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WP2

Organ-on-Chip

Work package leader:
Max Mastrangeli

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WP2 Pilar Coordinators

Smart well-plate - Bjorn de Wagenaar (**TUD**)

- TUD
- TU/e
- MIC-NL
- MCS
- MFCS
- PEN
- TNO
- FEMFT
- ITAV
- BESI-AT
- BESI-NL
- EVG
- AED
- IMT

HD e-Phys - Tim Stakenborg (**IMEC-BE**)

- IMEC-BE
- MIC-NL
- MCS
- FEMFT
- BESI-AT
- EVG
- (TNO)

Organ-on-chip devices - Nikolas Gaio (**BI/OND**)

- BI/OND
- MCS
- BCHIP
- TU/e
- TNO
- BESI-NL
- IISA
- UNIZAR
- INESC-MN

Smart multi-well lid – Sigfried Graaf (**CSEM**)

- MFCS
- BESI-AT
- CER
- AED
- CSEM
- INRO
- (IMT)

Cell sorting & sensors – Fabio Campi (**MSB**)

- MSB
- IISA
- TUD
- CER
- INESC-MN

TU Delft: Who is who and where

Max Mastrangeli
WP2 leader

Bjorn de Wagenaar
WP2 Pillar 1 leader

Janny vd Eijnden-v Raaij
hDMT managing director

Ronald Dekker
M4M mastermind

P. M. (Lina) Sarro
ECTM chair

The EEMCS building of the TU Delft campus, housing the class-100 cleanroom (Else Kooi Lab) and the research groups of the Microelectronics Department, wherein the ECTM.

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TU Delft: Our capabilities

- **Clean room-based microfabrication**
  - *Class 100*
  - *Multi-material*
    - silicon- and polymer-based
- **Characterisation**
  - *Inspection*
    - Optical
    - Electronic
    - Interferometric
  - *Chip- and wafer-level multi-probe stations*
    - Parameter (and network) analysers
    - 4-point

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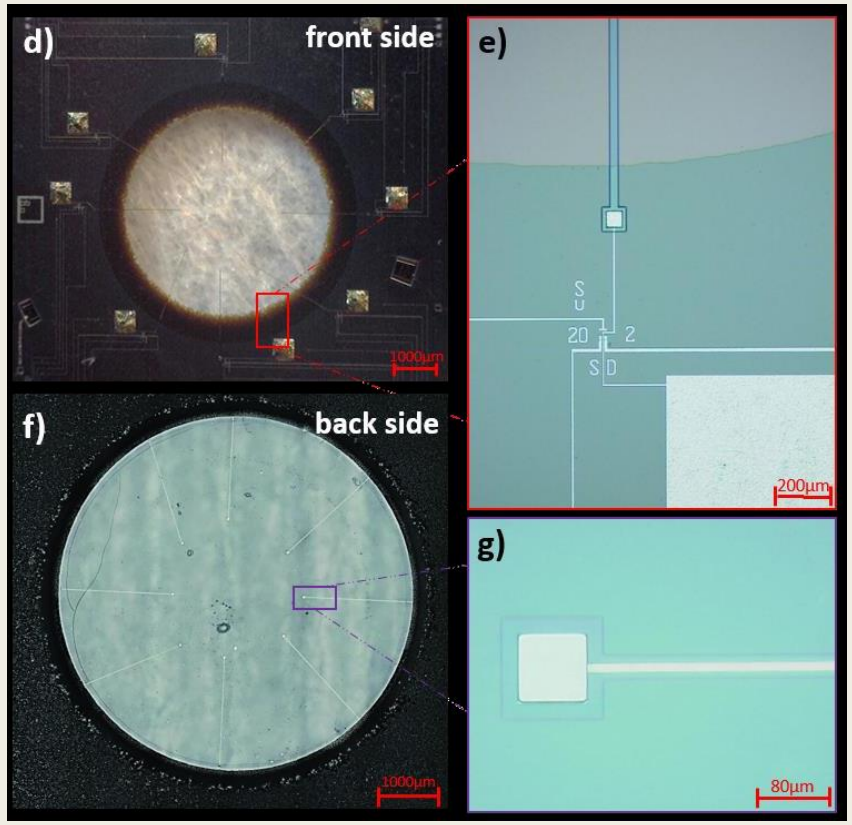
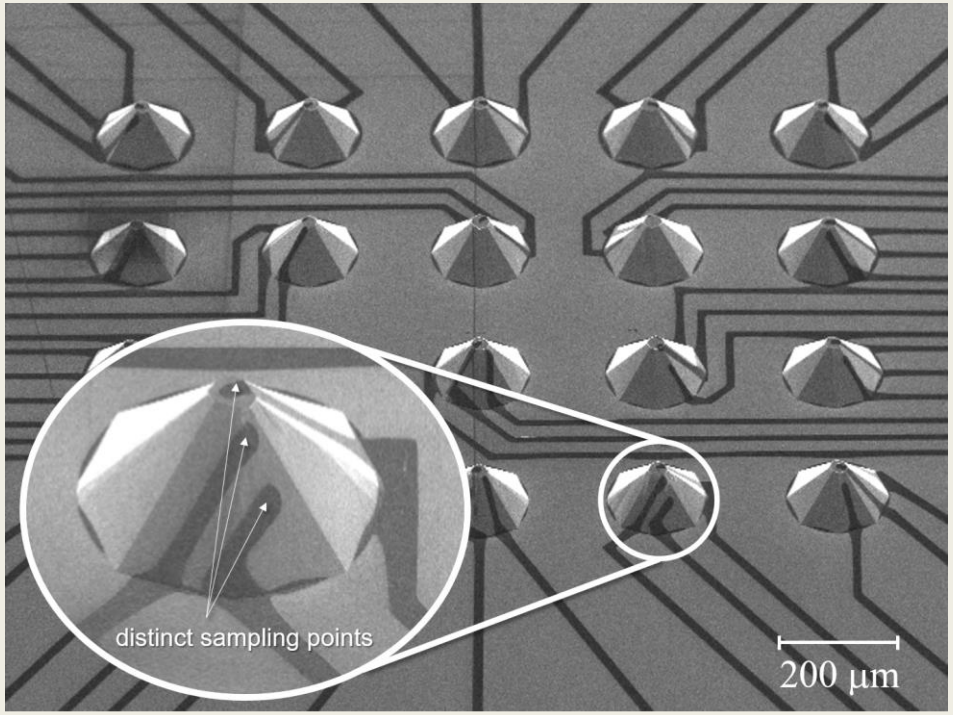
TU Delft: our planned contribution

WP2 & T2.1 lead + Microelectrode integration (T2.6)



Over polymer membranes



Three-dimensional

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TU/e Who is who and where

Jaap den Toonder

professor

Mohammad Jouybar

PhD student

Dino verhoef

MSc student

Microfab/lab @ TU/e campus, Eindhoven

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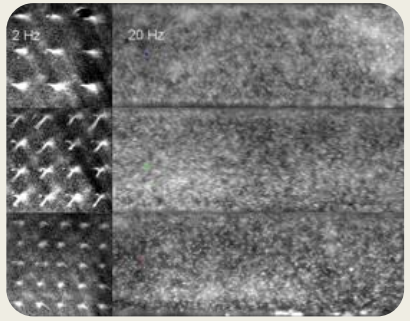
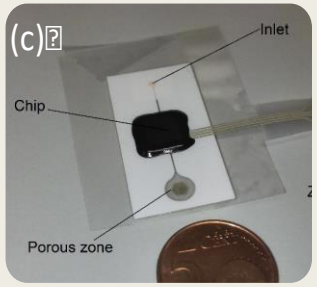
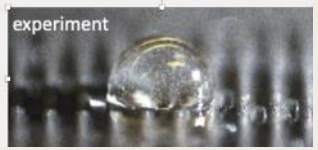
TU/e: our capabilities

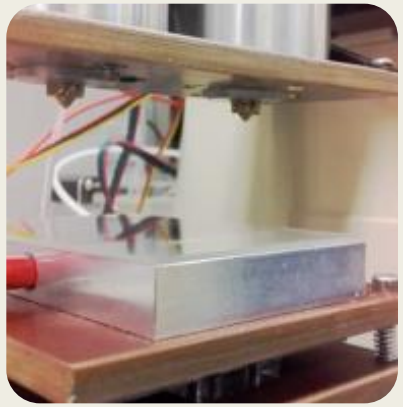
- Microfluidics: design, novel concepts, integration
  - *Experimental and supporting modelling*



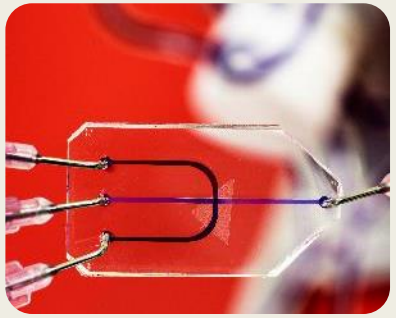


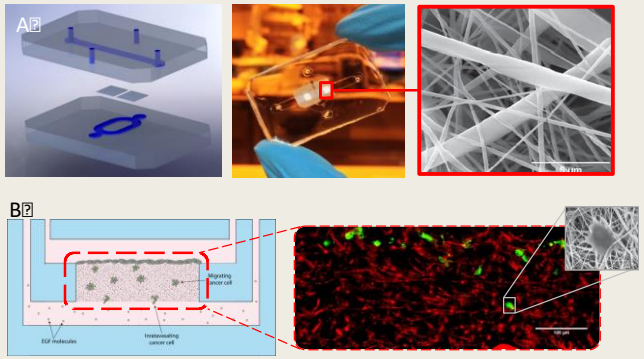


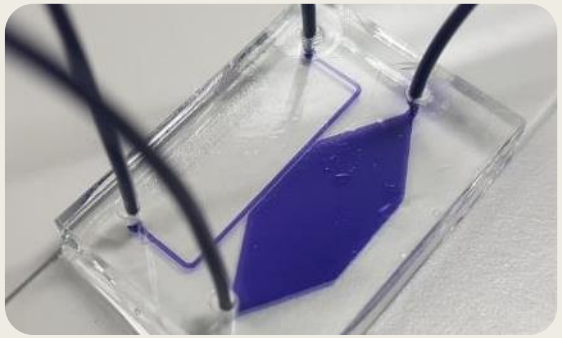
- Microfabrication: Microfab/lab
  - *Broad portfolio of technologies*
  - *Low-threshold access facilities*
  - *Development of novel research equipment*



- Organ-on-a-Chip
  - *Cancer*
  - *Brain*
  - *Blood-vessel*
  - *Kidney*







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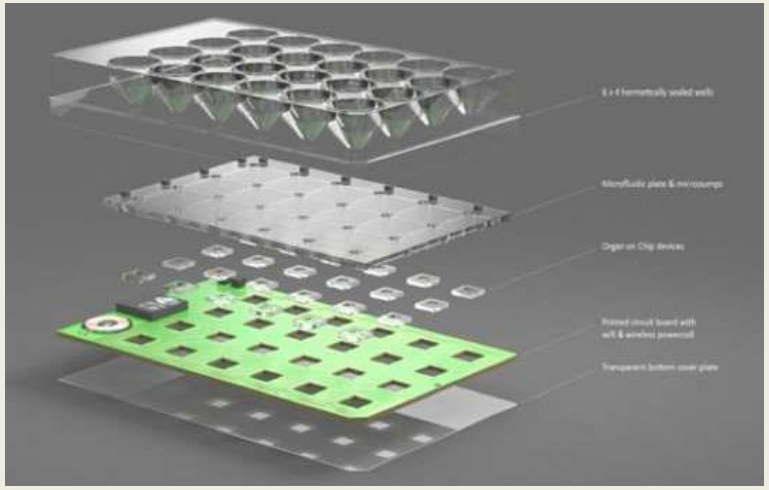
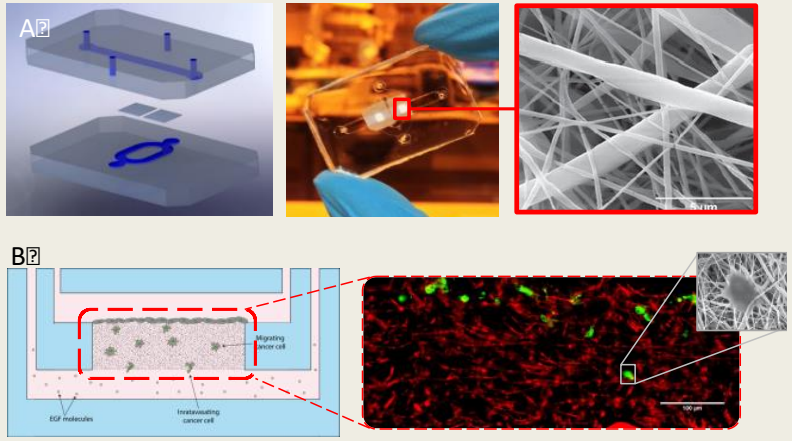
TU/e: our planned contribution

- Contribute to definition of
  - *Platform requirements*
  - *System architecture*
  - *Specifications*



- Develop innovative chip modules
  - *Cancer-on-a-Chip*
  - *Model metastasis*
  - *Understanding (R&D)*
  - *Personalized diagnostics*
  - *Drug resistance testing*



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Philips: Who is who and where





Rob van Schaijk Joost van Beek Paul Dijkstra Jacco Scheer Folkert Morsheim

Principal Architects Thin Film/MEMS/Assembly business development mgr.

Philips innovation services thin film facility

Philips innovation services micro devices facility

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PEN: Our capabilities

- High-end assembly equipment (SMT & Micro-electronic Assembly).
- Extensive knowledge and experience on interconnect technologies & materials.
- Process architecture and development experience with a wide range of medical devices such as catheter tips, US imaging components, detector modules (XRAY, CT), multi-well plates etc.
- Internal & External networks for components, materials & tooling.
- Capabilities to ramp-up from sample making to production (in-house).

PEN = Philips Electronics Netherlands BV (legal entity)
We are: Philips MEMS & Micro Devices

Moore4Medical

PEN: Our planned contribution

- Contribute to definition phase to include micro-electronics assembly experience (Design for Manufacturing).
- Develop and verify assembly processes.
- Demonstrator assembly.
- Provide industrially produced silicon parts for micropump fabrication.

TNO / Holst Centre

Auke Jisk Kronemeijer
Program Manager

Thiru Kanagasabapathi
Program Manager

Building HTC31 at the High Tech Campus Eindhoven

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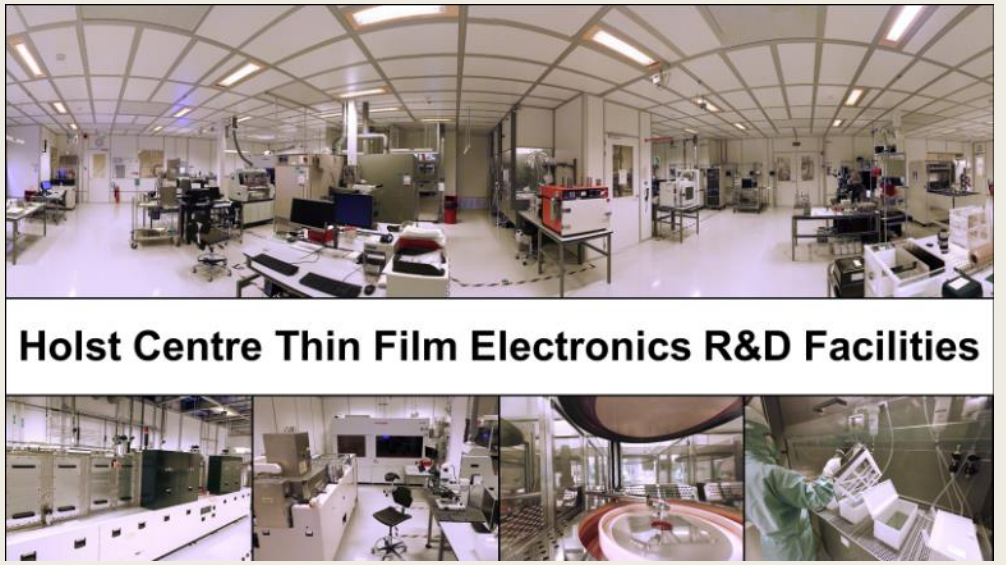
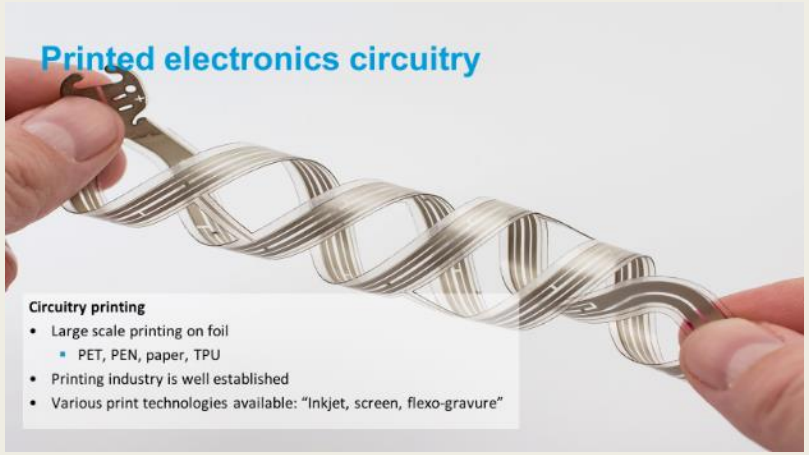
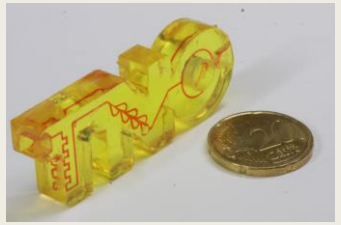
TNO / Holst Centre - Capabilities

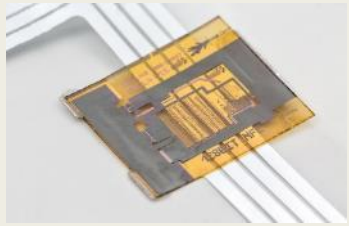
Research Institute on Flexible Electronics
Two technology platforms:

- Hybrid Printed Electronics
- Thin Film Electronics









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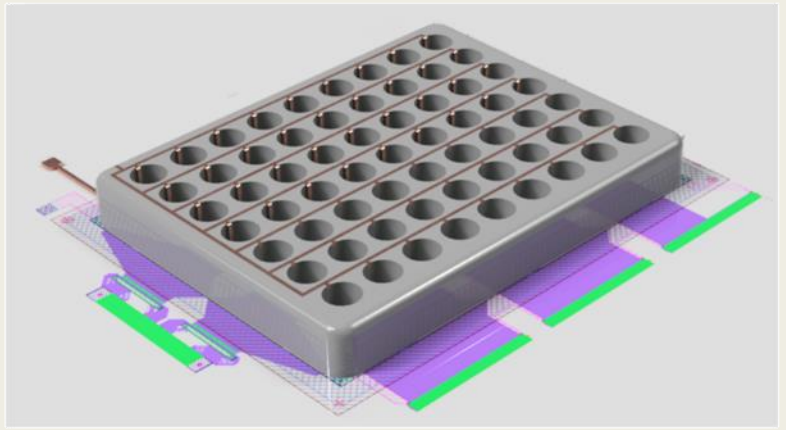
TNO / Holst Centre – Planned Contribution

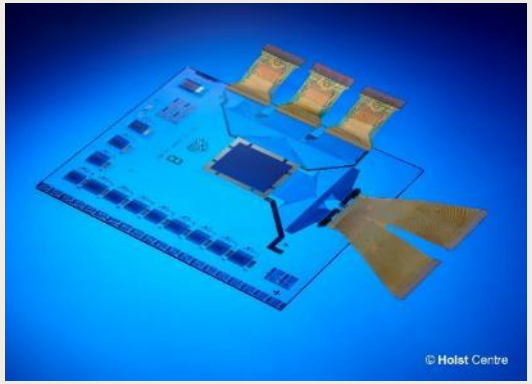
Goal: Connect with Organ-on-Chip Ecosystem & Investigate whether Holst Centre technology can bring Organ-on-Chip to Higher TRL by Scalable Realization Technology & Standardization

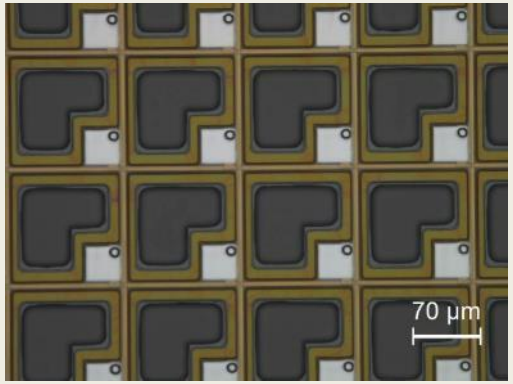
Envisioned as a first step: Integrated TEER Multiwell Plate

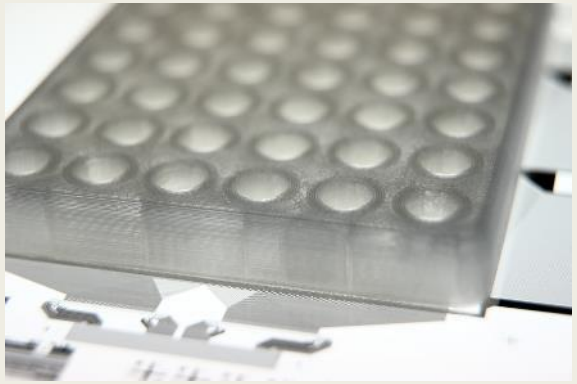
Work together with Imec, Bi/ond, Multi Channel Systems, Philips, TUE, TUD, Micronit, …. on this topic

Searching for Complementary Knowledge – Knowhow – Capabilities to (Flexible) Electronics









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BI/OND: Who is who and where

Nikolas Gaio

OOC Technology

Amr Othman

OOC Qualification

Cinzia Silvestri

Admin

BI/OND is currently based in the Faculty of Electrical Engineering, Mathematics and Computer Science building, in TU Delft.

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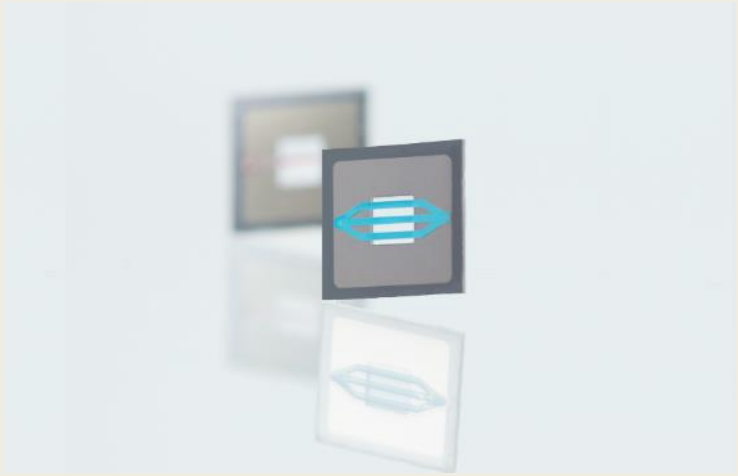
BI/OND capabilities

inCHIPit™



comPLATE™

- Silicon-based micro fabrication;
- Polymer processing,
- Microfluidics;
- MEA;
- In house qualification.

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BI/OND planned contribution

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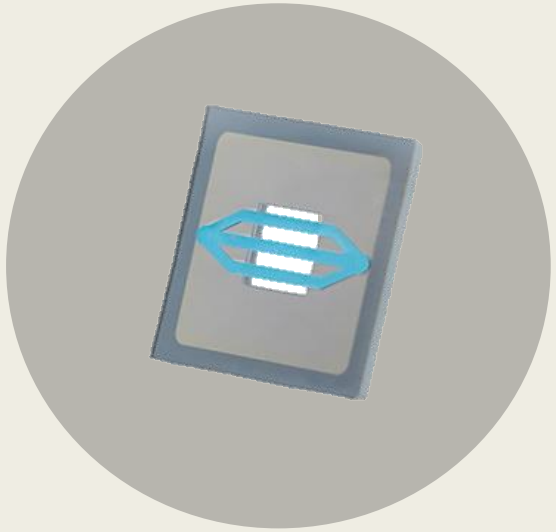
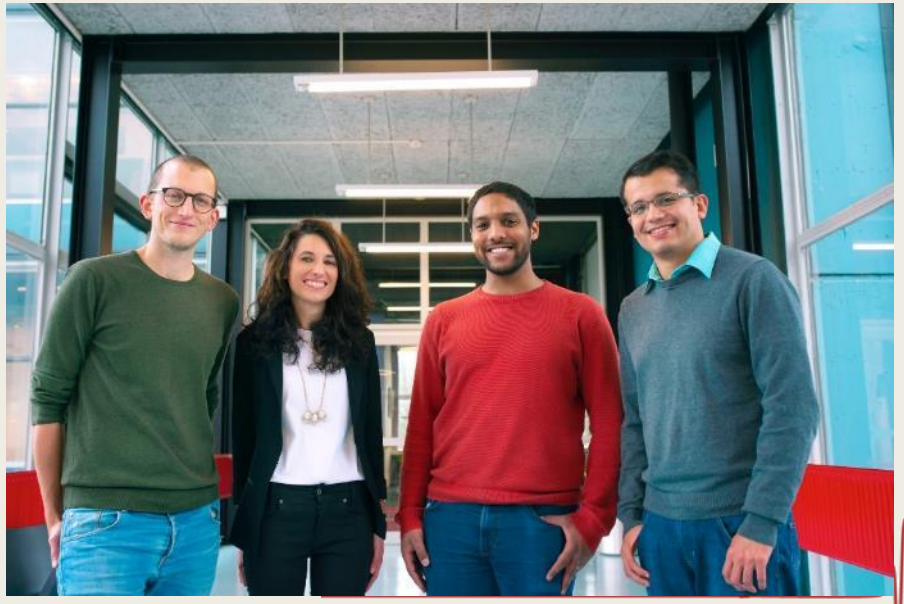
- Provide chips for the smart well plate (with and without electrodes);
- Share our know-how in the OOC field. Not only technical aspects: End-user point of view;
- Preliminary qualification (Heart-on-Chip);
- 3D electrodes for 3D tissues.

CHIP



PLATE



Besi Netherlands - Who is who and where

Sebastiaan Kersjes

Main contact

Niek van Haare

Deputy contact

Besi Netherlands B.V.
Ratio 6
6921 RW Duiven, the Netherlands
Tel. (31) 26 319 6100
Fax (31) 26 319 6200.

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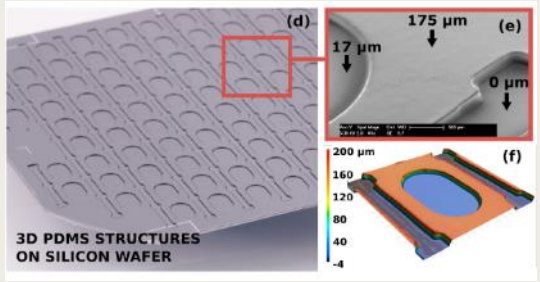
Besi Netherlands our capabilities

- Besi Netherlands is the innovation centre for Besi WW on the subject of (wafer level) encapsulation and saw singulation.
- Capabilities Besi-NL related to Moore4Medical are Transfer mold encapsulation using PDMS and Saw singulation technology for backend.



PDMS molding (Informed / Eurosensor 2018)

R&D transfer molding system

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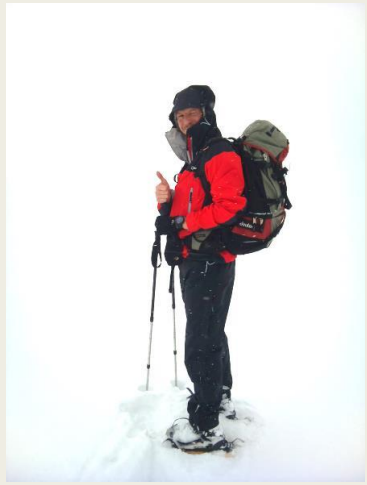
Besi Netherlands our planned contribution

- Besi NL will contribute w/r to encapsulation and singulation processes in WP2.
  - *T2.2; Encapsulation and Singulation technology for integrated systems needed for the Smart wellplate.*
  - *T2.3; On-wafer PDMS molding for OOC together w BIOND (proceeding on Informed)*
- Expected results; process development by obtaining state-of-the-art materials from the project partners
- Main contact
  - *Sebastiaan Kersjes*
  - *Sebastiaan.kersjes@Besi.com*
  - *Tel.: +31 26 319 4542*



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Micronit - who is who and where

Sandro Meucci
R&D Scientist

Maciej Skolimowski
Research Manager

Marko Blom
CTO

New HQ and merging of Enschede locations for product development and manufacturing

Contribute to an improved quality of life and work environment compliant with GMP and MDR

Ambition to achieve fully CO_2 neutral activity

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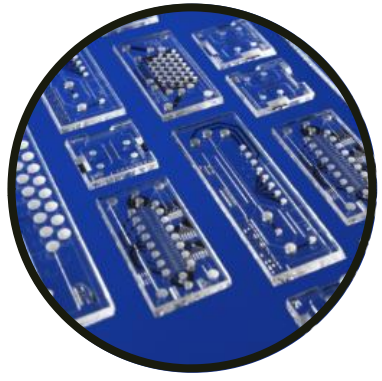
Micronit – our capabilities

Feasibility studies

Material know-how

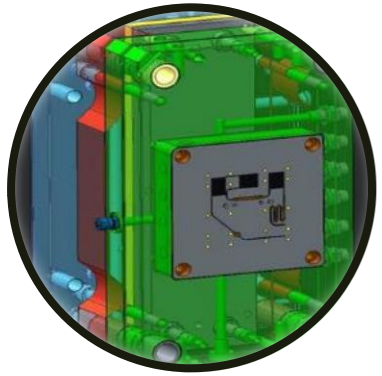


Fluidic design

Surface (bio)functionalisation

Rapid prototyping

Bonding



Mould development

Injection moulding

Assembly

flow alliance HOUSE OF MICROFLUIDICS

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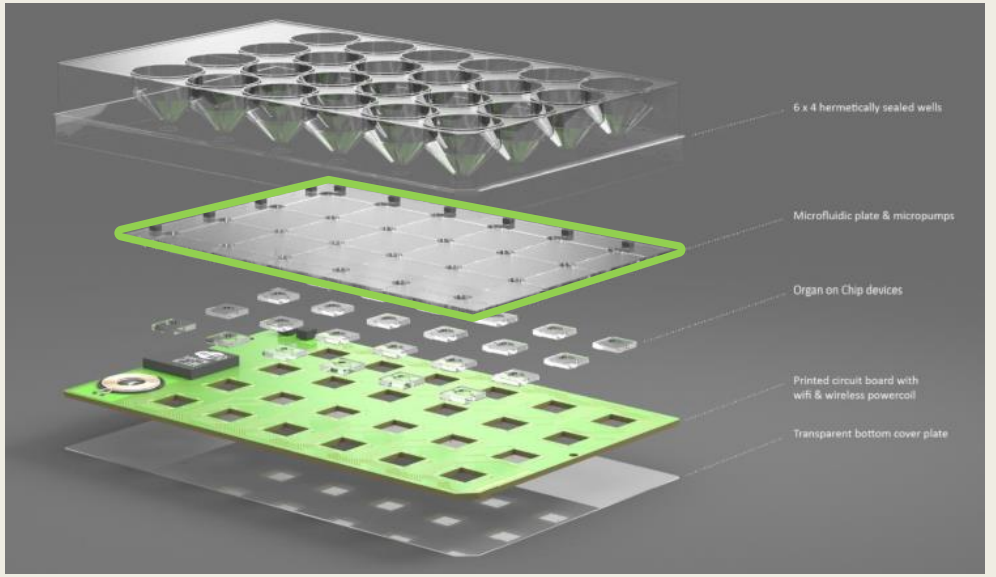
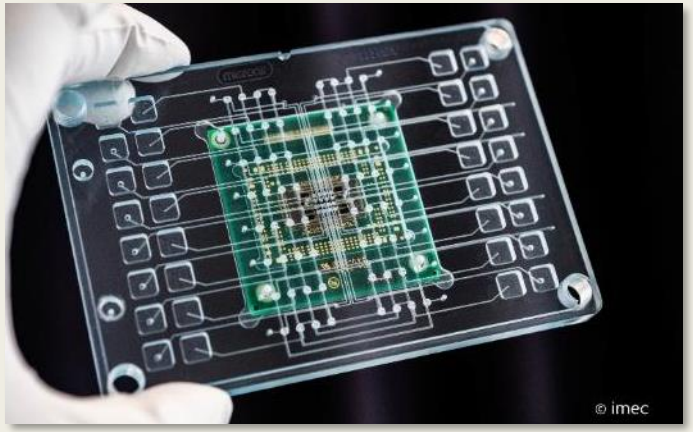
Micronit –our planned contribution

- WP2 Organ-on-Chip
  - *Input on all the tasks, for design and integration*
- Lead of Task 2.2 Smart multiwell plate: manufacturing
  - *In this task the smart multiwell plate will be realized. The work in the task breaks down into four subtasks executed by the respective specialists in this work package:*
    - Main activity : Manufacturing of the microfluidic layer (integrating the micropumps)
- Task 2.4 High definition electrophysiology multiwell plate
  - *Fabrication of the microfluidic layer (with perfusion) of the plate*
- Task 2.5 Smart multiwell lid realization
  - *Provide input on design and fabrication*





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Imec WP2 – organ on chip

Dries Braeken
R&D manager

Tim Stakenborg
Group lead Biodevices

Andy Miller
Dept. Director 3D integration

- World-leading R&D in nanoelectronics & digital technology
- 3500 international R&D top talents
- Unique € 2B leading-edge semiconductor fabs
- serving 500+ companies
- Created 40 spin-off companies and incubated 100+ start ups
- 8 sites worldwide

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ABOUT IMEC LIFE SCIENCE TECHNOLOGIES

Who we are

IMEC performs world-leading research in nano-electronics and leverages scientific knowledge with the innovative power of its global partnerships in several application domains.

IMEC Life Science Technologies (LST) leverages smart chip technology and systems solutions to take your tools to the next level

Who we work with

We partner with companies across the Life Sciences, Pharma and Healthcare value chain for development of next generation

- Laboratory analytical instruments
- IVD devices and Point of Care
- Pharma R&D and manufacturing
- Consumer health devices
- Medical devices

Our unique strengths

Customised chip solutions in four core areas: microfluidics, optics, sensors&actuators, and electronics

Strong **multidisciplinary teams** with experience on system design, multiphysics, process integration, testing and biology

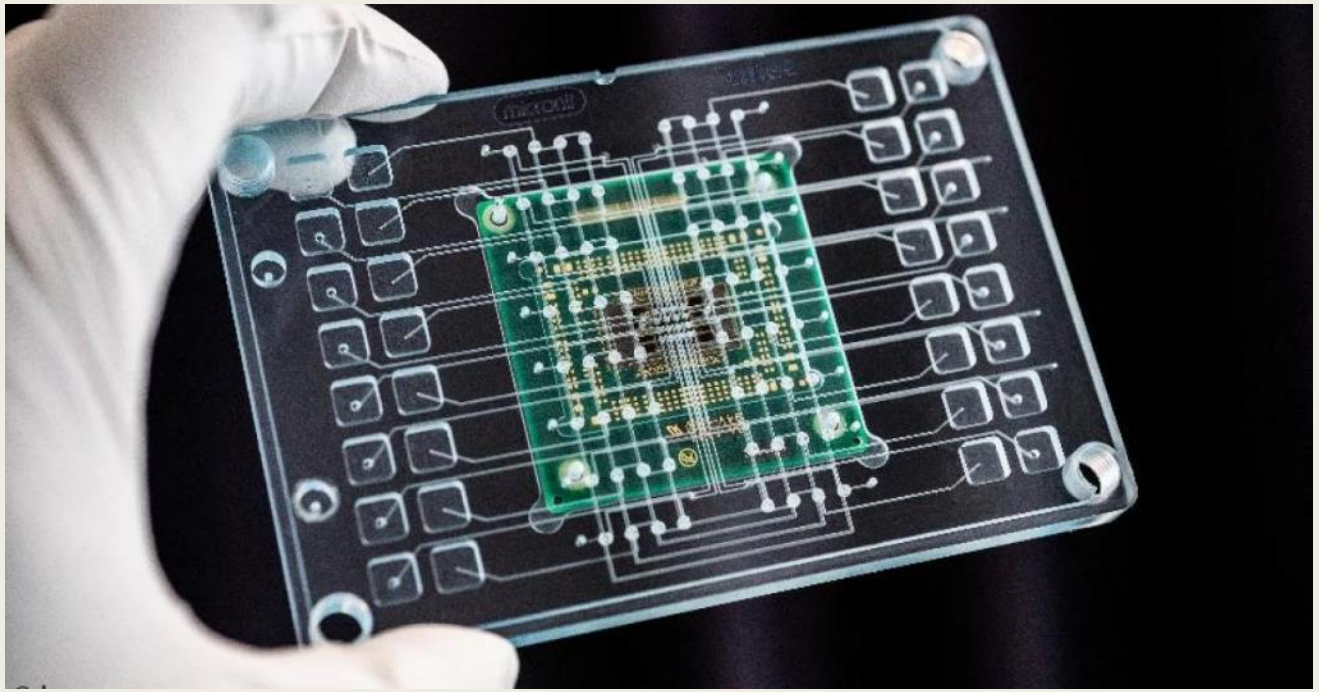
Volume manufacturing capability to bridge the gap from the lab to the market and compatible with high-volume foundries

imec WP2 contribution

Development of Multiwell OoC by supplying MEA chips
Explore reconstructed wafers (CMOS die fan-out)
Testing of multiwell plate in cardiotoxicity application

Teaming up with:

- Micronit
- EVG
- BESI
- MCS



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Multi Channel Systems (MCS) – Who is who and where?

Karl-Heinz Boven
CEO

Jannis Meents
Head of Research Projects

Christoph Jeschke
Head of Hardware development

multichannel systems
Innovations in Electrophysiology

Multi Channel Systems MCS GmbH
A subsidiary of Harvard Bioscience

Aspenhaustrasse 21
72770 Reutlingen
Germany
Fon +49-7121-90925-0
Fax +49-7121-90925-11
sales@multichannelsystems.com
www.multichannelsystems.com

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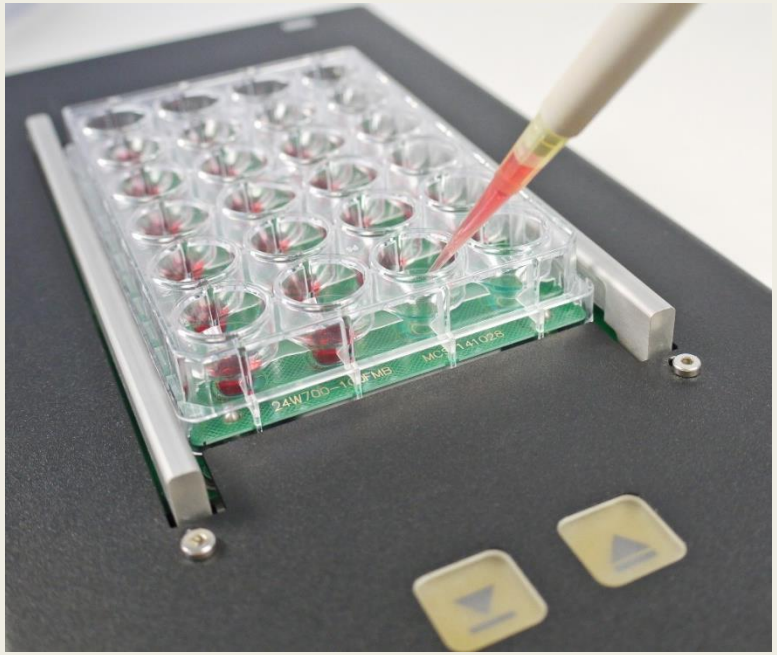
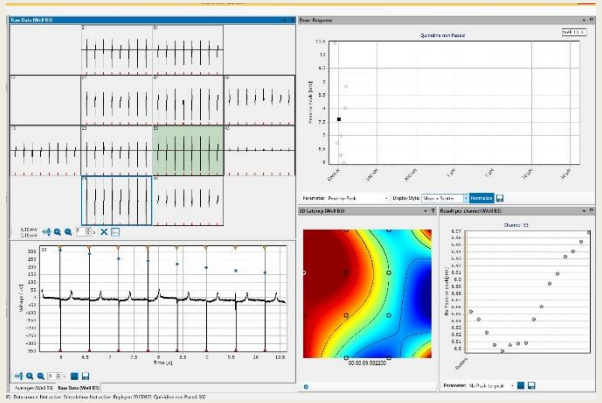
Multi Channel Systems (MCS) – Our capabilities

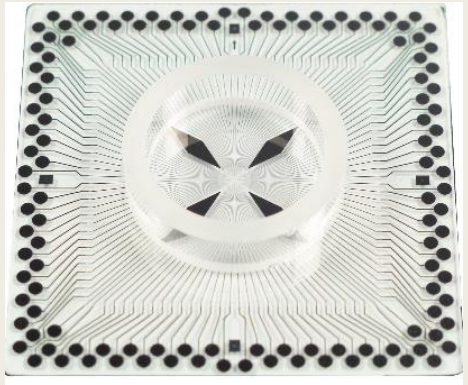
- Highly customized measurement systems for the E-Phys world
- Multiwell-MEA-System

  https://www.multichannelsystems.com/products/multiwell-mea-system
- Fluidics: Peristaltic Perfusion System

  https://www.multichannelsystems.com/products/pps2
- Years of experience in the field of electronics for inductive power- and bi-directional data transfer
- Data processing and transfer to the PC (USB or wireless) for data recording and further analysis
- Firmware development
- Windows Software development







Jannis Meents (jmeents@multichannelsystems.com)

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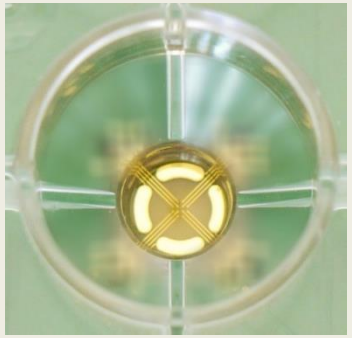
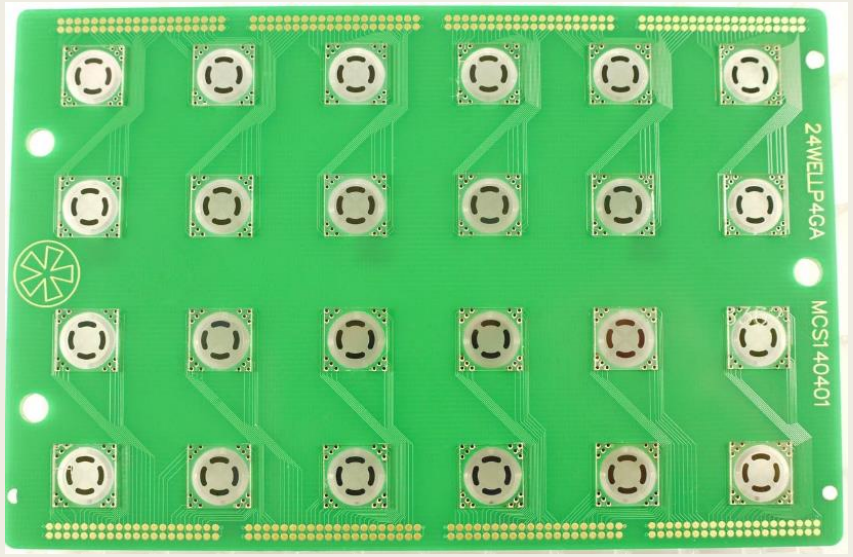
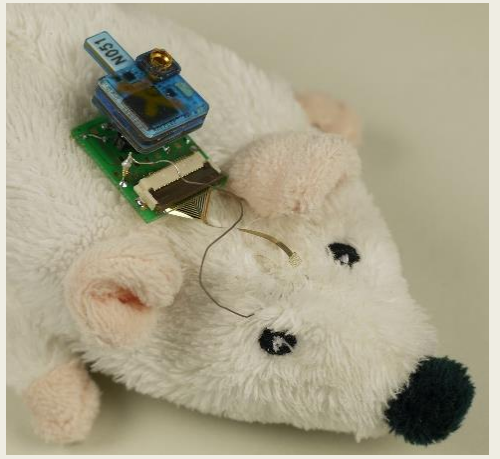
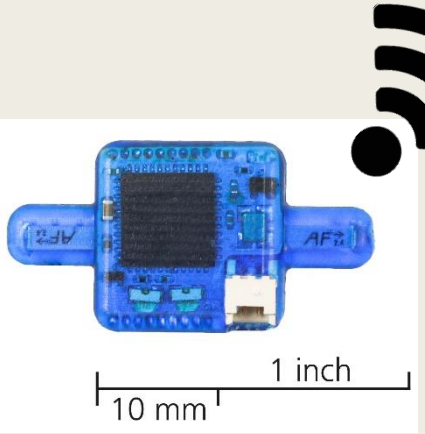
Multi Channel Systems (MCS) – Our planned contribution

- Share our expertise in the areas of
  - *Multiwell-Systems and MW-Plates*
  - *Wireless (Inductive) Power Transfer*
  - *Wireless data transmission*
  - *Control of pumps for microfluidics*
- Plan, develop and fabricate custom electronics or test systems needed for WP1 & WP2.
- Develop custom software needed for WP1 & WP2.
- Provide technical assistance for potential in-vivo experiments.
- Provide existing MCS hardware/systems for the consortium if needed.









Jannis Meents (jmeents@multichannelsystems.com)

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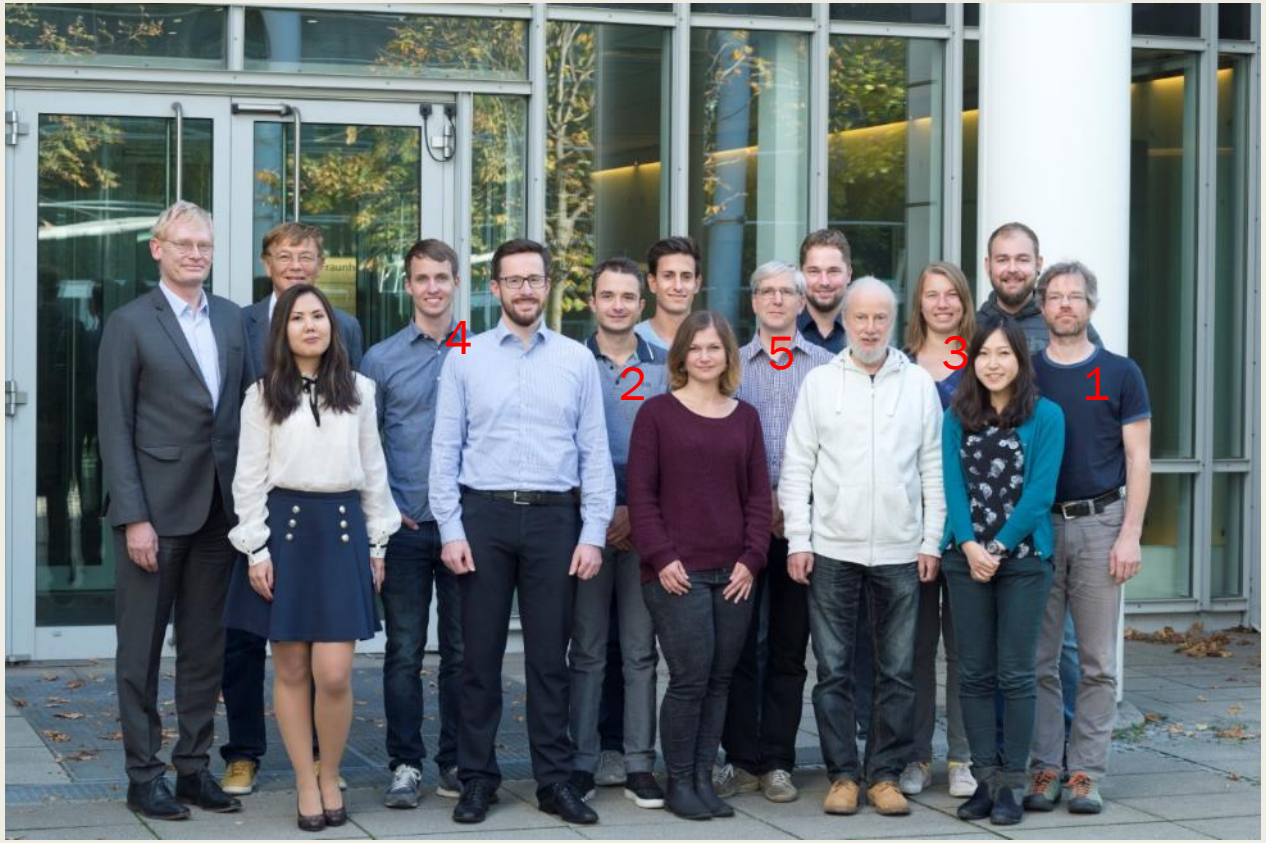
Fraunhofer EMFT, who is who and where?



1. Axel Wille (WP Coordinator)
2. Henry Leistner (Fab Transfer and Lead)
3. Agnes Bußmann (Interaction btw. Pump and Drug)
4. Thomas Thalhofer (Demonstrator)
5. Martin Wackerle (Safety Valve)

Fraunhofer EMFT at Hansastraße 27D in in Munich with over 100 employees, close to Fraunhofer HQ

EMFT our capabilities

- Team
  - *Martin Wackerle*
  - *Henry Leistner*
- Consulting microfluidics / micro dosing
- Design and demonstrator production of micro pump

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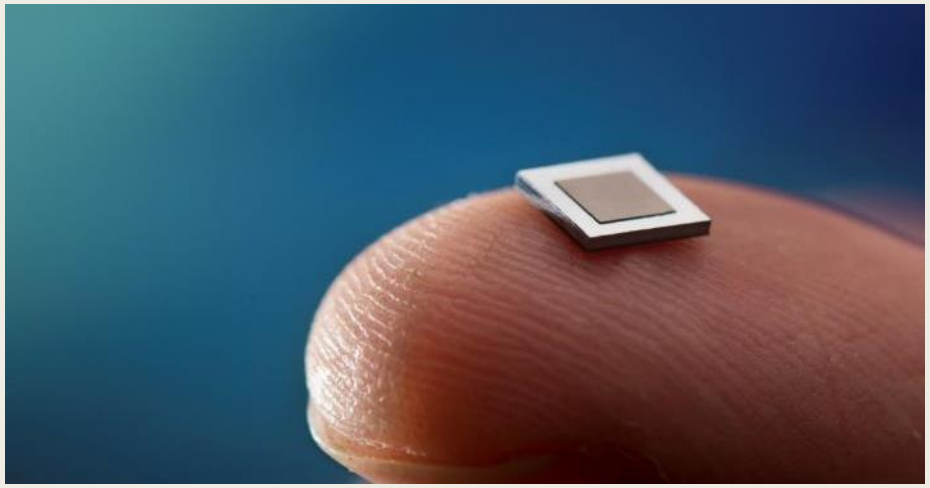
EMFT our planned contribution

- Supply of micro pumps
- Consulting regarding micro fluidics



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microfluidic ChipShop GmbH

Holger Becker
project leader

Sebastian Schattschneider
project scientist

Own 5000 sqm facility (with class 7 cleanrooms and biolabs) in Jena, one of the high-tech centers in Germany (mainly optical, photonic and biomedical instrumentation)

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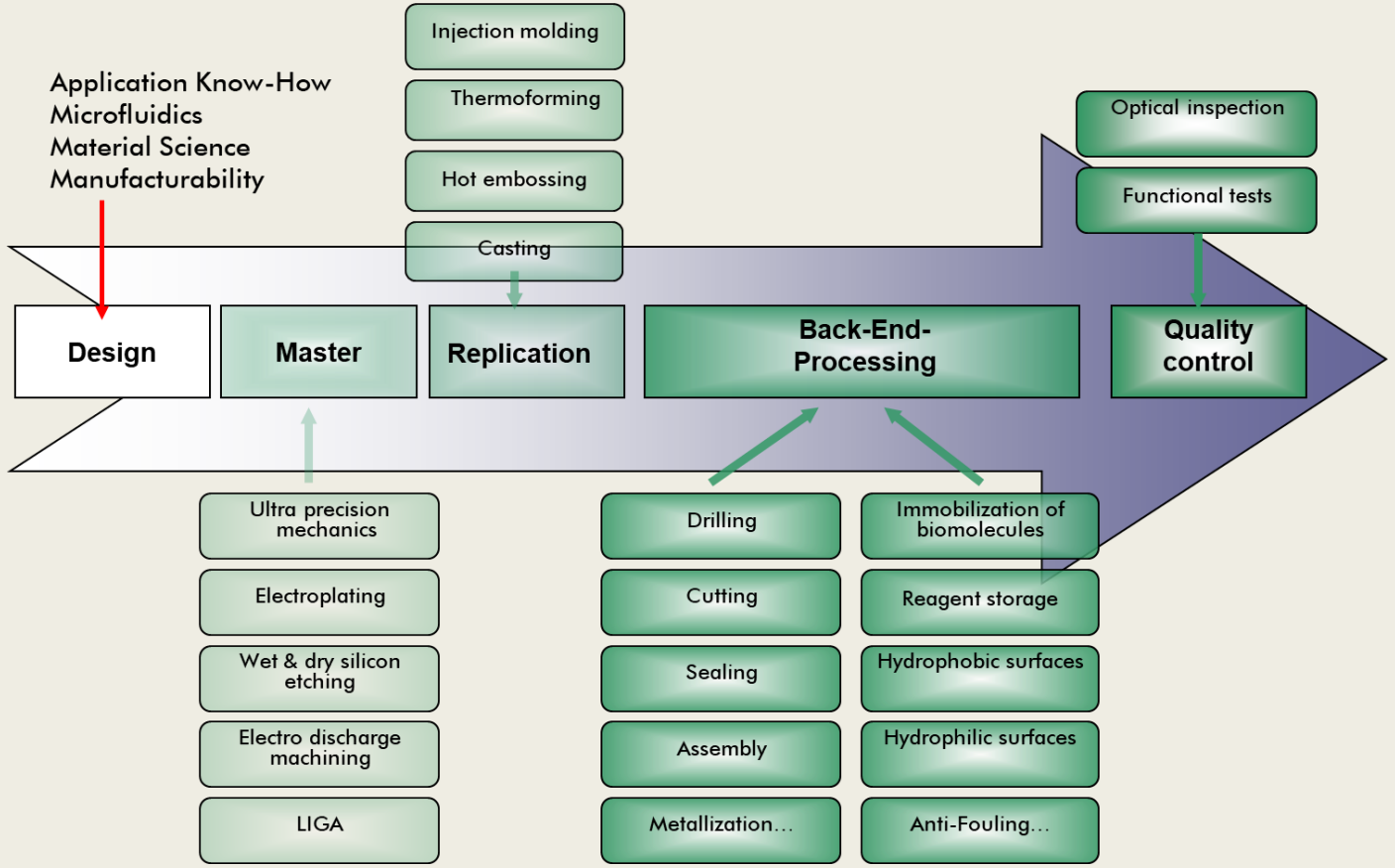
microfluidic ChipShop: our capabilities

- Complete technology chain for the development and industrial manufacturing of microfluidic devices in polymer (disposables)



- Application labs for fluidic validation
- ISO 13485

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microfluidic ChipShop: our planned contribution

- Task 2.1 Definition of platform requirements, system architecture, specifications for Smart Wellplate: Emphasis on manufacturability
- Task 2.2 Smart multiwell plate: manufacturing: Hybrid integration and polymer microfabrication
- Task 2.3 Smart multiwell plate: organ-on-chip devices: provision of parts to OoaC partners
- Task 2.4 High definition electrophysiology (HD e-Phys) multiwell plate: Hybrid integration (imec Si components)
- Task 2.5 Smart multiwell plate lid realization: design and realization
- Task 2.6 Innovative sensor and organ-on-chip modules: Provision of additional modules (e.g. with sensors) to partners
- Task 2.7 Validation of the smart multiwell plate platforms: Provide parts as well as fluidic experiments
- WP7 Innovation management

Anyone who needs microfluidic support or polymer microstructures

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MSB Who is who and where

Gianni Medoro
Company CTO

Maximilian Sergio
ICD Team Leader

Fabio Campi
M4M Main Contact

MSB Main Site, Castelmaggiore (Bologna), Italy.

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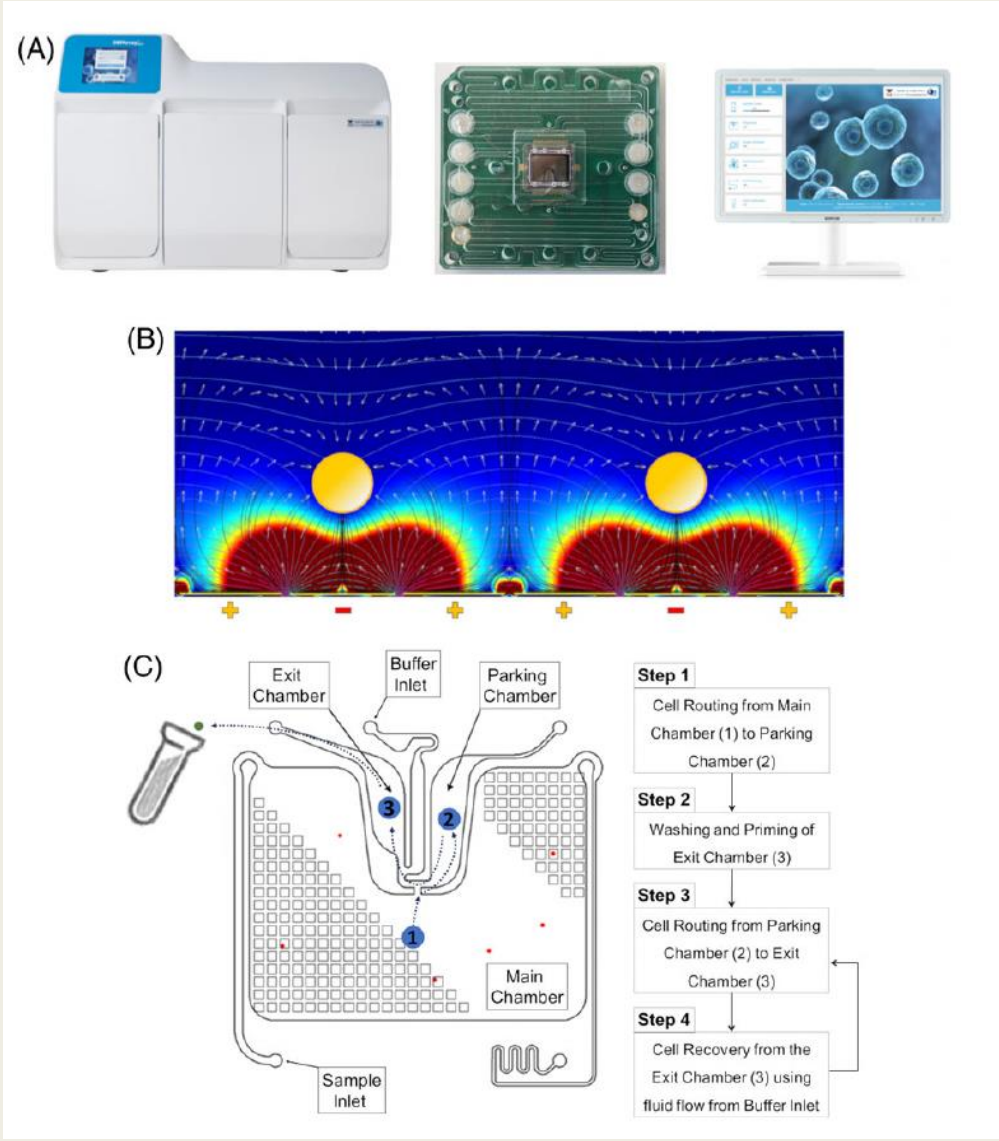
MSB our capabilities

- MSB has developed a ***proprietary technology*** (DEPArray™) that combines microelectronics and microfluidics to create a simple and reliable way of isolating and manipulating pure, single, viable rare cells from heterogeneous samples for cell culture or molecular analysis.
- DEPArray™ offers unprecedented capability to study rare cells and determine the biological significance of distinct subpopulations of cells within a sample

<u>This provides unique opportunities to develop new diagnostic and therapeutic strategies to improve patient outcomes and address unmet medical needs (e.g. personalized medicine for cancer).</u>



MENARINI silicon biosystems

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MSB: planned WP2 contribution

- In the innovation track, the “DEPArray” technology of MSB for the isolation of 100% pure single live cells from heterogeneous samples will be improved by a dedicated sensing platform for the detection and classification of rare cells.
- This sensing platform will enable the enhancement of throughput and yield provided by the DEPArray technology in order to “streamline” experiments workflows for applications with live cells, including those involving Organ-On-Chip devices.

MENARINI silicon biosystems

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BEONCHIP Who is who and where

Rosa Monge
BEOC-project leader

Luis E. Serrano
Product Develop. Engineer

Lara Pancorbo
R&D Technician

CEMINEM- University-Companies Joint Research Centre. Río Ebro Campus. Zaragoza (Spain)

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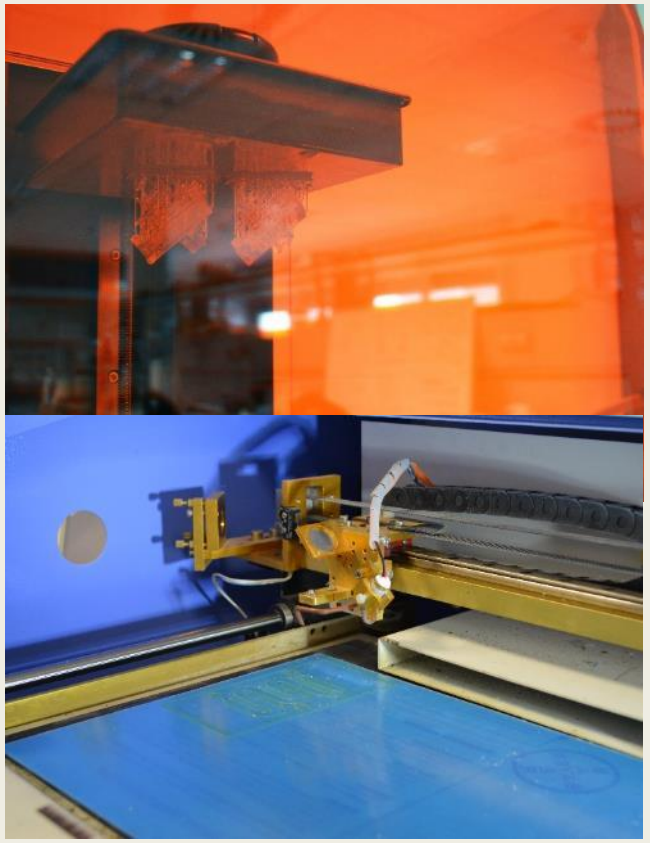
Beonchip S. L. our capabilities

We assist our customer from idea to mass production

- Lithography (SU8, PDMS, metal evaporation)
- 3D chip design
- Laser ablation
- 3D printing (biocompatible materials)
- Plastic bonding
- Surface functionalization (UV, O2 plasma)
- Plastic injection (mold design, injection test runs)
- Micromachining
- Broad variety of materials (COP, COC, PMMA, PET, Glass, PDMS…)



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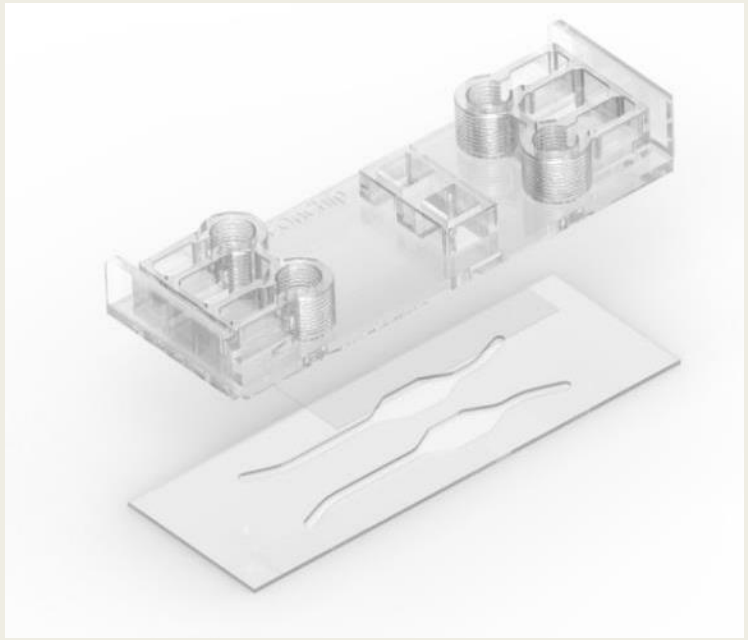
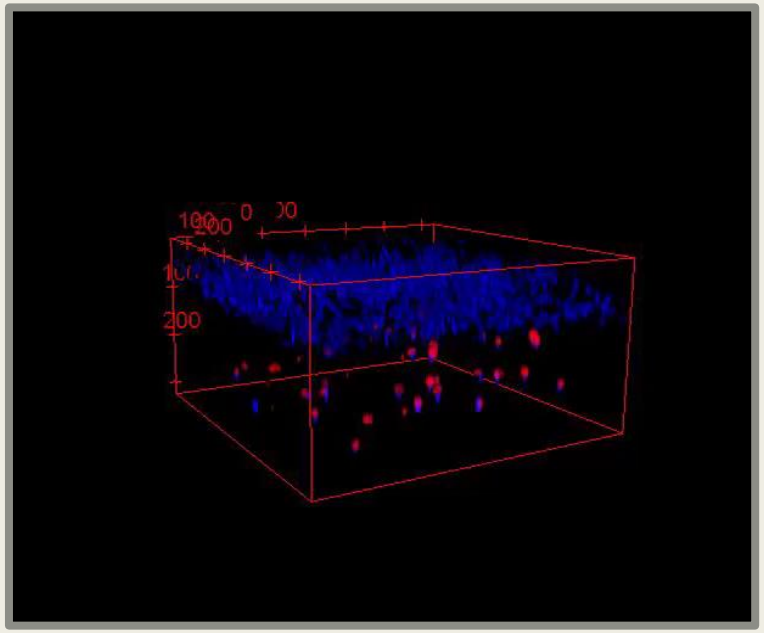
Beonchip S. L. our planned contribution

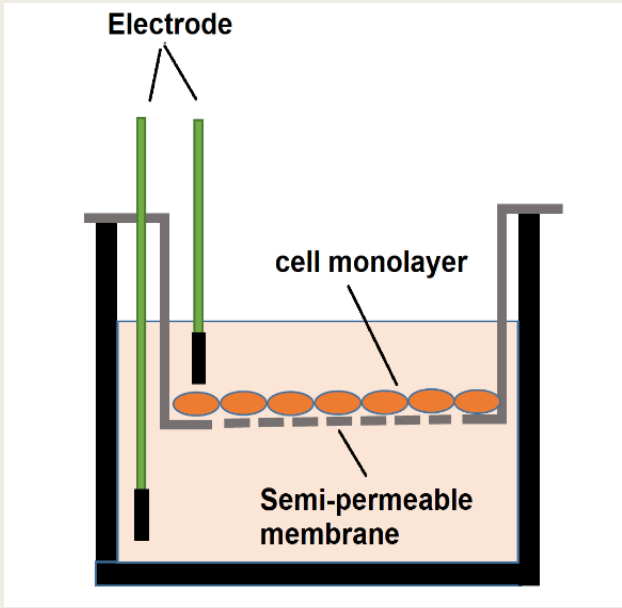
- BE-Transflow

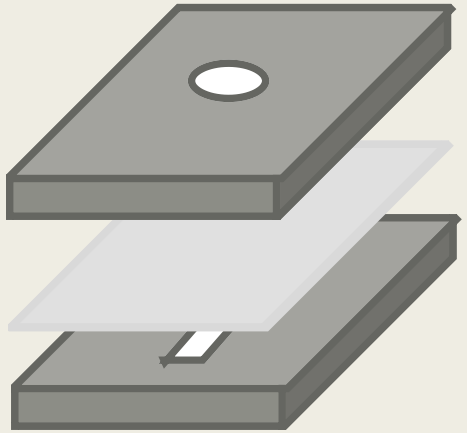


- Skin culture on chip



- TEER measurements





- Culture well
- Porous membrane
- Microchannel

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IISA: Who is who and where

Institute for Health Research

Antonio Antón

Project leader and clinical advisor

Estela Solanas

Project coordinator and basic research scientist

Institute for Health Research Aragon (IISA): joint biomedical research centre integrated by the hospital complex (Miguel Servet University Hospital (HUMS) and Lozano Blesa University Clinical Hospital (HCULB) and Primary Health Care), the University of Zaragoza and Health Sciences Institute of Aragón (IACS). It is located at CIBA building, Zaragoza (Spain).

Basic and applied research and innovation are joint to generate and transfer results to Health Service.

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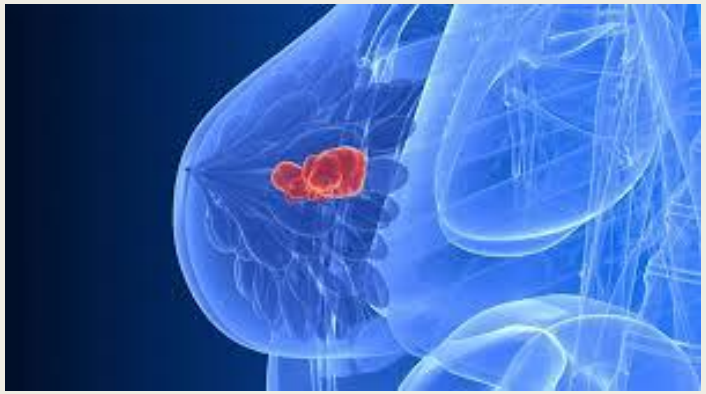
IISA our capabilities

Institute for Health Research

- Medical Oncology and Pathology Departments of the biggest hospital in our region with more than 1200 beds.
- Almost 1000 breast cancer patients per year.
- Multidisciplinary team with more than 40 clinicians and 20 basic researchers.
- Full equipped cell culture and molecular labs.



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IISA our planned contribution

Institute for Health Research

- Clinical-based perspective to the multiwell plate design.
- Improve the cell culture protocol to include breast cancer patient cells inside the platform
- Test different treatment strategies.
- Other tumors will be also tested to assess the versatility of the platform

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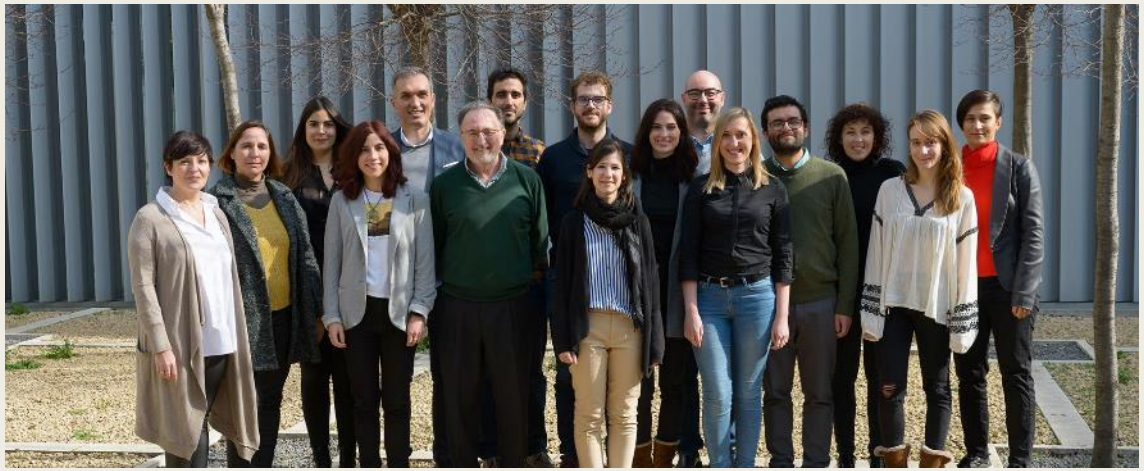
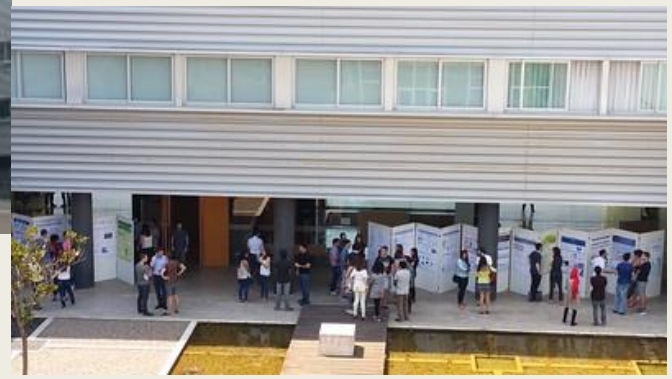
UNIZAR Who is who and where

Ignacio Ochoa
project leader

Roxana Subaseanu
project Coordinator





R&D Building at the Ebro river Campus (University of Zaragoza), housing the Aragon Institute of Engineering Research (I3A) and the Tissue Microenvironment (TME) Lab

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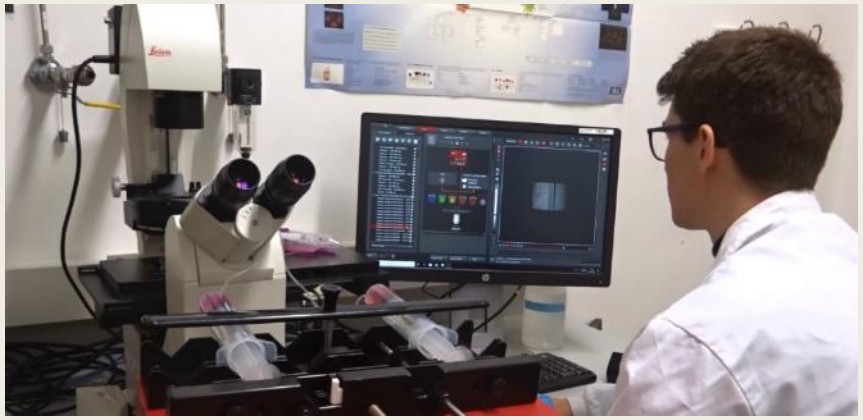
UNIZAR our capabilities

- Full equipped cell culture lab
- Confocal microscope
- Different perfusion systems (peristaltic, syringe and pressure)
- Biorreactors (CO2 incubators with integrated peristaltic pumps)



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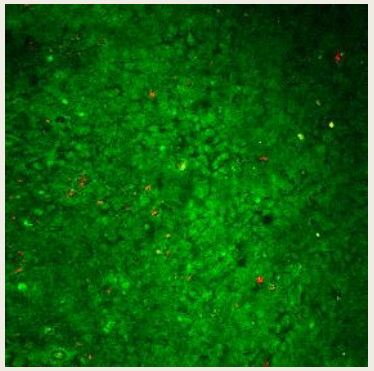
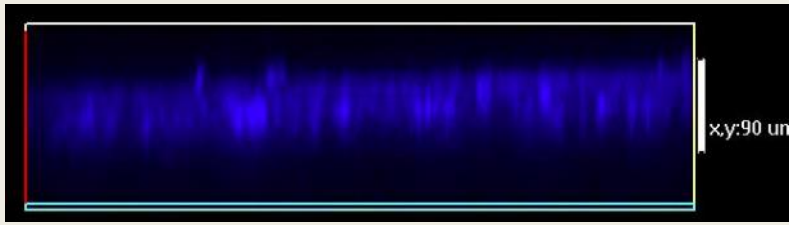
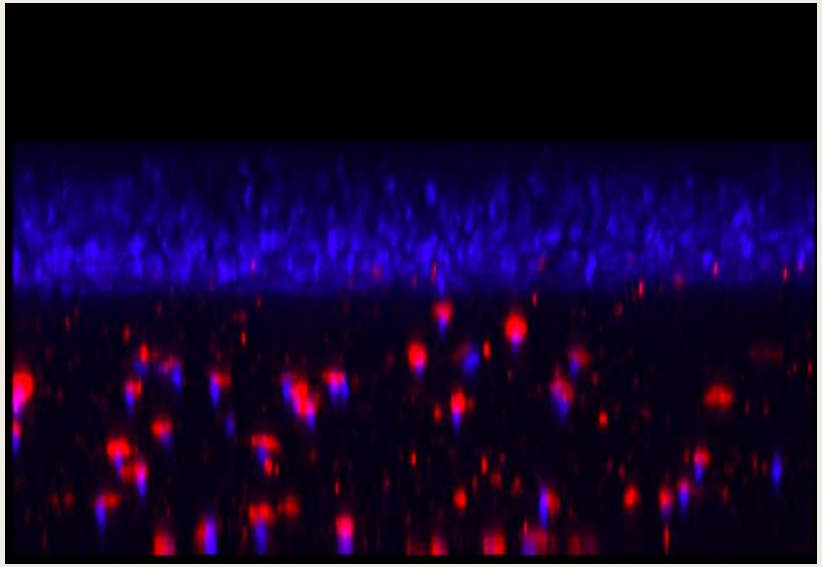
UNIZAR our planned contribution

- Validation of the cell seeding protocol to reconstruct the skin inside the BEOC microfluidic chip.

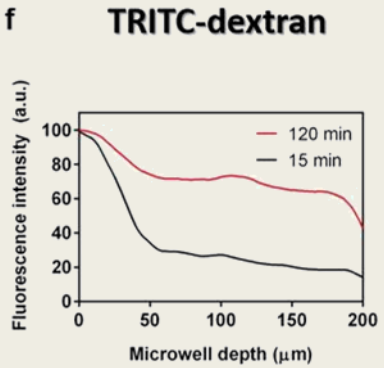




- Implement the cell culture conditions to achieve long term experiments (15 days)



- Permeability test with different fluorescent molecules to evaluate its permeability.



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ITAV – Who is who and where

Issa Tamer Elfergani
RF antennas expert

Joaquim Bastos
team leader

Jonathan Rodriguez
Mobile Systems group leader

IT-Aveiro 1, headquarters of Instituto de Telecomunicações, inside the University of Aveiro campus, in Portugal. It hosts several labs, such as RF and Networking labs.

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ITAV's capabilities

instituto de telecomunicações

- RTO with core expertise in design and implementation of diverse communication systems, as well as the integration of the respective components
  - *Secure and efficient short-range wireless technologies and their optimization or customization to specific use cases, applications and scenarios*
- Group of researchers with expertise in secure, reliable and efficient wireless communication solutions and techniques
  - *Energy efficient short-range wireless RF communication front-end, namely customised antennas*
- Fully equipped RF labs and easy access to University's RF anechoic chamber for testing and validation of antenna prototypes

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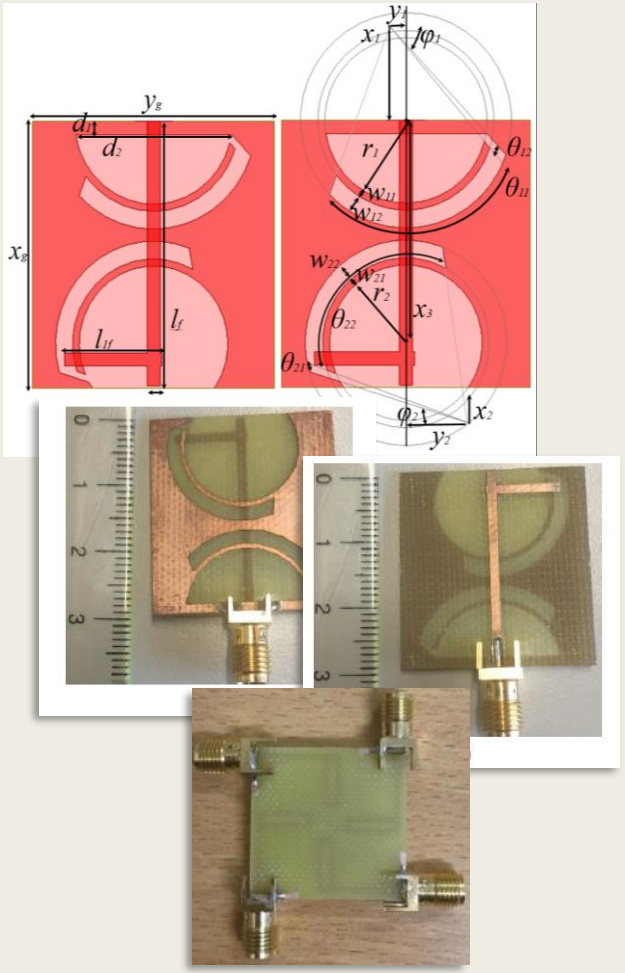
ITAV's planned contribution

instituto de telecomunicações

- ITAV contributes to WP2, with 21 PM of allocated effort
  - *Task 2.1: Def. of platform requirements, system arch., specs.*
    - Contribution to the definition of the overall system specification, namely focusing on wireless communication aspects and components, namely in the RF frontend
  - *Task 2.2 Smart multiwell plate: manufacturing*
    - Participation in "*2. Realization of the electronic layer including wireless power, pump control and communication*", contributing with customized antenna(s) design
      - *Assuring appropriately robust wireless data transport to and from the smart multiwell plate*
      - *Energy efficient high-gain antenna(s) design*
- Antenna(s) design, implementation and numerical simulations to evaluate standalone performance, using HFSS and CST tools
- Antenna(s) prototyping and physical measurements, including radiation pattern, to validate proposed designs



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INESC-MN, Lisbon Portugal

Susana Cardoso Freitas
Scientific coordinator

Veronica Romão
Biotechnology expert

Sara Viveiros
PhD student

350 m^2
INESC-MN Clean room
Lisbon

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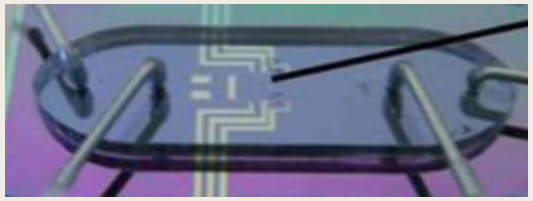
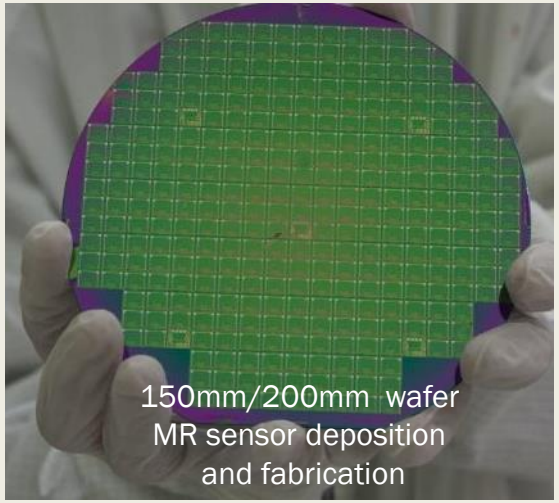
INESC MN
Microsystems and Nanotechnologies

INESC-MN capabilities

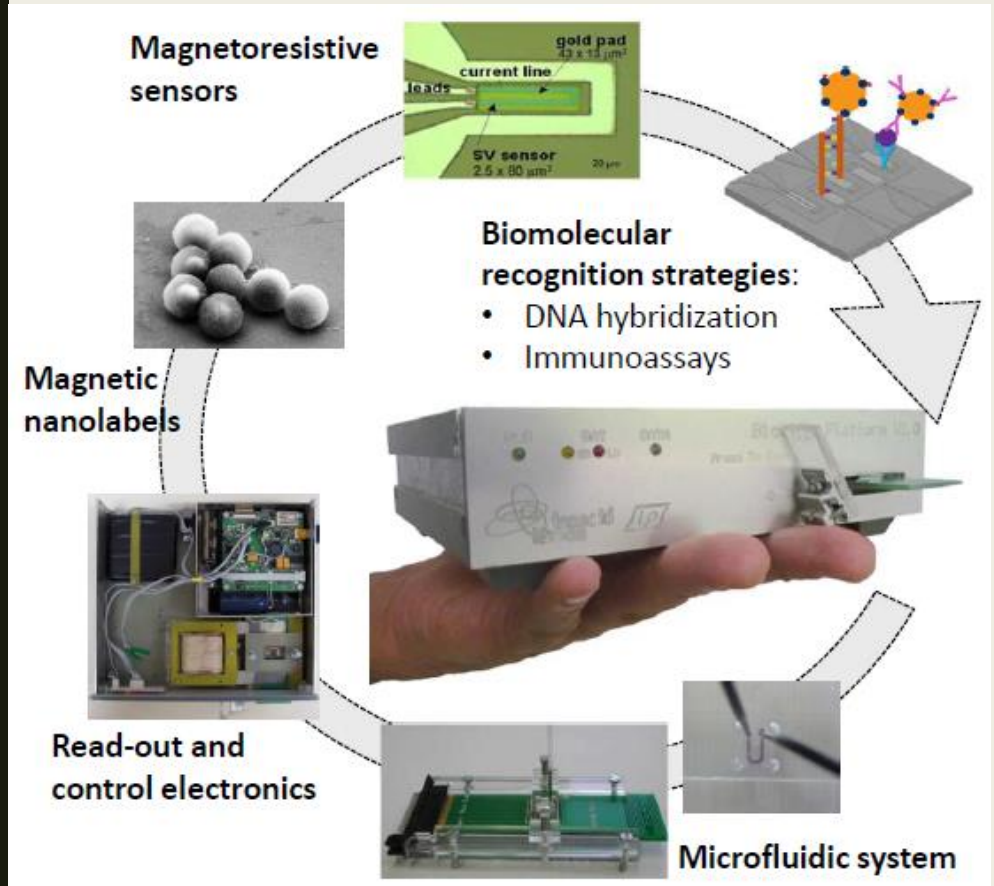
Microfluidic devices



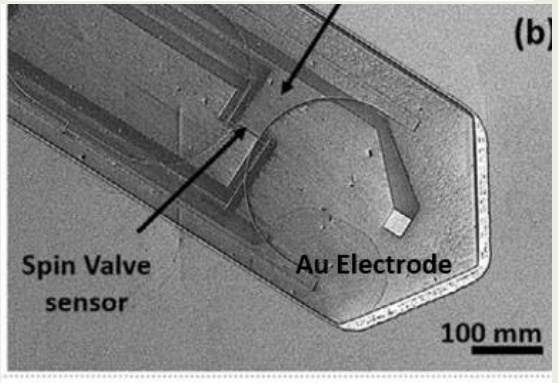


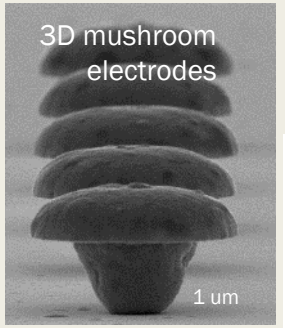
On-chip cell Cytometer

Lab-on-chip- Magnetic Biochips

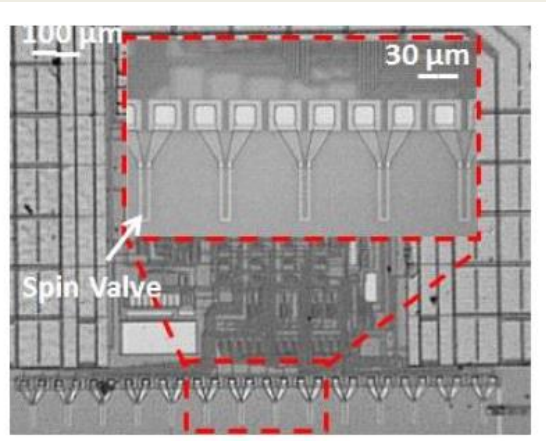


Flexible and Si needles with electrodes and sensors





Magnetic sensors on CMOS (magnetic camera and Biochips)



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INESC-MN planned contribution

Task 2.1 Definition of platform requirements, system architecture, specifications.

Task 2.6 Innovative sensor and organ-on-chip modules
New organ-on-chip modules and sensors will be developed for the future generation smart well plates.
Task 2.7 Validation of the smart multiwell plate platforms

INESC-MN role: to develop sensors for detection and quantification of magnetic labelled cells

- Flowmeter
- pH sensors
- Temperature sensors
- Oxygen sensors

Exploratory:

- glucose sensors
- sensors to measure contractibility of cells (in cardiac organ-on-chip)

Besi AT - Who is who and where

Thiago Moura
Main contact and technical responsible

Birgit Brandstätter
Project responsible

Damir Hajdarevic
Financial responsible

Besi Austria in Radfeld, Tirol:
The site houses equipment development for die attach flip chip and multi chip as well as process R&D.

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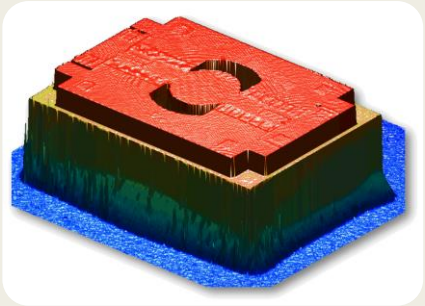
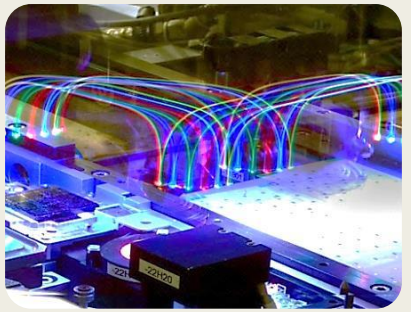
Besi AT capabilities

- Assembly equipment provider
- Fully automated pick & place
- Standard high accuracy down to ±3µm @ 3σ
- 6-axis bond head with tilt capability
- Cleanroom kit,
- UV curing

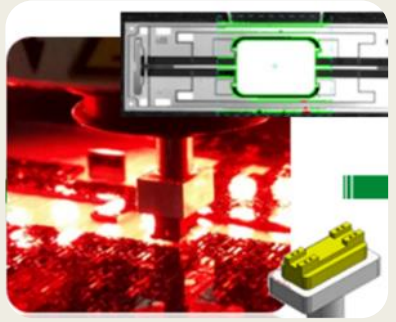


Advanced vision & 3D inspection

Accurate epoxy dispensing & jetting



Industry 4.0 & factory automation



MEMS handling and handling of fragile and complex structures

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Besi AT planned contribution

- Develop assembly machine for medical systems
- Machine focus on
  - *High cleanliness*
  - *Handling of*
    - complex and fragile medical elements
    - Large size objects
  - *Precise glue dispense and hermetic gluing for microfluidic assemblies*
  - *Low cost high volume production*

- Industrial assembly of
  - *multiwell plate and organ-on-chip devices*
  - *High-definition electrophysiology multiwell plate*
  - *Smart mulitwell plate lid*

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EV Group (EVG)

Bernd Dielacher
Business Development Manager - Biotechnology and MEMS

Anneliese Pönninger
Business Development Manager - Funded Projects

Philipp Peter
Process Technology Engineer - Bonding

Peter Urban
Process Technology Engineer - Bonding

Harald Rohringer
Product Manager - Bond Aligners and Integrated Bonding and Litho Systems

EV Group Headquarters
St.Florian am Inn, Austria

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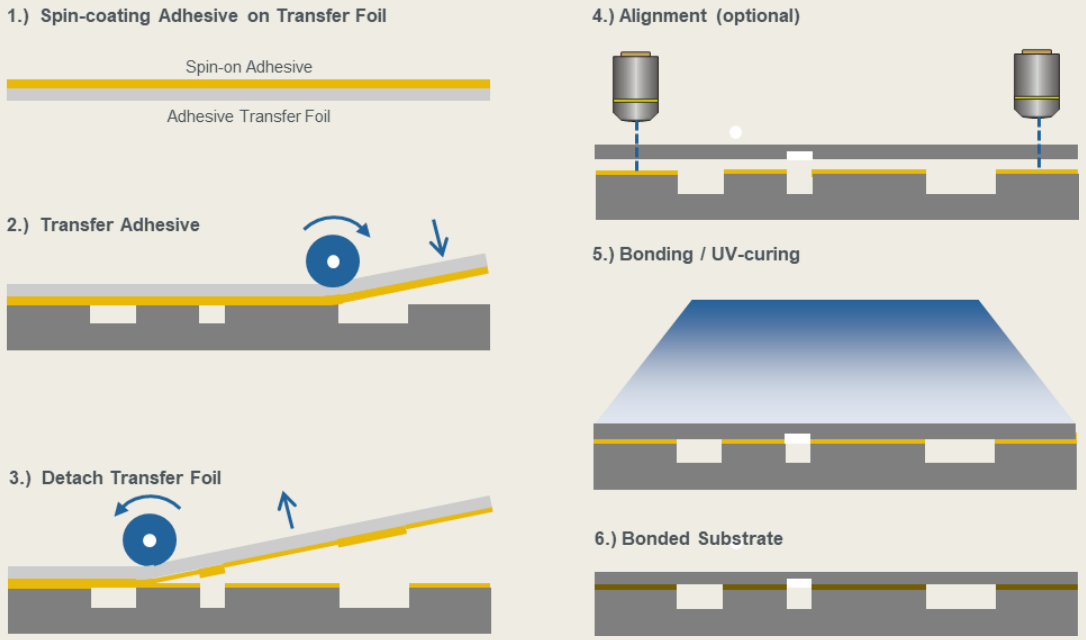
EVG - our capabilities

- EVG is a leading supplier of wafer processing equipment for the MEMS, nanotechnology and semiconductor markets.
- Technologies include Wafer bonding, Coating & Lithography, Nanoimprint Lithography and Metrology
- Process development in world-class clean room environment (ISO 4)

M4M Focus:

Adhesive Layer Transfer Bonding

- Ultrathin adhesive layers
- Room-temperature process
- Hybrid integration



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EVG - our planned contribution

- Bonding activities using adhesive layer transfer technology
  - *Wafer-level CMOS / Microfluidic (glass interposer) integration for high-definition electrophysiology multiwell plate (main task)*
  - *System integration for smart multiwell plate and lid*

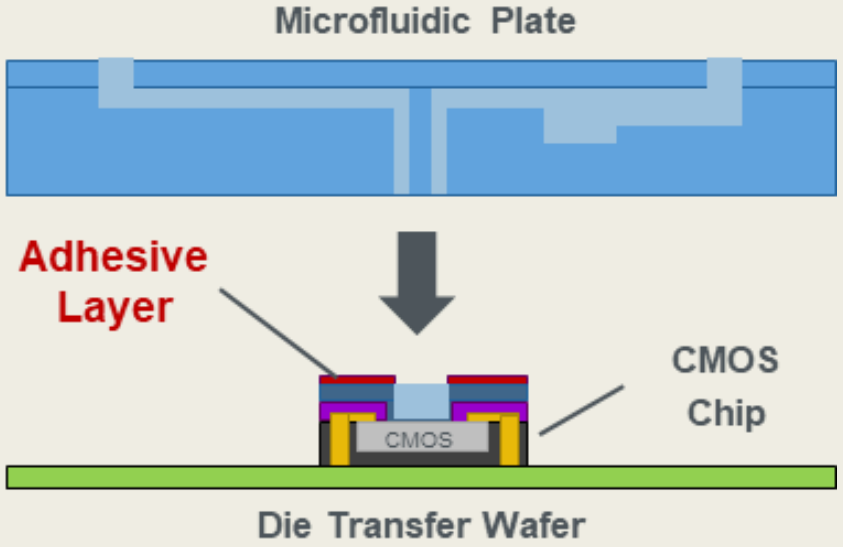
Activities:

→ Material evaluation

→ Process development

→ Equipment adaptions with focus on industrialization

CMOS / microfluidic integration concept



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CSEM: Who is who and where in WP2

Sigi Graf
Fluidics
WP responsible

Sarah Heub
Bio-Validation
Deputy

Felix Kurth
Bio-Chemical sensing

Nicolas Glaser
Sensing & Printing

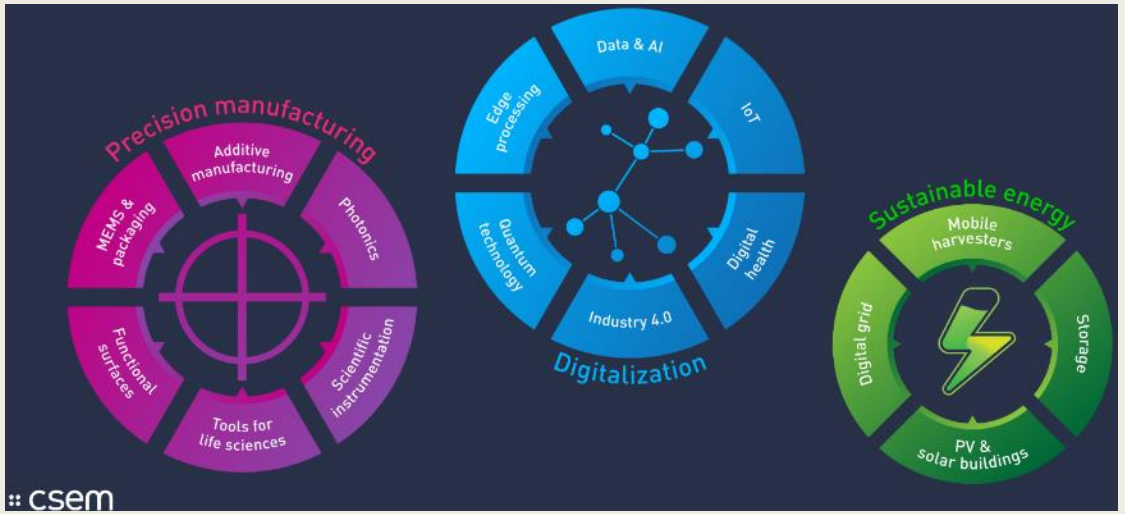
Erika Györvary
Technology Coordinator

Vincent Revol
Project Manager

Lead of Task 2.5 “Smart multi-well plate lid realization”

CSEM - our capabilities

- Swiss Research and Technology Organisation (RTO) focused on Technology Transfer (TT)
- Three main technology focus: Precision manufacturing / Digitalization / Sustainable Energy
- Relevant capabilities for Moore4Medical WP2
  - *Biosensors (design, prototyping and bio-validation)*
  - *Microfluidics (design, prototyping and testing)*
  - *Hybrid bonding and sensor packaging (process development)*
- Relevant infrastructure for Moore4Medical WP2
  - *Microfluidics prototyping facility*
  - *Surface functionalization*
  - *Sensor printing (clean rooms)*
  - *Biosafety lab II*



:: csem

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CSEM - our planned contribution

- Support Task 2.1 Definition of platform requirements, system architecture, specifications
- Lead Task 2.5 – Smart multi-well plate lid realization
  - *Development of a printed Glucose biosensor on polymer foil (focus on operational stability, manufacturability / scalability, simplification of calibration)*
  - *Development of active and passive fluid handling system (microfluidic design, component integration, manufacturability / scalability of assembly step)*
  - *Coordination of system integration with other manufacturing partners*
- Support Task 2.7 Validation of the smart multiwell plate platforms
  - *Final testing of smart multi-well plate lid*
  - *Integration and biovalidation on InSphero spheroid models*

Table 1-8 Specifications for the smart multiwell plate lid and spheroid demonstrator.

Smart Lid			**Multi-spheroid demonstrator**	
Number of Channels	24 (sequential readout)		Spheroids per channel	≥ 10
Glucose conc. range	0 – 1.5 g/l (res. 0.05 g/l)		Flow range	1-20 µl/min
Sample volume	10 µl		Culture volume	80-200 µl
Shelf life	> 3 months		Functional co-culturing	> 2 weeks
Stability in culture	> 8 hrs			

Moore4Medical

Who is who and where

Olivier Frey
Head

Lisa Hölting
Scientist

Özlem Yavas
Engineer

Currently moving to out new head quarters in the Bio-technopark in Schlieren, Zurich, Switzerland

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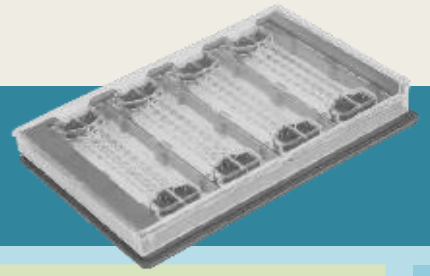
insphero our capabilities



Organ on a chip
Akura™ Flow Technology

Liver Toxicology
- 3D InSight™ Liver Platform
- Investigative Toxicology Platform (Causality Toolbox)

Diabetes & NASH/Fibrosis
(Metabolic Diseases)
- 3D InSight™ Liver Disease Platform
- 3D InSight™ Islet Platform
- T1D and T2D modeling

Oncology
- 3D InSight™ Tumor Platform

Akura™ 96- and 384-well Technology

3D microtissue co-cultures from
- Human
- Rat
- Dog
- Monkey
- Minipig
- Cell lines

- Human/rat pancreatic islets
- Human liver fibrosis
- Human fatty liver/steatosis
- NASH

- Cell-line-based co-cultures of human tumors
- PDX-derived primary tumor
- Immuno-oncology platform (cell lines and PDX)

- DMPK (low-clearance)
- Metabolic model
- Tissue-tissue interaction studies
- Pro-drug activation, therapeutic index

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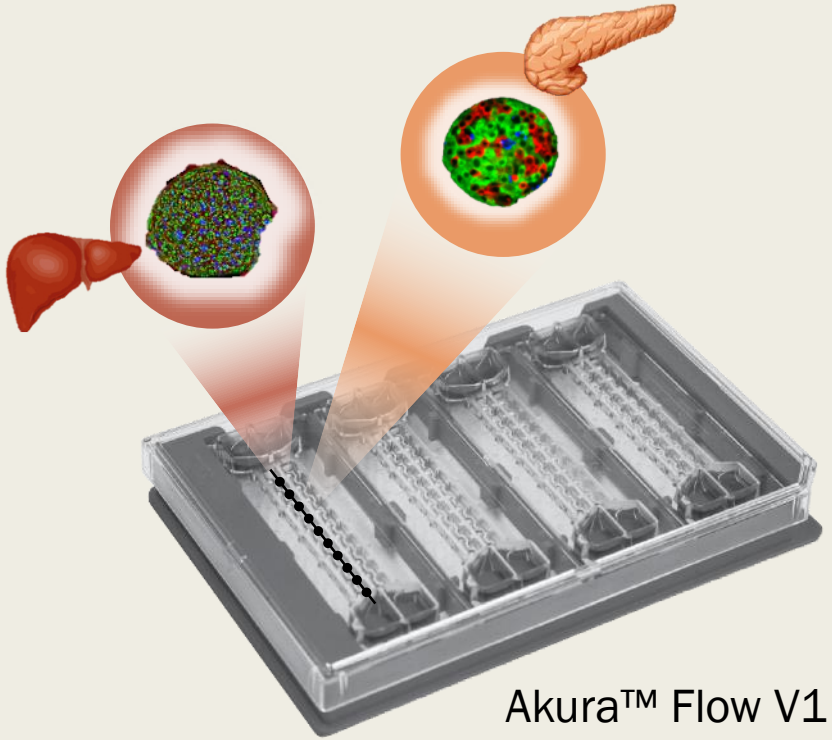
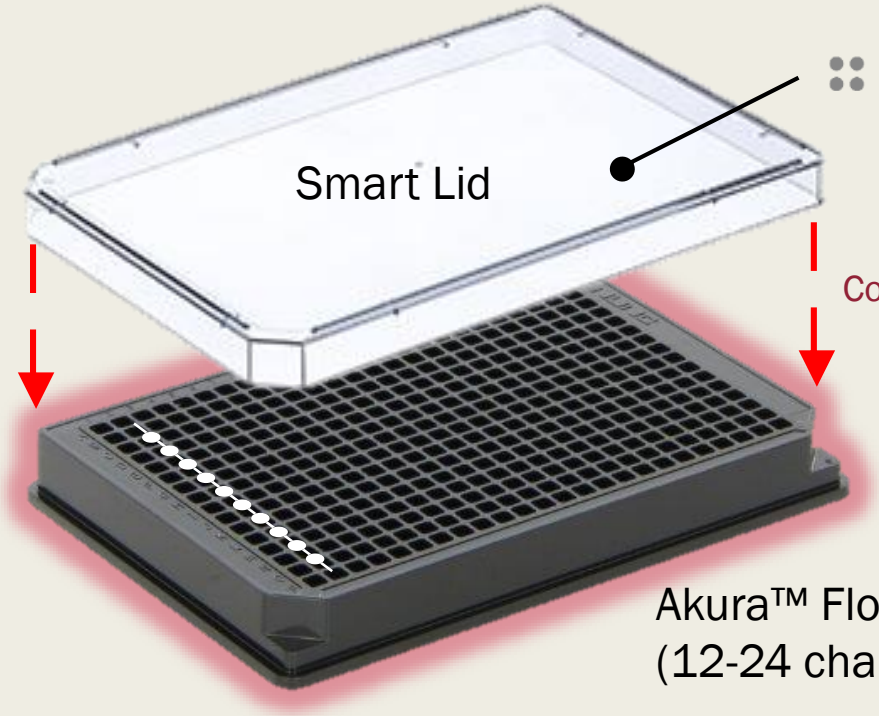
insphero our planned contribution

- Extend the currently Akura™ Flow platform toward compatibility with the Smart Lid with 24 multi-spheroid channels
- Provide use cases in the field of the Metabolic Syndrome (Islet-Liver interaction) for long-term culturing and metabolite monitoring (platform specification and validation)



Akura™ Flow V1
(8 channels)

csem



Akura™ Flow V2
(12-24 channels)

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IMT: Who is who and where

Carmen Moldovan
WP1

Bogdan Firtat
WP2

IMT: Main Building (left) and the new facility – CENASIC (right)

Location: 126A Erou Iancu Nicolae, Bucharest, Romania

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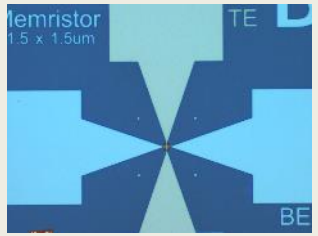
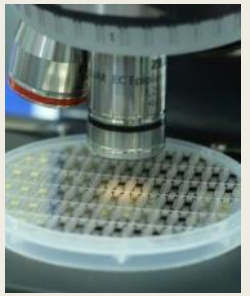
IMT: our capabilities

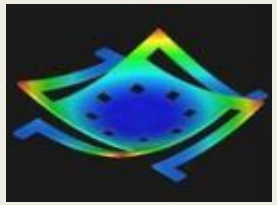
- The National Institute for Research and Development in Microtechnologies – IMT Bucharest was set up in 1996, and it is coordinated by the Ministry of Education and Research, acting basically as an autonomous, nonprofit research organisation.
- IMT is involved in research and development of micro- nano-biotechnologies and nano-electronics.
- The main competences are in closed connections to KETs and target the following research fields:
  - *Electronic Micro-and Nano-devices;*
  - *Photonic Micro-and Nano-devices;*
  - *Micro- electro-mecanical systems (MEMS), micro-and nano-fluidics;*
  - *Micro-nano-devices and systems for bio-medical applications (BioMEMS);*
  - *Advanced Materials and nanotechnologies*

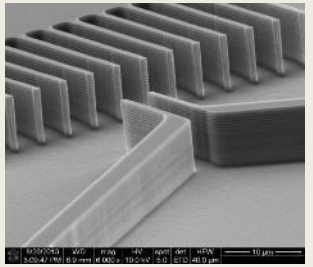




Laboratory of Microsystems for Biomedical and Environmental Applications, CINTECH Research Center

- Micro-nanosensors (chemoresistive, resonant gas sensors, accelerometers, microarrays, nanowire based ISFET), biosensors (electrodes, ISFET), microprobes for neuronal electrical activity recording: simulations/modelling, technological development and characterisation.
- MEMS devices for energy harvesting and sensors
- Microfluidic platforms - Simulation, modelling and fabrication
- Multisensor and microsystems integration; MicroPlatforms
- Signal conditioning; Data acquisition, processing and analysis;
- Autonomous and portable systems;





Main interests: bio – chemo sensors, MEMS technology, implantable devices, signal processing and data acquisition, energy piezoharvesters, Autonomous and portable systems, flexible electronics IoT for ICT, Space, Health and Environment

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IMT: our planned contribution

- Task 2.1 – General fluidic system modelling, for a first glance with relevant inputs to the initial specifications.
- Tasks 2.2 and 2.3 – In-depth microfluidic modelling and optimization:
  - *potential mixing issues, if several fluids (or different phases of the same fluid) are pumped through the fluidic system;*
  - *thorough analysis of the flow parameters (fluid velocity, flow rate, pressure), depending on the inlet parameters provided by the micropumps;*
  - *fluidic channels optimization (path and geometry) in order to meet the needed requirements (pressure and time needed around the cells area);*
  - *dead-spots identification (areas with zero velocity in the fluidic path);*
  - *any other fluidic analysis required by the WP2 members.*
- Tasks 2.5 and 2.6 – Multiwell plate, Sensors & modules:
  - *Contribution to design and optimization for the multiwell plate sensors on glass substrate;*
  - *Sensors fabrication.*
- Task 2.7 – Validation:
  - *Validation of the analyses through measurements;*
  - *Potential recalibration of the simulation parameters.*

MICROLIQUID Who is who and where

Luis Fernandez

CTO
Microliquid coordinator

Andreu Llobera

Head of Innovation
Technical lead

Borja Barredo

CEO
Administrative

microLIQUID
experts in microfluidics

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MICROLIQUID: our capabilities

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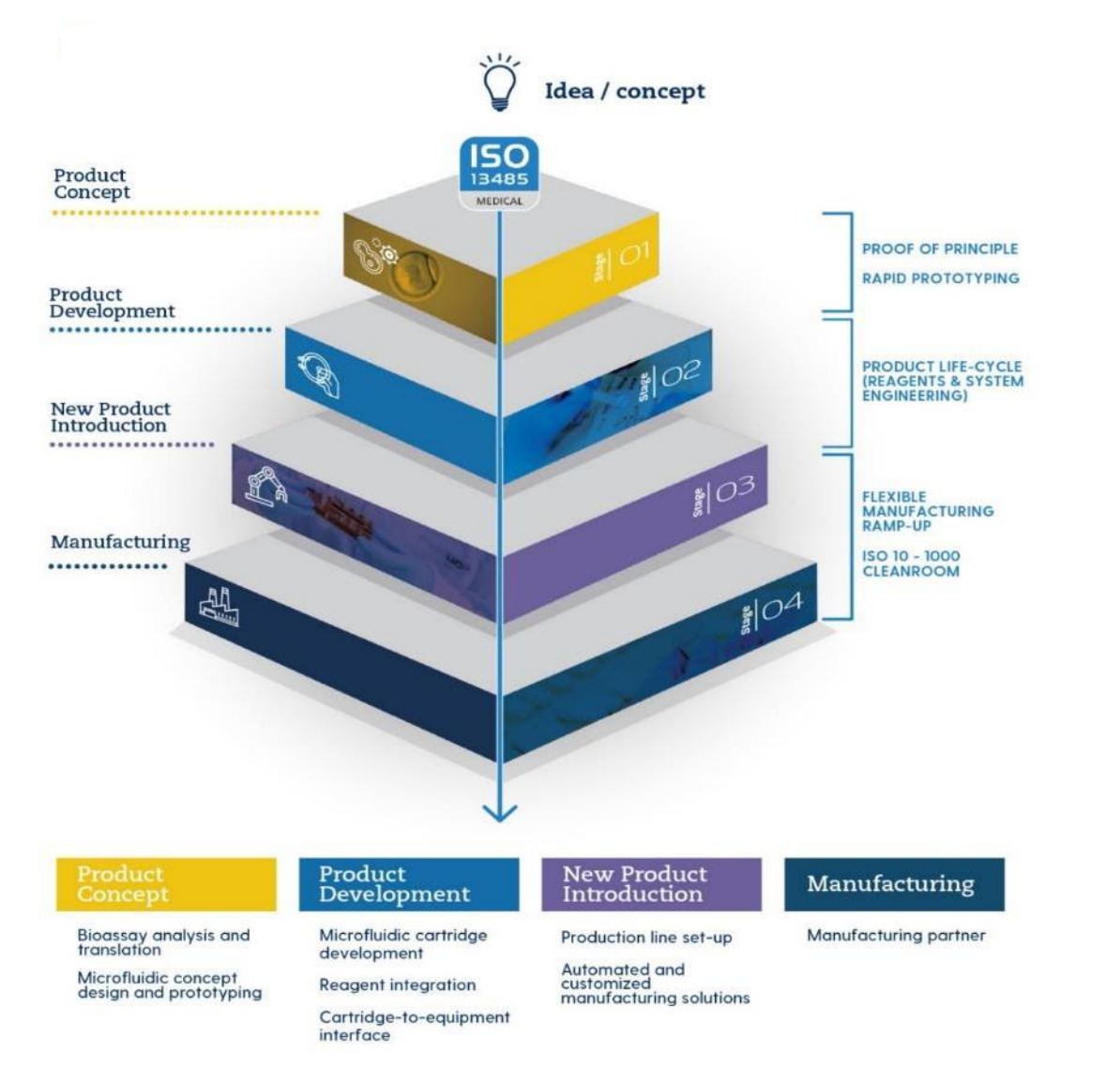
MICROLIQUID: our capabilities



Our Services

We work side-by-side with our customers

- Microfluidic contract design and manufacturing
- Capability to start working on a project **at any stage**
- Biomedical assay transfer and reagent integration
- Transfer to manufacturing and Flexibility in ramp-up

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Centre for Energy Research (CER)
Microsystems Laboratory

Péter Fürjes

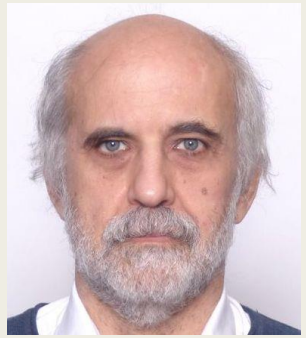
head of Lab

project management

Zoltán Szabó

researcher

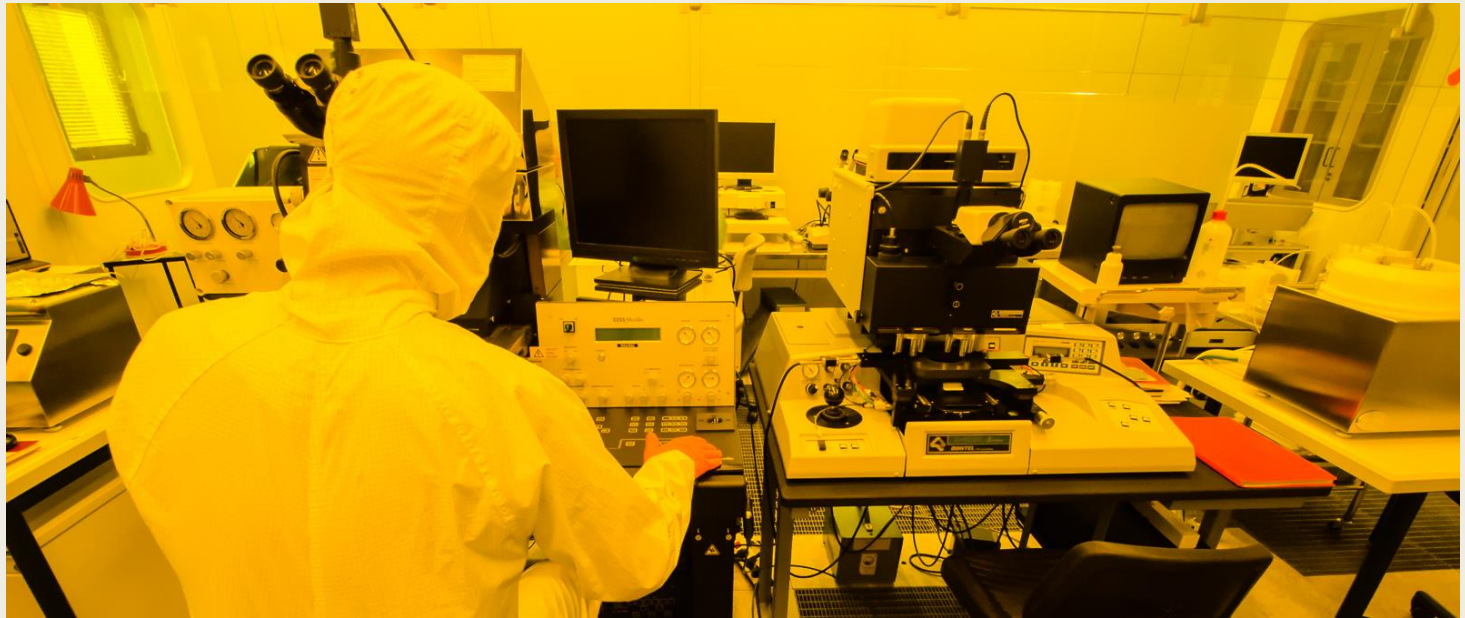
IR LED development



Csaba Dücső

tech. head of Lab

technology development



Budapest KFKI Campus

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CER MRL - our capabilities

300+150sqr meter **clean room** (for 4inch wafers) for (Si, polymer) **micromachining**

- 1μm resolution lithography (mask / direct writing / nanoimprinting / soft litgraphy with laser PG (mask shop)
- physical and chemical layer deposition (evap., sputt., APCVD, LPCVD, ALD),
- RIE, DRIE
- wafer bonding / dicing, packaging
- technology – device simulation / multimodal FEM modeling

Nanoscale fabrication:

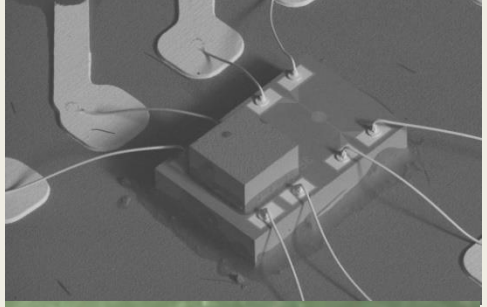
- E-BEAM (Raith 150), FIB (ZEISS, SCIOS), EBAD, IBAD

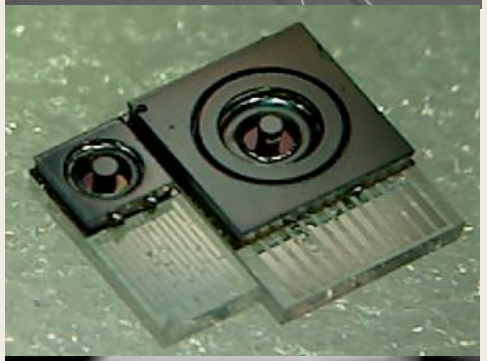
Characterisation:

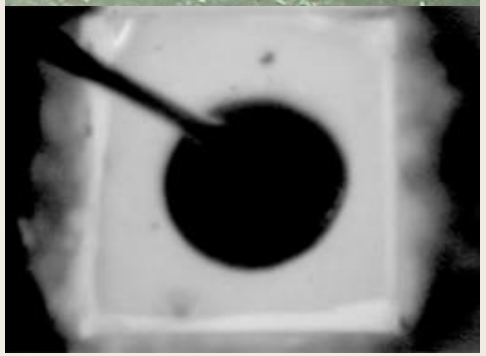
- microscopy, stylus surface profiling, SEM, TEM, AFM, STM
- XPS, EDS, Auger, SIMS, FTIR, EIS,

Devices

- **Gas sensors** (pellistor, TGS)
- Vectorial **force sensors** for medical and automotive applications
- Specific **IR LED** for spectroscopic applications
- **micro- and nanofluidic systems** for LoC applications and POC diagnostics
- Implantable **cortical and brain surface (EcOG) electrodes**







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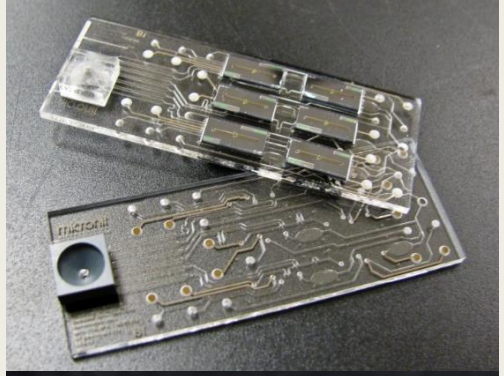
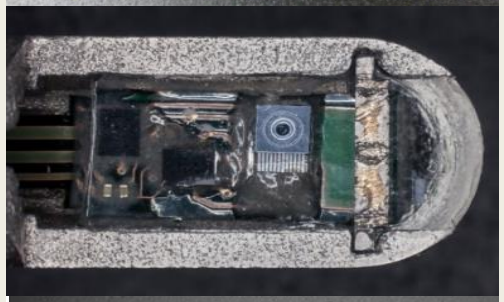
CER MRL – ECSEL projects

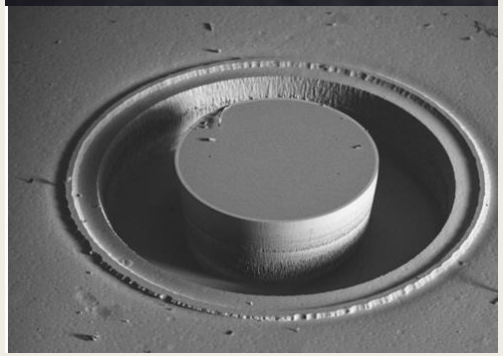
Chip Architectures by Joint Associated Labs for EUropean diagnostics
CAJAL4EU (ENIAC project)
leader: NXP (Belgium), partners: BME SZAKT, SE, 77 Elektronika, CEA-LETI (France), Micronit (the Netherlands)
coordinator sensor platform development (nanopore through transport modulation based biosensing)

Intelligent Catheters in Advanced Systems for Interventions
INCITE, (ENIAC project)
leader: Philips Research (the Netherlands)
partners: BME ETT, SE, Fundacja Rozwoju Kardiochirurgii (Poland)
national coordinator, workpackage leader (contact force sensor for Minimal Invasive Surgery robots)

A pilot line for the next generation of smart catheters and implants
POSITION-II, (ECSEL project)
leader: Philips Research (the Netherlands)
partners: SALVIA (NL), MTA TTK (HU) …
national coordinator, develepment F2R compatible capacitive force sensor integrable in catheter, biocompatibility test structures







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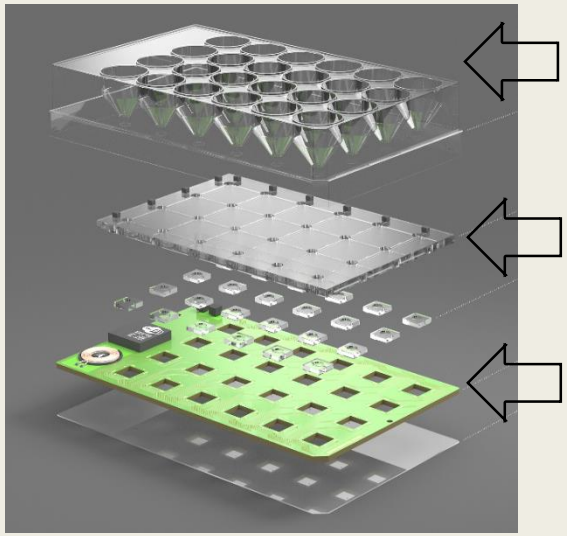
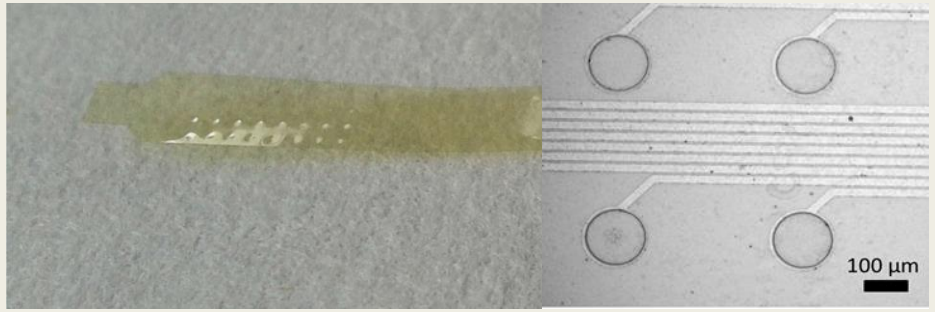
CER MRL – our planned contribution in **WP2**



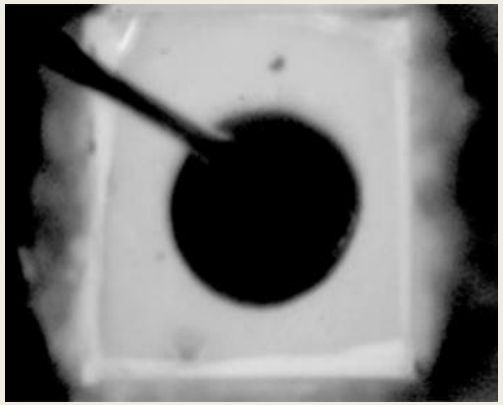
… „SMART LID”
flexible polymer multi-electrode systems

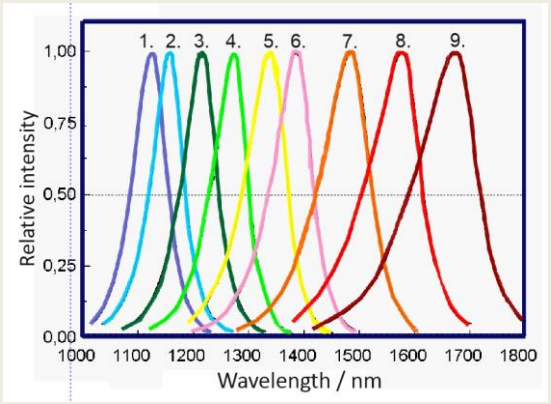
… **microfluidic layer**

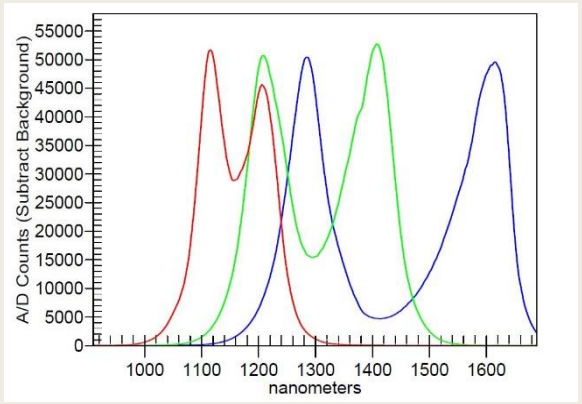


… development **near IR LED sources and spectroscopic solution** for monitoring nutrient composition (e.g. glucose concentration) in microfluidic channels

Patents:
2015 / P1500642 / Wideband IR source optimized for mobile spectroscopic applications
1999 / P9904539 / Integrated optical device, wavelength selective device for milti-channel multiplexer systems







Single wavelength and wideband NIR LEDs

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AEDUS Ltd. (AED)

Szabolcs Bella
CEO
chemical industry engineer
laser micro processing

Ilka Garai
mechanical engineer
polymer technologist
laser micro processing

Budapest
Office

Székesfehérvár
Factory

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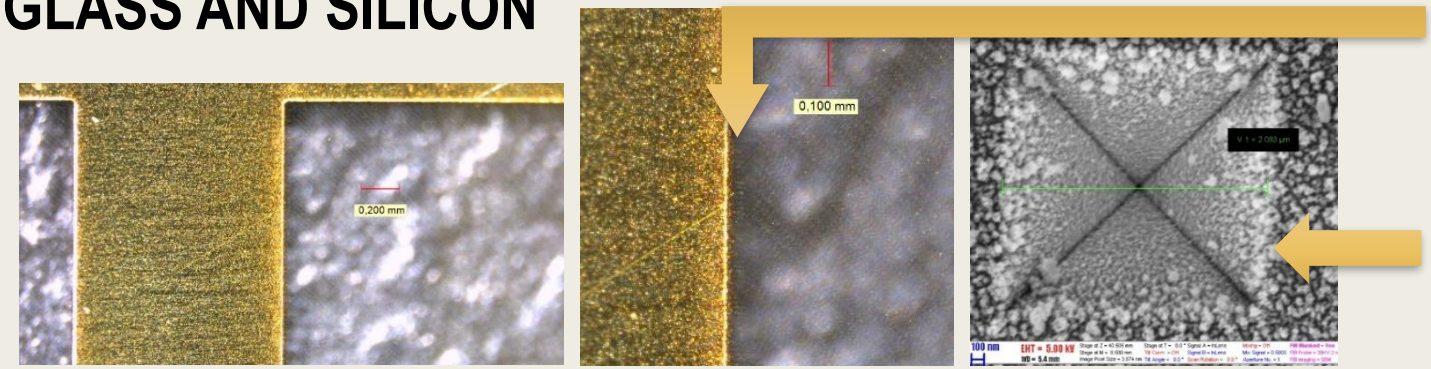
AED - our capabilities

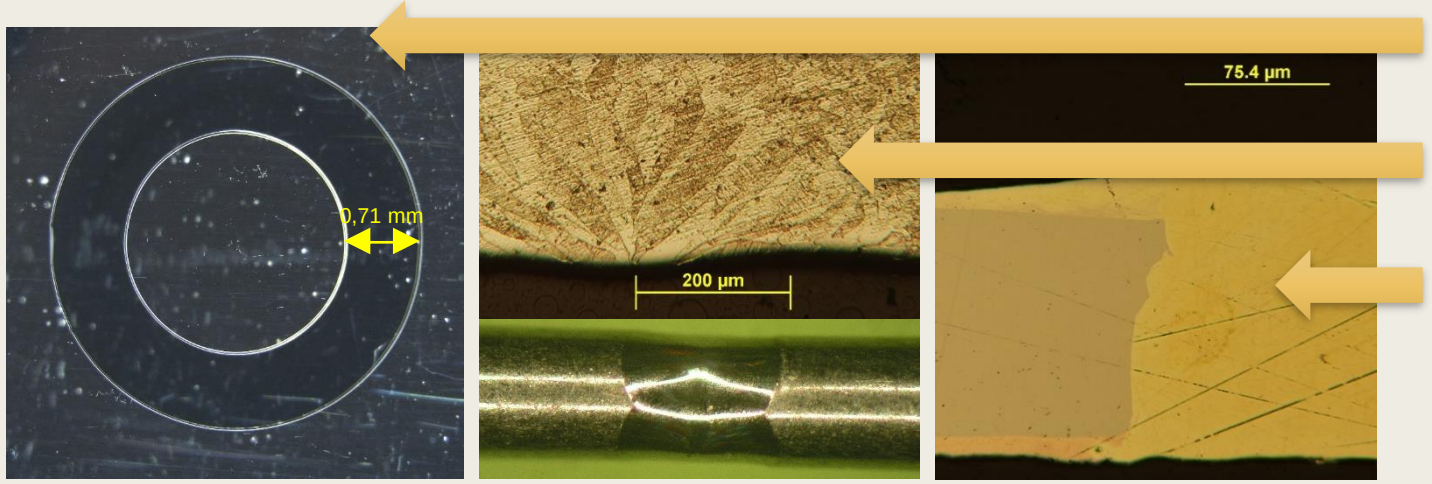
MICROPROCESSING OF COATINGS ON POLYMER, GLASS AND SILICON



Electrode design, ***development and manufacturing*** on special nano coated COP, PC and glass targets

New ***raman spectroscopy chip*** process development (Non colloid nano particle surface treatment)

MICRO WELDING OF POLYMERS AND METALS



Plastic welding of COP and PC for LOC with biology insert as well

Micro welding of Niobium rod and the crosssection of the welding area

Micro welding of coated Dumet-brass

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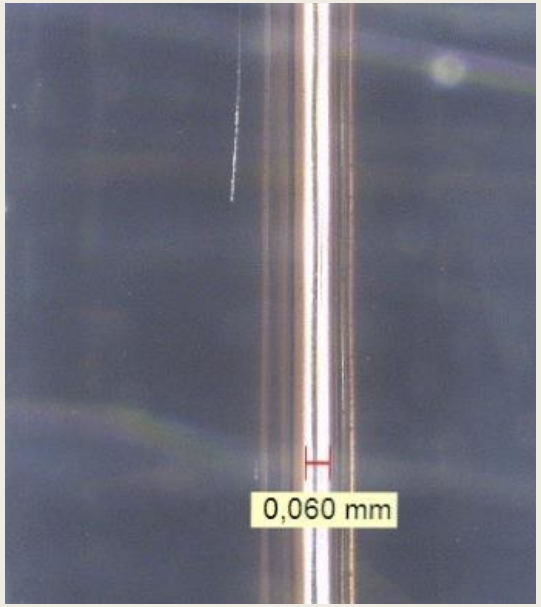
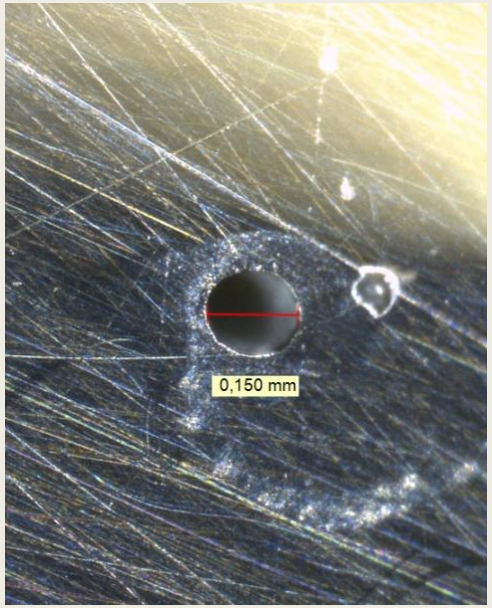
AED - our capabilities

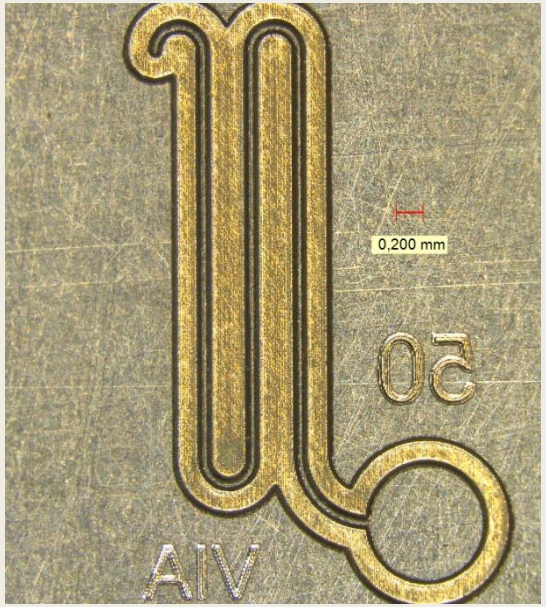
RAPID PROTOTYPING OF LAB ON CHIPS

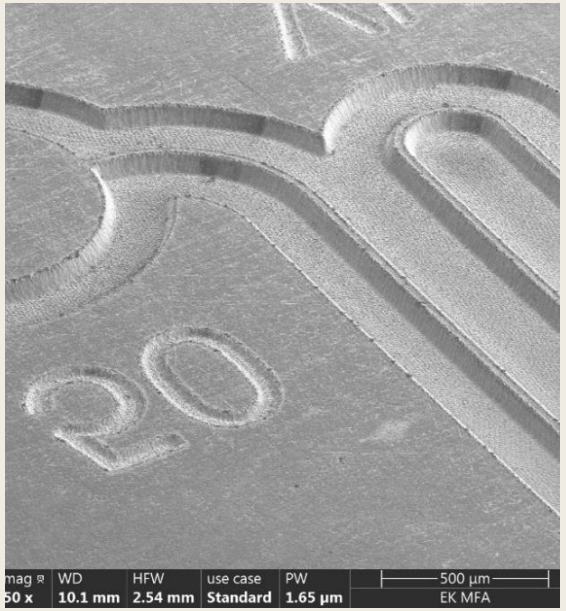




Microchannels direct in plastic for LOC

The aim of the project to build channel structures without using injection moulding process. With this technology the we can manufacture LOC instantly (in minutes) without the cost of the mould. The other advantage that we can build round shape channels instead of the rectangular to better simulate the cardiovascular system.





Rapid prototyping of micro channel structure in mould

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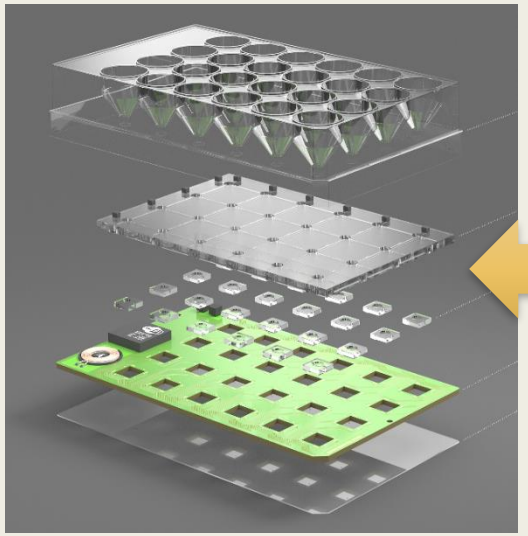
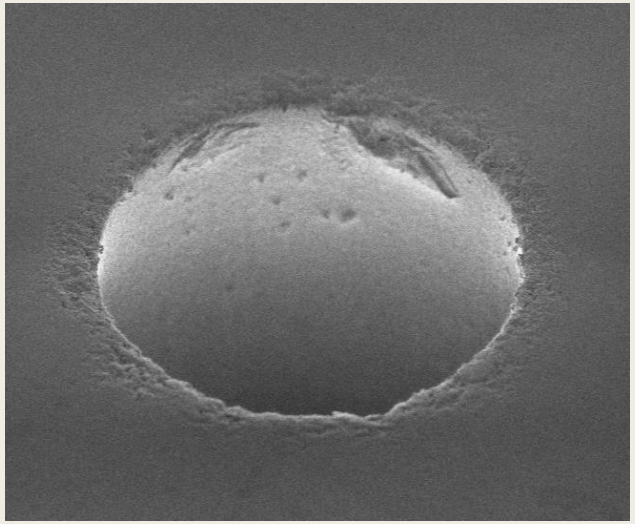
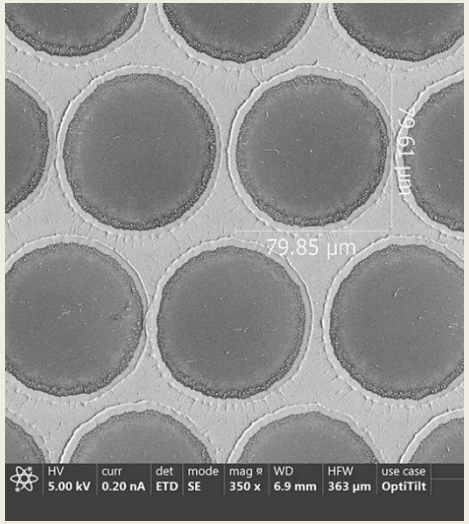
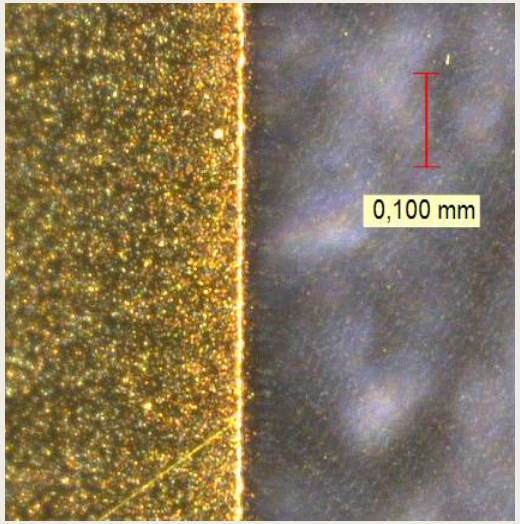
AED – our planned contribution in **WP2**



Aedus Space will contribute in **fabrication microfluidic layer by development high-precision laser drilling and sealing / welding technology for polymer substrates**. Sample transport subsystems will be also fabricated for polymer based electrodes and NIR spectral sensor for functional test.







AEDUS micro

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