Microfluidics InnovationHub

WEBINAR: WE GET MICROFLUIDICS ROLLING

Advantages of Roll-to-roll Replication

JANINE BROMMERT
Temicon

ANJA HAASE
Joanneum Research

JAN KAFKA
Inmold

ALVARO CONDE
Micronit

13 OCTOBER 2022

15:00-16:30 CEST

www.microfluidicshub.eu

Webinar Content

Microfluidics InnovationHub

INTRODUCTION
Ronald Tingl – Microfluidics Innovation Hub

Part I MASTERING & TOOLING
Janine Brommert – Temicon GmbH

Part II ROLL-TO-ROLL UV IMPRINTING
Anja Haase – Materials Institute, JOANNEUM RESEARCH
Mirko Lohse – micro resist technology GmbH

Part III ROLL-TO-ROLL EXTRUSION COATING
Jan Kafka – Inmold A/S

Part IV BACK-END PROCESSING
Alvaro Conde – Micronit BV

SUMMARY
Ronald Tingl – Microfluidics Innovation Hub

Q & A

The NextGen Microfluidics (NGM)

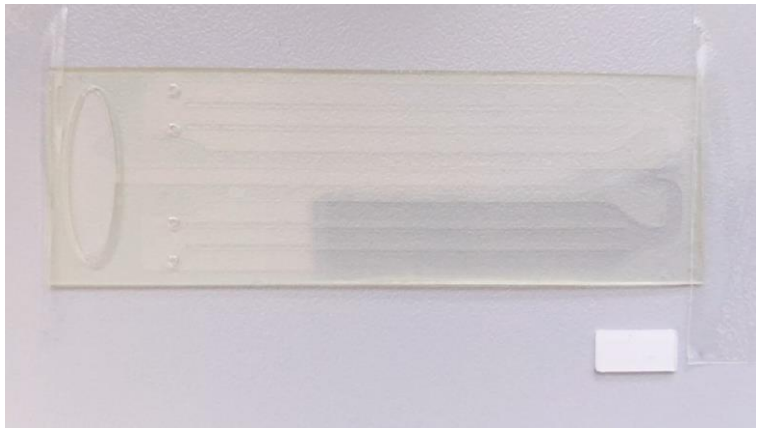
- NGM is an Open Innovation Test Bed
- Combining the competencies of 21 companies & research organizations
- The biggest platform worldwide for upscaling and testing microfluidic devices

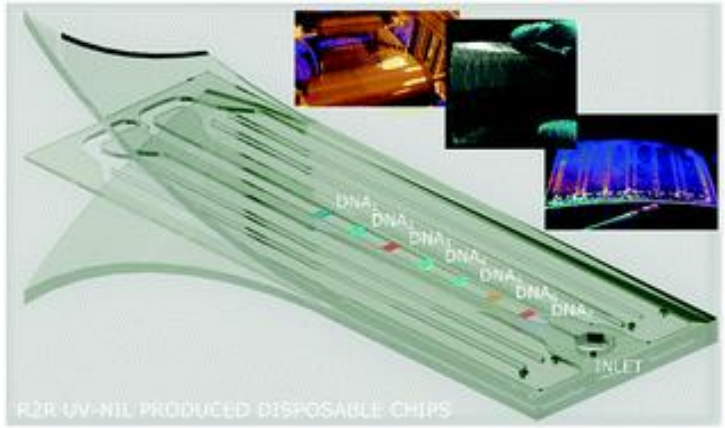
Design & Simulation	Electronics Manufacturer	Process Development	Medical Sensors	Research
BIONIC SURFACE TECHNOLOGIES	Infineon	INMOLD, SCIENION A BICO COMPANY, temicon micronano solutions, RESCOLL Société de Recherche	Erba Technologies Austria GmbH, Erba Mannheim, GENSPEED BIOTECH	JOANNEUM RESEARCH, BRFAA BIOMEDICAL RESEARCH FOUNDATION ACADEMY OF ATHENS, tecnalia MEMBER OF BASQUE RESEARCH & TECHNOLOGY ALLIANCE, BNN, TU Graz, Švédský institut

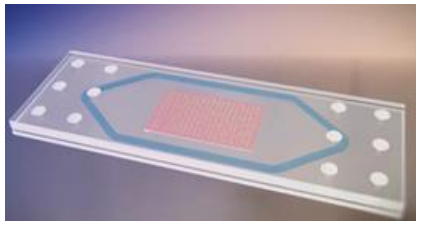
Materials	Bioprocess	Microfluidics Development & Manufacturing	Cell Culture Solutions
condensia Passion for chemistry, micro resist technology	NST WIRBELSCHICHTTROCKUNG	bi.FLOW systems biofluidic integration, micronit	ibidi cells in focus, Innoprot Speeding up drug discovery

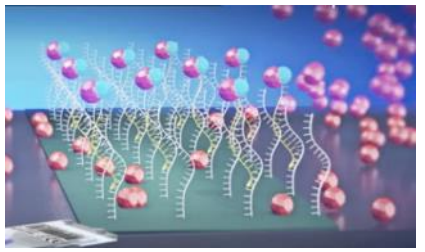
Talking Microfluidics

- We talk chips / cartridges / plates
- with microchannels, micro reaction chambers (µl, µm)
- performing chemical, biochemical, biological processes
- useful for medical diagnostics, chemical analysis, environmental monitoring, cell culture devices
- Lab-on-Chip, Organ-on-Chip, Soil-on-chip, Point-of-care









MIH – Single Entry Point to NGM Services

MIH is a non-profit association that includes 20 NGM members

Research
Development
Production

Program Management

Partner Coordination

Single Entry Point

MIH OPERATIONS

Marketing & Sales

Business Fulfillment

MARKETS

USE CASES

CUSTOMERS

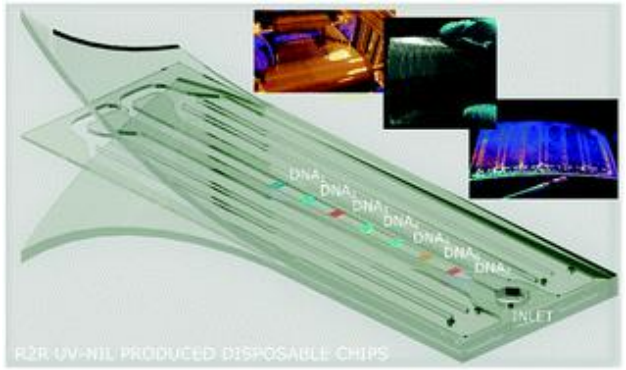
EXTERNAL PARTNERS

MIH Service Portfolio

Primary Components

Assay | Design | Mastering | Patterning | Surface functionalisation | Electrodes Sensors | Backend Services | Read Out Device System Integration | QM

IVD - ELISA, LAMP, PCR
ENZYME Detection
CELL analysis
Water, Food analysis

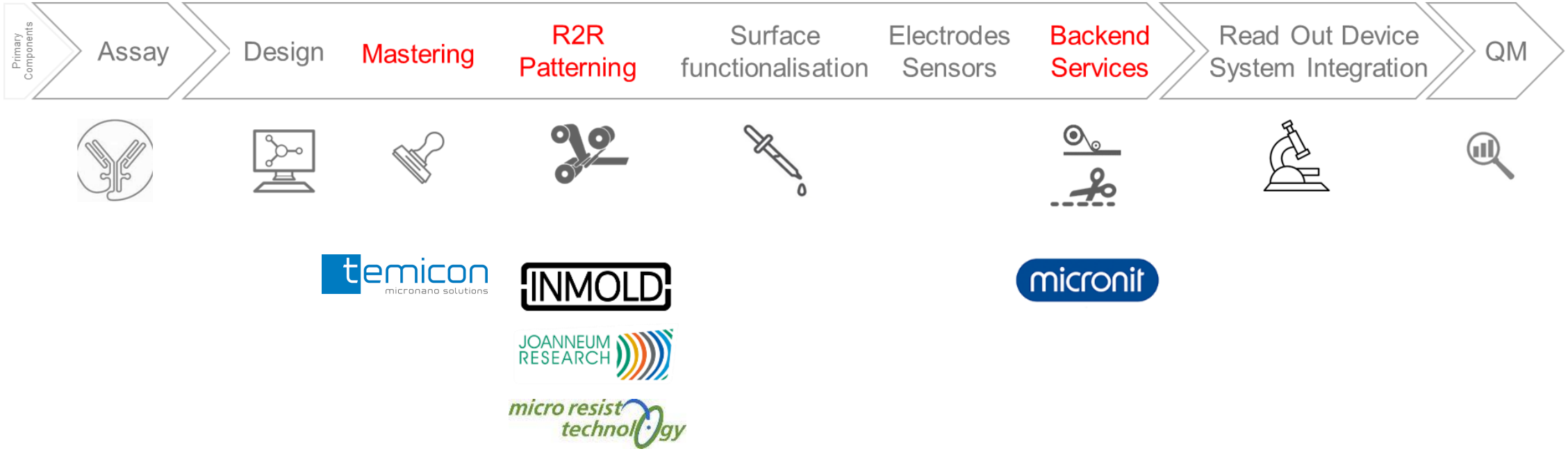


Active & Passive Microfluidics
Single units to millions of units
From Milling over Inj. Mold to Roll-to-roll

Microfluidic Chip

Microfluidic Solution

Spotlight on 3 Topics



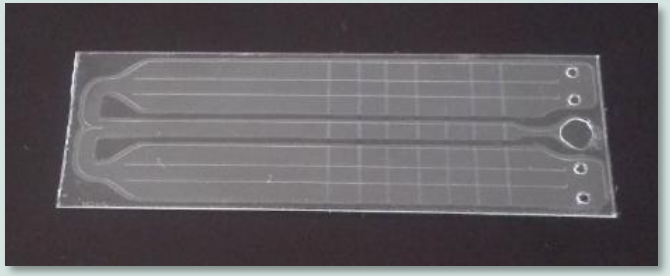
Why Roll-to-Roll Production for Microfluidic Chips?

Traditional manufacturing Microfluidic Chips

Micromilling, Soft & Hot Embossing, Injection Molding

Roll-to-Roll

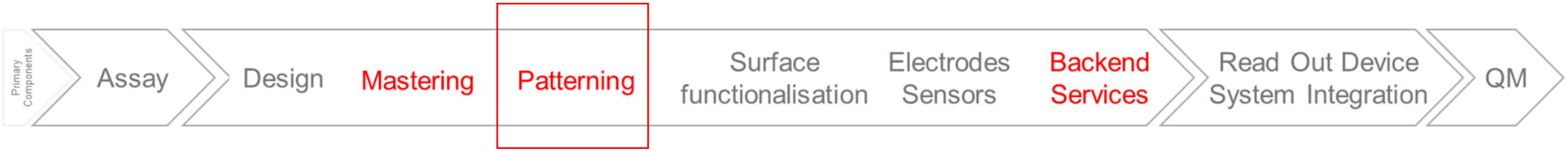
- High Volume / Low Cost
- Specific Microfluidic Chip Design Requirements



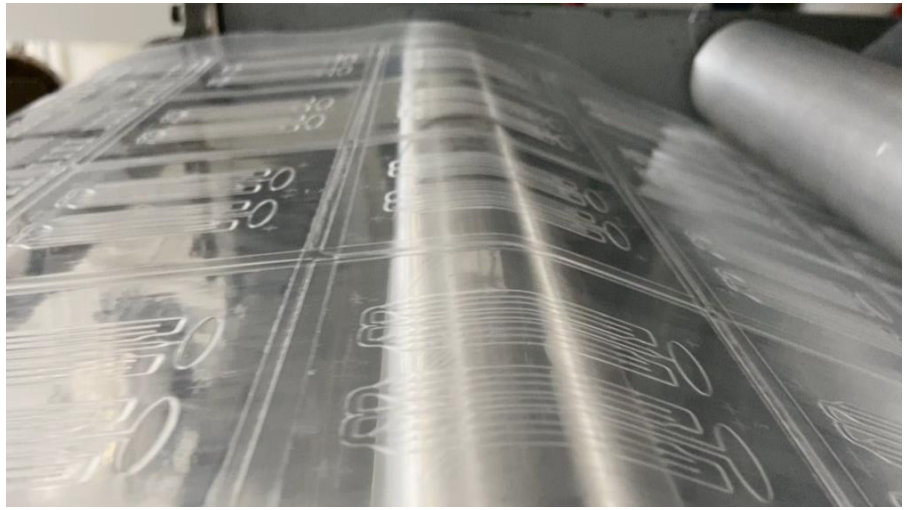
Overview Imprinting Technology

	PDMS	Micromilling	Hot Embossing	Injection Molding	R2R Replication
Throughput	Single digit	Single digit	Several 100k	Less than 1Mio	> 100k
Production costs	High	High	Medium	Low	Lowest
Flexibility	High	High	Medium	Medium	Medium
Time to prototype	Days	Days	4-6 weeks	4-6 weeks	4-6 weeks
Materials selection properties	Low	Low	High	High	Highest
Available in MIH	✓	✓	✓	✓	✓

Roll-to-Roll Patterning Technologies

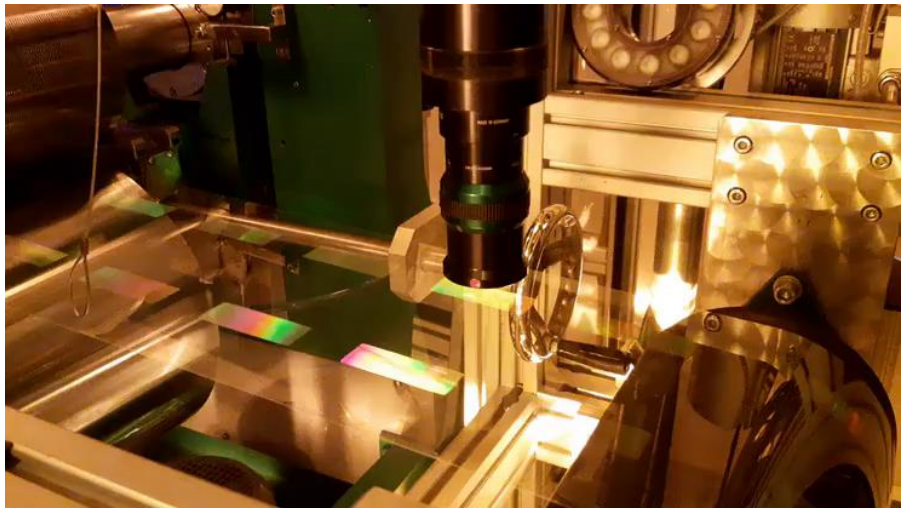


Roll to Roll Extrusion Coating



Patterning of thermoplastic foils

Roll to Roll UV-Imprinting



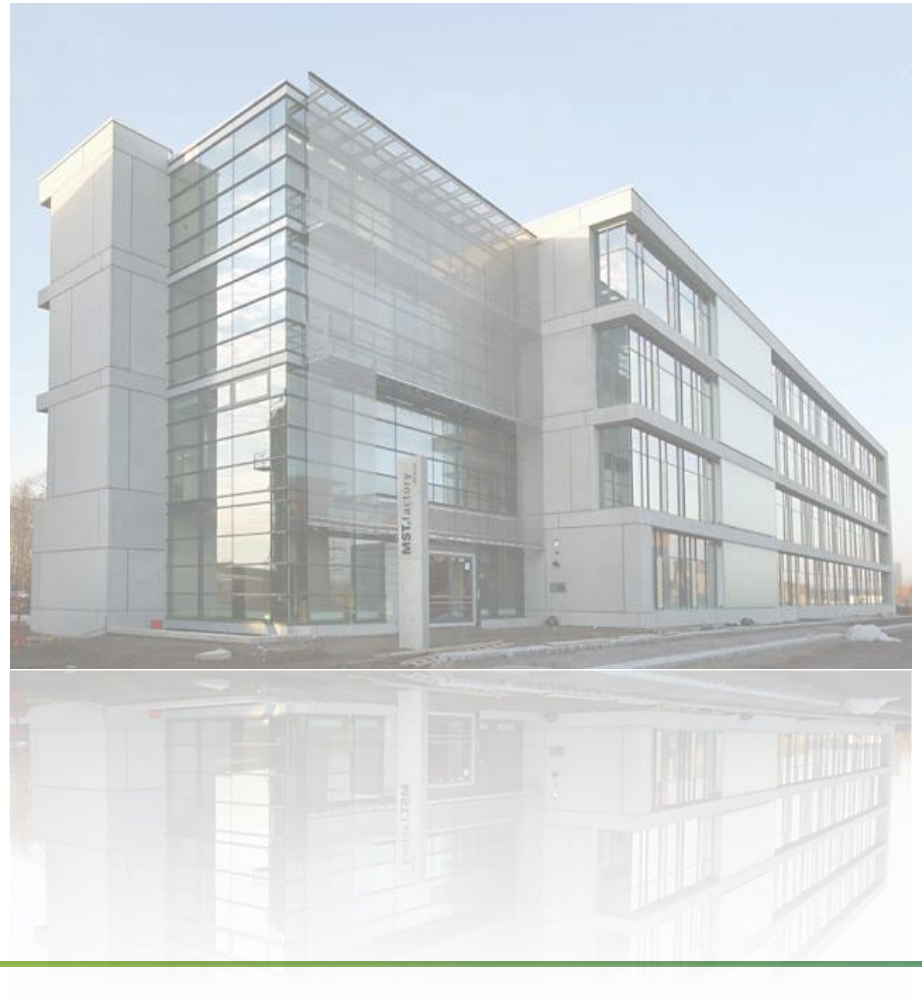
Patterning of UV photopolymers on substrate foils

Microfluidics InnovationHub

Mastering and Tooling

temicon
micronano solutions

temicon Company Profile

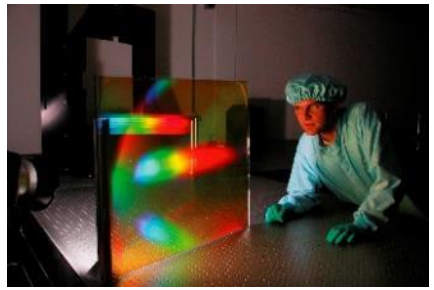


temicon is worldwide leading in series production of micro structured and nano structured components, films and functional surfaces.

- Founded in 2005 by Oliver Humbach
- Located in Dortmund, Freiburg (Germany) and Shenzhen (China)
- 70 Employees
- Clean Room Production ISO 5
- Worldwide Markets in Lighting, Display, Solar, Optics and Life Science

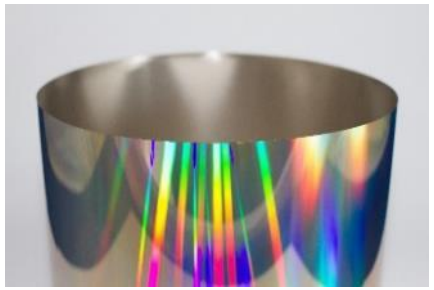
temicon Company Profile

Lithography



- Laser Interference Lithography (250 nm upwards), up to 1 m^2
- UV Lithography (2 µm upwards), up to 20“x 24“

Electroforming

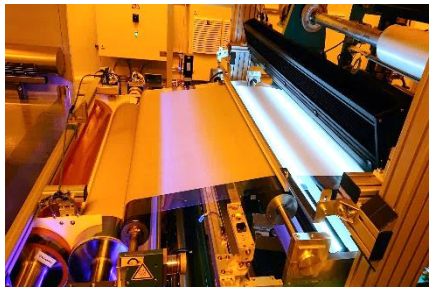


- 4“ – 20“x 24“
- 50 µm – 3 mm thickness
- Soft Ni (250 Hv), Intermediate Ni (450Hv) & Hard Ni (650 Hv)

Injection Molding

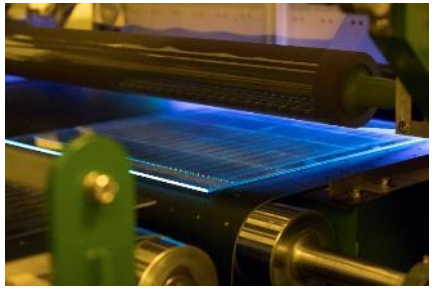
- Flexible Prototyping Tool
- PMMA, PC, COC/COP, PP, ABS
- Automated part removal

R2R Imprint



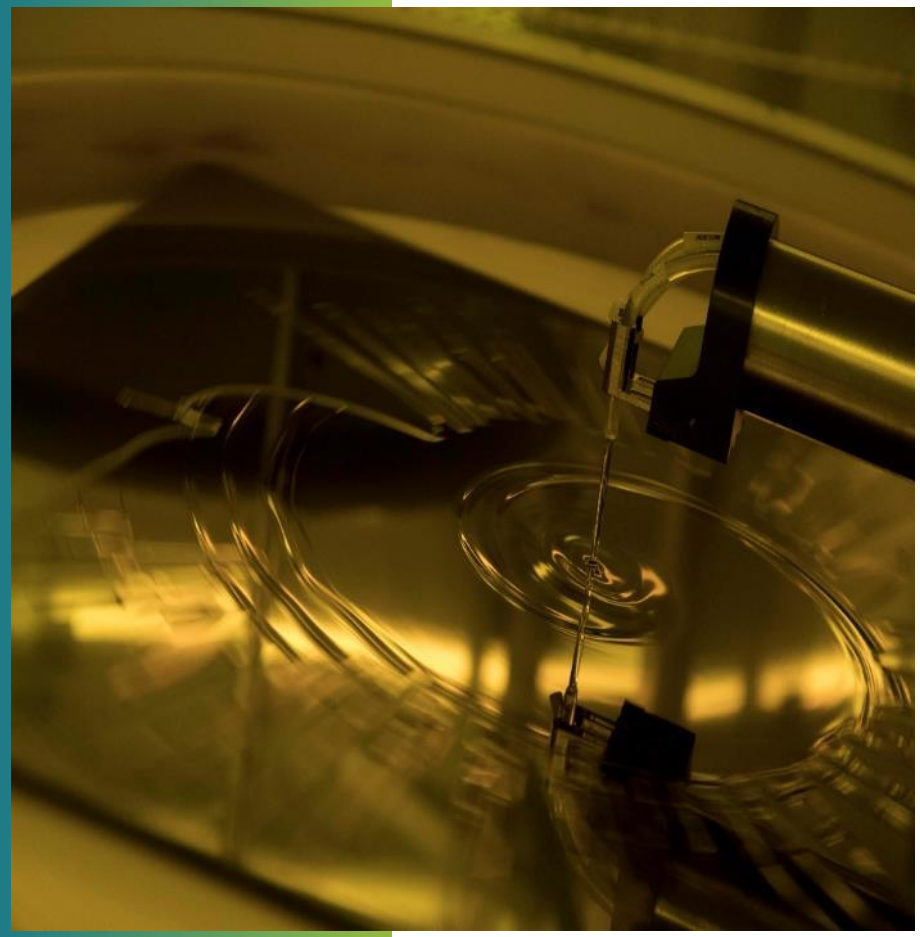
- 1m production width
- Up to 60 m/min production speed
- Film thickness 20 µm – 250 µm
- Inline Quality Control

R2P Imprint



- PMMA, PC and Glass substrates
- Up to 1,1 x 1,6 m substrates

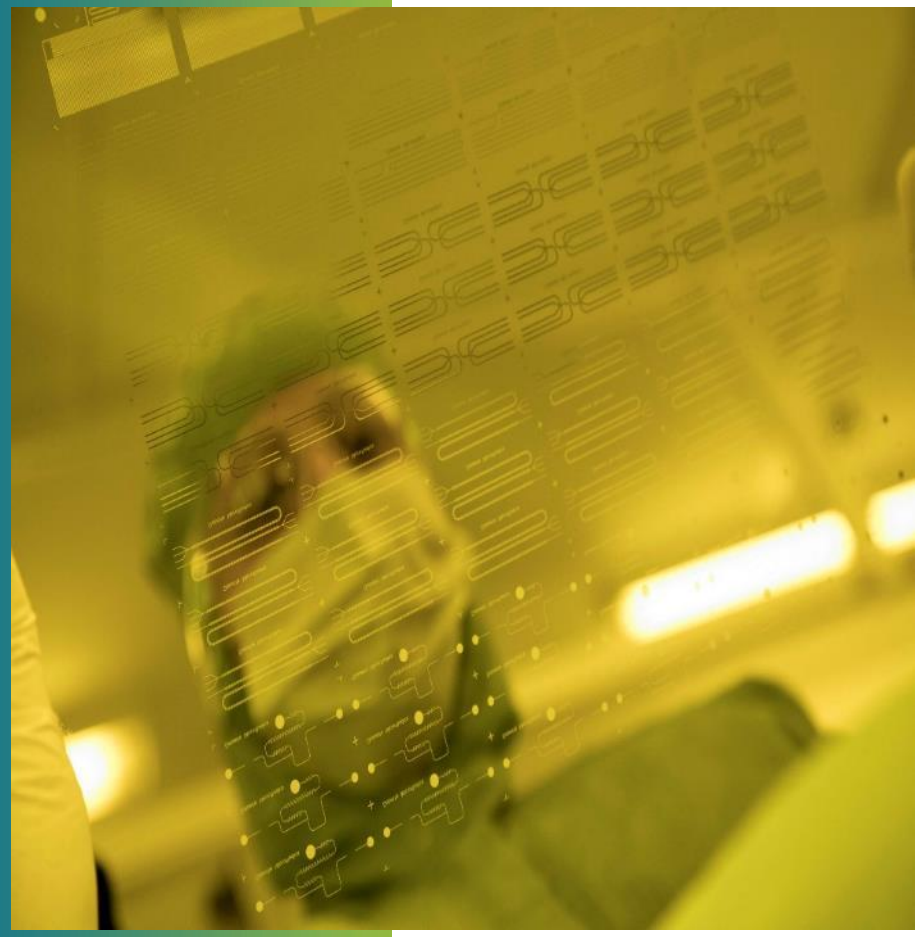
UV Lithography Mastering



Spincoating of the resin

The given design is transfered into a lithography mask. This structure is optically imprinted via UV irradiation into a photoresist. After development of the resist the non cured areas can be removed and only the cured parts of the structure remain. The created cavities can filled up with Ni during the electroforming process.

Electroforming

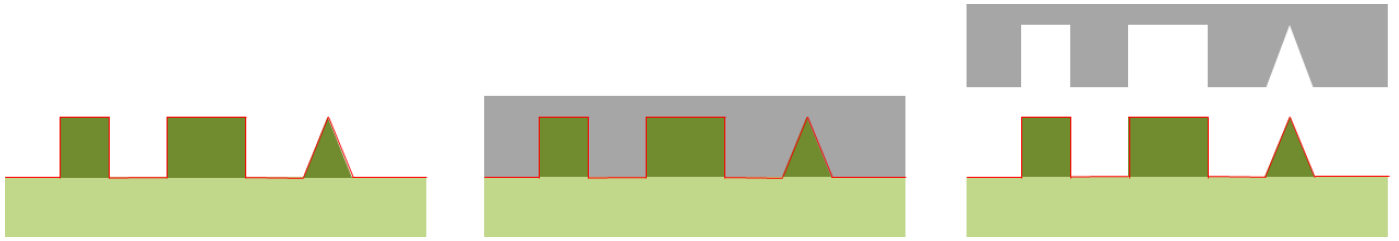


Sputtered Master

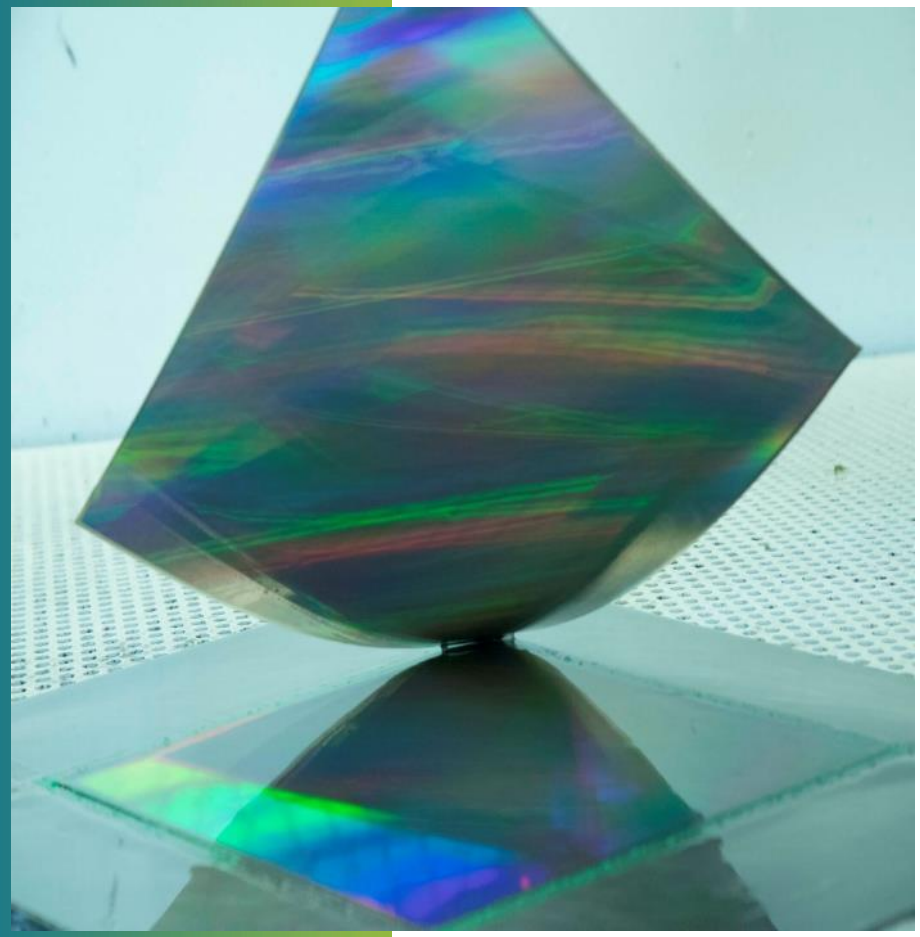
The master is sputtered to become conductive contacted and processed within an electroforming plant. Nickel growth on top the given masterstructures.

This 1st Ni-Shim is called the „Father“. The master is usually destroyed during the separation from the father, but the father can be used directly or is origin of many copys.

Male members of a family have the inverted structure of the master, females the original one.



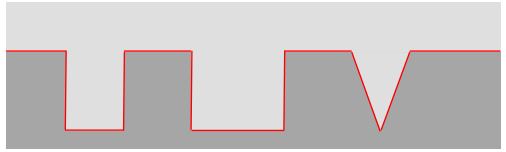
Electroforming – Family Process



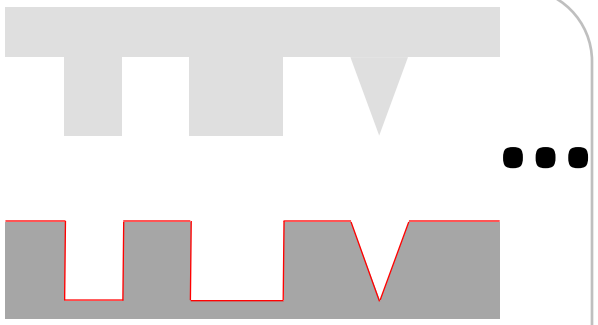
Separation

1st Electroforming
(Father)

Passivation

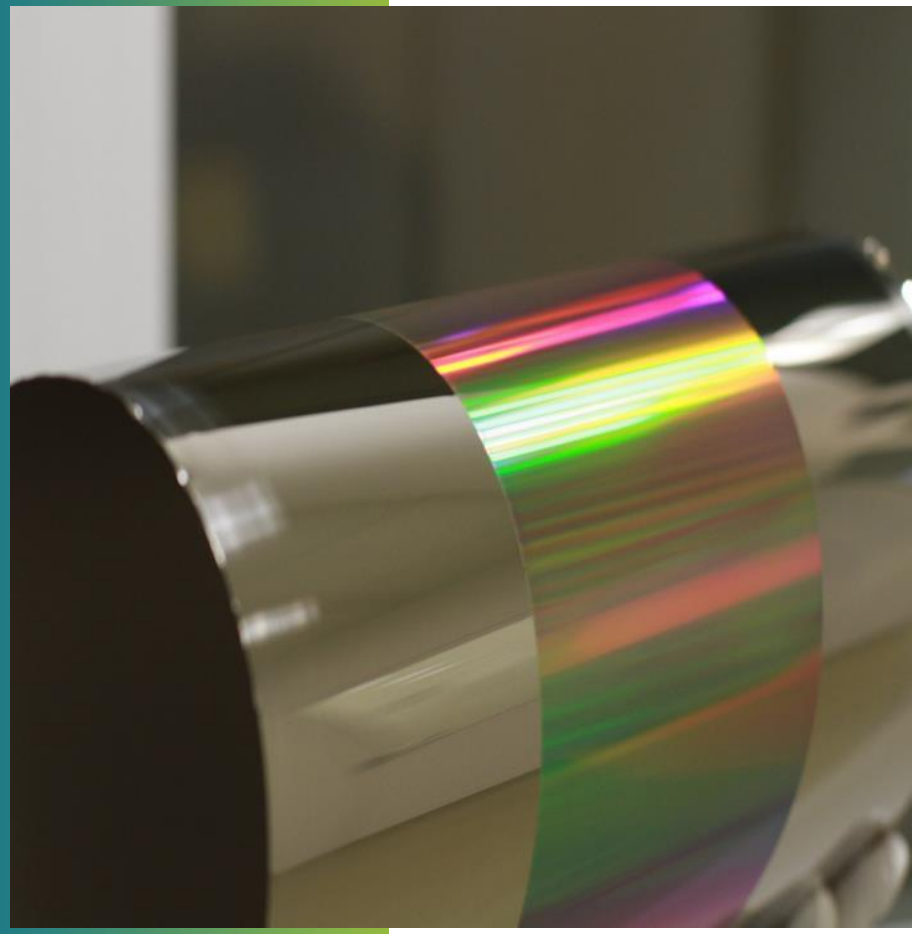


2nd Electroforming
(Mother)



Separation

Tooling – Sleeves

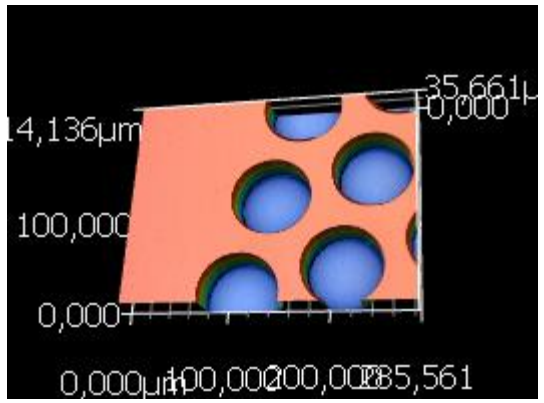


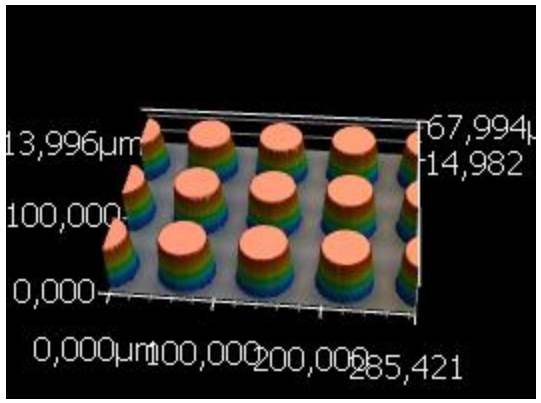
Sleeve

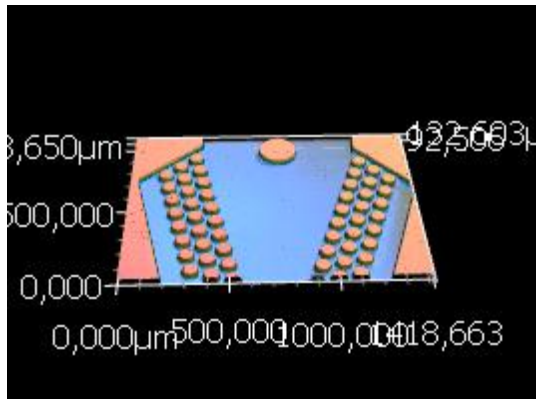
The intermediate product resulting from the electroforming is a flat shim. To come to a R2R tool it is necessary to transfer it into a cylindric form. Therefore the shim is bend and welded at the two connecting edges.

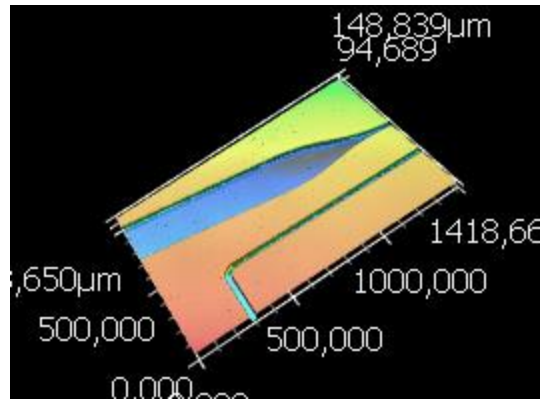
To grant a sufficient flexibility of the shim the thickness is usually between 150 -200 µm. By connecting several shims, a tool area of more than 1m^2 can be realized while the seam lines can be reduced down to 30 µm width and 10 µm height.

Typical structure examples









General Data

- Feature sizes 250 nm-200 µm
- 2-layer structures possible
- Draft angle 85° ± 3°
- Aspect ratio up to 3
- Different coatings for shims and sleeves available

Microfluidics InnovationHub

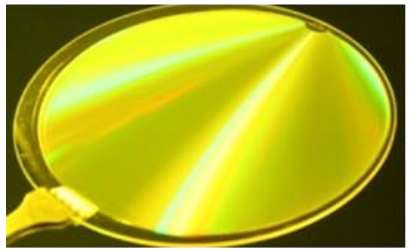
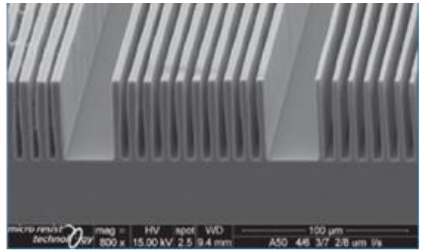
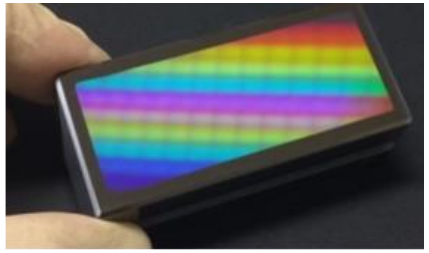
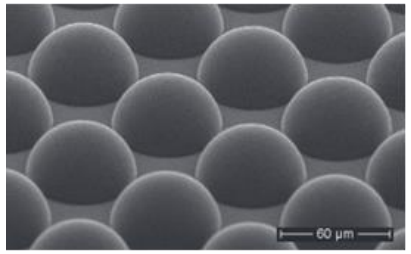
Roll-to-Roll UV Imprinting

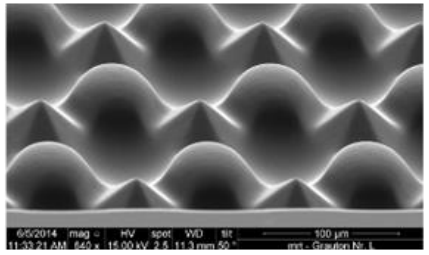
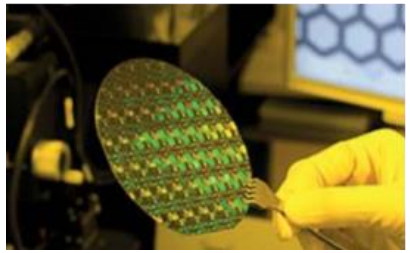
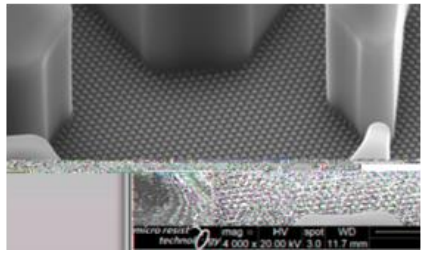
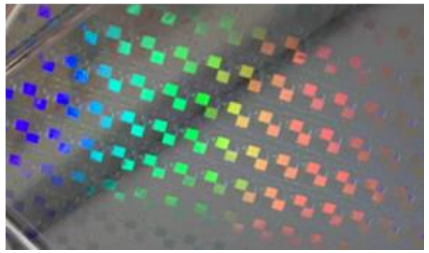
micro resist technology

JOANNEUM RESEARCH




micro resist technology GmbH

Specialized in providing **innovative resists**, **polymers,** and **photopolymers.** We support our high-tech costumers as a single-entry point to high performance materials, technologies and process solutions

- Established: 1993 (Berlin, Germany)
- Employees: 50+ (2022)
- Facility: 3.450 m^2 incl. clean room (300 m^2)
- Certifications:
  ISO 9001:2015
  ISO 14001:2015

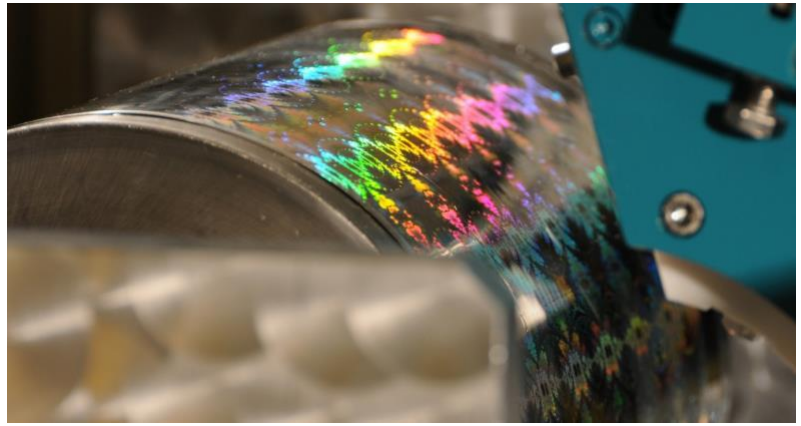
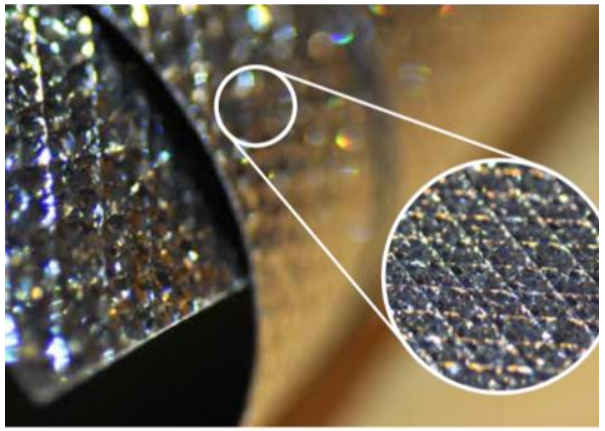
Fields of business activities:

- Manufacturing: formulation / synthesis
- Researching advanced materials and processes
- Lithographic Services

Strategic Distributorship in Europe:

DUPONT · KAYAKU ADVANCED MATERIALS · DJ MICROLAMINATES, Inc Dry Film Sheets · ShinEtsu

The Materials Institute
JOANNEUM RESEARCH Forschungsgesellschaft mbH


Austrian research company
500 Employees
7 Research units
20 People in
Microfluidics area

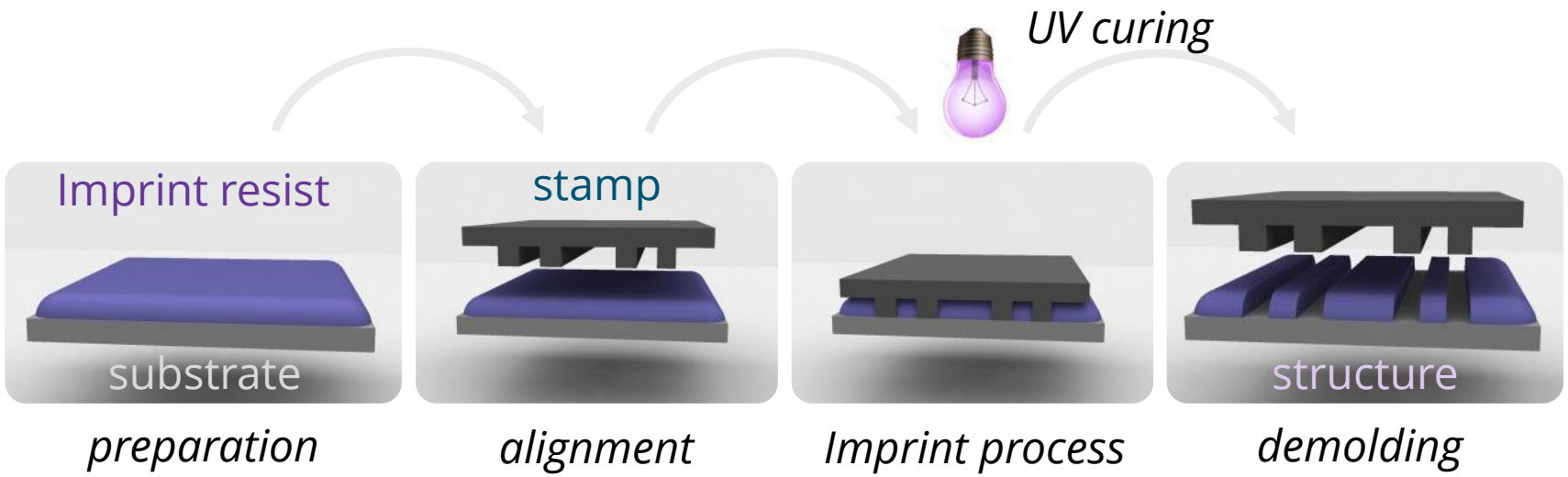
R2R-UV imprinting Pilot line

- Material (NIL - Cure®)
- Design (Simulation)
- Mastering & Tooling (Step & Repeat)
- Pilot line production

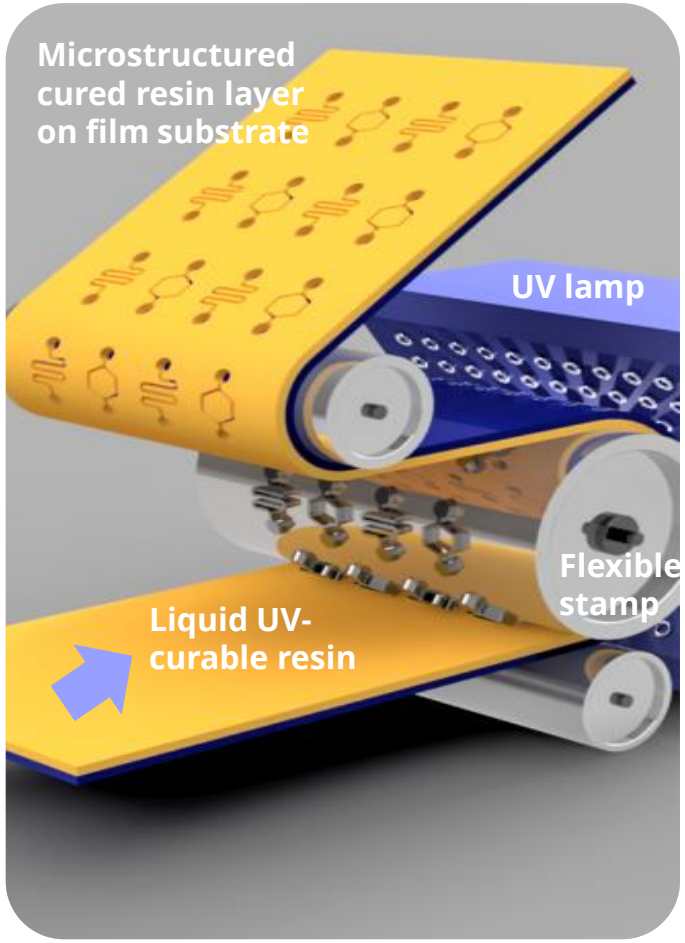
Various Applications
- ✓ Bionic Surfaces
- ✓ Decorative Films
- ✓ **Microfluidic Films**
- ✓ (freeform) Micro-optic Films

Micro and Nano - UV Imprinting

- Very simple method for replication of micro- and nanostructures
- Curing process either with UV light or temperature
- Very flexible with respect to geometries, sizes, and forms
- Lateral resolution independent on optical wavelength



Roll-to-Roll UV Imprinting



Key features

- Aspect ratio (H/W): 2:1
- Web speed: 0.5-30 m/min

Substrates

- Polymer, PET, PEN,COC, etc.
- Transparent
- Thickness: 20 µm to 250 µm

Resin

- UV-curable resin

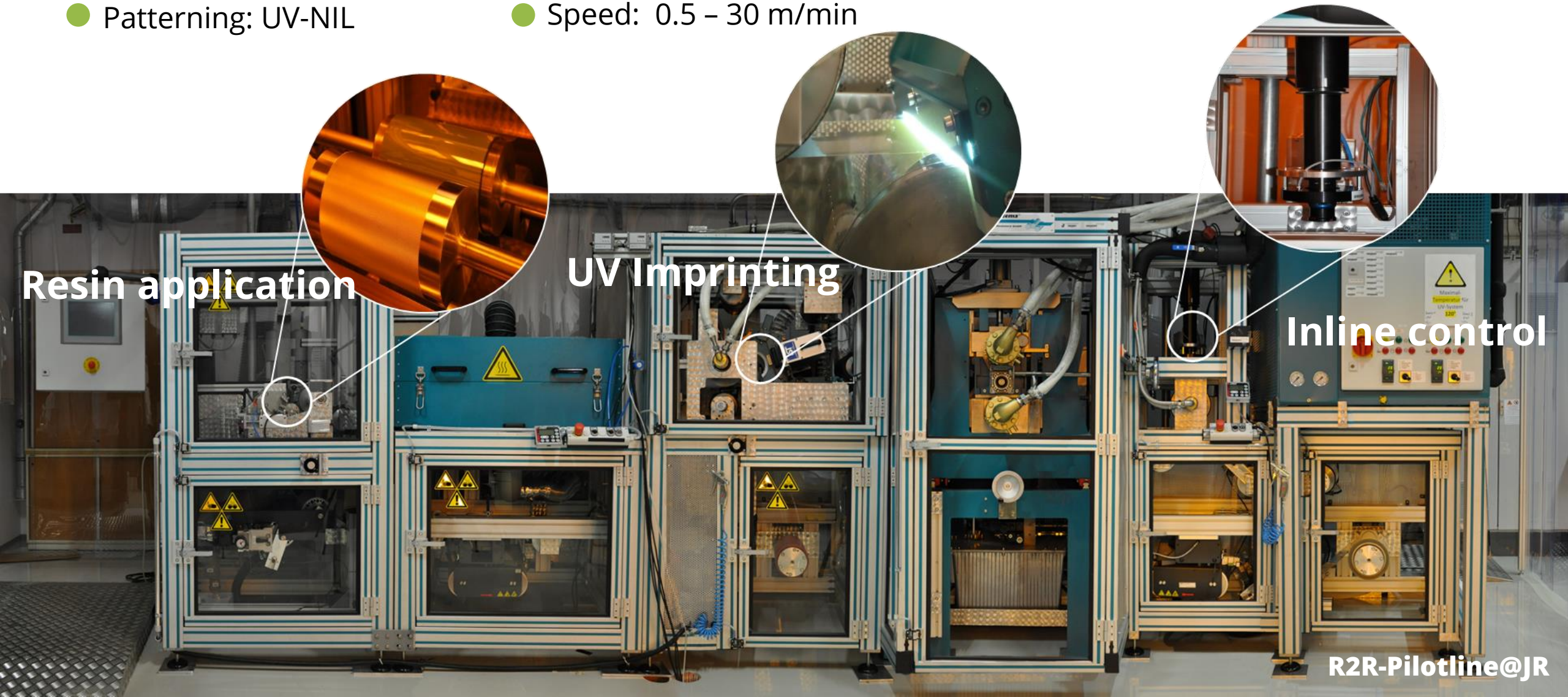
Structures

- 2.5D, several layers
- Up to 150 µm depth

Roll-to-Roll UV Imprinting

Roll-to-Roll UV Imprinting

- Coating: Gravure, Slot Die
- Patterning: UV-NIL
- Web Width: < 290 mm
- Speed: 0.5 – 30 m/min
- In-line camera, wet thickness control



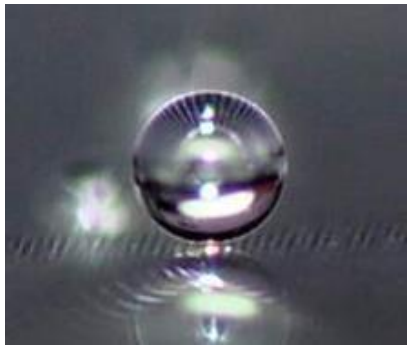
Resins for R2R UV Imprinting

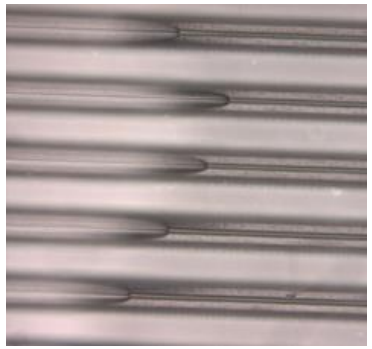
Resin properties relevant for µ-fluidics:

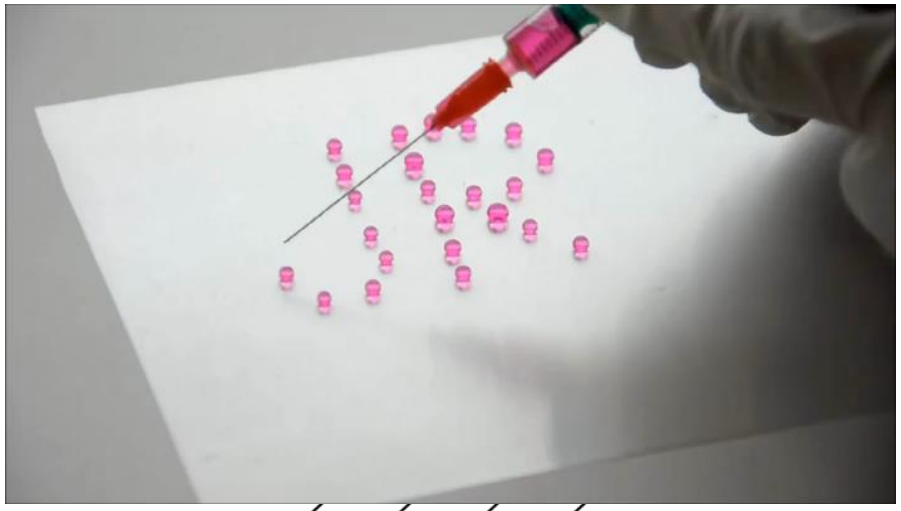
- Fast curing, low viscosity
- Low water contact angle
- No significant swelling
- Low cytotoxicity
- Low auto-fluorescence
- Providing “anchor-groups” for bio-functionalization
- Tunable elasticity
- Possibly biobased materials

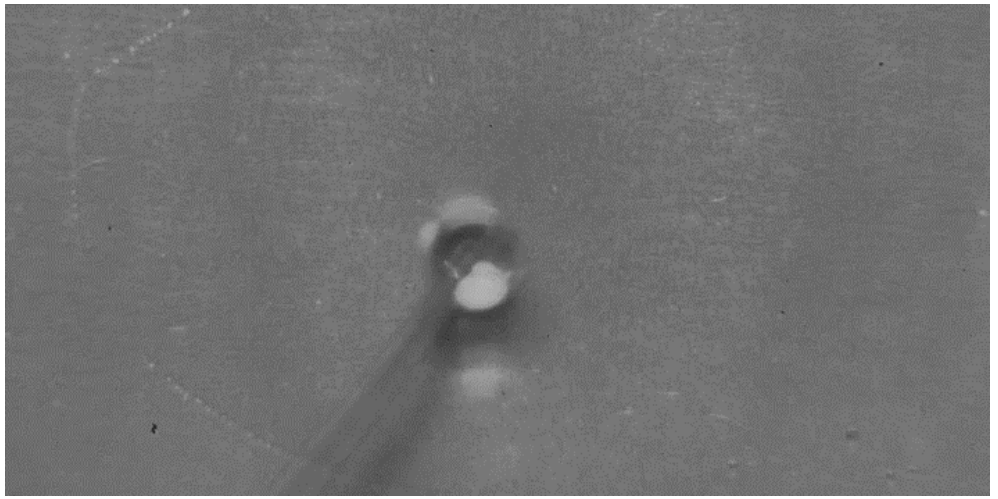
Parameters can be adjusted to customers‘ needs

Customizable properties by material choice

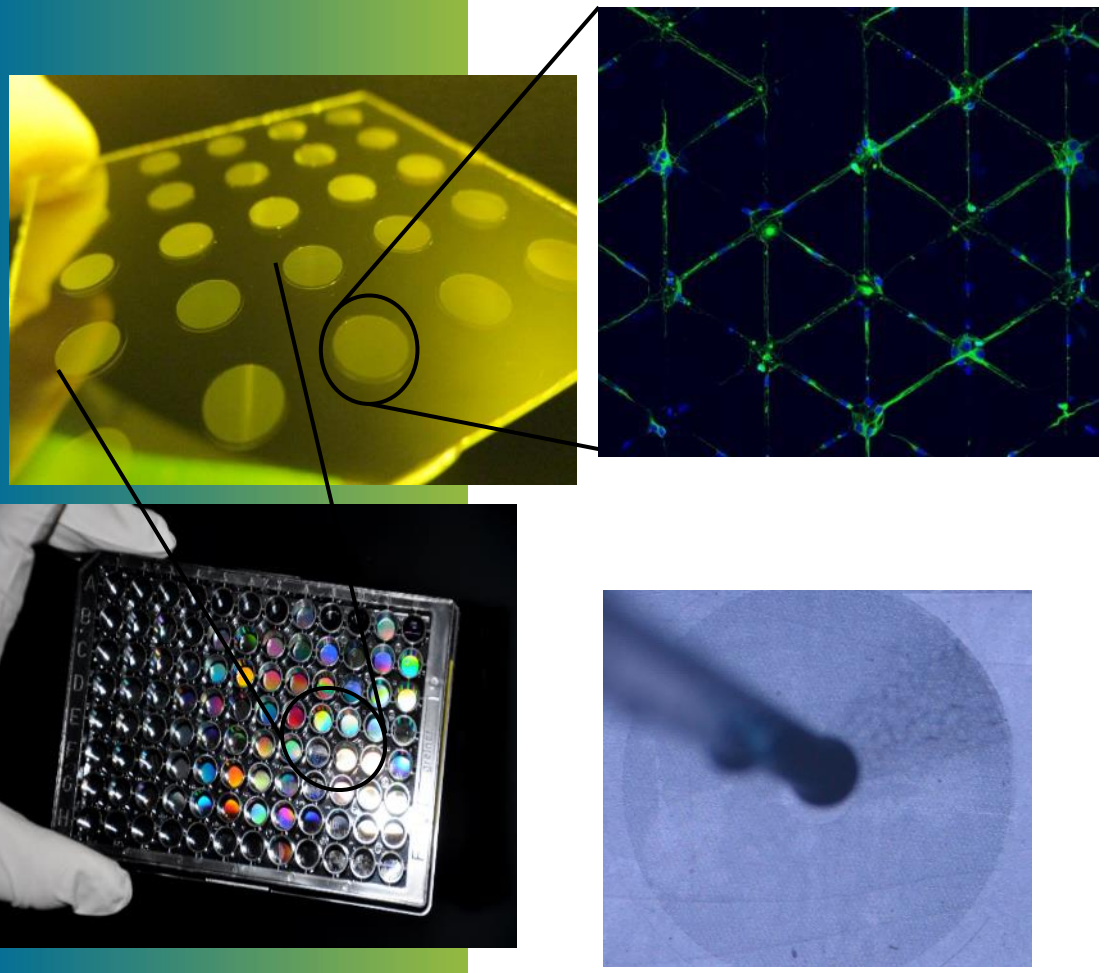








Example 1: Neuronal cell assay



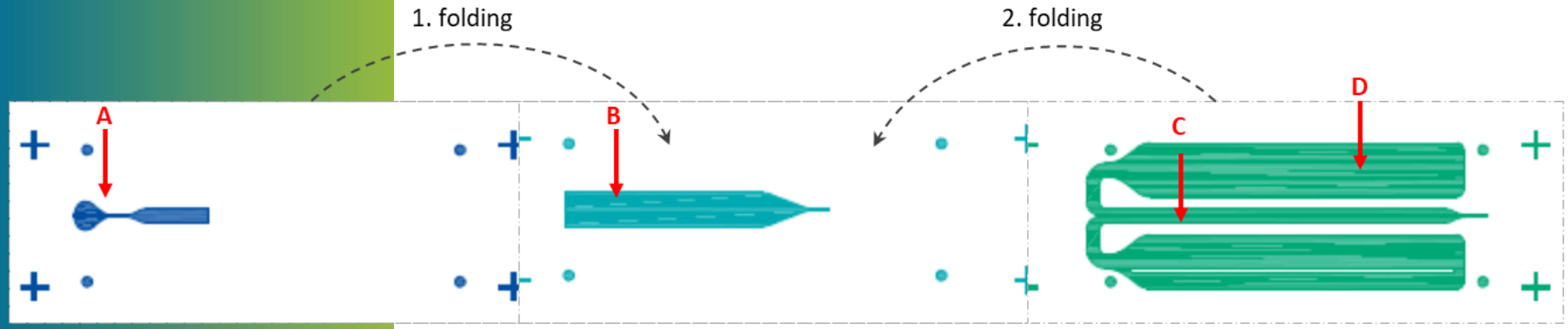
µ-fluidic pattern for guidance of neuronal cells

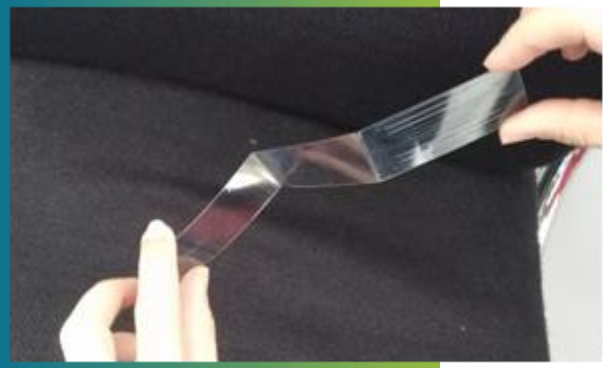
- Drug and assay testing
- Imprint pattern: µ-fluidic mesh with 17µm height, 5-10 µm width
- Fabrication speed: 1m/min
- Imprint resist: mr-UVCur26SF

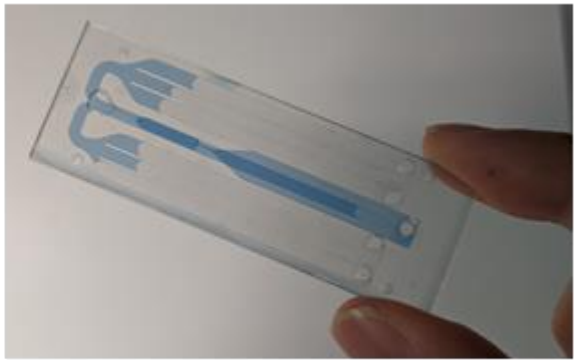
- ✓ Excellent cell compatibility towards neurons and other cells
- ✓ Low background signals due to optimized auto-fluorescence
- ✓ Improved signal deviation in preliminary assay testing due to well separated neurons

M.Lohse et. al, Nanomaterials 2021, 11, 902. https://doi.org/10.3390/nano11040902

Example 2: Origami Chips for 3D Microfluidics





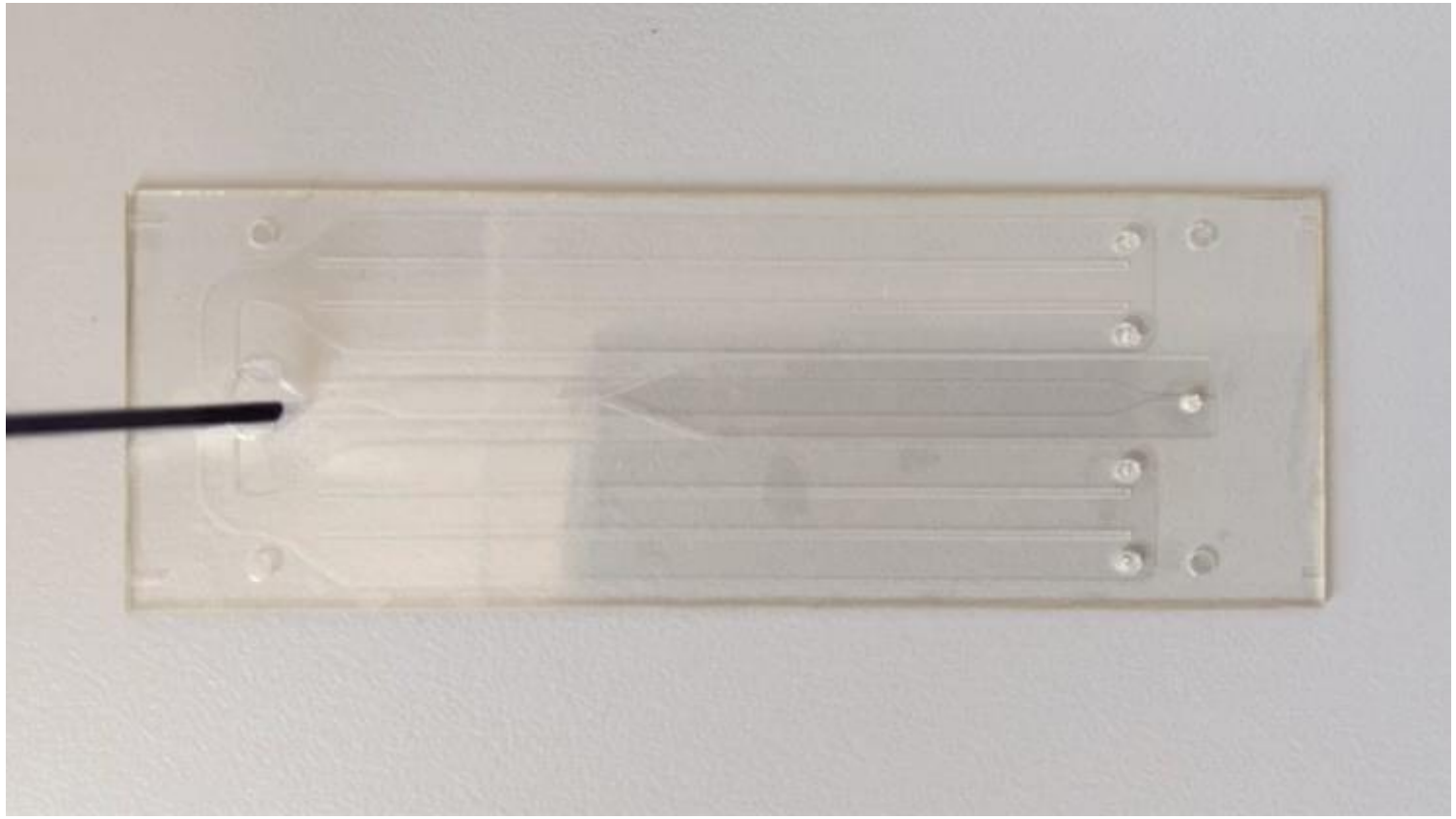


µ-fluidic channel imprinted on one side of substrate

- Possibility to integrate several functionalities
- Imprint pattern: µ-fluidic channels with 120 µm depth, mm wide
- Folding after laser engraving
- Fabrication speed: 1m/min
- Imprint resin: NILcure_JR21

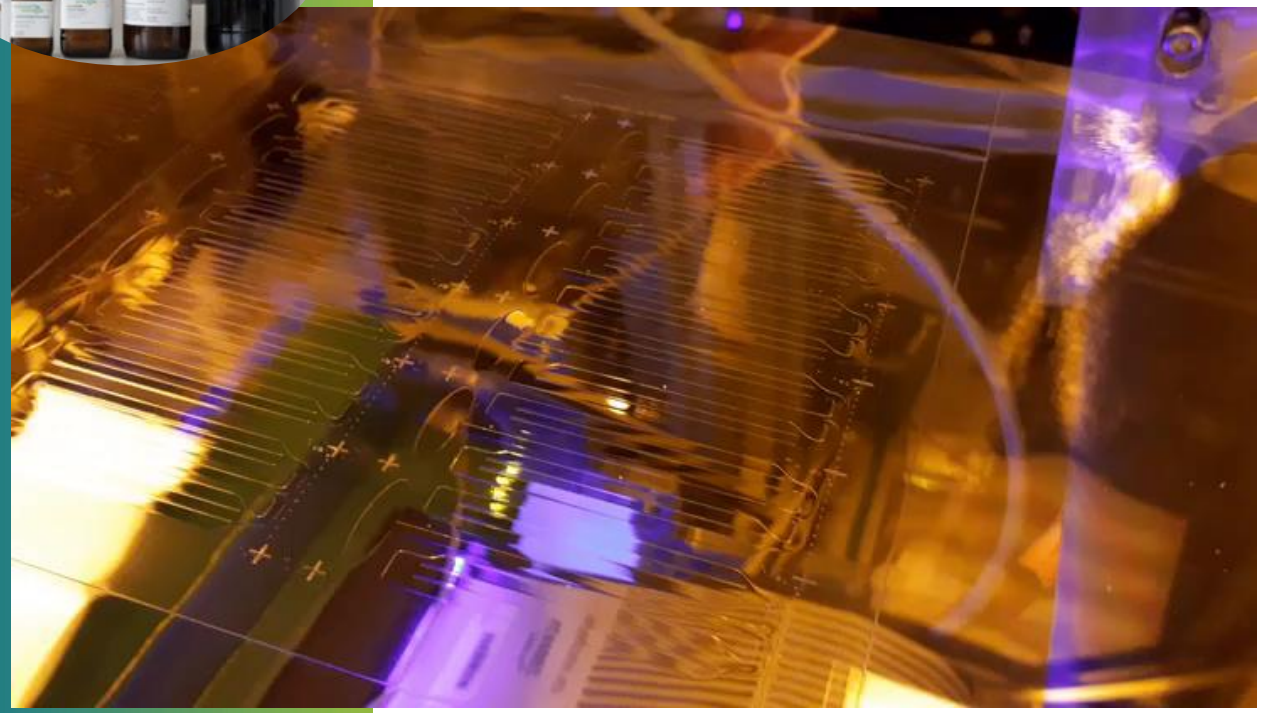
EP21157898.4

Example 2: Origami Chips for 3D Microfluidics



EP21157898.4

Example 3: Roll-to-roll based production of Lab-on-a-Foil



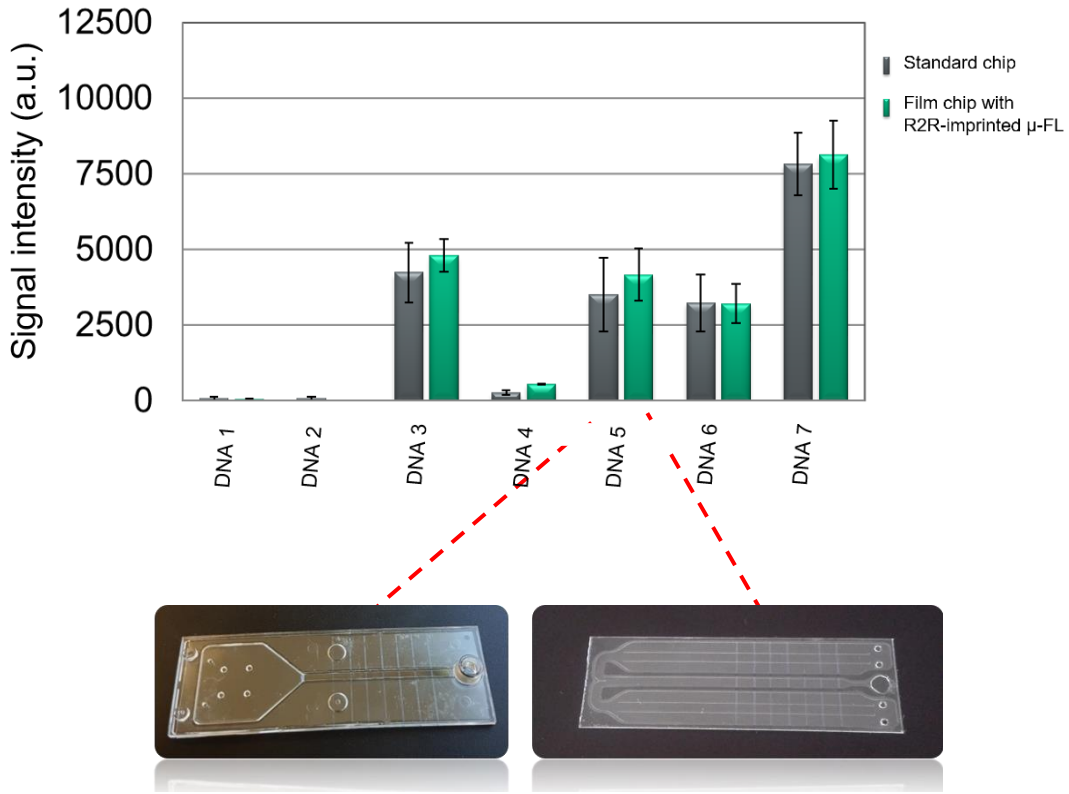
Fabrication of LoC Chip via R2R UV-NIL

- Imprint pattern: µ-fluidic chip with 150 µm height
- Fabrication speed: 4m/min
- Imprint resist: mr-BioNIL100SF_XPA

- ✓ Commercial readout system based on chemoluminescence
- ✓ Transfer of fluidic structures from injection molding to R2R-produced µF-channels
- ✓ Excellent filling of bonded chip due to intrinsic hydrophilicity
- ✓ Adjusted surface chemistry allows direct spotting of antigens
- ✓ Fast R2R fabrication with up to 1000 chips/hour

P. Tören et al., MRS Advances 2021, https://doi.org/10.1557/s43580-021-00064-7;
P. Tören et al., Lab on Chip 20, 4106 (2020)

Example 3: Roll-to-roll based production of Lab-on-a-Foil

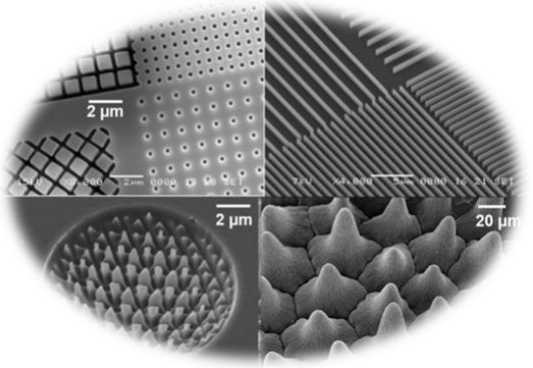


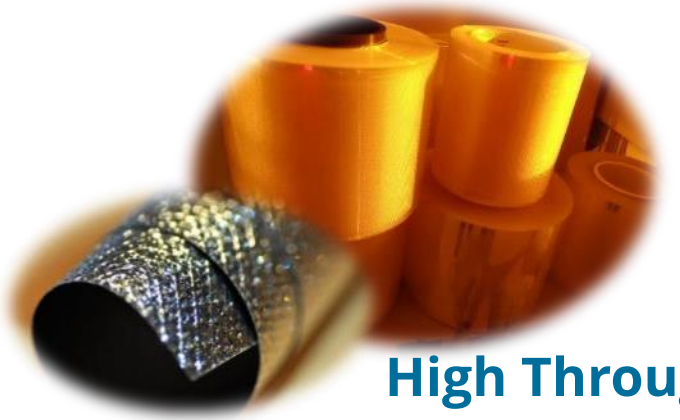
Transfer of fluidic structures from injection molding to R2R-produced µF-channels

Conclusion of Roll-to-Roll UV Imprinting

Adjustable Properties

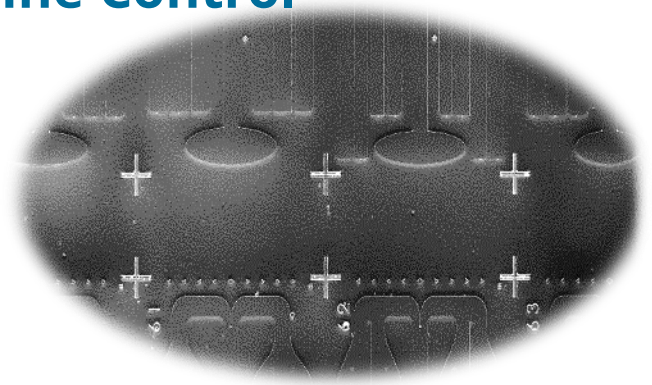
Multiple structures





High Throughput

Inline Control



Microfluidics InnovationHub

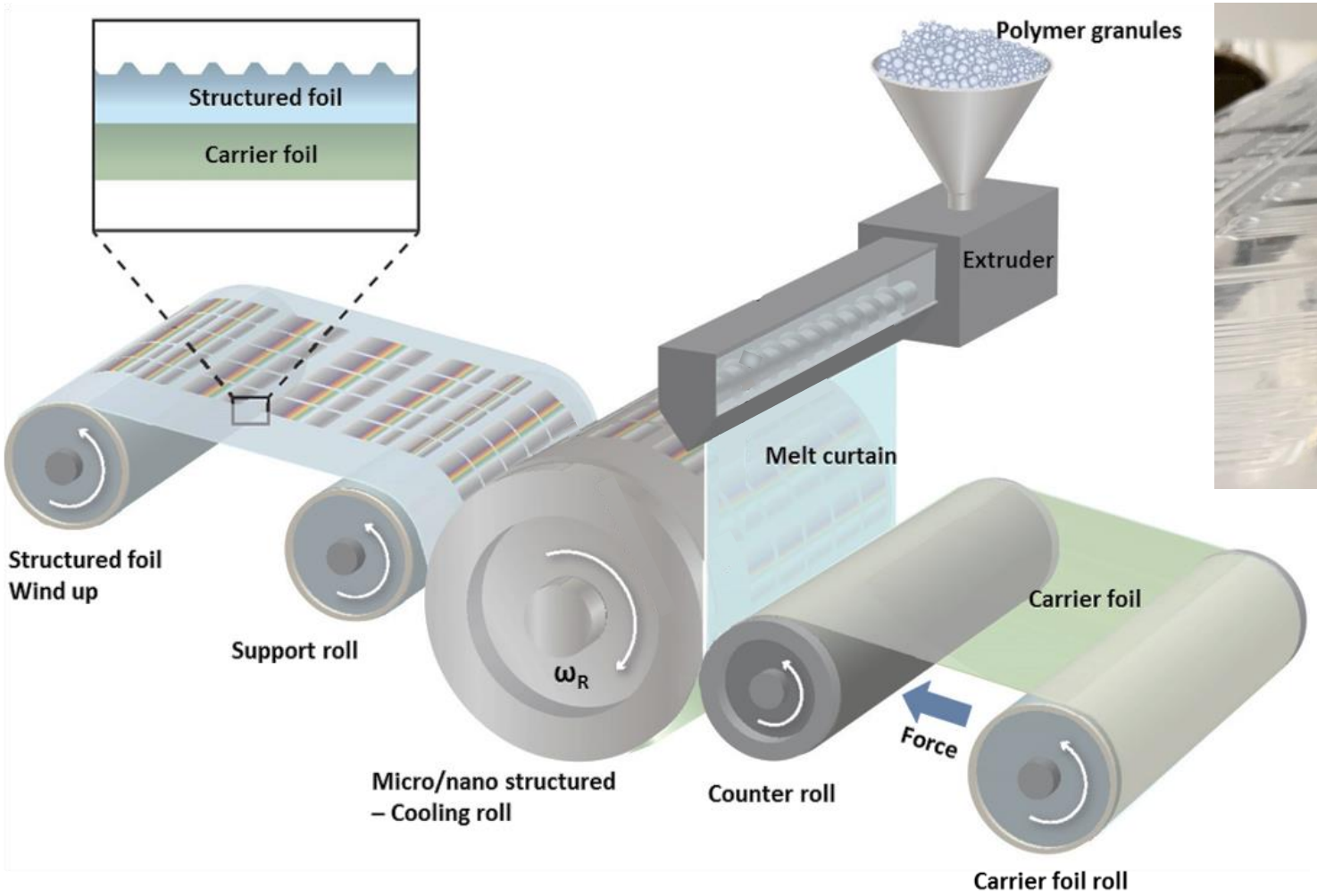
Roll-to-roll Extrusion Coating

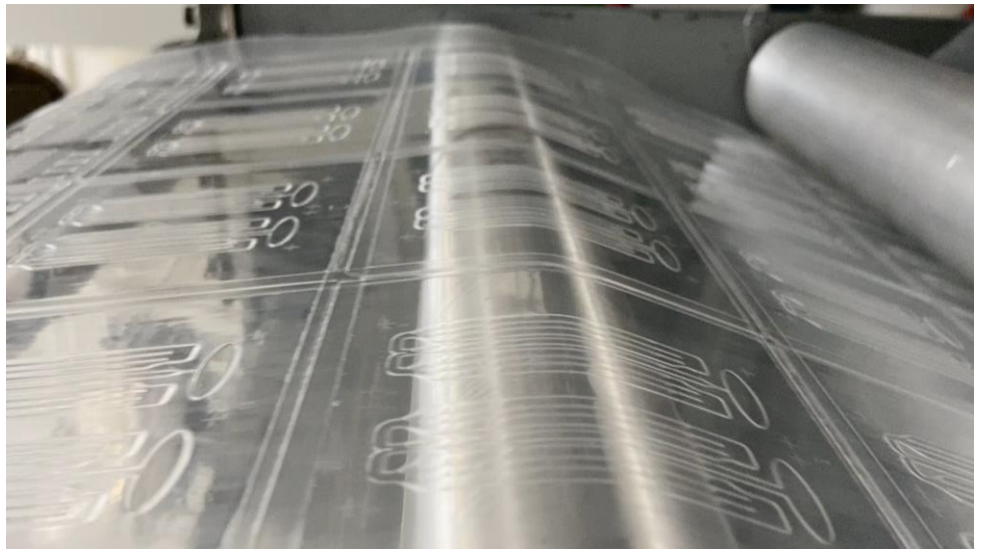
INMOLD



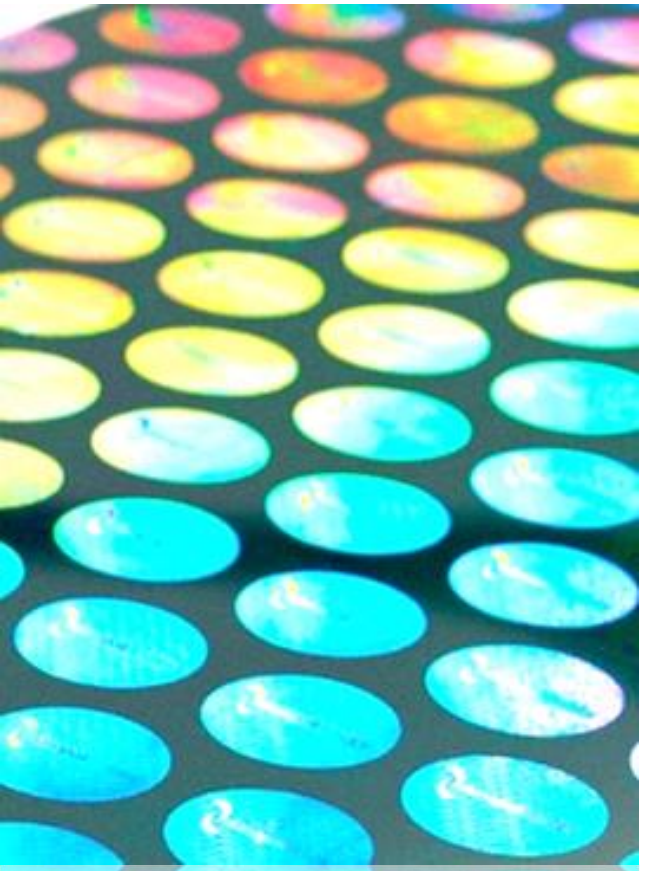

Inmold A/S

Principle of R2R-Extrusion Coating



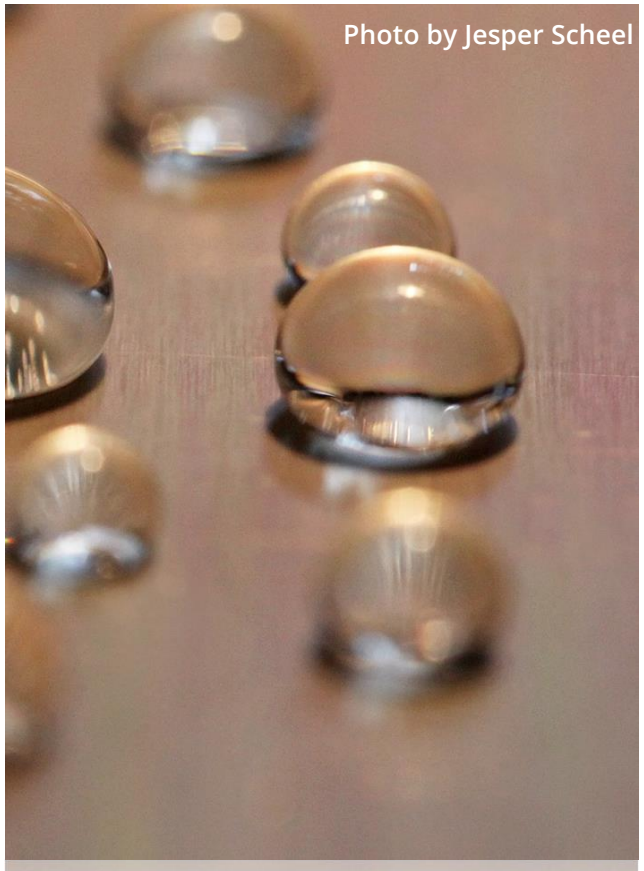


Surface patterning for surface functionalization

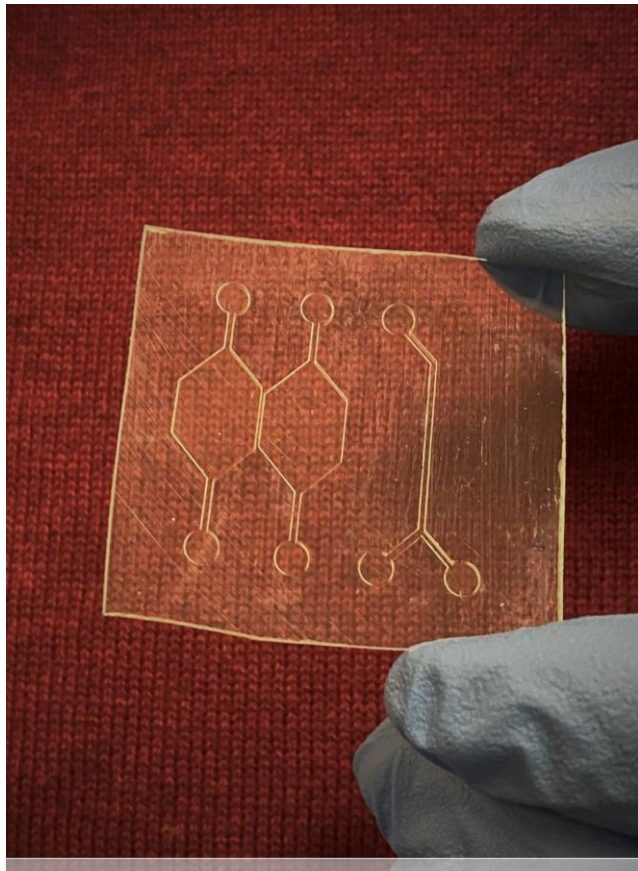


Decorative films

Plasmonic films



Hydrophobic films



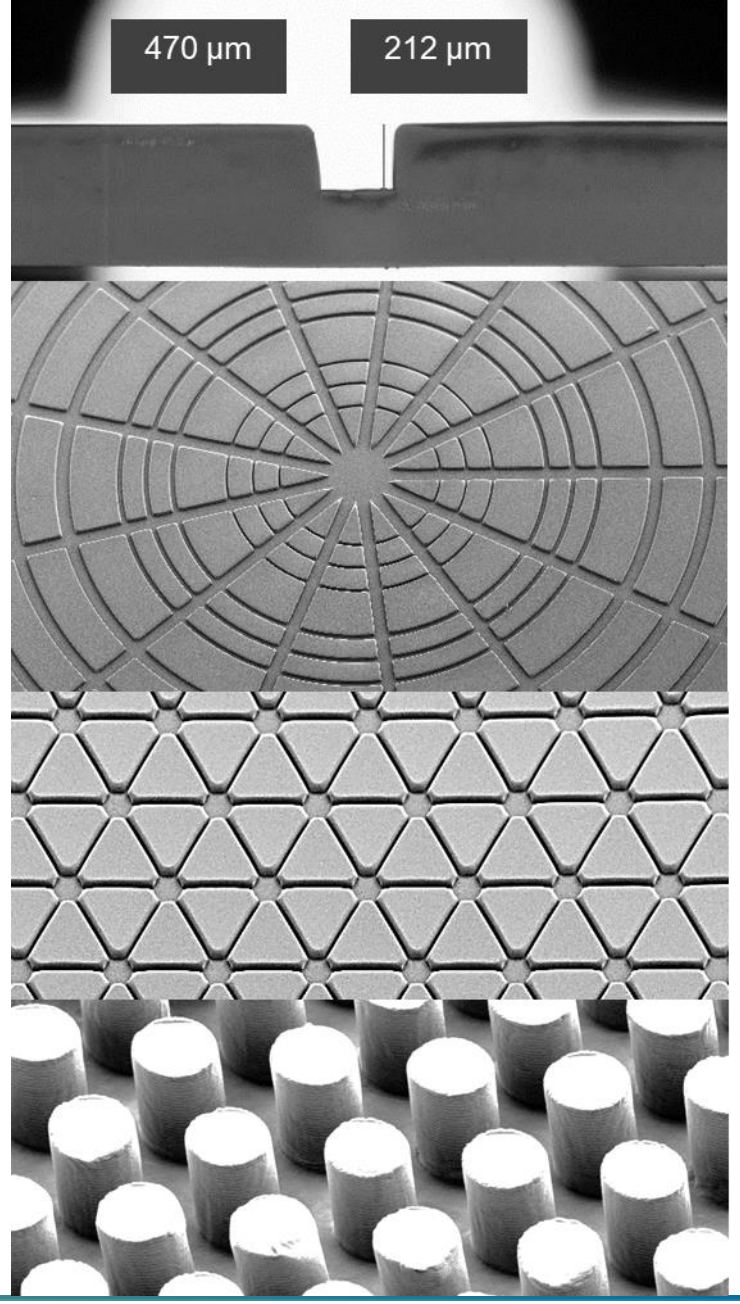
Life-science applications

Why R2R-EC for life-science?

- Thermoplastic polymer (TP):
  - Polypropylene (PP)
  - Polystyrene (PS)
  - Cyclic Olefin Copolymer (COC)
  - Other materials on request
- Chemical surface functionalizations established for TP are applicable
- Traditional bonding methods useable
- High production speeds of several m/min fulfill increasing demand of microfluidic market

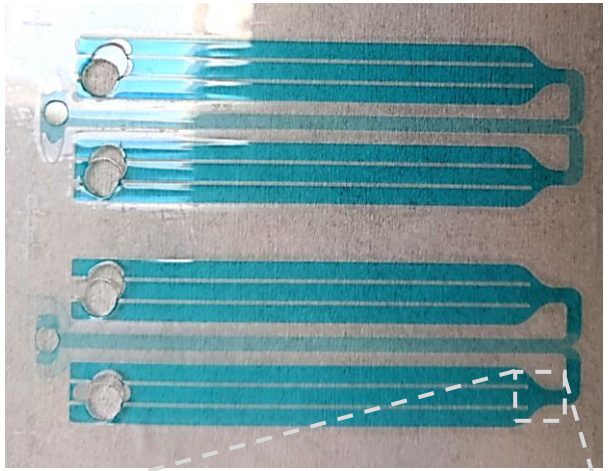
Advantages of R2R-EC

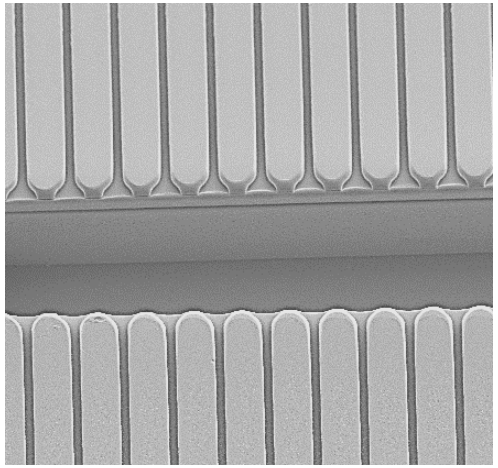
- Film production with thicknesses up to 500µm (structure imprint depth of up to 300µm)
  - High rigidity of produced films
  - Less material due to exclusion of bulk
  - Short distance between samples and detector
- Patterning of large surface areas possible allowing upscaling of microfluidic design
- High directional freedom of design (for AR ≤1)
- No draft angle necessary

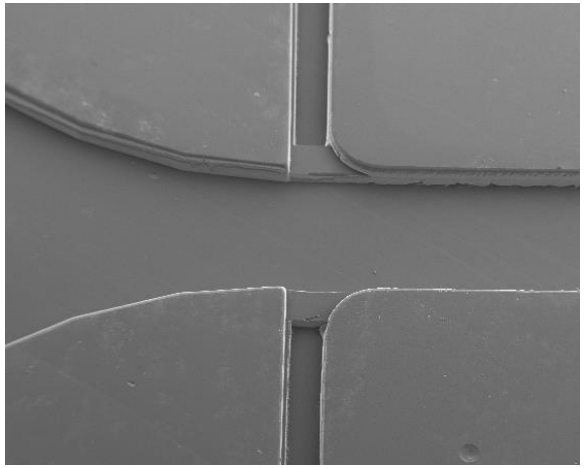


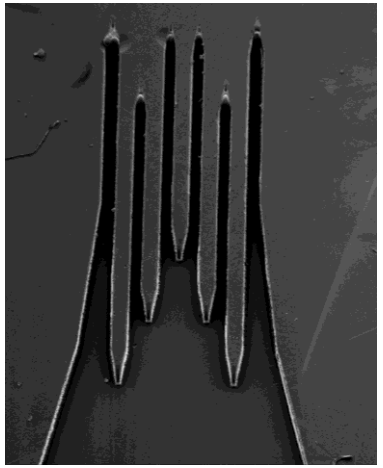
Imprint technology for complex microfluidic designs

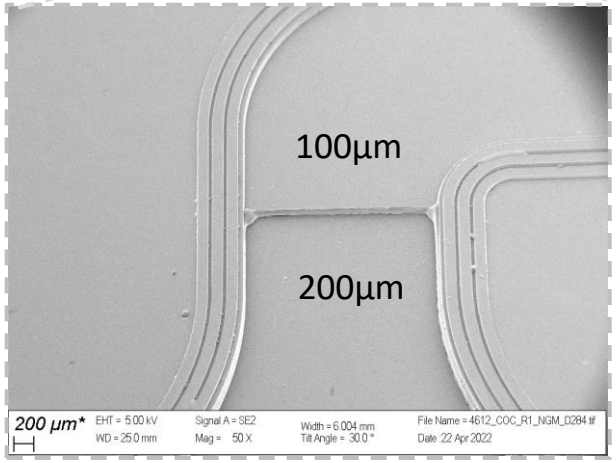
- Implementation of energy directors for bonding
- Multiple-level fluidic networks
- High through-put filters
- Large area mixers for life-science application





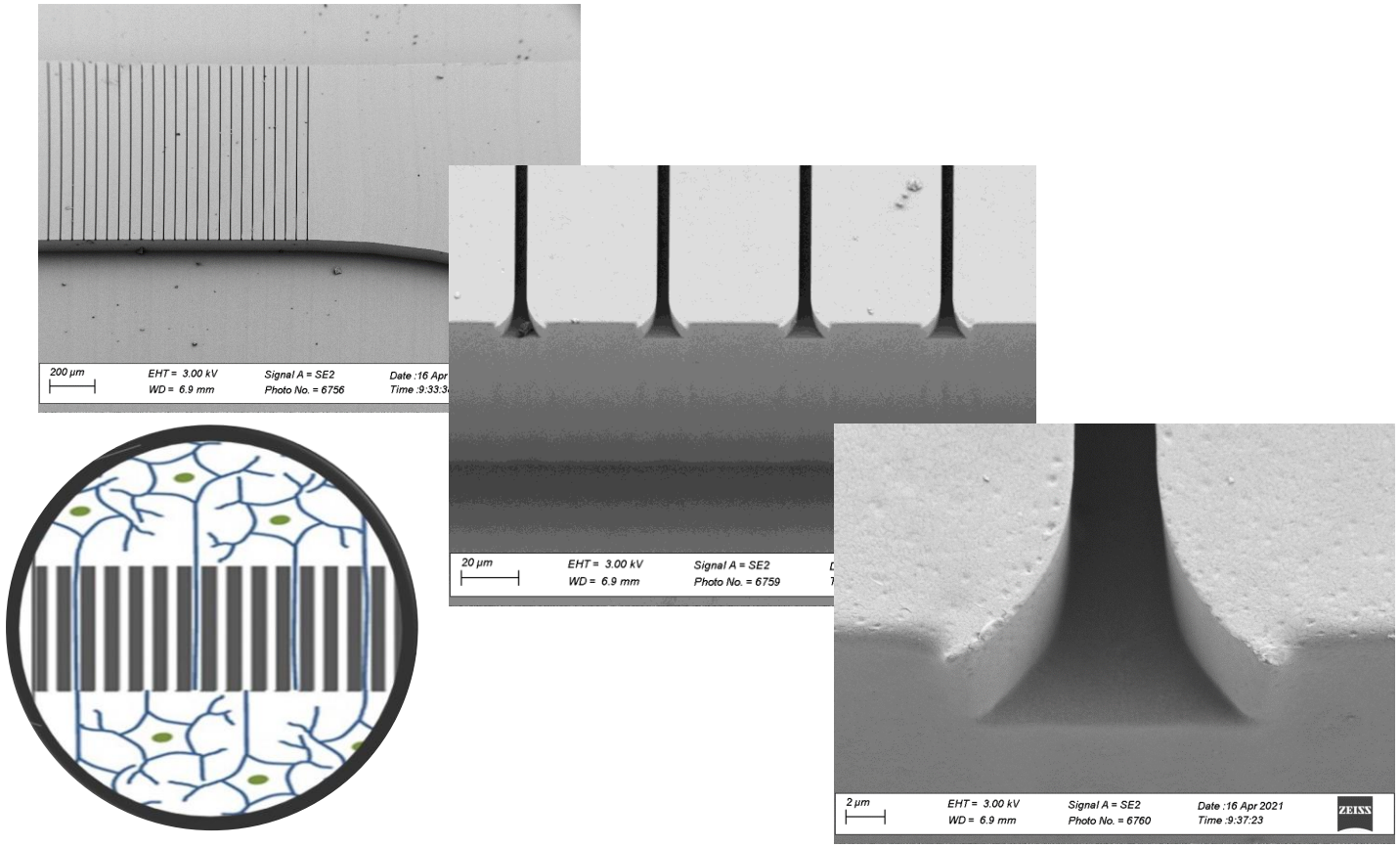




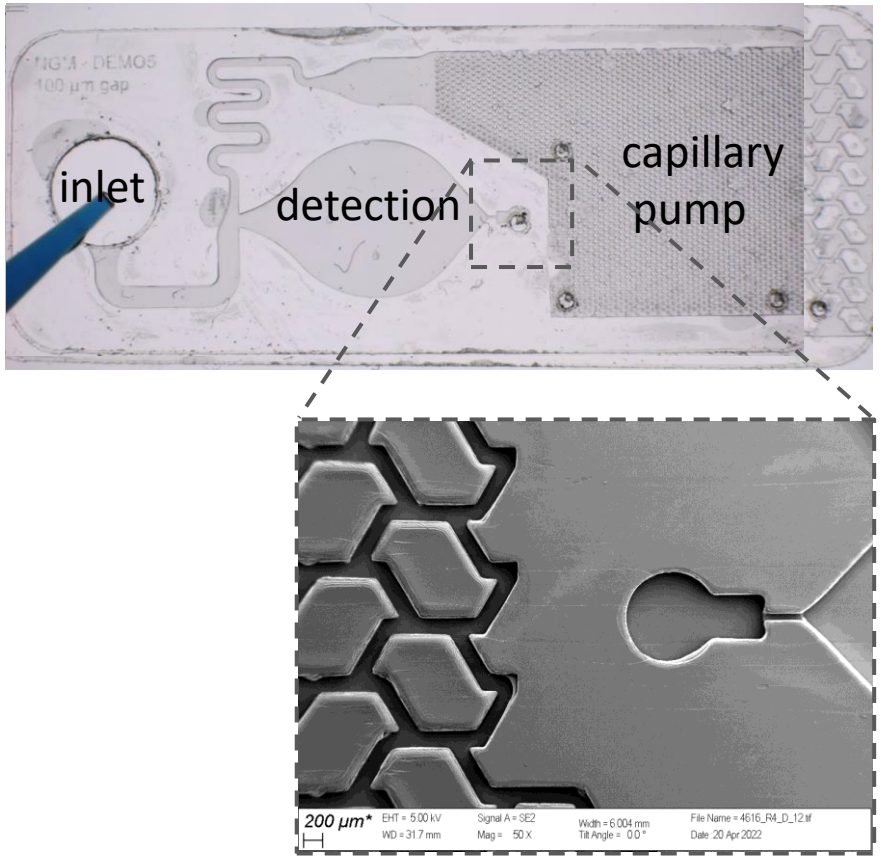


Examples of high aspect replication

Cell culture device

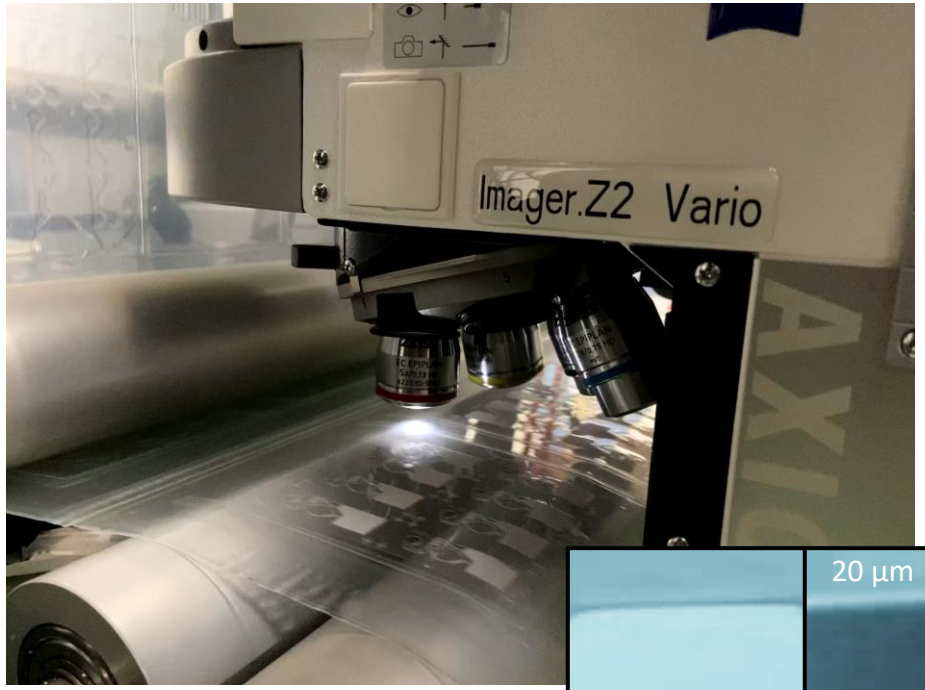


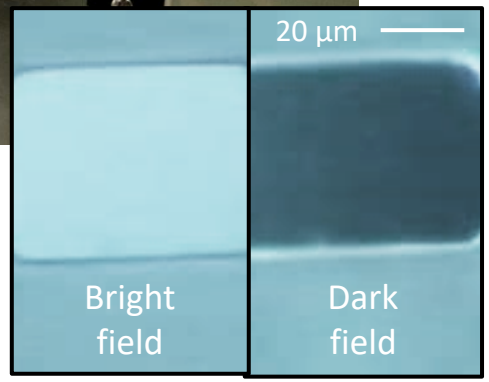
Sensor for Bioreactor Control



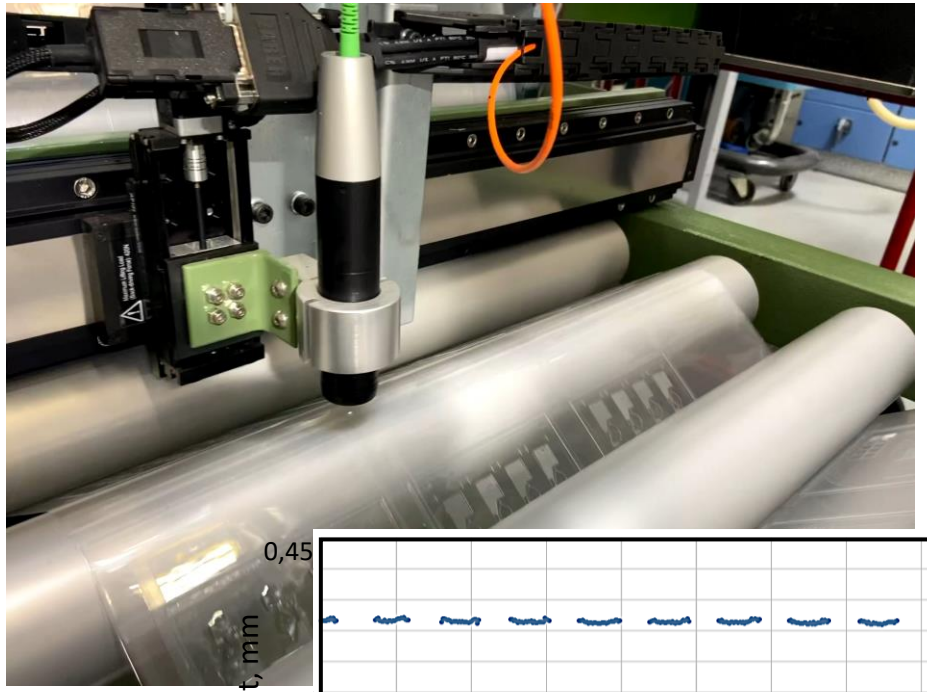
In-line Quality Control

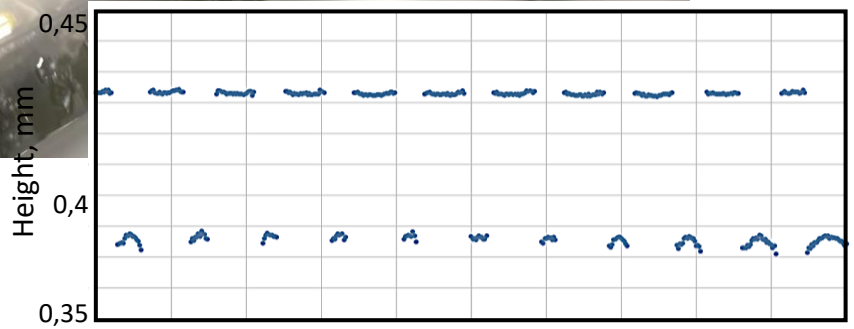
Optical Microscope





Confocal Microscope





50 µm structures imaged at a speed of 5 m/min

Summary R2R-Extrusion Coating

- Large-scale replication technique using thermoplastic polymer
- Surface functionalization and bonding techniques developed for thermoplastic polymers are compatible with R2R-EC
- Unique imprint regime allows replication of complex fluidic systems with substrate thicknesses up to 500µm
- Inline control allows quality control and parameter adjustment during production

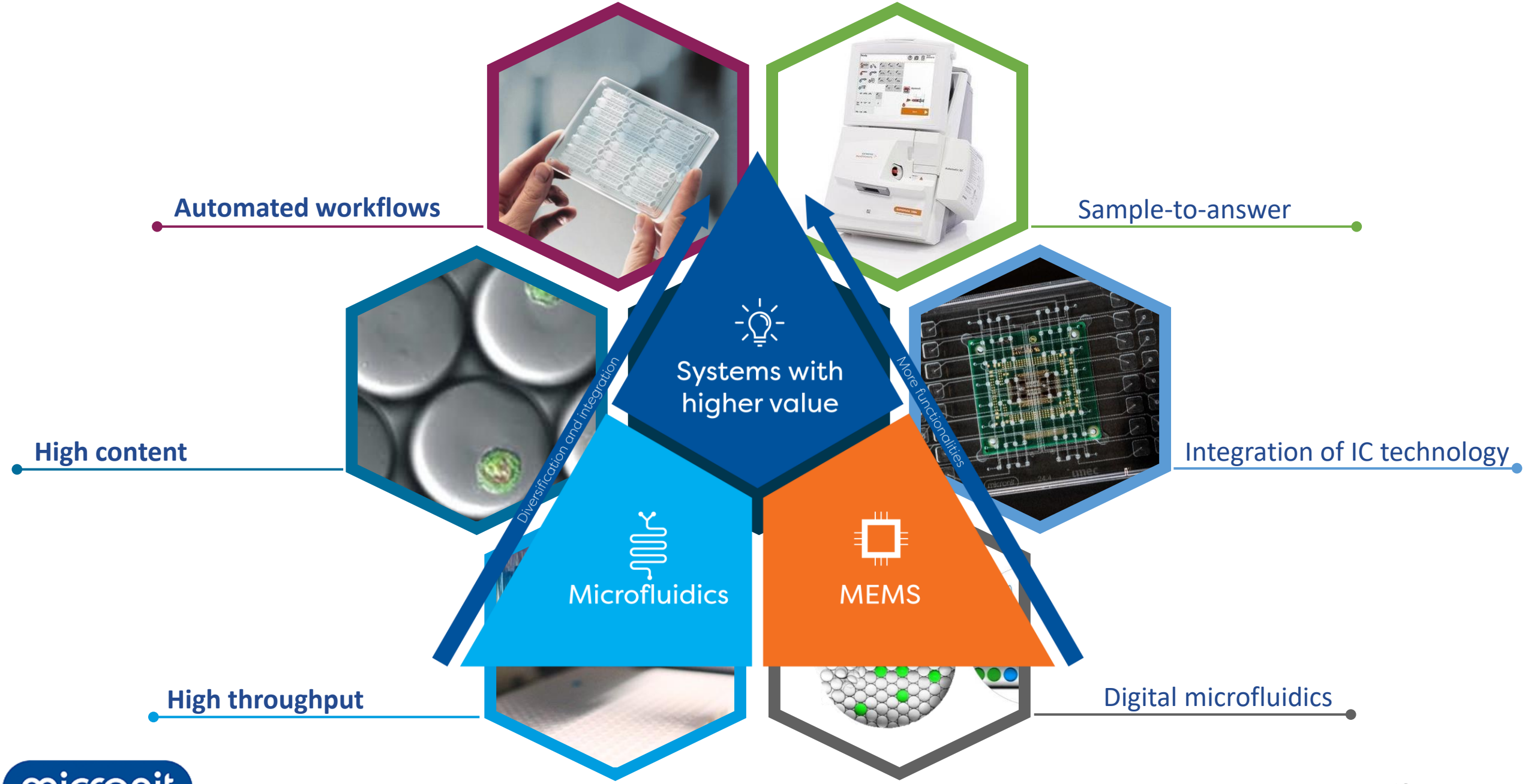
Microfluidics InnovationHub

Back-end Processing

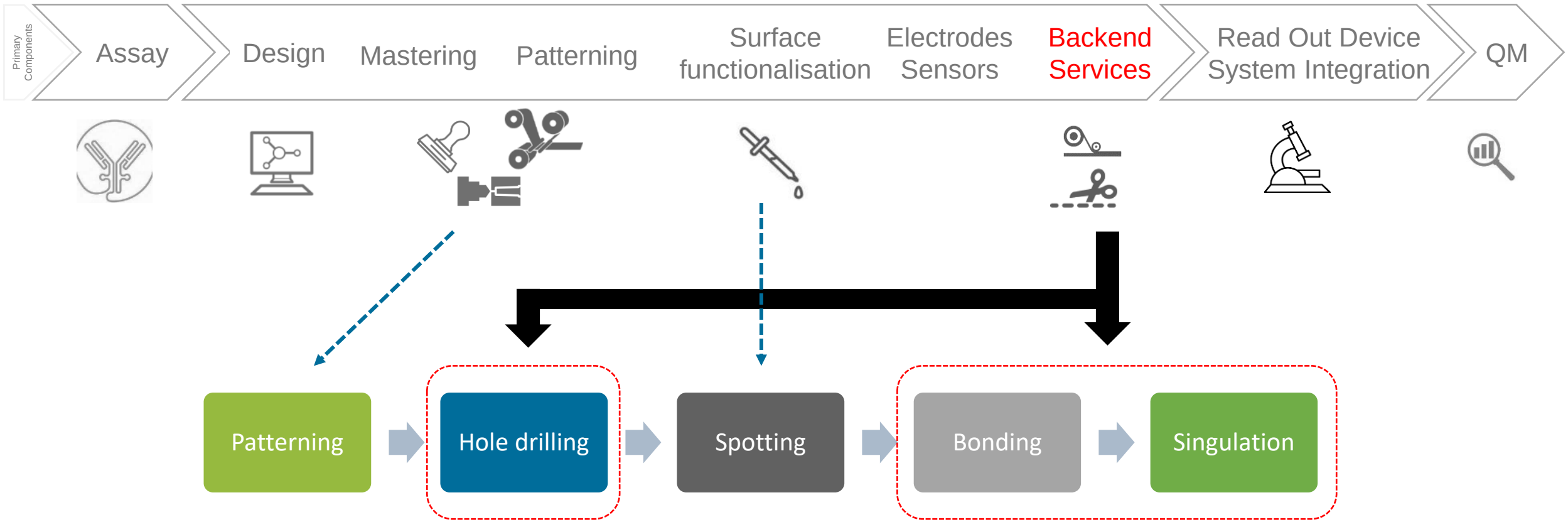
micronit

Micronit BV

- Founded in 1999
- Located in Enschede, the Netherlands and Dortmund, Germany
- 1000+ customers in 50+ countries
- We serve leading companies in the top 25 of life science, diagnostics and biotechnology industries and world's top 10 technical universities
- 120+ highly educated, multi-disciplinary employees, 15+ nationalities
- ISO 9001 and ISO 13485 certified


Automated workflows
Sample-to-answer
High content
Integration of IC technology
High throughput
Digital microfluidics
Systems with higher value
Microfluidics
MEMS
Diversification and integration
More functionalities

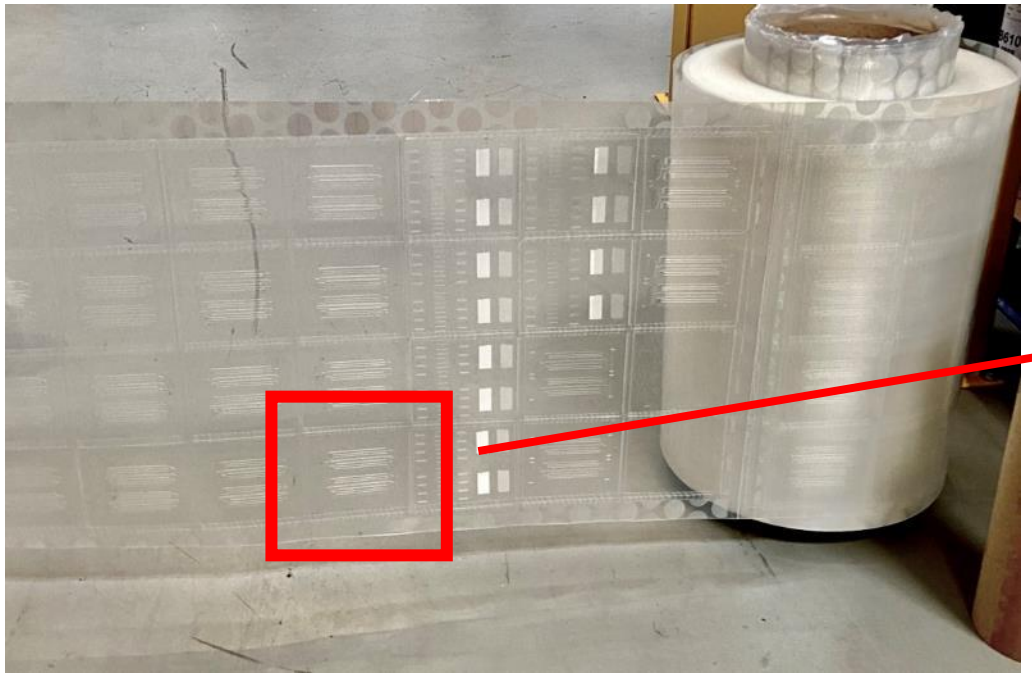
Process overview

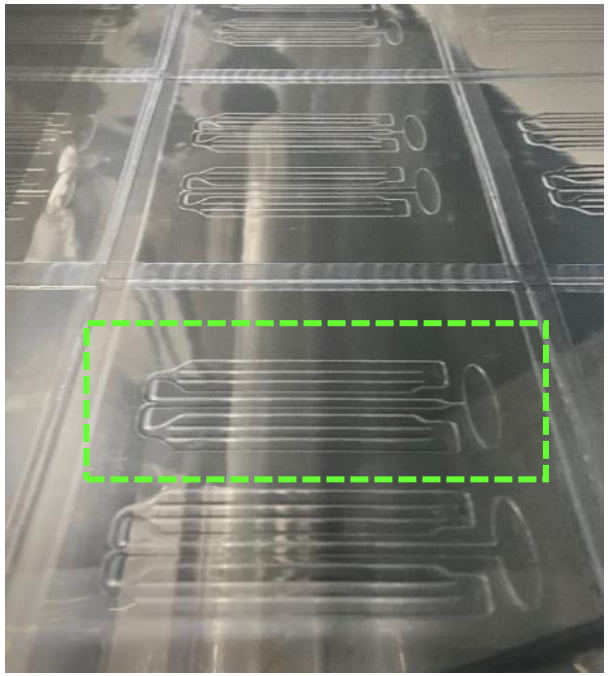


The foils – Example EC COC

Patterning

Un-winded roll

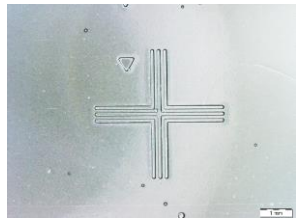




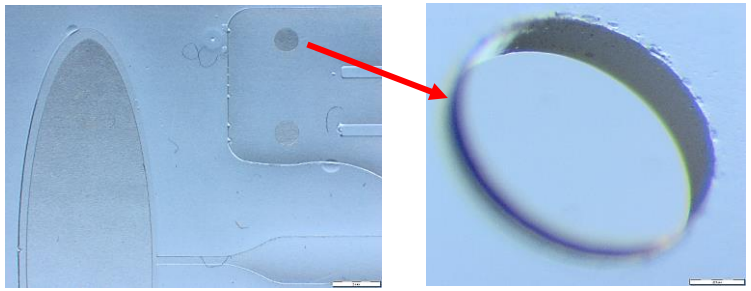
“Chip”

Hole drilling

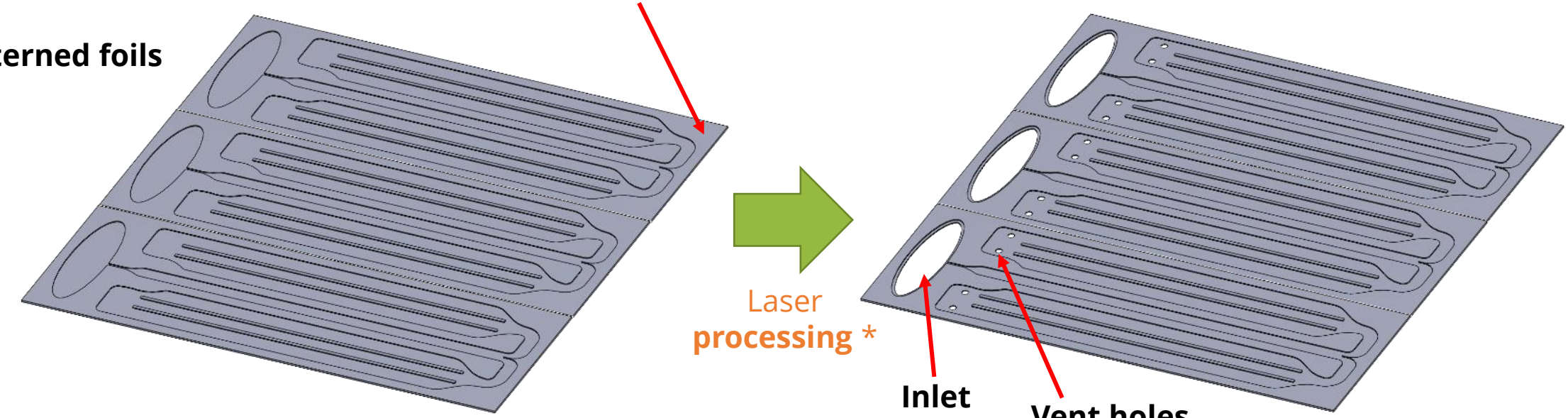
Fiducial in transparent material



Example of laser-drilled holes



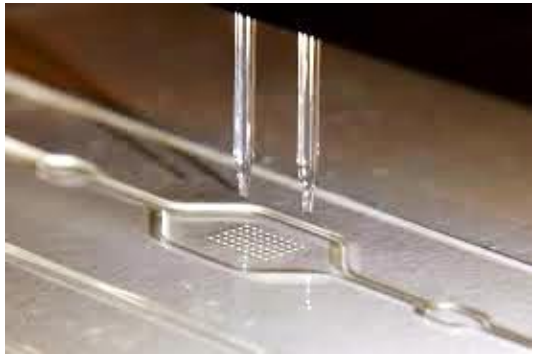
Patterned foils



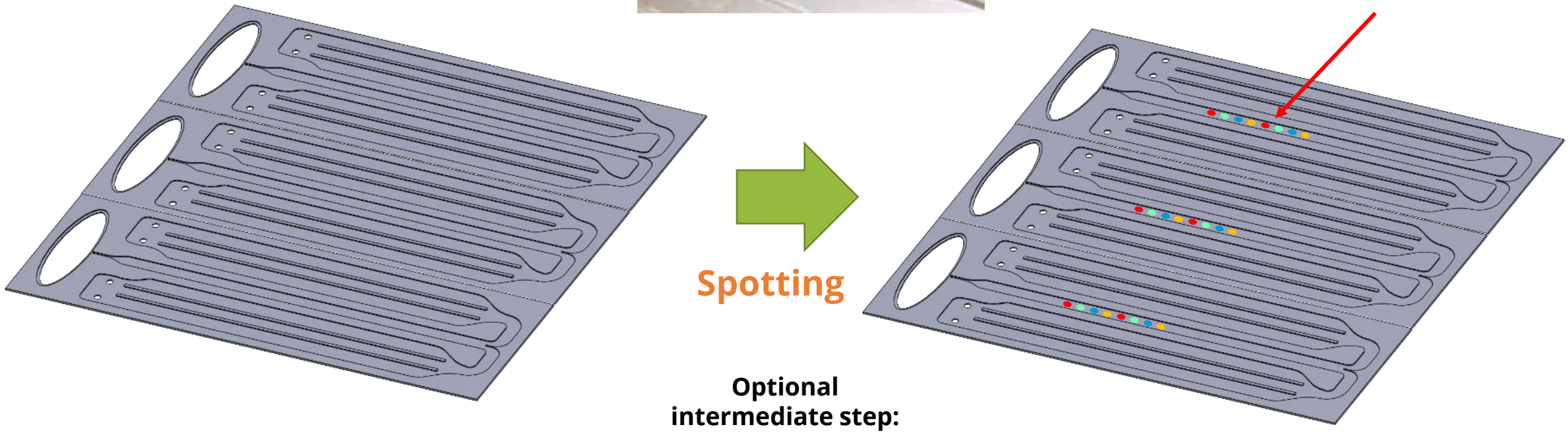
* including vision system to align on imprinted fiducials

Spotting

Example of a spotting process

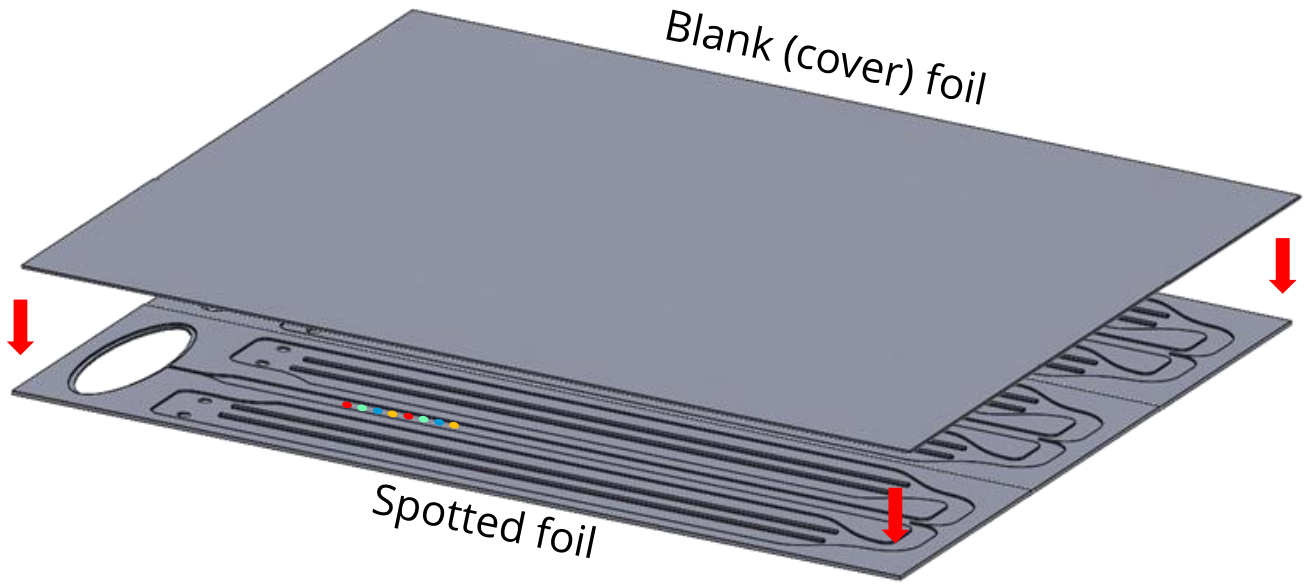


Spotted antibodies



Optional intermediate step:
surface activation

Bonding



Available bonding techniques

1. Extrusion coating
   - Solvent-assisted bonding
   - Ultrasonic welding
   - Thermal lamination
   - Laser welding *
2. UV-NIL
   - Partially cured resin

* Method under investigation

Bonding - EC

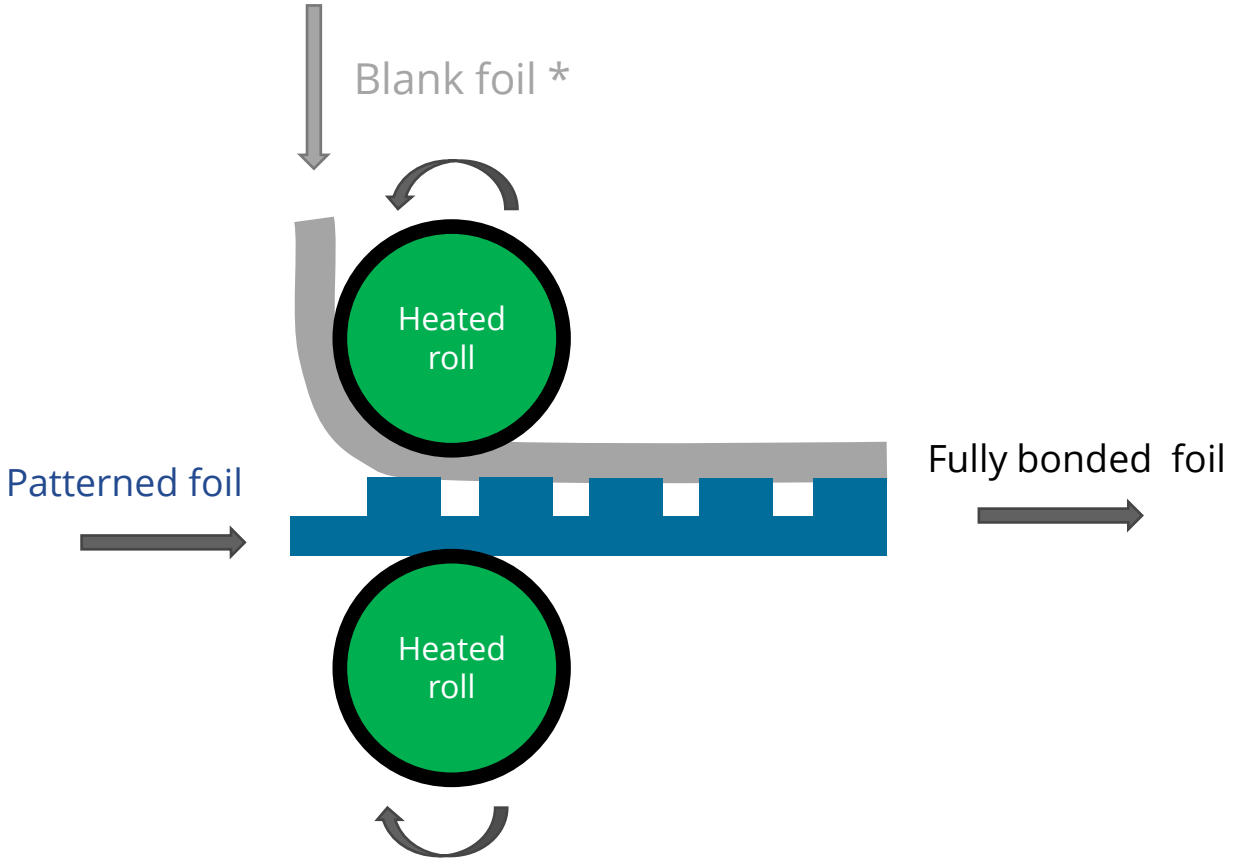
Bonding

R2R thermal lamination

- High throughput and simple process
- Temperatures above the Tg of the material → integrated biology degradation

R2R solvent-assisted bonding

- High throughput yet complex process (dangerous solvent vapors)
- Temperatures below the Tg of the material → integrated biology degradation preservation
- Solvent residues might alter cell-based assays and/or biology

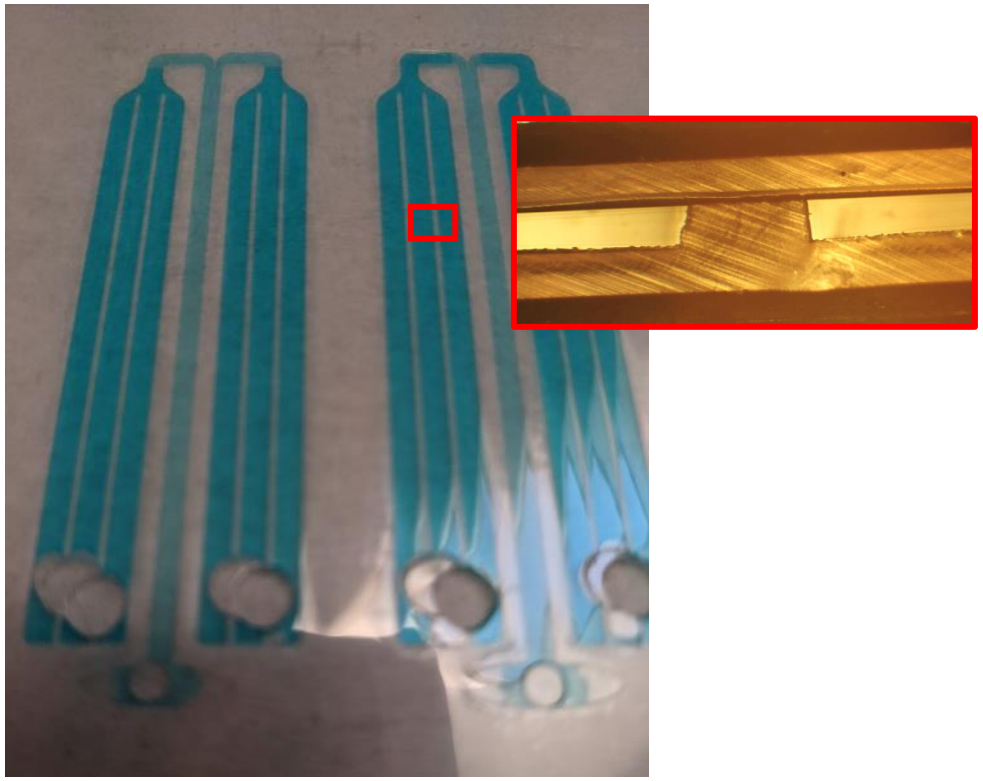


* Previously exposed to solvent for the solvent method

Bonding - EC

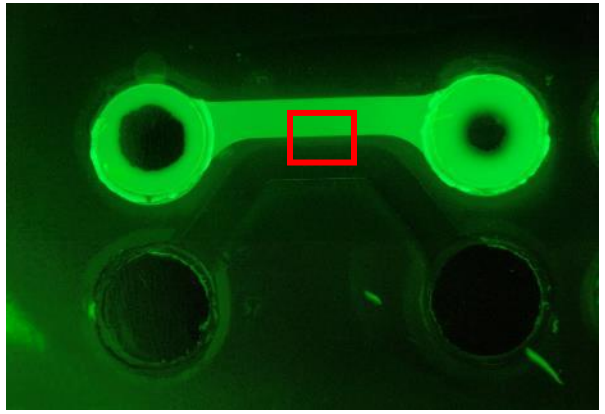
Examples R2R thermal lamination

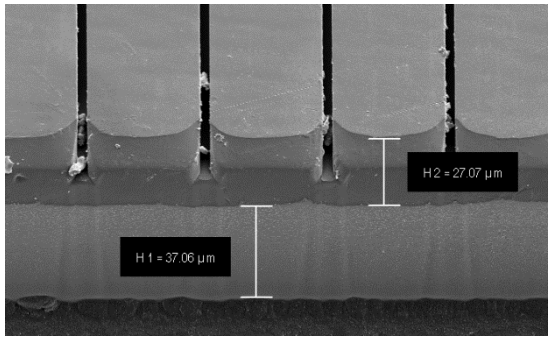
Antibody SARS-CoV2 test

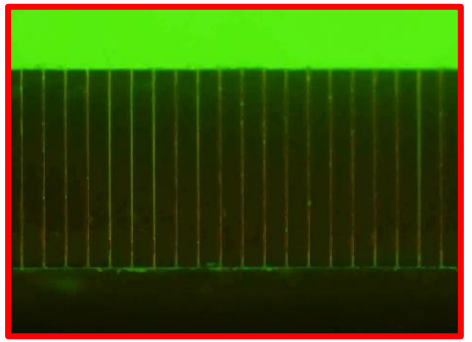


Examples R2R solvent-assisted bonding

Neural cell culture device



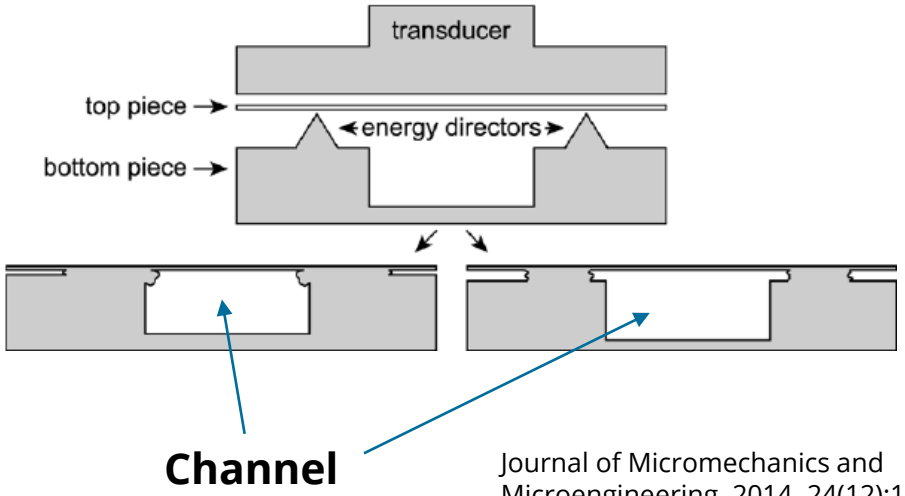




Bonding - EC

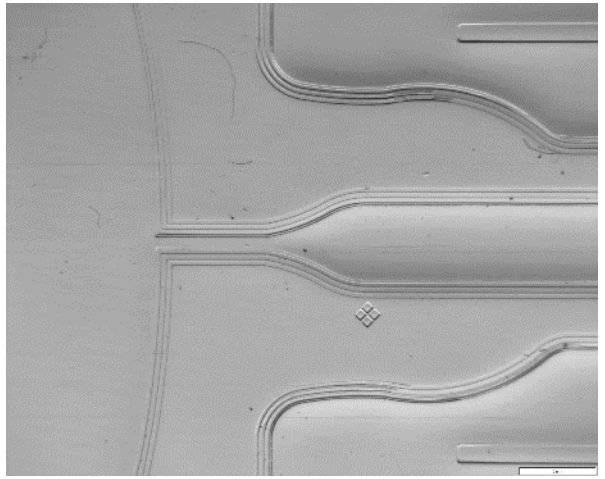
Ultrasonic welding

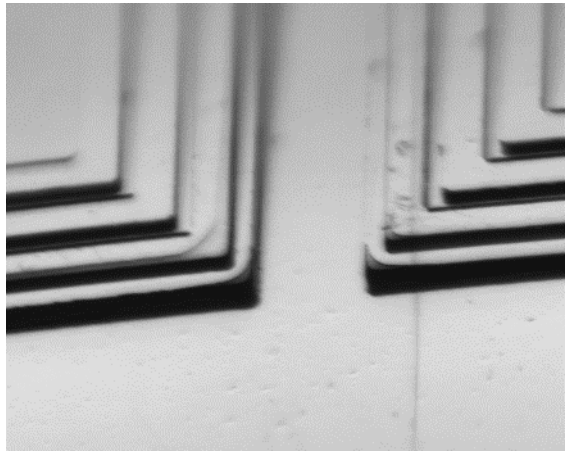
- Mid throughput process (can be implemented R2R in a stop & go fashion)
- Low-temperature process → preservation of biology
- No solvents/promotors involved

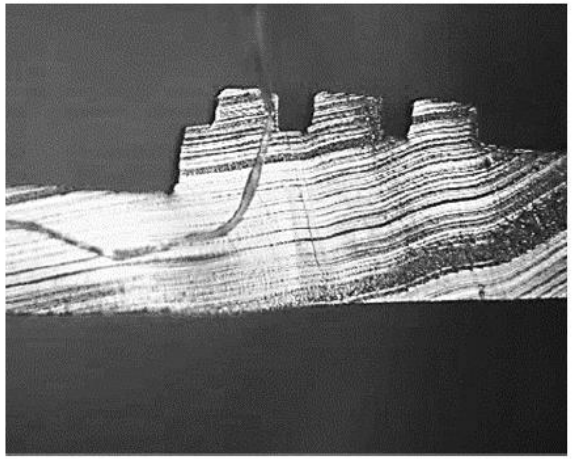


Journal of Micromechanics and Microengineering, 2014, 24(12):125007

Energy directors patterned directly on foils

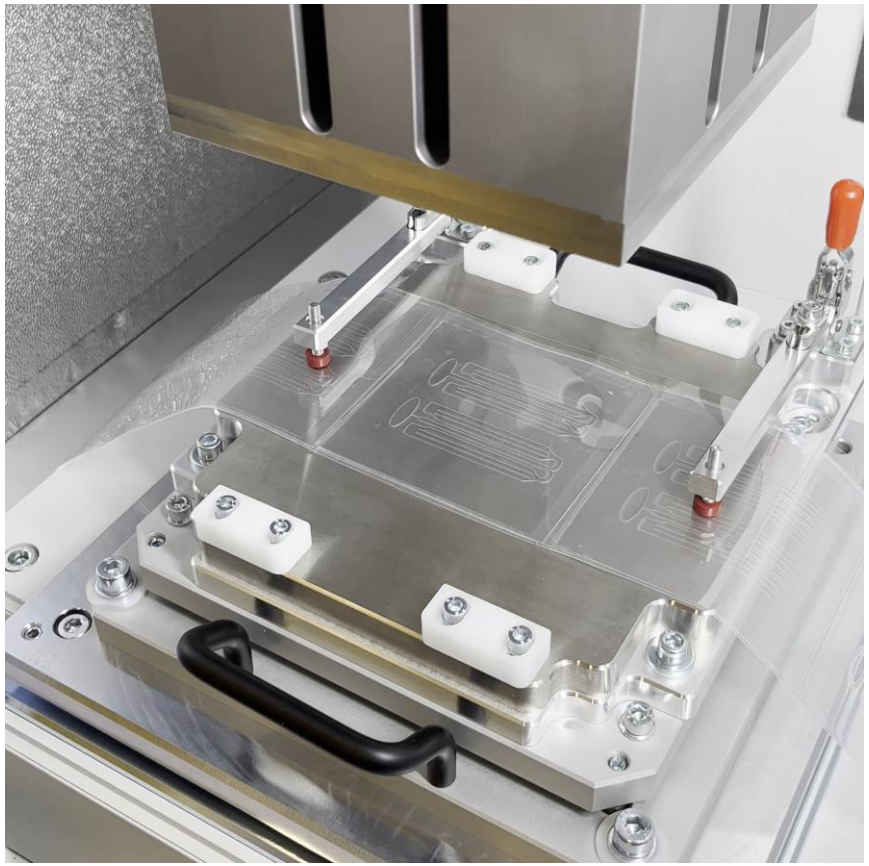


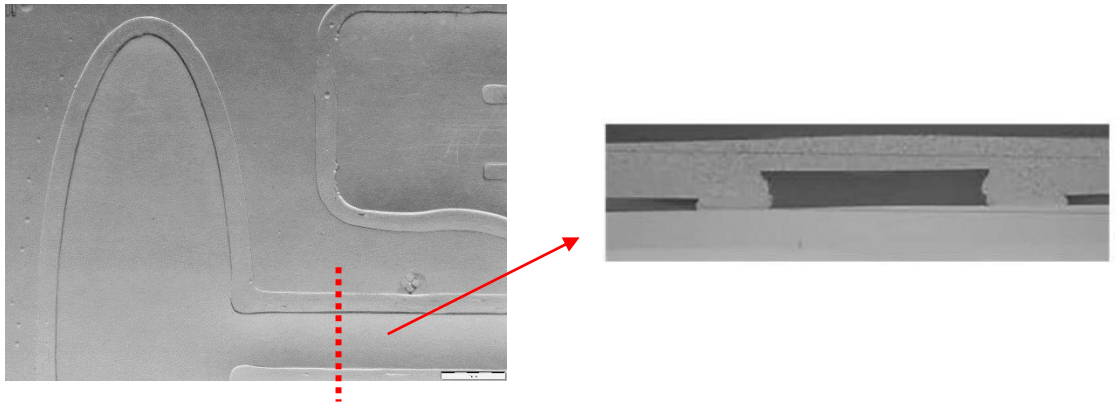




Bonding - EC

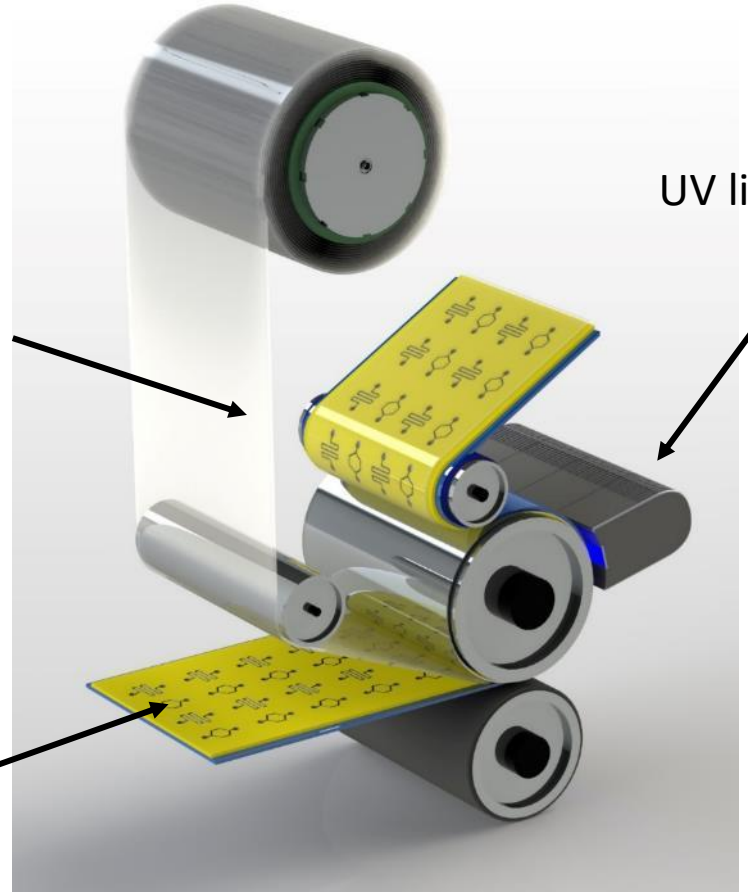
Results





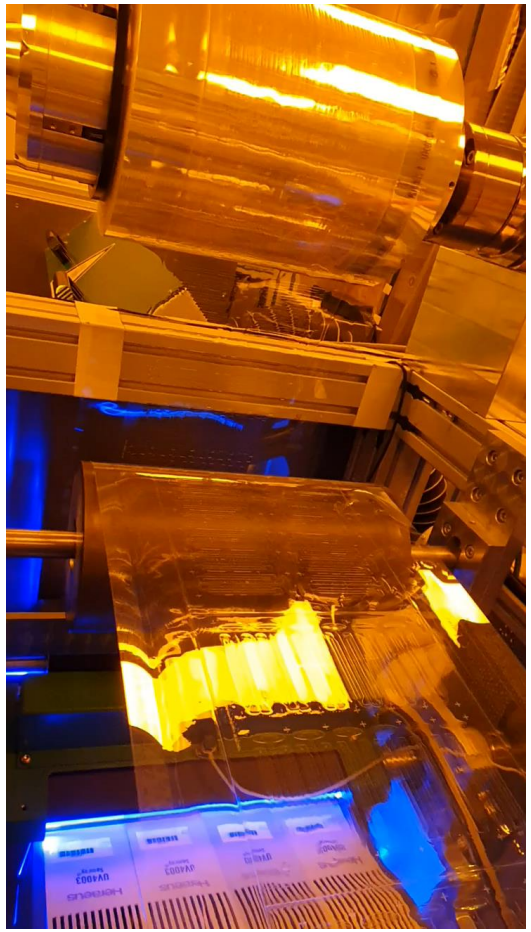
Bonding – UV Imprinting

Foil with a very thin (~µm) uncured same resin



UV light + pressure

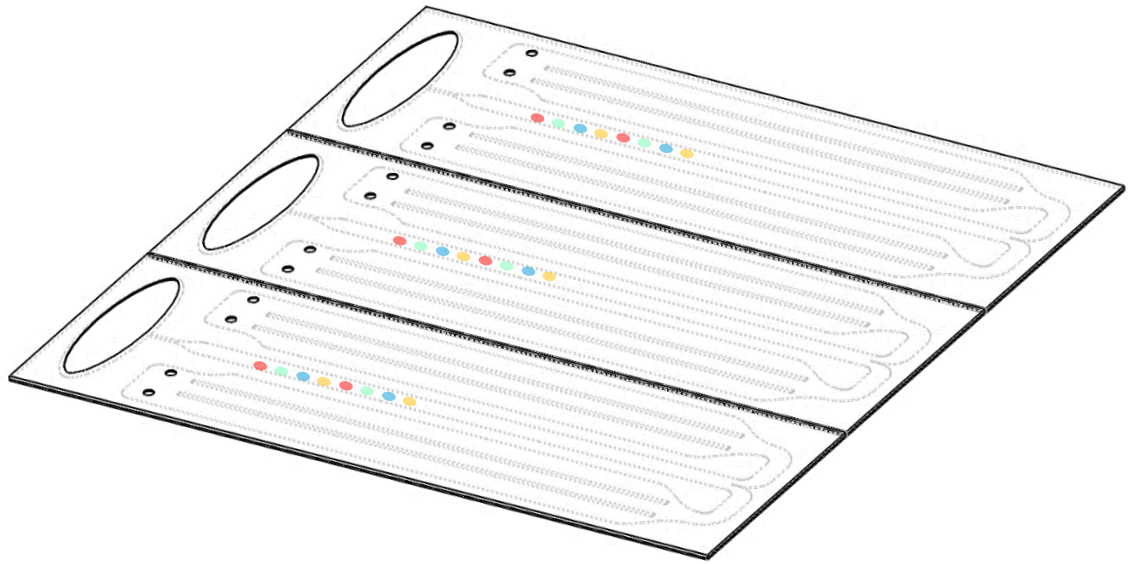
Partially cured structures



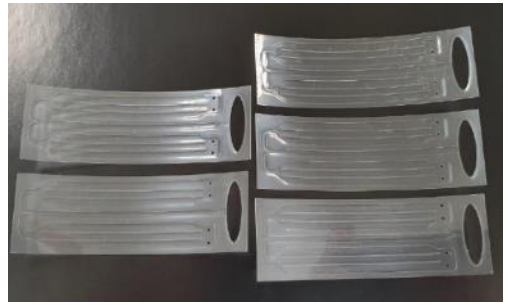
DE102020114621A1
WO2021244796A1

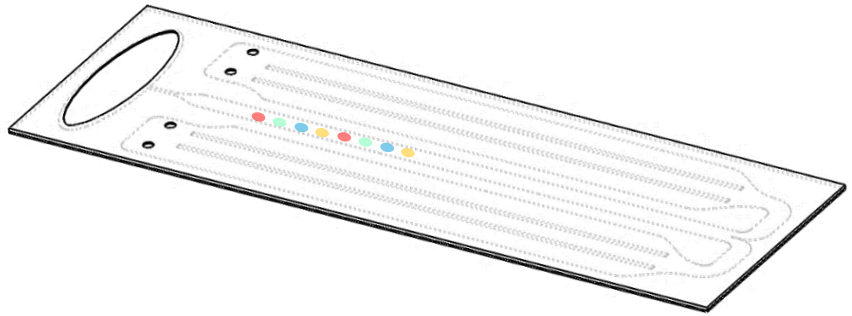
Singulation

Singulation



Laser processing *

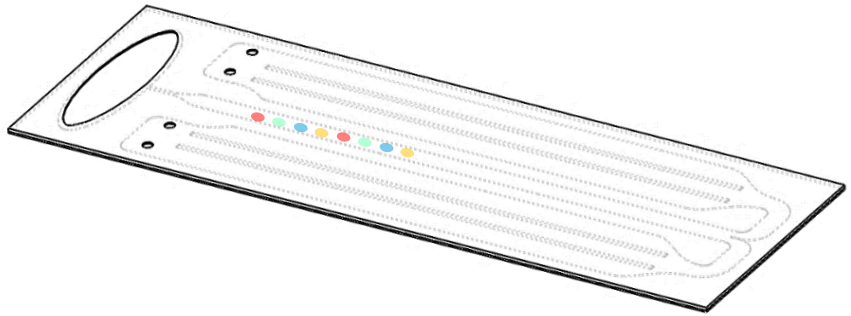


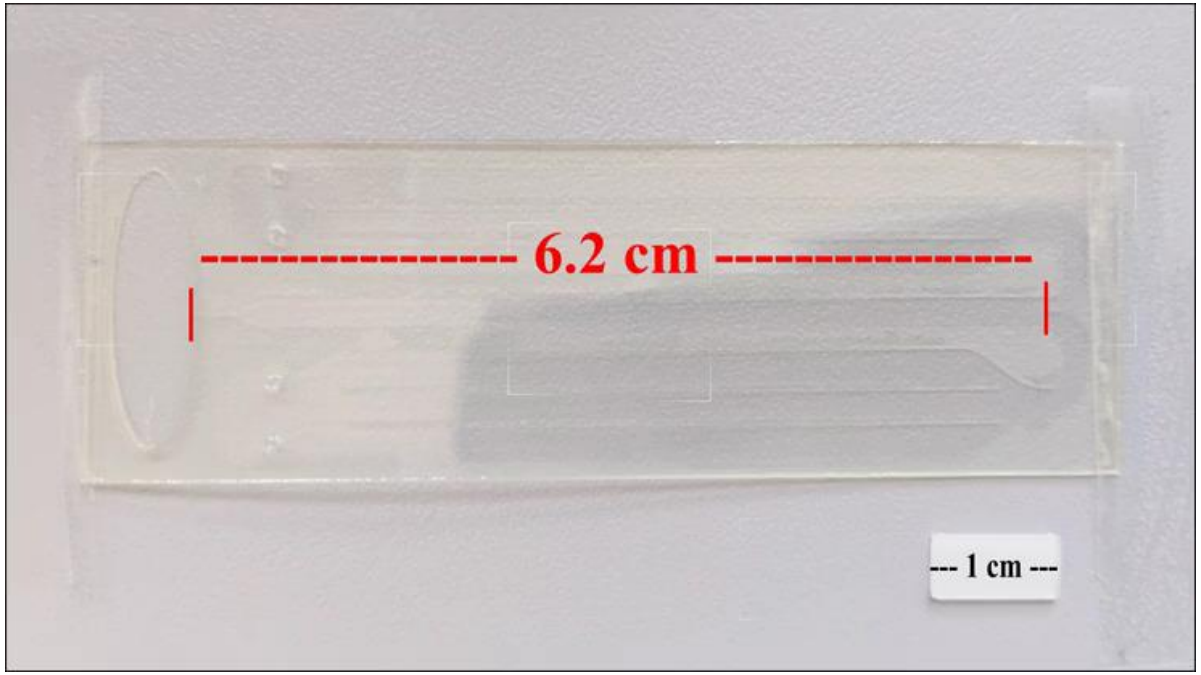


* including vision system to align on imprinted fiducials

Singulation

Final lab-on-a-foil





Microfluidics InnovationHub

SUMMARY

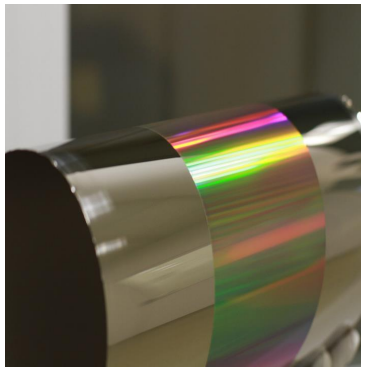
Topics Presented

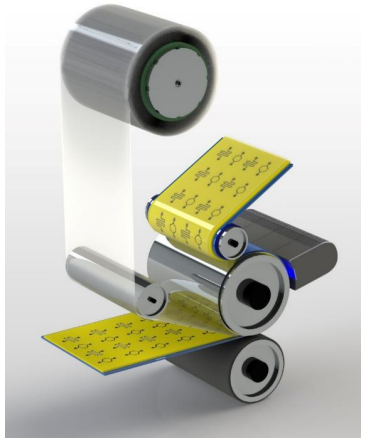
Primary Components | Assay | Design | Mastering | R2R Patterning | Surface functionalisation | Electrodes Sensors | Backend Services | Read Out Device System Integration | QM

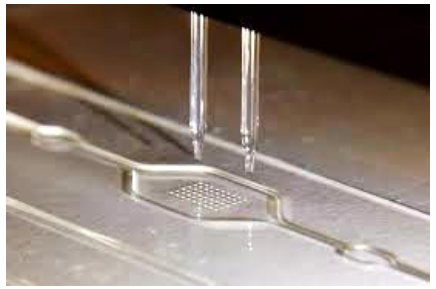
temicon micronano solutions INMOLD

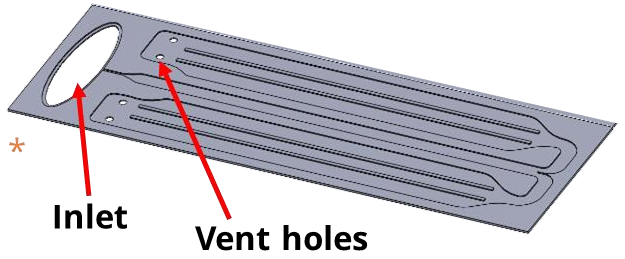
micronit

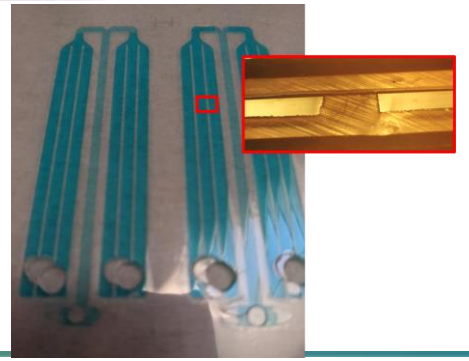
JOANNEUM RESEARCH micro resist technology

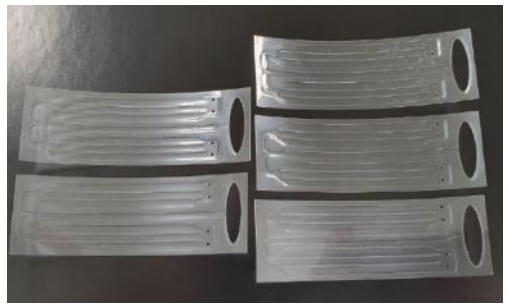












Microfluidics InnovationHub

WE DEVELOP AND PRODUCE

Microfluidic Lab-on-a-Foil Systems

- Single entry point to research & development services
- Comprehensive service portfolio
- Fast prototyping and scale up
- Multiple funding opportunities
- Quality assurance

We offer funding to scale up your application

- ✓ Open Call applications accepted on a rolling basis until September 2023
- ✓ Access to all services of the EU Horizon Europe project NextGenMicrofluidics
- ✓ Funding rate of up to 92% for European SMEs and 50% for Large Enterprises

Find out more at www.microfluidicshub.eu

Microfluidics Innovation Hub is the single entry point of the European project NextGenMicrofluidcs which received funding from the European Union's HORIZON 2020 research & innovation programme under grant agreement no. 862092.

Microfluidics InnovationHub

Questions & Answering