Light Propagation through Biological Tissue

and Other Diffusive Media

THEORY, SOLUTIONS, AND VALIDATION

SECOND EDITION

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Preface

THIS manual is intended as an in-depth introduction to light propagation through biological tissues and diffusive media. After having treated the general theory of light diffusion and its physical and biological interpretation, the text presents the derivation of tens of already reported and newly derived analytical and/or semi-analytical solutions. These solutions are "ready to use" and represent the most employed algorithms appearing in tissue optics and related fields, where light is used to probe the optical and/or biological properties of diffusive media. By studying these examples, the readers should be able to directly apply the solutions to real laboratory problems or to develop their own specific solutions.

In a dedicated part of the manual, the solutions are tested against "gold standard" reference data, and their domain of validity is carefully discussed. This part also serves as a tutorial explaining how to generate suitable reference data and how to test new algorithms obtained, e.g., by the reader.

The text is particularly well suited for skilled master students but also for advanced scientists searching for rapid solutions, eliminating the problem of repeating cumbersome calculations in diffusive optics, and bypassing the need to search among hundreds of published papers.

Thus, to summarize, the present manual offers: **I**) A general introduction to the theory of photon migration; **II**) Ready-to-use analytical and/or semi-analytical solutions, derived from the general theory of photon migration, associated with problems typically encountered in biomedical optics and related domains; **III**) A validation of the proposed solutions by means of comparisons with Monte Carlo (MC) simulations; **IV**) A tutorial software package, implementing the most representative analytical and semi-analytical solutions of the manual (see supplemental material 🔗) and **V**) A set of pre-calculated MC data serving as a gold-standard reference and allowing the reader to personally check the presented exact/approximated solutions (see 🔗).

New to this edition

The manual is a completely revised version of the former published book titled *Light Propagation through Biological Tissue and other Diffusive Media: Theory, Solutions and Software*.[1] The new text wants to get closer to the novelties of the theoretical modeling in photon transport that have appeared in recent years, thus putting the reader in the ideal conditions to comprehend the recent evolution of the theoretical modeling techniques. For this reason, together with an in-depth revision and expansion of the old chapters, eight new chapters have been included, covering new solutions and new aspects of the theory.

Theoretical Background

A simplifying hypothesis

The theoretical background of this book is the general theory of photon transport. The propagation of light through turbid media (i.e., media with scattering and absorption properties) can be accurately described in the mesoscopic and macroscopic scales with the radiative transfer equation (RTE). The RTE is a complex integro-differential equation of which analytical solutions are available for some geometries of practical interest.[2] Such solutions usually suffer from longer computation times and higher complexity compared to the solutions of other approximated theories such as the diffusion equation (DE). The DE is obtained from the RTE by making some simplifying assumptions. Compared to the solutions obtained with the RTE, the solutions derived from the DE, for the same problem, are certainly more efficient but may be approximated. For this reason, for each application in which the DE solutions are used, it is necessary to check their accuracy to ensure that the approximations are sufficiently small. This check can be performed by comparing the approximate solutions against the correspondent reference solutions obtained with the RTE (usually solved by the "gold standard" MC methods).

Why then the diffusion equation?

At this point, the obvious question remains: why to adopt the DE instead of an exact RTE? Diffusive media are turbid media for which the solutions of the DE provide a sufficiently accurate description of light propagation. Through these media, photons propagate in a diffusive regime. In fact, the paths followed by these photons, migrating, e.g., from a source to a detector, look like a random walk (zigzag trajectory). Thus, when these photons undergo a sufficiently high number of scattering events (generating the zigzag trajectory), we obtain a diffusive regime. The important point here is that in daily life we can find a long list of media for which a diffusive regime of propagation can be assumed. This list includes, for example, highly scattering media such as biological tissues, agricultural products, wood, paper, plastic materials, sugar, salt, and milk, for which the diffusive regime can be reached even when the volume of the medium is smaller than a cubic centimeter. The list can also include slightly scattering media, such as clouds of gas and dust in the interstellar medium; in these cases, an extremely large volume is necessary to obtain the diffusive regime. This book is devoted to the study of light propagation through scattering media with a special emphasis on biological tissues and diffusive media. This is the reason why the DE becomes of fundamental interest. Moreover, the diffusive regime of light propagation is a reference and limit regime under which forward solvers can be obtained with extraordinary simplified characteristics. We will see that the above described limits of the DE actually represent its main advantages, which can be fruitfully used in applied science.

Why present solutions in the time domain?

In our study we have given special emphasis to studying light propagation in the time domain,[3] i.e., providing solutions of the DE for a temporal Dirac delta source, and this fact requires a comment. This choice is motivated by the fact that this domain of analysis is widely spread in many applications where short-pulsed laser sources are used. However, the literature includes commonly used solutions in other transformed domains such as the temporal-frequency and spatial-frequency Fourier domains[4,5] where temporal and spatial modulated sources are used. It is important to note that solutions in other transformed domains, such as the temporal-frequency and spatial-frequency domains, can be fully reconstructed by making use of the solutions in the time domain and in the continuous wave (CW) domain[3] (a "special" case of the time domain where a continuously emitting source is used).[5] Thus, the solutions presented in this book can, in principle, cover all the domains of analysis.

For the time domain, it is also finally important to note that it has, in principle, the maximum information content since absorption and scattering effects can be more easily decoupled while studying the RTE in this domain. Indeed, when looking at measurable time-domain quantities, such as time-resolved detected light, the absorption and scattering terms can be identified as affecting very different and independent parts of the measured temporal profile. In fact, absorption interactions are progressively affecting late times, while scattering strongly affects the early part of the detected signal. This fact can lead to an evident advantage in terms of understanding the different physical phenomena and the measurement techniques of the optical properties. For this reason, the time domain represents a primary regime for studying and understanding photon transport. However, the time domain and CW domain can be extremely accurate in measuring the optical properties of diffusive media, showing that through designed experiments absorption and scattering can be decoupled also in the CW domain.[6,7] In this book, the time domain (including the special CW case) is the background for studying photon transport. In any case, for tutorial purposes, in this manual few examples of solutions will be discussed in the other domains.

Note that the expressions "time (temporal) domain" and "CW domain," utilized for simplicity in this manual, in general should be more precisely written with the longer expressions "spatial time (temporal) domain" and "spatial CW domain."

Using this manual in everyday practice

Solutions of photon transport can find a natural use in the assessment of the optical properties (absorption and scattering) of scattering media. In fact, these measurements often need, in the inversion procedure, a forward model that describes the dependence of the detected light on the values of the optical properties. Moreover, in the biological domain, the optical properties may in turn be linked to biological quantities important for the understanding of related underlying physiological mechanisms (see Fig. 1). The latter biological application is made possible by the fact that near-infrared light (typical light utilized for biological measurement) can penetrate deeply into tissues (some centimeters) and is sensitive to several tissue constituents.

More specifically, any biological tissue represents a complex random medium wherein light undergoes many scattering events and where, in many practical cases, its propagation may be suitably described as a diffusion process. The interaction of the near-infrared light with a biological tissue is dominated, with few exceptions, by scattering effects (the distance between two subsequent scattering events is on the order of ≈100 μm). However, most of the physiological information is led by the absorption of chromophores (e.g., oxy- or deoxy-hemoglobin) naturally present in the tissues. The

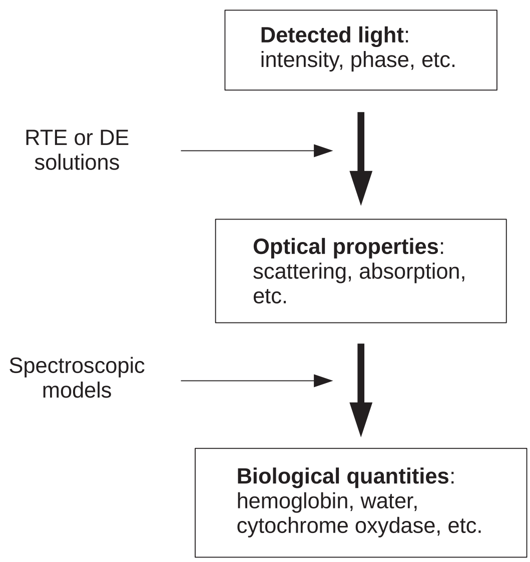

Figure 1 General approach allowing one to extract biological quantities from light that has traveled through a tissue.

possibility to treat this problem as a diffusion process, allows us to assess the small contribution of the absorption by isolating it in a very efficient manner from scattering. It is in this sense that the DE solutions proposed in this manual may represent a very powerful tool for the physiologist, the medical doctor or the engineer involved in the development of new instrumentation for biomedical optics.[3,8,9] These reasons are also why the solutions reported in this manual are already at the core of well-known instrumentation, such as near-infrared spectroscopy (NIRS) and diffuse optical tomography (DOT).[10,11]

Organization of the Manual

The text is organized in three main parts: I) General theory of photon migration; II) Analytic and semi-analytic solutions; and III) Validation of the solutions.

Part I

Part I introduces the whole book and describes the theories that will be used. This part ranges from Ch. 1 to Ch. 4.

- In Ch. 1, the general concepts and the physical quantities necessary to describe light propagation through absorbing and scattering media are introduced.
- In Ch. 2, the RTE and its main properties are described and discussed.
- In Ch. 3, the DE is derived starting from the RTE, and the reader is introduced to the general properties of the DE.
- In Ch. 4, the classic anisotropic diffusion equation (ADE) is derived from the anisotropic generalized RTE.

Part II

In part II, specific analytical and semi-analytical solutions derived from the theories presented in part I are carefully described. This part ranges from Ch. 5 to Ch. 14.

- Chapter 5 is devoted to solutions of the DE for homogeneous media.
- Chapter 6 is dedicated to ballistic and quasi-ballistic radiation and to a heuristic solution designed to model the effect of scattering in ballistic photon detection.
- Chapter 7 provides a general introduction to the calculation of the penetration depth in scattering media delivering analytical solutions for a diffusive slab.
- Chapter 8 focuses on the radial and lateral penetration depth in a homogeneous slab.

- Chapter 9 analyzes the detector-free propagation of light through a scattering and absorbing medium.
- Chapter 10 represents a special topic: hybrid solutions for a homogeneous slab, based on solutions of the RTE and the telegrapher equation.
- In Ch. 11, a solution of the DE for a two-layer medium is described.
- In Ch. 12, solutions for *N*-layered media are presented.
- In Ch. 13, solutions of the perturbed DE, when small defects are introduced into the medium, are obtained with the Born approximation.
- In Ch. 14, time-domain DE solutions for the Raman and the fluorescence signals are presented.

Part III

In part III, the obtained solutions are validated by means of comparisons with the results of reference MC simulations. This part ranges from Ch. 15 to Ch. 18.

- In Ch. 15, elementary MC methods typically utilized to describe photon migration in biomedical optics and, in general, in turbid media are presented.
- In Ch. 16, the different MC codes implemented to generate the reference data utilized to test the analytical and semi-analytical solutions proposed in this manual are carefully described in detail.
- Chapter 17 is dedicated to the validation of the solutions presented in part II. The validations are done by means of comparisons with the MC reference data of Ch. 16, and the results of the comparisons are described and discussed.
- In Ch. 18, the software included in 🔗 is described (MATLAB functions). The collection of MATLAB functions estimates almost all the solutions of photon transport presented in the manual. A large set of reference MC data (Excel *.xlsx format), which can be used as a standard reference, is also included in 🔗. Note that the old software named *Diffusion&Perturbation* together with the FORTRAN codes of the solutions of Ref. 1 can always be found in 🔗.

Beyond Photon Migration and Biomedical Optics

It is worthwhile at this point to conclude this preface by recalling that diffusive processes can be placed in a more general context that goes beyond biomedical optics. This fact may be better appreciated by noting that mathematical equations are in a way quite similar to words; i.e., they acquire their real meaning only when immersed in a precise context. This appears to be also the case for the DE. In fact, many media (agricultural products, wood, food, plastic materials, paper, pharmaceutical products, etc.) have optical properties at visible and/or near-infrared wavelengths for which light propagation in the diffusive regime can be established. Therefore, the same techniques used to study biological tissues can be applied to the monitoring of industrial processes, for quality control,[12–17] or in completely different fields.

Indeed, the theories presented in this manual, i.e., the RTE and the DE, arise from the more general transport theory.[18,19] Transport theory concerns the transport of "particles" through a "background medium" and is used in several applications where the transported particles and the host medium can have a very *different nature* and be represented by very *different physical quantities*. Thus, in general, the transport equation takes its sense depending on the physical phenomenon we want to describe. The advent of personal computers has made several numerical methods affordable to solve transport theory, and the availability of numerical solutions has further encouraged the use of this theory to solve a panoply of practical problems. The list of applications is surprisingly long and eclectic. Duderstadt and Martin[19] summarized for us some of the most relevant applications of transport theory:

> Neutron transport in nuclear reactors, Shielding of radioactive sources, Penetration of X-ray through matter, Brownian motion, Sound propagation, Propagation of light through the atmosphere, Propagation of light through stellar matter, Gas dynamics, Plasma dynamics, Transport of natural aerosols in the atmosphere, Diffusion of molecules in gases and fluids, Multiple scattering of electrons, Diffusion of holes and electrons in semiconductors, Photon transport through biological tissues, Transport of particles air pollution, Traffic flow, etc.

Thus, despite the different kinds of particles (neutrons, gas molecules, atoms of plasma, electrons, photons) or quantities that may be involved in the transport processes, all of these phenomena can be studied and described by using the same basic equation. When the transport process becomes diffusive, the transport equation can be simplified through the DE. Given a physical quantity u representative of the physical process studied (for instance, the particle density), whenever u is described by the equation

$$\frac{\partial}{\partial t}u(\vec{r},t) - k_1\nabla^2 u(\vec{r},t) + k_2 u(\vec{r},t) = 0, \tag{1}$$

we are dealing with a diffusive process. The coefficient k_1 is related to the spatial and temporal scale of the diffusive phenomenon studied, and the coefficient k_2 is related to the probability that the transported particles will be absorbed.

For example, for radiative transfer processes, k_1 will be related to the transport coefficient or diffusion coefficient of photons through the medium. For neutron transport processes, k_1 will be related to the transport coefficient of neutrons through the medium. For the diffusion of electrons and holes in semiconductors, k_1 will be related to the electrical conductivity. For the diffusion of molecules in gases, k_1 will be related to the transport coefficient of the molecules through the gas. The above equation with $k_2 = 0$ can be also used to describe the conduction of heat in solid isotropic materials, where u will be the temperature of the medium, and k_1 will be the thermometric conductivity of the substance, i.e., a material-specific quantity depending on the thermal conductivity, the density, and the specific heat of the substance.[20] The same equation is thus associated with very different physical concepts.

Usually, a diffusion process is associated with the random movement of a certain kind of particles. However, in some situations this is not so evident, as in the case of the physical diffusion of heat or the diffusion of fluids through porous materials.[21] This fact manifests the dichotomous nature of the diffusion process.[21] The dichotomous nature of diffusion theory has been noted by Narasimhan,[21] who showed how the equations of physical diffusion, i.e., Fourier theory of heat conduction,[22] and stochastic diffusion, derived from the Laplace theory of probability,[23] arose. Later, Albert Einstein obtained a single molecular-kinetic heat theory[24,25] wherein the equivalence between the diffusion coefficient of the physical process and of the random event was used. In physics, the work of Fourier inspired the use of the diffusion equation to study electricity phenomena, diffusion of molecules, and fluid flow.[21] The probability theory of Laplace inspired, at the end of the nineteenth century, scientists, economists, and statisticians to formulate a stochastic diffusion equation wherein the concept of probability density was used.[21] Given the high number of diffusion processes that can be observed in natural phenomena, we can view diffusion as a multi-fold theory that can assume very different physical meanings depending on the nature of the processes.

The above few examples and comments clearly show us that with the same mathematical tool different physical processes can be studied; however, given the intrinsic differences between the physical processes involved, each one requires a different physical interpretation of Eq. (1). These considerations want to emphasize that the solutions presented in this manual may have a quite larger field of use than that of tissue optics. Indeed, it is a characteristic of nature to show sometimes similar physical laws when processes involve different physical quantities.

We finally point out that the theories and solutions presented in this book have been obtained with reference to media illuminated by unpolarized light. However, the solutions are also applicable to media illuminated by polarized light, which commonly occurs when laser sources are used. In fact, multiple scattering randomly changes the polarization of scattered light so that light detected after a sufficiently large number of scattering events is completely depolarized. The previous state of polarization only remains near the source where photons arrive after a small number of scattering events. It has been shown with numerical simulations[26,27] and experiments[27] that when propagation occurs in the diffusive regime (i.e., when the solutions presented in this book become applicable), received photons have lost almost all traces of the initial state of polarization, and the results for polarized light become almost identical to those obtained for unpolarized light.

Thousands of papers on the diffusion of light have been published in scientific journals. For this reason, the references presented in this manual cannot *a fortiori* be exhaustive. Thus, we will mention only a few good introductory references, such as the monograph dedicated to the diffusion of light by Ripoll.[4] This reference, mainly refers to publications in the field of biomedical optics and more precisely to the field of NIRS and diffuse optical tomography. In order to have a more complete view of photon transport, we also suggest the reader to refer to other books on light propagation.[18,19,28–33]

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Chapter 1
Scattering and Absorption Properties of Turbid Media

THIS chapter clarifies the main framework under which this manual is developed. It provides the background for understanding the theories and solutions presented in the next chapters.

1.1 Approach Followed in This Manual

The collection of analytical solutions reported in this manual concerns the propagation of light through turbid media, such as biological tissues. Measurements on turbid media can be performed in the diffusive regime, where the photons have interacted many times so that the diffusion equation is a good approximation. Diffusive media are turbid media where photon propagation is measured in the diffusive regime; i.e., propagation is dominated by multiple scattering, and photons undergo many scattering events before being detected. In particular, the solutions presented in this manual describe how the energy (photons) propagates through turbid media in which light–matter interaction can be modeled with elastic or inelastic scattering, and absorption. Elastic scattering interaction deflects photons along new directions of propagation, but the energy of scattered photons, and their wavelength and frequency, remains unchanged. Inelastic scattering interaction affects both the direction and wavelength of the re-emitted photon. Absorption interaction causes the disappearance of photons.

The turbid media described in this manual are considered random media,[1,2] where absorption and scattering interactions can be treated through a proper definition of scattering and absorption coefficients of the medium. Media that have an extremely complex structure but are not necessarily random in the real sense of the word, can often also be mathematically described as random media. This is the case for many biological tissues. In practice, under the condition of random media, it is possible to provide a statistical description for both light propagation and media. Thanks to this

this manual allows one to suitably "describe" light propagation in the presence of inelastic scattering without needing to model the exact underlying physics.

1.2 Optical Properties of a Turbid Medium

The concepts of scattering and absorption coefficients are introduced by operative definitions based on their physical effects. In this way, like any physical quantity, these coefficients can in principle be measured by appropriate procedures.

1.2.1 The basic definitions

Light–matter interaction due to absorption is described by the absorption coefficient μ_a.

- The optical parameter μ_a is defined as the ratio between the power absorbed in the unit volume and the power incident per unit area; measured in mm^{-1}.

The interaction due to scattering is described by the scattering coefficient μ_s and by the phase function $p(\hat{s}, \hat{s}')$.

- The optical parameter μ_s is defined as the ratio between the power scattered in the unit volume and the power incident per unit area; measured in mm^{-1}.

The change in direction of the photon after a scattering event is described by $p(\hat{s}, \hat{s}')$.

- The scattering phase function $p(\hat{s}, \hat{s}')$, or simply the phase function, is defined as the probability density that a photon traveling in direction $\hat{s}$ is scattered within the unit solid angle around the direction $\hat{s}'$; measured in sr^{-1}.

As mentioned in the Preface, the theories and solutions presented in this manual pertain to media illuminated by unpolarized light, and so the scattering properties of the medium are introduced with reference to unpolarized radiation. In this case, if we consider spherical particles or randomly oriented non-spherical particles, the scattering function only depends on the scattering angle θ, i.e., the angle between directions $\hat{s}$ and $\hat{s}'$. So $p(\hat{s}, \hat{s}') = p(\hat{s} \cdot \hat{s}') = p(\cos(\theta)) \equiv p_\theta(\theta)$. The following normalization for the scattering phase function is thus assumed:

$$\int_{4\pi} p(\hat{s}, \hat{s}')d\hat{s}' = \int_0^{2\pi} \int_0^{\pi} p_\theta(\theta) \sin\theta d\theta d\varphi = 1. \tag{1.1}$$

heterogeneity and/or spatial correlations between the scatterers. These factors may generate anomalous light propagation on a macroscopic scale.[42]

In short, media structured with a fractal-like geometry represented by sudden changes of refractive indexes, have the right characteristics to generate an anomalous behavior for light transport. In the biomedical context, two tissues have these characteristics: human trabecular bone and lung. The trabecular bone is structured as a complex mineralized matrix surrounding an organic structure[3] with very different optical properties. It is also known that this structure has a fractal geometry.[43,44] The lung is constituted by a matrix of living tissue surrounding an intricate network of holes containing air,[3] clearly defining a fractal-like structure.[45] The presence of air in a scattering matrix recalls the appearance of a "Lévy glass"-like medium. Thus, for the moment we leave this as an open question, but these few lines show that particular care must always be taken when applying theoretical models to experimental data coming from biological tissues.

1.3 Statistical Meaning of the Optical Properties of a Turbid Medium

1.3.1 Mean free paths between scattering and absorption events

The optical properties of turbid media have a simple statistical meaning.[24,46] The scattering phase function $p(\hat{s}, \hat{s}')$ is defined as the probability that a photon traveling in direction $\hat{s}$ is scattered within the unit solid angle around the direction $\hat{s}'$. With the assumption of unpolarized radiation and an ensemble of scatterers that are spherical, or which are non-spherical but randomly oriented, the scattering phase function only depends on the scattering angle θ (obviously, the single scatterer must be made of isotropic material). The probability density functions $f_1(\theta)$ and $f_2(\varphi)$ for the angles θ and φ that specify the direction $\hat{s}'$, with reference to $\hat{s}$, are therefore simply given by

$$f_1(\theta) = 2\pi p_\theta(\theta)\sin(\theta) \tag{1.23}$$

and

$$f_2(\varphi) = \frac{1}{2\pi}, \tag{1.24}$$

where

$$\int_0^{2\pi}\int_0^{\pi} f_1(\theta) f_2(\varphi) d\theta d\varphi = \int_0^{2\pi}\int_0^{\pi} p_\theta(\theta)\sin(\theta) d\theta d\varphi = 1, \tag{1.25}$$

compatible with the normalization in Eq. (1.1).

In conclusion, the presence of scattering interactions progressively modify the characteristics of photon migration from the pure ballistic region (un-scattered radiation) up to the diffusive regime of propagation (multi-scattered radiation). The distinction between ballistic, quasi-ballistic, and non-ballistic photons cannot be exactly mathematically defined. In fact, the boundaries separating these different regimes depend on the considered physical context. In practice, we will see that these definitions serve, above all, as a mean to facilitate the description of specific problems, where the exact range of validity of these words naturally appears.

1.6 Examples of Diffusive Media

In this section, we provide some examples of diffusive media in daily life. In order to discuss diffusive media, we need a definition of the diffusive regime of propagation. As will be shown in Ch. 2, light propagation through turbid media can be described by the RTE. For many turbid materials, propagation can be described by a simpler but more approximate equation, the diffusion equation, for which relatively simple analytical solutions are available. Turbid media in which propagation can be described with good accuracy by the DE are named diffusive media. As will be shown in subsequent chapters, the conditions necessary to establish a diffusive regime of propagation for photons migrating from the source to the receiver depend both on the optical properties of the turbid medium and on the geometry. In Sec. 17.10, these conditions will be indicated for establishing a diffusive regime of propagation in homogeneous media: **(1)** $\mu_a/\mu'_s \lesssim 0.1$, **(2)** the volume of turbid medium $\gtrsim (10\ell')^3$, and **(3)** photons should have traveled paths with length $\gtrsim 4\ell'$, and the corresponding number of scattering events should be $\gtrsim 4/(1-g)$. When these conditions are satisfied, the largest part of radiation detected at distances $\gtrsim 2/\mu'_s$ is due to diffused photons, and solutions of the RTE based on the diffusion approximation can be therefore properly used for the analysis of experimental results.

At visible and/or near-infrared wavelengths, the condition $\mu_a/\mu'_s \lesssim 0.1$ is satisfied for many turbid materials, and a diffusive regime of propagation can therefore be established, provided their volume is sufficiently wide. By means of examples, we report here typical values for the optical properties of some turbid media observable in daily life.

Solid materials are often strongly scattering media and have a reduced scattering coefficient ≈ 1 mm^{-1}. This is the case for biological tissues and agricultural products. Measurements of the optical properties for biological tissue show a significant inter-subject variability and a dependence on the spectral range considered.[51] Typical values of μ'_s reported at near-infrared wavelengths range between ~0.5 and 1 mm^{-1} for muscle;[52–54] ~1 and 1.6 mm^{-1} for subcutaneous adipose tissue;[52,53,55] ~0.5 and 2.5 mm^{-1} for

Chapter 2
The Radiative Transfer Equation

As noted by Ishimaru,[1] two distinct theories have been developed to deal with multiple-scattering problems. One is based on Maxwell's equations, and the other is based on the radiative transport theory. The first theory starts from Maxwell's equations governing the electromagnetic field.[1] This theory is mathematically rigorous since, in principle, one can account for all the effects of multiple scattering within classical physics, including dependent scattering and dependent absorption, diffraction, and interference. A variety of analytical solutions for relevant scattering problems exists. Among them, the solutions for a sphere and for a cylinder and solutions of multi-spheres and multi-cylinders can be cited.[2] For complex geometries solutions of Maxwell's equations can be found by numerical procedures.[3–5] For instance, there are classical procedures such as the finite difference method and finite element method. Unfortunately, with theses numerical solutions the light propagation can be calculated only in small volumes (smaller than 1 mm^3) even when using high-performance computers. In addition, an enormous amount of information concerning the optical properties of the involved microstructure has to be known, with a resolution better than the light wavelength.

The radiative transfer equation (RTE) (also called the transport equation in other fields where the generic transport of particles is considered) is a phenomenological and heuristic theory describing the transport of energy through a scattering medium that lacks a rigorous mathematical formulation able to account for all the physical effects involved in light propagation. The RTE is actually obtained with the assumption that the intensities, not the fields, add up at a point in the medium. However, it has been demonstrated that under certain simplifying assumptions, the RTE can be derived from the electromagnetic theory of multiple scattering in discrete random media.[6–12] Solutions of the RTE have been compared with analytical solutions of Maxwell's equations, and a pretty good agreement was found between the two theories for relatively have the same unit difference. When we refer to the radiance as a general solution of the time-dependent or CW RTE, we have the same physical units [$Wm^{-2}sr^{-1}$] in both cases.

2.4 Probabilistic Interpretation of the Solutions

The Green's functions, i.e. the solutions obtained when unitary Dirac delta sources are considered, allow a useful interpretation of the solutions of the RTE in terms of probability density functions to detect photons. This interpretation is largely employed when studying real problems. Intuitively, if a unitary source is injected inside the medium, then the light detected at any point of the external boundary must obviously be a fraction of the source intensity (a value between 0 and 1). This fact can be used to represent the detected light (usually the photons flux) as the probability per unit surface and per unit time to detect photons. In this section, the concept of detection probability is at first introduced in general, and then the results are applied to the special case of a unitary source.

Let's consider a medium of volume V, delimited by a boundary Σ, containing a distribution of sources (they can also be on the boundary, but generated photons must always go into the medium) that at time zero are switched on for a finite time Δt (the light intensity does not need to be constant during Δt). The solution of the RTE, $I(\vec{r}, \hat{s}, t)$, allows one to calculate the solution for the photon flux, $\vec{J}(\vec{r}, t)$, according to Eq. (2.8). Moreover, the term $\mu_a I(\vec{r}, \hat{s}, t) d\vec{r} d\hat{s} dt$ gives us the energy extracted by absorption in $d\vec{r}$, $d\hat{s}$, and dt around $(\vec{r}, \hat{s}, t)$ (see Sec. 2.2.1). Now, the total energy E produced by the sources during a time Δt, must be equal to the total flux of energy, E_Σ, passing through Σ, plus the energy, E_A, absorbed in V, i.e.,

$$E = E_\Sigma + E_A. \ [\mathrm{J}] \tag{2.22}$$

By denoting $\hat{q}(\vec{r})$ the unit vector normal to Σ, at point $\vec{r} \in \Sigma$ directed outward we can express

$$E_\Sigma = \int_0^{+\infty} dt \int_{\vec{r} \in \Sigma} \vec{J}(\vec{r}, t) \cdot \hat{q}(\vec{r}) dS, \tag{2.23}$$

where $dS \subset \Sigma$ is a small surface around $\vec{r} \in \Sigma$, and

$$E_A = \mu_a \int_0^{+\infty} dt \int_V d\vec{r} \int_{4\pi} I(\vec{r}, \hat{s}, t) d\hat{s} = \mu_a \int_0^{+\infty} dt \int_V \Phi(\vec{r}, t) d\vec{r}. \tag{2.24}$$

Note that the above time integrals go from 0 to $+\infty$ (i.e., a time larger than Δt) to ensure that, after the source is switched off, all of the photons have enough

$$I_2(\vec{r}, \hat{s}_2) = R_{21}(\theta_2)I_0 + (1 - R_{21}(\theta_2))\left(\frac{n_2}{n_1}\right)^2 I_1(\vec{r}, \hat{s}'_1)$$
$$\forall \vec{r} \in \Sigma \text{ and } -1 \leq \hat{s}_2 \cdot \hat{q} \leq 0. \tag{2.92}$$

It can be verified that a solution of the RTE in a non-absorbing medium, i.e., a solution of Eq. (2.88), with boundary conditions of Eqs. (2.91) and (2.92) can be written as

$$I_1(\vec{r}, \hat{s}_1) = \left(\frac{n_1}{n_2}\right)^2 I_0; \qquad \forall \hat{s}_1 \text{ and } \vec{r} \in V,$$
$$I_2(\vec{r}, \hat{s}_2) = I_0; \qquad \forall \vec{r} \in \Sigma \text{ and } -1 \leq \hat{s}_2 \cdot \hat{q} \leq 0, \tag{2.93}$$

where $I_1(\vec{r}, \hat{s})$ is the internal radiance, and $I_2(\vec{r}, \hat{s})$ is the radiance leaving the boundary Σ. In fact, a constant radiance verifies Eq. (2.88). On the other hand, the constant value of Eq. (2.93) gives a radiance in agreement with the boundary conditions of Eqs. (2.91) and (2.92). We note that in Eq. (2.93), $\vec{r}$ positioned at the surface Σ means that the boundary is approached from the non-scattering medium. Given the above solutions for the radiance, it is possible in a straightforward way to also obtain solutions for the fluence rate and the photon flux.[26]

The internal radiance is thus uniform and isotropic, and its value is determined by the incoming radiance I_0 and by the refractive index mismatch between the internal (1) and external (2) medium. Also, the re-emitted radiation is uniform with a Lambertian distribution and with an intensity identical to the incoming radiance, i.e., $I_2(\vec{r}, \hat{s}) = I_2(\vec{r}, \hat{s}')$.

The obtained solution gives a full prediction of the radiance inside the medium and at its boundary Σ. This fact will be useful to predict the important invariance properties of the RTE described in Sec. 2.7.6.

2.7 Properties of the Radiative Transfer Equation

The general properties of the RTE are of great help when explicit solutions of this integro-differential are sought. The primary place is occupied by the scaling properties of the solutions, that are invariance properties under various types of coordinate transformations. Secondly, the reciprocity principle in radiative transfer is considered. Then, the particular dependence of the RTE solutions on absorption also represents information often used to solve the RTE with the typical scaling relationships of the RTE solutions with absorption.

This section is mainly dedicated to these points, with a final section dedicated to the mean chord theorem and to the invariance property of mean pathlength in scattering non-absorbing media.

method,[72] with the finite element method,[19,66,73–80] or others such as the discrete ordinates method,[19,81–83] the spherical harmonics method,[19,68,84] the finite difference method,[85] the integral transport methods,[19] and the path integral method.[86] Among the numerical procedures there are also stochastic methods such as the MC,[87] which is largely used to reconstruct solutions of the RTE.[19,68,88]

The several numerical methods used to treat the RTE are a consequence of the high complexity of this equation, and simpler approximate models are usually sought.[75,76,89–91] When propagation is dominated by multiple scattering, the most widely and successfully used model employs the diffusion approximation to yield a variety of solutions for both steady-state and time-dependent sources.[92–95] The diffusion equation is a parabolic-type partial-differential equation primarily applied in several physics fields. In the next chapter, its derivation from the RTE will be reviewed and discussed.

Notwithstanding the complexity of the RTE, recently relevant analytical solutions of the RTE were obtained for the infinite scattering medium by applying the P_N method and the method of rotated reference frames.[28,96–100] Solutions for semi-infinite (or slab) media were reported for refractive-index matched boundary conditions.[97,101] Recently, the radiative transport equation was solved for the case of semi-infinite media and mismatched boundary conditions.[102] The obtained solutions of the radiative transport equation were, furthermore, validated by comparison with the results obtained by Monte Carlo simulations.[103] This model was, in addition, applied to the spatial frequency domain.[104] Also in this domain, the derived analytical solutions were successfully verified against numerical solutions. Recently, analytical solutions of the layered geometry were found in all relevant measurement domains and for scattering media exhibiting fluorescence, and reported in Ref. 105. These developments have opened the possibility to have available analytical solutions of the RTE with a significant impact on future applications in biomedical optics.

2.10 Anisotropic Media and Anomalous Radiative Transport

2.10.1 Anisotropic media

In this introductory manual, we will mainly consider media for which it is assumed that the light scattering coefficient and the scattering phase function are independent of the light's incident direction.[1,8,106] However, we must be aware that many real media have an aligned microstructure that causes an anisotropic light propagation; examples include liquid crystals,[107–110] textile materials,[111] and biological tissues such as skin,[112,113] dentin,[114] muscles,[115,116] and wood.[117]

In the literature, the anisotropic diffusion theory is used often to describe the light propagation in these particular scattering media.[107,109,110,118–123] The

Chapter 3
The Diffusion Equation for Light Transport

THE diffusion equation (DE) for describing light transport in highly scattering media is an approximated theory obtained from the RTE under the hypothesis that detected light is subjected to a high number of scattering interactions and few absorption events. Under these conditions, a simplified expression for the exact radiance can be used, yielding the DE that represents the most widely used approach to the study of photon migration through highly scattering media, i.e., media in which the light propagation is dominated by multiple scattering. In this chapter, the main framework of this theory is reviewed. This chapter is focused on the diffusion of light; however, the theory here can be in principle extended to any diffusion process that may involve different kinds of particles.

3.1 Diffusion Equation and History

The DE has become one of the most used equations in applied science, and it is related to different kinds of physical phenomena. The main advantage of this theory is the relatively simple form of the equation, offering a large number of analytical solutions as testified by dedicated monographs[1–3] and the huge number of papers dedicated to the solutions of this equation (for an incomplete list, see the references of Ch. 5). The use of the DE crosses different research fields, and its origin goes back to the nineteenth century with the work of scientists such as Fourier,[4] Brown,[5] Laplace,[6] and Fick,[7,8] related to the heat equation, Brownian motion, stochastic diffusion and liquid diffusion, respectively. The very origin of the theory is in the works by Fourier and Laplace.[4,6] Laplace in his work introduced a partial differential equation, usually known as Laplace's equation, that, as noted by Narasimhan,[9] is in practice the first version of the DE that can be found in literature.[6] Laplace was probably inspired by the work of Fourier on the heat equation since he was one of the reviewers of Fourier's monograph on that subject in the first where k_o is a real constant that depends in a complex manner on μ_a (and also on μ_s and g). The exact expression for k_o has been proposed, e.g., in Ref. 33 (appearing in a form not so obvious to recognize). Note that Eqs. (3.25) and (3.26) represent a well-tested and more practical approximation of the k_o found in Ref. 33, and thus we may also write

$$D_{CW} \approx D_{RTE}. \tag{3.34}$$

To summarize, it clearly appears in this section that a modal analysis of the RTE allows us to demonstrate that the diffusion coefficient for the time-dependent DE does not depend on μ_a [Eq. (3.32)], whereas the diffusion coefficient for the time-independent DE is μ_a-dependent [Eq. (3.33)]. This result is obtained because *two different hypotheses must be made* to derive D_{TD} and D_{CW} with the corresponding DE. In the first case (D_{TD}), large scales of space and time must be considered, whereas in the second case (D_{CW}), only the condition of a large space scale is necessary. Thus, the two different hypotheses imply two different results. The practical consequence is that it is not sufficient to integrate the time-dependent solution for $\Phi(z, t)$ to obtain the time-independent solution $\Phi(z)$. A substitution of the diffusion coefficient D_{TD} with the parameter D_{CW} is also necessary. Note that contrary to the results in Ref. 34, and to be coherent with the physical units of this manual, the parameter v does not appear in Eqs. (3.32) and (3.33).

As previously explained, when working on typical biological tissues (e.g., bone, muscle, brain) in the red and infrared wavelength range, the difference between D_{TD} and D_{CW} is often small, and thus the parameter D_{TD} can be used in general. Of course, suitable experimental or MC tests must be performed to check unclear situations. This is what is done methodically in the present manual (see part III).

3.5 Properties of the Diffusion Equation

The DE shows some general properties like the RTE.

3.5.1 Scaling properties

Following the same procedure used to obtain Eq. (2.94), it is possible to show that if $\Phi(\vec{r}, t)$ is the solution of the DE with a Dirac delta source $\varepsilon_0(\vec{r}, t) = \delta(\vec{r})\delta(t)$ for a homogeneous diffusive medium characterized by μ_s' and μ_a, then $\overline{\Phi}(\bar{\vec{r}}, \bar{t})$, defined as

$$\overline{\Phi}(\bar{\vec{r}}, \bar{t}) = \left(\frac{\overline{\mu}_s'}{\mu_s'}\right)^3 \Phi(\vec{r}, t), \tag{3.35}$$

Chapter 4
Anisotropic Light Propagation

In this chapter, we will derive the classic anisotropic diffusion equation (ADE) from the anisotropic generalized RTE described by Eq. (2.205). Various mathematical approaches can be followed to obtain the ADE from the anisotropic GRTE. Here, we have chosen a relatively simple one, proposed by Vasques and Larsen,[1] and based it on two assumptions/rules.

The first assumption states that

- The solution $I_\ell(\vec{r}, \hat{s}, \ell)$ of the anisotropic GRTE [Eq. (2.205)] can be approximated by means of an asymptotic expansion.[2]

In other words, $I_\ell(\vec{r}, \hat{s}, \ell)$ can be expressed as

$$I_\ell(\vec{r}, \hat{s}, \ell) \asymp \sum_{n=0}^{+\infty} \epsilon^n I_\ell^{(n)}(\vec{r}, \hat{s}, \ell) \quad \text{for } \epsilon \ll 1\,, \tag{4.1}$$

where the symbol $\asymp$ is an equality in the asymptotic sense. In practice, the index n will not be taken to $+\infty$, but only to a given N, depending on the desired approximation order. By substituting Eq. (4.1) in the anisotropic GRTE and by equating the terms of the same order in ϵ, we obtain a set of N equations that, theoretically, can be solved to obtain the wanted $I_\ell^{(n)}(\vec{r}, \hat{s}, \ell)$. However, this procedure does not yet contain the constraints defining the diffusive regime (see Sec. 3.2) and thus simplifying the anisotropic GRTE. These constraints must now be included. To do so, use the following rule:

- Multiply by ϵ^n, with $n > 0$, the terms in the anisotropic GRTE [Eq. (2.205)] that provide little contribution in the energy balance. Multiply by ϵ^n, with $n < 0$, the terms in the anisotropic GRTE [Eq. (2.205)] that provide a large contribution in the energy balance. The value of n depends on the estimated "importance" of the considered term.

For example, the term in the anisotropic GRTE describing the scattering phenomenon will be multiplied by ϵ^n with $n < 0$, while the term describing the

Chapter 5
Solutions of the Diffusion Equation for Homogeneous Media

IN this chapter, an overview of solutions of the diffusion equation for homogeneous geometries is provided. Green's functions for the infinite medium, the laterally infinitely extended slab, the semi-infinite medium, the parallelepiped, the infinite and finite cylinder, and the sphere are presented. The solutions are obtained with the method of images, the eigenfunctions method, the integral transform method, or the separation of variables method. The solutions of the DE are approximate solutions of the RTE. Information on the accuracy of the solutions can be obtained from comparisons with the results of MC simulations that will be presented in Ch. 17.

5.1 Solution of the Diffusion Equation for an Infinite Medium: Separation of Variables and Fourier Transform Method

The infinite medium is a relevant geometry for photon migration, since it is the reference geometry when studying approximated theories of photon migration. In an infinite medium, photon migration occurs in the most general conditions without restrictions due to boundary effects. For this reason, when approximate theories such as the diffusion equation are used in this geometry, the effects of the approximations show their intrinsic properties and can be studied in all generality. Moreover, several solutions in more complex geometries are based on the solution for the infinite geometry.[1–4] In addition, some applications directly use the solutions for the infinite geometry.[5] Thus, the infinite medium represents a fundamental tool necessary for the comprehension of photon transport in any type of turbid medium.

Let us consider an infinite homogeneous medium characterized by absorption coefficient μ_a, reduced scattering coefficient μ'_s, and diffusion

$$D_M \nabla^2 \psi(\vec{r}) - \mu_a \psi(\vec{r}) = -\frac{\mu_s}{\mu_t}\delta(\vec{r}). \tag{5.40}$$

By considering the spherical symmetry of the problem and expressing Eq. (5.40) in spherical coordinates, we then obtain

$$D_M \left[\frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2 \frac{\partial \psi(r)}{\partial r}\right)\right] - \mu_a \psi(r) = -\frac{\mu_s}{\mu_t}\frac{\delta(r)}{2\pi r^2}. \tag{5.41}$$

Finally, by applying the Fourier transform [Eq. (5.38)] for radially symmetric functions to Eq. (5.41), we recover the DE, i.e., Eq. (5.39). This means that the solution of Eq. (5.39) in the spatial domain, i.e., $\psi(r)$, is also the solution of Eq. (5.41) for *a problem with spherical symmetry*, a solution that we already know from the classical DE. In fact, after comparing Eq. (5.40) with Eq. (3.20), it can be noted that they differ by the single-scattering albedo μ_s/μ_t multiplying the source term. This gives again Eq. (5.36), as expected.

Complete solution: The complete solution $\Phi(r)$ can thus be expressed as [Eqs. (5.20) and (5.36)]

$$\Phi(r) = \phi_0(r) + \Phi_d(r) \approx \phi_0(r) + \psi(r) = \frac{e^{-\mu_t r}}{4\pi r^2} + \frac{\mu_s}{\mu_t}\frac{1}{4\pi}\frac{e^{-\sqrt{\frac{\mu_a}{D_M}}r}}{D_M r}. \tag{5.42}$$

5.3 Solution of the Diffusion Equation for a Slab: Method of Images

The problem of light propagation through random media bounded by parallel planes has been a subject of interest for decades because many physical systems are likely to be represented in this way.[27–32] The slab is used, for example, for applications of the radiative transfer in the atmosphere[28,30,33–36] and in biological tissues.[1–3,17,31,32,37–43] For this reason, the solutions for the slab are widely used in photon migration studies.

To obtain the solutions reported in this section and in Sec. 5.3.2, we follow the so-called "method of images" (or mirror images)[27,44,45] that is commonly used for the slab.[1–4,17] Actually, the method of images is a very general method widely applied in electro-magnetism. In the present context, we apply the method to the particular case of diffusion of light. The method of images can be used equally in combination with the zero boundary condition (ZBC[1,2]) or the extrapolated boundary condition (EBC[3,4,17,46]). The ZBC assumes that the fluence equals 0 on the physical boundary of the diffusive medium. The EBC assumes the that the fluence equals 0 (Sec. 3.7.1) at the extrapolated surface at distance $2AD$ [Eq. (3.50)] from the physical boundary (EBC). The advantage of the EBC is that, thanks to the term A, it can account for a possible refractive index mismatch. In the following examples, only the EBC will be used. Further, the EBC is intrinsically more accurate than the

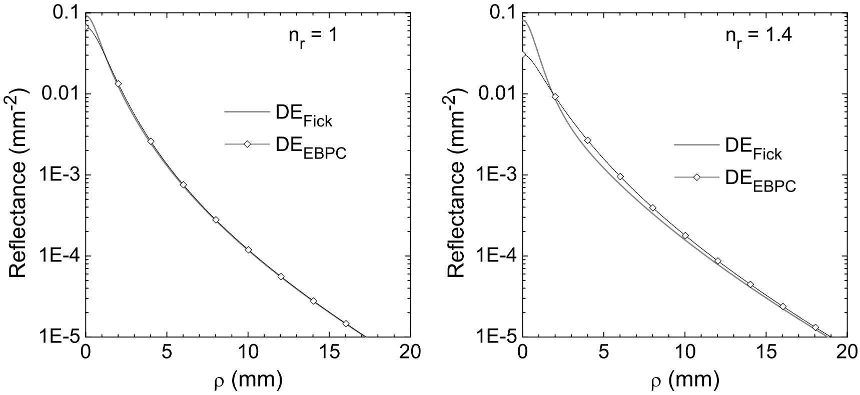

Figure 5.10 CW reflectance from a slab with $s = 40$ mm, $\mu_s' = 1\ \text{mm}^{-1}$, $\mu_a = 0.01\ \text{mm}^{-1}$, $z_s = 1$ mm, and $n_i = 1.4$. Comparison between results obtained using the Fick and EBPC approaches for matched ($n_r = 1$) and mismatched ($n_r = 1.4$) refractive indexes.

the expression of the fluence obtained with the EBC [Eq. (5.44)]. r_3 is independent of the source-receiver distance and $\lim_{t\to+\infty} r_3 = 1$.[58,64] Moreover, r_3 for typical values of the optical properties of biological tissue differs from 1 by a negligible amount if the early times are excluded. Therefore, the differences between PCBC and EBC are confined to the initial part of the temporal range. In Refs. 58 and 64, the ratio $r_4 = R_{PCBC}/R_{DE_{Fick}}$ was also studied, showing that $\lim_{t\to+\infty} r_4 = 1$, while for early times, when the time variation of the photon flux is very strong, r_4 differs from 1 significantly more than r_3. Thus, for long times, all the different expressions used to describe the outgoing flux tend to give the same description against time, whereas for early times, the use of Fick's law with the EBC shows different behavior with respect to the other expressions obtained with the PCBC and the EBPC.

5.8 Analytical Green's Function for a Parallelepiped

In this section, we present the Green's functions for the parallelepiped, both for the time domain and the continuous-wave domain.

5.8.1 Time domain

We consider a diffusive parallelepiped of dimensions L_x, L_y, and L_z with a spatial and temporal isotropic Dirac delta source with a unitary strength at $\vec{r}_s = (x_s, y_s, z_s)$, as shown in Fig. 5.11. The procedure used in Sec. 5.3 for the slab, based on the method of images and on the extrapolated boundary condition, is extended to three dimensions to obtain the solution for the parallelepiped.[4] Thus, instead of an infinite line of positive and negative point sources, a three-dimensional lattice of positive and negative point sources is

$$R_{beamEBPC}(\vec{r},\, t) = \frac{v\mu_s'}{A\pi a'^2 s'} \sum_{n=1}^{\infty} \sum_{l=1}^{\infty} \frac{J_0(\rho\lambda_l)}{J_1^2(a'\lambda_l)} \sin(K_n z_e) \frac{1}{(\alpha_{ln}^2 + \beta_n^2)}$$
$$\times \left\{ \exp(\alpha_{ln} s)[\alpha_{ln} \sin(K_n(s + z_e)) - K_n \cos(K_n(s + z_e))] + \right.$$
$$\left. - [\alpha_{ln} \sin(K_n z_e) - K_n \cos(K_n z_e)] \right\}$$
$$\times \exp[-(\lambda_l^2 + K_n^2) D v t] \exp(-\mu_a v t). \tag{5.163}$$

The calculation of the above formulas shows for the higher values of the indexes l and n some computational problems when the value of $\exp(\alpha_{ln} s)$ becomes larger than the limit value supported by the software used. At the moment, this fact may be a limitation in the real use of these formulas. The propagation of the light beam through the cylinder is characterized by the survival at the largest depth s of a residual of ballistic photons. Their effect on the energy balance has not been accounted for because it is usually negligible for sufficiently thick cylinders. The above formulas can become preferable in terms of accuracy to the DE solutions obtained by approximating the pencil beam to an isotropic source when the effect of such approximation is significant. This happens at very early times and short source–detector distances.

5.12 Ohm's Law for Light

In this section, the CW DE solutions for the total transmittance and reflectance from a diffusive slab are presented for different kind of light sources and slabs. One of the main purposes here is to introduce an Ohm-like law for light[60,69] that holds for the total CW transmitted light through a diffusive non-absorbing slab. This result stands out for its simplicity and establishes a similitude between the diffusion of photons in highly scattering materials and the diffusion of electrons in conductors so that they obey the same attenuation law. Like any approach based on the diffusion equation, Ohm's law for electrons is only an approximation. More exact results should be obtained by a transport equation for electrons in conductors.[70]

5.12.1 Isotropic source case

In Sec. 5.3.2, we obtained the solution for the total transmittance by the method of image sources for an isotropic source placed at $\vec{r}_s \equiv (0,\, 0,\, z_0)$, i.e., Eq. (5.73). The analytical form of this solution, given by an infinite series, does not allow it to be intuitively interpreted as a kind of Ohm's law for the transmitted light. To show the Ohm-like behavior, it is useful to exploit the

Chapter 6

Ballistic and Quasi-Ballistic Radiation

At the opposite of the diffusive regime of light propagation in scattering media, there is the ballistic regime. The intent of this chapter is to provide the basic solutions for the ballistic and quasi-ballistic regime of propagation[1,2] and a model for their detection in a collimated transmittance configuration. The ballistic regime shows complementary characteristics compared to the diffusive regime. The analysis of ballistic radiation is paradigmatic for understanding the complementary peculiarities of the diffusive regime and to describe the transition from ballistic light to diffusive. In the diffusive regime, radiance expresses a quasi-isotropic angular distribution, but in the ballistic regime, photons move along their initial direction of propagation. These complementary characteristics of ballistic and diffusive photons reveal the need of studying ballistic solutions for a complete understanding of photon migration in radiative transfer processes where often ballistic and diffusive photons coexist. A distinction between ballistic and diffusive photons is particularly required in applications based on ballistic detection. Ballistic light, by definition, is directly linked to the extinction coefficient of the medium, and for imaging purposes, the photons' paths can thus be precisely identified without resorting to complex reconstruction techniques.[3–6] Therefore, measurements of ballistic light are largely used in spectrophotometric applications aimed to extract information from the extinction coefficient of the medium and in imaging applications for media with small optical thicknesses (see Chapters 7 and 8 of Ref. 1 for some examples of applications). For these reasons, the study of ballistic radiation is an important part of photon migration in scattering media.

6.1 Solution of the RTE for Ballistic Radiation

In this section, the general solutions of the RTE for ballistic radiation are derived for a pencil beam and an isotropic source of unitary strength in an unbounded medium.

Chapter 7
Statistics of Photon Penetration Depth in Diffusive Media

DEPTH information is implicitly included in any theory of photon migration, and it regards, e.g., the maximum or the average depth probed by the detected light. In biomedical optics applications, the penetration depth can be extremely useful, since it can help to define the part of tissue actually probed by the measurements. Historically, the statistics of photon penetration depth is a topic of great interest.[1–16] In this chapter, we provide a comprehensive view of the subject, describing the penetration depth of light in random and diffusive media for the TD and CW domains. The main frame of the theory is provided by the RTE, and then explicit analytical formulas are derived for diffusive media by using the DE. This theory exploits the concept of pdf $f(z|\rho, t)$ for the maximum depth reached by the photons that are eventually re-emitted from the surface of the medium at distance ρ and time t. Analytical formulas for f, the mean maximum depth $\langle z_{\max}\rangle$, and the mean average depth $\langle \bar{z}\rangle$ reached by the detected photons at the surface of a diffusive slab are derived within the framework of the DE, in the TD and CW domains. Validation of the theory, by means of comparisons with the results of Monte Carlo simulations, will be presented in Ch. 17, which is dedicated to validations. The analytical formulas presented in this chapter are of interest for many research fields such as biomedical optics,[17] advanced microscopy[18], and disordered photonics.[19]

7.1 Statistics of Photon Penetration Depth inside an Infinite Laterally Extended Slab

The general framework of the theory presented in this section holds within the RTE. The theory is first addressed without reflections at the external boundary of the slab (matched refractive index between slab and external medium) and then generalized to the case of refractive index mismatches at the external boundary.

Chapter 8
Statistics of Transversal Penetration Depth in the TD

In this chapter, the concept of longitudinal penetration depth is extended to the transversal dimension of a laterally infinite homogeneous slab. Thus, a statistical tool is provided to study how light penetrates the lateral dimensions (x or y) of a scattering medium when a pencil beam impinges on it. The radial (transversal with a cylindrical symmetry r) penetration depth is also addressed in an infinite homogeneous medium that represents its natural geometry of analysis. The approach adopted is an extension of the content of Ch. 7. Therefore, the text will address the maximum radial penetration depth or the maximum lateral penetration depth. In the literature, while several publications dedicated to the longitudinal penetration depth can be found,[1–16] to the extent of our knowledge, investigations dedicated to the transversal (radial or lateral) penetration depth are not available.

8.1 Statistics for the Radial Penetration Depth in a Laterally Infinite Slab

The radial penetration depth is addressed by comparing the changes in reflectance from a finite cylinder, when its radius is increased by an infinitesimal quantity, to the reflectance from an infinitely extended slab of the same thickness. The ratio of these two quantities characterizes the light radially propagated through the slab. Thus, we will see that by means of such comparison and of the approach developed in the previous chapter it is possible to statistically define the radial penetration depth of the detected light. This study is carried out in the TD.

The maximum radial penetration depth in a laterally infinitely extended slab of thickness s_0, reduced scattering coefficient μ_s', and absorption coefficient μ_a is considered. The light source is a pencil beam impinging perpendicularly on the top cover of the slab (i.e., at the axis origin, along the z axis). To account for the light propagation through the radial dimension of difference between $\langle r_{\max}|\rho = 0, t\rangle|_{DE}$ and $\langle z_{\max}|t\rangle_{DE}$ is roughly within 12%. The process of photon penetration in the radial direction follows a similar behavior to that in the longitudinal direction of the semi-infinite medium.

8.2 Statistics for the Lateral Penetration Depth in a Laterally Infinitely Extended Slab

In analogy to the radial penetration depth, the approach of Sec. 8.1 is here applied to the lateral penetration depth. For this purpose, we consider a parallelepiped (in place of the cylinder) and an infinitely extended slab of the same thickness s_z. Following this approach, the pdf for the maximum lateral penetration depth can be defined.

The maximum lateral penetration depth in a laterally infinitely extended slab of thickness s_z, reduced scattering coefficient μ_s', absorption coefficient μ_a, where a pencil beam impinges perpendicularly (along z axis) to the entrance surface of the slab, is considered. To account for the light propagation through the lateral dimensions of the slab, a homogeneous parallelepiped of thicknesses s_x, s_y, and s_z (see Fig. 8.3), with its main z axis at half the distance between source and receiver ρ, is drawn inside the slab. The lateral penetration depth can be defined for both the lateral directions x and y. The fraction of outgoing photons at time t and distance ρ from the source with maximum lateral penetration $x_{\max}$ between x and $x + \Delta x$ is

$$\frac{R_{paral}(s_x = 2(x + \Delta x),\, s_y,\, s_z,\, \rho,\, t) - R_{paral}(s_x = 2x,\, s_y,\, s_z,\, \rho,\, t)}{R_{slab}(s_z,\, \rho,\, t)}, \qquad (8.17)$$

where $R_{paral}(s_x = 2x,\ s_y,\ s_z,\ \rho,\ t)$ is the reflectance from a parallelepiped of thickness s_z, dimension $s_x = 2x$ in direction x, and s_y is in direction y. In analogy to Sec. 8.1, we can define $R_{paral}(s_x = +\infty,\ \ s_y = +\infty,$

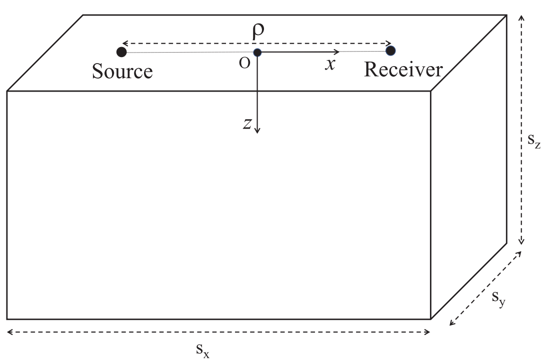

Figure 8.3 Schematic for studying the lateral penetration depth. It is considered a parallelepiped with the z axis at half the distance between source and receiver.

Chapter 9
Average Photon Distance from Source and Relative Moments

In this chapter, the *detector-free* propagation of light through a scattering and absorbing medium is analyzed. The term *detector-free* propagation refers here to the propagation of light undergoing scattering and absorption interactions, not restricted only to light detected by specific detectors. This makes a distinction with the analysis generally done in this book that usually refers to the detected light in a particular detector. This study involves the analysis of all emitted photons from the source, and thus it provides an overview of the evolution of the cloud of photons through the space. In this chapter, the general case of the infinite scattering medium will be addressed, and finally a view of the slab geometry will be provided. The knowledge of the photon fluence rate gives information about the energy density distribution inside a scattering and absorbing medium. The concept of TD and CW photon fluence rate, i.e., $\Phi(\vec{r}, t)$ and $\Phi(\vec{r})$, is exploited to express general statistical relationships, such as the mean displacement and the mean square displacement of photons from the source and the mean penetration depth regarding the *detector-free* photon migration through an infinite medium and a slab.

9.1 Statistical Relationships: Displacement of Photons from the Source in an Infinite Homogeneous Medium

This section examines how photons move away from an isotropic point-like source in an infinite medium. Therefore, the positions of all the emitted photons are considered, and the analysis is not simply restricted to those that reach a specific receiver. Analytical expressions for the average distances $\langle r \rangle(t)$ (mean displacement) and the average square distance $\langle r^2 \rangle(t)$ (mean squared displacement), where the photons can be found at time t, have been obtained. Analytical formulas for the CW average distances $\langle r \rangle(\mu_a)$ and average square distances $\langle r^2 \rangle(\mu_a)$ are also obtained. The intent of this section is to obtain

For symmetry reasons, when considering a point-like source inside an infinite medium, the above results for the penetration depth along z can also be considered valid for the penetration depth along x and y, which will be $\langle|x|\rangle(t) = \langle|y|\rangle(t) = \langle|z|\rangle(t)$.

9.2.2 Mean penetration depth in the CW domain

To obtain $\langle|z|\rangle(\mu_a)$ and $\langle z^2\rangle(\mu_a)$ also for the CW domain, or in general for $\langle|z|^n\rangle(\mu_a)$, the pdf $U(z, \mu_a)$ for the penetration, is needed. By using the same reasoning employed in previous sections 9.1.2 and 9.2.1, $U(z, \mu_a)|_{DE}$ in the diffusion approximation can be written as

$$U(z, \mu_a)|_{DE} = \mu_a \Phi_{DE}(z, \mu_a) = \frac{1}{2}\mu_{eff} \exp(-\mu_{eff}|z|). \tag{9.42}$$

It is straightforward to verify that $\int_{-\infty}^{\infty} U(z, \mu_a)|_{DE} dz = 1$.

The different moments can be calculated as

$$\begin{aligned} \langle|z|^n\rangle(\mu_a)|_{DE} &= \int_{-\infty}^{\infty} |z|^n U(z, \mu_a)|_{DE} dz \\ &= 2\int_0^{\infty} z^n \frac{1}{2}\mu_{eff} \exp(-\mu_{eff} z) dz = \frac{n!}{\mu_{eff}^n}. \end{aligned} \tag{9.43}$$

In particular,

$$\langle|z|\rangle(\mu_a)|_{DE} = \frac{1}{\mu_{eff}}, \tag{9.44}$$

$$\langle|z|^2\rangle(\mu_a)|_{DE} = \frac{2}{\mu_{eff}^2}. \tag{9.45}$$

Thus, the inverse of μ_{eff} represents the average penetration depth of detector-free propagation through an infinite medium where a CW point source is injected. Recalling the value calculated for $\langle r^n\rangle(\mu_a)$, it is interesting to show that

$$\frac{\langle|z|^n\rangle(\mu_a)|_{DE}}{\langle r^n\rangle(\mu_a)|_{DE}} = \frac{1}{n+1}. \tag{9.46}$$

9.3 Penetration Depth for all Photons Propagating through a Slab

The *detector-free* propagation can also be studied in bounded geometries such as the slab. Following a similar approach to that used for the infinite medium

Chapter 10
Hybrid Solutions of the Radiative Transfer Equation

BESIDES the approximate solutions of the RTE obtained by making use of the DE, few analytical solutions are available for studying light propagation through highly scattering media. In order to solve the RTE without simplifying assumptions, we have to resort to numerical methods. These methods convert the integral form of the transport equation into a system of algebraic equations that can be treated numerically by using a computer. The finite element method, the discrete ordinates method, and the spherical harmonics method are examples of numerical procedures for reconstructing solutions of the RTE.[1–7] Among the numerical procedures, there are also statistical methods like the MC method,[1,8] which offers a way to simulate the physical propagation of photons in scattering media. With the MC method, the physical quantities that describe photon migration, such as the flux and the fluence rate, are calculated after running a large number of photon trajectories. The MC can be considered a numerical method to solve the RTE even though the equation itself is not implemented in the code, as is usually done in other numerical methods.

Approximate analytical solutions subjected to similar limitations of those of the DE are also obtained with a random walk method.[9–12]

Solutions based on the DE are affected by the intrinsic approximations of this theory that show different consequences for steady-state and time-dependent sources. For steady-state sources, solutions based on the DE cannot describe photons detected at short distances.[8,13] For time-dependent sources, DE solutions provide a poor description of early received photons since the DE is well established only for photons undergoing many scattering events.[14]

The limitations of the DE can present a serious problem in modeling photon migration, especially when small volumes of diffusive media are considered. To overcome these limitations, several improved solutions of the DE have been proposed.[13,15–26] For this reason, the availability of analytical unscattered radiation, there is a logarithmic singularity due to radiation that has undergone a single forward-scattering event. This singularity, explicitly mentioned in the work of Paasschens,[27] has been denoted as a tail of the ballistic peak.

10.2.2 Heuristic time-resolved Green's function of the RTE for an infinite medium with non-isotropic scattering

When an infinite medium with a non-isotropic scattering phase function is considered, Eq. (10.9) cannot be rigorously used. Following a heuristic approach, which is justified by the similarity relations introduced in Sec. 1.4, the Green's function for an infinite homogeneous medium can be rewritten for the case of anisotropic scattering ($g \neq 0$) using μ_s' instead of μ_s for the scattered component as follows:

$$\Phi_{RTE\_i}(r,\,t) \simeq \frac{v\exp[-(\mu_s+\mu_a)vt]}{4\pi r^2}\delta(vt-r)+\Theta(vt-r)\frac{v\left[1-\left(\frac{r}{vt}\right)^2\right]^{\frac{1}{8}}}{\left(\frac{4\pi vt}{3\mu_s'}\right)^{\frac{3}{2}}}$$
$$\times\, G\left\{\mu_s' vt\left[1-\frac{r^2}{(vt)^2}\right]^{\frac{3}{4}}\right\}\exp[-(\mu_s'+\mu_a)vt]. \tag{10.12}$$

In Eq. (10.12), the effect of absorption has been included according to the general property of the RTE [Eq. (2.114)], multiplying the solution for the non-absorbing medium by $\exp(-\mu_a vt)$. Since $\mu_s' = \mu_s(1-g)$, for isotropic scattering Eq. (10.12) is identical to Eq. (10.9). Equation (10.12) can be heuristically used to represent the Green's function of the medium for anisotropic scattering and can be used to implement a hybrid model for the slab geometry, assuming $\Phi_{MODEL\_i} = \Phi_{RTE\_i}$.

10.2.3 Time-resolved Green's function of the telegrapher equation for an infinite medium

The TE, like the DE, is derived by using an approximation of the RTE. The TE in a region with no sources is a second-order differential equation for the fluence of the type

$$\alpha\frac{\partial^2}{v^2\partial t^2}\Phi(\vec{r},\,t)+\beta\frac{\partial}{v\partial t}\Phi(\vec{r},\,t)-\frac{1}{3}\nabla^2\Phi(\vec{r},\,t)+\gamma\Phi(\vec{r},\,t)=0, \tag{10.13}$$

where α, β, and γ are constants that assume different values, depending on the derivation used to obtain the TE. Some derivations of the TE use the so-called P_1 approximation[2,31] [Eq. (3.2)]. In this case, the TE is obtained from the RTE following a procedure similar to the one used for the DE but using only the P_1 approximation[2] (without Fick's law). Other alternative derivations can be used to obtain the TE.[28,32] In particular, in this section we report the TE

Chapter 12
The Diffusion Equation for an *N*-Layered Cylinder

In this section, we present a solution of the DE for a *N*-layered cylinder. This extends the findings of Ch. 11, where only a two-layered cylinder was considered. Contrary to Ch. 11, the method used to implement the solutions is based on transformed domains.[1–5] The reason for this choice is given by the fact that the eigenfunction method (Ch. 11) shows an increase of complexity in its implementation when used with a high number of layers. In fact, for a three-layered cylinder, the solution requires us to consider seven combinations of eigenvalues in the different layers.[6] This means that the implementation of the method for an arbitrary number of layers becomes prohibitively complicated. For this reason, we have opted for the transformed domains approach to solve the DE in a cylinder with an arbitrary number of layers. The DE is solved for an *N*-layered finite cylinder (see Fig. 12.1). Solutions are given in the steady-state, frequency, and time domains.

12.1 Photon Migration through an *N*-Layered Cylinder

Solutions of the DE for an *N*-layered cylinder are derived in the frequency domain, from which the solutions in the time domain are obtained. The steady-state solutions are derived from the special case at zero modulation frequency. We will solve the DE for two types of light sources: (1) a pencil beam normally incident onto an arbitrary location of the first layer is taken as a light source; i.e., the beam can be directed onto the cylinder cover as well as onto the cylinder barrel of the first layer; and (2) a circular flat beam incident on the middle of the cylinder cover.

Figure 12.1 shows a scheme of the considered *N*-layered cylinder. The thickness, the refractive index, the reduced scattering, and the absorption coefficients of layer k are denoted by s_k, n_k, μ'_{sk}, and μ_{ak}, respectively. The radius of the cylinder is indicated with L. As usual, it is assumed that the

Chapter 13
Solutions of the Diffusion Equation with Perturbation Theory

THE study of photon migration in heterogeneous media is an important issue since most of the diffusive media encountered in nature are inhomogeneous, and solutions of the DE for such media are needed especially for imaging applications.[1] Heterogeneous media are often represented as background media with constant optical properties and some defects in their interior (e.g., a localized tumor). Perturbation theory is a classical method for finding the solution of a differential equation as the superposition of an unperturbed solution for the background medium plus a small perturbative solution due to the presence of small defects. Perturbation theory has become a general-use approach in almost all the fields of physics. In particular, the solutions of the DE obtained with the Born approximation[2] (see Sec. 13.1) of perturbation theory are largely used in many applications because of their simplicity.

This chapter is dedicated to applying perturbation theory to the DE. Perturbation theory has been widely used to represent the effects on photon migration of defects embedded within diffusive homogeneous[3–11] and inhomogeneous[12–15] media. The general formalism of perturbation theory applied to the DE was first developed by several authors for time-dependent sources,[4,6] steady-state sources,[3,4] and modulated sources.[3,5] To overcome the limitations of the Born approximation, several approaches have been proposed. Ostermeyer and Jacques[5] suggested that perturbation theory could be implemented in an iterative manner to calculate the fluence rate at higher orders of approximation than the Born approximation. One of the first attempts to implement high-order perturbation theory for diffusive media was performed by Boas.[16] In the works of Wassermann[10] and Grosenick et al.,[11] the authors found useful solutions of higher-order perturbation theory in the time domain for a slab geometry, while Sassaroli et al.[14,15] considered the CW

Chapter 15
Elementary Monte Carlo Methods in Turbid Media

THE Monte Carlo (MC) method has been employed through the years as a *gold-standard* method to reconstruct numerical solutions of the RTE. The MC method provides a physical simulation of light propagation; i.e., photon trajectories are generated by using the same statistical rules that govern propagation in random media. In practice, the MC method estimates the expected characteristics of the photon population as *statistical averages* over a large number of case histories of photon life that are simulated by a computer.[1] These average statistical characteristics of the photon population are exactly what the RTE describes, and, intuitively, this is why the MC method allows one to estimate numerically solutions of the RTE. In fact, comparisons of MC-based results with exact analytical solutions of the RTE demonstrate that for the limit of an infinite number of photons used, the simulated data converge rigorously to the analytical results.[2] The existing literature shows that the MC method can be implemented by using different approaches. In this chapter, the approaches usually employed are briefly reviewed by illustrating their main peculiarities. These approaches are also the basis of more complex MC procedures, such as perturbation MC methods,[3–7] voxel-based MC methods,[8,9] mesh-based MC methods,[9–15] or GPU-accelerated MC codes.[16–22]

15.1 Photon Packets

The MC method can provide a physical simulation of light propagation that is expressed through trajectories numerically generated by using probability laws that govern light propagation through a turbid medium. However, we have seen that, in the present context, the main aim is to reproduce the average statistical characteristics of the photon propagation. We simply search for a numerical "solution" of the RTE, no matter if each single step of the simulation can be strictly interpreted in physical terms or not. Depending

Chapter 16

Reference Monte Carlo Results

ALMOST all the analytical solutions reported in Chs. 5–14 and the related software described in Ch. 18 are approximate solutions of the RTE. Thus, before using them, it is useful to know the level of their accuracy in order to establish their applicability in different fields of interest. For this purpose, the reader can find in the supplemental materials for this book large data sets that represent examples of solutions of the RTE obtained with MC simulations. In fact, with MC simulations, the RTE can be solved without the need of simplifying assumptions and with an accuracy only limited by the statistical fluctuations related to the stochastic nature of the method. The MC results can therefore be used as a standard reference for comparison. This chapter is mainly devoted to describe the MC results found in (Sec. 18.2.1). The MC results have been obtained using several different MC programs. For a better understanding and the proper use of the MC results, a description of the MC programs we used is reported in Secs. 16.1–16.4. Examples of comparisons will be shown in Ch. 17.

16.1 General Remarks

The MC programs that we used can work with scattering phase functions generated both with the HG model and with Mie theory.

The HG scattering phase function, defined as

$$p(\theta) = \frac{1}{4\pi} \frac{1 - g^2}{(1 + g^2 - 2\, g \cos\theta)^{3/2}}, \tag{16.1}$$

is completely characterized by the parameter g. It is possible to show that g corresponds to the asymmetry factor of the function, i.e., $\langle \cos\theta \rangle = g$, and that $\langle \cos^2\theta \rangle = \frac{1+2g^2}{3}$. For $g = 0$, the function is isotropic. For $g > 0$, the function decreases monotonously as θ increases. The corresponding cumulative probability function is

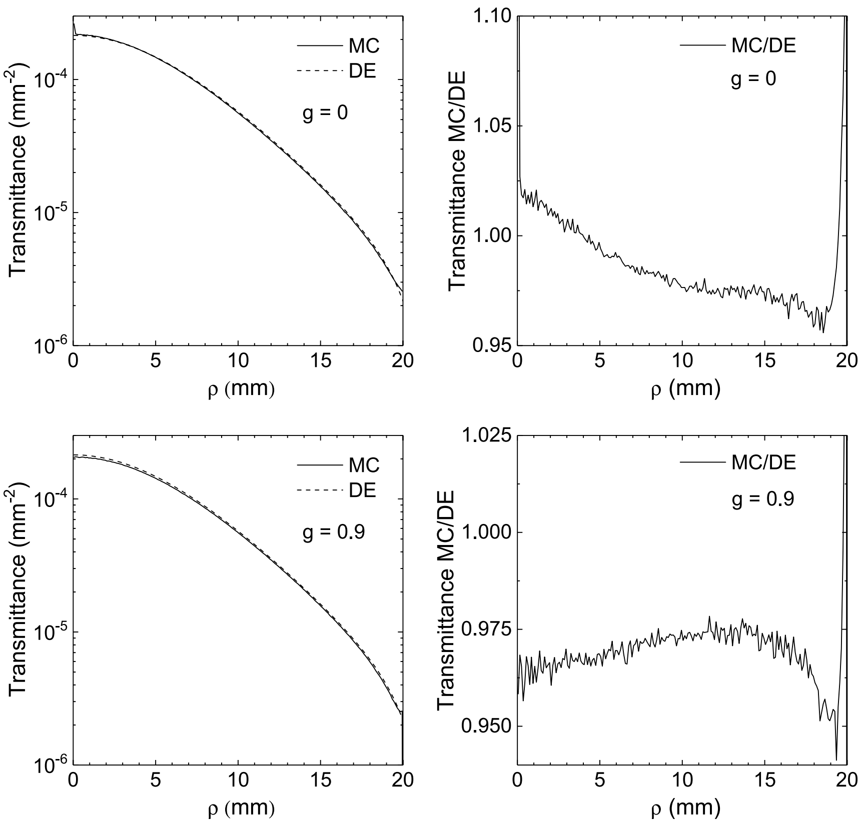

Figure 17.35 CW transmittance for a four-layered cylinder. DE data have been assessed using Eqs. (12.29), (12.38), (12.43), (12.44), and Fick's law. For the optical parameters, see text.

17.6 Comparisons between MC and Hybrid Models

In this section, comparisons are shown between the solutions of the RTE obtained with the hybrid models of Ch. 10 and MC results. Comparisons are shown for TR results plotting the ratios MC/RTE (hybrid models), MC/TE (telegrapher equation), and MC/DE (diffusion equation). All the figures will be focused on the response at short times and small source–receiver distances; times and distances at which the larger differences between the models are expected.

17.6.1 Infinite homogeneous medium

We refer to a non-absorbing medium with $\mu_s' = 1\,\text{mm}^{-1}$ and refractive index $n = 1$. Figure 17.36 reports comparisons for the fluence for $r = 1$, 2, and 5 mm for both $g = 0$ and 0.9. It is particularly interesting to compare RTE and MC results for the isotropic scattering phase function ($g = 0$) since, in this specific case, MC results are compared with a hybrid solution corresponding to an almost exact analytical solution.[4] The comparison shows that, apart from very

Chapter 18
Numerical Implementations and Reference Database

This manual comes with supplemental materials containing: (1) a series of MATLAB® functions implementing almost all the analytical and semi-analytical solutions appearing in the text; (2) previous FORTRAN subroutines together with the old software named *Diffusion&-Perturbation* that were included in the first edition[1] of the manual, and; (3) the reference database, generated by "gold standard" Monte Carlo simulations.

18.1 Numerical Implementation of the Solutions

18.1.1 MATLAB® functions

Why MATLAB software? Pedagogical reasons explained

For certain, the content of this manual can be perfectly taken up without the need of the included software. However, the possibility to generate numerical data may give some advantage during the learning phase. Let's report a few advantages that may be generated by the numerical approach: (1) It may allow us to visually investigate the behavior of the different solutions, e.g., as a function of their optical parameters' values. This behavior is often very difficult to foresee only by using the abstract mathematical formalism, with which all the solutions are presented in the manual. (2) It may allow us to easily experiment with different ranges of parameters' values, and make comparisons of the obtained solutions with, e.g., reference data. In other words, this may allow us to better understand, in practical terms, the conditions for which a given solution/model can be used. This is what the experimenter needs, and, for the majority of the cases, this information cannot be deduced only from the pure mathematical formalism. (3) It may allow us to become aware of the numerical problems that are often hidden behind an algorithm. In fact, many analytical solutions can be expressed only by using infinite mathematical series. This means that in real calculations, the series

Appendix A
Intuitive Justification of the Diffusion Approximation

To obtain Eq. (3.2), the specific intensity $I(\vec{r}, \hat{s}, t)$ can be expanded in spherical harmonics retaining only the first two terms (isotropic and linearly anisotropic) (see Ref. 1 for a detailed description). In this appendix, an intuitive physical justification of Eq. (3.2) is provided following the scheme proposed by Ishimaru.[2] In the diffusive regime of propagation, due to multiple scattering, the radiance has an almost isotropic angular distribution and consequently can be represented as

$$I(\vec{r}, \hat{s}, t) = \alpha\Phi(\vec{r}, t) + \beta\vec{J}(\vec{r}, t) \cdot \hat{s}, \tag{A.1}$$

where $I(\vec{r}, \hat{s}, t)$ is the sum of two terms: a first isotropic term, and a second term that accounts for the weak anisotropy of the specific intensity. The coefficient α can be determined according to the definition of $\Phi(\vec{r}, t)$ as

$$\Phi(\vec{r}, t) = \int_{4\pi} I(\vec{r}, \hat{s}, t)d\Omega = \alpha 4\pi\Phi(\vec{r}, t) \Rightarrow \alpha = \frac{1}{4\pi}\,. \tag{A.2}$$

Therefore, the first term of Eq. (A.1) is the average value of $I(\vec{r}, \hat{s}, t)$ over the solid angle. The value of β is determined by using the definition of $\vec{J}(\vec{r}, t)$: if $\hat{s}_J$ is the direction of $\vec{J}(\vec{r}, t)$, then

$$\left|\vec{J}(\vec{r}, t)\right| = \vec{J}(\vec{r}, t) \cdot \hat{s}_J = \int_{4\pi} I(\vec{r}, \hat{s}, t)\hat{s} \cdot \hat{s}_J d\Omega. \tag{A.3}$$

Appendix C
Boundary Conditions between Diffusive and Non-Scattering Media

WHEN an interface between a diffusive and a non-scattering medium is considered (see Fig. 3.2), the boundary condition for radiative transfer can be summarized by Eq. (3.43), which we rewrite as

$$-\int_{\hat{s}\cdot\hat{q}<0} I(\vec{r},\, \hat{s},\, t)(\hat{s}\cdot\hat{q})d\Omega = \int_{\hat{s}\cdot\hat{q}>0} R_F(\hat{s}\cdot\hat{q})I(\vec{r},\, \hat{s},\, t)(\hat{s}\cdot\hat{q})d\Omega, \tag{C.1}$$

where I is the specific intensity at the boundary Σ of the diffusive medium, R_F is the Fresnel reflection coefficient for unpolarized light, and $\hat{q}$ is the unit vector normal to the boundary surface. To solve the integrals of Eq. (C.1), we make use of the first simplifying assumption of the diffusion approximation [Eq. (3.2)]. By writing the flux as $\vec{J}(\vec{r},\, t) = J_u\hat{u} + J_q\hat{q}$ with $\hat{u}$ unit vector tangential to the boundary surface, with $\hat{s}\cdot\hat{q} = \cos\theta$ and $\hat{u}\cdot\hat{s} = \cos\varphi\sin\theta$, the first integral of Eq. (C.1) becomes

Appendix E
Diffusion Equation with an Infinite Homogeneous Medium: Separation of Variables and Fourier Transform Methods

This appendix is dedicated to the Green's function of the DE for an infinite homogeneous medium. The Green's functions for the fluence are obtained for a time-dependent source and for a steady-state source. The Green's function for the photon flux is obtained for a non-absorbing medium with a steady-state source.

E.1 Time-Dependent Source

The DE for an infinite homogeneous medium, in an orthogonal coordinates system (x, y, z), with a spatial and temporal Dirac's delta source of unitary strength $\delta(\vec{r})\delta(t)$ in the origin $\vec{r}_s = (0, 0, 0)$, can be written as

$$\left(\frac{1}{v}\frac{\partial}{\partial t} - D\,\nabla^2 + \mu_a\right)\Phi_G(\vec{r}, t) = \delta(\vec{r})\delta(t). \tag{E.1}$$

The solution will have the form

$$\Phi_G(\vec{r}, t) = \Phi_0(\vec{r}, t)\exp(-\mu_a vt), \tag{E.2}$$

where $\Phi_0(\vec{r}, t)$ is the solution for the non-absorbing medium, i.e., Eq. (E.1) with $\mu_a = 0$. The spherical symmetry of the problem and the separation of variables method allow us to express

$$\Phi_0(\vec{r}, t) = \Phi_{0x}(x, t)\Phi_{0y}(y, t)\Phi_{0z}(z, t) \tag{E.3}$$

with the corresponding DE equation

Appendix N
Relationship between the Inverse Fourier Transform and Inverse Laplace Transform

N.1 Inverse Fourier Transform Expressed as an Inverse Laplace Transform

THE aim of this section is to express the inverse Fourier transform (FT), $\Theta(t)f(t)$, of the function $F(i\omega)$ as an inverse Laplace transform (LT).[1] We have opted here to give only an intuitive demonstration of the problem, and thus some mathematical finesses not so important for our scope are not included. The demonstration will be related to a function of the form $\Theta(t)f(t)$, where $\Theta(t)$ is the Heaviside function. This is typical for most of the time-dependent functions found in this manual, where, in principle, negative times are not 'physical', and thus the contribution is in a sense nil. The reader interested in a more in-depth mathematical approach can refer to Refs. 1, 2.

To this aim, let's write the Fourier transform of $\Theta(t)f(t)$ as

$$F(i\omega) = \mathcal{F}\{\Theta(t)f(t)\}(i\omega) = \int_{-\infty}^{+\infty} \Theta(t)f(t)e^{-i\omega t}dt. \tag{N.1}$$

Now, the frequency-shifting property of the FT and the definition of the LT allow us to write the relations

$$\int_{-\infty}^{+\infty} \Theta(t)f(t)e^{-\sigma t}e^{-i\omega t}dt = F(\sigma + i\omega) = F(z), \tag{N.2}$$

where $\sigma \in \mathbb{R}$ is chosen such that the integral exists, and $z = \sigma + i\omega$. Equation (N.2) can also be written as

$$\int_{-\infty}^{+\infty} \Theta(t)f(t)e^{-\sigma t}e^{-i\omega t}dt = \int_{0}^{+\infty} f(t)e^{-zt}dt = \mathcal{L}\{f(t)\}(z). \tag{N.3}$$

Fabrizio Martelli graduated from the Physics Department of the University of Florence, Italy, in 1996, studying photon migration through biological tissue. He received his Ph.D. in physics from the University of Electro-communications (UEC), Tokyo, Japan, in 2002, with a thesis on photon migration through homogeneous and layered diffusive media for applications to tissue optics. He is currently an appointed researcher in the Department of Physics and Astronomy of the University of Florence. His major research topic is the modeling of light propagation through diffusive and scattering media and the development of inversion procedures to retrieve the optical properties of diffusive media from time-resolved and spatially resolved measurements. He has studied the modeling of photon transport with numerical simulations and with analytical theories, i.e., using both Monte Carlo simulations and analytical solutions derived from the diffusion equation or the radiative transfer equation. He has conducted extensive research on the determination of optical properties of biological tissues using time- and space-resolved near-infrared spectroscopic measurements. He has experience in the inverse problem implemented with standard nonlinear regression procedures and analytical solutions of the diffusion equation. He has published 100 papers in peer-reviewed journals and a monograph on light propagation through biological tissue.

Tiziano Binzoni received his master's degree at the Department of Physics of the University of Geneva with the thesis topic "Renormalization of the SQED model (supersymmetric quantum electrodynamics) without auxiliary fields." He obtained his Ph.D. degree at the Department of Physiology of the Faculty of Medicine of Geneva, with interdisciplinary work on "A dynamical approach to human skeletal muscle bioenergetics." He was appointed Privat-Docent at the Faculty of Medicine of Geneva with the "Study of the human skeletal muscle energy metabolism by means of non-invasive techniques." He regularly participated in the teaching activities at the Faculty of Medicine, with a particular interest in topics related to human physiology. He has accumulated extensive experience on non-invasive measurement techniques and in-depth theoretical and experimental knowledge on nuclear magnetic resonance spectroscopy/imaging and biomedical optics applied to the investigation of human skeletal muscle and bone. He is currently with the Department of Radiology and Medical Informatics of the Geneva University Hospital and with the Department of Fundamental Neurosciences at the Faculty of Medicine of Geneva. His main research topic is the experimental and theoretical development of optical techniques that allow non-invasive investigation of the mechanisms controlling human musculo-skeletal hemodynamics, with a focus on the influence of temperature. His background in theoretical physics and human physiology has allowed him to relate the theory of photons migration in living tissues to the underlying physiological phenomena. He has authored more than 90 peer-reviewed articles.

Samuele Del Bianco received his master's degree at the Physics Department of the University of Florence, Italy, in 2002, with a thesis on the methodologies for measuring the optical properties of biological tissues using both homogeneous and layered models. He received the Ph.D. from the Leonardo da Vinci Engineering School of the University of Pisa, Italy, in 2008, with a thesis on radiative transfer and inversion model of atmospheric measurements in the far infrared for cloudy conditions. He is a researcher at the Institute of Applied Physics "Nello Carrara" (IFAC) of the National Research Council (CNR). His major topic is the modeling of light propagation through the atmosphere to retrieve the physical and chemical properties of atmospheric constituents. He has experience in modeling light propagation by means of Monte Carlo (MC) simulations and using analytical theories derived from the radiative transfer equation. He has developed several MC codes for light propagation through scattering media using both unpolarized and polarized light. He also has vast experience in modeling light propagation through diffusive media such as biological tissues. He has conducted several experimental investigations on measuring the optical properties of diffusive media and of biological tissues by using time-resolved and spatially resolved measurements. He has used standard nonlinear regression procedures to retrieve the optical properties of diffusive media with a special reference to biological tissues. He has authored more than 50 peer-reviewed articles and of a monograph on light propagation through biological tissue.

André Liemert received the diploma in mechatronics from the University of Applied Sciences, Ulm, in 2007. In 2011, he received the Dr.-Ing. degree in electrical engineering from the University of Ulm. From 2011 until present, he has been working as a postdoctoral researcher in the Quantitative Imaging and Sensors department at the Institute of Laser Technologies in Medicine and Metrology in Ulm. His research activity spans all phenomena of radiative transfer in turbid media and its applications in medicine, physics, and engineering sciences. He has analytically solved the radiative transfer equation and the diffusion equation in several geometries, providing a wide set of analytical and semi-analytical solutions. His interest also touches some aspects of applied mathematics and many mathematical physics problems such as fractional radiative transport, the fractional diffusion equation, and the fractional Schrödinger equation. He has authored more than 50 peer-reviewed articles.

Alwin Kienle studied physics at the University of Ulm, Germany. During his doctoral thesis entitled "Light propagation in biological tissue," he worked at the Institute of Laser Technologies in Medicine and Metrology in Ulm (ILM), Germany, and at the Hamilton Regional Cancer Centre in Hamilton (HRCC), Canada. As a postdoctoral researcher, he was with research groups at the HRCC, and at EPFL in Lausanne, Switzerland. During his habilitation period at the University of Ulm, he studied theoretical and experimental issues concerning the determination of optical properties of scattering media. Currently, he is speaker of the board of directors at ILM and head of the department “Quantitative Imaging and Sensors.” In addition, he is a professor at the University of Ulm. The topics of his research activities are theoretical investigations of the light propagation of scattering media on microscopic, mesoscopic, and macroscopic scales, the determination of the optical properties of scattering media and, based on this, various applications in medicine, physics, and engineering sciences. He has published more than 100 papers in peer-reviewed journals.