



Microfluidic and Transducer Technologies for Lab on a Chip Applications

Lab on a Chip platforms

Some examples:

SABIO

InTopSens

Positive

Acknowledgements

Addressing the questions

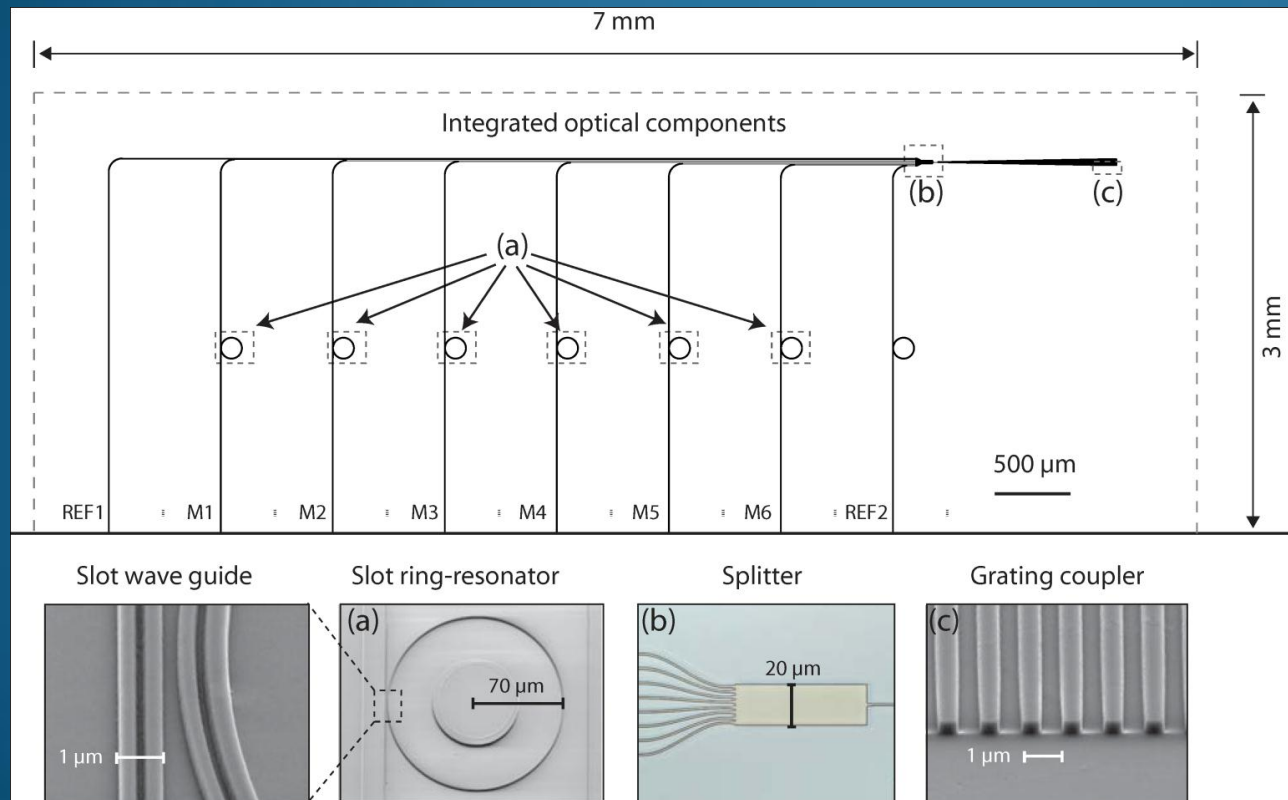
Daniel Hill,
MST Lab

Planar waveguide ring resonators are attractive for label-free biosensing due to their **small footprint**, **high Q-factors**, and **compatibility with on-chip optics and microfluidics**.

SABIO

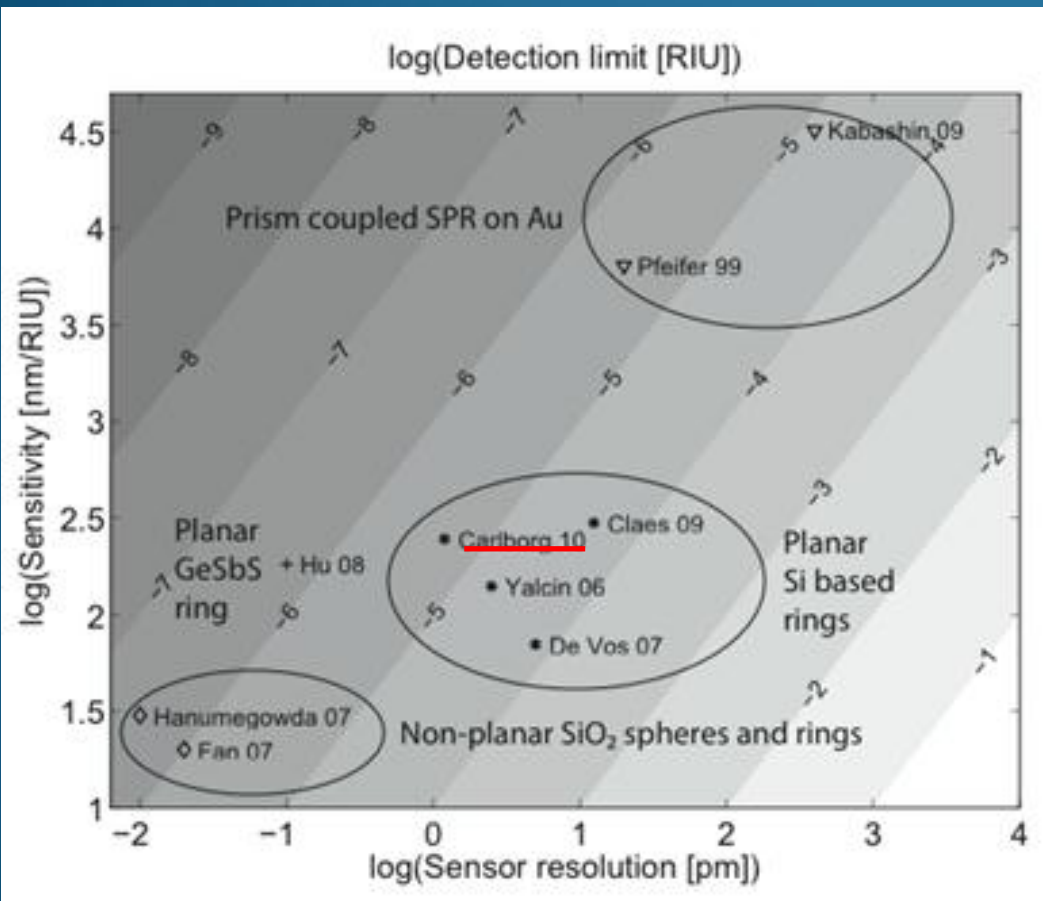
With RR for a good resolution we need:

- Large $d\lambda/dRI$.
- Low ring losses for sharp dips
- Efficient dip position determination
- Suppression of RI changes from unwanted influences e.g. T



Integrated nanophotonic slot-waveguide biosensor with simultaneous 6-plex readout for 6 biomarker **label-free hepatitis diagnosis**.

SABIO



- **DL** $> 5 \times 10^{-6}$ RIU, **sensitivity** < 240 nm/RIU over 7 K, without need of external temperature control or individual sensor calibration.

- **Bulk concentrations down to 100 ng/ml** of anti-BSA were measured, with a **surface mass density detection limit** for a glutaraldehyde-antiBSA model assay of **0.9 pg/mm²**.

■ Partners:

- UPVLC, UPM, KTH, Multitel, Kherion, Farfield, Zeptosens, Innsbruck Medical University, UPS

■ Main objectives:

- Integrated nanophotonic slot-waveguide biosensor with simultaneous 6-plex readout for 6 biomarker label-free hepatitis diagnosis.

■ Big innovation:

- Slot waveguide for biosensing (Opt. Lett.33, 708-710 (2008).)
- Multi-slots (Optics Express 16, 22 (2008) 17237-17242)
- MUI found new strain of Hep B not previously picked up by commercial instruments
- PDMS based vias
- Innovation of bonding in PDMS to acrylic polymer
- Demonstrated label free Hep C assay in sera on Analight for 80% activity with 0.2pg/mm²

■ Main challenges:

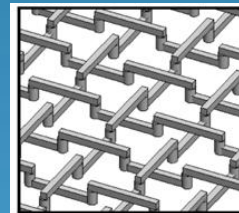
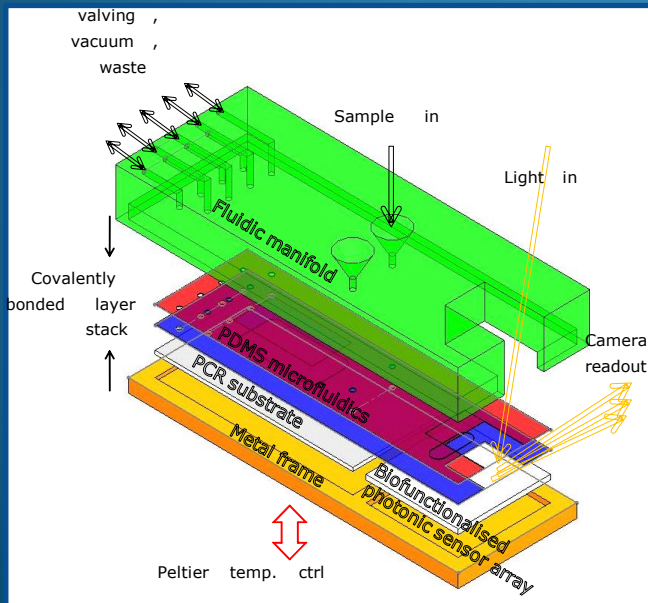
- Integration of microfluidics, biochemistry, photonics to keep biomolecules active on slotwaveguide.

■ Who will use the results when the project is finished? How are the end-users involved?:

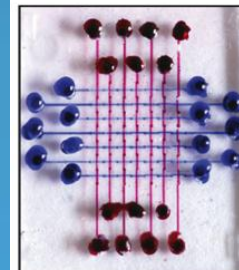
- Roche diagnostics have used MUI results to improve diagnostic tests
- Explosion of interest in slot waveguides as biosensors
- Technologies have been taken advantage of for head starts in other projects e.g. InTopSens.
 - 3D vias
 - Slot waveguides

InTopSens

- Similar nano-photonic sensors used in the PoC solution for the detection of sepsis and the antibiotic resistance profiling of the bacteria.
 - SOI RR starting point: 70 nm/RIU sensitivity for bulk changes in RI, a LOD of 10^{-5} RIU, which for biotin-avidin sensing corresponds to 3.8 ng/ml.
 - Slightly poorer all round than SiN slot RR, but still much more than sufficient for detecting typical DNA concentrations at 10^4 ng/ml for 46 PCR cycles taking 90'.
- Our initial target is 1ng/ml, equivalent to 3ng/mm², for DNA hybridisation.

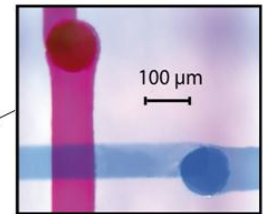
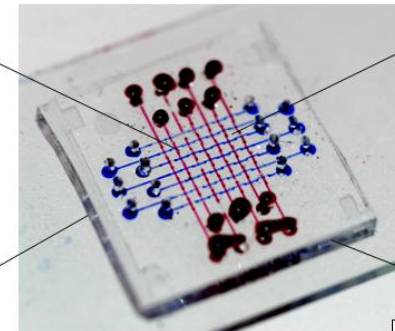


Basket weave



4 cm² large

Two level PDMS device with high level of vertical integration

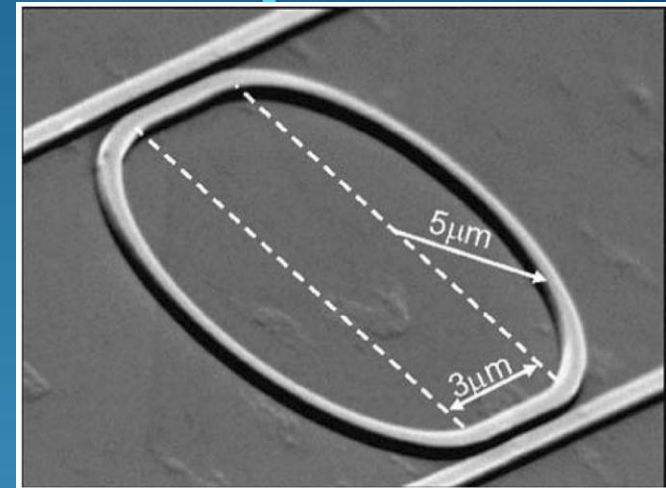
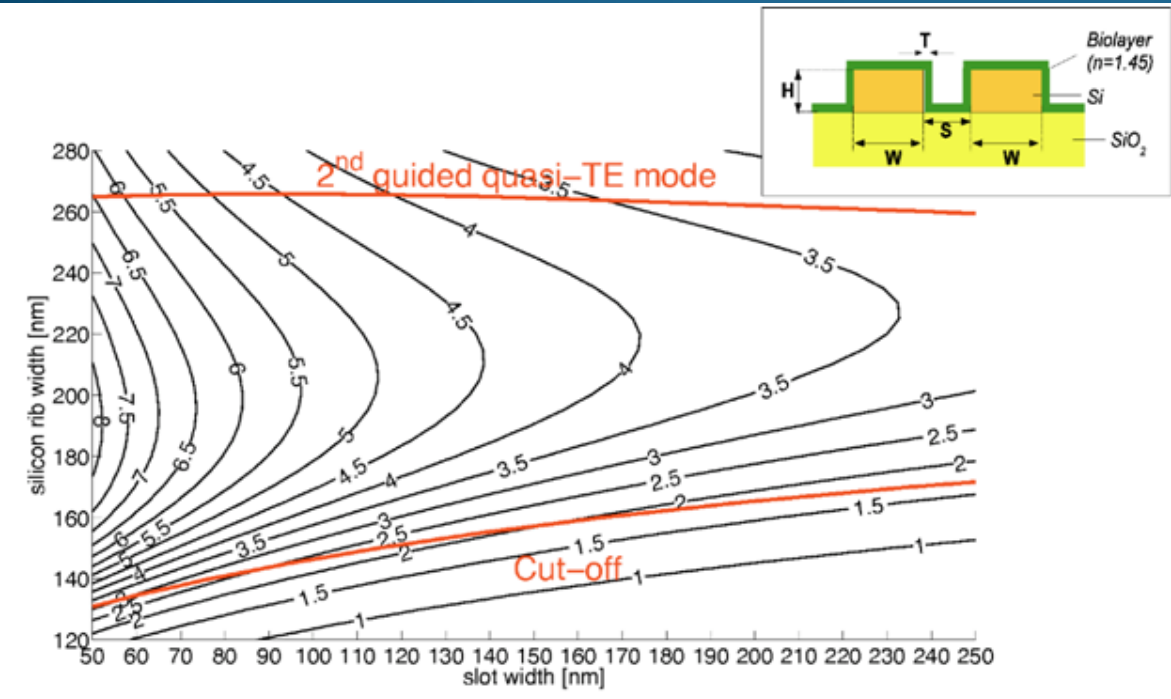


Overpass crossing



Direct leak tight adhesion to top layer because the "sticky" surface

InTopSens



- Slot sensor design parameters chosen as:
 - Ring radius of only 5 μm,
 - a slot width of 104 nm,
- fabricated by deep-UV (193 nm) lithography.

■ Sensitivity is 3.5x greater, 298 nm/RIU, but bending and mismatch losses led to a poorer Q and resolution, and therefore LoD, 4.2×10^{-5} RIU.

■ MZI with folded arms, Cascaded ring resonators based on Vernier effect,....

■ In parallel been working with PhC WG sensors

Sensing experiments

InTopSens

RI (WP2)

Protein (WP2)

ssDNA (WP3)

Main configurations

Configuration	RI (WP2)	Protein (WP2)	ssDNA (WP3)
RR	10^{-5}	5pg/mm ²	40nM (Aptes) ~ 27*Conc _{min}
PCW	3×10^{-4}	2pg/mm ² (BSA/antiBSA)	20nM (ICPTS) ~ 54*Conc _{min}

Alternative configurations (for better detection limit)

Vernier	8×10^{-6} (2170nm/RIU)
Modified PCW	Design
TM RR	Design (1pg/mm ² estimated)
4µm Disk resonator	Design (1pg/mm ² estimated, 10x smaller)
TE-TM RR	Proposed

■ Partners

- KTH, UPVLC, Aarhus University, Antwerpen University, Mobidiag, Farfield, UGent.

■ Main objectives:

- Development of a **point-of-care solution for the detection of sepsis and the antibiotic resistance profiling of the bacteria.**

■ Big innovation:

- A generic, novel thiol-ene based polymer microfluidic technology was developed that can be used for both rapid prototyping and for medium-scale production
- 3D microfluidic network
- Macro to micro fluidic interface
- Dual polarisation ring resonator (->overlapping consortium)
- Vernier ring resonators
- Small disc resonators with similar sensitivity, better for dual polarisation
- ssDNA hybridization sensing on PhC - Opt. Lett. 35, 3673-3675 (2010).
- Flood illumination/Parallel readout
- 4 patents +1
- 13 peer reviewed papers, so far!

■ Main challenges:

- On chip sample preparation (lysis) and bacteria sensing. 0.1ng/ml DNA hybridization sensing
- DNA sensing in general
- From lab-around-a-chip (clutter of wires, lasers, tubings) to lab-on-a-chip

■ Who will use the results when the project is finished? End-users involvement?:

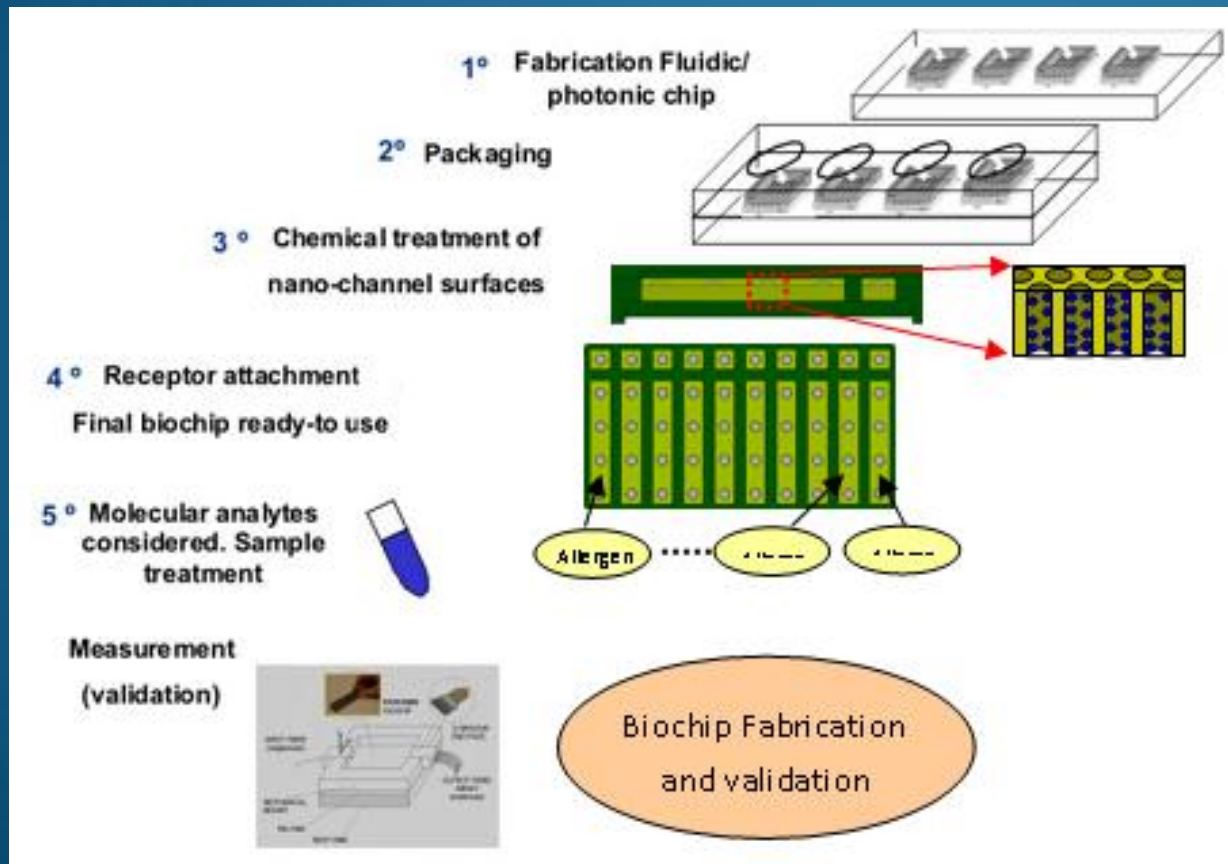
- Start-up from consortium, Licence, SME take up and/or Sell technology.
 - For either principal or alternative sepsis diagnostic the third is the most likely given that Mobidiag already has products in this very market.
 - For the various generic technologies???
- A large IMI project approved (RAPID) ensuring transfer of technology to large pharma (EFPIA) for bacteria and DNA screening

Porous silicon based bio-photonic sensors for **point of care food allergy determination.**

Positive

- **High surface:vol ratio** of porous silicon permits very high surface densities of bound AB-AG complexes in a reduced volume.

- + a novel optical interaction -> **scores of sensing areas / 1 cm² chip with detection-limits down to 0.1 pg/mm²**



■ Partners

- KTH, CSEM, UVEG, UTrento, CNR, Charité, Phylogene, Farfield.

■ Main objectives:

- Demonstrate a safe and rapid low cost diagnostic test for food allergies at point of care such as in a GP's office or hospital.

■ Big innovation:

- Starting 4 months before the project did!
- Use of porous silicon as a biosensor
- Polarimetry based biosensor

■ Main challenges:

- Agree on meeting locations!
- Bio-clogging of pores

■ Who will use the results when the project is finished? How are the end-users involved?:

- Farfield would use the generic biomolecular capture surface if successful.
- Phylogene interested in diagnostic device.

Thank you for your attention!

And thank you to

- The KTH, SABIO, InTopSens and Positive teams.
- Juan Martínez Pastor (Universidad de Valencia) and all of my other past, current and future collaborators.

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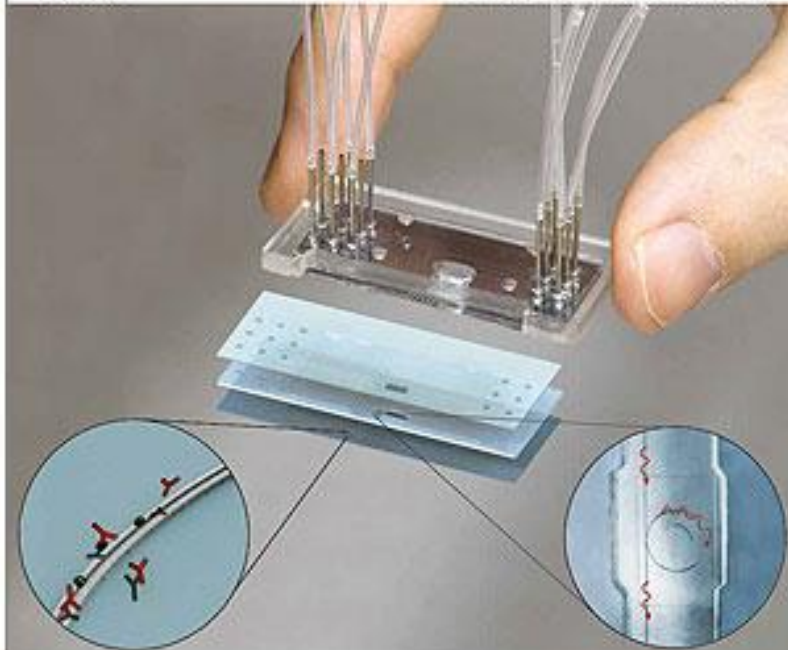
Gylfason et al, Lab-Chip, 2010

Lab on a Chip

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Carlberg
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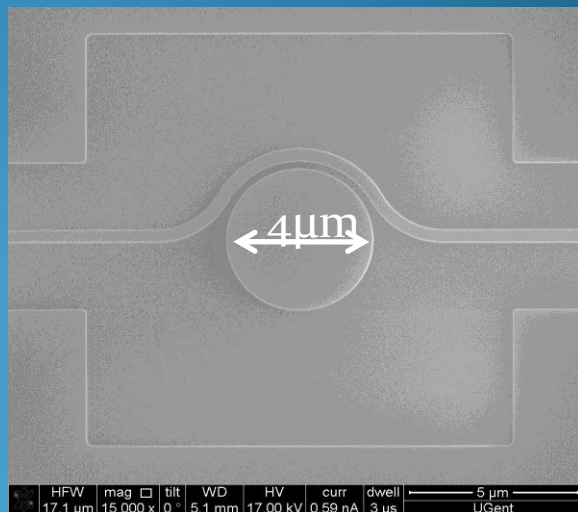
Qian
Agent-based simulation of droplet flow
McKinnon and Tucker
Bianchi et al

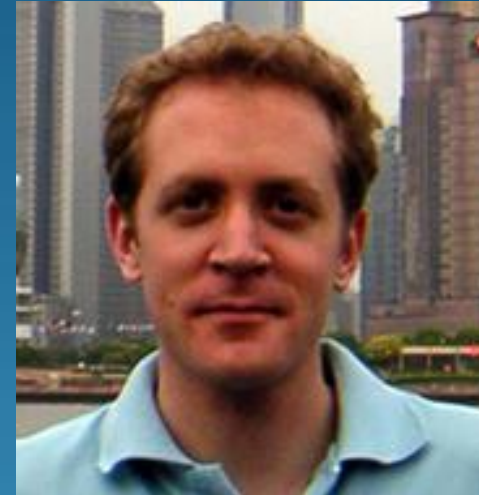
Experimental characterization of a silicon photonic biosensor consisting of two cascaded ring resonators based on the Vernier-effect and introduction of a curve fitting method for an improved detection limit

Tom Claes,* Wim Bogaerts, and Peter Bienstman
 Photonics Research Group, Department of Information Technology
 Ghent University - imec, Sint-Pietersnieuwstraat 41, 9000 Gent, Belgium



- Number 1 international conference in Microsystem technology / MEMS
- Acceptance rate: 5
- OH6: Carlborg et al, IEEE JMEMS, 2010





Oral presentations at MicroTAS, Oct. 3-7 2010 Groningen:

- Number 1 International conference series in lab-on-a-chip
- Acceptance rate for oral presentations: 10%
- After the presentation, the audience asked 10 (!) questions
- Approached by 1 multinational company, 1 SME and 2 universities for material samples and collaboration
- We are considering a KTH spin-off company