

## **Development and Implementation of an Interactive Instructional Module of Light Distribution in Tissue**

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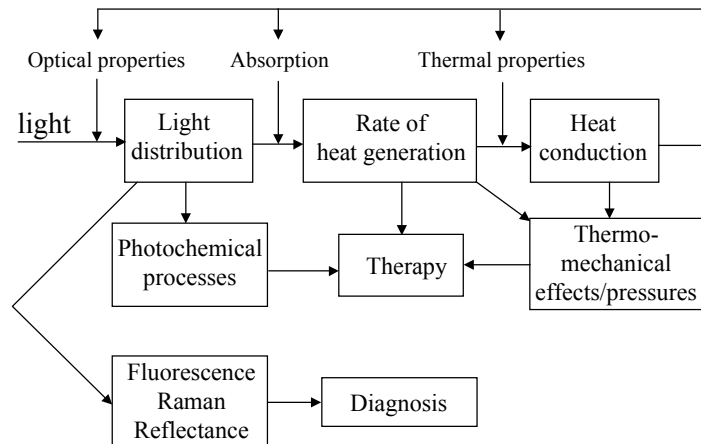
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### Abstract

At the very core of the field of biomedical optics (defined as the use of light from far-ultraviolet through the visible into the infrared for diagnostic, therapeutic and sensing applications in medicine and biology) lies a thorough understanding of light distribution in biological tissue. Courses in this field typically put significant emphasis on student's understanding of light transport in tissue. Analytically this process is described by the light transport equation which has little utility in helping students who are novices in this field obtain a conceptual understanding of light distribution in tissue. Students at all levels struggle with the concepts and have difficulty obtaining a working knowledge of the role of the various tissue properties, boundary conditions and laser parameters on light transport. The goal of this project was 1) to develop an interactive and visual learning module based on Monte Carlo simulations as education tool; 2) design learning activities to help students systematically explore the properties of light and tissue interaction relative to specific goals; and 3) to implement this module and its graphical interface in a Biomedical Engineering course in Biomedical Optics. Preliminary evaluations suggest that the hands-on experience of students using this module results in an increased conceptual understanding of light distribution in tissue. In addition, this method exposes students to the value, capabilities, as well as difficulties and limitations of numerical modeling of processes in Biomedical Engineering in general.

### 1. Introduction

The field of Biomedical Optics has become an important area for medicine and biology in which Biomedical Engineering professionals play a key role. Whether students pursue careers in Biomedical Engineering research centers, biomedical companies, or go on to the medical professions, they are almost certain to encounter optical technologies for diagnosis, sensing and therapy. It is expected that optical science and optical technology will be at the forefront of development of new enabling technologies and devices both in the basic science labs as well as in a clinical setting. Thus, several programs around the country, including ours, are actively working on course development in the area of Biomedical Optics. At Vanderbilt University we have developed a senior Biomedical Engineering elective course entitled 'Introduction to Biomedical Optics'. In this context, Biomedical Engineering is defined as 'the use of light from the far-ultraviolet through the visible into the infrared for diagnostic, therapeutic and sensing applications in medicine and biology'.



**Figure 1:** Block diagram illustrating the interrelationships between optical properties and ensuing therapeutic, diagnostic and sensing applications.

At the very core of all the interactions shown in figure 1 lies a thorough understanding of the interaction of light with biological matter governed by the optical properties. The levels of absorption, scattering and scattering directionality determine where light goes and how much of it ends up at which location. Courses in this field typically put significant emphasis on student's understanding of light transport in tissue. Analytically this process is described by the light transport equation, a rather complicated differential equation which has little utility in helping students, who are novices in this field, obtain a conceptual understanding of light distribution in tissue. Hence we identified and formulated a clear didactic problem: Students at all levels struggle with the concepts and have difficulty obtaining a working knowledge of the role of various tissue properties, boundary conditions and laser parameters on light transport.

The goal of this project was 1) to develop an interactive and visual learning module based on Monte Carlo simulations as education tool; 2) design learning activities to help students systematically explore the properties of light and tissue interaction relative to specific goals; and 3) to implement this module and its graphical interface in a Biomedical Engineering course in Biomedical Optics.

Abstract concepts like the properties of light, electricity, chemical reactions etc., are difficult for students to understand because they are invisible. Often the behaviors of these concepts are represented mathematically. For example, experts interviewed about the behavior of basic electrical circuits commonly resort to equations to explain the phenomenon of electricity. For the experts the mathematics elegantly describes the behavior of electricity they experience time and time again when they design and analyze various electrical systems [Schwartz, et. al. 2000; Schwart, et al. 1998]. Their experiences have provided an additional resource for interpreting the mathematical representation. Therefore, the natural course for instruction is to use this representation to explain how electricity works. However, students lack both the experience of seeing the various applications of electricity experts possess and they lack the mathematical sophistication to appreciate the elegance the equations provide for representing the behavior of

electricity. However, simulations and models can begin to supply students with a mechanism to obtain the experiences experts use to interpret the mathematics.

The challenges for understanding the properties of light and how it behaves are similar to those of electricity. Equations and probabilistic models are used to predict the behavior of light and its interaction with other materials such as human tissue. A user friendly Monte Carlo simulation has been developed to model the interaction of light with tissue for students use to explore these behaviors. However, like many models and simulation used in instruction, students are uncertain about how to interpret the output of these models. They will often ask questions like “Is the intensity of the light right?” or “Is this the only wavelength of light that will work for this problem?” In addition, they have trouble identifying if the model is providing reasonable results for a given set of input parameters. That is, they have trouble identifying when to use a model for a particular situation. Students need contexts to provide them with appropriate goals to interpret the results of a model. Therefore, we have focused on creating learning activities that compare and contrast various therapeutic and diagnostic situations for students to systematically explore the interaction of light and tissue.

The follow discussion begins by describing the light distribution in tissue using the mathematical representation. This serve two purposes, 1) to demonstrate why students have difficulty using the mathematics a sole description of light and tissue behavior and 2) to articulate the various parameters of light and tissue we would like to students to understand. These parameters are the same ones students vary as part of the input to the Monte Carlo model. The last section provides several examples of learning activities students engage in to explore and evaluate the properties of light with either a therapeutic or diagnostic challenge as the focus of their investigation.

## 2. Light Distribution in Tissue

A detailed treatment of optical properties and various models to describe light propagation in tissue is beyond the scope of this paper but is treated in detail in the book by Welch and van Gemert [Welch and van Gemert, 1995a]. In brief, since neither the absolute quantities (concentrations) nor the individual optical properties (absorption and scattering) of tissue constituents are known, these optical properties are typically formulated in a probabilistic context: the absorption coefficient,  $\mu_a$ , the scattering coefficient,  $\mu_s$  and the anisotropy factor,  $g$ . These are defined as follows:

<i>Symbol</i>	<i>units</i>	<i>description</i>
$\mu_a$	$\text{cm}^{-1}$	probability of absorption per infinitesimal path length $\Delta x$ is $\mu_a \Delta x$ ( $1/\mu_a$ is the mean free path length for absorption event)
$\mu_s$	$\text{cm}^{-1}$	probability of scattering per infinitesimal path length $\Delta x$ is $\mu_s \Delta x$ ( $1/\mu_s$ is the mean free path length for scattering event)
$g$	--	average (expected) cosine of the scattering angle, $\theta$

It is essential to realize that these properties are wavelength dependent and tissue specific. When absorption is dominant over scattering, scattering can be ignored and light distribution in absorbing tissues is simply described by the spatial distribution of the light source (i.e. typically

uniform or Gaussian) and an exponential decay in the direction of light propagation. This relationship is known as Beer's law:

$$E(z) = E_0 e^{-\mu_a z} \quad \text{Equation (1)}$$

Where  $E(z)$  is the irradiance ( $\text{W}/\text{cm}^2$ ) at depth  $z$  and  $E_0$  is the irradiance at the tissue surface. A few simple concepts can be derived from this relationship. It provides an accurate measure for the depth to which light can penetrate into the tissue (in fact, a depth of penetration can be defined as the depth at which the irradiance has been reduced to  $1/e$  of the incident irradiance), and the amount of light reaching each depth can be calculated exactly. However, in most tissues scattering cannot be ignored and contributes significantly to light distribution. In this case it is no longer possible to use a simple, intuitive model like Beer's law to predict light distributions. In its most general form for situations where both absorption and scattering play a role, spatial light distribution is described by the light transport equation which relates the gradient of radiance at some position 'r' in direction s to losses due to absorption and scattering and gain due to scattering from all other directions s' into s.

$$\frac{dL(r, \hat{s})}{ds} = -\mu_a L(r, \hat{s}) - \mu_s L(r, \hat{s}) + S(r, \hat{s}) + \mu_s \int_{4\pi} p(\hat{s}, \hat{s}') L(r, \hat{s}') d\omega' \quad \text{Equation (2)}$$

In this rather complex differential equation the terms represent:

$\frac{dL}{ds}$             the change in radiance at r in the direction s.

$L(r, s)$             the radiance defined as the propagation of photon power

$\mu_a L(r, \hat{s})$         losses due to absorption

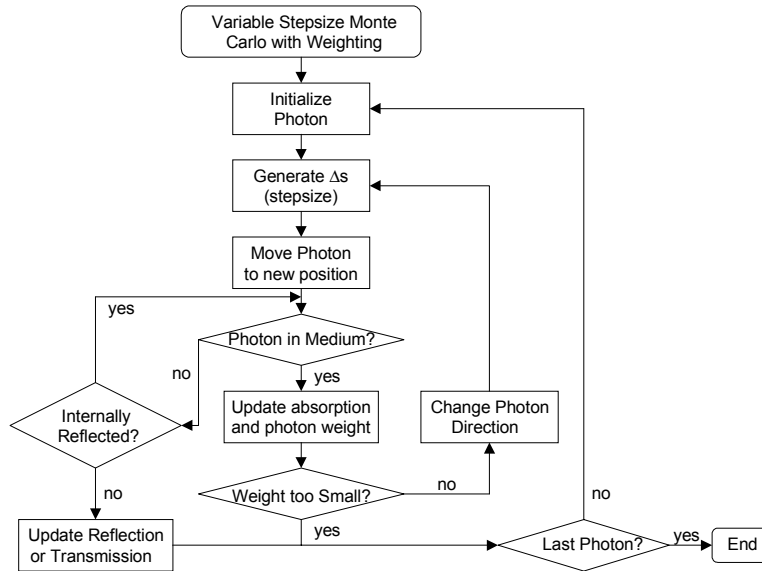
$\mu_s L(r, \hat{s})$         losses due to scattering

$\mu_s \int_{4\pi} p(\hat{s}, \hat{s}') L(r, \hat{s}') d\omega'$         gain due to scattering from all directions s' into direction s

where  $p(s, s')$  is the phase function.

$S(r, s)$             source of power generated at r in the direction s (which may be due to fluorescence or due to some kind of internal light source)

There are no useful analytical solutions to this equation. However, various models and approximate solutions have been developed [Welch and van Gemert, 1995b]. One of the most intuitive and practical solutions is a numerical simulation based on probabilistic principles, known as Monte Carlo simulation.



**Figure 2:** A simplified flow diagram for the Monte Carlo simulation of photon propagation (adapted from Welch and van Gemert [Welch and van Gemert, 1995c]).

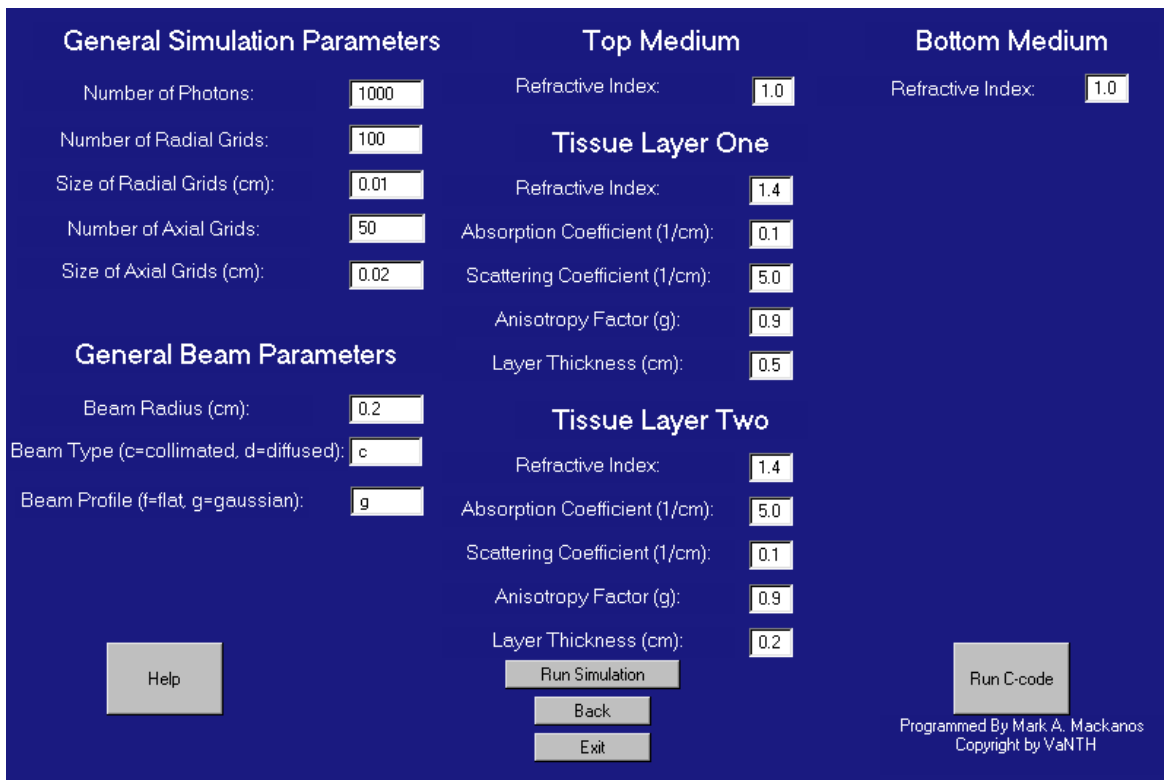
### 3. Principles of Monte Carlo Simulations

Monte Carlo simulations are used extensively as computer (numerical) models which provide a probabilistic approach to light propagation in tissue. At the core of Monte Carlo simulations lies a random number generator routine that forms the basis for the ‘rolling the dice’ probability approach in the Monte Carlo simulation. Monte Carlo simulations of photon propagation offer a flexible yet rigorous approach toward photon transport in turbid tissues. This method simulates the “random walk” of photons in a medium that contains absorption and scattering. The method is based on a set of rules that govern the movement of a photon in tissue. The two key decisions are (1) the mean free path for a scattering or absorption event (i.e. how far does the photon travel before scattering or absorption occurs), and (2) the scattering angle (i.e. in which direction does the photon continue after the scattering event). At boundaries, a photon is reflected or moves across the boundary. The rules of photon propagation are expressed as probability distributions for the incremental steps of photon movement between sites of photon—tissue interaction, for the angles of deflection in a photon’s trajectory when a scattering event occurs, and for the probability of transmittance or reflectance at boundaries. Monte Carlo light propagation is rigorous yet very descriptive. However, this method is basically statistical in nature and requires a computer to calculate the propagation of a large number of photons. The simulation keeps track of the fraction of the total number of photons that is absorbed in each grid element, thus providing a map of spatial energy distribution [Welch and van Gemert, 1995c].

The number of photons required in a simulation depends largely on the question being asked, the precision needed, and the spatial or temporal resolution desired. For example, to simply learn the total reflectance,  $R_t$ , from a tissue of specified optical properties, typically about 3,000 photons can yield a useful result. To map the spatial distribution of photons in a radially symmetric problem, at least 10,000 photons are usually required to yield an acceptable answer. To map spatial distributions in a more complex three-dimensional problem such as a finite-diameter beam irradiating a tissue with a buried blood vessel, the required photons may exceed 100,000. The main point is that Monte Carlo simulations are rigorous, yet statistical and therefore require

significant computation time to achieve a specified precision and resolution. Nevertheless, the flexibility of the method makes Monte Carlo modeling a powerful tool.

Monte Carlo simulations have been used in the research setting for decades even applied to the problem of light distribution in tissue. In addition, in a graduate course at The University of Texas at Austin on optical aspects of laser-tissue interaction, a major component of the course is writing a Monte Carlo simulation (in Pascal or C) [Welch, 1999]. While this is a worthwhile exercise that contributes to the basic understanding of light distribution in tissue, it is not suitable for an introductory course at the undergraduate level. Yet, the numerical simulation of light distribution in and by itself can be an effective means to expose students to the challenges and problems surrounding light distribution in tissue. The visual nature of these simulations is expected to make it easier for students to grasp the intricacies of this problem. Thus we elected to develop a Monte Carlo simulation written in MatLab where the students interact with a Graphical User Interface (GUI) without having to concern themselves with the underlying algorithms and programming. Instead they are presented with an interactive menu in which they can select the input parameters for the simulation. The results are displayed directly on a window showing the light distribution for the simulation they are running in near-real time. These results represent the fraction of the total photons absorbed at any position (grid volume element) in the tissue (i.e. spatial distribution of light absorption). Additionally, the fractions of light reflected and transmitted are calculated.



**Figure 3:** Interactive screen. This MatLab graphical user interface (GUI) is used to input optical properties to be used in the simulation as well as simulation parameters (number of photons, grid size, number of grids, etc.).

#### 4. Learning Objectives

The learning objectives are to 1) foster the students' understanding of the role of optical properties on the light distribution in tissue; 2) create an understanding that allows students to solve problems and design systems based on these properties and their effects on light-tissue interaction. The modeling environment described above suits itself to create a learning environment that can meet these objectives. However, the classical limitation of such an approach is that without clear objectives of what the student should learn, the hands-on experience could be no more than following a list of procedures (the classical 'cook-book lab') and never understanding the underlying principles. Studies have shown that implementation of such an hands-on learning activity can greatly enhance the learning experience by using (real life) challenges that focus the students attention and the use of contrasting cases to help students attune to the specific features of each of the relevant parameters.

Thus parallel with the development of the modeling environment itself we aim to 1) implement this simulation-based learning tool in a problem- or challenge-based environment; and 2) define interesting (real life) challenges that help the students focus on the interaction of light with tissue to achieve a specific goal (rather than simply asking them to notice the effects of various input conditions on the output).

Finally, there are several additional benefits to using this method that are not primary learning objectives or goals by themselves. First, the very nature of the Monte Carlo numerical statistical approach provides a practical context for revisiting basics of probability in an application that is meaningful to the students. Secondly, embedded in the use of the model are exercises aimed at learning the value of numerical modeling in biomedical problems. This is not only advantageous for the problems at hand but it exposes students to the value, capabilities as well as difficulties and limitations of numerical modeling of processes in Biomedical Engineering in general.

#### 5. Implementation

The implementation of this learning tool is placed in the context of specific challenges. A few examples are shown here. The presented challenges can be grouped into two categories. First there are several (2 shown here: challenge 1 and 2) that aim at introducing the students to the Monte Carlo simulation Graphical User Interface (GUI) and present contrasting cases in which the effect of varying a specific parameter is investigated. The second group (challenge 3 and 4) present real life medical challenges that can be modeled using the Monte Carlo simulation.

*Challenge 1* – Effect of beam profile on energy distribution in a non-scattering medium. Students will simulate this problem using Monte Carlo simulation. They can pick any spot radius,  $\omega_L$  as long as they use the same for the uniform and Gaussian simulations. Uniform intensity profile is described by:

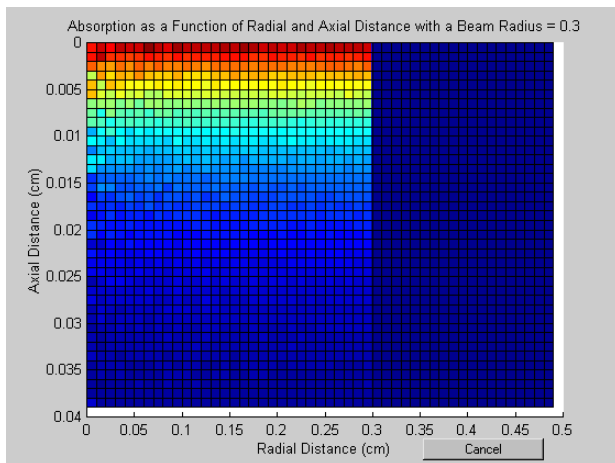
$$\begin{aligned} E(r) &= E(r = 0) & \text{for } r &\leq \omega_L \\ E(r) &= 0 & \text{for } r &> \omega_L \end{aligned}$$

Gaussian intensity profile is described by:

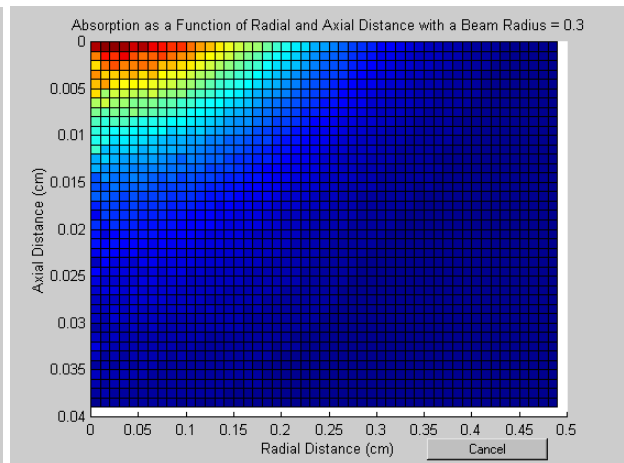
$$E(r) = E(r=0) e^{-2r^2 / \omega_L^2}$$

They can use any absorption coefficient provided they use the same in both cases. Suggested is to use an absorption coefficient,  $\mu_a = 100 \text{ cm}^{-1}$ .

Objectives: become familiar with the simulation interface; investigate the effect of spatial beam profile on energy distribution; learn to set up the simulation parameters such that adequate sampling is achieved; verify model results with that obtained from the analytical solution using Beer's law (since this is a simulation with no scattering, this is feasible). The issue of setting up adequate simulation parameters for a given set of optical properties is essential and fosters the building of a physical understanding of the values of the optical properties (i.e. what is a 'good' number of photons to run, what is a 'good' number of grid elements in the depth and axial direction and what is a 'good' size for each grid).



**Figure 4a:** Light distribution as function of depth and radius for a collimated, uniform light beam with a beam radius of 3 mm. Uniform tissue with  $\mu_a = 100 \text{ cm}^{-1}$ ;  $\mu_s = 0 \text{ cm}^{-1}$ ; 100,000 photons.



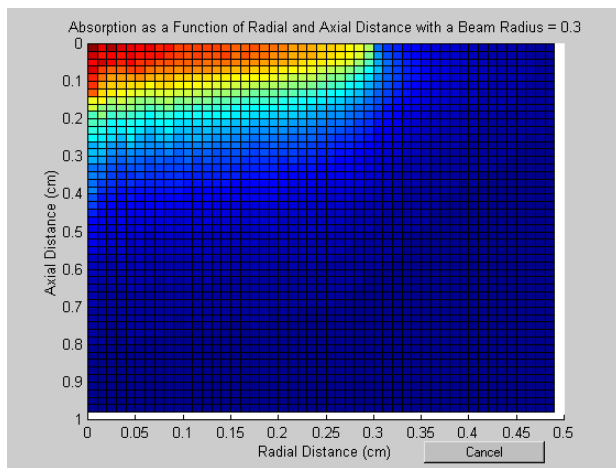
**Figure 4b:** Light distribution as function of depth and radius for a collimated Gaussian light beam with a beam radius of 3 mm. Uniform tissue with  $\mu_a = 100 \text{ cm}^{-1}$ ;  $\mu_s = 0 \text{ cm}^{-1}$ ; 100,000 photons.

*Challenge 2 – Effect of scattering direction (anisotropy) on light distribution.*

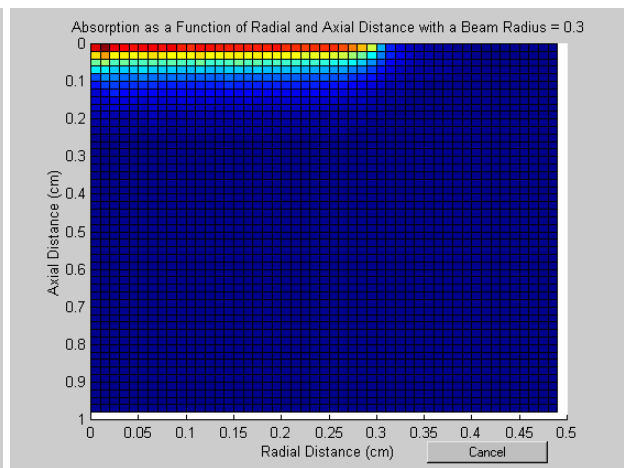
Students will simulate this problem using Monte Carlo simulation. They can pick any spotsize, as long as they use the same for both simulations and a uniform beam profile should be used. In this simulation scattering will dominate absorption by 100:1 (i.e.  $\mu_s = 100 \text{ cm}^{-1}$ ;  $\mu_a = 1 \text{ cm}^{-1}$ ).

Two simulations will be performed, the first with the anisotropy factor,  $g = 0.9$  (primarily forward scattering), the second with the anisotropy factor,  $g=0$  (isotropic scattering).

Objectives: investigate the effect of scattering and scattering direction on light distribution in tissue; further familiarization with the model interface and output expanded to simulations that can not easily be verified by a simple analytical model; setting up adequate simulation parameters for a given set of optical properties is essential and foster the building of a physical understanding of the values of the optical properties (i.e. what is a 'good' number of photons to run, what is a 'good' number of grid elements in the depth and axial direction and what is a 'good' size for each grid given the input parameters).



**Figure 5a:** Light distribution as function of depth and radius for a collimated, uniform light beam with a beam radius of 3 mm. Uniform tissue with  $\mu_a = 1 \text{ cm}^{-1}$ ;  $\mu_s = 100 \text{ cm}^{-1}$ ;  $g = 0.9$ ; 100,000 photons.

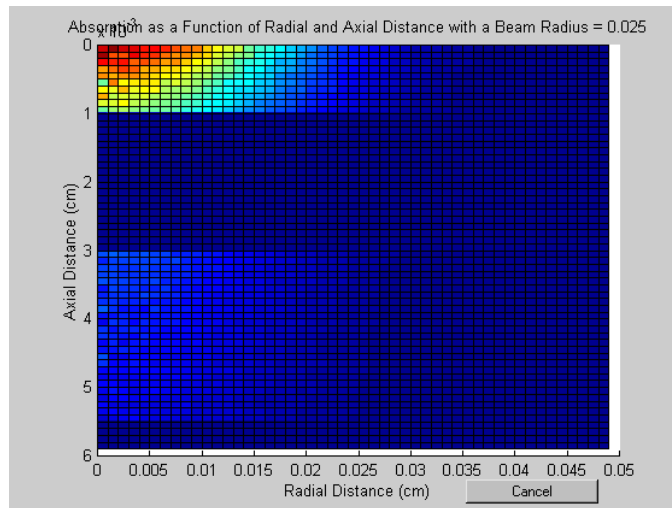


**Figure 5b:** Light distribution as function of depth and radius for a collimated, uniform light beam with a beam radius of 3 mm. Uniform tissue with  $\mu_a = 1 \text{ cm}^{-1}$ ;  $\mu_s = 100 \text{ cm}^{-1}$ ;  $g = 0$ ; 100,000 photons.

### Challenge 3 – Laser photocoagulation of the retina.

In this challenge students are presented with the medical problem of diabetic retinopathy, a medical complication in diabetic patients in which blood vessels become leaky and new blood vessels (neovascularization) form in response to oxygen deprivation of the retina. The treatment of choice for diabetic retinopathy is a laser procedure called pan-retinal coagulation (PRP). With PRP, the surgeon uses laser to destroy oxygen-deprived retinal tissue outside of the patient's central vision. While this creates blind spots in the peripheral vision, PRP prevents the continued growth of the fragile vessels and seals the leaking ones. The goal of the treatment is to arrest the progression of the disease. This problem is an interesting instructional problem because it lends itself to investigation of optical properties of the various layers in the back of the eye, effect of spot size, effect of beam profile, and effect of laser intensity on the distribution of laser energy in the retina. Ultimately, this dictates the heat source produced which in turn is directly responsible for the coagulative effect and thus the clinical efficacy of the procedure.

Objectives: formulate the medical problem and translate it to a problem that can be modeled using the Monte Carlo simulation; determine parameters of interest (anatomy of retina, thickness of individual layers – retinal pigment epithelium, avascular choroid, vascular plexus of choroid, sclera – as well as the wavelength dependent optical properties of each layer); determine relevant boundary conditions; implement problem in Monte Carlo simulation; interpret results in context of clinical objective.



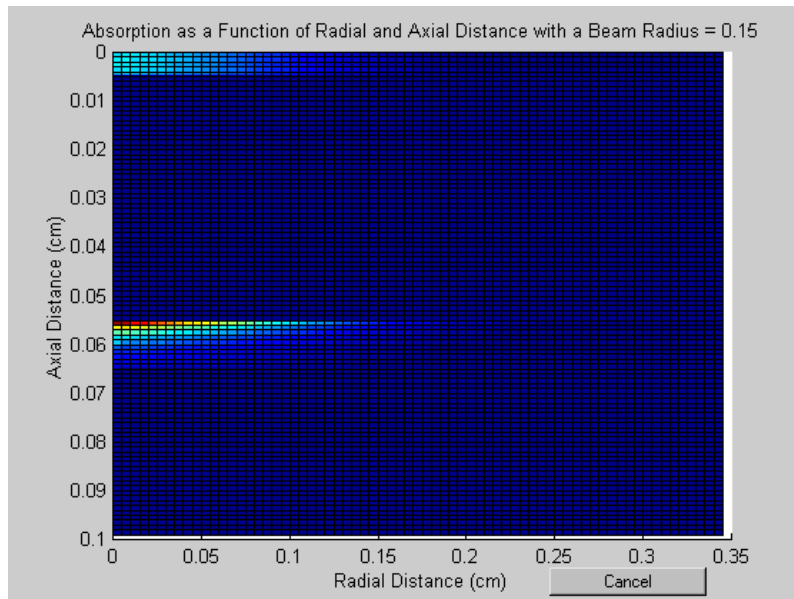
**Figure 6:** Light distribution as function of depth and radius for a collimated, Gaussian light beam with a beam radius of 0.25 mm. The retina is modeled as a three layered tissue with layer 1 representing the retinal pigment epithelium ( $d = 0.01$  mm;  $\mu_a = 693$   $\text{cm}^{-1}$ ;  $\mu_s = 100$   $\text{cm}^{-1}$ ;  $g = 0.9$ ), layer 2 presenting the avascular choroid ( $d = 0.02$  mm;  $\mu_a = 0$   $\text{cm}^{-1}$ ;  $\mu_s = 100$   $\text{cm}^{-1}$ ;  $g = 0.9$ ), and layer 3 representing the vascular plexus of the choroid ( $d = 0.025$  mm;  $\mu_a = 270$   $\text{cm}^{-1}$ ;  $\mu_s = 100$   $\text{cm}^{-1}$ ;  $g = 0.9$ ); 500,000 photons.

In the context of this paper, the main objective is to foster an understanding of the effects of optical properties on the initial light absorption in tissue, this challenge can easily be expanded to include calculations of actual energy density, ensuing temperature rise and may even be coupled to heat diffusion concepts and calculations.

#### Challenge 4 – Laser treatment of Port Wine Stain (PWS)

Port wine stains (PWS) are vascular malformations that present at birth. Because a vast majority of these birthmarks occur in the head and neck regions they are readily visible and may give rise to social and psychological problems, in particular in children and young adolescents. PWS occur in approximately 0.3% of the population (or 750,000 people in the US). While treatment of PWS is medically necessary only in rare occasions, the treatment for the aforementioned social and psychological reasons is more prevalent. Anatomically, PWS are made up of enlarged dermal blood vessels which gives the skin the reddish ('port-wine') appearance. Besides camouflaging with make-up, there were no satisfying treatments of PWS prior to introduction of the laser. The clinical goal of laser treatment of PWS is irreversible damage to the ectatic (enlarged) vessel walls without any to the other skin constituents. This specifically focuses the students attention to the wavelength dependence of optical properties in the different layers of skin. In particular the challenge reduces to the question: how can one effectively coagulate the blood vessels without causing major damage to the superficial epidermal layers where melanin is abundantly present.

Objectives: determine optimal wavelength to treat PWS with a laser; formulate the medical problem and translate it to a problem that can be modeled using Monte Carlo simulation; determine parameters of interest (anatomy of PWS – as well as the optical properties of each layer and the effect of wavelength on these properties); determine relevant boundary conditions; and consider assumptions that need to be made as well as the implications of model assumptions; implement problem in Monte Carlo simulation; interpret results in context of clinical objective.



**Figure 7:** Light distribution as function of depth and radius for a collimated, Gaussian light beam with a beam radius of 1.5 mm. The PWS is represented as a three layered tissue and the optical properties of light with a wavelength of 585 nm is selected. Layer 1 represents the epidermis ( $d = 0.05$  mm;  $\mu_a = 18$   $\text{cm}^{-1}$ ;  $\mu_s = 470$   $\text{cm}^{-1}$ ;  $g = 0.79$ ), layer 2 presents the dermis ( $d = 0.5$  mm;  $\mu_a = 0.24$   $\text{cm}^{-1}$ ;  $\mu_s = 129$   $\text{cm}^{-1}$ ;  $g = 0.79$ ), and layer 3 representing blood in the ectatic blood vessels (i.e. blood layer) ( $d = 0.1$  mm;  $\mu_a = 191$   $\text{cm}^{-1}$ ;  $\mu_s = 467$   $\text{cm}^{-1}$ ;  $g = 0.995$ ); 500,000 photons.

Additionally, this challenge brings out the various aspects of this type of medical laser procedure: the art (clinician's skills versus the variability and unpredictability of patients), the psychology (the patient and clinician's objective and subjective assessment of the cosmetic result), the biology (or the body's response to the laser radiation), and finally the physics which is mostly what we are concerned with here and which forms the basis for engineering and design issues. In addition, this challenge lends itself to include discussions on ethics of laser treatment for cosmetic versus medical indications as well as issues surrounding regulatory aspects of medical laser devices.

## 6. Conclusions and Recommendations

This interactive instructional module for light distribution in tissue has been developed and has been used for one semester in a senior elective Biomedical Engineering course in Biomedical Optics. It has been found to stimulate the students interest in Biomedical Optics and Biomedical Engineering in general by giving them hands-on activities that apply engineering, physics and mathematical principles to real-life problems and with significant visual feedback. With only one semester experience we can conclude the following: 1) The use of numerical simulations to a difficult analytical problem proves to increase understanding of the role and importance of specific optical properties; 2) use of the simulations enhances the development of student's intuition (conditioned subject knowledge) of the role of optical properties and the practical consequences of their numerical values; 3) presenting the simulation as a tool to address specific questions in the challenges that are posed proved to stimulate students interest and provided a context for the problem at hand; 4) the exercise of taking a clinical problem and translating it to a geometry and boundary condition problem that can be numerically simulated proved extremely

valuable by making it easier for the instructor to talk with students about these concepts, and by making it easier for students to comprehend and apply these problem to new situations.

While this module has been quite successful and effective, our experience in using it is still young and improvements can be made. In its current form, the use of the model is largely qualitative (where does most light end up, and what is the effect of optical properties on the relative distribution of light). Certainly in the future expansion to quantitative simulations can be made. In this scenario, the relative photon distribution can be used to calculate true energy densities and thus the ensuing temperature fields. This in turn can be the starting point for similar models of heat transfer simulations. A second problem is the implementation of the model in good, medically relevant challenges that can be modeled effectively using this module. The Port Wine Stain and retinal photocoagulation problems are quite amenable to this but we strive to implement more challenges. Finally, it is our goal to implement the use of the module in a problem-based learning environment for the entire course. We are currently working on modules based on the Legacy cycle in the context of a HPL (how people learn) framework [Bransford et al, 2000]. In this manner students will engage in problem-based educational activities that not only teach them subject specific content knowledge but help them develop into life-long learners and problems solvers.

## 7. Acknowledgements

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