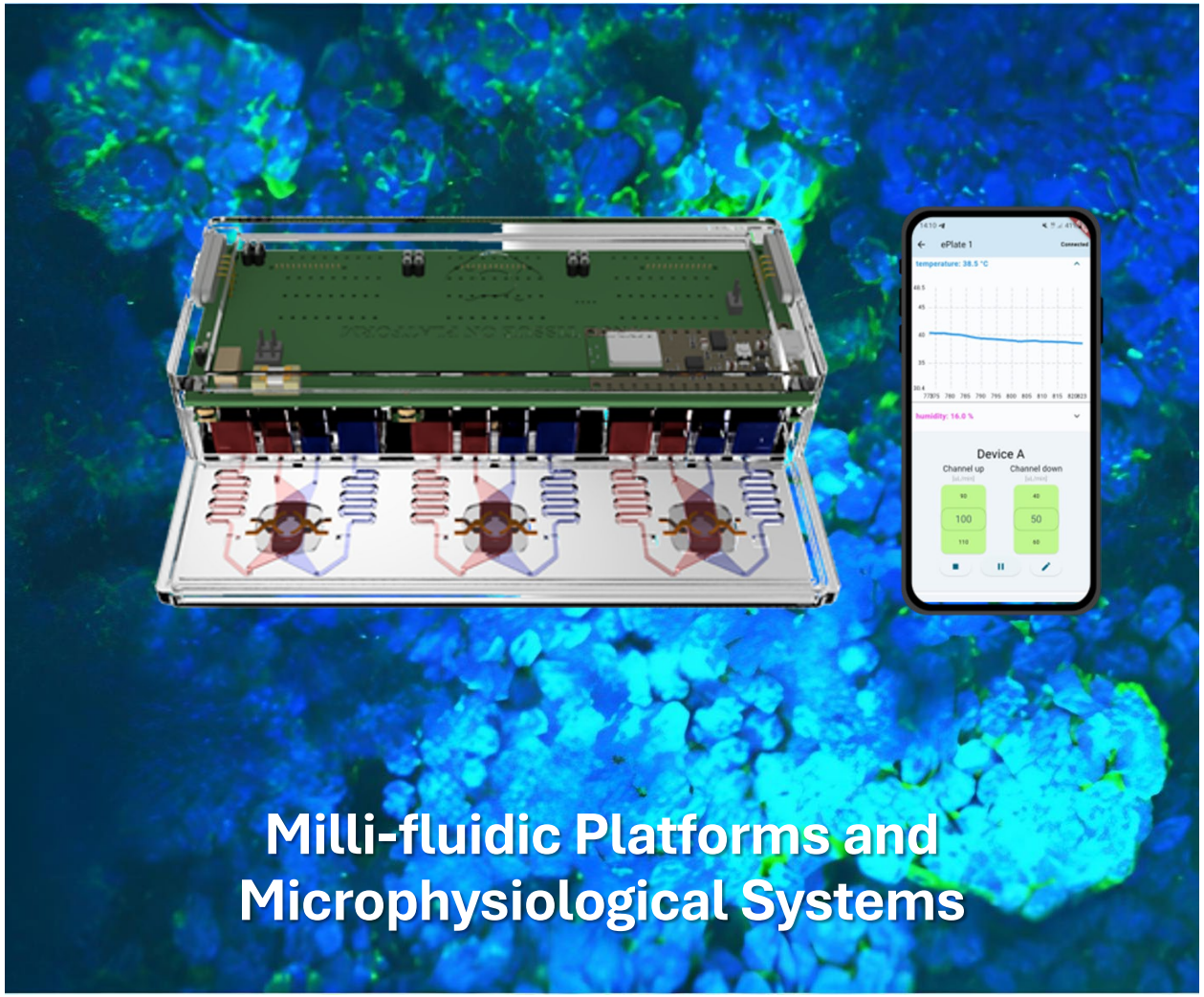
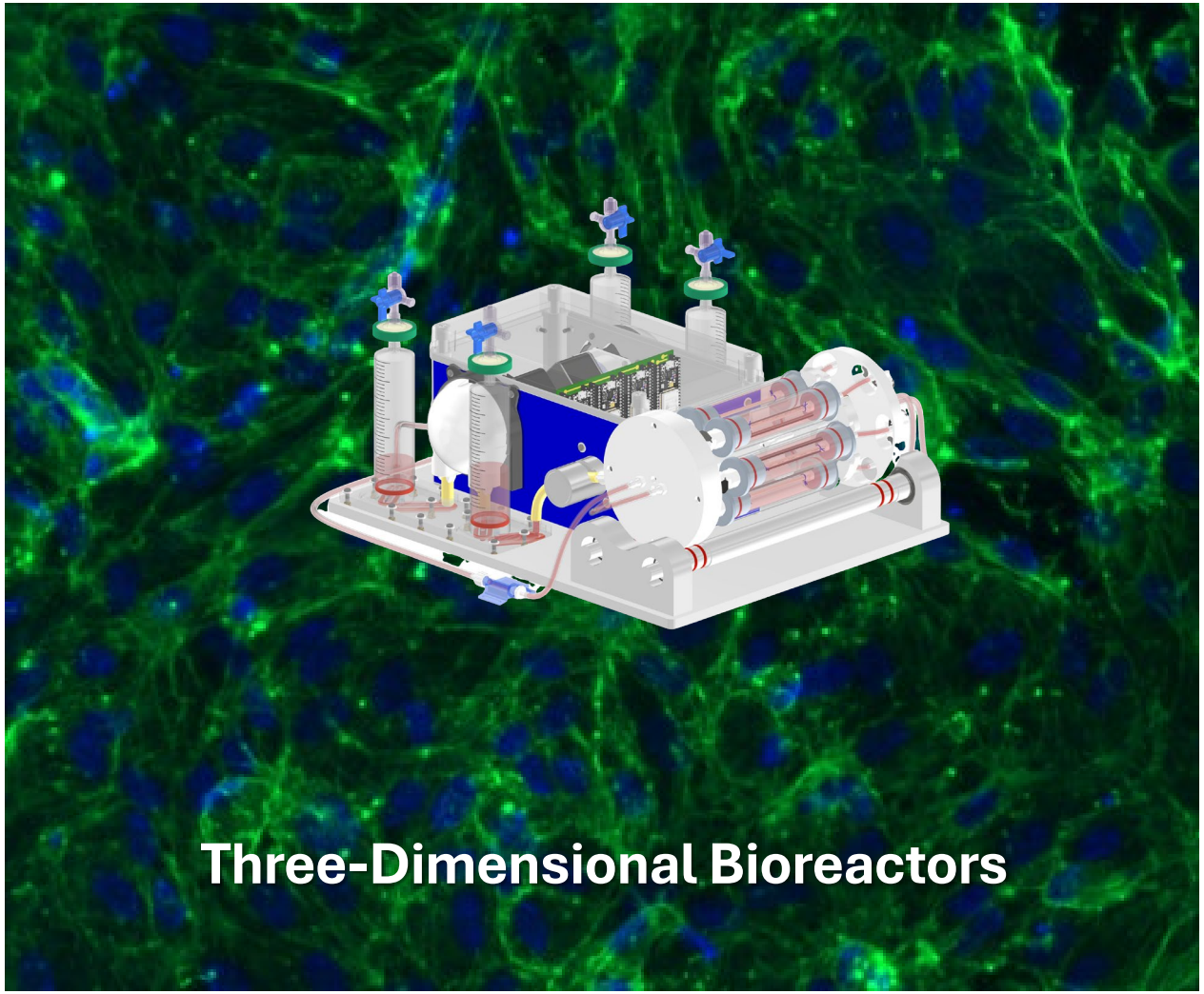
ADVANCED CULTURE SYSTEMS
Activities & Thesis Projects

Research Activities



Milli-fluidic Platforms and Microphysiological Systems

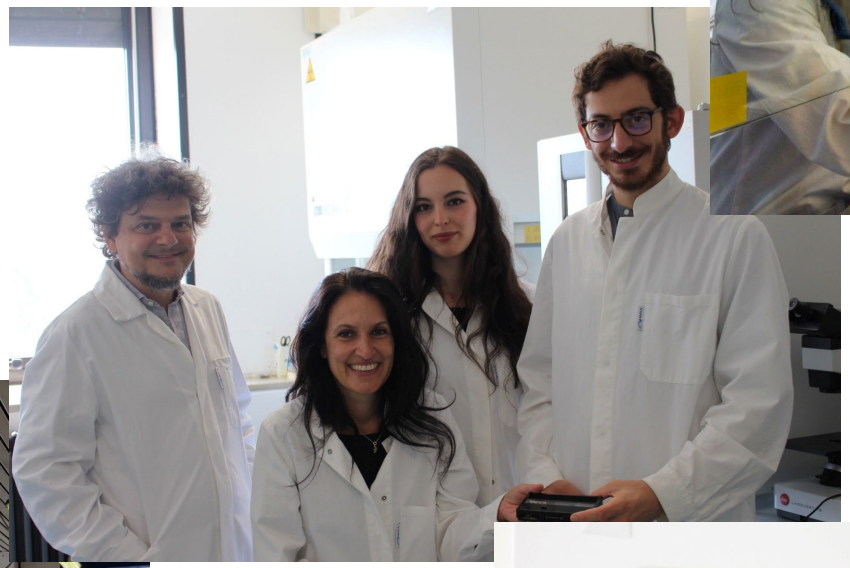


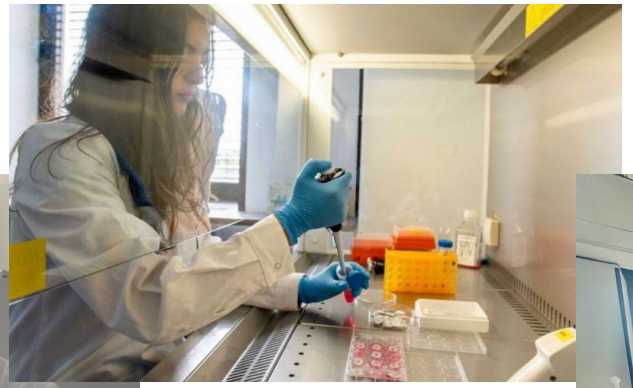
Three-Dimensional Bioreactors

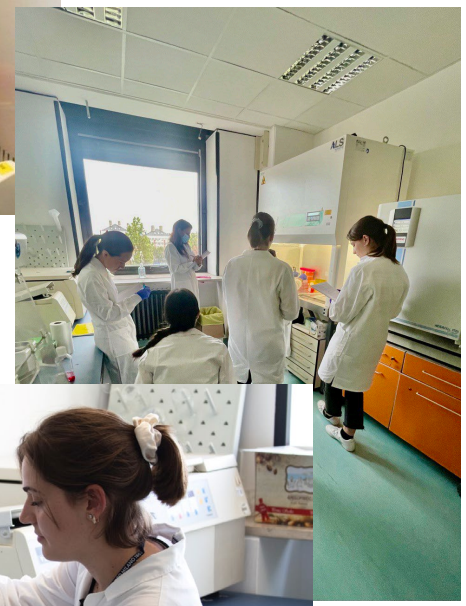
Biomechanics Research Group

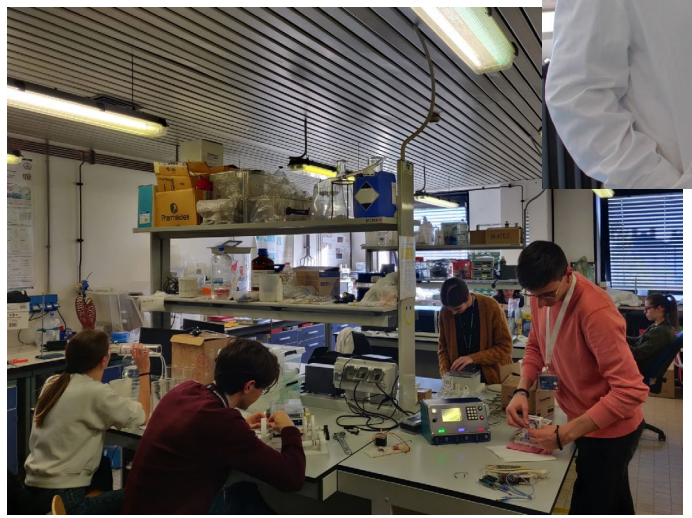
Advanced Culture Systems

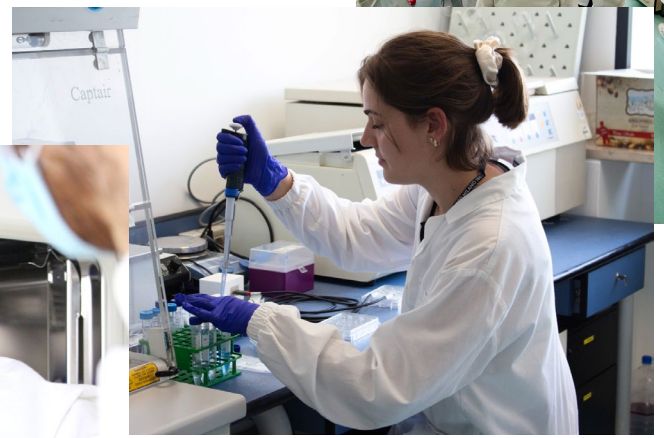
ATTiC Lab
Advanced Technology for Tissue Culture











Biomechanics Research Group

Advanced Culture Systems

Team


Monica Soncini


Gianfranco B Fiore


Lorenzo Coppadoro


Elia Pederzani


Alessandra Rando

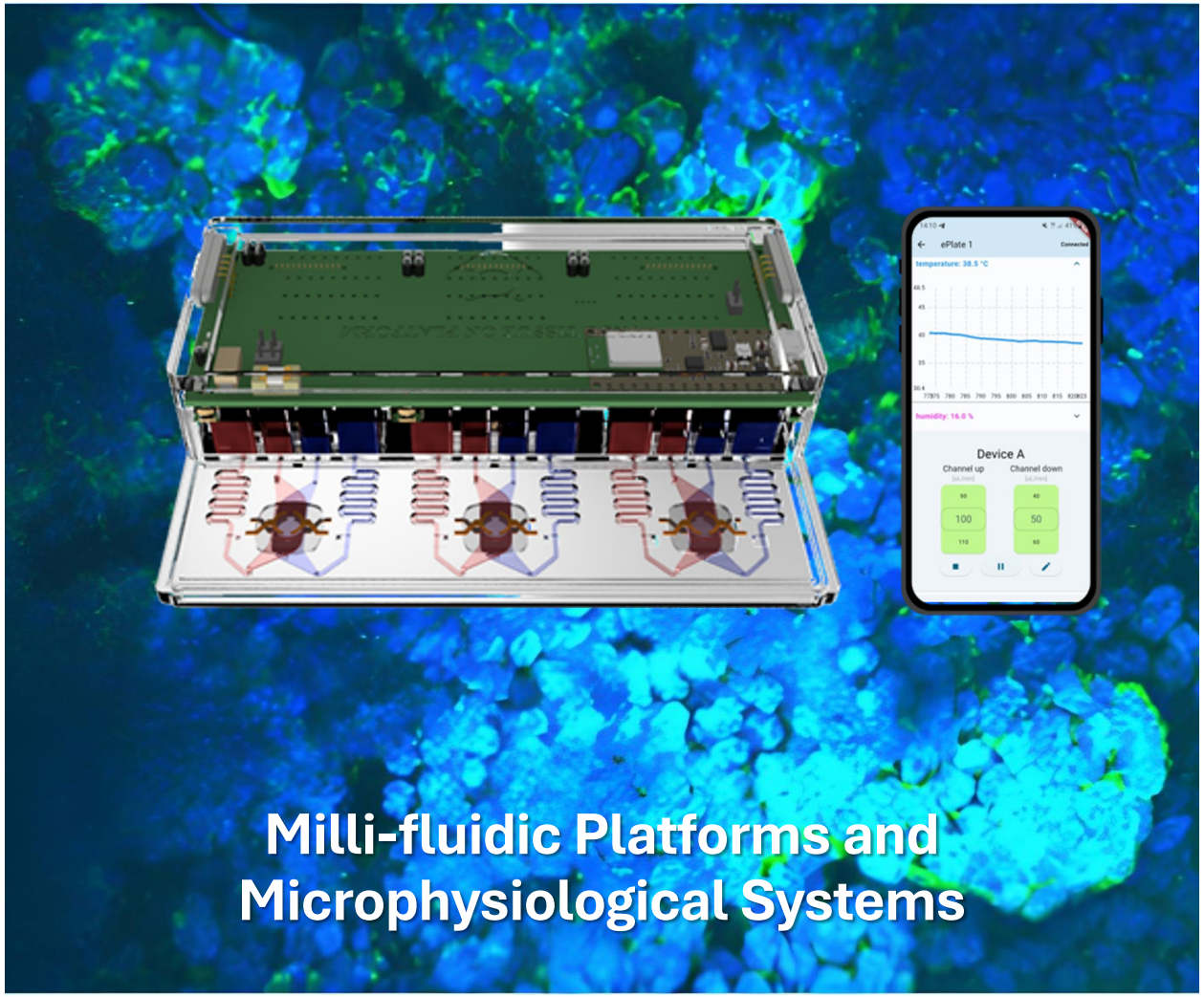

Giordana Marsili


Chiara Russo

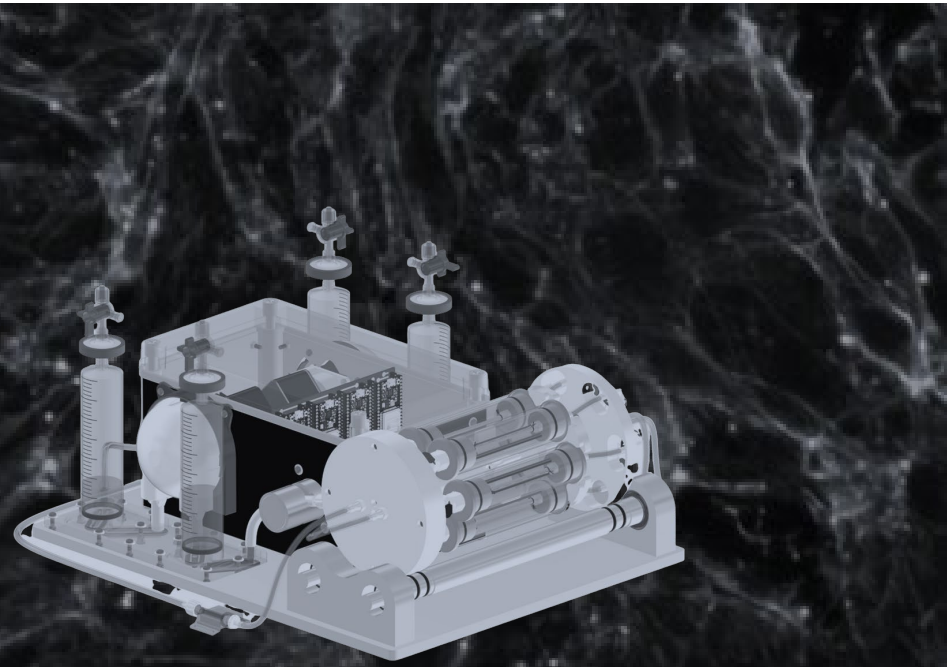

Martina Poppa


Alessandro Marchesini

Research Activities



Milli-fluidic Platforms and Microphysiological Systems



Three-Dimensional Bioreactors

Biomechanics Research Group

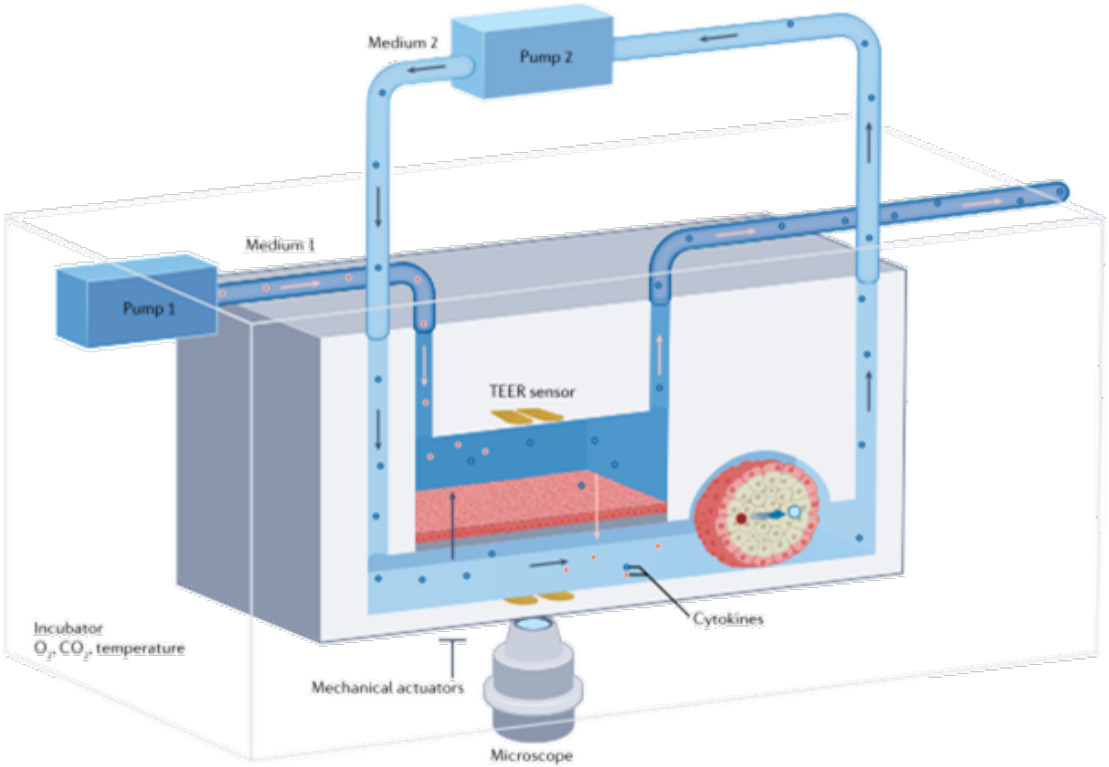
Advanced Culture Systems

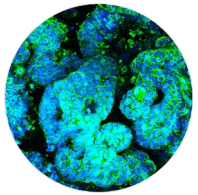
Milli-fluidic Platforms and Microphysiological Systems: The TTOP project

Human based, advanced in vitro/ex vivo models mimicking the human complexity

≠

87% of preclinically valid drugs **fail in clinical trials**





Choice of the **biological sample** and **culture substrate**

Choice of the **biosensors** and **monitoring parameters**

Choice of **device functionalities, usability** and **manufacturability**

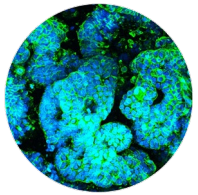
Advanced in vitro/ex vivo systems can increase of about **40%** the **probability** of a drug **to success** in clinical trials

Reference:
Leung 2022, Nature Reviews Methods Primers
Paul 2010, Nature Reviews Drug Discovery

Contacts:
lorenzopietro.Coppadoro@polimi.it

Milli-fluidic Platforms and Microphysiological Systems: The TTOP project

TTOP a modular, versatile and easy to use microphysiological system

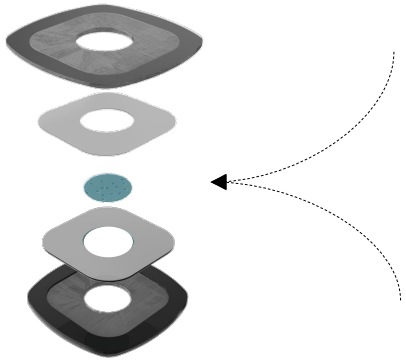


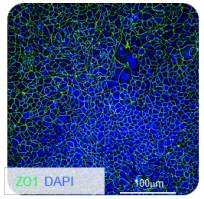
Tunable biological model
and culture substrate

Device unique features

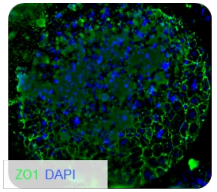
- Optical accessibility
- Contact co-culture
- Standard design
- Versatility in choosing the biological sample
- Sample retrieval and reuse in different configurations

TTOP culture insert

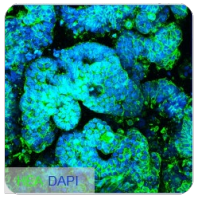




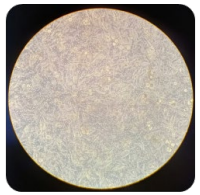
2D CELL CULTURES



3D CELL CULTURES

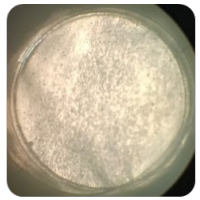


ORGANOTYPIC CULTURES

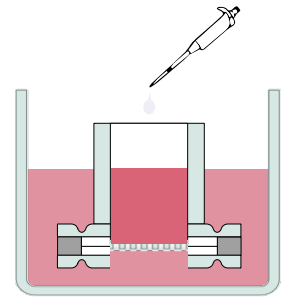


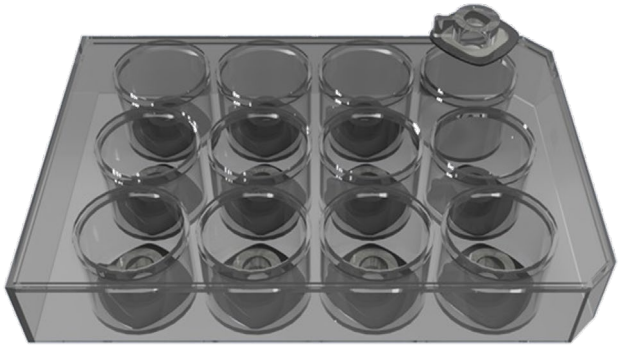
POROUS MEMBRANES

3D SCAFFOLDS



PATIENT DERIVED
BIOPSY SLICE





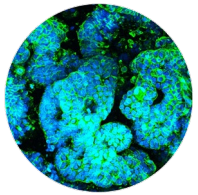
Activities

- In vitro barrier tissue state of the art analysis
- Key design parameters identification
- Device customization
- Technical and biological preliminary testing
- Device optimization and large scale manufacturing

Contacts:
lorenzopietro.Coppadoro@polimi.it

Milli-fluidic Platforms and Microphysiological Systems: The TTOP project

TTOP a modular, versatile and easy to use microphysiological system



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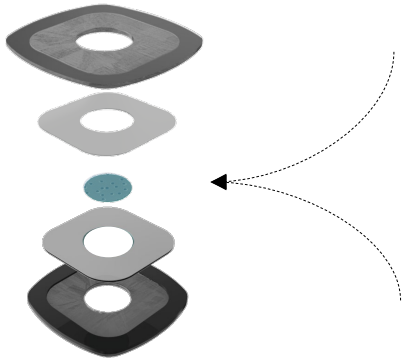

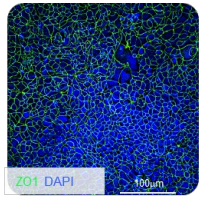

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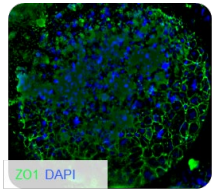
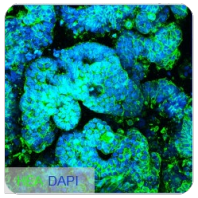
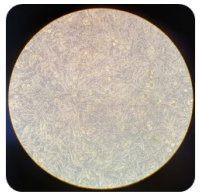


3D CELL CULTURES

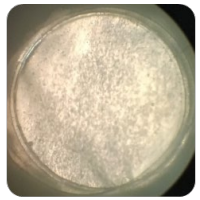


ORGANOTYPIC CULTURES



POROUS MEMBRANES

3D SCAFFOLDS



PATIENT DERIVED BIOPSY SLICE

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People involved:

Lorenzo Coppadoro

Giordana Marsili

Martina Poppa

Alessandro Marchesini

Alessandra Rando

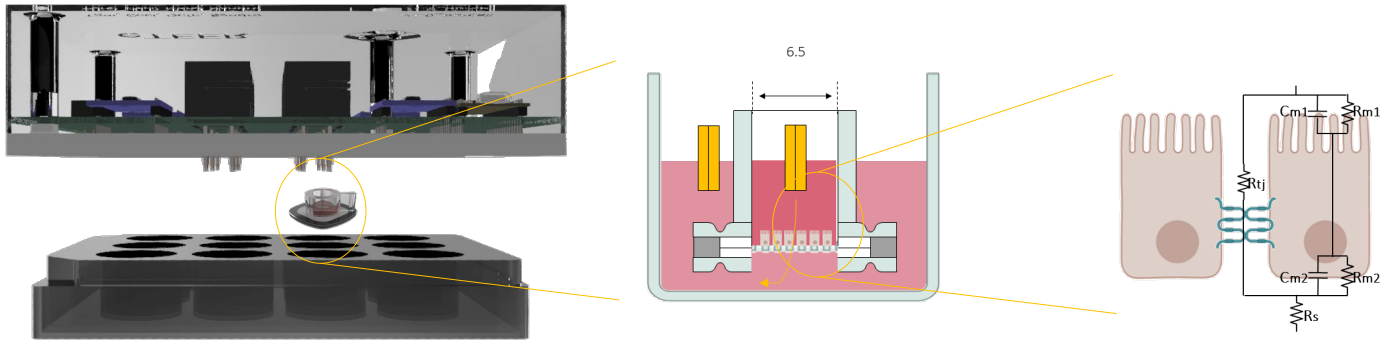
Chiara Russo

Contacts:
lorenzopietro.Coppadoro@polimi.it

Milli-fluidic Platforms and Microphysiological Systems: The TTOP project

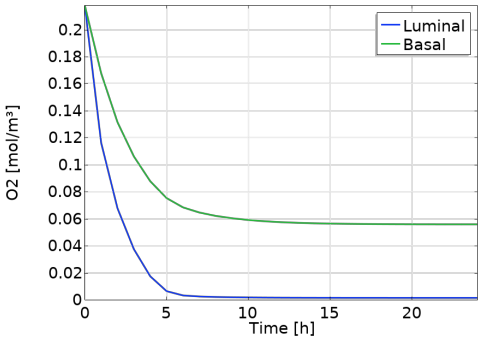
TTOP a modular, versatile and easy to use microphysiological system, with **integrated biosensors**

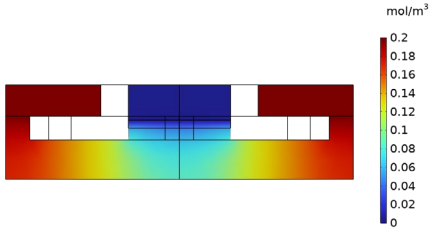
Resistance, impedance, oxygen biosensors integration



Device unique features

- No temperature or positioning artifacts
- Biocompatible
- Mini invasive
- Quantitative
- Automated data sampling with wireless approach





Activities

- Design and prototyping for ALI cultures
- Electronic design and prototyping
- 3D printing and manufacturing
- IOT programming
- Protocol definition and scale up
- Technical and biological validation

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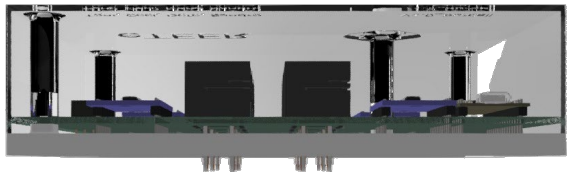

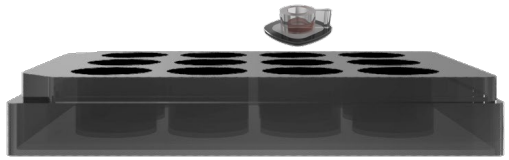

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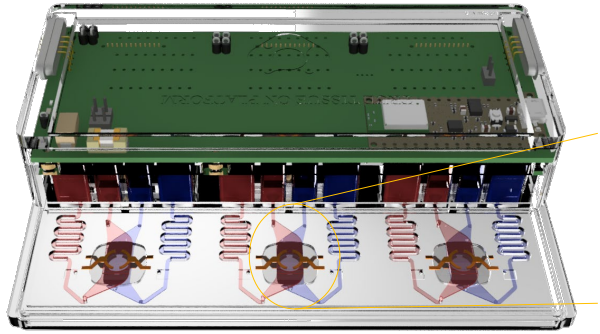
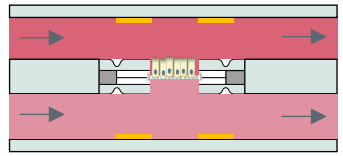
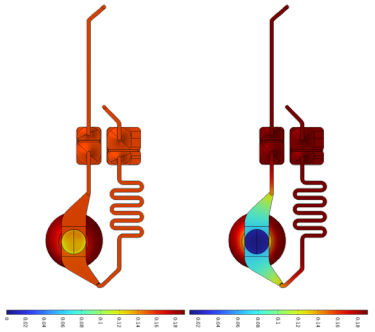
Milli-fluidic Platforms and Microphysiological Systems: The TTOP project

TTOP a modular, versatile and easy to use microphysiological system, with integrated biosensors, **mimicking the human microenvironment**

Modular design to mimic complex dynamic physio-pathological environments with a plug & play approach

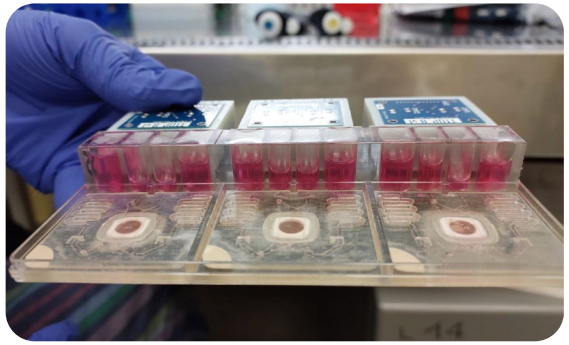


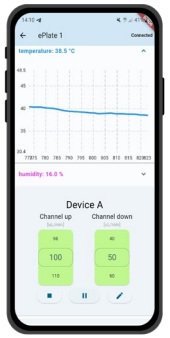


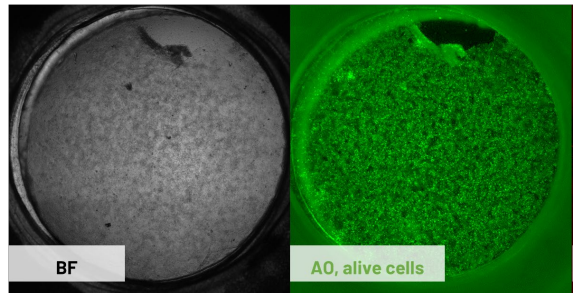


Device unique features

- Reuse of the culture insert for sequential treatments
- Programmable apical and basal perfusion conditions
- Scalable and automated design
- Automated data sampling with wireless approach







Activities

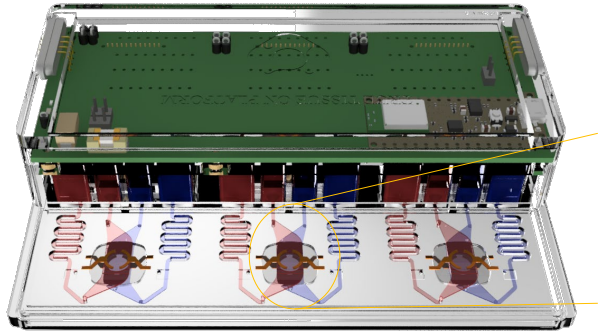
- Electronic design and prototyping
- Comsol multiphysics FEM modeling
- 3D printing and manufacturing
- IOT programming
- Protocol definition and scale up
- Technical and biological validation

Contacts:
lorenzopietro.Coppadoro@polimi.it

Milli-fluidic Platforms and Microphysiological Systems: The TTOP project

TTOP a modular, versatile and easy to use microphysiological system, with integrated biosensors, **mimicking the human microenvironment**

Modular design to mimic complex dynamic physio-pathological environments with a plug & play approach



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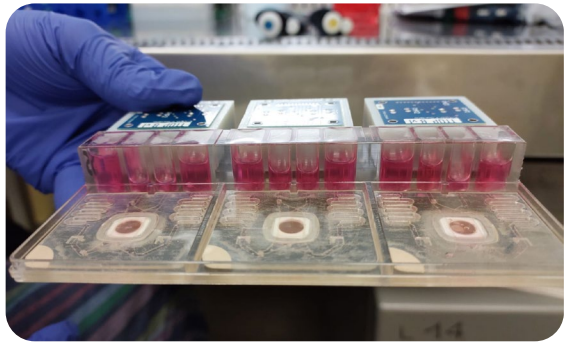

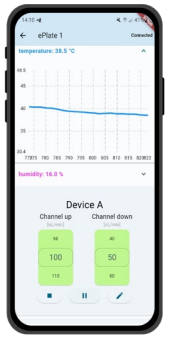

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- Technical and biological validation

People involved:

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Milli-fluidic Platforms and Microphysiological Systems

International partners and current project lines

- Co-cultures Epithelia-Endothelium for absorption studies — I.R.C.C.S. Ospedale San Raffaele
- Intestinal Organoids integration — IEO Research, Istituto Europeo di Oncologia
- Mechanical substrate properties effect on cell's maturation — University of Glasgow
- Integration of 2.5D primary cardiac decellularized patches — Centro Cardiologico Monzino
- Recirculation system for automated medium change for alginate 3D scaffolds — Universitat Politècnica de València
- PBMC migration/chemotaxis assay — I.R.C.C.S. Ospedale San Raffaele
- PBMC activation and TTOP pyrogenicity — Istituto Superiore di Sanità
- 3D villi-like scaffolds integration for intestinal advanced models — IBEC
- Multi-organ platform for cardiac-liver toxicity — University of Bradford, UCC University College Cork, Ireland

Contacts:
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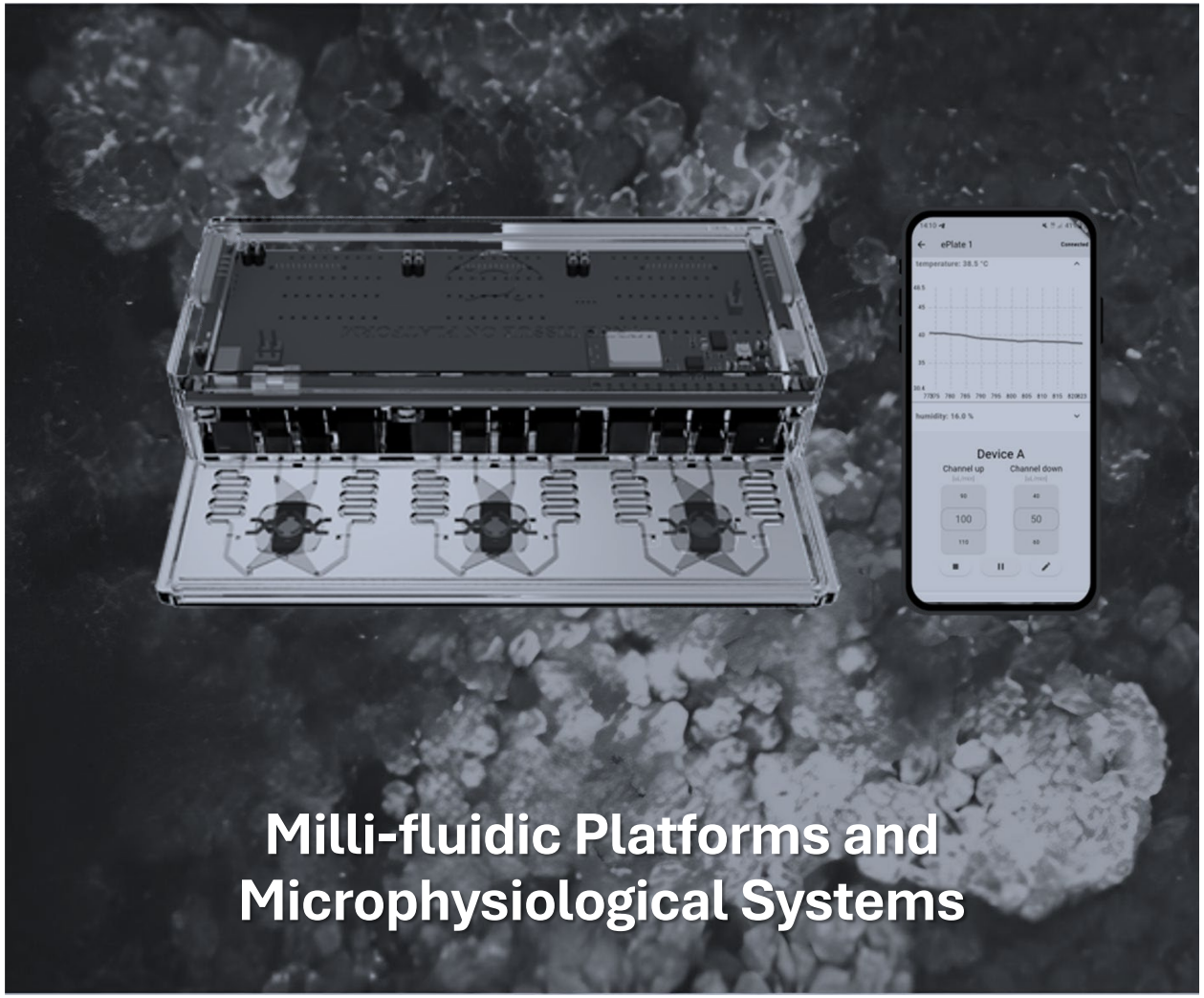
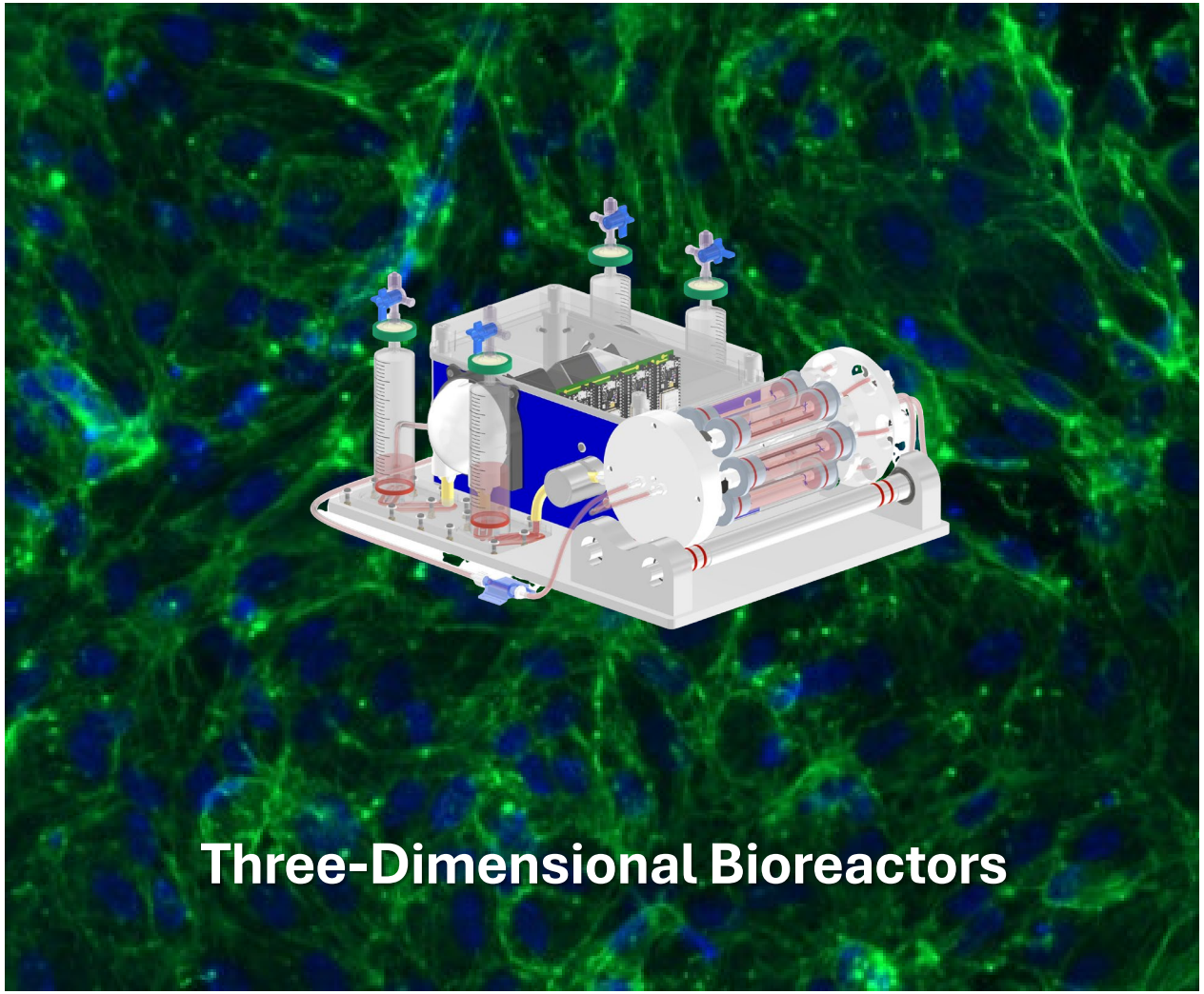
Research Activities



Milli-fluidic Platforms and Microphysiological Systems



Three-Dimensional Bioreactors

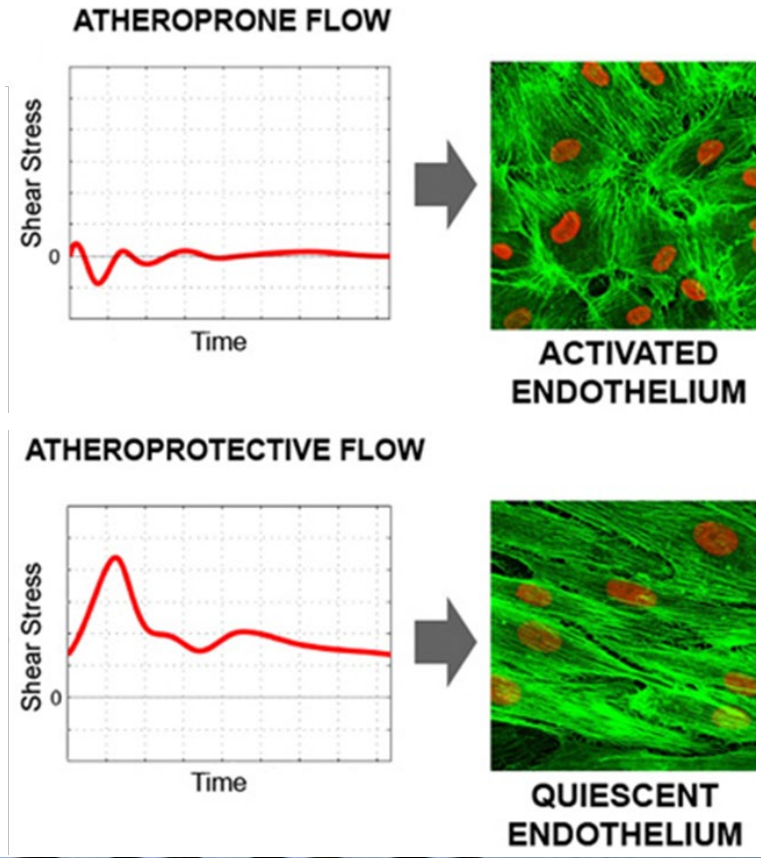
Biomechanics Research Group

Advanced Culture Systems

Three-Dimensional Bioreactors

elia.pederzani@polimi.it

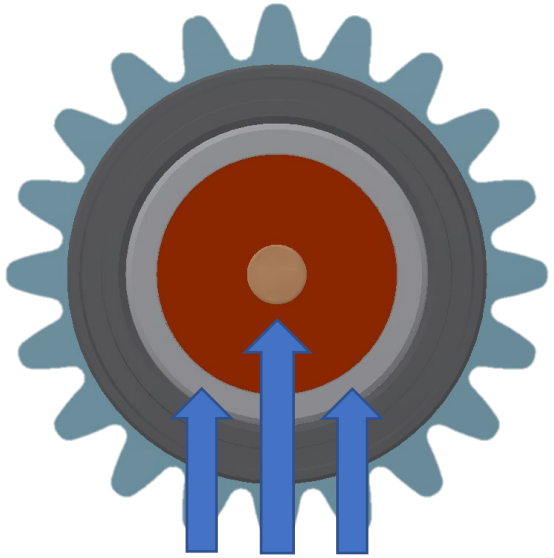
Bioreactors for complex hydrodynamic stimulation

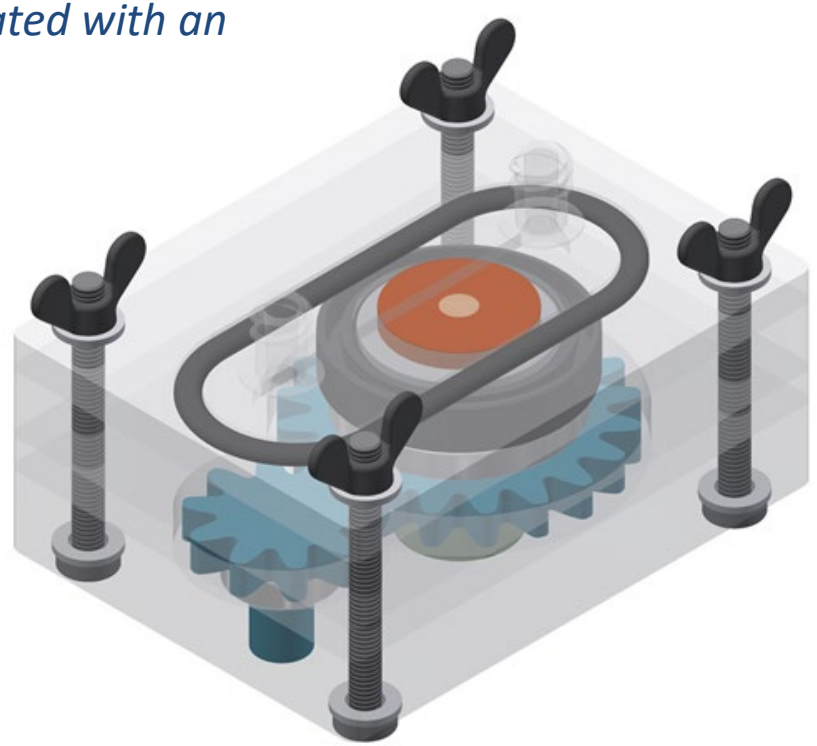


Characteristics

*- Controlled **hydrodynamic multidirectional stimulation** for studying vascular endothelial disfunctions*

*- **Modular** and **versatile**, integrated with an **electronic control unit***





Three-Dimensional Bioreactors
Bioreactors for complex hydrodynamic stimulation

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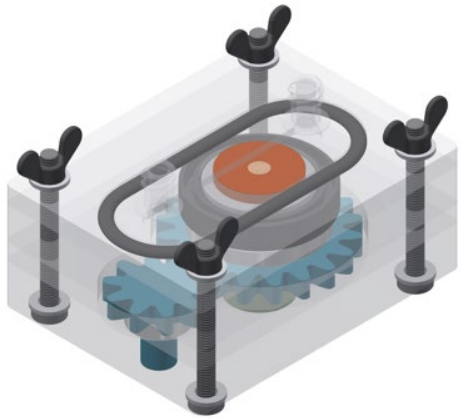
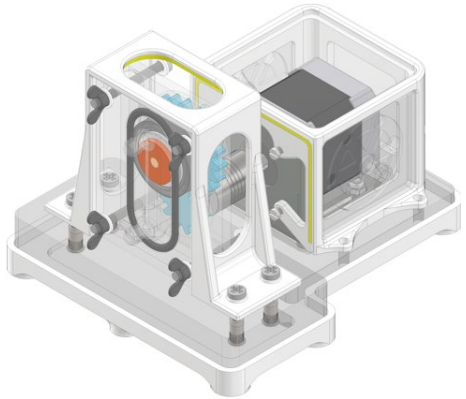
Bioreactors for complex hydrodynamic stimulation

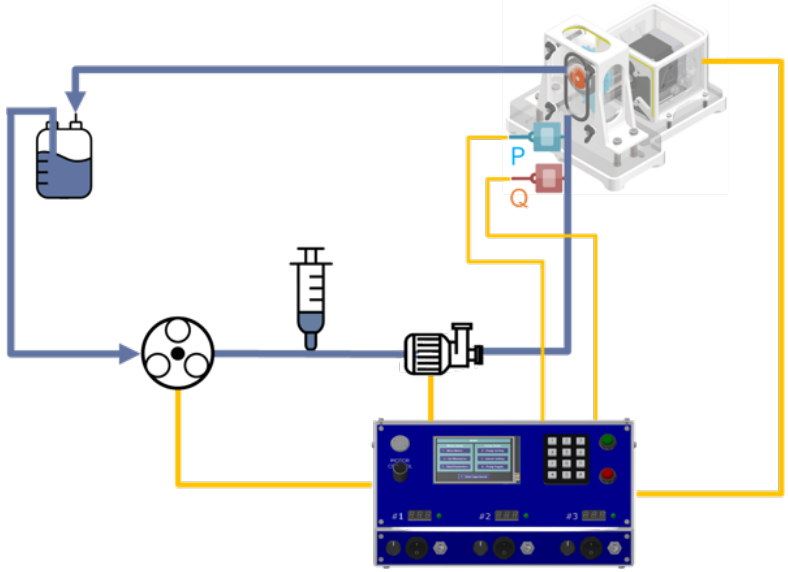
Activities

- *TECH: **hardware** and **software** optimization*
  - *CAD design of new bioreactor versions*
  - *rapid prototyping*
  - *microntrollers' managing*
  - *fluid dynamic simulations*
- *BIO: **biological validation** on **cell monolayers** and **biological tissue samples***
  - *cell culture on 2D acrylic cartridge*
  - *flow-induced stimuli application*
  - *immunostaining analysis*

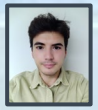
In collaboration with OSPEDALE SAN RAFFAELE







Three-Dimensional Bioreactors



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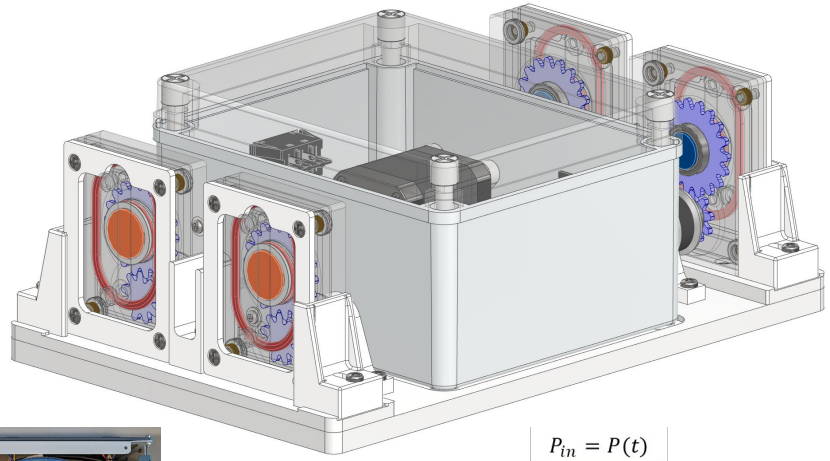
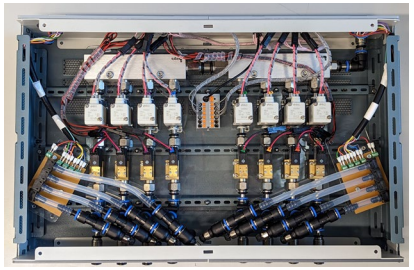
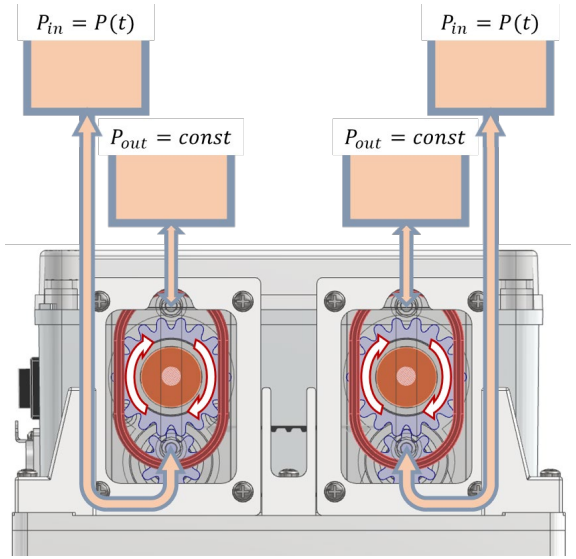
Bioreactors for complex hydrodynamic stimulation



Activities

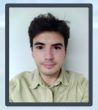
- *TECH: **hardware** and **software** optimization*
  - *pressure-driven system development*
  - *state-machine Labview VI design*
  - *fluid dynamic simulations*
- *BIO: **biological validation** on **cell monolayers***
  - *cell culture on 2D acrylic cartridge*
  - *flow-induced stimuli application*
  - *immunostaining analysis and permeability assay*





In collaboration with Imperial College London

Three-Dimensional Bioreactors



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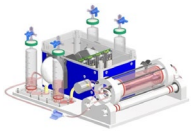
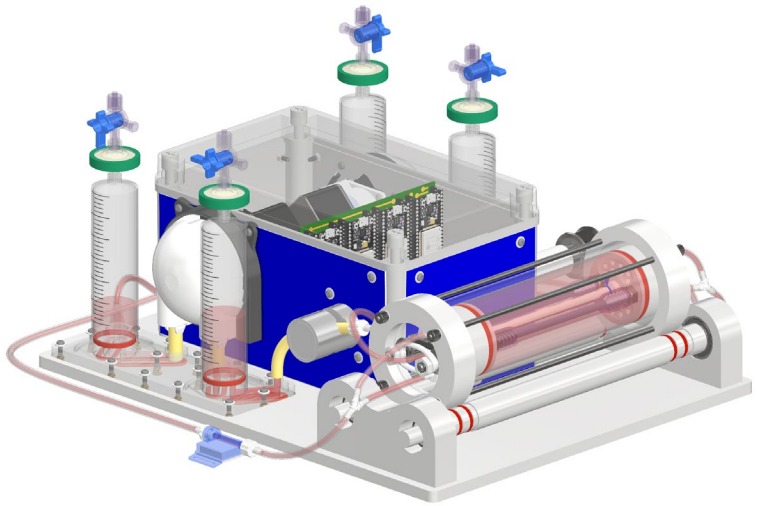


Advanced platform for recapitulating vascular phenomena

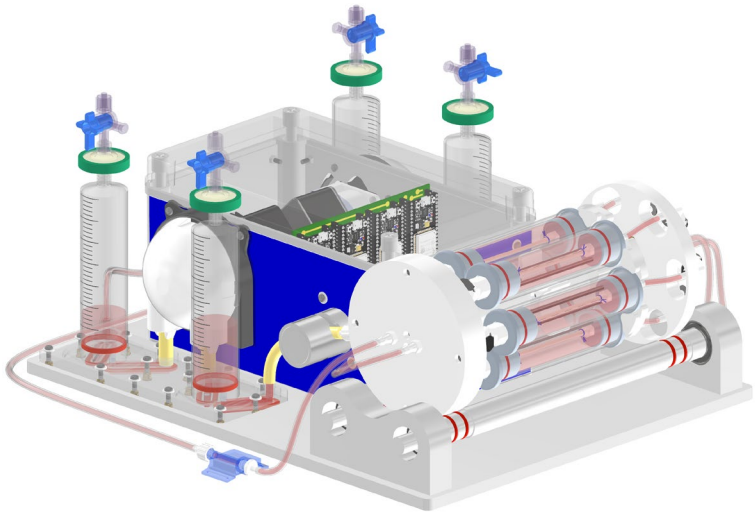


BRAVE

Automatic cell seeding

Fine pre-tensioning

Dynamic flow-induced stimuli

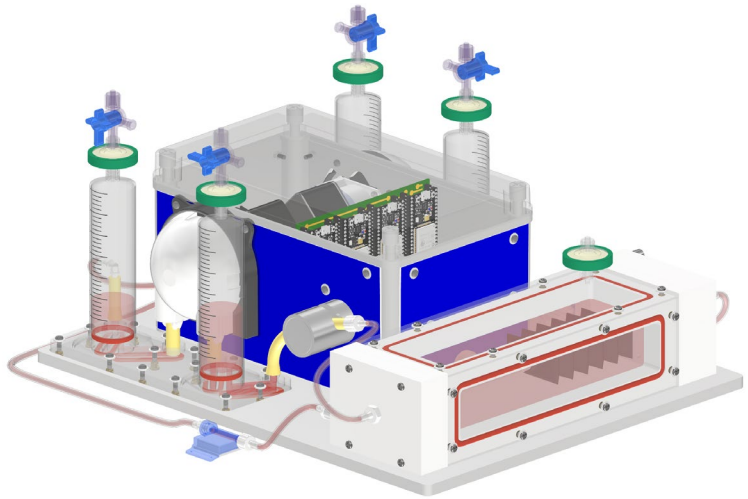


BRAVE-R

Automatic cell seeding

Multi-samples

Coronary flow-induced stimuli



BRAVE-RY

Mechanical test (ISO 7198)

Anastomosis geometries

Large vessels' flow-induced stimuli

Three-Dimensional Bioreactors

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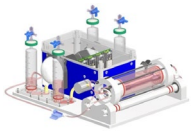
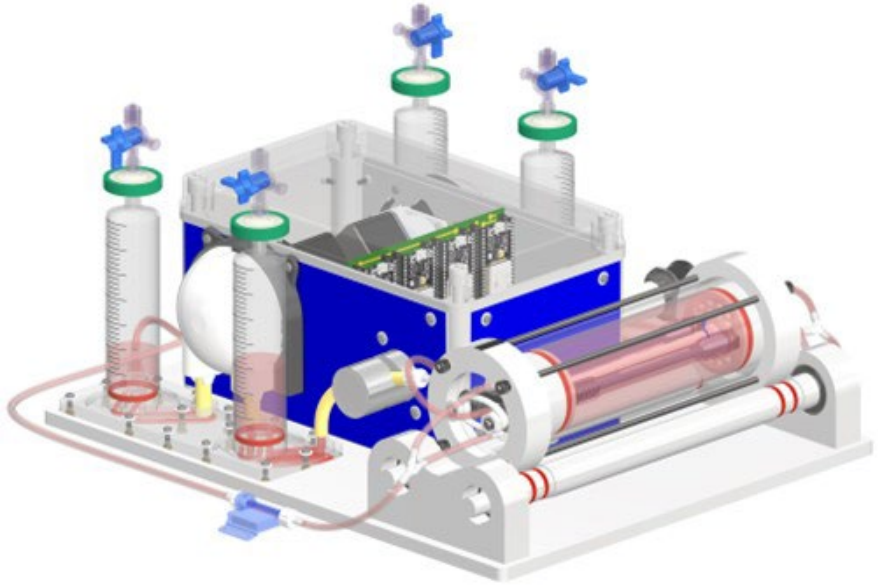


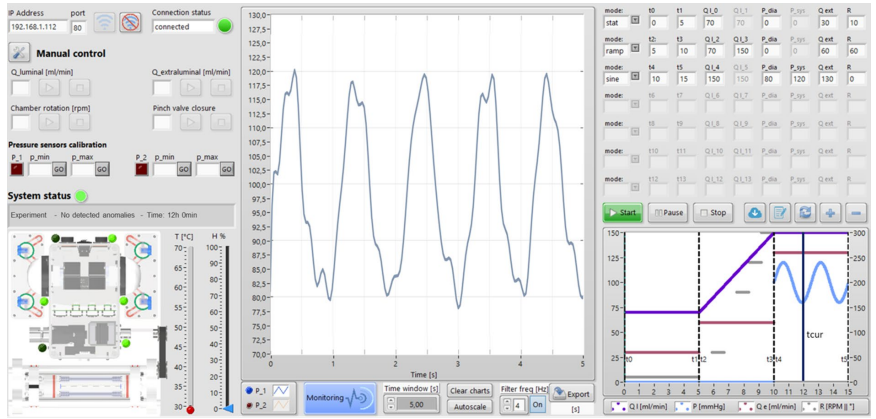
Advanced platform to establish a physiologically-relevant vascular model

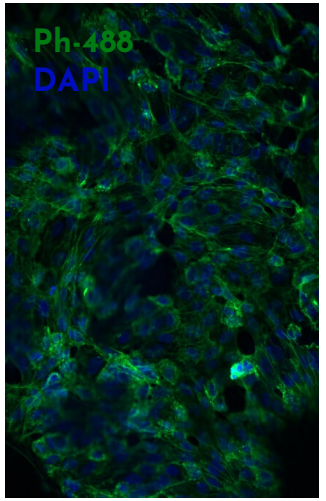
Activities

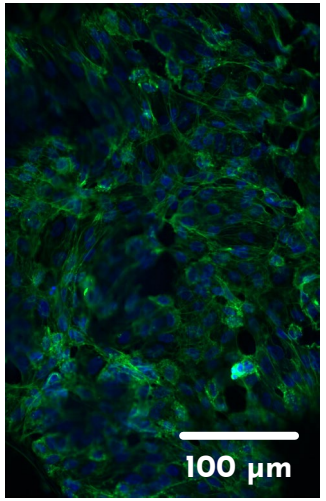
- *TECH: **hardware** and **software** optimization*
  - *CAD design of new culture chambers*
  - *rapid prototyping*
  - *microntrollers' managing*
  - *state-machine Labview GUI design*
  - *fluid dynamic simulations*
- *BIO: **3D vascular model***
  - *seeding protocols for graft co-culture*
  - *flow-induced stimuli application*
  - *immunostaining analysis*

In collaboration with ISTITUTO DI RICERCHE FARMACOLOGICHE MARIO NEGRI · IRCCS









Three-Dimensional Bioreactors

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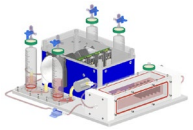
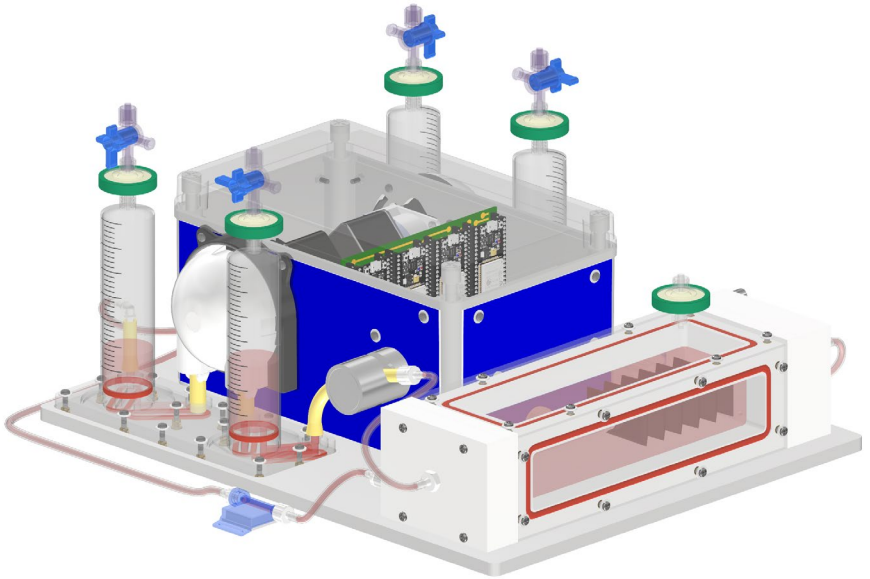


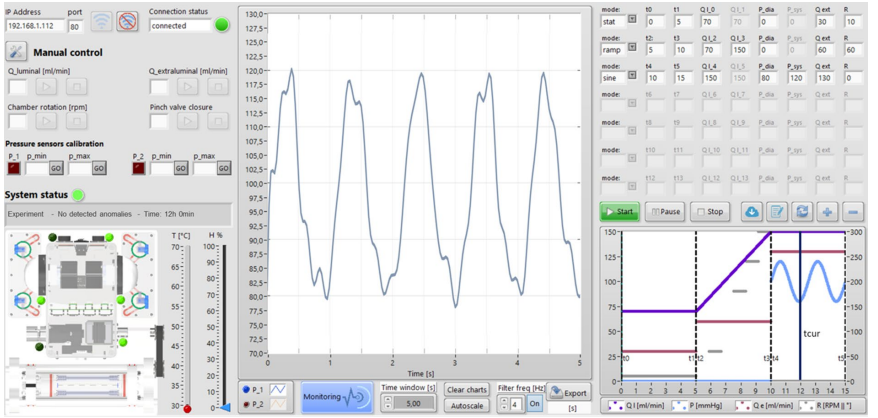
Advanced platform to simulate arteriovenous fistula behaviors

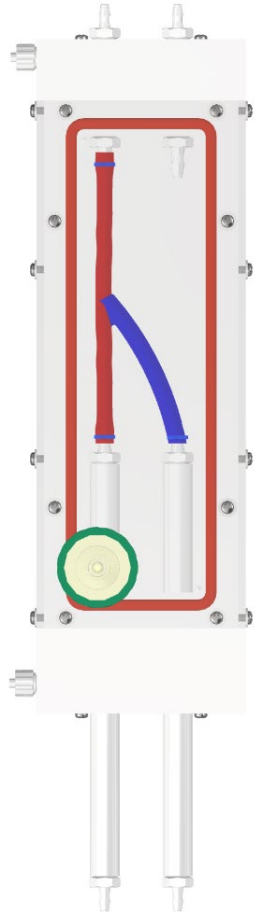
Activities

- *TECH: **hardware** and **software** optimization*
  - *CAD design of new culture chambers*
  - *rapid prototyping*
  - *microntrollers' managing*
  - *state-machine Labview GUI design*
  - *fluid dynamic simulations*
- *BIO: **biological experiments** for the **ex vivo replica** of **arteriovenous fistula***
  - *native vessels harvesting*
  - *AVF flow-induced stimuli application*
  - *immunostaining analysis*

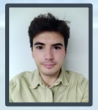
In collaboration with ISTITUTO DI RICERCHE FARMACOLOGICHE MARIO NEGRI · IRCCS







Three-Dimensional Bioreactors



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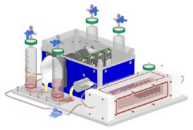
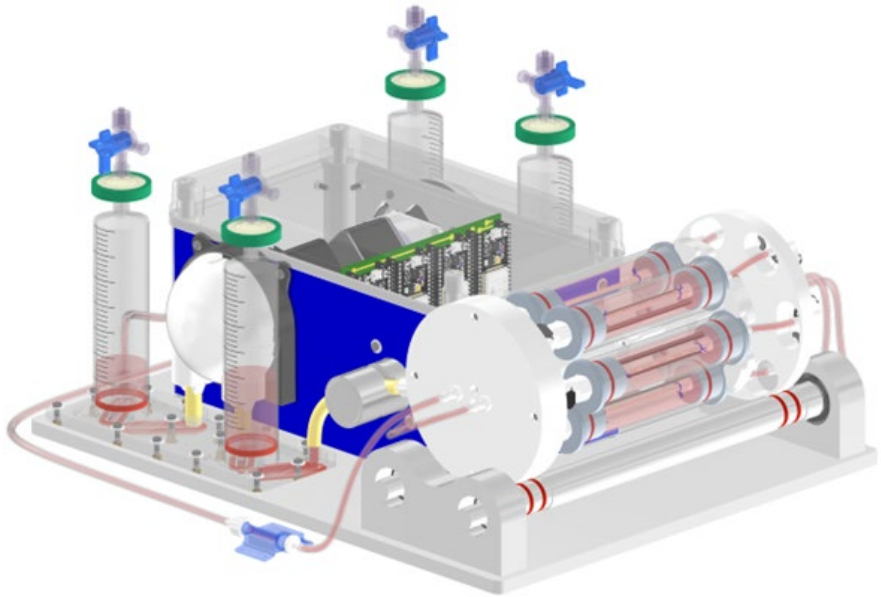


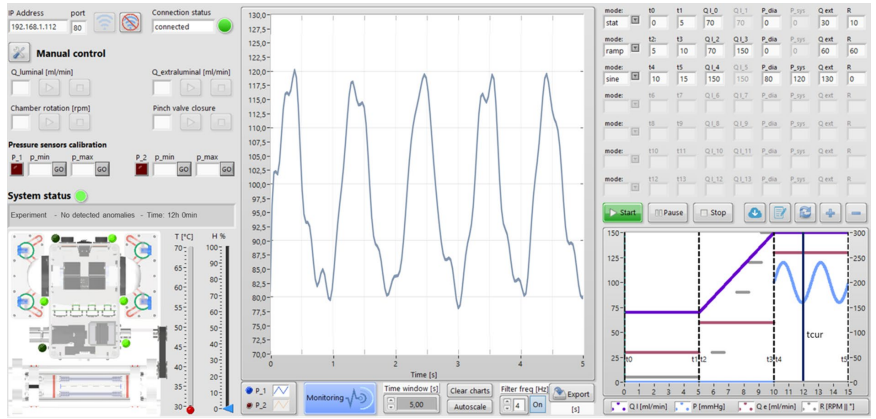
Advanced platform to validate a very small caliber vascular model

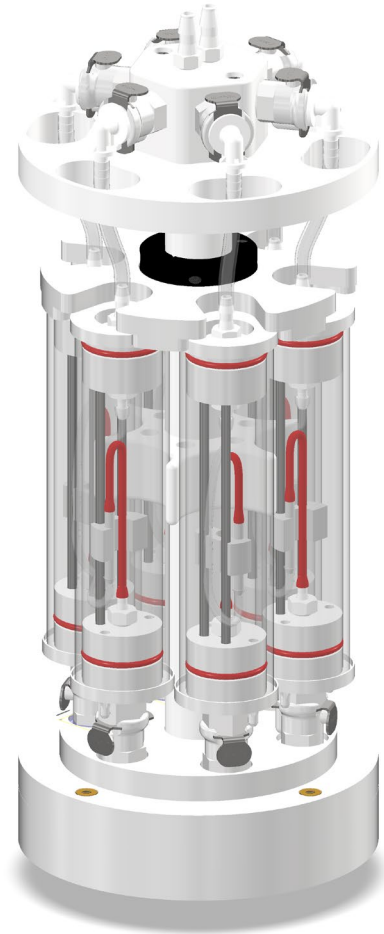
Activities

- *TECH: **hardware** and **software** optimization*
  - *CAD design of new culture chambers*
  - *rapid prototyping*
  - *microntrollers' managing*
  - *state-machine Labview GUI design*
  - *fluid dynamic simulations*
- *BIO: **biological experiments** for the **decellularization** and **recellularization** of **rat aorta***
  - *decellularization protocols*
  - *recellularization protocols*
  - *flow-induced stimuli application*

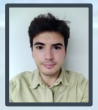
In collaboration with Centro Cardiologico Monzino







Three-Dimensional Bioreactors
Advanced platform as pulmonary simulator



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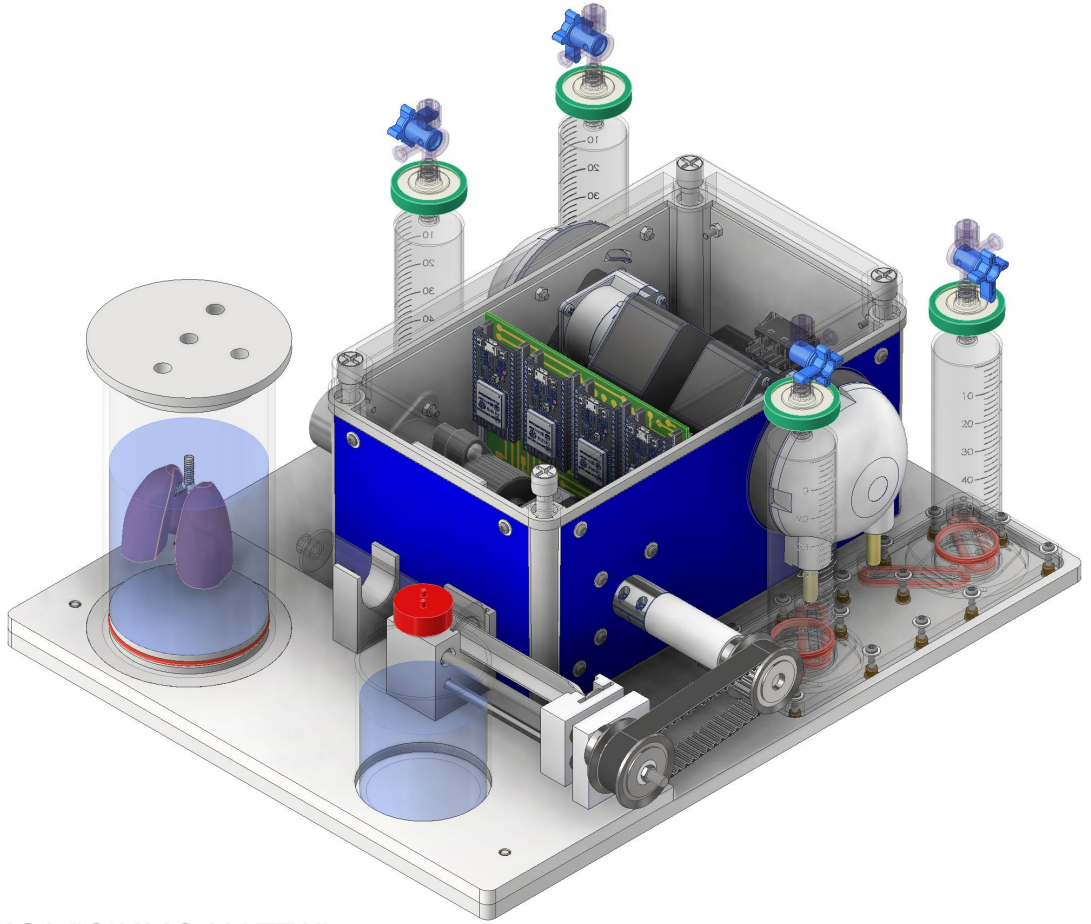
Advanced platform to simulate pulmonary physiological functions

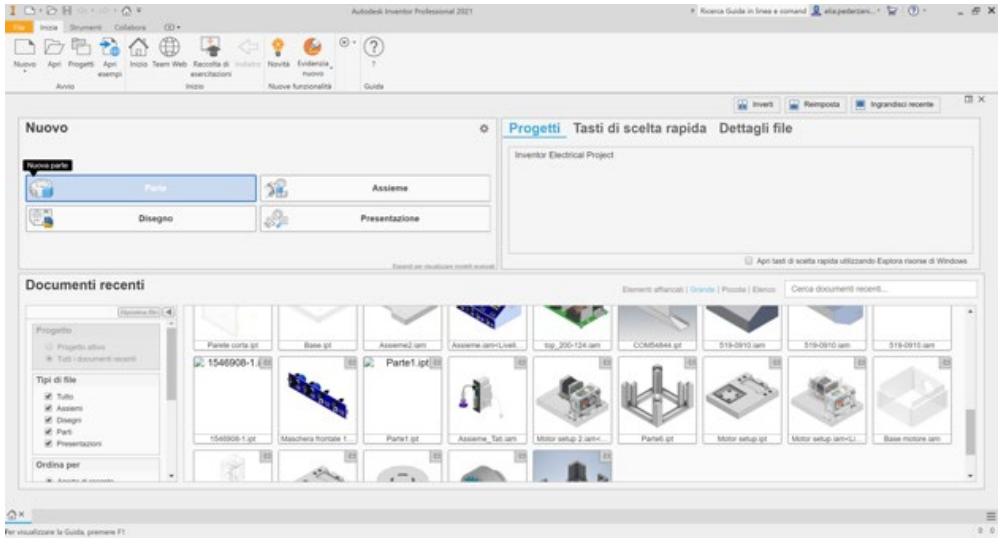
Activities

- *TECH: **hardware** and **software** optimization*
  - *CAD design of 2D and 3D (organ dimension) chamb*
  - *rapid prototyping*
  - *microntrollers' managing*
  - *state-machine Labview GUI design*
  - *fluid dynamic simulations*
- *EXP: **simulator** (silicone phantom model) **testing***
  - *lung phantom model manufacturing*
  - *setup validation*
  - *dynamic stimuli application*



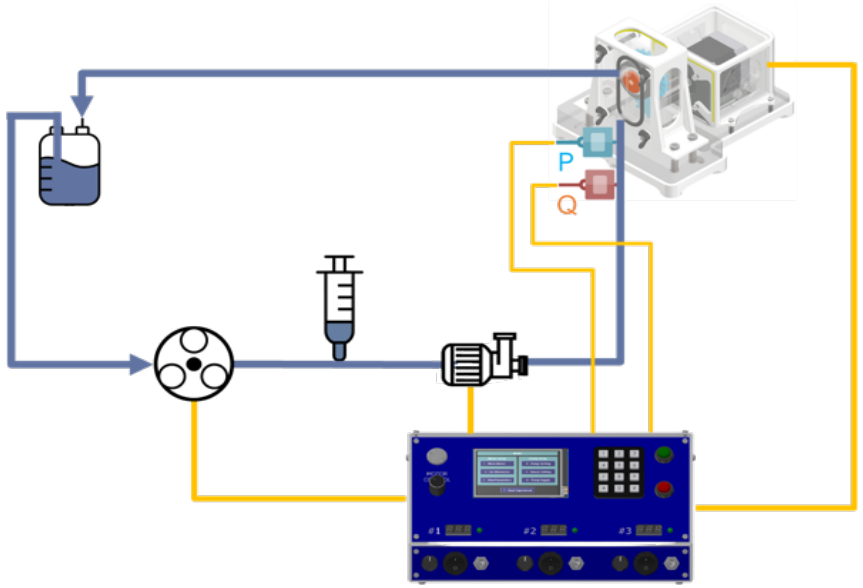
In collaboration with DIPARTIMENTO DI CHIMICA, MATERIALI E INGEGNERIA CHIMICA "GIULIO NATTA"

Workflow and main activities



*1. **Design and prototyping of** culture chambers/components/supports*

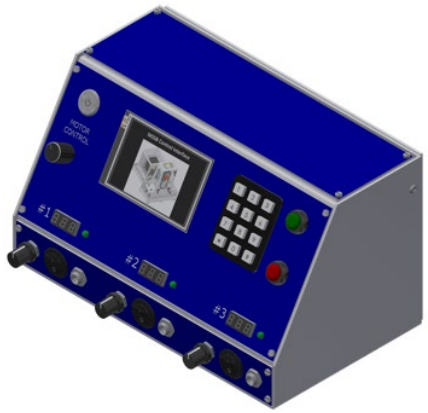
- *Design with **CAD** (Inventor)*
- ***simulations***
- ***prototyping** (laser, drilling machine, 3D printing)*

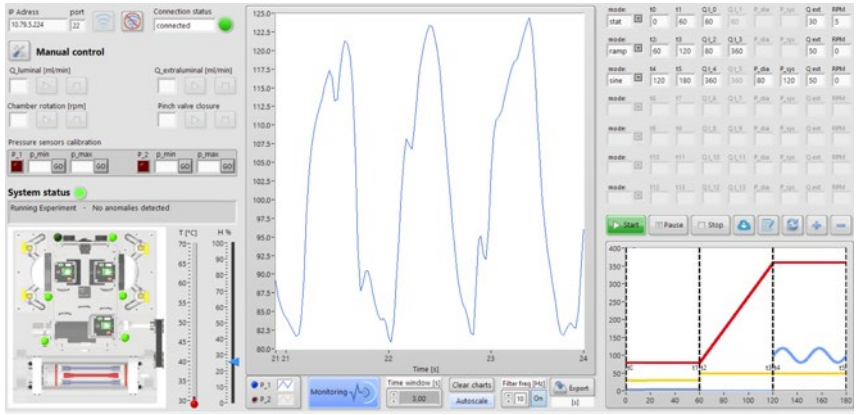


*2. **Design and realization of the hydraulic circuit***

- *Choosing the **actuation components***
- *Design of the **hydraulic circuit***
- ***Process automations** (seeding, mediun change)*

Workflow and main activities





*3. **Control system** development*
- Arduino programming
- Control unit realization

*4. **Bench tests***
- Phantom
- Biological tissues/prototissues

*5. **Experimental campaign**: in vitro model development (**ATTIC Lab**)*
- cell / tissue cultures
- culture post processing and analyses (hysto, IF):
tissue morphology,
cell density and proliferation,
cell / tissue characterization