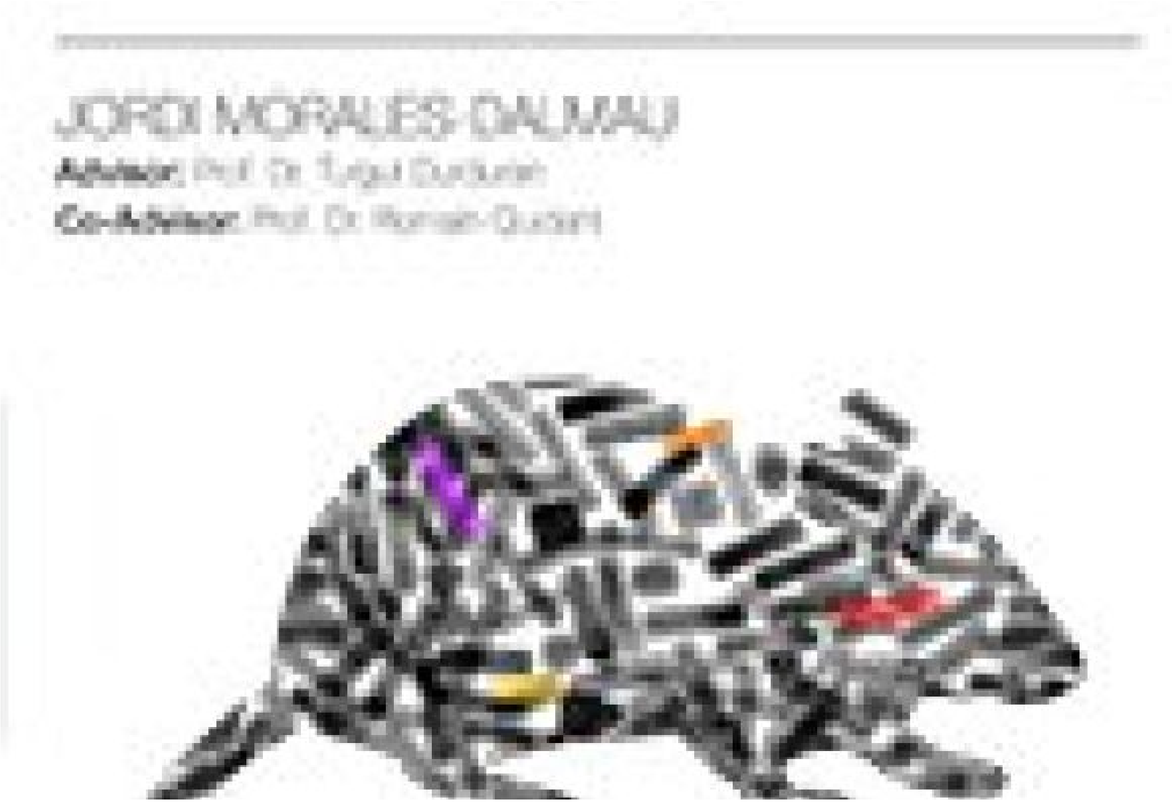

PhD Thesis Defense JORDI MORALES DALMAU 'From Cells to Tissues, Microscopy to Modeling: Towards Precise, Data-Driven Photothermal Therapy with Gold Nanorods'

JORDI MORALES DALMAU

February 15, 2019

Friday February 15, 11:00, ICFO Auditorium

JORDI MORALES DALMAU

Medical Optics

ICFO-The Institute of Photonic Sciences

Suspensions of gold nanorods (GNRs) are emerging as potential drugs to address some of the limitations in traditional biomedical sensing,imaging and therapy.

They are inorganic nanoparticles with good biocompatibility, with established protocols for flexible surface functionalization, with scalable production methods and with tunable light absorption. Of particular relevance for this thesis work, GNRs turn into efficient nano-sources of heat when illuminated at the wavelength of their maximum absorption peak, which is due to their longitudinal surface plasmon resonance (LSPR).

This property has been exploited, for instance, in plasmonic photothermal therapy (PPTT) to produce controllable and localized cellular death. Nevertheless, the introduction of PPTT in the clinics has been slow owing to the complexity of its implementation involving biochemistry and physics across multiple scales and disciplines.

Therefore, this work aimed at developing a set of tools capable to study, control and optimize the different mechanisms involved in PPTT, ranging from experiments on cell cultures to small animal models.

By carrying out a systematic study with ten different types of GNRs in suspension.
I have delimited the optimal shape and surface chemistry of GNRs for PPTT in terms of heating generation efficiency, cellular internalization and cytotoxicity. I have measured their heat generation over time at different laser powers and concentrations, and compared it with simulations. I have studied their accumulation in vitro and in vivo by developing a protocol to use two-photon luminescence microscopy as a quantitative tool, validated it against the standard inductively coupled plasma mass spectroscopy, and observed their toxicity over time.
Then, I have developed a hybrid platform to study different in vivo PPTT conditions with integrated therapeutic and monitoring modules. The therapeutic module controlled the irradiation area, power density and exposure time of the
laser emitting at the LSPR of GNRs. The monitoring module combined thermal imaging and non-invasive diffuse optical spectroscopy, including diffuse correlation and diffuse reflectance spectroscopies. In the specific case of murine renal tumors, the results have shown the feasibility using the hybrid, diffuse optical hand-held system to monitor changes of in vivo physiology under different PPTT conditions.

I have quantified and related the significant physiological changes to post-therapy tumor volume and histology measurements, which has been validated with Monte Carlo simulations of photon propagation in tissues coupled to the three-dimensional solutions of the bioheat equation.

With this work, I have laid the foundations towards personalized plasmonic photothermal therapy research on animals and its potential translation to humans.

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Thesis Advisor: Prof Dr Turgut Durduran