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New Photosensitizers Based on Cyanoaryl Porphyrazines Enabling Strong Antitumor, Rigidochromic and Immogenic Effects in Photodynamic Therapy

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Abstract. New type of rigidochromic cyanoaryl porphyrazines (CAPzs) had been developed in IOMC RAS. Being incorporated into various nano-sized macromolecular carriers they are found to be highly effective photosensitizers and reducing agent of tumors during photodynamic therapy (PDT). The main stractural feature of cyanoaryl porphyrazine (CAPz) macrocycles is associated with the structure of their peripheral frame which consists entirely of dipolar structural elements of the D- π -A type, where D is an aromatic π donor, A is the strongly electron-deficient CN group, and $-\pi$ - is π -conjugated space of porphyrazine macrocycle. On this reason CAPzs enable to form the specific molecule comformation termed twisted intramolecular charge transfer state (TICT) accessing the mobility of some molecule fragments (molecular 'rotors') upon photoexcitation. In the low rigidity environment TICT state is carried out through the 'rotor' motion leading to weak or negligible emission. On the contrary, higher rigidity settings introduce a significant energy barrier to TICT state formation favoring radiative decay and a switching on of fluouorescence emission. CAPz macrocycles demonstrate very weak emission in the low viscosity solutions but due to a binding of dye to intracellular biomolecules they show the noticeable fluorescence when they accumulate in cancer cells. PDT leads to a significant increase in the rigidity of the intracellular space of damaged cells, leads to an increase in the fluorescence lifetime of cyanoarylporphyrazines. Thus, dynamic fluorescence lifetime imaging of rigidochromic photosensitizer using FLIM setup allows us to track intracellular viscosity changes upon PDT. In other words, we enable real time monitoring the dynamics and effectiveness of PDT, which provides a specifically personalized therapeutic effects. To our best knowledge CAPzs are the first and unique macrocyclic π -conjugated framework that combine the strong photodynamic and rigidochromic properties. In addition, the recent in vitro and in vivo investigations have shown that some of

CAPzs are found to be the efficient inducers of various types of immunogenic cell death during PDT [1]. Involving the body's immune system in the fight against cancer prevents therapy resistance effect and significantly improves treatment outcomes.

Keywords: cyanoaryl porphyrazines, photosensitizer in PDT, twisted intramolecular charge transfer, rigidochromism

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INVITED SPEAKERS

Id-576

Visualization of the Sub-Wavelength Structure of Biomedical Objects with Nano-Sensitivity to Structural Alterations

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Abstract: Visualization of nanoscale structural changes in biological samples for early detection of different pathologies poses a significant challenge to both researchers and healthcare professionals. The spectral encoding of spatial frequency (SESF) approach permits visualization of the sub-wavelength structure in 2D microscopy imaging [1-5]. Optical coherence tomography (OCT) facilitates label-free, depth resolved structural and functional imaging of living tissues. However, the structural sensitivity and resolution of intensity-based OCT imaging are fundamentally limited to microscale. Here, we present the SESF approach and an adaptation of the SESF approach for depth resolved visualization of the sub-wavelength structure with nano-sensitivity to structural alterations. We called this novel technique nano-sensitive OCT (nsOCT) [6-13]. In our talk we will describe the principles of the SESF approach and nsOCT, and demonstrate different applications which show advantages of these novel techniques.

Keywords: Biomedical optics; Label free imaging; Optical coherence tomography; Nano-sensitivity; submicron structure; Depth resolved imaging.

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ld-578

Biomechanics of the Eye: From the Cornea to the Lens to the Retina

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Abstract: Several optical methods are emerging as powerful tools for noninvasive quantification of viscoelastic properties of ocular tissues such as the cornea, the lens, the sclera, the iris, and the retina. In this presentation, I'll overview recent progress made on the development and application of Optical Coherence Elastography (OCE) and Brillouin Spectroscopy techniques for quantification of mechanical properties of ocular tissues in normal and pathological states.

Perceptually Calibrated Scale of Optical Aberrations Generated by Multifocal Corrective Lenses

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Abstract. One of the problems associated with the use of modern vision correction is undesired optical phenomena in the form of halo and glare. These effects are a consequence of the use of multifocal techniques in lenses, such as higher-order diffraction or division of the surface into zones with different optical powers. Such lenses restore patients' near and far vision, but creates also visual disturbances in the form of light scattering and illusory bright rings. These phenomena significantly affect the quality of life and safety of functioning at night (especially during road traffic). There are a variety of methods for measuring and classifying them. Some of them are based on the subjective qualitative assessment of the size and intensity of halo and glare phenomena by patients. Others rely on the optical measurement of the imaging properties of a lens. None of them are accurate enough to reliably determine the magnitude and intensity of photopsies in the field of view. We have developed a new psychophysical measurement method and scale based on an computer algorithm that generates optical elements introducing model halo and glare phenomena in the field of view. The study involved a group of patients using multifocal methods of vision correction and a reference group of people with monofocal intraocular lenses. We measured the patients' field of view at a distance in the presence of bright spots provoking photopsies. We then modeled these photopsies with simplified but fully controlled optical elements with parameters that quantitatively describe a given visual disturbance.

Keywords: MFIOL; EDOF; photopsy; halo; glare.

Acknowledgment: The research was supported by the National Center for Research and Development under the LIDER LIDER/15/0061/L-9/17/NCBR/2018 programme and by the Warsaw University of Technology in the "Excellence Initiative - Research University" programme.

Using Laser Trapping for the Optimization of the Therapeutic Ratio

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Abstract: Cancer is the leading cause of death worldwide. It is treated with methods such as radiotherapy (RT) is administered. There is a growing concern for radiation-induced tissue toxicity. Radiation is most dangerous to cells during certain phases of the cell cycle within other phased. It damages cells by causing DNA breaks on both single- and double-stranded strands, resulting in cell death through various mechanisms. Thus, radiotherapy requires dosing that balances the killing of cancer cells with the radiotoxicity of healthy cells, and this is referred to as the *therapeutic ratio*. Determining the optimal dose is a great unmet and complex need. To obtain a favorable tradeoff between treatment benefit and morbidity, there must be a balance of radiation effectively destroying cancerous cells while preventing the detrimental effects of radiotoxicity on the healthy cells.

Using laser trapping technique, the present work contributes to advancing radiotherapy, a leading treatment method for cancer. A single, 2-cells, 3-cells, 4-cells, and 5-cells were trapped using the high-intensity gradient infrared laser at 1064nm and allowed to become ionized. In this work, a systematic study of Threshold Ionization Energy (TIE) and Threshold Radiation Dose (TRD) versus mass for both single and multi-cell ionization using Laser trapping techniques on neuroblastoma is presented. The results show that TIE increased as the mass of cells increased, meanwhile TRD decreased with the increase of cell mass. We observed an inverse correlation between Threshold Radiation dose and cell mass. We demonstrate how to compute the maximum radiation dosage for cell death using the laser trapping technique. Results show a possible blueprint for computing the Threshold Radiation Dose in vivo. The use of multiple cell ionization to determine radiation dosage along with better data accuracy concerning the tumor size and density will have profound implications for radiation dosimetry.

Keywords: Laser Trapping; Radiotherapy; Therapeutic ratio.; Chemotherapy, Oligostilbene

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Nanobiophotonics in the Studies of Drug-Chromatin Interactions: Single-Particle Fret Microscopy Approach

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Abstract. Many anticancer drugs target chromatin. Modes of action of such drugs include disturbance of chromatin structure and/or impairment of interactions between chromatin and proteins responsible for DNA reparation, replication and transcription. Understanding the mechanisms of antitumor action and evaluating their effectiveness are key tasks in the studies of both recognized and new drugs. Here we present nanobiophotonics approach based on single particle Förster resonance energy transfer (spFRET) microscopy and discuss its benefits in the study of drug interactions with nucleosomes and nuclear proteins. We designed a set of fluorescently labeled nucleosomes of different structure, assembling them from core histones and DNA of variable length containing a strong nucleosome-positioning sequence. A donoracceptor pair of fluorescent labels attached to neighboring gyres of nucleosomal DNA or to linker DNA enables probing of changes in a nucleosome structure. spFRET analysis is performed in a very diluted solution of nucleosomes by measuring fluorescence from freely diffusing single nucleosomes crossing the focal volume of a laser beam under microscope. Analysis of FRET efficiency at the level of single nucleosomes offers a unique opportunity to recognize various types of complexes with drugs and nuclear proteins, which are simultaneously formed in solution. spFRET analysis helps to find out the mechanisms of drug action revealing unwrapping of nucleosomal DNA, changes of nucleosome conformation, modulation of interactions between nucleosomes and nuclear proteins, and alterations in the structure of such complexes and enzymatic activities of nucleosome-interacting proteins.

Keywords: Nanobiophotonics; Drug; Nucleosome; spFRET; Fluorescence.

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INVITED SPEAKERS Id-591

Optical Imaging Technologies for Skin Diagnostics

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Abstract. A brief review on imaging methods and devices for non-invasive skin diagnostics and monitoring, recently developed at the Biophotonics Laboratory (https://www.asi.lu.lv/en/labs/biophotonics-laboratory/) in Riga, will be presented. The innovative methods include bi-modal multispectral - autofluorescence imaging for skin melanoma detection [1] and multispectral - thermal imaging for sepsis diagnostics [2], as well as tri-modal multispectral – autofluorescence lifetime – Raman band imaging for complex examination of skin malformations [3]. Besides, significant improvements in high-resolution spectral imaging [4, 5] and remote photoplethysmography imaging of skin [6] have been proposed. All above-mentioned methods have been implemented in portable prototype devices which have passed primary clinical tests on volunteers. Results of the clinical measurements and potential future applications of the developed technologies will be discussed.

Keywords: Skin diagnostic imaging, multispectral, melanoma, sepsis, photoplethysmography imaging.

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Functional Brain Imaging with Dynamic Light Scattering Imaging

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Abstract. Presently, Dynamic Light Scattering (DLS)-based modalities, including laser Doppler flowmetry (LDF), Diffusing Wave Spectroscopy (DWS) and laser speckle contrast imaging (LSCI), are widely used for non-invasive optical sensing and diagnostic imaging of blood flow in medical and biomedical applications, including neuroimaging. It should be pointed out that the majority of biological tissues are the highly heterogeneous media composing mixture of static and dynamic structural inclusions. The presence of static areas exhibit non-ergodic features providing systematic uncertainty in the quantitative interpretation of the measured DLS optical signals. In fact, various DLS-based imaging experimental systems are extensively used for imaging and quantitative assessment of blood flows within biological tissues, whereas the issues associated with the non-ergodicity are typically ignored. Based on the simple phenomenological model we present a justification for the applicability of DLS-based imaging technique for monitoring of blood flows within brain under the formally broken ergodicity conditions [1]. In addition, we introduce a time-space Fourier Kappa-Omega filtering approach for stabilization of fast dynamic brain images *in vivo* [2]. The proposed approach improves the quality of DLS-based imaging, avoiding the discrepancies in oscillations of blood flow associated with the heart and respiratory activities [3].

Keywords: Dynamic Light Scattering; Brain imaging; Blood flow; Ergodicity; Laser speckles.

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POSTER SESSIONS Id-574

Viburnum Opulus L. Extracts with Gold Nanoparticles as Photosensitizers for PDT

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have been studied and their use as a potential photosensitizers of singlet oxygen for photodynamic therapy has been approved. The presence of long-lived excited states in the extract molecules was established by spectral methods and time-resolved spectroscopy methods and the dependences of the absorption capacity and luminescence intensity of the extract molecules on the concentrations of oxygen and ablative gold nanoparticles in the reverse micelles of AOT (sodium dioctyl sulfosuccinate) have been established. Extract molecules' luminescence plasmonic enhancement and the processes of their complexation with oxygen have been also established. Furthermore, the rate constants of the processes of conversion of exciting energy in complexes have been determined.

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POSTER SESSIONS Id-581

Stereoscopic Depth Perception in Binocular Vision Corrected by Light Sword Lenses

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Abstract. There is an ongoing and promising research regarding use of Light Sword Lens (LSL) for presbyopia correction. The optical power in an LSL is modulated angularly along its aperture, which allows for formation of a continuous segment of focus, instead of one or multiple points in case of monofocal and multifocal intraocular lenses, respectively. However, one of the downsides of the imaging properties of the element is a slight transversal shift of the focal point along optical axis, which depends on the object vergence. In this study, we investigated this phenomenon, in order to estimate how it may interfere with depth perception based on stereopsis when both eyes are equipped in an LSL. A relative angular misalignment of the LSLs positioned on both eyes may create different depth perception errors, since the element does not possess rotational symmetry. The study is performed subjectively on patients using proprietary "VIDO" dynamic visual optics simulator.

Keywords: LSL; EDOF; dynamic optics; stereopsis; preception research

Acknowledgment: The research was supported by the National Center for Research and Development under the LIDER LIDER/15/0061/L-9/17/NCBR/2018 programme and by the Warsaw University of Technology in the "Excellence Initiative - Research University" programme.

POSTER SESSIONS Id-582

Position Tolerance of Light Sword Lens in Presbyopia Correction

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Abstract. Light Sword Lens (LSL) is a promising type of optical element with potential application in the correction of presbyopia due to extending the depth of light focusing. However, in a possible real-world situation, as an implant in the patient's eye or used as a contact lens, there exists a possibility of movement of the element with respect to the optical axis of the eye. Since the LSL is highly asymmetric, this can affect the performance of vision correction. In this study, we investigate the impact of this movement on the optical performance and vision acuity. For instance, certain ranges of movement may improve vision quality of the elements in a specific range of defocus values, leading even to enhance the overall usefulness of the LSL. The performance of the optical elements will be compared in terms of the Strehl ratio, PSF shape, and acuity of vision. The presented results will allow for better understanding of the LSL optical element performance and its application in human vision correction. The study is performed subjectively on patients using proprietary "VIDO" dynamic visual optics simulator.

Keywords: LSL; LSOE; presbyopia; visual acuity; visual optics

Acknowledgment: The research was supported by the National Center for Research and Development under the LIDER LIDER/15/0061/L-9/17/NCBR/2018 programme and by the Warsaw University of Technology in the "Excellence Initiative - Research University" programme.

ALL SUBMISSIONS & TOPICS

Topics	Submissions
	Id 575 - New Photosensitizers Based on
Photochemistry	Cyanoaryl Porphyrazines Enabling Strong
	Antitumor, Rigidochromic and Immogenic
	Effects in Photodynamic Therapy
	Id 590 - Nanobiophotonics in the Studies of
	Drug-Chromatin Interactions: Single-Particle
	Fret Microscopy Approach
Optical Coherence Tomography	Id 576 - Visualization of the Sub-Wavelength
	Structure of Biomedical Objects with Nano-
	Sensitivity to Structural Alterations
	Id 578 - Biomechanics of the Eye: From the
	Cornea to the Lens to the Retina
Optical Biomedical Diagnostics	Id 580 - Perceptually Calibrated Scale of
	Optical Aberrations Generated by Multifocal
	Corrective Lenses
	Id 591 - Optical Imaging Technologies for Skin
	Diagnostics
	Id 584 - Using Laser Trapping for the
Lasers and Tissue Interactions	Optimization of the Therapeutic Ratio
Monitoring of Brain	Id 594 - Functional Brain Imaging with
	Dynamic Light Scattering Imaging
Photodynamic Therapy	Id 574 - Viburnum Opulus L Extracts with
	Gold Nanoparticles as Photosensitizers for Pdt
	Id 581 - Stereoscopic Depth Perception in
	Binocular Vision Corrected by Light Sword
Optics And Photonics	Lenses
	Id 582 - Position Tolerance of Light Sword
	Lens in Presbyopia Correction