

funded by the
European Commission



CONTENT

- 2 Mission and Vision
- 3 Industrial User Club
- 4 Inside
- 8 Technology Breakthroughs
- 10 Tutorial
- 13 Events

Dear Reader,

one year has passed since the Network of Excellence for Biophotonics (PHOTONICS4LIFE) started to operate, therefore it is time for a short résumé of this first year.

We had already a first interim review meeting and we were pleased to hear that the reviewers are convinced that we are on track. In several cases we even think that we are ahead of schedule. This concerns especially our so-called "P4L-projects", which will not only interlink the research activities within P4L but also create excellent scientific output. They will also be employed to involve "Associate Partners". Some of these potential new partners of P4L participated already in our Annual Meeting, which was just held in Florence at CNR IFAC. It was collocated with an important meeting of the European Technology Platform Photonics21 WG 3 (Life Sciences and Health), which involves many of our partners discussing future possibilities for photonic solutions in Life Sciences and Health.

When you are holding this newsletter in your hands the first summer school of Biophotonics under collaboration with P4L will have just taken place in Ven, Sweden. We collaborated with the already existing "International Graduate summer school".

Only four months have passed since our first newsletter was published. The reason for this rush is not only that we have plenty of news to tell, but that we wanted to have this issue be finished for the LASER World of PHOTONICS taking place in June, 15th to 18th in Munich. Photonics4Life will be present not only at the congress but also at the fair in an area which is dedicated completely to Biophotonics. In addition, P4L organizes a workshop entitled "Visions for future diagnostics". More details on these topics and also more information on how you can get a member of P4L's industrial user club you can find in the following pages.

Best wishes,
Jürgen Popp



Photonics4Life – First Year of Operation

In its first year of operation the Network of Excellence for Biophotonics (PHOTONICS4LIFE) started to integrate the very broad field and subdivisions of Biophotonics. This was done by setting-up the structure of a comprehensive database, which is currently filled with information by the partners. The main branches of the database are medical domains, fabrication and enabling technologies, biological processes, data analysis, and biophotonics techniques. Each branch is subdivided in more than ten subbranches. Using keywords different entries can be linked to each others. This will help to browse through the database and to find relations between technologies, bio-photonic methods, diseases, etc. In the near future this database will develop to a powerful tool and helps to structure and integrate the fragmented area of biophotonics.

The value of this database was also recognized by the reviewers during the interim review meeting of Photonics4Life held in Brussels on February 27. Ten months after the start the review meeting served especially the aim to get the reviewers of Photonics4Life acquainted with the aims and the structure of the network. The reviewers are Dr. F. Tooley and Prof. Dr. H. J. C. M. Sterenberg (Prof. Dr. Brian MacCraith will join the reviewer team with the first official review meeting). After the general introduction by the coordinator of P4L, Prof. Dr. J. Popp, the P4L research oriented activities and the integrating as well as the spreading of excellence oriented activities were discussed in detail. The reviewers were especially impressed by the clinical view of the research oriented activities presented by Prof. Dr. K. Svanberg. Overall the reviewers decided that “the Project is on track and

should proceed”. The P4L members are convinced that this will also be the conclusion after the first regular review meeting which is scheduled for the 16th July in Barcelona.

To foster scientific collaboration among the different disciplines and between different partners within a workpackage or from different workpackages Photonics4Life initiated so-called “P4L projects”. These projects will be employed to form new partnerships in research and to enlarge activities in existing partnerships. They enable the partners to focus on their core expertise by coupling complementary capabilities. P4L gives special preference to interdisciplinary projects to promote the breaking down of barriers between the different disciplines working in the field of biophotonics.

In addition to promoting structuring and integration, the generation of cutting-edge scientific output can be expected from the P4L-projects. Therefore these projects embody efficient use of the funds offered by the EU and the taxpayer.

At the beginning of May the first nine P4L-projects were granted and initialized. These can be roughly categorized by assigning them to four topics, namely cancer research, biochips, new multifunctional or multimodal approaches and pharmaceuticals research.

» www.photonics4life.eu

P4L Projects	
Title	Leading Organisation
In vivo hyperspectral lifetime measurements of skin cancer autofluorescence	IMPERIAL
Morpho-chemistry characterization of collagen disorders	CNR-IFAC
Comparison between fluorescence and SPR imaging biochips for immuno-based and DNA-based assays	IPHT
Towards identification of molecules by means of Raman spectroscopy using lab-on-a-chip micro-optical detection systems	VUB
Comparison between fluorescence and SPR imaging biochips for immuno-based and DNA-based assays	IPHT
Integrated zebrafish detector “EmbryoSort”	FZK
Novel Bioworkstation: Optical trapping meets digital holographic microscopy, dynamic phase contrast microscopy and fluorescence lifetime imaging	USTAN
Label free holographic and AFM imaging of human neural cells under synchronized electrical stimulation	UoM
Photonic control of nanocontainers to investigate interactions with cells	UoM

Membership in P4L's Industrial User Club

Beside structuring and integration of Europe's Biophotonics R&D activities P4L also aims in linking up the research organisations with industry to foster innovation by learning about the industrial needs as well as by transferring R&D results to industry. P4L's Industrial User Club (IUC) is this short link between industrial companies and the academic partners in P4L. It is an easy opened door to the knowledge in biophotonics presented in P4L's database; it stimulates the dialogue between industry and academics in biophotonics; it enables companies to make use of the synergies, produced by the network. Being a partner in the IUC, companies will easily find – among several hundred researchers in P4L – experts in biophotonics which are prepared to solve their problem in technology, in biophotonic methods in the product development and also in clinical applications.

To get a member in P4L's industrial user club you can choose out of two options: **Level one members** will get access to the knowledge management centre without any membership fee. First class information is available on the huge amount of capabilities in P4L to support

development, fabrication, commercialization and clinical use of biophotonics developments. It allows to find the unknown expert, the missing instrumentation, the right potential to fill the gap in the development as well as in the fabrication process line. The only request is to sign up as a member and to provide info on your expertise and activity leading to at least one entry in the P4L database.

In addition to this, **level two members** benefit from:

- Using the priority service of the IUC to find the appropriate expert, knowledge or instrumentation to solve the specific problems of the company.
- Getting reduced registration rates for P4L's workshops and tutorials on technologies, methods, fabrication and medical use of biophotonics.
- Being the first to be invited to new common research initiatives of the P4L partners.
- Advertising the company business and products on the P4L web site by displacing the company logo with a link to the companies website.
- Describing the companies profile in P4L's newsletter which is distributed

to more than thousand people active in biophotonics.

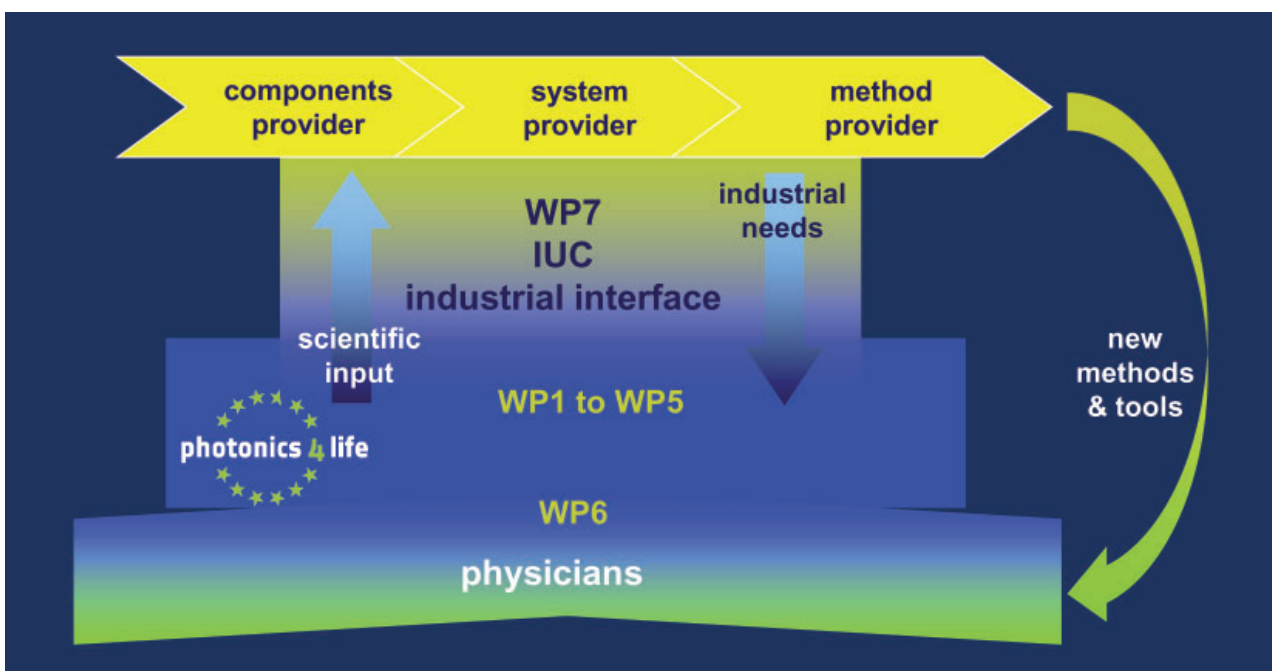
- Placing job offers on the P4L portal to get the first touch to the best qualified young scientists in the European Biophotonics community.
- Getting in touch to other industrial IUC partners through the IUC communication as well as in routinely organized IUC events.
- Joining P4L's booth at fairs for a special fee.

As an IUC member companies will be associated to the European network which drive the hot and innovative field of biophotonics. IUC members participate in the discussion about the future direction of Biophotonics and its applications.

If you are interested in an IUC membership visit the P4L IUC web site <http://industry.photonics4life.eu> or contact:

Contact

Tom Guldemont
Vrije Universiteit Brussel (VUB)
P4L IUC Officer
tom.guldemont@tona.vub.ac.be



Workpackage 6 in P4L – The Doctors' View on Photonics

Within the Network of Excellence for Biophotonics (Photonics4Life) the development of various techniques to be implemented into the clinical use is of high priority. Workpackage 6 entitled "Clinical applications and applications in doctors practices" works explicitly towards this goal. Looking to the application under "real-world-conditions" ensures that the developed tools do have the appropriate robustness, product safety and versatility for use in different clinical situations. These conditions fulfil the demands for easy-to-use systems, also for the clinicians. In oncology, e.g., there is a need to develop techniques for enhanced possibilities to detect early cancer and precancer and to demarcate tumour borders. Photodynamic therapy (PDT) utilising red laser light and photosensitising agents is a selective treatment modality for certain types of thin malignancies. By using optical fibres inserted into the tumour mass also deep lying tumours can be treated. A combined use of optical detection and PDT can, when fully developed, offer to the patients a highly selective, safe and minimal-invasive modality in the management of tumours.

It is of importance to get the doctor's view on the development and possible

application of the techniques and also to develop new methods along the lines where there are clinical problems still to be solved. This means that there should be a "medical pull" in the development of the industrial competence rather than looking at the techniques, which are there and try to find applications. This still existing "technology push" aspect may be less effective in bringing photonics into the clinic and to the favour for our patients. The "medical pull" approach applies to many of the techniques we are developing and planning to develop within WP6 in Photonics4Life.

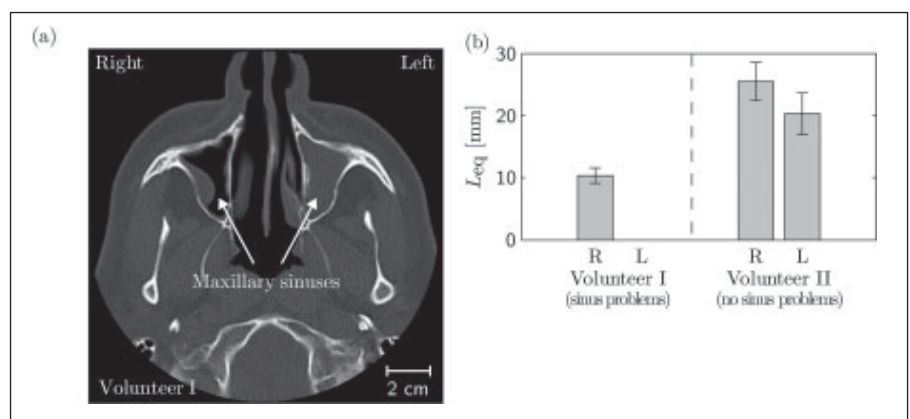
Traditionally in tumour diagnosis, tissue is sampled by invasive biopsies. The sample is put in formalin for fixation and then cut and stained for histopathological examination. The whole procedure takes up to several weeks before the clinician has the result. A new optical non-invasive probing technique is under development and clinical evaluation at the Department of Oncology in collaboration with the Atomic Physics Division, both at Lund University. Fully developed this technique will give real-time optical characterisation data in conjunction with the clinician's visual judgment for better and more precise diagnosis of the patients.

WP6 ensures the "medical pull" for the development in P4L by strengthening the feed-back between physicians, biomedical health personal and representatives of patients with the scientists and engineers developing new biophotonic methods and tools. Thus, the end-users are part of the development right from the start taking into account their needs in an appropriate manner. It guarantees a complete dealing with the innovation process starting from a medical problem and its technological solution via construction and integration of prototypes for proof of concept to clinical pilot studies and clinical trials at various levels.

Contact

Katarina Svanberg
Lund University Hospital (LLC)
Katarina.Svanberg@med.lu.se

Niels Bendsoe
Lund University Hospital (LLC)
Niels.Bendsoe@med.lu.se

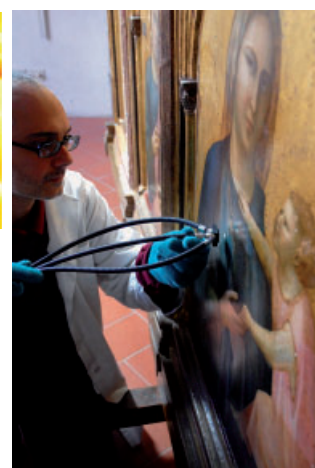
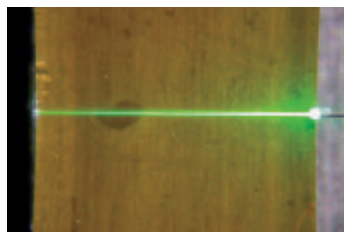
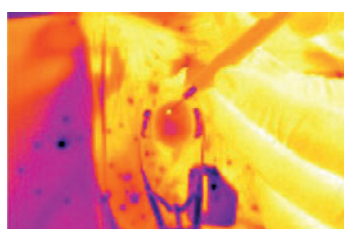


Institute of Applied Physics (IFAC)

The Institute of Applied Physics (IFAC) is part of the Italian National Research Council (CNR), the largest public research organization in Italy. IFAC is located in the CNR Area of Research of Florence. This location is part of the Scientific Pole of Florence, a campus hosting the scientific faculties of the Florence University and other scientific initiatives, like LENS.

IFAC staff is composed of about 80 permanent and 50 contract employees. Research aims are devoted to applied research in fields of optics, photonics, nanotechnology, electromagnetism, atmospheric physics, environmental sensors, industry production and cultural heritage. The research activities involve these competences in several research groups:

- The research group on **Sensors** is mainly devoted to the design and development of optical sensors for the detection of physical, chemical and biochemical parameters. In the last years the group focused its activity to the development of optical sensors for clinical diagnostics.
- The research group on **Materials and Devices for Photonics** has wide experience in the fabrication and characterisation of integrated optical devices, such as integrated optical amplifiers. The activity also includes material research, mainly focussed on glasses. More recently, activity on optical microresonators for sensing and light emission applications is being carried out.
- The research group on **Biophotonics and Nanomedicine** has extensive expertise in the technology of new biomedical lasers, in pre-clinical and clinical applications of minimally invasive laser surgery and therapy, and in microscopy techniques for analysis of biotissue (autofluorescence, multi-photon, AFM). More recently the group has developed and synthesized new nanostructured chromophores based on gold nanoparticles for PDT, laser welding and diagnostics.
- The research group on **Laser Systems** is studying novel solid state laser materials in both crystal and ceramic phase, for development of advanced performance lasers. High efficiency Ce and Yb based lasers have been achieved. Laser processing is also studied for industrial applications.
- The research group on **Lasers in Conservation** is studying novel applications of laser ablation, laser spectroscopy and neutron diffraction for archaeometry and conservation of cultural heritage. The group developed successful techniques for side-effects-free laser cleaning of stone, metals and wall paintings.
- The research group on **Aerospace Optical Systems** studies and develops optical instruments for space mission, and airborne remote monitoring of ground. Remote monitoring is also studied by means of radiometry in the microwave range.
- **Remote sensing** is studied by means of fluorescence LIDAR systems (FLIDAR), with specific prototypes employed for



environmental studies and for historic buildings remote diagnostics, detecting biodeteriogens and identifying stone materials.

IFAC has broad experience in coordination of cooperative projects at national and EU levels, and in transfer of innovation towards Hi-Tech industries and end users in the biomedical field. It owns facilities including a class 100 clean room with photolithographic apparatus and thin film deposition (thermal evaporator and RF magnetron sputtering), plasma etching and characterisation equipment, many standard and ultra-fast laser sources, optical and fluorescence microscopes, TEM, SEM, spectrometers, fast imaging systems, instrumentation for cell manipulation and tissue biopsy.

Contact

Roberto Pini
R.Pini@ifac.cnr.it
www.ifac.cnr.it

Saratov State University (SSU)

The SSU is one of the largest educational, scientific and cultural centers in Russia supporting education and research in biophysics, medical and biochemical physics, biomedical optics and biophotonics, nanotechnologies, computer science, nonlinear processes, and materials science & bioengineering. The University campus is shared with Saratov State Medical University, which is affiliated with specialized clinics and hosts clinical research and investigation.

R&D in Photonics and Biophotonics as well as educational programs are concentrated in two major SSU divisions: **Chair of Optics and Biophotonics (COBP)** and **Research-Educational Institute of Optics and Biophotonics (REIOB)**.

Around 60 research and faculty members of these two divisions are involved in photonics and biophotonics studies and education, including 10 full professors and 30 PhD and MD. Two student Chapters of SPIE and OSA are well operating on the basis of COBP and REIOB.

- **COBP** has a 63-year history. One of the first books on laser physics was published in 1964 by faculty members. The COBP's faculty is well-known in the world due to numerous publications in international journals and a number of issued monographs, tutorials and handbooks on tissue optics and biophotonics.
- **REIOB** was founded in 2004 to provide integration of research-educational programs of SSU into the global system of education and science in the field of optics, biomedical optics, and biophotonics, including basic and

applied science and commercialization of the basic R&D. The institute consists of the following laboratories: Biophotonics, Optics of Dispersive Media, Optical Medical Diagnostics, Spectroscopy, Biomedical Optics, and Photonic Crystal Fibers and Biosensors. Major scientific directions are: optics and spectroscopy of dispersive media; physics of optical measurements; laser and fiber-optic physics and technology; complex dynamics of optical systems and fractal optics; holographic measurements; interaction of laser and optical radiation with biological tissues and cells; complex dynamics and fluctuations in biomedical photonics; biophysical grounds of optical medical diagnostics and therapy; coherence and polarization-sensitive medical tomography; medical lasers, fiber-optical, photonic crystal fiber and light diode systems and sensors.

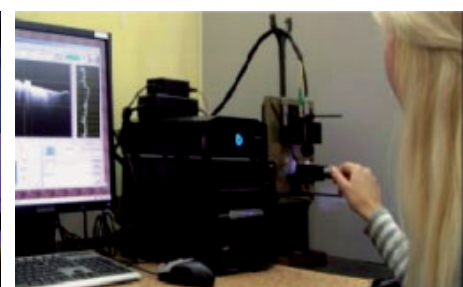
REIOB and COBP have well-developed national and international links with more than 60 leading research and educational centers in optics and biophotonics. In 2007 on the basis of REIOB and COBP and in the framework of Russian Federation Program "Innovative Universities" the International Research-Educational Center on Optical Technologies in Industry and Medicine was created.

SSU BP group is one of the pioneers in the field of combined reflectance/fluorescence spectroscopy of various tissues, in particular human skin (see Handbook of Optical Biomedical Diagnostics, V.V. Tuchin (ed.), SPIE Press, Bellingham, WA,

2002). SSU BP group pioneered also the field of controlling of tissue optical properties using tissue impregnation by biocompatible optical clearing agents. Technologies of measurements and extraction of optical parameters of soft and hard tissues were designed by this group and many new and updated data for skin, fat, bone, mucous and some other tissues are summarized in the monograph (V.V. Tuchin, *Tissue Optics: Light Scattering Methods and Instruments for Medical Diagnosis*, 2nd ed., SPIE Press, Bellingham, WA, 2007). In collaboration with "Nanostructured Glass Technology," Ltd. SSU developed a polycapillary glass technology for producing optical elements, including production of X-ray lenses, holey optical fibers, photonic crystal fibers, and substrates for biochips. The BP group also has a prolonged experience in designing and manufacturing of optical instrumentation for quantification of skin optical properties and color. Together with the Institute of Biochemistry and Physiology of Plants and Microorganisms RAS some pioneer results have been generated on designing of gold nanoparticle technology and their application to photothermal therapy and labeling and detection of blood components in circulating blood in vivo. Recently this group was among the first groups which provided gold nanoparticle trapping and imaging.

Contact

Vallery Tuchin
tuchin@sgu.ru



Photonics4Life – Annual Meeting

From 25 – 27 May 2009 the 13 Network Partners together with young researchers and interested potential new members met for their annual meeting in Florence, the City of Medici in Tuscany. Host faculty was the CNR - Istituto della Fisica Applicata. Its chair Prof. Roberto Pini stated that the event was “a brilliant combination of excellent networking, highly interesting talks and best Italian conditions.”

After an internal programme on the first day, the second day was all about science. More than 40 Junior Researchers of the network took their chance to present their latest findings in poster sessions and scientific talks. 16 of them showed the whole bandwidth and importance of Biophotonics. From the application of fluorescence lidars to prevent the loss of cultural heritage to fundamental research in nano Biophotonics various topics fascinated the audience.

As Photonics4Life is always eager to grow, several institutions were invited as potential new members. These were the Wrocław University of Technology represented by Henryk Kasprzak, FORTH IESL Heraklion represented by Maria Farsari, the Joint



Research Centre Ispra represented by Maurice Whelan and The Don Gnocchi Foundation Milano represented by Michele Casella. They as well gave interesting insights into their work and thereby showed how they could enrich the networks portfolio of competences.

Photonics21 – WG3 Meeting in Florence

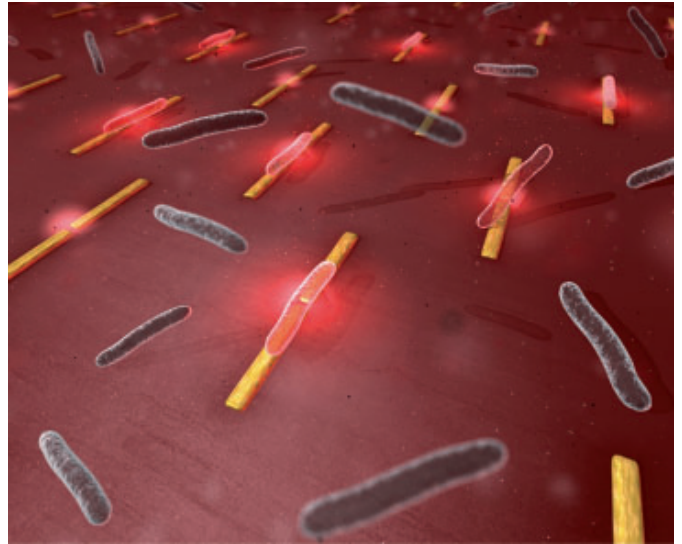
Collocated with the Annual Meeting of Photonics4Life the WG3 “Life Sciences and Health” of the European Technologie Plattform Photonics21 held a meeting in Florence to update the Strategic Research Agenda and to discuss and focus research priorities. The meeting was organized by Prof. Roberto Pini from the local partner of Photonics4Life CNR-IFAC who is also member of the Photonics21 WG3. Aside from the fact that nearly half of the participants are also involved in Photonics4Life, P4L members also contributed to this meeting by organizing and conducting 8 workshops together with the Zeiss AG where physicians and end-users of Biophotonics tools presented the most important trends and problems in their fields. The results of these workshops served as a basis for the more application-oriented approach the WG3 decided to take in the future. Accordingly, the WG3 plans to focus on the research on photonic solutions for the three most urgent problems connected with the increasing age of the population, namely, cancer, eye related diseases and pre-clinical research for all diseases.



Nano Optical Tweezing with Plasmonic Antennas

Researchers from the Plasmon nano-optics group in ICFO-The Institute of Photonic Sciences in Barcelona developed a novel generation of integrated optical tweezers able to immobilize and orientate individual living E-coli bacteria at a surface with low laser intensities.

The concept of optical antennas is applied to design a sub- λ optical well capable of efficiently trapping in water Rayleigh objects with small refraction index contrast. This way, parallel trapping of 200 nm polystyrene beads was achieved with a single laser beam under intensities at least 3 orders of magnitude weaker compared to prior works. Beyond, the method was applied to non-invasive trapping of living E-coli bacteria. The elongated optical well of the antennas enabled trapping of each bacteria along a predefined orientation during several hours. Despite this long exposition to the antenna fields, the bacteria keep growing and dividing in the same way as a reference population of unexposed specimens, revealing no observable damage induced by trapping. The performance of these nano-optical tweezers pave the way toward a new generation of analytical devices where the analyte would be non-invasively manipulated, selectively arranged and analyzed at the chip surface for low cost and parallel bio-analysis.



3D schematic of parallel trapping of living E-Coli bacteria at a surface patterned with gold nanoantennas.

Contact

Institut of Photonic Sciences (ICFO)
<http://www.icfo.es>

Stretching Blood Cells Releases Oxygen

Researchers from the Optical Tweezers Group at ICFO - the Institute of Photonic Sciences in Barcelona have recently combined optical tweezers and Raman spectroscopy to monitor the oxygen release of single red blood cells.

The ability to trap and manipulate a single cell or biomolecule while simultaneously exciting the Raman scattering is exploited to study the effect of force and deformation on the conformational structure of biomolecules and physiological states of cells. On blood cells a mechanical stress is applied to simulate the stretching and compression that cells experience as they pass through vessels and smaller capillaries. The tweezers action on cells can be seen similar to squeezing water out



Red blood cell being held in a dual-spot optical trap while the local Raman spectral changes upon stretching are monitored.

of a sponge. A transition between the oxygenation and deoxygenation states in response to such stretching has been demonstrated by spectroscopic methods. This transition is due to enhanced hemoglobin-membrane and hemoglobin neighbor-neighbor interactions. It is assumed that stretching and compressing is a way the body has to promote release of oxygen from blood cells.

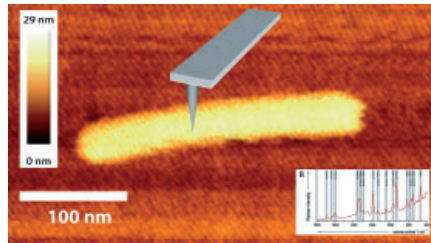
Contact

Optical Tweezers Group at ICFO
 Dimitri.Petrov@ICFO.es

Novel Approach: Tip Enhanced Raman Spectroscopy (TERS) for Virus Detection and Determination

Together with groups from the Robert Koch Institute in Berlin and the Institute for Analytical Sciences in Dortmund scientists from the Institute of Photonic Technology in Jena have found a way to detect and determine single viruses. They used the combination of two existing techniques of microscopy to reach this new level of viral imaging.

The researchers took advantage of the strong electromagnetic field enhancement near the silver coated tip of an atomic force microscope to combine the nanometer resolution with the molecular information provided by Raman spec-



TERS spectroscopic examination of a single tobacco mosaic virus. An AFM scan with the special tip is performed before each TERS measurement to position the AFM tip directly on the virus.

troscopy. This technique allows assigning single viruses to a certain species by their molecular fingerprint.

In life sciences, medicine, and food control it is important to warrant a fast and certain identification of viruses, because highly contagious diseases such as Ebola can already be caused by a handful of viruses. Classic viral detection methods are mostly based on microbiological processes that are usually complex and time consuming. Furthermore these techniques only allow the detection of large concentrations but not of one single organism.

Contact

Institute of Photonic Technology (IPHT)
<http://www.ipht-jena.de>

Glass Multichannel Capillary Tip for Extraction of Nucleic Acids

A new, robust technology for extracting nucleic acids has been invented by researchers from the "Nanostructured Glass Technology" group at Saratov State University, Russia. The method is based on the ability to adsorb nucleic acids on a glass surface. As a glass surface a well-developed internal surface of a regular glass multichannel capillary (MC) is used. The MC tip (Fig 1, lower) is integrated into a standard polypropylene pipette tip allowing to pump the sample and buffers through the multichannel capillary. The process to extract nuclei acids (Fig. 2) is extremely simple and could be easily automated. It will be about 8 times faster in comparison with a commonly used spin-column tech-

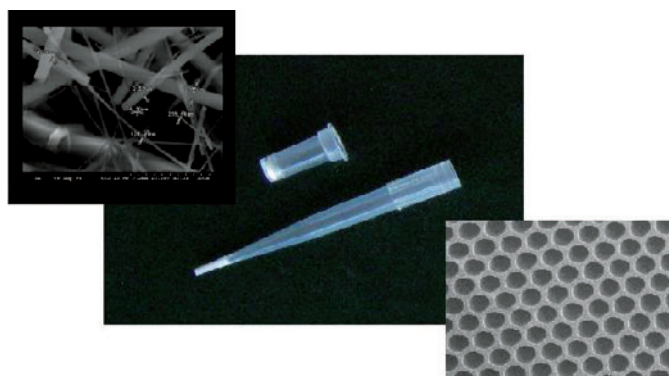


Fig 1. Comparison of a commonly used spin-column and the MC pipette technology for extraction of nucleic acids: electronic micrograph of fiber glass layer used in a spin-column technique and general view of a spin-column (upper); general view of MC tip pipette and optical image of MC tip (lower).

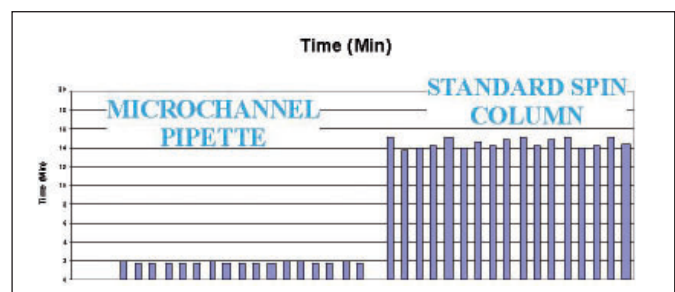


Fig 2. Comparison of DNA extraction time using MC pipette and spin-column technologies, 17 independent tests.

nique which explores a polypropylene tube (Fig 1, upper) with a fiber glass layer as an adsorbent where pumping of the sample and buffers through a spin-column is carried out by rotation in a centrifuge. Manual extraction took 2 min and could be improved in automatic mode. Additional benefits of MC technology are: 1) no damage of big biological molecules at pumping due to MC regular structure with a high quality of internal walls of capillaries; and 2) the possibility to be integrated in an optical measuring platform on the basis of microfluidic/holey fibers.

Contact

Julia Skinina, Saratov State University
 SkibinaJ@yandex.ru or
 Vallery Tuchin, Saratov State University
 tuchin@sgu.ru, tuchinw@mail.ru

Optical Tweezers: Novel Photonics for the Life Sciences

David J Stevenson, Tomáš Čížmár and Kishan Dholakia

The photon description of light and its associated properties of energy and momentum was a major turning point in the early part of the 20th century. It was realised that light possesses a linear momentum of h/λ per photon, where h is the Planck constant and λ the wavelength of light. This is a minuscule quantity but important for objects at the microscopic size scale or smaller where such a momentum may exert appreciable forces. This article introduces the principles of a single beam trap, commonly termed optical tweezers¹. We discuss how a plurality of tweezers and advanced beam shapes may be generated and highlight some of the significant applications of optical tweezers in the life sciences.

The area of optical manipulation properly emerged in the 1970s following the ad-

vent of the laser. The geometry of optical tweezers uses a tightly focused Gaussian beam produced by a high numerical aperture (NA) microscope objective. For particles of higher refractive index than their surroundings, the gradient force attracts the particle to the beam focus and the scattering force pushes the object downstream (in the beam propagation direction), so the stable trap position occurs on the axis behind the focus, where these forces are balanced. Figure 1 demonstrates this optical trapping in the Mie regime in a simplified form where the weak reflections at the particle boundary are not taken into account. In the lateral confinement (a) the off-axis particle refracts the beam thus changing the momentum of the beam. The law of action and reaction shows us that a force is exerted on the particle in the opposite

direction to the final beam direction, thus attracting the particle to the axis (region of highest light intensity). In the longitudinal confinement (b) the particle acts rather like a collimating lens. Since the axial momentum of the collimated beam is larger than the original diverging beam, the refraction of light by the particle attracts the particle towards the focus.

Whilst visually evocative and powerful just moving or trapping objects is insufficient. The success of optical tweezers has been its ability to be a calibrated force transducer: the particle is trapped in a harmonic potential well and the force of the particle is proportional to displacement (rather like a microscopic version of a Hookean spring). By measuring the stiffness of the trapped particle, and recording its displacement in the trap, the

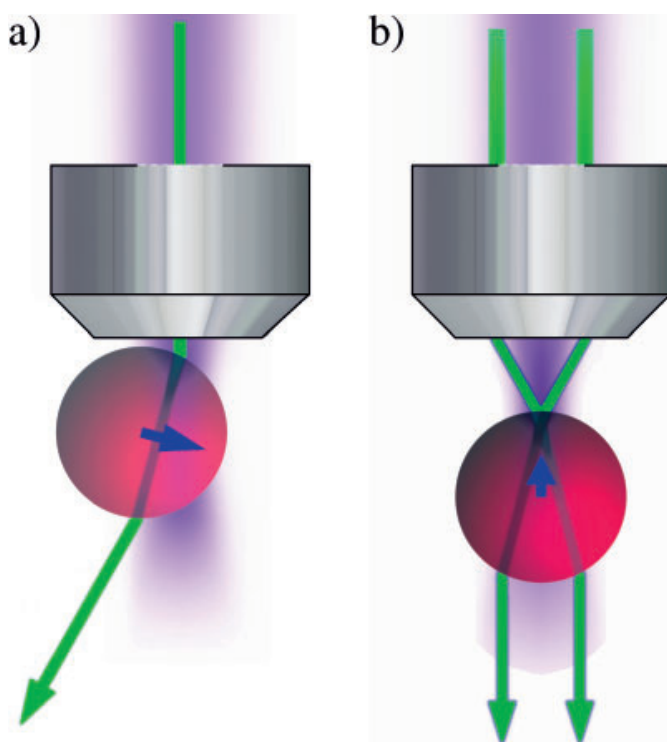


Figure 1. Optical trapping in lateral (a) and longitudinal (b) confinement.

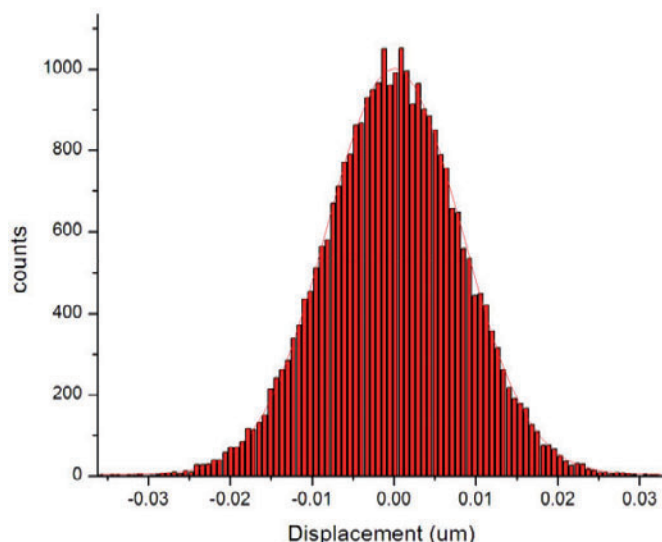


Figure 2. Particle position distribution in optical tweezers (Image courtesy of Steven Lee, University of St Andrews).

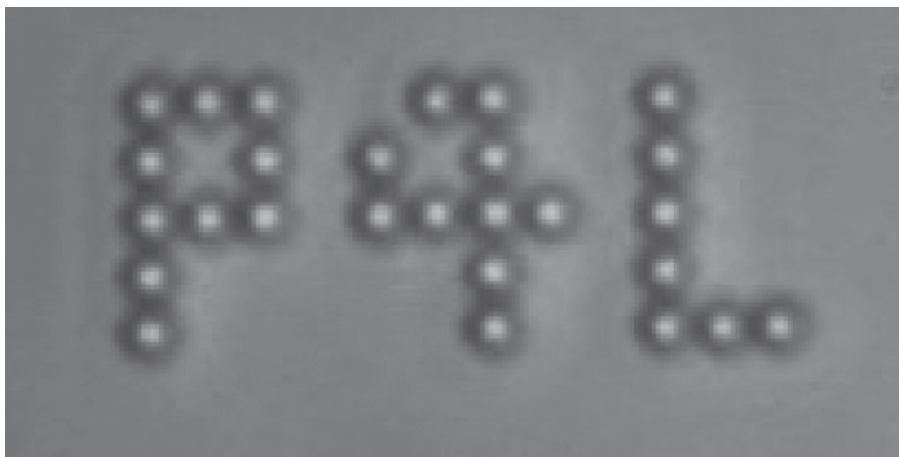


Figure 3. Photonics4Life logo of 2 μm polymer particles dynamically moved and trapped (Image and video courtesy of Tomáš Čizmár, University of St Andrews).

force acting upon the particle can be calculated. Switchable forces as low as 25 fN have been measured directly². In figure 2 a typical power spectrum measurement for a 50 nm diameter polymer sphere is demonstrated. The measured particle position in an optical trap is Gaussian distributed within ± 20 nm, which is in good agreement with equipartition theorem. A detailed examination of how to calculate trap stiffness may be found elsewhere^{3,4}.

For some experiments, it is desirable to have not just a single optical tweezers but a pattern of trap sites or even a more exotic beam shapes sculpted in amplitude and phase. One way to create an array of optical tweezers is to timeshare the beam between each of the individual trap sites⁵. The use of an acousto-optical deflector (AOD) is a powerful way to generate such time-shared traps. To generate figure 3 of the PHOTONICS4LIFE (P4L) logo 2 μm polymer particles were dynamically moved and trapped using an Acoustic Optical Deflector at St. Andrews. The trapping process can be watched online in the supplementary online video on the P4L web site. Alternatively one may avoid time sharing and simultaneously create all the trap sites by suitably shaping the incoming light field using holography. This more powerful method encodes the incoming phase of the incident laser beam prior to entering the back aperture of the objective using a computer controlled

Spatial Light Modulator (SLM)⁶ such that any optical shape in the imaging plane can be generated.

Optical tweezers have found a myriad of applications in the arena of biophotonics, including the elucidation of step sizes and forces of kinesin movement along microtubule tracks⁷⁻⁹, myosin movement along actin tracks^{10,11}, RNA polymerase transcription¹², and ribosome translation¹³. Figure 4 shows a concept to stretch a dsDNA molecule. The DNA is tagged with two microbeads which are used as “handles” to allow optical manipulation. In a force measurement experiment, one of the microspheres would be held still in a highly stiff trap and the position of the second microsphere would be monitored to calculate the forces acting by the DNA (or a molecule attached to the DNA such

as RNA polymerase) by the microsphere. Also a fascinating level of detail can be observed in these types of experiments, such as the amount of time a ribosome spends translating a codon ($<0.1\text{s}$), the translocation step size of a ribosome (equivalent to the distance of three base pairs, or one codon)¹³, and the step size of RNA polymerase (the distance of a single base pair – only a few angstroms!)¹⁴.

Optical tweezers is not restricted to single molecules but has seen much application at the cellular scale. As examples of experiments, optical tweezers enable the precise positioning of cells in defined culture patterns¹⁵, the sampling of single cells for proteomic analysis¹⁶, the dosing of single cells with multiple reagents¹⁷, the stretching of cells (as a diagnostic for cancer)¹⁸, the ablation or excision of subcellular material¹⁹, and the sorting of cells^{20,21}.

Optical tweezers has made major inroads in the last twenty years in the life sciences and is now a major tool in Biophotonics. From the humble single beam gradient trap, to multiple tweezers arrays, to more exotic beams such as the “non-diffracting” beams, sophisticated control and measurement for cellular and biomolecular systems is now possible. The sheer breadth of applications of the field is very exciting to behold: A bright future lies ahead!

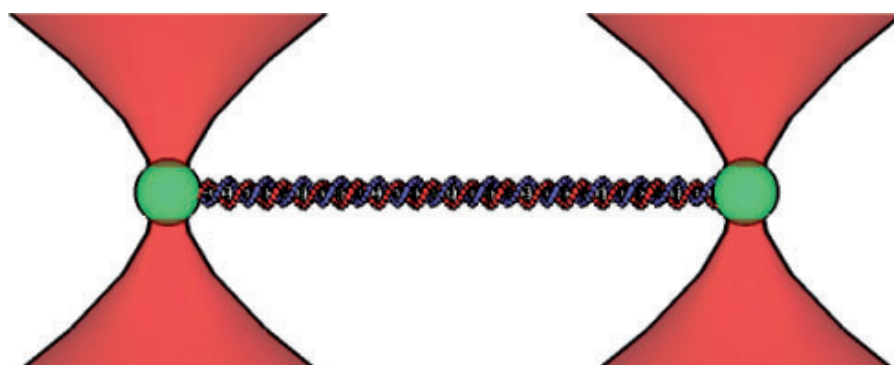


Figure 4. A concept diagram of a dsDNA molecule being stretched (not to scale).

Resources:

- <http://www.st-andrews.ac.uk/~atomtrap/Resources.htm>
A list of optical tweezers resources around the world.
- Lee, Reece et al, 20073
A guide to the construction and calibration of optical tweezers.
- Neuman and Block, 20044
A thorough review of optical tweezers.
- Greenleaf, Woodside, et al, 2007; Neuman, 200822, 23
Reviews of single molecule applications of optical tweezers.
- <http://tinyurl.com/p2th7g>
An example of DNA being stretched using optical tweezers.
- <http://tinyurl.com/qcd4y8>
An interactive way to understand the basics of optical tweezers.

References:

1. Ashkin, A. et al., *Optics Letters* 1986, 11, (5), 288-290
2. Rohrbach, A., *Opt. Express* 2005, 13, (24), 9695-9701
3. Lee, W. M. et al., *Nature protocols* 2007, 2, (12), 3226-3238
4. Neuman, K. C. and Block, S. M., *Review of Scientific Instruments* 2004, 75, (9), 2787-2809
5. Dholakia, K. and Lee, W. M., in *Advances In Atomic, Molecular, and Optical Physics*, 2008, pp. 261-337
6. Spalding, G. C. et al., *Holographic Optical Trapping in Structured light and its applications: an introduction to phase-structured beams and nanoscale optical forces*, edited by D.L. Andrews, Elsevier Press 2008
7. Svoboda, K. et al., *Nature* 1993, 365, (721-727)
8. Block, S. M., *Cell* 1998, 93, (1), 5-8
9. Fehr, A. N. et al., *Biophysical Journal* 2008, 94, (3), L20-L22.
10. Shepherd, G. M. et al., *Proc Natl Acad Sci U S A* 1990, 87, (21), 8627-8631
11. Finer, J. T. et al., *Nature* 1994, 368, (6467), 113-119
12. Yin, H. et al., *Science* 1995, 270, (5242), 1653-1657
13. Wen, J. D. et al., *Nature* 2008, 452, (7187), 598-603
14. Abbondanzieri, E. A. et al., *Nature* 2005, 438, (7067), 460-465
15. Akselrod, G. M. et al., *Biophysical Journal* 2006, 91, (9), 3465-3473
16. Lanigan, P. M. et al., *Journal of the Royal Society, Interface / the Royal Society* 2008, 5 Suppl 2, S161-168
17. Brown, C. T. A. et al., *Journal of Biophotonics* 2008, 1, (2), 183-199
18. Guck, J. et al., *Biophysical Journal* 2001, 81, (2), 767-784
19. Berns, M. W., *Methods in cell biology* 2007, 82, 1-58
20. Dholakia, K. et al., in *Methods in cell biology*, Academic Press, 2007, pp. 467-495
21. Paterson, L. et al., *Phys. Lett.* 2005, 87, (12), 123901
22. Greenleaf, W. J. et al., *Annual review of biophysics and biomolecular structure* 2007, 36, 171-190
23. Neuman, K. C. and Nagy, A., *Nature methods* 2008, 5, (6), 491-505

Industrial Workshop: LASER World of Photonics 2009

Munich, Germany – June 17, 2009

In the framework of the LASER World of Photonics 2009 in Munich Photonics4Life will conduct a workshop entitled "Visions for future diagnostics". The workshop is focused on oncology and will take place on Wednesday, 17th of June from 10:00 – 14:30 at the Biophotonics forum which is located in an area exclusively dedicated to Biophotonics. The aim of the workshop is to breakdown two barriers, which are the largest obstacles for increased growth of the Biophotonics industry: (1) missing understanding of users' needs and (2) missing understanding of technical possibilities. The concept is aimed to appeal not only to

the relatively few system providers, but should also be attractive for the many companies which are developing and fabricating photonic components and subsystems. The topic is by intent not technology- but application-oriented, since the workshop is not dedicated to present certain technologies for which applications are looked for. In contrast it is the approach of the workshop to start with concrete problems of the biomedical user and to search and develop in concert with them solutions based on photonic technologies.

Entrepreneurship in Biophotonics

Brussels, Belgium – September 7 – 18, 2009

To foster innovation in biophotonics Photonics4Life aims to generate an interest in entrepreneurship as well as to support business ideas, spin-outs from university, R&D organisations and from companies or start-ups and increase their chances of success. Within this scope P4L organizes a modular training course for everybody who is interested in entrepreneurship in biophotonics. Beside dedicated lectures on business economics, business ideas proposed by the participants are taken up and a business plan will be developed. The course is divided in 3 modules:

Module 1, 7. – 9. September Introduction to Business Economics

This module gives people, without any economic training, a comprehensive introduction to general business economics, with the emphasis on entrepreneurship. It covers a wide range of disciplines, including financial management, marketing and industry dynamics, it is the shortcut to a better understanding of the modern company.

Module 2, 10 & 11. September Business Economics of Biophotonics

Essential non-technological business aspects of the biophotonics industry are addressed. The focus is placed on two growing sectors in the industry: medical imaging and micro-optical systems in diagnostics. Presentations by industry leaders give a more complete understanding of these biophotonics markets. There will be an examination on modules 1 and 2, on the 12th of Sept., for those participants who would like to earn 3 ECTS-credits (prerequisite: general economics course).

Module 3, 14. – 18. September Biophotonics Business Project

The second week is focused on developing (parts of) a business plan for the participants biophotonics invention. Teamwork as well as individual work will guide the participants through some required components of a business plan: idea, product, market, value chain, strategy, etc. Since there is teamwork involved, every participant of this project will need to sign a NDA. Project topic should be submitted by Monday, August 17th. The organisation assesses whether the topic fits the scope of the business project and has the right to reject the project proposal. Acceptance of the project topic will be announced on Monday, the 17th of August.

The intensive training is open to everybody. Module 1 & 2 can be booked as a package for a fee of 750.– € for academic participants and level 2 IUC members. For other companies it will cost 1500.– €. If module 3 is added the price rises to 1000.– € and 2000.– € respectively.

For more information, visit www.photonics4life.eu
Registration and information by e-mail at tom.guldemont@vub.ac.be

To register, please provide your Name, Institute/Company, Invoicing Address, VAT, Phone, Fax and E-mail.

Dutch Photonic Event 2009

Nieuwegein, Netherlands – April 2, 2009



Reviewer Prof. H.J.C.M. Sterenberg (right) and Prof. Gert von Bally (left)

Photonics4Life was present at this year's number one Dutch Photonics Event on April 2nd through the attendance of the groups from Munster and Enschede. Although considered as a rather local event in the small town of Nieuwegein, it eventually had a severe international impact as a lot of foreign representatives from industry and academia attended.

Industry was heavily engaged on the fairground and also in the scientific programme, where they presented their newest developments. Philips, e.g., showed non-toxic nano-particles trackable with magnetic fields. According to invited speaker Prof. h.c. Gert van Bally, Vicecoordinator of P4L, the contribution of industry was impressive. "This is amazing, industries efforts are even bigger here than on the fair of last year's Photonics Europe" van Bally said.

As Biophotonics was one of the most important topics on the event the resonance towards the Photonics4life contribution, giving scientific talks and presenting newest findings on the exhibition ground, was very high.

Saratov Fall Meeting 2009

Saratov, Russia – September 21 – 24, 2009

The XIII International School for Junior Scientists and Students on Optics, Laser Physics & Biophotonics will be held on September 21 – 24, 2009, Saratov, Russia, organized by Saratov State University, member of P4L.

The main goal of the School is to involve the international community of junior 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. More than 10 workshops and seminars will be organized on hot topics in Optics, Laser Physics & Biophotonics. Also an SPIE short course "Biophotonics in Microcirculation Imaging" will be given by Dr. Martin J. Leahy, University of Limerick and National Biophotonics and Imaging Platform, Ireland.

SFM has a prolonged experience in organizing of Internet sessions during last 11 years. In 2007 – 2008 such presentations have included plenary lectures made by major P4L partners. Participants from more than twenty countries have located their papers on the meeting website <http://optics.sgu.ru/SFM>

SPIE Photonics Europe 2010

Brussels, Belgium – April 12 – 16, 2010

Leading photonics researchers and industry developers will present up-to-the-minute research and technology innovations at SPIE Photonics Europe in Brussels 12 – 16 April 2010. Participants will gain support for new ideas, learn about new developments in photonics and network with peers and future R&D team members.

Photonics Europe will include a technical programme of conferences and hot-topic plenary sessions, an innovation showcase, student and entrepreneurship events, courses, workshops, and an exhibition featuring an expected 150 companies. Also the Photonics Innovation Village will be organized giving the opportunity to show new and innovative developments in photonics. Abstracts can be submitted for papers in:

- Micro/nano technologies: metamaterials, photonic crystal fibers and devices, MEMS, MOEMS, nanometrology
- Optics and photonics: sensors, silicon photonics, organic photonics
- Laser technology: semiconductors, solid state, fiber lasers, amplifiers
- Applications: solar, biophotonics, automotive, image processing, multimedia.

Further information can be found under <http://spieeurope.org/photronics-europe.xml>

Event Calender

(co-)organized by photonics4life
 contribution from photonics4life partners

Date	Event	Location	Link
June 2009			
06 – 13 June	4 th International Graduate summer school – Biophotonics ,09	Ven, Sweden	http://www.biop.dk/biophotonics09/School/School.asp
08 – 11 June	Scandinavian Symposium on Chemometrics	Loen/Stryn, Norway	http://www.kj.uib.no/ssc11/index.htm
10 – 12 June	4 th EOS Topical Meeting on Advanced Imaging Techniques	Jena, Germany	http://www.myeos.org/jena
11 – 14 June	12 th International Conference on Photorefractive Materials, Effects and Devices – Control of Light and Matter	Bad Honnef, Germany	http://www.uni-muenster.de/Physik.PR09
14 – 18 June	ECBO – European Conference on Biomedical Optics	Munich, Germany	http://www.osa.org/meetings/topicalmeetings/ecbo
21 – 24 June	Nanophotonics Down Under 2009: Devices and Applications	Melbourne, Australie	http://www.smonp2009.com
July			
13 – 17 July	ICAVS-5: 5th International Conference on Advanced Vibrational Spectroscopy	Melbourne, Australia	http://www.chem.monash.edu.au/biospec/icavs/committee.html
August			
26 Aug – 03 Sep	ASCOS 2009 – Optical Chemical Sensors for Environmental and Food Safety	Madrid, Spain	http://www.ascos.org
28 Aug – 02 Sep	ECSBM2009 – XIII European Conference on the Spectroscopy of Biological Molecules	Palermo, Italy	http://www.ecsbm.eu
31 Aug – 03 Sep	International Conference “Micro- to Nano-Photonics II – ROMOPTO 2009”	Sibiu, Romania	
September			
07 – 18 Sep	Training on Entrepreneurship in Biophotonics	Brussels, Belgium	http://www.photonics4life.eu
21 – 24 Sep	Saratov Fall Meeting 2009 -XIII International School for Junior Scientists and Students on Optics, Laser Physics & Biophotonics	Saratov Russia	http://optics.sgu.ru/SFM
October			
07 – 09 October	ICO Topical Meeting on „Emerging Trends & Novel Materials in Photonics”	Delphi, Greece	http://www.ico-photonics-delphi2009.org
18 – 22 October	FACSS, the Federation of Analytical Chemistry and Spectroscopy Societies, conference	Louisville, USA	http://facss.org/facss/index.php
November			
02 – 06 November	Asia Communications and Photonics Conference and Exhibition	Shanghai, China	http://www.acp-ce.org
April 2010			
12 – 16 April	SPIE Photonics Europe 2010	Brussels, Belgium	http://spieeurope.org/photonics-europe.xml

P4L Partners

IPHT	Institute of Photonic Technology Popp Juergen, juergen.popp@ipht-jena.de	Germany
UoM	University of Muenster van Bally Gert, Ce.BOP@uni-muenster.de	Germany
MESA+	University of Twente Subramaniam Vinod, v.subramaniam@tnw.utwente.nl	Netherlands
CNR IFAC	Istituto di Fisica Applicata "Nello Carrara" Pini Roberto, R.Pini@ifac.cnr.it	Italy
IOGS	CNRS Institut d'Optique graduate school Canva Michael, michael.canva@institutoptique.fr	France
VUB	Vrije Universiteit Brussel Thienpont Hugo, hthienpo@vub.ac.be	Belgium
USTAN	University of St. Andrews Dholakia Kishan, kd1@st.andrews.ac.uk	United Kingdom
IMPERIAL	Imperial College of Science, Technology & Medicine Neil Mark, mark.neil@imperial.ac.uk	United Kingdom
ICFO	Institut de Ciencies Fotoniques, Fundacio Privada van Hulst Niek, Niek.vanHulst@ICFO.es	Spain
VTT	Valtion Teknillinen Tutkimuskeskus Känsäkoski Markku, markku.kansakoski@vtt.fi	Finland
FZK	Forschungszentrum Karlsruhe Mohr Jürgen, juergen.mohr@imt.fzk.de	Germany
LLC	Lund Laser Centre Svanberg Katarina, katarina.svanberg@med.lu.se	Sweden
SSU	Saratov State University Tuchin Vallery, tuchin@sgu.ru	Russian Federation

Editor

European Network of Excellence for Biophotonics – P4L

Coordinator

Prof. Dr. Jürgen Popp
Institute of Photonic Technology
Albert-Einstein-Straße 9
07745 Jena, Germany
juergen.popp@ipht-jena.de

Network support officer

Dr. Thomas Mayerhöfer
Institute of Photonic Technology
Albert-Einstein-Straße 9
07745 Jena, Germany
thomas.mayerhoefer@ipht-jena.de

Editorial staff

Dr. Jürgen Mohr
Forschungszentrum Karlsruhe, Germany

Georg Obermaier
Forschungszentrum Karlsruhe, Germany

Arrangement

Forschungszentrum Karlsruhe, Typography

Print

Elser Druck, Mühlacker, Germany

Next issue

November 2009

For additional information please visit
<http://www.photonics4life.eu>