*The **CREA**tion of the Department of Physical Chemistry of Biological Sys**TE**ms [CREATE]*

666295 — CREATE — H2020-WIDESPREAD-2014-2015/H2020-WIDESPREAD-2014-2

1st Report on tutoring and mentoring activity of ERA Chair holder towards his employees

[Deliverable D.2.4]

Level of dissemination: Public

Warsaw, March 2018

This project has received funding from the *European Union's Horizon 2020 research and innovation programme* under grant agreement No 666295

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1. Overview of tutoring and mentoring activity of ERA Chair holder towards his employees

This document contains specification of activities taken by the ERA Chair holder team in order to gain specific skills and knowledge, timetable and description of their course.

This report contains specification of study visits since the beginning of the project till the end of Febr. 2018 (M1 – M29).

Prof. Maciej Wojtkowski – ERA Chair holder, and his new employees of the Department of Physical Chemistry of Biological Systems took part in several international conferences and laboratory visits. Participation in these actions, besides the educational and training aspect, gave also an opportunity to establish new contacts and international cooperation with centers that conduct top-class research on optical imaging methods in biological systems.

Lab visit have been carried out to world-class research centers, including:

- Department of Pharmacology, School of Medicine, Case Western Reserve University, USA
- Neurophotonics Lab, Department of Biomedical Engineering, University of California, USA

2. Specification of activity carried out by ERA Chair holder

a) Conferences & Seminars

Lasers in Medicine & Biology, Gordon Research Conference, USA, Vermont

Name: Maciej Wojtkowski

Location: Mount Snow, West Dover, VT

Organizers: The Gordon Research Conferences

Type of event: conference **Date: 9-15/07/2016**

The Gordon Research Conferences provide an international forum for the presentation and discussion of frontier research in the biological, chemical, and physical sciences, and their related technologies. Gordon Research Conferences (GRC) are unique - intimate and small meetings created by „scientists for scientists" with opportunities to meet and talk about cutting edge, unpublished science with colleagues from around the world.

Prof Maciej Wojtkowski was invited to Gordon Lasers in Medicine & Biology conference as a session and discussion leader. He was responsible for organizing session entitled: „Propagation and Imaging Through Turbidity" (13.07.2016 9:00AM- 12:30PM). Prof Wojtkowski invited the following speakers:

1. **Hui Cao** (Yale University, USA) "Mesoscopic Transport of Photons"
2. **Wonshik Choi** (Korea University, South Korea) "Toward Super-Depth and High-Resolution Optical Imaging"
3. **Alwin Kienle** (Institute for Laser Technology in Medicine and Measurement Technique (ILM), Germany) "Light Transport in Biological Media"
4. **Monika Ritsch-Marte** (Innsbruck Medical University, Austria) "Lensless Imaging and the Computational Approach"

In addition prof Wojtkowski took part in an informal committee meeting for upcoming ECBO conference.

PROGRAMME

code::dive 2016

Name: Dawid Borycki

Location: Wroclaw, Poland

Organizers: Nokia Wroclaw

Type of event: conference **Date: 14-16/11/2016**

Dawid Borycki presented a talk entitled *Internet of Things. Building machine vision system supported by artificial intelligence*. The presentation was devoted to explain how to build low-budget machine vision system utilizing the Windows 10 IoT Core, machine learning, and custom image processing routines implemented with OpenCV. In general, wearable IoT devices can be used for remote telemetry of human's health, while the machine learning with custom image processing is found useful for semi- and automatic disease classifications.

In the introductory part, DB also presented research conducted by the CREATE group to broader audience. This was welcomed very well and several young researchers were interested in further details about the CREATE project with respect to imaging and sensing in biological systems. This was a perfect opportunity to promote the CREATE project.

Code::dive is the international conference organized by Nokia Wroclaw, which is one of the largest R&D institute in Poland. Dawid Borycki used this opportunity to discuss research projects of CREATE group with engineers and researchers from Nokia.

PROGRAMME

SPIE Photonics West 2017, Coherence Domain Optical Methods and Optical Coherence Tomography in Biomedi-cine XXI

Name: Maciej Wojtkowski

Location: San Francisco, CA, USA

Organizers: SPIE –international society for optics and photonics

Type of event: conference **Date: 27/01-3/02/2017**

This conference served as part of the SPIE Photonics West 2017 - the world's largest multidisciplinary event for photonics technologies collocated with one of the largest photonic exhibition.

Professor Wojtkowski was mainly involved as the program committee' member of this conference, as well as a co-author of three presentations:

- *Characterization of flowing blood cells using a novel OCT technique: rigorous three-dimensional computational study,*
- *Ultrasensitive detection of nanoparticles using dual optical lock-In microscopy,*
- *Resolution in two-photon infrared vision.*

In addition, Professor chaired a session dedicated to Functional OCT.

Moreover, Professor Wojtkowski participated in the organizational meeting of the European Conferences on Biomedical Optics - a congress, where he is organizing one of the sub-conferences: SPIE/OSA European Conferences on Biomedical Optics, Conference - Optical Coherence Imaging Techniques and imaging in scattering media II, which will take place in Munich, Germany, between 25-29.06.2017.

Professor Wojtkowski was responsible for organization of the session entitled : „ Functional OCT I" which took place on Tuesday 31 Jan.2017 1:30PM- 3:30PM. This session chaired by prof. Wojtkowski included the following

presentations :

1. A theoretical model for optical oximetry at the capillary-level by optical coherence tomography
2. Birefringence and vascular imaging of in vivo human skin by Jones-matrix optical coherence tomography
3. Depth analysis of collagen directionality on axial human uterine cervical tissue using optical coherence tomography
4. Correlation between polarization sensitive optical coherence tomography and SHG microscopy in articular cartilage
5. Parallel detection of Jones-matrix elements for polarization sensitive OCT
6. Polarization-sensitive plug-in optical module for a Fourier-domain optical coherence tomography system

PROGRAMME

SPIE Photonics West 2017, Coherence Domain Optical Methods and Optical Coherence Tomography in Biomedi-cine XXI

Name: Dawid Borycki

Location: San Francisco, CA, USA

Organizers: SPIE –international society for optics and photonics

Type of event: conference **Date: 27/01-3/02/2017**

Dawid Borycki participated in the SPIE Photonics West 2017 conference (Photonic West - PW'17). PW'17 is the world's largest multidisciplinary event for photonics. During this conference, Dawid Borycki gave a talk entitled: "*Quantifying time-of-flight-resolved temporal dynamics of optical field scattered from the turbid media with interferometric near-infrared spectroscopy (iNIRS)".*

Abstract of this presentation is as follows:

"Sensing and imaging methods based on the dynamic scattering of coherent light, including laser speckle, laser Doppler, and diffuse correlation spectroscopy quantify scatterer motion using light intensity (speckle) fluctuations. The underlying optical field autocorrelation (OFA), rather than being measured directly, is typically inferred from the intensity autocorrelation (IA) through the Siegert relationship, by assuming that the scattered field obeys Gaussian statistics. In this work, we demonstrate interferometric near-infrared spectroscopy (iNIRS) for measurement of time-of-flight (TOF) resolved field and intensity autocorrelations in fluid tissue phantoms and in vivo. In phantoms, we find a breakdown of the Siegert relationship for short times-of-flight due to a contribution from static paths whose optical field does not decorrelate over experimental time scales, and demonstrate that eliminating such paths by polarization gating restores the validity of the Siegert relationship."

Inspired by these results, prof. Wojtkowski group developed a method, called correlation gating, for separating the OFA into static and dynamic components. Correlation gating enables more precise quantification of tissue dynamics. To prove this, they show that iNIRS and correlation gating can be applied to measure cerebral hemodynamics of the nude mouse in vivo using dynamically scattered (ergodic) paths and not static (non-ergodic) paths, which may not be impacted by blood.

More generally, correlation gating, in conjunction with TOF resolution, enables more precise separation of diffuse and non-diffusive contributions to OFA than is possible with TOF resolution alone.

PROGRAMME

var Sovia = new Tech(),Microsoft

Name: Dawid Borycki

Location: Warsaw, Poland

Organizers: Microsoft

Type of event: conference **Date: 29/03/2017**

Dawid Borycki participated in ***var Sovia = new Tech*** meeting get updates on novel IT technologies provided by Microsoft. Specifically, Mixed Reality devices (HoloLens), Machine Learning (Microsoft Cognitive Services) and computation platforms (Biological Computing). A special interest was devoted to the Mixed Reality and Artificial Intelligence applications for healthcare.

PROGRAMME

Berlin BRAIN 2017

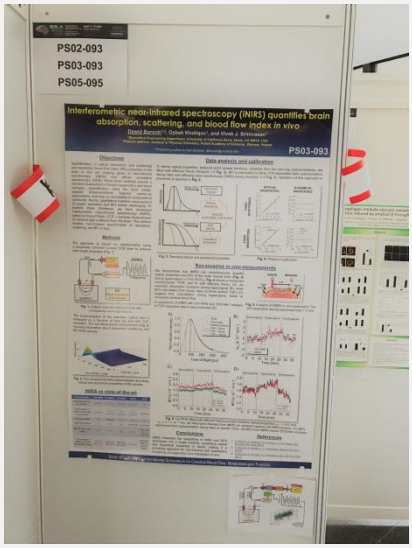
Name: Dawid Borycki

Location: Berlin, Germany

Organizers: ISCBFM – the International Society for Cerebral Blood Flow and Metabolism

Type of event: conference **Date: 1-4/04/2017**

Dawid Borycki presented a poster entitled "*Interferometric near-infrared spectroscopy (iNIRS) quantifies brain absorption, scattering, and blood flow index in vivo*". The presentation was devoted to explain a new method for quantifying optical (absorption and scattering) and dynamical (blood flow index, BFI). These are ongoing goals of near-infrared and diffuse correlation spectroscopies.



Dawid Borycki demonstrated that iNIRS can simultaneously quantify optical properties and BFI of the nude mouse brain during hypercapnia challenge by showing measured representative temporal point spread functions of light scattered from the brain and fits with diffusion theory. He showed that absorption increases during hypercapnia, while BFIs for three distinct path lengths suggest that vasodilation during hypercapnia leads to increased cerebral blood flow.

This poster presentation was also utilized to announce research results to broad audience of neuroscientists and interact with numerous researchers from top scientific institutions, e.g. University of Cambridge (UK), The Institute of Photonic Sciences (Spain), Harvard Medical School (USA).

PROGRAMME

2nd BE-OPTICAL School

Name: Monika Rapolu

Location: Toruń, Poland

Organizers: Nicolaus Copernicus University

Type of event: conference **Date: 2-5/05/2017**

The purpose of the visit was to attend the 2nd BE-OPTICAL School at the Institute of Physics of the Nicolaus Copernicus University and to discuss the characterization of the Bessel Beam OCT setup. The main topics of the lectures were :

- optical technologies for high-resolution imaging, metrology and sensing,
- tissue optics and bio photonics,
- statistics, data analysis and classification tools
- prepare a clinical trial,
- introduction to biostatistics and its applications in clinical studies.

Apart from scientific lectures there was also lecture on how to write a good science paper which was quite informative and useful for the near future. The lectures covered a wide range of topics like measurement and analysis of reflectance and fluorescence spectra, light transport in tissue, modelling and video techniques, laser therapy in field of tissue optics. There was also a brief overview of different imaging modalities and detection approaches, imaging devices such as microscopes, hand held probes and catheters, in vitro and in vivo studies. This particular talk was important course and taught to achieve the super resolution in the spectroscopy. There were courses on statistics, data analysis and classification tools describing the linear and nonlinear time series analysis, delay reconstruction, ordinal patterns, support vector machines, nearest neighbor's classifier, feature selection, surrogate data and hypothesis testing, information flow, statistics for clinical studies (t-test, ANOVA, Bland and Altman plots etc.). In conclusion, the school had covered the lectures which are quite useful in Monika Rapolu field of research and got some fruitful ideas during the discussions to implement in prof. Wojtkowski group's existing setup.

PROGRAMME

Microsoft Build 2017

Name: Dawid Borycki

Location: Washington State Convention Center, Seattle, USA

Organizers: Microsoft

Type of event: conference **Date: 10-12/05/2017**

Dawid Borycki participated in Microsoft Build 2017 conference to learn about new artificial intelligence, machine and deep learning toolkits, provided by Microsoft. Specifically, Professor Wojtkowski's team will utilize new modules of computer vision (CV) in several of ongoing projects. These CV modules can be manually trained (by providing own images along with their labels/descriptions) to the machine learning module. In this way CV module can be easily adjusted to specific applications. For instance to track and recognize objects in the optical coherence microscopy images at the cellular level.

PROGRAMME

CODE EUROPE 2017

Name: Dawid Borycki

Location: Warsaw, Poland

Organizers: Absolvent.pl Group

Type of event: conference **Date: 25/05/2017**

During this meeting, Dawid Borycki gave two talks:

1. *Implementing Internet of Things (IoT) solutions with Azure*. The story of this presentation was about the Azure cloud resources dedicated to the IoT. Specifically, Dawid described how to utilize and connect with each other the following Azure resources: IoT Hub, Stream Analytics, Storage, Event Hub, Notification Hub and Machine Learning to collect, process, and visualize data from remote IoT devices, and send alarms to mobile apps.
2. *Human emotion recognition and image content interpretation with Microsoft Cognitive Services*. The goal of this presentation was to present artificial intelligence capabilities of the Microsoft Cognitive Services (MCS) for building smart apps. After, short description of the MCS, Dawid explained how to develop an app utilizing MCS to recognize human emotions and read image content.PROGRAMME

European Conferences on Biomedical Optics ECBO 2017

Name: Maciej Wojtkowski/Dawid Borycki/Patrycjusz Stremplewski/Mounika Rapolu/Michał Hamkało

Location: Messe Munich, Munich, Germany

Organizers: OSA -The Optical Society/SPIE - International Society for Optics and Photonics

Type of event: conference **Date: 24-30/06/2017**

Prof. Wojtkowski's group, participated in the European Conferences on Biomedical Optics ECBO 2017 organized by the Optical Society-OSA and International Society for Optics and Photonics-SPIE. This conference was an international meeting of scientists, engineers, and clinicians who work with optics and photonics.

This conference was a continuation of "*Optical Coherence Tomography and Coherence Techniques*" and sought to broaden the scope to cover the general area of imaging in biological scattering media based on coherent light and its interactions with biological tissues. The conference provided an interdisciplinary forum for topics in research and development on a physical and theoretical basis of coherent imaging including techniques like optical coherence tomography/microscopy, adaptive optics ophthalmoscopy, nonlinear coherence imaging, photothermal and magnetomotive imaging and imaging with advanced wavefront control. In addition, this conference focused on the development of new light sources, new probes, new detection schemes and new signal processing algorithms for coherent imaging. Applications of coherent optical techniques for morphological as well as functional assessment in different living tissues and phantoms in various medical fields were also covered.

Prof Maciej Wojtkowski was invited to European Conferences on Biomedical Optics ECBO 2017 as a session and discussion leader. He was responsible for organizing sessions entitled: „*Optical Coherence Imaging Techniques*

and Imaging in Scattering Media (OCT) / Advances in Microscopic Imaging (AMI)" which took place on 26.06.2017 16:30AM- 17:30PM and 29.06.2017 10:00AM- 12:30PM.

Dawid Borycki gave a talk entitled "*Removing image distortions by spatio-temporal optical coherence manipulation*".

Shortened abstract of this talk was: "*Light propagating in turbid medium is randomly disrupted, causing image distortions. This issue was tackled by the sample-dependent wavefront shaping. Here, he present a technique of light modulation, in which image distortions are suppressed universally".*

Mounika Rapolu gave a talk on Bessel Beam OCM for analysis of Global Ischemia in Mouse Brain focusing talk mainly by presenting the in-vivo imaging of the global mouse brain ischemia using Bessel beam optical coherence microscopy. This method allows to monitor changes in brain structure with extra control of blood flow during the process of artery occlusion.

Patrycjusz Stremplewski presented of the poster entitled: "*Noninvasive two-photon imaging of murine retina in vivo"*. Presented results were acquired in collaboration with Department of Pharmacology, Case Western Reserve University, Cleveland.

PROGRAMME

Polish Optical Conference 2017

Name: Maciej Wojtkowski

Location: Gniezno, Poland

Organizers: Optics Division of the Polish Physical Society

Type of event: conference **Date: 3/07/2017**

Professor Maciej Wojtkowski participated in the Polish Optical Conference 2017 in Gniezno, with a plenary lecture entitled "*Time-frequency modulation of light phases in imaging*".

The Polish Optical Conference was organized by the Optics Division of the Polish Physical Society. The aim of this conference is to integrate the Polish opticians. Participation in Polish Optical Conference gave an opportunity to meet and exchange views with wide range of people, for whom the development of Polish scientific thought, engineering and teaching in the field of optics is important. This conference combined a high level of expertise with as wide range of subjects as possible to be representative for the entire Polish optics.

Lectures provided within the Polish Optical Conference covered the following topics: quantum optics; nonlinear optics; physics, optics and technology of lasers, and other sources of coherent radiation; optoelectronics and photonics; fiber optics; optical integrated circuits; medical optics; instrumental optics; optical spectroscopy; optical metrology and applications of optics.

PROGRAMME

The 44th Congress of Polish Physical Society

Name: Maciej Wojtkowski

Location: Wroclaw, Poland

Organizers: Optics Division of the Polish Physical Society

Type of event: conference **Date: 10-15/09/2017**

Professor Maciej Wojtkowski participated in the 44th Congress of Polish Physical Society in Wroclaw, with a plenary lecture entitled *"Journey from organs to cells: In vivo imaging by spatio-temporal optical coherence techniques"*.

The Congress of Polish Physical Society is the oldest Polish physics conference, with its history reaching back to the Inaugural Meeting held in Warsaw in 1923 and since then it has been organized in various cities in Poland by local branches of the Polish Physical Society. The 44th Congress took place at the Congress Centre of Wroclaw University of Science and Technology and was co-organized by the Wroclaw University of Science and Technology, the University of Wroclaw and the Institute of Low Temperature and Structural Research. This year it was held under the Honorary Patronage of both Ministry of Science and Higher Education of Poland and the Mayor of Wroclaw. The lectures selected for the Congress showcased the most important recent research advances in physics, with emphasis on achievements that involved Polish contribution. One of the specialized parallel afternoon sessions was devoted to optics, as a branch of physics especially strongly developed in the Department of Optics and Photonics of the Wroclaw University of Technology.

The plenary lecture, gave by Maciej Wojtkowski on 11.09.2017, has been focused on the most appealing and still unsolved problems in biological and medical imaging: *"The possibility of non-invasive visualization of tissue in vivo with an accuracy of microscopic examination".*

The Congress served as a great platform for exchanging knowledge and experience between various groups of physicists-researchers, which allows to broaden the perspective and start new collaborations.

PROGRAMME

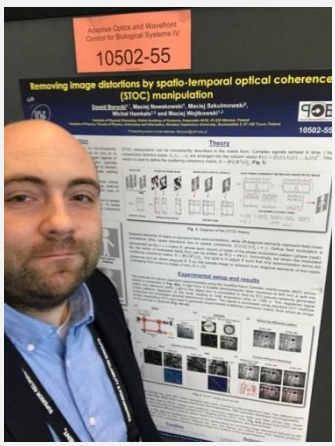
SPIE Photonics West 2018

Name: Dawid Borycki

Location: San Francisco, CA, USA

Organizers: SPIE –international society for optics and photonics

Type of event: conference **Date: 26/01-2/02/2017**



The purpose of this business trip was to present a poster entitled: "*Removing image distortions by spatio-temporal optical coherence (STOC) manipulation*". This was a great opportunity to present method, enabling seeing through opaque layers to a broad community, including scientists (from academia and industry) working on adaptive optics and wave front shaping. This work is of great importance for biomedical imaging, in which the goal is to non-invasively visualize microscopic tissue structure ex vivo or in vivo.

Apart from that Dawid Borycki was able to learn about new developments in microscopy, optogenetics (plenary lectures, delivered by top experts in the field, including Nobel laureates) and virtual, augmented and mixed realities. This year, SPIE Photonics West was hosting the largest event on AR/VR/MR. Importantly, the talks were delivered by principal engineers from the well-known corporations like Microsoft, Google, HTC, and so on.

PROGRAMME: here and here

Management of H2020 international projects

Name: Anna Pawlus

Location: Poznań, Poland

Organizers: SPIE –international society for optics and photonics

Type of event: training **Date: 11-12/12/2017**

This trip was dedicated to attend the "*Management of H2020 international projects*" training, organized by Regional Contact Point for EU Framework Programs in Poznań. Training was focused on several different aspects of managing H2020 projects, including project management rules, specification of projects in Horizon 2020, consortium agreement, management of tasks, people - partners, finances, and evaluation of good and bad management structure.

Training program was a useful "tool", which corresponds with one of the ERA Chair holder activities in the CREATE project – gaining funds for the research conducted at the Department of Physical Chemistry of Biological Systems. Knowledge and skills obtained during this training will be used in the coordination of the recently started H2020 project IMaging-based CUSTOMised EYE diagnostics — 'IMCUSTOMEYE'.

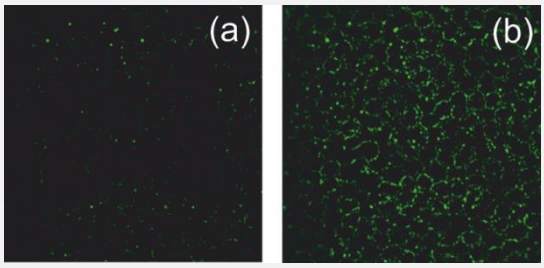
b) Lab visit

Department of Pharmacology, Case Western Reserve University

Name: Patrycjusz Stremplewski

Location: Cleveland, USA

Type of event: lab visit **Date: 29/09-10/10 & 7-12/11/2016**



The goal was to improve the quality of TPEF and reducing laser power needed for imaging by reducing duration of excitation pulse. It is known that the TPEF signal is inversely proportional to the excitation pulse duration, thus we can expect, that by using pulse of duration of 30 fs instead of 75 fs, centered at the same wavelength, we should obtain 2.5 fold higher signal. However reduced pulse duration is associated with increased bandwidth of the laser, thus dealing with the dispersion by the optical elements becomes more difficult. For such a short pulses as 30 fs the higher order dispersion (higher than group delay dispersion GDD) become significant, thus traditional dispersion compensation techniques, like chirped mirrors, pairs of gratings or prisms often fail to give satisfactory results, especially in the case of complicated, commercial microscope setup. Multiphoton intrapulse interference phase scan (MIIPS) setup seems well suited for this purpose, since it is capable of compensating higher order dispersion components, it might be easily adjusted when dispersion of the setup changes, and is capable of compensating huge amount of dispersion.

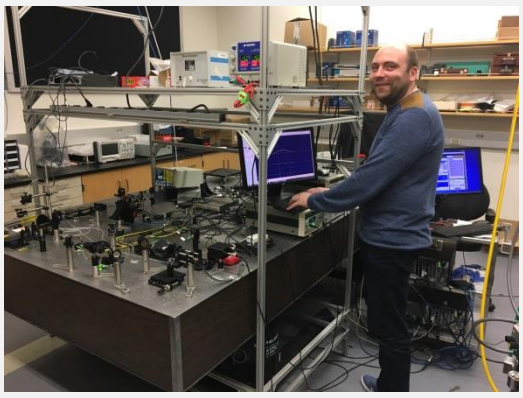
In order to compare results obtained with the lasers generating pulses of 75 fs and 30 fs, we introduced new excitation source and new dispersion compensation unit to our previously reported mutiphoton microscope. Switching between light sources was realized by changing the position of the mirror. Switching can be realized in approximately 30 seconds, so the conditions of the experiments, especially important when imaging live animals, can be preserved when comparing the intensities of the images collected with both lasers. Before imaging the power of both lasers was adjusted to the same level (at the output of the objective, and after the experiment (colleting images with both lasers) it was rechecked.

Neurophotonics Lab, Department of Biomedical Engineering, University of California

Name: Dawid Borycki

Location: Davis, USA

Type of event: lab visit **Date: 2/02-1/03/2017**



Noninvasive optical imaging in turbid media with microscopic resolution has multiple promising applications. For instance, such imaging can be used to visualize breast tumors to early detect and characterize any disorders and thus significantly increase the cure rate (because X-ray mammography cannot identify tumors at their early stage of development). The brain tractography (visualization of the axon maps) may help in characterizing demyelination in diseases of the central nervous system and complex neuropsychiatric disorders. However, as light penetrates deeper regions of the sample it is scattered multiple times. So, the resulting image instead of the pure sample structure, is confounded with noise from a diffusive photons.

There were multiple approaches developed among the past to tackle this problem. All of them isolate the ballistic component (which carries an information about the sample structure) from multiply scattered light (which introduces noise). To this end various properties of the scattered light are used to construct the so called gates.

For instance, multiply scattered light travels longer than ballistic photons (time gate), is depolarized (polarization gate), propagates off-axis (spatial gate), and under specific conditions has the greater chance of being absorbed than ballistic light (absorption gate).

In our previous works on interferometric near-infrared spectroscopy (iNIRS) we identified yet another way to distinguish ballistic light and this visit was to validate this idea. To this end I developed software components and we performed a series of ex vivo experiments. Acquired signals were processed digitally to determine a scattered field autocorrelations from which diffusive and ballistic components were extracted. Results of this research are being prepared as a manuscript.