

A scanning electron microscope (SEM) image showing a highly porous, honeycomb-like structure, likely a membrane or filter, with a regular array of small, interconnected pores. The structure is illuminated from the side, creating a strong sense of depth and texture. The background is dark, making the white, porous structure stand out.

# Precision manufacturing and functionalization for the life sciences

**Dr. Felix Kurth**

Head Integrated Flexible Sensors

OST Lectures

17.03.2022

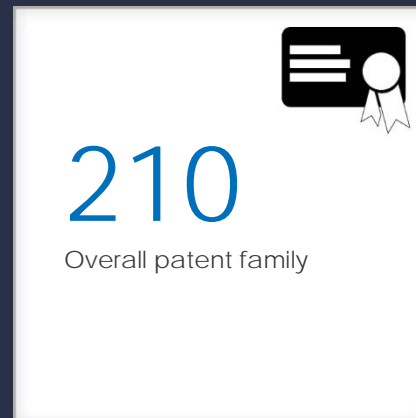
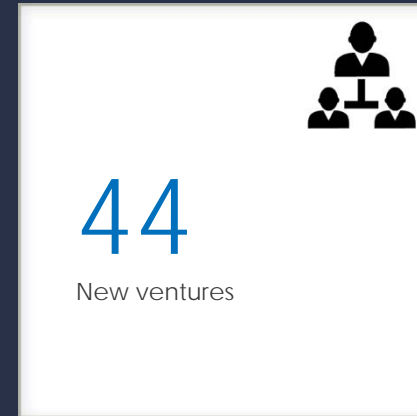
**:: csem**

CSEM  
SWISS TECHNOLOGY  
ORGANIZATION

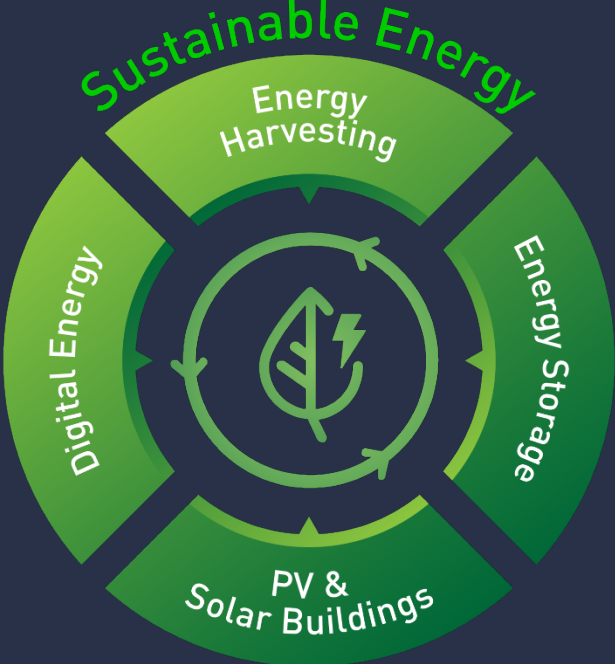
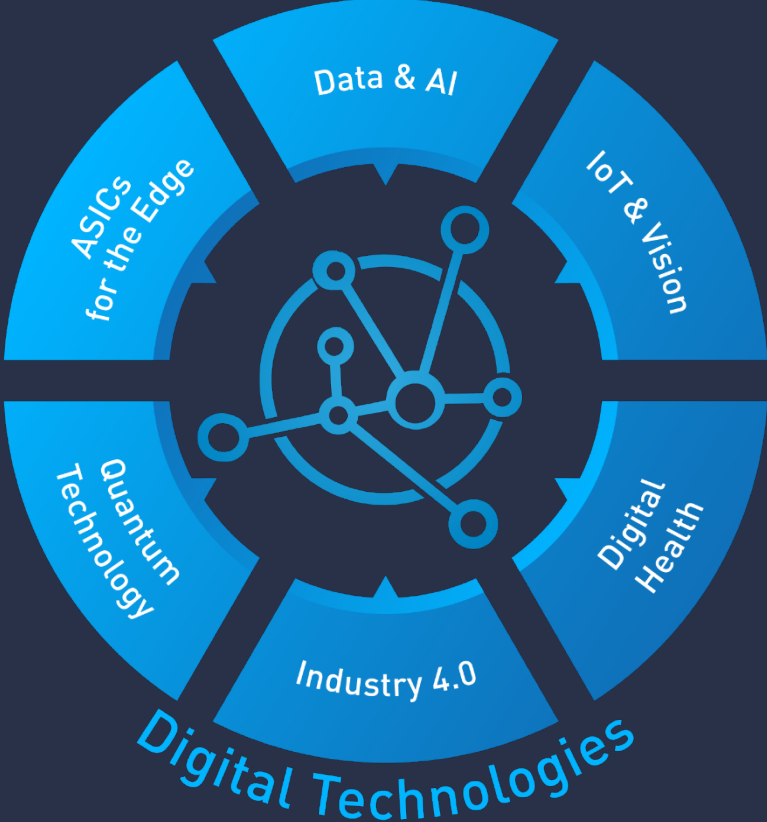
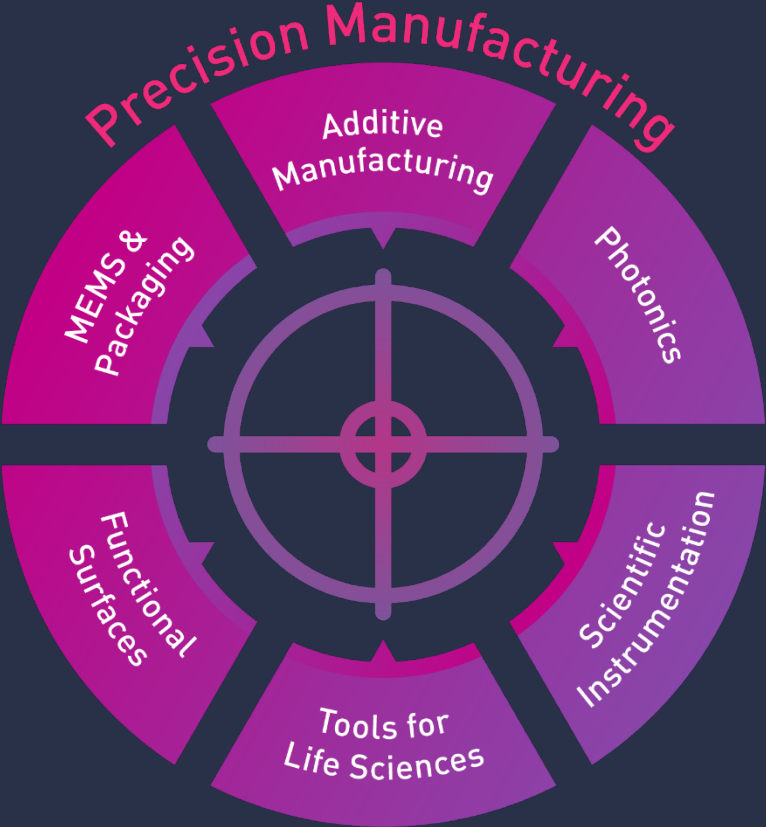


Technology Transfer to Industry

# CSEM at a glance



# Technologies **in focus** at CSEM





# Personalized Health

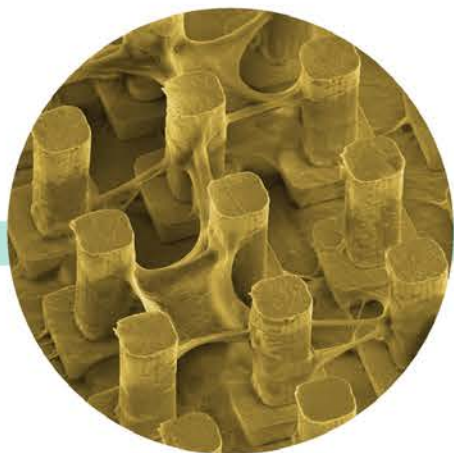
Specific Needs

- Health monitoring  
better data, anywhere, anytime
- Complex in-vitro models
- Regenerative medicine
- AI in Life Sciences

Increasing need for technology

# Tools for life sciences

Cell microsystems



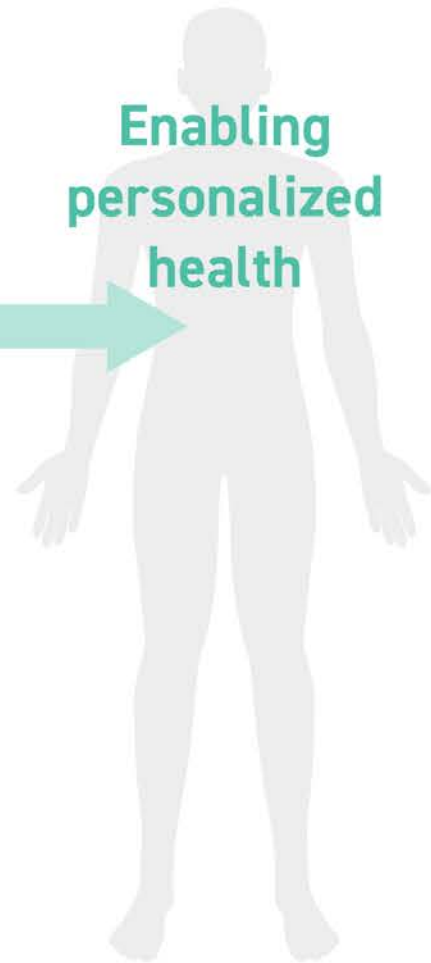
Biomonitoring



Lab automation



Enabling  
personalized  
health



Cells



Organoids

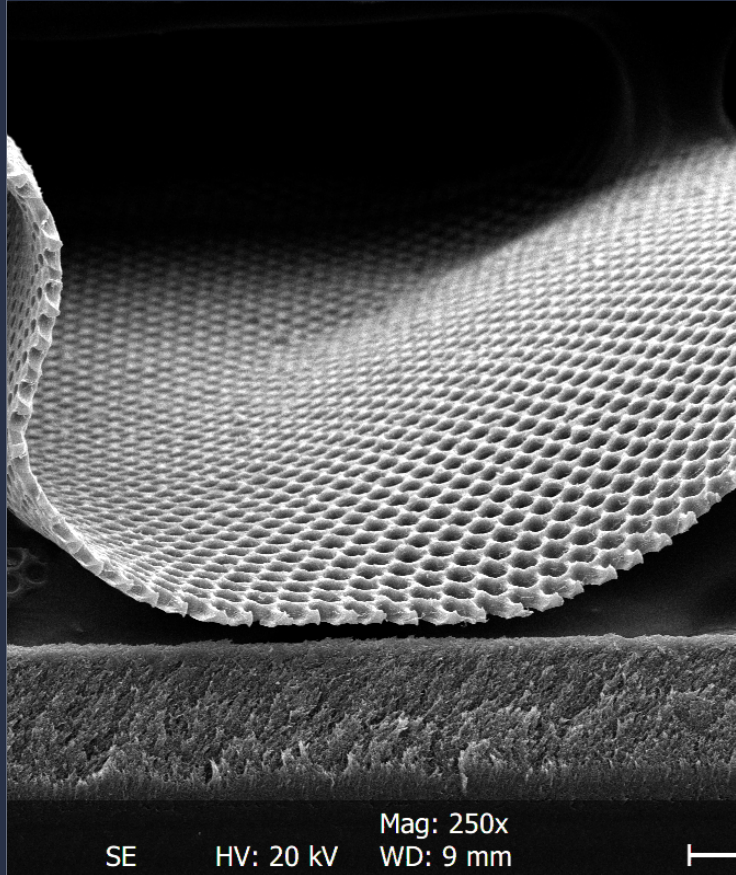


Tissues



Body fluids

## 1. Biosystems applications



Precision polymer membranes

## 2. Biomonitoring of biological fluids



Integrated printed sensors

Today's examples

## Large area & flexible high-precision membranes



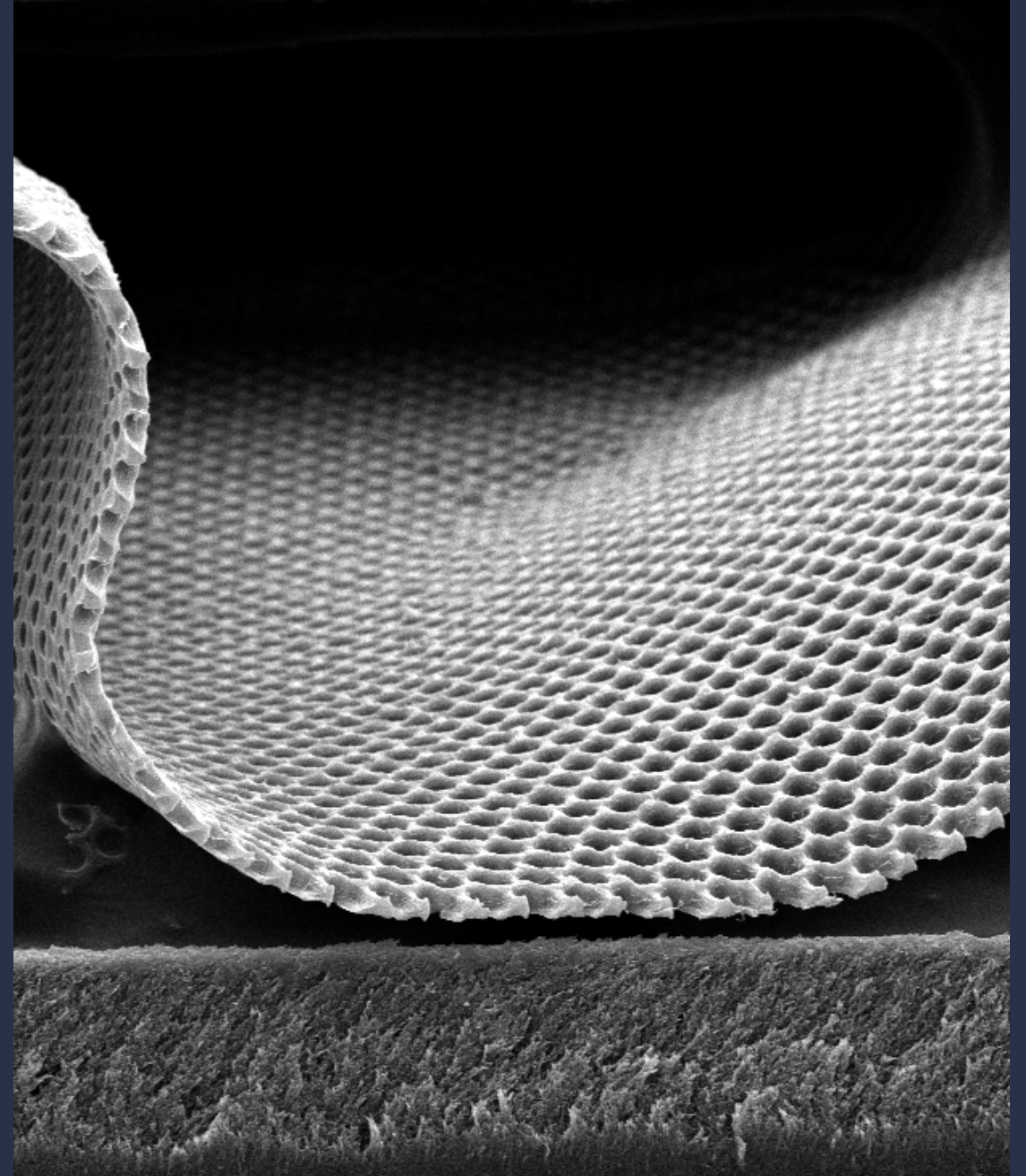
### Commercially available micro-filtration membranes

- Strongly limited and random porosity
- Small, stiff and expensive

### Polymer and metal precision membranes

- Scalable and cost-effective processes
- High density of precisely shaped and aligned pores

### Affinity membranes for specific binding

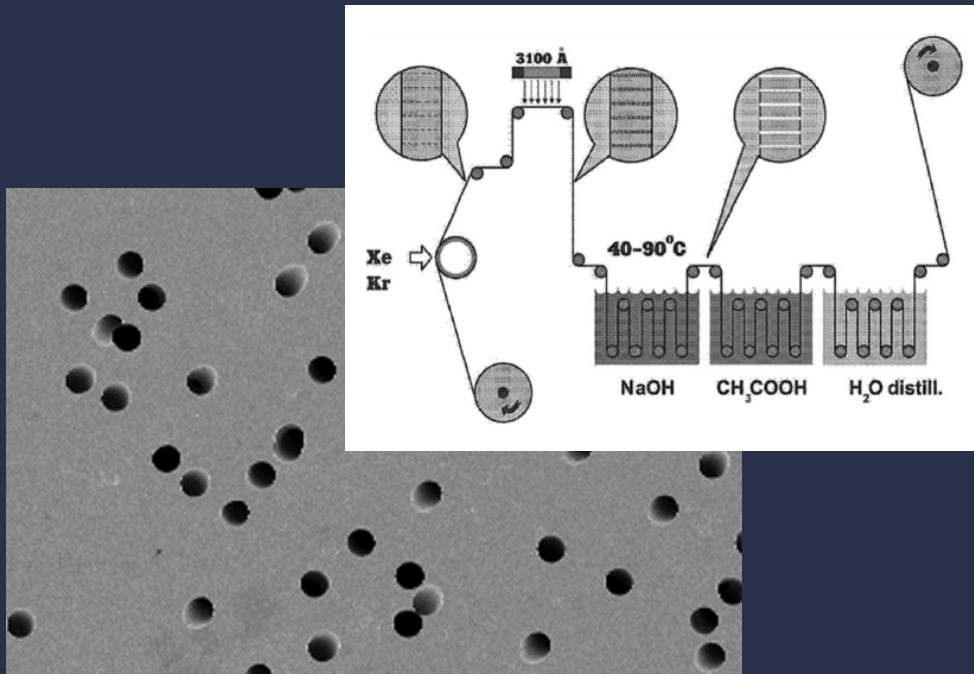




# State-of-the-art

## Track-etched membranes

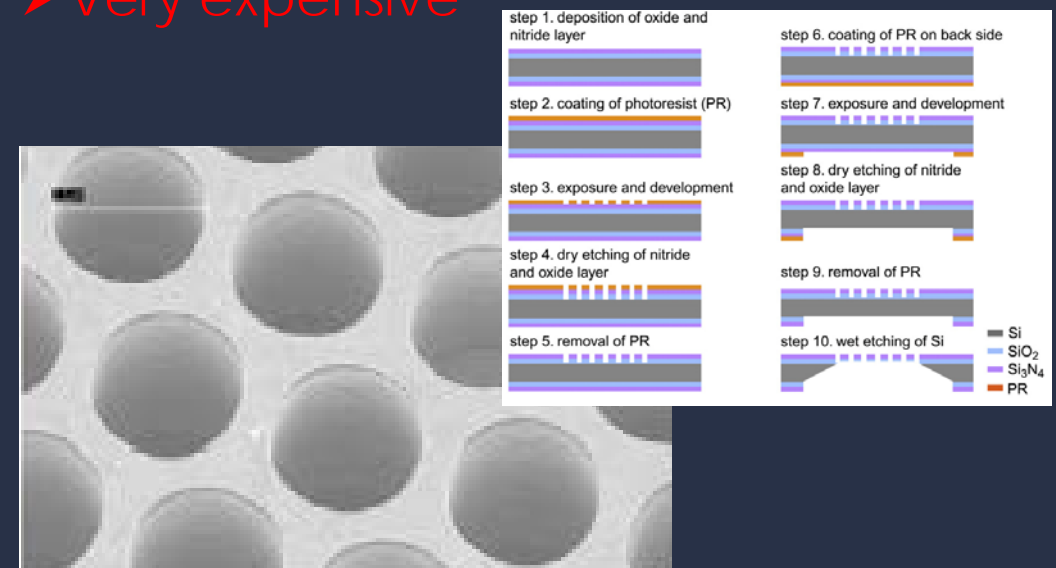
- Cost-effective
- Strongly limited and random porosity



Porosity: 5%

## Microelectromechanical systems (MEMS)

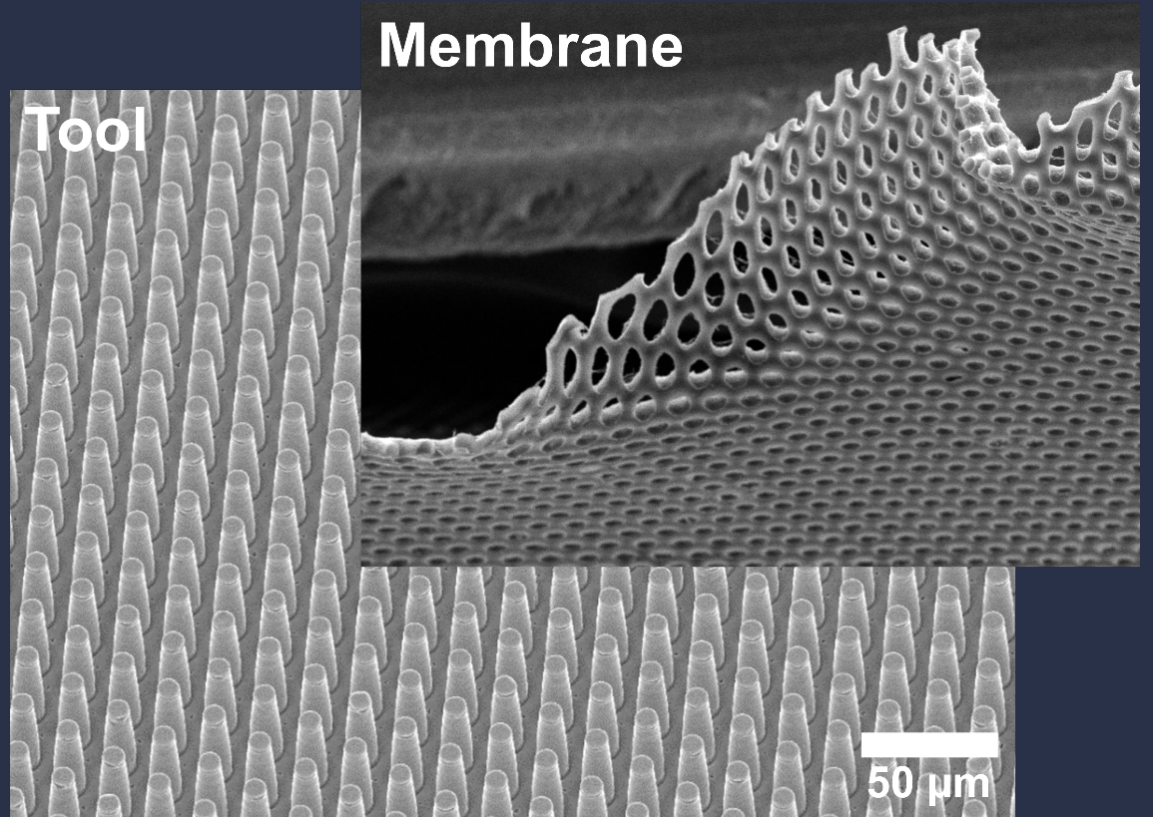
- High density of precisely shaped and aligned pores
- Small area, stiff and brittle
- Very expensive



# CSEM precision polymer membrane technology

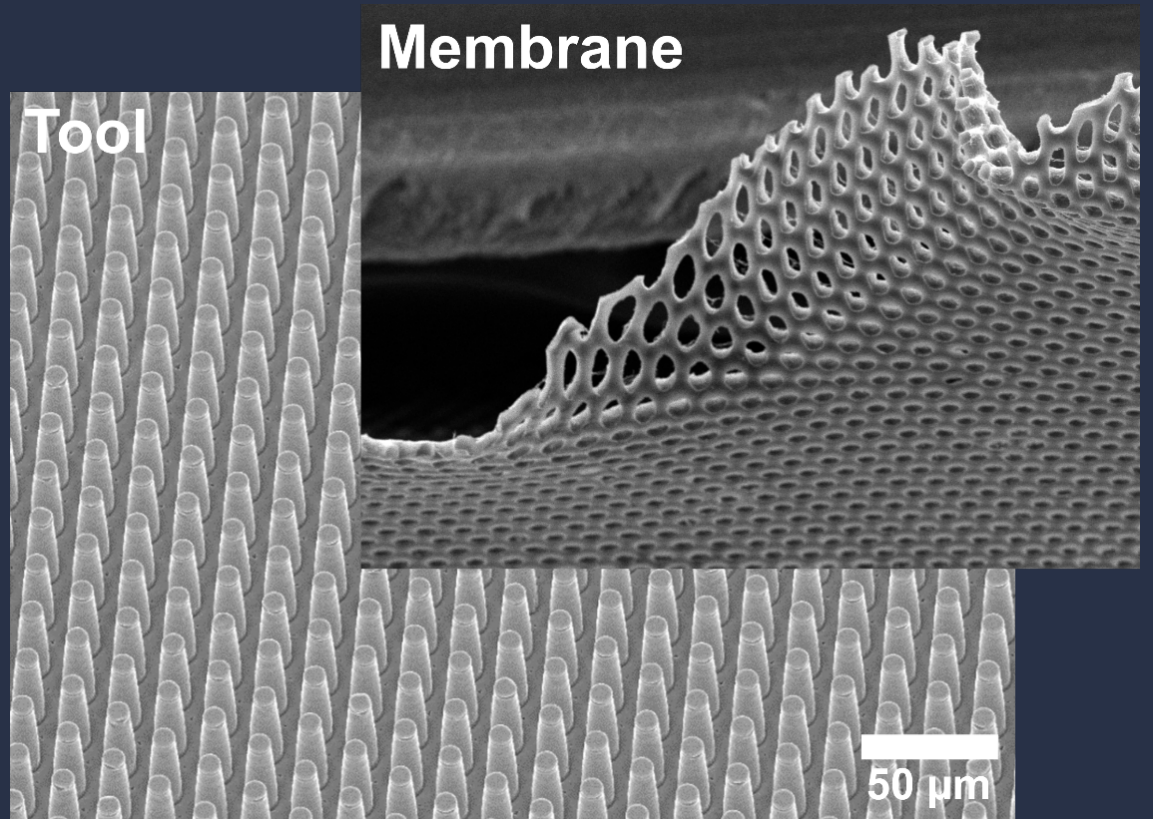
Fabrication of large area and flexible polymeric high-precision membranes

1. Design and fabrication of micro-structured tool
2. Membrane generation using scalable embossing approach



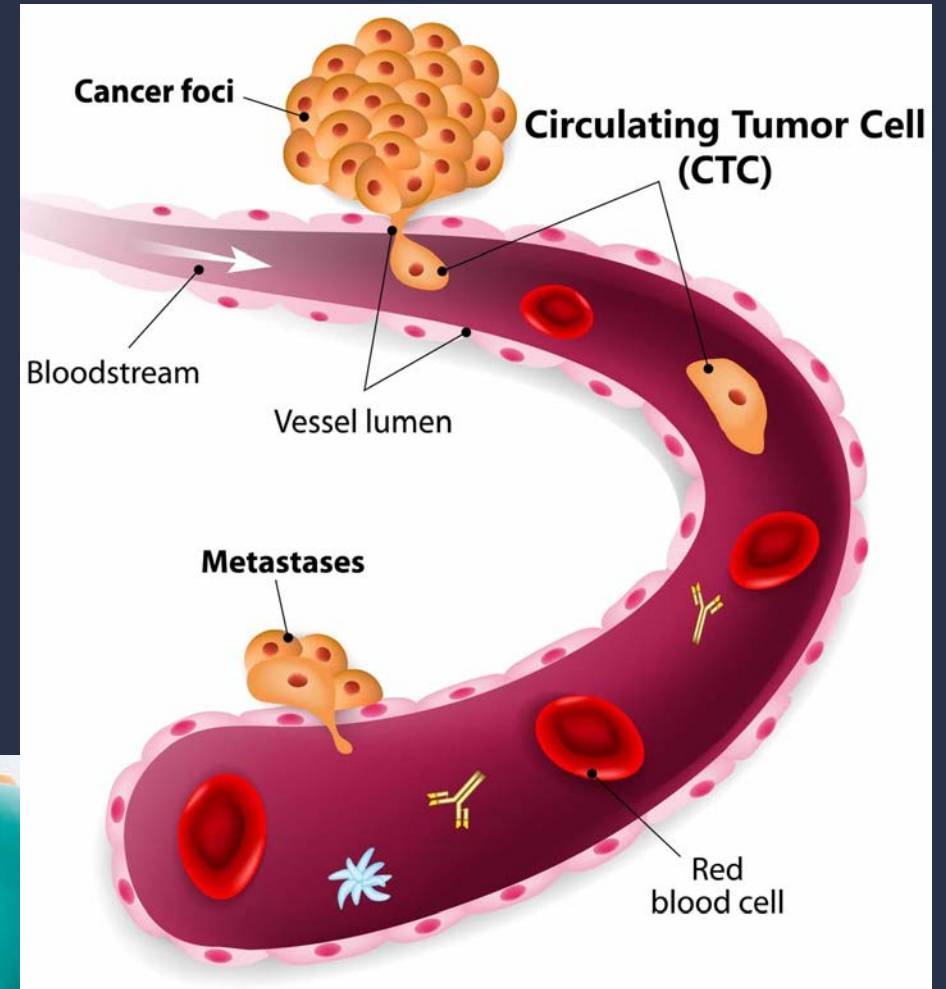
# CSEM precision polymer membrane technology

Material(s)	Polycarbonate (thermoplastics)
Size	50 mm disc
Thickness	10 $\mu\text{m}$
Pore size	5-7 $\mu\text{m}$ (min. $\sim$ 3 $\mu\text{m}$ )
Pore geometry	Cylindrical
Porosity	23 %
Fabrication process	Embossing



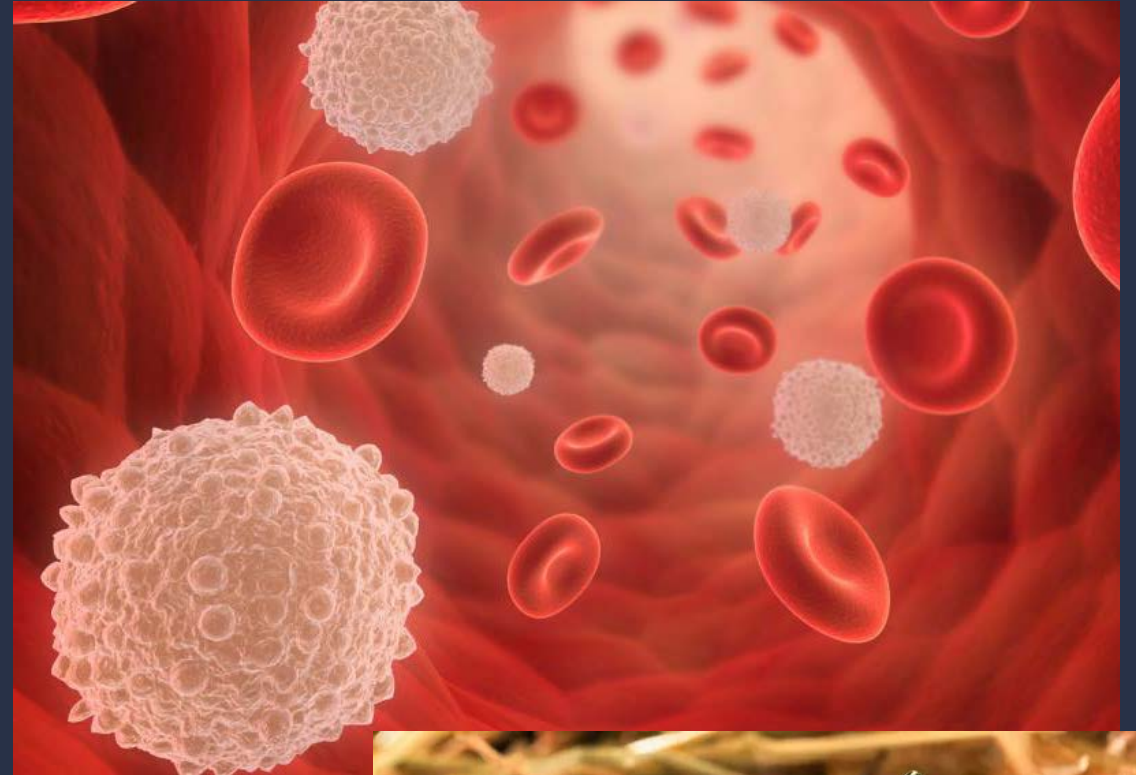
# Membranes for biosystems – liquid biopsy

- Analysis of circulating tumor cells (CTCs) in patient blood
  - ✓ Simple blood draw
  - ✓ Real-time view into systemic disease
  - ✓ Close disease monitoring
  - ✓ Enabling personalized cancer care



# The challenge

- Patients with early or pre-metastatic cancer have less than **1 CTC** per mL of blood
- Highly efficient CTC isolation from 60-100 mL of blood required
- Handle background of half a **trillion blood cells**

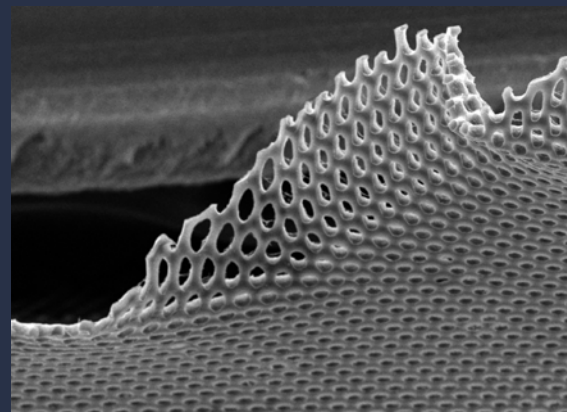
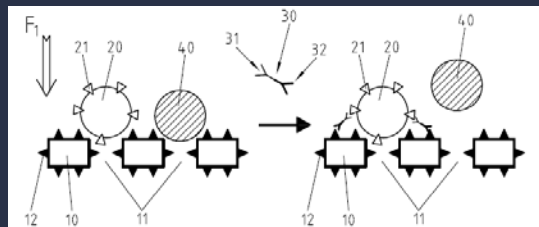


# Precision polymer membranes

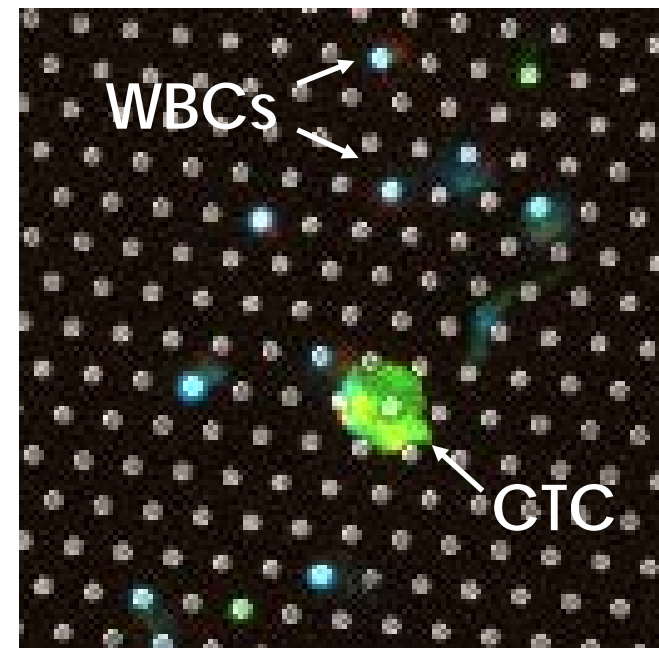
## Cell isolation for precision medicine



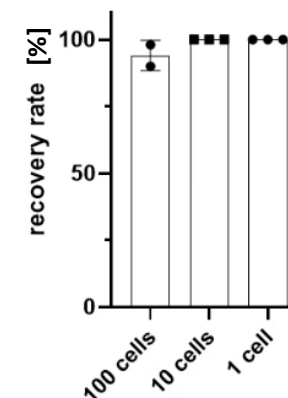
- **High-precision** polymer membranes for biosystems, e.g., rare cell isolation (CTCs)
- **Functionalization** of membranes for improved cell species selection
- **Metal-membranes** through galvanic processes
- **Integration-ready** with standard consumable components



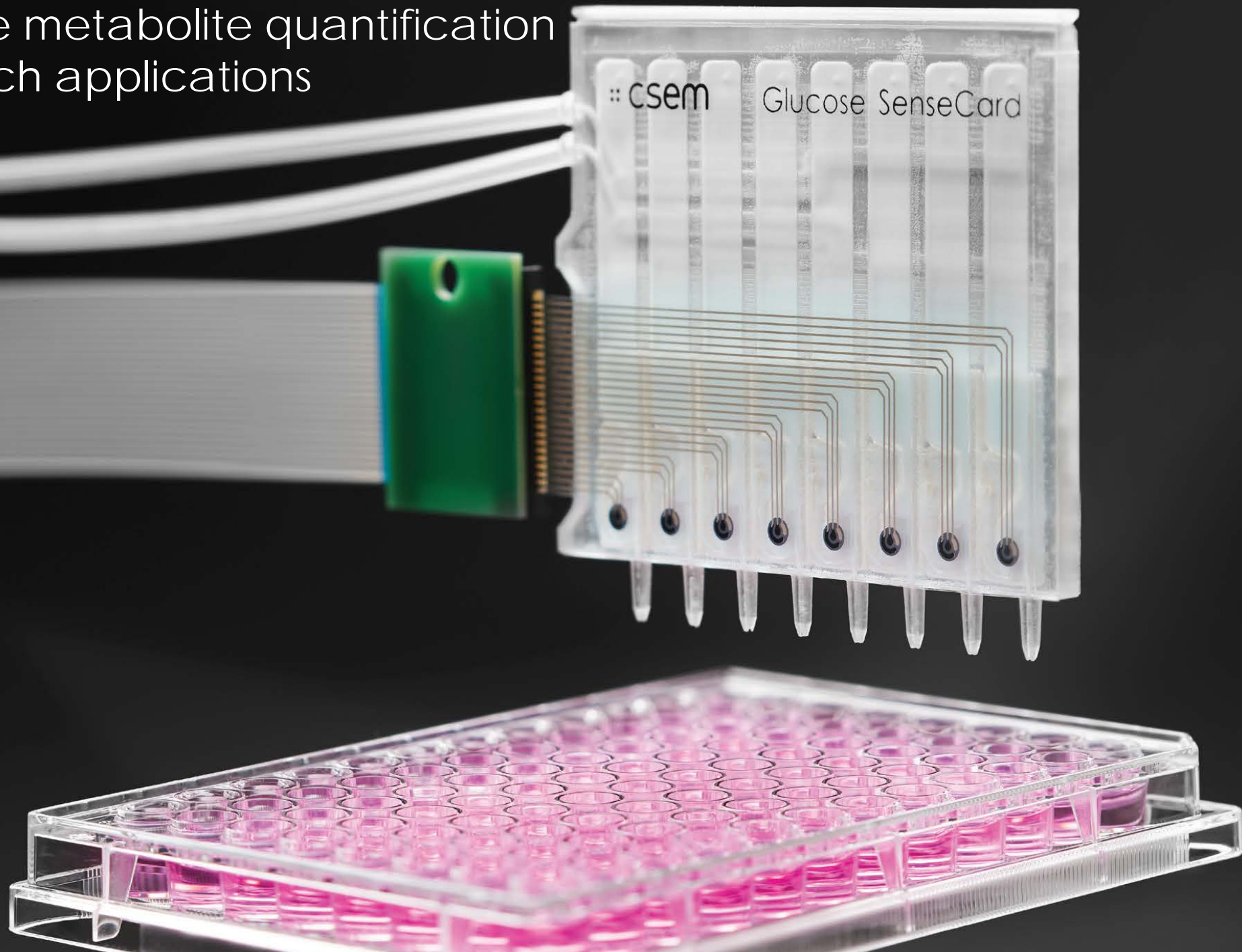
patent pending  
EP3770600A1  
US20210025871A1



"This is spectacular - clearly a world record!"  
Prof. Klaus Pantel, UKE



Real-time metabolite quantification  
for biotech applications



# Biosystems for personalized health



- **Alternatives to animal models** are strongly emerging (organoids, Organs-on-Chip)
- **3D tissue models** can replicate in vivo situation already very accurately
- These tissue models require highly **controlled microenvironments**
- **Multiplexed monitoring** of such microenvironments is crucial and highly demanding

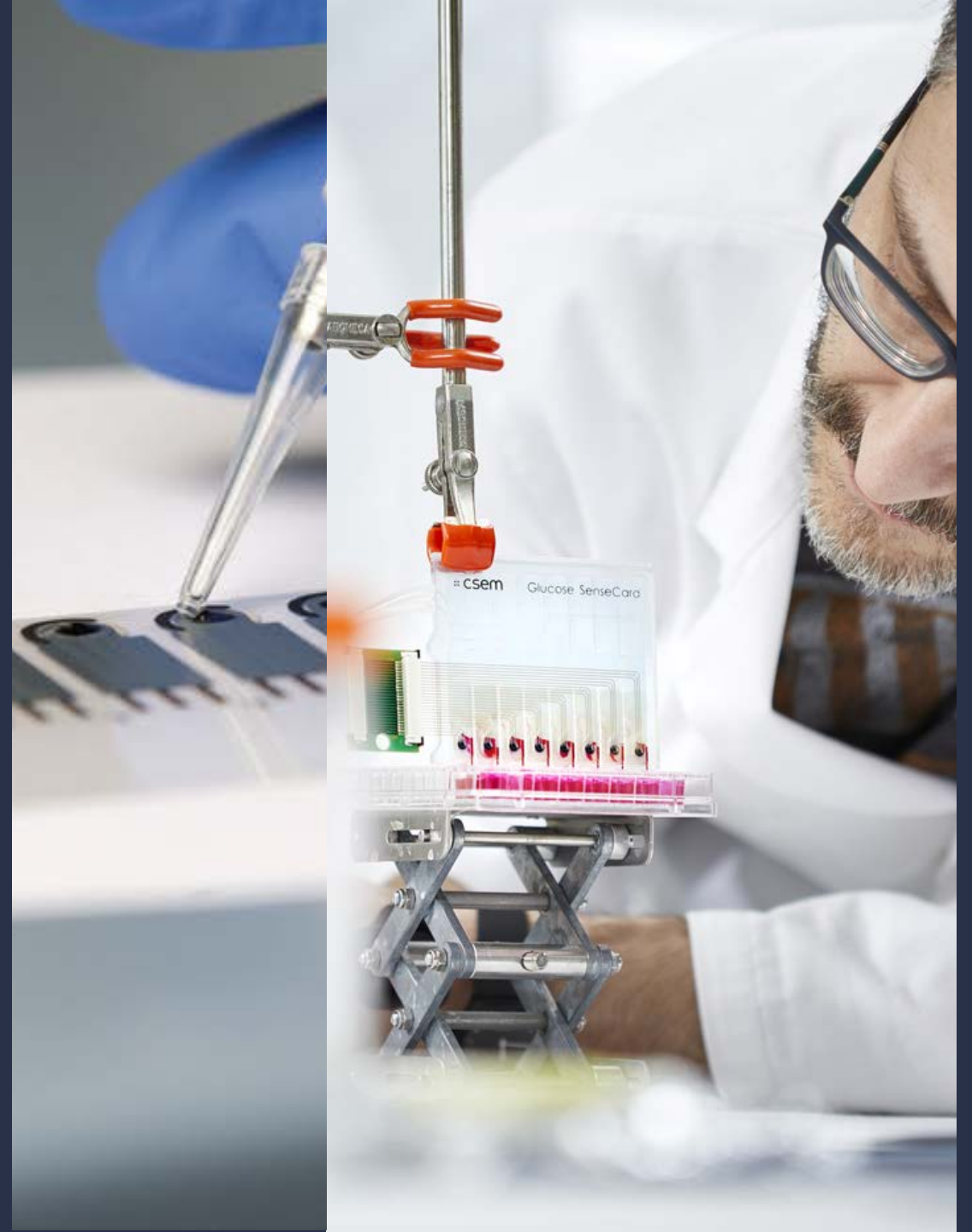




## Electrochemical sensors for biomonitoring



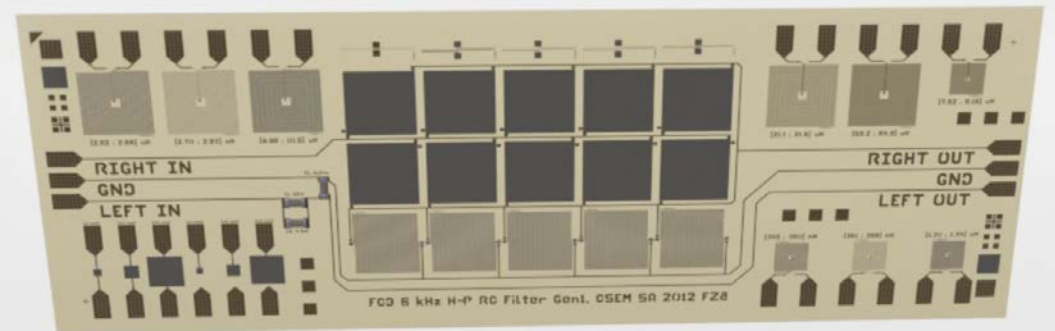
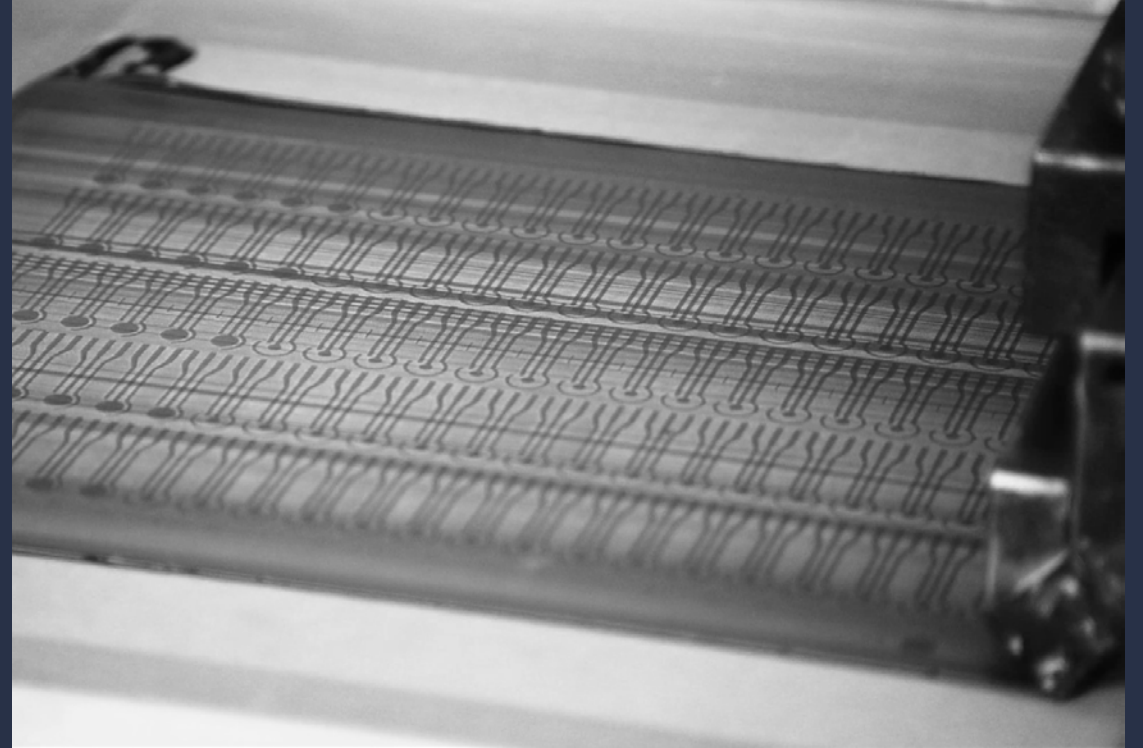
- Cheap and fast alternative to biochemical assays (e.g., ELISA)
- Highly specific and selective
- Single or reoccurring measurements per individual sensor
- Needed are (1) sensor & (2) readout module
- Sensors can be system-integrated or used "off-line"



# Printing of electrical circuits onto polymer substrates



- Printing of conductive metal inks (Ag, carbon, AgCl, Au, Pt) on plastic layer
- Screen-printing and inkjet printing
- Highly scalable production processes
- Printing resolution  $< 50 \mu\text{m}$ ; printing thickness from  $10 \mu\text{m}$  to  $> 200 \mu\text{m}$
- Flexibility of polymer substrate is preserved



Hybrid flexible printed circuit board

## Sensor **functionalization**



- High precision **liquid dispensing**
- **Polymer-based immobilization** and conservation matrices (e.g., OptoDex, PEGs, poly(dimethyl acrylamide, etc.)
- Stacking of layers – depending on sensor type and requirements
- Other functionalization layers can be derived by electrodeposition



## SenseCard

Long term metabolism monitoring for 3D tissues



- Small volume **sampling**
- Compatible with 96-SBS format
- **Electrochemical sensing** for glucose concentration (0 - 5 mM, tunable on request)



## Microfluidic-based **smart lids**



- Multiwell plate **cell culture automation**
- **Standardization** and parallelization
- Media exchange
- Pooling
- Perfusion
- **Injection molding** compatible
- **Integration of biosensors** possible





# Biomonitoring at CSEM



Biosystems

## Sensors for

pH, glucose, lactate, glutamate, lactic acid,  
ALT, LDH, ions (K<sup>+</sup>, Na<sup>+</sup>...), impedance,  
immunoassays, aptasensors

Urine



Saliva



Sweat



<https://www.medgadget.com/2020/06/sweat-sensor-gathers-large-samples-for-accurate-analysis.html>

# Delivering **innovation** to the life science industries

## CUTISS

Automated manufacturing of personalized skin grafts



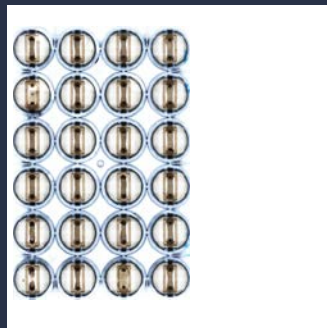
## Tecan

Liquid class free multi-channel pipetting



## Novartis

Automated contractility measurement



## IBIDI

Non-invasive optical gas sensor for cell culture media



## Helmholtz Institute

Early stage Zebrafish sorting



## INVENesis

Bioassays for drug testing in animal health



## Discover our Life Science Brochure



<https://www.csem.ch/pdf/157550>

