# MEDICAL DEVICE APPLICATIONS OF SILICON AND SILICON NITRIDE INTEGRATED PHOTONICS

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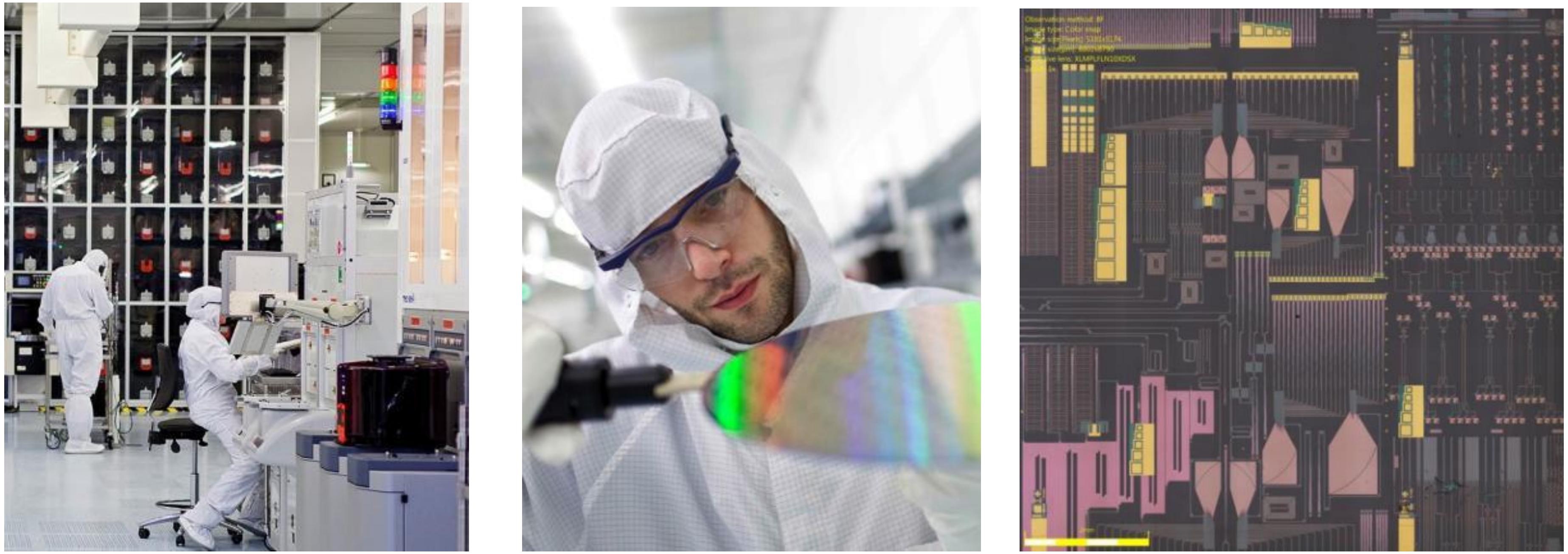
SPIE Optics and Optoelectronics, Prague, April 2019

GHENT UNIVERSITY

imec
embracing a better life

# WHAT IS SILICON PHOTONICS?

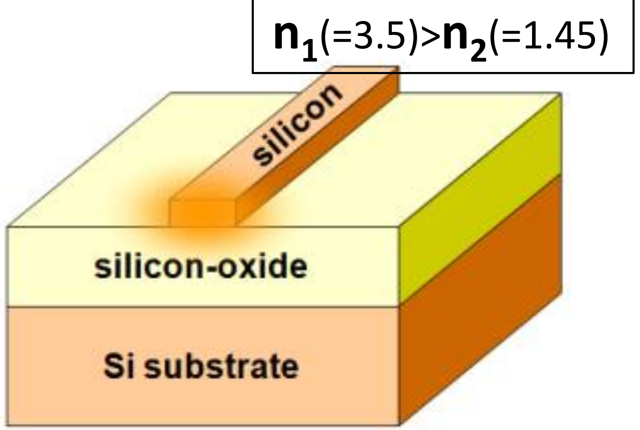
The implementation of high density photonic integrated circuits by means of CMOS process technology in a CMOS fab



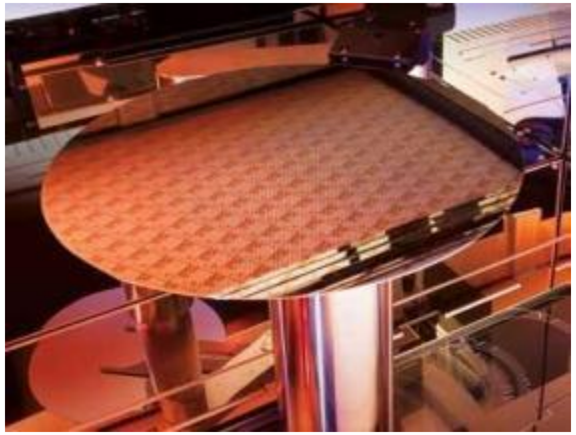
Pictures, courtesy of imec

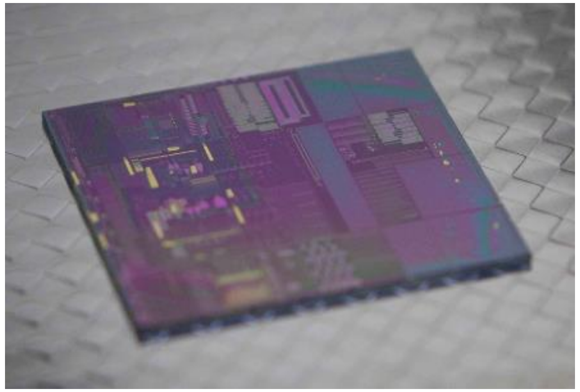
Enabling complex optical functionality on a compact chip at low cost

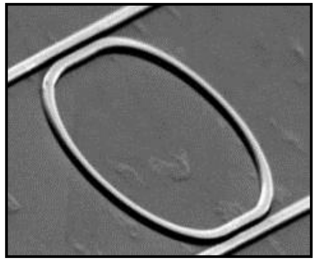
# WHY SILICON PHOTONICS

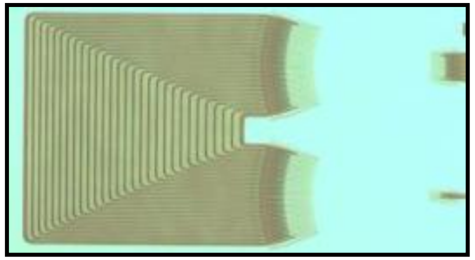


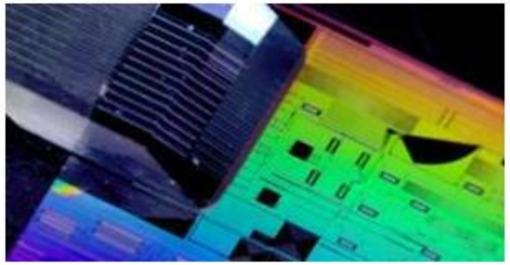
- High index contrast ⇒ very compact PICs
- CMOS technology ⇒ **nm-precision, high yield, existing fabs, low cost in volume**
- High performance passive devices
- High bitrate Ge photodetectors
- High bitrate modulators
- Wafer-level automated testing
- Hierarchical set of design tools
- Light source integration (hybrid/monolithic?)
- Integration with electronics (hybrid/monolithic?)











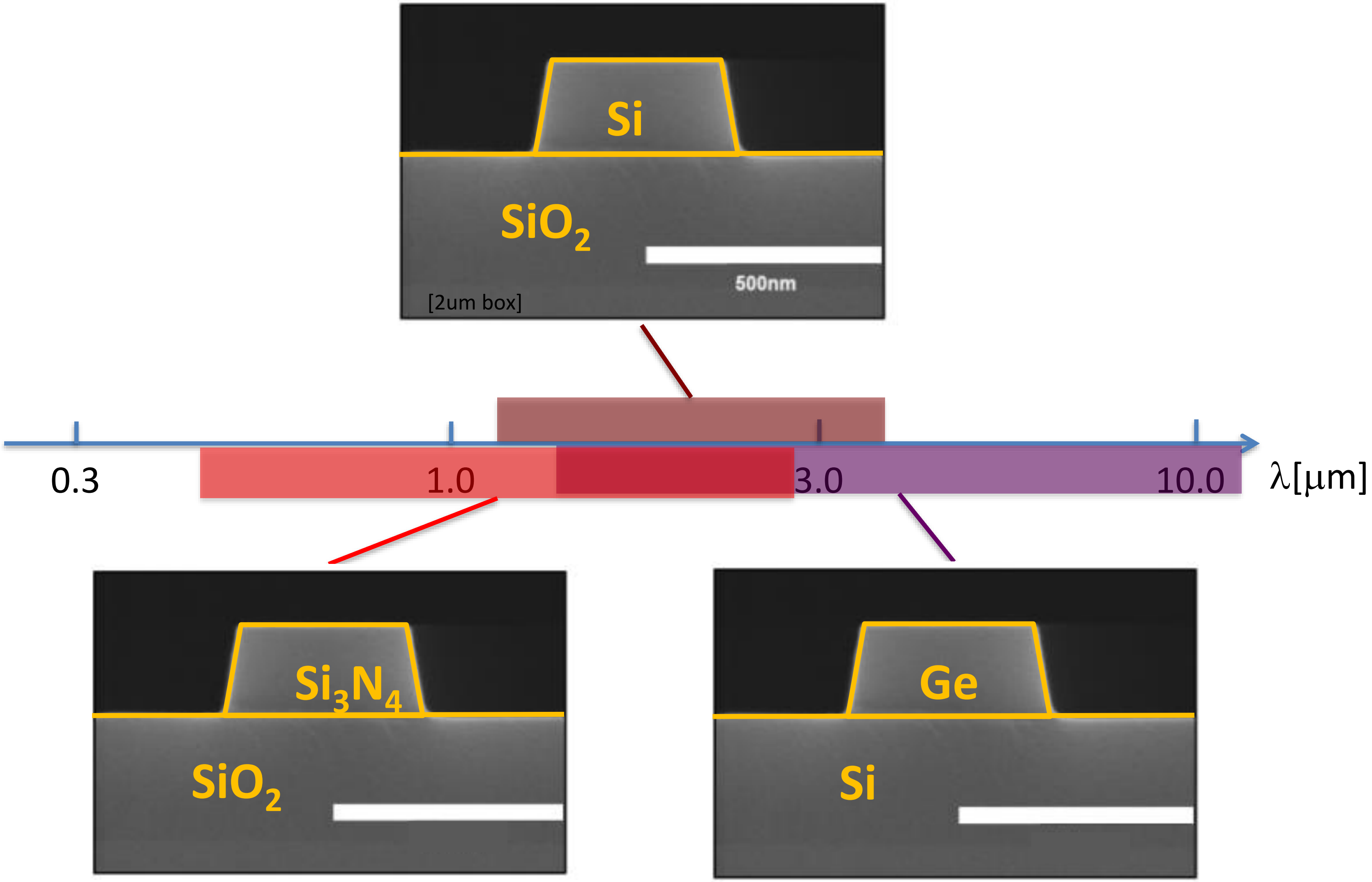
# THE PAST 5-10 YEARS: STUNNING INDUSTRIAL DEVELOPMENT IN SILICON PHOTONICS FOR TELECOM AND DATACOM

- active optical cables (eg PSM4: 4x28 Gb/s on parallel fibers)
- WDM transceivers (eg 4 WDM channels x 25 Gb/s on single fiber)
- coherent receiver (eg 100 Gb/s PM-QPSK)
- fiber-to-the-home bidirectional transceiver (eg 12 x 2.5 Gb/s)
- monolithic receiver (eg 16x20Gb/s)
- 40Gb/s, 50Gb/s and 100 Gb/s Ethernet (future: 400Gb/s)
- …

CompoundTek
tsmc
SILTERRA
amf ADVANCED MICRO FOUNDRY
Finisar
ACACIA COMMUNICATIONS, INC.
Inphi Think fast.
JUNIPER NETWORKS
KAIAM
Ayar Labs
aurrion
intel
Rockley PHOTONICS
ST
ELENION TECHNOLOGIES
IBM
SKORPIOS TECHNOLOGIES
TeraXion
sicoya
ciena
cisco
NVIDIA
GLOBAL FOUNDRIES
molex
Caliopa silicon photonics
HUAWEI
Mellanox TECHNOLOGIES
LUXTERA NANOPHOTONIC INTEGRATED CIRCUITS

# SILICON PHOTONICS: EXTENDING THE WAVELENGTH RANGE

WITHOUT LEAVING THE CMOS FAB



# MEDICINE AND LIFE SCIENCE

Enormous challenges:

- Ageing society
- Keep ever more performant health care affordable for society
- More focus on preventive medicine

Technology can help:

- Low-cost personal, bed-side and point-of-care medical devices
- Minimally invasive devices (cathetered approaches, implants, electronic pills)
- Rapid diagnostics (immuno-assays based on disposable use-once chips)

# ASSETS OF SILICON PHOTONICS FOR MEDICINE AND LIFE SCIENCE

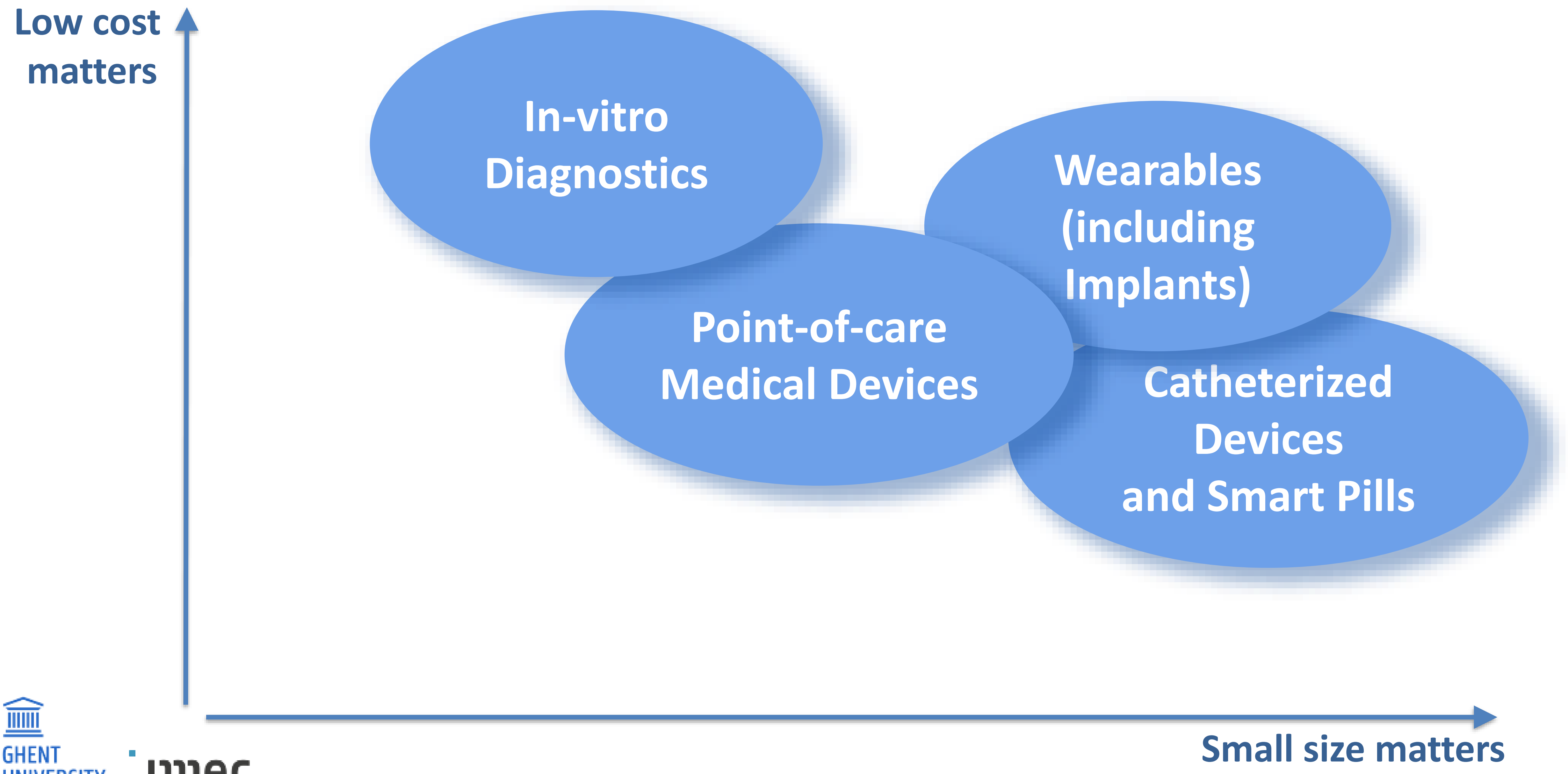
Low cost (even in moderate volume)

Very compact devices

Can address needs from visible to mid IR

Mature supply chain

# MAIN APPLICATIONS OF SILICON PHOTONICS IN MEDICINE



Low cost matters

In-vitro Diagnostics

Wearables (including Implants)

Point-of-care Medical Devices

Catheterized Devices and Smart Pills

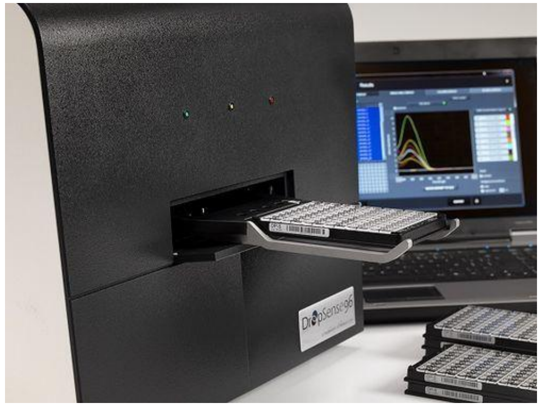
Small size matters

# THREE APPLICATION CASES

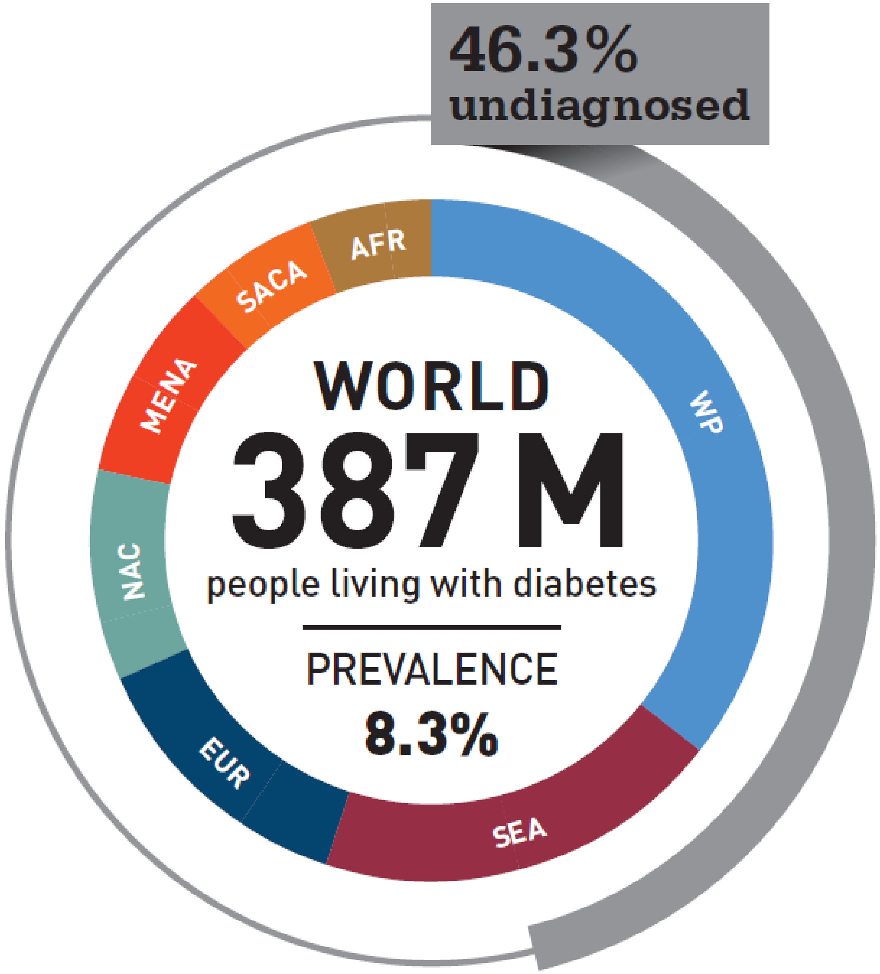
➡ Continuous glucose monitoring

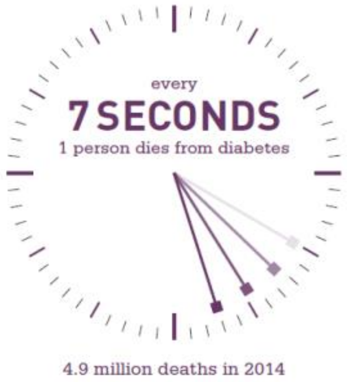
Cardiovascular monitoring

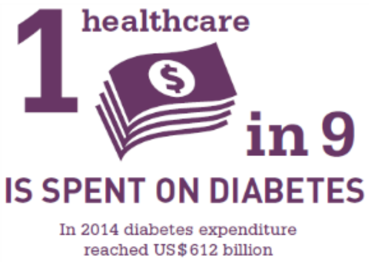
In-vitro diagnostics

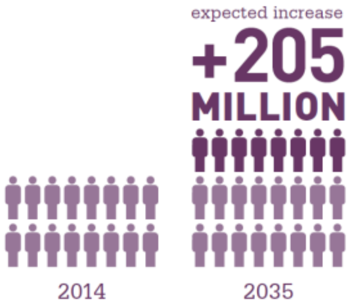


# DIABETES IS THE 21ST CENTURY HEALTH CHALLENGE







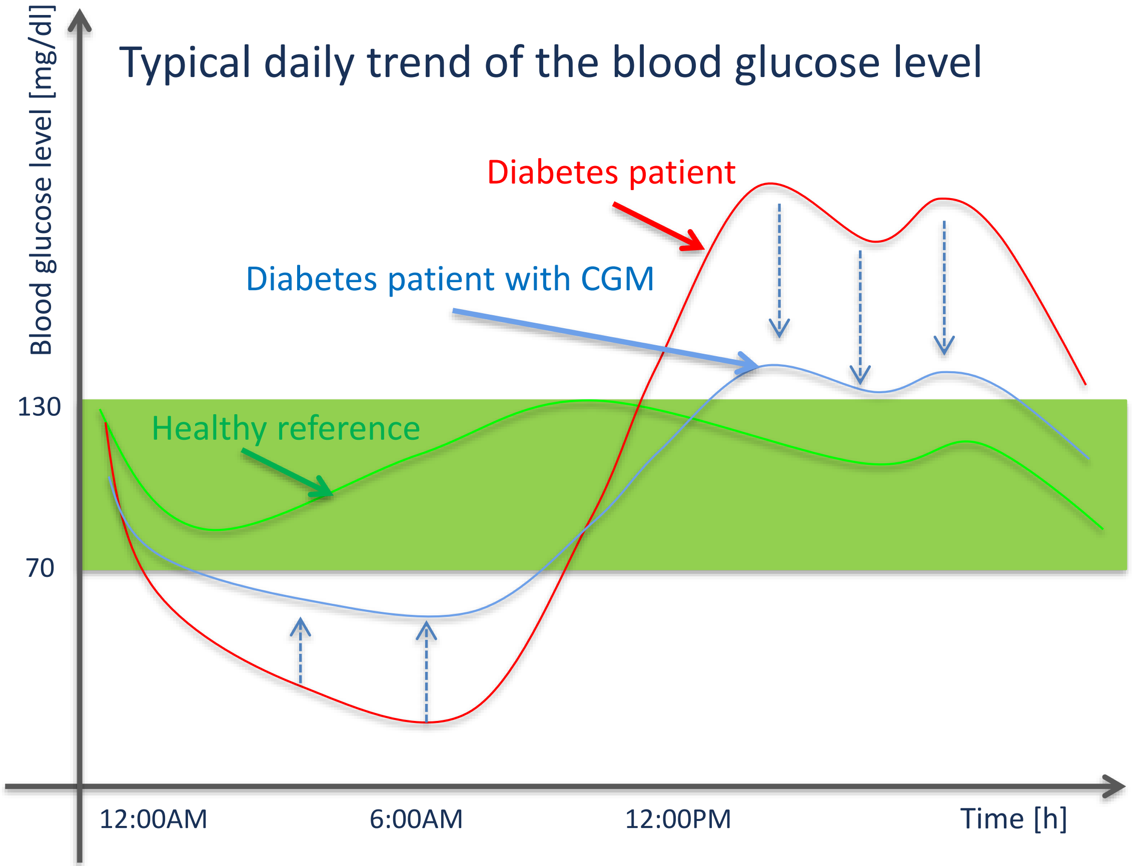


http://www.idf.org/diabetesatlas/update-2014

# CONTINUOUS GLUCOSE MONITORING (CGM) HAS PROVEN TO IMPROVE GLYCEMIC CONTROL OF DIABETES PATIENTS

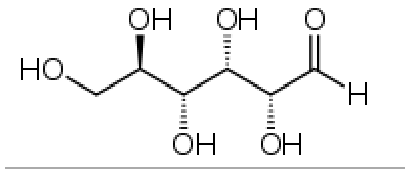
CGM systems show positive health impact *

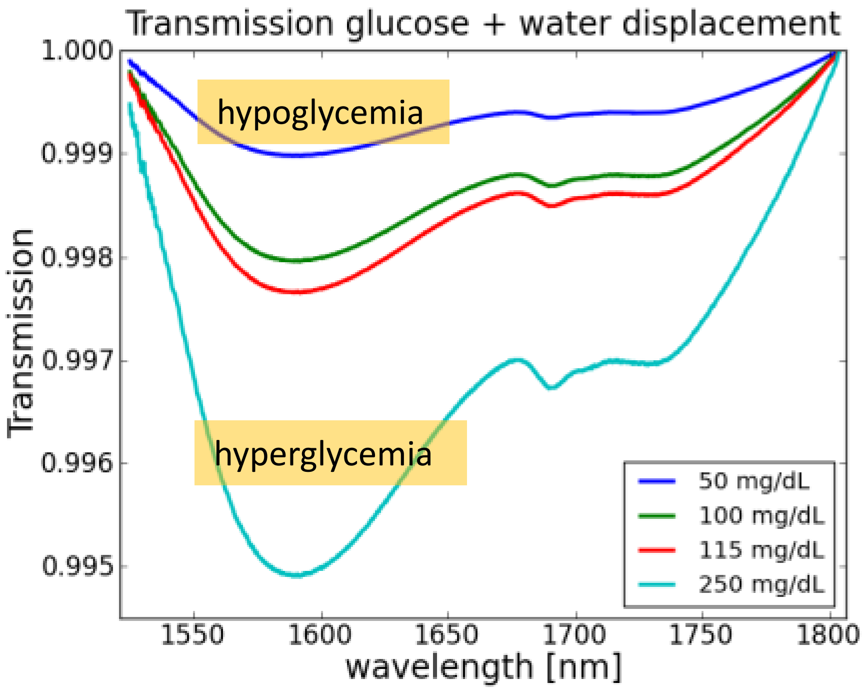
- lower average blood glucose levels
- decrease of hypoglycemic frequency



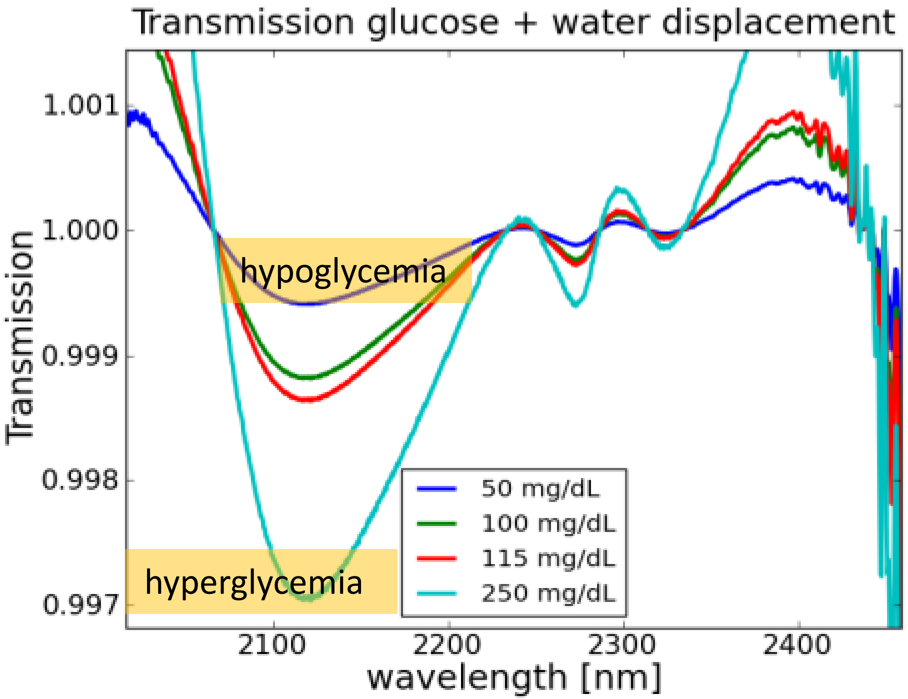
* Liebl A, Henrichs HR, Heinemann L, et al. Continuous glucose monitoring: evidence and consensus statement for clinical use. J Diabetes Sci Technol . 2013;7:500-519

# GLUCOSE ABSORPTION SPECTROSCOPY





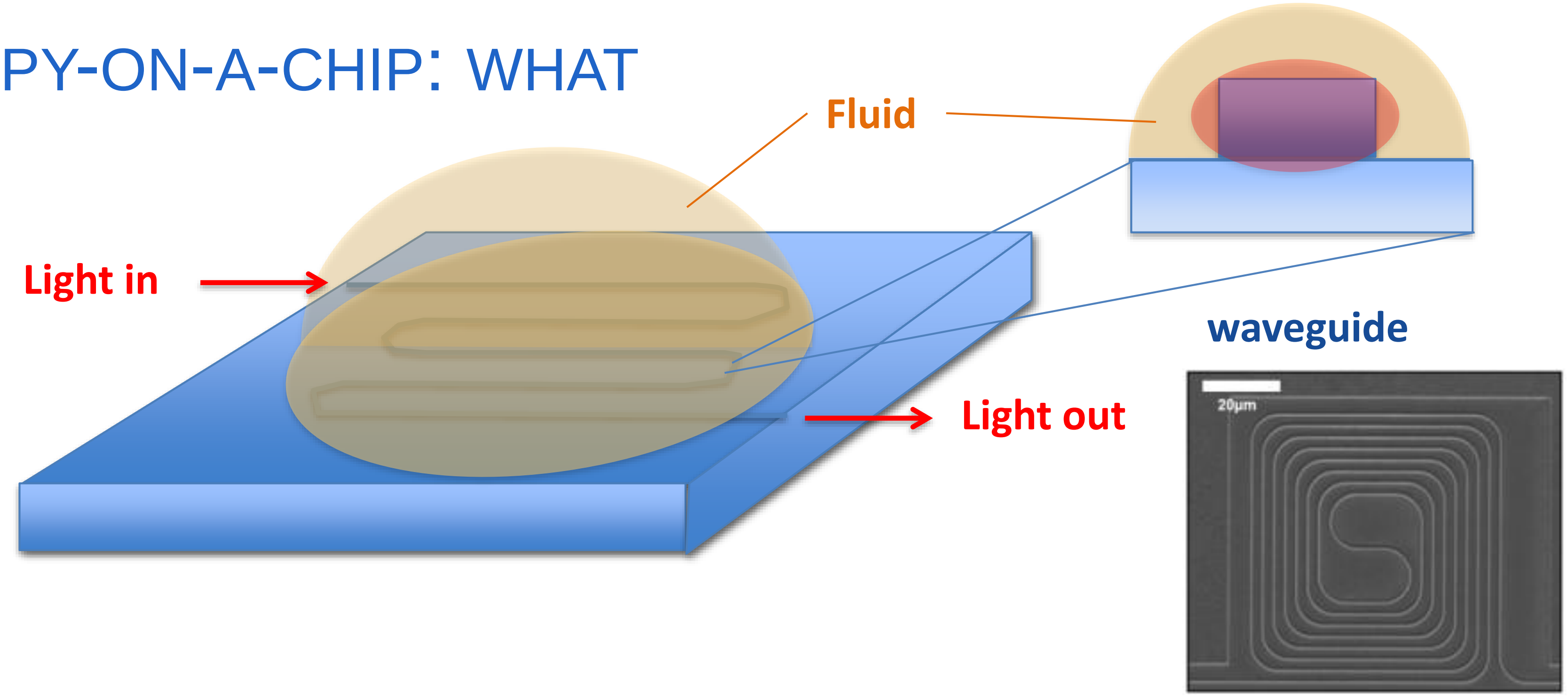
First overtone band: 1500 - 1800 nm

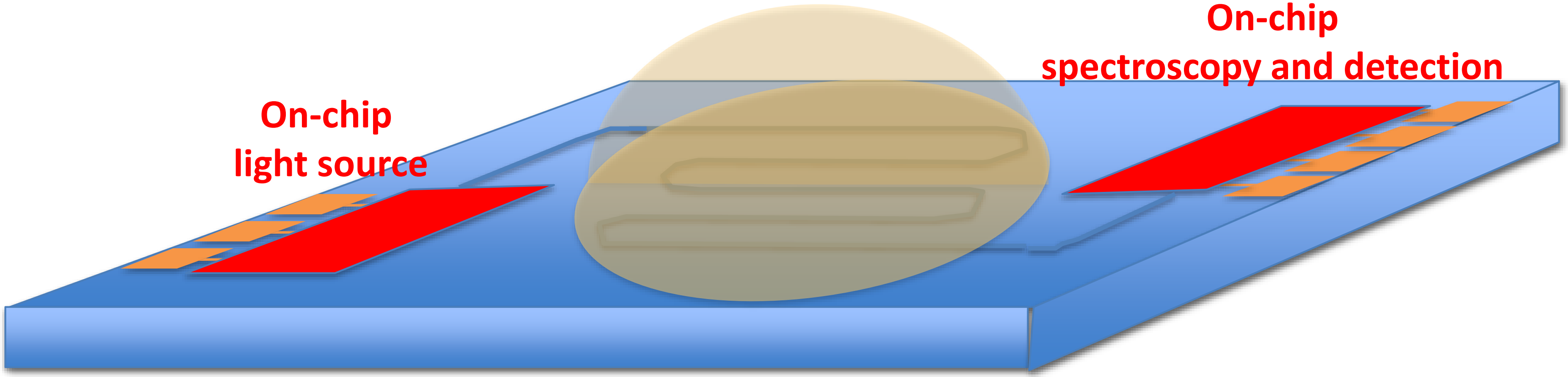


Combination band: 2000 - 2500 nm

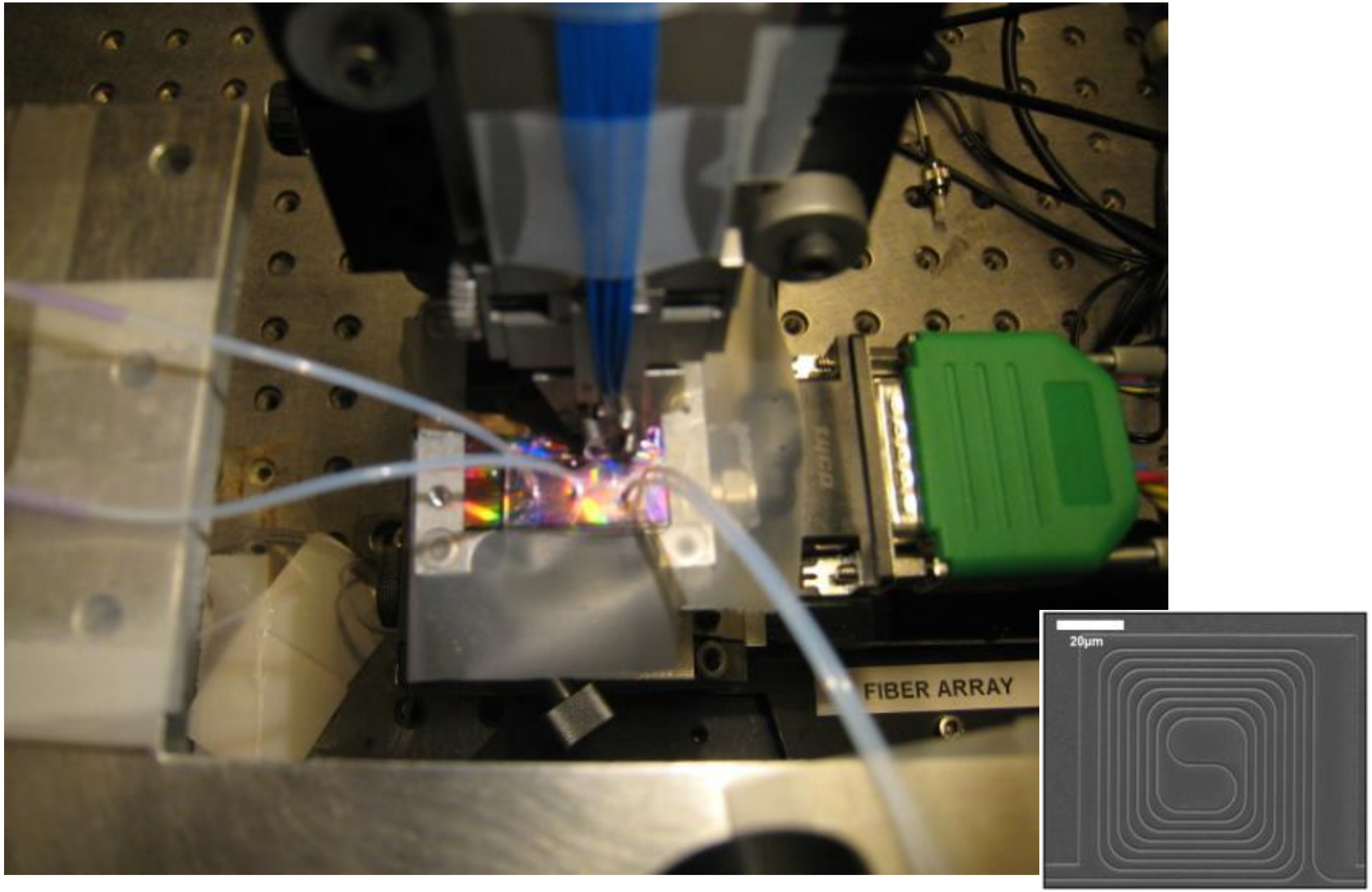
For glucose sensing in humans (3-15 mM): Largest change in transmission is 0.5 %
Required sensitivity : 0.02%

# SPECTROSCOPY-ON-A-CHIP: WHAT





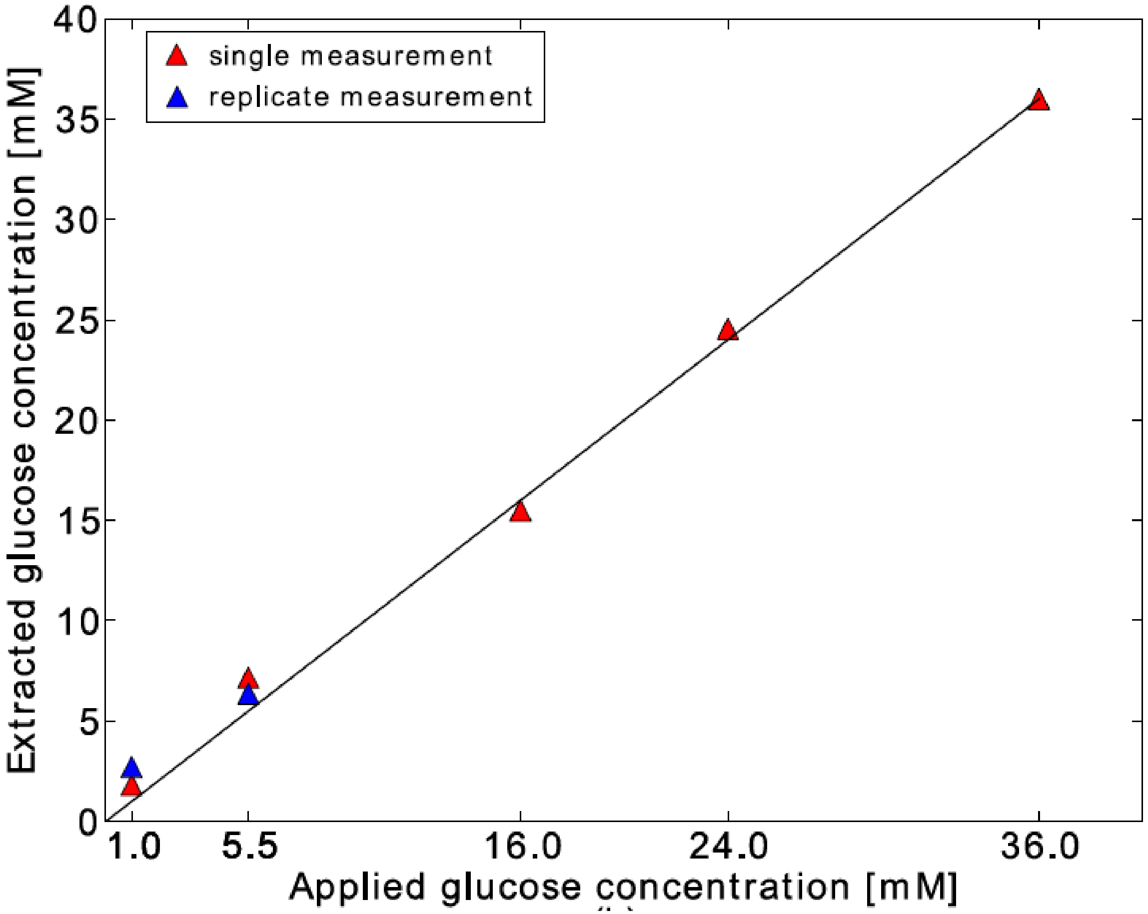
# PROOF-OF-CONCEPT DEMO OF GLUCOSE SENSING IN THE LAB



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

# GLUCOSE ABSORPTION SPECTROSCOPY: PROOF-OF-CONCEPT

Use measured spectrum of 36 mM solution as the basic vector

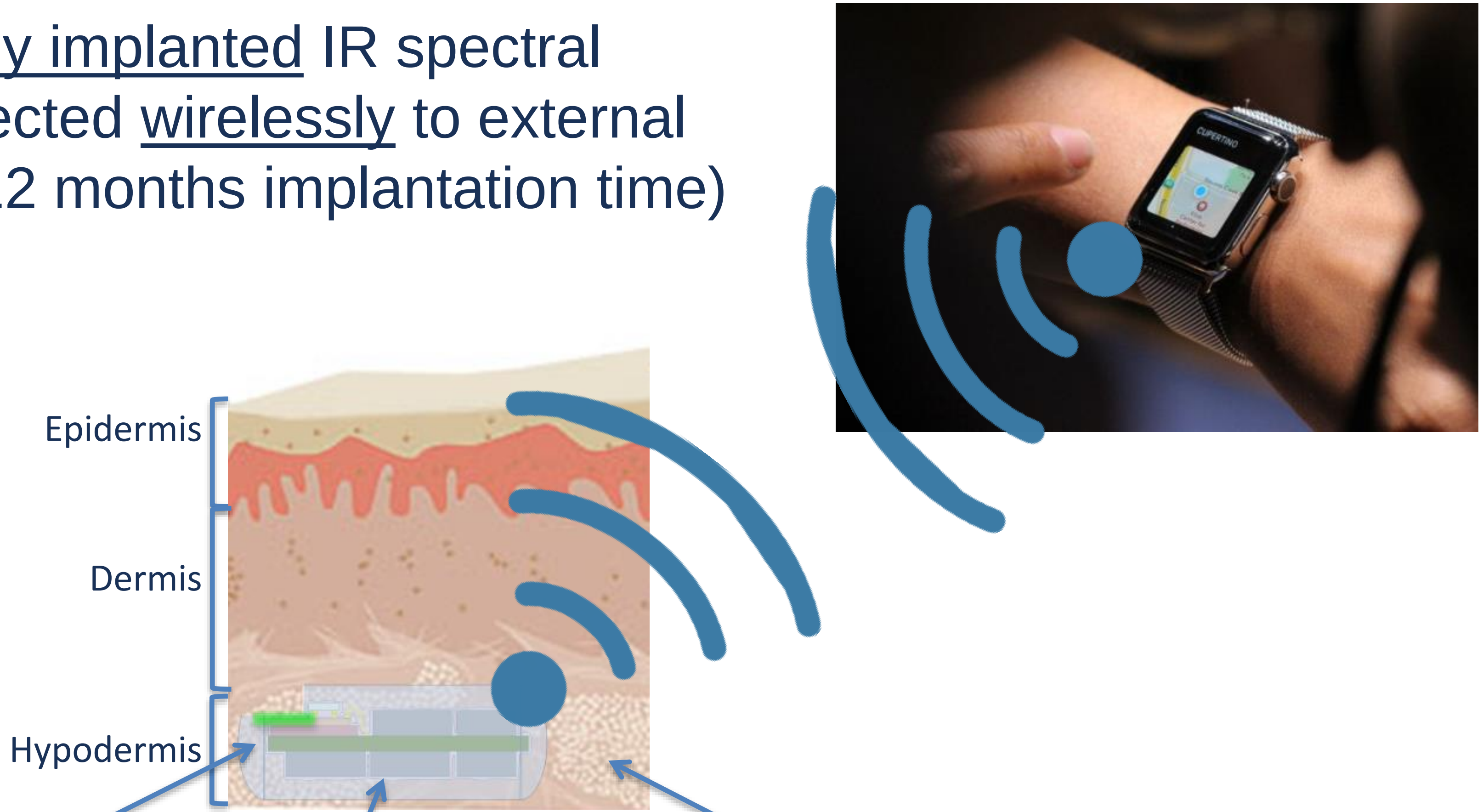


**Demonstrated sensitivity of 1mM**

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

# CGM ENABLED BY SILICON PHOTONICS

Subcutaneously implanted IR spectral analyser connected wirelessly to external transceiver (>12 months implantation time)



Light sensing glucose (in reality invisible IR)

GluCARE implant spectrally analysing interstitial fluid

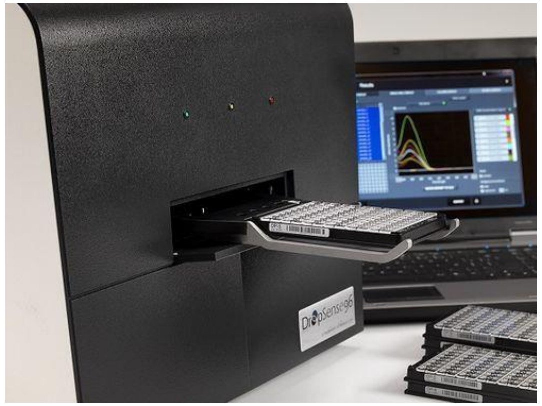
Adipose tissue with glucose containing interstitial fluid

# THREE APPLICATION CASES

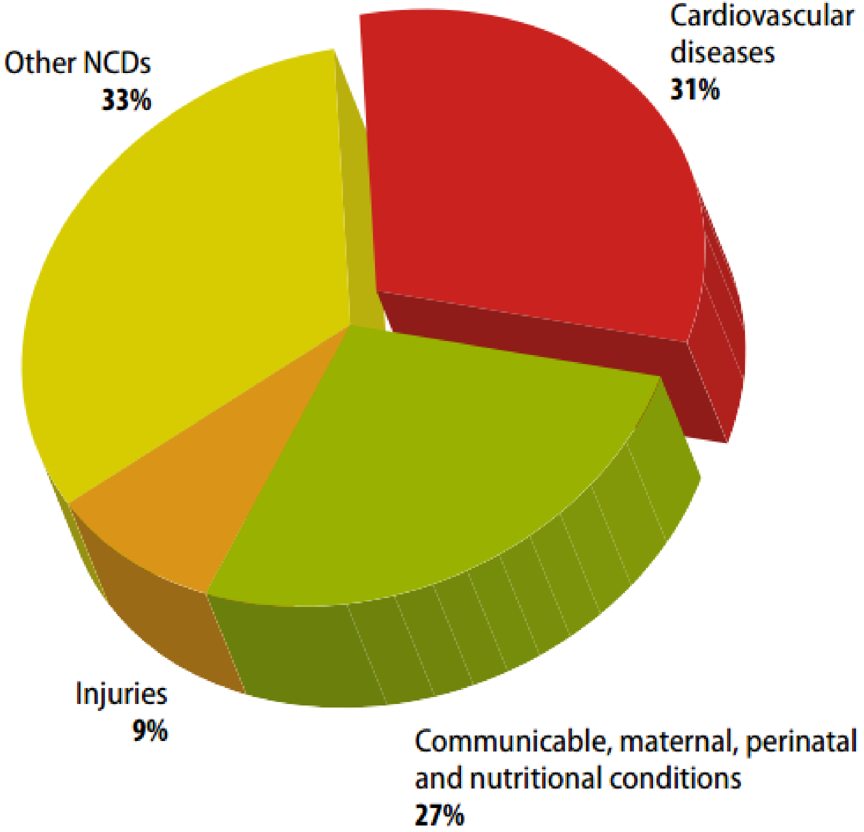
Continuous glucose monitoring

➡ Cardiovascular monitoring

In-vitro diagnostics



# CARDIOVASCULAR DISEASES



**Distribution of major causes of death including CVDs**

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

# CARDIOVASCULAR DISEASE (CVD)

Arteriosclerosis: stiffening of arterial walls

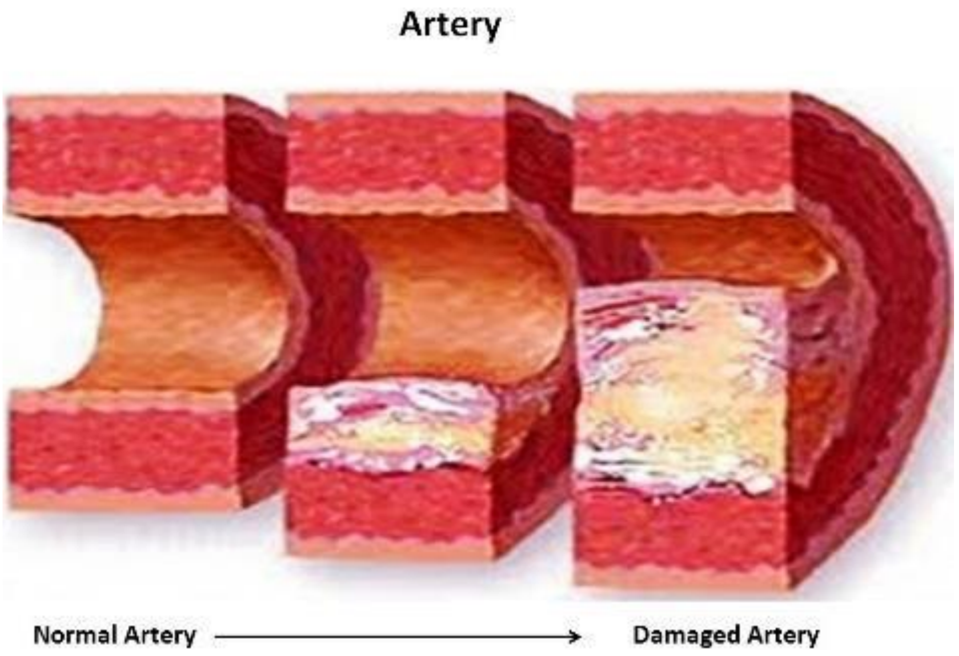
Atherosclerosis: deposition of plaque on the inner arterial walls (which can lead to stiffening)

Stenosis: abnormal narrowing in a blood vessel

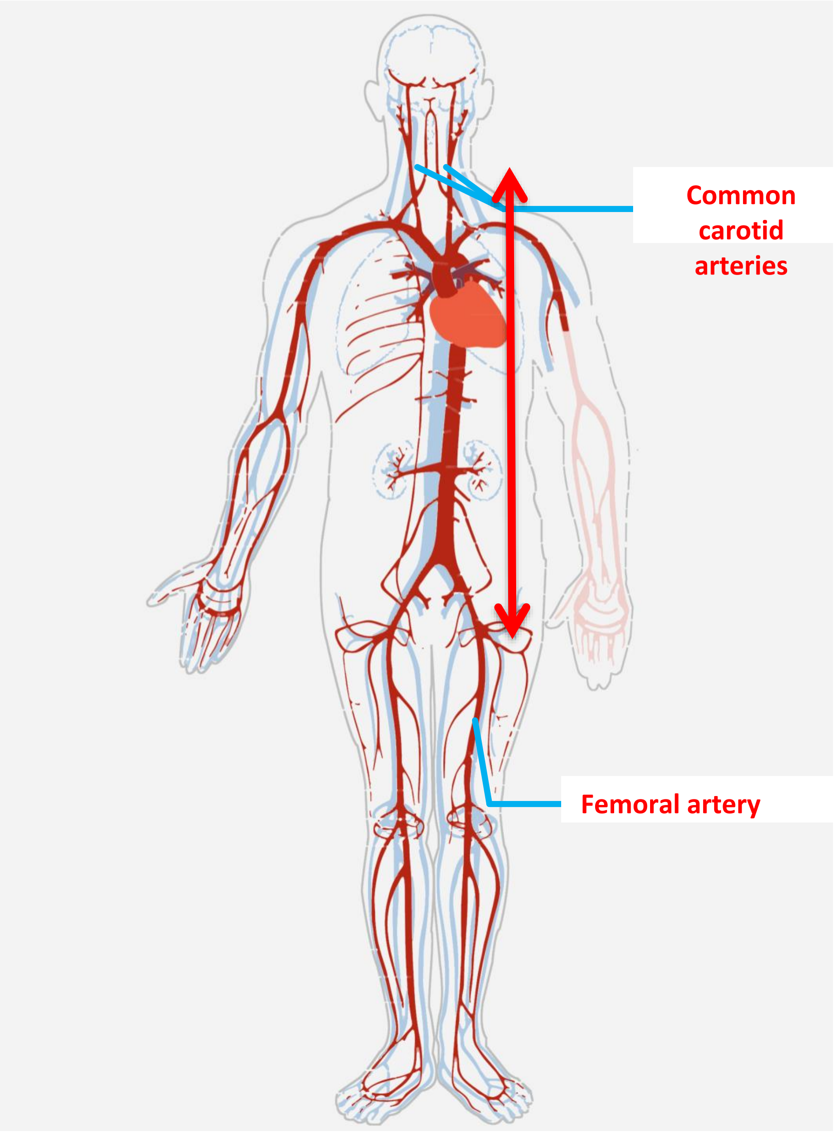
Heart Dyssynchrony: left and right part of the heart are not triggered synchronously

A **map of the skin displacement** above arteries can help for early diagnosis of these pathologies.

- Method: laser Doppler vibrometry
- Technology: silicon photonics
- Use: by general practitioner



# PULSE WAVE VELOCITY (PWV): MARKER FOR ARTERIAL STIFFNESS

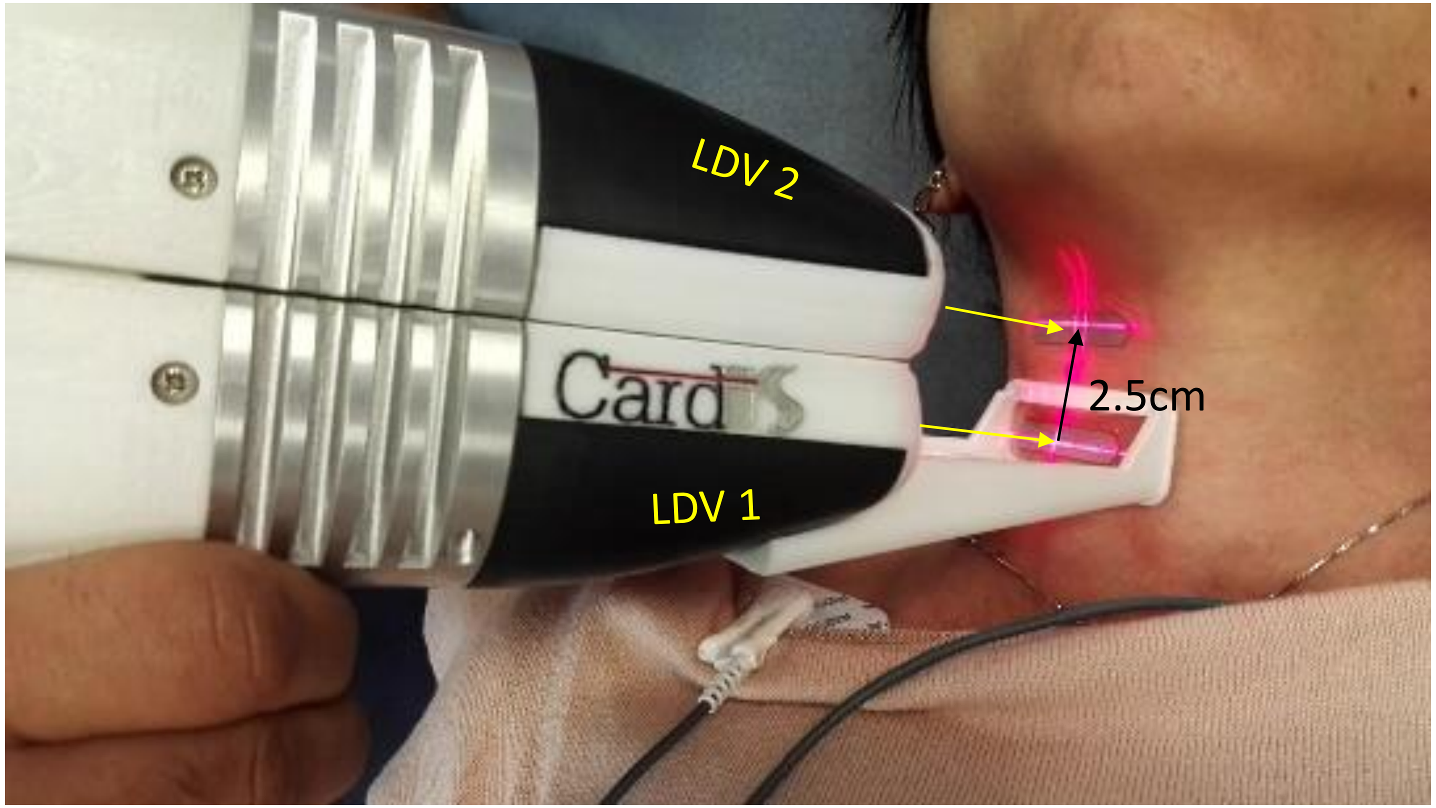


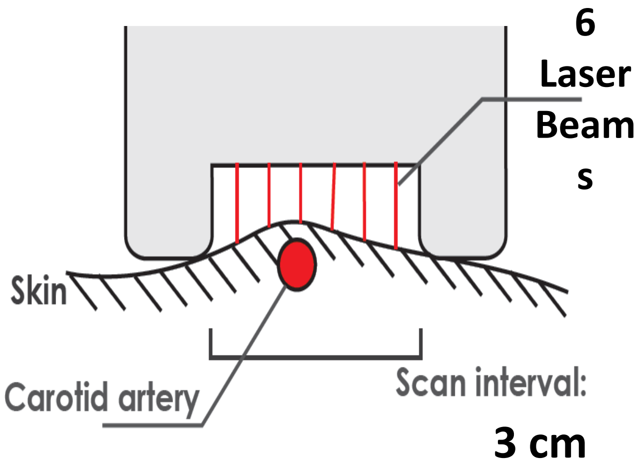
**Pulse Wave Velocity: speed by which the pressure wave caused by a heart beat travels in the arteries**

$$PWV = \frac{pulse\ travel\ distance}{pulse\ travel\ time}$$

**Larger PWV ->**
**Higher arterial stiffness ->**
**Higher risk of cardiovascular events**

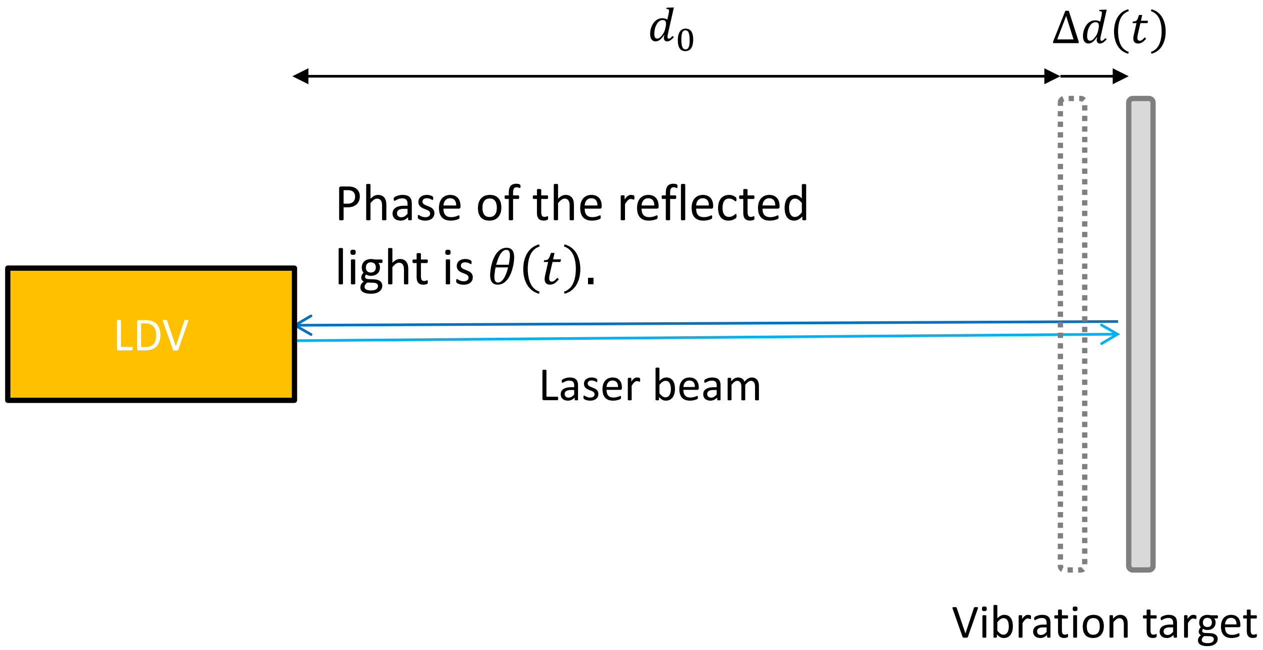
# APPROACH: MEASURE LOCAL COMMON-CAROTID PWV





Method used: measure skin movement by Laser Doppler Vibrometry (LDV)

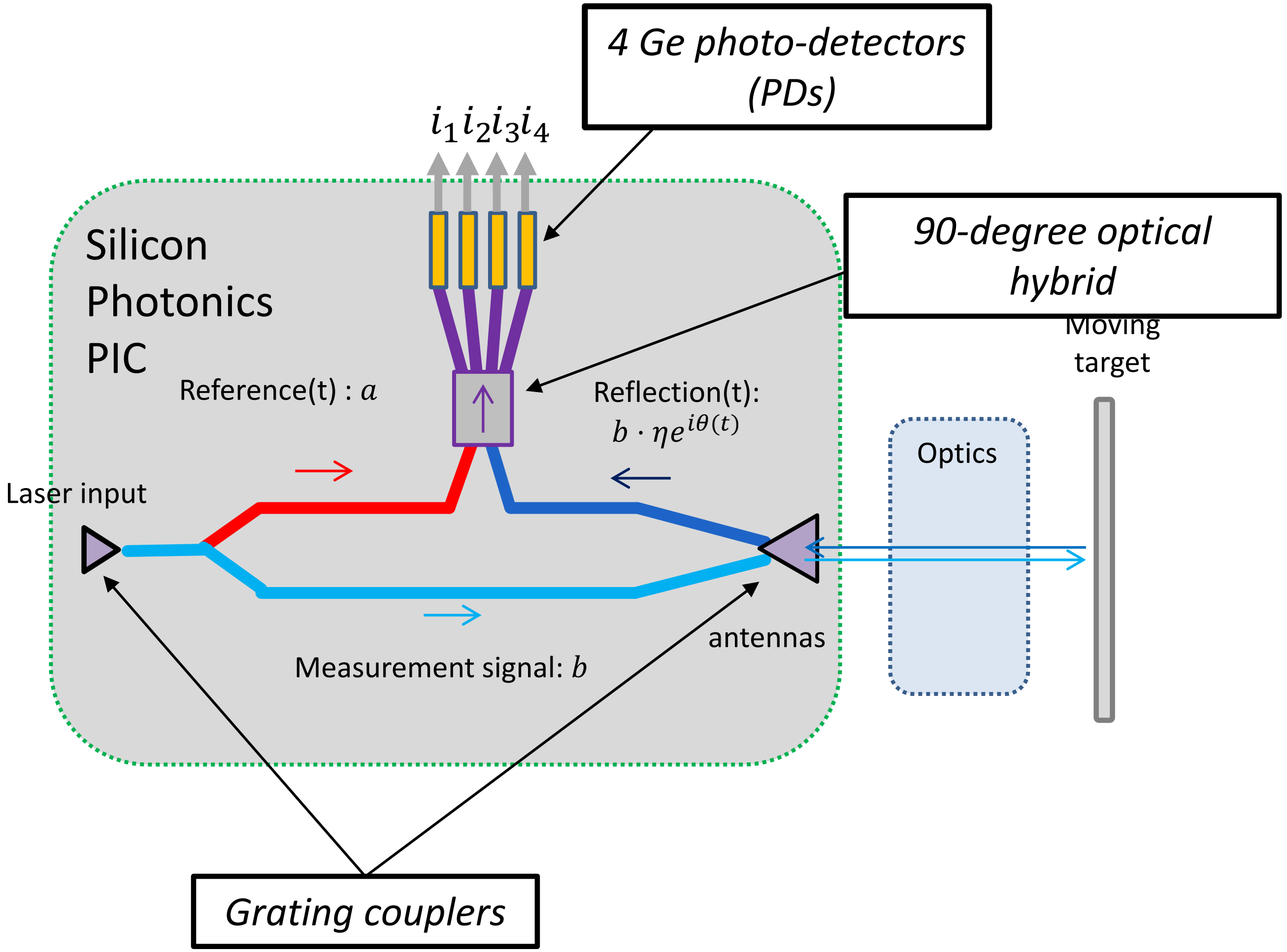
# WORKING PRINCIPLE OF LDV

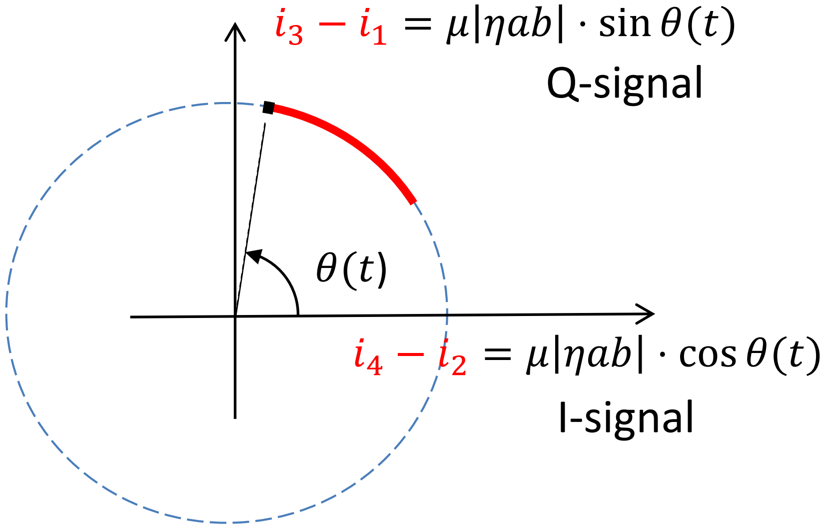


The displacement $\Delta d(t)$ can be retrieved by measuring $\theta(t)$, based on the relation

$$\theta(t) = \frac{2\pi}{\lambda_0} \cdot 2\Delta d(t) + \text{const.}$$

# WORKING PRINCIPLE OF LDV: HOMODYNE DETECTION

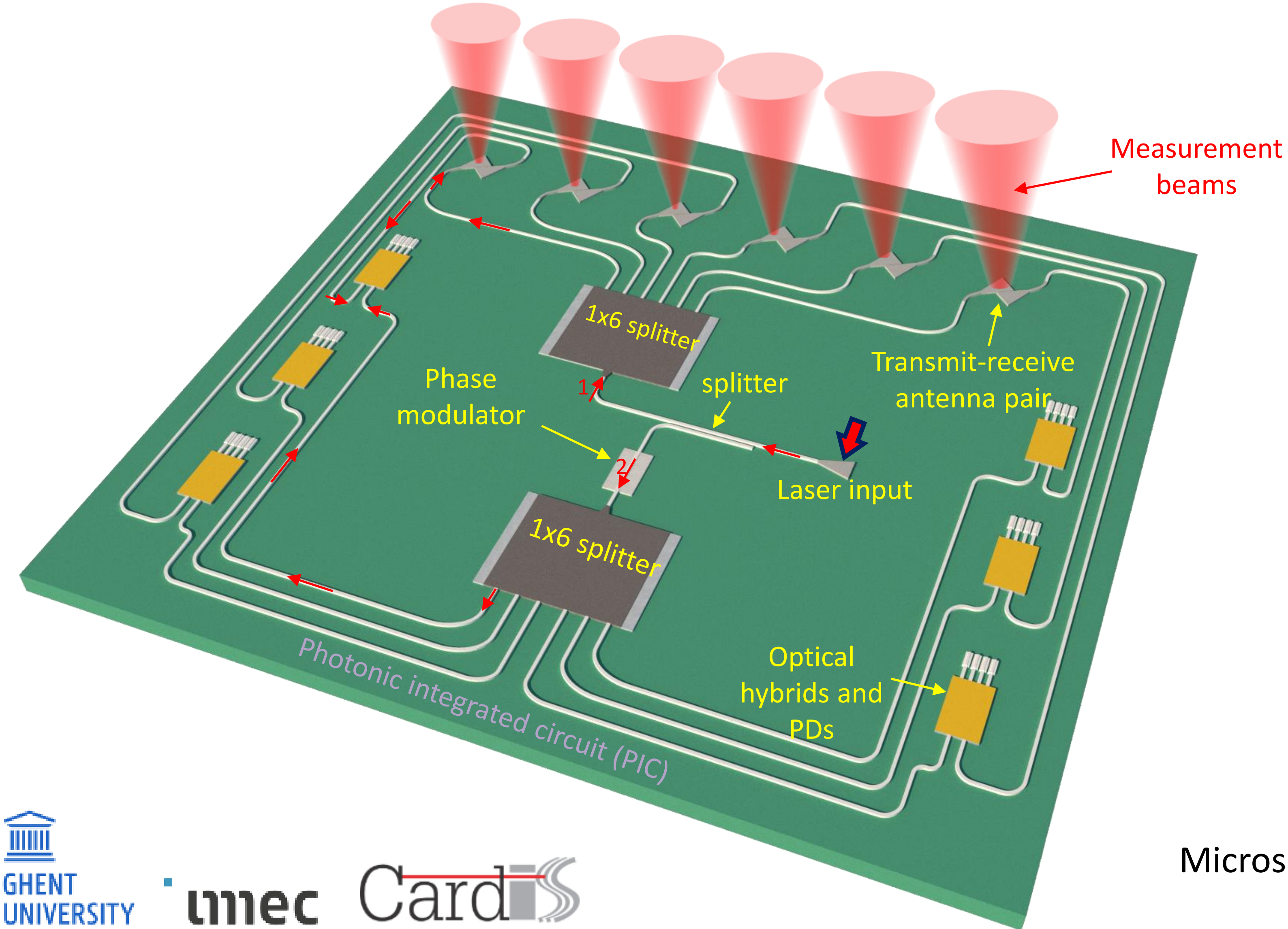


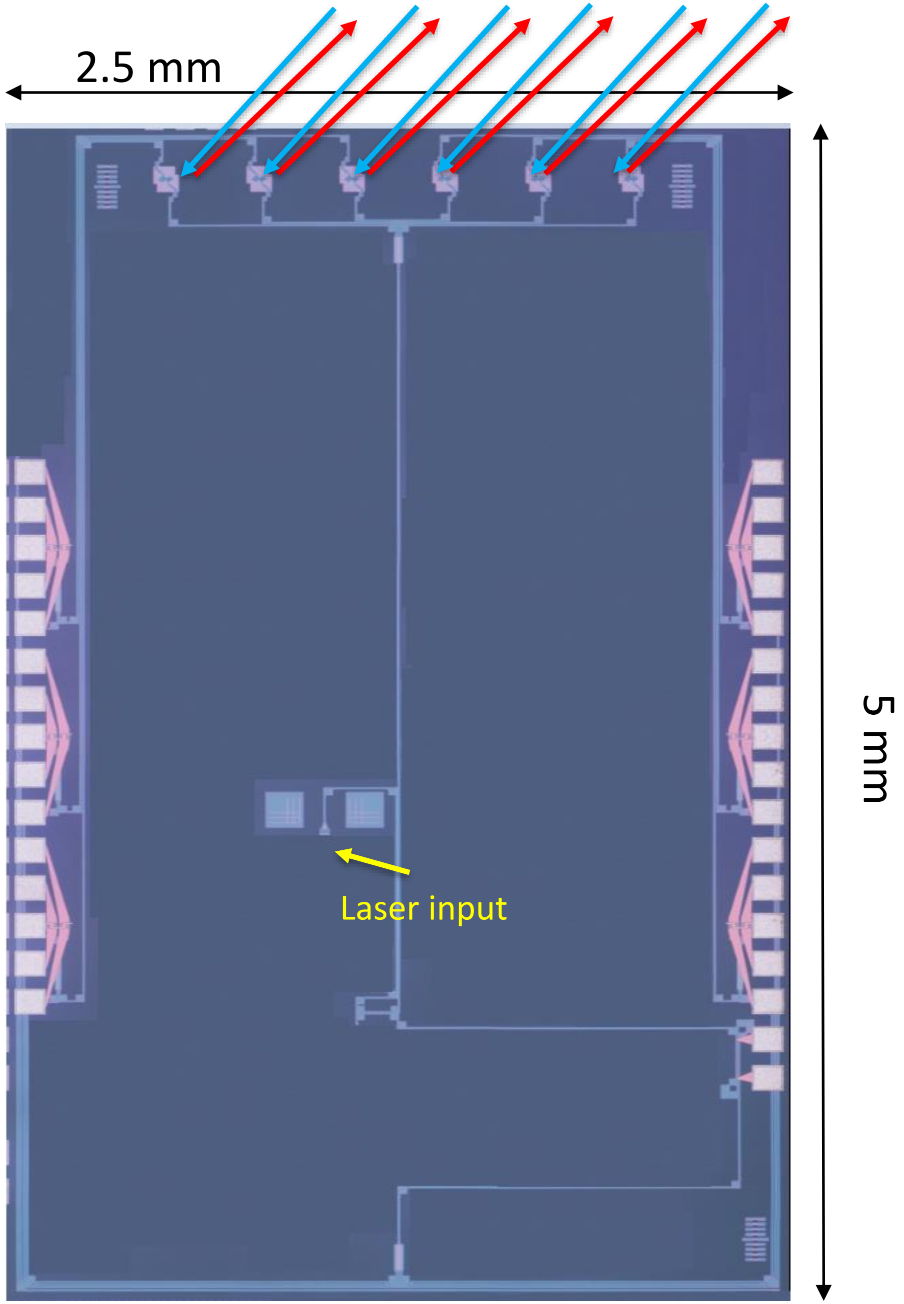


**Demodulation method:**

$$\theta(t) = \arctan\left(\frac{i_3 - i_1}{i_4 - i_2}\right)$$

# REALIZATION OF A SIX-BEAM LDV ON SILICON CHIP

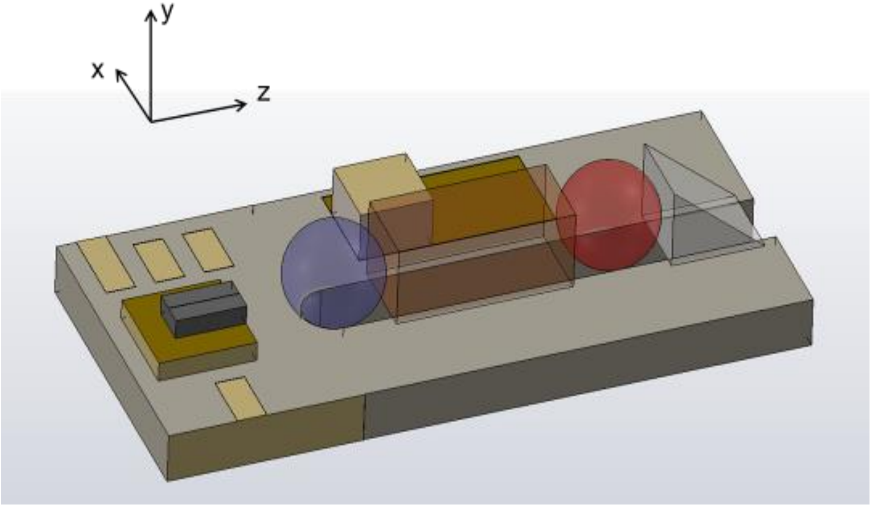




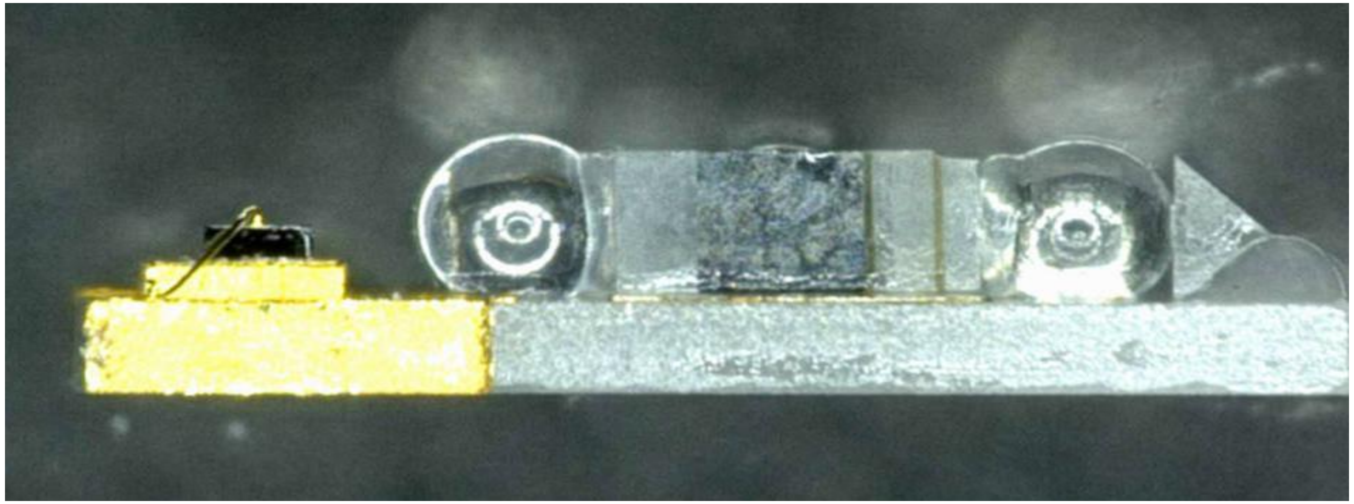
Microscope image of the photonic integrated circuit (PIC) in a silicon-on-insulator platform

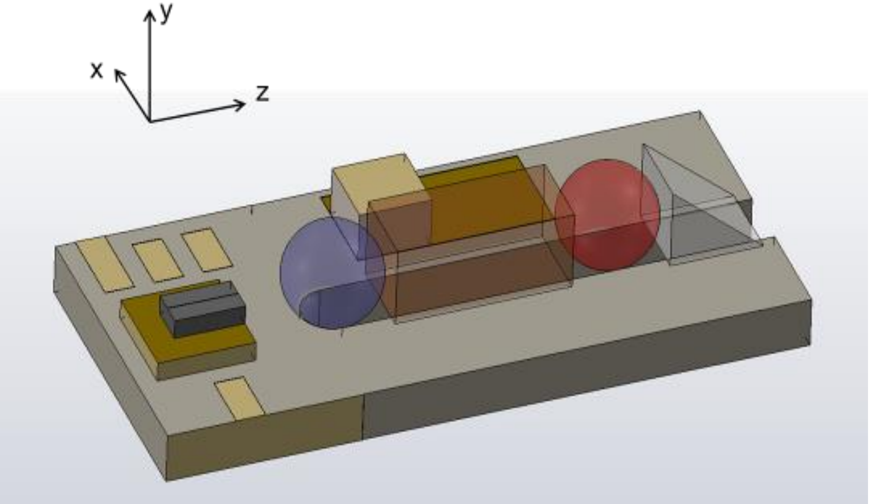
# PHOTONIC INTEGRATED CIRCUITS (PICS)

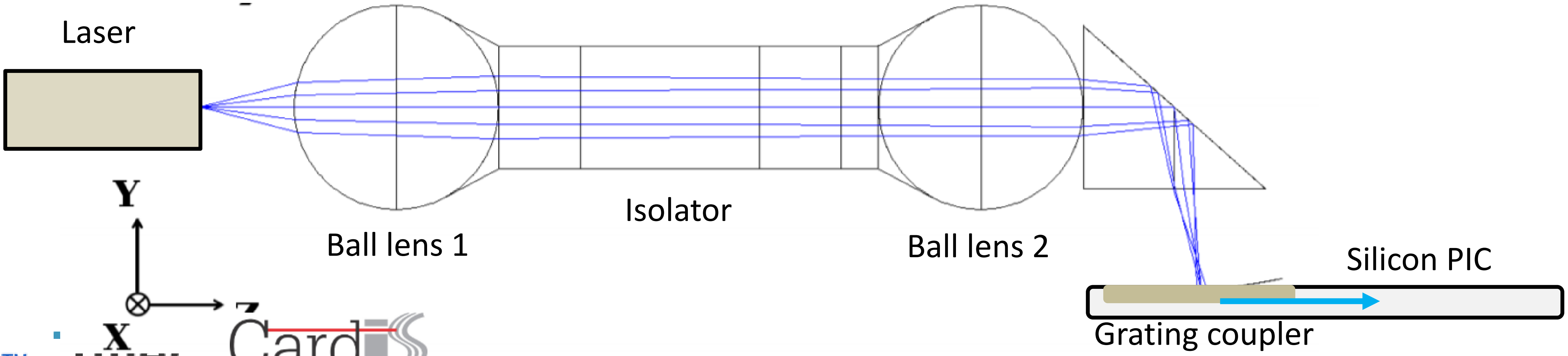
- PICs fabricated through Europractice MPW-service
- iSiPP50G SOI process at imec
- Laser diode is mounted on a Micro-Optic Bench (MOB) which is attached to the PIC



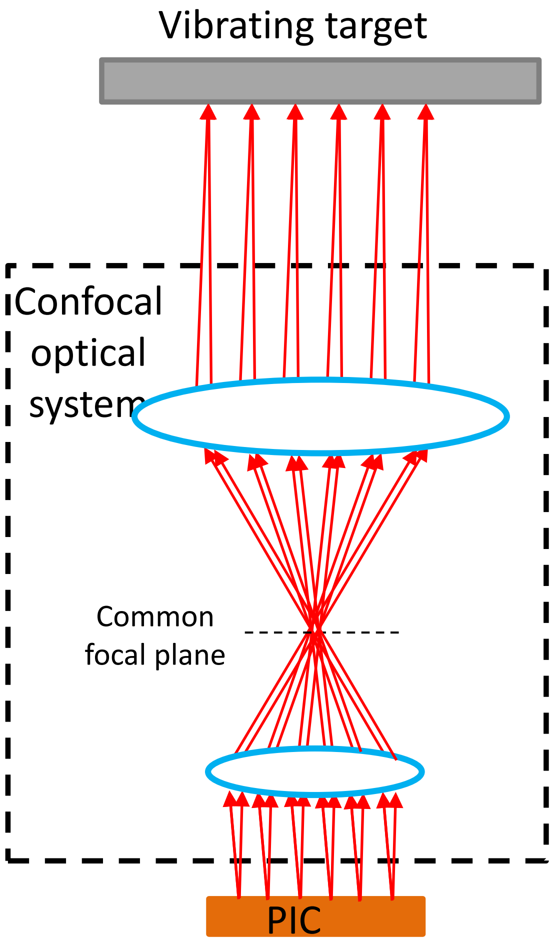
# HYBRID LASER INTEGRATION: MICRO-OPTIC BENCH APPROACH



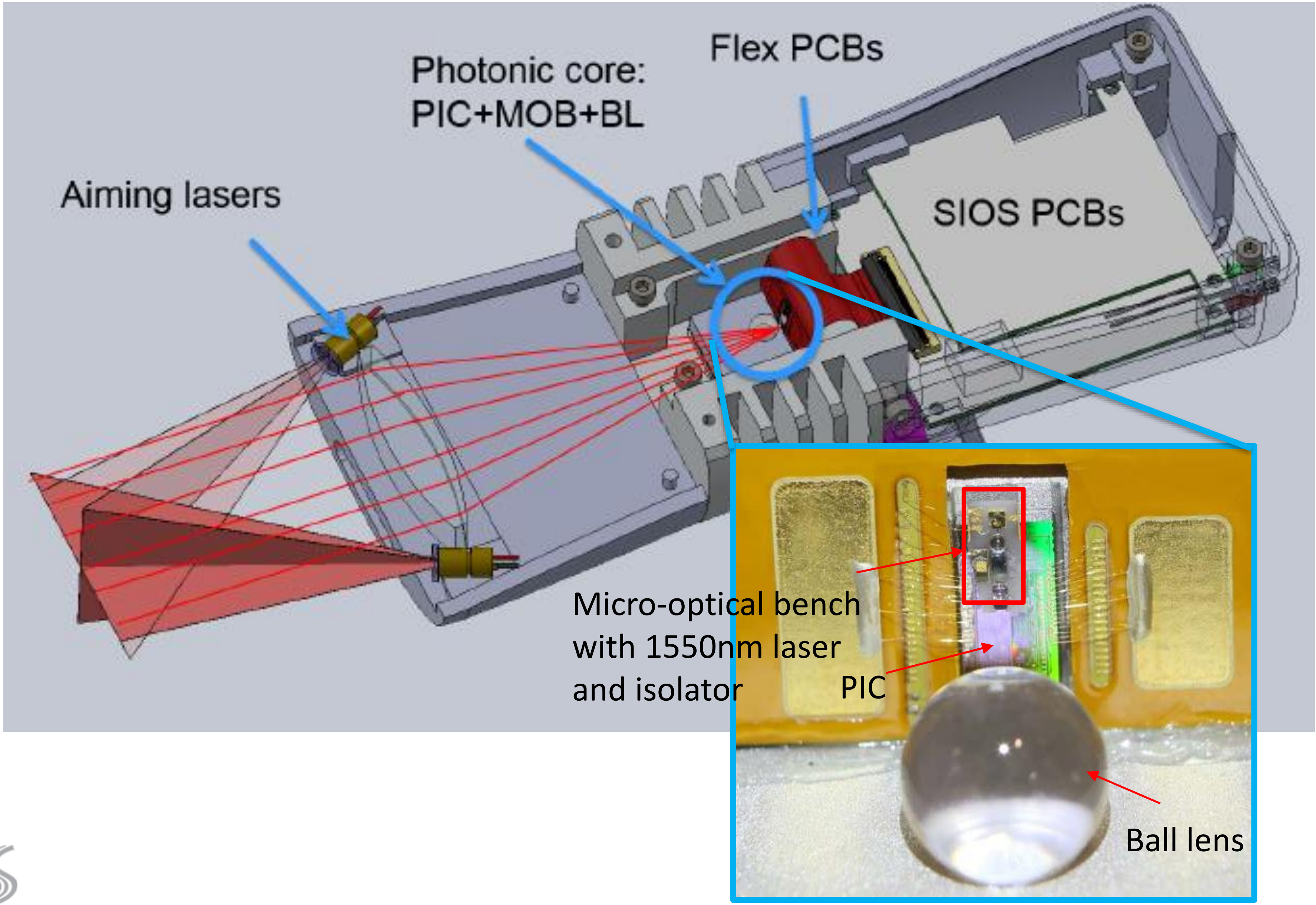




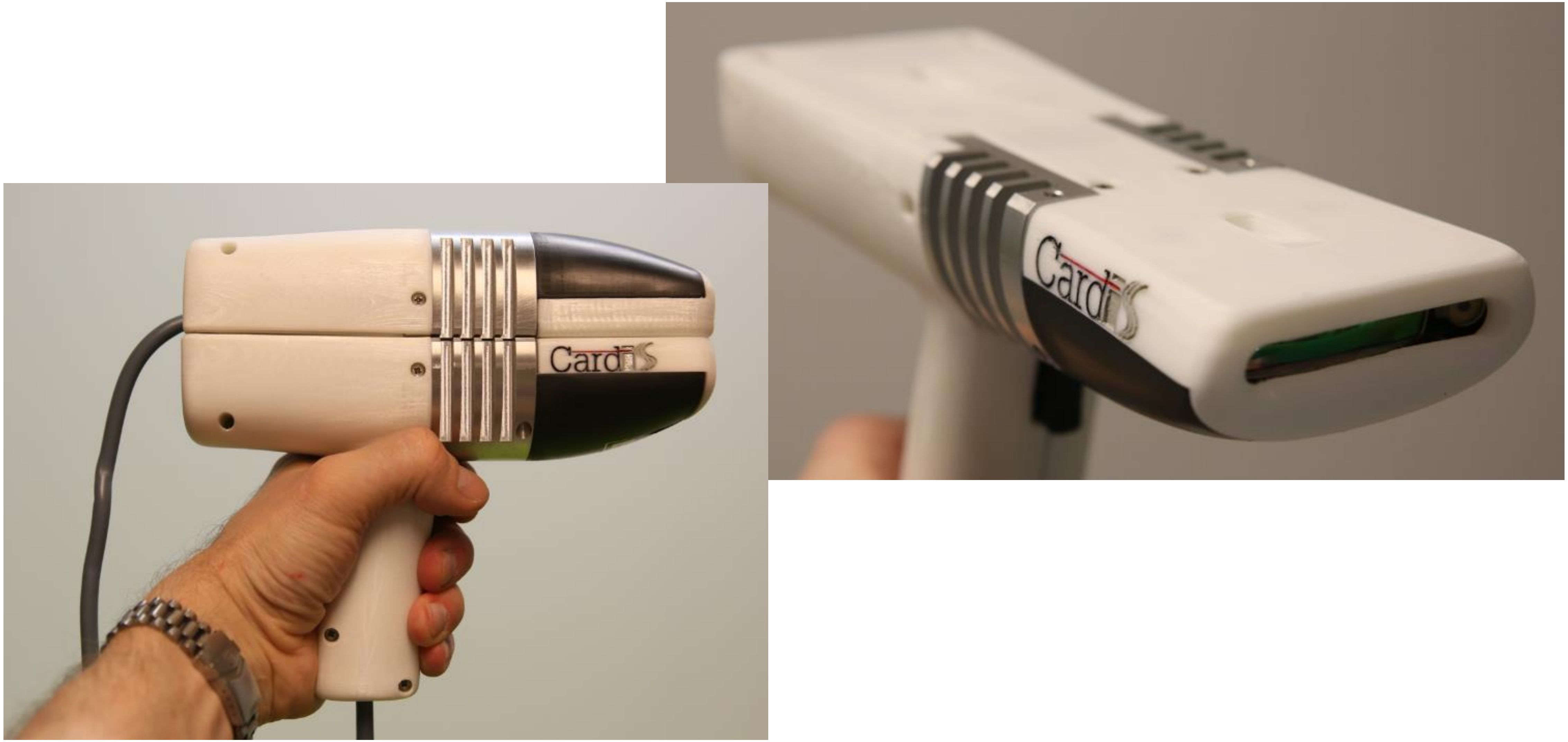
# PACKAGING OF THE 6-BEAM LDV



**PIC and external optics**

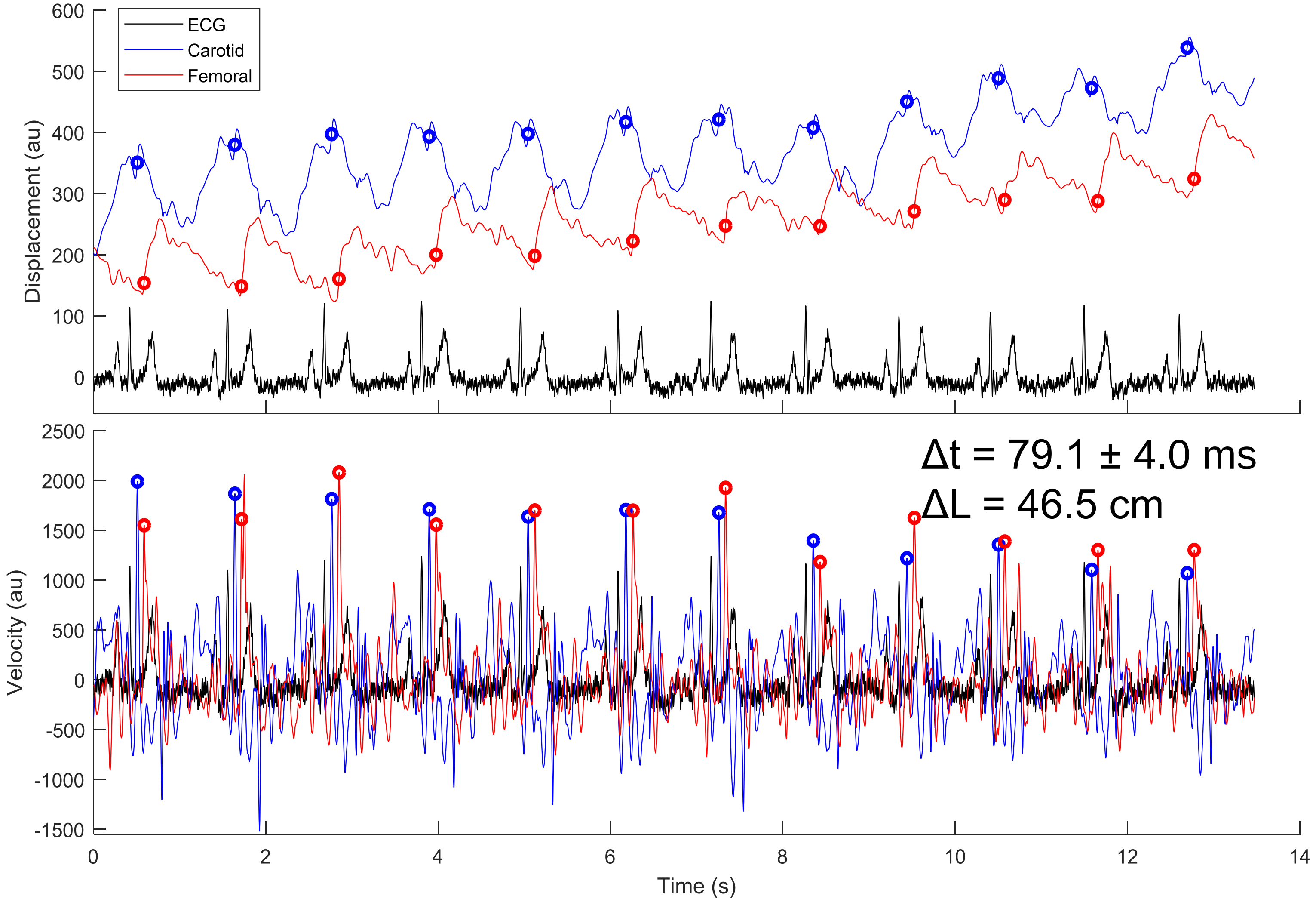


# THE EXTERNAL VIEW OF THE MULTI-BEAM LDVS



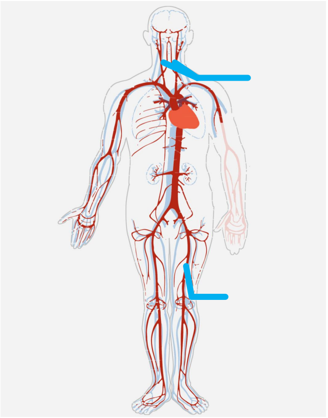
# CLINICAL TRIALS AT INSERM, PARIS

# CAROTID-FEMORAL (CF) PWV MEASUREMENT



Δt = 79.1 ± 4.0 ms
ΔL = 46.5 cm

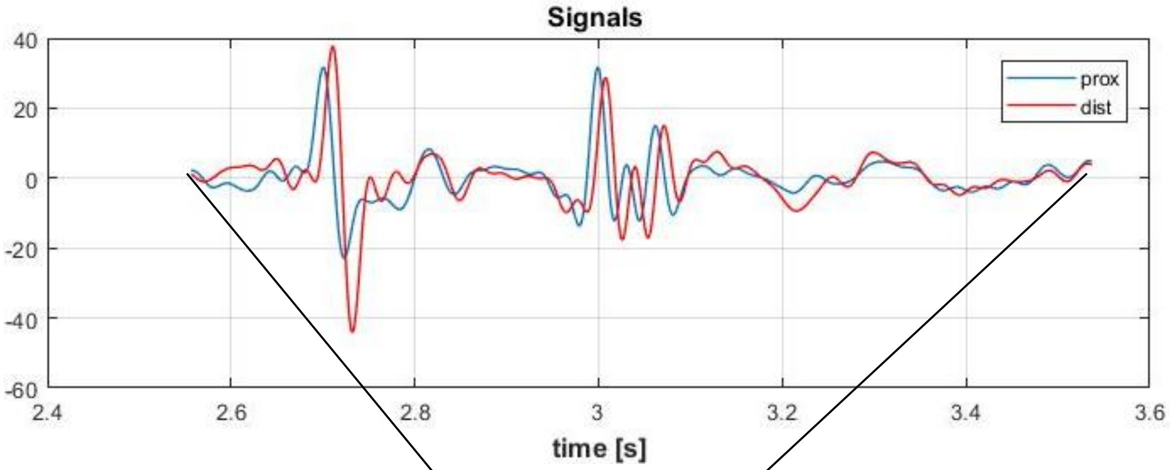
The cf-PWV is obtained with the 1st derivative signal on a healthy subject.

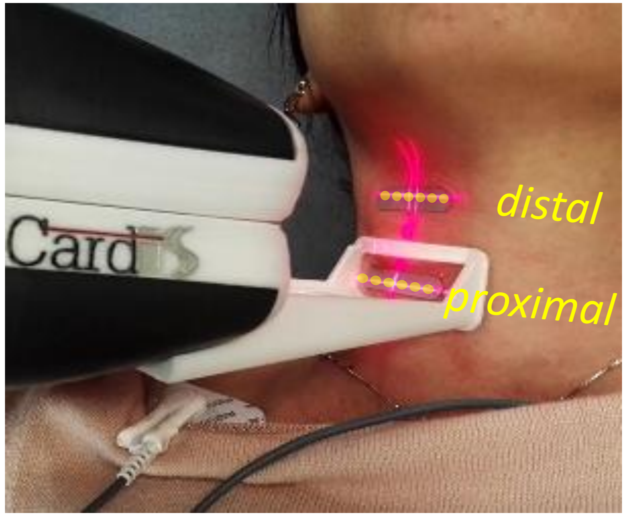


| Sensor | cf-PWV |
|---|---|
| CARDIS LDV | 5.88 ± 0.30 m/s |
| Commercial cf-PWV meter (Sphygmocor) | 5.96 ± 0.40 m/s |

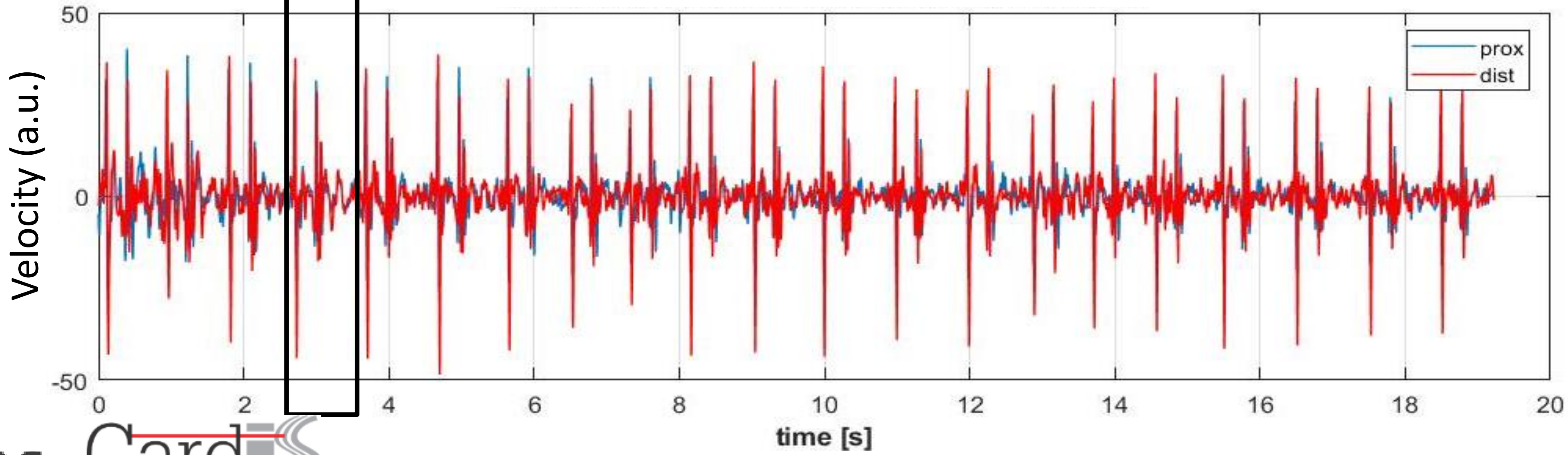
The cf-PWV measured by the CARDIS LDV is very similar to that measured by a commercial PWV meter.

# COMMON-CAROTID (CC) PWV MEASUREMENT RESULTS





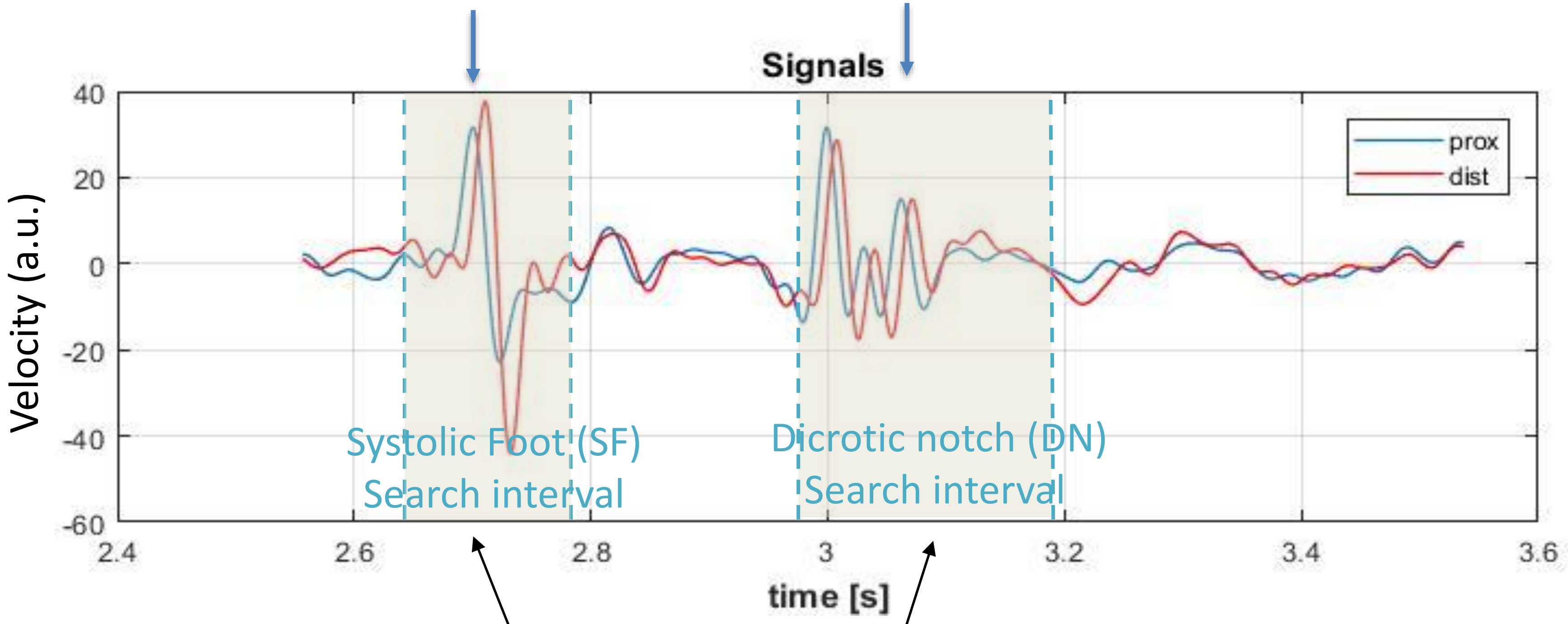
Data from two corresponding channels.



# MEASURED CC-PWV VALUES

Systolic Foot:
Aortic valve opens

Dichrotic Notch:
Aortic valve closes



Systolic Foot (SF)
Search interval

Dicrotic notch (DN)
Search interval

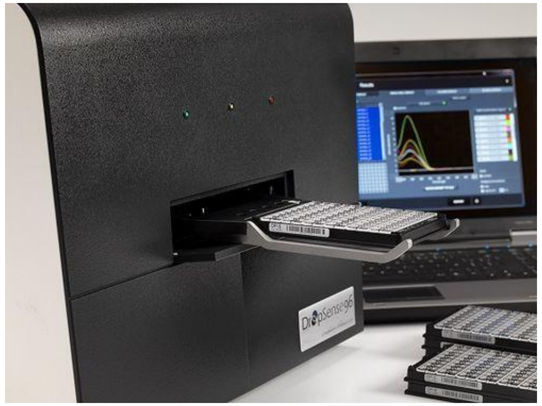
The time delays are calculated by using a cross-correlation method in these intervals.

# THREE APPLICATION CASES

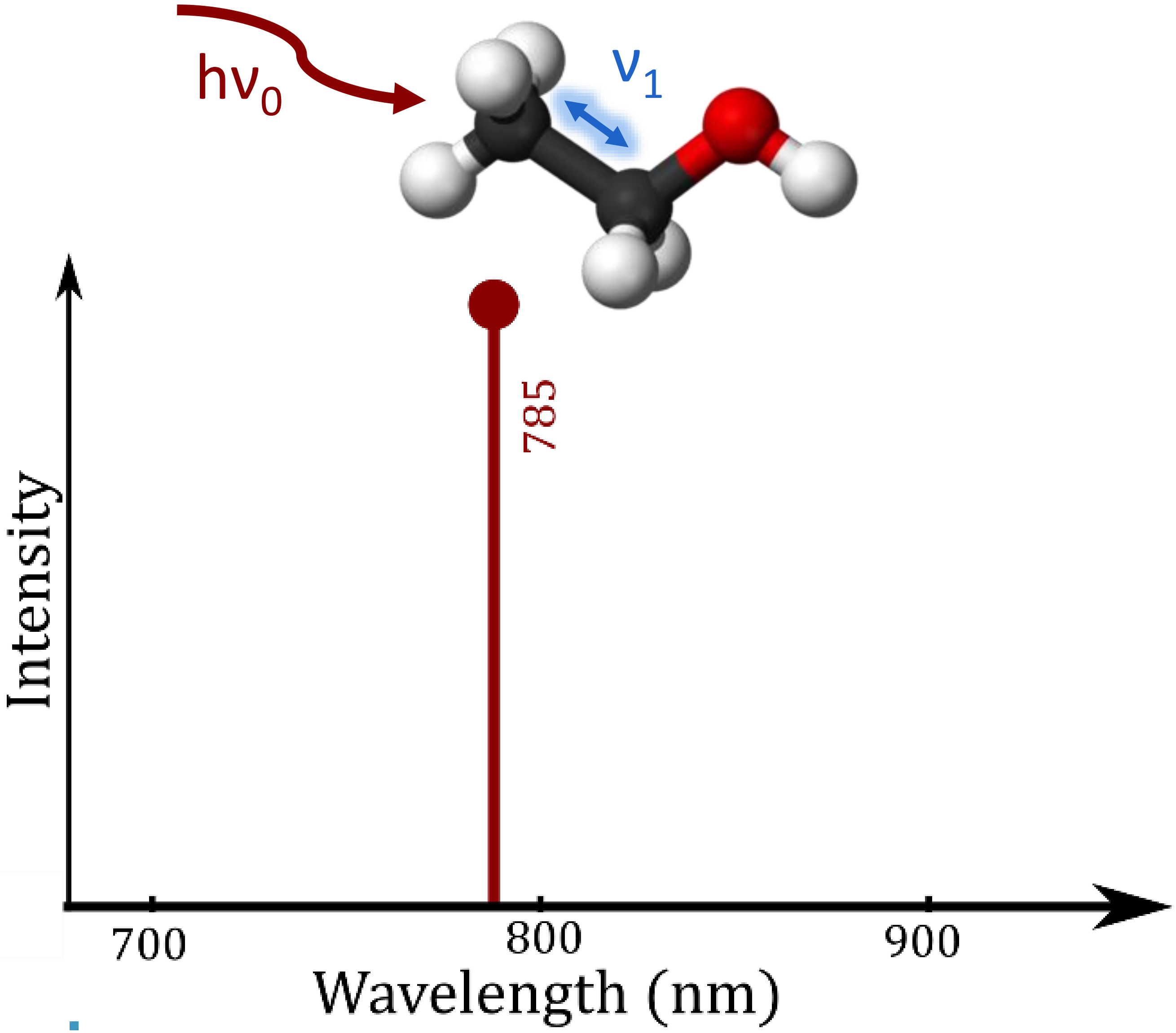
Continuous glucose monitoring

Cardiovascular monitoring

➡ In-vitro diagnostics by on-chip Raman



# THE RAMAN SPECTRUM IS A FINGERPRINT OF A MOLECULE'S VIBRATION



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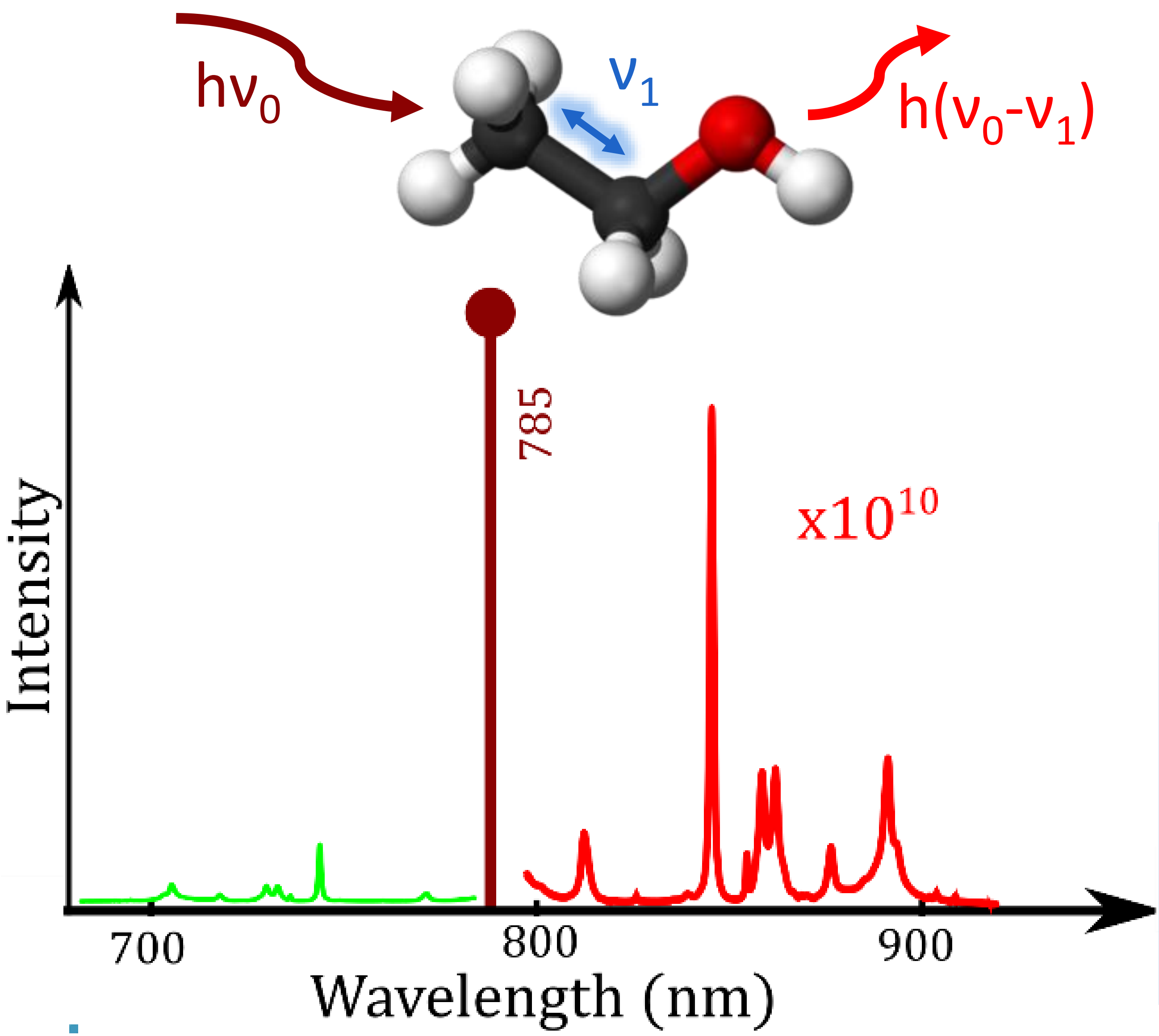


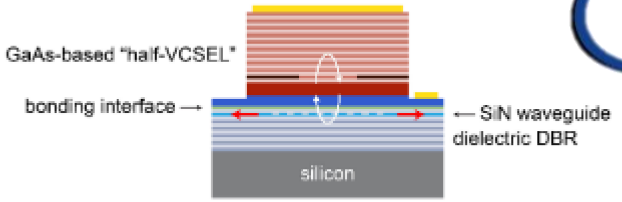
**+ Specific chemical information without any labeling or contact**

**- Weak signals**

# Towards a full integrated SiN platform for on-chip Raman

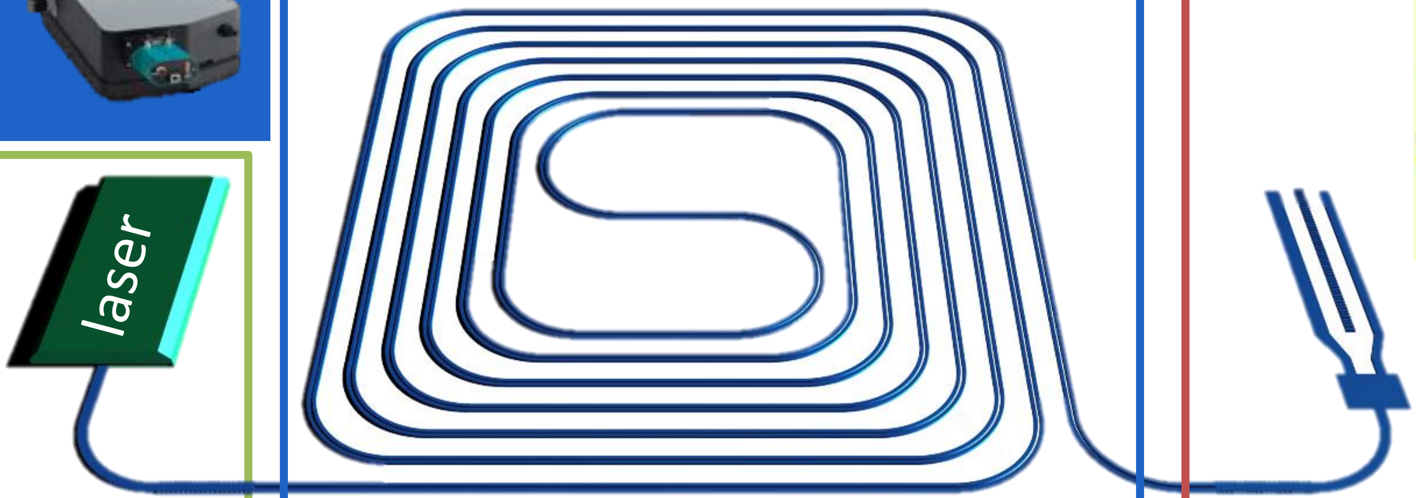
**PAST: a € 100.000, 1 m$^3$ microscope**

**III/V on SiN Pump Laser**

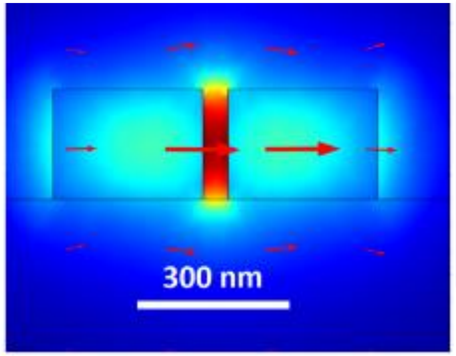


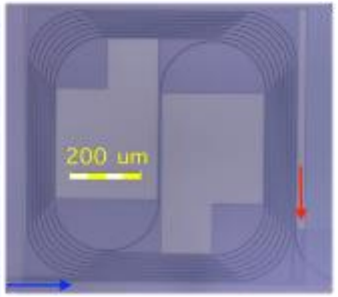
*Haglund, Kumari et al,*
*JSTQE 2017 (6)*

**FUTURE: a € 10, 10 mm$^2$ chip**



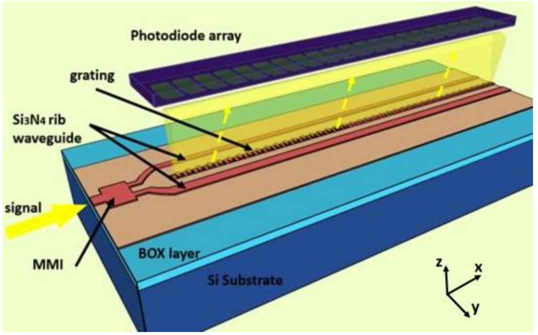
**Waveguide enhanced collection**





*Dhakal, Wuytens et al. ACS Photonics 2016 (3)*

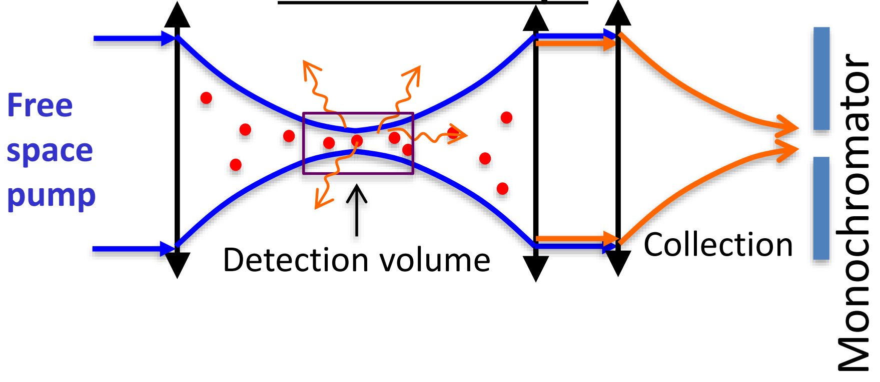
**CMOS integrated spectrometer**



*Nie et al.,*
*Optics Express 2017 (8)*

# WAVEGUIDE-ENHANCED RAMAN SPECTROSCOPY

## Free space excitation and collection in a microscope



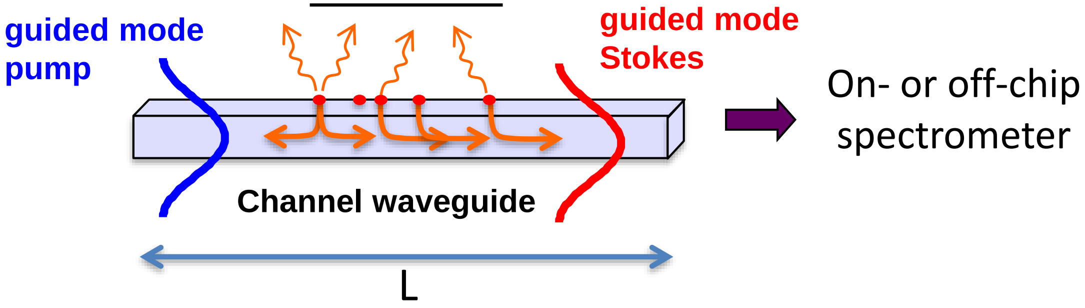
- Large étendue from particle cloud: $\Rightarrow$ Resolution - sensitivity - size compromise for the spectrometer
- In a confocal microscope:

$$\frac{P_{coll}}{P_{pump}} = 2\frac{\lambda_0}{n}\rho\sigma_{scat}$$

density

scattering cross-section

## Waveguide-based excitation and collection



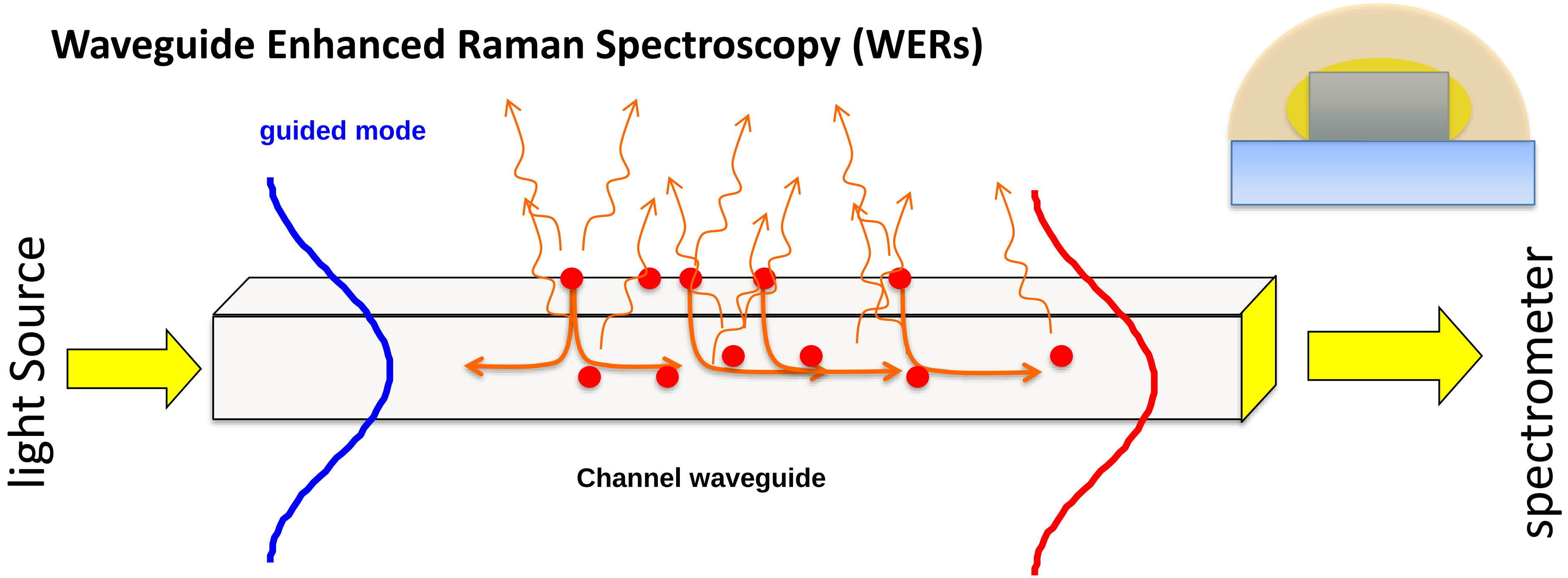
- Cloud couples to single waveguide mode: smallest possible étendue! $\Rightarrow$ Optimal performance of spectrometer

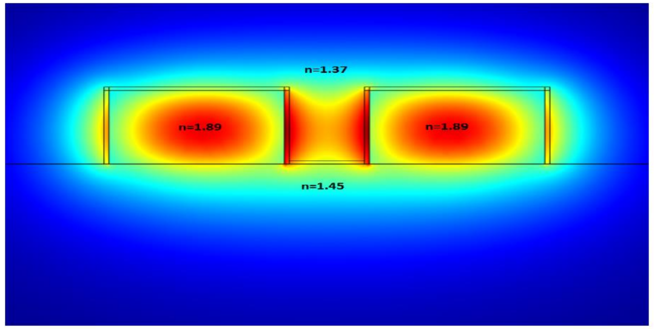
$$\frac{P_{coll}}{P_{pump}} = \boxed{L}\,\eta_0\rho\sigma_{scat}$$

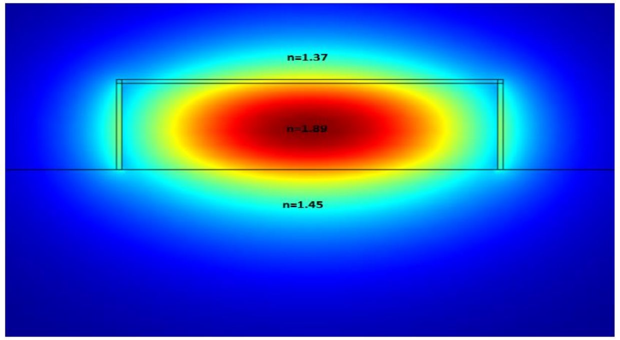
$$\eta_0 \equiv \frac{1}{n(\vec{r})k_\nu}\left(\frac{\pi n_g \lambda_0}{\varepsilon_0}\right)^2 \left(\frac{\iint_{Clad} \left|\vec{e}_m(\vec{r})\right|^2 d\vec{r}}{\iint_{\infty} \varepsilon(\vec{r})\left|\vec{e}_m(\vec{r})\right|^2 d\vec{r}}\right)^2$$

**High index contrast matters**

# Waveguide Enhanced Raman Spectroscopy (WERs)

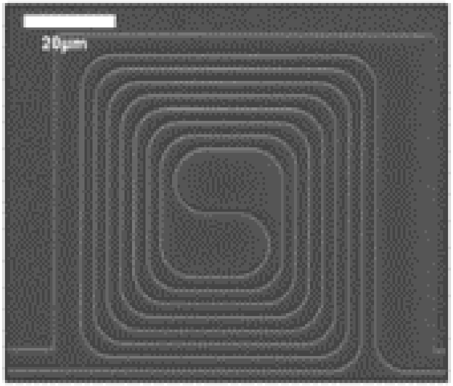


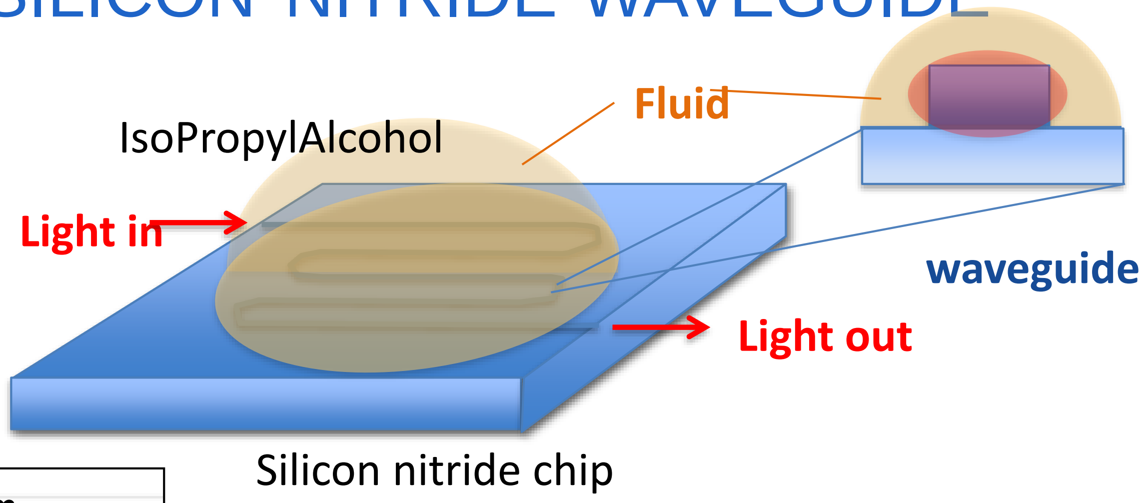


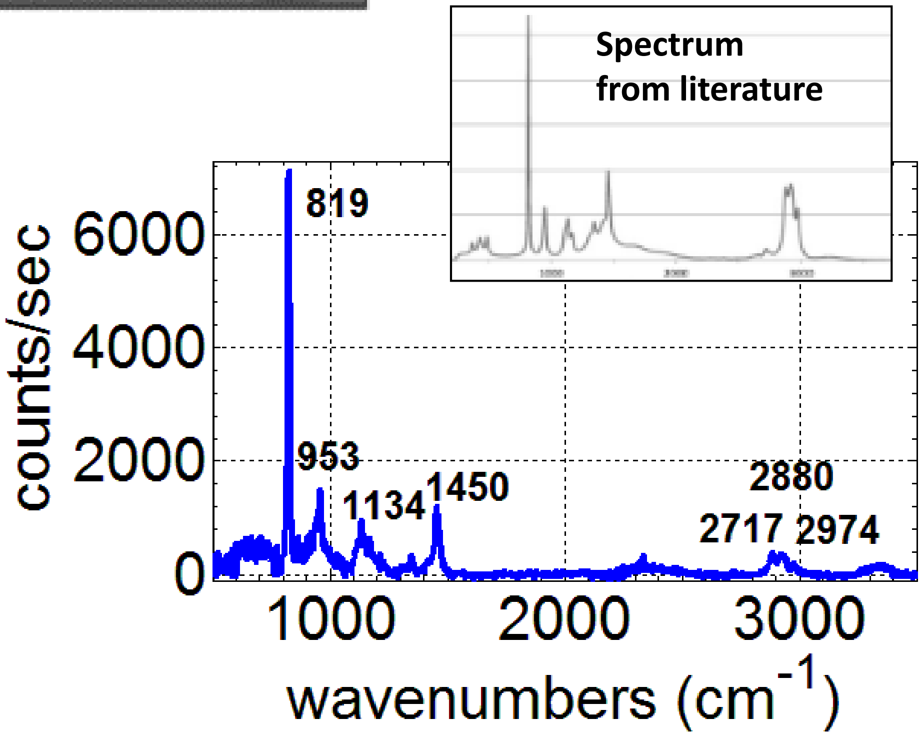


A. Dhakal *et al.*, ACS. Photonics. **3**, 2141-2149 (2016)
Z. Wang *et al.*, Opt. Letters. **41**, 4146-4149 (2016)
C.  Evans et al., ACS Photonics 3, 1662-1669 (2016)

# RAMAN SPECTRUM OF IPA ON SILICON-NITRIDE WAVEGUIDE





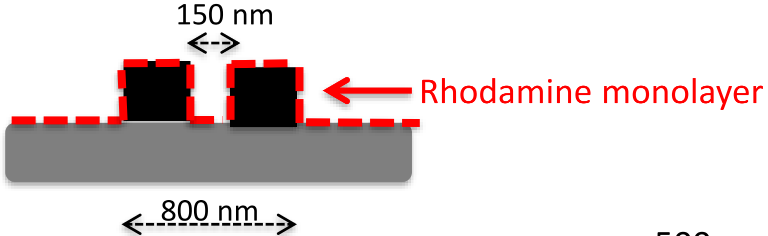


Efficiency of collection 10-100x better than in Raman microscope

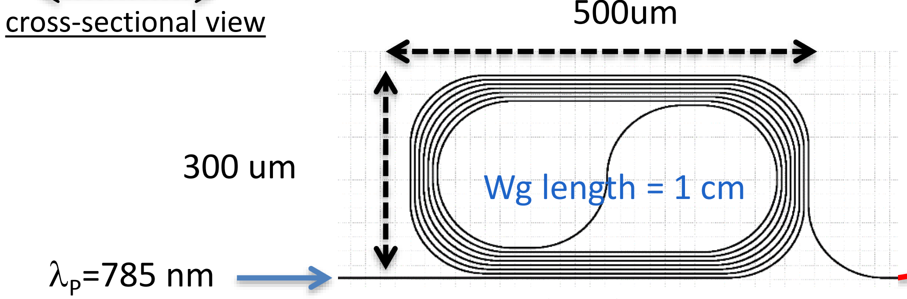
A. Dhakal et al, Opt. Lett. (2014)
A. Dhakal et al, Optics Express (2015)

# RAMAN SPECTROSCOPY OF RHODAMINE MONOLAYERS

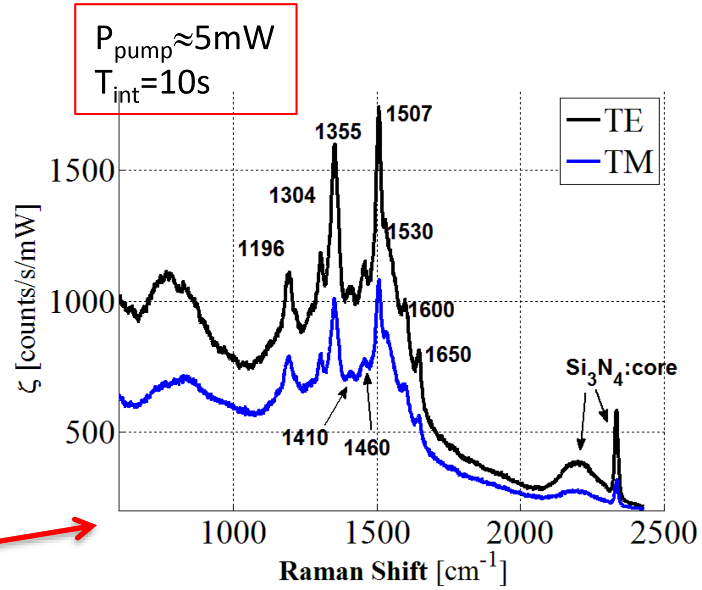
$Si_3N_4$ waveguides were silanized, reacted with amine-reactive NHS-Rhodamine and rinsed to get a monolayer of Rhodamine on the waveguide surface.



cross-sectional view



Top view of the functionalized chip

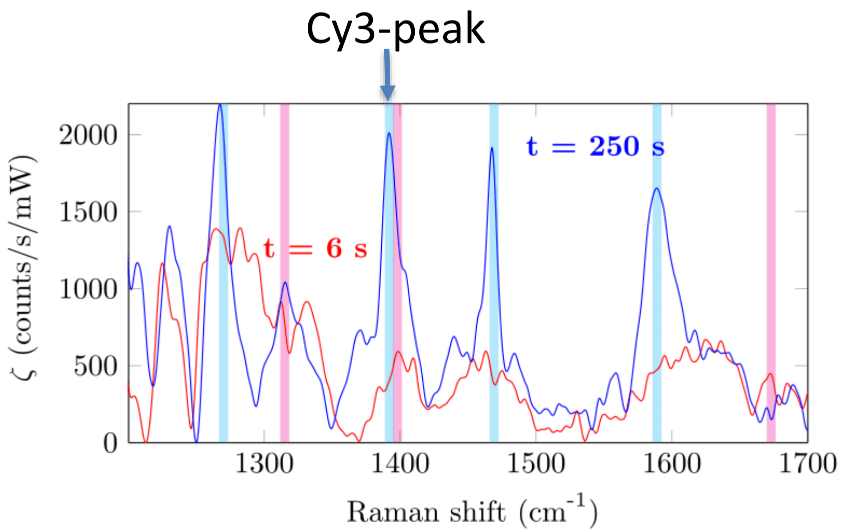


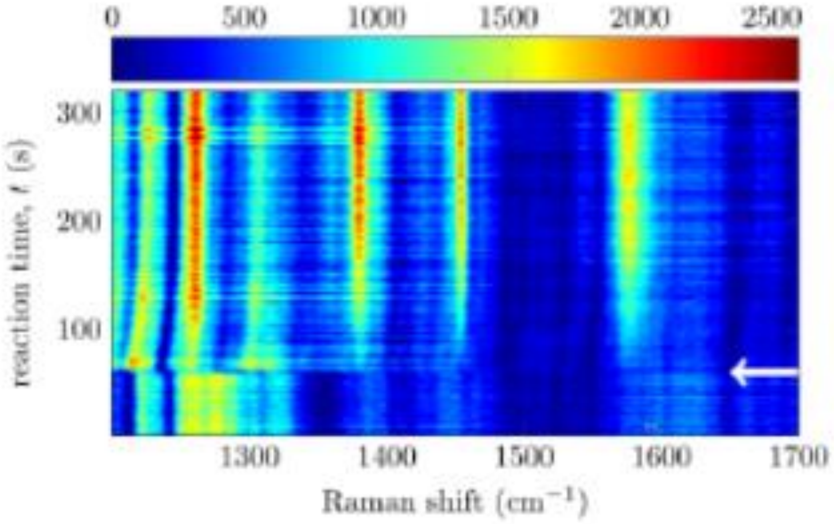
$P_{pump} \approx 5mW$
$T_{int}=10s$

>$10^4$ more collection efficiency than with Raman microscope.

A. Dhakal ea, ACS Photonics, 2016

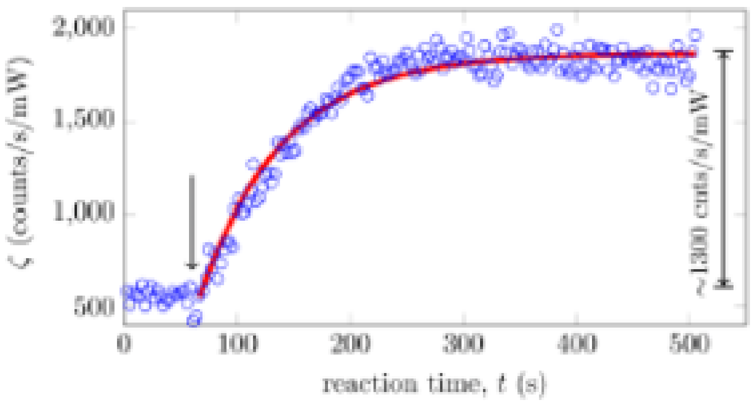
# DNA HYBRIDIZATION KINETICS





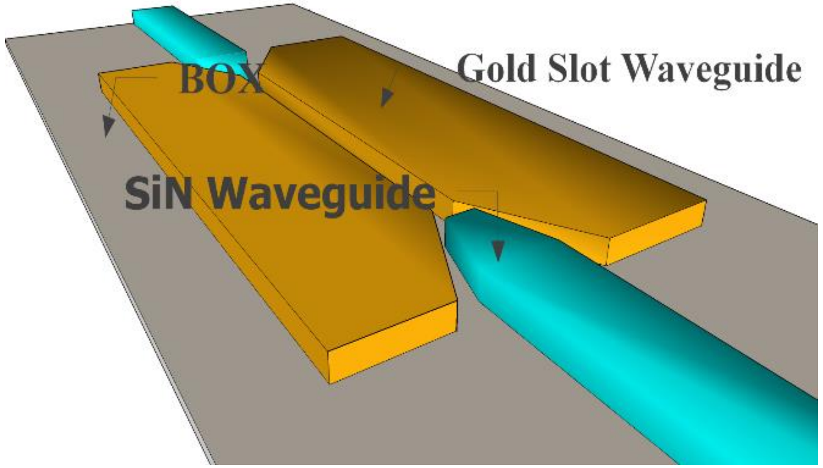
1. Waveguides functionalized with single strand DNA (here of a cancer-relevant gene K-Ras)

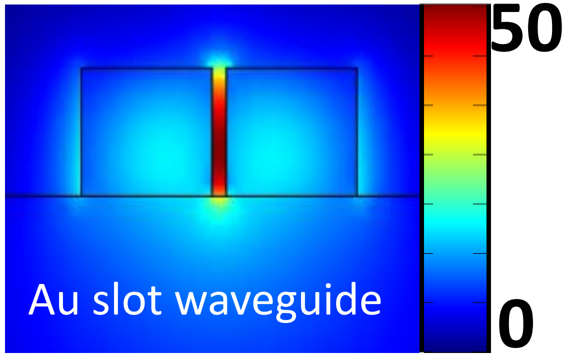
2. Real-time monitoring of the binding of complementary DNA, labeled with Cy3

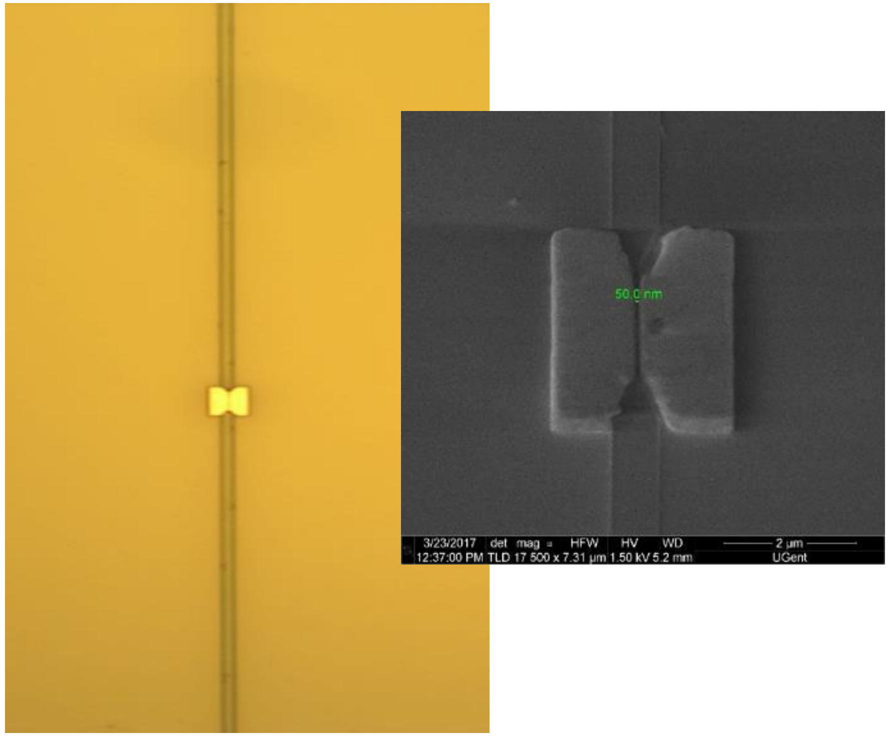


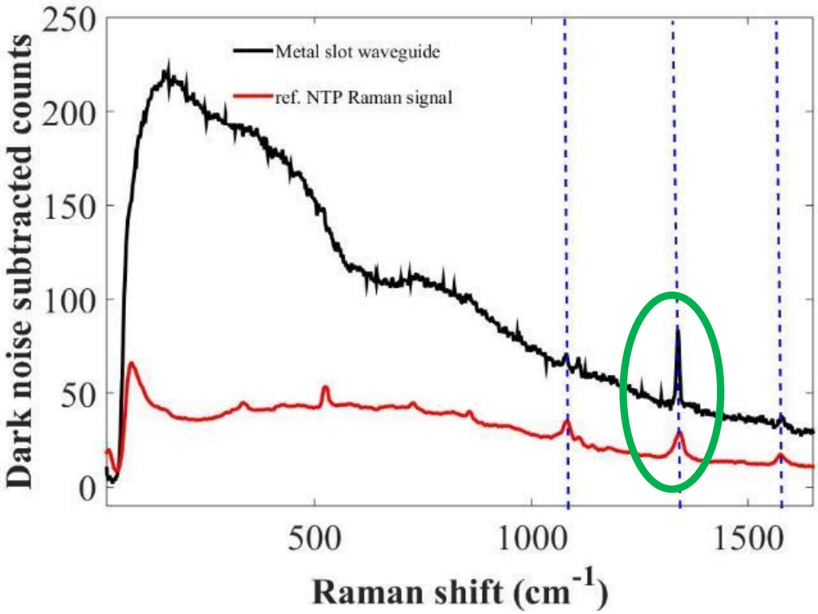
A. Dhakal ea, ACS Photonics, 2016

# USING METAL SLOT WAVEGUIDES TO ENHANCE THE RAMAN SCATTERING





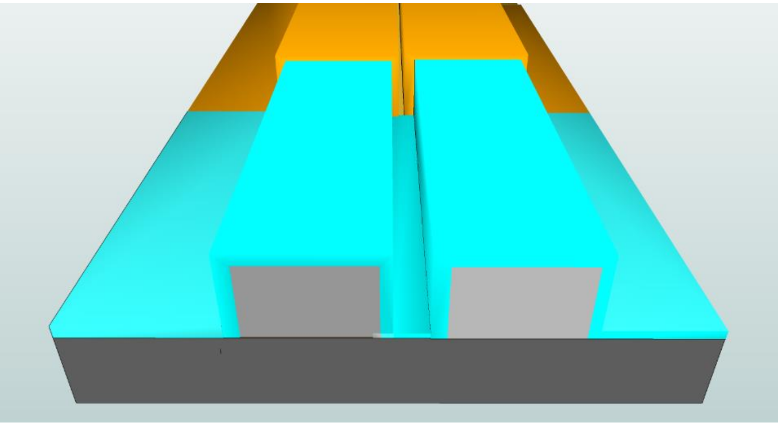


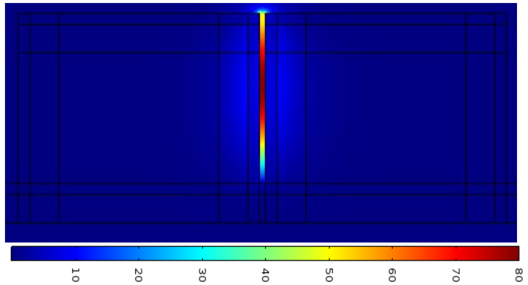


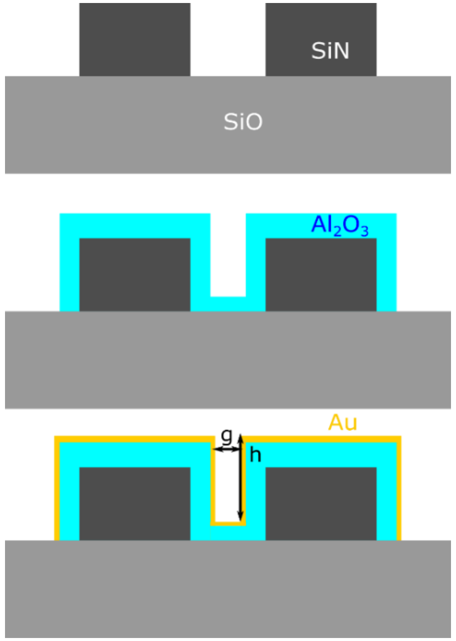
**Spectrum of NTP (4-NitroThioPhenol) bound to gold**

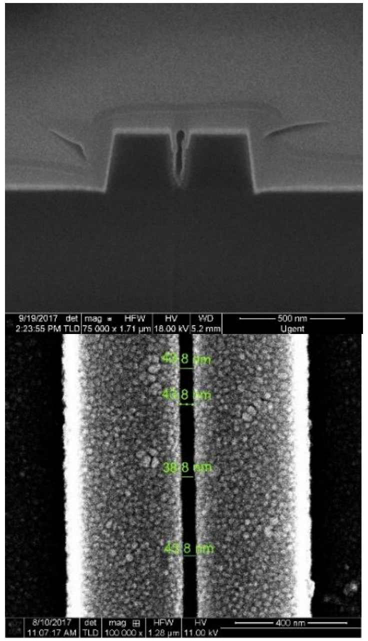
A. Raza et al, ECIO 2017

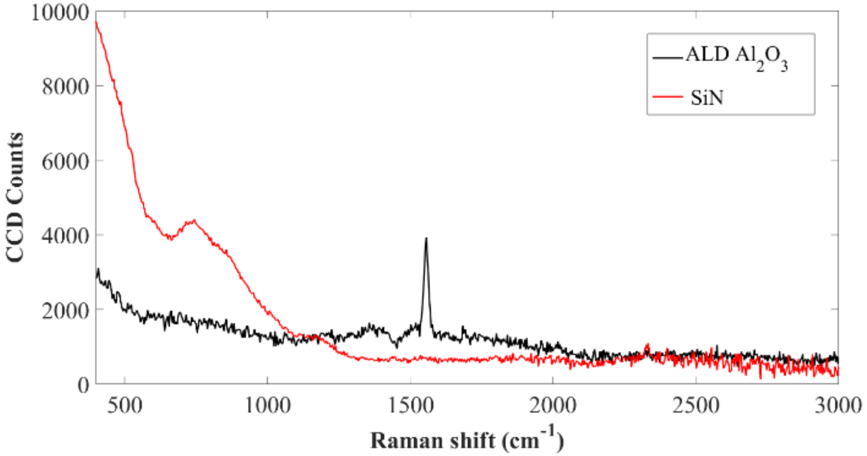
# ALL DUV FABRICATED HYBRID PHOTONICS PLASMONICS WAVEGUIDE:







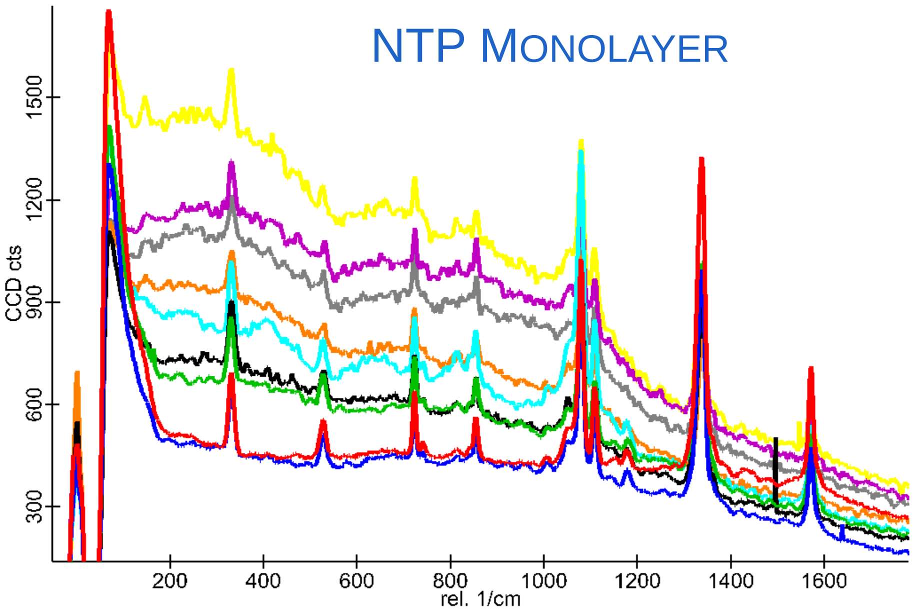


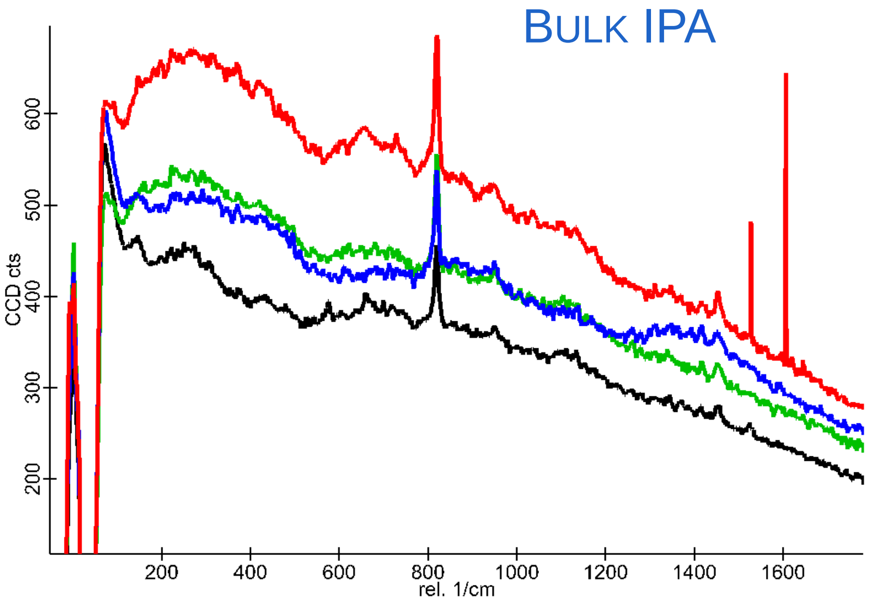


A. Raza et al, CLEO 2018

# ALL DUV FABRICATED HYBRID PHOTONICS PLASMONICS WAVEGUIDE

## STRONG ENHANCEMENT:





## VARIABILITY OF ENHANCEMENT: 5%

A. Raza et al, CLEO2018

# LESSONS LEARNED

Mature technology platforms

⇓

Limited degrees of freedom

Diverse medical applications

⇓

Many degrees of freedom

**Need for smart design**

In life science signals are typically noisy or weak relative to background

**Need for smart signal analysis**

# CONCLUSIONS

Silicon photonics has the potential of serving many medical applications, in particular for point-of-care, in-the-body devices and in-vitro diagnostics

Key assets: compact size and volume; low cost

Proof-of-concept demonstrated for:

- Continuous Glucose Monitoring

  absorption spectroscopy on a silicon chip

- Pulse Wave Velocity (PWV) measurement

  multi-beam Laser Doppler Vibrometry enabled by a silicon chip

- Selective detection of medically relevant molecules

  Raman spectroscopy on a chip

# ACKNOWLEDGEMENTS

## Funding

iWT

erc

THE FRAMEWORK PROGRAMME FOR RESEARCH AND INNOVATION
HORIZON 2020

CardiS

## Collaborations

Medtronic

Tyndall National Institute

SIOS Meßtechnik GmbH

Queen Mary University of London

Inserm

Maastricht University

## Video

Louise Marais and colleagues, Inserm

**Photonics Research Group of Ghent University – imec**

**imec Silicon Photonics platforms (SOI and SiN)**

GHENT UNIVERSITY

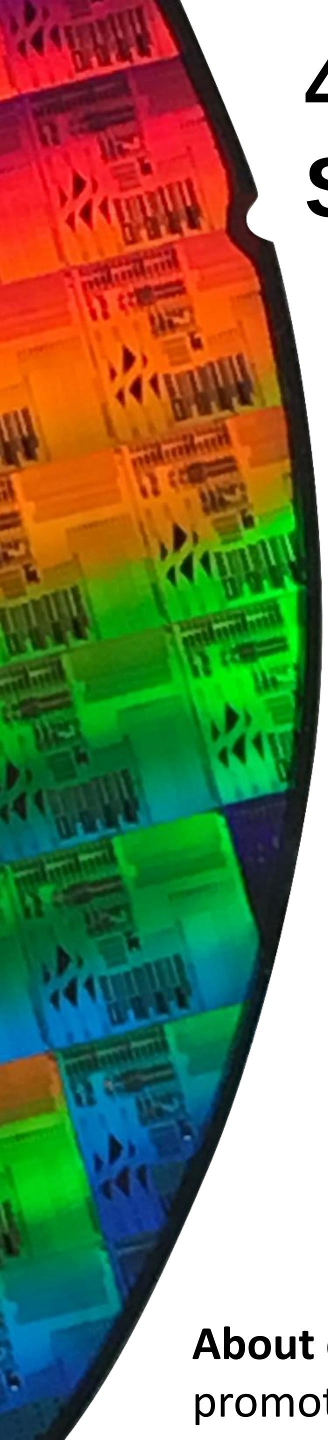
imec

GHENT
UNIVERSITY

# ECIO 2019

24th April - 26th April 2019
Ghent University, Belgium

## 21st EUROPEAN CONFERENCE ON INTEGRATED OPTICS



# 4th ePIXfab Silicon Photonics Summer School
# Scuola Superiore Sant'Anna Pisa, ITALY

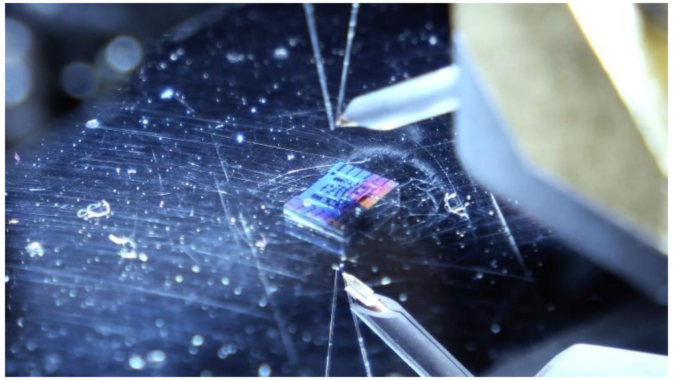
**DATE :**1st to 5th July, 2019

**KEY FEATURES**

- Geared towards industrial and academic participants
- Fundamentals to the latest developments in silicon photonics
- Emerging applications of silicon photonics.
- Interact with top-notch experts in the field of silicon photonics

**MORE INFO:**

e-mail: info@ePIXfab.eu
web: http://epixfab.eu/upcoming-trainings/spss19



**About ePIXfab:** ePIXfab is the European Silicon Photonics Alliance, with a mission to promote silicon photonics science, technology, and application through fabless model.