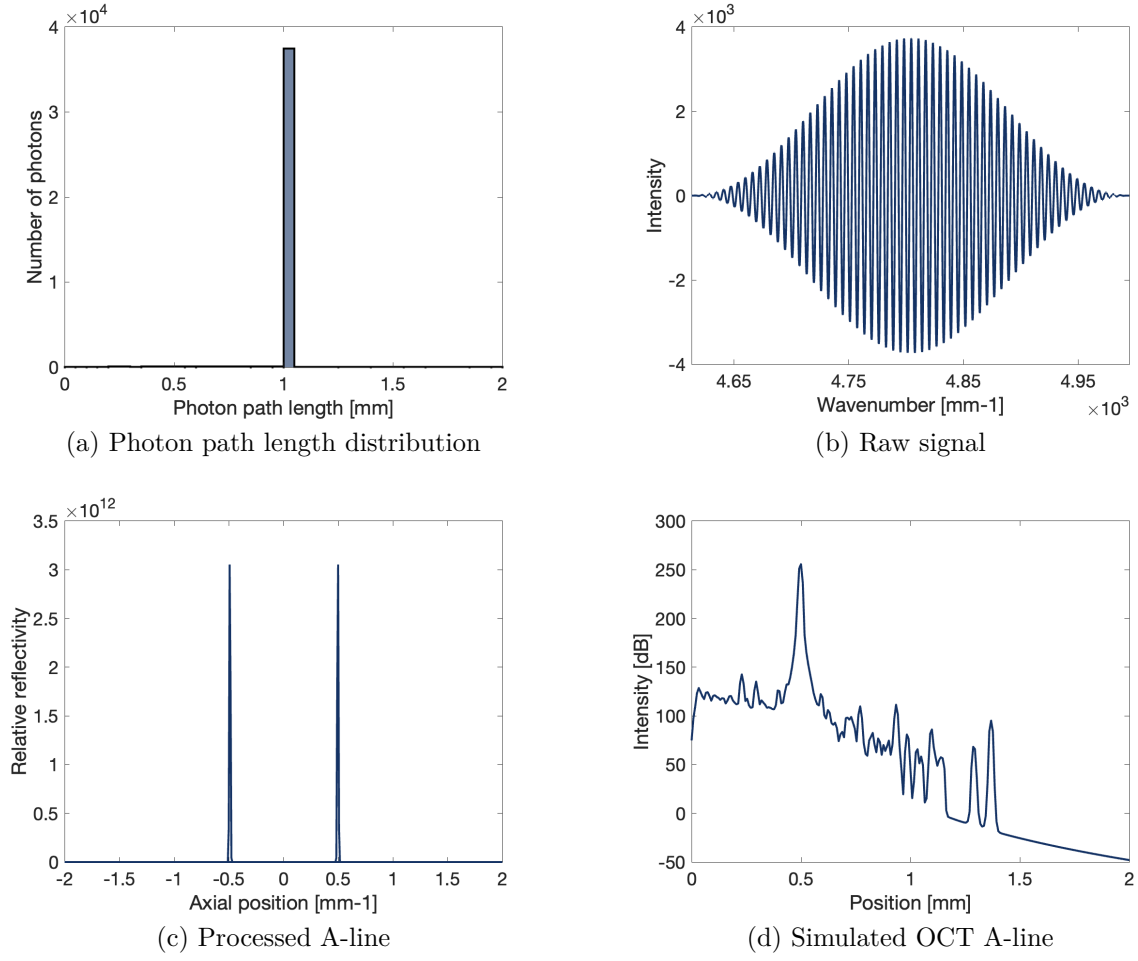


Figure 3.1 Example of the FD-OCT signal at the different stages of reconstruction

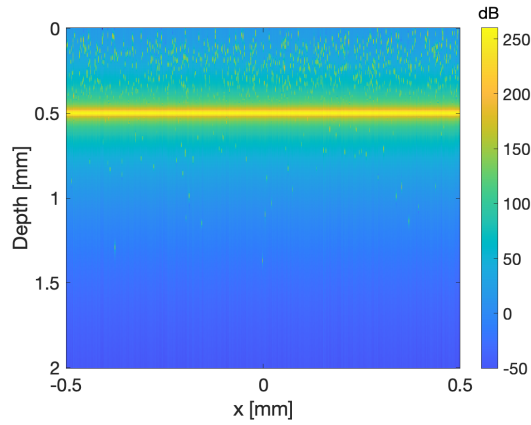


Figure 3.2 Simulated OCT B-Scan.

3.2 Validation of Gaussian beam

We then validated the implemented Gaussian beam-focusing algorithm for modeling the laser source. By matching the fluence with the theory, we wanted to ascertain the accuracy of the MCOCT code. In our simulator, the lens can be positioned at a distance $z_{f,I}$ from the surface of the medium, leading the focus point of the lens to be at a depth z_f . For the validation, the refractive index of the medium was set to unity with a scattering coefficient of zero. A focusing lens of the length $f = 1.5$ mm was positioned $z_{f,I} = 0.5$ mm above the tissue surface, i.e., the beam focuses at a position $z_f = 1$ mm inside the tissue. The beam width at the imaging lens was set to $D = 0.1$ cm.

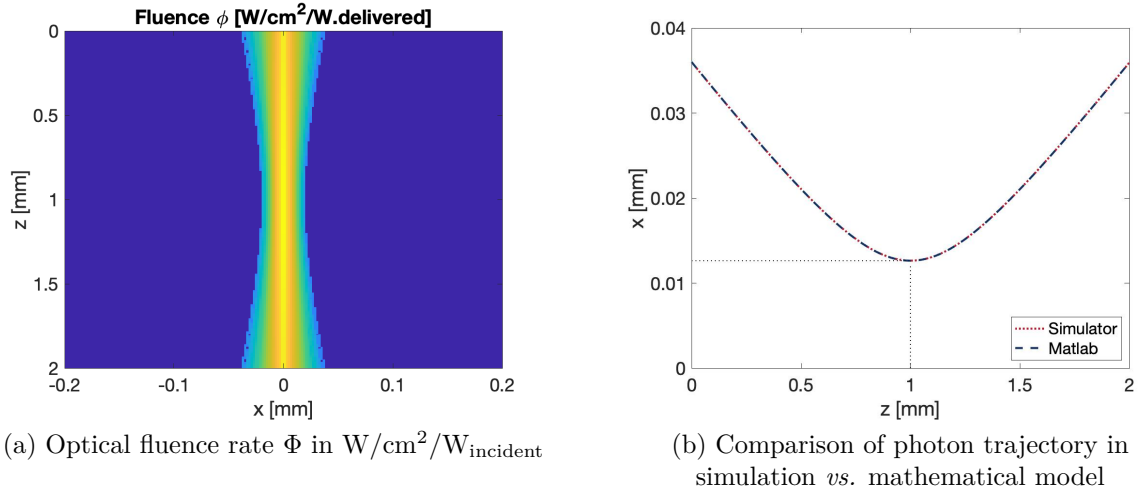


Figure 3.3 Photon propagation using Gaussian beam.

Figure 3.3 (a) shows the fluence output of the simulator, where we can clearly observe the focusing and curved trajectory of the beam. Figure 3.3 (b) shows the comparison between the path of a photon that was launched at the edge of the beam to the computed beam radius along the z -axis with equation 2.15. We can see that the photon propagates exactly according to the theoretical model described in Section 2.2. The beam focus position, the beam waist at the focus and at the tissue surface match the numerical solution calculated from the Equations 2.13 and 2.15. In the next step, we verified the correct implementation of the intensity distribution as shown in Figure 3.4. First, the fluence along the x -axis was normalized and compared to the computed intensity according to Equation 2.19 in Figure 3.4 (b). Then, we compared the intensity distribution along the z -axis using Equation 2.18 as depicted in Figure 3.4 (c). Both curves show a good match, so we can conclude that the Gaussian beam is accurately implemented in our simulator. The refractive index of biological tissue is $n \neq 1$,

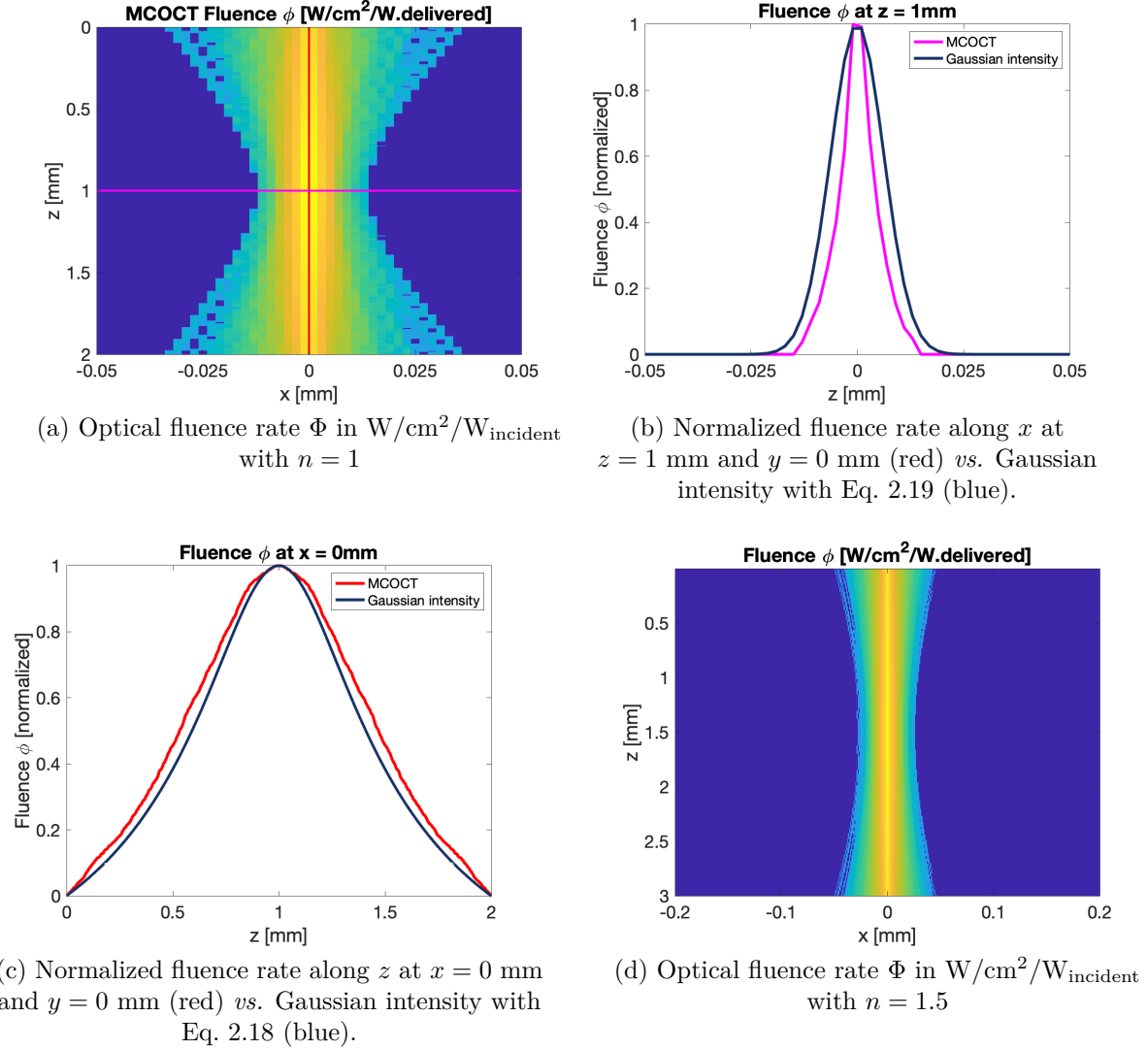


Figure 3.4 Optical fluence rates ϕ comparison using a Gaussian beam in the simulator between (a) $n = 1$ and (b) $n = 1.5$. Comparison of fluence rates with the simulator (red) vs. the mathematical model (blue) along x (b) and along z (c).

wherefore we checked the impact of the refractive index of the medium on the focal point. For that, the same tissue as earlier was used but with a refractive index of $n = 1.5$ this time. Figure 3.4 shows how the position of the focal point is changing. As the refractive index is 1.5 times higher than before, the optical path length of the photons should be longer by the same factor. The focus point should be at the position of $z = 1.5$ mm, which can be observed in Figure 3.4 (d). This means the impact of the refractive index of the medium regarding the photon propagation and beam waist position is properly implemented. A comparison to other beam implementations, such as pencil beam and geometric-focused beam will be

presented in Figure 5.3 of Chapter 5.

3.3 Effect of importance sampling

To improve computation time, we successfully incorporated the method of importance sampling as described before in Section 2.4.2 [49, 50]. We demonstrated in Section 4 through fluence comparisons to MCX, that the importance sampling method does not bias the simulation results. Here, we investigated the factor of acceleration this method is providing. For that, we ran the simulator twice in the same tissue, once with importance sampling and once without, i.e., the scattering follows the HG function. The tissue was described as a one-voxel slab of $1 \times 1 \times 0.1 \text{ cm}^3$ with $n = 1.4$, $\mu_a = 1 \text{ cm}^{-1}$, $\mu'_s = 10 \text{ cm}^{-1}$, and $g = 0.9$. The chosen values are common approximations for skin dermis [58, 66]. For the simulation, we used an amount of 500 illumination/detection probes launching a Gaussian beam at a wavelength of $\lambda = 1310 \text{ nm}$. The imaging lens had a focal length of $f = 30 \text{ mm}$ and was positioned 0.5 mm inside the tissue. First, we launched 10^7 photon packets to see in which range the simulation times are. All simulations were run on a computer equipped with an Apple M1 CPU at 3.20GHz and 8GB RAM. Afterward, 10^8 photon packets were launched to confirm the linear connection of launched photon packets, detected photon packets, and simulation time. In order to generate a satisfying OCT A-line, the goal was to detect at least $\sim 1.5 \times 10^6$ photon packets, as this was also the case for the optical phantoms in Section 4. From this, we extrapolated the simulation time and photon packets that needs to be launched in order to achieve this. The computation time and amount of photon packets are all summarized in Table 3.1.

Table 3.1 Computation time and quantity of launched and detected photons with and without importance sampling. IS refers to simulations with importance sampling and HG to those using only the HG function.

	IS	HG	Extrapolation			
			IS	HG	IS	HG
Photons launched	10^7	10^7	10^8	10^8	10^9	$\sim 1.1 \times 10^{12}$
Photons detected	1.5×10^4	13	1.5×10^5	140	1.5×10^6	1.5×10^6
Simulation time	6.585 min	3.3 min	69.132 min	33.163 min	11.5 h	$\sim 5921 \text{ h}$

We can see, that the ratio between launched and detected photon packets is ~ 0.15 when using importance sampling and ~ 0.00014 if not, indicating an increase by a factor of ~ 1000 . We launched 10^9 photon packets in order to get enough detected photons to create a satis-

fyng OCT signal, which took around 11 h. Figure 3.5 shows the simulation results using importance sampling. When the scattering process follows only the HG function, the amount of photon packets to be launched increases by a factor of ~ 1000 , as expected. From extrapolation, we can approximate that the simulation would then take almost 6000 h, wherefore this was not done in the scope of this thesis.

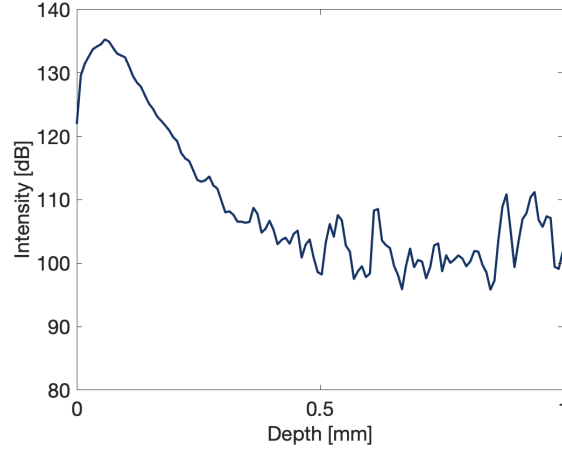


Figure 3.5 MCOCT generated A-line from 10^9 launched photon packets using importance sampling and averaged over 500 detection probes.

3.4 Optical phantom fabrication

The optical phantoms were fabricated using PDMS, nigrosine, and titanium dioxide as mentioned before. The homogeneity of the phantoms was confirmed by comparing the attenuation curves at various different location for each phantom. Figure 3.6 (a) shows an image of a phantom that we fabricated. In total, six optical phantoms with different recipes were created, from these four are one-layered, namely the phantoms #1, #2, #3, and #5. The other two, phantoms #4 and #6 were bi-layered, where for the top and bottom layer two separate recipe of a one-layered phantom was used. Figure 3.6 (b) shows the side view of phantom #4, where we can clearly observe the two different layers. We want to acknowledge Prof. Thomas Gervais here, who provided us access to all the equipment needed to fabricate these phantoms in his laboratory.

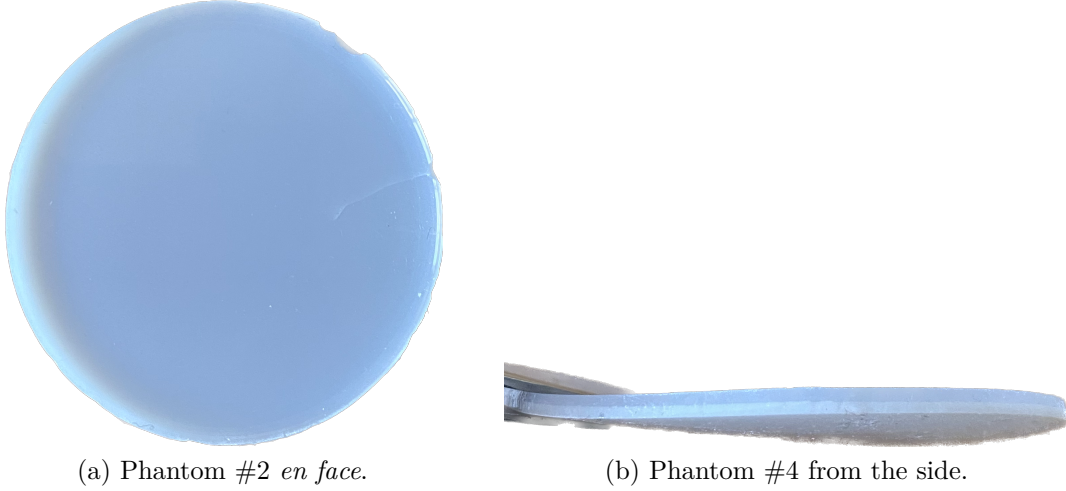
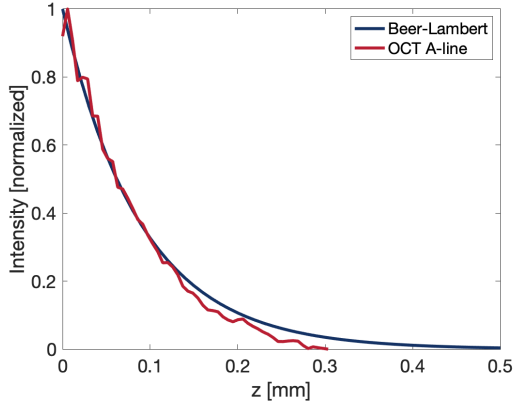


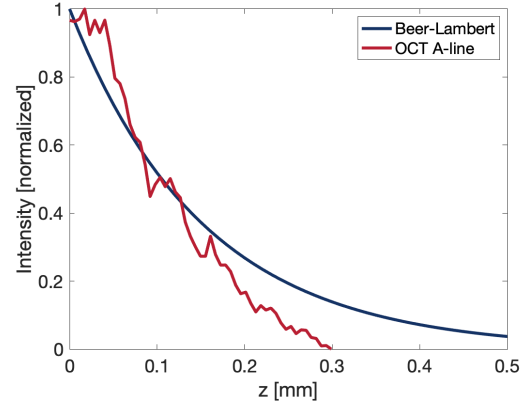
Figure 3.6 Images of optical phantoms

3.5 Determining the anisotropy coefficient

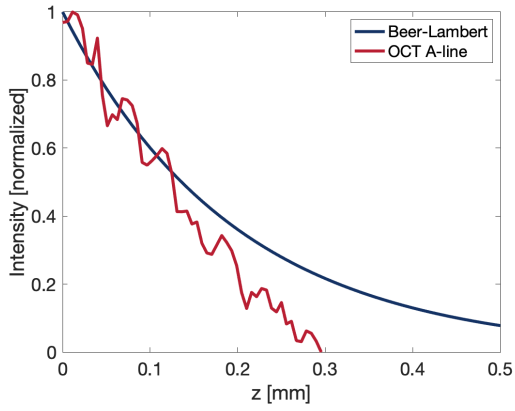
We used the IAD method and an OCT system to estimate μ_a , μ'_s , and n of each one-layered optical phantom. For simulating the propagation of photon packet using the Monte Carlo algorithm, the scattering coefficient μ_s and the anisotropy g need to be determined. These are needed to sample a new angle for photon propagation according to the anisotropy, as described in Section 2.4.1. Since μ'_s is known, determining g would give the scattering coefficient μ_s . The probability of absorption and scattering increase exponentially with the traveled distance in the tissue. The simplest method to model the OCT signal amplitude in a homogeneous turbid medium is using the single scattering model as described in Eq. 2.21. We fitted the single scattering model to the OCT signal in depth of the optical phantoms using an imaging lens with the focal length $f = 30$ mm. The selection of the fit was done after visual inspection and the range from $z = 0.2$ mm to $z = 0.5$ mm was chosen, where $z = 0$ refers to the phantom surface. Figure 3.7 shows the best fit we achieved between theoretical model and the experimental OCT signal for each one-layered phantom. From this, we determined the anisotropy as $g = 0.7$, $g = 0.8$, $g = 0.9$, and $g = 0.8$, for the phantoms #1, #2, #3, and #5, respectively. Using these, we can calculate the scattering coefficient with $\mu_s = \mu'_s / (1 - g)$ for each phantoms.



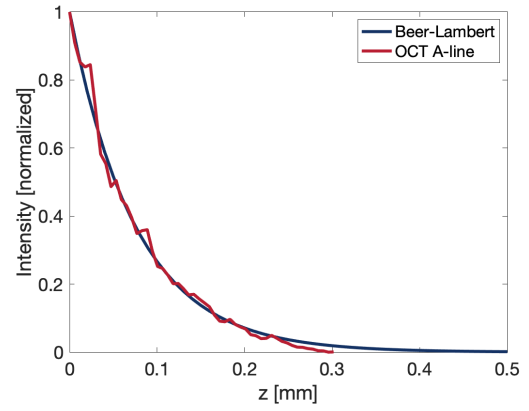
(a) Phantom 1



(b) Phantom 2



(c) Phantom 3



(d) Phantom 5

Figure 3.7 Single scattering model (blue) *vs.* Normalized OCT A-line (red) to estimate anisotropy g .

CHAPTER 4 ARTICLE 1 : MCOCT: AN EXPERIMENTALLY AND NUMERICALLY VALIDATED, OPEN-SOURCE MONTE CARLO SIMULATOR FOR OPTICAL COHERENCE TOMOGRAPHY

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Khaliun Erdenedalai, Raphaël Maltais-Tariant, Mathieu Dehaes, and Caroline Boudoux,
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for optical coherence tomography",

an article that was submitted to the journal *Biomedical Optics Express* on July 17th 2023.

Author contributions

Khaliun Erdenedalai is the principal author and did $\sim 90\%$ of the work. This includes literature research, translating mathematical equations into code and modifying the standard simulator algorithm, performing the validation of the simulator, analyzing the results, and writing the article. Raphaël Maltais-Tariant, the second author, developed the code for translating the simulation output into OCT signals and contributed to the writing of the article. Mathieu Dehaes and Caroline Boudoux were senior investigators and shared the senior authorship to equal parts. Both assisted in the manuscript revision (writing and editing).

Authors: Khaliun Erdenedalai, Raphaël Maltais-tariant, Mathieu Dehaes, and Caroline Boudoux.

Abstract

Here we present MCOCT, a Monte Carlo simulator for optical coherence tomography (OCT) incorporating a Gaussian illumination scheme and bias to increase backscattered event collection. MCOCT optical fluence was numerically compared and validated to an established simulator (MCX) and showed concordance at the focus while diverging slightly with distance to it. MCOCT OCT signals were experimentally compared and validated to OCT signals acquired in tissue-mimicking phantoms with known optical properties and showed a similar attenuation pattern with increasing depth while diverging beyond 1.5 mm and proximal to layer interfaces. MCOCT may help in the design of OCT systems for a wide range of applications.

4.1 Introduction

Optical coherence tomography (OCT) is a high-resolution, non-invasive imaging technique increasingly used for medical and biological applications. It is based on the principle of low-coherence interferometry, which relies on utilizing a light source with a broad wavelength bandwidth to ensure coherence gating, thus leading to a high axial resolution of a few microns [1]. In OCT systems, an interference spectrum is created by combining the reflected light from a reference mirror with that from the sample arm. This pattern is used to obtain a reflectance profile of the sample as a function of depth, namely an OCT A-line. OCT imaging primarily relies on detecting ballistic and quasi-ballistic backscattered photons from turbid environments, such as biological tissues. As light penetrates deeper into the tissue, its intensity decreases exponentially due to scattering and absorption, subsequently limiting the imaging depth to a few millimeters. OCT is now a standard diagnostic tool in the field of ophthalmology and a promising candidate in various other fields, including cardiology, dermatology, gastroenterology, and laryngology [5–8].

Light propagation in a turbid medium can be modeled in simple geometries by analytically solving the radiative transfer equation (RTE) [2]. However, when imaging biological tissue with high scattering properties, the mean free path of light within the tissue is short, which renders the RTE calculation and its inverse problem reconstruction too complex. In such cases, numerical simulation techniques using Monte Carlo (MC) methods have emerged as the gold standard for modeling photon interactions in biological tissue [19,20,30,46,67,68]. With MC, light is considered a collection of photon packets that are tracked as they undergo multiple events of reflection, refraction, absorption, and scattering while traveling through the turbid medium. Over the past years, several MC algorithms have been developed, amongst which Monte Carlo multi-layered (MCML) is the most widely known, forming the foundation of numerous other simulators for biomedical applications [20]. In MCML, an ensemble of photon packets is launched as a pencil beam, perpendicularly its surface into a multi-layered medium with a simulation geometry that is cylindrically symmetric around the z -axis. The use of voxels, tetrahedrons, and other 3D volumetric mesh further allowed the extension of planar and cylindrical geometries to model more realistic tissue structures [30,31,34,35,69]. To accelerate the speed and improve computational efficiency, it was also proposed to use a graphics processing unit (GPU), enabling simultaneous simulations of a higher number of photon packets [41,48].

Monte Carlo methods were previously applied to simulate OCT signals [37, 46, 50, 51, 70–73] and some open-source OCT simulators recently became available [36, 47]. Monte Carlo simulation for tissue layers with embedded objects for OCT (MCEO-OCT) is a modified version of MCML that embeds geometric shapes in the multi-layered tissue to mimic vessels and utilizes the method of importance sampling to accelerate the computation time [47]. The OCT massively parallel simulator (OCT-MPS) is based on an MC approach that exploits a tetrahedron mesh and GPU programming [36]. These two simulators were developed for time-domain OCT applications as only photons describing a path length difference with the reference path length smaller than the coherence length of the OCT system are tagged as contributing to the signal. For Fourier-domain applications, two MC simulators have previously been developed : one uses a layered tissue geometry with Gaussian beam focusing [45] whereas the other exploits a 3D voxel system with a pencil beam [53]. Neither model is however open-source. These tools can be used to better understand OCT signals, aid in the instrumental design and development of OCT-based applications, guide the development of OCT signal processing algorithms, and more recently train neural networks to improve OCT image reconstruction [36, 37, 45–47, 50, 51, 53, 70–75].

In this work, we propose an open-source Fourier-domain simulator, MCOCT, modified from MCML 3D voxel geometry *mcxyz* and implemented modifications to accommodate the particular requirements of Fourier-domain OCT. To achieve depth-resolved reflectometry in addition to simulating photon propagation, photon packets are simulated at a single central wavelength and tracked to record their traveled distance and extract phase as a function of wavelength. This strategy allows mimicking coherence gating. A photon detection system with an angle of acceptance was also implemented to mimic the numerical aperture of the imaging system [46]. To achieve a significant signal-to-noise ratio and expedite computation time, importance sampling was also employed [49, 50]. Gaussian illumination was further incorporated to model the light intensity profile and better represent OCT imaging. For numerical validation, the optical fluence rate generated by MCOCT was compared to the one simulated by Monte Carlo eXtreme (MCX) [41] using the same optical properties and geometry. For experimental validation, OCT signals generated by MCOCT were compared to OCT signals acquired at specific numerical apertures in synthetic phantoms with known optical properties.

4.2 Methods

In the following subsections, we will sequentially describe various parts of the MCOCT simulator.

4.2.1 Monte Carlo photon propagation

A standard MC simulation starts with the launch of a photon packet into a medium that is defined by its index of refraction n , absorption coefficient μ_a , scattering coefficient μ_s , and anisotropy coefficient g [20]. For voxel-based approaches, each voxel is associated with a tissue type and its optical properties. Photon packets randomly propagating through the geometry are associated upon launch with a weight $W = 1$ representing the packet intensity that decreases as it undergoes events. At the site of an absorption interaction, W is updated according to $W = W \cdot \exp(-\mu_a \cdot s)$, where s is the distance traveled by the photon in that step [20]. In the case of a scattering interaction, the diffusion direction is calculated from the azimuthal angle ϕ and the deflection angle θ_s [2]. ϕ is uniformly distributed in the range $[0, 2\pi]$, whereas θ_s is typically modeled by the Henyey-Greenstein (HG) function f_{HG} that depends on the optical properties of the medium [26, 76]. Since most biological tissues have an anisotropy coefficient $g \in [0.90, 0.95]$ at the clinically applied wavelengths of OCT, the photons are more prone to scatter in the forward direction [66]. When W is below a predetermined critical threshold, a roulette process begins in which the photon packet is associated with a probability to continue its propagation, otherwise, the sequence is terminated for this particular photon packet and W is zeroed [20]. The simulation ends upon the termination of all photon packets.

4.2.2 OCT signal simulation

In order to simulate OCT A-lines, we introduced a new beam-focusing method based on Gaussian beams, used statistical methods to increase the probability of photon detection, tracked photons path lengths, and incorporated a system mimicking photon illumination and detection.

beam waist w_0 . Employing the paraxial approximation, the beam waist can be described as $w_0 = (2 \cdot \lambda \cdot f) / (\pi \cdot D)$, relative to the focal length of the imaging lens f and the beam diameter at the lens D [39]. In OCT imaging, light propagates through several layers of different indices of refraction n_i with each layer affecting the axial position and the width of the beam waist, i.e., the beam curvature. Figure 4.1 illustrates the curved trajectory of such a beam depicting the individual parameters where $z = 0$ corresponds to the sample surface. The position of the focus in the tissue is given by z_f and the distance between the tissue surface and imaging lens by $z_{f,I}$, presenting a more general approach compared to assuming the focusing lens to be at $z = 0$ [39].

To implement this beam curvature in the MC method, the beam was focused by propagating photons along the trajectory by a small step s_{min} unit to the next position (x, y, z) . Thereby, the unit of the step size is defined by the optical properties of the tissue. After each step, the direction unit vector $\hat{u}$ is updated to ensure a precise photon tracing along the initial trajectory. Considering a photon propagation through two layers of differing refractive indices n_1 and n_2 , the beam waist of the initial beam in a medium with n_2 can be described as

$$w_{0,n_2} = \frac{\lambda_0 \cdot n_2}{\pi \cdot n_1 \cdot \arctan\left(\frac{D}{2f}\right)}. \quad (4.1)$$

The Rayleigh range of the beam z_R in the medium of n_2 is

$$z_{R,n_2} = \frac{\pi \cdot w_{0,n_2}^2 \cdot n_2}{\lambda_0} \quad (4.2)$$

and the radius of curvature of the beam $R(z)$ in the medium at a position z can be expressed as

$$R_{n_2}(z) = -z_{f,L} \cdot \left(1 + \frac{z_{R,n_2}}{z_{f,L}}\right)^2, \quad (4.3)$$

where $z_{f,L}$ is the axial distance between the focal plane in the medium and the photon position, which is updated after the photon moves. The resulting direction vector has an orientation perpendicular to the radius of the curvature of the beam and is consequently given by

$$\hat{u} = \frac{1}{\sqrt{1 + \frac{x^2 + y^2}{R_{n_2}(z)^2}}} \left(-\frac{x}{R_{n_2}(z)}, -\frac{y}{R_{n_2}(z)}, 1 \right). \quad (4.4)$$

The photon packet propagates by s_{min} until it undergoes its first scattering event, after which it propagates in accordance with a traditional MC simulation [20].

Importance sampling and photon splitting methods

To increase the probability of backscattering events, the method of importance sampling was implemented and combined with photon splitting (see flowchart in Fig. 4.2) [49, 50]. Importance sampling is a probabilistic method to accelerate MC simulations for OCT by biasing random events leading to backscattering, thereby increasing the probability of photon detection and thus enhancing computational efficiency. An updated biased scattering function f_B based on the HG probability density function f_{HG} was then introduced. After a scattering event, this function modified the photon propagation direction to be oriented towards the detector, i.e., the collecting fiber system. The resulting bias was corrected by introducing a corresponding likelihood ratio as

$$L(\cos \theta_B) = \frac{f_{HG}(\cos \theta_S)}{f_B(\cos \theta_B)}, \quad (4.5)$$

where L expresses the ratio between the probability of observing the biased scattering angle in an unbiased simulation θ_S and in a biased simulation θ_B . This likelihood ratio was tracked throughout all scattering events to ultimately adjust the weight of collected photon packets. Additional scattering, biased or unbiased, can be applied once the photon undergoes a first biased scattering event. To ensure the forward scattering of some photons, photon splitting was applied such that photons were split at each scattering event into two halves and both were tracked. One-half scattered in a biased manner towards the collecting fiber according to f_B with a likelihood of L and the other unbiased by continuing the forward propagation pursuant to f_{HG} with an assigned likelihood of $L' = 1 - L$, referred to as the continuing photon packet in Fig. 4.2 .

Optical configuration and tracking algorithm

Optical illumination and detection configurations were simulated using an illumination and a collection fiber probes with identical properties of numerical aperture (NA), geometry, and spatial locations. Simulations of multiple A-scans were achieved by varying the lateral positions of the illumination and detection fibers. When the backscattered photon returned within the fiber's NA and radius, the photon was labeled as detected. The traveled distance of the photon packet in each different layer was tracked as opposed to the fluence absorbed by the sample. This strategy allowed us to adjust the phase of the signal for media with different refractive indices afterward. Upon photon detection, the cumulative traveled distance (total pathlength TP), weight W , and likelihood L of each photon were saved.

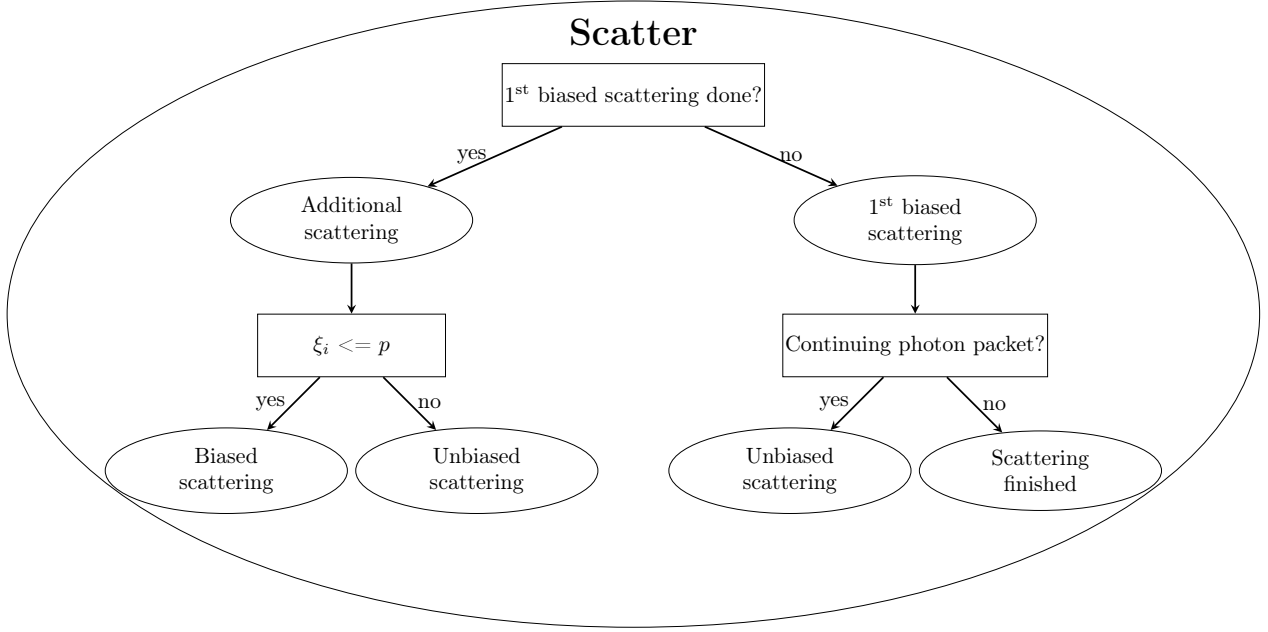


Figure 4.2 Flowchart describing the scattering process of the simulator. Variables are described in Table 4.5 of the Appendix.

This method was implemented by modifying an existing open-source C-language software package that is available on the website of the Oregon Medical Laser Center [31]. The MCOCT photon tracking algorithm flowchart is shown in Fig. 4.3 and describes the steps of a standard MC simulation (gray background) as well as our methodological contributions (white background).

4.2.3 OCT signal reconstruction

For each A-Scan defined by a lateral (x) position of the illumination/detection fiber module, a number N of detected photons with their corresponding weight, likelihood, and total pathlength was acquired. These parameters were then used to reconstruct the OCT signal following a series of mathematical processes described in Fig. 4.4. In order to calculate the signal across the spectral bandwidth $\Delta\lambda$ at a central wavelength of λ_0 , a discrete k array corresponding to the m^{th} wavenumber ($k_m = 2\pi n/\lambda_m$) was created with $\lambda_{min} = \lambda_0 - \Delta\lambda/2$ and $\lambda_{max} = \lambda_0 + \Delta\lambda/2$. The collected signal S_k from the sample was then reconstructed as a function of wavelength and for all j detected photon packets using this expression:

$$S(k_m) = \sum_{j=1}^N \sqrt{W_j L_j} \exp(i(k_m \cdot TP_j)) . \quad (4.6)$$

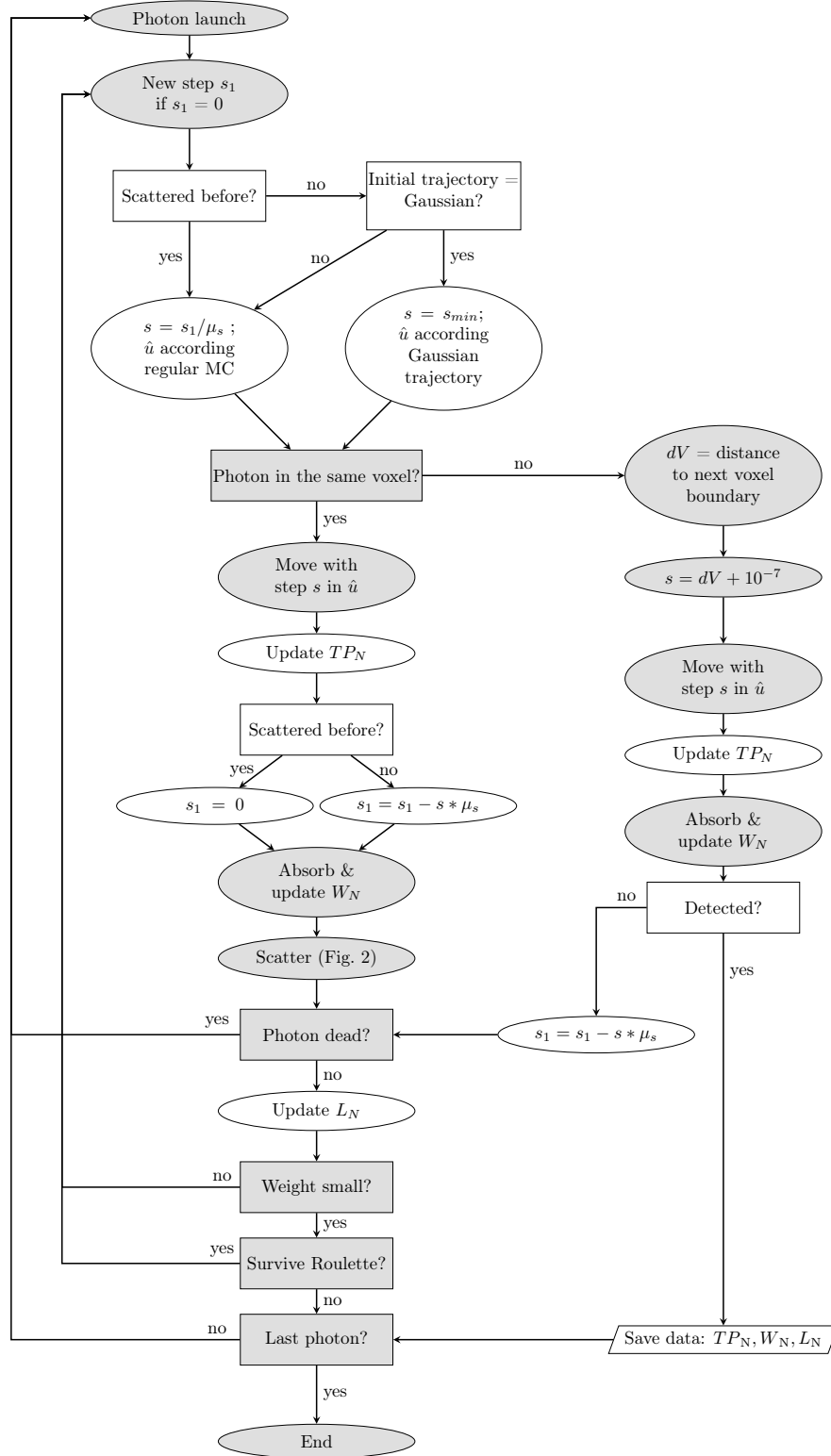


Figure 4.3 MCOCT Flowchart. Variables are described in Table 4.5 of the Appendix.

The reference arm signal amplitude was calibrated as the average of the modulus $|\cdot|$ of the signal amplitude of the sample arm to ensure comparable power in both arms :

$$R(k_m) = \text{mean}(|S(k_m)|) . \quad (4.7)$$

By emulating a balanced detection configuration, the signal at the detector was generated by interfering the sample arm signals $S(k_m)$ with the reference arm signals $R(k_m)$ and therefore creating the interference fringe signal $I(k_m)$ defined by

$$I(k_m) = |S(k_m) + R(k_m)|^2 - |S(k_m) - R(k_m)|^2 . \quad (4.8)$$

Consequently, $I(k_m)$ was defined as a function of the wavelength and required further Fourier-domain processing to generate the OCT signal as a function of depth by applying a Hanning window, zero padding, and Fourier transform. These processes were performed in Matlab (Version R2021a, Natick, MA, USA).

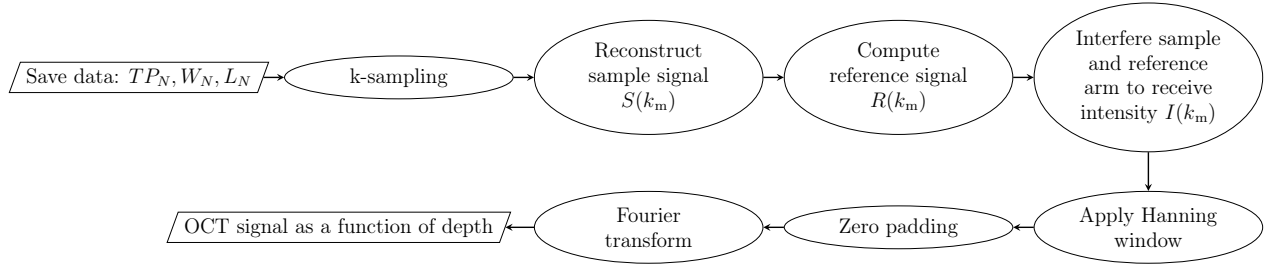


Figure 4.4 OCT signal reconstruction. Variables are described in Table 4.5 of the Appendix.

4.2.4 Tissue-mimicking optical phantoms

Optical phantoms at the optical properties of biological tissues were fabricated and characterized to validate this simulator.

Fabrication

To validate our simulator, optical phantoms mimicking biological tissue were developed with polydimethylsiloxane (PDMS) matrices. PDMS was selected for an accurate representation of the refractive index $n \sim 1.4$ of biological tissue [57]. The matrix demonstrates good durability and is visible with the OCT system at a wavelength of 1310 nm. Nigrosine was utilized as the absorbing agent and titanium dioxide powder as the scattering agent to mimic biological tissue (see Table 4.1). Three one-layer phantoms and one bi-layer phantom were

fabricated with different optical properties by varying μ_a , μ_s , n , and g . The bottom layer of the bi-layered phantom was created using the same recipe as the one-layered phantom 3, wherefore the properties of these layers are assumed equal.

Table 4.1 Concentrations of the scattering (titanium dioxide) and absorbing (nigrosine) agents of the phantoms.

	Phantom #				
	1	2	3	4: top layer	4: bottom layer
Titanium dioxide [mg/g of PDMS]	8.5	3	1.5	6	1.5
Nigrosine [mg/g of PDMS]	25	25	25	25	25

Optical properties characterization

The absorption coefficient μ_a and reduced scattering coefficient μ'_s defined as $\mu'_s = (1 - g)\mu_s$ were determined for the one-layer phantoms. To acquire the transmission and reflection spectra, a LAMBDA 1050 spectrophotometer from PerkinElmer (Waltham, MA, USA) was used. This commercial device is equipped with a single integration sphere capable of receiving both diffuse and specular lights. The collected spectra were processed using the Inverse Adding-Doubling method to estimate μ_a and μ'_s [62, 77]. The determination of the anisotropy parameter g was unattainable through direct measurement. To obtain an approximation of g , OCT signals were fitted to the Beer-Lambert model [2]. Measured optical properties are described in Table 4.2 and represent biological tissue for OCT imaging at 1310 nm [58, 66].

Table 4.2 Optical properties of the phantoms characterized by spectrophotometry.

Phantom #	Geometry	μ_a [cm ⁻¹]	μ'_s [cm ⁻¹]	n	g
1	one-layered	0.0922	16.79	1.4303	0.7
2	one-layered	0.147	6.58	1.4240	0.8
3	one-layered	0.118	2.55	1.4409	0.9
4	top layer of bilayered	0.0912	13.23	1.3844	0.5
	bottom layer of bilayered	0.118	2.55	1.4409	0.9

OCT imaging of phantoms

OCT imaging was performed with a VCSEL Fourier-domain system (Thorlabs, NJ, USA) at $\lambda_0 = 1310$ nm with $\Delta\lambda = 130$ nm. Two lenses of different focal lengths were used: a short one with $f = 30$ mm and a long one with $f = 75$ mm. The position of the focus inside each optical phantom z_f was determined separately for each focal lens and summarized in Table 4.3. For each experiment, OCT imaging generated 300 A-lines which were averaged for comparison with MCOCT.

Table 4.3 Position of focus z_f [mm] below the phantom surface for each focal lens f .

Focal length f [mm]	Phantom #			
	1	2	3	4
$f = 30$	0.618	0.552	0.602	0.9
$f = 75$	1	1.16	1.14	0.9

4.2.5 MCOCT simulations for comparison with MCX simulations

To validate the beam focusing performance, the flux output (optical fluence rate) generated by MCOCT was compared to the one from MCX [41]. The accumulated energy was stored within the 3D voxel matrix during the simulation. The 3D matrix with the deposited weight was normalized relative to the input power, resulting in the local absorption rate per watt (W) of the incident light in units of $\text{W}/\text{cm}^3/\text{W}_{\text{incident}}$. Dividing this rate by the absorption coefficients of the corresponding voxels resulted in the local fluence rate Φ in $\text{W}/\text{cm}^2/\text{W}_{\text{incident}}$. The tissue was represented in both simulators by a $200 \times 200 \times 300$ voxel geometry with isotropic voxels of 0.001 cm^3 . The distance between the imaging lens and tissue surface $z_{f,I}$ was set at 0.85 cm with a beam width at imaging lens $D = 0.1$ cm. In MCOCT, the illumination beam had a Gaussian profile at the imaging lens. In MCX, the trajectory was simulated as a hyperboloid of one sheet and the photon packets propagated in straight lines along the double-ruled surface, thereby mimicking a Gaussian-distributed photon launch [41]. For both simulations, optical properties were $\mu_a = 0.001 \text{ cm}^{-1}$, $\mu_s = 0.01 \text{ cm}^{-1}$, $n = 1$, and $g = 0.5$. MCOCT and MCX simulations were executed using 10^6 photon packets and were run on a desktop computer equipped with an Intel(R) Xeon(R) E5 CPU at 3.50GHz, 16GB RAM and an NVIDIA TITAN Xp card.

4.2.6 MCOCT simulations for comparison with OCT imaging in phantoms

Optical properties from Table 4.2 were used to generate OCT A-lines with MCOCT. Importance sampling was incorporated with a bias coefficient of $a = 0.9$ and an additional bias probability of $p = 0.8$, as defined in [49, 50]. A scheme of 1000 equidistant illumination and detector pairs along the x -axis from $x = -1$ cm to $x = 1$ cm was used and resulted in simulating 1000 A-lines for a single B-scan. To minimize simulation time, a one-voxel slab of $2 \times 2 \times 0.5$ cm³ was used to model the one-layered phantoms. For comparison with the bilayered phantom, the medium was modeled as a two-voxel slab of $2 \times 2 \times 1.8$ cm³. For all simulations, the incident light beam diameter at the focusing lens D was set to 0.07 cm for imaging at $\lambda_0 = 1310$ nm. For OCT signal reconstruction, $\lambda_{\min} = 1245$ nm and $\lambda_{\max} = 1375$ nm. Optical properties were approximated to be constant over the OCT reconstruction spectrum. All simulations were executed using between 10^8 and 10^9 photon packets and were run on the same desktop computer as above. Simulated A-lines are further averaged among detectors (1000) to reduce speckle contrast.

4.3 Results

Figure 4.5 (a) and (b) show the optical fluence rates Φ at $y = 0$ mm generated by MCOCT and MCX, respectively. In both simulations, the beam appears curved as expected for a Gaussian distribution. The simulation time was 60 seconds for MCOCT and one second using MCX. Figure 4.5 (c) shows a very good agreement between optical fluence rates simulated along the x -axis at the depth of the beam focus ($z = 1.5$ mm) by MCOCT (red) and MCX (blue). Figure 4.5 (d) presents the optical fluence rates simulated along the z -axis at a fixed x -position ($x = 0$ mm) by MCOCT (red) and MCX (blue). Both curves progress similarly around the beam waist but show more discrepancies with distance including a fastest decrease for MCX compared to MCOCT.

Figures 4.6 and 4.7 show the comparison between A-lines generated by MCOCT (blue) and those measured in the 4 experimental phantoms (red) using an imaging lens with a focal length of $f = 30$ mm and $f = 75$ mm, respectively. At $f = 30$ mm, the attenuation of the MCOCT A-line follows a similar pattern to experimental data in the one-layer phantoms except in a region close to the surface of the sample where the signal intensity is lower in experimental data. In the bi-layer phantom (phantom #4, (d)), the change of optical properties from the superficial layer to the deep layer is marked by a transient change in signal intensity at a depth corresponding to the interface between layers (0.9 mm). A change in the attenuation slope is also observed with the change of optical properties between layers.

For all comparisons, the accuracy of the simulated data also decreased with increasing depth as a result of lower signal intensity due to fewer collected photons. At $f = 75$ mm, signal intensity patterns were similar to that of $f = 30$ mm while signal intensity close to the surface presented a more accurate qualitative match.

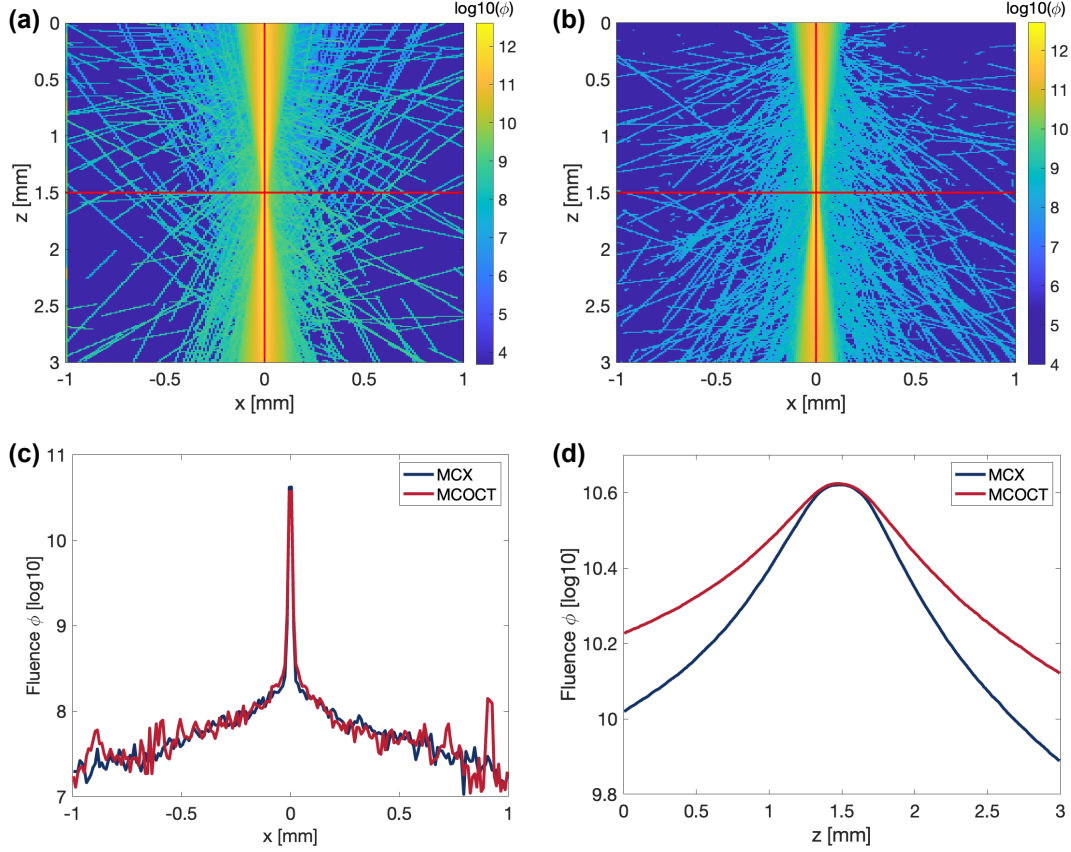


Figure 4.5 Optical fluence rates Φ [$\text{W}/\text{cm}^2/\text{W}_{\text{incident}}$] comparison between (a) MCOCT and (b) MCX simulated with the same optical properties. (c) Comparison of optical fluence rates along x at $z = 1.5$ mm and $y = 0$ mm generated by MCOCT (red) and MCX (blue). (d) Comparison of optical fluence rates along z at $x = 0$ mm and $y = 0$ mm simulated with MCOCT (red) and MCX (blue).

Table 4.4 reports computation times for generating a B-scan of the phantoms presented in Figure 4.6 and Figure 4.7 along with the quantity of simulated and detected photons. Detected photons varied between 1.5×10^5 to 2.9×10^6 for a number of photons launched varying between 10^8 to 10^9 , yielding a ratio of detected/launched between 0.0525 and 0.33%.

Table 4.4 Computation time and quantity of launched and detected photons for MCOCT simulations presented in Figure 4.6 and Figure 4.7.

	Figure							
	4.6a	4.6b	4.6c	4.6d	4.7a	4.7b	4.7c	4.7d
Photons launched	10^9	10^9	10^9	10^8	10^8	10^8	10^8	4×10^8
Photons detected	1.5×10^6	2.2×10^6	2.5×10^6	2.9×10^5	1.5×10^5	2.2×10^5	3.3×10^5	2.1×10^5
Total time (hours)	31.5	30.8	33.3	1.5	3	3	3.3	6.7

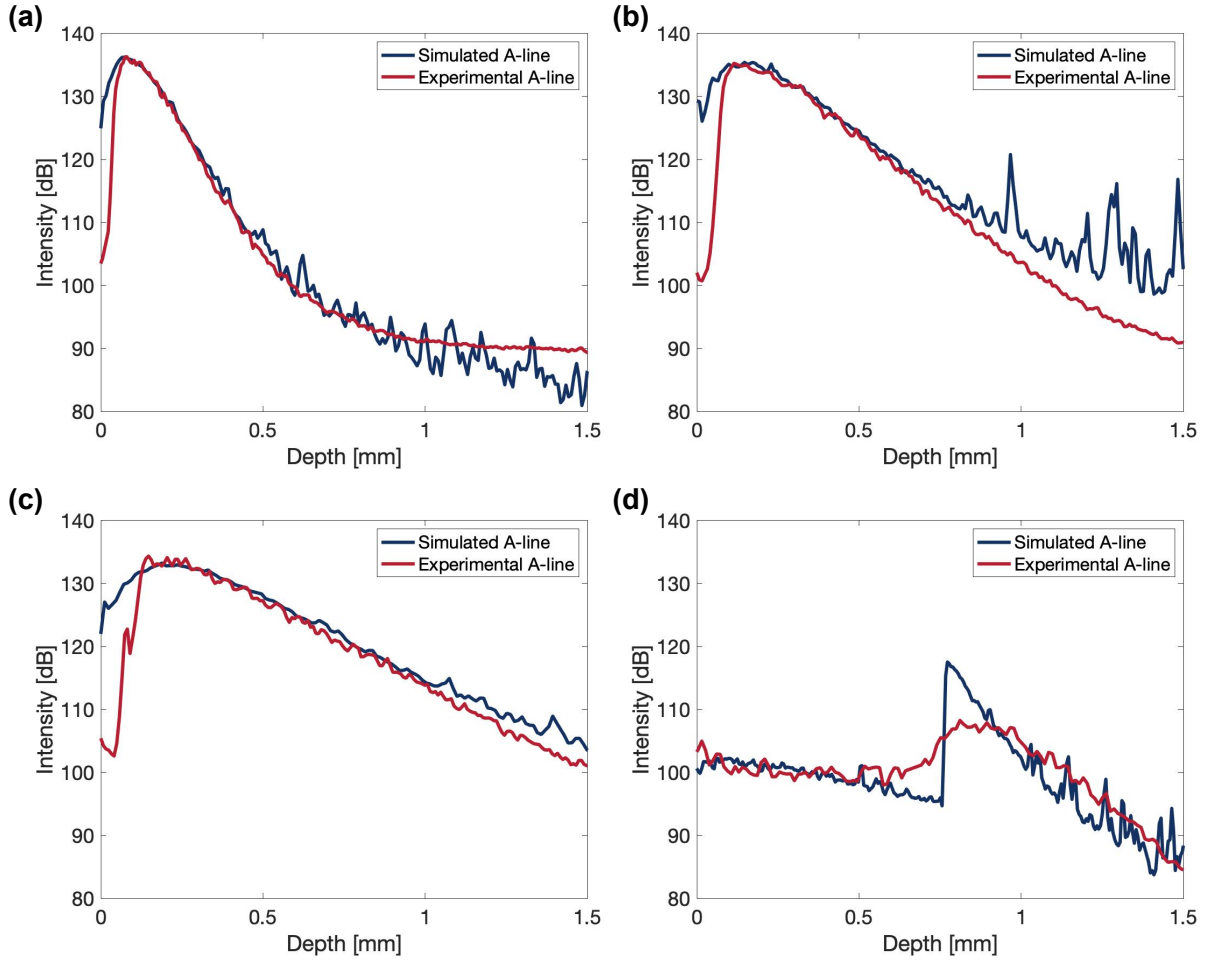


Figure 4.6 Experimentally obtained (red) *vs.* simulated (blue) OCT A-lines using an imaging lens of $f = 30$ mm of (a) Phantom #1 (b) Phantom #2 (c) Phantom #3 and (d) Phantom #4.

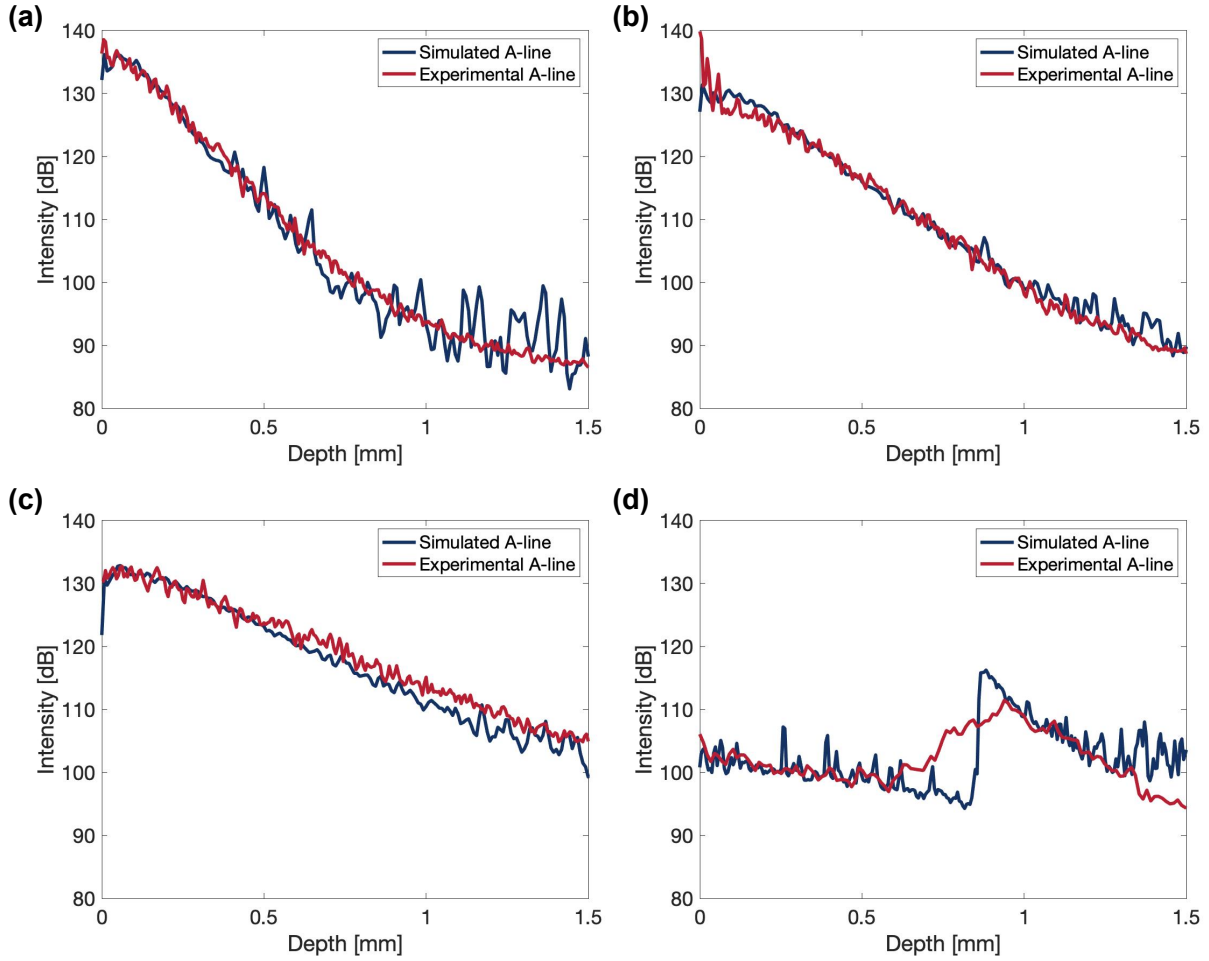


Figure 4.7 Experimentally obtained (red) *vs.* simulated (blue) OCT A-lines using an imaging lens of $f = 75$ mm of (a) Phantom #1 (b) Phantom #2 (c) Phantom #3 and (d) Phantom #4.

4.4 Discussion

In this work, an OCT simulator (MCOCT) based on Monte Carlo methods was implemented and validated. The simulator was based on a Gaussian illumination profile and the importance sampling method as well as signal reconstruction in the Fourier domain. The numerical comparison with MCX [41] and experimental comparisons with OCT imaging in phantoms with known optical properties allowed us to assess and validate the performance of MCOCT.

In OCT systems, the high lateral resolution is achieved through tight focusing of the probing beam, which can be performed by the implementation of a Gaussian focusing profile. A method considering the wave nature of photons was developed by focusing the light along the curved trajectories in accordance with Gaussian optics to a diffraction-limited focal spot. In the simulation, a low scattering coefficient was selected to better visualize the curved Gaussian trajectory of photons. When compared to MCX hyperboloid [41], the diffraction-limited spot size at the focus w_{0,n_2} matched well. Optical fluence rates from the two simulators showed an overlap in progression around the beam waist. With distance to the beam waist, the fluence rates varied, which is due to the different approaches used for mimicking the Gaussian photon trajectory. When focusing the light in MCOCT, the photon packet propagated by minimal steps allowing us to track the voxel in which the photon packet was located more accurately and adapt the direction in case of changing optical properties. This strategy allowed us to bypass the need to solve an equation of motion previously proposed [39, 45]. Then, only the size of $s_{\min}$ needs to be adapted and mainly depends on the voxel geometry. In MCOCT, the importance sampling method was used to increase the occurrence of backscattering, thereby reducing computational costs, while in MCX all photons scattered according to the HG function.

When compared with OCT A-lines acquired in phantoms using a short focal length (30 mm), A-lines reconstructed by MCOCT differed within the first ~ 0.2 mm. This pattern was not observed at a longer focus (75 mm), where MCOCT matched OCT imaging in the four phantoms. This discrepancy is likely due to the reflection of light at the phantom surface, which is not considered in the simulator. When the surface has slight tilts, the coupling of reflected light with the incident light is higher for shorter focal lengths, leading to enhanced distortions in the A-line at the surface. The decrease in OCT signals with increasing penetration depth is expected as the probability of photon absorption also increases with depth. A gradual deviation between A-lines generated by MCOCT and phantoms imaging occurred beyond a depth of about 1 to 1.5 mm. This difference is likely due to the fact that fewer photons reached these depths and were detected. The deviation was more prominent in one-layered phantoms imaged at the focal length of 30 mm compared to 75 mm. The reason behind this is unclear to us at present and is a current limitation of the simulator. For OCT applications in biological tissue, this limitation may not be a significant concern as typical OCT systems are designed to provide an imaging depth of approximately 1.5 mm [2].

The accurate characterization of signal intensity at interfaces is challenging when modeling complex geometry with multiple layers. When the change in refractive index occurs at

the interface of two layers, photons undergo either reflection or refraction, which are mathematically described by Fresnel equation [2]. MCOCT signal intensity simulated proximal to the interface of the two layers in the bi-layered phantom did not match the one from OCT imaging at both focal lengths. Fresnel reflection was not implemented in MCOCT and this discrepancy may be mitigated by considering such reflections as in previous works [45].

Minimizing computational cost is challenging when considering complex media with optical properties mimicking biological tissue. The computation time was higher for phantoms with higher scattering coefficients as these simulations presented more scattering events. For example, generating the OCT signal with the same quantity of detected photons for phantom #1 required higher computational resources than for phantom #3 as scattering was ~ 6 times higher (see Table 4.4). Also, the quantity of photon packets launched when initiating the simulation is dictating the computation time as well as the ratio of detected photons (0.0525 to 0.33%) that contribute to the OCT signal. As expected, simulations that used 10^9 photon packets (one-layered phantoms at $f = 30$ mm) were ~ 10 times longer than simulations that launched 10^8 photon packets (one-layered phantoms at $f = 75$ mm). For the bi-layered phantom, a similar pattern was observed as the simulation using 4×10^8 photon packets (at $f = 75$ mm) took ~ 4 times longer than one using 10^8 photon packets (at $f = 30$ mm).

In addition to the computational efficiency of the MC process, the number of voxels included in the geometry also affected the computational time of MCOCT. Each time a photon packet propagates by the distance prescribed by $s_{\min}$, MCOCT estimates its distance to the voxel boundary, which represents several occurrences when considering a geometry with a high number of voxels. This step is essential for geometry designed with multiple layers as optical properties have to be modified when propagating through different tissues. The voxel size also dictates the spatial resolution of the optical fluence rates. A strategy to minimize the number of crossing-boundary events is to use one voxel for each layer with the voxel size in the axial direction to be equal to the layer thickness. This simple design can be used for simpler geometry such as rectangular slabs but is less appropriate for complex media. The axial resolution of the simulated OCT data is achieved through the imaging spectrum, whereas the quantity of simulated source/detector positions dictates the lateral resolution of the B-scan. The use of large voxels for simple geometry did not affect the lateral resolution of the OCT image. Another factor that influenced the computation time was the minimal step used to generate the Gaussian focusing beam. The selection of a short minimal step will increase the accuracy of individual photon trajectories but also increase the occurrences with which the trajectory has to be updated. Previous methods have been proposed to automatically

adjust the step size during the simulation [39]. In MCOCT, an adjustable step could be implemented but it is not clear how it would reduce computation time while maintaining high accuracy. Another time-consuming procedure in the Monte Carlo module was the random number generation that is needed for each scattering event. Generating one random number each time could be substituted with an *a priori* array of random numbers generated prior to the simulation.

Our work has several limitations. MCOCT simulations were run on a single CPU thread, which limited speed compared to GPU-based simulators [36,41]. Accelerating methods such as parallel computing by Compute Unified Device Architecture (CUDA) will be explored for future versions of MCOCT. Using this architecture would also allow performing the initialization, simulation running, postprocessing, and visualization entirely in Matlab. Therefore, users would not need a separate UNIX-emulating console shell to run a compiler and the MC executable, nor is there a need for intermediate input/output files, which additionally would save storage space. Parallelization would allow simulating a higher quantity of photon packets leading to higher accuracy of the OCT signals at higher sample depths. Noise and/or dispersion were not added to MCOCT signals before reconstruction, but could be added to the reconstructed OCT signal in future works. MCOCT used a scheme of 1000 illumination and detector probes along the x -axis to generate a B-scan image. Since the geometry is described using a 3D voxel system, it is also possible to simulate a scan over the y -axis to reconstruct 3D volumes. However, a 3D scan would currently result in a significant increase in computation time. The demonstration of the ability to generate 3D volumes would be more relevant with a code based on parallelization using GPU.

While further enhancements remain necessary, our open-source simulator can be employed for model validation and system optimization by generating OCT signals across a wavelength spectrum to ascertain the appropriate NA to achieve the desired contrast and its observable depth. Simulating the impact of varying NA or different modes of a photonic lantern [78] can determine the feasibility of achieving a substantial contrast. Our tool can also contribute to the planning of *in vivo* experiments to provide preliminary estimates of specific biomarkers such as changes in retinal layer thickness to characterize particular physiological/pathological conditions [79]. Previous applications [36, 37, 45–47, 50, 51, 53, 70–73] and more recent ones involve the generation of OCT image datasets that can be used in the training of neural networks aimed at tackling the inverse problem in OCT. Some groups already proposed Monte Carlo simulation platforms to generate realistic OCT images for predictive model training [74, 75].

4.5 Conclusion

In this work, a novel Monte Carlo simulator for Fourier-domain OCT (MCOCT) was introduced. The incorporation of a Gaussian light illumination scheme and the ability to increase backscattered event collection allowed us to achieve a more realistic approach to OCT imaging. Optical fluence rates generated by MCOCT were compared with an established MC simulator (MCX), which provided a numerical validation. OCT signals generated by MCOCT were also compared to OCT signals acquired at specific focal lengths in tissue-mimicking phantoms with known optical properties, which provided experimental validation. Future work involves leveraging GPU acceleration for enhanced computational efficiency and speed, as well as considering Fresnel reflections proximal to interfaces in multi-layered geometries. MCOCT may further allow the designing of OCT system hardware and image processing for various medical and biomedical applications.

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Portions of this work were presented at the SPIE BIOS 2021 conference in an oral presentation and as a poster at the Optica Biophotonics Congress: Optics in the Life Science in 2023 [80,81].

Disclosures

The authors declare no conflicts of interest.

Data Availability

The source code for MCOCT will be available on GitHub upon publication of the manuscript. Raw data used in this work are available upon appropriate request.

4.6 Appendix

Table 4.5 Variables used for Figures 4.1, 4.2, 4.3, and 4.4

Tissue optical properties		OCT signal reconstruction	
n	refractive index of tissue	k	wavenumber
μ_a	absorption coefficient	$S(k)$	sample signal
μ_s	scattering coefficient	$R(k)$	reference signal
g	anisotropy coefficient	$I(k)$	interference signal
Scattering		Illustration	
θ_S	scattering angle	λ	wavelength
θ_B	scattering angle	f	focal length
f_{HG}	Henyey-Greenstein function	z_f	distance between tissue surface and focus in medium
f_B	bias function	$z_{f,I}$	distance between tissue surface and imaging lens
L	likelihood value	$z_{f,L}$	distance between focus in medium and photon position
p	probability value	D	beam width at imaging lens
ξ_i	random generated number [0,1]	w_s	beam width at tissue surface
Flowchart		w_{0,n_2}	beam waist in medium
s_1	propagating distance	$w_{n_2}(z)$	beam waist in medium at position z
s	step size of photon packet	z_{R,n_2}	Rayleigh range in medium
$s_{\min}$	predefined step size	$R_{n_2}(z)$	radius of curvature at position z
dV	distance to voxel	θ_{n_1}	half divergence angle in medium of n_1
N	number of collected photon packets	θ_{n_2}	half divergence angle in medium of n_2
TP_N	total pathlength	$\hat{u}$	direction unit vector
W_N	weight	x, y, z	x, y, z position of photon
L_N	likelihood	n_1	refractive index of first layer
		n_2	refractive index of second layer

CHAPTER 5 ADDITIONAL FINDINGS

This chapter presents supplementary results and findings that were made within the framework of this master's research project. We present two additional phantoms that were developed but not featured in the earlier article. Subsequently, we conduct a comparison to analyze the impact of various initial beams utilized in the simulator.

5.1 Additional phantoms

The first phantom, that was not included in the article is phantom #5. Its optical properties were estimated and using these, we ran simulations for the two different NA. Figure 5.1 shows the comparison between A-lines generated by MCOCT (dark blue) and those measured in phantom #5 using an imaging lens with the focal lengths $f = 30$ mm and $f = 75$ mm. For

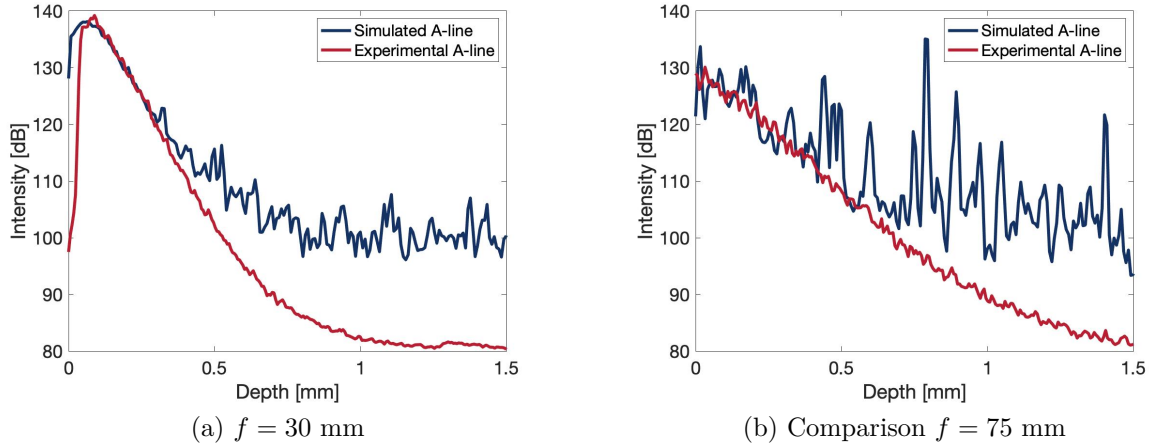


Figure 5.1 Experimentally obtained (red) *vs.* simulated (blue) OCT A-lines using an imaging lens of f of phantom #5

both lenses, the attenuation of the MCOCT A-line follows a similar pattern to the experimental data until a depth of about 0.4 mm. Afterward, the deviation gets more prominent, especially when images at the focal length of 30 mm compared to 75mm, as was the case for the other one-layered phantoms. One plausible explanation for this deviation could stem from the inaccuracy of the measured optical properties, though a good match was observed when determining the anisotropy g . As a consequence, it is possible that the scattering coefficient μ_s is accurate, while this is not the case for the parameters g and μ'_s , which influences the simulation. To confirm this, a potential course of action would involve conducting a

reevaluation of the optical properties through remeasurement.

Phantom #6 was the second bi-layered phantom that we created. The top and bottom layers were made using the same recipe as phantom #5 and phantom #2, respectively. Figure 5.2 (a) shows a B-Scan of the phantom using the OCT system. The OCT A-line is an average of 300 A-lines in the range that is shown by the red lines in the B-Scan.

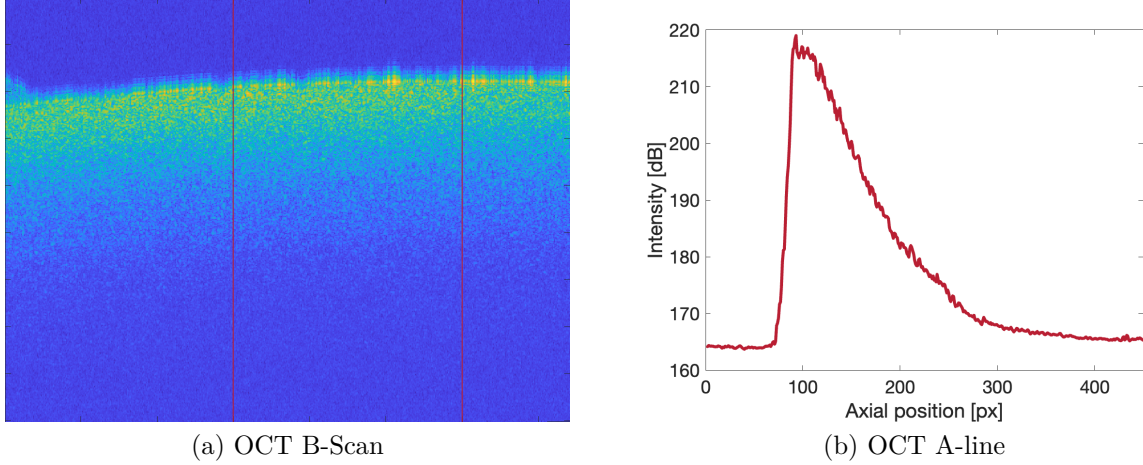


Figure 5.2 OCT images of phantom #6

In both images, we cannot observe the change of optical properties from the top layer to the bottom layer. The interface between layers could not be detected or measured, thereby precluding us from accurately simulating light propagation within this phantom. It is possible that the two layers probably got mixed with one another during the fabrication process resulting in the absence of distinct layers. To address this challenge, an alternative approach could involve considering the phantom as a singular layer and subsequently measuring its optical properties. However, prior to this procedure, the homogeneity of the phantom, i.e., the uniform merging of the previous layers must be validated.

5.2 Effect of different beams

In our simulator, it is possible for the user to choose the type of beam of the laser source. One is a pencil beam, where the photons initially propagate orthogonal into the sample, i.e. only in the axial (z)-direction and according to $\hat{u} = (0, 0, 1)$. We also implemented the geometric-focused beam, where the initial photon propagation is towards the geometrical focus of the beam at the axial position z_f . To see how significant the accuracy gain through proper implementation of a Gaussian beam is, we simulated phantom #4 using the different beams.

Figure 5.3 shows the comparison between the simulation results and the experimental OCT A-lines for both focal lengths of phantom #1. We can see that implementing a Gaussian beam with its curved trajectories is essential to achieve an accurate simulation of OCT signals. In contrast, when utilizing the geometric-focused beam, the simulated A-line aligns closely with the experimental one only within the initial ~ 0.2 mm, after which deviations become evident. Surprisingly, the results for the pencil and geometric-focused beams exhibit a considerably larger discrepancy than anticipated. According to expectations, the OCT signals should progressively decrease with increasing penetration depth due to the exponential increase in photon absorption probability. This does not seem to be the case as we detected still a lot of signals from deeper regions. The A-lines should be closer to the experimental and fewer photons should reach increasing depths. This discrepancy necessitates further investigation to identify and resolve any underlying bugs in the simulator code.

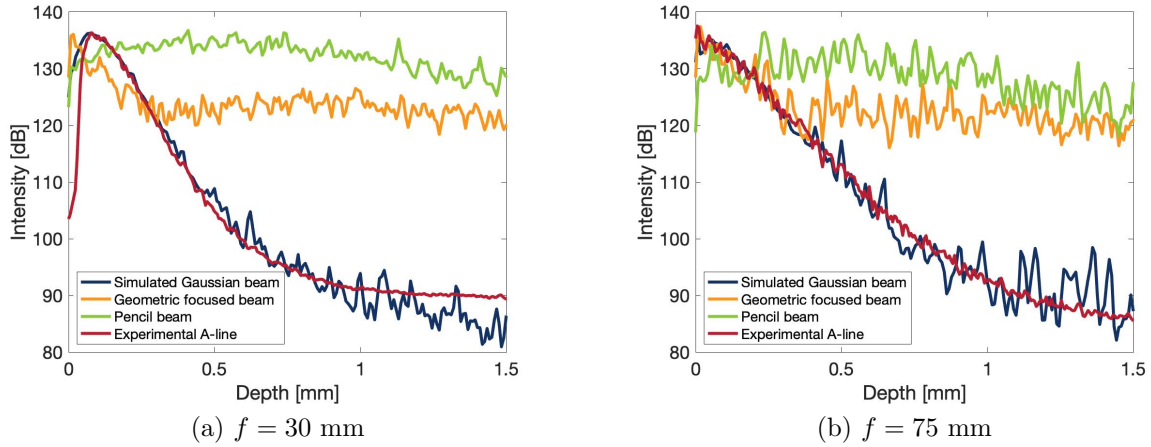


Figure 5.3 Experimentally obtained (red) *vs.* simulated using a Gaussian beam (blue) *vs.* geometric focused (orange) *vs.* pencil (green) beam OCT A-lines using an imaging lens of with the focal length f of phantom 1.

CHAPTER 6 GENERAL DISCUSSION

During this research project, we successfully developed a simulator based on the Monte Carlo method to simulate FD-OCT signals. We successfully incorporated a scheme for detecting backscattered photons and developed an algorithm to create the OCT signal from these. For enhanced accuracy, we incorporated Gaussian beam focusing and validated our simulator experimentally with optical phantoms and numerically using other simulators. Here, we discuss our additions and possible further modifications of the simulator.

6.1 Modifications to standard MC

In our developed simulator MCOCT, the representation of tissue geometry adopts a 3D voxel matrix to allow the simulation of tissue with laterally varying optical properties. While this representation sufficed for homogeneous and layered phantoms, it falls short in describing biological tissue due to its irregular shapes. To accurately model domains with curved boundaries and meshes with complex types, it is possible to change to a tetrahedron-based mesh approach. Doing so, we could use the simulator to generate OCT images of more complex media, bringing us a step closer to model very realistically biological tissue.

Simulating FD-OCT signals entails considering two fundamental requirements. Firstly, since OCT relies on detecting backscattered photons from tissue, it is essential to determine which photon packets are detected. To address this, we implemented an optical configuration and detection system with identical geometry and lateral positioning. Here, it is crucial to ascertain whether the photon's angle is suitable for detection, as it determines whether the photon will be coupled back into the fiber. To achieve this, our imaging and detection configuration also possess identical NA. We assume that any photon with the same NA as the imaging lens will be detected. However, in reality, the coupling efficiency into single-mode fibers depends on the field overlap, which we have not accounted for as we do not know how to represent it as of now. This could be explored in future investigations, as our used approximation could be a source of error. The second requirement involves recording the phase of the detected photons, which we accomplished by recording the distance traveled by each photon packet.

To achieve a more accurate representation of a real focusing beam, we implemented a Gaussian beam with its focus. In our method, the photon propagates by a predefined small step s_{min} following the Gaussian trajectories until it undergoes its first scattering event. It is

worth noting that an avenue for future research is finding out whether this method of enforcing s_{min} is more time-consuming compared to solving the equation of motion. Another alternative approach involves representing the Gaussian trajectories as a hyperboloid. This was not implemented for simulating OCT signals thus far, though it would be worthwhile to investigate whether this approach achieves sufficient accuracy and, if so, whether it offers improved computational efficiency. In the scope of this master’s project, this avenue was not explored owing to time constraints.

Importance sampling was successfully implemented to run the simulation faster. Since only a minority of the photons participate in the OCT signal, to obtain better signals from deeper regions, an enormous amount of launched photons was needed even with the bias scattering, thereby increasing computational time. Minimizing computational cost is challenging when considering complex media with high optical coefficients, such as biological tissue. A possible and validated approach for MC is using a GPU, allowing parallel launch of multiple photon packets, thereby decreasing computation time significantly. In our simulator, the number of voxels in the voxel system also severely affects the computational time. Modeling the medium with tetrahedrons is more complex than with voxels and is expected to demand higher computational resources. Consequently, changing the MCOCT code to run it on a GPU would be the immediate next step, albeit with the anticipation of increased computational intensity. This was not done yet, as this would involve changing the whole code to another programming language, namely CUDA. This task is notably demanding in terms of time, particularly considering my non-programmer background, necessitating a greater allocation of time.

6.2 Possible modifications to MCOCT code

In MCOCT, the simulator does not take into account the phenomenon of reflection occurring between layers, i.e., reflection at the tissue surface as well as between layers in the tissue. Due to the disparity in refractive indices between tissue and air, a significant portion of the incident light is reflected at the surface of the tissue. In our simulator, we represent the tissue surface as flat and even, despite its actual irregularity. This simplification is employed because an accurate model describing the reflection of light on a tilted and uneven surface was not available at the time and we did not find a way to model it. Finding such a model that represents properly the surface orientation and the roughness of the tissue would contribute to the accuracy of such a simulator.

In an OCT system, noise and dispersion can arise from various sources and impact the quality and reliability of the acquired images. In the simulations presented here, the effects of noise and dispersion were not incorporated into the MCOCT signals prior to reconstruction. Our post-processing algorithm though includes these options, where noise is described as an additive component of the spectrum. Dispersion in an OCT system affects the axial resolution by broadening the coherence length and reduces the precision in measuring the depth information accurately. To simulate dispersion, modifications to the k-array can be made, which is currently linear, to reflect a non-linear behavior corresponding to the desired dispersion characteristics.

In an MC approach for simulating light-tissue interaction, the scattering is commonly modeled using the HG function. This function is a simplified model that makes certain assumptions and approximations using only a single parameter, namely g . However, in scenarios involving complex scattering, such as multiple scattering events, strong anisotropy, or highly heterogeneous media like biological tissue, the HG function may not provide sufficient accuracy. To address these limitations, it is worthwhile to explore alternative models, such as the two-term HG or Mie theory. Using the Mie theory offers more flexibility in customizing the scattering function. It allows for a more detailed consideration of factors such as emission shape, detector shape, and the customization of the scattering function itself. By incorporating the Mie theory into the simulation framework, higher levels of accuracy can be achieved when dealing with intricate scattering scenarios and highly heterogeneous media. This could be a possible modification of the code, where the user can select the desired scattering model depending on the accuracy needed for the simulation.

6.3 Phantoms

Due to the unavailability of commercial optical phantoms characterized at the wavelength of $\lambda = 1310$ nm, we undertook the task of constructing these phantoms in-house. As the pouring process was performed manually, the resulting phantoms exhibited surface irregularities, rendering them not completely flat. Given the absence of a suitable model to account for this issue, the phantom's position was corrected manually upon visual inspection to reach an even surface by placing an appropriate object beneath the sample during imaging. Additionally, despite using the same concentration of absorbing agent, the measured absorption coefficients displayed variations, ranging between $\mu_a = 0.0912 \text{ cm}^{-1}$ and $\mu_a = 0.147 \text{ cm}^{-1}$. This phenomenon can be attributed to the minute value of the absorption coefficient, which renders accurate measurement challenging. One significant limiting and time-consuming factor we

encountered was the determination of the anisotropy parameter g , which could not be directly measured. We used a simple model to determine g which does not account for multiple scatterings that occur in the sample, making the determined parameter less accurate.

CHAPTER 7 CONCLUSION

The aim of this master’s project was to develop a validated, open-source Monte Carlo simulator for Fourier-domain optical coherence tomography signals. In this final chapter, we build upon the groundwork laid by our current research to propose potential future directions and enhancements.

7.1 Summary of Works

We successfully developed a first-generation Monte Carlo simulator tailored for generating FD-OCT signals, that is open-source and available to the community. To do so, we implemented relevant specific features to the standard MC algorithm to accommodate for simulating OCT imaging. We incorporated a photon illumination and collection fiber system in the simulator for labeling the photon packet as detected if it returned within the fiber’s NA. Additionally, a post-processing algorithm was devised to derive OCT signals from the simulator’s output, based on signal formation in an actual FD-OCT system. For a more realistic and accurate approach, we integrated a Gaussian illumination beam into the simulator. To speed up the algorithm, we implemented importance sampling and observed acceleration of the simulator by a factor of ~ 1000 . Numerical validation was conducted through comparison of fluence rates generated by MCOCT with those produced by MCX. We fabricated optical tissue-mimicking phantoms *in vitro* and estimated their optical properties at the wavelength relevant to OCT. With these, OCT signals generated by MCOCT were compared to OCT signals acquired from the phantoms at different focal lengths, providing experimental validation.

7.2 Limitations

The MCOCT simulator exhibits some limitations that warrant consideration. Presently, the tissue is described as a 3D voxel system, which has sufficed for the experiments so far but lacks the desired accuracy to realistically model biological tissue. To address this, an evolution to a mesh-based tissue geometry representation appears necessary, as this offers the most precise representation available in current literature. Another limitation pertains to the photon detection system, which currently labels all photon packets as detected if they return within the fiber’s NA and radius. In an actual OCT system, the coupling efficiency into the fiber depends on the field overlap, a complexity not considered currently. In our simulations, the

A-lines generated by MCOCT exhibit gradual deviations from the experimentally obtained ones from the phantoms beyond a depth of about 1 to 1.5 mm. A possible reason for this discrepancy is the scattering model used, which should be further investigated. Additionally, inaccuracy in the characterization of the optical phantoms could also lead to this, wherefore more phantoms of reliable optical properties are needed for further validation. Furthermore, we observed a more pronounced deviation when using an imaging lens of a shorter focal length $f = 30$ mm compared to a longer one $f = 75$ mm. The underlying reasons for that remain elusive to us and necessitate further investigation. The most prominent limitation of the simulator lies in the computation speed, wherefore this is of primary focus in future research. To address this, we successfully added importance sampling methods to speed up the algorithm, which significantly improved efficiency. However, given the exponential increase in scattering and absorption with tissue depth, a substantial number of photons must be launched to achieve a satisfactory SNR as fewer photons are detected from deeper regions. Moreover, when simulating more complex shapes which require more computation, even with importance sampling, simulation times remain high. Another time-consuming factor involves our method of photon packet propagation, wherein minimal steps are taken along Gaussian trajectories until their first scattering events. Since the implementation of a Gaussian beam is necessary for simulation accuracy, alternative approaches need to be investigated to find one that is precise enough as well as less computationally intense.

7.3 Future Research

We achieved developing an open-source MC simulator for generating FD-OCT signals. Moving forward, our first priority is to transition the programming environment to enable code execution on a GPU. This is expected to significantly accelerate the simulator's performance. Afterward, the geometric representation of the tissue is to be modified to realistically model biological tissue by considering curved boundaries and embedded objects. Subsequently, to achieve more realistic modeling of biological tissue, we intend to modify the geometric representation by incorporating curved boundaries and embedded objects. For that, the voxel geometry will be transitioned to a tetrahedron-based mesh. As this simulator is for generating OCT signals, the more aspects of OCT are considered, the closer the simulator becomes to reality. Notably, the implementation of a Gaussian beam has proven crucial for accurately simulating photon propagation in OCT. However, exploring alternative approaches, such as solving the equation of motion or utilizing a hyperboloid approach, may potentially offer computational advantages without compromising accuracy, which needs to be investigated. Another aspect is including the effects of noise and dispersion, which are present in

any OCT image. Moreover, developing a method to account for the field overlap and the resulting coupling efficiency is another step. As mentioned, the surface of biological tissue is not perfectly even and flat. Finding a model to represent the surface orientation and the rough structure of the tissue would also contribute to the accuracy of such a simulator. In the current implementation, we utilize the Henyey-Greenstein scattering function, which is a good approximation for various applications and faster to compute than others. However, in the case of OCT, it might be good to explore other scattering models to see if these give a more realistic representation of reality. The experimental validation of MCOCT could be done more extensively for which more complex optical phantoms are needed. In this regard, fabrication and reliable characterization of optical properties while ensuring repeatability are essential. Though improvements are still needed, our simulator marks a valuable step in generating OCT signals and represents the first MC-based OCT simulator that is provided open-source to the community. After improvement, such a simulator could generate realistic OCT images with known samples, contributing to model validation, system optimization, and dataset creation for training neural networks to address the inverse problem in OCT. We believe that this work holds potential for advancing OCT research and applications in various biomedical fields.

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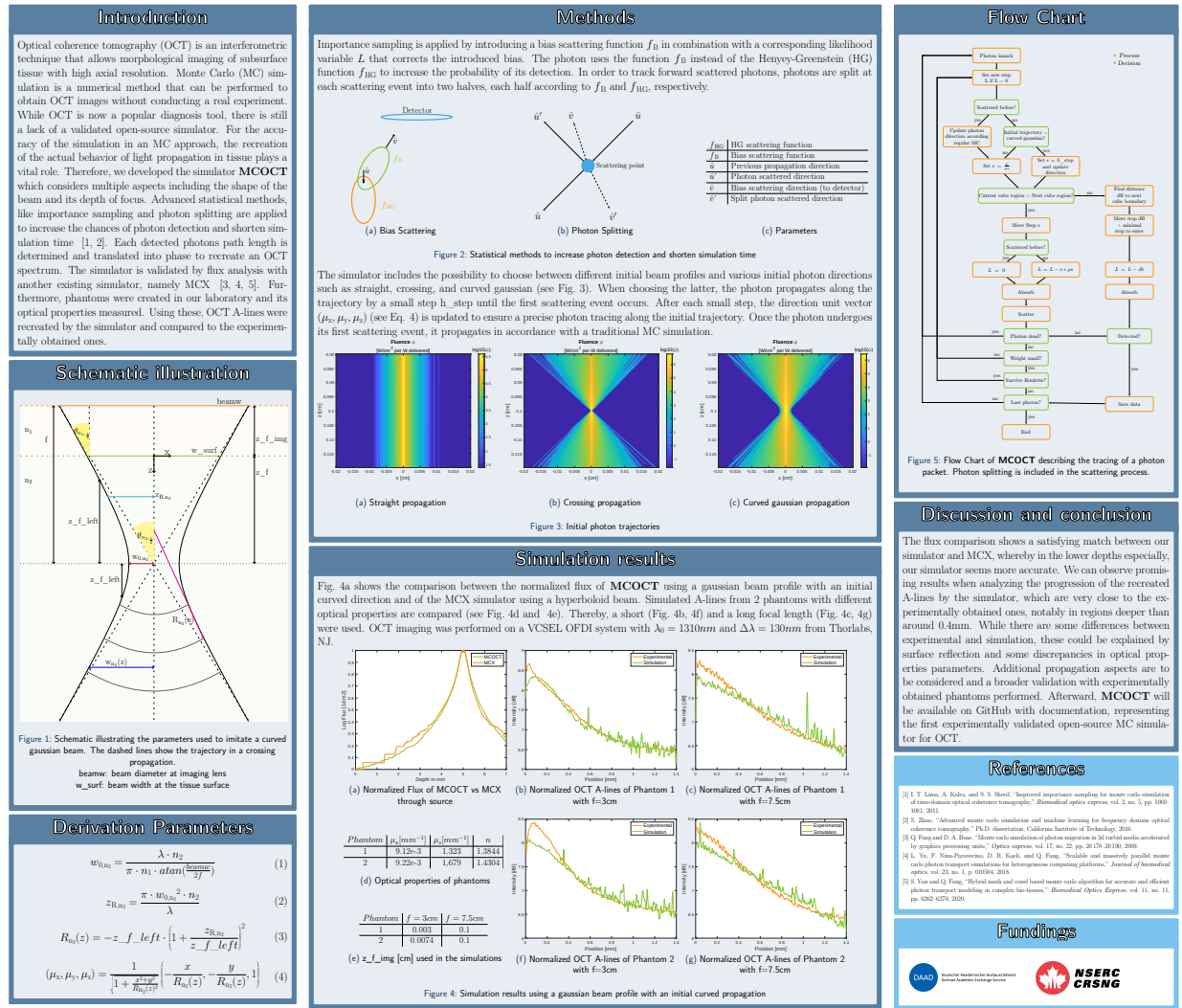
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APPENDIX A GRS/GRC POSTER

A part of this work was presented at the Gordon Research Seminar and the Gordon Research Conference on Optics and Photonics in Medicine and Biology. The presented poster is shown below in Figure A.1.



Simulation results

Fig. 4a shows the comparison between the normalized flux of **MC²OCT** using a gaussian beam profile with an initial curved direction and of the MCX simulator using a hyperboloid beam. Simulated A-lines from 2 phantoms with different optical properties are compared (see Fig. 4d and 4e). Thereby, a short (Fig. 4b, 4f) and a long focal length (Fig. 4c, 4g) were used. OCT imaging was performed on a VCSEL OFDI system with $\lambda_0 = 1310nm$ and $\Delta\lambda = 130nm$ from Thorlabs, NJ.

Figure 4: Simulation results using a gaussian beam profile with an initial curved propagation

Discussion and conclusion

The flux comparison shows a satisfying match between our simulator and MCX, whereby in the lower depths especially, our simulator seems more accurate. We can observe promising results when analyzing the progression of the recreated A-lines by the simulator, which are very close to the experimentally obtained ones, notably in regions deeper than around 0.4mm. While there are some differences between experimental and simulation, these could be explained by surface reflection and some discrepancies in optical properties parameters. Additional propagation aspects are to be considered and a broader validation with experimentally obtained phantoms performed. Afterward, **MC²OCT** will be available on GitHub with documentation, representing the first experimentally validated open-source MC simulator for OCT.

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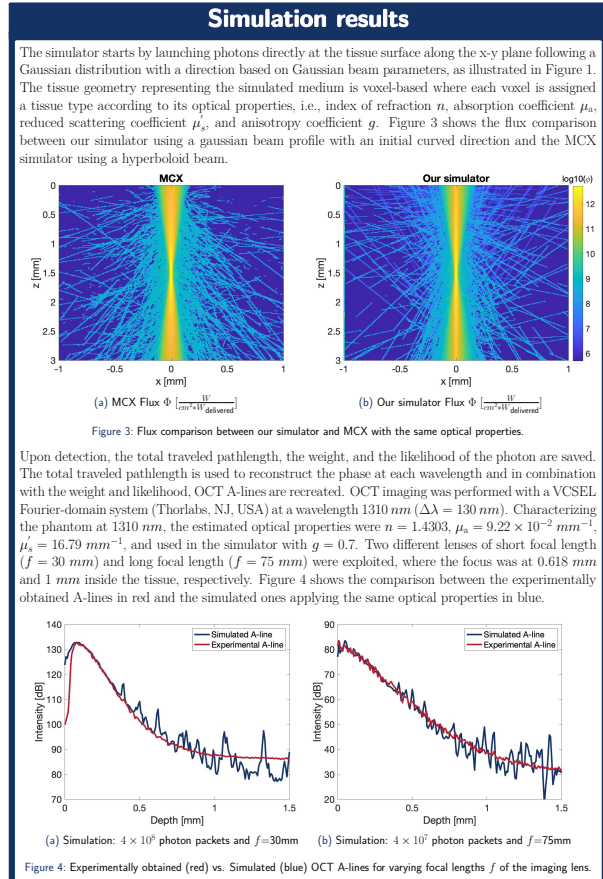
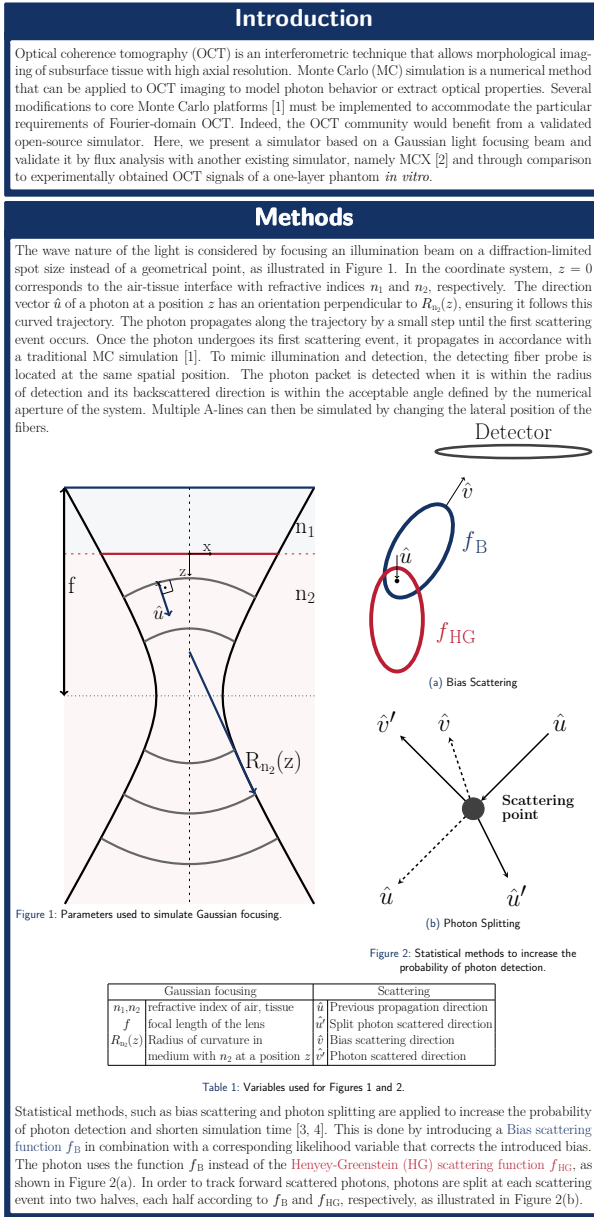
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Fundings

Figure A.1 Poster presented at the Gordon Research Seminar and Conference.

APPENDIX B OPTICA POSTER

A part of this work was presented at Optica Biophotonics Congress: Optics in the Life Science. The presented poster is shown below in Figure B.1.



Discussion and conclusion

We can observe promising results for both lenses when analyzing the progression of the recreated A-lines by the simulator, which is very close to the experimentally obtained ones. Figure 4 indicates a decrease in the accuracy of the simulator with imaging depth, which is to be expected as a result of lower signal intensity. The flux comparison shows a satisfying match between our simulator and MCX, whereby in our simulator the effects of the biased scattering are visible. Our future work involves a broader validation considering different optical properties and multiple layers in the tissue medium. A potential limitation of this simulator is the enhanced computational cost, which can be addressed by launching multiple photon packets in parallel using a graphics processing unit to ensure efficient and fast computation. This simulator will be available on GitHub, representing to our knowledge the first experimentally validated open-source MC simulator for OCT.

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Figure B.1 Poster presented at the Optica Biophotonics Congress: Optics in the Life Science.