1st International Biophotonics Meeting in Israel
Dates: Sunday-Tuesday 9 - 11 December 2012

Conference Chairs
Bruce J. Tromberg, Beckman Laser Institute and Medical Clinic (United States); Israel Gannot, Tel Aviv Univ. (Israel)

Program Committee
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Sunday 9 December

Coffee and Registration
Date: Sunday 9 December Time: 08:00 - 08:30

Welcome and Opening Remarks
Date: Sunday 9 December Time: 08:30 - 09:00

Prof. Bruce Tromberg and Prof. Israel Gannot – Conference chairs
Prof. Joseph Klafter – President of Tel-Aviv University
Prof. Daniel Hershkowitz - Minister of Science and Technology

Award Presentation 09:00 - 09:15

Lifetime Achievement Award: Prof. Abraham Katzir
Date: Sunday 9 December Time: 09:00 - 10:00

Shedding new light on old diseases
Paper BPI12-1
Time: 09:15 - 10:00

Author(s): Abraham Katzir, Tel Aviv Univ. (Israel)
Biomedical optics is a very new field, but it actually originated thousands of years ago. Medicine is as old as mankind and diseases of today were discovered in mummies in ancient Egypt and are a continuation of diseases of creatures that preceded man. Man may have used surgical tools in the Neolithic period (~ 7000 BC). Physicians in Ancient Egypt, around 3000 BC, used a fire-drill, a heated sharp utensil, as a surgical tool. It was used, for example, to drill holes in the jaw to
relieve abscesses and for cauterization – a predecessor to laser surgery. The sun was worshipped by many ancient cultures, and their physicians discovered its curative powers. The use of specific chemicals to augment the therapeutic effect of sunlight dates back several millennia. Extracts from plants containing psoralen were used in Ancient Egypt to treat skin affected by disease. This was followed by exposure to sunlight. Skin depigmentation, such as vitiligo, was treated in this way in Egypt and in India – an early example of photomedicine. At the time of Hippocrates sun bathing was prescribed in Ancient Greece for curing of diseases (heliotherapy). During the Middle Ages sun worship was associated with Paganism and therefore not used. But in the beginning of the 19th century in Europe researchers started developing artificial light sources for medical diagnosis and therapy. They also developed photomedicine that led to modern photodynamic therapy (which still uses psoralen). Man-made glass dates to 3000 BC, when glass beads were made in ancient Egypt and Mesopotamia. Glass has been gradually developed to form lenses and optical fibers and endoscopes, which are widely used now by physicians. In the 20th century there were other major discoveries in the area of electro-optics, including the lasers, detectors, imaging and display systems etc. All of these had enormous impact on medicine. Biomedical optics is thus the culmination of five thousand years of the use of light in medicine.

Coffee/Exhibition Break 10:00 - 10:30

Keynote and Plenary Session
Date: Sunday 9 December  Time: 10:30 – 12:00

Optically probing the nano-architecture of cells and tissues (Keynote Presentation)
Paper BPI12-2
Time: 10:30 - 11:15

Author(s): Steven L. Jacques, Oregon Health & Science Univ. (United States)
Optical measurements are sensitive to structures on the size scale of a wavelength of light. Hence, cellular and extracellular structures with sizes in the range of 200-2000 um dominate optical measurements of biological tissues. The contribution from very small structures (<200 um) is still apparent, however, as apparent "Rayleigh scattering" which is significant in tissues with collagen. Two measurements are able to discern the size distribution: (1) Confocal reflectance measurements as the depth position (z) of the focus is scanned down into the tissue, R(z) = rho exp(-mu z). In this case, the factor rho is especially sensitive to the size distribution of the scattering structure within a tissue. Using rho, we have detected a single gene mutation (osteogenesis imperfecta) in mouse skin. We have detected the degradation of collagen fibers into fibrils by metal-metalloproteinases. We have detected the effects of "optical clearing" of dermis when dermis is soaked in glycerol. (2) Wavelength dependence of diffuse light reflectance. In this case, the size distribution of structures in a tissue is described by A (d/1nm)^-B, a fractal distribution of sizes (d = diameter of structure). Such a distribution yields a wavelength (lambda [nm]) dependent reduced scattering coefficient, mus'(lambda) = a (lambda/1nm)^-b. The relationship of b versus B will be shown, along with values of b and apparent B for soft tissues and skin from the literature. Such measurements offer an opportunity to assess and monitor the nanoarchitecture and microarchitecture of skin and other tissues. Detecting the effects of pathology, actinic damage, and pharmaceuticals on the skin are potential applications of these non-invasive optical methods.

Functional optical imaging of the retina (Invited Paper) (Plenary)
Paper BPI12-14
Time: 11:15 - 12:00

Author(s): Amiram Grinvald, Weizmann Institute of Science (Israel) and Optical Imaging Ltd (Israel)
Optical imaging proved to be a useful tool in functional studies of the retina providing early diagnosis of the prevalent retinal diseases. Retinal reflectance changes in the absence of photic stimulations, or in its presence, yield information obtained none invasively about red blood cell blood velocity, capillary images of richer information relative the gold standard FA (but without any contrast agent), qualitative oximetry, choroidal visualization and in response to photic stimulation, information is provided about metabolic processes underlying responses in the retina. The quantitative images of these parameters are obtained using an FDA approved Retinal Function Imager (RFI).

Lunch/Exhibition Break 12:00 - 13:20
Applying biophotonics techniques to reveal a new treatment for complete protection from stroke
Paper BPI12-4
Time: 13:30 - 13:50
Author(s): Ron D. Frostig, University of California Irvine (United States)
In this talk I will describe how using complementary biophotonics techniques including intrinsic signal optical imaging (ISOI), laser speckle imaging (LSI), and optical coherence tomography (OCT), revealed a surprising new way by which a mild sensory stimulation completely protects the brain from an impending ischemic stroke following permanent occlusion of the middle cerebral artery in an adult rat model. These techniques helped revealing the underlying mechanism responsible for this new type of protection: stimulus-induced neurovascular plasticity that leads to massive reorganization in blood-flow patterns. I will describe the advantages and limitations of this protection strategy and its potential translational implications.

Multimodal optical neural imaging monitoring blood oxygenation and flow (Invited Paper)
Paper BPI12-5
Time: 13:50 - 14:20
Author(s): Ofer Levi, Hart Levy, Dene Ringuette, Yaaseen Atchia, Raanan Gad, University of Toronto (Canada); Suzie Dufour, Ctr. de Recherche de l'Univ. Laval Robert-Giffard (Canada) and Univ. of Toronto (Canada)
We present the development of a multi-modality optical neural imaging system, to image blood flow velocity and oxygenation in a rat brain, using a fast CCD camera and miniature VCSEL illumination. We have demonstrated the use of this system in tracking ischemia and with adding a fluorescence modality, in evaluating the disruption of a blood-brain barrier and tracking seizure activity in the brain. We will also review our progress towards a portable imaging system as a minimally invasive method for long-term neurological studies in un-anesthetized animals, which should provide a better understanding of progression and treatment efficacy of various neurological disorders.

Quantitative monitoring of brain hemodynamic and morphology after head trauma using structured near-infrared illumination through intact mouse head
Paper BPI12-6
Time: 14:20 - 14:40
Author(s): David Abookasis, Boris Volkov, Ariel Univ Ctr (Israel); Marlon S. Mathews M.D., Beckman Laser Institute and Medical Clinic, University of California, Irvine (United States)
Structured near-infrared (NIR) illumination system capable of imaging and quantitatively map changes in tissue hemodynamic properties and morphological features in non-contact and scan-free fashion was used in this study pre-and post head injury in mice brains (n=10). Injury was induced in anesthetized male ICR mice by weight-drop model using ~50gram cylindrical metal falling from a height of 90cm onto the intact scalp. During experiments, NIR structured light was projected at different spatial frequencies and wavelengths before and after injury on the mouse head and CCD camera positioned perpendicularly above the head acquired the reflected light. Computer analysis on the captured data reveals spatiotemporal changes in the distribution of brain tissue optical properties namely absorption and reduced scattering coefficient. Using Beer's law and Mie theory, hemodynamic (hemoglobin, oxygen saturation, lipids) and morphological changes were clearly observed in comparison to baseline measurements. Overall, results confirm measurable and quantifiable changes over time on both parameters and demonstrate our ability to detect variation in intact head physiological parameters during injury. To the best of our knowledge, this is the first demonstration of using NIR structured light based system on intact head in response to head trauma.

Temporally focused imaging of a bio-engineered neuronal network "Optonet"
Paper BPI12-7
Time: 14:40 – 15:00
Author(s): Shy Shoham, Hod Dana, Anat Marom, Shir S. Paluch, Inbar Brosh, , Technion Institute of Technology (Israel)
Planar neural networks and interfaces serve as a versatile in vitro model of central nervous system (CNS) physiology. Here, we demonstrate volumetric functional imaging in a bio-engineered brain-like neural tissue growing in a transparent hydrogel, by introducing complementary new developments in nonlinear microscopy and neural tissue engineering. Our system uses a novel multiphoton microscope design with a 3D scanning-line temporal-focusing (SLITE) subsystem to provide an unprecedented rapid volumetric imaging performance: dense 3D sampling at tens of volumes/sec of structures
with mm-scale dimensions containing a network of over 1000 developing cells with complex spontaneous activity patterns.

**Temporally focused illumination is inherently robust against scattering**

Paper BPI12-8  
Time: **15:00 - 15:15**

Author(s): Ben Leshem, Weizmann Institute of Science (Israel); Eirini I. Papagiakoumou, Paris Descartes University, (France); Aurélien Bègue, Paris Descartes University (France); Osip Schwartz, Weizmann Institute of Science (Israel); Valentina Emiliani, Paris Descartes University (France); Dan Oron, Weizmann Institute of Science (Israel)


**Coffee/Exhibition Break** 15:15 - 15:35

**Session 3: Tissue Interactions [In honor of Prof. Sol Kimel]**

Date: **Sunday 9 December**  Time: **15:35 - 17:25**  
Session Chair: Bruce J. Tromberg, Beckman Laser Institute and Medical Clinic (United States)

**Online computational tool for the needs of biophotonics and biomedical optics (Invited Paper)**

Paper BPI12-9  
Time: **15:35 - 16:05**  
Author(s): Igor Meglinski, Univ of Otago (New Zealand)

An opportunity of direct simulation of influence of structural variations of biological tissues on the probing light makes Monte Carlo (MC) a primary tool for biomedical optics and optical engineering. Due to the diversity of optical modalities utilizing various properties of light and mechanism of light-tissue interaction different MC models are required to be developed to describe image/radiation transfer for the particular diagnostic application and/or experimental system. Introducing an object oriented concept of Monte Carlo modelling and utilizing modern web applications we present the generalized and unified computational tool suitable for the major applications in Biophotonics and Biomedical Optics.
The dependence of light absorption in tissue on blood vessels diameter and distribution: a computer simulation study
Paper BPI12-10
Time: 16:05 - 16:25
Author(s): Hamootal duadi, Dror Fixler, Bar Ilan university (Israel)

In this work we investigated the influence of blood vessel diameter on the transmission profile of tissue. The photon propagation path was calculated from the absorption and scattering constants via Monte Carlo simulation of photon migration within irradiated tissues. Several simulations were done where a different vessel diameter was chosen but the blood volume was kept constant. The mean fraction of photons that exited the tissue at several central angles was presented for each vessel diameter. The main result is that for central angle lower than 1350 the photon transmission is lower for vessels of lower diameter while for central angle higher than 1350 the photon reflection is smaller for vessels of higher diameter. This result was achieved in the 2-D and 3-D simulations.

Image-guided ultrafast laser microsurgery probes
Paper BPI12-89
Time: 16:25 - 16:55
Author(s): Adela Ben-Yakar, The Univ. of Texas at Austin (United States)

Ablation with ultrashort laser pulses provides unrivaled microsurgical precision and has gained increasing clinical acceptance in ophthalmology. Most clinical applications of this method would benefit from accessing the surgical site through a flexible, miniaturized probe. To achieve this goal, we have developed MEMS-based miniaturized surgery probes with 18-mm and 9.6-mm diameters and overcome the challenge of delivery of ultrashort pulses through an optical fiber with pulse energies large enough for surgery. Using these probes, we can now perform femtosecond laser microsurgery combined with nonlinear imaging. I will present our recent advancements on this topic and introduce how we are planning to apply this method for the treatment of vocal fold scarring and other applications.

Addressing unresolved clinical problems with subsurface ultrafast laser tissue alteration with minimal collateral damage
Paper BPI12-13
Time: 16:55 - 17:25
Author(s): Aaron D. Lewis, Hebrew University (Israel)

Ultrafast manipulation of light to address the general needs of clinical disorders is a field that is in its infancy. A specific area of clinical intervention that our group has been focusing on is those areas of medicine in which solutions are required for a variety of diseases in which subsurface tissue manipulation with minimal collateral damage is essential. Our laboratory over several decades has developed a variety of techniques for ultralow collateral damage. One of the first examples of the development of a laser technology with minimal surrounding damage was to capture the argon fluoride excimer laser for manipulation of the zona pellucida in oocytes or in vitreoretinal surgery. This was followed by realizing that glass probes developed for scanned probe microscopy had a structure where conducting material surrounded by a dielectric coating could be used to emulate argon fluoride excimer laser pulses and those of other lasers by imposing on the tip of such structures a submicrosecond electrical discharge that produced an electron avalanche. However all of these techniques with ultralow collateral damage were surface techniques and this statement could be extended nearly universally to even those lasers that had more extensive collateral damage in their application. Thus, although lasers in general have revolutionized the use of light in clinical settings, depth selective tissue manipulation has been difficult to impossible to accomplish when overlying layers of tissue were either absorptive or scattering. This arose from the fact that laser based laser tissue interactions are mostly based on one photon processes that provide a cone of excitation where the energy density is sufficiently high to excite heat or fluorescence in the entire cone. Thus, it is difficult to excite a specific depth of a tissue without affecting the overlying surface. Nonetheless, a wide variety of clinical disorders require subsurface tissue manipulation with ultralow collateral damage. Examples are age-related macular degeneration (AMD), fungal infections, tumors surrounded by overlying tissue etc. The advent of femtosecond (fsec) lasers has caused a revolution in multiphoton microscopy and fabrication. With such lasers and their associated non-linear interactions, the photon energy density is only
high enough in the focal volume, and this opens a new direction to address subsurface tissue manipulation. Over the past decade we have shown in intradermal DNA delivery, in fungal infections and in an age related macular degeneration (AMD) animal model that these disorders can be addressed with the depth selection capable of fs-picosecond laser interactions with tissue even in ultraclose proximity to overlying and surrounding tissue. Pathological evidence indicates the lack of collateral damage to the overlying or surrounding tissue. Our work advances the use of ultrafast manipulation of light and from a physical perspective we are aware that there are numerous ways to manipulate ultrashort pulses. Thus, this gives us great hope when we see that simply using the energy density of an ultrashort pulse one can impress such spatial selectivity in tissue alteration. In essence, our results indicate that this form of ultrafast laser clinical intervention, which is virgin territory, should have a very bright future.

Poster Session and Reception
Date: Sunday 9 December Time: 17:30 - 19:00
Opening: Ehud Heyman, Dean of Engineering, Tel-Aviv University (Israel)

Imaging of TiO2 and ZnO nanoparticles in human tooth dentine and enamel in vitro using optical coherence tomography and multiphoton microscopy
Paper BPI12-58
Author(s): Natalia A. Trunina, NG Chernyshevsky Saratov State University (Russian Federation); Alexey P. Popov, University of Oulu (Finland); Jürgen Lademann, Charité – Universitätsmedizin Berlin (Germany); Valery V. Tuchin, NG Chernyshevsky Saratov State University (Russian Federation); Risto Myllylä, University of Oulu (Finland); Maxim E. Darvin M.D., Charité – Universitätsmedizin Berlin (Germany)
Two-photon autofluorescent (AF) and second-harmonic generation (SHG) multiphoton microscopy (MPM), and optical coherence tomography (OCT) were used to image ultrasound-promoted penetration (USP) of TiO2 and ZnO nanoparticles from aqueous suspension into human tooth dentine and enamel sections in vitro. After short-term USP, the MPM revealed ZnO nanoparticles at a depth of 45 μm, the penetration depth of TiO2 nanoparticles was 5 μm. Long-term USP of TiO2 nanoparticles caused significant (up to 5 dB) increase of the OCT signal from the depth 300–600 μm of dentine which can be attributed to nanoparticle penetration.

Cell-targeted holographic retinal photo-stimulation in vivo
Paper BPI12-59
Author(s): Adi Schejter, Limor Tsur, Nairouz Farah, Technion Institute of Technology (Israel); Inna Reutsky-Gefen, Ruppin Academic Ctr. (Israel) and Technion Institute of Technology (Israel); Shy Shoham, Technion Institute of Technology (Israel)
Artificial photo-stimulation of retinal ganglion cells (RGCs) in retinas with outer retinal degeneration could be the key to developing retinal neuroprosthetic devices, which will restore patients' vision. In previous work, we demonstrated patterned photo-stimulation of RGCs in-vitro, using optogenetic and photo-thermal mechanisms. Here we present and characterize a system which integrates precise spatiotemporal holographic photo-stimulation of RGCs with high resolution fundus imaging, towards in vivo stimulation of retinas. Finally, the system's application to functional calcium imaging of neuronal population activity as part of the development of a novel optical retinal prosthesis is described.

Skin optical properties in the wavelength range from 350 to 2500 nm
Paper BPI12-60
Author(s): Daria Tuchina, Alexey Bashkatov, Elina Genina, Vyacheslav Kochubey, Valery Tuchin, NG Chernyshevsky Saratov State Univ (Russian Federation)
Diffuse reflectance and total and collimated transmittance spectra were measured by LAMBDA 950 (Perkin Elmer, USA) spectrophotometer with an integrating sphere in the spectral range 350 – 2500 nm. Inverse Monte Carlo technique has been used for processing the experimentally measured spectra of the skin samples; wavelength dependence of absorption and scattering coefficients, and anisotropy factor has been obtained. Skin optical model based on fractal distribution of skin scatterers and spectral dependence of skin chromophores has been developed. The presented results can be used for the development of the optical imaging technologies and can be useful in photodynamic and photothermal therapy.
Quantitative phase imaging of fingerprints using a low-coherence, dual channel interferometric imaging system
Paper BPI12-61
Author(s): Haniel Gabai, Natan T. Shaked, Tel Aviv University (Israel)

We introduce a new, off-axis, wide-field, low-coherence and dual-channel imaging system which is based on simple-to-align common-path interferometer for fingerprint imaging. In contrast to the two-arms interferometers, the proposed system requires no optical path matching in order to obtain interference with low-coherence source. Fingerprint topology is a challenging target for phase imaging due to phase unwrapping ambiguities. To overcome this problem, we used a tunable low-coherence source to implement the two-wavelength phase unwrapping method. Next, we processed the two 180 degrees phase shifted, off-axis interferograms to a single noise-reduced interferogram from which we obtained high-quality depth profiles.

Portable low-coherence interferometric module for quantitative phase microscopy and nanoscopy
Paper BPI12-62
Author(s): Pinhas Girshovitz, Natan T. Shaked, Tel Aviv University (Israel)

We present an interferometric module to be attached to a simple inverted microscope, enabling the recording of the full wave-front of light emitted from a transparent or semi-transparent samples, without the strict stability and the highly-coherent illumination that are usually required for interferometric microscopy setups. The device is portable and inexpensive, built using off-the-shelf optical elements and can easily operate with low-coherence illumination, with remarkably-high optical thickness accuracy. We believe that this new setup will make interferometric phase microscopy more accessible and affordable for biologists and clinicians, while significantly broadening its range of applications.

Quantitative parameters obtained by integrating simultaneous interferometric phase and fluorescence microscopy
Paper BPI12-63
Author(s): Irena Frenklach, Pinhas Girshovitz, Natan T. Shaked, Tel Aviv University (Israel)

Biological cells are transparent objects which cannot be observed using conventional microscopy and require labeling. One of the solutions is phase microscopy, which records the complex amplitude of light passing through the sample. Integration of fluorescence in phase microscopy allows using the advantages of both methods to characterize cell dynamics. If we fluorescently label the cell nucleus, and subtract the cytoplasm phase profile from the area in the phase image where the nucleus is stained, the nucleus phase profile can be extracted. Based on this profile, we can calculate the nucleus dry mass and uniquely learn about the cell lifecycle.

Optical mechanical signatures of cancer cells measured by interferometry
Paper BPI12-64
Author(s): Yael Bishitz, Tel-Aviv University (Israel)

We propose to establish a cancer biomarker based on the unique optical mechanical signatures of cancer cells measured in a non contact manner by optical interferometry. Using interferometric phase microscopy, we quantitatively measured in-vitro the nanometer-scale optical thickness fluctuation maps, time-dependent, for live cancer cells and for similar but healthy cells. We found that cancer cells fluctuate significantly more than healthy cells, especially in the membrane area. To support our results, we used atomic force microscopy to measure the cell stiffness. These results show the potential of interferometric phase microscopy as a simple tool for diagnosis and monitoring of cancer.

Transcutaneous delivery of micro- and nanoparticles with laser microporation
Paper BPI12-65
Author(s): Elina A. Genina, Alexey N. Bashkatov, Leonid E. Dolotov, Institute of Optics and Biophotonics, Saratov State University (Russian Federation); Valery V. Tuchin, Institute of Optics and Biophotonics, Saratov State University (Russian Federation) and Institute of Precision Mechanics and Control of RAS (Russian Federation) and University of Oulu (Finland); Ilya V. Yaroslavsky, Gregory B. Altshuler, Palomar Medical Technologies Inc. (United States)

We are presenting results of delivery of PEGylated TiO2 nanoparticles and ZnO and Al2O3 microparticles in skin. Fractional ablation was provided by a 2.94 µm-Er:YAG laser. Suspensions of TiO2 nanopowder with the particle size 100 nm, ZnO micropowder with the particle size 5 μm and Al2O3 micropowder with the particle size 27 μm in PEG were used. In vivo human skin was investigated. Quantitative analysis of skin sites using OCT was used. Monte Carlo technique has been used for analysis of angular and spatial distribution of backscattering radiation from the skin tissue in the visible and near-infrared spectral range.
Wide-field interferometric sensing of gold nanoparticles at the subcellular level
Paper BPI12-66
Author(s): Nir A. Turko, Ania Peled, Natan T. Shaked, Tel Aviv Univ (Israel)
A novel method for imaging photothermally activated gold nanoparticles (AuNPs) by wide-field interferometry is presented. To obtain this goal, we built a reflection-mode wide-field interferometric phase microscope and modified it for the excitation of plasmonic resonance in AuNPs, while recording their resultant phase signatures. On the first stage, the AuNPs were conjugated to a glass coverslip and excited with a laser at a wavelength corresponding to their absorption spectral peak. We then acquired an image sequence of the sample phase profile in time and analyzed the entire field of view using a Fourier analysis, creating a map of the locations of the AuNPs without the need for lateral scanning. We obtained a strong photothermal (PT) signal at AuNPs central locations, exponentially dependent on the distance from their centers. This enables identification of the central locations of the AuNPs in the chosen field of view. On the next stage, AuNPs were conjugated to breast cancer cells using EGFR antibodies. We recorded a PT signal in these live cells, which was not present on non-cancerous cells of the control group. To support these results, we also performed the same experiments on fixed dead cells with our PT phase microscopy system and verified them with plasmon scattering-based confocal microscopy. To the best of our knowledge, we are the first to record wide-field PT signals at the subcellular level without the need of total-internal-reflection prisms.

Optical modulation of transgene expression in retinal pigment epithelium (Invited Paper)
Paper BPI12-67
Author(s): Daniel V. Palanker, Daniel Lavinsky M.D., Stanford University (United States); Thomas W. Chalberg, Avalanche Biotechnologies, Inc. (United States); Yossi Mandel M.D., Philip Huie, Roopa Dalal, Michael F. Marmor, Stanford University (United States)
A challenge for gene therapy of the retina is down-regulation of transgene expression in case of adverse reaction to the therapy. We present an optical method to down-regulate transgene expression in RPE. Microsecond exposures produced by scanning laser selectively destroy a predetermined fraction of RPE cells without retinal damage. RPE continuity is restored within days by migration and proliferation of adjacent RPE, but the transgene not integrated into the nucleus is not replicated. Thus, the decrease in transgene expression is precisely determined by laser pattern density and can be further reduced by repeated treatment without affecting retinal structure and function.

Femtosecond laser-assisted cataract surgery with liquid immersion optical interface (Invited Paper)
Paper BPI12-68
Author(s): Daniel V. Palanker, Stanford University (United States); Philip Gooding, David Angeley, Georg Schuele, Dan E. Andersen, George R. Marcellino, Emma Essock-Burns, OptiMedica Corp. (United States); William W. Culbertson, Bascom Palmer Eye Institute (United States); Juan Batlle, Rafael Feliz, Laser Centro (Dominican Republic); Jonathan H. Talamo, Talamo Hatch Laser Eye Consultants (United States)
Femtosecond lasers have added unprecedented precision and reproducibility to cataract surgery. However, traditional application approach to optomechanical interface with the patient’s eye introduced significant folding of the posterior corneal surface. These folds result in beam defocusing, thereby leading to incomplete cutting of the lens capsule. To avoid corneal folding we developed a liquid immersion interface, and compared its performance with the curved contact lens interface ex-vivo and in a clinical trial. The liquid immersion interface allows avoiding the corneal folding presented with the contact lens, it improves the globe stability, reduces the subconjunctival hemorrhage, and decreases the intraocular pressure rise.

OCT quantified morphology of adipose tissue at photodynamic/photothermal treatment
Paper BPI12-69
Author(s): Irina Y. Yanina, Natalia A. Trunina, NG Chernyshevsky Saratov State Univ (Russian Federation); Valery V. Tuchin, NG Chernyshevsky Saratov State Univ (Russian Federation) and Institute of Precise Mechanics and Control RAS (Russian Federation) and University of Oulu (Finland)
Structural changes of the adipose tissue at photodynamic/photothermal treatment were studied with OCT. The 100-150 µm fat tissues slices were used in in vitro experiments. Water-ethanol solutions of indocyanine green (ICG) and brilliant green (BG) of 1 mg/ml and 6 mg/ml concentration, respectively, were used for fat tissue staining. CW diode laser (ACCULASER, 810 nm) and dental diode irradiator Ultra Lume Led 5 (442 and 597 nm) were used for irradiation of tissue slices. Laser irradiation time was 1 min, and for lamp - 5 min. The observed change in the tissue structure was associated with fat cell lipolysis and destruction caused by photodynamic/photothermal action.
Overall heating of the samples from room to physiological temperature leads to stronger (in depth) and faster tissue morphology change at the similar other processing conditions. These data evidence in favor of the hypothesis that the photodynamic/photothermal treatment induces fat cell lipolysis for some time-period follows up after the treatment.

Recent progress in the imaging of lymph and blood microcirculation (Invited Paper)
Paper BPI12-70
Author(s): Vyacheslav Kalchenko, Department of Veterinary Resources, Weizmann Institute of Science (Israel); Igor Meglinski, Univ of Otago (New Zealand); Yuri Kuznetsov, Alon Harmein, Department of Veterinary Resources, Weizmann Institute of Science (Israel)
The blood and lymphatic vascular systems play a key role in the human body. Abnormalities in vascular networks, blood and lymph microcirculation are typically associated with various diseases, such as diabetes, arteriosclerosis, venous leg ulceration, anemia, ischemia and tumors development. Therefore, the techniques for advanced monitoring and characterization of vascular networks, blood and lymph microcirculation are instantly required. We overview the results and recent progress in the development of hybrid optical-based imaging approach for various vascular applications. Using Dynamic Light Scattering modality with fluorescent intravital microscopy is highly promising in studies of vascular biology, tumor biology and immunology.

On-chip optical stimulation and electrical recording from cells
Paper BPI12-71
Author(s): Alexey Yakushenko, Forschungszentrum Juelich GmbH (Germany); Zheng Gong, mLED Ltd (United Kingdom); Vanessa Maybeck, Forschungszentrum Juelich GmbH (Germany); Boris Hofmann, Aesculap AG (Germany); Erdan Gu, Martin Dawson, Institute of Photonics, University of Strathclyde (United Kingdom); Andreas Offenhaeusser, Bernhard Wolfrum, Forschungszentrum Juelich GmbH (Germany)
We demonstrate an optoelectrical device capable of bidirectional optical stimulation and electrophysiological recording. It consists of an array of micropixellated InGaN light-emitting diodes coupled to a custom-made ultrathin planar microelectrode array. Electrogenic cells (HL-1) were transfected with a light-sensitive protein and cultured directly on the chip. We monitored action potentials of individual spontaneously beating HL-1 cells by extracellular electrical recordings. On-chip light stimulation of non-beating HL-1 cells triggered network activity that was recorded using calcium imaging. We see the potential of our chip for electrophysiological experiments of optogenetically-modified cells with single cell resolution without complex optics or external light sources.

Gold nanoparticles-based biosensing of single nucleotide DNA mutations
Paper BPI12-72
Author(s): Pazit Polak, Zeev Zalevsky, Orit Shefi, Bar Ilan University (Israel)
Detection of DNA mutations is critical for scientific research and diagnostic procedures. We propose a novel method for rapid detection of mutations. We found that heating of a solution containing DNA and gold nanoparticles results in degradation of the DNA. The DNA is protected against degradation, if an oligonucleotide that matches the DNA is added. The level of degradation indicates the presence of mutations in the DNA. Detection of two common mutations leading to cystic fibrosis is demonstrated. The method is sensitive enough to indicate even a single nucleotide difference, and has potential to ultimately replace initial medical genetic tests.

Photon efficiency optimization in time correlated single photon counting technique for fluorescence lifetime imaging systems
Paper BPI12-73
Author(s): Lior Turgeman, Dror Fixler, Bar-Ilan Univ (Israel)
In time correlated single photon counting (TCSPC) systems the maximum signal throughput is limited by the occurrence of pile-up and other effect. High repetition rate light sources (in the range of 50 to 100 MHz) that are used in fluorescence lifetime imaging (FLIM) experiments enable minimization of classical pile-up related distortions. However, these systems suffer from dead time related distortions that cause unpredictable distortions of the fluorescence signal. In this work, we optimize F-value which is the relation of the relative standard deviation in the estimated FLT to the relative standard deviation in FI measurements to minimize signal distortions.

Diagnostics and treatment of biological tissues using laser IR thermography
Paper BPI12-74
Author(s): Alexander P. Sviridov, IPLIT RAS (Russian Federation); Dmitry A. Zimnyakov, Saratov State Technical University (Russian Federation); Andrey V. Kondyuri, Institute on Laser and Information Technologies (Russian
The integration of programmable laser heating, IR thermography and modeling of laser induced temperature fields is considered as a tool for diagnostics and treatment of biological tissues. Experiments in vivo on 20 volunteers demonstrated high sensitivity of laser thermography for control of blood perfusion. By varying the laser wavelength around water absorption band the depth mapping of the perfusion effectiveness could be performed. The programmable laser heating of tissues could be used to distant control of enthalpies of energetic thermal processes induced in tissue by the laser.

Looking through scattering media and around corners with incoherent light
Paper BPI12-75
Author(s): Eran Small, Weizmann institute of science (Israel)
Imaging with optical resolution through highly scattering media is a long sought after goal with many practical implications, e.g. for deep tissue imaging. This goal was considered impractical until recently, mainly because of the large number of scattered modes involved. This conception changed after the demonstration by Vellekoop and Mosk of focusing coherent light through turbid media by wavefront-shaping. Here we show that although wavefront-shaping techniques are based on interference, imaging through multiple-scattering media is possible with incoherent thermal light. We demonstrate that wavefront-shaping with incoherent illumination enables speckle-free, wide-field imaging in real-time, without the need for raster-scanning or off-line computational reconstruction and can be done in both transmission and reflection.

Neural activity extraction from blurred light sheet microscopy images
Paper BPI12-76
Author(s): Shir Paluch, Romi Elbaz, Hod Dana, Shy Shoham, Faculty of Biomedical Engineering, The Technion – I.I.T., Haifa (Israel)
Significant enhancement of data acquisition rate in functional neuronal microscopy may be obtained by using light sheet excitation methods, such as temporal focusing (TF). However, since these methods usually detect the fluorescent signal using a camera, they are sensitive to tissue scattering effects. Here we present a simple algorithmic approach for data extraction from blurred images acquired by a dual TF-two photon laser scanning microscope, which offers additional information regarding the cells’ geometrical location. Simulations predict that the presented approach is capable of extracting functional information for depths of more than 700μm inside brain-like tissues, even in cases of severe noise.

Measurement of blood perfusion by laser speckle imaging cellphones
Paper BPI12-77
Author(s): Itay Remer, Alberto Bilenca, Ben-Gurion Univ of the Negev (Israel)
Laser speckle imaging has proven to be a useful tool for the noninvasive assessment of tissue blood perfusion at high spatiotemporal resolution. In particular, laser speckle imaging of the retinal blood vessels has gained much interest in recent years due to its ability to detect anomalous alterations of the microcirculation blood flow. In this presentation, we will introduce hand-held non-invasive laser speckle imaging instrument based on standard camera-cellphone technology. This cellphone-based imager enabled us to detect microvascular changes in mouse retinal blood vessels in murine model of cerebral malaria.

Mathematical modeling of skin response on combined action of electromagnetic radiation in UV- and other frequency ranges
Paper BPI12-78
Author(s): Mikhail M. Stolnitz, NG Chernyshevsky Saratov State Univ (Russian Federation)
Mathematical model of processes in skin under action of UV-radiation and electromagnetic waves of other spectral ranges (in particular, terahertz one) is presented. Some mechanisms of such interactions on molecular, cell and tissue levels are hypothesized. Biological and biomedical consequences are discussed.

Light penetration depth for deep tumor detection using FDPM measurements of targeted gold nanorods
Paper BPI12-79
Author(s): Rinat Ankri, Dror Fixler, Bar-Ilan Univ (Israel); Soroush Mirzaei-Zarandi, Beckman Laser Institute, Irvine University, California (United States)
A new method for cancer detection based on diffusion reflection (DR) measurements of targeted gold nanorods (GNR) was recently reported by us. The detection method is based on the increase in the tumor absorption properties due to the
attachment of the GNR to the tumor. Till far, intensity-based DR measurements detected cancer cells that are adjacent to the skin surface. In this work, we use the Frequency Domain Photon Migration (FDPM) method for the GNR detection, enabling higher penetration depth in the tissue. The results can serve as the first step for the simple detection of deep tumors, such as breast cancer, based on DR measurements of targeted GNR.

**Fractality vs contrast of laser speckle image: A tool for assessing flow velocity and scatterer concentration in phantom body fluids**

Paper BPI12-80

Author(s): Cerine Lal, Arnab Banerjee, Sujatha Narayanan Unni, Indian Institute of Technology Madras (India)

Techniques based on laser speckle provide non invasive and whole field ways of assessing tissue microcirculation, which is an important parameter in the staging of various related diseases. This paper investigates assessment of flow velocity as well as scatterer concentration from the fractal nature of the obtained flow channel speckle pattern. Fractal dimension is found to vary with changes in flow velocity as well as concentration of the phantom solution. The results are also compared with analyzing the contrast of the same speckle pattern.

**Modeling severity levels of psoriasis skin disease using non invasive hyperspectral sensor**

Paper BPI12-81

Author(s): Simon Adar, Yaron Ogen, Yoel Shkolnisky, Tel Aviv University (Israel); Yoram Soroka, Marina Frušič-Zlotkin, Hebrew University of Jerusalem (Israel); Eyal Ben-Dor, Tel Aviv University (Israel)

Psoriasis disease is an autoimmune disease which has an effect on skin cells and causes their rapid growth. In this study, we quantify the clinical severity of this disease by using non-invasive method. This method exploits reflected light spectrometer measurements in the wavelength range of 350-2500nm. The recently proposed Diffusion Maps mathematical framework followed by Support Vector Machine (SVM) classification algorithm were used to discriminate between the required clinical psoriasis severity classes. Results show that the clinical status of the psoriasis disease can be evaluated with this approach, avoiding long delay by waiting for biochemistry analysis.

**In vivo assessment of HER2 receptors expression, using Affibody-based fluorescent probes (Invited Paper)**

Paper BPI12-82

Author(s): Victor Chernomordik, National Institutes of Health (United States); Moinuddin Hassan, Food and Drug Administration (United States); Yasaman Ardeshirpour, National Institutes of Health (United States); Rafal Zielinski, The University of Texas MD Anderson Cancer Center (United States); Jacek Capala, Amir Gandjbakhche, National Institutes of Health (United States)

Application of NIR fluorescence imaging to study HER2 overexpression in tumors in vivo is presented. Affibody-based fluorescent probes target HER2 in mice with subcutaneous xenografts of human tumors. Necessary information on binding kinetics is provided by a sequence of fluorescence images, taken after probe injection. Linear correlation between initial rates of the dye accumulation in the tumor, revealed by the fluorescence, and ex vivo ELISA assays allows to quantify/monitor HER2 expression in vivo. Alternatively, noticeable decrease in the fluorescence lifetime, related to binding in the tumors with high HER2 expression makes time-resolved imaging a promising tool to characterize HER2.

**Single-pulse stimulated Raman scattering spectroscopy**

Paper BPI12-83

Author(s): Hadas Frostig, Weizmann Institution of science (Israel)

Stimulated Raman scattering (SRS) spectroscopy is a label-free spectroscopy method that has proven useful for biological imaging. Conventionally, SRS spectroscopy requires a multibeam setup. In this work we demonstrate the acquisition of SRS spectra with the use of a single femtosecond pulse. High-resolution vibrational spectra are obtained by shifting the phase of a narrow band of frequencies within the input pulse spectrum, using spectral shaping. The vibrational lines are resolved via amplitude features formed in the spectrum after interaction with the sample. Using this technique, low-frequency Raman lines (<100 cm⁻¹) are observed on both the Stokes and anti-Stokes sides.

**Quantitative probing of collagen fiber spatial orientation by SHG polarization microscopy**

Paper BPI12-84

Author(s): Vladimir A. Hovhannisyan, Po-Sheng Hu, Chen-Yuan Dong, National Taiwan University (Taiwan)

Polarization-sensitive second harmonic generation (PSSHG) microscopy is a noninvasive label-free optical tool for probing of some structural features of noncentrosymmetric macromolecules and their supramolecular organization in
biotissues such as skin, muscle, tendon, cartilage, cornea. We develop a simple method based on PSSHG microscopy that allows pixel-resolution mapping of collagen fiber spatial orientation in tissues. Using this approach collagen fiber orientation imaging in tendon, cornea and sclera is performed and the potential of the method for biomedical diagnostics is discussed.

**Characteristics of photo-absorber induced neuro-thermal stimulation (PAINTS)**

Paper BPI12-85

Author(s): Nairouz Farah, Alaa Zoubi, Suhail Matar, Inbar Brosh, Shy Shoham, Technion Institute of Technology (Israel)

We characterize a novel physical method for optical neural stimulation which relies on the absorption of focused laser beams by exogenous micron-scale photo-absorbers introduced in the vicinity of target cells. Laser pulses of varying durations (CW or femtosecond IR) absorbed by the photo-absorbers, led to rapid thermal transients with a well-defined and highly-localized dynamics, which matched theoretical predictions. The threshold activation energy, induced by the thermal transients, decreased as a strong function of pulse duration and the threshold behavior for short pulses was found to be highly dependent on laser properties. The overall behavior matched a quantitative model's prediction.

**Exploiting ocular properties for simple retinal imaging at high resolution**

Paper BPI12-86

Author(s): Nizan Meitav, Erez N. Ribak, Physics Depaertment, Technion - Israel Institute of Technology (Israel)

Imaging the retina at high resolution requires a dilated pupil, which exposes more corneal irregularities. Consequently wave front aberrations are added, which blur the image. In this talk we will present various methods to improve retinal imaging by taking advantage of the dynamics of the ocular high order aberrations, the corneal refractive index and the geometry of the retinal cones and rods. Using these methods we have obtained a resolution of single photoreceptor cells.

Though being demonstrated with a simple optical setup, without adaptive optics, these methods can be also integrated with other schemes of retinal imaging.

**Determination of coherence length, depolarization of light and estimation of flow rate and direction in biological tissues**

Paper BPI12-87

Author(s): Dror Fixler, Bar-Ilan Univ (Israel)

Lately in phototherapy the use of diodes instead of lasers was suggested for economical and practical reasons. It has been argued that lasers have no preference over diodes since they lose their coherence and polarization once penetrating into biological tissues. In this work we have experimentally validated the conditions affecting the spatial coherence and depolarization of a laser illumination going through a biological tissue. We found that the coherence of the laser is partially lost when there is a flow of fluid through the tissue. Since the biological tissue is not static and contains many blood vessels and capillaries, the polarization of the laser may be lost as well. By inspecting the spatial shape change in the spot of light the direction and flow rate can be fully extracted.

**A Combined Thermal and Fluorescence Method for Targeted Hyperthermic Cancer Treatment Monitoring.**

BPI12-88

Authors: Asaf Shoval, Tel-Aviv University (Israel),

Targeted hyperthermic treatments were developed to overcome the disadvantages of cancer treatments. Our objective is to develop a method for monitoring such treatments that will overcome disadvantages of current monitoring methods. The first modality of our method utilizes fluorescence markers and provides information about apoptotic death by a simple optical measurement. The second modality thermally estimates the power of the induced heat source by measuring skin surface temperature and can provide information about tumor eradication by quantifying the conjugation of biospecific agents. This method has the advantages of being fast, low cost, easy to use and non-invasive.

**A Method for Electron Therapy using a High-Intensity Laser**

BPI12-89

Authors: Michal Tepper, Tel-Aviv University (Israel)

Radiotherapy is a common cancer treatment method. However, it also affects neighboring healthy tissues, causing short and long term side-effects. The objective of this study is to develop a laser-based localized electron therapy method for internal tumor treatment. In this method, an intense laser beam is transmitted to the tumor's vicinity, creates an electron source and accelerates the
electron toward the tumor, causing its destruction. The penetration profile of the electron radiation can be controlled and manipulated to fit the treated tumor.

The research includes developing a theoretical simulation of the method in relevant scenarios and gradual experimental validation.

**Multimodal Monitoring of Psoriasis Treatment Using Various Optical Techniques**

BP112-90

Mikhail M. Stolnitz¹, Alexey N. Bashkatov¹, Elina A. Genina¹, Maria A. Reznikova², Natalia A. Slesarenko², Natalia A. Trunina¹, Sergey R. Utz², Maxim A. Vilensky¹, Valery V. Tuchin¹,³,⁴

¹Saratov State University, Saratov, Russia; ²Saratov State Medical University, Saratov, Russia; ³Institute of Precise Mechanics and Control RAS, Saratov, Russia; ⁴University of Oulu, Oulu, Finland

Psoriasis is a chronic recurring inflammatory skin disease. In spite of long history, monitoring of psoriasis treatment efficacy frequently has subjective character. Now optical methods are being widely established as a useful investigative tool in skin research. The aims of in vivo skin imaging are to study physiological as well as pathological processes and to monitor the same body site noninvasively along with and after treatment.

Goal of this study is the developing of various optical methods for multimodal monitoring of psoriasis treatment efficacy. Patients with untreated, chronic plaque psoriasis were included in the study. Three optical methods, namely the optical coherence tomography (OCT), the reflectance spectroscopy and the full-field speckle correlation technique, were used for multimodal monitoring of psoriasis treatment by PUVA-therapy.

OCT images of lesional and non-lesional psoriatic skin were observed in patients before and after treatment. The difference between first and second skin type is clearly seen in the shape of averaged A-scans. The hemodynamic monitoring has been performed on the base of the speckle contrast method. Contrast changing due to blood flow reducing in the process of treatment is demonstrated.

Reflectance measurements have been performed using fiber-optic spectrometers. From these experimental data the blood oxygenation degree and water volume fraction of treated skin area has been estimated. Mathematical model of psoralen-sensitized psoriatic epidermis dynamics under UV-radiation action is developed. Model predictions are compared with experimental data. Pilot study proved that indicated above optical methods and its combination can be diagnostically valuable in psoriasis treatment monitoring.

**Plasmonic manipulations of cancer cells**

Paper BPI12-91

Dvir Yelin, Daniella Yeheskely-Hayon, and Limor Minai, Technion – Israel Institute of Technology (Israel)

Ultrashort laser pulses irradiating malignant cells that were targeted by gold nanoparticles have been shown effective in causing cell damage at high specificity and minimum toxicity to surrounding tissue. While the exact mechanism that affects the cells is often unknown, membrane rapture due to the shock waves emanating from the particles is likely to be the main cause of cell damage. In this study, we show that various types of cancer cells, which were specifically targeted by antibody-coated gold nanoparticles and irradiated by resonant femtosecond pulses, exhibit a variety of phenomena, depending mainly on the number of irradiation pulses. These include the generation of reactive oxygen species (a few laser pulses), fusion between neighboring cells (2-6 pulses), and widespread cell necrosis (ten or more pulses). Moreover, we have found that antibodies, which were released from the nanoparticles following irradiation, have successfully triggered the complement-dependent cytotoxicity system, causing additional long-term damage among the irradiated cells. The talk will discuss the range of possible mechanisms that could lead to these phenomena, present potential applications, and put this approach in the context of other common methods for selectively manipulating or damaging cancer cells.
Noninvasive optical imaging of action potential propagation in neuronal networks (*Invited Paper*) (*Plenary*)
Paper BPI12-3
Time: 08:00 – 08:45

Author(s): Irving J. Bigio, Boston Univ (United States)

Invited: Vital to the study and treatment of important neuropathies, such as epilepsy and stroke, is an understanding of the neuronal network processes that are perturbed by disease, and the changes in response to treatment. Intracortical parallel processing may be investigated, ideally, with a minimally invasive technology having both high temporal and spatial resolution. The objective of this work is the development of a minimally-invasive method of imaging neural activity in isolated nerves and in small animal brain slices. The method is based on imaging the change in optical birefringence that is induced by the electric field of the action potential itself. The method targets near-real-time, single-axon-resolution imaging of action potentials and the important parallel processing that occurs in complex neuronal networks, and should ultimately be able to provide moving-picture images of complex action potential propagation. Preliminary results with isolated nerve fibers will be described.

Session 5: Neuro-Optics and Vision II

Date: Monday 10 December
Time: 08:45 - 10:50

**Session Chair:** Dror Fixler, Bar-Ilan Univ. (Israel)

Photovoltaic subretinal prosthesis for restoring sight to the blind: in-vivo performance (*Invited Paper*)
Paper BPI12-15
Time: 08:45 - 09:15

Author(s): Daniel Palanker, Yossi Mandel, Georges Goetz, Daniel Lavinsky, Philip Huie, Theodore Kamins, Richard Manivanh, James Harris, Keith Mathieson, Stanford University (United States)

We have developed a wireless photovoltaic retinal prosthesis, where captured images are projected onto the retina using pulsed near-IR light. Each pixel in the subretinal implant converts pulsed light into pulsed electric current to stimulate the nearby inner retinal neurons. Photovoltaic arrays were successfully implanted subretinally in rats. Optical Coherence Tomography and fluorescein angiography demonstrated normal retinal thickness and vasculature above the implants upon 6 months follow-up. NIR stimulation of the implant elicited robust visual evoked potentials at safe irradiance levels. This wireless modular system offers a promising approach to restoration of sight in patients blinded by retinal degenerative diseases.

Principles of spatiotemporal optogenetic control over neural activity (*Invited Paper*)
Paper BPI12-16
Time: 09:15 - 09:45

Author(s): Nir Grossman, Massachusetts Institute of Technology (United States) and Harvard University (United States)

Optogenetics offers an unprecedented ability to spatially target neuronal stimulations. However the dynamics of stimulating photosensitized neurons with light is still poorly. Herein we examine experimentally and theoretically the underlying principles that govern and limit the light-to-spike process with Channelrhodopsin-2 (ChR2) and discuss their impact on our ongoing efforts to develop an optogenetic retinal prosthetics. We show that both the spatial and temporal patterns of the illumination have an important role in determining the efficiency of the stimulation and the kinetics of the spiking output.

New channelrhodopsin flavours for your optogenetic research (*Invited Paper*)
Paper BPI12-17
Time: 09:45 - 10:15

Author(s): Matthias Prigge, Weizmann Institute of Science (Israel); Franziska Schneider, Satoshi P. Tsunoda, Humboldt Universität zu Berlin (Germany); Ofer Yizhar, Weizmann Institute of Science (Israel) and Weizmann Institute of Science (Israel); Karl Deisseroth, Stanford University (United States); Peter Hegemann, Humboldt Universität zu Berlin (Germany)

Channelrhodopsins (ChRs) have been used as a genetically-encoded probe to precisely trigger and manipulate membrane potential in excitable cells. Here we present a new generation of ChRs in respect to colour, speed and activity. A systemically chimeric analysis of different ChRs from Volvox carteri and Chlamydomonas reinhardtii led to a well expressing variant called C1V1 25. A subsequent widespread mutational study led to a fine-tuned arsenal of ChRs. First we change absorption properties of C1V1 25 and ChR2 yielding new colour-tuned ChRs, spanning the visual spectrum from 380 – 630 nm. Secondly, we diversify kinetic properties of each colour-mutant into fast ( < 20 ms ), moderate ( ~ 100 ms) and slow (> 3000 ms). Each mutant was then expressed in dissociated hippocampal neurons to test its applicability in...
optogenetic experiments. All new colour-mutants show higher photocurrents in neurons than their widely used precursor ChR2 WT, ChR2 H134R or VChR1. To demonstrate the possibility of dual-excitation, we targeted ChR2 and our most red-shifted version into two distinct cell populations and specifically activated each population by applying either 405 nm or 560 nm. In combination with genetically-encoded calcium sensors like GCaMP and cameleon our colour-shifted versions show lower cross-activation than in the case of ChR2. This highlights the possibility to optically trigger neurons by ChRs and simultaneously record its activity by fluorescence reporters.

How vision begins: the effect of light propagation in the retina on human vision
Paper BPI12-18
Time: 10:15 - 10:30
Author(s): Amichai M. Labin, Department of Physics, Technion - Israel Institute of Technology (Israel); Shadi K. Safuri, Department of Physiology and Biophysics, Technion - Israel Institute of Technology (Israel); Erez N. Ribak, Department of Physics, Technion - Israel Institute of Technology (Israel); Ido Perlman, Department of Physiology and Biophysics, Technion - Israel Institute of Technology (Israel)
The most primary step of vision is the absorption of light by the visual pigment molecules in the outer segments of cone and rod photoreceptors. However, the cells in the retina are organized in a seemingly reverse order in respect to the light path, in which the photoreceptors are located at the bottom of the retina behind the entire neuronal structure. Here we address the process of light propagation in the retina by natural optical fibers - Müller cells. We show that low inter-cell light coupling, determined by the cells optical properties are optimized to preserve visual acuity and image resolution.

Holographic patterned photo-stimulation of neuronal activity for vision restoration
Paper BPI12-19
Time: 10:30 - 10:50
Author(s): Inna Reutsky-Gefen, Ruppin Academic Center (Israel) and Technion - Israel Institute of Technology (Israel); Lior Golan, Limor Tsur, Shy Shoham, Technion - Israel Institute of Technology (Israel)
When natural photoreception is disrupted, artificial stimulation of surviving nerve cells offers a potential strategy for bypassing compromised neural circuits. Recently, opto-genetic strategies inspired early development of optical retinal prostheses. Here, we demonstrate holographic photo-stimulation strategies for bionic vision restoration. We also demonstrate reliable patterned optogenetic stimulation of ChR2-expressing retinal ganglion cells with millisecond temporal precision and cellular resolution. The responses are strongly dependent on the amount of light delivered to cell’s membrane. Holographic excitation strategies could enable flexible control over distributed neuronal circuits, potentially paving the way towards high-acuity vision restoration devices and additional medical and scientific neuro-photonics applications.

Coffee/Exhibition Break and Poster Viewing 10:50 - 11:10

Session 6: Funding
Date: Monday 10 December Time: 11:10 - 12:00

Session Chair: Ibrahim Abdulhalim, Ben-Gurion Univ. of the Negev (Israel)
Life sciences industry in Israel: the chief scientist challenges
Paper BPI12-20
Time: 11:10 - 11:30
Author(s): Ora Dar,
This presentation will cover the activities of the chief scientist of the ministry of industrial affairs to support Research and Development in the hi-Tech Bio-Tech Industries; Magnet programs (Industry-Academy collaborations), R&D fund, International collaborations. R&D centers, Biomed Fund and the unique Israeli incubators program.
Paper BPI12-21
Time: 11:30 - 11:45
Author(s): Fadel Salah, Ministry of Science and Technology (Israel)
The ministry of Science and Technology, supports research within Israel through R&D centers, infrastructure and bi-national research collaboration through bilateral agreements with various countries, including. Germany; France, Italy, China, Korea, India, Great Britain.as well as others.

The U.S.-Israel bi-national science foundation (BSF) as a source for funding for U.S. and Israeli scientists
The US-Israel Bi-National Science foundation operates for a long time already and supports collaboration between American and Israeli Scientists. Recently, The BSF has joined forces with the American National Science foundation to extend the options of joint research between the two countries. This talk will describe those options.

**Lunch/Exhibition Break 12:00 - 13:30**

**Session 7: Industrial Session – In honor of Prof. Nathan Croitoru for his 85th birthday.**

*Date: Monday 10 December  Time: 13:30 - 15:30*

**Session Chair: Israel Gannot, Tel Aviv Univ. (Israel)**

**Miniature cameras: the big picture (Invited Paper)**
Paper BPI12-23
Time: **13:30 - 13:50**
Author(s): Tsafrir Kolatt, Medigus Ltd. (Israel)

Biophotonics is not only the ability to decipher the photonic information from the human body, but also the ways to obtain it. In medicine, using natural orifices for inner visual impression is very attractive. Miniature cameras provide ways by which this goal can be accomplished, and doing so, overcome a few challenges. We will present the state of the art smallest video camera in the world and demonstrate how its integrations into various medical apparatus address current needs of modern medicine.

**Laser accelerators as route to viable proton therapy (Invited Paper)**
Paper BPI12-24
Time: **13:50 - 14:10**
Author(s): Shmuel Eisenmann, HIL Applied Medical (Israel)

Proton radiation (PT) treatment for most solid cancers is notably superior in comparison to standard radiation therapy (x-ray). It deposits energy in a confined area, reducing the damage to surrounding healthy tissue. Still, nowadays there are less than 40 PT facilities worldwide – in fact, existing facilities address only 2-5% of the clinical demand. This is entirely due to prohibitively expensive construction ($150-250M) and annual operation. HIL Applied Medical harnesses cutting-edge approaches to laser-based particle-acceleration. These breakthroughs enable us to dramatically reduce the size, complexity and cost of a proton accelerator, thus becoming a key enabler of compact, cost-effective PT facilities.

**Nano retina update on artificial retina development (Invited Paper)**
Paper BPI12-25
Time: **14:10 - 14:30**
Author(s): Ra’ananan Gefen, Nano Retina (Israel)

Nano Retina Inc., a joint venture of Rainbow Medical Ltd. and Zyvex Labs LLC, is developing a bionic retina designed to restore sight to millions blinded by retinal degenerative diseases. Nano Retina’s solution includes all the necessary functionality of a retinal prosthesis on one tiny implant, i.e. 600 pixels of image reception, and transformation to neural stimulation with the required energy and control utilities. The epi-retinal implant is powered by means of a unique infrared energy technique, and implantation is a 30-minute procedure involving local anesthesia, after which the natural eye’s own mechanics, including eye movement, are used again.

**Monitoring cerebral blood flow autoregulation using ultrasound modulated diffused light (Invited Paper)**
Paper BPI12-26
Time: **14:30 - 14:50**
Author(s): Michal Balberg, Noam Racheli, Avihai Ron, Revital Shechter, Moshe Kamar, Ornim Medical Ltd (Israel)

Blood flow to the brain is regulated to provide constant flow over a range of blood pressures. Recently it was shown that patients with impaired autoregulation during bypass surgery, are at increased risk to develop stroke We hereby demonstrate, for the first time, a non-invasive and continuous measurement of cerebral blood flow (CBF) in a swine
model, using a novel technology that is based on detection of ultrasound modulated diffused light (UT-NIRS) as a function of blood pressure. By measuring CBF as a function of variations of blood pressure, the autoregulation range can be delineated in patients.

**Full-field OCT: a new addition to the pillcam story**
Paper BPI12-27
Time: 14:50 - 15:10
Author(s): Gabriel Iddan,

Ever since Michelson introduced his ubiquitous interferometer it has been applied in many ways and forms of optics and electro-optics. One of the most exiting areas of application has been OCT which has the potential of complimenting the present biopsy coloring technique. The present paper introduces a new way of creating a single shot full transverse interferometry images of any desired subsurface tissue layer without the need of mechanical transverse scanning. The new approach is based on adding telecentric optics in the optical path.

**The use of multiple modalities for noninvasive monitoring of blood parameters**
Paper BPI12-28
Time: 15:10 - 15:30
Author(s): Aharon Weinstein, O Herzenstein¹, E Gabis¹, L Maayan¹ and A Korenberg²
1. OrSense LTD, Petah Tikva, Israel, 2. Department of Hematology and Blood Bank, Assaf Harofeh Medical Center, Zerifin, Israel

Hemoglobin (Hb) tests are routinely used in in blood donation centers and hospital wards (such as ER, ICU and operating room), and are essential for the detection of hemorrhage and anemia. Current measurement methods are invasive, off-line and discrete, and the introduction of non-invasive Hb measurement has many advantages. In addition to the prevention of pain and the freedom to take multiple measurements continuously, it also reduces the time of measurement and protects the patients and staff from potential transmission of infectious diseases.

The NBM-200 (OrSense Ltd.) is a non-invasive system for monitoring of Hemoglobin, based on Occlusion Spectroscopy technology in the red/near-infrared range. At the core of this technology is the generation of a new bio-physical signal, resulting from temporarily occluding the blood flow to the measurement site. This signal replaces the natural pulsation as a basis for calculation and is less influenced by low perfusion and weak pulse. The measurement is performed by using an annular, multi-wavelength probe with pneumatically operated cuffs, with which an over-systolic pressure is produced at the finger base. This technique is also applicable for the non-invasive monitoring of other blood analytes such as Oxygen saturation and glucose [O. Amir et al., J. Diab. Sci. Tech., 1(4), 2007].

**Coffee/Exhibition Break** 15:30 - 15:50

**Session 8: Plenary Session**
Date: Monday 10 December Time: 15:50 - 16:30

**Monitoring of mitochondrial function in vivo: past overview and future clinical perspectives** *(Invited Paper)*
Paper BPI12-29
Time: 15:50 - 16:30
Author(s): Avraham Mayevsky, Bar-Ilan Univ (Israel)

Normal mitochondrial function is a critical factor in maintaining cellular bioenergetics and homeostasis in the body. Cellular bioenergetics depends upon the integrity of the respiratory chain located in the inner membrane of the mitochondria. Real-time optical monitoring of mitochondrial NADH is an indicator of intra-cellular oxygen levels. Mitochondrial dysfunction was recognized as a key element in the pathogenesis of various illnesses. Hence, it was necessary to bridge the gap between the significant body of knowledge, derived from animal studies, into daily utilization of tissue's NADH monitoring in humans exposed to critical conditions. such as severe operations, shock or sepsis.

**Session 9: Imaging and Sensing I**
Date: Monday 10 December Time: 16:30 – 19:55
**Real-time intraoperative assessment of microsurgery using 3D Doppler Fourier-domain optical coherence tomography** *(Invited Paper)*

**Paper** BPI12-30  
**Time:** 16:30 - 17:00  
**Author(s):** Jin U. Kang, Johns Hopkins Univ (United States)

In this talk, I will describe the development of an ultrafast 3-dimensional (3D) optical coherence tomography (OCT) imaging system that provides real-time intraoperative video images of the surgical site to assist surgeons during microsurgical procedures. The system is based on a full-range non-uniform Fourier-Domain OCT (FD-OCT). The system was built in a CPU-GPU heterogeneous computing architecture capable of video OCT image processing. The system displays at a maximum speed of 10 volume/second for an image volume size of 160×80×1024 (X×Y×Z) pixels. We have used this system to visualize and guide two prototypical microsurgical maneuvers; microvascular anastomosis of the rat femoral artery and ultramicrovascular isolation of the retinal arterioles of the bovine retina. Our preliminary experiments using 3D-OCT-guided microvascular anastomosis showed optimal visualization of the rat femoral artery (diameter < 0.8 mm), instruments, and suture material. Real-time intraoperative guidance helped facilitate precise suture placement due to optimized views of the vessel wall during anastomosis. Using the bovine retina as a model system we have performed “ultra microvascular” feasibility studies by guiding handheld surgical micro-instruments to isolate retinal arterioles (Diameter ~ 0.1 mm). Isolation of the microvessels was confirmed by successfully passing a suture beneath the vessel in the 3-D imaging environment.

**Direct and hybrid methods in optical biomedical imaging**

**Paper** BPI12-31  
**Time:** 17:00 - 17:30  
**Author(s):** A. Claude Boccara, Institut Langevin (France)

In order to image through scattering media such as biological tissue various approaches showed advantages and drawbacks in term of contrast, resolution, depth and signal to noise ratio. Optical Coherence Microscopy that uses singly backscattered photons matches imaging at shallow explorations with transverse diffraction limited resolution and better in sectioning. Nevertheless the contrast is limited to the level of backscattering and it would be nice to complement this information. Deeper explorations one has to rely on diffuse Tomography that is difficult because human or animal bodies are highly heterogeneous at various scales: resolution is thus practically limited to about one third of the depth. In this context coupling optics and acoustics using acousto-optics or photoacoustics was found useful to get acoustic resolution (typically < 1mm) at a few cm depths in order to reveal an optical contrast. We will illustrate the principles and some applications of these two techniques in imaging that are based on fairly different physical basis. In astronomy wavefront engineering has been very helpful to correct aberrations induced by atmosphere turbulence (in optics) or body induced aberrations in acoustics. We will point out the progresses that have been achieved these last years in term of wavefront control in the space domain or in the time domain and the perspective that they open to image through aberrating and scattering media and we will show examples using time reversal photoacoustics. In conclusion, based on recent publications dealing with wave mastering in scattering media we will discuss how these wavefront controls could help to renew the field of optical tomography.

**Development of integrated intravascular OCT/US/PAT for cardiovascular and neurovascular imaging** *(Invited Paper)*

**Paper** BPI12-32  
**Time:** 17:30 - 18:00  
**Author(s):** Zhongping Chen, Beckman Laser Institute, University of California, Irvine (United States)

This presentation reports the development of integrated multiple modality intravascular imaging techniques for the identification and evaluation of venerable plaques. The integrated imaging modality combines high resolution capability of optical coherence tomography (OCT), deep penetration depth of intravascular ultrasound (IVUS), molecular sensitivity of photoacustics (PA) imaging, and mechanical contrast of phase resolved acoustic radiation force optical coherence elastography to quantify plaques.

**Coffee/Exhibition Break, 18:00-18:15**

**Trimodal detection of early childhood caries using laser light scanning and fluorescence spectroscopy: first clinical experiences** *(Invited Paper)*
Optical detection of tooth decay at early stages of the caries process assesses risk and monitors natural healing. Previous attempts of optically diagnosing caries have demonstrated greater sensitivity than X-ray imaging, but the associated low specificity has reduced clinical impact of these devices. A laser scanning imaging and spectroscopy device is used for the first time in pediatric dental clinics, the scanning fiber endoscope (SFE). Originally developed for cancer diagnosis, SFE provides integrated reflectance and fluorescence imaging for red-flagging early caries. Between video imaging frames, SFE is switched to measure laser-induced fluorescence spectroscopy, distinguishing subsurface disease from stains and plaques.

Multispectral photoacoustic transfer function to measure bone strength and functionality

Paper BPI12-34
Time: 18:45 – 19:00
Author(s): Idan Steinberg, Avishay Eyal, Israel Gannot, Tel-Aviv Univ (Israel)
The risk of osteoporotic bone fracture depends on the bone mineral density, microstructure and functional status. We have developed a multispectral photoacoustic technique to simultaneously measure the bone functionality and biomechanical strength. Initial ex-vivo experiments were performed on rat tibia bone using a tunable Ti:Sapph laser and an acousto-optic modulator. A spectrum analyzer was used to accurately map the bone transfer function. Analysis of this complex function yields important clinical measures related to the composition and strength of each bone constituent. Preliminary results show the clinical potential and added value of such method to complement current clinical practice.

Optical bio-imaging systems assisted by liquid crystal devices (Invited Paper)

Paper BPI12-35
Time: 19:00 – 19:20
Author(s): Ibrahim Abdulhalim, Ben-Gurion Univ of the Negev (Israel)
Liquid crystal devices are under extensive study for photonic and optical non-display applications. One of the important areas where they can significantly improve applications is in optical imaging in which they can function as spatial light modulators for wavefront correction, tunable filtering, tunable focusing and polarization control with their distinct advantage of being miniature. Recently we have been investigating liquid crystal devices for this special purpose for biomedical imaging applications. Several novel devices will be described and their integration into the specific system: 1. Discrete wavelength tunable filter. 2. Continuous high dynamic tunable filter. 3. Continuous wavelength independent polarization rotator. Spectropolarimetric imaging system that uses these devices will be described with application for skin cancer detection. In addition using a fast liquid crystal phase modulator we developed a high resolution full field optical coherence microscope capable of observing 3D microbiological structures as small as 0.4x0.4x1.0 μm³ (xyz) using quasi monochromatic light.

Photoacoustic flowmetry system based on laser diodes excitation

Paper BPI12-37
Time: 19:20 – 19:35
Author(s): Adi Sheinfeld, Avishay Eyal, Tel Aviv University (Israel)
A photoacoustic system based on a pair of fiber-coupled 830nm laser-diodes enabled implementation of two different flowmetry methods. One (Photoacoustic Doppler flowmetry - PAD) was based on the PA Doppler effect and the other (Photoacoustic Thermal Diffusion Flowmetry – PA-TDF) on PA monitoring of the heat clearance rate. In PAD, tone-burst optical excitation allowed simultaneous mapping of the Doppler shift and axial position in a phantom vessel filled with flowing blood with indocyanin green. In PA-TDF temperature oscillations were photothermally induced in a blood vessel phantom and photoacoustic measurement of the heat clearance time constants was used for calculation of the fluid velocity.

Wide-bandwidth time of flight spectroscopy for biomedical and industrial process control applications

Paper BPI12-38
Time: 19:35 – 19:55
Author(s): Dmitry Khoptyar, Arman Ahamed Subash, Department of Physics, Lund University (Sweden); Otto Heijager Attermann Nielsen, Department of Informatics and Mathematical Modeling Technical University of Denmark (Denmark); Alfi Shaharin, Department of Physics (Sweden); Muhammad Saleem, National Institute of Lasers and Optronics
We report on outstanding performance characteristics of the ultra-broadband photon time of flight absorption/scattering spectrometer for evaluation of the optical properties of turbid media. The device is now operating in the range from 400nm up to 1400nm and provides less than 1% errors in determination of absorption and scattering spectra. The key factor in achieving superior precision of the system was to implement advanced timing stabilization scheme that enables suppression of the source temporal drifts causing the errors. We illustrate the excellent instrument performance by presenting number of experimental studies in biomedical and pharmaceutical applications.

Tuesday 11 December

Session 10: Plenary Session
Date: Tuesday 11 December Time: 08:30 - 09:15

Lensfree on-chip microscopy and tomography toward telemedicine applications (Invited Paper) (Plenary)
Paper BPI12-39
Time: 08:30 - 09:15
Author(s): Aydogan Ozcan, Univ of California Los Angeles (United States)
The massive volume of wireless phone communication brings an enormous cost-reduction to cellphones despite their sophisticated hardware and software capabilities. Utilizing this advanced state of the art of the cell phone technology towards point-of-care diagnostics and/or microscopic imaging applications can offer numerous opportunities to improve health care especially in the developing world where medical facilities and infrastructure are extremely limited or even do not exist. Centered on this vision, in this talk I will introduce new imaging and detection architectures that can compensate in the digital domain for the lack of complexity of optical components by use of novel theories and numerical algorithms to address the immediate needs and requirements of Telemedicine for Global Health Problems.

Session 11: Microscopy I: In honor of Prof. Vasilios Sarafis
Date: Tuesday 11 December Time: 09:15 - 12:05
Session Chair: Yuval Garini, Bar-Ilan Univ. (Israel)

In honor of Prof. Vasilios Sarafis
Paper BPI12-40
Time: 09:15 - 09:25
Author(s): Zeev Zalevski,
Digital holographic microscopy
Paper BPI12-41
Time: 09:25 - 09:50
Author(s): Stefenn G. Lipson, Technion and Ort-Braude College (Israel)
The original idea of wavefront reconstruction by holography was conceived by Denis Gabor in 1948 in order to overcome the limitations in quality of the electron lenses available at that time. Optical holography was implemented in the 1960's using photographic film as the recording medium, and one of its most important aspects, creating three-dimensional images from a single two-dimensional photograph, was demonstrated. In the last two decades, the question of replacing the photographic film by a digital camera has been addressed, and the topic of digital holographic microscopy has developed. However, the use of a digital camera presents new challenges. The camera resolution (pixel size) is an order of magnitude larger that that of holographic film, while the typical number of pixel available (tens of Mpixels) is several orders of magnitude smaller than that of a typical film hologram. But the sensitivity of the digital camera is much higher, and the use of computational reconstruction opens up new possibilities. I will discuss the new concepts and ideas which have developed in order to take into account these changes, illustrated with some experimental results. The outcome is a new imaging technique which can provide high-speed monochromatic recording and analysis of three-dimensional microscopic objects.

Super resolved photoactivated localization microscopy (Invited Paper)
Paper BPI12-42
Time: 09:50 - 10:15
Author(s): Carl G. Ebeling, Department of Physics and Astronomy, University of Utah (United States); Amihai Meiri, Bar-Ilan Univ (Israel); Rajesh Menon, Department of Electrical and Computer Engineering, University of Utah (United States); Erik M. Jorgensen, Howard Hughes Medical Institute, Department of Biology, University of Utah (United States); Jordan
Localization-based super-resolution techniques utilize photo-activated state-switching to individually isolate single emitting fluorophores and localize their position below the diffraction limit of classical optical microscopy. In conventional localization algorithms, the uncertainty in the position of the fluorophore scales inversely with the square root of the number of photons collected. For probes with a limited photon budget, this constrains the ‘resolving’ capabilities of pointillist-based imaging systems. Here, we examine a methodology based on using the phase information of the emitted photons to enhance the localization sensitivity in a laser-scanning photo-activation localization microscope by utilizing photon self-interference to generate a modified detection intensity distribution.

Coffee/Exhibition Break 10:15 - 10:40

Soft x-ray cryo-tomography: imaging in 3D with very short photons
Paper BPI12-43
Time: 10:40 - 11:05
Author(s): Michael Elbaum, Weizmann Institute of Science (Israel)

With short wavelength and long penetration, microscopic imaging with X-rays has been a long-standing but elusive goal. Developments were hampered by the lack of refractive lenses. With modern improvements in nano-fabrication technology it is possible to produce high-quality diffracting optics. Both scanning and wide-field microscopes have been constructed based on Fresnel zone plates. Practical resolutions reach 25 nm or less in synchrotron-based instruments. Thus X-ray imaging now offers a bridge between transmission electron microscopy, with its high resolution but restriction to thin samples, and visible light microscopy with relatively low resolution for imaging of phase objects. A particularly interesting part of the X-ray spectrum for biological imaging is the “water-window” between absorption edges of carbon and oxygen at 284 and 543 eV, respectively. Membranes and lipids show a natural contrast against the aqueous medium, related to the atomic absorption. Indeed the contrast is quantitative and can be evaluated as a signature for protein or lipid composition. Close to the oxygen K edge the absorption length of water is approximately 10 μm, meaning that many cellular specimens can be examined whole, without sectioning. As the internal structures of interest are much smaller, however, tomography is required in order to obtain a three-dimensional map of the sample. The talk will discuss the implementation of soft X-ray cryo-tomography at the BESSY II synchrotron, and our recent application to study the nucleation of heme-rich crystals (hemozoin) in the digestive vacuole of the malaria-causing parasite *Plasmodium falciparum*.

Biomedical optical nanoscopy without florescence labeling using interferometry
Paper BPI12-44
Time: 11:05 - 11:25
Author(s): Natan T. Shaked, Tel Aviv Univ (Israel)

Microscopy and nanoscopy of live cells provide a powerful research tool for cell biology studies and a means for medical diagnosis and monitoring of diseases. Exogenous fluorescent labels can be used to enhance the cell contrast or obtain imaging of features below 150 nm (the optical diffraction limit). However, these agents might be cytotoxic and influence the cell behavior. In addition, fluorescent agents might photobleach, limiting the imaging duration. The contrast and resolution-limit problems when imaging cells can be solved by using phase nanoscopy. Novel interferometric phase nanoscopy techniques will be presented in this lecture.

Analyzing the morphology of neuronal cells as a tool for studying neuronal growth and development
Paper BPI12-45
Time: 11:25 - 11:45
Author(s): Orit Shefi, Bar-Ilan Univ. (Israel)

All-optical-histology: a combined multi-photon microscopy and plasma-mediated ablation method and its implementation in large-scale study of brain anatomy
Paper BPI12-46
Time: 11:45 - 12:05
We study the structure of cortical vasculature and its relationship to neuronal units across large volumes of contiguous, undistorted histological samples (several cubic millimeters at an isotropic um per voxel resolution). These unique datasets are obtained by means of a combining tiled two-photon volumetric imaging and plasma-mediated ablation to overcome the limits imposed by light-scattering in fixed tissue (about 200μm). Armed with these datasets we showed that—opposed to the commonly accepted view— the structure of the cortical vasculature is largely independent of the location of neuronal units.

Session 12: Microscopy II
Date: Tuesday 11 December Time: 13:30 - 16:15
Session Chair: Natan T. Shaked, Tel Aviv Univ. (Israel)

In living motion: tissue dynamics imaging in 3D tissue culture (Invited Paper)
Paper BPI12-47
Time: 13:30 - 14:00
Author(s): David D. Nolte, Purdue Univ (United States)

Motion is an intrinsic characteristic of all living systems, and scattered light is particularly sensitive to motions inside living tissue through phase modulation and low-frequency Doppler effects. In this talk, I will describe motility contrast imaging and tissue dynamics spectroscopy that use intracellular motions as functional biomarkers for applications such as drug screening, viability assessment, proliferative potential, and cancer therapy selection, among others. Tissue dynamics imaging uses low-coherence off-axis digital holography to volumetrically section scattered light in tissues, and converts fluctuating speckle intensities into spectral power densities that correspond to different types of intracellular motion.

Dynamics studies by live-cell imaging: from diffusion to cell-cycle processes
Paper BPI12-48
Time: 14:00 - 14:20
Author(s): Yuval Garini, Bar-Ilan Univ. (Israel)

Modern microscopy methods have made a “dream come true” by allowing to measure dynamic processes in live cells. This is made possible initially thanks to the colorful world of fluorescent protein and the genetic engineering that permits to label almost any molecular specie with a fluorescent tag. Further, different microscopy methods were developed for observing dynamic processes at different time-scales. These includes fluorescent correlation spectroscopy (FCS) for measuring rapid processes such as diffusion, continuous photobleaching (CP) for measuring the dynamics of both free and bound particles (and the ratio between them), fluorescence recovery after photobleaching (FRAP) for measuring mainly the kinetics of bound states (as well as diffusion) and finally single particle tracking (SPT) for measuring longer-term dynamic processes. We will demonstrate the use of these methods for two important cases: 1. Studying mechanisms of chromatin dynamics that maintains the chromosome territories and 2. Dynamic processes of splicing factors in live cells and their spatial localizations.

Multimodal optoacoustic and multiphoton fluorescence microscopy
Paper BPI12-49
Time: 14:20 - 14:40
Author(s): Gali Sela, Technion-Israel Institute of Technology (Israel); Daniel Razansky, Helmholtz Center (Germany); Shy Shoham, Technion-Israel Institute of Technology (Israel)

Multiphoton microscopy is typically used to measure fluorescence contrast. Optical resolution optoacoustic microscopy measures absorption contrast utilizing the absorber’s non-radiative relaxation properties, thus providing complementary
information to that given by the fluorescence. We have developed a system for simultaneous multimodal optoacoustic and multiphoton fluorescence 3D imaging. The system is based on integrating an ultrasonic transducer into a two-photon laser scanning microscope with a NIR femtosecond laser with a high repetition rate (80MHz). Superposition of the optoacoustic images of markers that are highly absorbant in the NIR spectrum with the fluorescence images provides complementary structural and functional information.

Infrared surface plasmon and waveguide modes for label-free sensing of live cell morphology  
Paper BPI12-50  
Time: 14:40 - 14:55  
Author(s): Victor Yashunsky, Alexander Zilbershtein, Vladislav Lirsman, The Racah Institute of Physics, the Hebrew University of Jerusalem (Israel); Amir Bein, School of Nutritional Sciences, Institute of Biochemistry, the Hebrew University of Jerusalem (Israel); Michael Golosovsky, The Racah Institute of Physics, the Hebrew University of Jerusalem, Israel (Israel); Benjamin Aroeti, Department of Cell and Developmental Biology, the Hebrew University of Jerusalem (Israel); Bertha (Betty) Schwartz, School of Nutritional Sciences, Institute of Biochemistry, the Hebrew University of Jerusalem (Israel); Dan Davidov, The Racah Institute of Physics, the Hebrew University of Jerusalem (Israel)  
We demonstrate that a live epithelial cell monolayer can act as a planar waveguide for mid-infrared waves. Our infrared reflectivity measurements show that epithelial cells, which maintain tight intercellular connectivity, support waveguiding of the infrared light in the spectral region of 1.4-2.5 μm and 3.5-4 μm. We measure infrared reflectivity of p-polarized spectrum at oblique angle from living cells cultured on a semitransparent gold film on high-refractive index prism and utilize the unique properties of the confined infrared waves (i.e., waveguide modes and surface plasmon polaritons) traveling through the cell layer. By tracking the resonant wavelength and attenuation of these waves we study morphological changes in living cells with extremely high precision. The waveguide mode resonances disclose quantitative and dynamic information on epithelium thickness and connectivity when the surface plasmon resonance provides complementary information on cell-substrate adhesion. Our method enables monitoring of submicron variations in cell layer morphology in real-time, and in the label-free manner.

A new paradigm for parallelized STED microscopy (Invited Paper)  
Paper BPI12-51  
Time: 14:55 - 15:15  
Author(s): Yael Roichman, Omer Wagner, Ori Cheshnovsky, Tel Aviv Univ (Israel)  
Stimulated emission depletion microscopy (STED) is one of the first super-resolution imaging techniques. It stands out in its ability to create fast, high resolution, multiple-color image sequences, provided the scan area is small and suitable fluorophores are chosen. These features make STED a desirable imaging technique for live cell imaging, as proven by the new scientific discoveries that were made using STED. We propose a new design for a multi-color, parallelized STED microscope, capable of multiple beam scanning,. Our design is based on multi-wavelength holography used to split, and shape, both the excitation beams as well as the depletion beams.

Equivalent physical parameters of organelles in the 'phase portrait' of a T-lymphocyte  
Paper BPI12-52  
Time: 15:15 - 16:15  
Author(s): Alexander Shtil, MIREA (TU) (Russian Federation)  
We developed a method of identification of structural elements (zones) in the phase images of eukaryotic cells. The method is based on differential optical density of the zones. Using a simple optical model ~20 physical parameters (including refractivity and the size of organelles) were calculated. The values of these parameters were attributed to the equivalent parameters of the cytoplasm, mitochondrion, nucleus and nucleoli of the T-lymphocyte. Furthermore, we presented the algorithm of evaluation of numerical values of equivalent parameters. A big number of these parameters in the 'phase portrait' of the T-lymphocyte allowed for biophysical interpretation of T-cell dynamics in response to phytohemagglutinin and in disease. Our approach is applicable for other cell types and treatments. Thus, the detailed quantitative analysis of the phase image of cells can improve the efficacy of cellular diagnostics and shorten the time of measurements.

Coffee/Exhibition Break 16:15 - 16:35  

Session 13: Imaging and Sensing II
Date: Tuesday 11 December  Time: 16:35 - 18:20

**Novel serial intravital imaging technique in a murine lymph node reveals unexpected dissemination patterns in lymphoma progression** *(Invited Paper)*

**Time:** 16:35 - 17:05  
**Author(s):** Bryan R. Smith, Ken Ito, Masakatsu Kotsuma, Stanford University (United States); Cornelius Miething, Scott Lowe, Memorial Sloan Kettering (United States); Sanjiv S. Gambhir, Stanford University (United States)

Non-Hodkin’s Lymphoma (NHL) is a highly disseminated disease. It is not well-understood how cancer, including NHL, disseminates (or metastasizes) from one organ in the body to another. Metastasis is what typically leads to patient mortality rather than primary tumor. Here, we developed a novel technique for intravital microscopy to serially observe the lymphoma patterns in a mouse model of lymphoma over several weeks. We observed evidence at odds with the current paradigm of metastasis when we found that lymphoma cells “burst” from other organs to seed metastasis in the lymph nodes. We uncovered the molecular mechanism responsible for this burst.

**Normative database of judgment of complexity task with functional near infrared spectroscopy: application for traumatic brain injury (TBI)** *(Invited Paper)*

**Paper BPI12-36**  
**Time:** 17:05 - 17:30  
**Author(s):** Amir Gandjbakhche, National Institutes of Health (United States)

The ability to assess frontal lobe function in a rapid, objective, and standardized way, without the need for expertise in cognitive test administration might be particularly helpful in mild traumatic brain injury (TBI), where objective measures are needed. We are combining fNIRS and frameless stereotaxy which allowed us to co-register the functional images with previously acquired anatomical MRI volumes. In our experiment, the subjects were asked to perform a task, evaluating the complexity of daily life activities, previously shown with fMRI to activate areas of the anterior frontal cortex. We reconstructed averaged oxyhemoglobin and deoxyhemoglobin data from 20 healthy subjects in a spherical coordinate. The spherical coordinate is a natural representation of surface brain activation projection. Our results show surface activation projected from the medial frontopolar cortex which is consistent with previous fMRI results. With this original technique, we will construct a normative database for a simple cognitive test which can be useful in evaluating cognitive disability such as mild traumatic brain injury.

**Simulation analysis of imaging through biologic turbid media using compressive digital holographic sensing**  
**Paper BPI12-55**  
**Time:** 17:30 - 17:45  
**Author(s):** Yair Rivenson, Adrian Stern, Joseph Rosen, Ben-Gurion Univ of the Negev (Israel)

In a recent work, an imaging method for the recovery of partially obscured objects was presented. The method was implemented with a single aperture holographic acquisition combined with a computational reconstruction. The object recovery problem was recast as a compressive sensing (CS) problem. Here, we use simulations to study the ability of our proposed method to reconstruct objects which are set behind biological turbid media, often regarded too complex and considered opaque. By measuring the physical properties of the media, the number of object features which can be reconstructed is theoretically determined.

**Toward real-time volumetric optoacoustic tomography**  
**Paper BPI12-56**  
**Time:** 17:45 - 18:00  
**Author(s):** Luis Dean Ben, Daniel Razansky, Technical University of Munich and Helmholtz Center Munich (Germany)

Using optoacoustic excitation, complete volumetric tomographic datasets from the imaged object can in principle be generated with a single interrogating laser pulse. Yet, multiple technical limitations, related to lack of appropriate ultrasound detection technology, digital sampling and processing capacities, hindered so far effective implementation of fast three-dimensional optoacoustic imaging and tomography. Herein, we developed a system capable of acquiring volumetric optoacoustic data in real time. Current implementation can generate ten three dimensional optoacoustic image frames every second, mainly limited by the pulse repetition rate of the excitation laser.

**Nano-particles meet nanoscopy: quantum-dots for nano-bio-photonics**  
**Paper BPI12-57**
The unique photophysical properties of single nano-crystal quantum-dots (QDs) are utilized to enhance optical resolution and allow precise mapping of protein binding sites on stretched genomic DNA. QDs are used to specifically label proteins bound to DNA, allowing multicolor, nm-resolution localization. Protein-DNA complexes are linearly extended in a flow chamber resulting in a "beads on a string" like structure that may be directly visualized under a fluorescence microscope. Fluorescent spots (designating bound proteins) are mapped by registering their position relative to a known sequence-specific genomic marker such that the precise locations of the protein binding sites are determined. The method is demonstrated by detecting individual QD-labeled T7-RNA polymerases on the T7 bacteriophage genome. In addition we show how physical extension of long DNA molecules on surfaces and in nanofluidic channels reveals genetic information in the form of a linear, optical "barcode" and discuss the relevance of such information and its' potential applications.