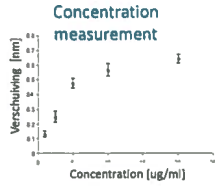
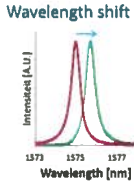


Label-free ring resonator biosensor through refractive index sensing of antigen-antibody binding



Biosensors

Detect presence and concentration of

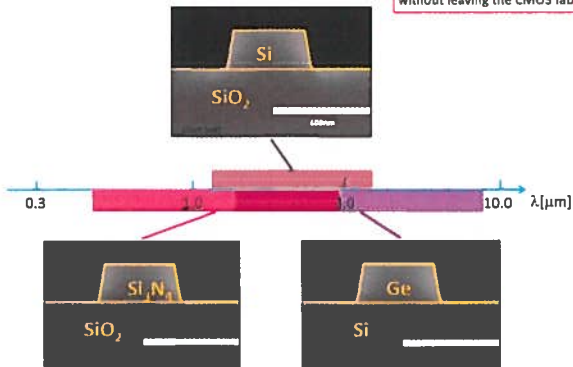
- Proteins
- Viruses
- Bacteria
- DNA
- ...

Two classes:

- Labeled: detection of label bound to biomolecule
- Label-free: direct detection of biomolecule

Silicon photonics: extending the wavelength range

without leaving the CMOS fab



R. Soref, Nature Photonics 2010

Outline

An introduction to silicon photonics

➔ Refractive index biosensors for immunoassays

Spectroscopy-on-a-chip

Absorption spectroscopy: Continuous Glucose Monitoring

Raman spectroscopy: virus detection?, enzyme detection?, exosome detection?, amyloid detection?

Point-of-care Pulse Wave Velocity measurement

What is silicon photonics?

The implementation of high density photonic integrated circuits by means of CMOS process technology in a CMOS fab



Enabling complex optical functionality on a compact chip at low cost



Silicon Photonics and its applications in life science

Roel Baets

Photonics Research Group, Ghent University – imec
Center for Nano- and Biophotonics, Ghent University
roel.baets@ugent.be



Outline

An introduction to silicon photonics

Refractive index biosensors for immunoassays

➔ Spectroscopy-on-a-chip

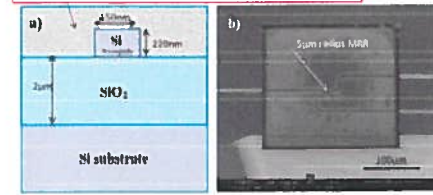
Absorption spectroscopy: Continuous Glucose Monitoring

Raman spectroscopy: virus detection?, enzyme detection?,
exosome detection?, Amyloid detection?

Point-of-care Pulse Wave Velocity measurement

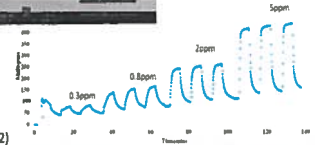
Selective, reversible and fast ammonia gas detection

Microporous silica layer, pores: 2nm; porosity: 45%
Functionalized for ammonia-selectivity



Sensitivity down to 100ppb demonstrated

No interference from H₂O and CO₂



N. Yebo et al, Optics Express, 20(11), pp. 11855 (2012)

Application:

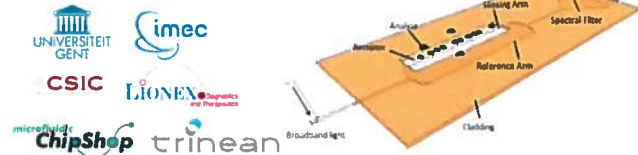
breath analysis



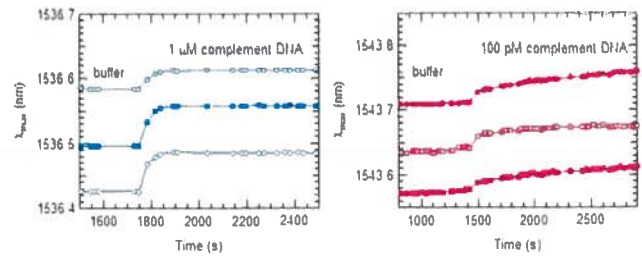
Pocket project (FP7)



- Detection of Tuberculosis biomarkers in urine
- SiN PIC-platform in visible: cheaper sources and detectors
- Cheap readout: broadband source + sensor + on-chip spectrometer
- Coordinator: UGent (P. Bienstman)
- Spin-off plans

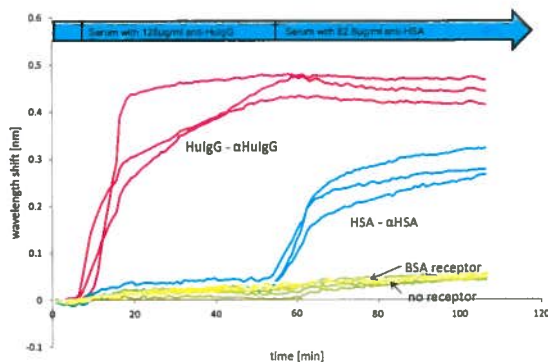


DNA hybridisation



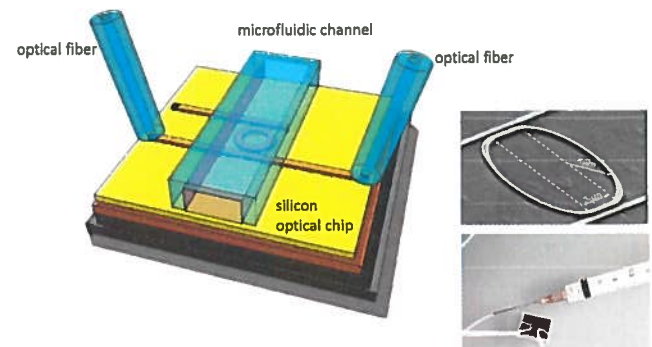
Concentrations down to 100 pM can be detected

Multiplex sensing results

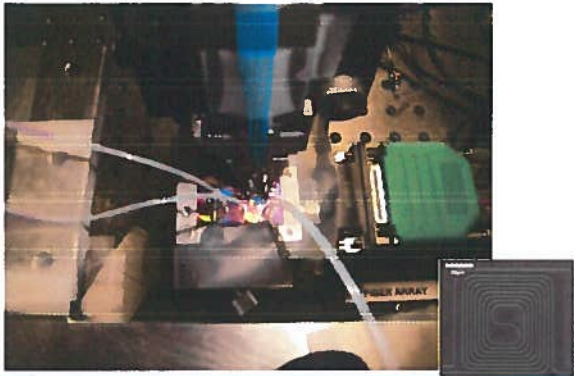


K. De Vos et al, Optics Express (2007)

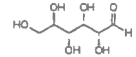
Lab-on-chip concept



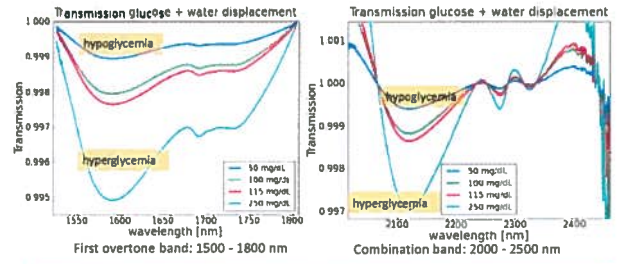
Proof-of-concept demonstration in the lab



Glucose absorption spectroscopy



Objective: Continuous Glucose Monitoring by means of subcutaneous implant

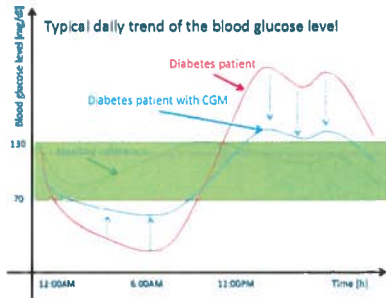


For glucose sensing in humans (3-15 mM): Largest change in transmission is 0.5 %
Required sensitivity : 0.02%

Continuous Glucose Monitoring (CGM) has proven to improve glycemic control of diabetes patients

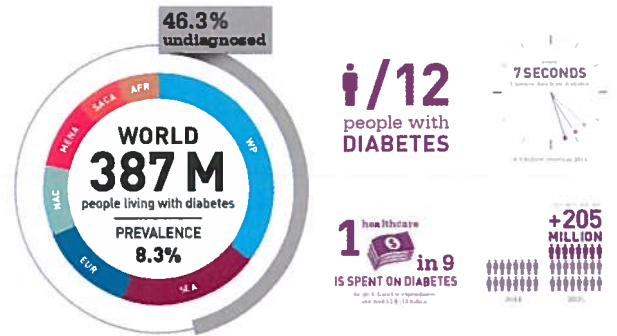
Multiple randomized, controlled studies* with usage of CGM systems show positive health impact:

- lower average blood glucose levels (reduction in HbA1c compared to the baseline value)
- Decrease of hypoglycemic frequency



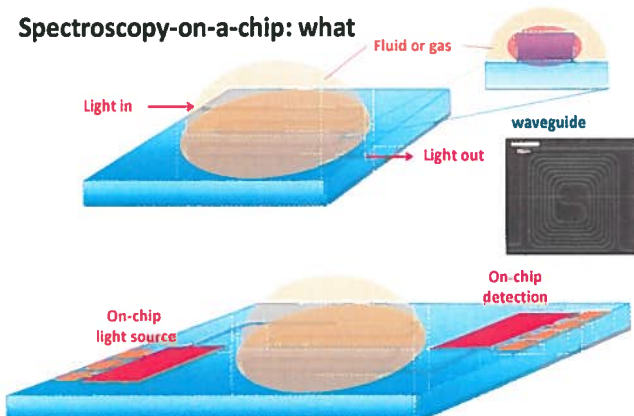
* Liebi A, Henrichs HR, Hainemann L, et al. Continuous glucose monitoring: evidence and consensus statement for clinical use. J Diabetes Sci Technol. 2013;7:500-519

Diabetes is the 21st century health challenge

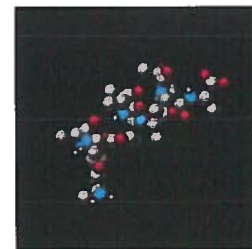


<http://www.idf.org/diabetesatlas/update-2014>

Spectroscopy-on-a-chip: what



Vibrational spectroscopy



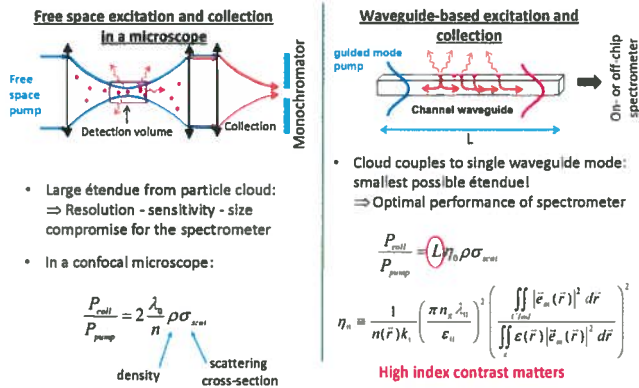
Infrared absorption spectroscopy

Very sensitive
"Poor" sources and detectors
Less compatible with biology

Raman spectroscopy

Very insensitive (but there are tricks)
Mainstream sources and detectors
More compatible with biology

Waveguide-enhanced Raman spectroscopy

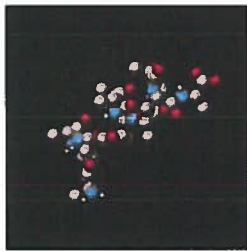


Raman signal strength: extremely weak

Typical molecular scattering cross-section: 10^{-29} cm^2

After propagation through 1 cm of 100% dense analyte, one photon is scattered for $10^6 - 10^7$ input photons

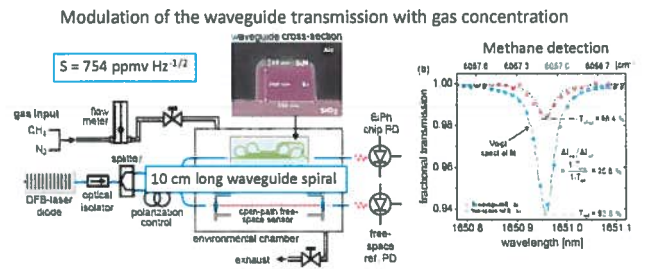
Vibrational spectroscopy



Infrared absorption spectroscopy
 Very sensitive
 "Poor" sources and detectors
 Less compatible with biology

Raman spectroscopy
 Very insensitive (but there are tricks)
 Mainstream sources and detectors
 More compatible with biology

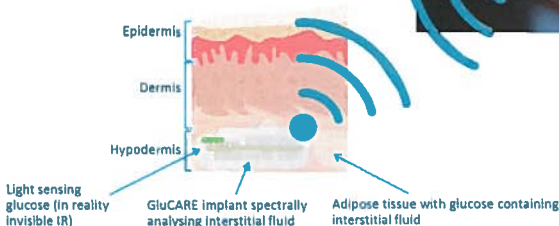
Trace gas sensing with evanescent absorption spectroscopy



Zhang, Eric J., et al. CLEO 2016.

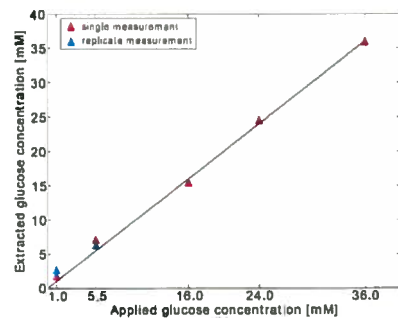
GluCARE enabled by "silicon photonics"

Subcutaneous implanted IR spectral analyser connected wireless to external transceiver (>6 months implantation time)



Glucose absorption spectroscopy: proof-of-concept

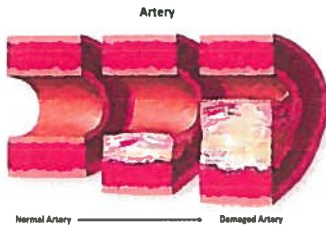
Use measured spectrum of 36 mM solution as the basic vector



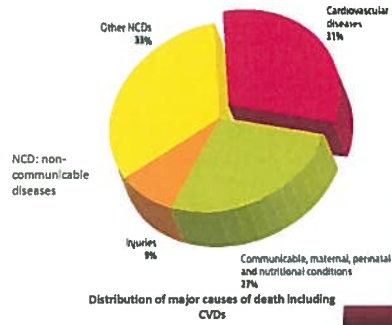
E. Ryckeboer et al, Biomedical Optics Express (2014)

Atherosclerosis

Deposition of plaque ⇒ higher arterial stiffness ⇒ higher pulse wave velocity



Cardiovascular diseases



Cardiovascular disease: The biggest killer in the world, responsible for 30% of deaths (WHO, 2011)



Outline

An introduction to silicon photonics

Refractive index biosensors for immunoassays

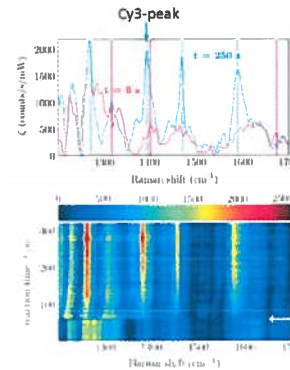
Spectroscopy-on-a-chip

Absorption spectroscopy: Continuous Glucose Monitoring

Raman spectroscopy: virus detection?, enzyme detection?, exosome detection?, amyloid detection?

➡ Point-of-care Pulse Wave Velocity measurement

DNA hybridization kinetics



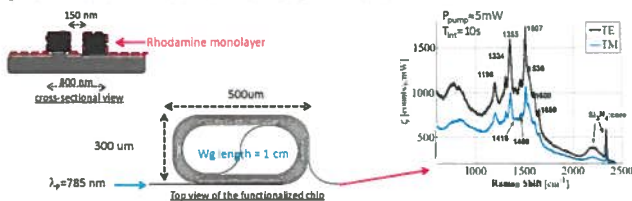
1. Waveguides functionalized with single strand DNA (here of a cancer-relevant gene K-Ras)

2. Real-time monitoring of the binding of complementary DNA, labeled with Cy3

A. Dhakal et al, <http://arxiv.org/abs/1608.08002>, 2016

Raman spectroscopy of Rhodamine monolayers

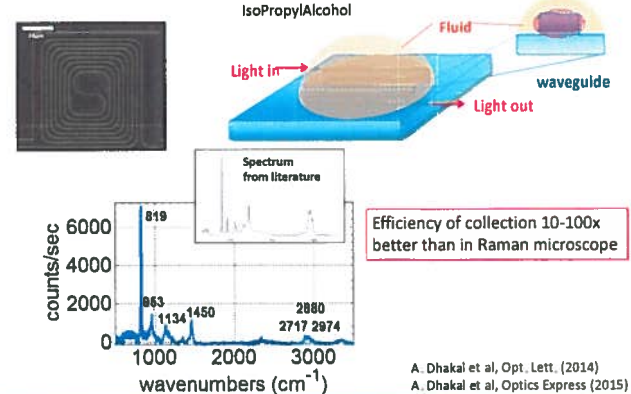
Si₃N₄ waveguides were silanized, reacted with amine-reactive NHS-Rhodamine and rinsed to get a monolayer of Rhodamine on the waveguide surface.



>10⁴ more collection efficiency than with Raman microscope.

A. Dhakal et al, <http://arxiv.org/abs/1608.08002>, 2016

Raman spectrum of IPA on silicon-nitride waveguide



Efficiency of collection 10-100x better than in Raman microscope

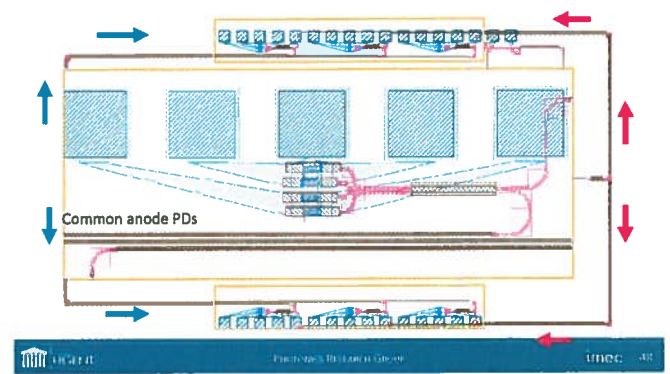
A. Dhakal et al, Opt. Lett. (2014)
A. Dhakal et al, Optics Express (2015)

Conclusion

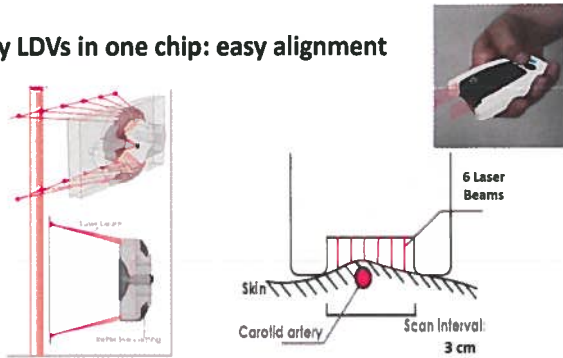
Silicon photonics:

- Mature technology in CMOS-fab, low cost in high volume
- Strong industrial traction for telecom/datacom/interconnect applications
- From visible to mid-IR
- Very large potential for lab-on-chip applications, body implants and PoC tools
 - refractive index sensing for immunoassays
 - spectroscopic sensing
 - absorption spectroscopy
 - Raman spectroscopy
 - point-of-care diagnostic tools (LDV, OCT, ...)

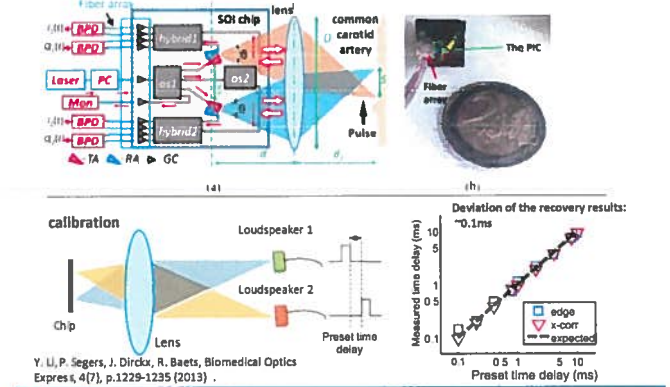
Photonic integrated circuit



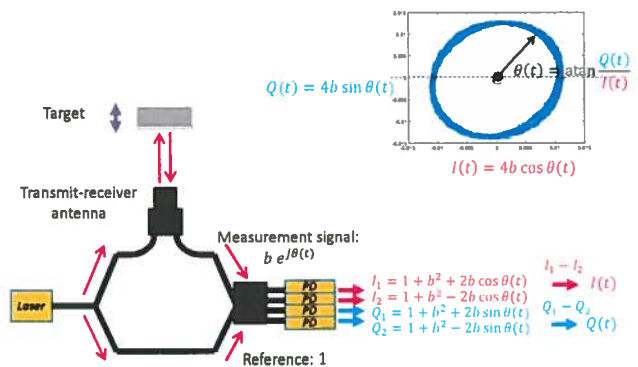
Many LDVs in one chip: easy alignment



Our previous work: Dual-homodyne LDV for PWV measurements



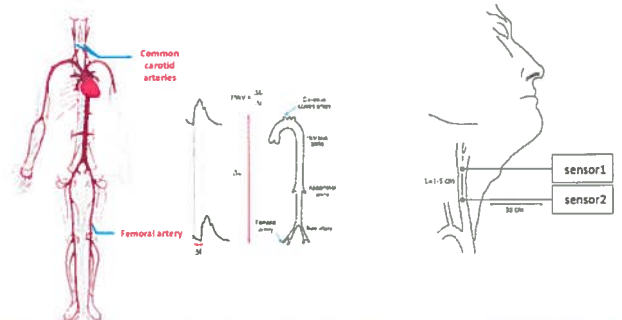
Principle of Homodyne Laser Doppler Vibrometry



Pulse wave velocity

Gold standard: Carotid-femoral PWV

Point-of-Care approach: Local PWV



Acknowledgements

Photonics Research Group
professors P. Bienstman, W. Bogaerts, B. Kuyken, G. Morthier,
G. Roelkens, N. Le Thomas, D. Van Thourhout
many postdocs and PhD's



IMEC CMOS process line
and ePIXfab www.epixfab.eu

Funding and collaborations through national and EU research projects





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Overview and details of the sessions of this conference. Please select a date or location to show only sessions at that day or location. Please select a single session for detailed view (with abstracts and downloads if available).

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baets

Presentations

IOI 1 S01: Silicon Photonics and Guided-Wave Optics: Integrated silicon and silicon-hybrid photonics

Time: 29/Sep/2016: 1:30pm - 3:00pm Location: Newton Cabinet

1:30pm - 2:00pm

Invited

Silicon photonics and its applications in life science

Roel Baets

Ghent University - imec, Belgium

A variety of silicon photonics applications such as refractive index biosensors and lab-on-a-chip sensors in a life science context will be given

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