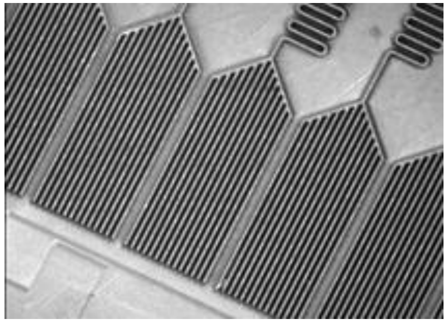
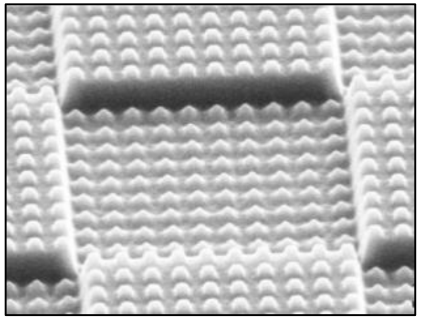
Fachhochschule Nordwestschweiz
Hochschule für Technik

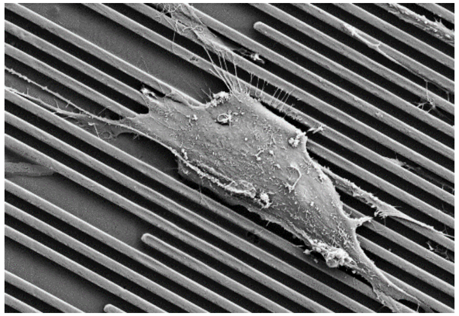
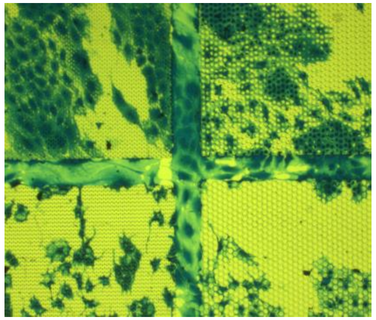
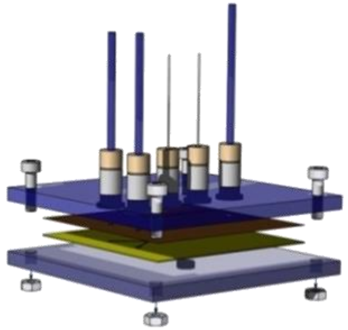
PAUL SCHERRER INSTITUT

Mikrofluidik 4.0 – Erwartungen an die Diagnostik von morgen

Trends in Micro Nano – 30.11.2017, Technologie Park Basel




Prof. Dr. Per Magnus Kristiansen, INKA Institute of Polymer Nanotechnology
FHNW University of Applied Sciences and Arts Northwestern Switzerland & PSI

Outline

- Short Intro to INKA – Institute of Polymer Nanotechnology
- Motivation for thermoplastic microfluidics
- Why Microfluidics 4.0 – Trends and Challenges
- Injection molded microfluidics – an older example
- Next generation(s) - Potential of surface topographies and more
- Summary

INKA – a meanwhile 13 year old „joint (ad)venture“ between FHNW & PSI

FHNW - IKT & INKA

10 km

LMN – Laboratory for Micro- und Nanotechnology

INKA

IKT
Institute of Polymer Engineering (IKT)

INKA
Institute of Polymer Nanotechnology (INKA)

INKA-PSI

SwissFEL Nanoengineering

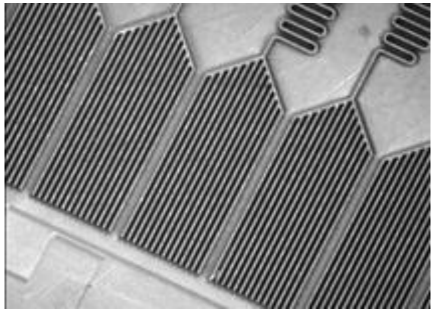
X-ray optics

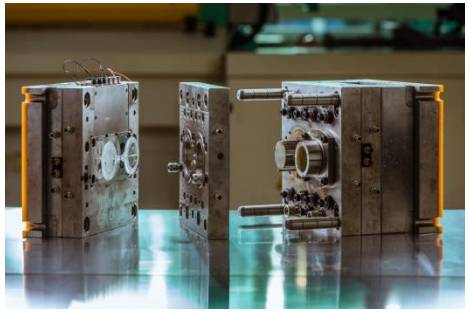
Nano-Magnetics

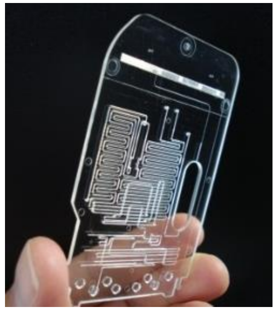
etc.

Functionalization of polymer materials by
- **micro- and nanostructured surfaces**
- **chemical surface modification (grafting)**
- **nanoscale additives**

The value chain of micro- & nanostructured polymer devices





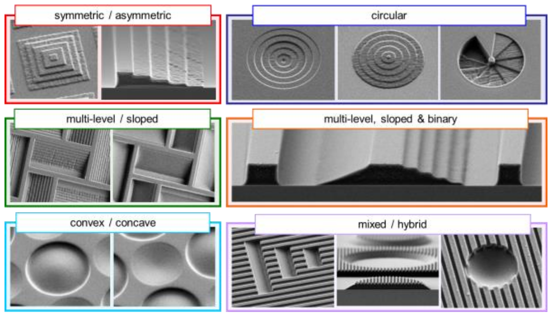


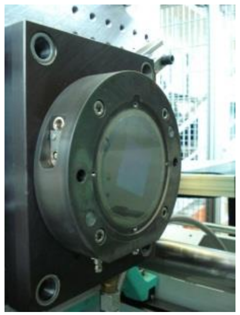
Master generation by lithography or laser ablation

Tool design, construction and realization

Industrial replication technologies

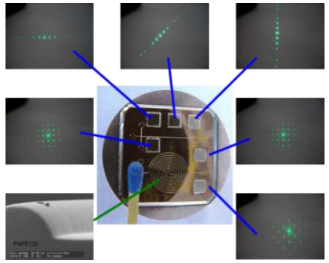
Focused application development

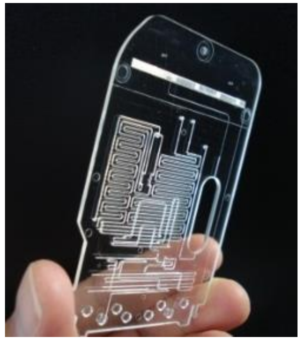


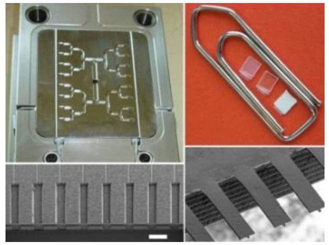


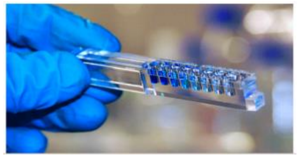
Diagnostics development history at INKA

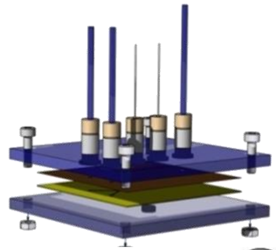
- **De-wetting analytical test tubes**
  - Realized 3D lotus effect by laser machining
- **DOEs for QC in microfluidic chip (MFC) production**
  - Proven correlation between DOE and channel quality
- **MFC with 2-side structuring for blood diagnostics**
  - Tooling & process development ; succesful transfer to industry
- **Polymeric Microcantilevers for diagnostics applications**
  - PhD project Prabitha Urwyler (Uni Basel); molding the «impossible»
- **Whole blood (evancescence-based) diagnostics chip**
  - Optical surfaces combined with difficult part design
- **PEEK microfluidics for membrane protein research**
  - Laser drilling, embossing & thermal bonding
- **Highly integrated MFC (custom specific design)**
  - Combination of a multitude of different design features
- **Most recently: Sample environments for photon sciences**

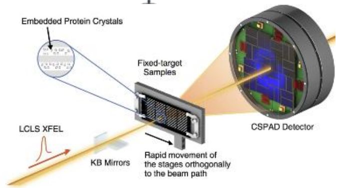










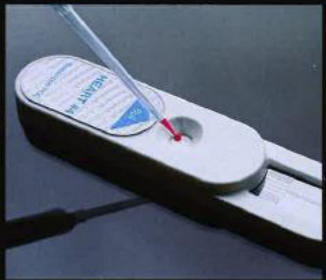


Disclaimer – Microfluidics 4.0 / Point-of-care diagnostics 2.0

Event promotion flyer of CSEM

Einladung
microTalk

Montag, 4. Dezember 2017
CSEM Zentrum Alpnach



Point-of-care diagnostics 2.0
Microfluidics for mobile health

Dr. Emmanuel Delamarche
IBM Research - Zuerich

csem in Zusammenarbeit mit mccs Micro Center Central-Switzerland

WILLKOMMEN BEIM CSEM IN ALPNACH

Point-of-care diagnostics 2.0
Microfluidics for mobile health

Diagnostics are ubiquitous in healthcare because they support prevention, diagnosis and treatment of diseases. Point-of-care diagnostics are particularly attractive for identifying diseases near patients, quickly, and in many settings and scenarios. IBM Research works on the development of capillary-driven microfluidic chips for highly miniaturized immunoassays. This presentation will review how to program capillary flow and encode specific functions to form microfluidic elements that can easily be assembled into self-powered devices for immunoassays, reaching unprecedented levels of precision for manipulating samples and reagents. This technology can also be augmented using peripherals and smartphones for flow control and monitoring with sub-nanoliter precision. Is the next generation of point-of-care devices finally coming?

Dr. Delamarche is leading activities on Precision Diagnostics at IBM Research - Zurich. One of his main projects deals with the development of portable and precise diagnostic devices using microfluidic concepts and smartphones. He is also a Lecturer at ETH Zurich and a contributor to scientific panels for grant agencies and governments. He published over 120 papers and is co-inventor on more than 70 patent families. He has received numerous awards from IBM, was named "Master Inventor" by IBM, and received the Werner prize of the Swiss Chemical Society in 2006.

Freundliche Grüsse

Philippe Steiert
Direktor CSEM Regionalzentren

Helmut F. Knapp
Leiter CSEM Zentrum Alpnach

PROGRAMM

Montag, 4. Dezember 2017

17.00	**Begrüssung**
	Helmut Knapp Leiter CSEM Zentrum Alpnach
17.10	**Point-of-care diagnostics 2.0** **Microfluidics for mobile health**
	Emmanuel Delamarche IBM Research - Zuerich
18.00	**Diskussion**
18.15	**Apéro**
19.00	**Ende der Veranstaltung**

For a broader perspective on PoC diagnostics, join next Monday in Alpnach !

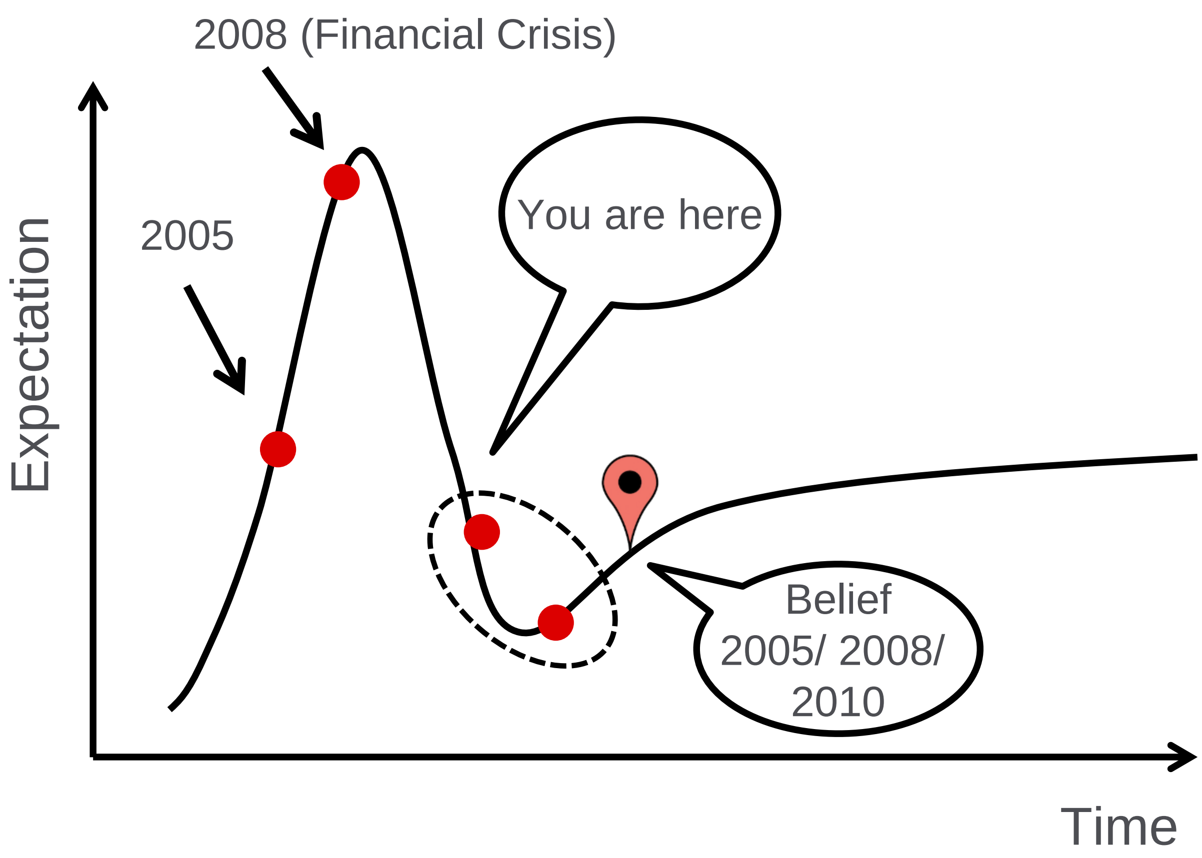
→ Note: Registration closes today!

Motivation for thermoplastic microfluidics

- Nice review paper* highlighting some of the remaining issues in microfluidics
- «**in the industry** (…) **thermoplastics** have been **preferred as low-cost and mass-producible alternatives** to PDMS as well as to silicon and glass.
- «**PDMS microfluidic devices or silicon-based** (e.g. CMOS) **sensors are** widely adopted in the academic community because they are **easy to apply for proof-of-concept purposes, but** typically **manufacturability and economy of scale are not as favorable as plastic chips.**»
- «**Packaging and interfacing microfluidics remain a significant technical challenge** and obstacle for the commercialization and wide-spread use of microfluidics»

* Ref: Y. Temiz, R.D. Lovchik, G.V. Kaigala, E. Delamarche, Microelectron. Eng. 132, 156-175 (2015)

Gartner Hype Cycle of microfluidic cartridges



Where are we really?

- Some applications are on the market
- Tremendous amounts of R&D with up to pre-serial production
- However, there is still no killer application… Yet.

Ref: C. Denier, *Microfluidics Workshop* 2016, Basel

Why Microfluidics 4.0 – Trends & Challenges

Observed trends in microfluidics

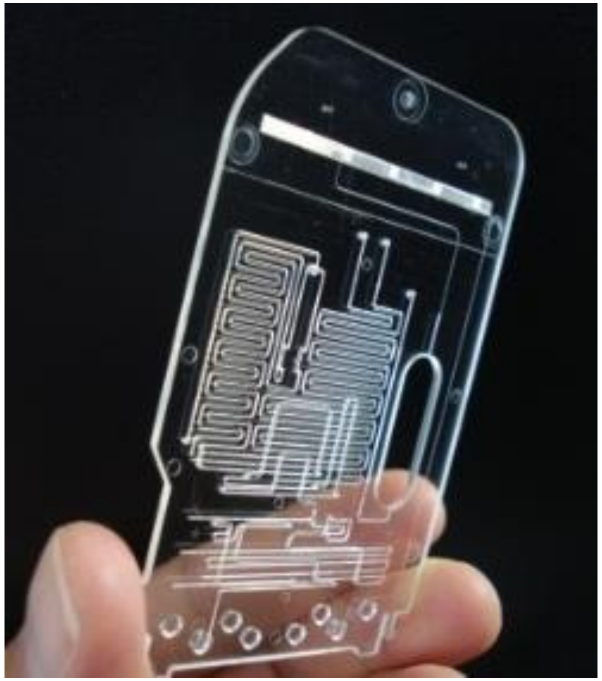
- Increasing complexity of MF designs
- MF building blocks become smaller
- Handling of small sample volumes
- Requests for added functionalities
- Platform «spirit» - same designs for different purposes
- Hybridization attempts, e.g. for sensor and electronics integration

Challenges in manufacturing

- Robust manufacturing processes, reliably reaching tight tolerances
- Process feedback loops required
- Quality control both in- and off-line
- Efficient functionalization methods and related novel approaches
- Interface connection to the outside (→ standardization efforts)

What industry is looking for requires «Industry 4.0» manufacturing approaches

A meanwhile old microfluidic chip for point-of-care blood analysis

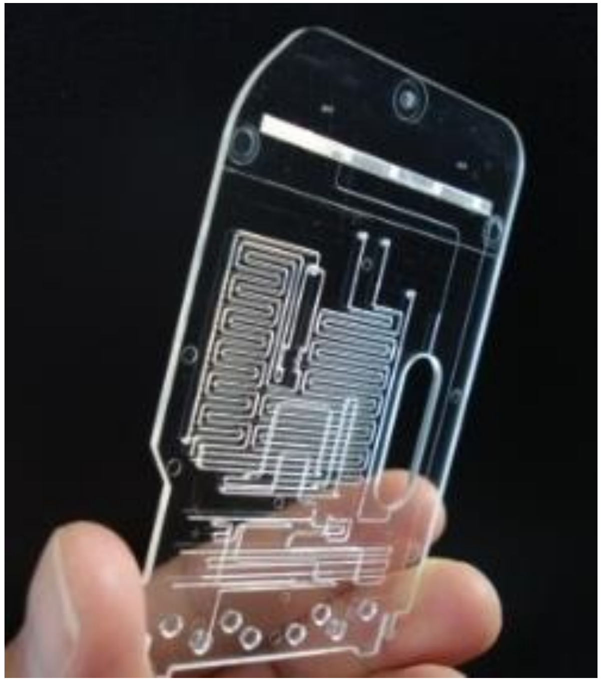


Chip & photo by FHNW

KunststoffXtra, 12,64-67 (2016)

- True 2-side structured microfluidic chip
- Channel dimensions 100-500 µm
- Multiple connecting through-holes
- 5 integrated optical read-out zones
- Material: cyclo-olefin copolymer (COC)
- Hybrid mold concept (Nickel only where needed)
- Very narrow process window

A meanwhile old microfluidic chip for point-of-care blood analysis



Chip & photo by FHNW

KunststoffXtra, 12,64-67 (2016)

Claros® 1

OPKO Health

In-Office Immunoassay • Lab Quality Without the Lab

Results in 10 Minutes from finger-stick of whole blood sample

The Claros® 1 in-office analyzer and Sangia™ microfluidic assay cassettes are a complete immunoassay solution for the physician's office

- Obtain quantitative lab-quality results
- Achieve fast turn around time (10 minutes)
- Sample from a small drop of blood - no venipuncture
- Enables rapid clinical decision-making
- Defines course of patient treatment in a single office visit

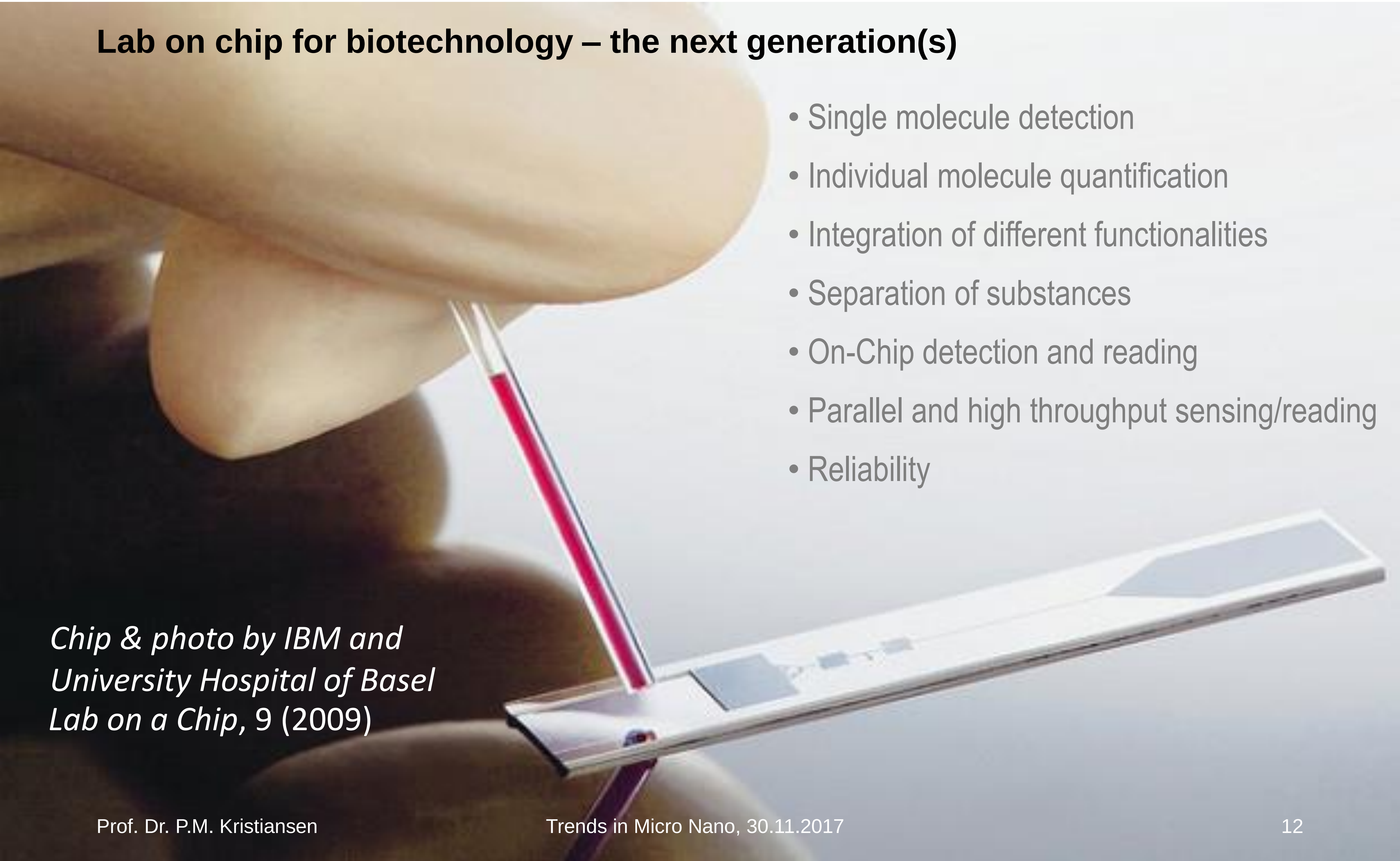
Ref: http://claros1.opko.com/

Claros 1 and Claros 1 Total PSA are CE Marked and Pending FDA Clearance

OPKO Diagnostics
a Division of OPKO Health, Inc.

Lab on chip for biotechnology – the next generation(s)

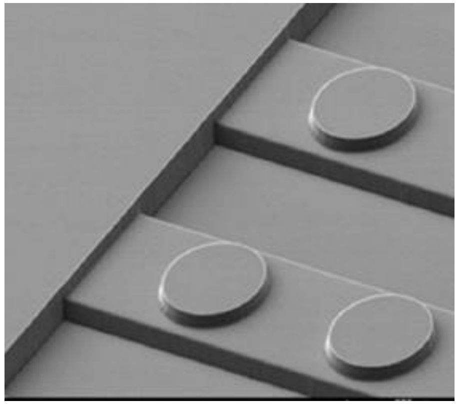
- Single molecule detection
- Individual molecule quantification
- Integration of different functionalities
- Separation of substances
- On-Chip detection and reading
- Parallel and high throughput sensing/reading
- Reliability



Chip & photo by IBM and
University Hospital of Basel
Lab on a Chip, 9 (2009)

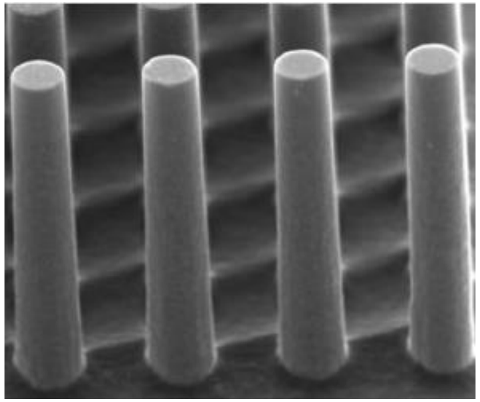
Typical topography requirements of modern microfluidic biosensors

Multi height features



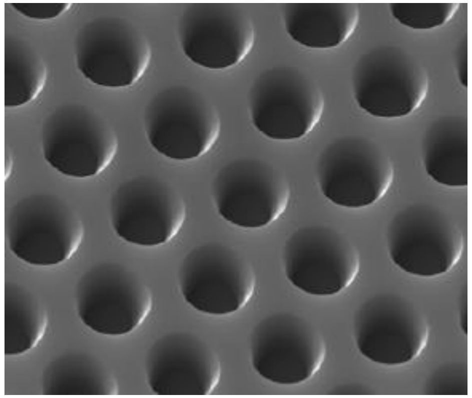
- combining fluidic channels with detection areas and reservoirs
- filtering
- removing bubbles
- changing the flow characteristics (e.g. hydrodynamic focusing

High aspect ratios



- filtering
- mixing
- cell sorting
- increasing shear flow
- increasing cell-antibody interaction
- making surface superhydrophobic

High density arrays



- beads trapping
- localization of DNA and proteins
- high density reaction chamber
- localized surface plasmon resonance
- diffractive elements

Realizing microfluidics by variothermal injection compression molding

High fidelity replication is possible with

- Variothermal process control
- Injection compression molding

Dedicated moulding tools

- Variothermal / isothermal + compression
- Online viscosity control

Peripheral equipment & subsequent processes

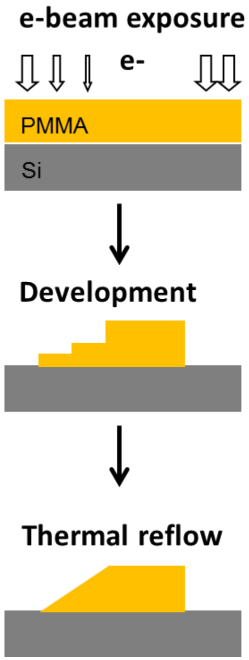
- Handling robots, pick-up systems
- Bonding technologies, surface treatment

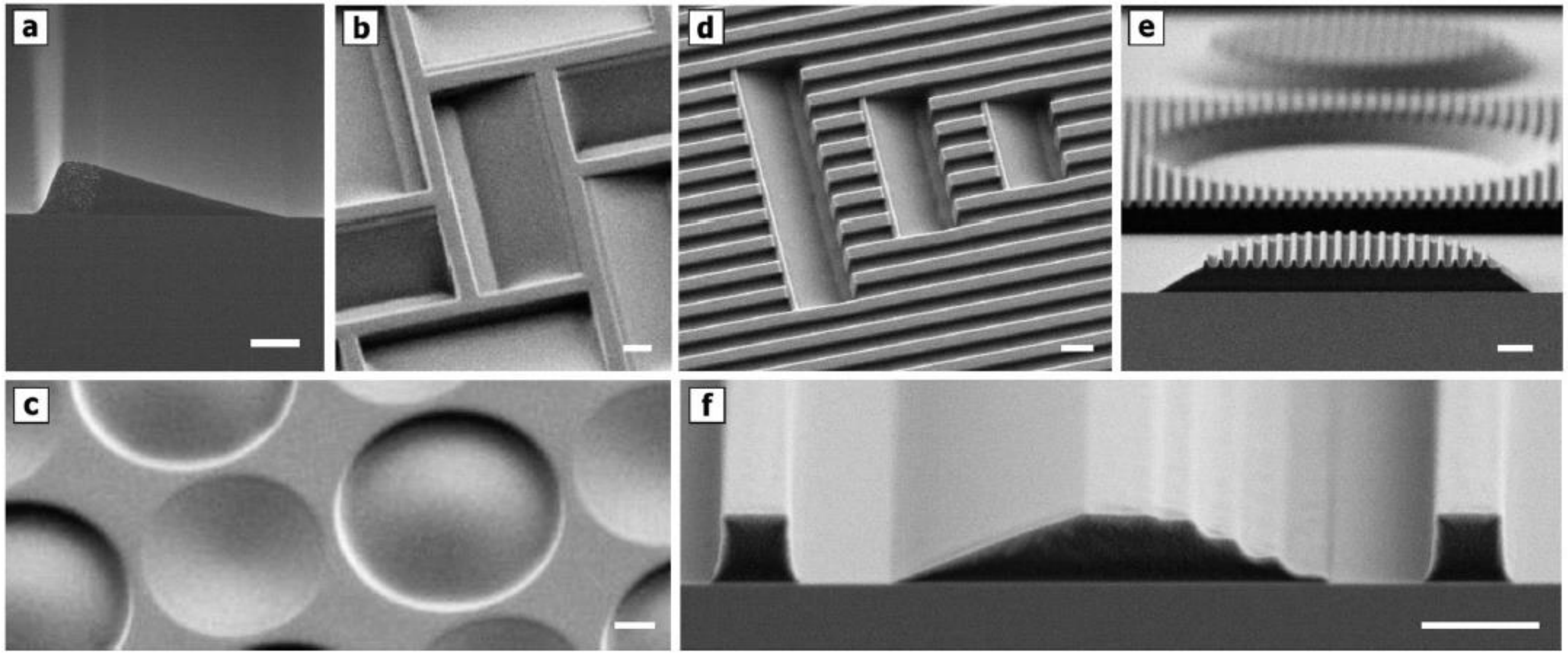
It is impressive what can be injection molded – but can we go even further?

Courtesy of Helmut Schift, INKA-PSI

TASTE – “Thermally activated selective topography equilibration”

Enabling technology for complex submicron 3D patterning
(grayscale electron beam lithography + thermal reflow)

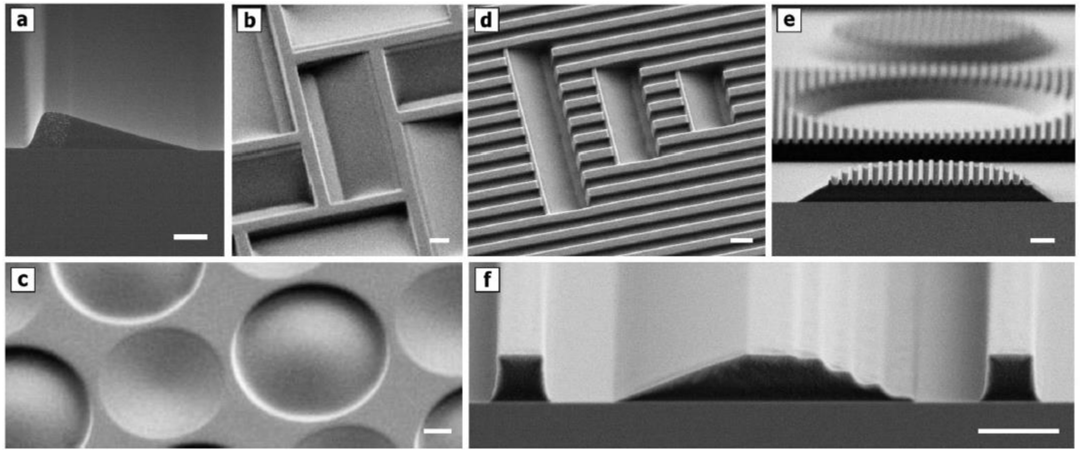




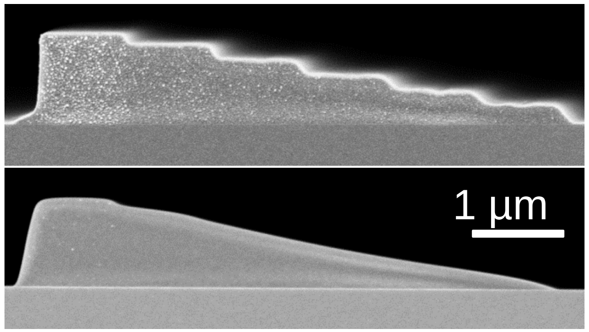
Ref: A. Schleunitz et al. Nano Convergence 2014, **1**:7

Scale bars: 1µm

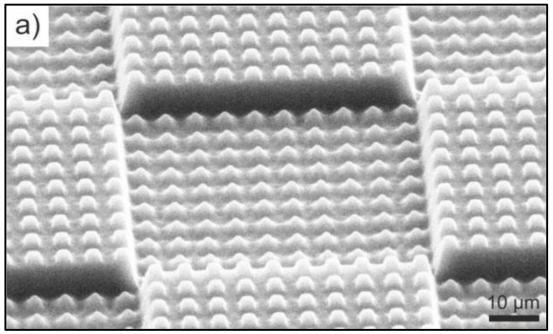
TASTE technology – outreach into industrial applications



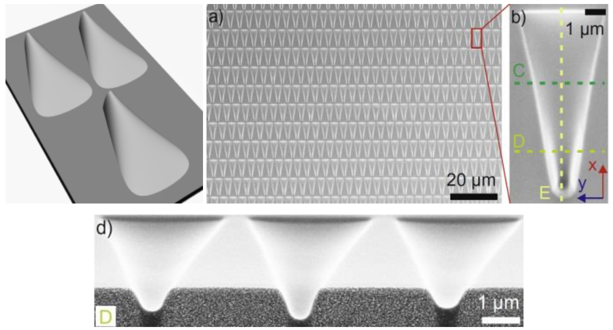
Selected topics exploited in more detail within funded industrial R&D projects



microprisms



hierarchical surfaces

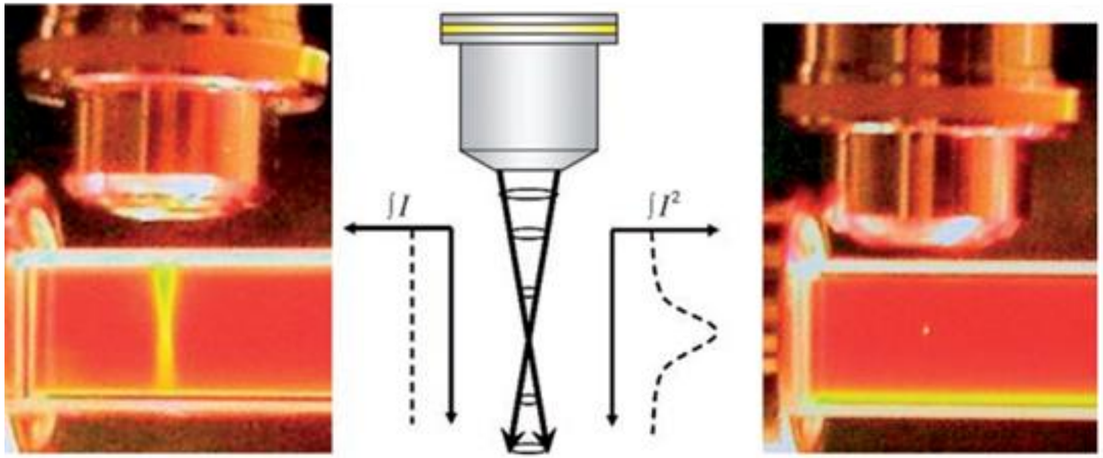


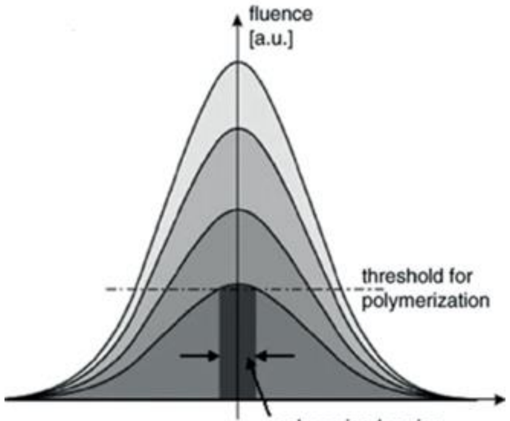
bioinspired surfaces

Courtesy of Jonathan Schmidli, INKA-FHNW

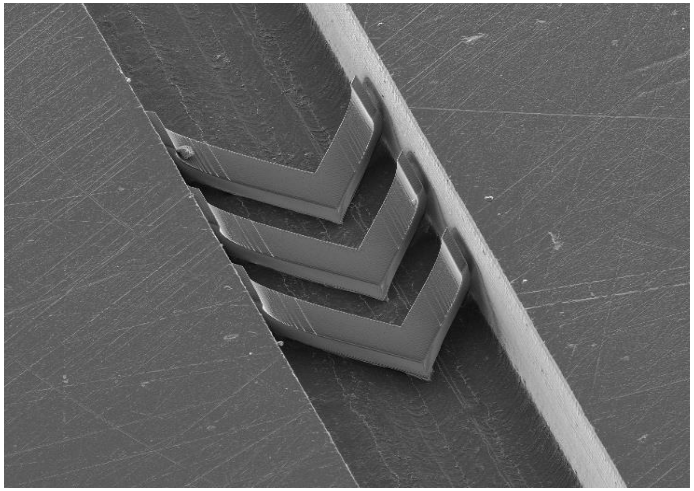
Sequential addition of functional features (here by 2-photon polymerization)

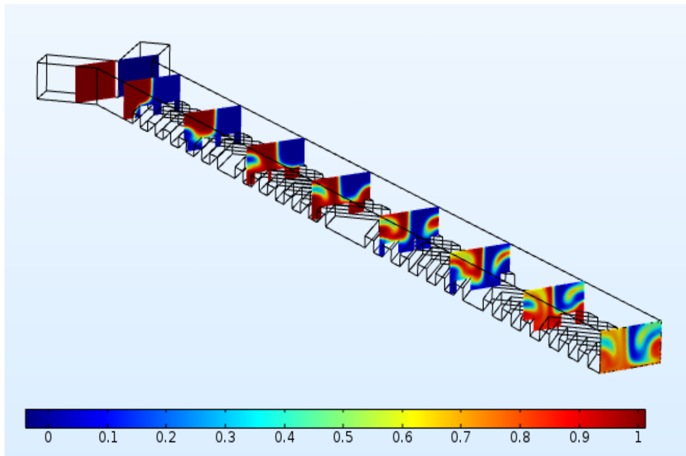
Single vs. 2-photon exposure



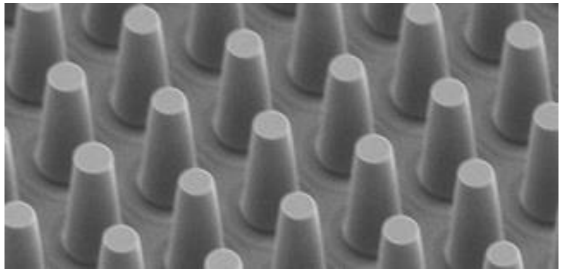


Staggered herringbone mixers





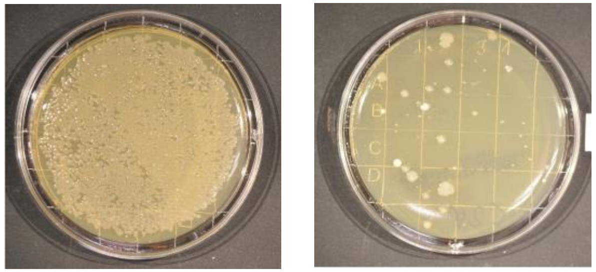
Functional polymer surfaces - further options to be explored



PASSIVE

Surface properties induced by topography *and/or chemistry*

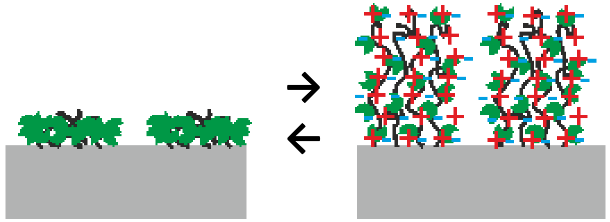
- Adapted wetting behavior, embedded capillary effects
- Self-cleaning, Antifouling
- Scratch resistance
- Haptics, e.g. soft touch



ACTIVE

Surface property plays an active role, modifying interaction

- Antimicrobial (biocidal), antifungal, etc.
- Light management
- Cell interaction, e.g. guiding



SMART / RESPONSIVE

Surface properties change upon external stimulation

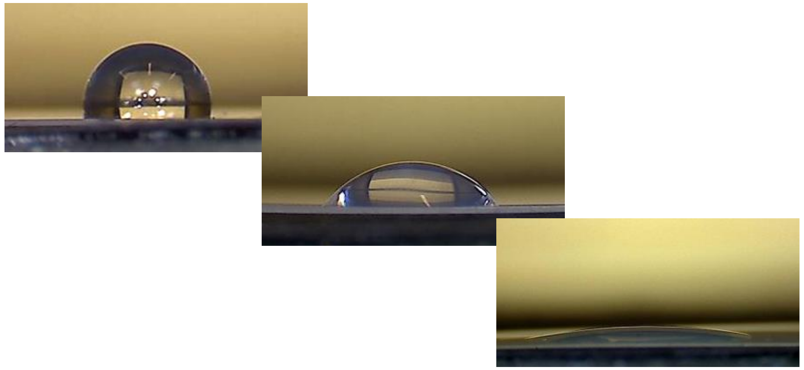
- External stimuli: pH, light, temperature, magnetic field ..
- Biomolecule interaction
- Sensing / Actuation
- Self-healing

There is tremendous room at the top and the bottom of your imagination

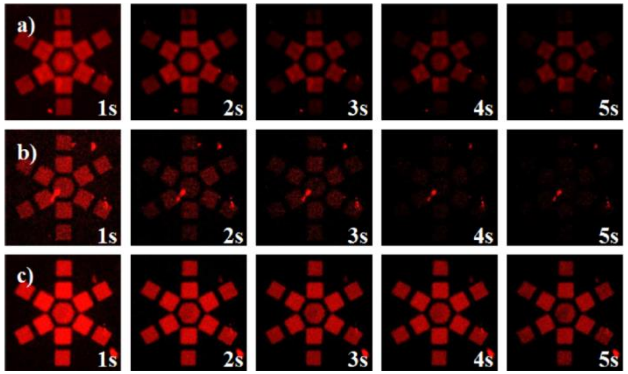
Courtesy of S. Neuhaus and C. Padeste, INKA-PSI

Functional polymer surfaces achieved by chemical modification (grafting)

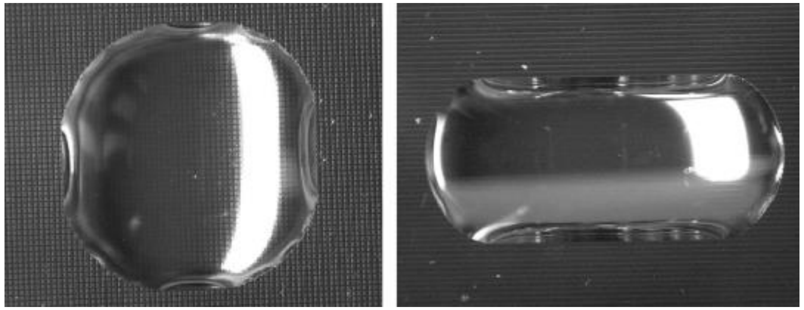
Wettability control (optionally triggered)



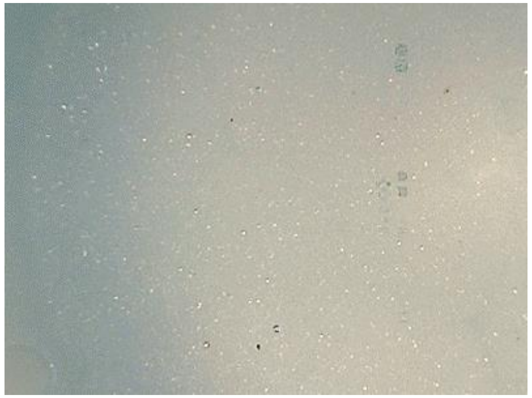
Photoresponsive brushes



Anisotropic wetting



Enzymatic activity



Summary and Outlook

- **Industrial replication of complex micro-/nanostructures is possible**
  - Functionality without change in material (regulatory advantage)
  - Where is the ultimate limit for complexity?
- **Additional functionalities can be implemented «on-mold»**
  - Integrated optics, e.g. for in-coupling or readout
  - Functional micro/nanostructures, e.g. hydrophopic barriers
- **Or we can further modify the parts themselves (if feasible)**
  - Laser-based modifications, i.e. for «writing» waveguides or conductors
  - Altering surface chemistry in addition, i.e. grafting, photochemistry, …
- **What else? – Your imagination is a good starting point for a discussion**

Contact Details

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