Book Review

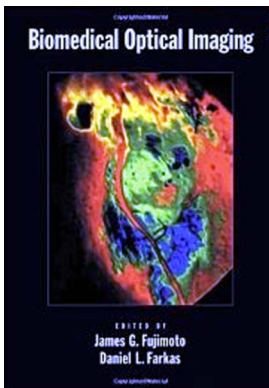**Biomedical Optical Imaging**

James G. Fujimoto and Daniel L. Farkas, Editors, 422 pages + xii, ISBN: 978-0-19-515044-5, Oxford University Press, New York (2009), $90.00, hardcover.

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Biomedical Optical Imaging is edited by two eminent and distinguished educator-scientists. Professor James G. Fujimoto is with the Department of Electrical Engineering and Computer Sciences at the Massachusetts Institute of Technology and also an adjunct professor of ophthalmology at the Tufts New England Medical Center. Professor Daniel L. Farkas is the vice chairman for research in the Department of Surgery and the director of the Minimally Invasive Surgical Technologies Institute at the Cedars-Sinai Medical Center in Los Angeles; he is also a research professor in biomedical engineering at the University of Southern California and an adjunct professor with the Robotics Institute at Carnegie Mellon University. The editors designated eminent researchers and their colleagues to contribute chapters on the application of optical imaging to the field of biomedicine. The editors state that their choice of topics in this book is focused mainly on reviewing technologies that are currently used in research, industry, or medicine, rather than those that are being developed. The interests of the editors and the space limitations of a 400-page book limited the scope of the chapter selections; other editors would have provided a different table of contents. Notably there are no chapters that cover the modern important advances in photoacoustic imaging.

The field of biomedical optical imaging consists of a myriad of techniques, devices, instruments, probes, computer algorithms and software, animal studies, and clinical trials. While the potential clinical benefits of optical imaging are enormous, a large divide exists between animal studies performed in a laboratory setting and the rigor of large double-blind, randomized clinical trials that factor in differences of ethnicity, age, and sex, as well as national, dietary, cultural, and genetic differences. The goal of biomedical researchers is to bridge the difficult gap between a working laboratory device and a device approved by the Food and Drug Administration that is commercially and clinically viable, safe, and efficacious. While this goal is exceedingly difficult, the potential benefits for patient health care are enormous.

Nevertheless, there is the potential for enthusiastic investigators, many with real and potential conflicts of interests due to commercial interests and intellectual property rights, to overstate the potential benefits and to concomitantly understate or to ignore a critical appraisal of the limitations of the methodology and additionally to ignore the explicit comparisons of sensitivity, selectivity, complexity, and cost analyses of competing technologies. The problems of real and potential conflicts of interest could be mitigated by accurate financial disclosure of the contributors with regards to their potential benefits and connections. A reading of the chapters in this book failed to indicate compliance with this across-the-board requirement of financial disclosure as is typically required by highly regarded scientific and medical journals. Additionally, careful editing is required to insure that the contributions from one group are not overstated and are put into context with the contributions of other groups.

In their preface, the editors state that the intended audience for *Biomedical Optical Imaging* consists of beginning researchers in the field or graduate students who will use it as a textbook for a graduate course in optical imaging. If the book's purpose is to serve the former group then it would have to include additional introductory materials in dedicated chapters that cover the following topics: the interaction of light and tissues, the principles of spectroscopy, the design of instrumentation including noncoherent and coherent light sources, intermediate optics, detectors, signal processing, and the development of probes and other contrast materials. While some of these topics appear in the book, they are scattered in various chapters and thus diminish the book's utility for beginning researchers. As for the latter group of graduate students, *Biomedical Optical Imaging* does not provide the fundamentals of the mathematical and the physical background that would be required as a textbook for a graduate course in biomedical optical imaging.

What is my critical review after reading the book's chapters, analyzing their pedagogical content, and evaluating their usefulness for the intended audiences? I present some commentary on several representative chapters of the book. The first chapter that presents work from Tony Wilson's group is a clear and concise review of image formation in the microscope, which serves as a prerequisite for the subsequent chapters on optical microscopy. If this book is to be used as a textbook then this section on image formation needs to be expanded. The sections provide solutions to the following questions: how to design a light-efficient, real-time, three-dimensional imaging system based on structured illumination; how to correct for optical aberrations via an adaptive optics Hartmann-Shack wavefront sensor coupled to a deformable mirror or a spatial light modulator; and most interestingly,

how to use a spatial light modulator to generate arbitrary vector wavefronts. The chapter provides one example of the latter technique by demonstrating the generation of radially polarized light for fluorescent imaging with a concomitant improvement of resolution.

The second chapter describes spectral optical imaging. This is a field that derives from hyperspectral imaging in airborne and satellite surveillance systems in which each pixel of the digital image contains spectral information. This development in biology and medicine is presented in an extensive chapter that is replete with informative and colorful illustrations from Farkas' group. The strength of this chapter is a balanced presentation of theory, instrumentation, computational techniques, classification algorithms, and biological applications of spectral imaging. The materials presented in this chapter may have applications in a variety of optical imaging techniques since spectral imaging enhances the information content of images and therefore may improve both the contrast and the ability to segment biomedical images.

Fujimoto's group contributed a chapter that highlights their seminal contributions in the field of optical coherence tomography (OCT), but also cites key and important contributions from other groups. Their chapter is a very clear presentation of the theory and the instrumentation (including light sources and detectors), and it is focused on important applications (illustrated in color images) in ophthalmology, developmental biology, and optical biopsy. Their contribution is enhanced by a discussion of detection sensitivity, noise, and signal processing. The chapter is a sound introduction to several types of OCT based on both time-domain and spectral or Fourier domain detection; but a more detailed discussion of polarization-sensitive OCT would be useful. A major problem in biomedical optical imaging is how to differentiate normal and abnormal cells and tissues. Their inclusion of OCT images juxtaposed to classical histopathology is an exemplar that should be followed in other biomedical imaging studies.

From the group of Petra Schwille there is an extensive contribution on two-photon correlation spectroscopy. Their contribution, which includes clear and colorful figures, is an excellent student tutorial that is current up to the year 2002 on the subject of single-molecule fluorescence correlation spectroscopy (FCS). While FCS is not an optical imaging technique, it is an extremely sensitive technique to probe particle movement, molecular dynamics, and chemical reactions in solution and in cells. The use of kinetic models in the analysis of the autocorrelation function (for a single fluorescent species) is the basis of the technique. This contribution provides a good introduction to the ancillary techniques of dual volume and dual color cross-correlation analysis with two-photon excitation to investigate molecular dynamics.

A review of the field of nanoscopy (optical methods to provide wide-field imaging with nanometer resolution) is contributed from Stefan Hell's group. The fundamental problem that the Hell group addresses is how to improve the optical resolution (that was formerly limited by diffraction) in a wide-field optical microscope. While all of the references date from 2002 or earlier (there is one citation from 2007 together with

a brief mea culpa) the chapter can serve as a good tutorial for students who are not familiar with the field. The chapter is augmented by very clear colored figures that present the student with an easily understood physical and analytical picture of the instrumentation, the theory, and the analysis. Nevertheless, due to the dated nature of the citations, much of the more recent technical developments and applications of super-resolution optical microscopy, both from the Hell group and more importantly from other groups, is not included in this chapter.

Biomedical Optical Imaging contains several important contributions on the applications of various optical technologies to medical diagnostics; these contributions range from near-infrared fluorescent probes and contrast agent development to fluorescence and spectroscopic markers of cervical neoplasia. Additionally, there are useful contributions on imaging in thick tissues using broadband diffuse optical spectroscopy, the use of near-infrared light to detect brain activity, and a recent chapter with citations up to the year 2008 on optical reporter genes.

I selected one contribution to discuss in this review. Perusal of the literature indicates the clinical importance of optical spectroscopy in both diagnostics and therapeutics, i.e., photodynamic therapy (PDT). Photomedicine is a real success story and is a strong motivation for scientists and engineers to pursue fundamental research in biomedical optics in all its manifestations. Katarina Svanberg's group contributed an extensive review of fluorescence imaging in medical diagnostics. As the authors correctly state in their chapter, "early diagnosis of malignancies remains the most important prognostic factor in the treatment of cancer." Here is a rich field for biomedical optics; the impact and success of this research is literally saving and improving lives. The authors describe several important advances in fluorescence techniques and clinical instruments up to the year 2003. As the authors clearly demonstrate with the aid of colored clinical images, the design and utility of the clinical techniques include the optical detection of tumors in the lower urinary tract, the bronchus, the female genital tract, skin, the head and neck, and the gastrointestinal tract.

I now present my summary of the many positive features of *Biomedical Optical Imaging*. The editors selected eminent contributors who represent a range of scientific, technical, and clinical interests. Each of the contributor's groups made a series of seminal contributions to the advancement of biomedical optics. Their contributions are well illustrated with numerous color figures that illustrate the theory, instrumentation, methods of analysis, and biomedical applications.

At first glance the combination of two outstanding scientists who served as editors, the outstanding scientific reputations of the principal contributors, and the imprimatur of Oxford University Press with its reputation of excellence in scholarly publishing elicits the image of a book that is clearly written, well illustrated, easily read, and meets the high standards of scholarly publishing that is commensurate with the reputations of the editors, the contributors, and the publisher.

While the quality of the contributions is consistent with the above expectations, there are two caveats that belie these expectations. First, there exist an extraordinarily high number of typographical errors, which occur throughout the book: in the preface, in the individual chapters, and in the index. In a book of 422 pages I recorded a minimum of 402 typographic errors. Second, my reading of the references in the book indicates that although the book was published in 2009, most of the references and much of the content of the chapters are from the period prior to 2002. For example, the chapter from the group of Winfried Denk ends with the quotation: "…reflects the status of the field in 2003." An exception is the book's final chapter on the topic of optical reporter genes that contains references up to the year 2008.

In summary, the onerous number of typographical errors due to typesetting that occurs in the book is a distraction to the reader. In addition, the severely dated content of the book, the insufficient physical and mathematical detail in the introductory materials of each chapter, the lack of financial disclosure from corporate partners, and the lack of contextual analysis (the discussion of each group's contributions in relation to the works of other groups) of the various techniques together with a discussion of their validation and limitations forces me to withhold my recommendation for *Biomedical Optical Imaging*.

Barry R. Masters is a visiting scientist in the Department of Biological Engineering at the Massachusetts Institute of Technology and a visiting scholar in the Department of the History of Science at Harvard University. He was formerly a professor in anatomy at the Uniformed Services University of the Health Sciences. He is a Fellow of the Optical Society of America, SPIE, and the American Association for the Advancement of Science. Professor Masters has published 81 refereed research papers and 128 book chapters and articles. He is the editor or author of *Noninvasive Diagnostic Techniques in Ophthalmology; Medical Optical Tomography: Functional Imaging and Monitoring; Selected Papers on Confocal Microscopy; Selected Papers on Optical Low-Coherence Reflectometry and Tomography; Selected Papers on Multiphoton Excitation Microscopy; Confocal Microscopy and Multiphoton Excitation Microscopy: the Genesis of Live Cell Imaging*; and (with Peter So) *Handbook of Biomedical Nonlinear Optical Microscopy*. He is currently writing a new book to be published by Cambridge University Press: *Superresolution Optical Microscopy*. Professor Masters is a member of the editorial board of *Graefe's Archive for Clinical and Experimental Ophthalmology*. His research interests include the development of in vivo microscopy of the human eye and skin, biomedical imaging and spectroscopy, and the fractal analysis of branching vascular patterns.