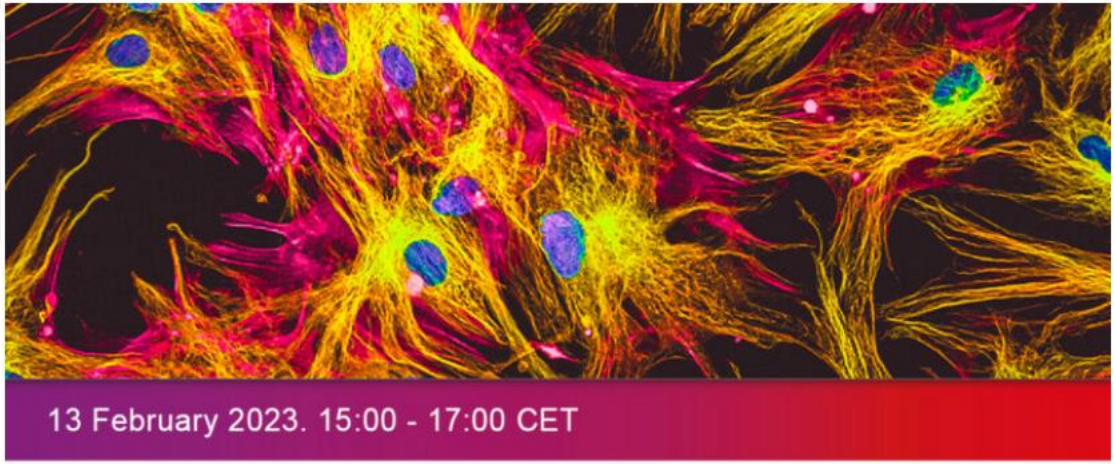
INTERNATIONAL IBERIAN NANOTECHNOLOGY LABORATORY

Advanced functional optical microscopy for nanoscale sensing and bioenergetic imaging

Jana B. Nieder

Research Group Leader

Ultrafast Bio- and Nanophotonics



EPIC
EUROPEAN PHOTONICS INDUSTRY CONSORTIUM

INTERNATIONAL IBERIAN NANOTECHNOLOGY LABORATORY

47,000 sqms

100 MEur investment

23 R&D Groups

100's Collaborations with companies

State-of-the-Art Electron Microscopy Imaging and Spectroscopy Facilitiy

1000 m² **State-of-the-Art** Cleanroom Facility

State-of-the-Art Nanophotonics Flagship Facilitiy

Vision

To be a recognised Leading Global Nanotechnology Innovation Hub

Mission

Exploring Interfaces

Interdisciplinarity

Technologies, Applications, and Resources under one same roof

24 Research groups working in 6 research clusters

FACILITIES

Open Access Facilities

The INL user facilities allow access not only to their infrastructure and systems but also to microsystems and nanotechnology experts and their knowledge with considerable flexibility. Access is open to both internal and external users. The user facilities provide support throughout all research and development chain in cleanroom processes (device modelling and design, process integration and device fabrication, packaging and testing) as well as in advanced microscopy and spectroscopy, X-ray diffraction and scattering techniques, photonics and bioimaging and magnetic resonance imaging.

Another impacting factor is the heterogeneous set of techniques available under the same roof leading to competitive integration of different technologies and rapid prototyping thus paving the way to methods and devices with performances out of reach of a given single technology.

The full list of equipment available at INL can be consulted here.

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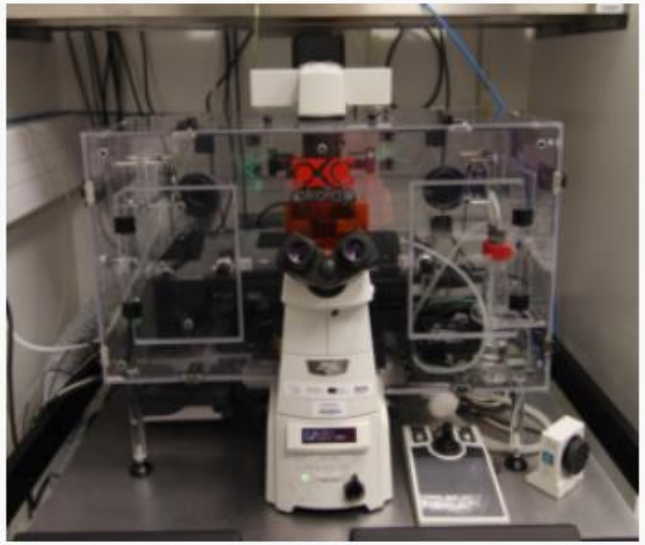
Commercial Bioimaging – Advanced Optical Microscopes

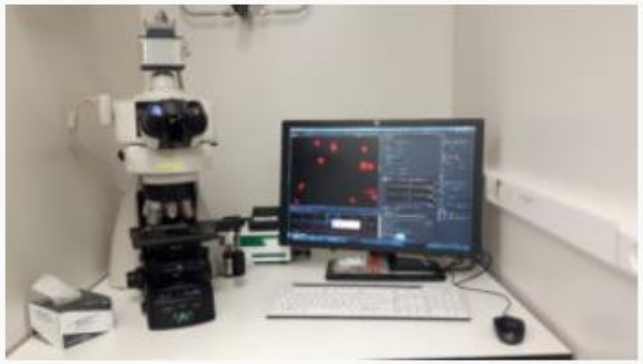
Access and user support

Nikon Ti-E TIRF/dSTORM – Widefield microscope



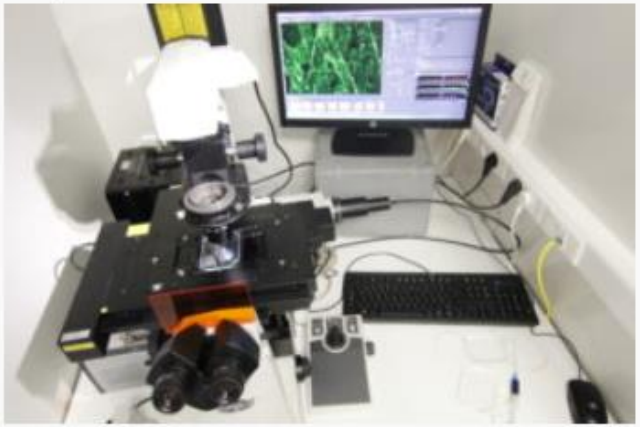
Zeiss LSM 780 – Confocal microscope

Nikon Eclipse Ni-E – Upright fluorescence microscope

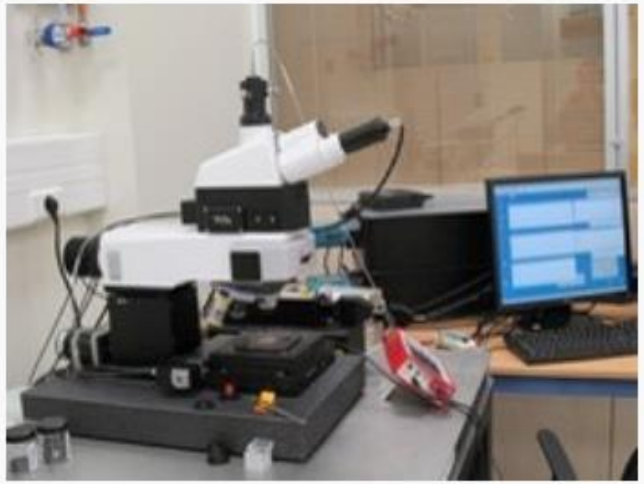


Nanolive 3D Cell explorer

Nikon Eclipse Ti-E – Inverted fluorescence microscope



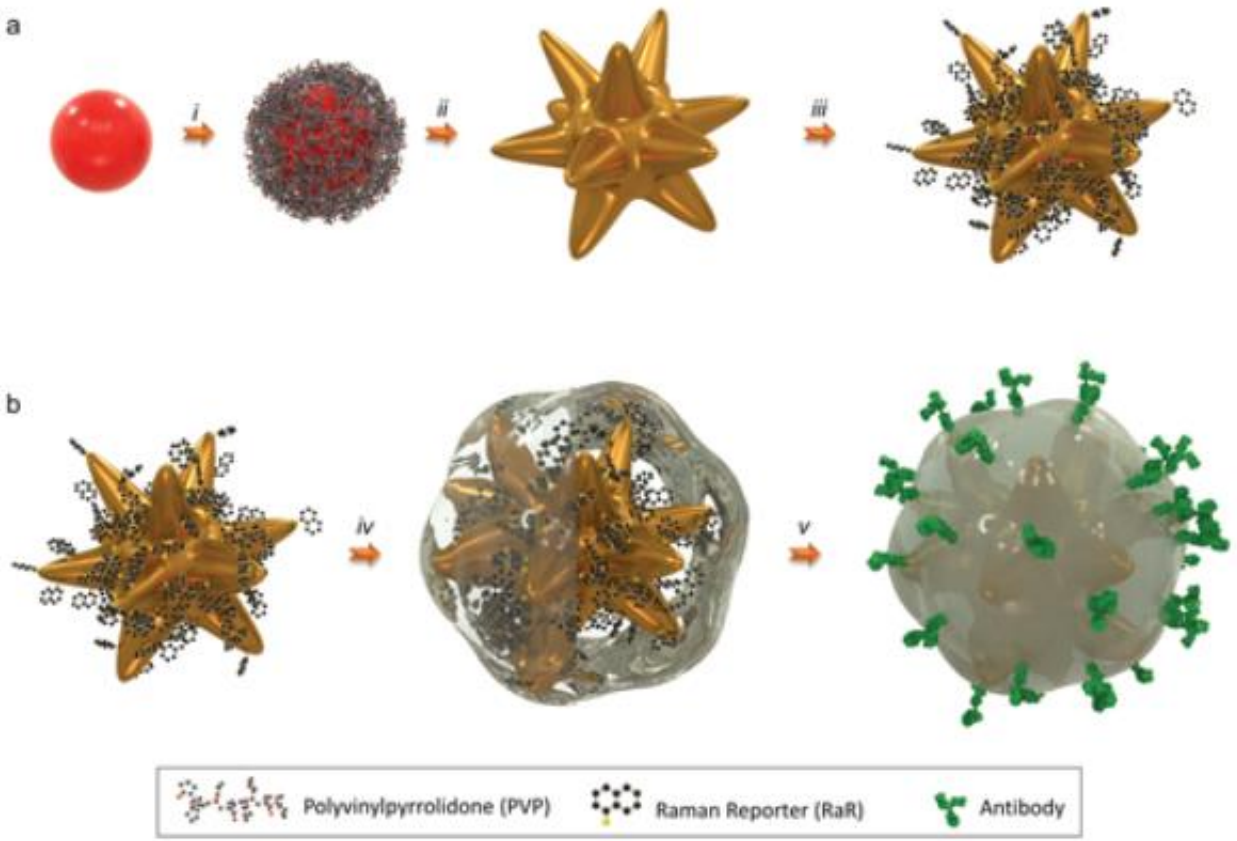
Witec Alpha 300R – Confocal Raman microscope



Example - Bioimaging Solutions for R&D in Precise Personalized Health Tech

Example

SERS-Based Single-Cell Multiplex Phenotyping

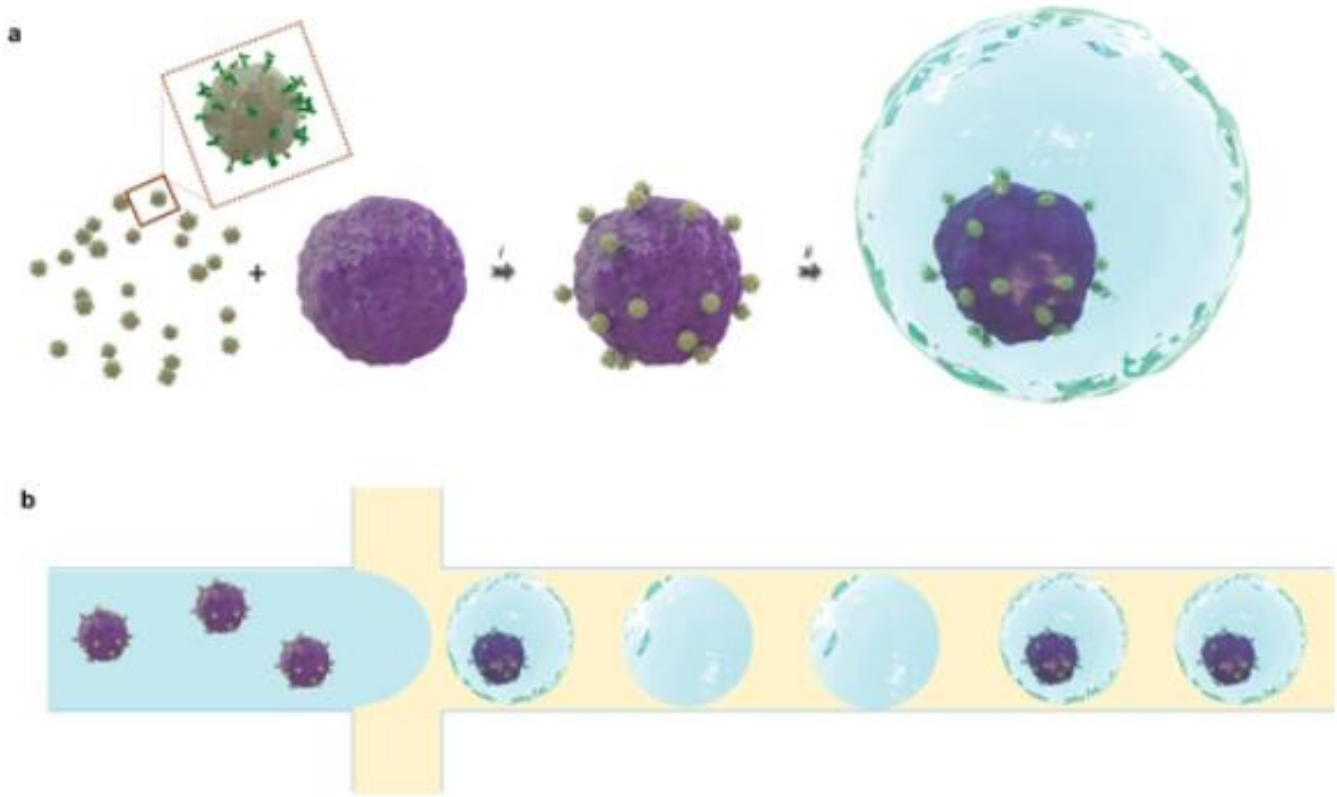


Oliveira, K., .. Diéguez, L., Abalde-Cela, S., Multiplex SERS Phenotyping of Single Cancer Cells in Microc
Optical Mater. **2023**, 11, 2201500

Example - Bioimaging Solutions for R&D in Precise Personalized Health Tech

Example

SERS-Based Single-Cell Multiplex Phenotyping



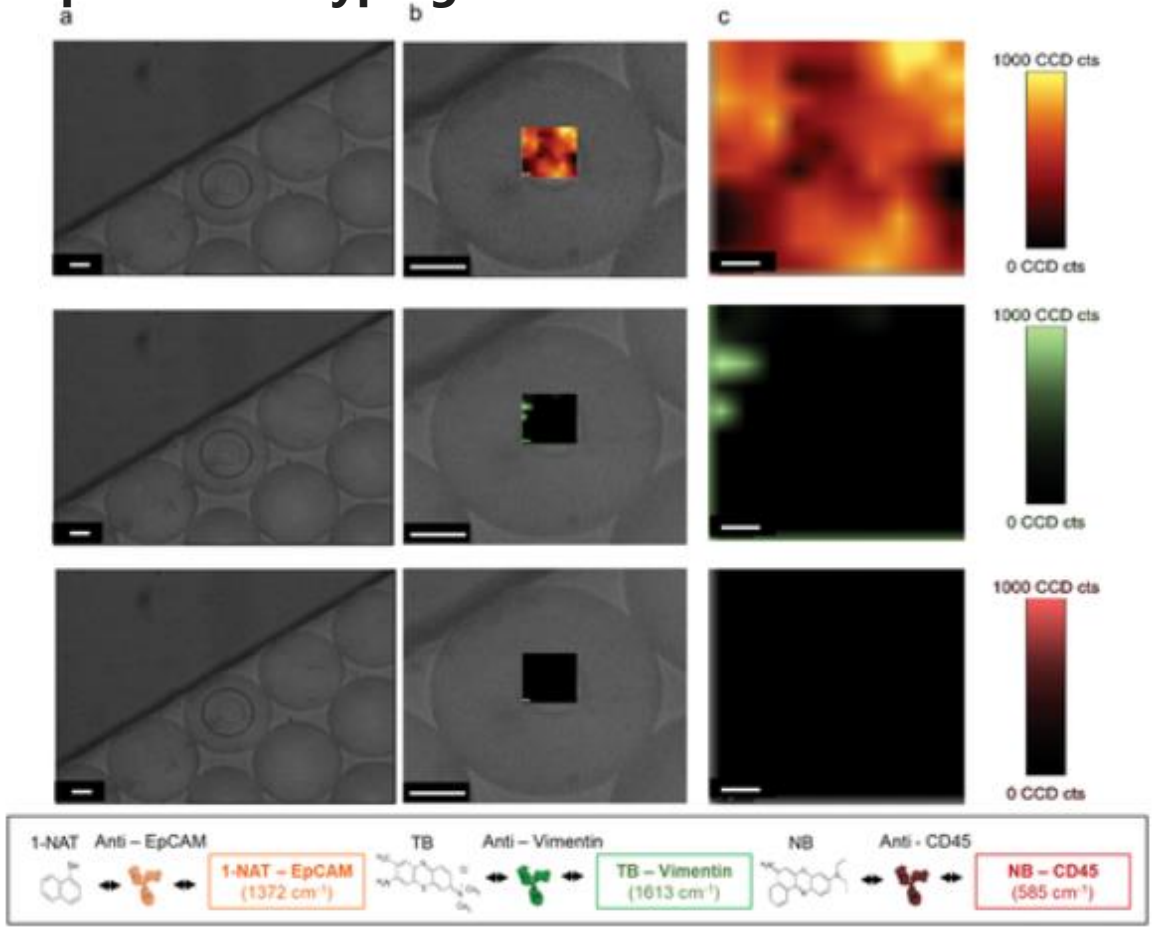
Oliveira, K., .. Diéguez, L., Abalde-Cela, S., Multiplex SERS Phenotyping of Single Cancer Cells in Microdroplets. *Adv. Optical Mater.* **2023**, 11, 2201500

Example - Bioimaging Solutions for R&D in Precise Personalized Health Tech

Example

SERS-Based Single-Cell Multiplex Phenotyping

Cancer cells are labeled with different SERS tags that recognize membrane proteins and encapsulated individually in microdroplets. Afterward, single cells within microdroplets are imaged by SERS spectroscopy.



SERS Characterization

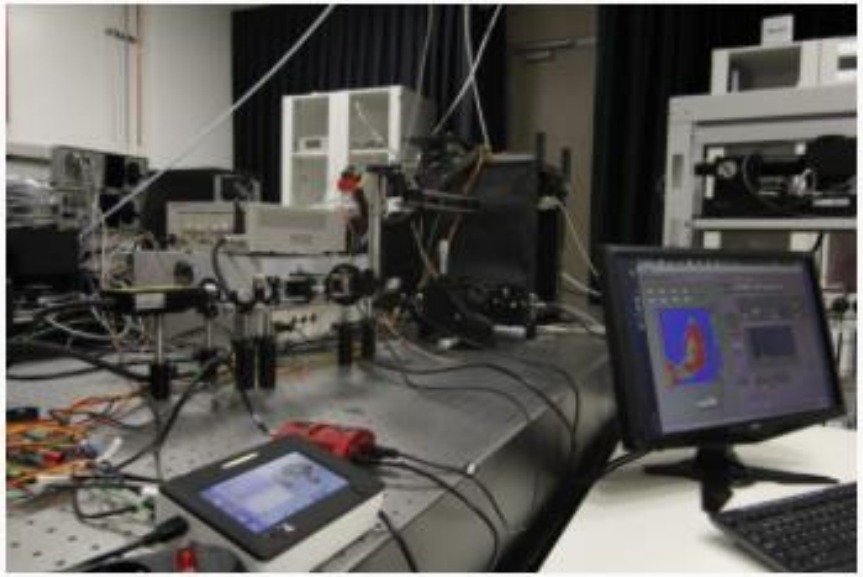
Raman measurements were carried out in a 300R Confocal Raman microscope (WITec) using a 785 nm laser line grating (600 gr cm^{-1}) as the excitation source and 10× and 20× objectives. Acquisition of liquid samples, normalized to obtain a final concentration of Au of 1 mm, were performed for 1 s and five different scans (using objective 10×). The Raman power was set at 70 mW.

Oliveira, K., .. Diéguez, L., Abalde-Cela, S., Multiplex SERS Phenotyping of Single Cancer Cells in Microdroplets. *Adv. Optical Mater.* **2023**, 11, 2201500

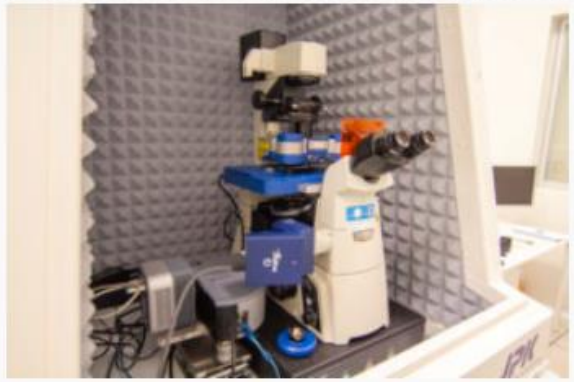
Customized Bioimaging – Advanced Optical Microscopes

Dedicated development for specific needs, resolution, multifunctionality

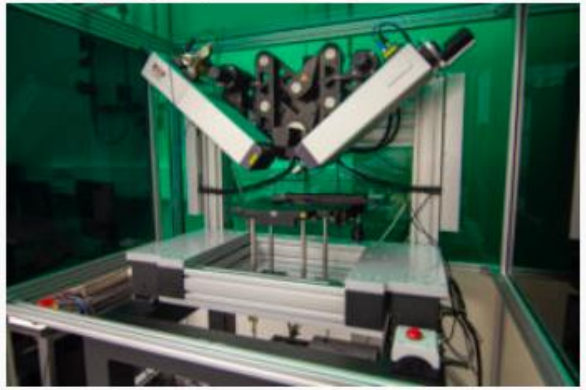
Multiphoton, Second Harmonic Generation and Fluorescence Lifetime Imaging Microscopy (FLIM) – Inverted microscope platform –



Andor Revolution DSD combined with JPK Nanowizard 3 Combined fluorescence and atomic force microscopy



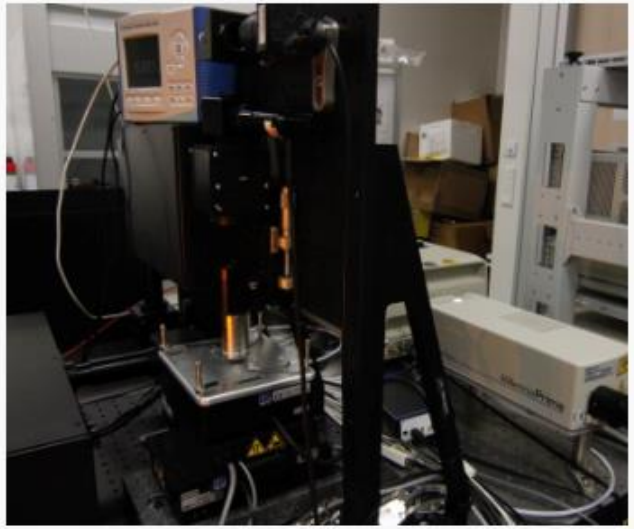
Spectral imaging ellipsometer AccurionNanofilm_ep4



Nano-/ Microfabrication & Bioimaging

Combination of Nano-/Microfabrication and advanced Bioimaging tools

Microfabrication work station and ultrafast femtosecond laser



Example 3D scaffolds fabricated by two photon polymerization

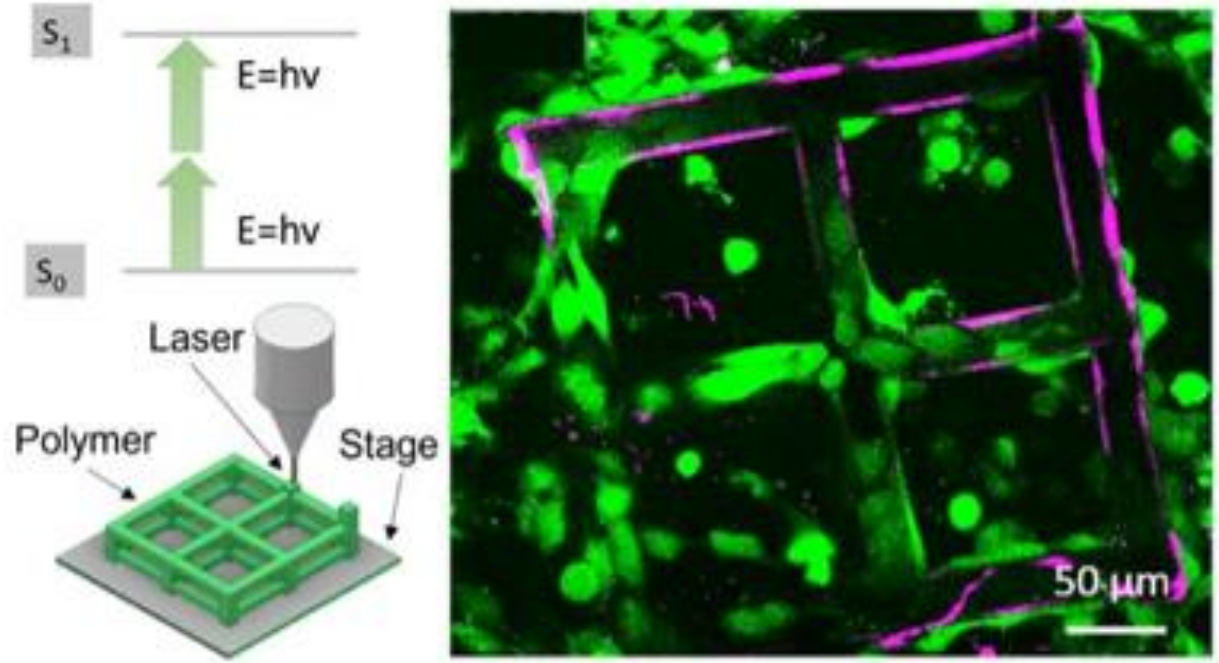
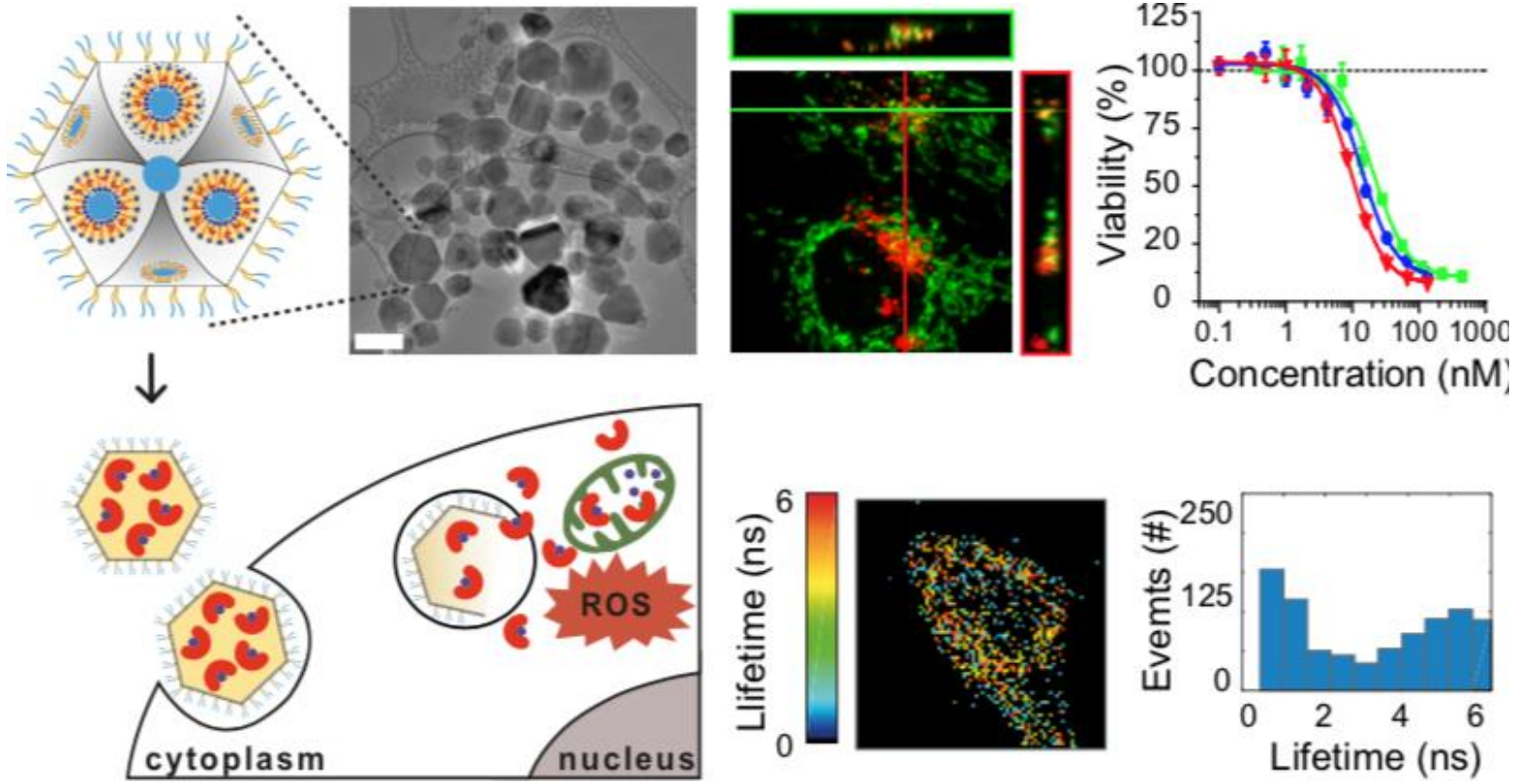


Figure 1: Top left: Schematic of the two-photon absorption process for Two-Photon Polymerization (TPP). Bottom left: Schematic representation of the TPP process tracing a log pile cell scaffold. Right: Confocal fluorescence images of bone marrow mesenchymal stem cells interacting with SZ2080 structures functionalized with fibronectin taken with a 20× microscope objective, reproduced from [1].

Costa B.N.L., Adão R.M.R., Maibohm C., Accardo A., Cardoso V.F., Nieder J.B. Cellular Interaction of Bone Marrow Mesenchymal Stem Cells with Polymer and Hydrogel 3D Microscaffold Templates. *ACS Appl. Mater. Interfaces.* 2022;14:13013–13024.

Label free cellular bioenergetics via Multi-Photon Fluorescence Lifetime Imaging Microscopy (MP-FLIM)

Example – label free mapping of a drug delivery system's efficacy to deliver anti cancer drugs



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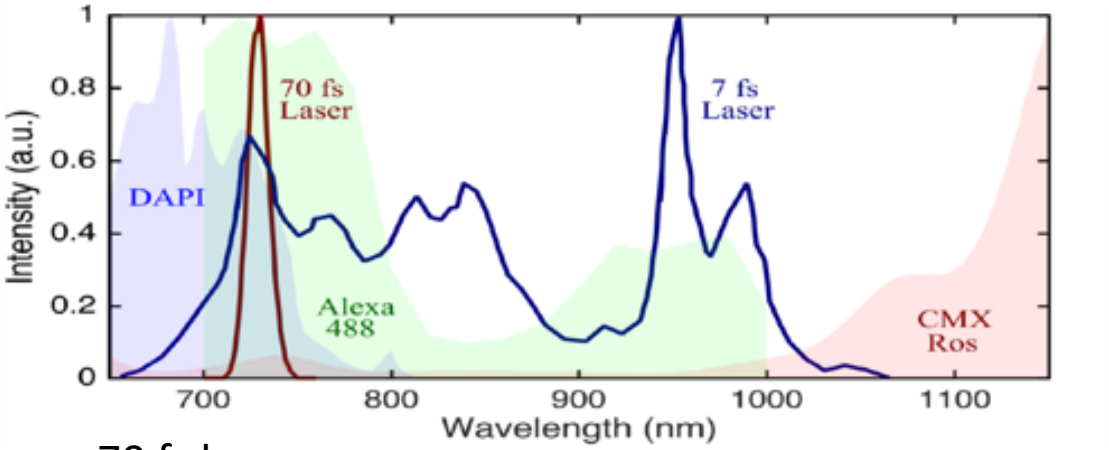
Faria, A.R.†; Silvestre, O.F.† et al., (2019) ***Nano Research, Vol** 12; 5.*

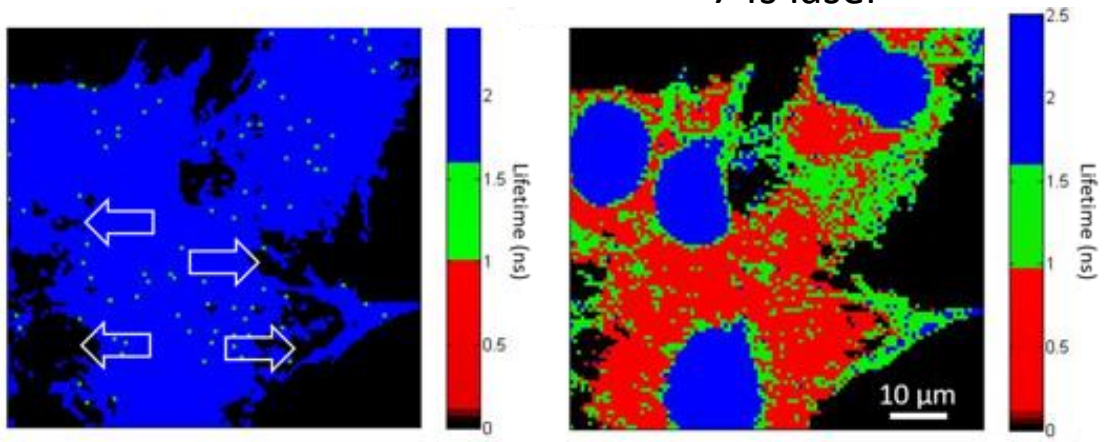
Label free cellular bioenergetics via Multi-Photon Fluorescence Lifetime Imaging Microscopy (MP-FLIM)

SyncRGB-FLIM Method based on ultrabroadband few cycle fs laser and FLIM detection

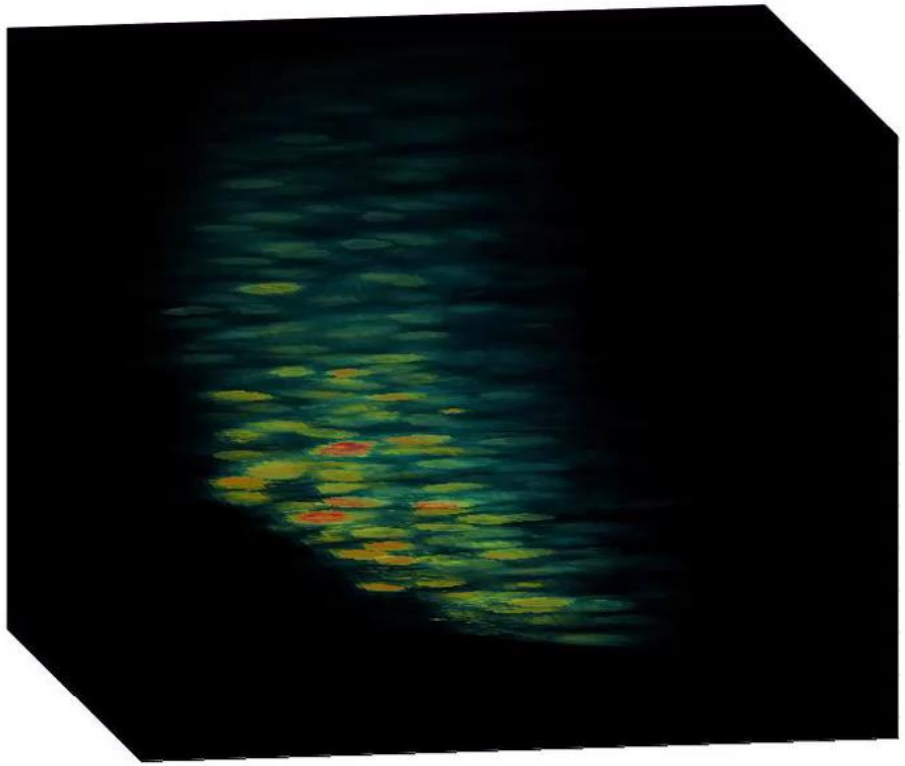


70 fs laser

7 fs laser



Maibohm et al. Biomed. Opt. Express, **2019**



140x140 µm x112µm Spheroid of A469 cells exposed to anticancer drug

SyncRGB-FLIM a bioimaging technique for a label free 3D in vitro biomedical imaging

Consortium:

Project: ExtreMed

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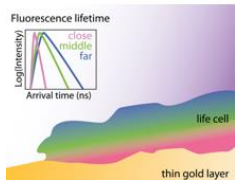
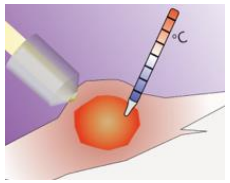
EP 19724610 (Europe) and EP 17047249 (US).

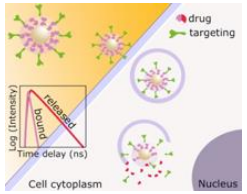
Current and emerging research lines

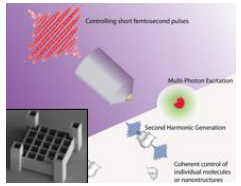
Advanced Bioimaging and sensing

- Near-field super-resolution
- Nanothermometry
- Applications in nanomedicine
- Nonlinear few cycle lasers





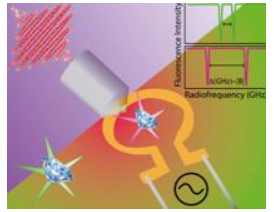




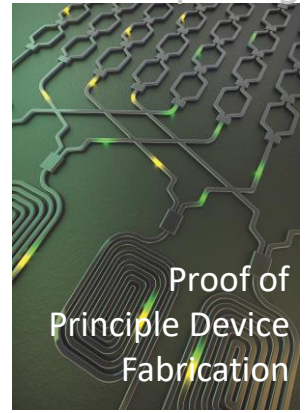
- 3D scaffolding for 3D disease models

Quantum Photonics

- Single Quantum emitters in 2D materials
- NV center in diamond based nanomagnetometry

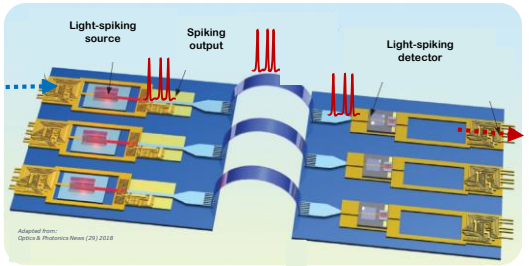


Quantum photonic computing



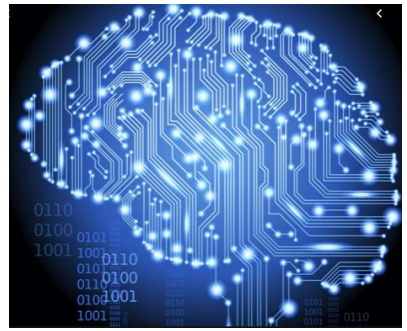
Photonic Integrated Devices

- Photonic Integrated Circuits



NanoLEDs, Photonic Sensors based e.g. on Mach Zehnder Interferometers, 3D microfabricated optical interconnects

Neuromorphic photonic computing



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#600375

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