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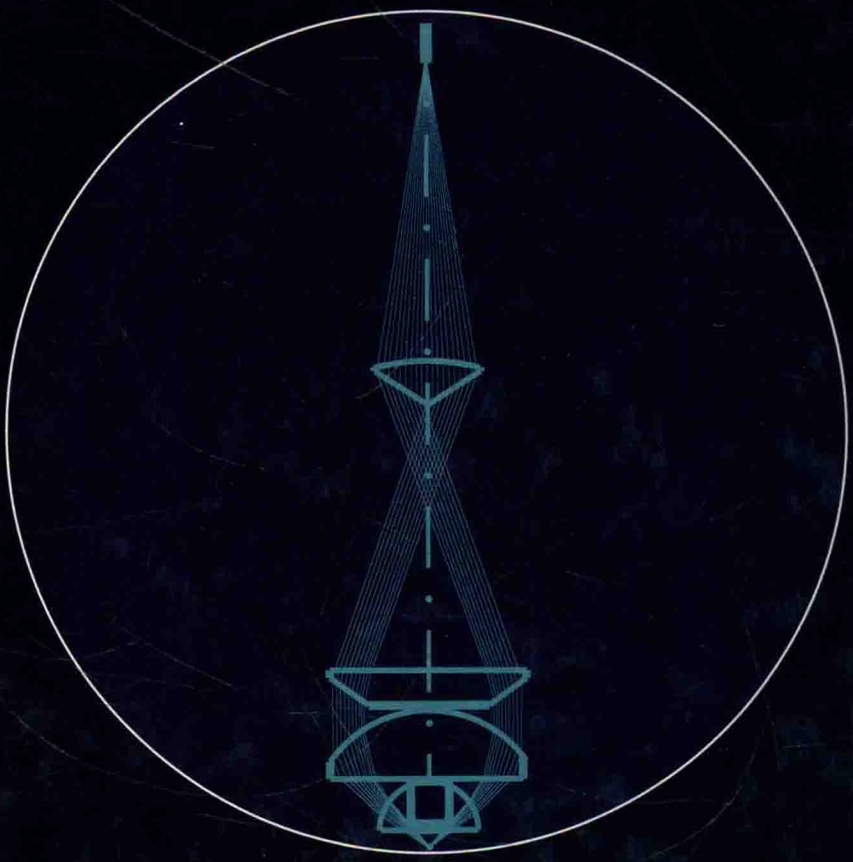
Biomedical Optics

Principles and Imaging



LIHONG V. WANG
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BIOMEDICAL OPTICS

PRINCIPLES AND IMAGING

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BIOMEDICAL OPTICS

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To our families, mentors, students, and friends

PREFACE

Biomedical optics is a rapidly growing area of research. Although many universities have begun to offer courses on the topic, a textbook containing examples and homework problems has not been available. The need to fill this void prompted us to write this book.

This book is based on our lecture notes for a one-semester (45 lecture hours) entry-level course, which we have taught since 1998. The contents are divided into two major parts: (1) fundamentals of photon transport in biological tissue and (2) optical imaging. In the first part (Chapters 1–7), we start with a brief introduction to biomedical optics and then cover single-scatterer theories, Monte Carlo modeling of photon transport, convolution for broadbeam responses, radiative transfer equation and diffusion theory, hybrid Monte Carlo method and diffusion theory, and sensing of optical properties and spectroscopy. In the second part (Chapters 8–13), we cover ballistic imaging, optical coherence tomography, diffuse optical tomography, photoacoustic tomography, and ultrasound-modulated optical tomography.

When the book is used as the textbook in a course, the instructor may request a solution manual containing homework solutions from the publisher. To benefit from this text, students are expected to have a background in calculus and differential equations. Experience in MATLAB® or C/C++ is also helpful. Source codes and other information can be found at ftp://ftp.wiley.com/public/sci_tech_med/biomedical_optics.

Although our multilayered Monte Carlo model is in the public domain, we have found that students are able to better grasp the concept of photon transport in biological tissue when they implement simple semiinfinite versions of the model. For this reason, we encourage the use of simulations whenever appropriate.

Because a great deal of material beyond our original lecture notes has been added, two semesters are recommended to cover the complete textbook. Alternatively, selected chapters can be covered in a one-semester course. In addition to serving as a textbook, this book can also be used as a reference for professionals and a supplement for trainees engaged in short courses in the field of biomedical optics.

We are grateful to Mary Ann Dickson for editing the text and to Elizabeth Smith for redrawing the figures. We appreciate Sancy Wu's close reading of

the manuscript. We are also thankful to the many students who contributed to the homework solutions. Finally, we wish to thank our students Li Li, Manojit Pramanik, and Sava Sakadzic for proofreading the book.

LIHONG V. WANG, PH.D.
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CHAPTER 1

Introduction

1.1. MOTIVATION FOR OPTICAL IMAGING

The most common medical imaging modalities include X-ray radiography, ultrasound imaging (ultrasonography), X-ray computed tomography (CT), and magnetic resonance imaging (MRI). The discovery of X rays in 1895, for which Roentgen received the first Nobel Prize in Physics in 1901, marked the advent of medical imaging. Ultrasonography, which is based on sonar, was introduced into medicine in the 1940s after World War II. The invention of CT in the 1970s, for which Cormack and Hounsfield received the Nobel Prize in Medicine in 1979, initiated digital cross-sectional imaging (tomography). The invention of MRI, also in the 1970s, for which Lauterbur and Mansfield received the Nobel Prize in Medicine in 2003, enabled functional imaging with high spatial resolution. Optical imaging, which is compared with the other modalities in Table 1.1, is currently emerging as a promising new addition to medical imaging.

Reasons for optical imaging of biological tissue include

1. Optical photons provide nonionizing and safe radiation for medical applications.
2. Optical spectra—based on absorption, fluorescence, or Raman scattering—provide biochemical information because they are related to molecular conformation.
3. Optical absorption, in particular, reveals angiogenesis and hypermetabolism, both of which are hallmarks of cancer; the former is related to the concentration of hemoglobin and the latter, to the oxygen saturation of hemoglobin. Therefore, optical absorption provides contrast for functional imaging.
4. Optical scattering spectra provide information about the size distribution of optical scatterers, such as cell nuclei.
5. Optical polarization provides information about structurally anisotropic tissue components, such as collagen and muscle fiber.

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TABLE 1.1. Comparison of Various Medical Imaging Modalities

Characteristics	X-ray Imaging	Ultrasonography	MRI	Optical Imaging
Soft-tissue contrast	Poor	Good	Excellent	Excellent
Spatial resolution	Excellent	Good	Good	Mixed[a]
Maximum imaging depth	Excellent	Good	Excellent	Good
Function	None	Good	Excellent	Excellent
Nonionizing radiation	No	Yes	Yes	Yes
Data acquisition	Fast	Fast	Slow	Fast
Cost	Low	Low	High	Low

[a]High in ballistic imaging (see Chapters 8–10) and photoacoustic tomography (see Chapter 12); low in diffuse optical tomography (see Chapter 11).

6. Optical frequency shifts due to the optical Doppler effect provide information about blood flow.
7. Optical properties of targeted contrast agents provide contrast for the molecular imaging of biomarkers.
8. Optical properties or bioluminescence of products from gene expression provide contrast for the molecular imaging of gene activities.
9. Optical spectroscopy permits simultaneous detection of multiple contrast agents.
10. Optical transparency in the eye provides a unique opportunity for high-resolution imaging of the retina.

1.2. GENERAL BEHAVIOR OF LIGHT IN BIOLOGICAL TISSUE

Most biological tissues are characterized by strong optical scattering and hence are referred to as either *scattering media* or *turbid media*. By contrast, optical absorption is weak in the 400–1350-nm spectral region. The mean free path between photon scattering events is on the order of 0.1 mm, whereas the mean absorption length (mean path length before photon absorption) can extend to 10–100 mm.

Photon propagation in biological tissue is illustrated in Figure 1.1. The light source is spatially a pencil beam (an infinitely narrow collimated beam) and temporally a Dirac delta pulse. The optical properties (see Appendix A) of the tissue include the following: refractive index $n = 1.37$, absorption coefficient $\mu_a = 1.4\ \text{cm}^{-1}$, scattering coefficient $\mu_s = 350\ \text{cm}^{-1}$, and scattering anisotropy $g = 0.8$. The mean free path equals 28 μm, corresponding to a propagation time of 0.13 ps. The transport mean free path equals 140 μm, corresponding to a propagation time of 0.64 ps. Note how widely the photons spread versus time in relation to the two time constants mentioned above. This diffusion-like behavior of light in biological tissue presents a key challenge for optical imaging. Various techniques have been designed to meet this challenge.

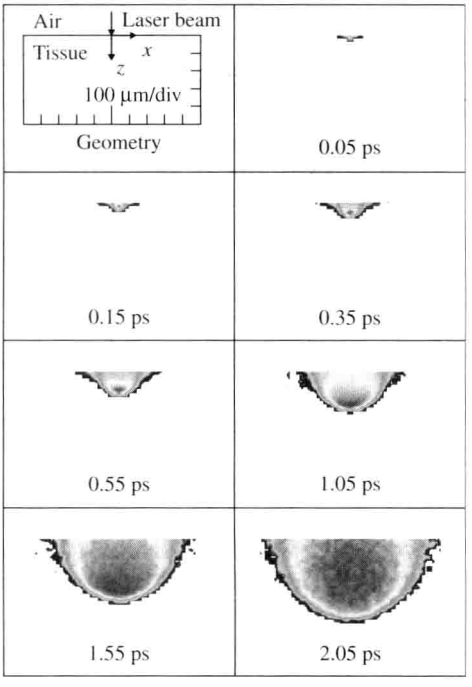

Figure 1.1. Snapshots of the simulated photon density distribution in a piece of biological tissue projected along the y axis, which points out of the paper.

1.3. BASIC PHYSICS OF LIGHT–MATTER INTERACTION

Absorption of a photon can elevate an electron of a molecule from the ground state to an excited state, which is termed *excitation*. Excitation can also be caused by other mechanisms, which are either mechanical (frictional) or chemical in nature. When an electron is raised to an excited state, there are several possible outcomes. The excited electron may relax to the ground state and give off luminescence (another photon) or heat. If another photon is produced, the emission process is referred to as *fluorescence* or *phosphorescence*, depending on the lifetime of the excited electron; otherwise, it is referred to as *nonradiative relaxation*. *Lifetime* is defined as the average time that an excited molecule spends in the excited state before returning to the ground state. The ratio of the number of photons emitted to the number of photons absorbed is referred to as the *quantum yield of fluorescence*. If the excited molecule is near another molecule with a similar electronic configuration, the energy may be transferred by excitation energy transfer—the excited electron in one molecule drops to the ground state while the energy is transferred to the neighboring molecule, raising an electron in that molecule to an excited state with a longer lifetime. Another possible outcome is photochemistry, in which an excited electron is actually transferred to another