Issue 23 | July 2017

Laserlab Europe

Laserlab Forum

Newsletter of LASERLAB-EUROPE:
the integrated initiative of European laser infrastructures funded by the European Union's Horizon 2020 research and innovation programme

Laser Careers

In this Issue

Editorial

Tom Jeltes

Science and technology are sometimes like inseparable twins. There are probably few areas where this is more true than in the field of photonics. It goes without saying that most of the science conducted within Laserlab-Europe would be unimaginable without laser technology (technology for science). On the other hand, no progress in laser technology is possible without a thorough knowledge of the specific interactions between light and matter (science for technology).

The thin line between laser science and laser technology becomes apparent in this issue of Laserlab Forum. A clear example is the Access Highlight, which describes a comparison of several varieties of a laser-based imaging technique, Light Sheet Fluorescence Microscopy, which is increasingly used by life scientists to study artificially grown three-dimensional tissue. I would call this project a *scientific* study of laser *technology*.

In addition, in this issue's focus section on Laserlab careers, one can not only read about scientists who carved a career path within academia, but also about several people who started their careers as users of laser technology, to become developers or product managers at companies producing lasers and related devices later on. From their scientific endeavours they either know the precise requirements of those technological devices, or they gained the scientific expertise to develop new equipment for a company that serves their former community.

In any case, the careers focus provides a modest sample of people whose careers have been influenced in a positive way by their involvement in the Laserlab consortium. This shows, in my view, that the value of Laserlab-Europe extends much beyond the confines of its partners' labs.

Tom Jeltes

News

Katarina Svanberg honoured with SPIE Gold Medal of the Society

© Sune Svanberg

Katarina Svanberg

Katarina Svanberg, professor and chief consultant of oncology at Lund University Hospital, received the 2017 Gold Medal of the Society, awarded by SPIE, the international society for optics and photonics. The award recognises her contributions to biophotonics, in particular clinical work exploring and verifying the efficacy of phototherapy and in vivo diagnosis in treating cancer patients.

According to 2016 SPIE President Robert Lieberman, Katarina Svanberg's work on laser-induced tissue fluorescence has made 'optical biopsy' a reality for many forms of cancer, and her deep commitment to the practical application of optics and photonics for the diagnosis and treatment of disease has helped save and improve the lives of hundreds of individuals. The award also acknowledges Svanberg's dedication to building scientific and medical infrastructure in Africa and inspiring young people across the world. Svanberg has trained medical personnel in the poorest regions of Africa in biomedical optical techniques.

The Gold Medal of the Society is the highest honour SPIE bestows. Beginning in 1977, it has been awarded annually in recognition of outstanding engineering or scientific accomplishments in optics, electro-optics, or photographic technologies or applications, to recipients who have made exceptional contributions to the advancement of relevant technology. During these 39 years, this is the first time that the Gold medal is awarded to a female scientist alone.

Michael Krieg brings ERC Starting Grant to ICFO

© ICFO

Michael Krieg

Michael Krieg, a former postdoctoral researcher at Stanford University, has come to Laserlab-Europe partner ICFO, Barcelona, with an ERC Starting Grant. His newly established research group at ICFO will use the roundworm *Caenorhabditis elegans* as a model to study the importance of the mechanical properties of cells for health and disease.

For his Starting Grant project, which is titled 'How to build a brain? Engineering molecular systems for mechanosensing and protection in neurons', Krieg will exploit microfluidic and nanotechnological tools to apply precise forces to single cells or animals. His group will also try to make a so-called optogenetic neurotransmitter system – where light is used to control neural activity – to rewire neural circuits in diseased animals. Michael Krieg arrives from Stanford University where, for the past years, he has focused his postdoctoral research on deciphering the mechanical basis of the sense of touch in the lab of Miriam Goodman in the Department of Molecular and Cellular Physiology.

© HZDR / Rainer Weisflog

High-power laser DRACO at HZDR

HZDR and Weizmann Institute found laser laboratory in Israel

In order to combine their expertise in the field of laser-particle acceleration, Laserlab-Europe partner Helmholtz Center Dresden-Rossendorf (HZDR) and the Israeli Weizmann Institute of Science are building a joint laboratory in Rechovot, Israel. The Weizmann-Helmholtz Laboratory for Laser Matter Interaction (WHELMI) is the first laboratory co-financed by the Helmholtz Association on the campus of a foreign partner.

The agreement on the cooperation was signed on 26 April 2017 at the official launch of the project in Israel. Over the next five years, WHELMI will receive funding of a total of five million euros. The laboratory is to bridge the gap between basic and applied research. The new facility will mainly focus on targets – in addition to the laser itself the most important component in laser-particle acceleration.

With the help of high-energy lasers, different particles such as protons, ions or electrons can be accelerated. The resulting intense electron pulses can produce secondary radiation in a wide energy range. This allows researchers on the one hand to observe, for example, ultrafast chemical or biological processes. On the other hand, acceleration by laser power could also reduce the huge and costly equipment required to bring protons or ions to maximum speeds. This could, among other things, simplify the use of particle radiotherapy for the treatment of tumours.

What is Laserlab-Europe?

Laserlab-Europe, the Integrated Initiative of European Laser Research Infrastructures, understands itself as the central place in Europe where new developments in laser research take place in a flexible and co-ordinated fashion beyond the potential of a national scale. The Consortium currently brings together 33 leading organisations in laser-based inter-disciplinary research from 16 countries. Its main objectives are to maintain a sustainable inter-disciplinary network of European national laboratories; to strengthen the European leading role in laser research through Joint Research Activities; and to offer access to state-of-the-art laser research facilities to researchers from all fields of science and from any laboratory in order to perform world-class research.

Ulrich Schramm from the HZDR and his colleague Victor Malka from the Weizmann Institute and Laserlab-Europe partner LOA will act as founding directors of WHELMI.

Central Laser Facility celebrates its 40th anniversary

The UK's Central Laser Facility (CLF), partner of Laserlab-Europe, was founded 40 years ago. The CLF's 40th anniversary was celebrated with a one day conference on the 'Impact and Importance of UK Laser Science on the Global Stage' on 20 June 2017. Speakers included Andrew Taylor, Executive Director of STFC National Laboratories, Sir Peter Knight, Imperial College London, STFC Chief Executive Brian Bowsher and Claes-Göran Wahlström, Coordinator of Laserlab-Europe.

Based at Science and Technology Facilities Council's (STFC) Rutherford Appleton Laboratory site in Oxfordshire, the CLF organisation has grown from a handful of people working on a single laser to a facility with more than 100 full-time staff, involved in hundreds of international collaborations. The lasers developed by the CLF over the past forty years are in use at many research facilities in the UK and abroad. In addition, the CLF has a strong background in innovation, technology transfer and spin-out companies.

Recent innovations involving the CLF team have included developing a scanning technology that detects the chemical contents of aircraft passengers' unopened containers, and work developing laser tweezers to enable researchers to better understand the structure and function of a molecule.

© STFC

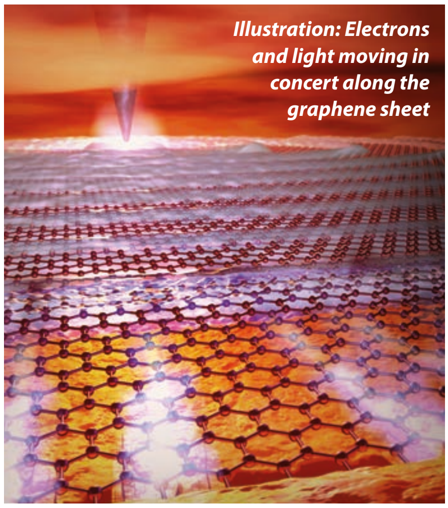


Illustration: Electrons and light moving in concert along the graphene sheet

© ICFO / F.Vialla

Seeing electrons surfing the waves of light on graphene

Researchers from Laserlab-Europe partner ICFO, Barcelona, have studied how light can be used to 'see' the quantum nature of an electronic material. They managed to do that by capturing light in a net of carbon atoms and slowing it down so that it moves almost as slow as the electrons in the graphene. The results of the project carried out by an ICFO team led by Frank Koppens in collaboration with researchers from Italy, Spain and the US, was published in Science.

The experiments were performed with ultra-high quality graphene. To excite and image the ultra-slow ripples of light in the graphene (also called plasmons), the researchers used a special antenna for light that scans over the surface at a distance of a few nanometers. With this near-field nanoscope they saw that the light ripples on the graphene moved more than 300 times slower than the speed of light, and dramatically different from what is expected from classical physics laws.

This technique now paves the way for exploring many new types of quantum materials, including superconductors where electricity can flow without energy consumption, or topological materials that allow for quantum information processing with topological qubits.

ERC Advanced Grants

Two Laserlab-Europe researchers each have been awarded an ERC Advanced Grant of 2.5 million euros this year. Both of them are from the Max Planck Institute of Quantum Optics (MPQ) in Garching, Germany. Thomas Udem will use his grant to build a laser system producing coherent extreme ultraviolet radiation to study singly ionised helium for tests of Quantum Electrodynamics, whereas theorist Ignacio Cirac is planning to investigate the physics of quantum emitters coupled to unconventional baths.

Thomas Udem: High Resolution Extreme Ultraviolet Laser Spectroscopy

At the precision frontier of Quantum Electrodynamics (QED), comparisons between theory and experiment have so far been performed almost exclusively with atomic hydrogen. According to Thomas Udem, it is of fundamental importance to proceed to other, hydrogen-like systems that can be computed with very good accuracy.

In his ERC Advanced Grant project, Udem therefore proposes to study singly ionised helium (He^+) with high resolution laser spectroscopy. In addition of representing a hitherto unexplored system, he argues, He^+ allows for a far better test than atomic hydrogen due to the QED power series expansion of its energy levels in terms of $Z\alpha$. With the nuclear charge Z and the fine structure constant α, the disputed terms are of the order of $(Z\alpha)^6$.

Unlike ordinary hydrogen, He^+ can be readily stored in an ion trap and sympathetically cooled by co-stored ions with an accessible cooling transition. This approach eliminates essentially all dominating experimental uncertainties that are faced with ordinary hydrogen today. The 1S-2S resonance is the sharpest and hence most interesting transition. Its observation requires highly coherent extreme ultraviolet radiation at 60.8 nm, which can be generated through high-order harmonics from a mode-locked laser. The resulting frequency comb is most suitable for a two-photon transition, as photons from pairs of modes can combine to deliver the excitation energy. According to Udem, other applications of such a new laser source are foreseeable as well.

Ignacio Cirac: Quantum Emitters in Non-conventional Baths

The coupling of two-level quantum emitters to a zero temperature electromagnetic reservoir (or bath) is a central problem in quantum optics. For a single emitter, the bath, having infinite degrees of freedom, may induce dissipation (via spontaneous emission), and other basic phenomena of Quantum Electrodynamics, like Lamb shifts. For many emitters, it may lead to collective phenomena, such as superradiance and dipole-dipole interactions. If the electromagnetic bath has some structure – meaning it has a non-linear dispersion relation, with gaps at certain energy intervals – new and intriguing phenomena may arise. This holds even more so for a bath with a tailored dispersion relation for the electromagnetic field. These unconventional baths can be found, for instance, in photonic crystals made of dielectric materials, where the (quasi)periodic structure gives rise to dispersion relations in the bath akin to those occurring in solid state physics. Thanks to the advances in nano-fabrication, it is possible nowadays to build photonic crystals with arbitrary patterns, and thus to tailor the dispersion relations.

In his Advanced Grant project, Ignacio Cirac will develop new theoretical techniques in order to investigate the physics of emitters coupled to these unconventional baths. In addition, specific physical setups will be proposed and analysed, starting with atoms close to photonic crystals.

Workshop on metrology of high-power, ultrashort pulse lasers

A Laserlab-Europe workshop on the "Metrology of high-power ultrashort pulse lasers: user and supplier perspectives" took place at the Max Born Institute, Berlin, on 10 May 2017. The workshop, which was part of the Laserlab work package *"Innovation Management and Industry Relations"*, focussed on characterisation and metrology techniques used to define the parameters of high-power, ultrashort laser pulses, and discussed the need for developing metrology standards in this area. The half-day meeting was attended by 50 people from both academia and industry.

Recent progress in the development of high-power, ultrashort pulse lasers has given rise to a wide range of new physics and applications of high-intensity laser technology. This rapid development is driving a need for systematic and standardised characterisation of high-power lasers, which would allow direct comparison between different laser systems and contribute to fully quantifying experimental results obtained at laboratories across the globe.

The procedures used to characterise high-power lasers have yet to be standardised; they are currently being developed and applied independently by different laboratories. This lack of standardisation was the main reason why this workshop on the metrology of high power, few-cycle laser systems was organised.

The main objective of the event was to facilitate discussion through a joint workshop involving users and suppliers, to consider the primary requirements for characterising the performance of high-power ultra-short pulsed lasers. The workshop also aimed to provide an overview on metrology standards and the traceability of measurements, and considered the potential of establishing a future activity to coordinate and develop this area.

The event was divided into three parts, respectively focussing on pulse duration and laser intensity measurements, and metrology. Each session was followed by long discussions. In the first part, Tobias Witting from MBI, Berlin, stressed that ignoring space-time coupling in measurements of the electric field strength of laser pulses can introduce large systematic uncertainties. He discussed spectral-based techniques that have been developed to directly characterise the spatio-temporal properties of laser pulses. Jean-Marc Heritier from Coherent Inc., USA, gave an overview of the tools his company offers to users of its laser systems, such as the single-shot autocorrelator.

The second part started with a talk by Fabien Quéré, from IRAMIS-SPAM, Saclay, France, who introduced methods for spatio-temporal characterisation of collimated and focussed beams, respectively. Felix Mackenroth, from Max Planck Institute for the Physics of Complex Systems in Dresden, Germany, discussed the use of free, relativistic electrons as a non-destructible sensor for high-power laser pulses, and Mathieu Paurisse from Amplitude Technologies talked about contrast measurements and the impact of saturation effects in cross-correlators.

The final part comprised a presentation by Michael de Podesta from the UK's National Physical Laboratory, who discussed metrology standards and how to make a measurement traceable. He stressed the importance of propagating and reporting systematic and statistical uncertainties in all measurements, which are often omitted from publications.

The workshop was chaired by Roman Spesyvtsev and Dino Jaroszynski (University of Strathclyde, Scotland, UK).

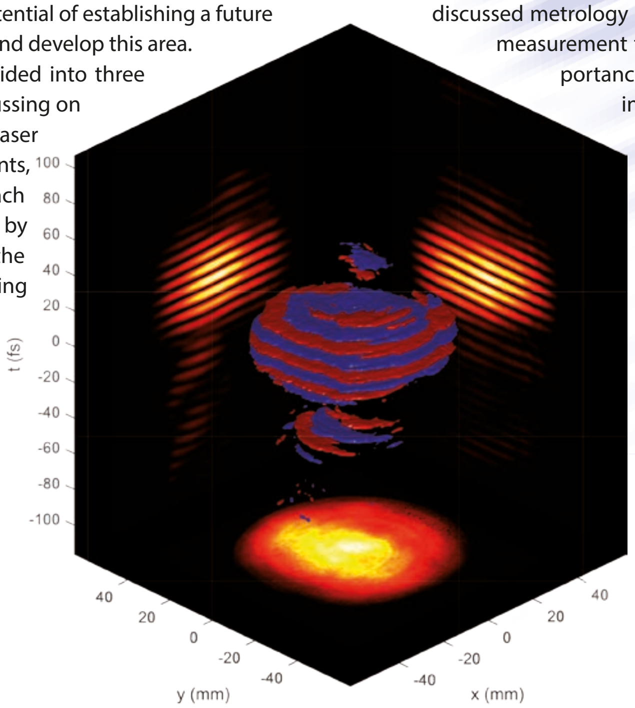


Illustration: Spatio-temporal E-field of a 100 TW-25 fs laser pulse from the UHI100 laser (Amplitude Technologies) at CEA Saclay, measured in the near-field (collimated beam).

Careers in laser science

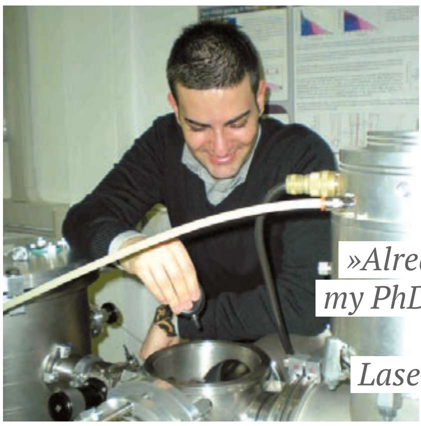
One of the main objectives of Laserlab-Europe is to strengthen the leading role of Europe in laser research. Evidently, providing a stimulating and nourishing environment for (young) researchers is an important aspect of this task. In this focus section a number of European laser scientists give some insight into their past and current occupations, and the influence Laserlab-Europe has had on their careers.

Matteo Negro

2017-present: Head of Optical R&D at BIOS Group, Milan
2014-2017: Researcher at CNR – Institute for Photonics and Nanotechnologies (IFN), Milan
2013: Postdoc at CNR-IFN, Milan
2013: PhD in Physics at Politecnico di Milano (Cum Laude)
2009: MSc in Physical Engineering at Politecnico di Milano

"For my PhD I worked in the group of Prof. Salvatore Stagira and Dr. Caterina Vozzi at POLIMI. Research there is at top level; I had the opportunity to put my hands on cutting-edge laser sources and to perform complex experiments with ultra-intense laser pulses. Already in the first weeks of my PhD I had the opportunity to benefit from the Laserlab-Europe network, through a CUSBO project involving the Imperial College. Thus, I rapidly got in contact with the international community, doing amazing experiments on ultrafast molecular spectroscopy – a topic which, together with attosecond pulse generation, has accompanied me along my whole scientific experience. Many successful collaborations enabled by the Laserlab network would follow, including ones with the Weizmann Institute in Rehovot, the INCDTIM in Cluj, and DESY in Hamburg.

Recently, I started to feel ready for a new experience, where I could exploit all the skills I developed as a scientist – both technical and soft skills – in a commercial setting. This is why I decided to accept an offer from BIOS, which is a rapidly growing SME in the field of aesthetic medical devices that is investing in development of home-built laser sources and platforms."



»Already in the first weeks of my PhD I had the opportunity to benefit from the Laserlab-Europe network.«

»I performed many Laserlab-funded experiments and found two of my positions via the Laserlab-Europe website.«

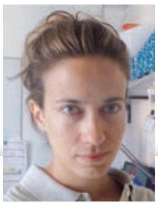
"Even though I only started to study physics when I was 26 years old already, I am now responsible for the scientific programme of the Centro de Laseres Pulsados (CLPU) in Salamanca, and I hold the Laser-Plasma chair at the University of Salamanca.

Laserlab-Europe has been very helpful for my career, because I performed many Laserlab-funded experiments. This started in 2009 with an experiment about fast electron transport in shock-compressed targets at LULI (Paris) and was followed by projects at CELIA (Bordeaux), PALS (Prague), and GSI (Darmstadt). Today, my students are involved in Laserlab experiments at LULI and GSI as well.

In addition, I found two of my positions via the Laserlab-Europe website: the call for senior scientists at ELI-ALPS in 2013 and for the Laser-Plasma chair at CLPU in 2014. I am currently involved in the Laserlab Joint Research Activity LEPP, and I organised workshops of the Networking Activity on Ultra-intense Ultrafast Lasers (NAUUL) and the Networking activity on Extreme Intensity Laser Systems (NEILS), both in Salamanca in 2016 and 2017, respectively."

Luca Volpe

2014-present: CPLU chair at University of Salamanca
2014: Senior Scientist at ELI-ALPS
2013: Postdoc at CELIA, Bordeaux
2009-2012: Postdoc at University of Milan-Bicocca
2008: PhD at University of Milan



Livia Lancia

2016-present: Researcher at CNRS (LULI, Palaiseau)
2010-2016: Postdoc and Teaching Assistant at Sapienza University of Rome
2010: Joint PhD at Ecole Polytechnique Palaiseau and Sapienza University of Rome
2006: MSc at Sapienza University of Rome

"I have been a Laserlab user since 2012, when as a postdoc at the University of Rome 'La Sapienza' I submitted, as Principal Investigator, a proposal to realise an experiment on laser amplification mediated by ion waves in a plasma. I applied for access to a Laserlab facility, LULI, with a group of colleagues from Italy, Germany and France.

Since then Laserlab-Europe supported three other experimental campaigns at LULI, which were motivated by the encouraging results obtained on the way. In these projects, we have demonstrated the possibility to amplify a sub-picosecond pulse up to a factor five, through interaction between two laser beams and a plasma ion wave. This plasma-based laser amplification has become an important part of my scientific production, carried out in parallel to other research activities – including other Laserlab partnerships.

The possibility to develop this project has allowed me to gain a unique expertise in this domain, which has been acknowledged by invited conferences and workshops and a Young Scientist prize in 2015. It certainly played a major role as well in my recruitment at CNRS in 2016."

»Since 2012 I have been involved in four experimental campaigns supported by Laserlab-Europe.«

»Our project with the Cancer Research Centre of Marseille funded by the Laserlab-Europe Transnational Access programme led to a publication in Nature.«

"I obtained my PhD in the Physics of Living Systems group at LaserLaB Amsterdam, partner of Laserlab-Europe, where I worked on techniques combining optical tweezers with super-resolution (STED) microscopy, Acoustic Force Microscopy (AFS) and Optical Pushing. These methods are used to manipulate and study single biological molecules (such as DNA and proteins) and their interactions in order to create a deeper understanding of how life works, and they were developed partly within the Laserlab Joint Research Activity BIOAPP and predecessors.

In 2016, our investigation into how DNA is repaired when a double-stranded break occurs led to a publication in Nature. This project was part of a collaboration with the Cancer Research Centre of Marseille, funded by the Laserlab-Europe transnational access programme.

At the end of my PhD I joined LUMICKS, a spin-off company of LaserLaB Amsterdam, as a cofounder to bring the technologies that I co-invented to the market. This enables life scientists around the world to perform groundbreaking research with tools that until recently were only available in advanced biophysics labs. We have already installed over twenty instruments world-wide in two years, allowing us to grow to a business with over twenty-five employees. As a product manager, my role is to set out the technology roadmap of LUMICKS."

Gerrit Sitters

2014-present: Product manager and cofounder at LUMICKS, Amsterdam
2016: Best Thesis Award in the area of Biophysics and Biomedical Engineering (BIOPM)
2015: PhD in Biophysics at LaserLaB Amsterdam, VU University
2010: MSc in Applied Physics at Eindhoven University of Technology, The Netherlands

Francesca Calegari

2016-present:	Full Professor of Physics at the University of Hamburg and Leading Scientist at DESY
2014:	ERC Starting Grant
2014:	Visiting Scientist at MPSD, Hamburg
2013-2016:	Adjunct Professor of Physics at Politecnico di Milano
2011-2016:	Staff Researcher at IFN-CNR, Milan
2009-2011:	Postdoc at Politecnico di Milano and CNR-INFM
2009:	PhD at Politecnico di Milano

"The main focus of my research is to track, and ideally control, in real time the electron dynamics occurring in matter. To this purpose, my group develops table-top light sources providing attosecond time resolution. The Laserlab node CUSBO/POLIMI provided me with a unique and exciting environment, which triggered ground-breaking experiments – crucial for my career.

Within Laserlab-Europe I had the chance to collaborate with well-known international research groups, leading to results that have been published in high-impact journals. All of this contributed to the opportunity of being successful in the Helmholtz Recruiting Initiative, which allowed me to get a full professor position at Hamburg University and a staff position at DESY, where I currently lead the Attosecond Science Division.

Recently, I have been also awarded a European Research Council (ERC) Starting Grant to understand the role of the electron dynamics in the photo-induced chemical changes that occur in our own biomolecules (e.g., DNA and proteins) in a bottom-up approach. This important research is conducted in collaboration with the CUSBO/POLIMI node."

© F. Calegari

»The Laserlab node CUSBO/POLIMI provided me with a unique and exciting environment, which triggered ground-breaking experiments – crucial for my career.«

»My postdoctoral fellowships at Laserlab-Europe partners ISMO and LUMAT-LASERIX gave me the opportunity to explore my research topic through different approaches.«

"I am working on the spectral and temporal characterisation of plasma-based XUV lasers, which is crucial for the development of advanced architectures involving external seeding with high-order harmonics (so-called 'seeded XUV lasers'), and which is one of the objectives of the Laserlab Joint Research Activity ILAT. During my PhD thesis, I have shown that the temporal and spectral properties can be simultaneously retrieved from the measured linear autocorrelation of the pulse. As a postdoc at ISMO, I have been able to further clarify the physical interpretation of this feature.

My postdoctoral fellowships at Laserlab-Europe partners ISMO and LUMAT-LASERIX gave me the opportunity to explore my research topic through different approaches: I worked on the characterisation and on the improvement of the source properties, while using and developing both theoretical and experimental tools. I also had the opportunity to perform experiments at LASERIX: first as a Principal Investigator for the ISMO team and now as a staff member of the facility, where I am directly involved in developing and operating the seeded XUV laser source.

In these experiments I have used a variety of methods, techniques and tools, which broadened my range of skills: in numerical simulations, as an experimentalist, and more generally in conducting collaborative projects."

Andréa Le Marec

2017:	Postdoc at LUMAT – LASERIX (Université Paris-Sud, CNRS)
2016-2017:	Postdoc at ISMO (Université Paris-Sud, CNRS)
2016:	PhD at ISMO (Université Paris-Sud, CNRS)
2012:	MSc 'Science of Fusion', Université Pierre et Marie Curie, Paris

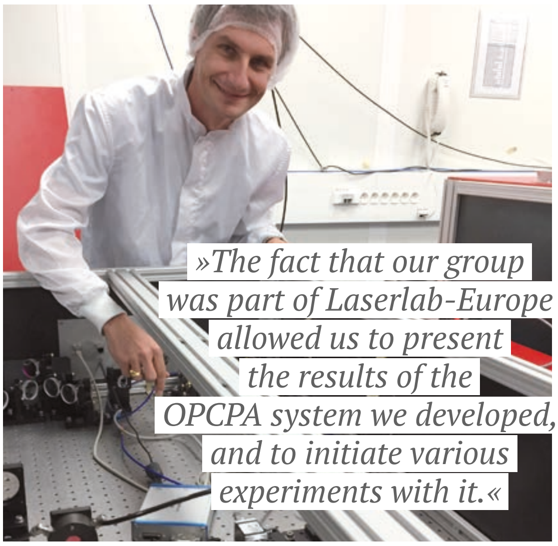
Olivier Chalus

2010-present: Product Manager / R&D Scientist at Thales, France
2007-2010: Postdoc at ICFO, Barcelona
2007: PhD at University of New Mexico and Université Louis Pasteur, Strasbourg
2003: MSc at École Nationale Supérieure de Physique de Strasbourg

"After my PhD I joined the Attosecond and Ultrafast Optics (AUO) group of Jens Biegert at Laserlab-Europe partner ICFO, where we developed a 100 kHz Optical Parametric Chirped Pulse Amplifier (OPCPA) system operating at a wavelength of 3 microns. The fact that the group was part of Laserlab-Europe allowed us to present the results of the system and to initiate various experiments with it, for example on surface plasmon enhanced strong-field photoemission with the group of Peter Dombi from Budapest, Hungary. In the group we also had a Ti:Sapphire system, allowing us to explore strong-field physics and High Harmonic Generation.

When I joined the Laser Department of Thales in France, I worked on the first commercial 1Hz Petawatt laser system (BELLA). I am now involved in the development and completion of a 2x10 PW laser system with very high contrast for ELI-NP. This laser system uses hybrid OPCPA/Ti:Sapphire technology, meaning that I can combine my expertise of both techniques gained at ICFO.

The link with my previous work does not stop here, as we even have established a partnership between Thales and ICFO for developing a new 7 µm OPCPA source able to deliver ultrashort pulses at 100 Hz with several millijoules of output energy."



»The fact that our group was part of Laserlab-Europe allowed us to present the results of the OPCPA system we developed, and to initiate various experiments with it.«

»Contact with my current employer originates at Laserlab-Europe partner ICFO: we were a very good customer of TOPTICA with our ion trap experiment.«

"Contact with my current employer, TOPTICA Photonics AG in Munich, originates at Laserlab-Europe partner ICFO, where I obtained my PhD studying quantum networking with remote ion traps in the group of Jürgen Eschner: we were a very good customer of TOPTICA with our ion trap experiment. I stayed in touch with the people that installed our laser system, and I visited the company at their booth at conferences.

There are several things that I learned at ICFO that are very useful for me now. For instance, I am responsible for the frequency comb product line at TOPTICA, and cold atom and ion trap experiments are users of frequency comb technology. It is essential for me as product manager to understand the applications of our technology, and to be able to communicate to the customers on the same technical level.

In addition, I feel that the experience of building a technically very challenging experiment from scratch gives me a very broad understanding and confidence with optics, fine mechanics, software control, laser physics, fiber optics, etc.

Finally, I have a network from my time at ICFO. Since I am still working in photonics, I do meet people from ICFO wherever I go. Some of them are customers now, others are useful contacts for technical counsel or might become an interesting option when it comes to recruiting good people."

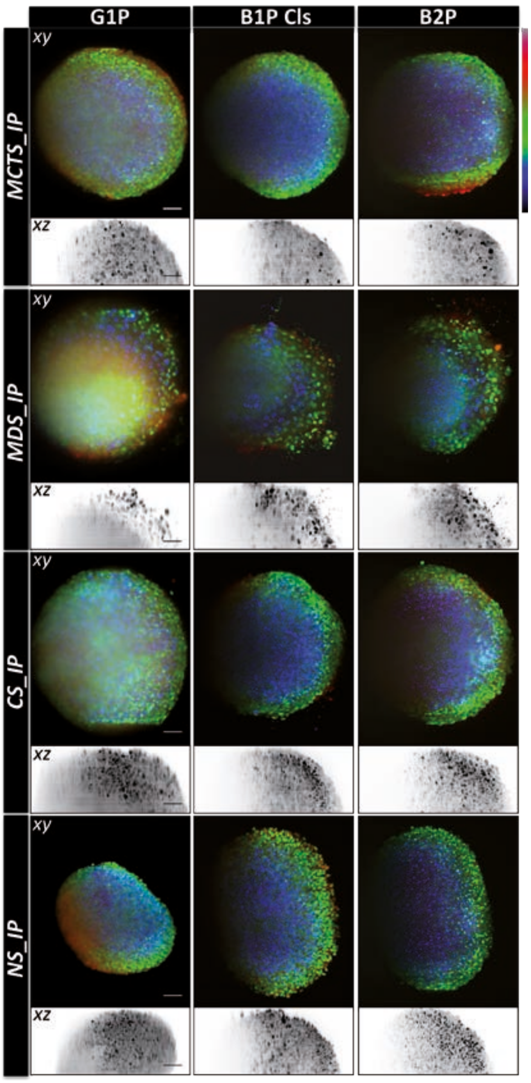
Felix Rohde

2014-present: Product Manager Frequency Combs and Laser Reference at TOPTICA Photonics AG
2012-2014: Postdoc at PTB Braunschweig, Germany
2010-2012: R&D Product Manager at Cosingo, Barcelona
2009-2010: Postdoc at ICFO, Barcelona
2009: PhD at ICFO, Barcelona

Imaging tissue mimics with light sheet microscopy

Artificially grown three-dimensional pieces of tissue are increasingly used to study cell growth and disease progression in biomedical research. These so-called tissue mimics can be observed using a technique called Light Sheet Fluorescence Microscopy. In a recent Laserlab transnational access project, the groups of Pablo Loza-Alvarez (ICFO) and Corinne Lorenzo (ITAV, Université de Toulouse) collaborated to compare the effectiveness of different light sheet illumination modalities for complex 3D samples. The findings of their study were published in Scientific Reports.

Tissue mimics such as microtissues, spheroids and organoid cultures have become increasingly important in life science research, as they provide a physiologically more relevant environment for cell growth, tissue morphogenesis and stem cell differentiation. In contrast to cell lines cultured in monolayers, these 3D models can be engineered to display most of the hallmarks of native tissue in terms of architecture, cell heterogeneity and self-renewal properties. They thus have great potential for modelling tissue development and disease progression in the context of cancer, heart, and stem cell research, as well as in neurobiology, drug discovery and toxicity testing.



Over the last decade, Light Sheet Fluorescence Microscopy (LSFM) has emerged as a powerful solution for long-term live 3D imaging of organism models and many other application fields, including tissue mimics. However, due to their thickness, inhomogeneity and high light-scattering properties, observing tissue mimics at high resolution, in-depth (beyond 100 µm) and in real-time remains a major technical challenge.

To address these problems, several image processing tools and hardware have appeared. In a recent study we have presented a unified and objective comparison of different Light Sheet Fluorescence Microscopy techniques in terms of practicality and performance in the specific context of 3D tissue mimics imaging.

For this purpose, Corinne Lorenzo and Pablo Loza-Alvarez have worked in collaboration with two associated groups, the Département Optique Théorique et Appliqué at Onera in Toulouse and the Quantitative Image Analysis Unit at the Paris Pasteur Institute, to formally assess the performance of the different light sheet microscopy modalities to study tissue mimics. All groups involved have complementary skills and expertise in cancer biology, cell imaging, image processing, biophotonics and optics.

We generated four types of tissue mimics representing samples with different cell morphology (volume, density, shape, etc.) and cell population heterogeneity. Our tissue mimics correspond to samples generally used in different fields of investigation such as cancer biology (mammary duct spheres, multicellular tumour spheroids), cardiac biology (cardio-spheroids) and neurobiology (neurospheres).

In a first approach, we tested six different light-sheet modalities using a single type of tissue mimics. This allowed us to highlight and select the modalities of choice based on:

i) Resolution: 3D Point Spread Function using fluorescence in the tissue mimic sample;
ii) Signal-to-noise: Ratio between the signal and the background;
iii) Contrast: The Normalised Contrast Index as the differences between adjacent pixels.

The light sheet was produced using a cylindrical lens or by Digitally Scanning Light Sheet Microscopy (DSLM). With DSLM the used modalities were linear (one-photon) and nonlinear (two-photon) excitation regimes, under Gaussian or Bessel beam excitation profiles. Finally, the system included a sCMOS camera in which the digital scan was synchronized using the 'rolling shutter' mode to achieve confocal line detection.

Figure 1: Maximum intensity projection of different tissue mimics imaged by different light sheet modalities. Maximum projections along (x-y) and (x-z) of 3D image stack obtained using the indicated one-side light sheet illumination modality of 400 images (z spacing 1µm) of multicellular tumour spheroids (MCTS), mammary duct sphere (MDS), cardio-sphere (CS) and neurosphere (NS) tissue mimics measuring around 400 µm in diameter and stained with PI are displayed with depth lookup table for (x-y) and inverted grey lookup table for (x-z). For a good visualisation, scale intensity signals were set independently for each modality. Scale bar: 50 µm. (Image taken from Andilla et al., 2017)

All measurements were automatically extracted from the images using a set of robust and user-friendly image analysis and quantification protocols, available through the open-source Icy platform.

We first observed that the transversal resolution was similar for all modalities. However, the axial resolution was twice as large in the one-photon Bessel case, due to the side-lobes of the Bessel beam. In terms of standard deviation, two-photon modalities presented sharper resolutions than their one-photon counterparts, reflecting the good performance of the nonlinear versus the linear regime in terms of reducing scattered and out-of-focus light.

We then plotted the histogram of the overall signal-to-noise obtained for each illumination and observed that one-photon modalities were significantly superior to two-photon modalities in terms of fluorescence emission efficiency. On the other hand, when observing the local contrast measures (given by the Normalised Contrast Index), we saw that non-linear modalities yielded the largest values in comparison to any other linear modality. Finally, taking both metrics into account, it was interesting to observe that the linear modalities provided similar signal-to-noise and Normalised Contrast Index, despite the negative impact of the out-of-focus light from the side-lobes of the Bessel beam.

From this first set of results, we selected the three most representative techniques and we then further characterised the performance of the systems when imaging the different types of tissue mimics.

In the second set of experiments, we considered only the gold standard Gaussian with linear excitation and Bessel modalities with filtering capabilities. Here different tissue mimic models, including multicellular tumour spheroids, mammary duct spheres, cardio-spheroids and neurospheres were used to assess the imaging capabilities of the light sheet illumination modalities. In addition to the quantitative measures used in the first stage of evaluation, here we developed an additional set of quality metrics specific to LSFM: penetration depth and the Contrasted Imaging Volume or CIV, also using the Icy platform.

We observed that tissue mimics differed in term of nuclear size, cell density and level of heterogeneity (Fig. 1). However, the signal-to-noise was relatively stable across tissue mimics and light sheet illumination modalities. Nonetheless, non-linear Bessel excitation generally displayed lower signal-to-noise than linear modalities.

In terms of the Normalised Contrast Index, variability in behaviour was notably greater across tissue mimics, showing a maximum NCI for non-linear Bessel excitation regardless of the tissue mimic imaged. In the case of cardio-spheroids and neurospheres, linear Bessel excitation looked like non-linear excitation, providing a similar level of Normalised Contrast Index.

When looking at the resolution, the results were consistent with the first stage of experiments and no significant differences in behaviour appeared among the tissue mimics investigated herein.

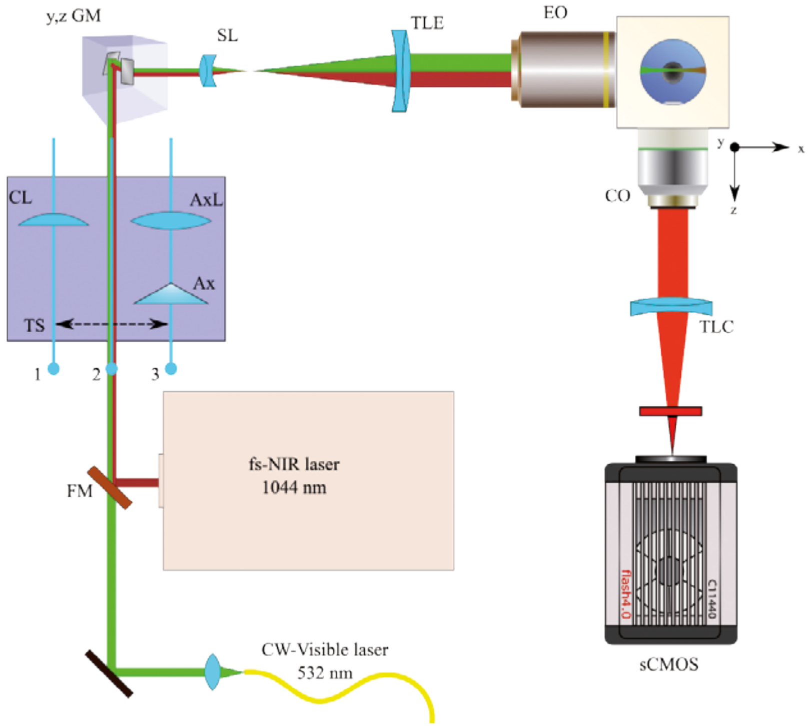


Figure 2: Schematic representation of the multimodal LSFM setup used. A CW and an ultrashort pulsed laser, both aligned to the same optical path, were used for linear and nonlinear excitation, respectively. A cylindrical lens (1) free beam propagation (2) and an axion lens (3) could be also included in the setup for accessing the different LSFM modalities. The light sheet was generated using a 10x, NA=0.3 objective and the images were taken using a 20x, NA=0.5 objective. (Image taken from Andilla et al., 2017)

By measuring the penetration depth achieved by the different illumination modalities, we observed that the nonlinear Bessel excitation offered better overall penetration depth, independent from the tissue mimic type.

As expected, there is no clear winner among the various techniques tested, and the choice of modality typically depends on the application at hand. Linear Gaussian excitation gives the best signal-to-noise, but lacks on contrast and sectioning capabilities. In comparison, linear Bessel excitation provides fair signal-to-noise, but a larger field of view and better sectioning capabilities. Finally, nonlinear Bessel excitation provides the largest field of view and a highly homogeneous x,y,z resolution, but it does not perform as well in terms of signal-to-noise. Overall linear Bessel excitation seems to provide the best compromise among all measured criteria if the uniformity of the sectioning capabilities is not demanding for the measurements.

Pablo Loza-Alvarez

Andilla, J., et al., Imaging tissue-mimic with light sheet microscopy: A comparative guideline, *Sci. Rep.* 7, 44939 (2017)

Buildings of Hungarian pillar of ELI opened officially

On 23 May 2017, the Grand Opening Ceremony of the Extreme Light Infrastructure – Attosecond Light Pulse Source (ELI-ALPS) buildings took place in Szeged, Hungary in the presence of Hungarian Prime Minister Victor Orbán. ELI-ALPS will partially open to users in 2018 before reaching full operation in 2020.

The main scientific mission of ELI-ALPS is to enable visualisation of ultrafast structural dynamics of matter and therefore to give international users access to research equipment with the highest resolution in both space and time. In addition, the technological mission of ELI-ALPS is to contribute to the science and development of high-peak-power and high-average power light sources.

Designed to provide the international scientific user community with access to some of the most advanced particle and radiation sources in the world, ELI is implemented as a distributed infrastructure with three pillars: ELI Nuclear Physics (ELI-NP) in Magurele, Romania, ELI-Beamlines (ELI-BL) in Dolní Břežany, Czech Republic, and ELI-Attosecond Light Pulse Source (ELI-ALPS) in Szeged, Hungary.

ELI-ALPS' primary laser sources are specifically engineered to drive cutting-edge secondary particle and radiation beamlines. Highly specialised user instrumentation, such as reaction microscopes, ion microscopes, surface science end-stations, and VMI spectrometers complement the technological arsenal of ELI-ALPS.

Among the laser systems commissioned by ELI-ALPS are a high-repetition-rate (HR) system, based on fibre laser technology, delivering TW peak power and < 6 fs pulses at 100 kHz; the future single-cycle (SYLOS) system, providing 20 TW and < 6 fs pulses based on optical parametric amplification; and the PW-class high-field (HF) laser operating at 10 Hz repetition rate with close to 15 fs pulse duration.

The performance of the above laser systems operating with central wavelengths in the range of 750 to 1030 nm is complemented by the mid-infrared (MIR) laser system, providing sub-4 cycle, tunable laser pulses at 100 kHz repetition rate with over 15 W average power.

Young Researcher Travel Bursaries for ICUSD 2017

EUCALL, the network of leading large-scale user facilities for free electron laser, synchrotron and optical laser radiation, among them Laserlab-Europe, provides travel bursaries for up to 20 young researchers to attend the International Conference on Ultrafast Structural Dynamics – ICUSD in Trieste, Italy, 5-7 December 2017.

ICUSD is a platform for discussing the latest methodological, theoretical and scientific developments aimed at understanding real-time structural changes in materials science, chemistry and biology. While these various communities have their scientific rationale, they share a variety of techniques including

- Ultrafast EUV and x-ray diffraction, scattering and spectroscopy,
- Ultrafast multidimensional vibrational and electronic spectroscopies,
- Ultrafast electron diffraction, scattering and microscopy,

which all aim at visualising the dynamics of assemblies of atoms at the atomic-scale resolutions of space (the sub-Å) and time (the femtosecond). The conference aims at building bridges to better connect these communities and to foster the exchange of information and expertise.

Applications may be submitted at *www.eucall.eu*.

Forthcoming events

Training School on Laser Applications for Biology and Biomolecular Systems
3-7 July 2017, Coimbra, Portugal

Summer School
Lasers in Medicine and Life Sciences – LAMELIS 2017
12-21 July 2017, Szeged, Hungary

Laserlab User Meeting
27-29 August 2017, Vilnius, Lithuania

To find out more about conferences and events, visit the Laserlab online conference calendar.

How to apply for access

Interested researchers are invited to contact the Laserlab-Europe website at www.laserlab-europe.eu/transnational-access, where they find relevant information about the participating facilities and local contact points as well as details about the submission procedure. Applicants are encouraged to contact any of the facilities directly to obtain additional information and assistance in preparing a proposal.

Proposal submission is done fully electronically, using the Laserlab-Europe Proposal Management System. Your proposal should contain a brief description of the scientific background and rationale of your project, of its objectives and of the added value of the expected results as well as the experimental set-up, methods and diagnostics that will be used.

Incoming proposals will be examined by the infrastructure you have indicated as host institution for formal compliance with the EU regulations, and then forwarded to the Access Selection Panel (ASP) of Laserlab-Europe. The ASP sends the proposal to external referees, who will judge the scientific content of the project and report their judgement to the ASP. The ASP will then take a final decision. In case the proposal is accepted the host institution will instruct the applicant about further procedures.

Laserlab Forum Contact

Professor Claes-Göran Wahlström
Coordinator – Laserlab-Europe
Email: *Claes-Goran.Wahlstrom@fysik.lth.se*
The Coordinator's Office
Daniela Stozno
Max Born Institute
Max-Born-Str. 2A | 12489 Berlin | Germany
Phone: +49 30 6392 1508
Email: *stozno@mbi-berlin.de*

Editorial Team:
Tom Jeltes (*tomjeltes@gmail.com*)
Julia Michel, Daniela Stozno
Layout: unicom Werbeagentur GmbH

If you would like to subscribe to this publication or find out more about the articles in this newsletter, please contact the editorial team at *office@laserlab-europe.eu*

Visit us on