LASER SPECTROSCOPY AND OPTICS GROUP (LSO)
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**COMPETENCES**

* Laser spectroscopy of milli-, micro- and nano-droplets.
* Microdroplet lasers.
* Laser beams unresonant interaction with microdroplets: optic, elastic and mechanical phenomena.
* Biomedical applications of lasers: basic science and applications in biomedicine and environment control.
* Laser methods in fighting multiple drug resistance on earth and in outer space.
* Generation, spectroscopy and optics of foams and emulsions.
* Droplets in pollution control.
* Foams and emulsions in life sciences.
* Lasers in optofluidics and microfluidics.
* Droplets spectroscopy and optics in outer space.
* Nanospectroscopy and nanooptics.
* Laser methods in energy saving materials and systems.
* Chaotic properties of laser beams: fundamentals and applications.
* Materials characterisation by spectroscopic and optical methods: UV-VIS-NIR absorption, standard fluorescence, laser induced luminescence (fluorescence and phosphorescence), Raman, FTIR, interferometry, microscopy, holography, spectrometry.
* Laser methods in conservation of cultural heritage: picture, sculpture, ephemeral opera and graffiti, music, archaeology, buildings preservation.
* Spectroscopy and optics in extreme natural and laboratory environment.
* Thin layer chromatography (TLC) and LC-TOF/MS to monitor complex molecular systems.
* Spectroscopic methods in monitoring environment pollution of gases, liquids, soil and biosphere: cavity ring down spectroscopy (CRDS), optoacoustic spectroscopy, laser induced breakdown spectroscopy (LIBS), laser induced luminescence (LIL: LIF&LIP), autofluorescence.
  ● Wave and beam testing of optical and mechanical components by laser interferometry.
  ● Nanomaterials, nanoparticles obtained by LAL.
  ● Lasers, plasma and radiation methods and techniques for development of emerging technologies in health, energy, security and environment.
  ● Observing the outer and Earth space with systems in the THz or visible field.
  ● Spectroscopy and imaging in THz.
  ● Optics of standard and new materials: metamaterials, nanostructures, biomaterials.
  ● Development and applications of hyperspectral systems.
  ● Testing power and high-power waves.
  ● Structuring azopolymeric materials for applications in biosensors and electronics.
  ● Applying mathematical formalisms calculation for optical propagation in normal and extreme optical phenomena.
UPDATED RESULTS

1. Generation of nano- and micro- droplets which propagate at supersonic and hypersonic speeds by unresonant interaction of a laser beam with millimeter-sized droplets

   The unresonant interaction of pulsed laser beams with liquid microliter droplets takes place when droplet material is not absorbing the laser beam. Results:
   * damped deformations and vibrations of parent droplet;
   * emissions of aerosols (nano-, micro-droplets);
   * emission of jets of liquid at supersonic speeds and of microdroplets (microbullets) and nanodroplets (nanobullets) at supersonic and hypersonic speeds;
   * production of cylinder channels in parent droplet that leads to formation of air bubbles inside it.

2. Microspheric lasers with liquid active medium.

   Lasers based on resonant interaction of pumping laser beams with droplets.

   Selected organic fluorophores are an ideal platform to build micro-lasers, based on high cross sections of light absorption that generate high emission efficiency. Micro-lasers may have high quality factor, low threshold energy and emission band tuning.
Micro-spherical particles and resonance cavities have distinct spectroscopic properties compared to centimeter active media.

Micro-laser characteristics depend on chemical composition of active media and their shape and dimensions. Resonant optical phenomena obtained in such geometries are known as cavity or morphologically dependent resonances i.e. whispering gallery modes (WGMs).

3. Microfluidic measurements of medicine solutions (surface tension and contact angles).

Droplets are components of daily life with multiple roles. A droplet “component” which plays a role in understanding its behaviour, is the surface it “shows” to environment. The shape of an unperturbed droplet is determined by surface tension that tends to decrease surface/volume ratio and gives its spherical shape and gravity that tends to deform it. There is an increased interest to use droplets with milli-, micro-, and nano-meter dimensions in industry, medicine, space science. This created new research domains in which small volumes behaviour at interaction with light beams is studied. The droplets may contain not only liquids but foams and emulsions as well.

The properties of micro and nano-droplets are not entirely known and measurements of surface or interfacial tension are needed due to its effects such as: leaves floating on lake surface, a drop of water climbing to the edge of a surface until its mass is high enough so that the weight defeats adhesive forces that keep it on the surface and it falls down, an insect “walking” on water, etc.

Another characteristic is the contact angle made by liquids with a solid surface. It allows quantitative measurements of a material surface wettability and highly depends on surface tension value: small surface tension is associated with high wettability.
A liquid may be wetting (contact angle smaller than 90°) or not wetting (contact angle between 90° and 180°) a surface. A hydrophilic surface belongs to a material with a special affinity to water, on which the water spreads. In contrast, a hydrophobic surface is repelling water and therefore it has a contact angle higher than 90°. Superhydrophobic surfaces have contact angles higher than 150° for the same kind of substrate.

Within the LSO at INFLPR the surface tension and contact angle measurement are performed with a Drop and Bubble Shape Tensiometer PAT-1 from Sinterface.

4. **Study of microfluidic properties of millimetric droplets which contain laser irradiated drugs in hypergravity conditions.**

Experiments have been carried out under the effect of simulated hypergravity conditions regarding the interaction of laser modified medicine solutions with hydrophilic and hydrophobic target surfaces by using the Large Diameter Centrifuge facility under the aegis of the European Space Agency.

**Droplets shapes at different gravitational acceleration values**

Medicine impregnated target surfaces may play a significant role in developing new drug delivery systems. Since microorganisms can survive, grow and even proliferate under high g-level conditions causing threats to health of astronauts as well as to the reliability of spacecraft, such wetting processes under increased gravity may constitute a useful tool in space medicine.
5. Generation of drugs foams and emulsions and their spectroscopic and microscopic study.

a. Eighteen years ago, our partners Instituto Medico Laser (IML, Madrid, Spain) and Instituto Medico Villafortuny (Cambrils, Spain) observed that applying Nd:YAG laser beam and irradiate tissue immediately after injection of Polidocanol microfoam, the venous lesions cleared almost completely, and the effects achieved appeared to be permanent. Several trials demonstrate these extraordinary performances and the protocol was added to their daily practice as a recommended complementary treatment for large areas of varicose veins. Extensive optical studies were made to better understand physical processes involved in the evolution of foaming Polidocanol but also laser beam influence on this sclerotic agent. Experimental observations allow to set new treatment conditions to assure a better penetration of laser radiation in the tissue and more efficient modification of drug molecules, there.

b. Emulsions were generated by Tessari method by combining STS and Vitamin A. The stability of these emulsions was analyzed.

![Stability over time of vitamin A and STS emulsions obtained by Tessari method within the first 24 hours of preparation](image1)

![Microscopic reflected image (AxioCamMR5, Zeiss, 20x) of a STS-vitamin A (1.6: 0.4) foam](image2)

![Microscopic reflected images (AxioCamMR 5, Zeiss, 50x) of a STS-vitamin A (1.6-0.4) foam](image3)
6. Development of new, laser related methods to generate stable foams and emulsions containing medicines

Studies on foam generation by exposure of Vancomycin solutions in water to pulsed laser beam emitted as 4\textsuperscript{th} harmonic of a Nd:YAG laser beam were made. Foams generation in Vancomycin solutions during laser irradiation imply bubble nucleation, most probably generated by transient acoustic waves induced by laser pulse. In the process, modifications of Vancomycin molecules are identified.

\textit{Foaming in droplets containing Vancomycin HCl solutions in ultrapure de-ionized water produced by irradiation at 266nm & 532nm. Droplet volume: 5 \mu L.}

A new method to generate emulsions has a starting point in the Tessari emulsifying procedure, but is developed to be fully automated. We developed a software that controls a two-syringe Hamilton diluter/dispenser to mix a water – based surfactant/medicine (Polidocanol, STS) and an oily component (Vitamin A). The generated emulsion is then exposed to laser radiation in order to obtain nano-/micro-emulsions.

7. Interferometric microscopy systems with increased contrast in view of biomedical applications

Cells and biological tissues are mostly transparent under visible light due to their low absorption and weak scattering. Bright field microscopy provides intensity information regarding the analyzed sample. Since the samples analyzed by microscopy are very thin, the intensity of the incident light is not altered enough, but instead, a shift in phase is introduced due to variation of refractive index.

Recently, quantitative phase imaging (QPI) has emerged as a valuable tool for living cell imaging, especially because it is label-free and nondestructive. QPI relies on the principle of interference, whereby an image field is overlaid with a reference field. As a result, even the most transparent objects, such as unlabeled live cells, can be imaged with high contrast and sensitivity using phase information of the field. Since the phase of the image field is measured quantitatively, it can report on both thickness and dry mass density of the specimen. With the recent advances, QPI has become a significant method for studying live cells, such as red blood cell dynamics, cell growth, cell dynamics and cell tomography.
Phase maps of an unlabeled prostate biopsy obtained by wDPM, with the color bar indicating phase in radians

Quantitative phase image of an ChR2 active neuron with units in optical pathlength (OPL)

Using its multi-scale coverage and high sensitivity to sub-nanometer changes in optical pathlength, QPI has also found applications in neuroscience and enabled non-invasive studies of neurons at both single-cell level and network level. A system for QPI measurements is developed by LSO in collaboration with Quantitative Light Imaging Laboratory, University of Illinois at Urbana Champagne.

8. Laser systems with chaotic emission.

Semiconductor lasers which have nonlinear dynamics (e.g. in external optical feedback conditions) are studied as physical systems and are useful in engineering applications for encoding information transmission.

External feedback generates phenomena out of which the most studied is the chaotic behavior. When the laser is operated near emission threshold, the time evolution of the beam intensity shows low-frequency fluctuations (LFF). Chaotic synchronization regimes and optical spectrum behavior of two coupled lasers, one operating in LFF regime and other having free emission, depend on the similarity of spectral structures of the uncoupled lasers emissions. Dominant active laser modes of the coupled system emission coincide with the laser modes of the one or both uncoupled lasers emissions function of operating synchronization regime. Changes in optical spectrum of the coupled system are associated with synchronization regimes. Power repartition between the active modes of a coupled system allows identifying synchronization regime.

9. Light triggering of drug carrier systems for targeted delivery and controlled release

Photochemical and photophysical characterization of novel drug compounds are of interest for site specific and targeted delivery. Studies are performed using advanced laser spectroscopic techniques (LIF-laser induced fluorescence, time resolved phosphorescence, transient absorption, FTIR spectroscopy). These techniques have advantages: selectivity, high sensitivity, real time monitoring of products and intermediates during irradiation.
Basic data such as quantum yield of oxygen singlet generation, fluorescence lifetime, triplet quantum yield and lifetime, and reaction rates are obtained and may be used to optimize drug therapy by developing new drug delivery systems or therapeutic regimes. Data are provided for further in vivo testing of compounds, to establish optimal protocols for preclinical tests.

Linker cleavage by generated singlet oxygen. FTIR analysis of photoproducts.

Phosphorescence decay of singlet oxygen for conjugated SWCNT-Verteporfin compared standards

10. Hyperspectral systems

Experimental systems of imaging spectrometry or hyperspectral systems (for the UV-VIS field, 250-1100 nm) are developed, for applications in: biology, medicine, remote sensing, and mineralogy. Imaging spectrometer is a 3D recording system: two dimensional parameters and one spectral. The system does not provide a classical image. The recording systems are based either on classical dispersion (with gratings), or on interferometry systems (Mach-Zehnder interferometer, polarization interferometer).

Hyperspectral system for NDT of emissive photonics elements developed with Czerny – Turner monochromator using „push broom“ system to scan the dimensional parameters.
The 3D hyperspectral experimental system, developed to-date, includes a Czerny – Turner monochromator which uses two gratins (with a pitch of 600 or 1200 l/mm) and a matrix camera CCD (1024 x 128 pixels). The system enables imaging recording in UV-VIS with spectral resolution of 0.156 nm or 0.078 nm. By design, the system can be adjusted for objects placed on a large distance (2-3 m), by using photo objectives with large focal distance but also for microscopic bio-systems, for which microscope objectives are used.

![A hyperspectral image from the registered “data cube”](image)

![The reconstructed 2D image of the object (three vertical color LEDs )](image)

For the dimensional scanning of the sample, it is set a „push broom” system that „brooms” with equal steps the sample (providing the image resolution).

The entire system and the 3D „data cube” are computered recorded.

11. THz-TDS system applied in imaging and spectroscopic analysis of compounds.

A THz-TDS system working in the (0.2-4) THz spectral range, may give information about vibrational spectra of molecules. Based on it, a number of systems were built and specific experiments were performed covering a large area of applications: imaging (2D or hyperspectral), spectra dedicated to detection of compounds (dangerous and hazardous substances, hidden and/or sensible objects) aiming security issues, forbidden signaling substances and/or spectra measurements for quality and quantity detection.
Beam profile of the THz beam in the focal plain

Thz beam profile through a super-resolution technique: a) convolution image b) image deconvolution

Absorption spectra of alcohol with different concentration (100%, 50%, 33%) and alcohol medicinal (70%-alcohol with some other substances: methyl salicylate, methylene blue)

Absorbance spectrum of Imidacloprid 4 g/l (a pesticide)

THz spectra for the E102 azoic food dye (in order up down: powder, liquid, and dried - last two were on a paper sheet)

Coumarin absorption spectra in THz domain
12. **Stylus Profiler XP-2 from Ambios Technology**

The XP-2 stylus-type surface profiler in our laboratory, provides precision surface topography measurements on a wide variety of substrates with 1.5 Å vertical resolution. The system is ideal to obtain high resolution for step height measurements, surface form and roughness, thin film stress, high resolution 3D surface imaging and for other geometrical surface measurements. It is noted that the instrument used optical deflection height-measurement sensor similar to that used in AFM systems and provides the lowest mass and inertia among any other commercially available instruments. The measurements are made with a stylus having 2 µm radius, stylus force range 0.05-10mg and sample stage 200mm.

![3D images on a metallic surfaces with the Profilometer](image-url)
Profile and 3D images on a polimeric surfaces with the Profilometer