Milano, 8 gennaio 2026

Biofisica

Presentazione degli argomenti di stage triennale

Perche'?

1. Lavorare in **ambiente interdisciplinare**
2. **Sistemi complessi** classici in condizioni di alto «rumore»
3. Sviluppo e applicazione di tecniche ottiche
4. Apprendimento dei principi della **microscopia ottica**
5. Apprendimento di tecniche **di image-analysis**
6. Apprendimento delle basi **dell'AI per analisi di large data sets**

Apre la strada a:

1. Data treatment in **noisy environments**
2. **AI for imaging**
3. Ricerca biomedica, neuroscienze, biotecnologie e **imaging medico**
4. Sviluppo tecnologico **in Vision Science**

BIOPHYSICS & BIOPHOTONICS @UNIMIB

Prof. Giuseppe Chirico (Biofotonica LM, Lab. Biofotonica II LM)
Prof. Maddalena Collini (Elementi di Biofotonica LT, Lab. Biofotonica I LM)
Prof. Laura D'Alfonso (Lab. Biofotonica I LM)
Prof. Laura Sironi (Esperimentazioni di Biofisica LT, Microscopia Ottica LM)
Dr. Luca Presotto (Esperimentazioni di Biofisica LT)
Dr. Margaux Bouzin (Lab. Biofotonica I LM)
Dr. Mario Marini (Lab. Biofotonica II LM)
Dr. Jennifer Riccio, Oumayma Alhou
Davide Panzeri, Letizia Marchesi, Riccardo Bolzoni

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Anthem
Advanced Technologies for Human-centered Medicine

MUSA

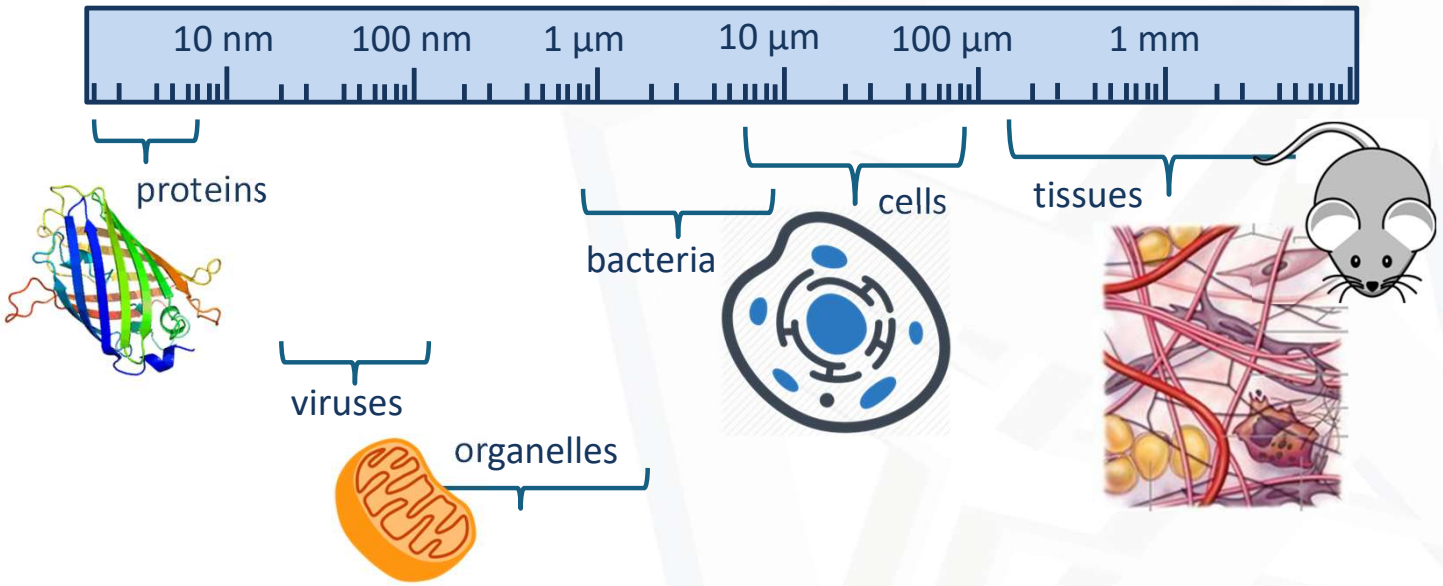
NQSTI
National Quantum Science and Technology Institute

Finanziato dall'Unione europea
NextGenerationEU

INSIGHT

FET Open project

COMPLEX BIOLOGICAL SYSTEMS



Biophysics: investigation of **complex** biological systems – from the tissue scale down to the sub-cellular level – by means of **physical laws** and **techniques**

Development of instrumentation and image processing methods for the quantitative characterization of biological systems by **theoretical, simulative and experimental** approaches in **optical microscopy**

RESEARCH LINES AND THESIS TOPICS

Development of instrumentation and image processing methods for the quantitative characterization of biological systems by theoretical, simulative and experimental approaches in **optical microscopy**

Machine Learning-based image processing

Image segmentation and processing algorithms for digital pathology and remote sensing
[L. Sironi, D. Panzeri]

Nanotechnology

Photo-thermal and photo-luminescent nanostructured devices
[L. D'Alfonso, G. Chirico, L. Marchesi]

Live-cell imaging and dynamics

Anomalous intracellular diffusion and transport processes
[M. Collini, M. Bouzin]

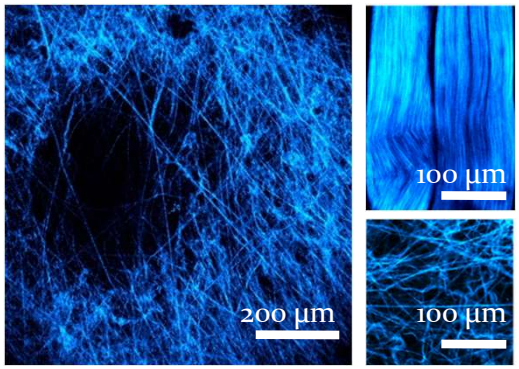
Development of (optical) imaging techniques

Image Scanning Microscopy, digital holography & adaptive optics
[G. Chirico, M. Collini, M. Bouzin, M. Marini, G. Meroni, R. Bolzoni]

Simulation and modelling of biophysical processes

Simulation of the immune response activation
[G. Chirico, L. Presotto, J. Riccio]

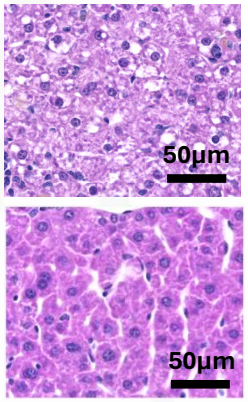
1. MACHINE LEARNING FOR DIGITAL PATHOLOGY



Two-photon excited fluorescence, second harmonic generation (SHG) microscopy, FLIM (fluorescence lifetime) imaging

Whole-slide Hematoxylin&Eosin Hepatocarcinoma (HCC) biopsy

H&E HCC Patch



H&E Healthy Tissue Patch

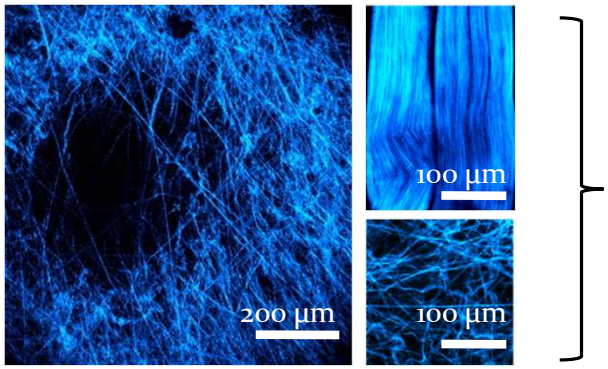
Machine Learning →

- ✓ Image Segmentation
- ✓ Image Virtual Staining
- ✓ Image Restoration

→ **Extraction of structural, textural, functional, metabolic information** to complement the color and texture analysis of histology images **(multimodal imaging)**

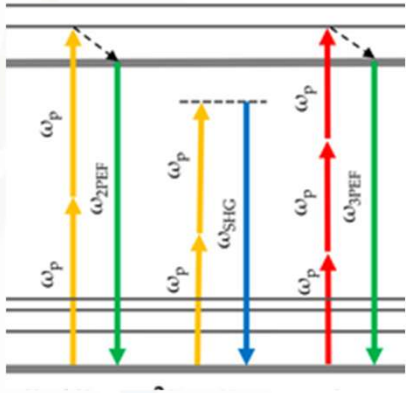
Collaboration with Dr. D. Inverso – *UniSR*
Prof. L. Di Tommaso – *Humanitas Research Hospital*
Prof. G. Castellani, Dr. E. Giampieri – *Università di Bologna*
Prof. G. Cerullo, Polimi and Carmbidge Raman Instruments
laura.sironi@unimib.it

1. MACHINE LEARNING FOR DIGITAL PATHOLOGY

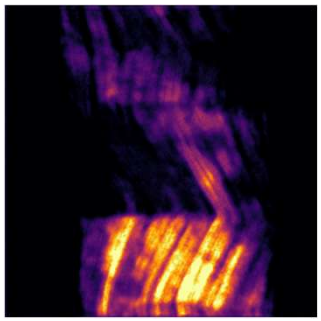


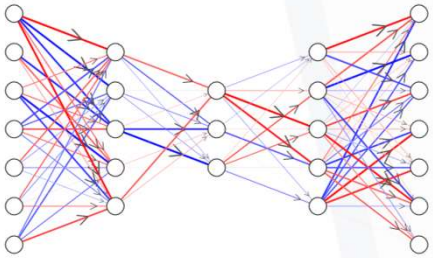
Polarized Second Harmonic Generation (P-SHG) imaging

1a. **Segmentation** and retrieval of biophysical parameters from Polarization-dependent Second Harmonic Generation microscopy

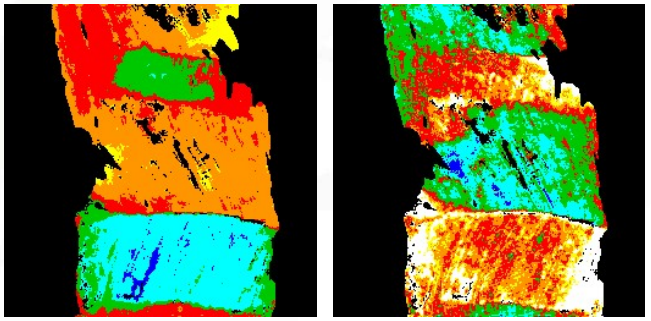


P-SHG image sequence





disorder map **orientation map**



characterization of collagen fibrils

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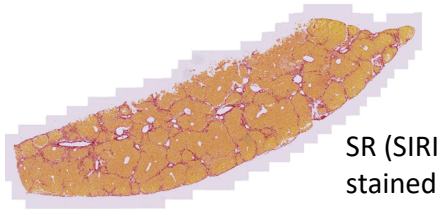
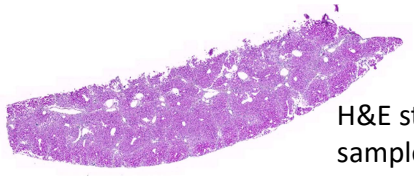
1. MACHINE LEARNING FOR DIGITAL PATHOLOGY

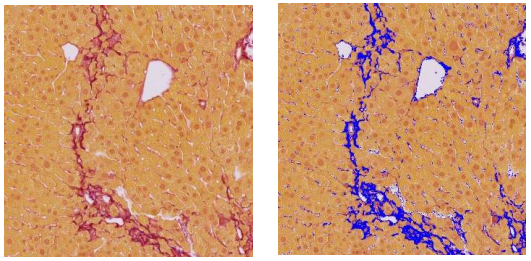
1b. Development of novel ML pipelines for automated disease diagnosis



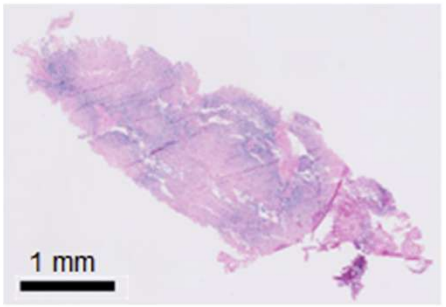
SR (SIRIUS RED)
stained sample image



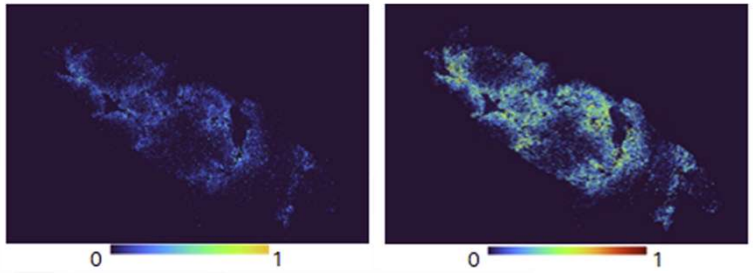
H&E stained
sample image



COLLAGEN SEGMENTATION
AND QUANTIFICATION



Human liver biopsy



IRON QUANTIFICATION
IN HEMOCHROMATOSIS DISEASE

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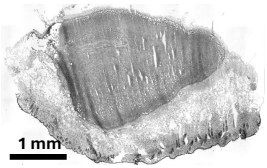
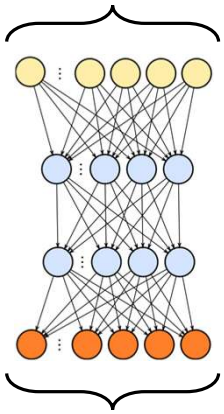
1. MACHINE LEARNING FOR DIGITAL PATHOLOGY

1c. Development of **virtual staining algorithms**

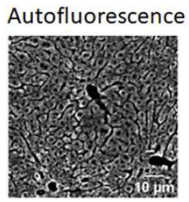


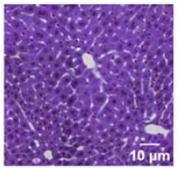
Unstained sample image

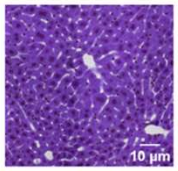
Deep Neural Network



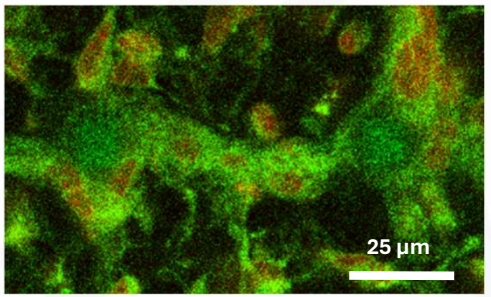
Virtually stained sample image







1d. **Image processing**



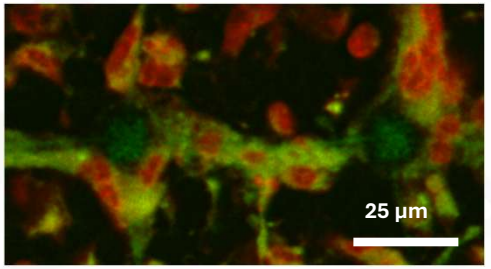


Image denoising

Improved recognition of relevant biological structures in-vivo

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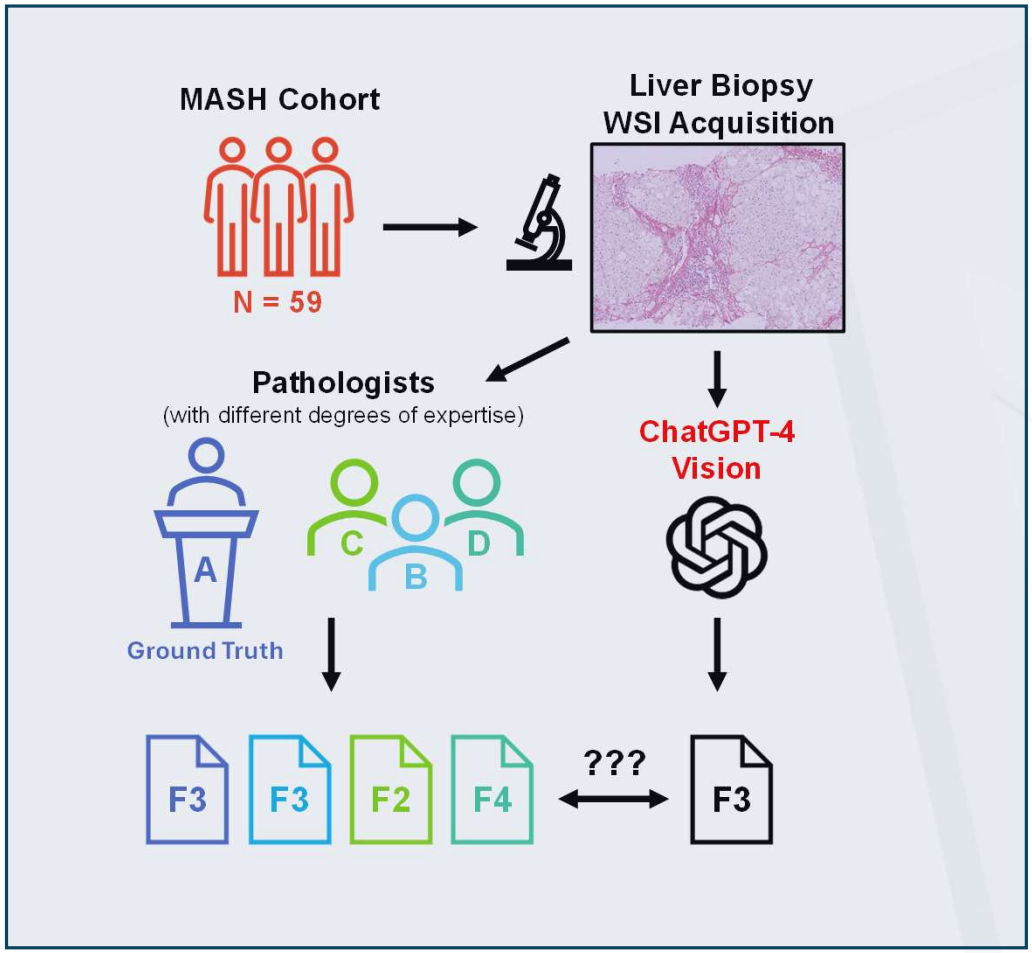
1. MACHINE LEARNING FOR DIGITAL PATHOLOGY



1e. Analysis of histopathological images by **Large Language Models** such as chatGPT and LLAMA

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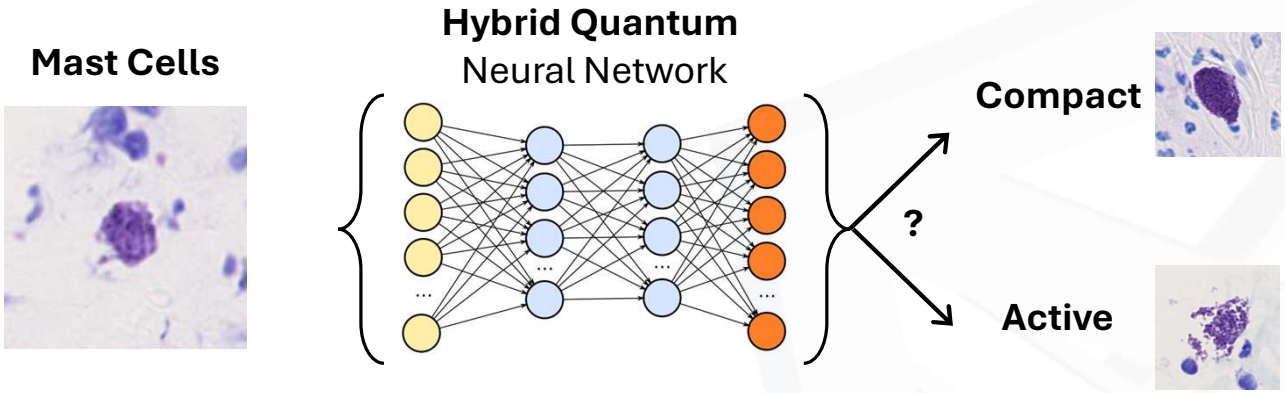
1. MACHINE LEARNING FOR DIGITAL PATHOLOGY



1f. Quantum Neural Networks for digital pathology and remote sensing

in collaboration with **prof. A. Giachero** (andrea.giachero@unimib.it)

Other projects and applications:

- Healthy / tumor cells classifications
- Remote-sensing vegetation spectra classification

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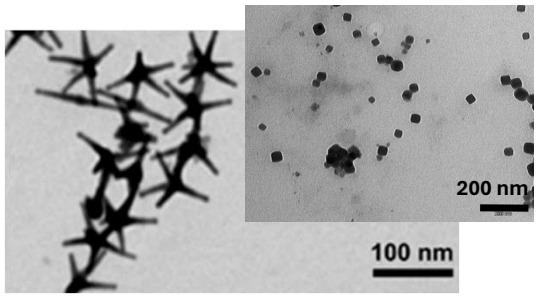
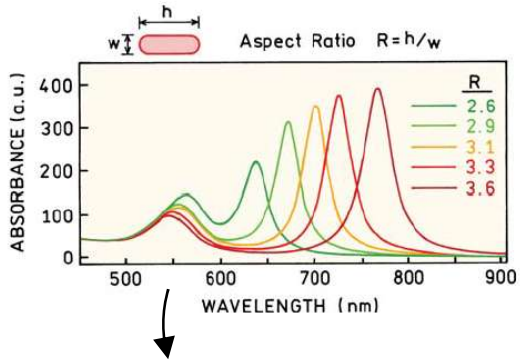
2. NANOTECHNOLOGY

Anisotropic gold/silver nanoparticles,
PrussianBlue (Fe) nanoparticles





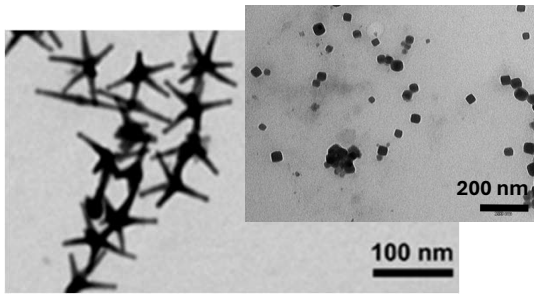
plasmonic resonance engineering

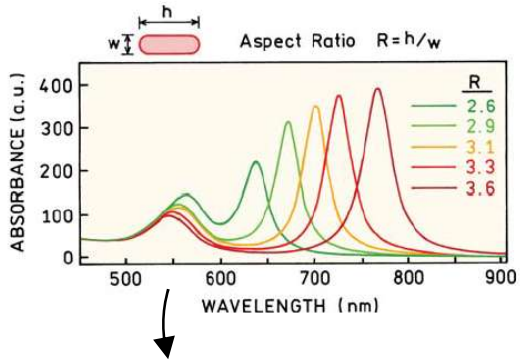
- ✓ **Optical (in-vivo) imaging**
- ✓ **Drug delivery**
- ✓ **Photo-dynamic and photo-thermal therapy**

Collaboration with Prof. P. Pallavicini Lab
Chemistry Dept. @ Università degli Studi di Pavia

2. NANOTECHNOLOGY

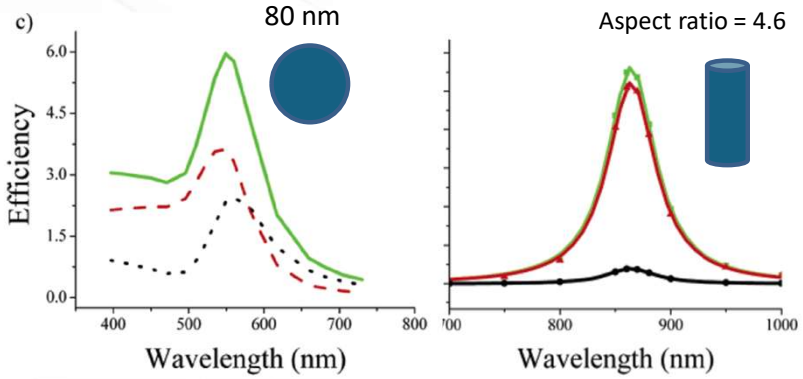
Anisotropic gold/silver nanoparticles,
PrussianBlue (Fe) nanoparticles





plasmonic resonance engineering

2a. Numerical simulation (multipole expansion) of the extinction (scattering and absorption) properties of the nanostructures



$$\varepsilon_s(a,\omega) = \varepsilon(\omega)_{\text{exp}} + \frac{\omega_p^2}{\omega^2 + i\omega\gamma_{\text{bulk}}} - \frac{\omega_p^2}{\omega^2 + i\omega\Gamma}$$

Collaboration with Prof. P. Pallavicini Lab
Chemistry Dept. @ Università degli Studi di Pavia

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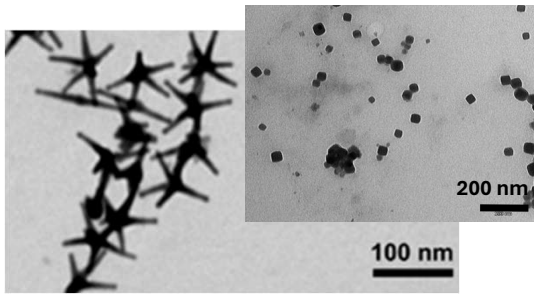
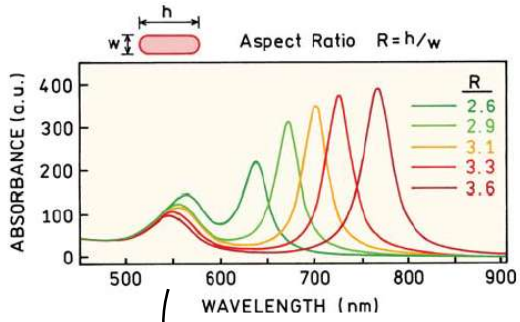
2. NANOTECHNOLOGY

Anisotropic gold/silver nanoparticles,
PrussianBlue (Fe) nanoparticles





plasmonic resonance
engineering

2b. Photo-thermal nanostructured devices for thermal eradication of bacteria

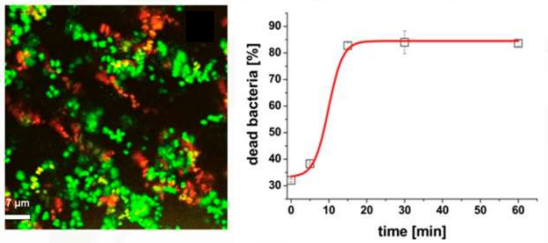
NIR radiation

↓

Localized temperature variation

↓

NIR-triggered bacteria ablation



Quantification of live/dead cell populations

Collaboration with Prof. P. Pallavicini Lab
Chemistry Dept. @ Università degli Studi di Pavia

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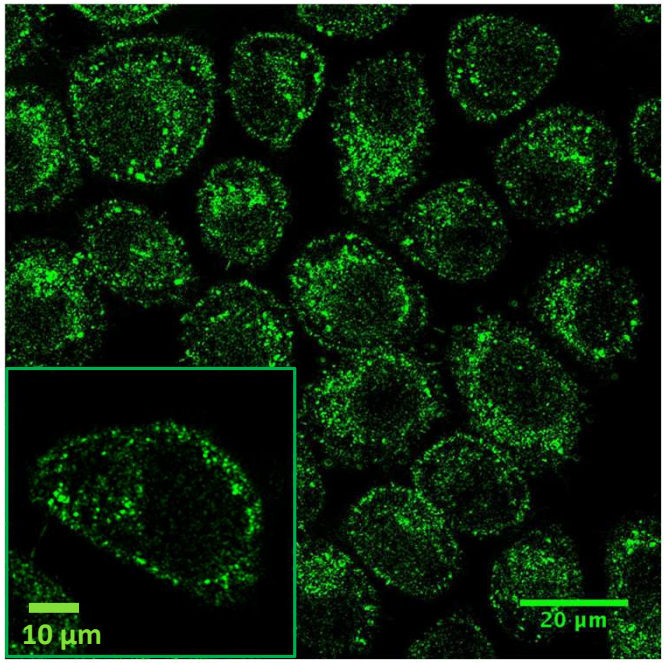
3. NANOTECHNOLOGY & LIVE-CELL IMAGING

Anomalous (intracellular) diffusion of nanostructures



Gold nanoparticles in HeLa cancer cells

→ How do nanostructures behave and get transported in the cellular environment?

→ General interest issue: How to characterize the dynamics and transport of receptors, organelles, cargoes, etc., in an extremely corralled and crowded environment?

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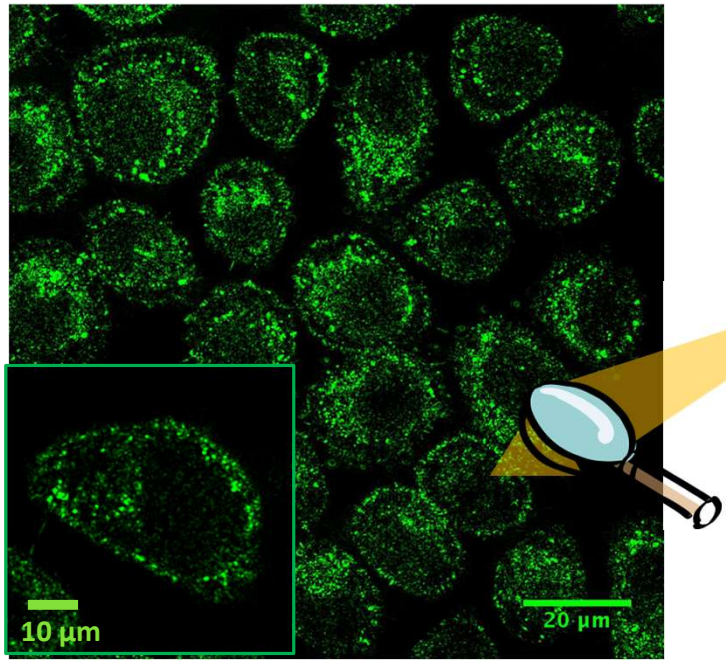
3. NANOTECHNOLOGY & LIVE-CELL IMAGING

Anomalous (intracellular) diffusion of nanostructures



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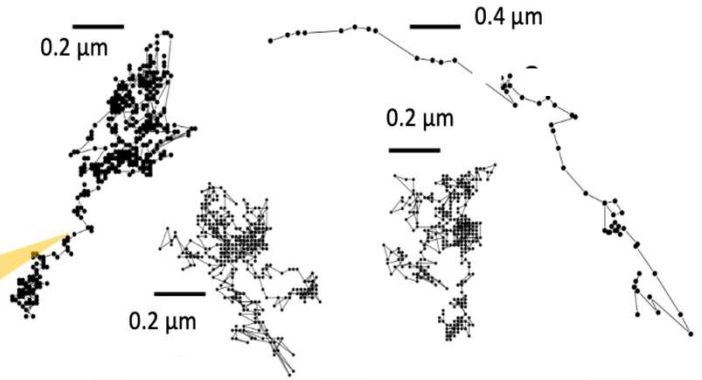

Analysis of time-lapse image sequences:

trajectories reconstruction &
Mean Square Displacement (MSD) analysis

- Properties of the environment (crowding, viscoelasticity, …)
- Type of transport (Brownian vs anomalous)

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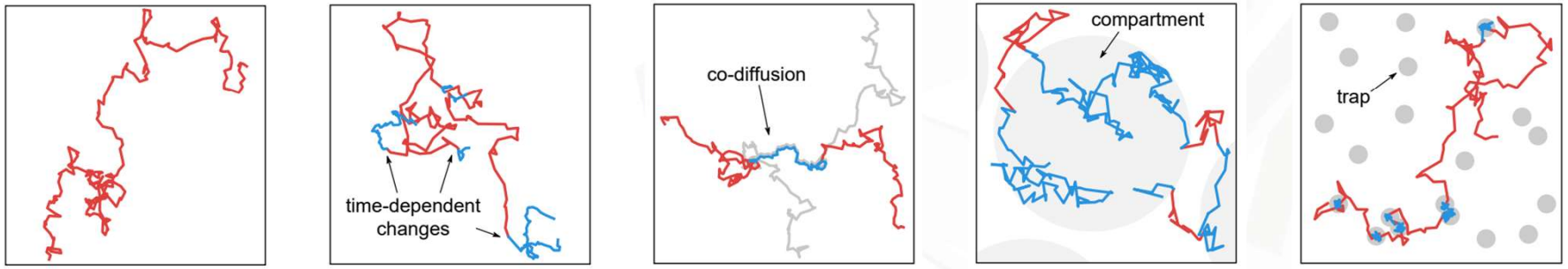
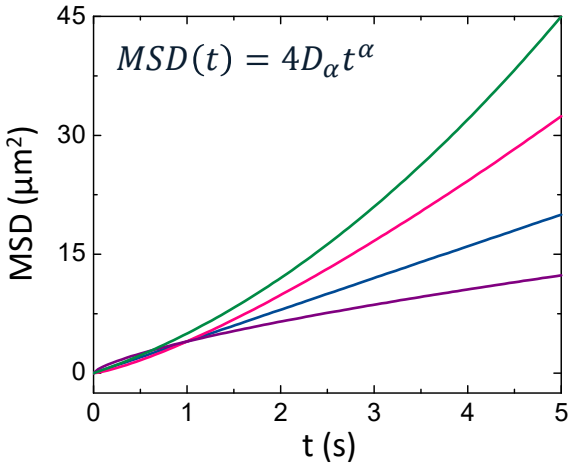
3. NANOTECHNOLOGY & LIVE-CELL IMAGING

Anomalous (intracellular) diffusion



Power-law time dependence for the MSD:



3a. Theoretical models reproducing the behavior of particles undergoing anomalous diffusion (Fractional Brownian motion, Lévy flights, etc.)

3b. Experimental investigation of sub-diffusion in cellular model systems (GUVs)

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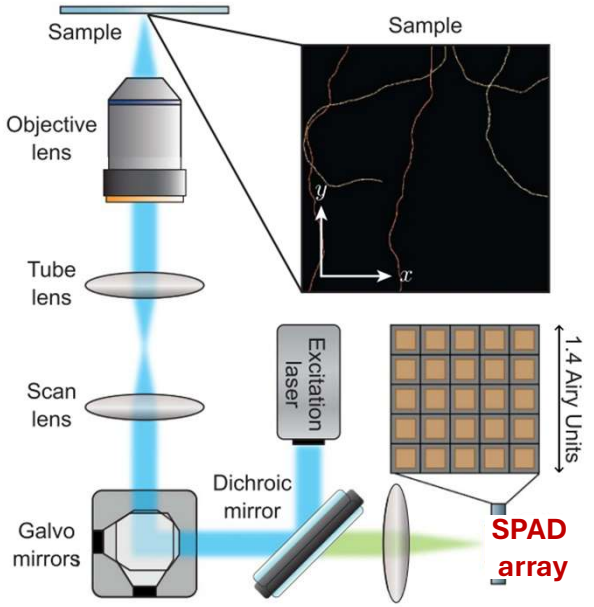
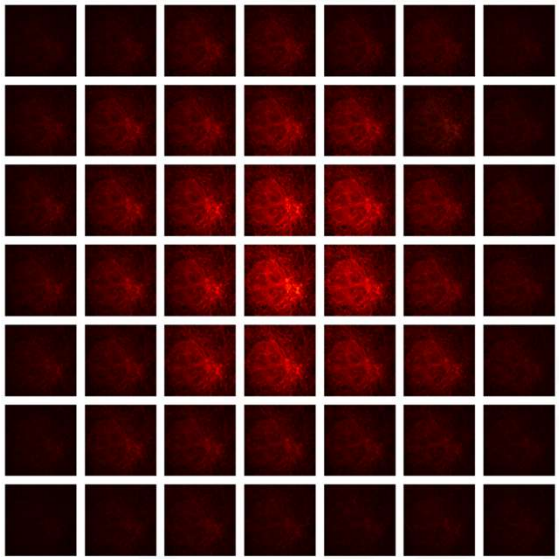
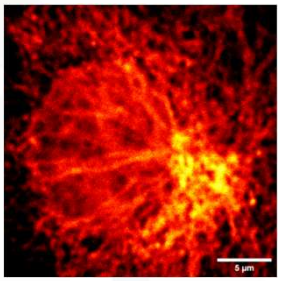
4. DEVELOPMENT OF IMAGING TECHNIQUES

4b. Super-resolution fluorescence imaging by Image Scanning Microscopy (ISM)

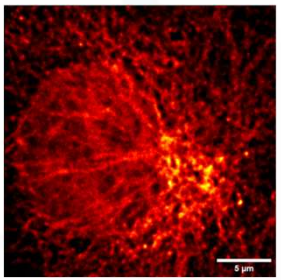




Conventional image



Super-resolution ISM image



Super-resolution imaging experiments on fluorescent reference samples and cells/tissue slides

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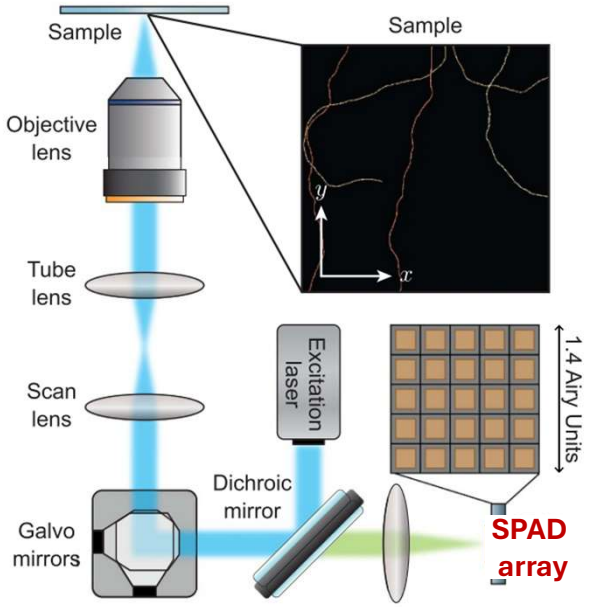
4. DEVELOPMENT OF IMAGING TECHNIQUES

4b. **Super-resolution** fluorescence imaging by Image Scanning Microscopy (ISM)



1. Application to cell cultures to **increase resolution in cellular compartments** visualization

2. Application to thick tissue to estimate the effect of **tissue scattering** on resolution

3. Fluorescence fluctuations spectroscopy for **anomalous diffusion detection**

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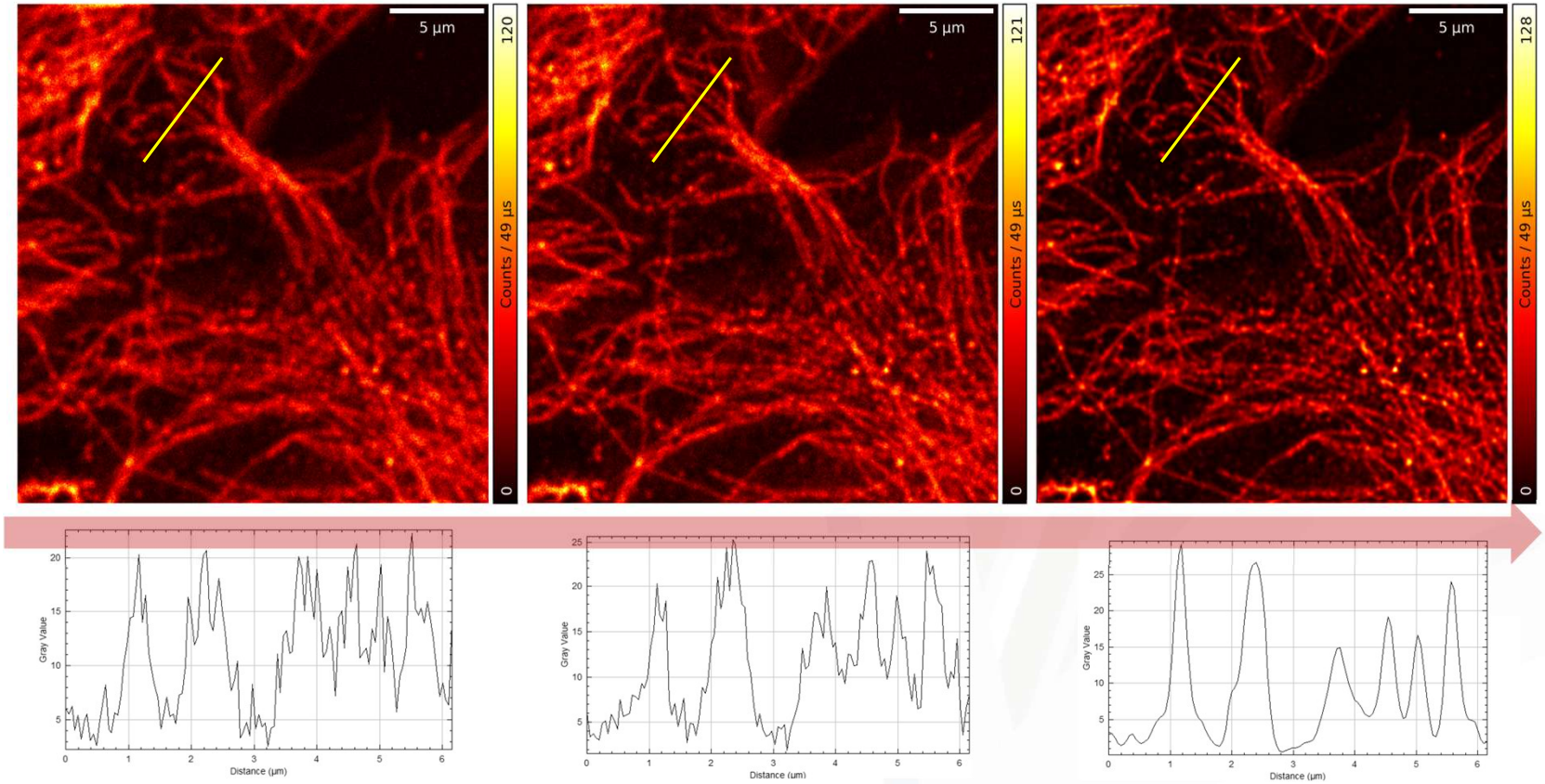
4. DEVELOPMENT OF IMAGING TECHNIQUES

4b. Application to cells : Bovine pulmonary artery cells

Confocal | Image scanning microscopy | ISM with out-of-focus-rejection



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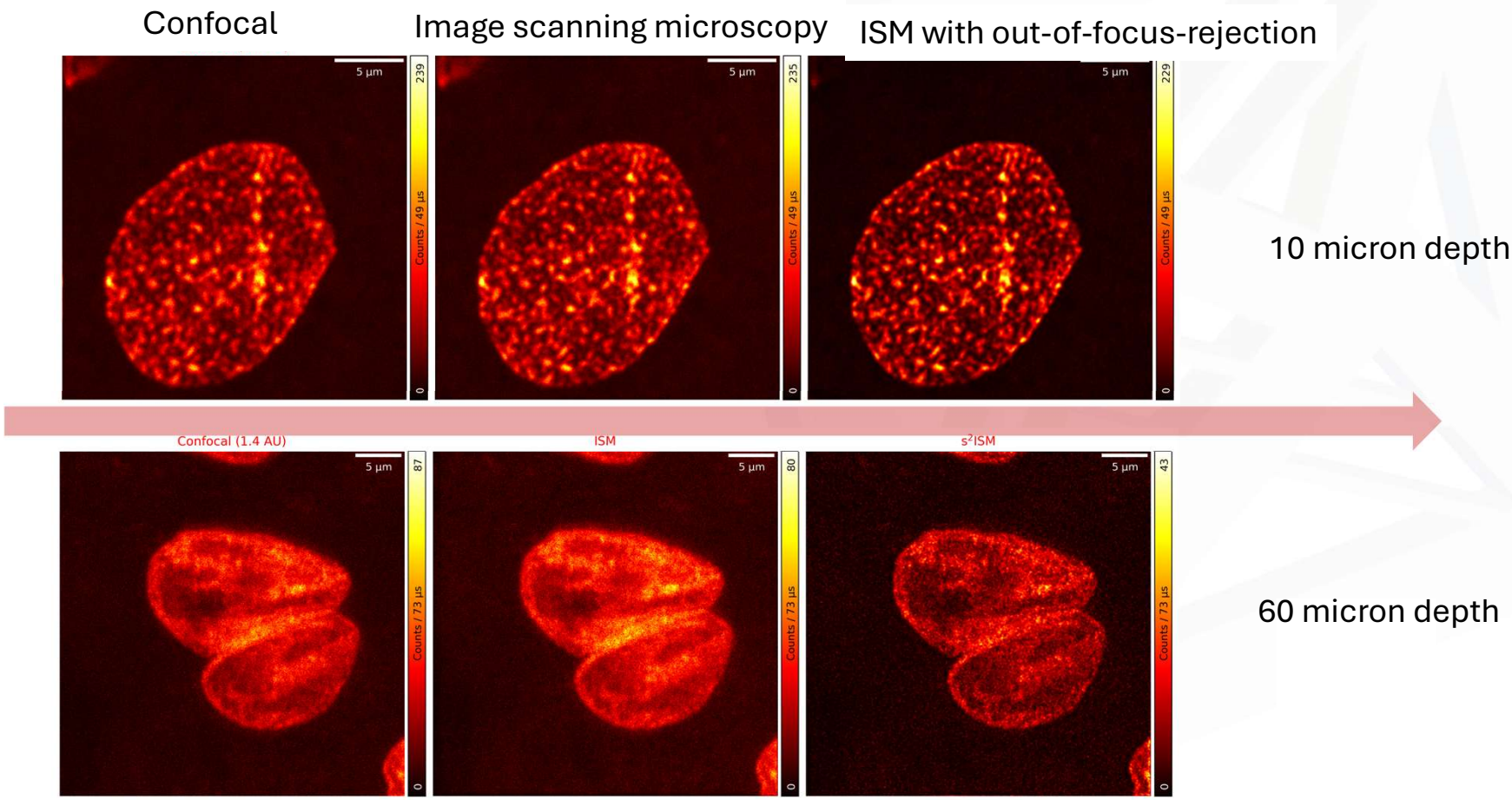
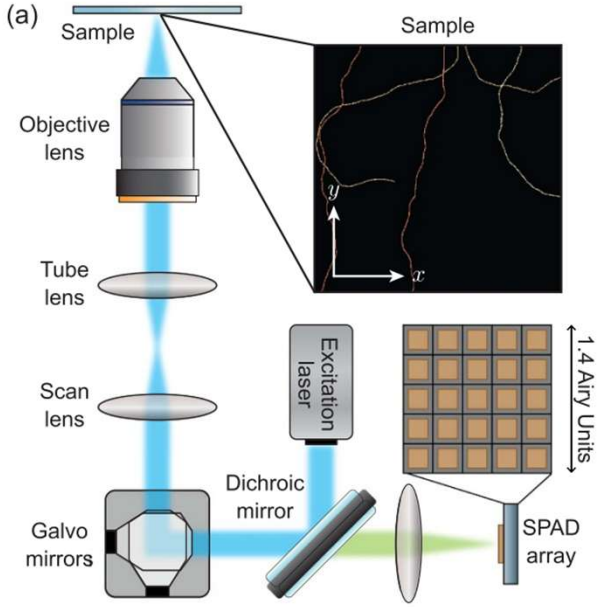
4. DEVELOPMENT OF IMAGING TECHNIQUES

4b. Application to tissue : Artificial skin – Nuclei staining

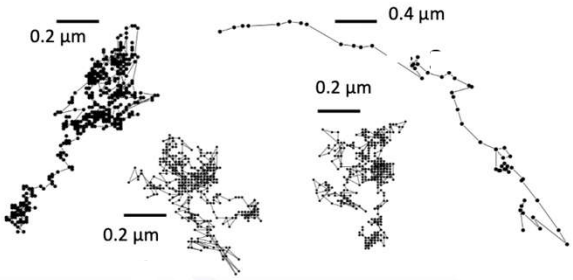


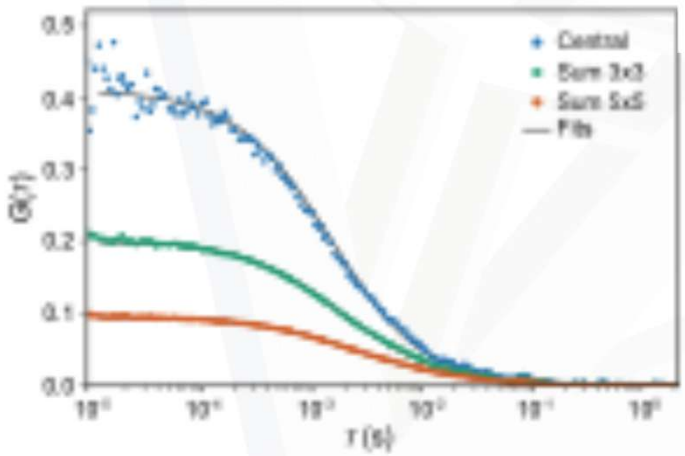
4. DEVELOPMENT OF IMAGING TECHNIQUES

4b. Application to anomalous diffusion by fluorescence fuctuations detection



General interest issue: How to characterize the dynamics and transport of receptors, organelles, cargoes, etc., in an extremely corralled and crowded environment?





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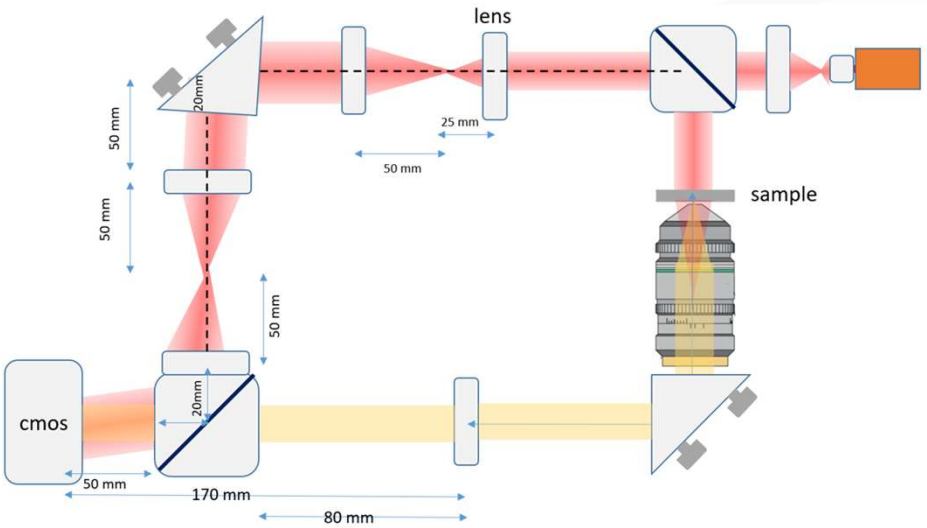
4. DEVELOPMENT OF IMAGING TECHNIQUES

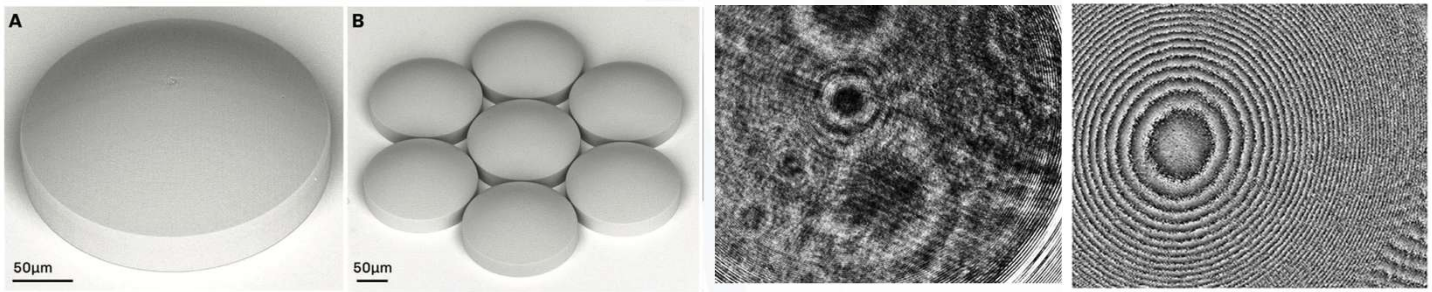
4c. digital holography → Micro-lenses characterization



Interferometric imaging method for the retrieval of both intensity and phase images

↓

Characterization of micro-optics (micro-lenses) for deep tissue imaging



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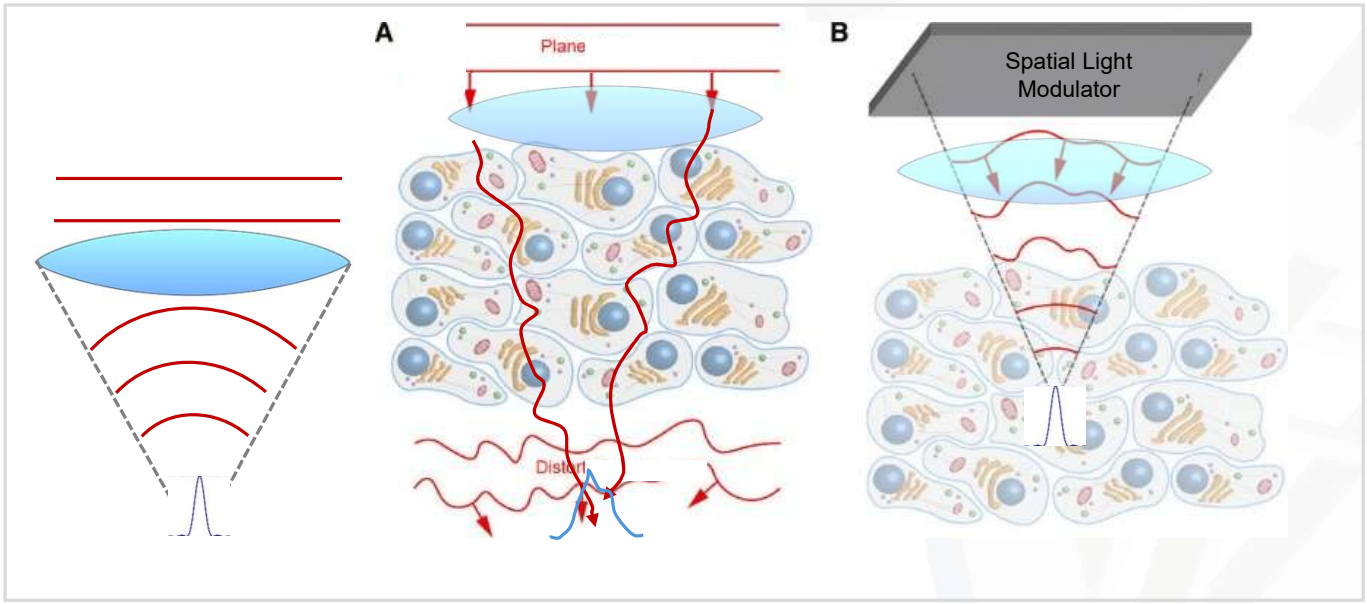
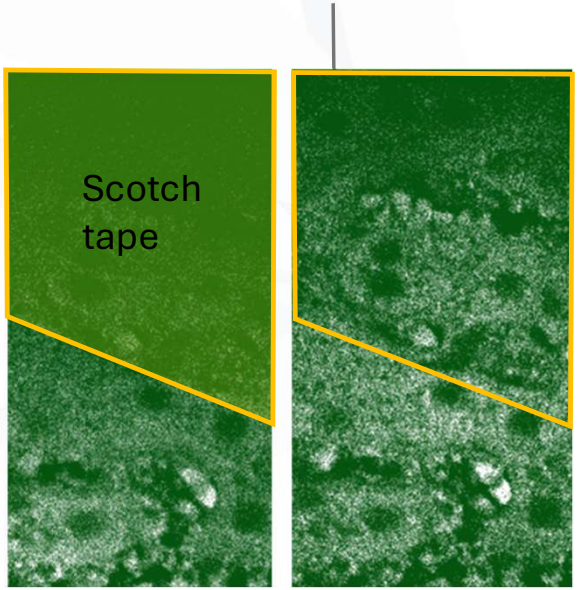
4. DEVELOPMENT OF IMAGING TECHNIQUES

Holographic Scattering Correction for Two-Photon Excitation Microscopy

Through water



Limited resolution depth achievable in turbid biological samples (~800 nm in murine brain)



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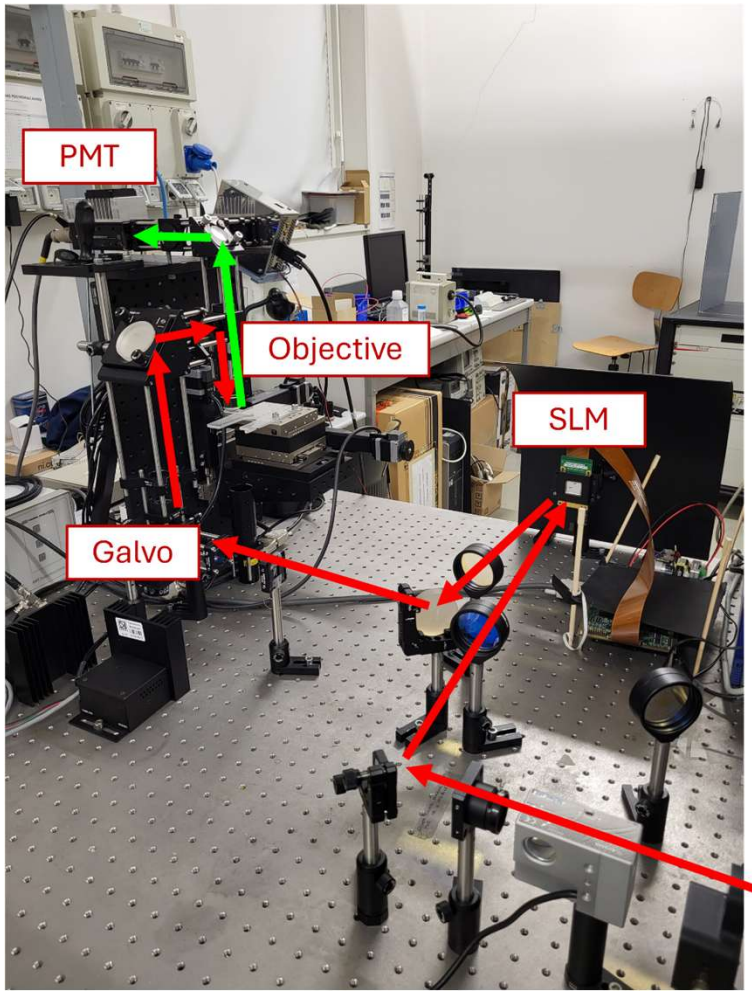
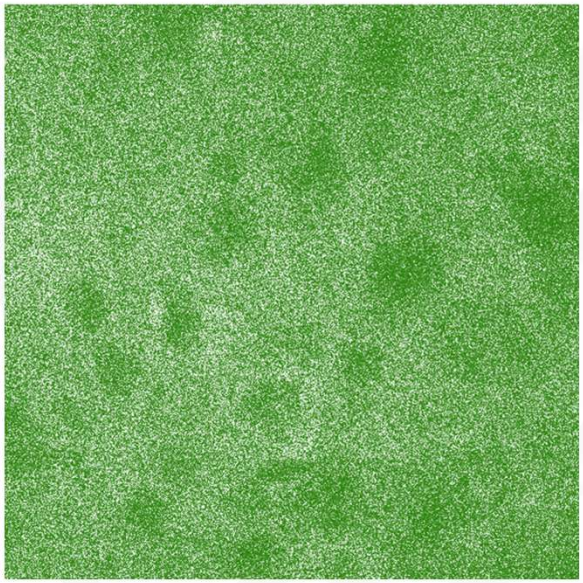
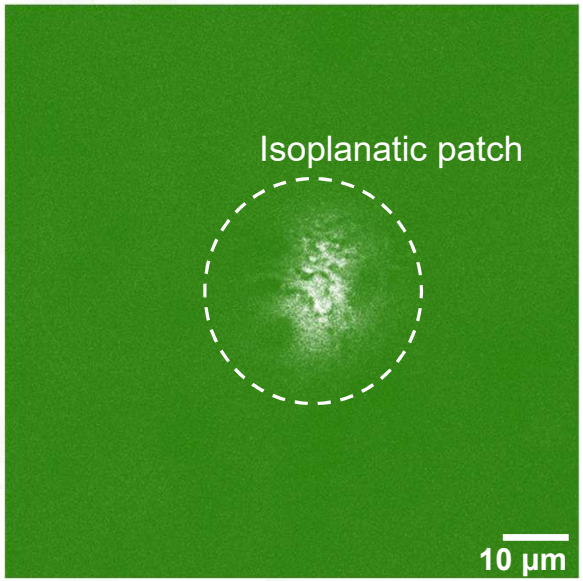
4. DEVELOPMENT OF IMAGING TECHNIQUES







Correction works on small (20x20 um) «isoplanatic» patches

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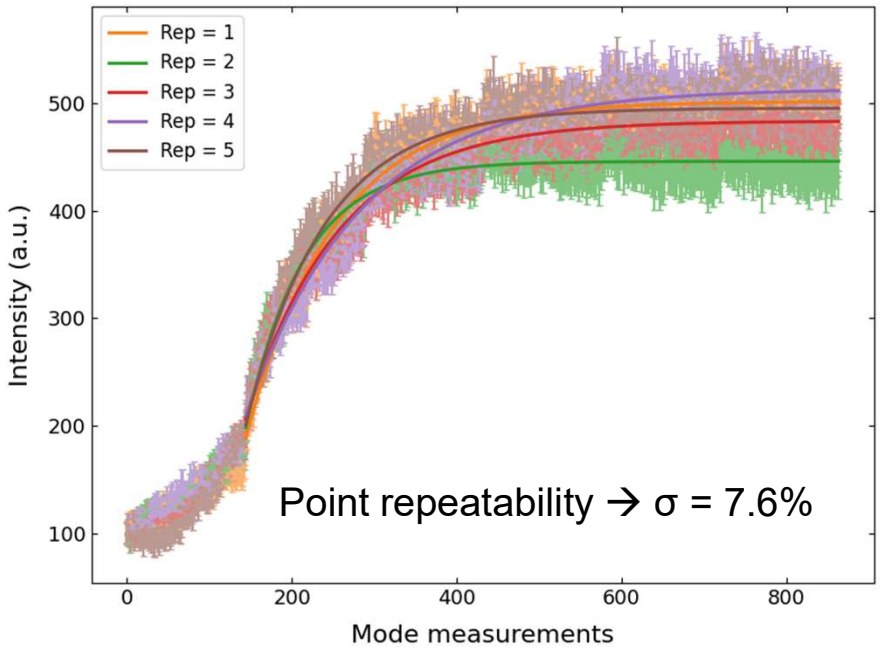
4. DEVELOPMENT OF IMAGING TECHNIQUES

Point-wise repetitions



Signal enhancement

$$\eta = \frac{I_{fin} - I_{init}}{I_{init}} \rightarrow 15\ times$$

- Effect of the turbidity on the isoplanatic patch
- Reduction of the photobleaching during correction
- Evaluation of the improvement of the optical resolution at depth in artifical tissues.

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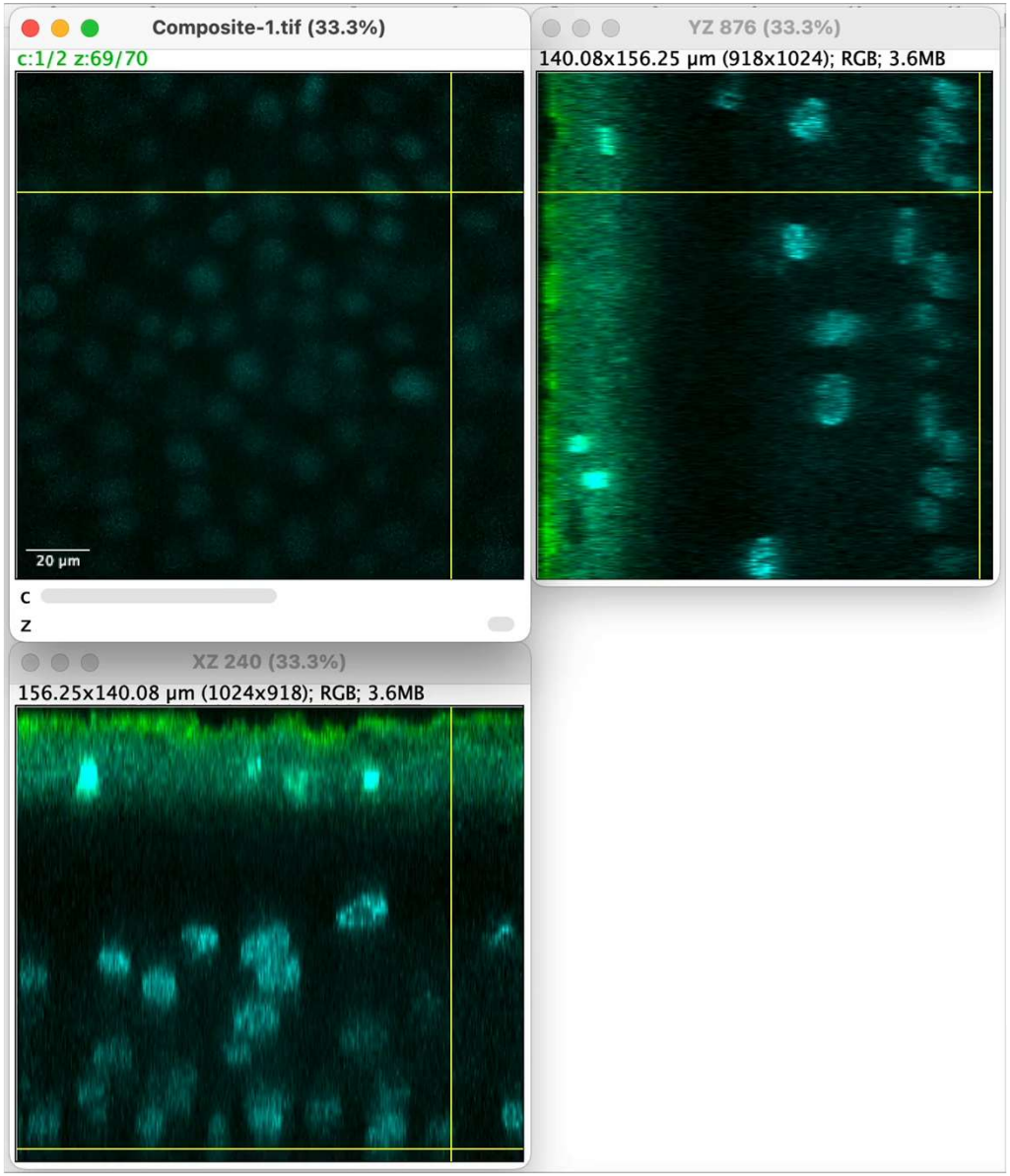
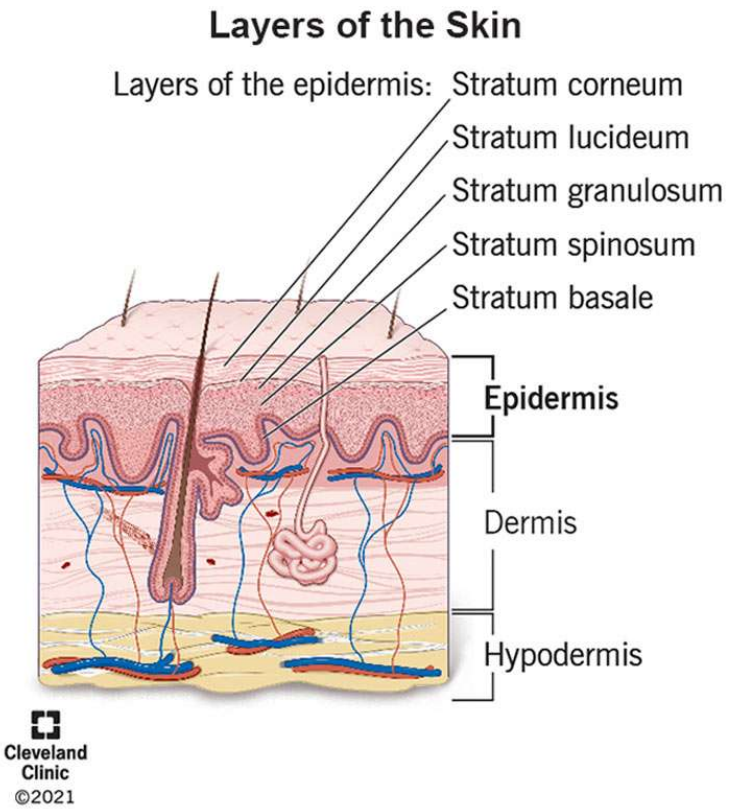
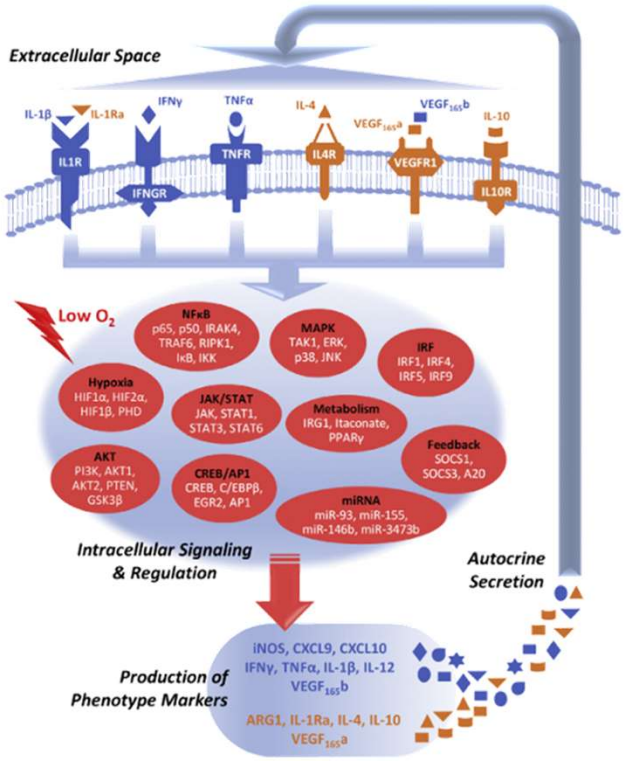

Composite-1.tif (33.3%)
c:1/2 z:69/70
20 µm
C
Z
YZ 876 (33.3%)
140.08x156.25 µm (918x1024); RGB; 3.6MB
XZ 240 (33.3%)
156.25x140.08 µm (1024x918); RGB; 3.6MB


Layers of the Skin
Layers of the epidermis:
Stratum corneum
Stratum lucideum
Stratum granulosum
Stratum spinosum
Stratum basale
Epidermis
Dermis
Hypodermis
Cleveland Clinic
©2021

5. SIMULATION AND MODELLING OF BIOPHYSICAL PROCESSES

5a. Simulation of the immune response



- Mathematical modeling of the host immune reaction upon a bioimplant
- Macrofage modeling through partial differential equations (chemical reactions)
- Output interpretation: link between hundreds of simulated variables and a few experimentally relevant and measurable quantities

→ «sensitivity analysis» of the model: identification of the relevant parameters for the dynamical evolution of the system

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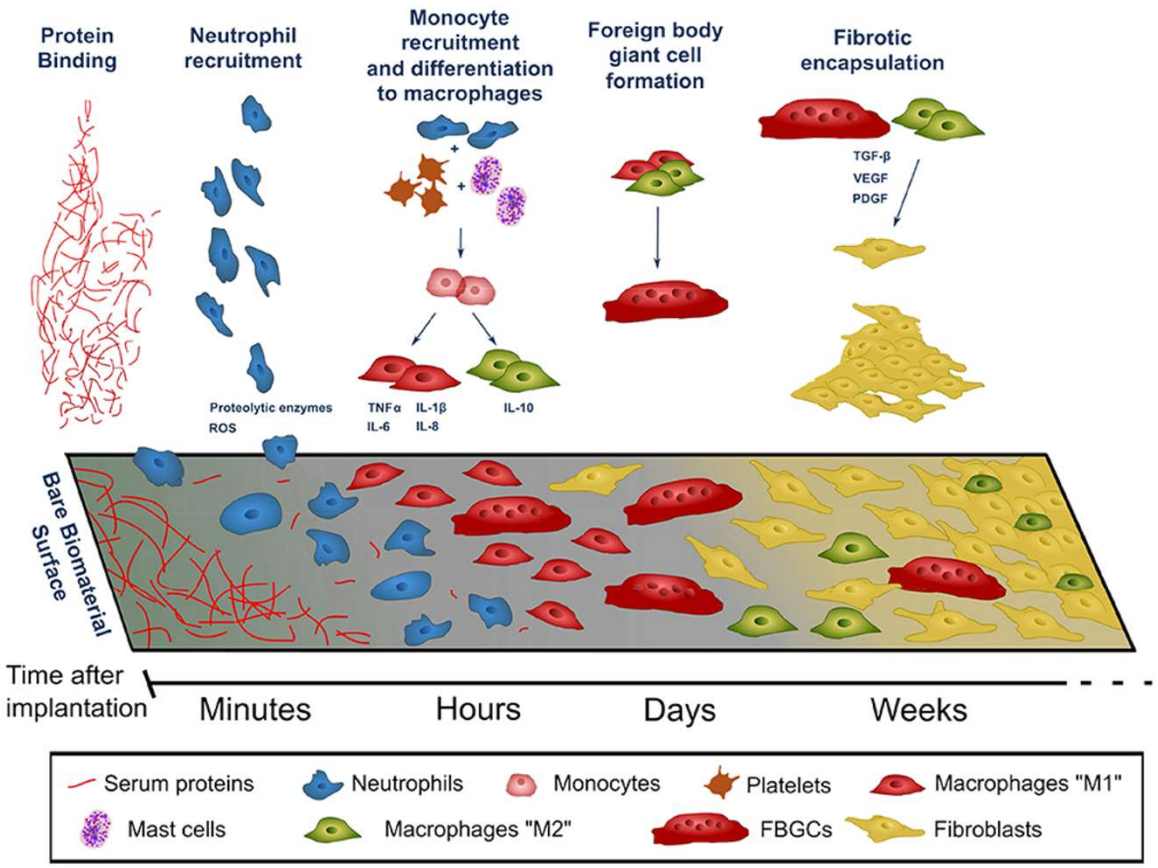
5. SIMULATION AND MODELLING OF BIOPHYSICAL PROCESSES



VASCULAR

↓

INFLAMMATORY

↓

FIBROTIC

Carnicer-Lombarte et al., Front. Bioeng. Biotechnol., 2021

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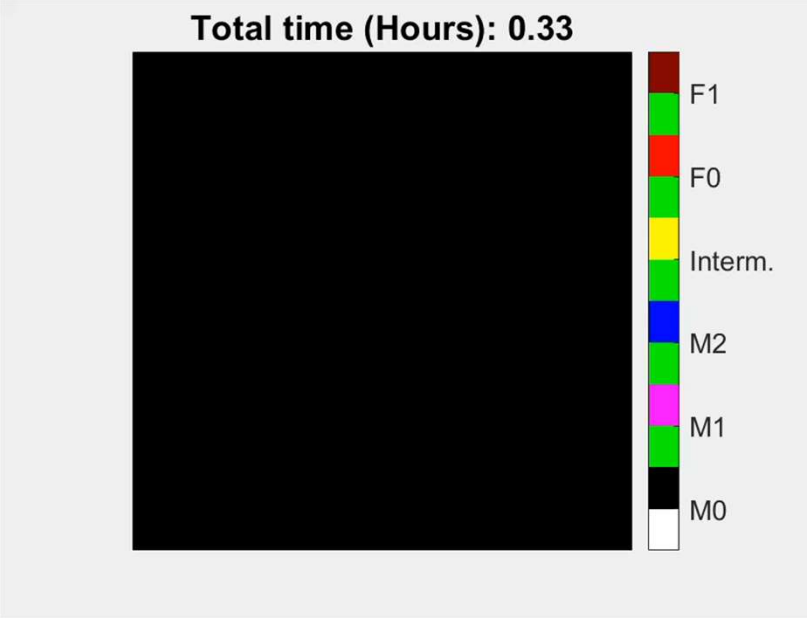
5. SIMULATION AND MODELLING OF BIOPHYSICAL PROCESSES

- Simulation of vessels and local sources of cells -> extravasation
- Simulation of angiogenesis and consequent vascularization
- Simulation of collagen deposition
- Collaboration with MERLN Institute (Belgium)
- Collaboration with Mattek (artificial epidermis)



- F1:fibroblasts
- F0 fibrocytes
- M0: Monocytes
- M1: pro-inflammatory macrophages
- M2: pro-healing macrophages

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