Advanced nanotechnologies for bio applications

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MATERIALS AND PROCESSES
FOR MICRO & NANO TECHNOLOGIES

https://areeweb.polito.it/ricerca/micronanotech/

INTRODUCTION

Nanotechnologies applied to medicine are proposed for monitoring, control, construction, repair, defence and improvement of all human biological systems, working from the molecular level using engineered devices and nanostructures.

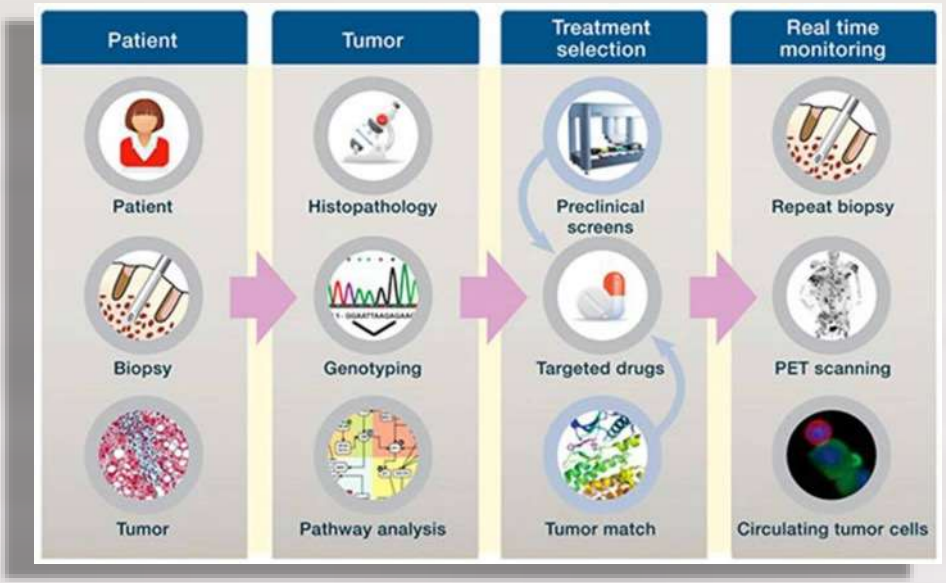
Opportunities include superior diagnostics and biosensing, improved imaging techniques – from molecules to human beings – and not least, innovative therapeutics and technologies to enable tissue regeneration and repair.

In the present talk, the most recent results in the field of biosensors, Lab-on-chip and Organ-on-chip of the Materials and Processes for Micro & Nano Technologies Labs of Politecnico of Torino will be presented and discussed.

A particular focus will be dedicated to

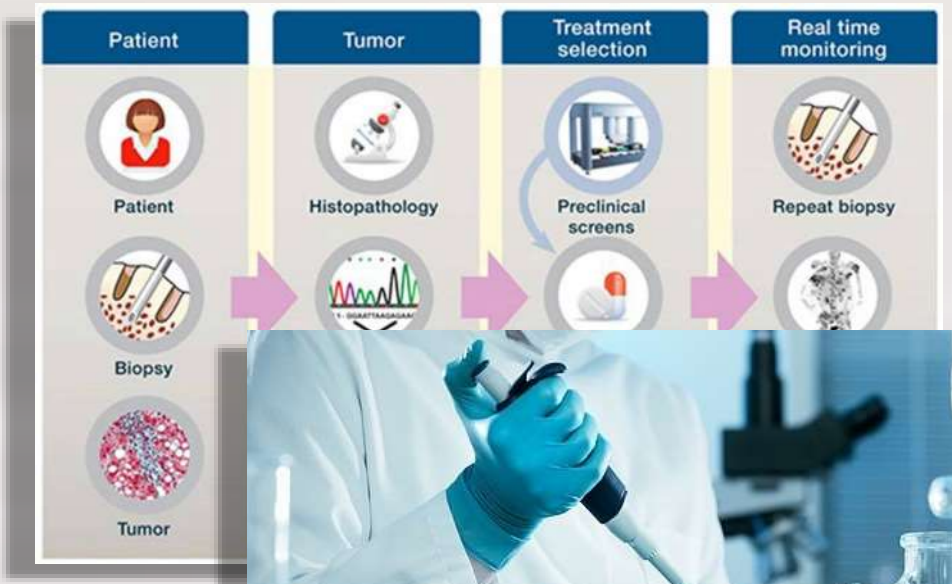
- rapid and low cost diagnostic devices and biosensors for detection of markers in tumor diseases;
- innovative solutions for in vitro drug testing and physiological scenarios mimicking.

New Challenges = New Solutions



Tools for precision medicine

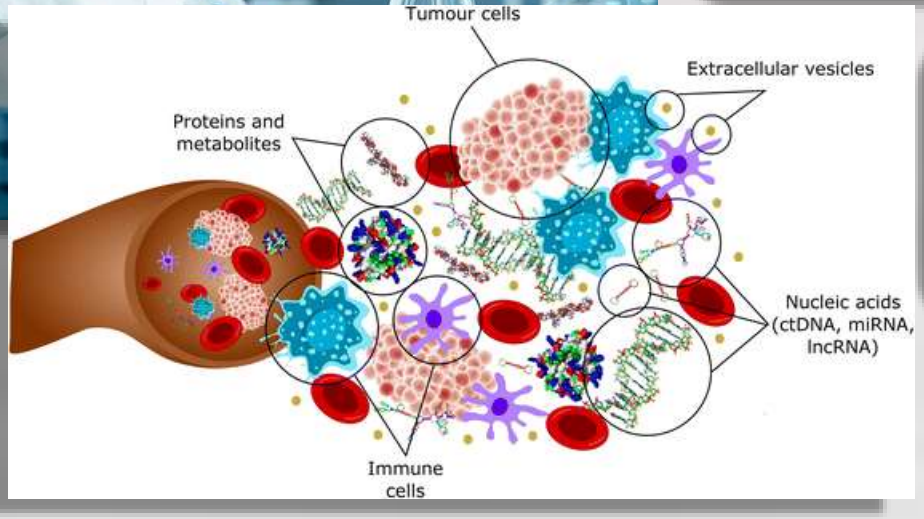
New Challenges = New Solutions



Tools for precise medicine

New Separation and Analytic platform

New Challenges = New Solutions



Tools for precise medicine

New Separation and Analytic platform

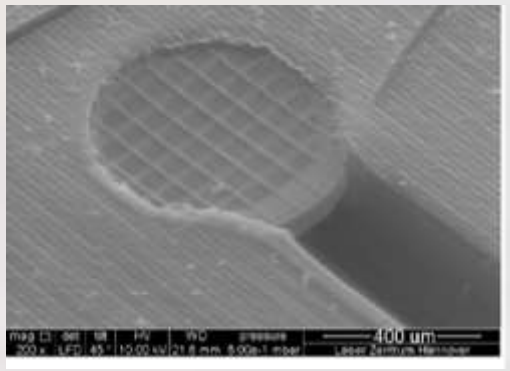
New biosensors for novel biomarkers

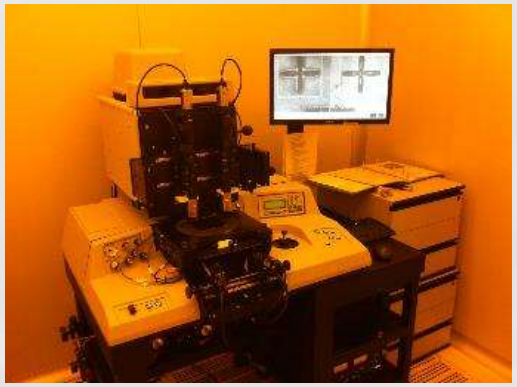
Smart Technologies

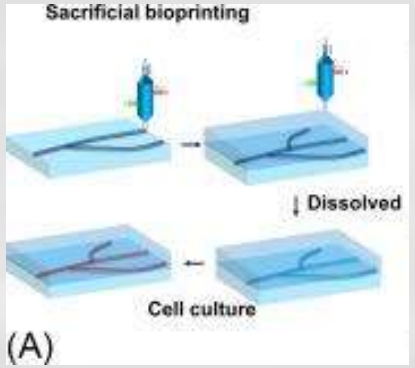
Micro & Nano technologies

Additive manufacturing

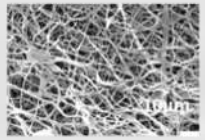
Nano materials and composites



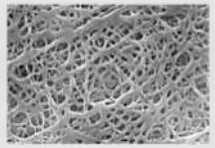




Degradation test in static condition



Degradation test in dynamic condition



IvTech bioreactor

Electrospun collagen membrane inside the holder

Our Team

http://www.polito.it/micronanotech

7 Professors

1 Administrative

12 Permanent Researchers

3 Technicians

17 Post Doc & Fellowships

28 PhD students

PIQUET
PIEMONTE QUANTUM ENABLING TECHNOLOGY

https://piquetlab.it/

POLITO BIO MED LAB

http://www.biomedlab.polito.it/

Our Facilities

- Nanofabrication LABS
- Advanced morpho./structur./composit. characterization (FESEM, XPS, AFM/STM, XRD, Raman, TEM, Fluorescence, FTIR, …)
- Advanced optical characterization (Time-Resolved Fluorescence Spectroscopy, Quantitative Phase Microscopy, Characterization of NanoPhotonic Structures, …)
- Chemical Functionalization and Biosensing

Our Facilities

PoliTo^{BIO}Med Lab - Biomedical Engineering InterDip Lab

https://www.polito.it/ricerca/centri

Quartz Crystal Microbalance (QCM)

Mission

From the bio world to the hard science, related to biomedical applications.

- Smart materials for 3D printing technologies
- Cell printing
- Organ-on-Chip – technologies for organ models, tissue growth and release of drugs

Confocal Microscope Spinning Disk

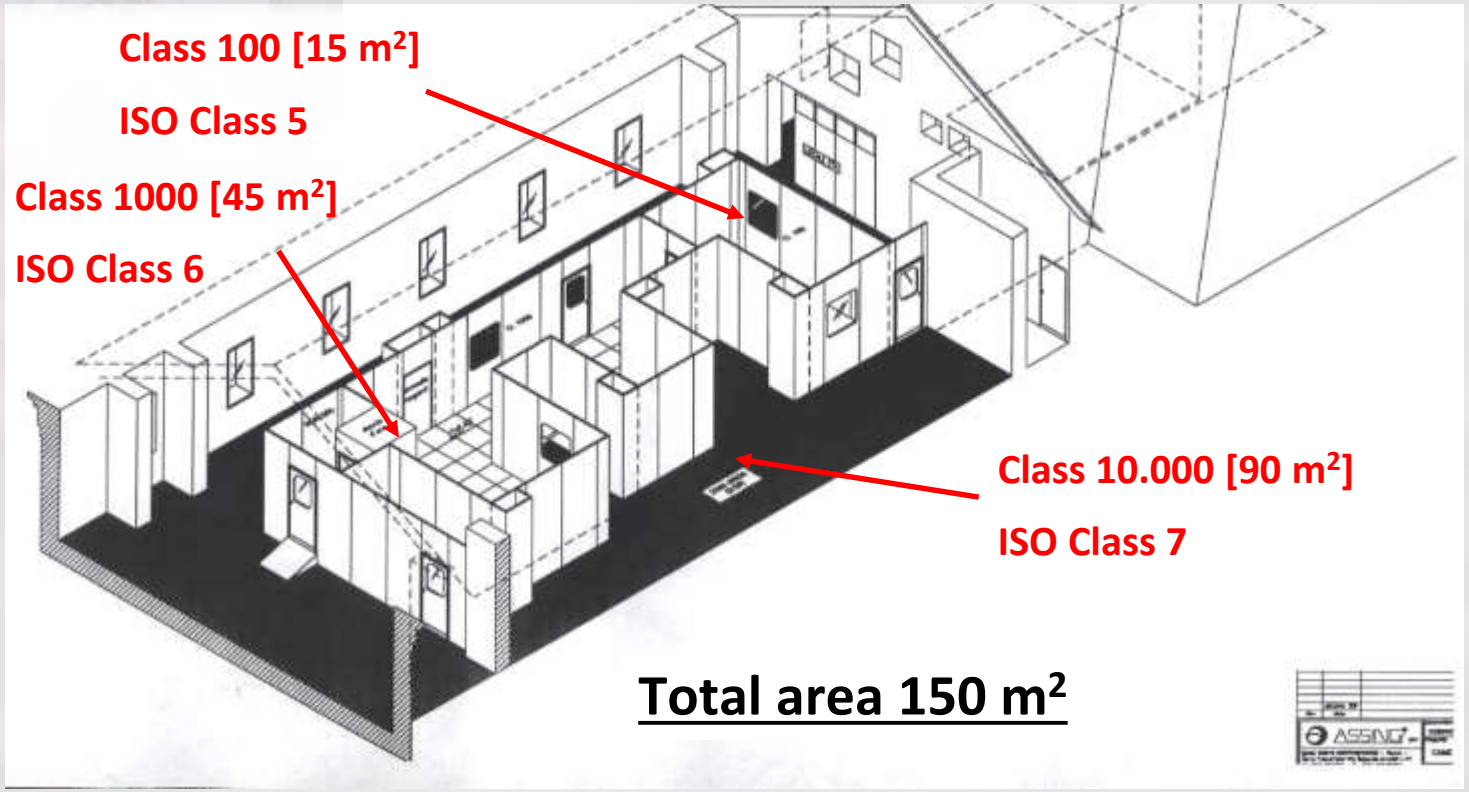
Bio printer

DLP 3D printing

Digital PCR

Our Facilities

Clean Rooms

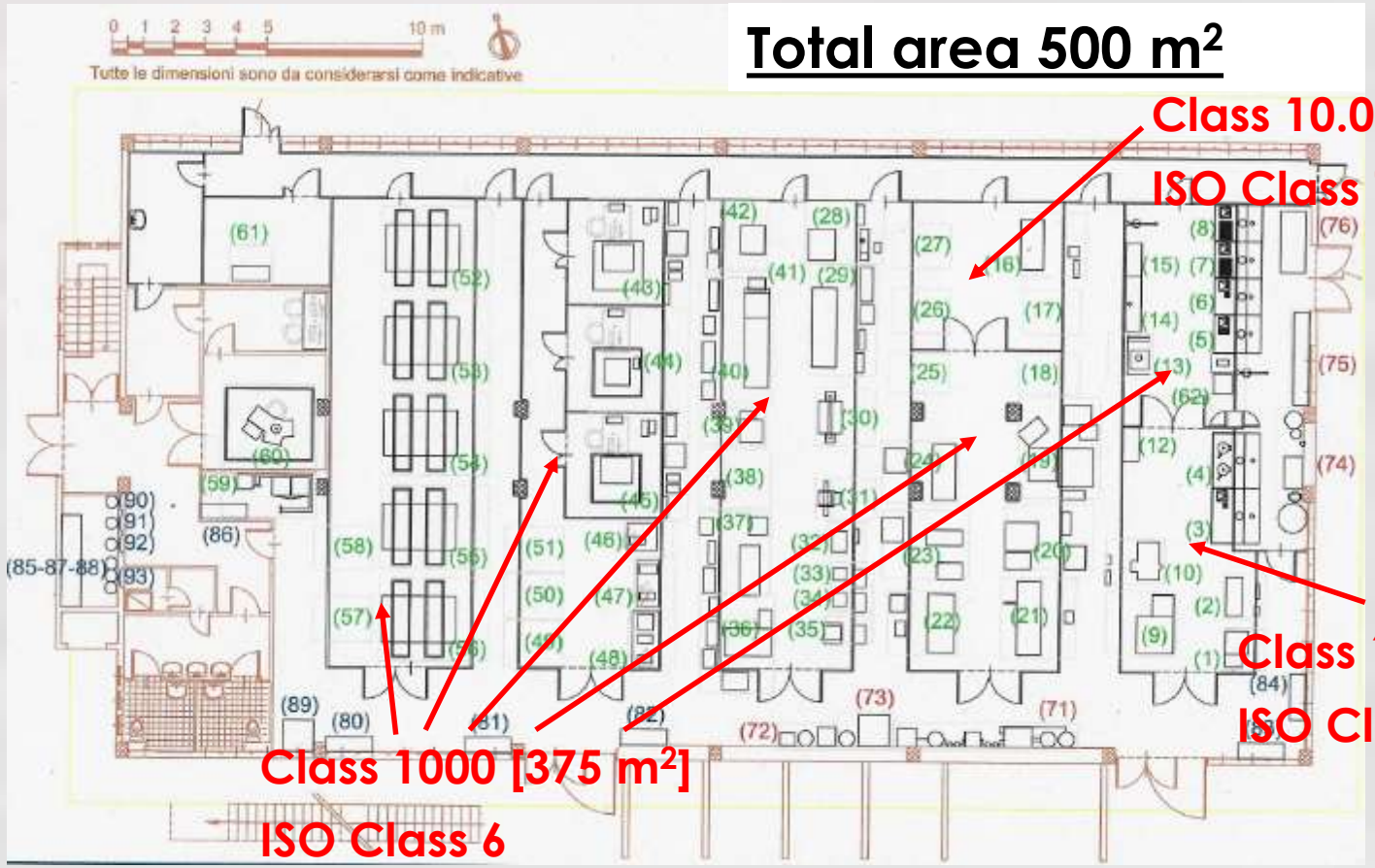


Total area 150 m²

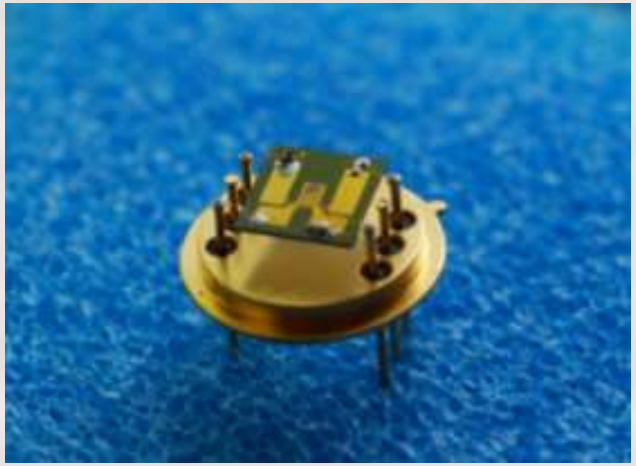
Our Facilities

CLEAN ROOMS end 2021

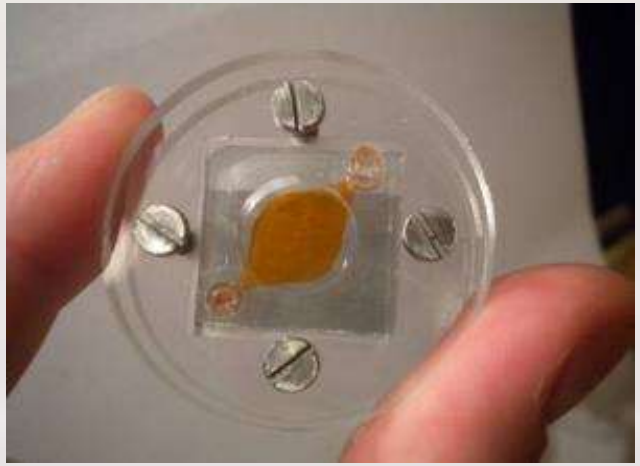
PIEMONTE QUANTUM ENABLING TECHNOLOGY



Our Expertise



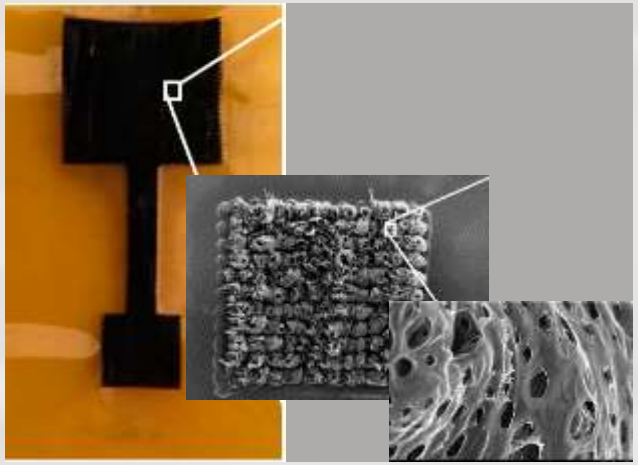
Microsensors



Lab-On-Chip & Microfluidics

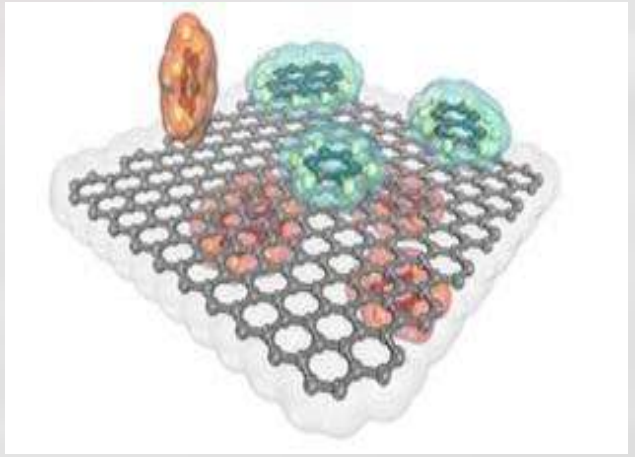
Energy & Sustainability

Electronic Systems

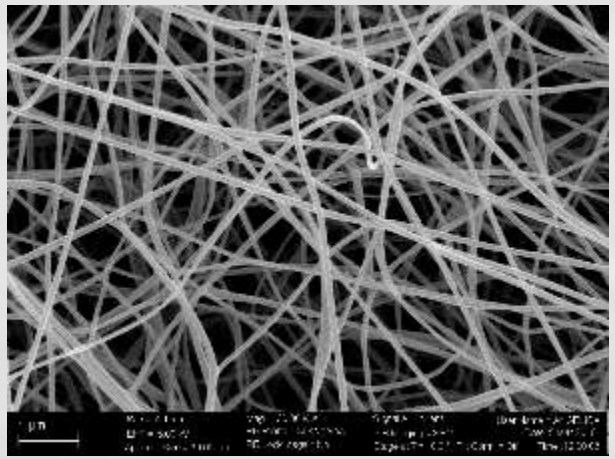


Laser Micromachining

Additive Manufacturing



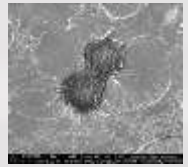
Chemical Functionalization

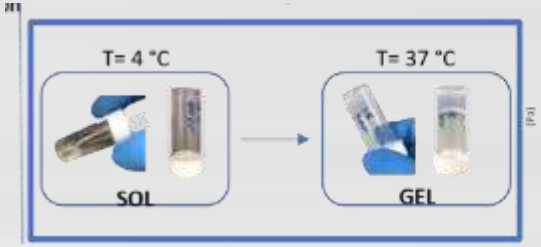


Nanomaterials Synthesis

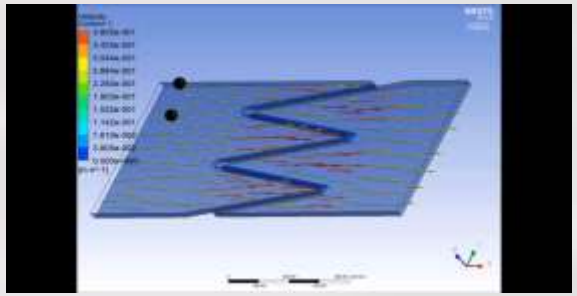
Next Generation Tools for bio applications

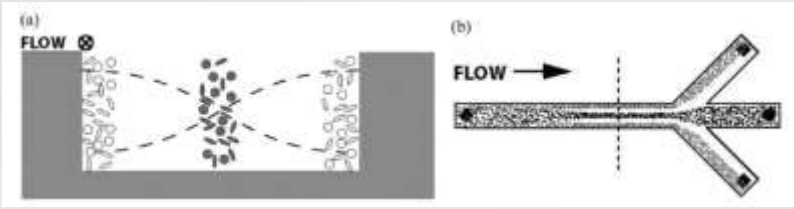
3D printing - Organ Models and Scaffolds



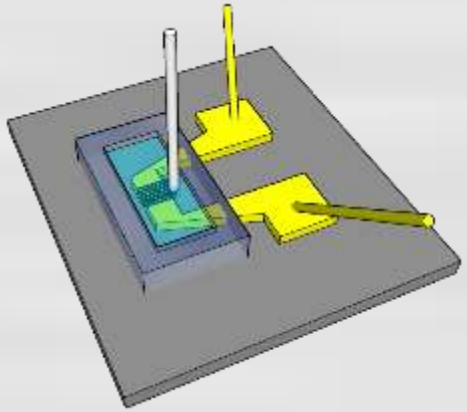


Microfluidics and LOC

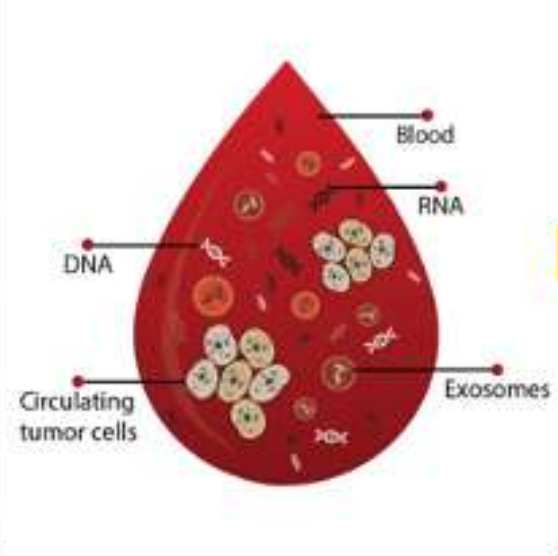




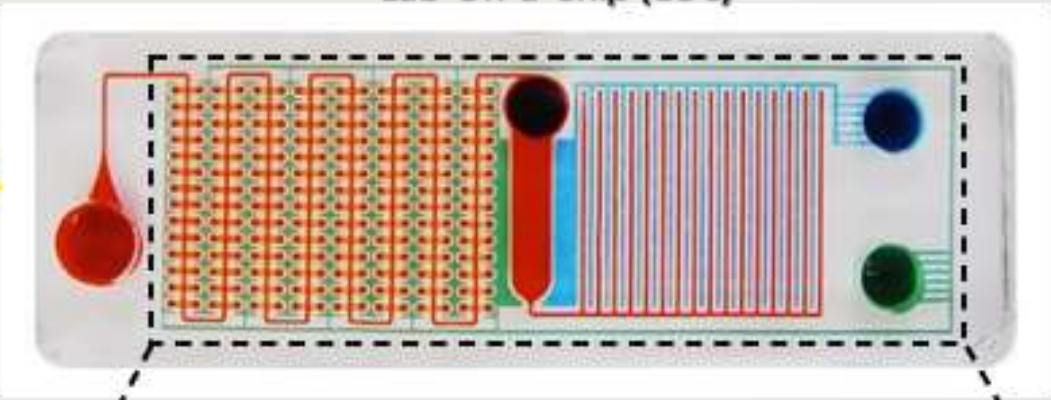
Sensors

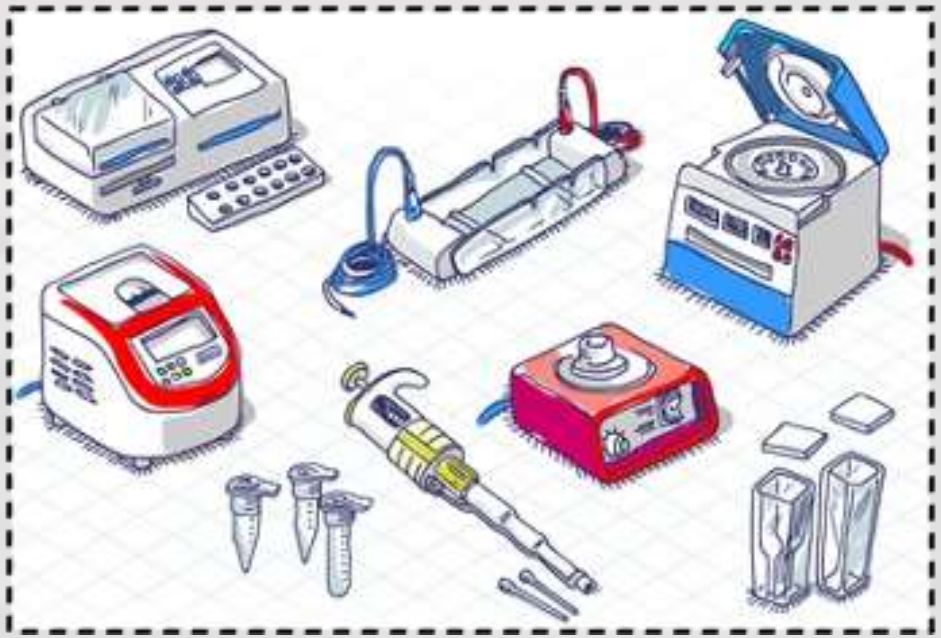


Microfluidics and LOC for Liquid Biopsy



Lab-On-a-Chip (LOC)





Microfluidics allows the miniaturization of laboratory instrumentations and procedure in portable, integrated and automated systems for **point-of-care** or **in-the-field detection**.

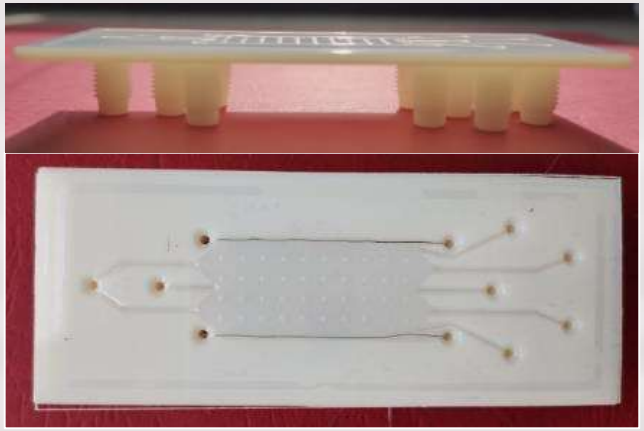
LOC features:

- ✓ Small sample volumes
- ✓ Low amount of reagents
- ✓ Rapid analyses
- ✓ High-throughputs and efficiencies
- ✓ Parallel analyses
- ✓ Low fabrication cost for high device throughputs
- ✓ Integration of multiple components
- ✓ User-friendly

Microfluidics and LOC for Liquid Biopsy

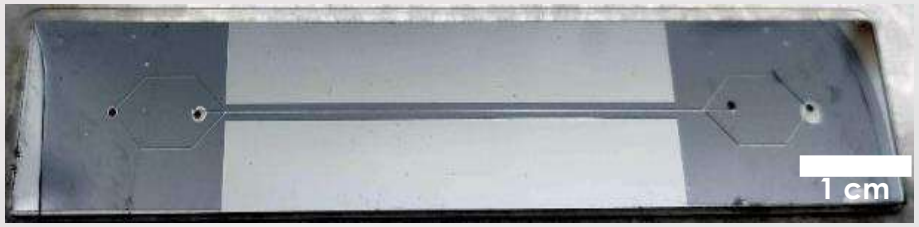
Development of three microfluidic devices for the analysis of various biomarkers as Lab-On-a-Chips for the early detection and diagnosis of lung cancer - DEFLECT Project framework

Micro-free flow electrophoresis device



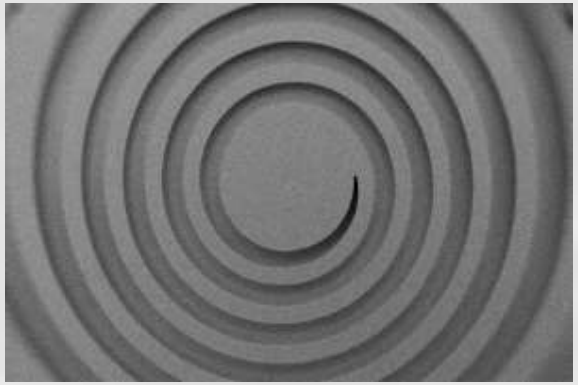
- Design and fabrication of a 3D printed microfluidic device
- Device manipulation performances of synthetic micro/nanoparticles and biological samples as extravesicles in a reduced volume

Bulk acoustic wave device



- Design and fabrication silicon-based microfluidic device
- Device separation performances of micro and nanoparticles
- Device separation performances with cells in a reduced time

MiRNA capture devices

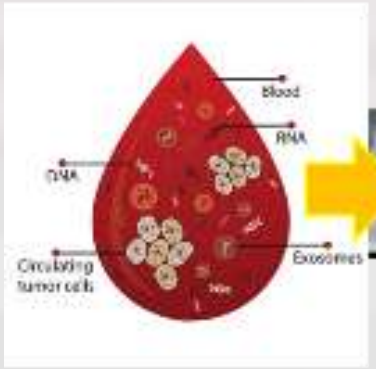


- Design and fabrication of two spiral shape PDMS-based microfluidic devices having a reaction chamber with an increased surface-to-volume ratio
- Customized and automatized on-chip detection protocol
- Capture low amount of microRNA molecules from biological fluids

Microfluidics and LOC for Liquid Biopsy

Improvement design or setting conditions to each microfluidic devices according to biological test results

Development of a rapid and integrated multi-analysis systems for liquid biopsy

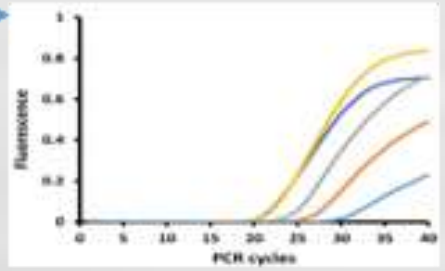


Circulating tumor cells

Nucleic acids

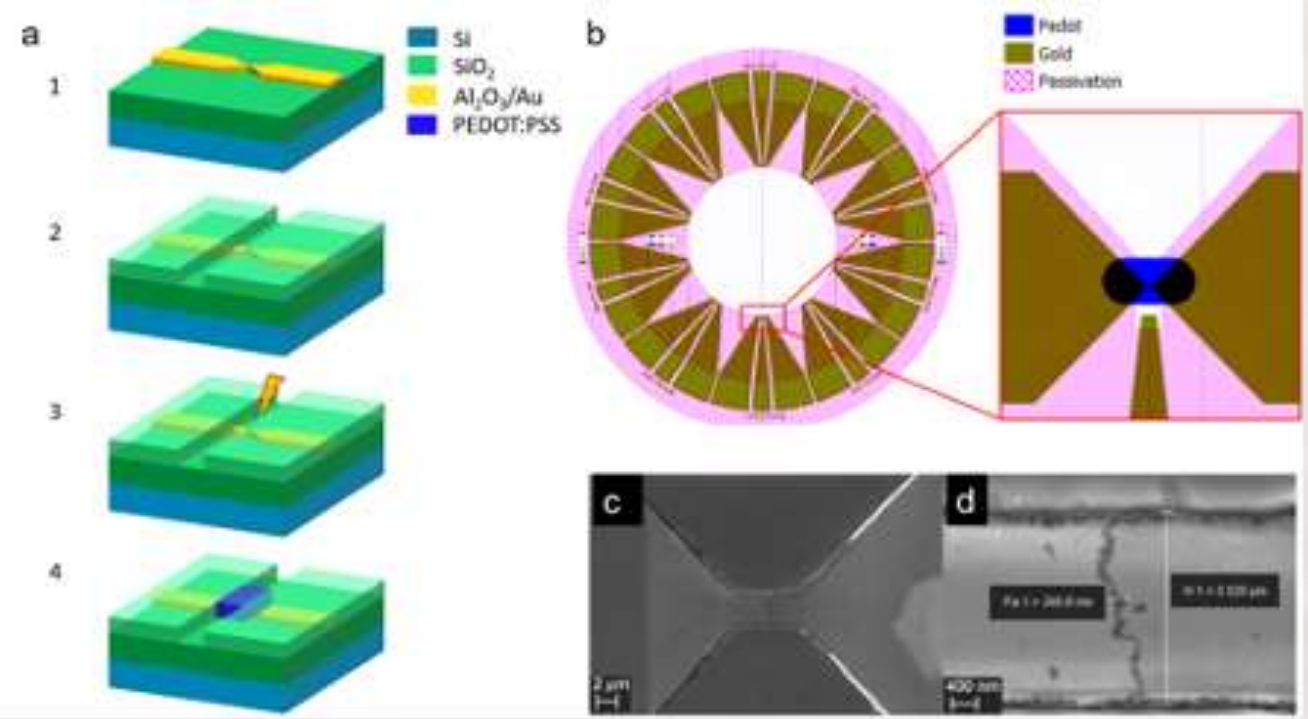
Extravesicles

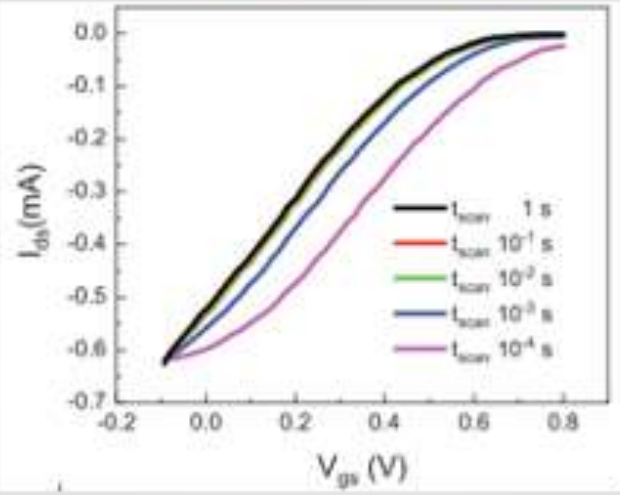
Proteins

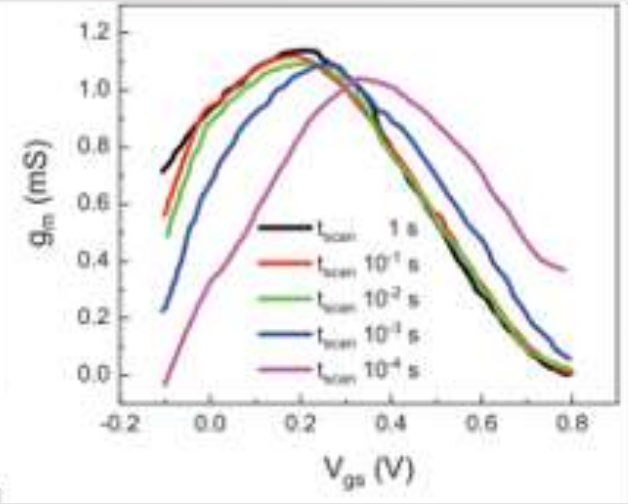


Nucleic acids capture

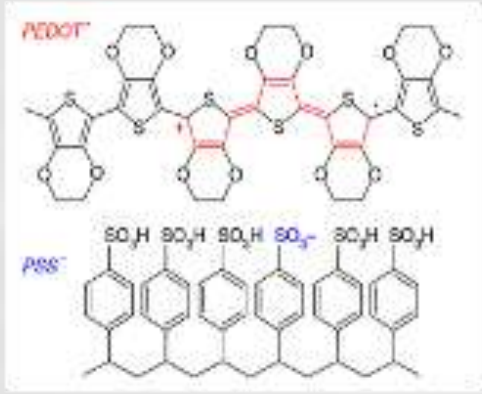
Biosensors: Scaling down to nanozised architecture







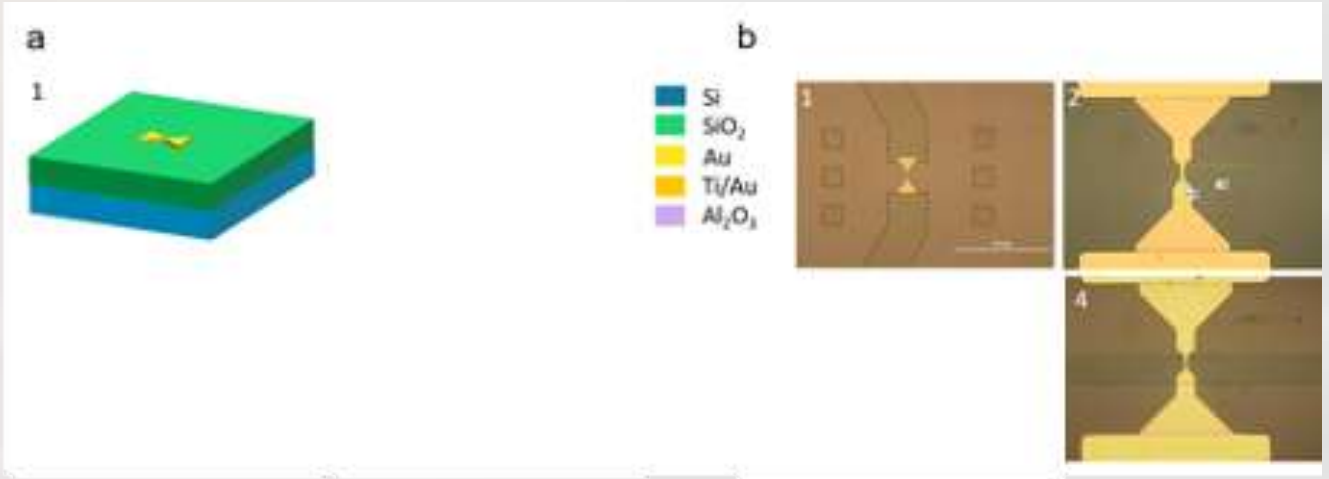
- PEDOT:PSS channel

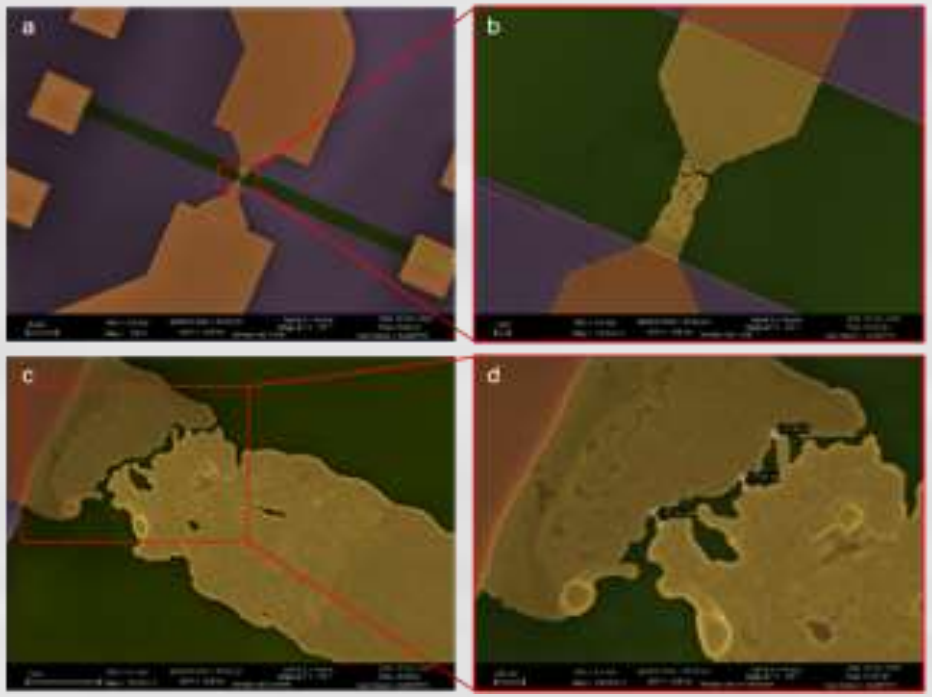


- Minimization of the role of ions diffusion on OECT operation:
  - Superior amplification fast-varying signal with respect to conventional µm sized OECT
  - Fast response (milliseconds scale)

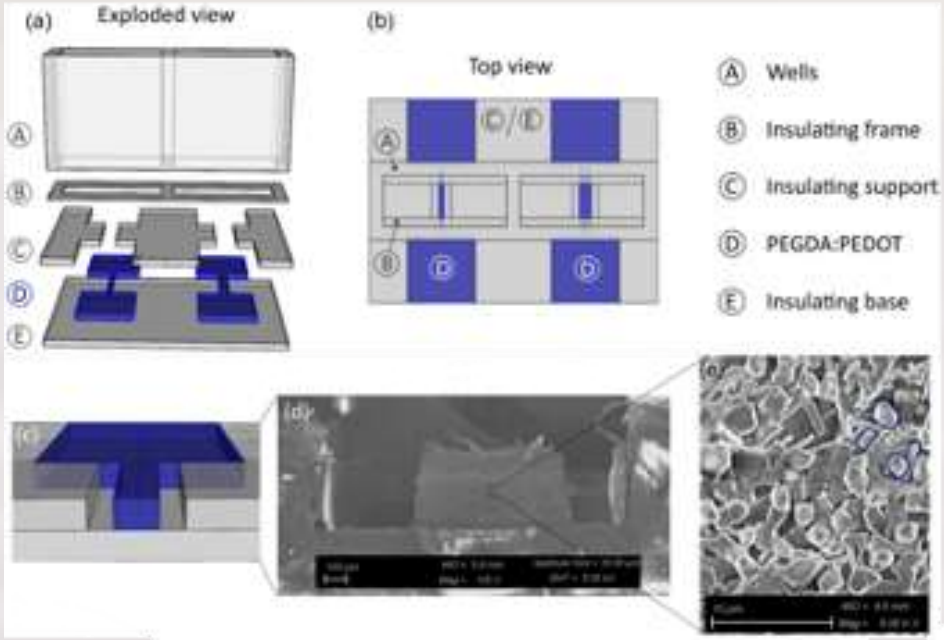
Biosensors: Scaling down to nanozised architecture

1. Microwire fabrication
2. Source/drain contact fabrication
3. Source/drain passivation
4. Nanochannel fabrication via EIBJ
5. Polymer deposition

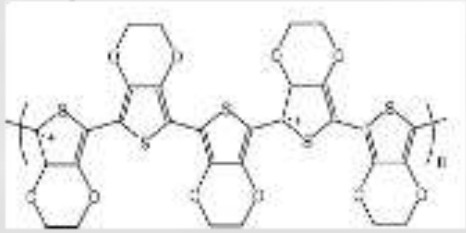




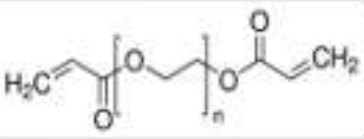
Biosensors by 3D printing of active resins



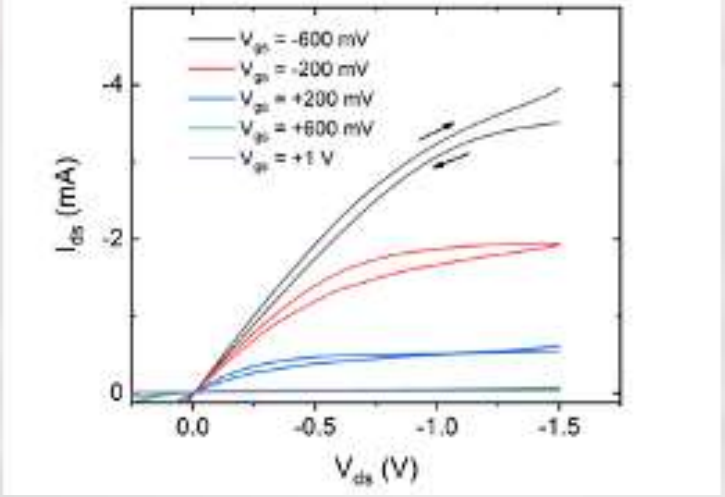
- Active material = PEGDA:PEDOT
  - Photocurable resin
  - Anionic PSS shell replaced by non-polar PEGDA matrix
- Depletion-mode OECT
- $\frac{I_{on}}{I_{off}} \simeq 10^3$
- $g_{m,max} = \max\left(\frac{\partial I_{ds}}{\partial V_{gs}}\right) \simeq 2.5\ mS$

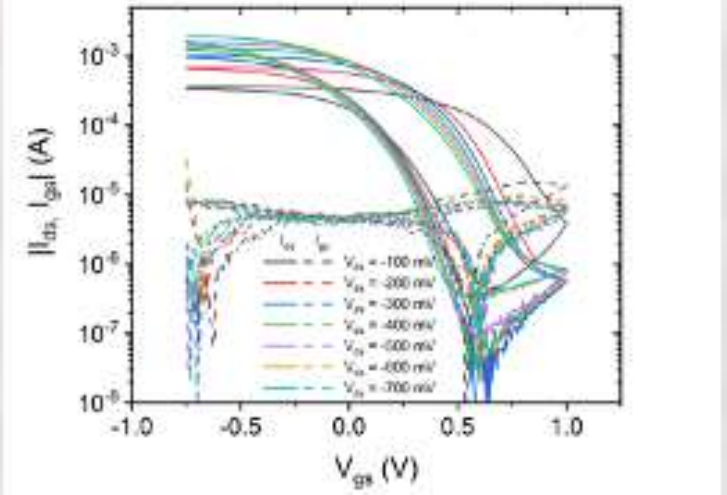


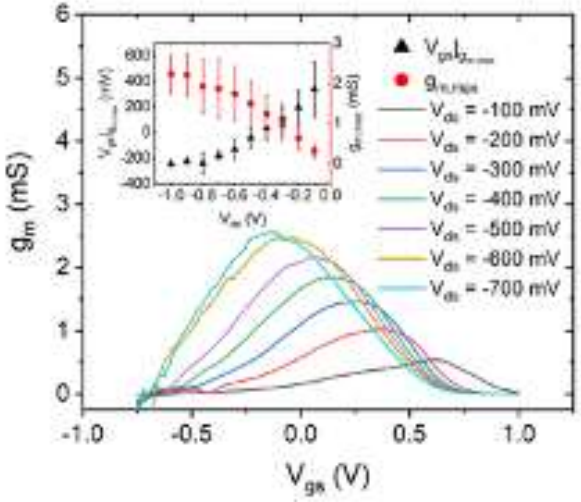
PEDOT



PEGDA



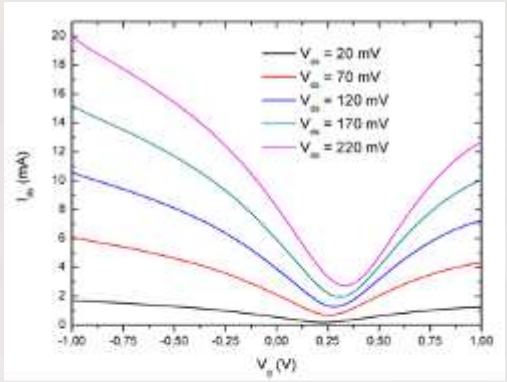


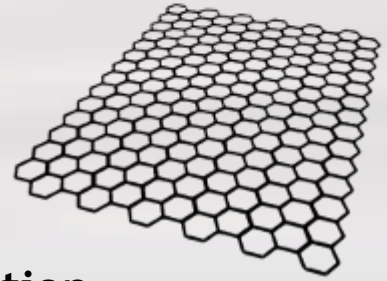


Biosensors: 2D nanomaterial based

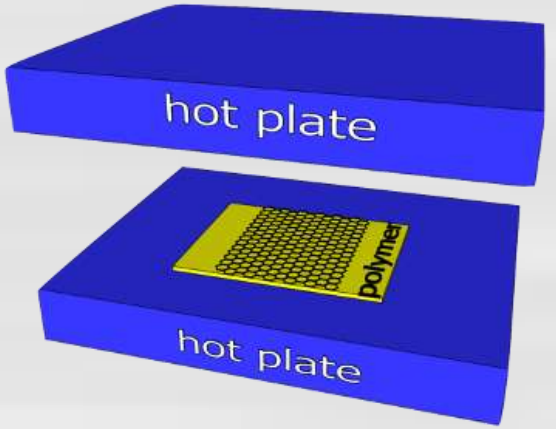
Graphene Field Effect Transistor

- Specific transcharacteristic, goes from conducting electrons to conducting holes
- Never turns off
- High sensibility where the slope is higher
- Easy to functionalize

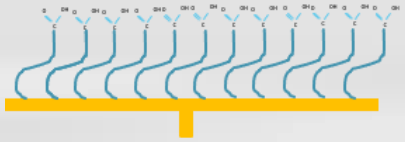


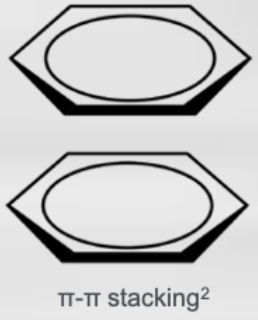


Hot Embossing graphene transfer

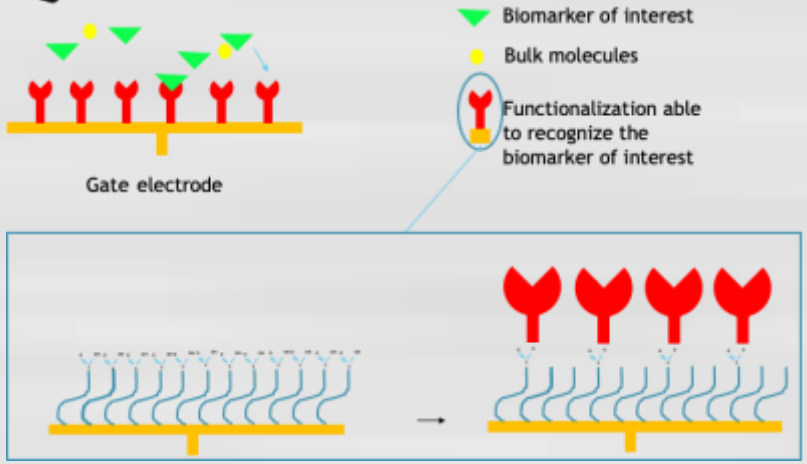


Functionalization



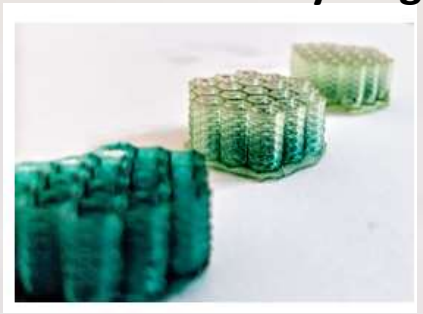


- Caffeic acid
- Triptophan
- Pyrene
- Indole-3-butyric acid
- Tran-cinnamic acid
- Thionine
- Protoporphyrin IX
- Benzophenone COOH



3D printing - Polymers

Hydrogels



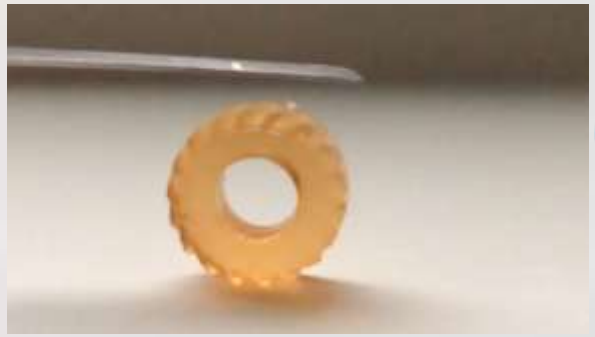
Proteins inclusion or grafting

Cells growth

Conductive polymers
In situ polymerization:
3D Printed
Conductive hydrogels

Fantino et al. **Macromol. Mat. Eng., 2018**. 1700356

Flexible materials

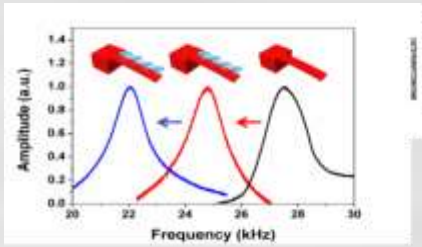


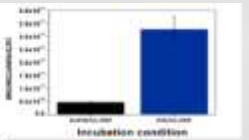
microfluidics

Monomers for easy post functionalization

Active Microfluidics
Channels functionalization

Functional Polymers for BIO

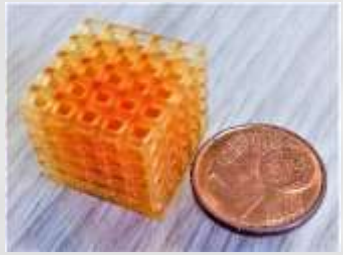




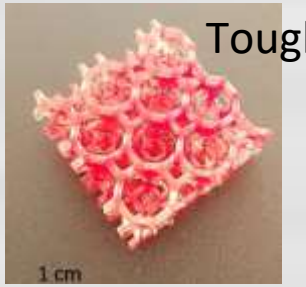
Fast production of sensors easy functionalization

Stassi, S. et al. , **ACS Appl. Mat Interfaces 2017**, 9, 19193-19201

CO_2 capture



Hybrid Epoxy-Acrylic



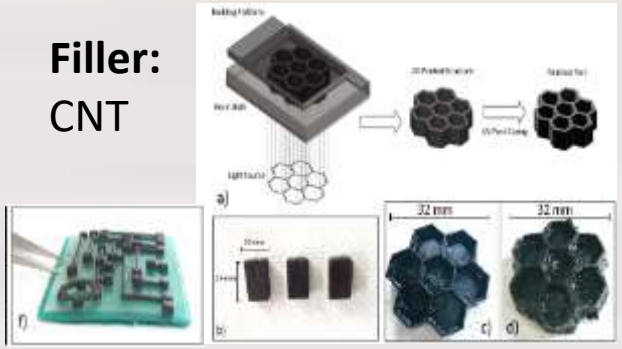
Toughness

Lantean et al. **Inventions 2018**.

3D printing - Use of FILLERS: nanocomposites

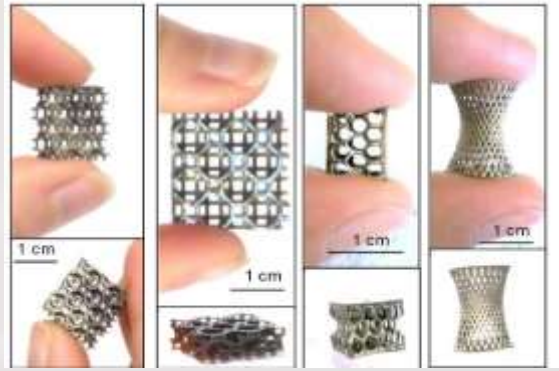
ELECTRICAL PROPERTIES

Filler: CNT



Gonzalez, G et al. **Polymer 2017**, 109, 246

Filler: In situ silica Silver NPs



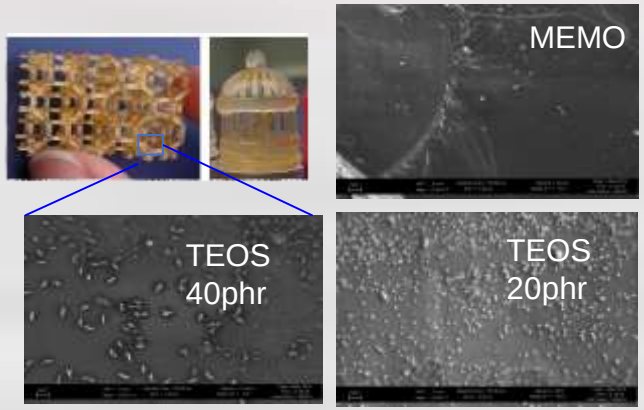
Fantino et al. **Adv Mat, 2016**. 28 (19),3712

MAGNETIC PROPERTIES

Filler: Magnetic NPs

MECHANICAL PROPERTIES

Filler: In situ silica NPs

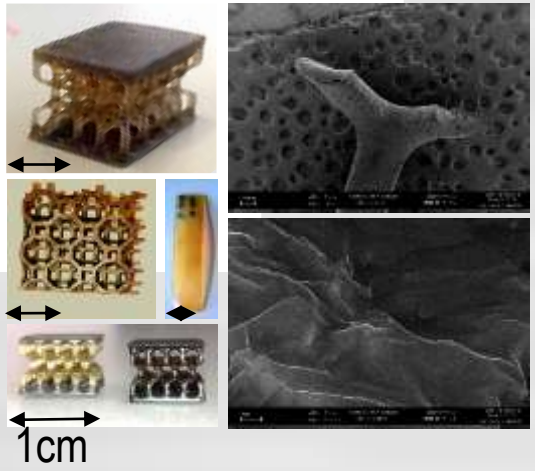


Chiappone, A.; et al. **ACS Appl. Mat Interfaces 2016**, 8, 5627

Filler: CELLULOSE NANOCRYSTALS

Wang J., et al. **Ang. Chem., 2018**. 57,2353

Filler: Graphene Oxide



A. Chiappone et al. **Composites part B 2017,** 124,9

3D printing - Use of Functional Dyes

Photoresponsive 3D printed structures

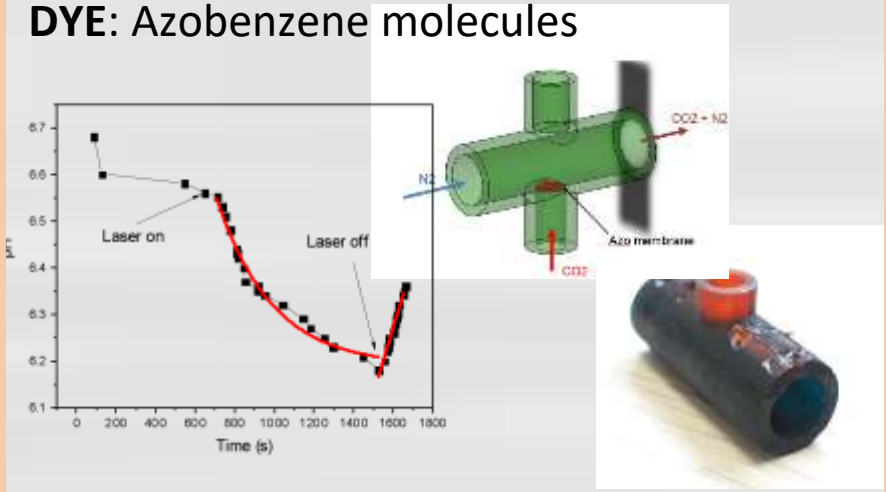
PHOTORESPONSIVE MECHANICAL PROPERTIES

DYE: Azobenzene molecules

Roppolo, I. et al. , **Materials Horizons (2017)** *4, 396-401*

PHOTORESPONSIVE CO_2 PERMEABILITY

DYE: Azobenzene molecules

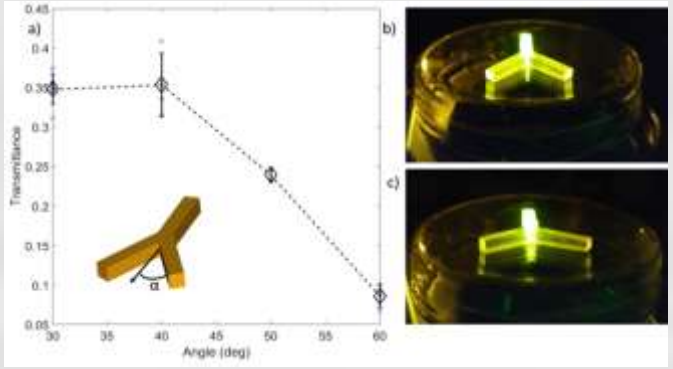


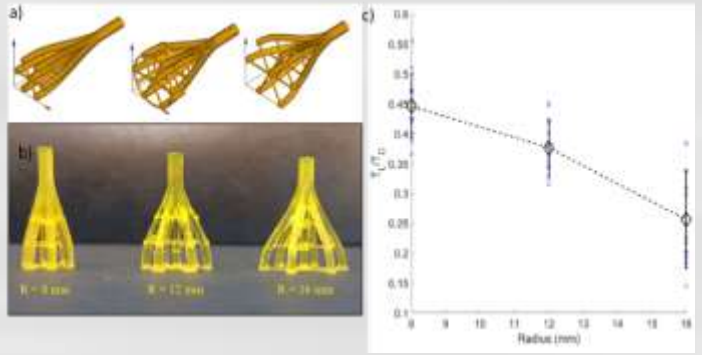
Gillono, M. et al. Applied Material Today (2020)

Photoluminescent 3D printed waveguides

OPTICAL PROPERTIES

DYE: photoluminescent molecule

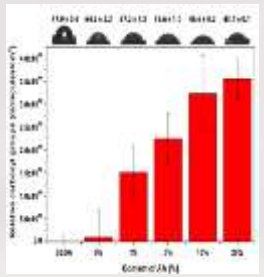




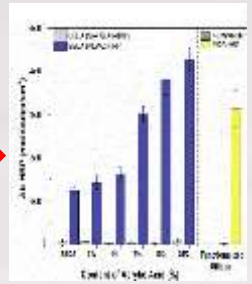
Frascella, F. et al. ACS Appl. Mat Interfaces 2018, 45, 39319-39326

3D printing - Biomaterials

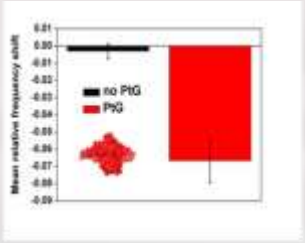
STUDY OF DIFFERENT MONOMERS + ADDITIVES

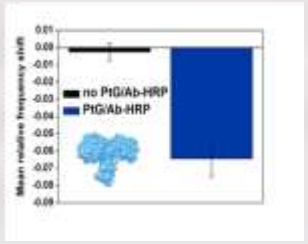


Evaluation of available - COOH groups

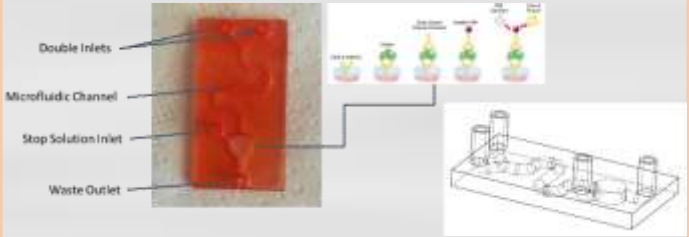


Bioassay functionalization

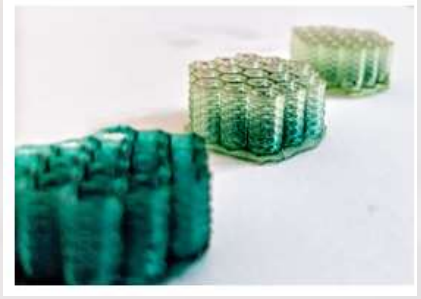


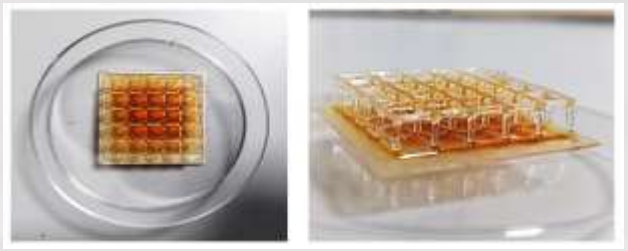


SURFACE FUNCTIONALIZATION FOR BIOMOLECULES DETECTION SMART MICROFLUIDICS

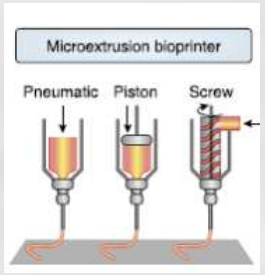


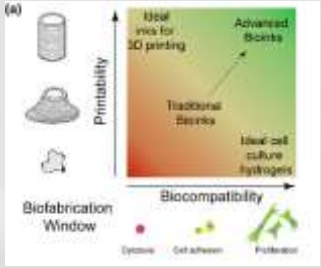
PRINTING OF PROTEINS OR ENZYMES IN HYDROGELS





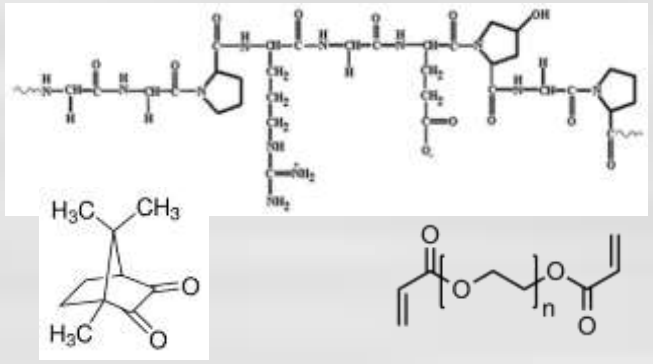
BIOPLOTTING

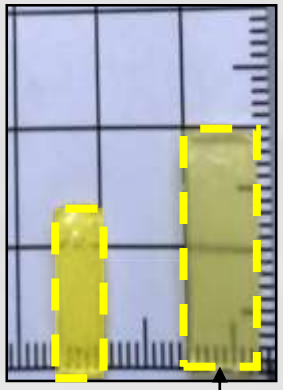




PHOTOCURABLES HYDROGELS

LIGHT INDUCED CROSSLINKING OF GELATIN for scaffolds

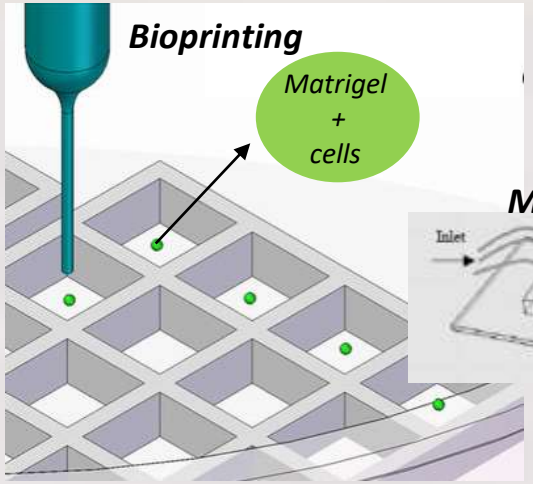


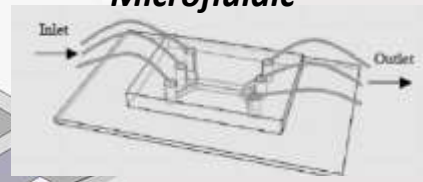


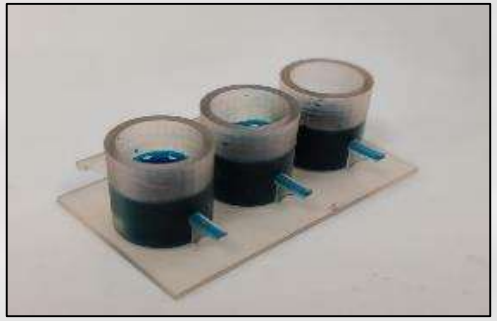
Organ Models and Scaffolds

SMART MULTIWELLS

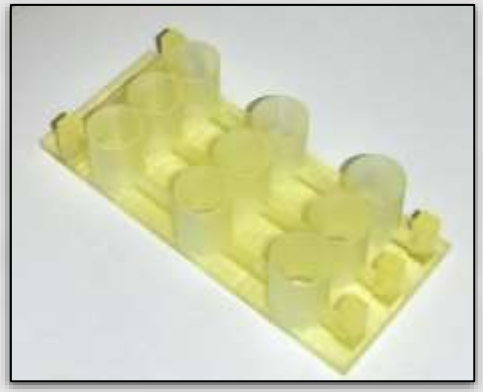
Study of bioinhert monomers for the production of smart multiwells







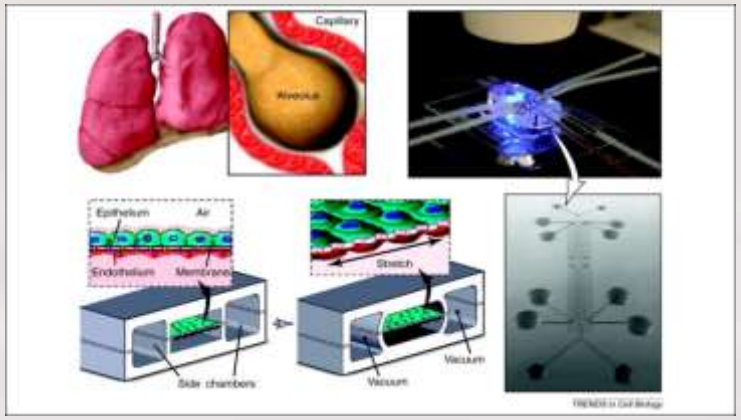
- Automated organoid culture
- High-throughput screen for drug candidates with patient-derived cancer organoids
- Multi material 3D printing device, with possible material spatial selective functionalization



Frascella, F. et al, Nanomaterial 2020

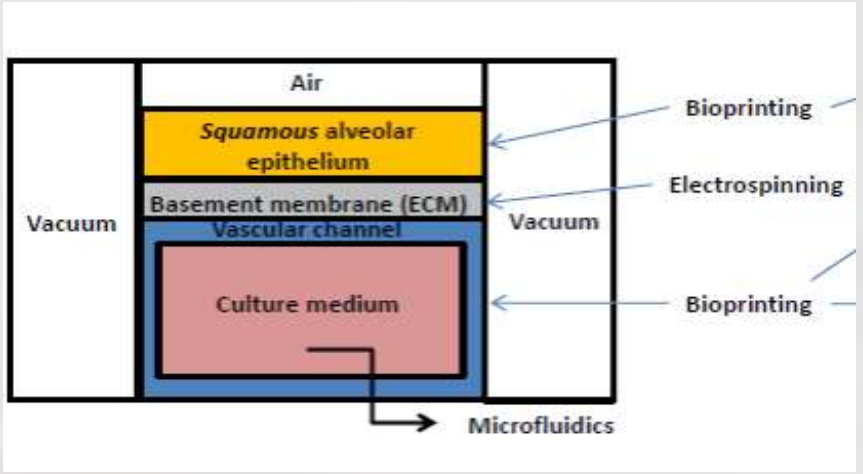
Organ Models and Scaffolds

LUNG ON CHIP

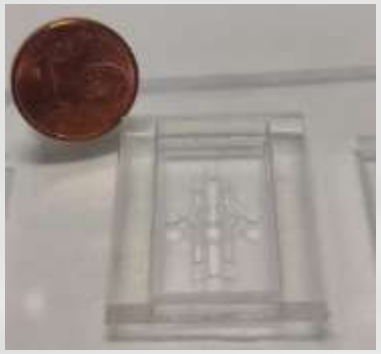


Science 2010;328(5986):1662-8

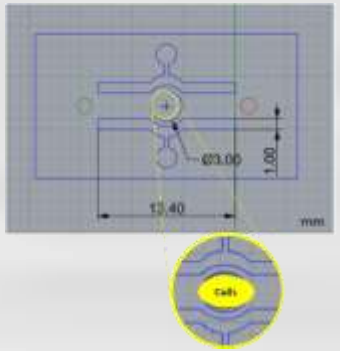
Microfluidic and biomimetic system of healthy and pathological lung tissue



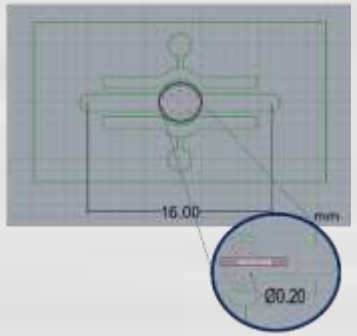
Prototipo dispositivo polimerico 3D (Organ on chip) per organoidi

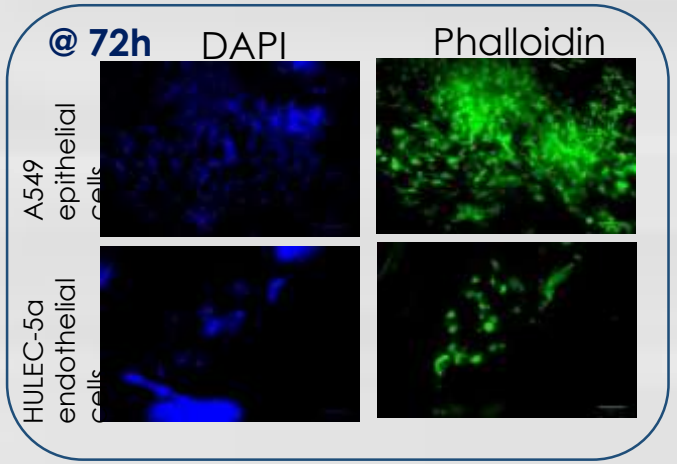


TOP LAYER



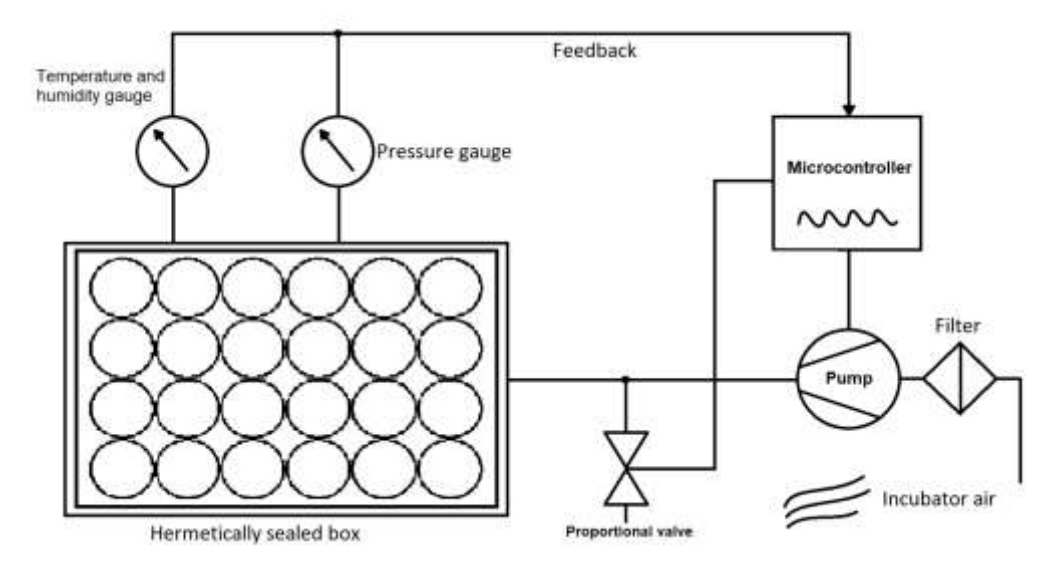
BOTTOM LAYER



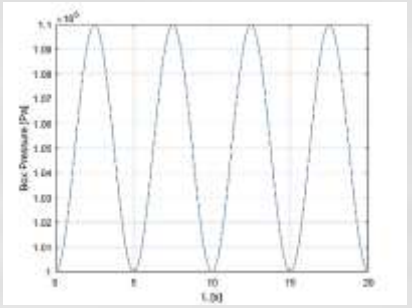


Organ Models and Scaffolds

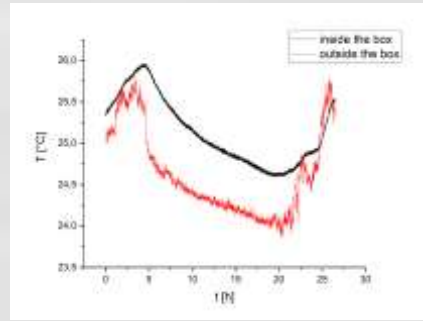
Mechanical stimulation of organoids



Pressure monitoring



Differential T monitoring



- Evaluation of the response of lung organoid cultures to an external mechanical stimulus pneumatically applied
- The system is designed to work in a standard CO_2 incubator

* in collaboration with Prof. Luca Primo, Dr. Valentina Monica (UniTO)

Organ Models and Scaffolds

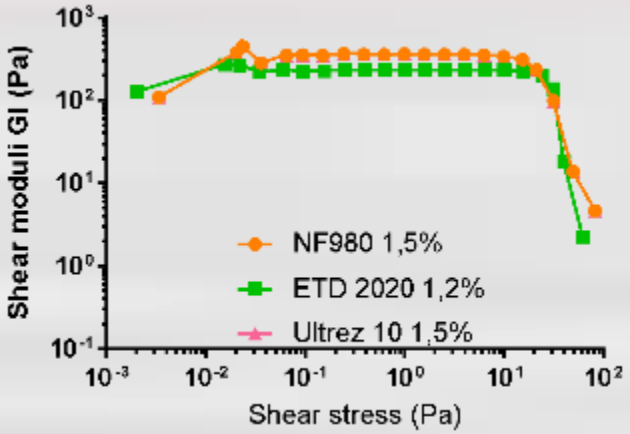
3D bioprinting of cell-laden bioinks – Lung on Chip

1 - CARBOPOL – sacrificial material

Ultrez 10 1,5% ETD 2020 1,2% NF980 1,5%

= 5 mm

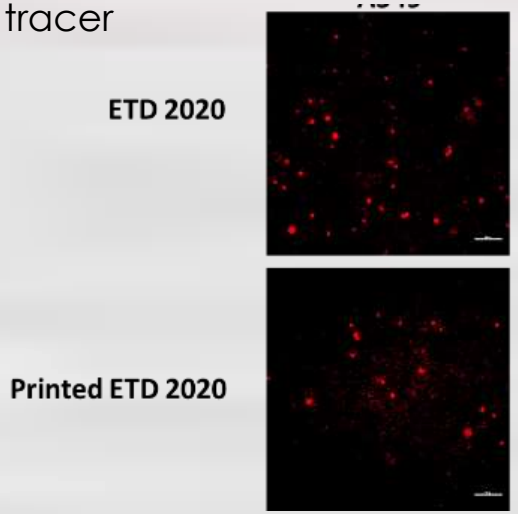
Printability test by means of reology



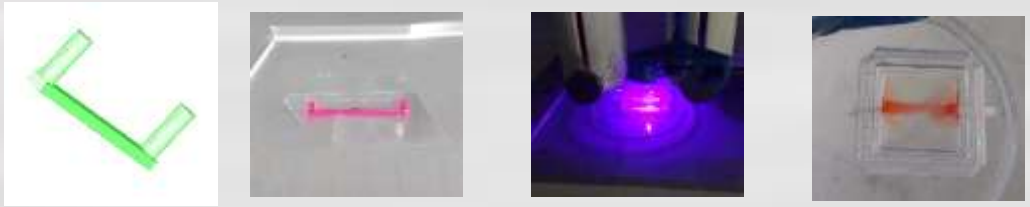
Baruffaldi D. et al. Bioprinting, 2021

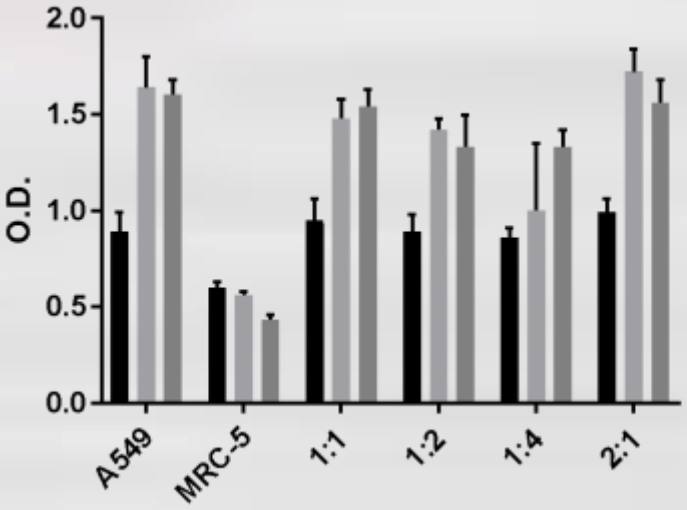
Cell lines tested:
- A549, lung cancer epithelial
- MRC-5 normal lung fibroblast

CYTO-ID® Red long-term cell tracer



2 - GelMA – matrix





co-colture in different GelMA – cell viability

THANK YOU FOR YOUR ATTENTION

C.F. Pirri

Politecnico, C.so Duca degli Abruzzi 24, 10129 Torino (ITALY)
Istituto Italiano di Tecnologia, Via Livorno 60, 10144 Torino (ITALY)

MATERIALS AND PROCESSES
FOR MICRO & NANO TECHNOLOGIES

https://areeweb.polito.it/ricerca/micronanotech/