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

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1st Report on study visits

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1. Overview of study visits

This document contains **specification of study visits carried out by the ERA Chair Holder, his team, and members of synergetic groups** (i.e. research groups selected by the ERA Chair holder for collaboration and development of the research goals adopted by the ERA Chair holder) 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).

Study visits are actions aimed at breaking barriers that inhibit international cooperation of IPC with foreign leading scientific units (through study and laboratory visits). The visits were attended by members of the newly established department and members of synergetic and perspective groups as well. Many of these visits 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
- University of Nevada Reno, USA
- Stanford University, USA
- School of Physics and Astronomy, University of Edinburgh, UK
- Soft Living Matter Group, Princeton University, USA
- Max-Planck-Institute for Dynamics and Self-Organization, Germany
- Institute for Biomedical Optics, University of Luebeck, Germany

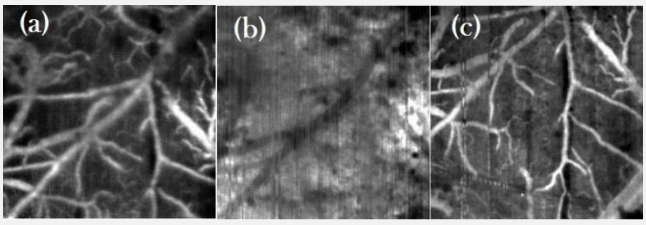
2. Specification of study visits carried out by ERA Chair holder

a) Professor Maciej Wojtkowski group

Name: Monika Rapolu

Place: Optical Biomedical Imaging Group Institute of Physics, Nicolaus Copernicus University

Type of event: study visit **Date: 9-10/01/2017**



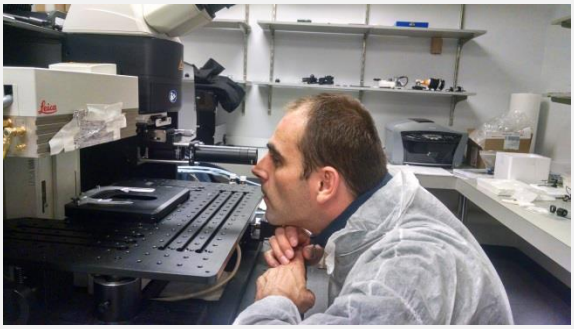
The goal of the visit was a deep analysis of the in-vivo imaging of the global mouse brain ischemia (GI) using Bessel beam optical coherence microscopy. This method allows to monitor changes in brain structure with extra control of blood flow during the process of artery occlusion. The results showed capability and sensitivity of OCM system with Bessel beam of analysing brain plasticity after severe injury within a period of 8 days. This visit has helped to analyse the angiographic and structural B-scan maps along with microscopic images of the mouse brain gives the GI information and allow to visually monitor the induced structural change in brain before global ischemic stroke, at the time of the stroke and up to at least 8 days after the stroke. The research provided a detailed understanding of underlying pathway and showed evidence that this particular mouse model survived the stroke. The deeper analysis of the structural changes after stroke is yet to be made. This experiment shed some light for better understanding global ischemia of the brain and may lead to findings saving many lives, disability reduction and improving quality of life. It may also serve as a convenient tool for testing new drugs against ischemia-induced neurodegeneration.

Name: Patrycjusz Strempewski

Place: Department of Pharmacology, School of Medicine, Case Western Reserve University

Date: 22-28/04/2017

Type of event: study visit **Date: 05-11/06/2017**



Two-photon excitation fluorescence (TPEF) imaging of the back of the eye allows visualization of subcellular structures in the living animal eye. This method is helpful for investigating mechanisms of retinal diseases and development of ophthalmic therapies. Endogenous fluorophores, necessary for replenishing visual chromophore, and thus sustaining vision have absorption maxima in the range from 320 – 400 nm. However, anterior optics of the animal eye poorly transmits light at those wavelengths. Two-photon excitation fluorescence imaging employing 75 fs laser pulses overcomes this barrier and visualizes subcellular organelles in the living animal eye.

The aim of the working visit was to improve the quality of TPEF and reduce laser power needed for imaging by further reduction of the duration of excitation pulses. 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 20 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. Dr Patrycjusz Stremplewski used Multiphoton Intrapulse Interference Phase Scan (MIIPS) technique to solve the problem of the setup dispersion. For shorter pulses and the same average excitation power we obtain signals more than 3.5 times higher than with the longer pulse excitation.

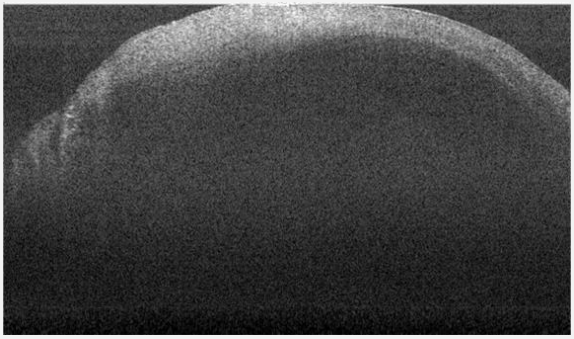
During this visit dr Patrycjusz Stremplewski performed both in vivo and ex vivo tests.

Name: Michał Hamkało

Place: 1) Max-Planck-Institute for Dynamics and Self-Organization, Goettingen

2) Institute for Biomedical Optics, University of Luebeck

Type of event: study visit **Date: 01-05/07/2017**



The goal of the visit was to carry first in the world investigation of full heart using of OCT system. For that Michał Hamkało acquired newly extracted hearts of mice from an authorized laboratory in Goettingen and took it to Luebeck (to next cooperator) with help of dr Jan Christoph. At the Institute for Biomedical Optics in Luebeck he was working with the OCT system (one of the fastest in the world) in order to specify parameters of heart imaging. Crucial part of the investigation was to specify the depth range in the heart muscle of a mouse or a rabbit and speed limits of OCT. This way of measuring is supposed to give an information about behaviour of the heart not only on the surface but also in its volume. Such information can be extremely important for studies of heart attacks (widely developed in Goettingen). As a result of tests, Michał Hamkało have shown that it is possible to acquired 3D images of mouse heart (around 2-3 mm depth of imaging) and similarly for rabbit heart. Since mouse heart is smaller, in this case one can go through the whole wall of the heart. Michał has also run the measurements with high volumes per second rate (requiring huge and fast data transfer). Such measurements are inevitable for beating heart imaging, since processes occurring there can be well observed with rates going up to 100 volumes/s.

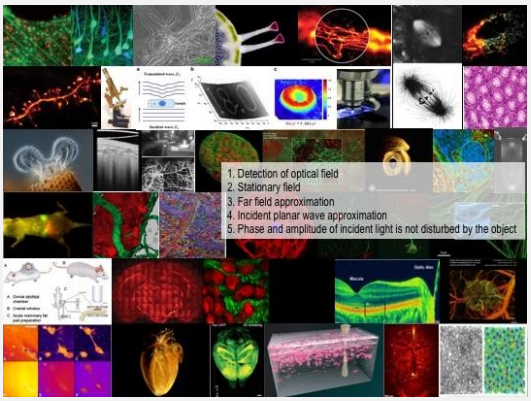
During his stay, Michał also had opportunity to visit laboratories in the Institute for Biomedical Optics, and take part in one seminar (04.07). Acquired results are very helpful for understanding application of OCT systems for heart imaging and moving to the next stage of experiments, which may result in a valuable publication.

Name: Maciej Wojtkowski

Place: 1) University of Gdansk,

2) Medical University Gdansk

Type of event: study visit **Date: 10/07/2017**



The main goal of the visit was to present the research activity of the Physical Optics and Biophotonics Group to the researchers from Medical University Gdansk and University of Gdansk, get to know their scope of research and search for potential areas of cooperation and joint research topics.

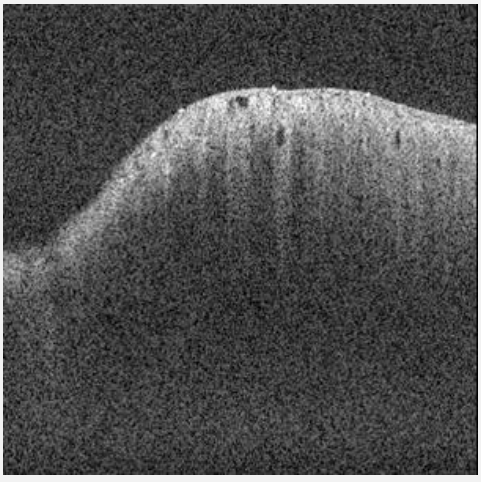
Maciej Wojtkowski gave a lecture entitled „From organs to cells - minimally invasive 3D imaging" at the Faculty of Chemistry of the University of Gdansk, briefly presenting main activities of his group and their main interests. Besides the lecture, this trip included a visit to the laboratories at the University of Gdansk and the Medical University Gdansk, where prof. Wojtkowski had an opportunity to meet and exchange research ideas with prof. Sylwia Rodziewicz-Motowidło, Head of Department of Biomedical Chemistry (University of Gdansk) and dr hab. med. Michał Pikuła, Chairman of the Gdansk Branch of the Polish Society of Experimental and Clinical Immunology (Medical University Gdansk).

Visit to University of Gdansk and Medical University Gdansk was a great basis for establishing future cooperation and an opportunity providing common ground for a joint research, especially taking in consideration the main research areas at the visited laboratories, like stem cell biology, tissue regeneration (human and animal tissue), breeding and analyzing skin cells, adipose tissue and lymphocytes (gene expression, flow cytometry).

Name: Michał Hamkało

Place: Institute for Biomedical Imaging at University of Luebeck

Type of event: study visit **Date: 13-16/12/2017**



This visit was scheduled in cooperation with one of the best group in the field of ultrafast Optical Coherence Tomography (OCT) of **prof. Huber group from Luebeck**. The purpose of the visit was to obtain results from ultrafast (up to 100 vol./s) OCT on rabbit and mice hearts. In order to do that, a cooperation with Max Planck for Dynamics and Self-Organization from Goettingen was established to give an adequate support from a biological point of view (incl. provision with well-prepared hearts).

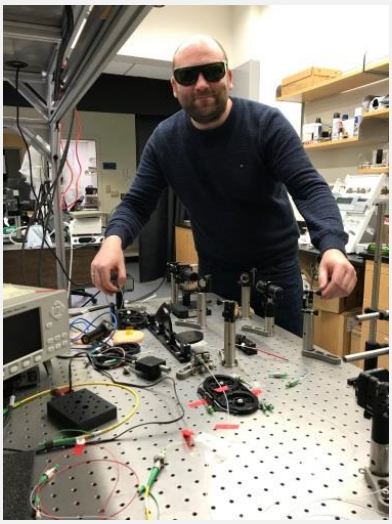
During the trip, both mice and rabbits hearts were measured with different rates (volumes per second) and obtained results were first of this kind (with such speed) performed on hearts (Fig). Based on the results penetration depth, and resolution were estimated and all possible configuration of the OCT set up. On top of that, hearts were artificially moved in order to simulate normal heart beating. Collected results from such experiments will be used to create proper tracking software (necessary for further studies). Thanks to these measurements, the research will move into the next stage – experiments with the use of ultrafast OCT for measuring heart beating in the Langedorff perfusion chamber. In such configuration heart is extracted from animal and can sustain living state for a few hours. Then arrhythmias and heart improper functioning is induced by application of proper medicine. Volumetric

scanning of heart beatining in such conditions will deliver new information about origin of heart diseases, which is ultimate goal of our research cooperation.

Name: Dawid Borycki

Place: Neurophotonics Laboratory, University of California Davis, Davis, CA USA

Type of event: study visit **Date: 18-26/01/2018**



The purpose of this business trip was to perform collaborative work on the interferometric near-infrared spectroscopy (iNIRS). More specifically, experiments to quantify optical properties in dynamic media were performed. Then, the data were processed numerically using the new method of correlation gating to separate ballistic and scattered light transmitted through thick samples. Given these components the optical properties of the dynamic medium from a single measurement were determined. Quantifying light transport in biological tissues and turbid media is an ongoing challenge. This challenge arises from the difficulty in experimentally separating unscattered, ballistic light from forward scattered light. Correlation gating is a new approach that numerically separates light paths based on statistical dynamics of the optical field. This method was applied to separate and independently quantify ballistic and scattered light transmitted through thick samples.

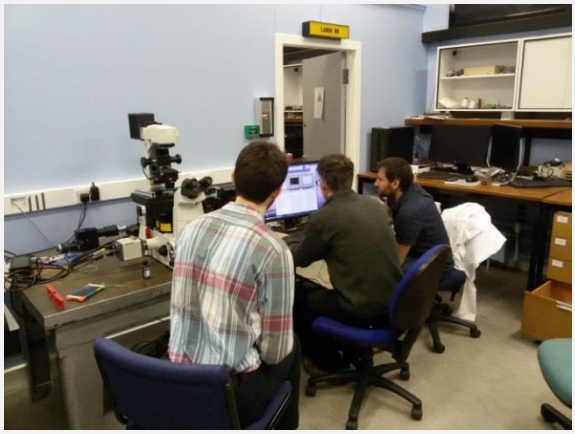
b) Synergetic group

- Department of photochemistry and spectroscopy - Laser Centre
- Soft Condensed Matter Group
- Surface Nanoengineering for chemo- and bio-sensors Group
- Charge transfer processes in hydrodynamic systems Group
- Photochemistry and Spectroscopy Department
- Microfluidics and Complex Fluids Group.

Name: Karina Kwapiszewska, Soft Condensed Matter Group
Krzysztof Szczepański, Soft Condensed Matter Group

Place: School of Physics and Astronomy, University of Edinburgh

Type of event: study visit **Date: 24-28/04/2017**

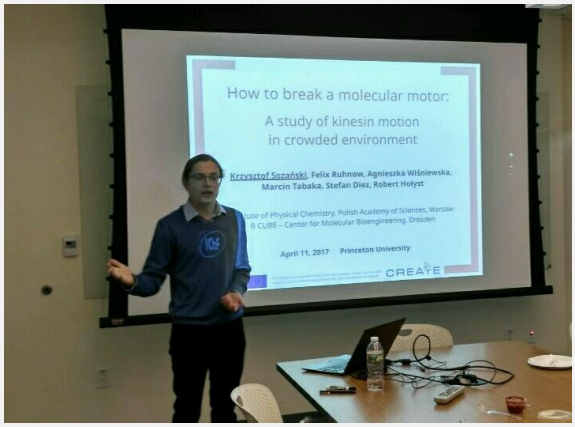


The goal of the visit was to perform experiments on human cells using novel microscopic technique: differential dynamic microscopy (DDM). The plan of the experiments contained quantification of movement of subcellular components in native HeLa cells and observation of changes of mobility during programmed cell death (apoptosis). Overall conclusion of the performed experiments is that limits of DDM method were reached. Single values that could have been obtained were consistent with those measured by fluorescence correlation spectroscopy (FCS) in IPC. However, repeatability was much worse and no additional information could have been obtained. The possible solution for those problems would be work using brighter (more dye molecules) and more stable (different dye) or bigger probes (nanoparticles). This needs more work concerning optimization of probe introduction to cell interior.

Name: Krzysztof Sozański, Soft Condensed Matter Group

Place: Princeton University

Type of event: study visits **Date: 10-13/04/2017**



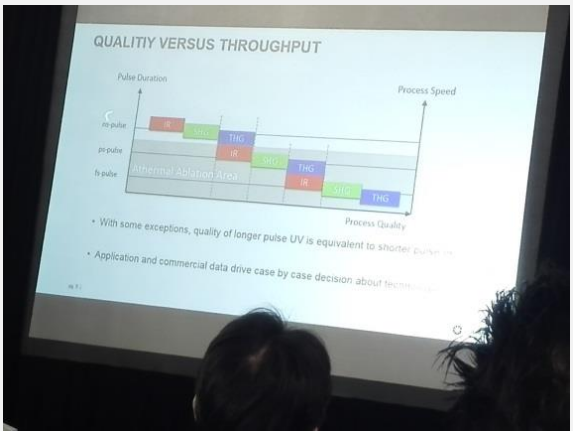
The purpose of the travel was to assess the perspectives for future collaboration with the Soft Living Matter Group run by prof. Clifford Brangwynne at the Princeton University. The group conducts cutting-edge research in the field of physicochemistry of soft matter in living systems. The group possesses a wide background and know-how concerning biophysical studies on model biological systems at all complexity levels (single cells, tissues and organisms). It is applied there, i.e., to studies of phase transitions in living systems and intrinsically disordered proteins, which play a key role in the pathogenesis of neurodegenerative diseases.

These topics are directly related to the research conducted currently at the Department of Physical Chemistry of Biological Systems and Department of Soft Condensed Matter at IPC as well as planned future projects of these departments. During his stay, Krzysztof Sozański gave a talk entitled: "*How to break a molecular motor: A study of kinesin motion in crowded environment*", which was met by a lively reception and sparked a compelling discussion. Krzysztof Sozański held meetings with the PI (prof. Brangwynne) and majority of the group members, talking about their current projects, experimental capabilities of the labs and areas where our scientific interests overlap, as well as the possibilities of the future collaboration with the group.

Name: Yuriy Stepanenko, the Laser Centre

Place: CLEO Laser Science to Photonic Application conference, the laboratory of Biological Imaging of prof. Mark J. Schnitzer in Howard Hughes Medical Institute, Stanford University, San Jose /USA

Type of event: conference and study visit **Date: 13-22/05/2017**

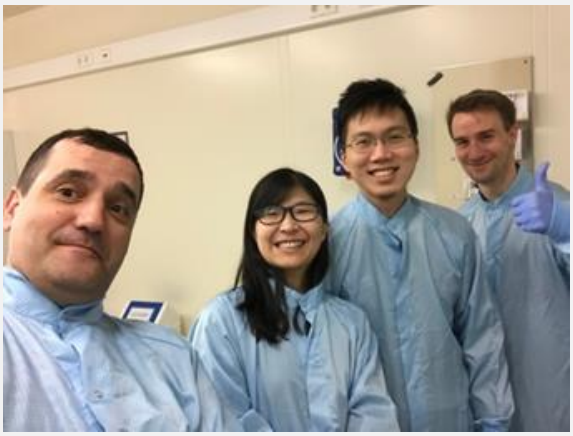


The presentation entitled "Ultrafast laser mode-locked using Nonlinear Polarization Evolution in Polarization Maintaining fibers" was presented during the attendance to the CLEO Laser Science to Photonic Application conference. Along with conference participation we visited the laboratory of Biological Imaging of prof. Mark J. Schnitzer in Howard Hughes Medical Institute, Stanford University. During our visit at Nevada Terawatt Facility, University of Nevada Reno stability of the parameters of our newly developed femtosecond oscillator was tested in the Z-pinch laboratory.

Name: Jan Guzowski, Microfluidics and Complex Fluids Group

Place: Lab at University of Freiburg, Germany

Type of event: study visit **Date: 9-10/01/2018**

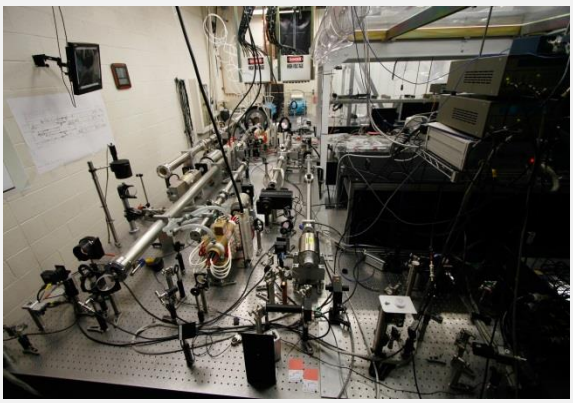


Together with other members of the group Jan Guzowski visited **Prof. Roland Zengerle Lab at University of Freiburg**, Germany. The agenda of the meeting included presentation by Prof. Zengerle as well as by other two group leaders in his lab, namely **Dr. Peter Koltay** and **Dr. Felix von Stetten**. The purpose of the visit was to establish long-term collaboration with prof. Garstecki lab, in particular associated with co-advising by prof. Zengerle of two PhD students, Yu-Ting Kao and Yu-Kai Lai. Jan Guzowski's contribution to the meeting was a presentation of previous research and brainstorming new ideas for the PhD theses. The hosts also provided the visitors with a guided tour around the lab as well as around the microfabrication facilities at Hahn-Schickard, a non-profit organization supporting industry in developing new products based on MEMS technologies.

Name: Yuriy Stepanenko, the Laser Centre

Place: University of Nevada Reno, USA

Type of event: study visit **Date: 1-5/02/2018**



Yuriy Stepanenko visited the University of Nevada, Reno. The purpose of this study visit was to continue the collaboration began in 2007 with the group of Laser-plasma interaction at Nevada Terawatt Facility, University of Nevada, Reno. The group uses advanced laser sources for plasma generation, particle acceleration and diagnostics of Z-pinch. During his stay Yuriy participated in experiments of high-energy plasma generation using the Z-pinch device. He presented diagnostic tools for ultrafast lasers developed at the Institute of Physical Chemistry in the context of its applications in experiments of laser-generated plasma. The visitors discussed the possibilities of further scientific cooperation in the field of stable femtosecond pulses generation using fiber optics.

c) Others

Name: Maciej Wojtkowski/Marcin Opałło/Aleksander Jabłoński/Robert Hołyst/ Hou Sen

Place: Nankai University in Tianjin, China

Type of event: study visit **Date: 6-8/03/2017**

Professor Maciej Wojtkowski, the ERA Chair holder, accompanied by the:

-Director of the Institute of Physical Chemistry PAS - professor Marcin Opallo,

-President of the Scientific Council of IPC - professor Aleksander Jablonski

-Project Coordinator - professor Robert Holyst, and

-former postdoc at Professor Holyst Group – Associate Professor Hou Sen, linking person with Nankai University,

visited Nankai University in Tianjin, China (the 6 – 8th March, 2017). The main aim of this event was to visit laboratories, which required presentation of current research of IPC, looking for joint research topics, and to sign a cooperation agreement between the **Institute of Physical Chemistry PAS** and **State Key Laboratory of Medicinal Chemical Biology Nankai University**.

The Nankai University, as one of the strongest scientific units, hosts two prestigious and well-funded State Key Laboratories: one of Medicinal Chemical Biology and the second - of Elemento-Organic Chemistry. The National Key Laboratories are private-public laboratories, currently receiving funding and administrative support from the central government of the People's Republic of China.

The State Key Laboratory of Medicinal Chemical Biology has an interdisciplinary character, and as such is a valuable partner for the IPC in the face of strong biological attributions of the ERA Chair project.