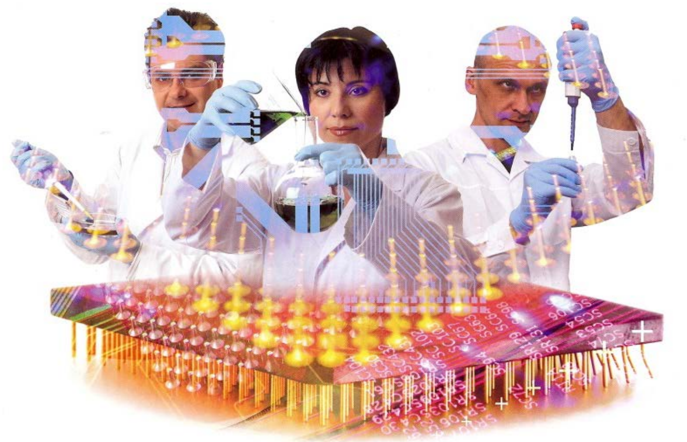
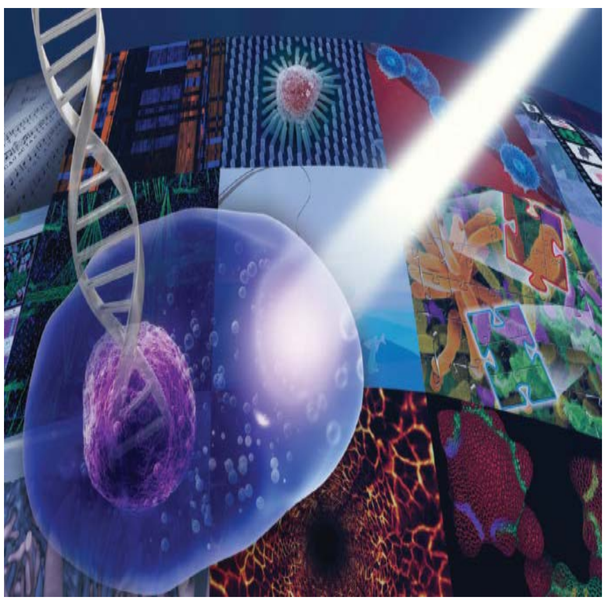
Photonics-enhanced Polymer Labs-on-Chips: from high-tech prototyping platform to applications

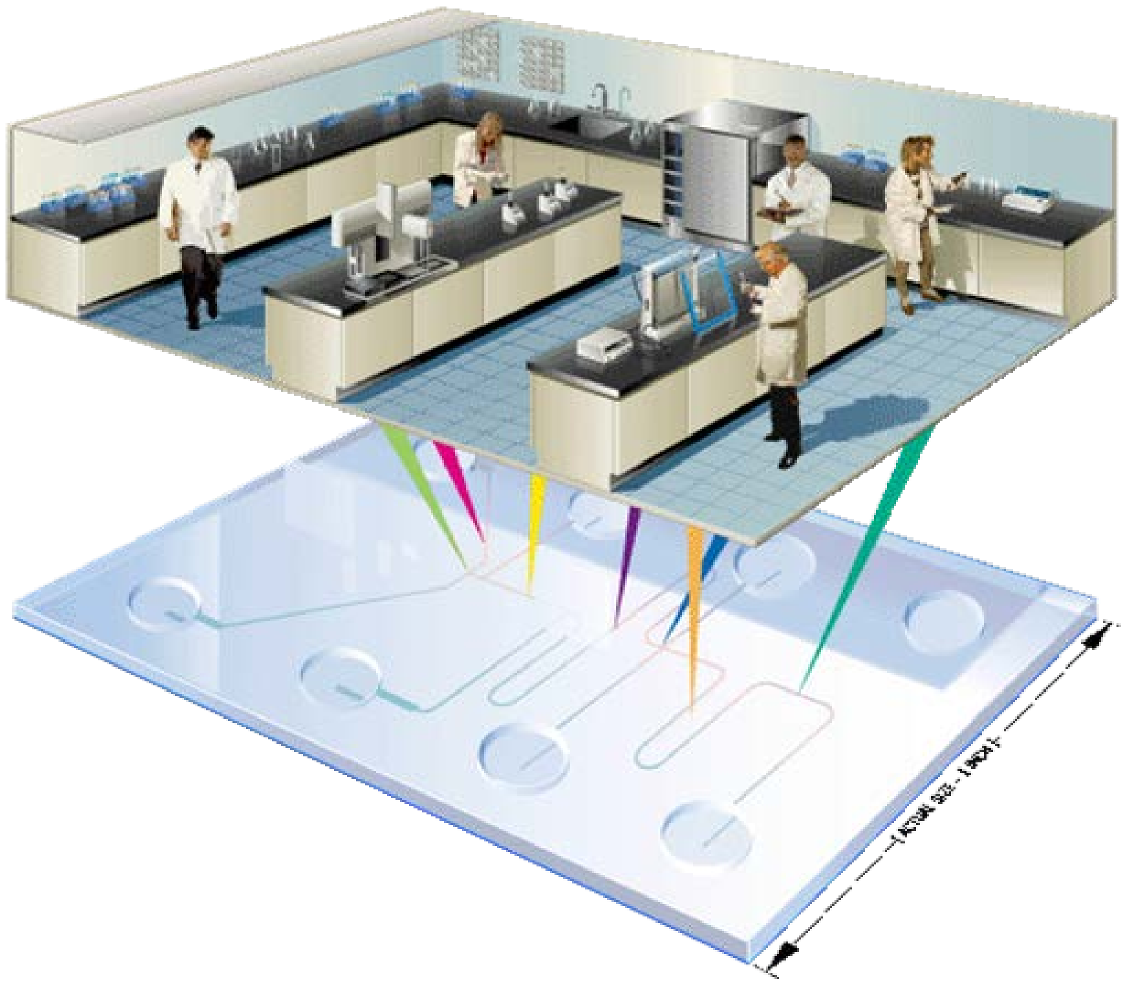
Jürgen Van Erps

Biosensors & Bioelectronics 2015
Hilton Atlanta Airport (USA)

Lab-on-a-chip







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Lab-on-a-chip for point-of-care diagnostics

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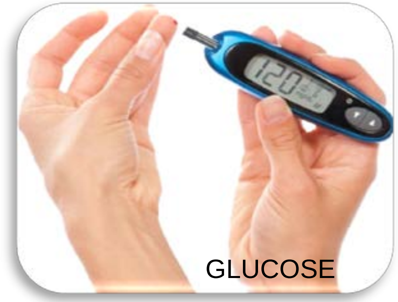
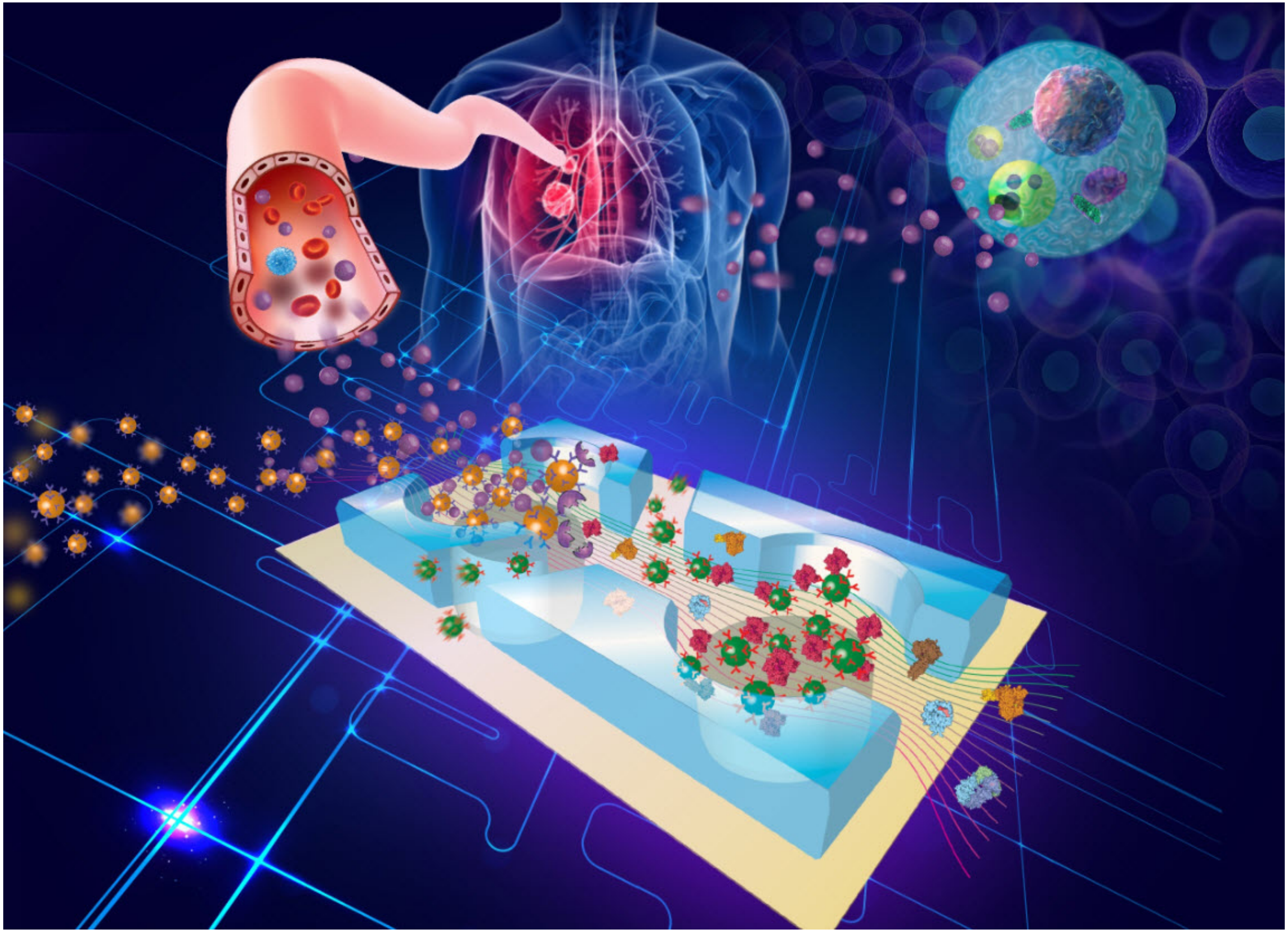
Multifunctional micro-systems



Health

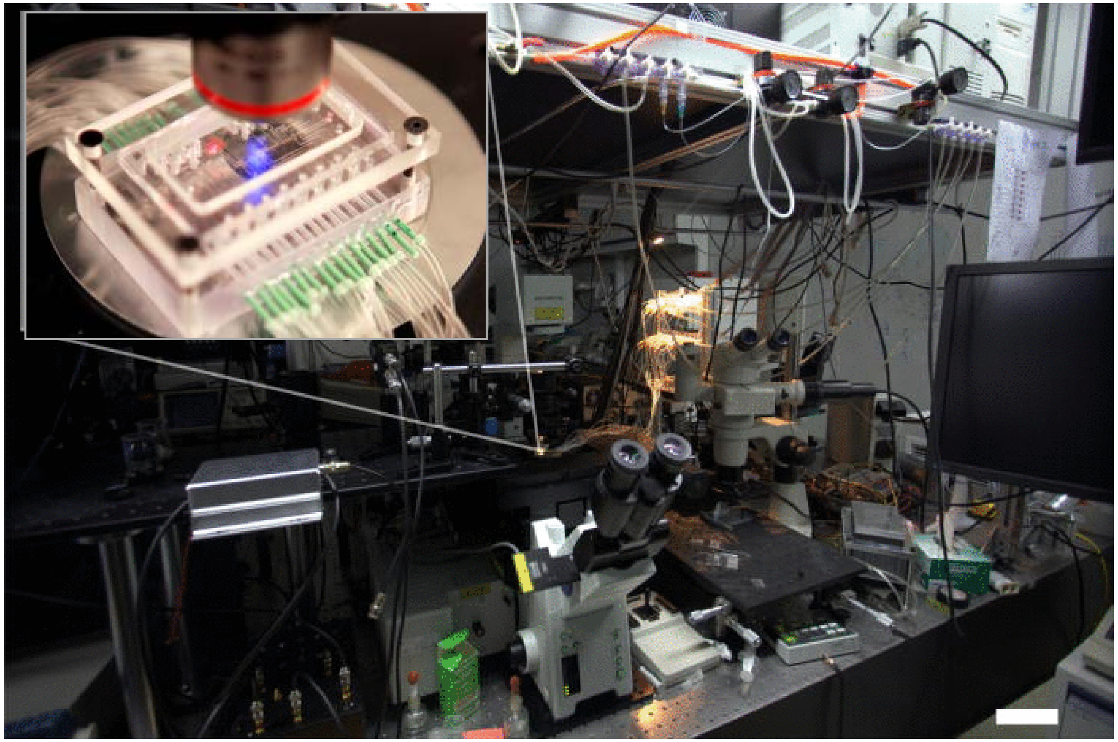
Water and food

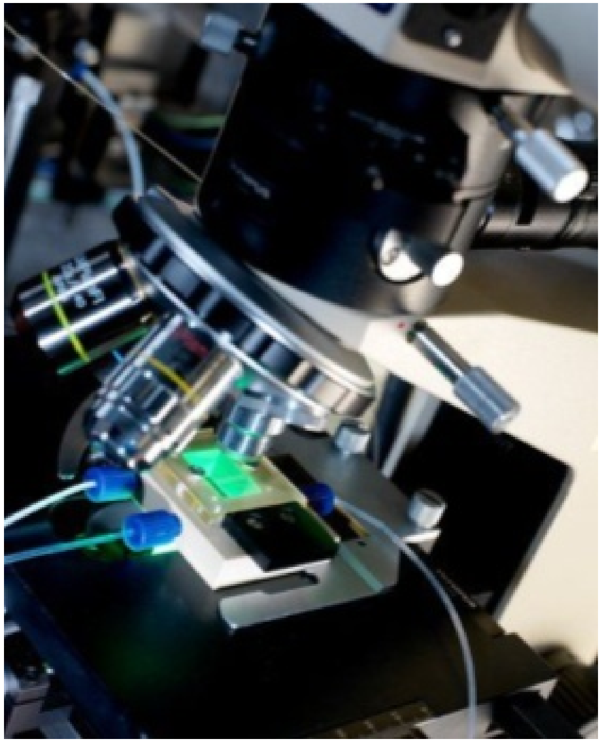
Human-on-a-chip



Lab-on-a-chip
Challenges

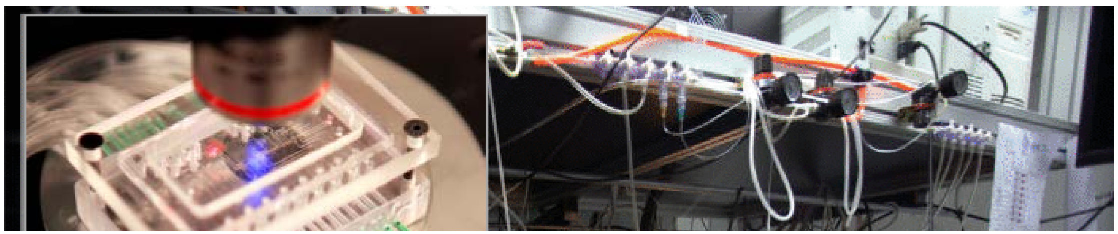
- Limited to laboratory prototypes without widespread use in clinical or high-throughput applications
  - Detection is done using bulky and expensive instrumentation: "chip-in-a-lab" rather than a lab-on-a-chip



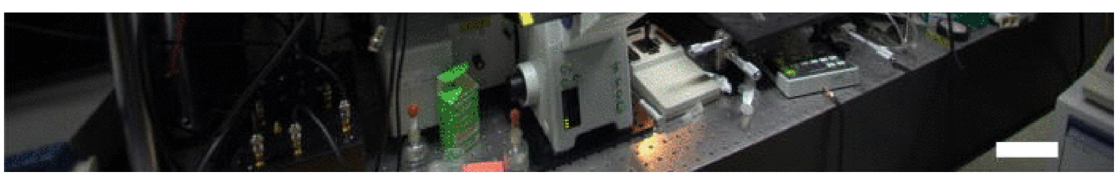


Lab-on-a-chip Challenges

- Limited to laboratory prototypes without widespread use in clinical or high-throughput applications
  - Detection is done using bulky and expensive instrumentation: “chip-in-a-lab” rather than a lab-on-a-chip



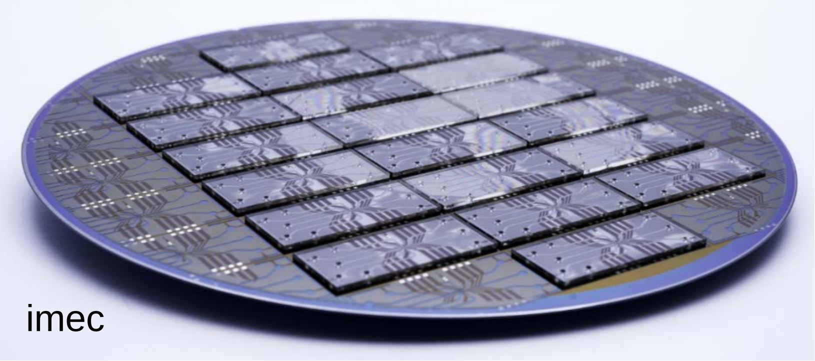
Need for miniaturized and integrated detection



Lab-on-a-chip Challenges

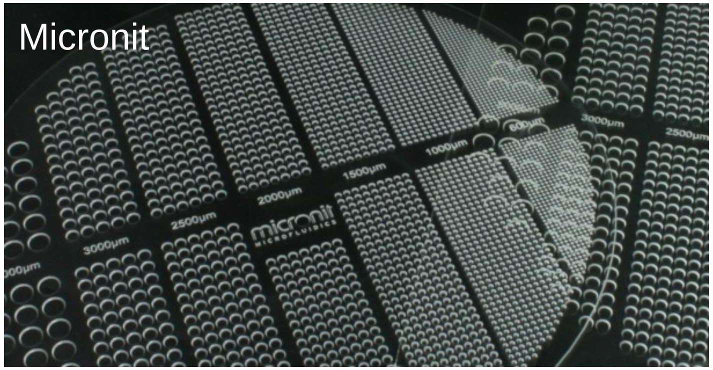
- Limited to laboratory prototypes without widespread use in clinical or high-throughput applications
  - A wide variety of approaches and competing material platforms

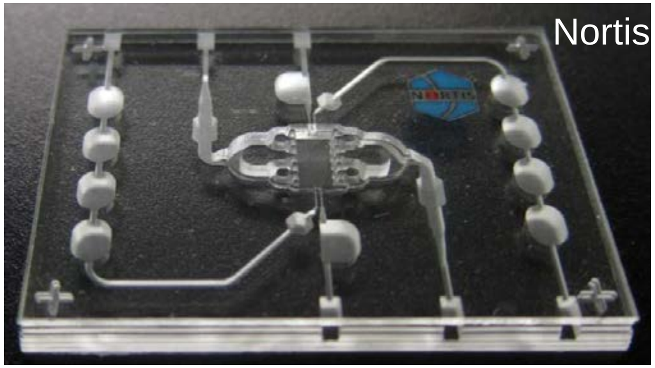
Si / SiN



Polymers

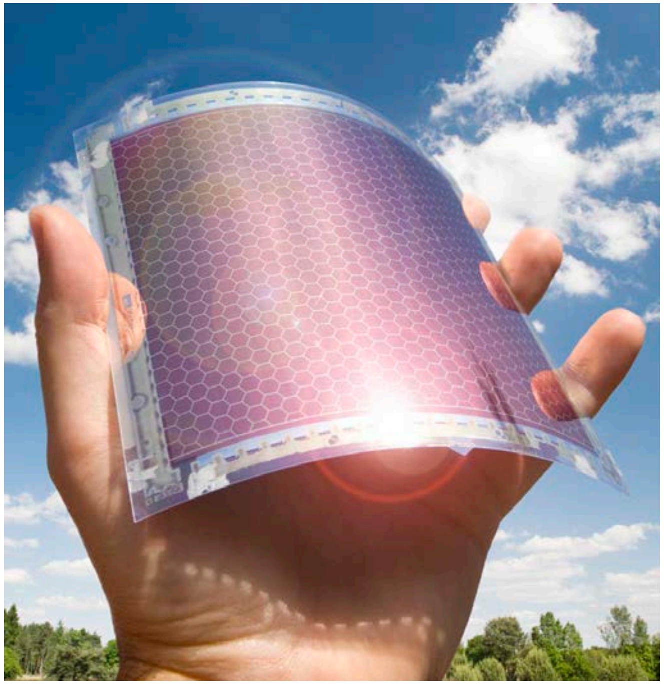
Glass





The future could be plastic...

- Flexible organic photovoltaics as a low-cost alternative to silicon photovoltaic cells

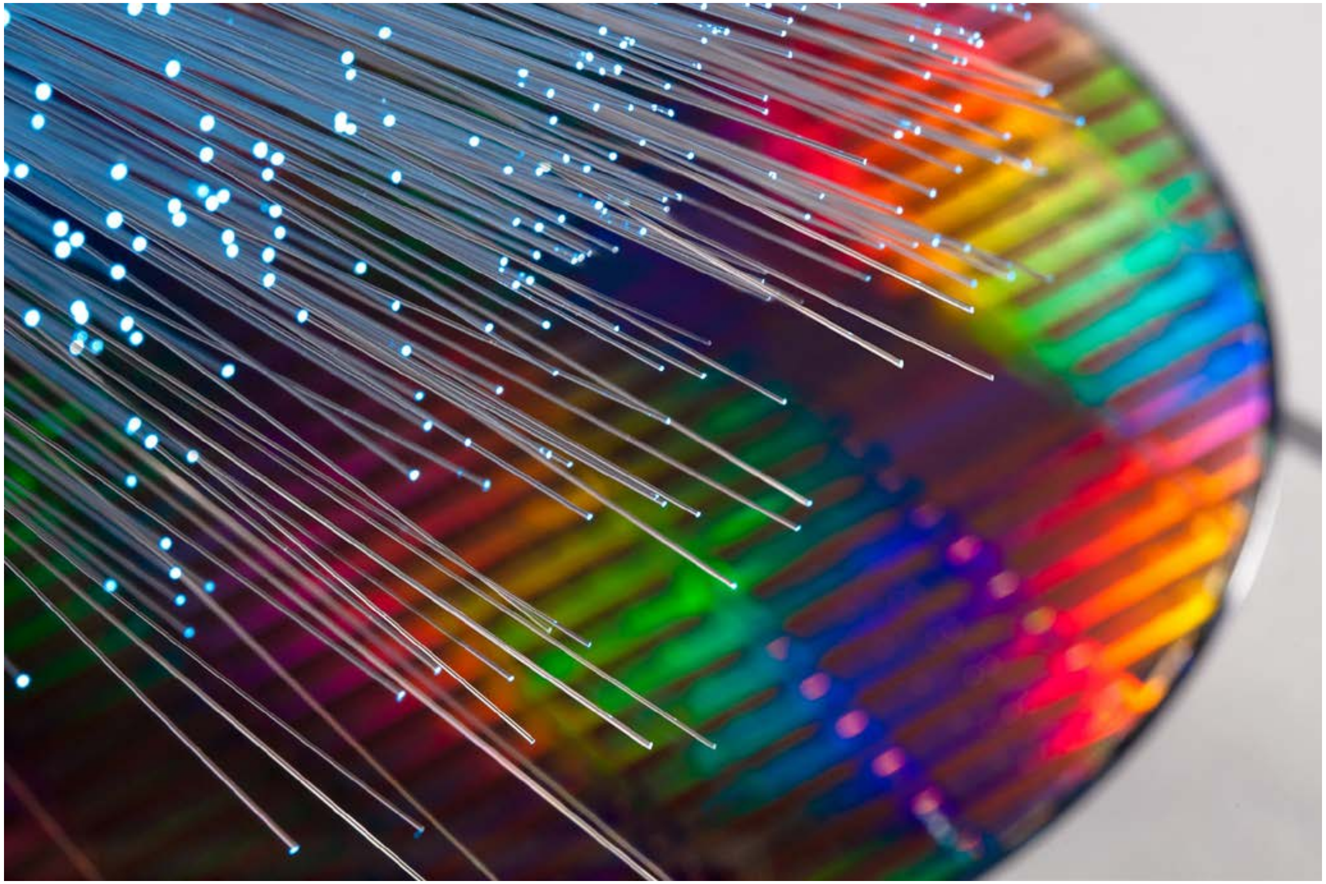


The future could be plastic...

- From rigid LCD displays to flexible OLED displays

The future could be plastic...

- From glass fiber for long-haul optical telecom to polymer optical fiber for short-distance interconnects



The future could be plastic...

- Towards ubiquitous polymer labs-on-chips?
  - Low-cost wafer-scale mass manufacturing
  - Wide range of material properties (e.g. T_g)
  - Biocompatible
  - Biodegradable
  - Disposable
  - Surface functionalization

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B-PHOT's micro-optics technology supply chain

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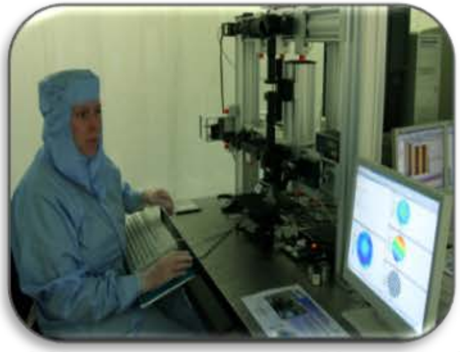
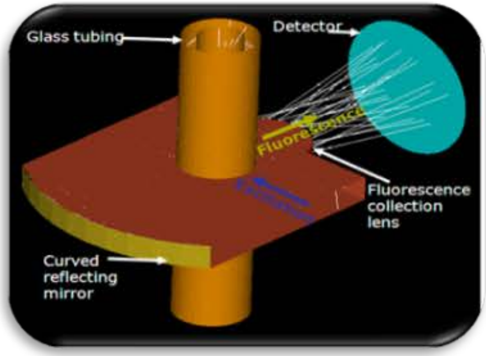
Mastering and Prototyping Technologies

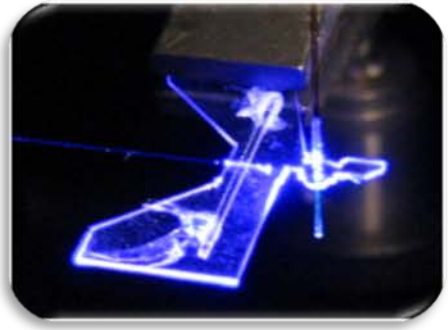


Optical Measurement and Characterization

Low-Cost Low-Volume Replication



Optical Modelling

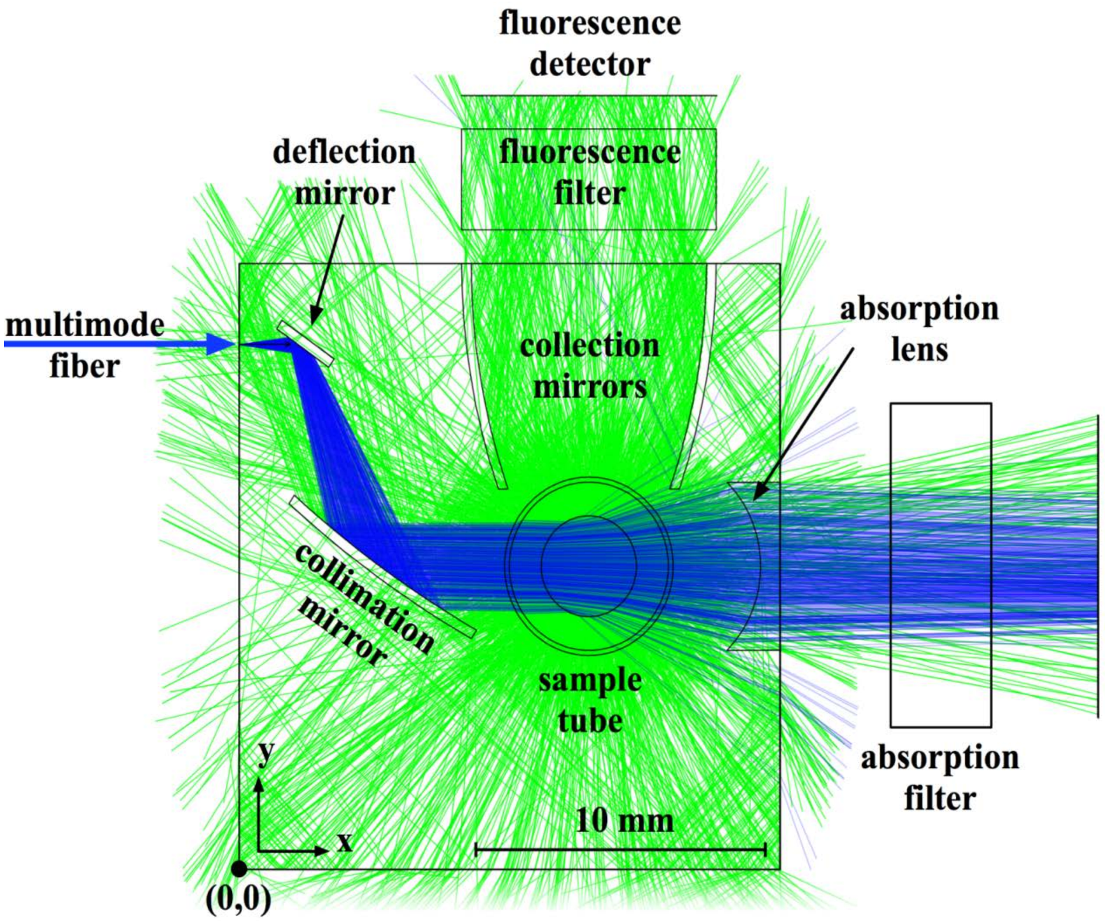


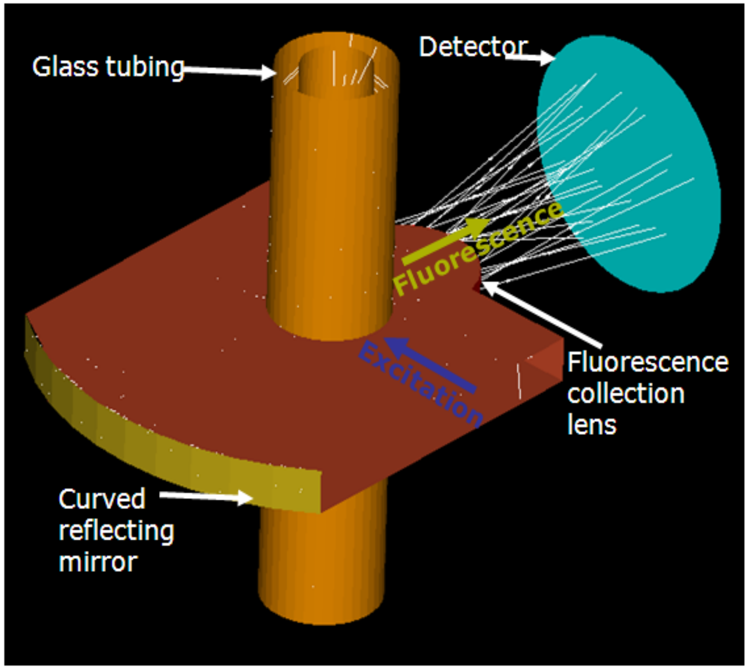
Demonstrators and Prototypes

Advanced Materials

PBM UGent

Optical modelling capabilities





Ray-tracing of polymer labs-on-chips

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We operate an advanced Polymer Prototyping Line

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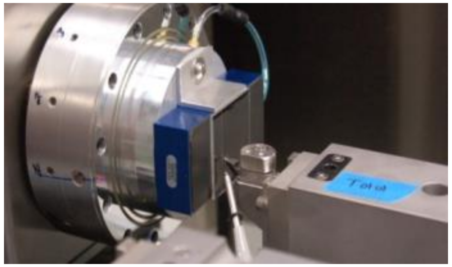
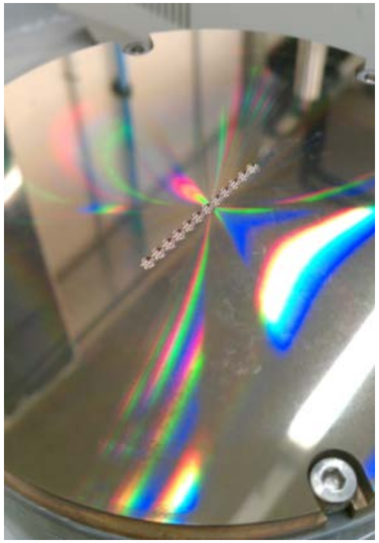
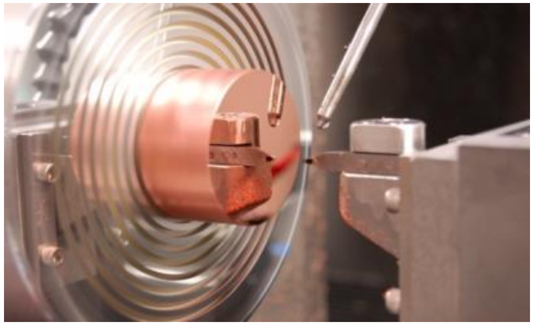
Mastering & Prototyping: Ultraprecision diamond tooling

- Ultraprecision machining: <140 nm PV and Ra < 5 nm
- Materials
  - Non-ferrous metals for mould formation
  - Polymers for direct prototyping
- Applications
  - Freeform one step optics
  - Micro-optics on non-flat substrates in diverse materials
  - Mould fabrication

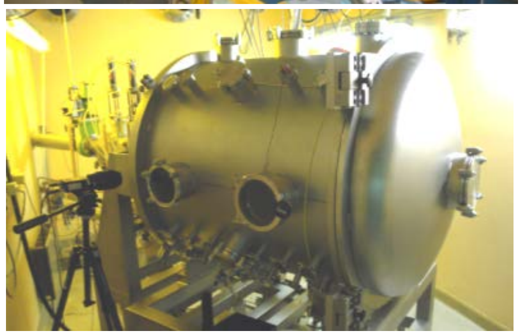




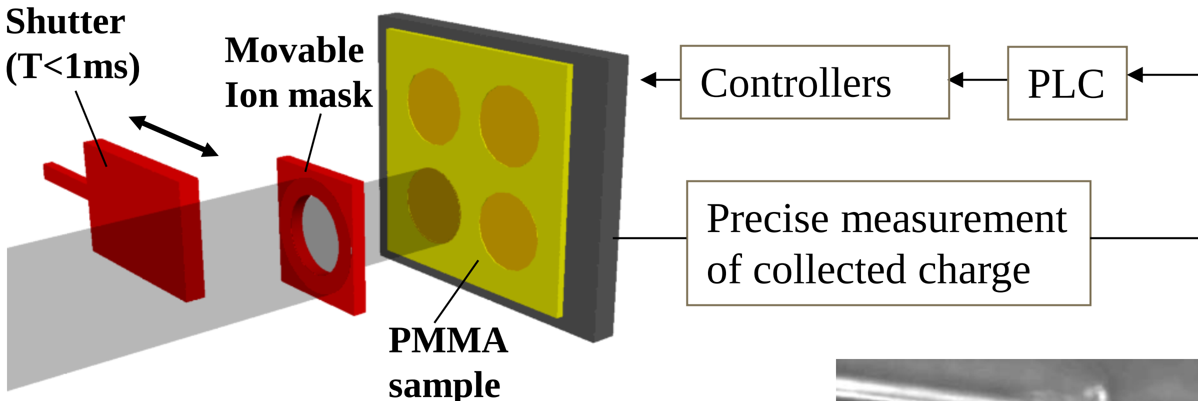


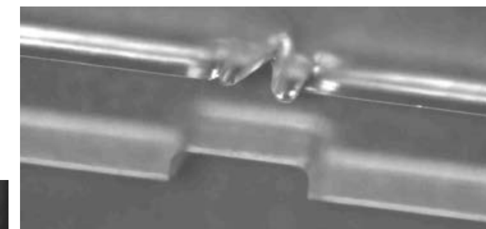
Mastering & Prototyping: Deep Proton Writing

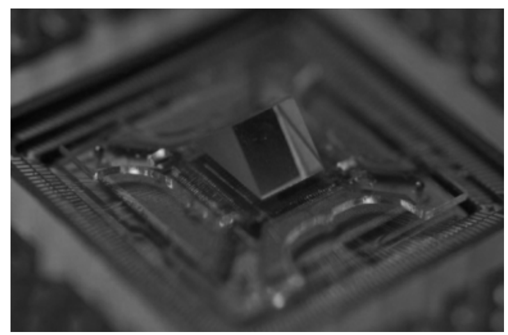
CGR-560 cyclotron

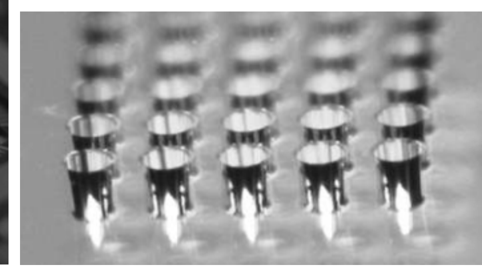


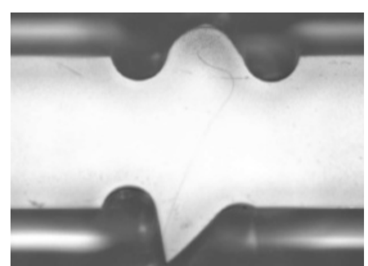
DPW vacuum chamber

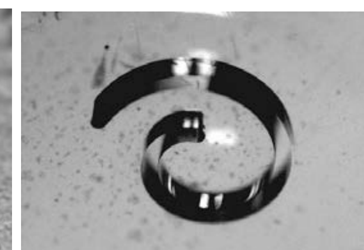












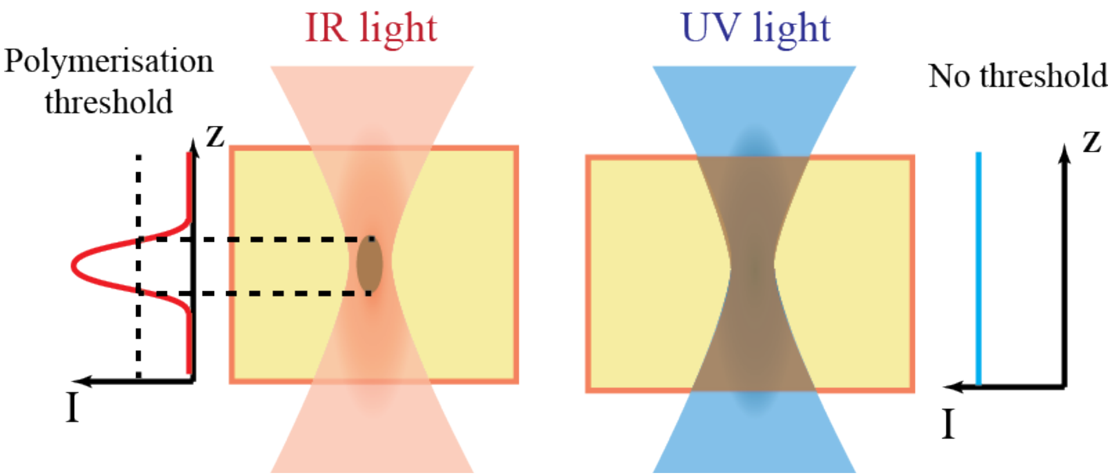
Selective proton irradiation of PMMA

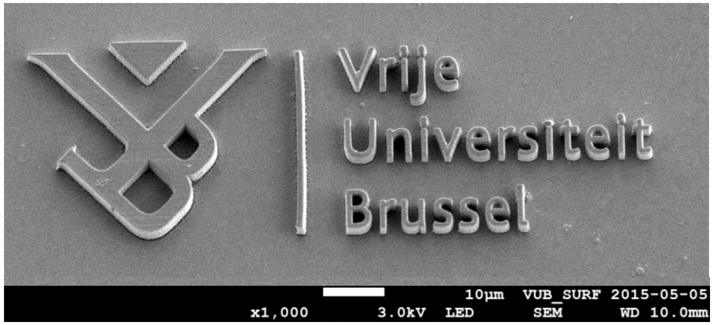
Local energy transfer of 12MeV proton beams results in highly defined degraded points and contours

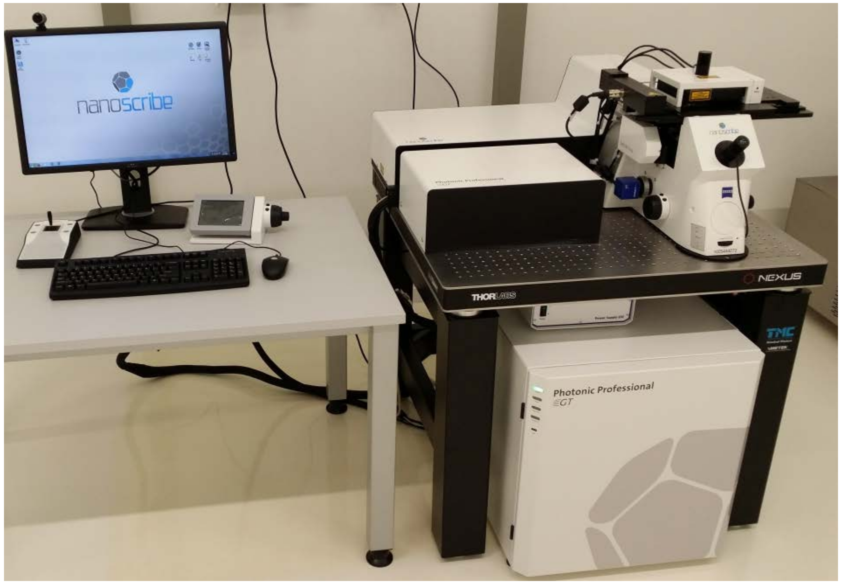
Proton beam size = 20µm – 300µm
Translation precision of PMMA plates = 50nm
Translation range = 50mm x 50mm
Process optimized up to 2mm thick PMMA plates

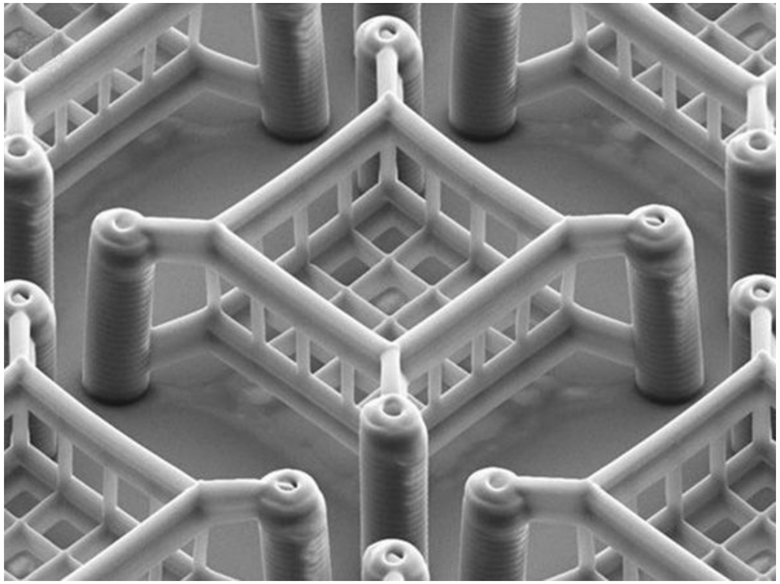
C. Debaes et al., New J. Phys., Vol. 8, No. 11, 2006.
J. Van Erps et al., Nucl. Instr. Phys. Methods B, Vol. 307, 2013.

We enter the next paradigm shift using 3D-laser lithography with biopolymers



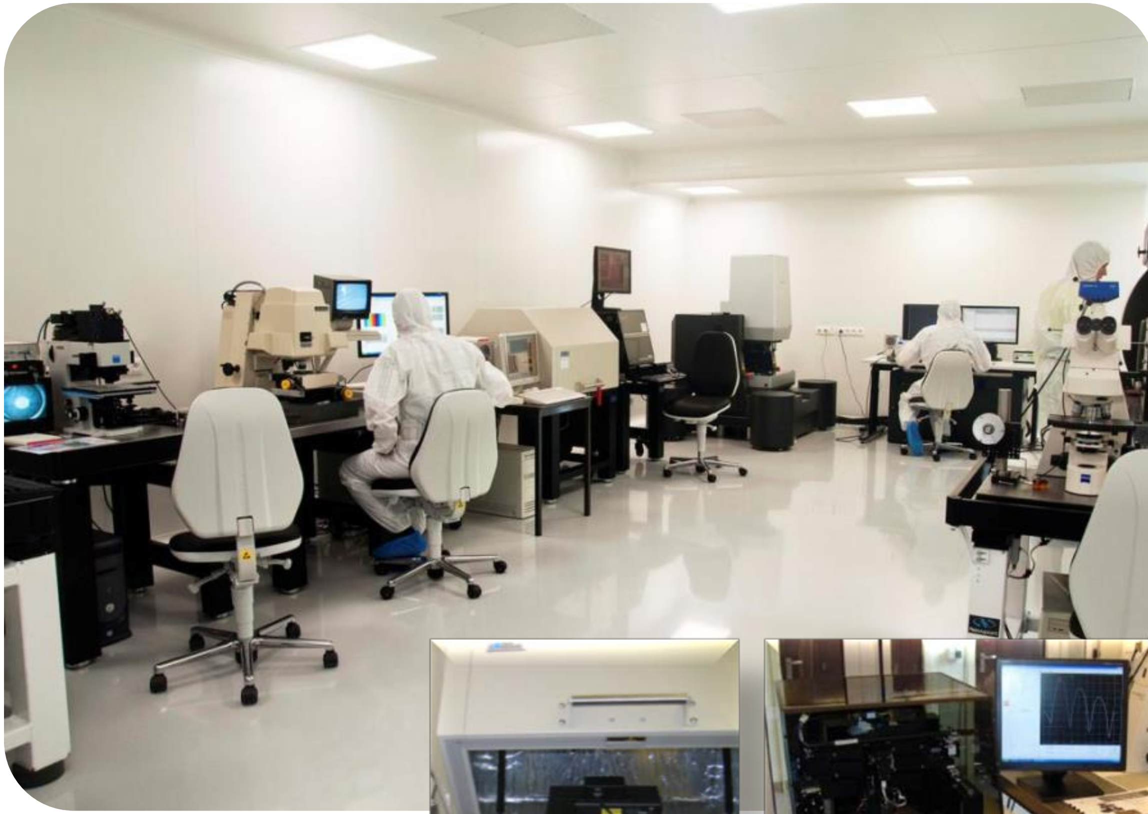


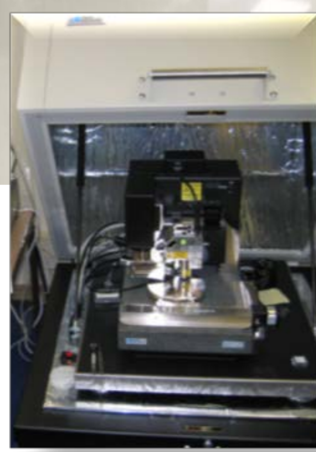


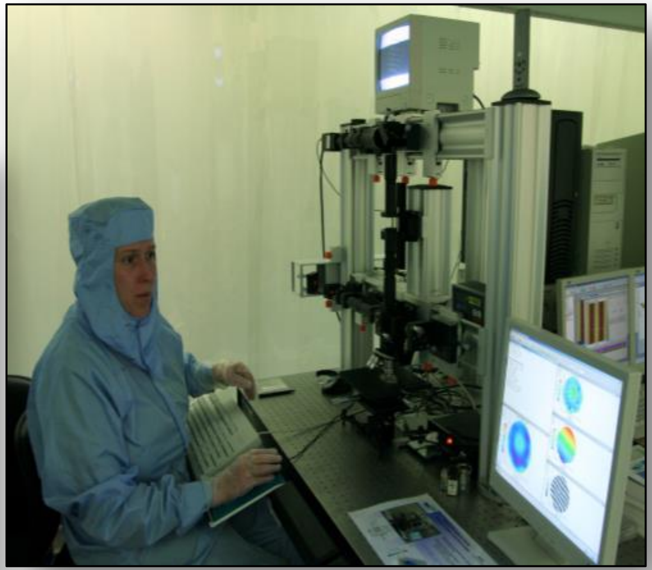


We characterize these components with professional optical instrumentation and metrology

ISO class 7 cleanroom facility

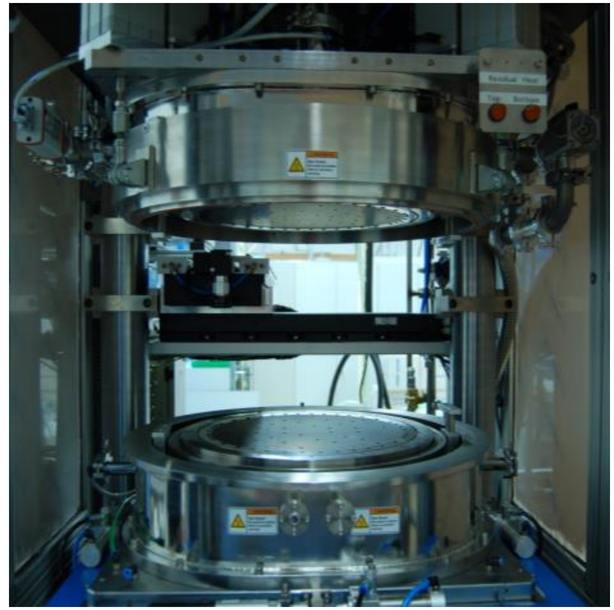


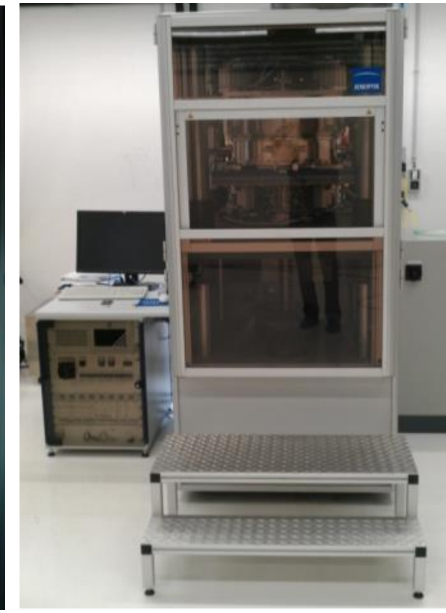


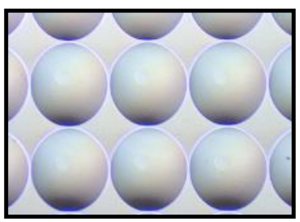


We test mass-manufacturability and fabricate low-volume series using hot embossing replication

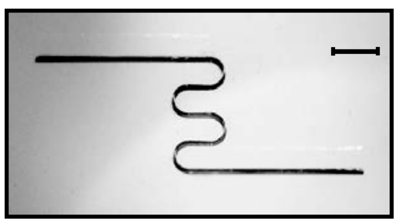
- 300 mm wafer capacity
- Double-sided embossing (Mould alignment <2 µm)
- Typical cycle times: 5 minutes
- Maximum temp.: (350±2)°C
- Maximum force: 450 kN
- Low- temperature UV embossing (nano-imprinting) possible



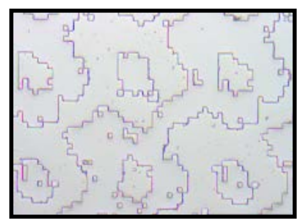




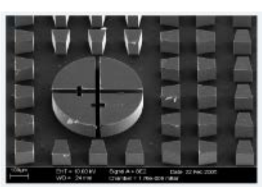
Micro-lenses

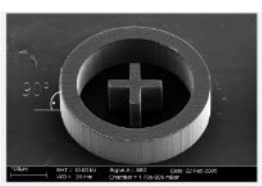


Microfluidic channels

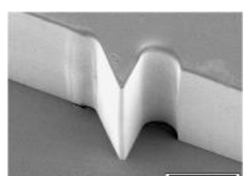


Diffractive optics

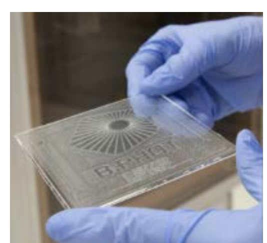


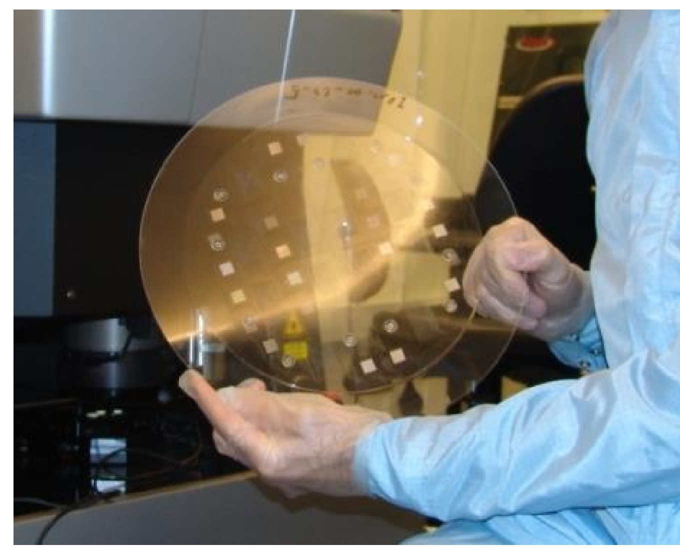


Pillars / Alignment marks

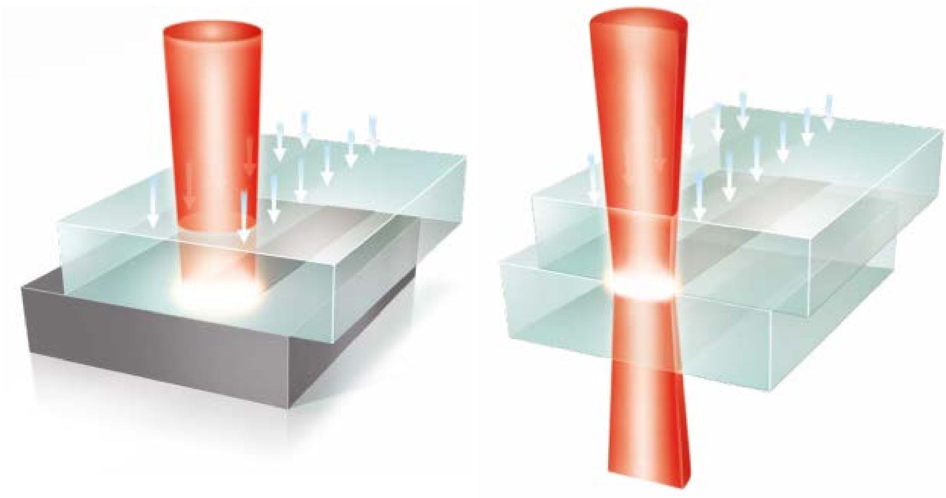


Micromirrors





We apply clear-to-clear laser welding of 300mm wafers to seal the microfluidic channels



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How can light be used to probe biochemical molecules in microfluidic channels?

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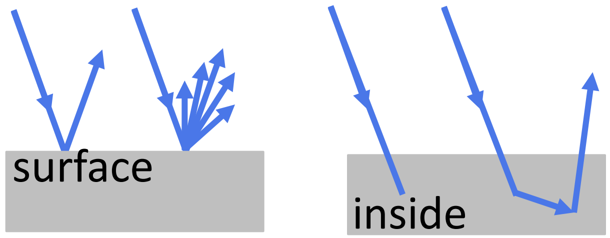
UV-VIS-NIR (250-1600nm)

specular/diffuse **reflection**

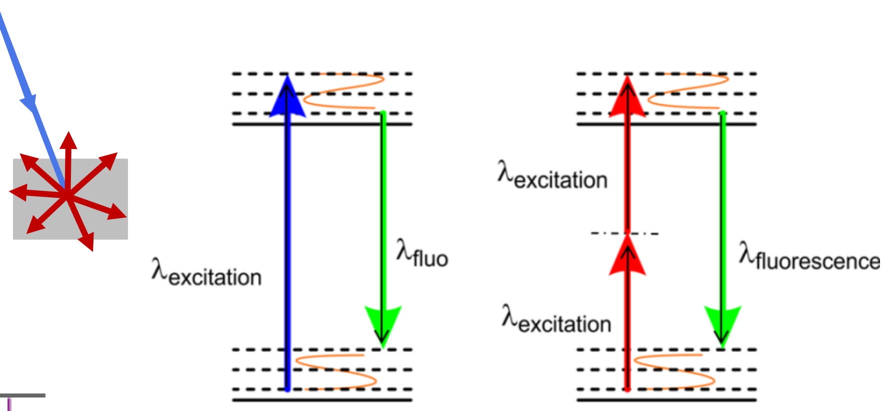


polarization

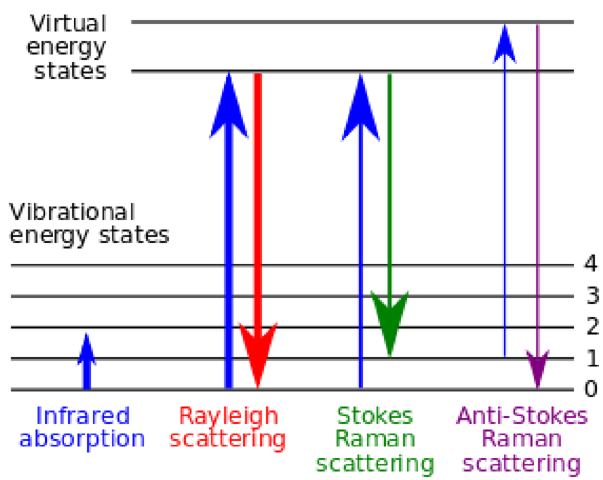
selective & vibrational absorption

internal scattering

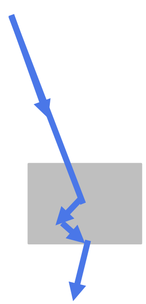
fluorescence (OPIF & TPIF)



Raman scattering

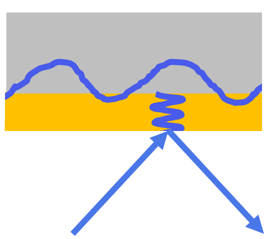


refraction



Transmission/ Absorption

Surface Plasmon Resonance (SPR)

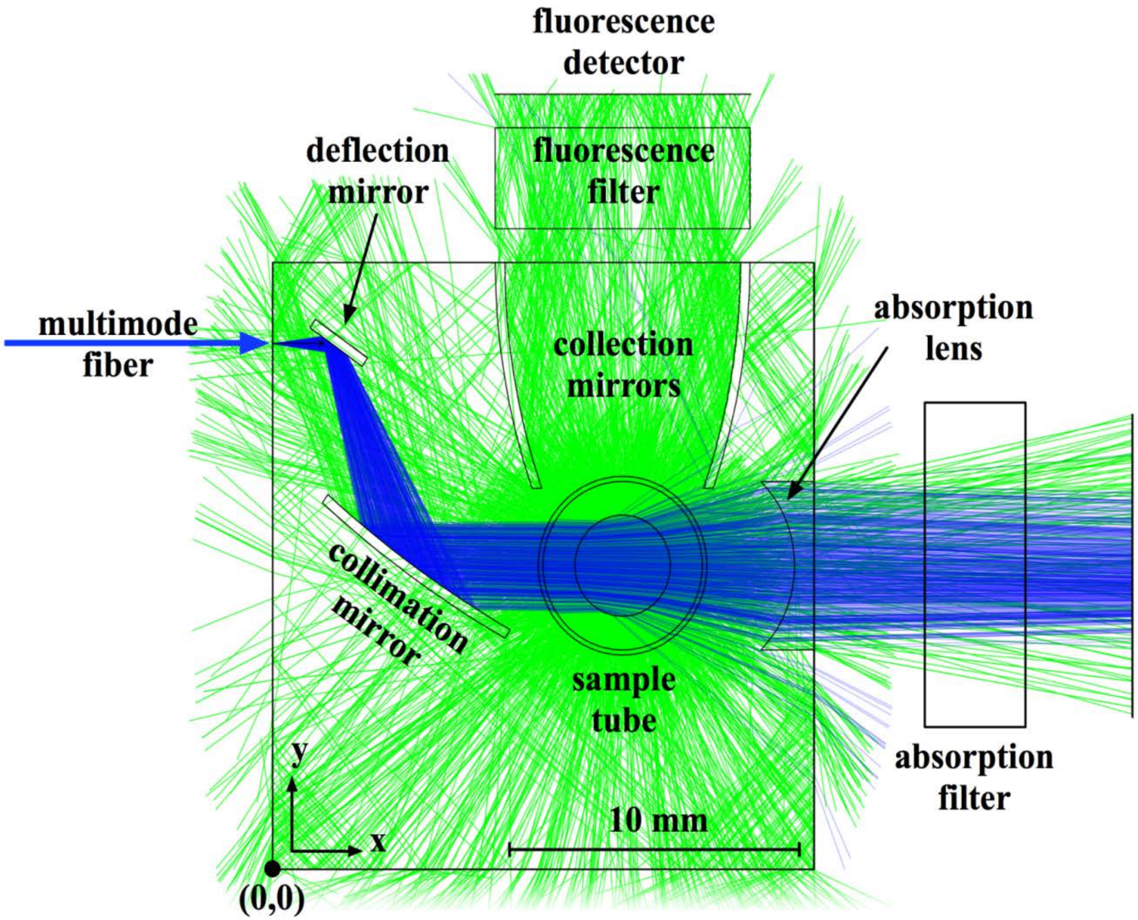


Let us highlight two practical lab-on-a-chip demonstrators

- **A combined absorbance and fluorescence detection module for lubricant oil monitoring**

- **A free-form optofluidic chip for confocal Raman spectroscopy measurements**

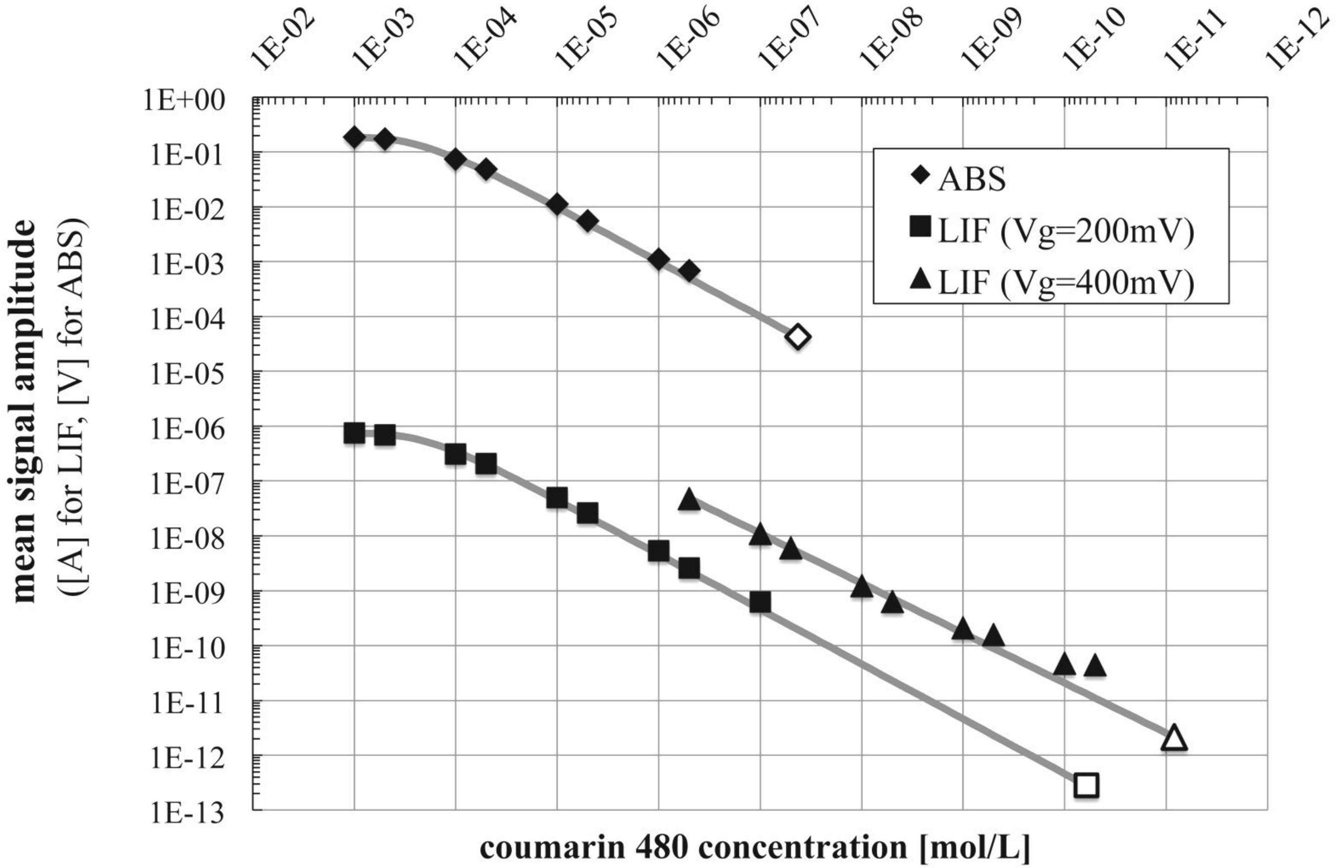
Combined absorbance and fluorescence detection module for lubricant oil monitoring



T. Verschooten et al., Journal of Micro-Nanolithography MEMS and MOEMS, 13(3), 2014.

Combined absorbance and fluorescence detection module for lubricant oil monitoring

- Calibration curves to define LoC performance



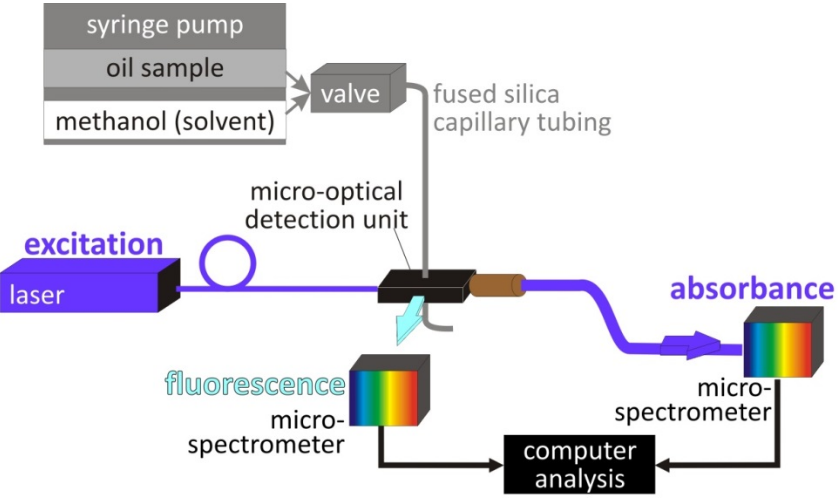
ABS: Experimental LOD = 500nM LIF: Experimental LOD = 50pM

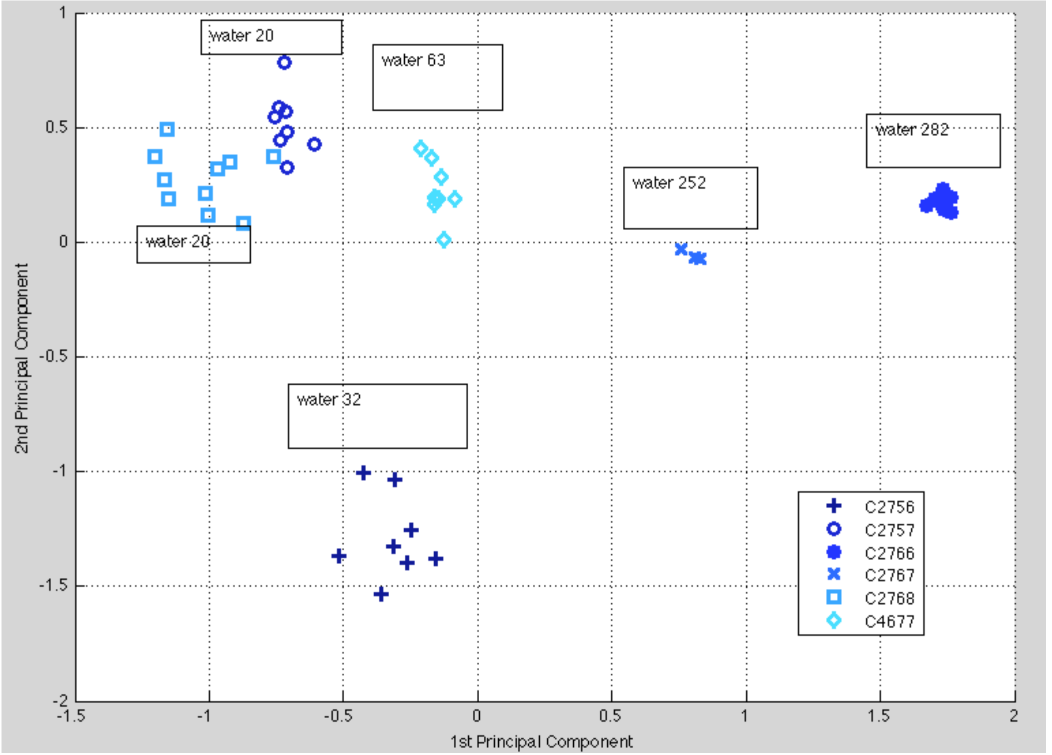
Limit Of Detection LOD = smallest concentration that can be measured with an SNR ≥ 3.3

T. Verschooten et al., Journal of Micro-Nanolithography MEMS and MOEMS, 13(3), 2014.

Combined absorbance and fluorescence detection module for lubricant oil monitoring

- Application of the LoC for lubricant oil monitoring





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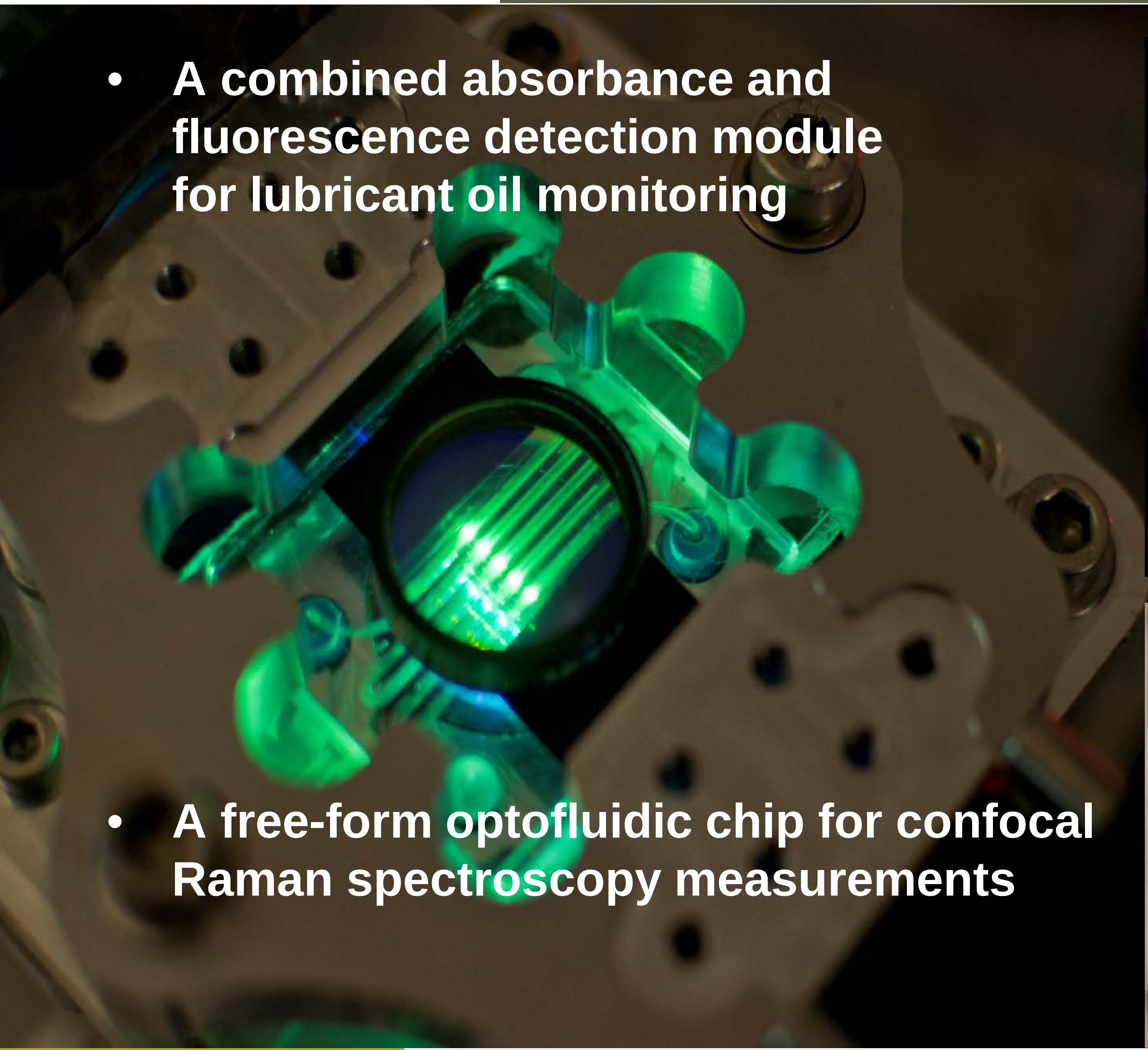

- **A combined absorbance and fluorescence detection module for lubricant oil monitoring**

- **A free-form optofluidic chip for confocal Raman spectroscopy measurements**

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Confocal Raman-on-chip measurement device

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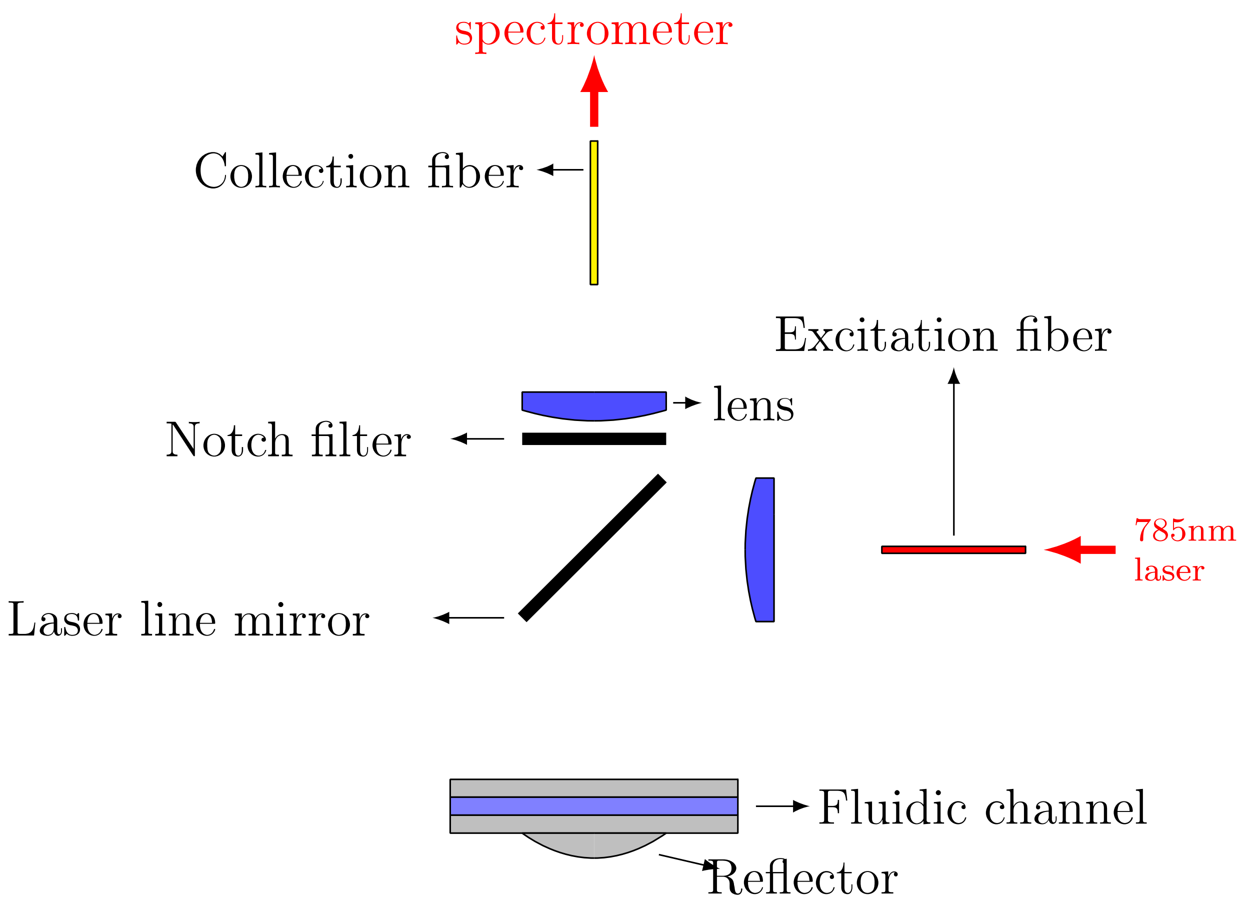
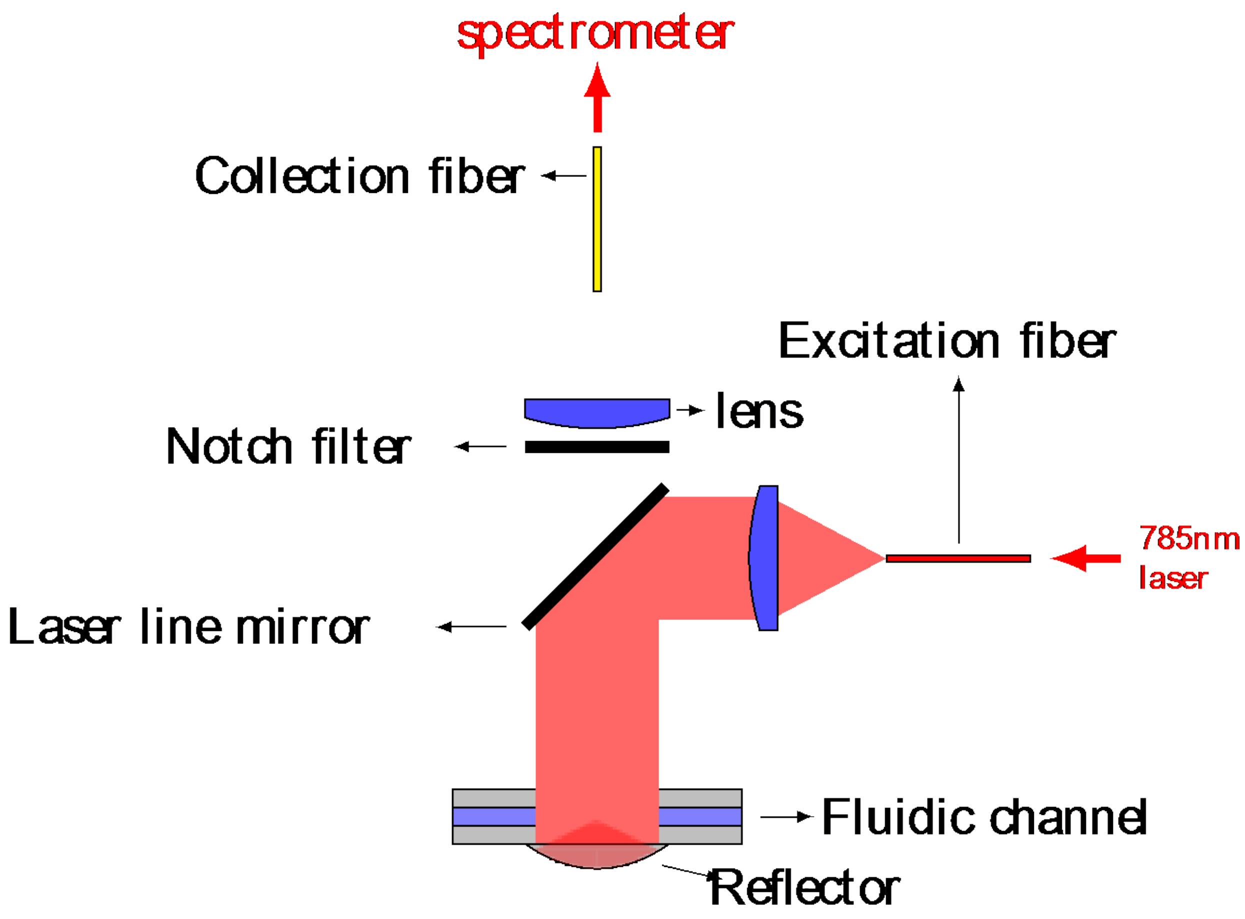


D. De Coster et al., IEEE J. of Sel. Top. in Quant. Electr., Vol. 21, No. 4. pp.1-8, 2015.

Confocal Raman-on-chip measurement device

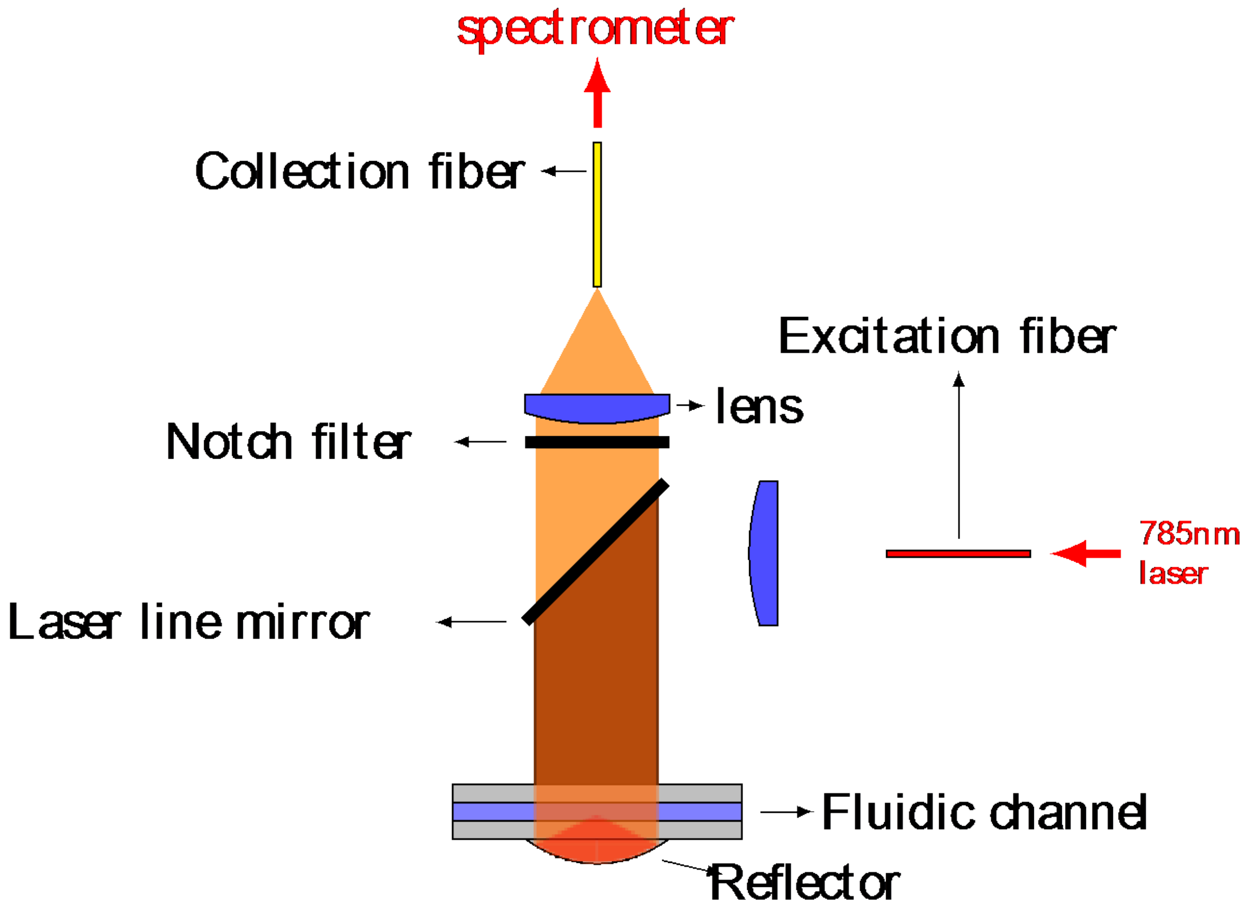
- Excitation path:



D. De Coster et al., IEEE J. of Sel. Top. in Quant. Electr., Vol. 21, No. 4. pp.1-8, 2015.

Confocal Raman-on-chip measurement device

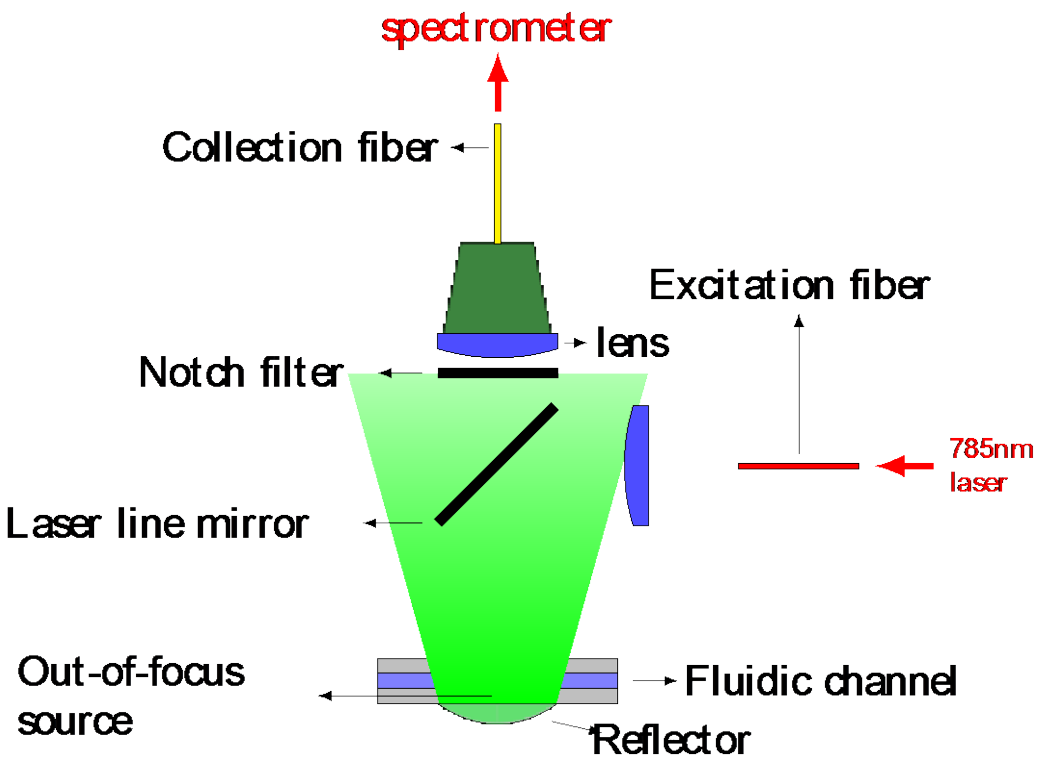
- Collection path:

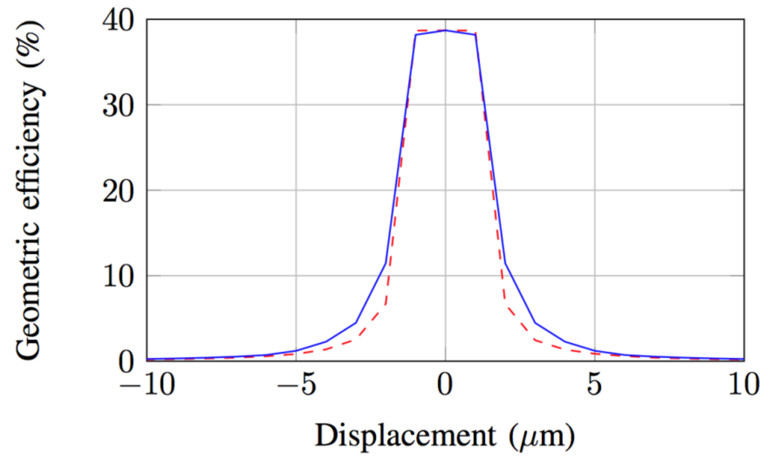


D. De Coster et al., IEEE J. of Sel. Top. in Quant. Electr., Vol. 21, No. 4. pp.1-8, 2015.

Confocal Raman-on-chip measurement device

- Minimize background by using the collection fiber as a pinhole:





- using the principle of confocal microscopy
- background light is not focused into the collection fiber

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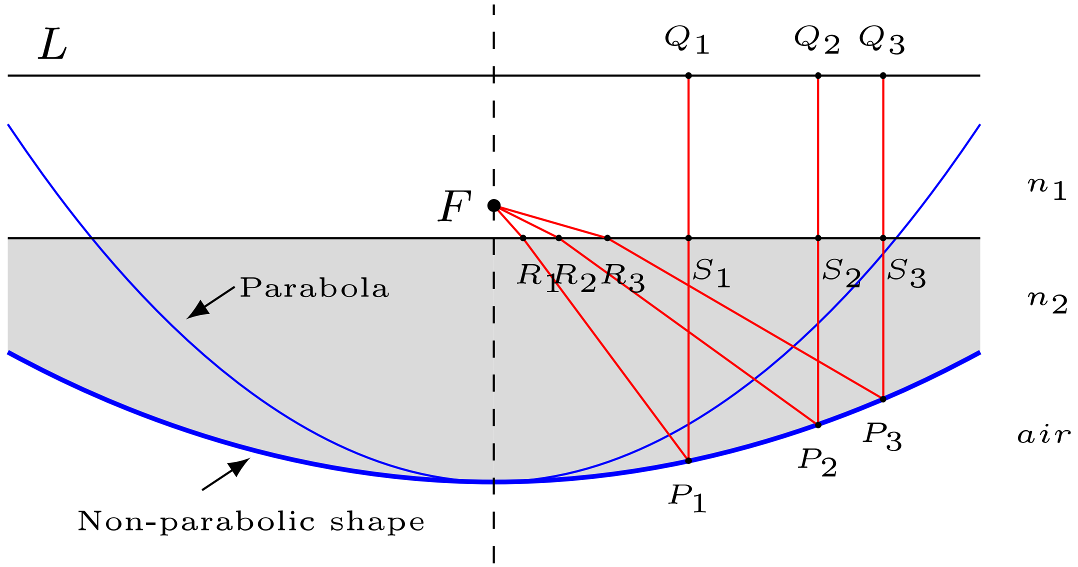
Confocal Raman-on-chip measurement device

- Maximize the throughput by using free-form reflector lens:



n_1 = water

n_2 = PMMA

- Non-parabolic reflector focuses a collimated incident light beam to the focal point ⇒ good performance

- geometry design based on the **principle of a parabolic reflector** and **Fermat's principle**, taking the refraction before focus into account:
  $n_1|Q_iS_i| + n_2|S_iP_i| + n_2|P_iR_i| + n_1|R_iF_i|$ = constant

- geometry is determined numerically ⇒ result: free-form reflector shape

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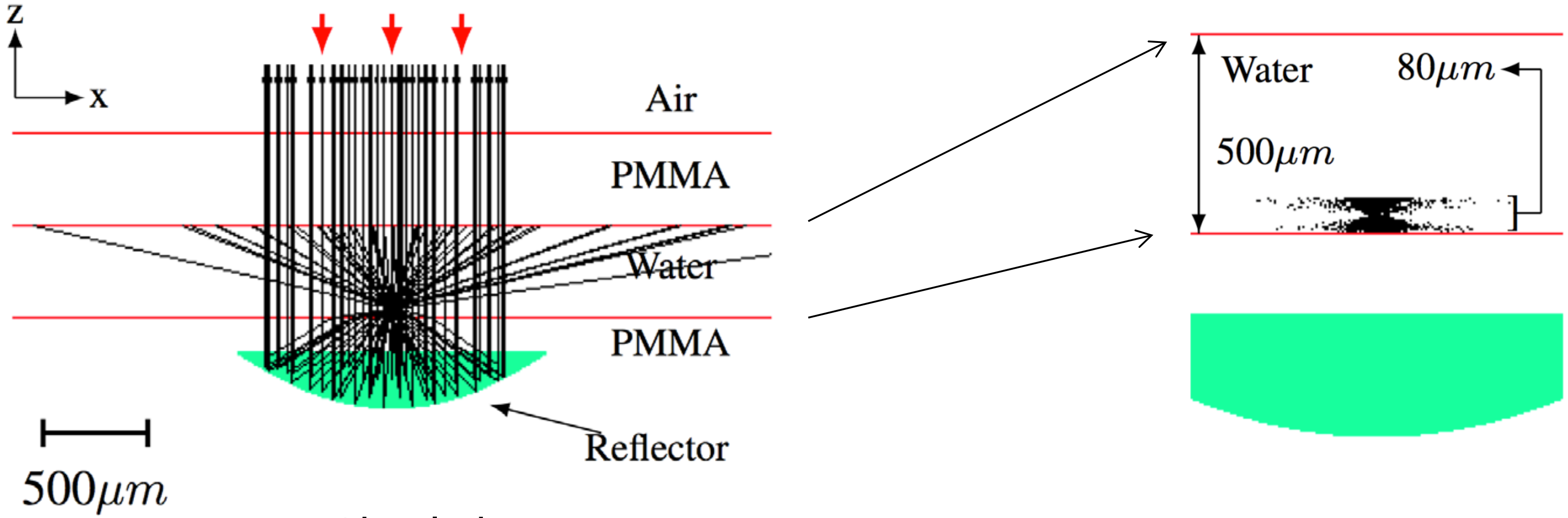
Confocal Raman-on-chip measurement device

- Maximize the throughput by using free-form reflector lens:



Simulation:
-non-sequential ray-tracing in Breault ASAP
-generation of Raman scattering in Matlab

Source:
-collimated Gaussian beam
-λ = 785nm
-beam waist is half of reflector diameter

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Confocal Raman-on-chip measurement device

- Maximize the throughput by using free-form reflector lens:

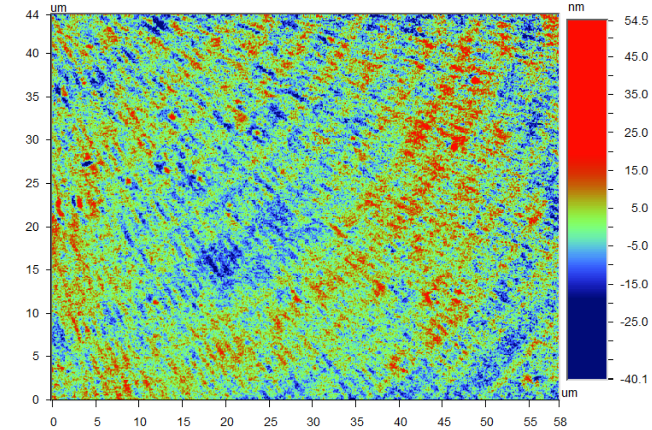
UDT used to prototype the free-form lens directly in PMMA:
-radius diamond tool: 221.3 µm

PMMA reflector:
-average ROC: 1.284 mm
-diameter: 1.6 mm
-height: 300 µm

200nm gold coating
(Chemical Vapor Deposition)

Characterization
(non-contact optical surface profiler)

RMS roughness = 9 nm (std = 1.24 nm)
22 evaluation areas (45 µm x 60 µm)



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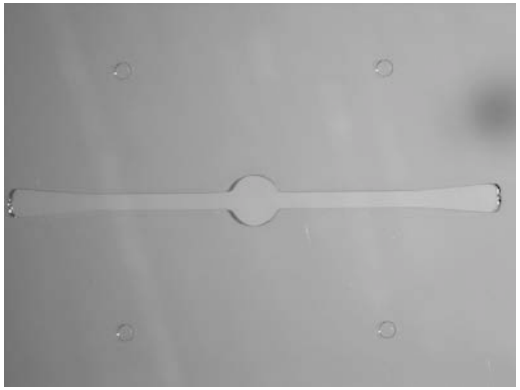
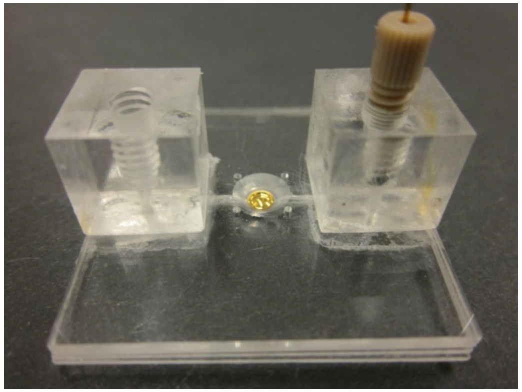
Confocal Raman-on-chip measurement device

- Assembly of the LoC:

Lab-on-chip consists of 3 PMMA layers:

- top layer (in- and outlet holes): milling
- middle layer (fluidic channel): milling
- bottom layer (reflector): diamond tooling





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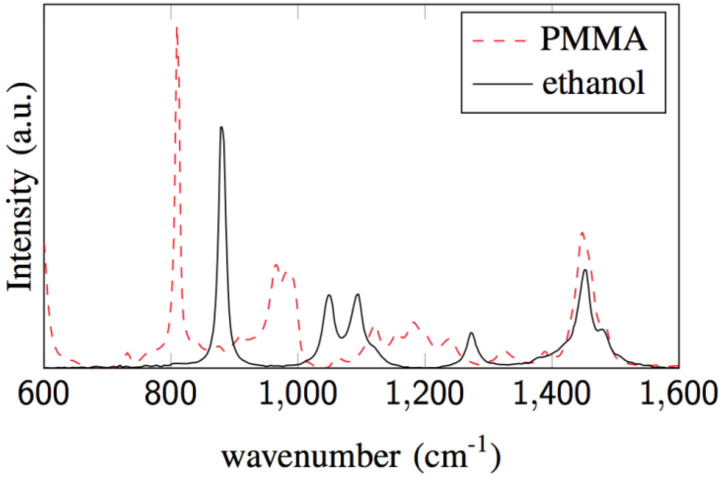
Confocal Raman-on-chip measurement device

- Proof-on-concept demonstration: reference measurement

Raman spectrometer



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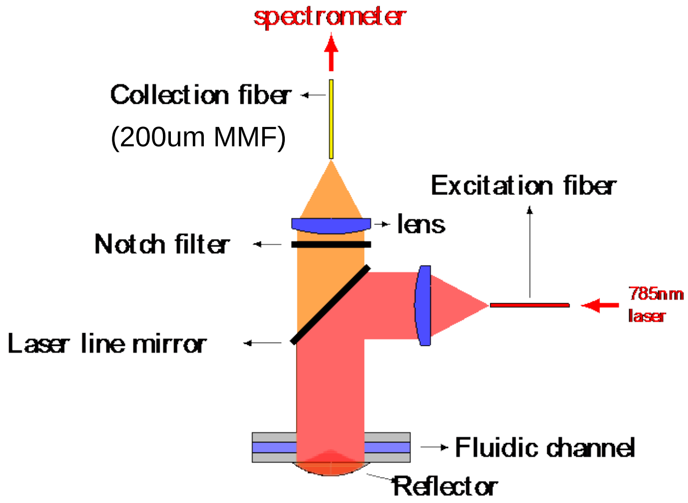
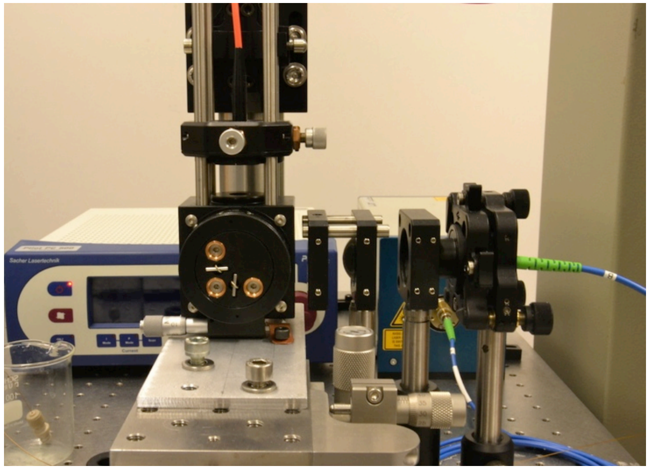
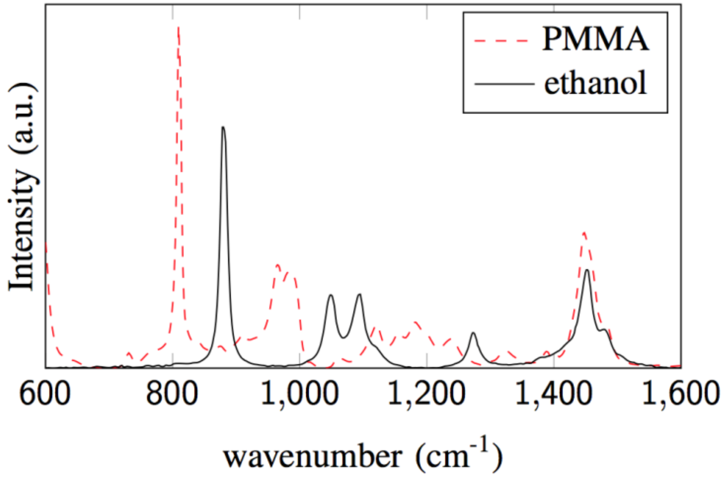
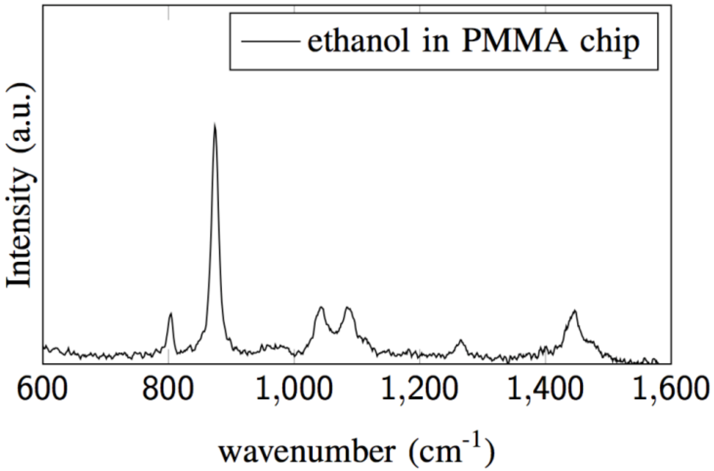
Confocal Raman-on-chip measurement device

- Proof-on-concept demonstration: background suppression









PMMA background suppression: factor 7

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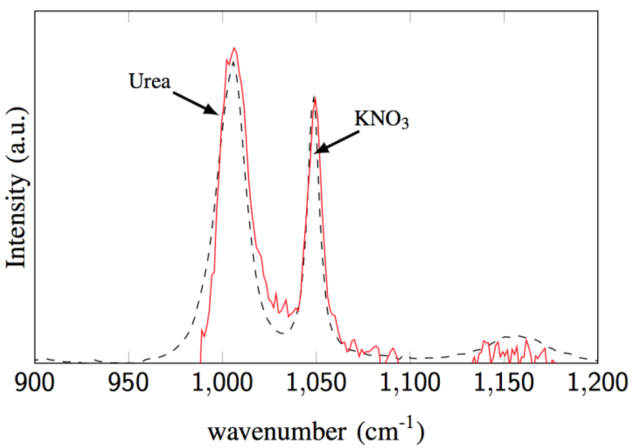
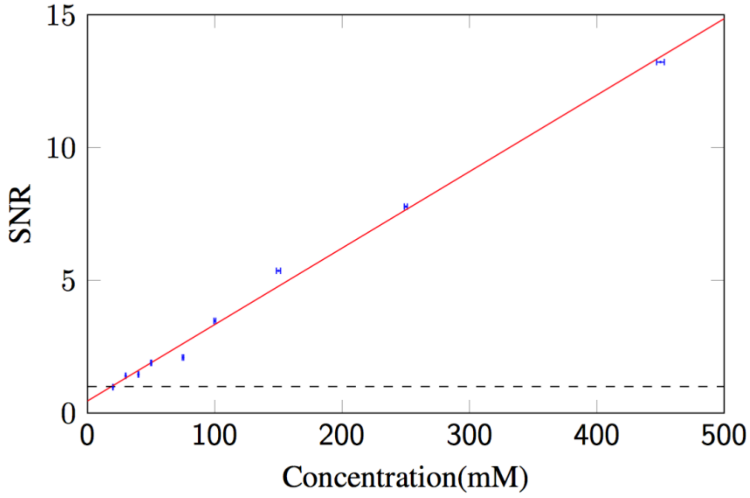
Confocal Raman-on-chip measurement device

- Proof-on-concept demonstration: Raman measurements on urea solutions

Calibration of the system:

- Raman measurements on urea solutions with known concentrations
- making use of an internal standard (KNO_3) for normalization





Mixture 450mM urea and 100mM KNO_3

reflector based Raman chip

commercial Raman spectrometer

Calibration curve for urea:

SNR = mean(peak area) / std(peak area) over 10 measurements

Noise Equivalent Concentration = 20mM
(acquisition time = 15s, power 190mW)

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Conclusion

Wafer-scale production of photonics-enhanced labs-on-chips holds tremendous potential for

- Low-cost mass production
- Wafer-scale integration with electronics for source/detector
- True disposability
- Biocompatibility / biodegradability
- Ubiquitous deployment

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