Enhancing One Health through Advanced Microfluidic Systems

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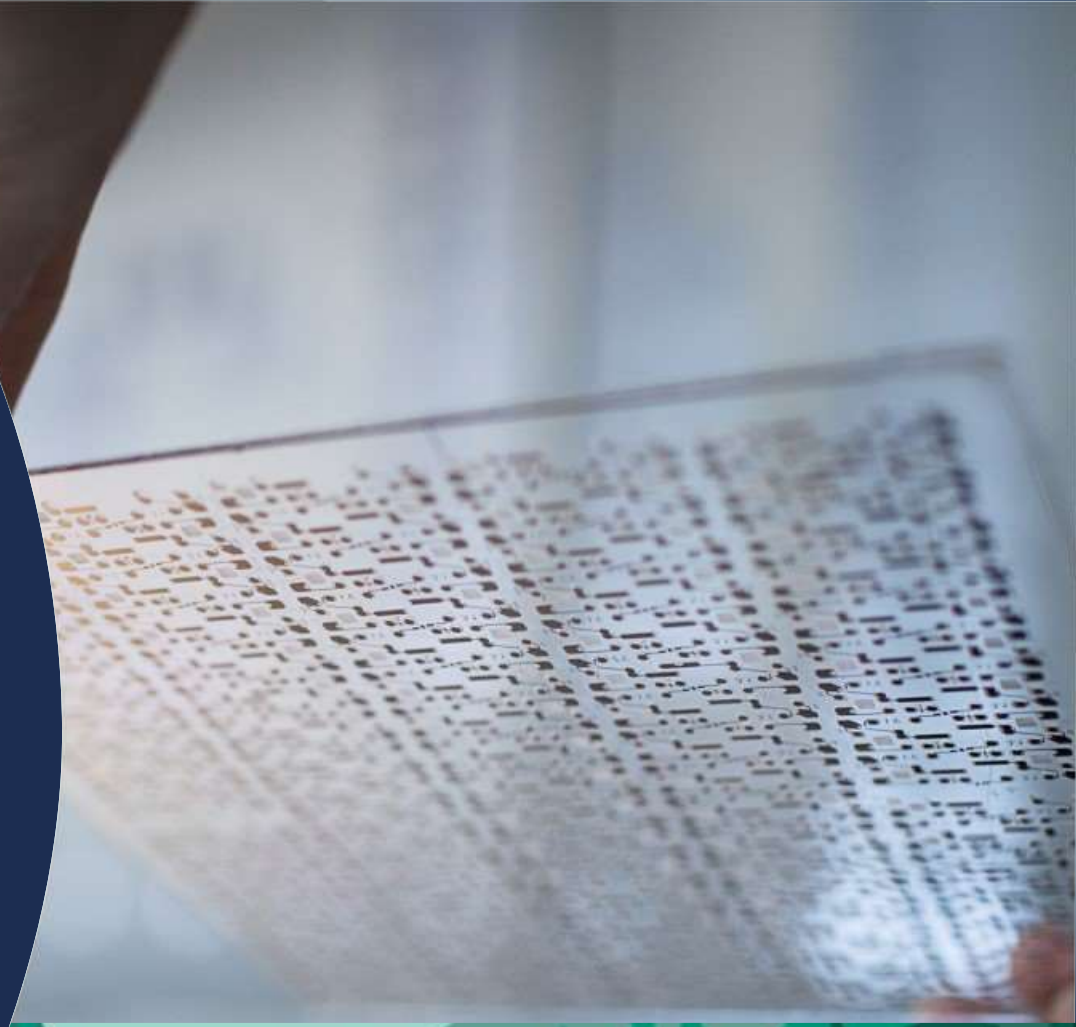
Business Development Manager

03/12/24

Talk at the 40th Chemnitz Seminar, "Sensor Systems for One Health”,

Session 3: Biosensors



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About Micronit

Micronit is the leading global contract development and manufacturing partner of microfluidics-based consumables. We enable products in life science and health applications.

Independent powerhouse of microfluidics

Serving top 10 leading companies in the fields of life science, diagnostics and biotechnology

1000+ customers in 50+ countries

100+ highly educated multi disciplinary employees
15+ nationalities

Facts & figures

20+ years of project experience

Located in Enschede the Netherlands

ISO 9001 and ISO 13485 certified

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Our Manufacturing facilities

- Production of Glass, Polymer, Silicon and integrated chips
- ISO 9001:2015 and ISO 13485:2016 processes.
- Focus on world class manufacturing and continuous improvement
- 600m2 Cleanroom space (class 5-8), total space 1000m2
- Manufacturing team: ~50 experienced and dedicated team members
- Low, medium and high volume up to 1M on consumable level
- >50 customers served in last 6 months
- Process Quality Control: direct insight via control charts/SPC

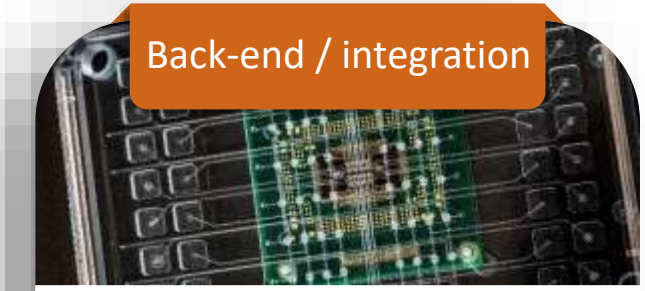
Manufacturing technologies

Glass / Silicon

- Lithography
- Wet etching
- Dry etching
- Deposition
- Bonding

Polymer

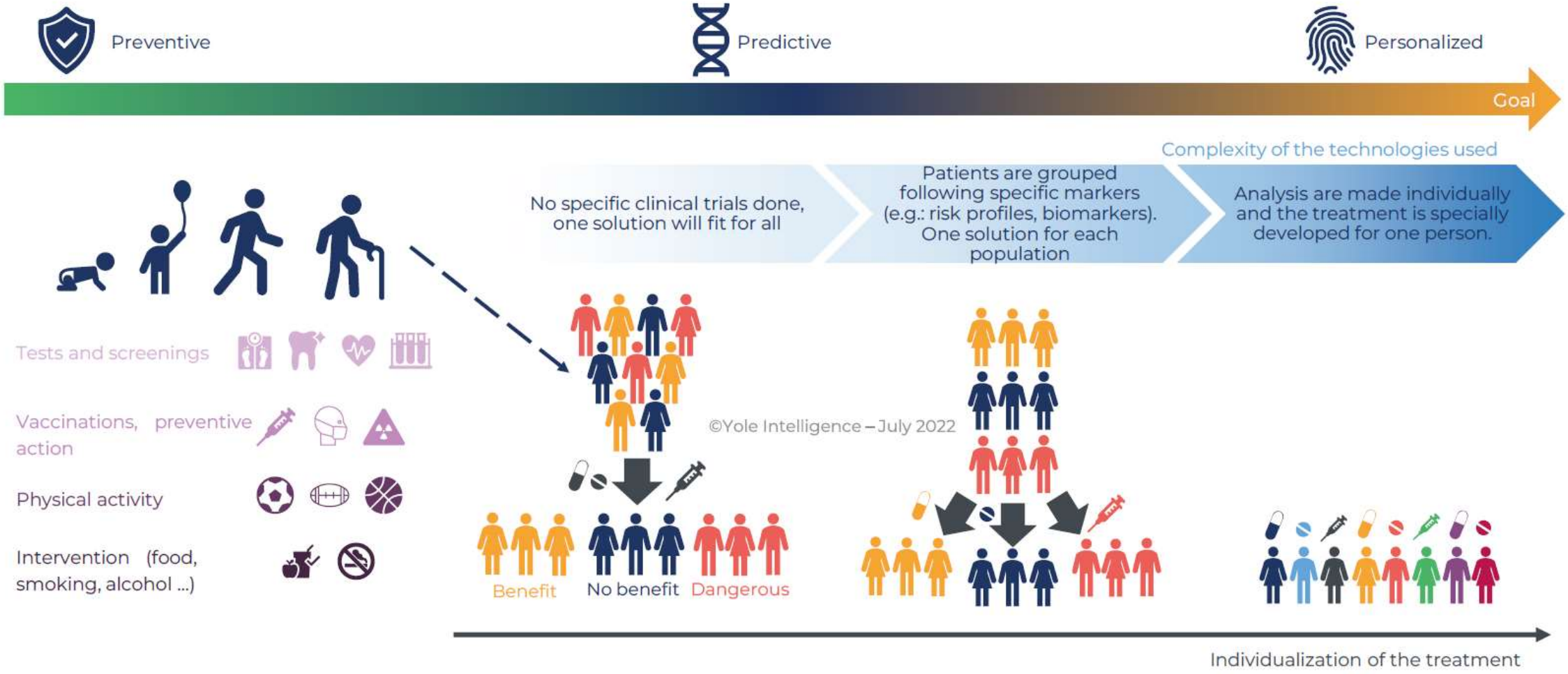
- Hot embossing
- Micromilling
- IM and HE mold (insert) fabrication
- Injection molding
- Bonding



Back-end / integration

- Coating
- Reagent deposition
- Hybrid assembly
- Flip-chip bonding
- Dicing / Packaging

Personalization of healthcare – towards 4P medicine



Yolé, Status of the Microfluidic industry, 2022

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The microfluidic field

From lab to near patients

Research

- in the lab (centralized)
- on multiple instruments
- Single flow cell chip

Clinical

- in the hospital (decentralized)
- automated lab workflow
- lab-on-a-chip

Point of Care

- at home
- personal handheld
- Autonomous lab-on-a-chip

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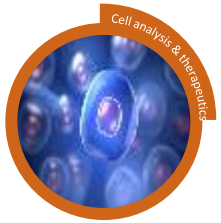
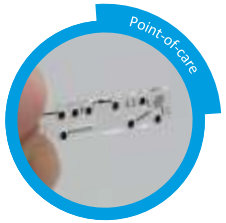
Micronit’s core segments in healthcare & life sciences

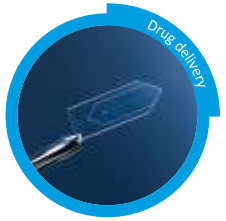
Multi-omics, with target applications such as DNA sequencing (including NGS) and Single Cell Genomics but also emerging derived applications such as Data Storage and Liquid Biopsy.



Microfluidics-based tools for cells sorting, manipulation and analysis are used more and more for diagnostics and therapeutics applications.



Point-of-Care (PoC) diagnostics is the largest segment within the Point-of-Need testing market. New opportunities in this market are offered by an increasing number of mid-/high-end molecular tests (DNA and RNA analysis) reaching the market. These require integrated lab on a chip consumables in turn for a better performance, ease of use and a higher average selling price.



Drug delivery is a market which Micronit addresses today based on existing capabilities (such as micro needles and nozzles).

Organ-on-Chip technology, used for Drug development (discovery & screening), are still in their early days but have the potential to enable personalized medicine and provide better models than currently used.

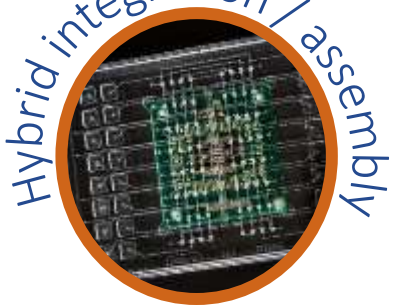
Micronit's unique selling points

Microfluidics development

- **Microfluidics design house** from idea to a full product running in (small-medium) series production
- End-to-end solution provider from prototyping to production of microfluidic based products, components and Lab-on-a-Chip consumables

Manufacturing

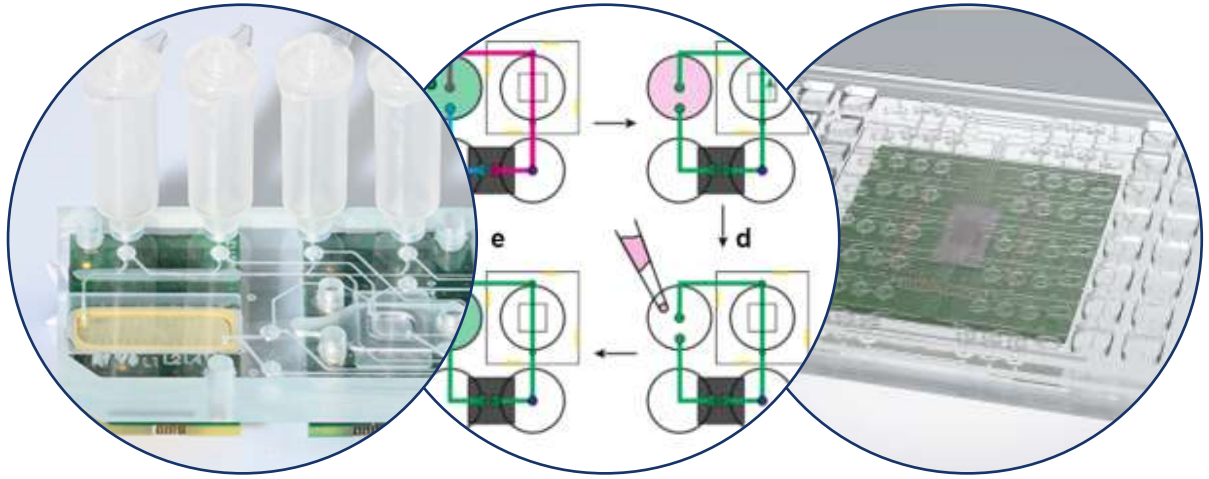
- Operating a **wafer-based microfabrication** cleanroom for 200 mm silicon and glass wafers, combined with a fully equipped pilot production line for polymer and hybrid consumables
- Multi-material processing expertise, IP and semiconductor-grade hybrid integration equipment all in-house

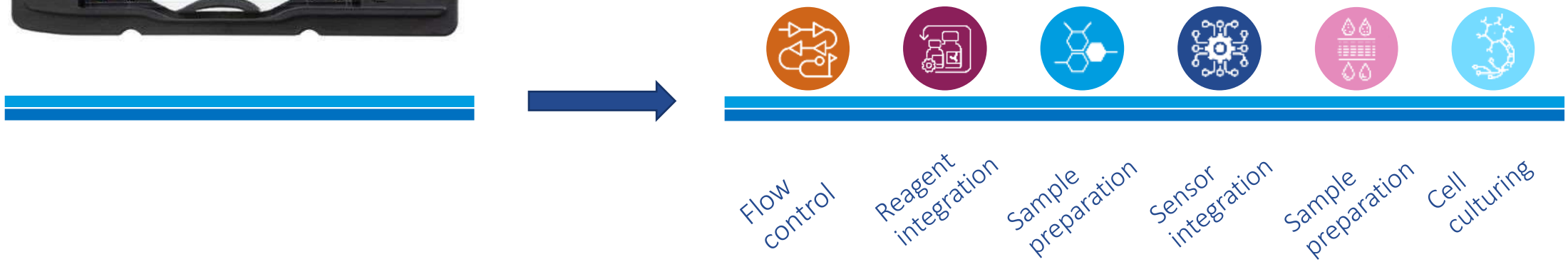


Platform technology approach

Development

From a single chip to platforms with multiple functionalities





LoaC platforms as optional starting point for development

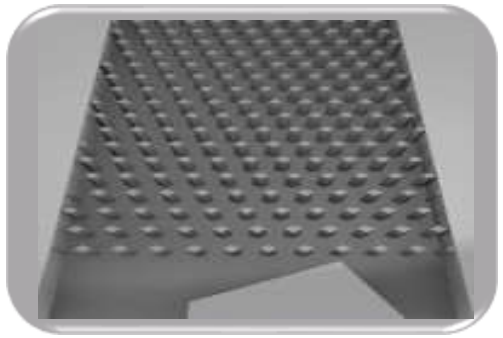
Point-of-Care Diagnostics

- Simple to use cartridge
- Fully or semi-autonomous
- Molecular diagnostics
- Strong Micronit IP position (manufacturing and design)

Clinical research and Diagnostics

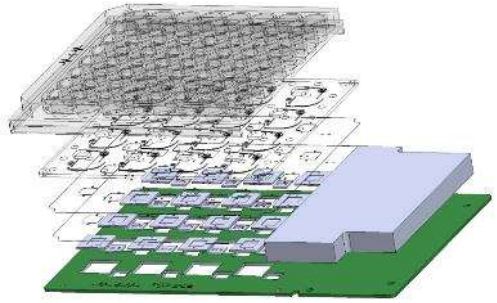
- Complex workflow automation
- PCR/qPCR/dPCR
- Next generation sequencing
- Manufacturing Micronit IP position

Pharmaceutical and Life science



- Cell and particle sorting with a variety of principles
- Clinical research
- Manufacturing Micronit IP position

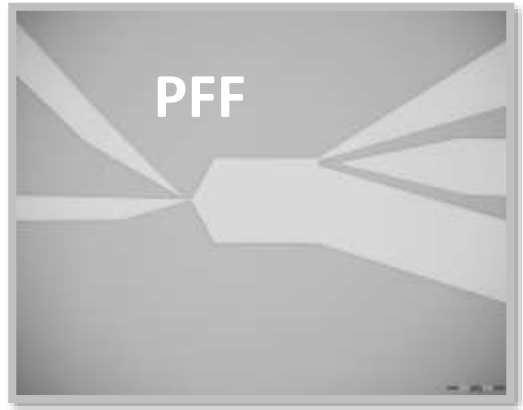
Personalized medicine and Cell therapies

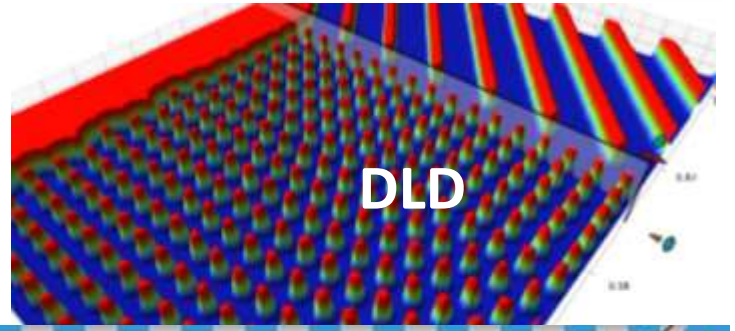


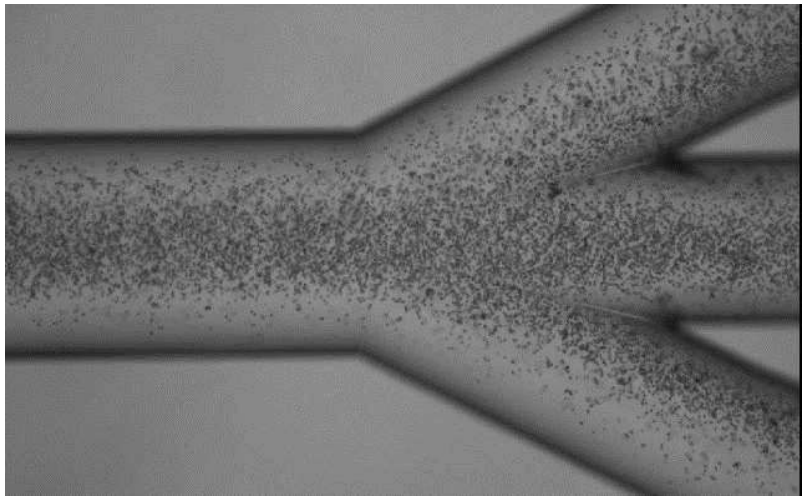
- Standard microtiter plate
- Hybrid integration of microfluidics / MEMS
- Biomimetics
- Manufacturing Micronit IP position

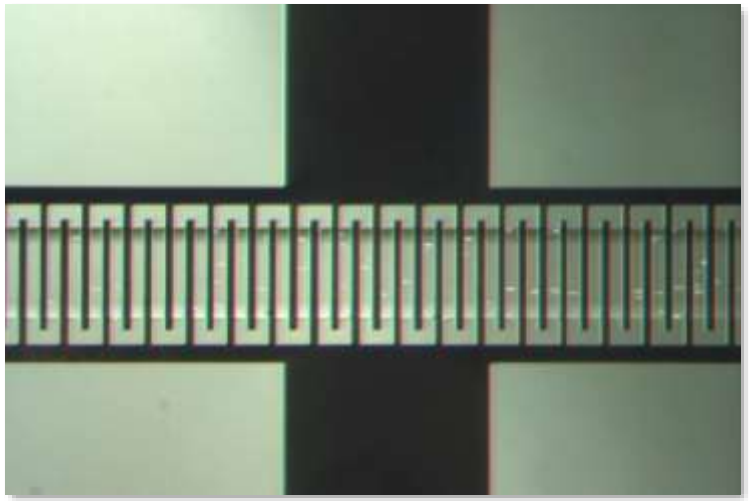
Microfluidic cell sorting technologies

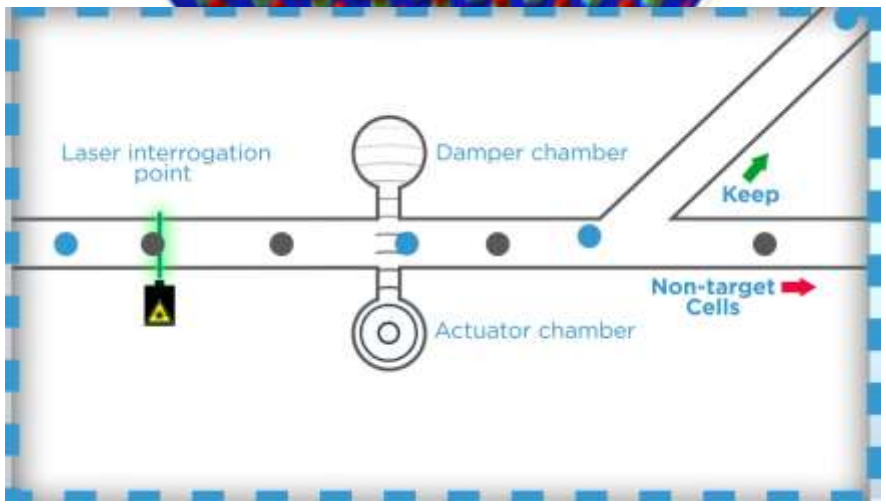
1. Acoustophoresis (SAW)
2. Dielectrophoresis (DEP)
3. Microfluidic switching
4. Pinched flow fractionation (PFF)
5. Deterministic lateral displacement (DLD)
6. Magnetic levitation







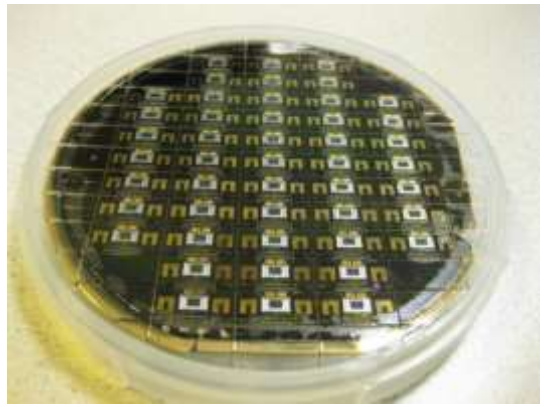




Considerations regarding “integration”

Manufacturing

- There are various integration “cross-sections”:
  - Die- / module-level vs. wafer-level: virtually always a hybrid / heterogeneous combination of materials
  - Permanent integration vs. temporary integration: the latter is often more an interfacing task
  - full integration of sensor functionalities but for instance also of flow control means
  - No integration but placing functionalities in an instrument



- For microfluidic cartridges, the challenges are often found in the permanent modular and in full integration or combinations thereof
- Choices are driven by various criteria:
  - Flexibility in the Development stage
  - Functionality
  - Cost (e.g. Dx platforms)
  - Robustness

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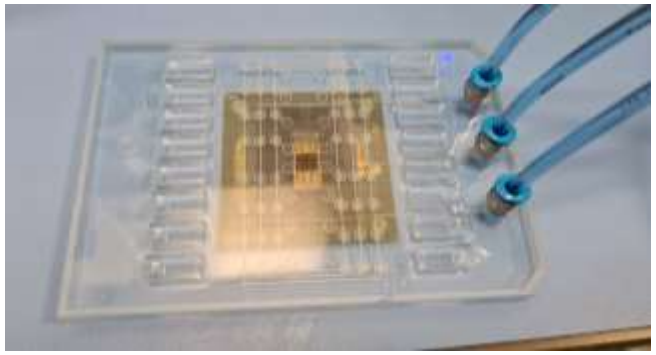
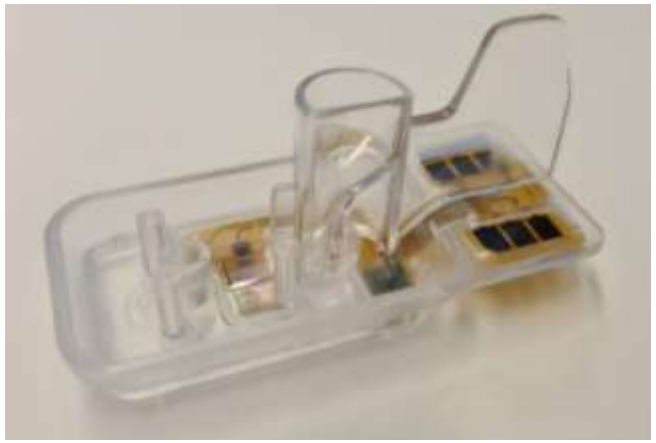
Modular integration and required competences

Integration around modular components:

- Fluidic manifold, often comprised of a thermoplastic polymer, providing (fluidic) access to glass/silicon/polymer modules (e.g. serving as a sensor)
- Integration of actuators, e.g. piezo components
- Integration of electronics / controls, e.g. in the form of a (flex-)PCB





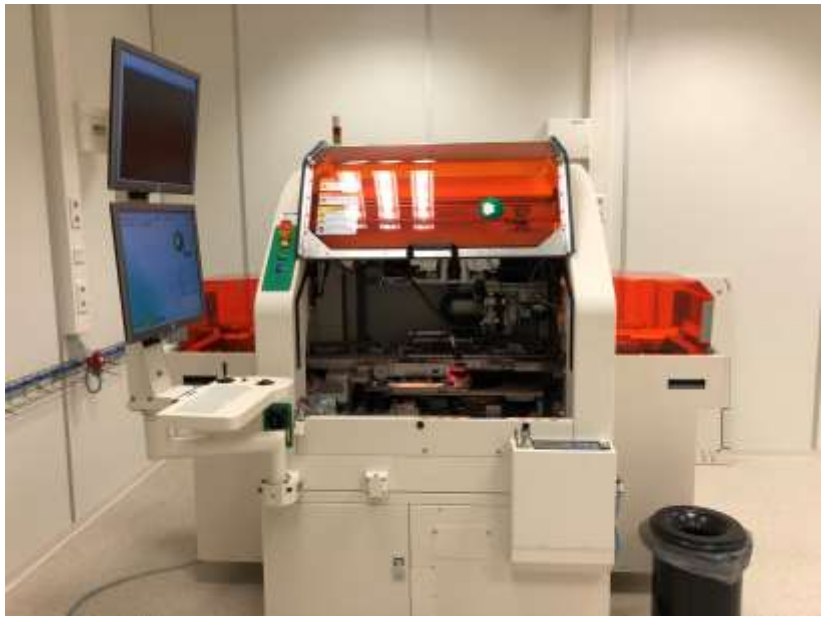
Required competences:

- Design and fabrication of manifolds
- Portfolio of integration technologies, most notably adhesive bonding
- Compliance with standards that guarantee robustness

Die-level integration competences

Manufacturing

- Adhesive printing
- Capillary underfilling via accurate dispensing
- Die bonder / pick-and-place
- Automatic tape / film placement

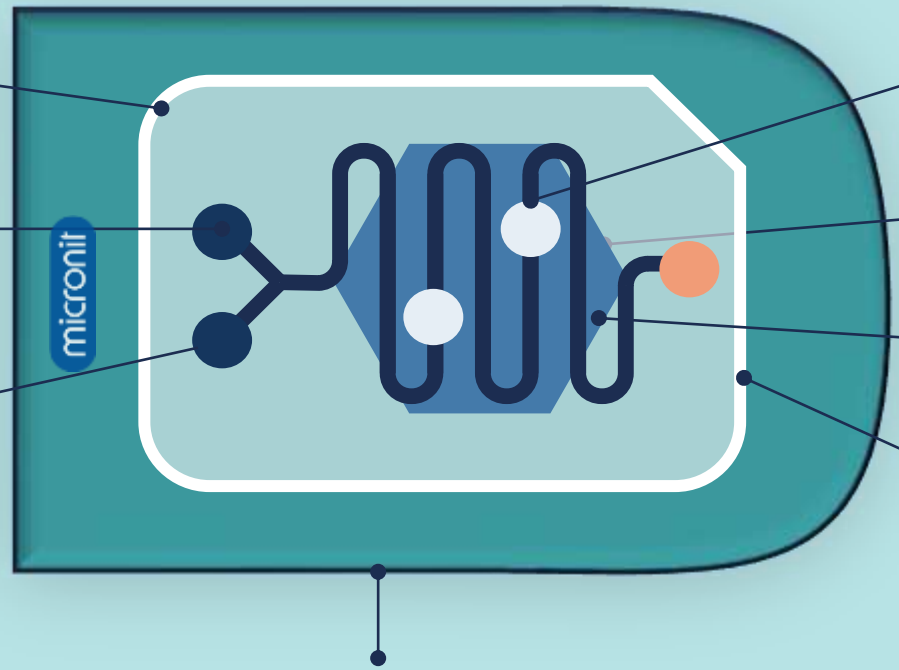


Integrated Laboratory Automation into lab-on-a-chip consumables

Multi-Material Components

Liquid Handling automation

Sample Preparation



Chemistry & Reagent Integration

Surface Functionalization

Sensor Integration

Interfacing & System integration

Overall Quality Control

Our gated approach gives you the best possible quality results. ISO 13485 and ISO 9001 compliant

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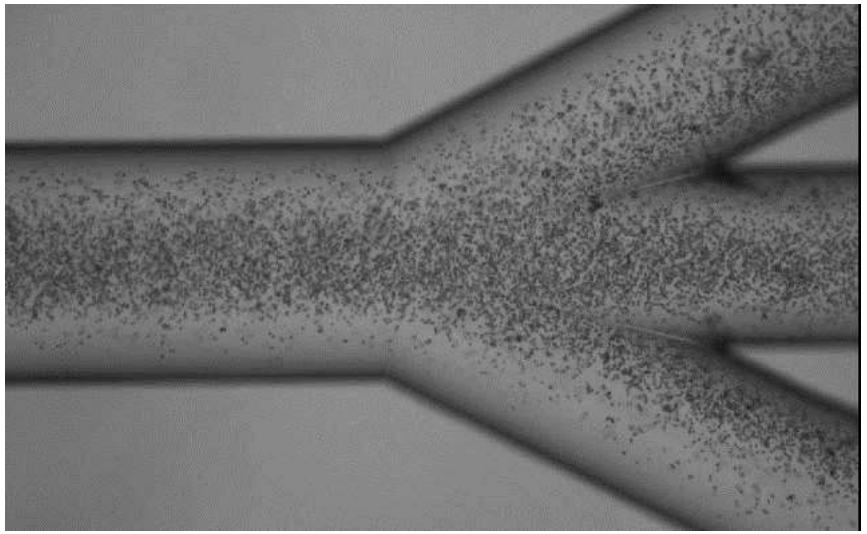
Showcases

Acousort - Acouwash

- Automated Cell and Blood Sample Separations
- Using Acoustophoresis
  - Surface Acoustic Wave (SAW) in microfluidic channel
  - Separate blood components and contaminations

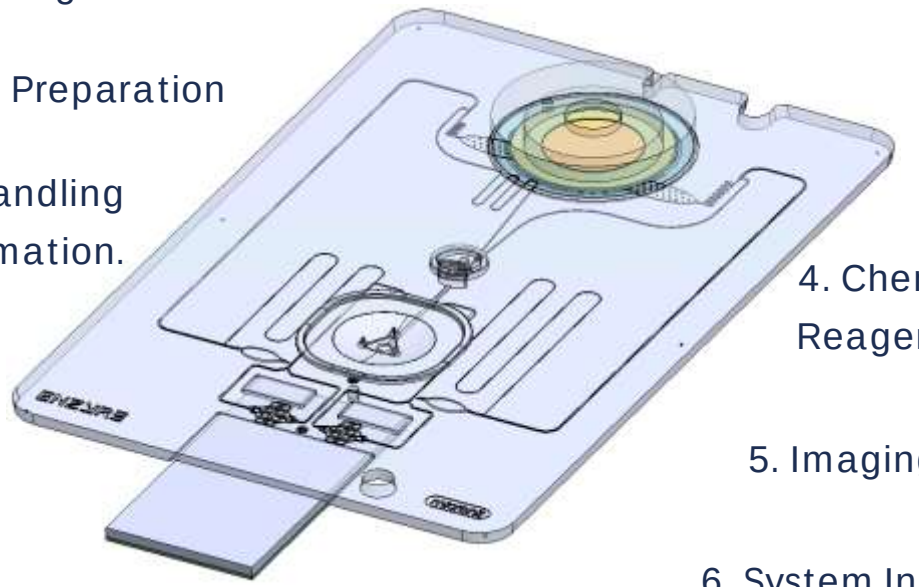


Near patient diagnostics: Enzycard

1. Assay Integration

2. Sample Preparation

3 Liquid handling automation.



4. Chemistry & Reagent Integration

5. Imaging & Analysis

6. System Integration

Handheld micro-laboratory to monitor blood coagulation status of any patient anywhere in the world, enabling fast action to prevent or stop bleeds.

ENZYCARD
Disposable cartridge
Test specific reagents

Enzyre: how to faster help patients with bleeding disorder?

EnzySystem; **polymer**-based **integrated** µf-card near patient blood coagulation diagnostics

Handheld micro-laboratory to monitor blood coagulation status of **any patient anywhere** in the world, enabling fast action to prevent or stop bleeds.

- Patients with bleeding disorders
  → monitor & guide therapy
- Critical care patients
  → identify cause of compromised coagulation
- Acute traumatic situations
  → understand status of coagulation
- Induced by medication (e.g. anti-coagulants)
  → monitor & guide therapy

Enzycard - advanced next generation diagnostics consumable

Focus on microfluidic development with specific integration challenges /requirements:

- High density fluidic access / non-contact
- Intimate optical access

> Blood filter for sample preparation

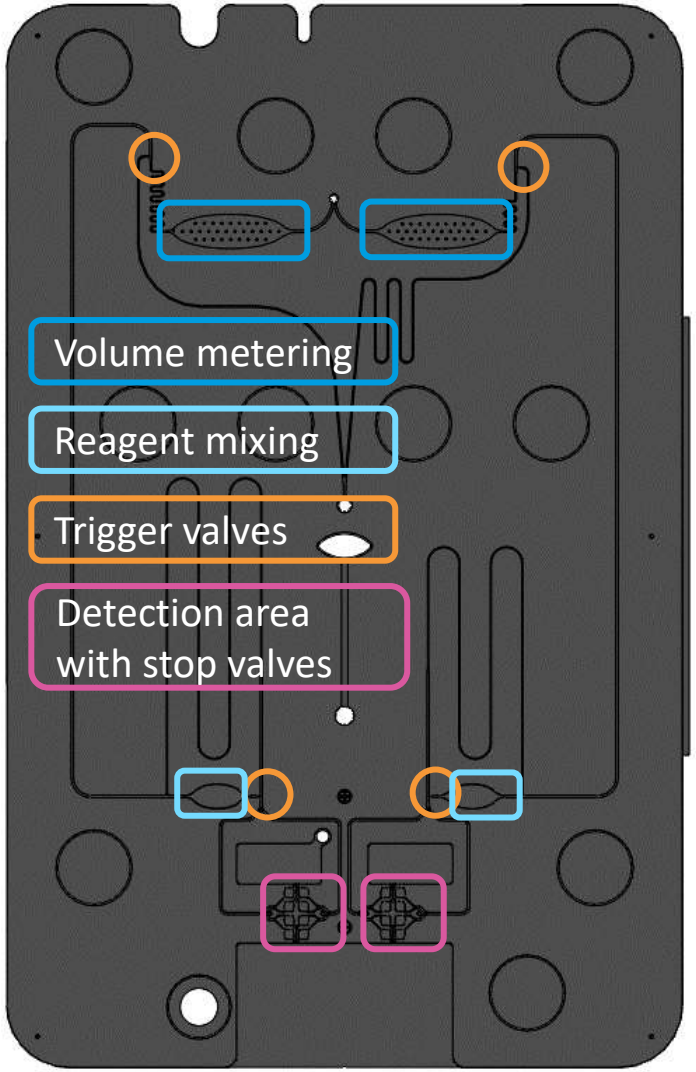
> Blister for buffer storage

> Capillary flow-based sample dilution

> Surface coating

> Spotted reagents

> Integrated CMOS sensors for detection



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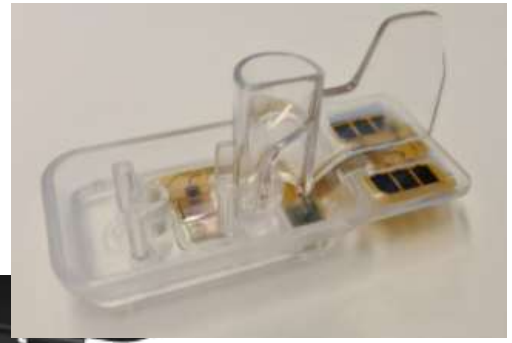
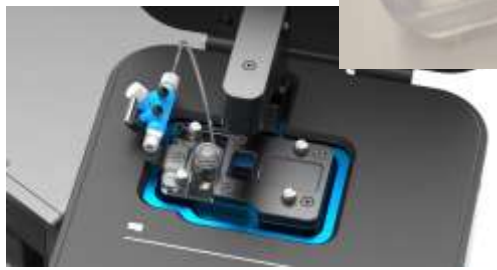
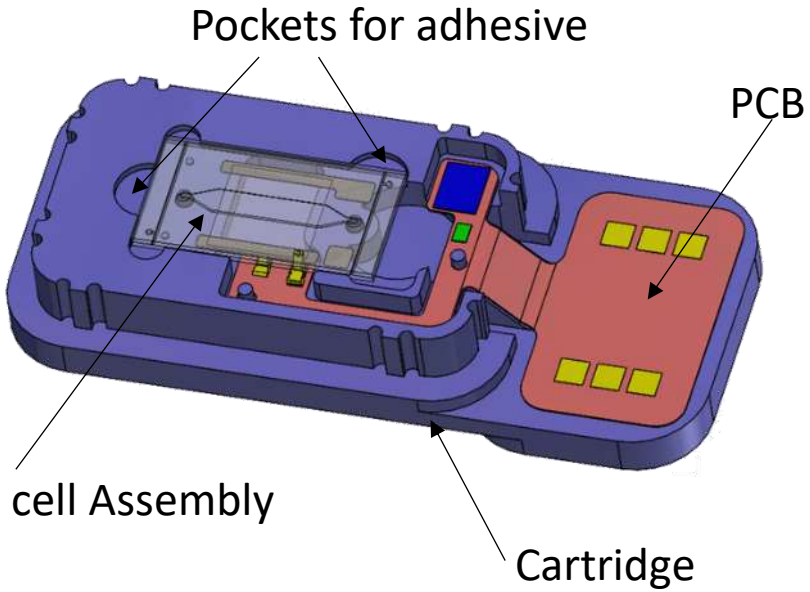
Injection molded manifold to flowcell-piezo assembly

Combination of competences required:

- Micron-accuracy placement of piezo actuator with sub-micron adhesive layer thickness
- Capillary adhesive underfilling for connecting a polymer manifold to the flowcell-piezo sub-assembly
- Robust processes, compatible with transportation standard IEC 60068-2-38





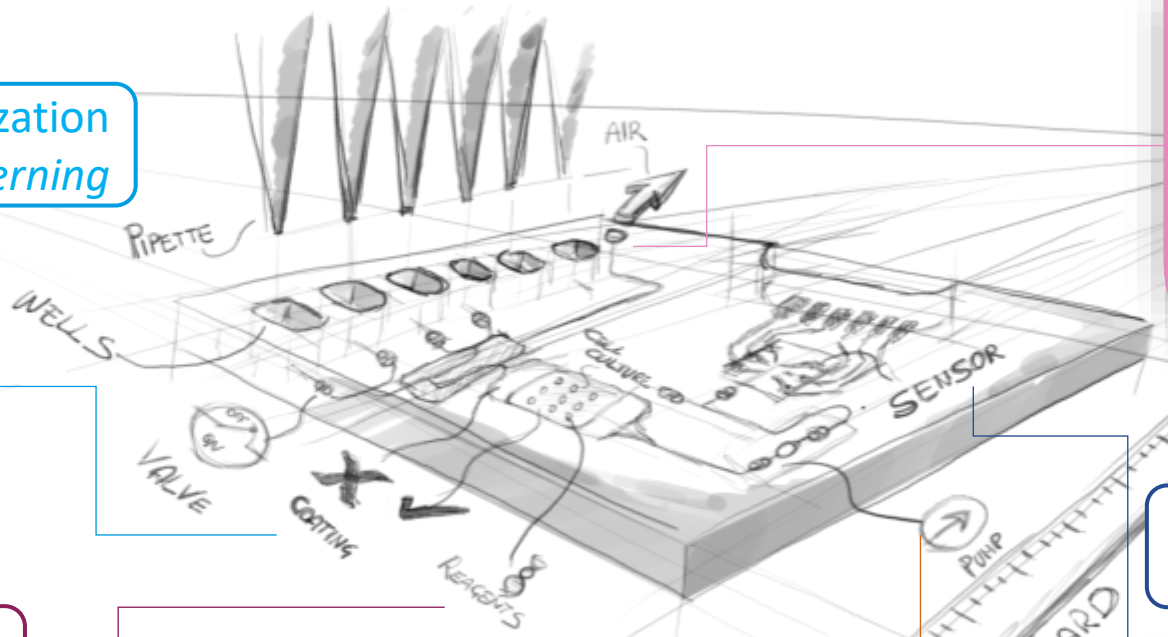


Product development and manufacturing with specific challenges:

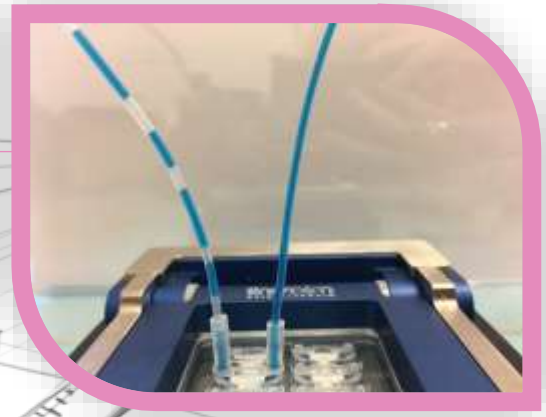
- Highly accurate glass flowcell
- Accurate piezo assembly
- Robust polymer-glass integration

Organ-on-a-Chip technologies

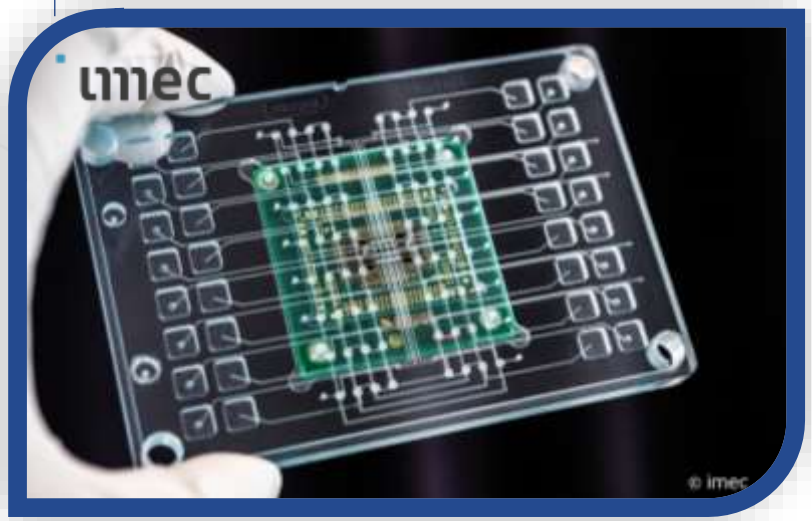
Surface functionalization
Adhesive protein patterning



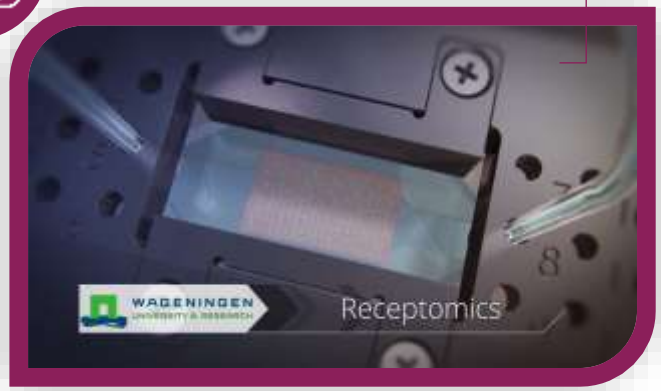
Sample preparation
Air bubble removal



Transducer integration
MEA chip integration



Reagent integration
On-chip transfection



Flow control
Unidirectional recirculation

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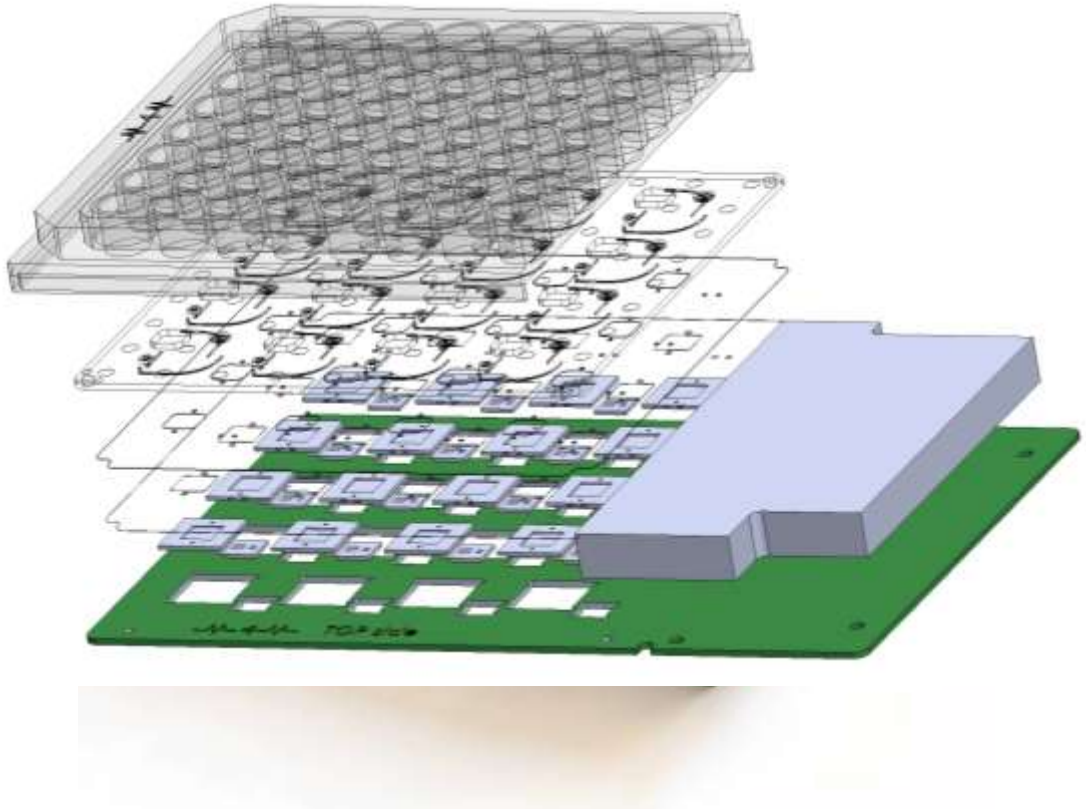
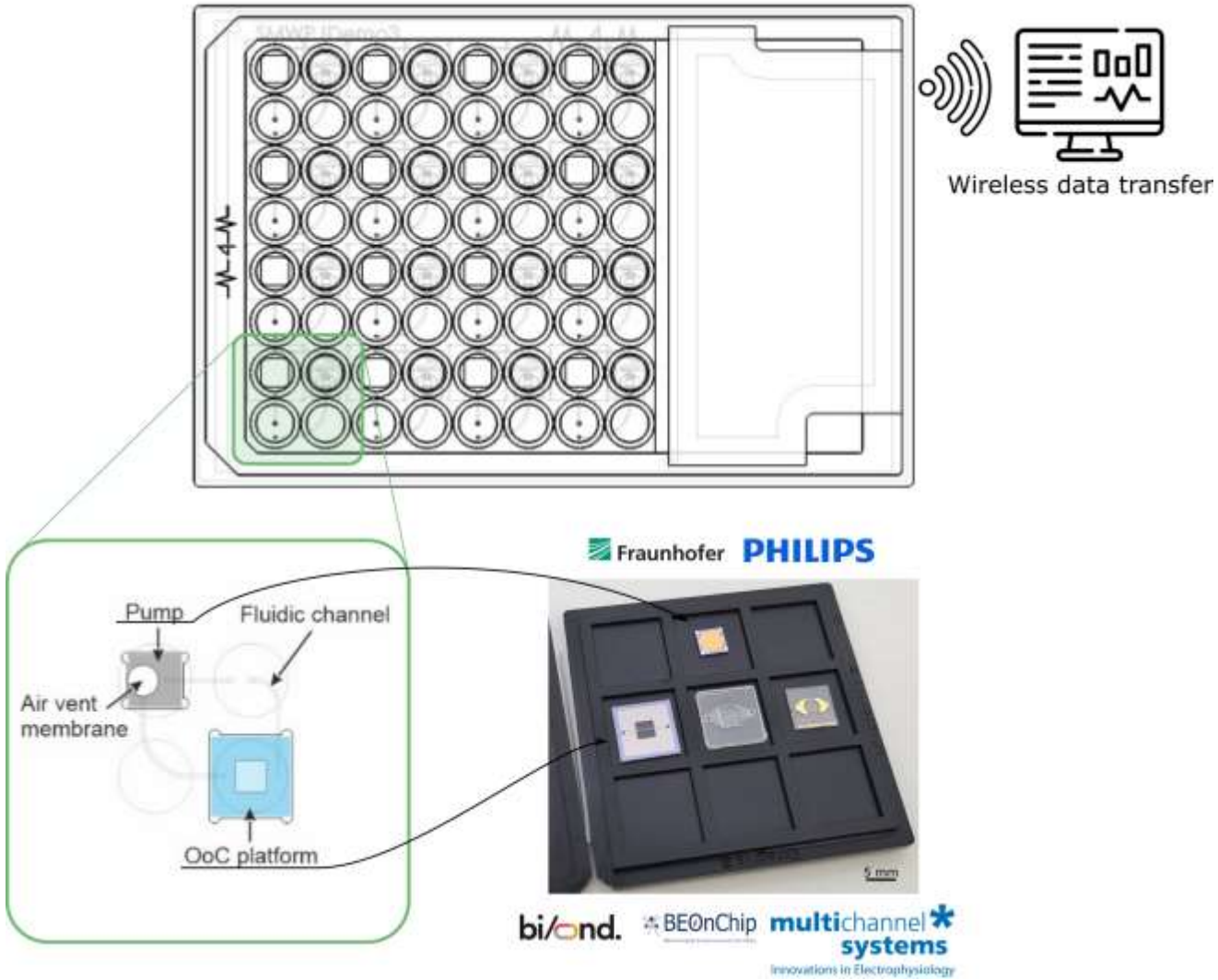
Smart Multi-Well Plate





Development with specific challenges:

- Multitude of different components for integration
- Long term fluid exposure

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Single point of contact

Scaling up your project from small volumes to larger quantities can be challenging.

Technical challenges

- Selection of the right materials and components
- Translating functionalities into a feasible design
- Gaining control over fluidics
- Integration with relevant instruments and workflows
- Reliability and feasibility
- Ensuring data-analysis and read-out options

Business challenges

1. Aligning diverse expertise of project members
2. Maintain product pricing within your business case
3. Keep the project on the timeline
4. Managing expectations for future growth
5. Ensuring market adoption
6. Quality & certification

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Summary

- Independent microfluidics expert center
- More than 20 years of experience from idea to production (Stage Gate approach; six sigma)
- ISO9001 and ISO13485 certified
- Cleanroom for 200 mm glass and silicon processing, running 2-shift manufacturing
- Installed base of equipment and infrastructure for polymer cartridge prototyping and repetitive small series
- In-house equipment and technologies for die-level and wafer-level integration

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Thank you for your Attention.

We look forward to working with you!

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www.micronit.com