1. PHD PROJECT DESCRIPTION (4000 characters max., including the aims and work plan)

Project title:

Parallel imaging techniques in optical coherence tomography for biomedical applications.

1.1. Project goals

A. To develop line-field spectral-domain OCT system for structural and angiographic imaging of the human eye in vivo.

B. To reduce the cross-talk effect in line-field OCT imaging of highly scattering tissue.

C. To test the developed solutions in the imaging of the human eye.

1.2. Outline

Optical Coherence Tomography (OCT) is an interferometric technique which uses partially coherent light to obtain three-dimensional images of various objects at microscopic scales. The vast majority of OCT applications is in biomedical imaging, including: ophthalmology, microscopy, endoscopy, dermatology, and many others. Each of the applications has its own requirements which lead to development of specific imaging setups and methods, data acquisition techniques, and even image analysis methods. However, one of the common requirements of all biomedical OCT applications is short imaging time to enable collection of all the data needed for the diagnosis, in just a few seconds. A typical OCT data acquisition method is a serial collection of image lines, each showing the structure or function of tissue in depth, underneath a single, few-micrometers-wide spot of the object. A set of such depth-lines is then arranged in 2D cross-sections and 3D data sets. To speed up the collection of data in this imaging regime, it is necessary to speed up the acquisition of the depth-lines. This is done by using faster cameras or special light sources. Another option are parallel detection techniques in which entire two-dimensional images consisting of hundreds or thousands of depth-lines are acquired depth-by-depth or side-by-side, and then arranged into 3D data sets. These methods are called full-field OCT (FF-OCT) when 3D data are acquired as “sheets” at increasing depths, or line-scan OCT (LS-OCT) when 3D data are acquired as side-by-side depth slices [1, 2]. FF-OCT and LS-OCT are faster than conventional OCT [2, 3, 4] and therefore provide more accurate data.

OCT is an interferometric technique providing information about amplitude and phase of the interferometric signals. The access to the phase information is especially valuable. It enables development of methods for the detection of functional processes in the living tissues, including the detection and measurement of the blood flow down to the smallest vessels [5], or detection of neural tissue activity due to functional stimuli [1]. But also, the phase information can be used to develop computational adaptive-optics techniques for sub-cellular imaging resolution [2, 6]. This combination of sensitivity to tissue function and sub-cellular imaging resolution promises new exciting possibilities to study many aspects of functional processes in tissues. However, this level of OCT detection sensitivity and accuracy can be only achieved if the acquired interferometric data has very low phase-noise. The full-field OCT and line-field OCT techniques with their superior

imaging speeds were shown to provide data with much higher phase-stability than the conventional OCT [1]. However, this advantage comes at a price. A phenomenon known as cross-talk [7] ("leaking" of signals from the neighborhood to the analyzed spot of the object) has been shown to degrade the visibility of fine tissue details nearly to zero in full-field OCT imaging of deep layers in [1, 8, 9] highly scattering tissues.

To make the full-field and line-scan OCT techniques fully useful in biomedical imaging, it is necessary to reduce the cross-talk effect, develop experimental methods for the imaging of the living tissue and test the developed solutions in a feasibility study, which are the goals of this project.

1.3. Work plan

- In the introductory phase of the project, the PhD candidate will learn under the tutorage of the supervisors the theoretical and experimental basics of the OCT technique. The candidate will study state-of-the-art full-field and line-field OCT techniques and research possible methods of practical implementation of these methods.
- In the intermediate phase, the candidate will take part in the design and construction of the line-field spectral-domain OCT system and will perform imaging tests of the constructed setups.
- The advanced phase will consist of researching and implementation of methods for the reduction of cross-talk in LF-OCT. The candidate will investigate the severity of cross-talk in line-field OCT depending on the light scattering properties of imaged object, will test the effect of coherence-gating on cross-talk reduction and develop, under the couching of the supervisors, dynamic phase modulation methods for cross talk suppression.

1.4. Literature

1. Hillmann, D. et al. In vivo optical imaging of physiological responses to photostimulation in human photoreceptors. Proc. Natl. Acad. Sci. 113, 13138–13143 (2016).
2. Ginner, L. et al. Noniterative digital aberration correction for cellular resolution retinal optical coherence tomography in vivo. Optica 4, 924 (2017).
3. Fechtig, D. J. et al. Line-field parallel swept source MHz OCT for structural and functional retinal imaging. Biomed. Opt. Express 6, 716 (2015).
4. Watanabe, Y. et al. Angular high-speed massively parallel detection spectral-domain optical coherence tomography for speckle reduction. J. Biomed. Opt. 16, 060504 (2011).
5. Gorczynska, I. et al. Comparison of amplitude-decorrelation, speckle-variance and phase-variance OCT angiography methods for imaging the human retina and choroid. Biomed. Opt. Express 7, 911–942 (2016).
6. Hillmann, D. et al. Aberration-free volumetric high-speed imaging of in vivo retina. Sci. Rep. 6, 35209 (2016).
7. Karamata, B. et al. Multiple scattering in optical coherence tomography. I. Investigation and modeling. J. Opt. Soc. Am. A 22, 1369–1379 (2005).

8. Udkamp, H. E. S. et al. In-vivo retinal imaging with off-axis full-field time-domain optical coherence tomography. 41, 1–4 (2016).
9. Stremplewski, P. et al. In vivo volumetric imaging by crosstalk-free full-field OCT. Optica 6, 608–617 (2019).

1.5. Required initial knowledge and skills of the PhD candidate

The candidate will develop all necessary knowledge and skills during the project realization. However, basic knowledge in at least one of the following areas is expected:

- basics in computer programming (preferably C++, Matlab, LabView),
- basics in imaging optics,
- basics in signal processing,
- basic knowledge in electronics, circuits and mechanical design..

1.6. Expected development of the PhD candidate's knowledge and skills

The PhD candidate will have an opportunity to learn, study and research various scientific and engineering topics, adjustable to his or her interests:

- selected problems in tissue optics: influence of scattering in biological tissues on light properties and light propagation,
- modeling of light propagation in turbid media (Monte Carlo, FDTD),
- image formation with partially coherent light,
- methods for controlling light properties and propagation,
- optical techniques in medical imaging and diagnostics,
- design (ZEMAX, OSLO) and construction of optical systems for biomedical imaging,
- biomedical data and image analysis methods,
- advanced programming (GPU, FPGA),
- development of data acquisition software,
- computer control of imaging devices.