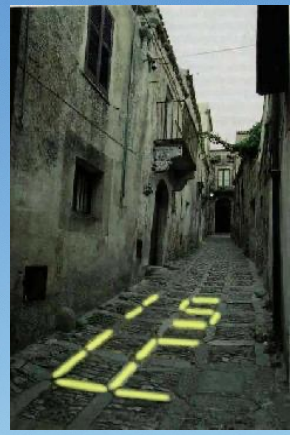


International School of Liquid Crystals
XXVI course

2nd International School of the
IEEE Photonics Society Italy Chapter
and the Italian Liquid Crystal Society

E. Majorana Centre for Scientific Culture, Erice (Italy), Italy
August 26- 31, 2023



Biophotonics at the nanoscale: from smart nanomaterials to advanced optical technologies for life, environmental science and nanomedicine

Book of abstracts

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A. d'Alessandro, P. Pasini, C. Zannoni
Directors of the course

C. Zannoni
Director of the School



SICL SOCIETÀ ITALIANA CRISTALLI LIQUIDI



Scheduled Topics

Advanced nanomaterials, including molecular composite materials with their optical properties, device and system technologies for bio-imaging and microscopy, chemical, biochemical and physical sensors, fiber sensors, lab-on-chip, optogenetics, optofluidics, and image sensors, photonic biosensing technologies, liquid crystal Biosensors, chip for biomedical application, Imaging and spectroscopy, Industrial applications and issues.

List of lecturers

Francesca Bragheri, CNR - Institute of Photonics and Nanotechnology, Milan, Italy

Nunzio Cennamo, University of Campania "Luigi Vanvitelli", Italy,

Gabriella Cincotti, University of Roma TRE, Italy,

Vincent Couderc, Université de Limoges, France,

Antonello Cutolo, "Federico II" University of Naples, Italy

Antonio d'Alessandro, Sapienza University of Rome, Italy

Luciano De Sio, Sapienza University of Rome, Italy

Massimo De Vittorio, , Italian Institute of Technology and University of Salento, Italy

Pietro Ferraro, Institute for Applied Sciences and Intelligent Systems (ISASI) – CNR Italy

Lorenzo Pavesi, University of Trento, Italy

Roberto Pini Institute of Applied Physics (IFAC) – CNR

Young Min Song, Gwangju Institute of Science and Technology (GIST), South Korea,

Claudio Zannoni, University of Bologna

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G. Cincotti – University of Roma TRE
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L. Lucchetti – Polytechnic University of Marche
A. Marino – Institute of Applied Sciences and Intelligent Systems CNR- ISASI
A. Melloni – Polytechnic of Milan
P. Pasini – INFN Section of Bologna, Co-Director of the course
S. Pietralunga – Istituto di Fotonica e Nanotecnologie – CNR Milan
S. Selleri – University of Parma
S. Wabnitz – Sapienza University of Rome,
C. Zannoni – University of Bologna “Alma Mater”, Director of the International School of Liquid Crystals

Organizing Committee

A. d’Alessandro, Sapienza University of Rome
L. De Sio, Sapienza University of Rome
A. Marino, Institute of Applied Sciences and Intelligent Systems CNR- ISASI
P. Pasini, INFN Section of Bologna

Biophotonics at the nanoscale: from smart nanomaterials to advanced optical technologies for life, environmental science and nanomedicine

Purpose of the course

The school is organized by the IEEE Photonics Society Italy Chapter in collaboration with the Italian Liquid Crystal Society (SICL) as the 26th course in the frame of the activities held at the International School of Liquid Crystals, one of the scientific advanced schools established at the "Ettore Majorana" Center in Erice. The school is aimed at PhD students and Post-docs in Engineering, Physics, Chemistry, Material Science and Photonic Technologies.

The course topics encompass advanced material properties, device design, technologies, and photonics applications in life science, environmental science, and high-precision medicine (i.e., nanomedicine). The school is mainly devoted to advanced nanotechnologies and biotechnologies in which photonics is the key enabling tool. Advanced nanomaterials, including molecular composite materials with their optical properties, will be among the school's topics. A specific focus will be devoted to device and system technologies for bio-imaging and microscopy, chemical, biochemical and physical sensors, fiber sensors, lab-on-chip, optogenetics, optofluidics, and image sensors. The industrial point of view will also be considered. Lectures will be given by international first-class scientists from prestigious Italian and foreign universities, research centres and industrial laboratories.

Purpose of the course is also to provide a forum to trigger cultural exchanges and foster new collaborations in Photonics. The school will provide a platform for interfacing basic science with applied engineering to track down a new frontier in Biophotonics. Students are encouraged to submit a scientific contribution to be presented in a poster during the course.

International School of Liquid Crystals 26th Course

Biophotonics at the nanoscale: from smart nanomaterials to advanced optical technologies for life, environmental science and nanomedicine

2nd School of IEEE Photonic Society - Italian Chapter and Italian Liquid Crystals Society

Erice, 26th August– 31st August, 2023

26th August

Afternoon: Arrival

21.15: Welcome Reception at the Marsala Lecture Hall (S. Rocco)

27th August

		C. Zannoni - Director of the ISLC
9.00-9.20	Welcome	
9.20 - 10.20	Lecture 1 Introduction on Liquid Crystals, Lecture 2	A. d'Alessandro (IEEE PS President) Claudio Zannoni , University of Bologna, Italy
10.20 - 11.20	Lecture 3 Advances in plasmonic nanovectors for tumors theranostics	Roberto Pini , Institute of Applied Physics (IFAC) – CNR, Italy
11.20 - 11.50		<i>Coffee Break</i>
11.50 - 12.50	Lecture 4 Early diagnosis of Alzheimer biomarkers by means of SERS nanostructured platforms,	Roberto Pini , Institute of Applied Physics (IFAC) – CNR, Italy
12.50 - 15.00		<i>Lunch break</i>
15.00 - 16.00	Lecture 5 Applications of nonlinear optics in multimode fibers for multiphoton imaging and CARS spectroscopy,	Vincent Couderc , Université de Limoges, France
16.00 - 17.00	Lecture 6 Nanotechnology for precision medicine using LC and nanoparticles,	Luciano De Sio , Sapienza University of Rome, Italy
		<i>Coffee Break</i>
17.00 - 18.30	Coffee and Posters	Coffee and Poster session

28th August

- 9.00 - 10.00** **Lecture 6**
Simple and highly sensitive Bio-Chemical Plastic Optical Fiber Sensors,
- 10.00 - 11.00** **Lecture 7**
Fiber optic biosensors for Nanomedicine I,
- 11.00 - 11.30**
- 11.30 - 12.30** **Lecture 8**
Fiber optic biosensors for Nanomedicine II,
- 12.30 - 15.00**
- 15.00 - 16.00** **Lecture 9**
On-chip integrated advanced 3D fluorescence microscopy,
- 16.00 - 17.00** **Lecture 10**
Super-Resolution Optical Imaging of Bacterial Cells,
- 17.00 - 18.30** **Coffee and Posters**

Nunzio Cennamo, University of Campania "Luigi Vanvitelli", Italy

Antonello Cutolo, "Federico II" University of Naples, Italy

Coffee Break

Antonello Cutolo, "Federico II" University of Naples, Italy

Lunch break

Francesca Bragheri, CNR - Institute of Photonics and Nanotechnology, Milan, Italy

Gabriella Cincotti, University of Roma TRE, Italy,

29th August

- 9.00 - 10.00** **Lecture 11**
Integrated silicon biosensor for aflatoxin detection,
- 10.00 - 11.00** **Lecture 12**
Functional colorimetric sensing platforms for measuring environmental changes,
- 11.00 - 11.30**
- 11.30 - 12.30** **Lecture 13**
Liquid biopsy by phase contrast tomography,
- 15.00 - 21.00** **Excursion**

Lorenzo Pavesi, University of Trento, Italy,

Young Min Song, Gwangju Institute of Science and Technology (GIST), South Korea,

Coffee Break

Pietro Ferraro, Institute for Applied Sciences and Intelligent Systems (ISASI) – CNR Italy

TBD

30th August

- 9.00 - 10.00** **Lecture 14**
Neuromorphic photonics and the brain,
- 10.00 - 11.00** **Lecture 15**
Technologies for optogenetics and neurophotonics
- 11.00 - 11.30**
- 11.30 - 12.30** **Lecture 16**
LC devices for biophotonics,
Concluding Remarks

Lorenzo Pavesi, University of Trento, Italy

Massimo De Vittorio, Italian Institute of Technology and University of Salento, Italy

Coffee Break

Antonio d'Alessandro, Sapienza University of Rome, Italy

20.00 Social Dinner and poster awards

31st August Departures

Abstracts of lectures

An Introduction to Liquid Crystals

Claudio Zannoni

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The talk will briefly introduce liquid crystals in terms of their molecular organisation and main properties [1, 2]. The focus will be on nematics and their sensitivity to a variety of external stimuli, which is key to their use as amplifiers of small perturbations and applications in sensors. We shall discuss, in particular, their sensitivity to chiral solutes, with the turning of a uniform nematic into cholesterics, their twisted version. While this has been known for a long time, as well as the demonstration of their ability to sense even minute structural molecular modifications like the substitution of a hydrogen with a deuterium, thus rendering a molecule chiral [3], a recent realisation is the huge twisting power enhancement obtained by linking chiral ligands to achiral gold nanoparticles of different size and shape (spheres, rods, discs, prisms, stars)[4-6]. The effect can be rationalised using a simple model of decorated nanoparticles chirality and solute-solvent shape compatibility. [6, 7]

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Advances in plasmonic nanovectors for tumors theranostics

*Roberto Pini, Fulvio Ratto, Francesca Rossi, Lucia Cavigli,
Sonia Centi, Francesca Tatini*

*“Nello Carrara” Institute of Applied Physics, National Research Council of Italy (CNR-IFAC)
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The combination of pulsed and CW near-infrared laser light with plasmonic particles is gaining relevance for the photoacoustic imaging and photothermal ablation of cancer. Selective targeting of malignant cells with these contrast agents may rely on complementary biochemical and biological strategies, including the use of specific probes or the exploitation of cellular vehicles.

Here we moved from a platform of PEGylated gold nanorods (GNRs) in a range of size from a few tens to a few hundreds of nanometers, with plasmonic near-infrared (NIR) bands that we activated with a NIR laser at 800 nm to perform hyperthermia and drug release of e.g. chemotherapeutic agents they may carry onboard. In fact, upon systemic injection, these nanoparticles tend to passively accumulate in the tumor according to the EPR (extravasation, permeation) effect due to high vascular permeability of the abnormal vasculature of the tumor.

In order to improve this figure, we implemented multiple approaches and strategies for active delivery of the GNRs to cancer cells by functionalization with ligands for specific cell phenotypes:

- (i) antibodies against cancer antigen 125 (CA125), which is a common biomarker for ovarian lesions [1];
- (ii) inhibitors of carbonic anhydrase 9 (CAIX), which are expressed by hypoxic cells such as those found in solid tumors [2]; and
- (iii) by introducing macrophages as a versatile model of cellular vehicles that would phagocytose the particles and home to inflammatory lesions [3].

All these approaches have the common feature to be biologically inspired and may be synergistically combined to target tumors.

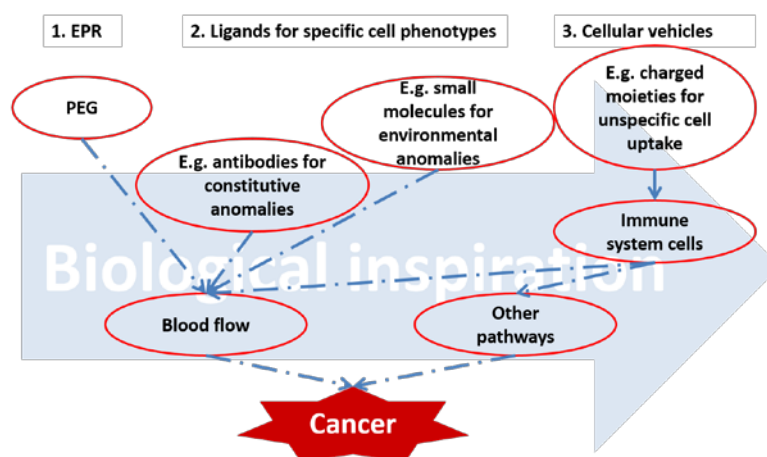


Fig. 1. Sketch of multiple approaches for targeting cancer tissue by means of laser-activatable plasmonic nanoparticles

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Early diagnosis of Alzheimer's biomarkers by means of SERS nanostructured platforms

*Roberto Pini, Paolo Matteini, Chiara Amicucci, Martina Banchelli,
Sonia Centi, Cristiano D'Andrea, Marella de Angelis*

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We report examples from our recent research activity on the development of plasmonic substrates (e. g. substrates supporting localized surface plasmon resonances featured by nanoscaled metallic surfaces or assembled nanoparticles) for surface-enhanced Raman spectroscopy (SERS) analyses of neurodegenerative diseases like Alzheimer's [1,2]. SERS is an ultrasensitive analytical technique that couples the unique features of Raman spectroscopy in providing a description of chemical composition and structure of molecules with a huge signal enhancement due to isolated or assembled silver or gold nanoparticles. As a result, identification of trace amounts of molecules, including those of biomedical interest, becomes feasible. In the last decade a great deal of efforts has been exerted in the development of functional SERS substrates obtained by simple, low cost, rapid and scalable fabrication methods, such as micropipetting, screen- and ink-jet printing, and filtration of colloidal solutions of plasmonic nanoparticles. Previous tests at the laboratory level have been mainly based on adding a biomolecule solution to a dispersion of noble metal colloidal nanoparticles and adding aggregating agents or imparting the particle with suitable surface charge, to induce the formation of interparticle gaps enclosing adsorbed molecules. Upon excitation with appropriate light, the Raman signal of an adsorbed species in the gaps is amplified to such an extent to provide characteristic fingerprint information [3]. However, the formation of particle clusters with highly divergent size causes scarce reproducibility with large signal variability, which remains a main obstacle of this approach. Alternative strategies have been aimed at obtaining more consistent and dependable SERS responses from biomolecules, designing suitable platforms with organized assemblies of plasmonic nanoparticles [4,5]. Recently, we demonstrated the possibility to take advantage of rapid, inexpensive fabrication techniques to produce disposable SERS substrates, by combining the self-assembly of filtered silver nanowires (AgNWs) and control over their cluster density with the laser ablation removal of predetermined areas from the SERS-active layer, obtaining spatially confined plasmonic spots, accommodating a high concentration of molecules. These SERS platforms can be integrated with a simple spot-on analysis specifically adapted for reliable detection and characterization of molecules of biomedical interest [6].

In a further development of SERS platforms based on silver nanowires, we devised and tested the use of graphene as a support for these plasmonic nanostructures to improve the signal detection, offering a flat background and imparting superior reproducibility. The proposed fabrication procedure relied on low-cost and facile aerosol deposition of AgNWs on graphene paper, still allowing biodetection of molecules at submicromolar concentration [7].

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Applications of nonlinear optics in multimode fibers for multiphoton imaging and CARS spectroscopy

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Supercontinuum sources are particularly interesting because of their ability to emit laser radiation simultaneously over a wide bandwidth from UV to infrared [1]-[2]. The development of microstructured optical fibers [3]-[5] has also stimulated these new sources development, which are capable of operating in a wide range of time domains, from femtosecond to continuous regimes. The first demonstrations of supercontinuum in a microstructured optical fiber were carried out with femtosecond pulses coupled at a laser wavelength close to the zero-dispersion wavelength of the fiber [6]. More recently, a spatially coherent supercontinuum has been demonstrated in multimode fibers thanks to Kerr and/or Raman spatial cleaning effects, opening up new avenues for high-power polychromatic laser sources and associated applications [7].

Currently, nonlinear imaging based on Raman scattering, fluorescence, harmonic generation... can be greatly enhanced using these supercontinua but may also require different temporal pulses ranging from femtoseconds to picoseconds, as has already been demonstrated for M CARS imaging [8-11]. This particular technique requires the synchronous nonlinear interaction between a narrow-band pump and a broadband Stokes spectrum at the sample level, and enables the simultaneous detection of all vibrational modes that are covered by the pump-Stokes spectrum. It is also possible to determine other parameters such as the nonlinear index of materials with this coherent system.

In this presentation, we will first introduce the nonlinear process capable of generating a broadband spectrum and present examples of supercontinua generation in $\chi^{(2)}$ and $\chi^{(3)}$ materials with the explanation of nonlinear mechanisms producing visible, infrared or UV radiations.

Next, we will explain the experimental approach to multimodal imaging mixing fluorescence, vibrational modes, and harmonics generation obtained in single- and multimode fibers.

New results obtained with graded-index multimode fibers in microspectroscopy and endomicrospectroscopy will be presented.

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Nanotechnology for liquid crystals biosensing and precision medicine

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Nanotechnology, with the support of nanomaterials, has the power to boost several innovative applications ranging from biotechnology to high-precision medicine. In this framework, plasmonic nanoparticles (NPs) such as gold and silver NPs play a crucial role thanks to their multifunctional properties, such as sensitivity to the surrounding refractive index (colorimetric change) and light-induced localized temperature increase (thermoplasmonic effect). With these premises, in this presentation, I report and discuss our recent achievements in label-free and liquid crystals (LCs)-assisted biosensing [1] and drug-free, radiopharmaceutical-assisted photo-thermal therapy. [2] In addition, unique opportunities in healthcare applications are presented thanks to the latest achievements in white light-assisted thermoplasmonics that enables a new technique in medical tools disinfection. [3] The presented results open new avenues for green and carbon-free medical applications.

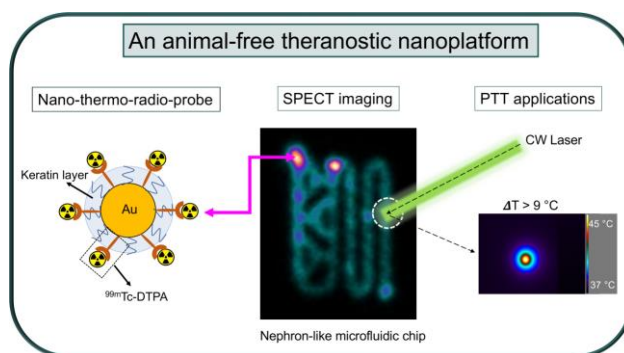


Figure 1. Gamma camera image of a nephron-like microfluidic chip filled with the ^{99m}Tc labeled and keratin-coated AuNPs

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Acknowledgments

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Simple and highly sensitive Bio/Chemical Plastic Optical Fiber Sensors

Nunzio Cennamo

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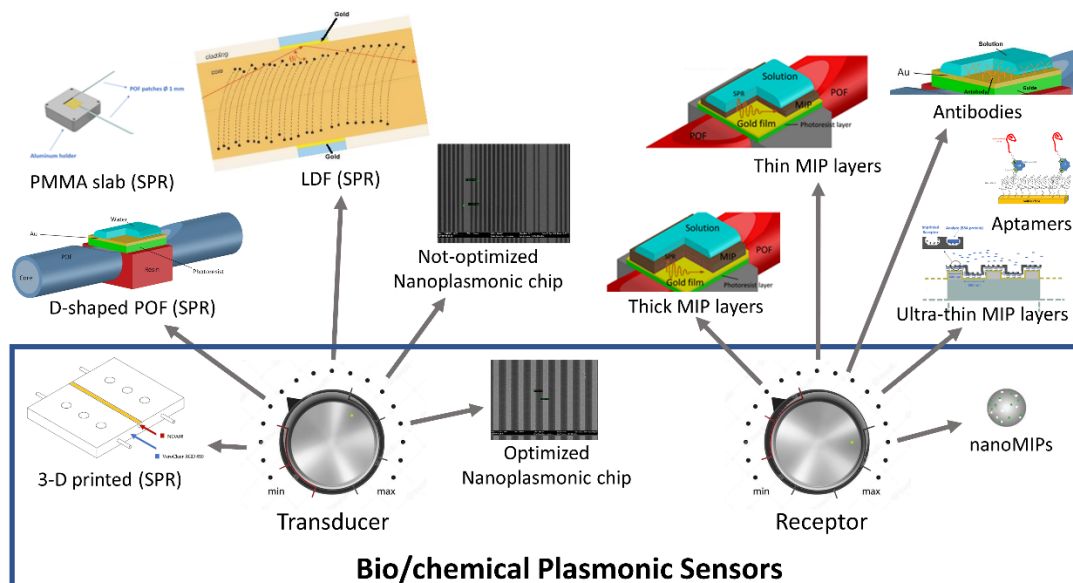
Abstract: Several developed low-cost, highly sensitive, simple-to-realize and to-use plasmonic sensor configurations are presented. In particular, the proposed sensor configurations are based on innovative platforms that efficiently excite the plasmonic phenomena (surface plasmon resonance (SPR) or Localized SPR) in gold nanofilms, continuous or nanostructured, such as planar polymer waveguides, polymer optical fibers (POFs), and specialty optical fibers (e.g., light-diffusing fibers).

The presented sensor configurations are extrinsic and intrinsic POF sensor types that, via POFs, excite the plasmonic phenomena (SPR or LSPR) in nanofilms, continuous or nanostructured, to measure analyte-receptor interaction. These sensor chips are monitored using a simple experimental setup based on a white light source and spectrometer. Moreover, they can be combined with different kinds of chemical and biological receptors for several application fields. In these cases, in fact, we can obtain the selectivity to the substances of interest via the use of specific Molecular Recognition Elements (MRE) in contact with the plasmonic sensing surfaces, such as those based on molecularly imprinted polymers (MIPs), antibodies, aptamers, nanoMIPs, etc. The substances that can be measured with the proposed approach are pollutants, viruses, bacteria, toxic metals, pesticides, biomarkers, or other molecules of interest to detect in aqueous solutions. In general, all the presented POF bio/chemical sensor configurations are highly sensitive, selective, small-size, and versatile.

The presentation proposes an overview of how a designer could use the bio/chemical sensor components, both the plasmonic transducer and the receptor, to modify the response of the bio/chemical sensor system in terms of substance and detection range of interest. The balance of the combination of these two components (transducer and receptor) would produce the desired optimal performance. For instance, the detection range can be changed from femtomolar to micromolar ranges.

So, the advantages and disadvantages of each bio/chemical sensor system are presented in detail. More specifically, extrinsic and intrinsic POF biosensor schemes will be reported in terms of plasmonic characteristics and application fields. For instance, these selective plasmonic optical fiber sensor systems (intrinsic or extrinsic) can be used for "Smart Cities" applications, as in water quality monitoring, through an IoT (Internet of Things) approach, or, alternatively, they can be used onboard of simple robots, based on an autonomous guide, for the mapping of specific substances or to follow increasing concentrations of pollutants in rivers or sea to identify the point of interest (the source), etc.

Similarly, these plasmonic bio/chemical chips can be used to realize interesting point-of-care tests (POCT), exploiting the same setup combined with different plasmonic bio/chemical chips, to monitor several both substances and detection ranges of interest for biomedical applications.



MULTIFUNCTIONAL OPTICAL FIBER SENSORS FOR MEDICAL AND INDUSTRIAL APPLICATIONS

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Summary

We shall discuss the large variety of applications of multifunctional optical fiber sensor. The talk is divided in two parts. In the first one, after briefly introducing the basic principles, we describe some applications to safety and security in transportations (railways and aerospace), environment monitoring, civil engineering and underwater inspection.

In the second part we focus our attention on many medical applications by introducing a new teranostic platform: the hospital in the needle as well.

Finally, after focusing our attention on some market applications, we describe the new Nanophotonic and Optoelectronic Center for Human Health and Industrial Applications "Emilia" (CNOS). This is a 3000 square meters center located in Benevento (Italy) the construction of which will be completed around the end of the year.

On-chip integrated advanced 3D fluorescence microscopy

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Single cell analyses (SCA) have been extensively exploited in different fields from cancer studies to embryogenesis, since they allow unravelling aspects in biological heterogeneity that might be hindered when evaluating a bulk population of cells. These methods require to be automatic and high throughput to acquire statistically significant results. The synergic integration of optical and microfluidic components on a chip enables high throughput imaging while guaranteeing device compactness, ease of use and alignment stability. For these reasons, in recent years we observed an increasing interest towards the development of microfluidic-based microscopes on a chip [1].

Recently, light sheet fluorescence microscopy (LSFM) opened new ways to image samples in 3D allowing the evaluation of cellular functionalities, with remarkably fast acquisition and low phototoxicity. The development of super-resolution imaging techniques, as structured illumination microscopy (SIM), enabled the visualizations into cells down to single molecules. The combination of these techniques and SCA would allow comprehensive analyses with high resolution.

An introduction to the implemented microscopy techniques as well as the realization and validation of the devices on biological samples will be introduced. In particular I will present different solutions to implement both LSFM and SIM in an optofluidic platform for super resolution 3D imaging of single cells. The used fabrication technique is femtosecond laser micromachining (FLM) [2], an advanced and enabling technique for 3D micromachining of glass substrates whose versatility allows easily prototyping of different microscope on-chip devices.

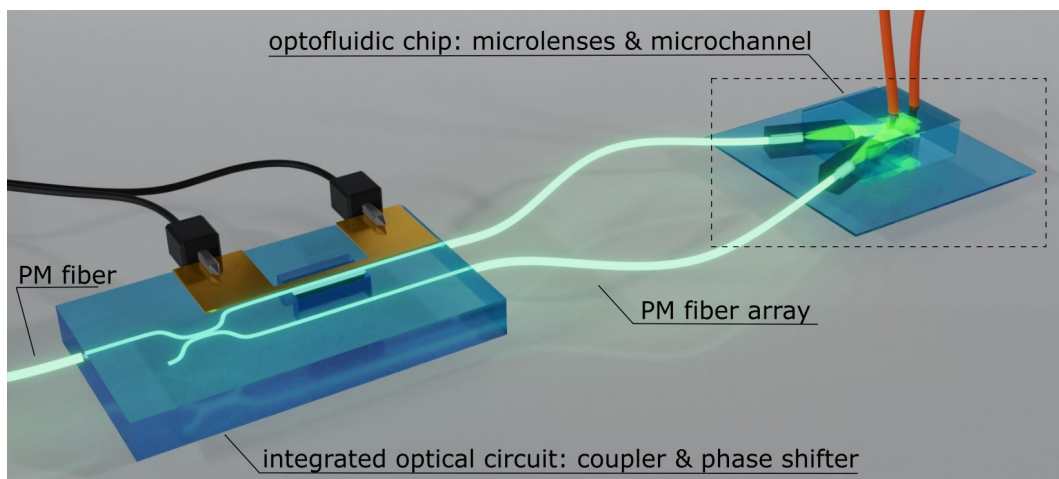


Figure 1. Schematic design of an integrated microscope.

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Super-resolution optical imaging of bacterial cells

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Microscopy is an essential tool in the field of microbiology, playing a crucial role in various applications, including the identification of microorganism in environmental samples and the diagnosis of infectious diseases. Nevertheless, due to the small size of bacterial structures, advanced super-resolution microscopy (SRM) techniques are necessary to achieve nanoscale resolution in imaging.

The significance of SRM in microbiology extends to the development of new antimicrobial drugs. The overuse of therapeutic antimicrobial and disinfectants is a major contributing factor, leading to the emergence of resistance in bacterial pathogens. It is estimated that by 2050, up to 10 million deaths could be caused by antimicrobial resistance. However, most discovery and preclinical development projects assess antimicrobial efficacy using conventional cell-based assays, which provide average responses from cell populations without considering individual cell phenotypes. This limitation can be overcome by employing single-cell studies based on SRM, which provide a deeper understanding of bacterial behavior, allowing for the identification of novel direct-acting molecules, new targets, and new mechanisms of action.

In this paper, we present a comprehensive review of various SRM approaches used to investigate bacterial cell morphology and functions. We highlight the achieved resolution and emphasize the importance of fluorophore selection and other critical imaging requirements [1]. Furthermore, we discuss recent applications of SRM that have yielded novel insights into bacterial cellular structures. We underscore the pivotal role that super-resolution microscopy can play in the near future in tackling the challenge of antimicrobial resistance.

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Integrated silicon biosensor for aflatoxin detection

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Aflatoxins (AF) are naturally occurring mycotoxins, produced by many species of *Aspergillus*. Among aflatoxins, Aflatoxin M1 (AFM1) is one of the most frequent and dangerous for human health. The acceptable maximum level of AFM1 in milk according to EU regulation is 50 ppt, equivalent to 152 pM, and 25 ppt, equivalent to 76 pM, for adults and infants, respectively. Here, I discuss the development of a photonic biosensor based on Si₃N₄ asymmetric Mach-Zehnder Interferometers (aMZI) [4] or microresonators [3,5], functionalized with aptamers or Fab' for AFM1 detection in milk samples (eluates). The design of the photonic circuits [1,2] the different passivation strategies [7,8] and the lab [6] as well as on-field testing of the integrated biosensing system [9] are all discussed. The minimum concentration of AFM1 detected by our aMZI sensors is 48 pM (16.8 pg/mL) in purified and concentrated milk samples which demonstrates the viability of photonic integrated biosensors.

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Neuromorphic photonics and the brain

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The interest in Artificial Neural Networks (ANNs) has considerably increased in recent years due to their versatility, which allows for dealing with a huge class of problems [1]. Nowadays, ANNs are mostly implemented on electronic circuits [2–4]. Very-large-scale ANN models have been elaborated which outperform human minds in given tasks [5, 6] at the expense of large training times and huge power consumption [7–9]. A possible solution to these limitations is provided by Photonic Neural Networks (PNNs) which enable high-speed, parallel transmission (Wavelength Division Multiplexing, WDM) and low power dissipation [10, 11].

In my talk, I will discuss a few simple PNNs implemented on a silicon photonics platform [12] that demonstrate the basic mechanism of silicon-based PNNs. Silicon photonics is particularly interesting since its easy integration with electronics allows for on-chip training of the network and for volume fabrication of the PNNs [13]. A simple optical neuron is discussed where different delayed versions of the input optical signal are made to interfere before the output port [14, 15].

Finally, I will show how it is possible to merge photonics neural network and biological neurons to perform joint experiments where light signals are transduced into neuronal stimulation to activate specific neuronal circuitries. In this way, hybrid intelligence can be achieved which opens interesting perspectives for neuromorphic computation and novel neurological therapies..

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Functional colorimetric sensing platforms for measuring environmental changes

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In addition to vital functions, more subsidiary functions are being expected from wearable devices. The wearable technology thus far has achieved the ability to maintain homeostasis by continuously monitoring physiological signals. The quality of life improves if, through further developments of wearable devices to detect, announce, and even control unperceptive or noxious signals from the environment. Soft materials based on photonic engineering can fulfil the abovementioned functions. Due to the flexibility and zero-power operation of such materials, they can be applied to conventional wearables without affecting existing functions [1]. Herein, the role that photonic engineering on a flexible platform plays in detecting or reacting to environmental changes is discussed in terms of material selection, structural design, and regulation mechanisms. In particular, as a simple platform, we focus on ‘ultra-thin films’ for measuring environmental changes, including humidity, temperature, chemicals, and bioparticles. Starting from the coloration from the thin-film coatings, this talk extends to how the colors change from the external stimuli. Future directions with deep learning approach is also discussed [2-3].

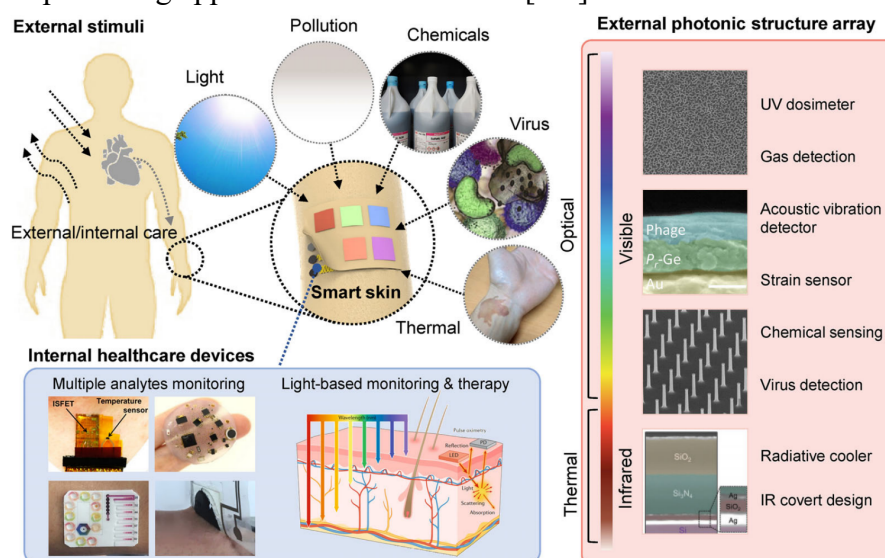


Figure 1. External/internal care facilitated through wearable devices capable of external interaction on environmental stimulus such as light, pollution, chemicals, thermal and virus, etc.

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Liquid biopsy by phase contrast tomography: *perspectives and real chances*

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The early identification of a circulating tumor cells in blood condition can be considered a priority in cancer research, as it can allow disruptive improvement of efficacy of therapeutic treatments. It takes the name of Liquid Biopsy. Nowadays, the standard method for cancer diagnosis is the biopsy of solid tumor tissue. However, tissue biopsy this procedure only reflects the situation in a single site of the tumor at a single time, and after the tumor has been developed to cm size. Moreover, it takes complex protocols. However, as the tumors shed parts of themselves into the human circulatory system, it is possible to reveal them by analyzing body fluids, such as blood and urine. Liquid Biopsy (LB) instead, could provide a completely non-invasive methodology for detecting specific biomarkers from body fluids. Usually, the emerging LB approaches try to identify and/or isolating specific biomarkers (i.e. circulating tumor DNA (ctDNA), tumor-derived exosomes (TDEs) or circulating tumor cells (CTCs)). Recently, an increasing attention has been focused on microscopy techniques for the detection and isolation of the CTCs based on label-free approaches and microfluidic devices. Recently, new perspectives have been opened for searching new strategies based on intelligent lab-on-a-chip for detecting tumor cells in body fluid samples. One possibility is to isolate CTCs using immunogenicity, positive enrichment, negative enrichment, enrichment based on biophysical properties (i.e., size, deformability, density). Particularly interesting is the latter approach that can enables label-free methodologies. It will be shown how microfluidic tomographic cytometry has a great potential to detect CTCs. Moreover, it is important to underline that the high-throughput of this new method is comparable to the standard image cytometry apparatus in conduct assays at the single-cell level. In fact, it will be shown how machine learning-powered tomographic phase imaging flow cytometry can be capable to provide high-throughput 3D phase-contrast tomograms of each single cell by demonstrating that discrimination of tumor cells against white blood cells is achievable with the aid of artificial intelligence in such label-free flow-cyto-tomography method. Description of methods that allow to obtain 3D tomograms of the cells' refractive index will be presented regarding experimental aspects as well as numerical processing pipelines. Various examples of the scenario with cancer cells will be illustrated and explained by addressing all the key-technology aspect of the label-free flow-cyto-tomography.

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Technologies for optogenetics and neurophotonic

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Optical techniques have found a broad range of applications for the brain. Neural activity can be controlled in optogenetics by genetically encoded light-sensitive ion channels, while fluorescent indicators of neural and molecular activity allow for optical recording and imaging of the brain dynamics. All these advanced photonic mediators are enabling the study of the brain circuitry with unprecedented specificity and accuracy. However, because of light absorption and scattering of the tissue, new optical tools and technologies are needed for accessing the deepest regions of the brain with high spatial and temporal resolution.

In this lecture, the typical photonic approaches to manipulate and record neural and molecular activity will be described. It will be shown how photonic probes can be used as minimally invasive bidirectional brain interfaces. Emphasis will be given to tapered optical fibers, recently applied to access deep brain regions in animal models with unprecedented versatility [1-3]. It will be also shown how tapered fibers can be employed in-vivo in Raman and SERS spectroscopy experiments for label-free neurotechnology.

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- and how micro and nanomachining them enable a multimodal interaction at cellular and molecular scale in behavioral experiments.

Liquid crystals devices for biophotonic applications

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Liquid crystal (LC) have many potential applications not limited to flat panel display because of their interesting linear and nonlinear optical properties [1]. In this lecture the basic optical and dielectric properties will be summarized in order to introduce some examples of device concepts for biosensor applications. LC random lasers have been proposed for medical diagnostics and biomedical imaging [2]. In another class of sensors, ions are widely distributed in nature and bionts, playing critical roles in many physiological activities and ecological cycles. Appropriate amount of ions is beneficial to the human body, while the excess ions can cause irreversible damages. As a result, a variety of LC sensors are proposed to detect the ion concentration in both body fluids and water samples [3]. LC have been also proposed to develop GRIN lenses able to show tunable focal lengths, tunable optical axis, tunable Zernike coefficients, and continuous wavefronts (not step-like wavefronts) [4-6]. Many applications are also developed using GRIN LC lenses, such as auto focusing for cell phones (tunable focal length), optical zoom for cell phones(tunable focal length), vision correction(eyeglasses) (aberration correction), varifocal images for augmented reality/virtual reality (change the location of virtual images), 3D integral images(tunable depth of field), tunable depth of field for endoscopes tunable depth of field , light concentrator for solar cells (tunable focal length), and low-level light therapy (tunable focal length).

LC can be used also to tune peaks of absorption of localized surface plasmon resonances in gold nanorods for photothermal therapies. Microstructures including PDMS microfluidic channels. a simple and effective design which combines optical and microfluidic channels to allow accurate investigation of gold nanorods (GNRs) potential in the development of light assisted antimicrobial therapies. The powerful combination allows the realization of innovative light-assisted antimicrobial treatments in a portable and biocompatible microsystems [7-9].

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Abstracts of posters

Fibertrodes for wide-volume optoelectrical neural interfaces in behaving mice

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Optical methods to study neural circuits are greatly supporting the neuroscience community to better control and monitor electrical and molecular events in the central nervous system, and implantable optoelectronic probes are playing an essential role in the development of complex experiments in which increasing the number of targeted neurons and reaching deep brain regions represent key challenges [1][2]. However photoelectric artifacts are often observed at light onset and light offset, mostly due to capacitive coupling from the driving lines in μ LED probes [3][4] or direct illumination of the recording pads. This effect is particularly relevant when seeking wide-volume light delivery and simultaneous electrophysiology, as the high number of delivered photons in the scattering brain tissue increases the probability to generate Becquerel photoelectric effect. In this work, we propose an optoelectrical device-based tapered fiber, able to deliver light for the entire depth of the hippocampus and simultaneously record local field potentials (LFP) with no photoelectric noise from mice running on a wheel. This has been achieved by engineering both the fabrication process as well as the photonic properties of the probe. The fabrication process involves the use of advanced microfabrication techniques translated onto the non-planar surface of the fiber [5], which is characterized by a narrowing region with diameters ranging from several micrometers down to sub-micron levels. With reference to *Fig. 1(a)* a TF (200 μ m core diameter and 0.66 numerical aperture) was coated with a conductive metal layer, except for a 1mm-long extent tailored for the hippocampus depth. The metal coating was deposited directly on the cladding, and its thickness was engineered to completely screen the recording pad from the evanescent field of the waveguide. After connectorization on a custom printed circuit board and insulation by a parylene layer, the recording site was obtained by employing the Focus Ion Beam milling to open a recess and locally deposit a platinum layer with ion beam induced deposition. The obtained devices were tested *in vivo* in head-fixed transgenic mice *Thy1-ChR2*, trained to run spontaneously in a wheel. We were able to collect spontaneous LFP, with a successful recording of theta and gamma oscillation (*Fig. 1(b)*). The same probe was used to deliver a 473 nm laser beam and activate ChR2 in stratum oriens of the dorsal CA1. Response to optogenetic laser stimulation is shown (*Fig. 1(c)*), with no sign of photoelectric artifacts.

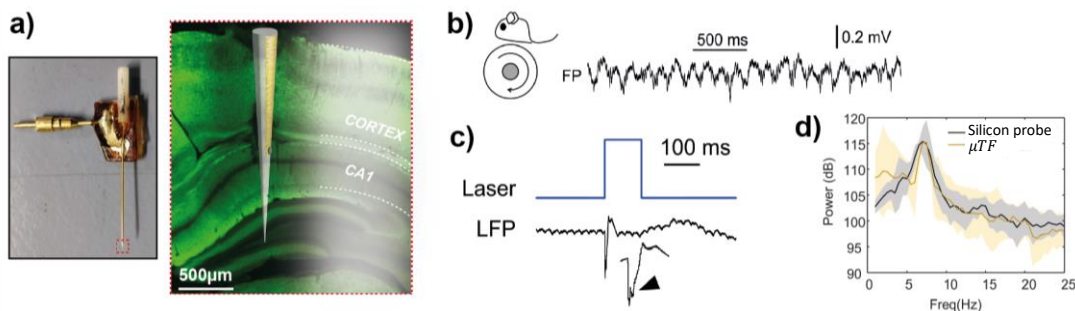


Fig. 1 *a)* μ TF employed for *in-vivo* electrophysiological and optogenetic experiments in hippocampus. *b)* Spontaneous LFP recordings from a head-fixed running mouse using the μ TF. *c)* Response to optogenetic laser stimulation. *d)* Comparison between LFP spectra from the μ TF and silicon probes in the low-frequency range. *e)* μ TF with uncovered tip and 360° optical aperture

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Semiconducting polymer bio-hybrid interfaces: an introductory bioelectrical investigation

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Keywords: Bioelectronics; Conjugated polymer; P3HT; Bio-hybrid opto-electrical interface; Characterization; Biocompatibility

Bioelectronics is an emergent multidisciplinary field that combines biology and electronics for therapeutic applications. In particular, bio-hybrid interfaces to investigate the electrical activity of living cells *in vitro* is at the forefront of bioelectronics. In this field, organic semiconductors are surely the most promising electronic materials. Among them, poly(3-hexylthiophene) (P3HT) is a widely used one that absorbs light in the visible light spectrum. It has gained attention, initially, for photovoltaic applications[1] and then for photoactivable interfaces [2] as a potential interactor with living systems. Therefore, its ability to absorb visible light is growing an increasing interest in light-mediated cell modulation and stimulation[3], which provides the great advantage of high selectivity and spatial resolution, and low/no invasiveness. Thus, it represents an alternative to electrical stimulation to elicit physiological responses for studying molecular mechanisms involved in basic and biomedical research. Photoinduced physiological effects mediated by P3HT have been observed in a number of *in vitro* [3] and *in vivo* models[4]. Based on these considerations, it is of utmost importance to characterize P3HT films in general, and specifically for these applications. The aim of this work is to compare the optoelectrical properties of P3HT bio-hybrid interfaces consisting of P3HT deposited on ITO glass substrates via spray coating technique, at three different concentrations (2,5,10 mg/ml). The P3HT sprayed film is characterized by considering: morphology, wettability, and optoelectrical properties. The morphological properties were evaluated through atomic force microscopy while the wettability was estimated determining the contact angle of a water drop. The optoelectrical properties were measured using a potentiostat and a LED light source ($\lambda=450, 520, 620\text{nm}$). The interchange of a dark phase(10s) and a phase of light exposition (10s) was used for the induction of photocurrent, measured through the chronoamperometry, and the induction of photovoltage, measured through the chronopotentiometry. Obtained results have shown the ability of the polymer to respond to specific wavelength of light in the visible spectrum(520nm) and gave the possibility to select the best concentration (2mg/ml) of the polymer for the interaction with *in vitro* biological systems, thus for optimal biohybrid interface. Biocompatibility of the spray-coated semiconductive polymer was investigated *in vitro* by measuring the growth curves of SH-SY5Y cells at three different time points (24, 48, and 72h). This experiment has highlighted that cells are able to survive and grow on the polymer confirming that P3HT is a suitable bio-hybrid interface for biological systems, paving the way to use it in more complex *in vitro* systems

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Electrowetting of chromonic liquid crystals

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Controlling of the shape and motion of liquid droplets on solid surfaces is a fundamental task for many applications [1]. It can be achieved by employing passive or active methods [2]. One of the most widely used tools for manipulating water droplets on surfaces is electrowetting on dielectric (EWOD) [3].

Here we present a characterization of the contact angle of sessile water-based chromonic liquid crystal (LC) droplets using EWOD. The contact angle of chromonic LC droplets is studied on different substrates, such as a polydimethylsiloxane coating and a liquid-infused surface [4] which is important in view of the variety of possible bioinspired applications, such as microfluidic biosensors or microtools for drug delivery [5].

As chromonic LC, we use disodium cromoglycate (DSCG) dissolved in water at different weight concentrations ranging from 4 to 13% (wt/wt). We studied the solution at various temperatures, in which the droplets show different liquid crystalline phases. The control of the wettability of DSCG droplets achieved in EWOD experiments is found to be quite efficient, leading to a variation of the contact angle as high as 70° up to voltages of 300 V on the liquid-infused surface. No major variations are observed by varying the temperature between 14 and 35 °C.

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Focusing wavelength-tunable, ultrashort supercontinuum pulses through a MMF: challenges and perspectives

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In the last decade, supercontinuum lasers (SC) gained the attention of the scientific community due to the combination of a broadband source with the properties of fs-pulsed single-mode lasers. These characteristics allow SC sources to be used in a wide range of applications including fluorescence lifetime imaging [1], the study of plasmonic structures [2] and optical coherence tomography [3]. On the other hand, wavefront shaping has been proven to be an important tool to manipulate the light inside a turbid media, and it can be employed to reconstruct the transmission matrix of multimode optical fibers (MMFs) in order to control the spatial behaviour of the output electromagnetic field [4]. This has enabled a set of applications, including the realization of low-invasiveness imaging endoscopes [5], controlling the coupling between guided modes and surface plasmon resonances [6] and far-field imaging based on photons time-of-flight [7]. The ability to focus super continuous pulses with either broad or narrow spectral bands through a MMF would extend the capabilities of the approach, allowing for multiwavelength fluorescence lifetime imaging or hyperspectral endoscopy through a MMF.

We have developed a wavefront shaping system (Figure 1) to focus ultra-short pulses (<100fs) through a MMF using a custom SC source with a tunable output. We performed a multi-parametric study to understand how the behaviour of the focused output spot depends on: the central wavelength, the spectral width and the number of phase modulation spots sampled on the input facet of the fiber. We view our approach as a promising method towards a set of endoscopic applications requiring coherent broadband light sources, including hyperspectral endoscopy and multi-wavelength fluorescence lifetime imaging.

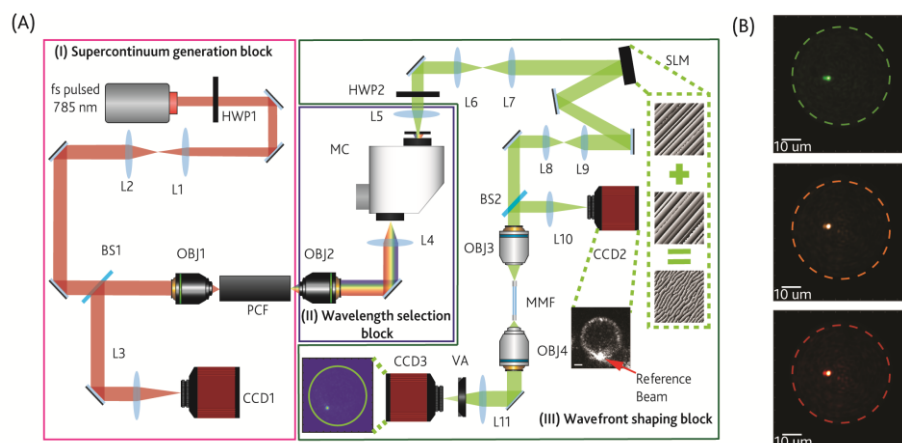


Figure 1: A) Schematic representation of the optical setup. Three main blocks can be identified: (i) the supercontinuum generation block, achieved by pumping a femtosecond laser inside a photonic crystal fiber, (ii) the wavelength selection block, obtained with a monochromator, and lastly (iii) the wavefront shaping block, where light modulation implemented with a phase-only spatial light modulator. B) Focusing spot obtained in a 50 μm core multimode fiber at three different wavelengths: 570 nm, 600 nm and 633 nm.

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Theoretical approach of electromagnetic energy conversion into heat via different types of light source

Part I – Determination of absorbed energy

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This work proposes the method how to describe theoretically the light conversion into heat via different light sources. As a test system, a glassy platform is selected where gold nanorods are deposited on the surface, and serve as a heat source. The total absorbed light intensity, \check{S}_e^{TOT} , which is directly responsible for the heat conversion, is calculated analytically following Rayleigh-Drude approximation, is based on the formula [1,2]:

$$\check{S}_e^{\text{TOT}} = \frac{\int_{\lambda_o}^{\lambda_k} \left(\sum_i^N \left(W_i \cdot (\sigma_{abs_i})_{\lambda, \phi_i, L_i} \cdot I_{abs_i} \right) \right) d\lambda}{\int_{\lambda_o}^{\lambda_1} d\lambda}$$

where: λ is the incident wavelength; I_{abs_i} is the intensity absorbed by the particles; W_i is the particles' polydispersity; σ_{abs_i} is the absorption coefficient; ϕ_i is particles spacing; L_i is the depolarization factor; N is the total number of particles and i is assigned to subsequent particle.

Figures 1 examine first results of the absorbance spectra so as to predict which of the nanoparticle's properties are crucial to reach the highest temperature, which may be applied in the future in germs' metabolism processes inactivation or energy processes.

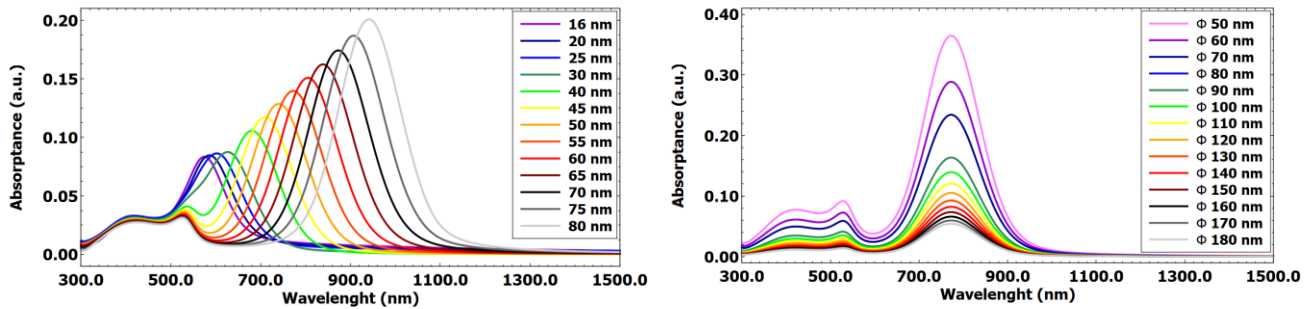


Figure 1. Calculated absorbance spectra for different nanorods' (left) aspect ratio and (right) distance from one another

Keywords: heat transfer, energy conversion, gold nanorods

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Enhancement of Circular Dichroism Response of Biological Chiral Molecules mediated by Plasmonic Nanoparticles

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Circular Dichroism Spectroscopy (CD) contribute to obtaining structural information of a several number of organics and biological molecules. CD define the phenomenon of a different absorption of circularly right-handed and left-handed polarized light given by a chiral molecule ^[1].

In biomedical context the interaction between light and chiral matter is significant not only for the influence on biological basic functions; using different enantiomeric forms of chiral biomolecules as biological markers permit the identification, the prognosis, and the monitoring of different diseases.

However, the biological molecules size is small compared to the wavelength of the incident light and as consequence the dichroic signals obtained are usually weak and difficult to measure ^[1].

This aspect is improved by considering the interaction of chiral biological molecule with plasmonic nanoparticles which enhance the dichroic signal (superchirality) and cause a shift of the CD bands in the visible region of the electromagnetic spectrum ^[2].

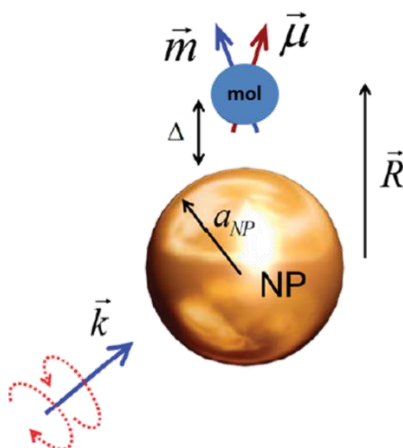


Figure 1: Representation of the interaction between a chiral biological molecule and plasmonic nanoparticle.

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Theoretical approach of electromagnetic energy conversion into useful heat via different types of light source

Part II – Source implementation into CFD numerical methods

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Computational fluid dynamics (CFD) brings a huge opportunity to solve many different and complicated mathematical formulas, which is commonly preferred for problems from advanced optics, thermodynamics or particle flow. In this work, the proposed model of absorbed energy determination, which has been being developing by the authors in Part I, allows to implement any electromagnetic source, throughout lasers, via white-light lamp, to the solar radiation. In this work, the general set of equations taking into account the balance of mass, momentum and energy along with the turbulence evolution formulae can be generally described as [1-3]:

$$\frac{\partial}{\partial t} \begin{pmatrix} \rho \\ \rho \vec{v} \\ \rho e \\ \rho \mathbb{k} \\ \rho \epsilon \end{pmatrix} + \text{div} \begin{pmatrix} \rho \vec{v} \\ \rho \vec{v} \otimes \vec{v} \\ \rho e \vec{v} \\ \rho \mathbb{k} \vec{v} \\ \rho \epsilon \vec{v} \end{pmatrix} = \text{div} \begin{pmatrix} 0 \\ \vec{\tau} - p \vec{I} \\ (\vec{\tau} - p \vec{I}) \cdot \vec{v} + k_t \text{grad}(T) \\ (\mu + \mu_t / \text{Pr}_k) \cdot \mathbb{k} \\ (\mu + \mu_t / \text{Pr}_\epsilon) \cdot \epsilon \end{pmatrix} + \begin{pmatrix} 0 \\ \rho \vec{g} \\ \check{S}_e^{\text{TOT}} \\ S_k \\ S_\epsilon \end{pmatrix} \quad (1)$$

where, the total irreversible momentum flux and energy source are defined, respectively, as:

$$\vec{\tau} = \text{grad}(\overline{X^\dagger}) - \frac{2}{3} \mu I_{\vec{d}} \vec{I} + 2\mu \vec{d} - \frac{2}{3} (\rho \mathbb{k} + \mu_t \cdot I_{\vec{d}}) \cdot \vec{I} + 2\mu_t \cdot \vec{d} \quad (2)$$

$$\check{S}_e^{\text{TOT}} = \frac{\int_{\lambda_0}^{\lambda_k} \left(\sum_i^N (W_i \cdot (\sigma_{abs_i})_{\lambda, \phi_i, L_i} \cdot I_{abs_i}) \right) d\lambda}{\int_{\lambda_0}^{\lambda_1} d\lambda} \quad (3)$$

Moreover, both particles and continuum media may be adjusted to different multiphase models in the future. Therefore, the electric-insulated system, mentioned in the part I, is examined using CFD numerical methods where different light source's types (laser, lamp, solar radiation), profiles (gaussian, flat-top, etc.) and time modes (continuous, pulse, etc.) are considered. Results reveal that gaussian pulse green lasers should be utilized in order to obtain the maximal temperature increase, whereas high-power white light lamps are appreciated to reach high average temperature in the system.

Keywords: heat transfer, energy conversion, gold nanorods

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Hybrid nanostructures for white light-triggered and thermoplasmonic-based healthcare applications

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The Covid 19 pandemic has promoted increased personal protective equipment (PPE) production. Face masks have been crucial in controlling the pandemic's spread among PPE. Face masks are classified according to the different sizes of pathogens and various transmission mechanisms. FFP2 face masks have rapidly become the first choice for indoor use since they provide 94% of filtering efficiency for viruses and bacteria. However, the difficulty of medical waste disposal contributed to environmental pollution. New methodologies are continuously developed to minimize the environmental impact, such as the decontamination methods that usually are more effective on surgical masks but often provoke damage to the thin device. This work presents our latest results in nanomaterials-based smart face masks. To this end, a new generation of broadband hybrid nanomaterials is integrated into FFP2 face masks. This highlights the extraordinary capability to produce innovative personal protective equipment with white-light-assisted and on-demand disinfection properties. The realized system is studied in optical, morphological, spectroscopic, and viability assay experiments. Our findings are pioneering a unique opportunity for personal protective equipment and healthcare facilities since the reported methodologies allow non-hazardous disinfection of medical devices by simply using a conventional white light lamp and, in the next near future, smartphone torches.

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