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Valery V. Tuchin
Editor

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Contents

xi Conference Committees
xv Introduction
xix Plenary Presentation: High-resolution Photoacoustic Tomography [6535-02]
L. V. Wang, G. K. Beare, Washington Univ. in St. Louis (USA)

PLENARY LECTURE

653502 Non-invasive in-vivo Raman spectroscopic measurement of the dynamics of the antioxidant substance lycopene in the human skin after a dietary supplementation [6535-01]
M. E. Darvin, Charité Universitätsmedizin Berlin (Germany); I. Gersonde, H. Albrecht, Laser and Medical Technology GmbH (Germany); W. Sterry, J. Lademann, Charité Universitätsmedizin Berlin (Germany)

SELECTED INVITED LECTURES

653503 Diffuse reflection imaging of sub-epidermal tissue haematocrit using a simple RGB camera [6535-03]
M. J. Leahy, J. O’Doherty, P. McNamara, Univ. of Limerick (Ireland); J. Henrikson, Linköping Univ. Hospital (Sweden); G. E. Nilsson, Linköping Univ. (Sweden) and WheelsBridge AB (Sweden); C. Anderson, F. Sjöberg, Linköping Univ. Hospital (Sweden)

653504 On the way to subcellular imaging of mechanotransduction in the developing vasculature [6535-04]
I. V. Larina, Baylor College of Medicine (USA); Y. Wang, Univ. of California, San Diego (USA) and Univ. of Illinois at Urbana-Champaign (USA); S. Chien, Univ. of California, San Diego (USA); M. E. Lane, Rice Univ. (USA); M. E. Dickinson, Baylor College of Medicine (USA)

653505 Femtosecond pulse propagation in biotissue-like scattering medium: theoretical analysis versus Monte Carlo simulations [6535-05]
E. A. Sergeeva, Institute of Applied Physics (Russia); M. Yu. Kirillin, Univ. of Oulu (Finland) and M.V. Lomonosov Moscow State Univ. (Russia); A. V. Priezzhev, M.V. Lomonosov Moscow State Univ. (Russia)

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The CID number appears on each page of the manuscript. The complete citation is used on the first page, and an abbreviated version on subsequent pages.
653506 The influence of human eye aberrations on the resolution and field of view of fundus-cameras [6535-06]
A. Dubinin, T. Cherezova, A. Belyakov, Moscow Lomonosov State Univ. (Russia); A. Kudryashov, Moscow State Open Univ. (Russia)

653507 Non-invasive diagnostics of several structural and biophysical parameters of skin cover by spectral light reflectance [6535-07]
A. P. Ivanov, V. V. Barun, B.I. Stepanov Institute of Physics (Belarus)

653508 Frequency-domain photon density wave setup with multicolor illumination at 684, 794, and 1060 nm [6535-08]
V. I. Plehanov, I. V. Turchin, E. A. Sergeeva, V. A. Kamensky, Institute of Applied Physics (Russia)

653509 Fluorescence diffuse tomography for tumor detection and monitoring [6535-09]
I. V. Balalaeva, Institute of Applied Physics (Russia) and Nizhny Novgorod State Univ. (Russia); A. G. Orlova, Institute of Applied Physics (Russia); M. V. Shirmanova, E. A. Kibraeva, Nizhny Novgorod State Univ. (Russia); E. V. Zagainova, Institute of Fundamental and Applied Medicine (Russia); I. V. Turchin, Institute of Applied Physics (Russia)

65350A Light diffuse reflectance for detection and differentiation of teeth caries lesions [6535-10]
E. Borisova, Institute of Electronics (Bulgaria); Tz. Uzunov, Medical Univ. Sofia (Bulgaria); S. Valkanov, Institute of Metal Science (Bulgaria); L. Avramov, Institute of Electronics (Bulgaria)

65350B Monitoring changes in the scattering properties of mouse skin with optical coherence tomography during an in vivo glucose tolerance test [6535-11]
M. Kinnunen, S. Tausta, R. Myllylä, S. Vainio, Univ. of Oulu (Finland)

65350C Optical coherence tomography among medical imaging modalities: potential and limitations [6535-12]
N. Gladkova, E. Zagaynova, Nizhny Novgorod State Medical Academy (Russia) and Institute of Applied Physics (Russia); N. Shakhtova, A. M. Sergeev, V. Gelikonov, Institute of Applied Physics (Russia); F. Feldchtein, Institute of Applied Physics (Russia) and Imalux Corp. (USA); G. Gelikonov, Institute of Applied Physics (Russia) and BioMedTech (Russia); E. Balandina, Nizhny Novgorod State Medical Academy (Russia)

65350D Effect of the width of the scattering indicatrix on the dispersion of the photon density waves in a strongly scattering medium [6535-13]
V. V. Lyubimov, A. V. Chemezov, Vavilov State Optical Institute (Russia)

65350E Image transfer through the complex scattering turbid media [6535-14]
I. V. Meglinski, E. Berrocal, Cranfield Univ. (United Kingdom); M. A. Linne, Lund Institute of Technology (Sweden); D. A. Greenhalgh, Cranfield Univ. (United Kingdom)

INTERNET INVITED LECTURES

65350F Concurrent NIRS-fMRI activation studies by using a new method for BOLD signal analysis [6535-15]
A. Sassaroli, Tufts Univ. (USA); B. deB. Frederick, McLean Hospital (USA); Y. Tong, Tufts Univ. (USA); P. F. Renshaw, McLean Hospital (USA); S. Fantini, Tufts Univ. (USA)
Effects of apertures on scattered light: a Monte Carlo study of confocal imaging [6535-18]
C. Tjokro, Singapore-Massachusetts Institute of Technology Alliance (Singapore); C. J. R. Sheppard, National Univ. of Singapore (Singapore)

Polarization sensitive optical coherence tomography for application conditions with external perturbations [6535-19]
V. Tougbaev, T.-J. Eom, C.-S. Kee, D.-K. Ko, J. Lee, Gwangju Institute of Science and Technology (South Korea)

Measuring of optical properties of biological samples by low cost goniometrical equipment [6535-20]
M. Hoffmann, O. Schewtschenko, Forschungszentrum für Medizintechnik und Biotechnologie e.V. (Germany); O. Minet, Charité Berlin (Germany)

Quantitative tissue polarimetry using polar decomposition of 3 × 3 Mueller matrix [6535-21]

In vivo flow cytometry and time-resolved near-IR angiography and lymphography [6535-24]
E. I. Galanzha, Saratov State Univ. (Russia) and Univ. of Arkansas for Medical Sciences; V. V. Tuchin, Saratov State Univ. (Russia); R. W. Brock, V. P. Zharov, Univ. of Arkansas for Medical Sciences (USA)

Perturbation model for photon migration imaging in the low scattering regime [6535-22]
V. Toronov, Ryerson Univ. (Canada)

Changes in capillary filling do not influence inspiratory-induced vasoconstrictive episodes [6535-23]
R. Rauh, E. Ochsmann, M. Kessler, Univ. of Erlangen-Nuremberg (Germany); M. Mueck-Weymann, Univ. of Erlangen-Nuremberg (Germany) and Univ. for Health Sciences, Medical Informatics and Technology (Austria)

Uptake of photosensitizers by bacteria is influenced by the presence of cations [6535-24]
A. Kishen, S. George, National Univ. of Singapore (Singapore)

Internal temperature distribution in blood vessel under the action pulse laser radiation [6535-25]
L. G. Astafyeva, G. I. Zheltov, B.I. Stepanov Institute of Physics (Belarus)

Monitor glucose induced changes in optical properties of rat skin in vitro [6535-26]
D. Zhu, W. Lu, Q. Li, H. Gong, Q. Luo, Huazhong Univ. of Science and Technology (China)

Changes in visible light transmission across the corneal stroma [6535-27]
J. Doutch, A. J. Quantock, K. M. Meek, Cardiff Univ. (United Kingdom)

Elasticity mapping of tissue mimicking phantoms by remote palpation with a focused ultrasound beam and intensity autocorrelation measurements [6535-28]
C. Usha Devi, R. S. Bharat Chandran, R. M. Vasu, A. K. Sood, Indian Institute of Science, Bangalore (India)
Optical fluorescence biosensor for plant water stress detection [6535-29]
J. P. C. Chong, O. W. Liew, Singapore Polytechnic (Singapore); B. Q. Li, A. K. Asundi, Nanyang Technological Univ. (Singapore)

Toward a methodology for studying the application of open source innovation practices in non-software domains [6535-30]
S. Tanev, Carleton Univ. (Canada)

Hemispherical imaging of skin with polarized light [6535-31]
J. C. Ramella-Roman, The Catholic Univ. of America (USA) and National Institute of Standards and Technology (USA); B. Boulbry, T. A. Germer, National Institute of Standards and Technology (USA)

Propagation of infrared wavelengths through the corneal stroma with reference to hydration changes [6535-32]
J. Doutch, C. Tucker, A. J. Quantock, P. A. R. Ade, K. M. Meek, Cardiff Univ. (United Kingdom)

Optical trapping near a charged surface: three-dimensional optical binding of colloids [6535-33]
S. Ahlawat, R. Dasgupta, P. K. Gupta, Raja Ramanna Ctr. for Advanced Technology (India)

Ultrasound assisted optical elastography for measurement of tissue stiffness: contribution to the measurement from scattering coefficient variation [6535-34]
R. S. Bharat Chandran, C. Usha Devi, R. M. Vasu, A. K. Sood, Indian Institute of Science, Bangalore (India)

Efficient noise tolerant reconstructions in diffuse optical tomography through computation of Jacobian in wavelet domain [6535-36]
B. Kanmani, B.M.S. College of Engineering (India); R. M. Vasu, Indian Institute of Science, Bangalore (India)

A high-resolution optical imaging system for obtaining the serial transverse section images of biologic tissue [6535-37]
L. Wu, B. Zhang, P. Wu, Q. Liu, H. Gong, Huazhong Univ. of Science and Technology (China)

Stratum corneum: a barrier of skin resistsants light [6535-38]
D. Zhu, Y. Hu, Z. Mao, Y. Zheng, W. Lu, Q. Luo, Huazhong Univ. of Science and Technology (China)

Concentration dependence of the optical clearing effect created in muscle immersed in glycerol and ethylene glycol [6535-39]
L. Oliveira, Ctr. de Ciências e Tecnologias Ópticas (Portugal); A. Lage, Porto Univ. (Portugal); M. Pais Clemente, Ctr. de Ciências e Tecnologias Ópticas (Portugal); V. Tuchin, Saratov State Univ. (Russia)

Oxygenation of biological tissue in vivo by laser irradiation [6535-40]
A. N. Korolevich, M. M. Asimov, B.I. Stepanov Institute of Physics (Belarus); E. E. Konstantinova, Republican Ctr. of Research and Service on Cardiology (Belarus)
Optical properties of human stomach mucosa in the spectral range from 400 to 2000 nm
[6535-35]
A. N. Bashkatov, E. A. Genina, V. I. Kochubey, A. A. Gavrilova, Saratov State Univ. (Russia); S. V. Kapralov, V. A. Grishaev, Saratov State Medical Univ. (Russia); V. V. Tuchin, Saratov State Univ. (Russia)

Monte Carlo study of skin optical clearing to enhance light penetration in the tissue
[6535-43]
A. N. Bashkatov, E. A. Genina, V. V. Tuchin, M. M. Stolnitz, D. M. Zhestkov, Saratov State Univ. (Russia); J. M. Lademann, Humboldt Univ. (Germany)

Optical clearing of human eye sclera under the action of glucose solution [6535-85]
A. N. Bashkatov, E. A. Genina, V. I. Kochubey, A. A. Gavrilova, Saratov State Univ. (Russia); T. G. Kamenskikh, V. A. Galanzha, Saratov State Medical Univ. (Russia); V. V. Tuchin, Saratov State Univ. (Russia)

Laser microinterferometer for estimation of red blood cell volume [6535-41]
G. Lazarev, A. Sedashev, Bauman Moscow State Technical Univ. (Russia)

Signal propagation in nerve fiber [6535-42]
Y. N. Zayko, Stolypin Volga Regional Academy of State Service (Russia)

Competitive intelligence information management and innovation in small technology-based companies [6535-44]
S. Tanev, Carleton Univ. (Canada)

COHERENCE-DOMAIN AND POLARIZATION METHODS IN BIOPHYSICS AND MEDICINE

Endoscopic laser Doppler flowmetry in the experiment and in the bleeding gastric and duodenal ulcer clinic [6535-45]
S. V. Kapralov, Y. G. Shapkin, Saratov State Medical Univ. (Russia); V. V. Lychagov, V. V. Tuchin, Saratov State Univ. (Russia)

Photonic crystal fiber with hollow-core for biosensing application [6535-46]
J. S. Skibina, V. V. Tuchin, Saratov State Univ. (Russia); V. I. Beloglazov, N. B. Skibina, M. V. Chainikov, Nano Structural Glass Technology Ltd. (Russia)

Application of LASCA for study of blood microcirculation in brain: testing of new prophylactic preparations [6535-47]
S. Ulyanov, Saratov State Univ. (Russia); Y. Ganilova, Saratov State Univ. (Russia) and Saratov State Medical Univ. (Russia); O. Ulianova, Saratov State Agrarian Univ. (Russia) and Saratov State Univ. (Russia); P. Li, D. Zhu, Q. Luo, Huazhong Univ. of Science and Technology (China)

Investigation of glucose-hemoglobin interaction by optical coherence tomography [6535-48]
O. S. Zhernovaya, A. N. Bashkatov, E. A. Genina, V. V. Tuchin, Saratov State Univ. (Russia); I. V. Meglinski, D. Yu. Churmakov, L. J. Ritchie, Cranfield Univ. (United Kingdom)
| 65351D | Investigation of formalin influence over hard and soft biological tissues fluorescent spectra in vitro [6535-49] |
| 65351E | Influence of multiple light-scattering on TiO2 nanoparticles imbedded into stratum corneum on light transmittance in UV and visible wavelength regions [6535-50] |
| 65351F | Optical model of thermo-sensitive heterophase medium (adipose tissue) [6535-52] |
| 65351G | Investigation of skin water loss and glycerol delivery through stratum corneum [6535-53] |
| 65351H | In vitro study of indocyanine green solution interaction with skin [6535-54] |
| 65351I | Estimations of complex refractive index of hemoglobin at its incubation with glucose [6535-55] |
| 65351J | Modification of terahertz pulsed spectrometer to study biological samples [6535-56] |
| 65351K | Dependence of optic disc parameters on disc area according to Heidelberg Retina Tomograph: Part II. [6535-57] |
| 65351L | 3D simulation of tissue pathological changes localization [6535-58] |
| 65351M | Definition of contribution of the endogen fluorophors in the fluorescence spectrum of the attacked cervical tissue [6535-59] |
| 65351N | Spectral kinetics of plant tissue [6535-60] |
Ultra-violet laser microbeam and optical trapping for cell micromanipulation [6535-76]
D. Kotsifaki, M. Makropoulou, A. A. Sarafetinides, National Technical Univ. of Athens (Greece)

Superresolution in optical diffuse tomography [6535-77]
A. G. Kalintsev, N. A. Kalintseva, Vavilov State Optical Institute (Russia); O. V. Kravtenyuk, Foundation for Research and Technology-Hellas (Greece); V. V. Lyubimov, Vavilov State Optical Institute (Russia)

OPTICAL AND CLINICAL BIOPHYSICS

Photooxygenation of singlet oxygen traps upon excitation of molecular oxygen by dark red laser radiation in air-saturated solutions [6535-62]
A. A. Krasnovsky, A.N. Bach Institute of Biochemistry (Russia) and M.V. Lomonosov State Univ. (Russia); I. V. Kryukov, A. V. Sharkov, P.N. Lebedev Physical Institute (Russia)

The role of Ca²⁺-related signaling in photodynamic injury of nerve and glial cells [6535-63]
A. V. Lobanov, Y. O. Petin, A. B. Uzdensky, Rostov State Univ. (Russia)

The involvement of MAP kinases JNK and p38 in photodynamic injury of crayfish neurons and glial cells [6535-64]
Y. O. Petin, M. Y. Bibov, A. B. Uzdensky, Rostov State Univ. (Russia)

The study of liquid water structure and transfer properties by molecular dynamics [6535-65]
V. Vl. Mitrofanov, Moscow State Univ. (Russia)

Internal temperature distribution in blood vessel under the action pulse laser radiation [6535-66]
L. G. Astafyeva, G. I. Zheltov, B.I. Stepanov Institute of Physics (Belarus)

Blood flow structure in patients with coronary heart disease [6535-67]
L. I. Malinova, Saratov Scientific Research Institute of Cardiology (Russia) and Saratov State Medical Univ. (Russia); G. V. Simonenko, Saratov State Univ. (Russia); T. P. Denisova, Saratov State Medical Univ. (Russia); V. V. Tuchin, Saratov State Univ. (Russia)

Gross protein influence upon blood plasma and serum self organization processes in patients with coronary heart disease [6535-68]
L. I. Malinova, Saratov Scientific Research Institute of Cardiology (Russia) and Saratov State Medical Univ. (Russia); U. V. Sergeeva, Saratov State Medical Univ. (Russia); G. V. Simonenko, Saratov State Univ. (Russia); T. P. Denisova, Saratov State Medical Univ. (Russia); V. V. Tuchin, Saratov State Univ. (Russia)

The effect of LED-light action on microbial colony forming ability of several species of staphylococcus [6535-69]
E. S. Tuchina, N. F. Permyakova, V. V. Tuchin, Saratov State Univ. (Russia)

Diffusion of Cortexin and Retinalamin in eye sclera [6535-79]
E. A. Genina, E. A. Zubkova, A. A. Korobko, I. Yu. Yanina, A. N. Bashkatov, Saratov State Univ. (Russia); T. G. Kamenskikh, V. A. Galanzha, Saratov State Medical Univ. (Russia); V. V. Tuchin, Saratov State Univ. (Russia)
653512  **Mathematical modeling of clearing liquid drop diffusion after intradermal injection [6535-81]**  
M. M. Stolnitz, A. N. Bashkatov, E. A. Genina, V. V. Tuchin, Saratov State Univ. (Russia)

653520  **Mathematical modeling of clearing liquid penetration into the skin [6535-82]**  
M. M. Stolnitz, A. N. Bashkatov, E. A. Genina, V. V. Tuchin, Saratov State Univ. (Russia)

653521  **Monte Carlo modeling of eye iris color [6535-83]**  
E. V. Koblova, Saratov State Medical Univ. (Russia); A. N. Bashkatov, L. E. Dolotov, 
Y. P. Sinichkin, Saratov State Univ. (Russia); T. G. Kamenskikh, Saratov State Medical Univ. 
(Russia); E. A. Genina, V. V. Tuchin, Saratov State Univ. (Russia)

653522  **Algorithm of the automated choice of points of the acupuncture for EHF-therapy [6535-71]**  
E. P. Lyapina, I. A. Chesnokov, Ya. E. Anisimov, N. A. Bushuev, E. P. Murashov, Federal State 
Unitary Enterprise SPE Almaz (Russia); Yu. Yu. Eliseev, Saratov State Medical Univ. (Russia); 
H. Syuzanna, Univ. of Applied Science (Russia)

653523  **Analysis of thermal damage in vocal cords for the prevention of collateral laser treatment 
effects [6535-75]**  
F. Fanjul Vélez, J. L. Arce-Diego, Á. del Barrio Fernández, Univ. de Cantabria (Spain); 
A. Borragán Torre, Ctr. de Foniatría y Logopedia (Spain)

653524  **Mid-infrared laser ablation of intraocular acrylic lenses [6535-78]**  
E. Spyratou, M. Makropoulou, C. Bacharis, A. A. Serafetinides, National Technical Univ. of 
Athens (Greece)

**MANAGEMENT IN BIOPHOTONICS RESEARCH AND EDUCATION**

653525  **Self-management for physics department graduates [6535-72]**  
B. A. Medvedev, Saratov State Univ. (Russia); K. R. Babayan, Saratov Juridical Institute 
(Russia)

653526  **Symbiosis of a telemedicine and neural net’s project as a new way of the decision of 
medical problems [6535-73]**  
O. V. Kasimov, E. V. Karchenova, Saratov Railroad Clinical Hospital (Russia); I. L. Maximova, 
Saratov State Univ. (Russia)

*Author Index*
Conference Committees

Annual International Multidisciplinary School for Young Scientists and Students on Optics, Laser Physics & Biophysics X

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Plenary Session IV
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Lecture Session II
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Lecture Session IV
Sergey S. Ulianov, Saratov State University (Russia)

Oral Session I: Tissue Optics and Spectroscopy
Alexander B. Pravdin, Saratov State University (Russia)

Oral Session II: Biophotonics and Imaging I
Alexander A. Stratonnikov, General Physics Institute, Moscow (Russia)

Oral Session III: Biophotonics and Imaging II
Sergey S. Ulianov, Saratov State University (Russia)

Oral Session IV: Workshop on Management of High Technologies Commercialization III
Valery V. Tuchin, Saratov State University (Russia)

Oral Session V: Seminar on Telemedicine - Opportunities, Applications, Prospects
Irina L. Maksimova, Saratov State University (Russia)
Alexander B. Pravdin, Saratov State University (Russia)

Poster Session
Alexander G. Akchurin, Saratov State University (Russia)
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Alexander V. Priezzhev, Moscow State University (Russia)
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Introduction

The Annual International Multidisciplinary School for Young Scientists and Students on Optics, Laser Physics and Biophysics X, Saratov Fall Meeting (SFM-06) was held in Saratov, Russia, 26–29 September 2006, with about 600 participants from Russia, FSU countries, USA, Canada, Europe, and Asia. It included the wide range of the modern problems of fundamental and applied optics, laser physics, photonics, and biomedical optics.

SFM-06 also contained ten international workshops and seminars:

- **Optical Technologies in Biophysics and Medicine VIII** (Valery V. Tuchin, Chair), SPIE Proc. 6535
- **Coherent Optics of Ordered and Random Media VII** (Dmitry A. Zimnykov, Chair), SPIE Proc. 6536
- **Laser Physics and Photonics VIII** (Leonid A. Melnikov and Vladimir L. Derbov, Chairs), SPIE Proc. 6537
- **Spectroscopy and Molecular Modeling VII** (Valentin I. Berezin, Lev M. Babkov, and Michael D. Elkin, Chairs), SPIE Proc. 6537
- **Electromagnetics of Microwaves, Submillimeter and Optical Waves IV** (Michael V. Davidovich, Chair), SPIE Proc. 6537
- **English as a Communicative Tool in the Scientific Community V** (Vladimir L. Derbov, Svetlana V. Eremina, and Alexander B. Pravdin, Chairs), SPIE Proc. 6537
- **Management of High Technologies Commercialization III** (Valery V. Tuchin, Chair), SPIE Proc. 6535
- **Luminescence II** (Vyacheslav I. Kochubey and Sergey N. Shtykov, Chairs), SPIE Proc. 6537
- **Nanostructures and Nanoparticles: Fabrication, Properties, and Applications II** (Nikolai G. Khlebtsov, Chair), SPIE Proc. 6536
- **Telemedicine: Opportunities, Applications, Prospects** (Irina L. Maksimova, Alexander B. Pravdin, Chairs), SPIE Proc. 6535

The main organizers of the Saratov Fall Meeting are Saratov State University (SSU), Research-Educational Institute of Optics & Biophotonics at SSU, and Research-Educational Center on Nonlinear Dynamics and Biophysics of CRDF and Ministry of Education and Science RF (REC-006).

The main goal of the school, workshops, and seminars is to inform young researchers and students in the field of recent developments and applications of laser and optical technologies in medicine and biology, coherent optics of random and ordered media, material and environmental sciences, nonlinear dynamics of laser systems, laser spectroscopy, and molecular modeling. The
primary focus was the discussion of fundamentals and general approaches of description of coherent, low-coherent, polarized, spatially and temporally modulated light interactions with inhomogeneous absorbing media, photonic crystals, tissue phantoms, and various types of tissues in vitro and in vivo. Such effects as static and dynamic light scattering, Doppler effect, optoacoustic and optothermal interactions, mechanical stress, photodynamic effect, etc., were also considered. On this basis the variety of laser and optical technologies for medical diagnostics, therapy, surgery, and light dosimetry, as well as for spectroscopy of random and ordered media, were presented.

SFM-06 was organized as morning plenary sessions, afternoon lecture and oral sessions, and evening poster presentations. The original oral reports and posters were presented by the junior scientists and students. Plenary lectures were listened to with great interest and were discussed by the audience.

Plenary and invited lectures and oral and poster presentations covered a wide area of topics including tissue optics, spectroscopy and imaging, controlling of optical properties of tissues, as well as biophysical and photo-chemical aspects of photo and laser therapy.

One main aspect of Saratov Fall Meetings is the one-day Internet session. In 2006 this session included the plenary lecture “High-resolution photoacoustic tomography” by Lihong V. Wang from the Washington University in St. Louis (USA).

Participants from USA, Russia, Austria, Australia, Bulgaria, Canada, Finland, Germany, Ireland, UK, Slovakia, Canada, China, Portugal, Italy, Japan, Ukraine, Belarus, Switzerland, Denmark, Spain, Singapore, the Netherlands, Poland, India, and other countries have placed their papers on the meeting website: http://optics.sgu.ru/SFM/, which was available during the meeting and will be available for a whole year up to the next meeting. Among the invited Internet lecturers were well-recognized experts in the fields of biomedical optics and light scattering: Steven L. Jacques (USA), S. Fantini (USA), Sean J. Kirkpatrick (USA), R. K. Wang (USA), Hong Liu (USA), Wei Chen (USA), Omar S. Khalil (USA), K. M. Meek (UK), J. Lademann (Germany), M. Hoffmann (Germany), O. Minet (Germany), Colin J. R. Sheppard (Singapore), A. K. Asundi (Singapore), A. Kishen (Singapore), Qingming Luo (China), P. K. Gupta (India), Christoph K. Hitzenberger (Austria), A. Kowalczyk (Poland), Vitali A. Tougbaev (South Korea), and O. V. Angelsky (Ukraine). A three-hour on-line Internet discussion was held on papers presented in the Internet session via a chat moderated by Alexander Priezzhev. Many of the presented Internet papers are published in this conference volume.

SFM-06 has gathered about 600 participants; a great number of presented materials are the result of collaboration between research groups from different countries supported by international scientific programs such as CRDF, INTAS, Royal Society and others.
The major portion of this volume includes papers presented in the workshop on Optical Technologies in Biophysics and Medicine VIII. However, a few of the most interesting papers (paper numbers 30, 44, 72, and 73) presented in the workshops on Management of High Technologies Commercialization III and Telemedicine: Opportunities, Applications, Prospects also are published in the volume.

This year SFM was held a few months after the XII Conference on Laser Optics in St. Petersburg (26–30 June 2006) with the Workshop on Lasers in Biomedical Diagnostics and Laser Tomography of Biomedical Objects (co-chairs, V. V. Lubimov, A. M. Sergeev, and V. V. Tuchin), with topics related to SFM-06. This opportunity allowed us to invite a few papers presented in the St. Petersburg Workshop to be published in this volume. These papers are numbers 75, 76, 77, and 78.

This year is also very important for organizers of the meeting, because 60 years ago the Chair of Optics of Saratov State University was organized by our teacher, Professor Mark L. Katz. We have dedicated SFM-06 to the memory of Professor Mark L. Katz on the 100th anniversary of his birth and the 60th anniversary of the Chair of Optics, founded by him in 1946. We are very proud that our Chair is recognized as a host of many international conferences and schools including SFM. We are very thankful to our numerous friends all over the world who sent us their congratulations and best wishes.

It is a great pleasure and privilege for the chair of SFM to thank all of the authors for their contributions to SFM-06, especially to the Internet lecturers for their exciting presentations, and to Alexander Priezzhev, a moderator of the Internet sessions for the last nine years, for his talent and impressive moderation.

The organizers of SFM are grateful to all of the sponsoring organizations and programs that supported this meeting very effectively: SPIE Russia Chapter, Executive Director Edmund Akopov; Russian Foundation for Basic Research; U.S. Civilian Research & Development Foundation for the Independent States of the Former Soviet Union (CRDF), grant REC-006 and mini-grant on the conference support; and Volga Region Center of New Information Technologies.

I would like to thank Elina Genina and Ivan Fedosov for their help with the preparation of this volume.

Valery V. Tuchin
High-resolution Photoacoustic Tomography

Lihong V. Wang, Gene K. Beare
Dept. of Biomedical Engineering Washington University in St. Louis

ABSTRACT

Novel photoacoustic tomography techniques, including, orthogonal-mode photoacoustic tomography, reflection-mode photoacoustic microscopy and deeply penetrating RF-based thermoacoustic tomography are presented.

Keywords: photoacoustic tomography, photoacoustic microscopy
Credits to Lab Members

CURRENT LAB MEMBERS
• A. Garcia-Uribe
• S. Hu
• X. Jin
• R. Kothapalli
• C. Kim
• G. Ku
• C. Li
• L. Li
• Y. Li
• K. Maslov
• E. Smith
• K. Song
• L. Song
• M. Todorovic
• X. Xu
• X. Yang
• R. Zemp
• H. Zhang
• S. Zhou

SELECTED FORMER LAB MEMBERS
• J. Ai, PhD
• D. Feng, MS
• J. Hollmann
• S. Jiao, PhD
• J. Li, PhD
• M. Li, PhD
• G. Marquez, PhD
• M. Mehrubeoglu, PhD
• J. Oh, PhD
• H. Sun, PhD
• Y. Pang, MS
• S. Sakadzic, PhD
• M. Sivaramakrishnan, MS
• X. Wang, PhD
• Y. Wang, MS
• X. Xie, MS
• M. Xu, PhD
• Y. Xu, PhD
• G. Yao, PhD
• W. Yu, MS
• X. Zhao, MS

Credits to Collaborators

• Texas A&M University (Animal study):
  • G. Stoica, DVM

• UT MD Anderson Cancer Center (Clinical study & molecular contrast agents):
  • M. Duvic, MD
  • B. Fornage, MD
  • K. Hunt, MD
  • C. Li, PhD
  • V. Prieto, MD

• Nanospectra (Nanoshells):
  • P. O’Neal, PhD
  • J. Schwartz, PhD
Motivation

Orthogonal-mode photoacoustic tomography

Reflection-mode photoacoustic microscopy

Deeply penetrating RF-based thermoacoustic tomography

Summary

Motivation for Optical Imaging

Safety — Non-ionizing radiation: photon energy is ~2 eV.

Physics — Related to the molecular conformation of tissue.

Optics — High intrinsic contrast:
  - Optical absorption: Angiogenesis, hyper-metabolism, apoptosis, necrosis, and exogenous contrast agents.
  - Optical scattering: Size of cell nuclei.
  - Optical polarization: Collagen, muscle fibers.
  - Spectroscopy: Wavelength multiplexing

Physiology — Functional imaging of physiological parameters:
  - Oxygen saturation of hemoglobin
  - Total hemoglobin concentration (related to blood volume)
  - Enlargement of cell nuclei
  - Denaturation of collagen
  - Blood flow (Doppler)

Physiology — Molecular imaging (exogenous contrast agents).

....
**Challenges in Optical Imaging**

- SNOM: Scanning near-field optical microscopy
- CFM: Confocal microscopy
- 2PM: Two-photon microscopy
- SHM: Second harmonic microscopy
- OCT: Optical coherence tomography
- DOT: Diffuse optical tomography
- UOT: Ultrasound-modulated optical tomography
- PAT: Photoacoustic tomography

**Outline**

- Motivation
- Orthogonal-mode photoacoustic tomography
- Reflection-mode photoacoustic microscopy
- Deeply penetrating RF-based thermoacoustic tomography
- Summary
Orthogonal-mode Photoacoustic Tomography

1. Laser pulse (<ANSI limit: e.g., 20 mJ/cm²)
2. Local heating (~ mK)
3. Ultrasonic emission (~ mbar)
4. Ultrasonic detection (scattering/100)


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Functional Photoacoustic Imaging of Rat Cortex in response to Whisker Stimulation In Vivo

PAT image (left stimulation) PAT image (right stimulation)


http://oilab.tamu.edu
Deeply Penetrating Photoacoustic Tomography
with NIR Excitation & ICG Contrast


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Reflection-mode Confocal Photoacoustic Microscopy: Illustration

Reflection-mode Dark-field Confocal Photoacoustic Microscopy: System

System Parameters

- Laser
  - Tunability: 570-770 nm
  - Repetition rate: 10 Hz
  - Pulse width: 6.5 ns
  - Optical fiber: 0.6 mm diameter
  - Energy per pulse: 0.2 mJ
  - Energy density at focus: \( \sim 6 \text{ mJ/cm}^2 < 20 \text{ mJ/cm}^2 \) (ANSI safety limit)
- High-frequency ultrasound transducer
  - Center frequency: 50 MHz
  - Nominal bandwidth: 70% of 50 MHz
  - NA: 0.44

Imaging Depth and Resolution

B-scan of a black double-stranded cotton thread embedded in rat

- Imaging depth: \( \sim 3 \text{ mm} \)
- Axial resolution: \( \sim 15 \text{ microns} \)
- Depth/resolution: \( \sim 200 \text{ pixels} \)
- Lateral resolution: \( \sim 45 \text{ microns} \)
- Acquisition time: 2 \( \mu \text{s/A-scan} \)
- No signal averaging

Volumetric Imaging of Microvasculature In Vivo

Maximum amplitude projection onto the skin

Volume: 10 mm x 8 mm x 3 mm

Imaging of Skin Burn in Pigs

Acute thermal (175 °C, 20 s) burn in pig skin in vivo.
Postmortem imaging at 584-nm optical wavelength.

Photograph

Healthy tissue
Coagulated tissue
Hyperemic ring 1 mm

Photoacoustic image

Hyperemic bowl

B-scan image

Hyperemic bowl

Histology

Hyperemic bowl

PA amplitude [a.u.]

Distance [mm]

Burn depth ~1.7 mm

Skin surface
Imaging of Skin Burns of Various Depths

Acute thermal (150 °C, various times) burn in pig skin in vivo.
Postmortem imaging at 584-nm optical wavelength.

Imaging of Hemoglobin Oxygen Saturation (SO₂) In Vivo

Total hemoglobin concentration  SO₂ in segmented venules and arterioles

**Hemodynamics In Vivo**

578, 584, 590, and 596 nm

Change in oxygenation

<table>
<thead>
<tr>
<th>Physiological states</th>
<th>Imaged SO₂</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypoxia</td>
<td>1</td>
</tr>
<tr>
<td>Normoxia</td>
<td>0.8</td>
</tr>
<tr>
<td>Hyperoxia</td>
<td>0.6</td>
</tr>
</tbody>
</table>

**Total hemoglobin**

**Oxygen saturation**

578, 584, 590, and 596 nm

**Imaging of Melanoma In Vivo**

Composite photoacoustic image acquired at 584 and 764 nm

B-scan image at 764 nm

**Contrasts:**
- Vessel: 13
- Melanoma: 69

**Nature Biotech.**
24, 848 (2006)

http://oilab.tamu.edu -- 40
Imaging of Human Palm In Vivo

Maximum amplitude projection onto the skin

Skin surface

B-scan image

Optical absorption


Modern High-resolution Optical Microscopy

<table>
<thead>
<tr>
<th>Modality</th>
<th>Year</th>
<th>Depth</th>
<th>Depth / Resolution</th>
<th>Contrast</th>
</tr>
</thead>
<tbody>
<tr>
<td>Confocal microscopy</td>
<td>1970s</td>
<td>~0.5 mm</td>
<td>&gt; 100</td>
<td>Scattering, fluorescence</td>
</tr>
<tr>
<td>Two-photon microscopy</td>
<td>1990s</td>
<td>~0.5 mm</td>
<td>&gt; 100</td>
<td>Fluorescence</td>
</tr>
<tr>
<td>Optical coherence tomography</td>
<td>1990s</td>
<td>~1 mm</td>
<td>&gt; 100</td>
<td>Scattering, polarization</td>
</tr>
<tr>
<td>Dark-field confocal photacoustic microscopy</td>
<td>2005*</td>
<td>~3 mm, scalable</td>
<td>&gt; 100</td>
<td>Absorption</td>
</tr>
</tbody>
</table>

Outline

- Motivation
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- Reflection-mode photoacoustic microscopy
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Thermo-acoustic Image of a Mastectomy Specimen

- 11 cm diam. X 9 cm thick
- ~5:1 contrast
- Invasive lobular carcinoma

Tech. in Cancer Res. & Treatment
4, 559 (2005).

Summary

- Physically combining ultrasonic and electromagnetic waves (light & RF) provides
  - improved spatial resolution compared with optical/RF imaging,
  - new contrast mechanisms compared with ultrasound imaging.
- Spatial resolution is determined by the ultrasonic parameters.
- Spatial resolution is scalable with the ultrasonic parameters.
- Contrast is provided by the electromagnetic properties.
- Deep (~cm) tissue imaging can be achieved.
- Speckle artifacts do not exist.
- Functional imaging can be accomplished with endogenous contrast.
- Molecular imaging can be accomplished with exogenous contrast agents.
- Non-ionizing radiation is used.
- Costs are comparable with those of ultrasound systems.
Funding Sources

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- NIH
  - R01 CA106728
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  - R01 CA092415
  - R01 EB000712
- NIST

RECENTLY COMPLETED
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  - CA83760
  - CA71980
  - CA68562
  - EB000319
- NSF
- US Army
- Whitaker Foundation

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Welcome to the Optical Imaging Laboratory, a research laboratory dedicated to the developments of novel non-ionizing tomography and spectroscopy for the early detection of various cancers.

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