Journal of Biomedical Optics

BiomedicalOptics.SPIEDigitalLibrary.org

Selected Topics in Biophotonics: Optical Coherence Tomography and Biomolecular Imaging with Coherent Raman Scattering Microscopy

Stefan Andersson-Engels
Peter E. Andersen

SPIE.

Selected Topics in Biophotonics: Optical Coherence Tomography and Biomolecular Imaging with Coherent Raman Scattering Microscopy

Stefan Andersson-Engels
Lund University
Department of Physics
Lund, Sweden
E-mail: stefan.andersson-engels@fysik.lth.se

Peter E. Andersen
Technical University of Denmark
Department of Photonics Engineering
Roskilde, Denmark
E-mail: peta@fotonik.dtu.dk

The Special Section on Selected Topics in Biophotonics: Optical Coherence Tomography and Biomolecular Imaging with Coherent Raman Scattering Microscopy comprises two invited review papers and several contributed papers from the summer school Biophotonics '13, as well as contributed papers within this general scope.

1 Motivation and Purpose of Biophotonics Graduate Schools

Over the past decade, lasers, optical methods, and instruments based on light interaction with tissues have emerged as powerful techniques for medical diagnostics, monitoring wide spectra of tissue function, and pathology. In biophysics and biology, optical sensing and manipulation of cells have strengthened understanding of basic cell function. Together with improved laser therapeutic techniques, optical sensing and cell manipulation form the basis for the increased interest in biophotonics. Throughout Europe, the U.S., and the rest of the world, major research centers are highly active in this field that in a broad sense may be labeled biophotonics. Therefore, education within this area is becoming increasingly important.

The main purpose with the biennial graduate summer school is to provide education within biophotonics for students and young scientists at the highest international level. Our aim is to attract internationally renowned researchers as lecturers who would attract the most talented young researchers worldwide in the field of biophotonics.

2 Format of the Biophotonics Graduate Summer School

The school mainly targets graduate students and postdoctoral fellows from around the world. The format of the school is a combination of lectures and student poster presentations, with time between lectures for discussions and exchange of scientific ideas. The lecturers cover one topic in a full session comprised of four lectures, which thoroughly covers the basics and state of the art of each topic. On one hand, this choice limits the number of topics taught at each school. On the other hand, the topics selected for the schools are covered in detail. Therefore, the range of topics taught will change from school to school.

An important feature of the school format is that students and lecturers spend the entire week together, which provides excellent opportunities for the exchange of scientific ideas, networking, and socializing.

The 6th International Graduate Summer School Biophotonics '13 covered the basics of lasers as well as supercontinuum sources and their application in medicine, tissue optics, photodynamic therapy, optical tweezers and their applications in biophotonics, optical biosensors, diffuse optical and molecular imaging, fluorescence nanoscopy, optical coherence tomography, and coherent Raman scattering microscopy.[1]

3 Special Section in the *Journal of Biomedical Optics*

We are pleased to introduce the contributions to this special section, comprised of two invited papers and nine contributed papers, mainly from the participants of the school, but also from other researchers in the field. Not all the contributions are strictly covered by the title of the special section, but all of the contributions reflect the core topics of the school and span the fields of biomedical optics and biophotonics. The invited papers are:

- W. Drexler et al., "Optical coherence tomography today: speed, contrast, and multimodality"
- A. Alfonso-García et al., "Biological imaging with coherent Raman scattering microscopy: a tutorial."

These two papers from lecturers at the school are review and tutorial in character, respectively, and provide an excellent background to the fields of optical coherence tomography, whilst also pointing to future challenges and coherent Raman scattering microscopy, respectively. These invited papers provide a natural continuation to previous tutorial papers on the foundation of diffuse optics,[2] imaging thick tissues with diffuse optics,[3] molecular imaging,[4] optical micromanipulation[5] and photodynamic therapy[6] published in special sections from previous schools. These papers all belong to a planned series of tutorial review papers from each biennial school that provide high-level, open-access educational material for the benefit of the scientific community and, in addition, fulfill our own motivation for creating the school in the first place.

Following the invited review papers, we have organized the contributed papers according to their main topic, starting

with papers categorized as contributions. Related to the topic of OCT at high speed, the first paper by Tankam et al. addresses a means for using a graphics processing unit for achieving high A-scan rate for volumetric, high-resolution images of skin. In a parallelized scheme, the authors demonstrate that the processing time for rendering the graphics was shorter than the data acquisition time paving the way for real-time volumetric imaging. Optical scattering reduces imaging penetration and scattering from blood may be particularly strong in certain wavelength ranges. Kinnunen et al. investigated so-called optical clearing by exogenous agents and by using optical tweezers (see tutorial on manipulation[5]), and they studied the effects at the cellular level. In this study, solutions of glucose were used as the optical clearing agent and the effects were investigated for polymer microspheres and red blood cells. Clearing agents that are biocompatible, such as solutions of glucose, could be of great importance for imaging through blood and therefore be of interest for intravascular imaging, for example OCT.

Related to coherent anti-Stokes scattering (CARS) microscopy, Galli et al. apply the CARS technique in brain imaging. The key aspect being investigated is the influence of tissue fixation (formalin and methanol-acetone) on the CARS image intensity and contrast. Label-free imaging of tissue *in vivo* would have high impact for clinical applications. Therefore, when investigating new modalities it is important to understand contrast mechanisms and to perform investigations on samples *in vitro*. The issue being dealt with in the work of Galli et al. is the effects of fixation and its impact on *in vitro* samples, providing some understanding of the expected *in vivo* behavior.

Another general area covered in this special section is to model light transport in tissue within specific biomedical applications. Several contributions are within this general area. Bürgermeister et al. evaluate antimicrobial photodynamic therapy (aPDT) using modelling of light propagation and photodynamical mechanisms. Here they use coupled equations for light propagation and chemical processes, as the treatment will have a clear influence on the tissue optical properties. The mathematical description provided may help to develop improved treatment protocols for aPDT possible with direct feedback. Bodenschatz et al. analytically investigate sources of errors in spatial frequency domain imaging (SFDM) to extract optical properties of tissues. They consider typical experimental errors in their analysis, providing interesting analysis of this promising technique. From the same group, Elmaklizi et al. employ finite difference time-domain techniques to study directly from the Maxwell Equations how light can be focused into tissue. Furthermore, Steinberg at el. evaluate a diffusion model for robust evaluation of hemodynamics in neonates. The model is benchmarked towards time-resolved Monte Carlo simulations, yielding only a few percent deviations in the evaluated parameters between the models.

The two remaining contributions to this special section concern the studies utilizing fluorescence substances. In an interesting study, Serebrovskaya et al. investigate the photocytotoxity of the fluorescence protein photosensitizer KillerRed targeted to cytoplasmic surface of lysosomes. They suggest that this substance might become of interest as an optogenetic tool to direct target selective cell populations to either apoptosis or necrosis. Xie et al. demonstrate a novel instrument based on both diffuse reflectance and fluorescence at multiple wavelengths to extract the intrinsic fluorescence signal, correcting for any influences of tissue optical properties. Quantitative assessment of molecular concentrations in tissue is essential in many applications, including *in vivo* pharmacokinetic studies.

Acknowledgments

The editors would first like to thank all the lecturers and participants of the summer school Biophotonics '13 for making the school a very fruitful and positive experience; the authors of all papers in this special section for their excellent contributions; and the many reviewers around the world who provided high-quality reviews of the manuscripts. Your dedicated efforts have made this high-quality special section possible. The editors would also like to thank the JBO publication staff, Rita Davis and Karolyn Labes in particular, for their invaluable support and prompt assistance in helping meet the JBO standards. Finally, the editors would like to thank Prof. Lihong Wang, Editor-in-Chief, for his never-ending support and stimulating encouragements during the entire process of making this special section.

References

1. Biophotonics '13 Website, 2013 www.biop.dk/biophotonics13/.
2. S. L. Jacques and B. W. Pogue, "Tutorial on diffuse light transport," *J. Biomed. Opt.* **13**, 041302 (2008).
3. T. D. O'Sullivan et al., "Diffuse optical imaging using spatially and temporally modulated light," *J. Biomed. Opt.* **17**, 071311 (2012).
4. E. M. Sevick-Muraca and J. C. Rasmussen, "Molecular imaging with optics: primer and case for near-infrared fluorescence techniques in personalized medicine," *J. Biomed. Opt.* **13**, 041303 (2008).
5. D. J. Stevenson, F. Gunn-Moore, and K. Dholakia, "Light forces the pace: optical manipulation for biophotonics," *J. Biomed. Opt.* **15**, 041503 (2010).
6. K. Svanberg et al., "Photodynamic therapy: superficial and interstitial illumination," *J. Biomed. Opt.* **15**, 041502 (2010).

Stefan Andersson-Engels is a professor in the Department of Physics, Lund University, Sweden, where he leads a research group within biomedical optics. He has more than 20 years of research experience in developing optical techniques to assist in diagnostic and therapeutic applications within medicine. Since 2003, he has co-organized the biannual International Graduate Summer School Biophotonics, held at the Isle of Hven, Sweden. He is an editorial board member of the *Journal of Biomedical Optics* and *Journal of Biophotonics*, respectively.

Peter E. Andersen is senior scientist and research professor at the Technical University of Denmark, where he leads research within biomedical optics. He has more than 15 years of research experience with light sources for biomedical optics and optical coherence tomography systems and their application. Since 2003, he has co-organized the biannual International Graduate Summer School Biophotonics, held at the Isle of Hven, Sweden. He is appointed Deputy Editor of *Optics Letters*, editorial board member of *Journal of Biomedical Optics*, and editorial board member *of Journal of Biophotonics*.