

# biofisica e biofotonica (in Bicocca)

## LABS (Laboratory of Advanced BiophotonicS



Biophysics (also biological physics) is an interdisciplinary science that employs and develops theories and methods of the physical sciences for the investigation of biological systems.



Mcrobes

1µm

100µm

 $10\mu m$ 

Cells

(Eq. blood cells)





alla permanente!





alla risposta immunitaria..









## gruppo di biofisica e biofotonica: le cose nuove..

Super-resolution photo-thermal imaging

Nanotechnology

Artificial Intelligence-based image processing

#### FET OPEN project: IN2SIGHT

An in-vivo bioengineered chip as a smart intravital multiphoton imaging window

## SUPER-RESOLUTION FLUORESCENCE & FAR-IR IMAGING

Super-resolved thermography & STED nanoscopy



#### Photo-thermal far-infrared imaging:

- Heat release in the sample upon visible laser light absorption
- Detection of the emitted thermal radiation by a thermal camera ( $\lambda$  = 7-13 µm)

grey-body approximation & Stefan-Boltzmann's law

### Time-dependent ~mm resolution limited by diffraction and heat diffusion





 $\sim$  mm spatial resolution (Abbe's law for diffraction + heat diffusion)

< 60 µm spatial resolution

5°C

<u>ن</u>

°°C













Model-based SR Presotto L. et al., Adv. Intell. Syst., 2300510, 2023

Development of hardware and software super-resolution (SR) strategies

### SUPER-RESOLUTION PHOTO-THERMAL IMAGING

#### — Thermal conductivity imaging

How to map temperature + thermal properties? Finite-element simulations + theoretical modelling of temperature rise-and-decay kinetics

 $\frac{k}{D}\frac{\partial T(\underline{r},t)}{\partial t} - k\nabla^2 T(\underline{r},t) = Q(\underline{r},t)$   $\begin{cases} -k\frac{\partial T(\underline{r},t)}{\partial z} \bigg|_{z=0} = -h[T(x,y,0,t) - T_m(\infty)] - \varepsilon\sigma[T^4(x,y,0,t) - T_m^4(\infty)] \\ -k\frac{\partial T(\underline{r},t)}{\partial z} \bigg|_{z=L} = h[T(x,y,L,t) - T_m(\infty)] + \varepsilon\sigma[T^4(x,y,L,t) - T_m^4(\infty)] \end{cases}$ 

Conservazione dei beni culturali Collab. with D. Di Martino, G. Gorini



Bouzin M. et al., Mat. Today Phys., 18, 100375, 2021

#### Space-resolved quantification of the melanin concentration in melanoma biopsies

Space-resolved quantification of the melanin concentration in melanoma biopsies to complement fluorescence, H&E staining and ABCDE rule





### NANOPARTICLES FOR TECHNOLOGY

metal nanoparticles (gold/silver/iron)















absorption VIS-NIR scattering VIS-NIR luminescence VIS





### NANOTECHNOLOGY

#### Photo-thermal bacteria eradication

Collaboration with Prof. A. Polissi Lab Pharmacological and Biomolecular Sciences Dept. @ UNIMI



Grisoli, P. et al. Nanomaterials 11, 6 (2021) Borzenkov, M. et al., Nanomaterials, 10,786 (2020) Borzenkov, M. et al., Bellstein J. Nanotechnol., 11,1 (2020)

#### Multi-photon fabrication

Collaboration with Dr. A. Zeynali University of Stuttgart





#### Neuron cells stimulation

Collaboration with Prof. M. Lecchi Lab Biotechnology and Biosciences Dept. @ UNIMIB



#### **Cell-nanoparticles interaction**

Collaboration with Prof. P. Bigini Mario Negri Institute for Pharmacological Research



Dynamics and transport of cargoes, receptors, proteins in crowded, heterogeneous, corralled environments



#### **Photo-thermal therapy**

"NanoThermoPatch" for medical applications M. Borzenkov, G. Chirico, M. Collini, P. Pallavicini

Patented



#### Photo-thermal nanomaterials for food packaging

"NanoFunPack" development of next-generation smart packaging solutions for food industry







### NANOTECHNOLOGY: Photo-thermal applications

#### Photo-thermal bacteria eradication



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



## Multi-photon fabrication



T<sub>C</sub>

 $T_H$ 



Collaboration with Dr. A. Zeynali University of Stuttgart, Germany



### ARTIFICIAL INTELLIGENCE-BASED IMAGE PROCESSING: Digital pathology

#### Label-free tissue characterization

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



Extraction of structural, textural, functional, metabolic information to complement the color and texture analysis of standard histology images

#### Multi-Level Predictions/Analysis

Prediction of: staining, molecular expression and gene mutations from label-free tissue images



VIRTUAL STAINING

Prediction of: disease progression from healthy tissue (e.g. liver fibrosis)



Healthy liver Fibrosis FIBROSIS PROGRESSION

- AI-aided disease diagnosis: segmentation, feature extraction and correlation with clinical information







Collaborations:

Dr. D. Inverso – San Raffaele Hospital Prof. L. Di Tommaso – Humanitas Research Hospital Prof. G. Castellani, Dr. E. Giampieri – Università di Bologna Prof. J. Calderaro, Henri Mondor Hospital, Créteil, France.



## ARTIFICIAL INTELLIGENCE-BASED IMAGE PROCESSING: Digital pathology

#### Label-free tissue characterization

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L. Sironi\* et al., Frontiers in Oncology, 2019 DOI: 10.3389/fonc.2019.00527 L. Sironi\* et al., Scientific Reports, 2017 DOI: 10.1038/s41598-017-17726-y)

#### **Multi-Level Predictions/Analysis**

Prediction of: staining, molecular expression and gene mutations from label-free tissue images



Prediction of: disease progression from healthy tissue (e.g. liver fibrosis)



**Healthy liver** Fibrosis **FIBROSIS PROGRESSION** 

#### Al-aided disease diagnosis: segmentation, feature extraction and correlation with clinical information



81% diagnostic accuracy Better results than junior pathologists





Panzeri et al., Frontiers in medicine, accepted



Autofluorescence Hematoxylin&Eosin

VIRTUAL STAINING

## ARTIFICIAL INTELLIGENCE-BASED IMAGE PROCESSING: Remote Sensing

Development of a MUlti-SEnsor remote sensing approach from drone to earLY detect plant diseases: A tool for sustainable agriculture and food security (MUSELY)



PRIN 2022 PNRR

DISAT, University of Milano-Bicocca

### FET OPEN project – IN2SIGHT

#### An in-vivo bioengineered chip as a smart intravital multiphoton imaging window for new validation protocols of biomaterials









### FET OPEN project – IN2SIGHT







## FET OPEN project – IN2SIGHT: **Optical set-up and image acquisition/analysis**



Imaging on stained fibroblasts through the microlenses



#### Label-free imaging of implanted In2Sight optical device









## FET OPEN project – IN2SIGHT: **Optical set-up and image acquisition/analysis**

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#### Imaging on stained fibroblasts through the microlenses



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## FET OPEN project – IN2SIGHT







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#### Collaborations:







dkfz. GERMAN CANCER RESEARCH CENTER























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