PHOTONICS RESEARCH GROUP

APPLICATIONS OF SILICON PHOTONICS IN LIFE SCIENCE AND MEDICINE

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Photonex SPIE Digital Forum, October 2020
(online presentation)

GHENT UNIVERSITY

imec
embracing a better life

HEALTH CARE

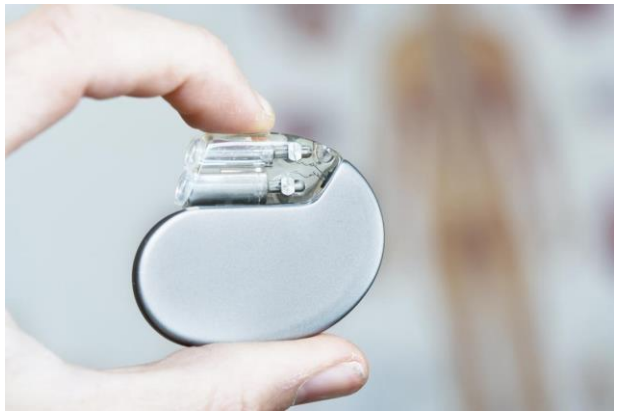
Enormous challenges:

- Ageing society
- Keep ever more performant health care affordable for society
- Pandemics

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)

MICRO-CHIPS: KEY FOR COMPACT AND LOW-COST MEDICAL DEVICES



Pacemaker

Electronic IC’s

Infrared fever thermometer

Mid-IR detector chip

Pulse Oximeter

Near IR LED and detector chips

ASSETS OF SILICON PHOTONICS FOR MEDICINE AND HEALTH CARE

Rich set of sensing modalities

Low cost (even in moderate volume)

Disposable (use-once) devices

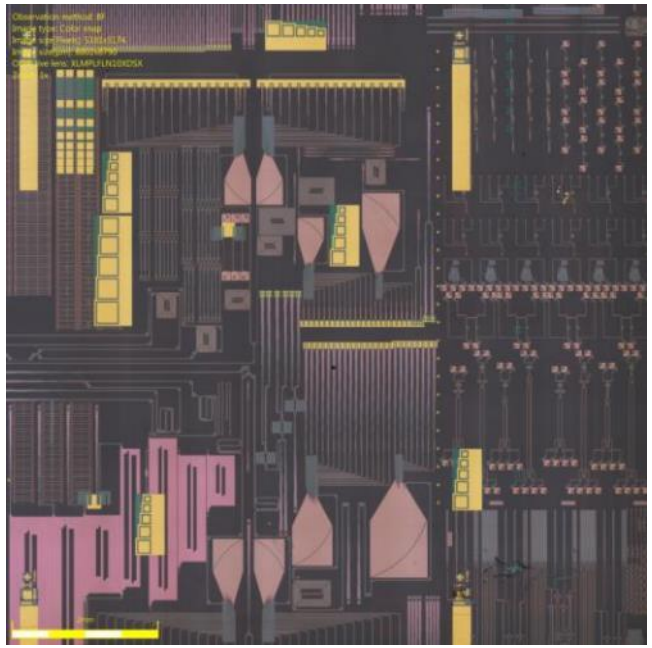
Very compact devices (even small enough for bodily implants)

Can address needs from visible to mid IR

Mature supply chain

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

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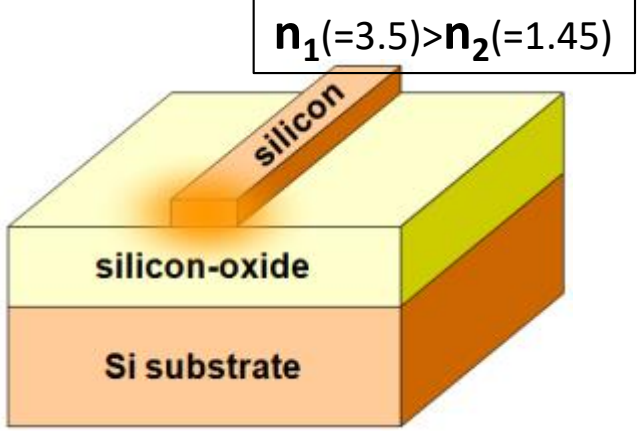
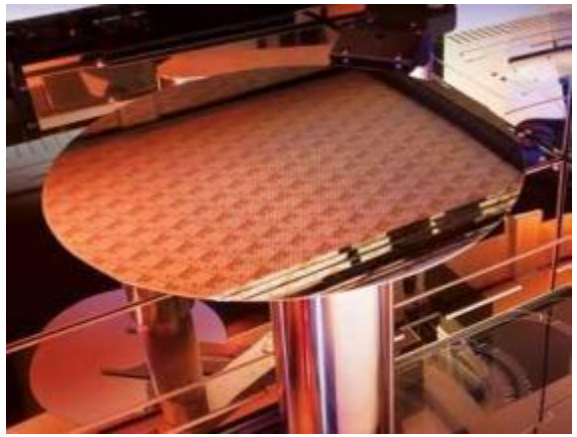
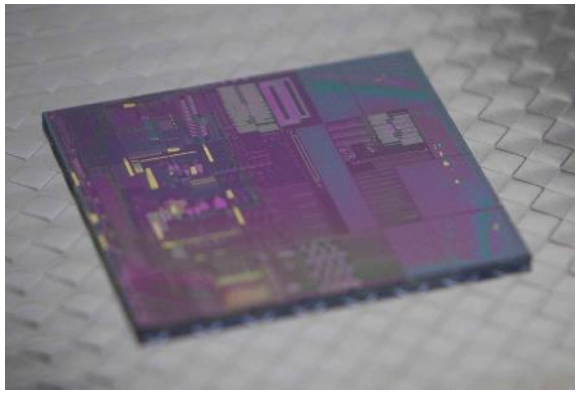
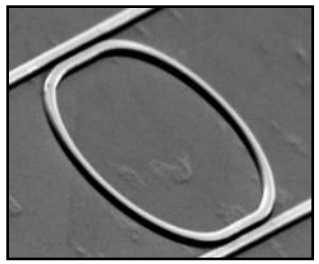
WHY SILICON PHOTONICS

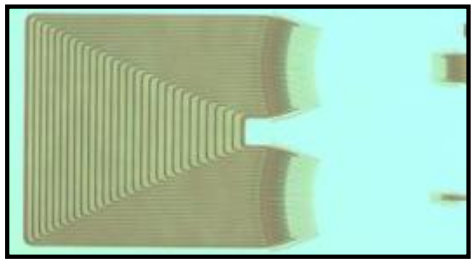
- High index contrast ⇒ **very compact PICs**
- CMOS technology ⇒ **nm-precision, high yield, existing fabs, low cost in volume**
- High performance passive devices
- High bitrate Ge photodetectors
- High bitrate modulators
- Wafer-level automated testing
- Hierarchical set of design tools
- Light source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











Transceivers for Data centers and for Telecom

Typical data rate: 100 Gb/s

Typical symbol rate: 25 GBaud

- PSM4 (4 parallel fibers)
- WDM (4 wavelengths)
- PAM4
- Coherent (2 polarisations + QPSK)
- Coherent (16-QAM)

Under development:

Data rate: 400-800 Gb/s

Symbol rate: 50-100 Gb/s

CompoundTek

SiLTerra

tsmc

amf Advanced Micro Foundry

Finisar

Acacia Communications, Inc.

Inphi Think fast.

Cisco

Juniper Networks

aurrion

Ayar Labs

TeraXion

sicoya

ciena

intel

Cisco Lightwire

ST

Xm Kaiam

Elenion Technologies

IBM

Skorpios Technologies

molex

Global Foundries

Mellanox Technologies

Kotura

Luxtera Nanophotonic Integrated Circuits

Cisco

Caliopa silicon photonics

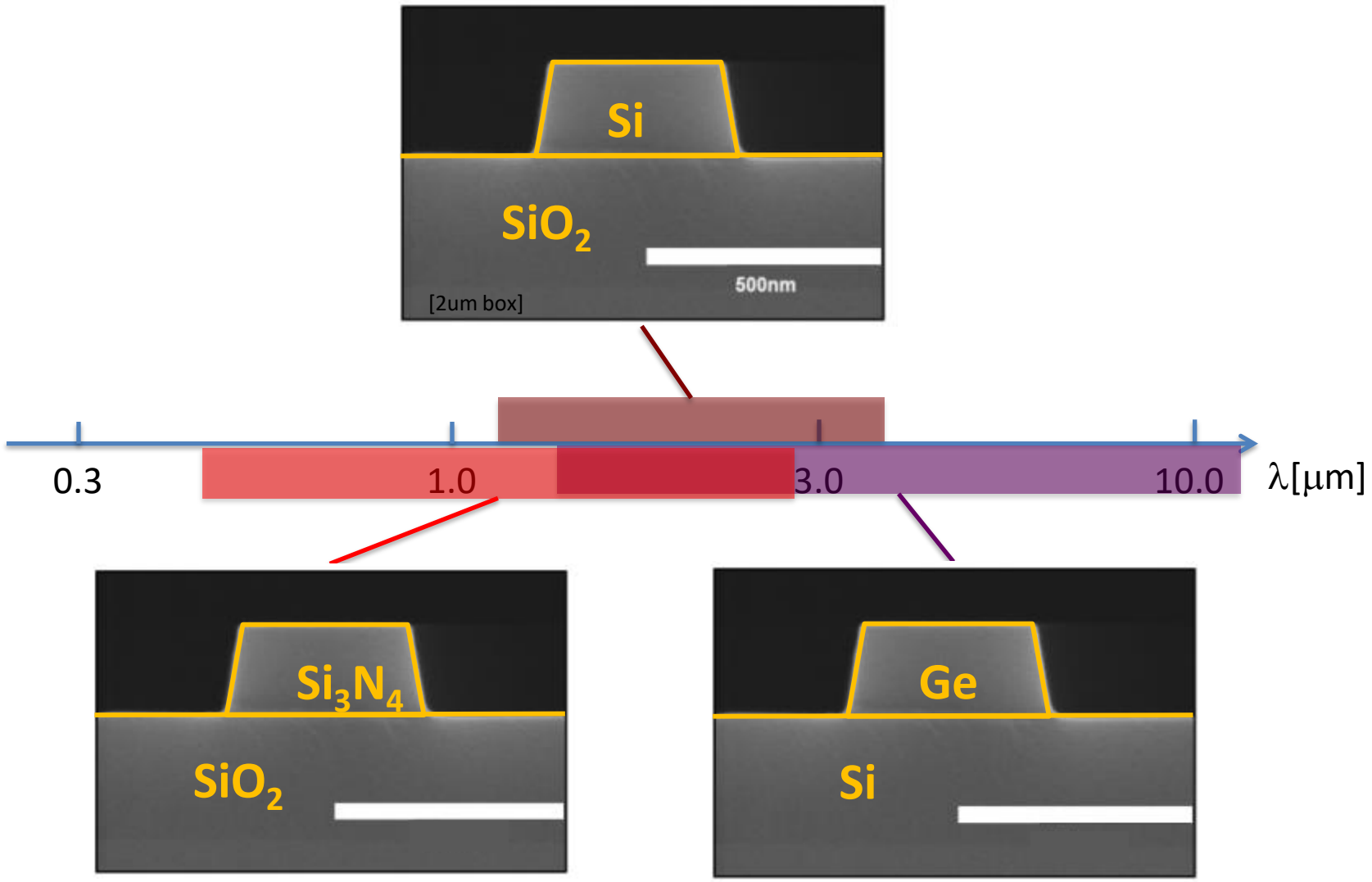
Huawei

Ghent University

imec

SILICON PHOTONICS: EXTENDING THE WAVELENGTH RANGE

WITHOUT LEAVING THE CMOS FAB



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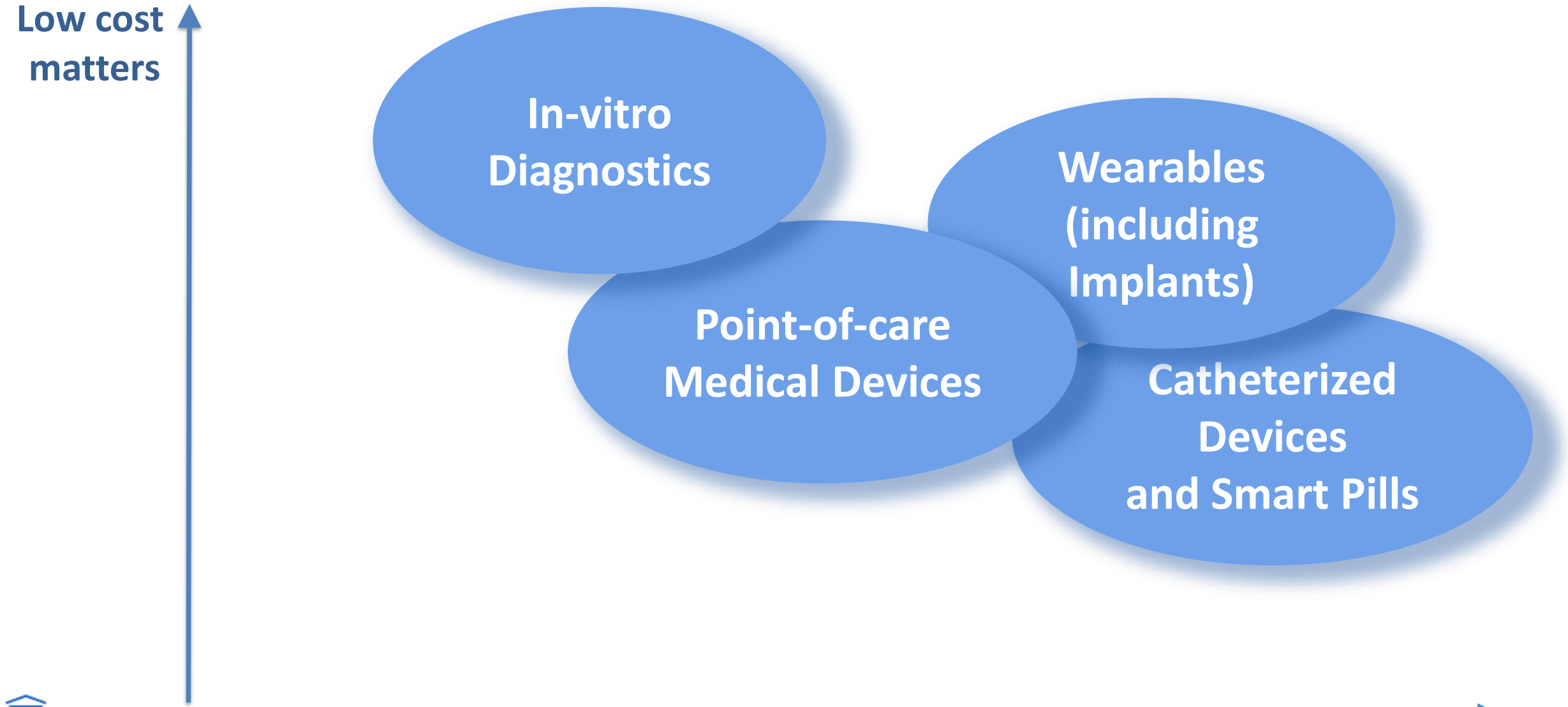
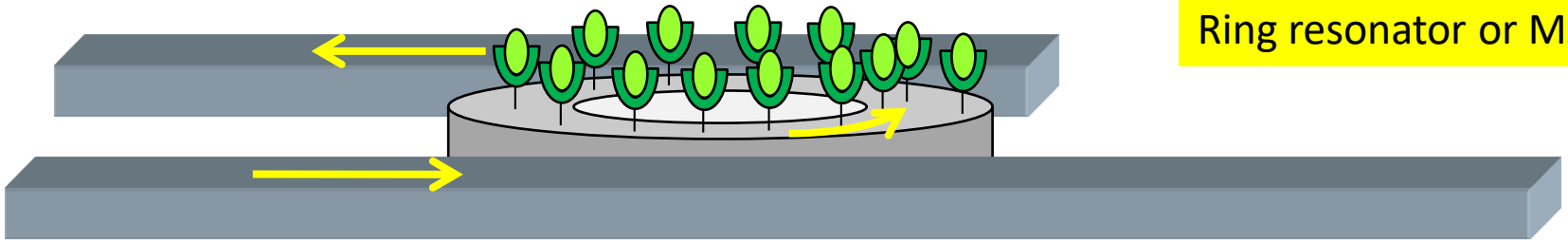
Main applications of Silicon photonics in Medicine

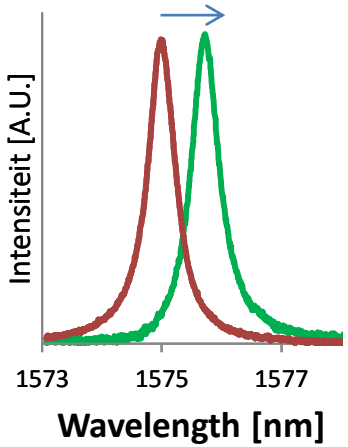


LABEL-FREE BIOSENSOR
THROUGH REFRACTIVE INDEX SENSING OF ANTIGEN-ANTIBODY BINDING



Ring resonator or MZI

Wavelength shift



19 Antibody Test

by genalyte | Apr 27, 2020 | Uncategorized

First Instrument-Based, Rapid Test Uses Multi-Antigen Approach to Achieve Best-in-Class Sensitivity and Specificity, U.S. FDA EUA Submitted

SAN DIEGO, April 27, 2020 /PRNewswire/ — **Genalyte**, the company empowering physicians and patients with real-time diagnostics and healthcare analytics, announced today the availability of its rapid COVID-19 serology panel on its Maverick™ platform. The panel tests for the detection of IgG and IgM antibodies that the body produces in response to the novel coronavirus (SARS-CoV-2).

Genalyte's U.S. Food and Drug Administration (FDA)-cleared Maverick™ Diagnostic System

Genalyte

https://www.genalyte.com/

COVID-19 Multi-Antigen Serology Panel

Semi-Quantitative detection of antibodies to SARS-CoV-2

Who We Are

Genalyte is a CAP accredited, CLIA certified lab specializing in large scale serology testing. Our Maverick™ SARS-CoV-2 Multi-Antigen Serology Panel uses a multiplex format to test patient samples for antibodies to five SARS-CoV-2 proteins. The result is unparalleled accuracy across a variety of patient populations.

Our Platform

The Maverick™ Diagnostic System (MDS) uses silicon chip based photonic ring resonance technology to perform multiple simultaneous rapid tests on a small volume of whole blood. The system is cloud-connected for assay protocol retrieval and clinical oversight. Results are available in 20 minutes. FDA Cleared in 2019 .

General Population: 7-14 days

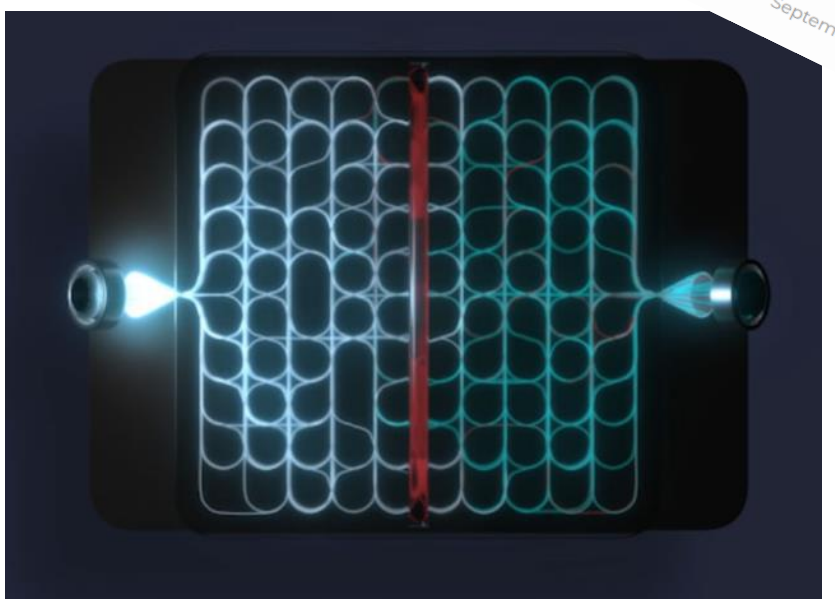
	PCR Result		
MAVERICK	Pos	Neg	
Pos	46	0	46
Neg	7	303	310
	53	303	

Post Seroconversion: >14 days

	PCR Result		
MAVERICK	Pos	Neg	
Pos	86	0	86
Neg	2	303	305
	88	303	

Biosensors for Home and PoC use

- Consumer price
- Rapid test
- First product: STD self-test from urine sample



Belgian startup Antelope Dx raises €9M to fund development of at-home self tests for STDs and COVID-19

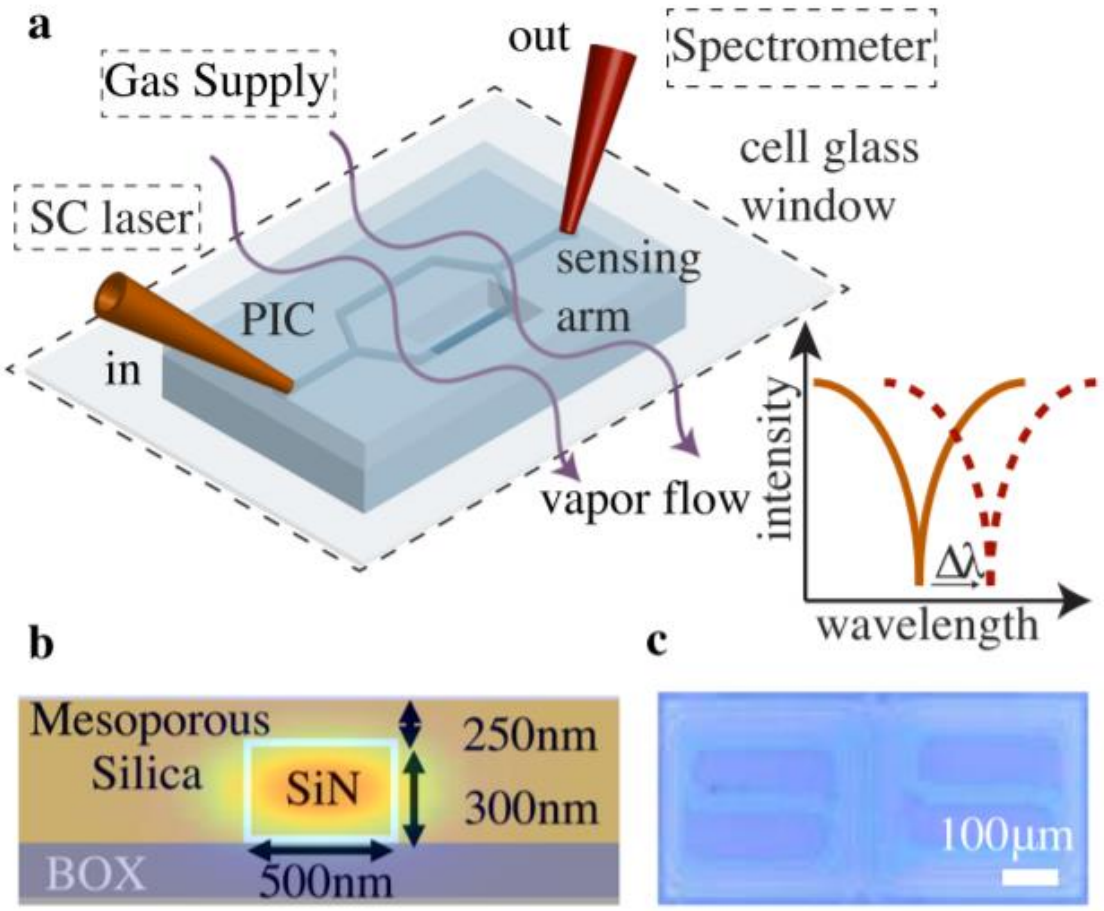
by Editorial team — September 16, 2020 in (Crowd)funding, Health & Medtech, News, Startups

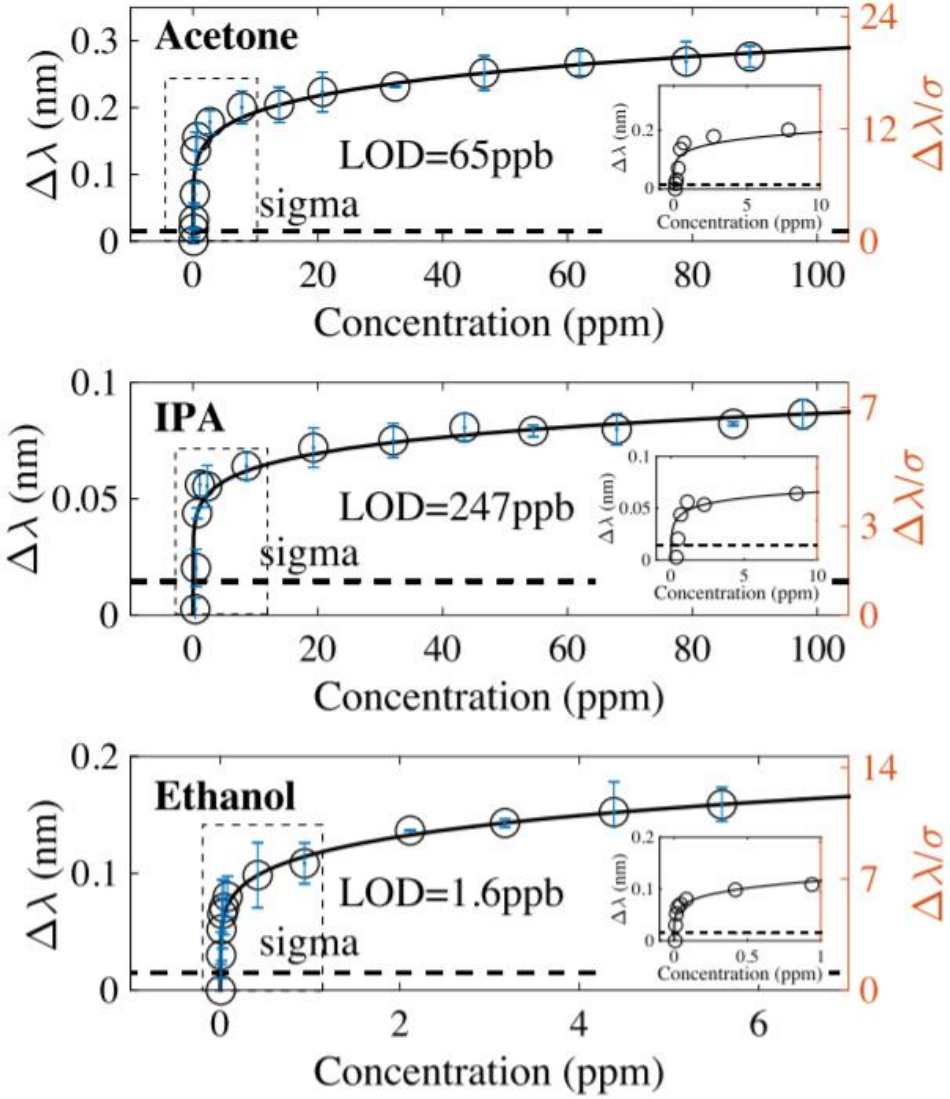
https://www.antelope-dx.com/

ANTELOPE DX

ULTRASENSITIVE GAS SENSING WITH REFRACTIVE INDEX SENSORS

Medical application: breath analysis





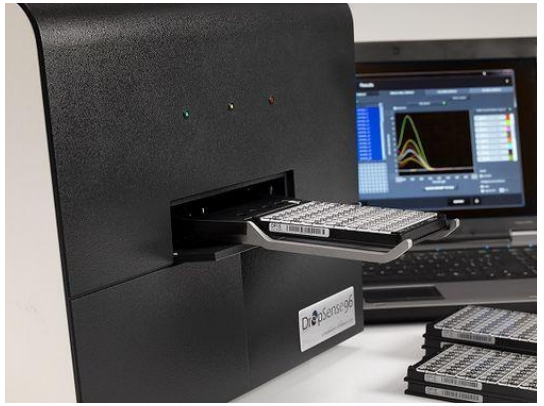
G. Antonacci et al, APL Photonics 2020

Exploration of New Application Cases

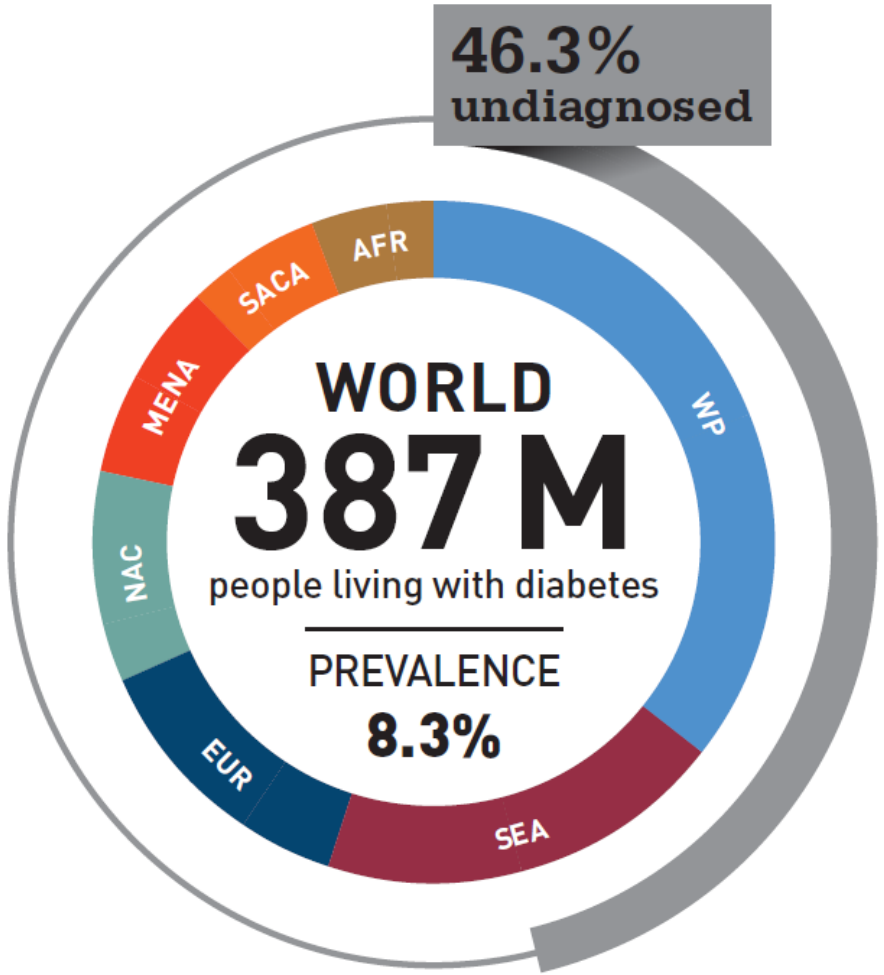
- Continuous glucose monitoring

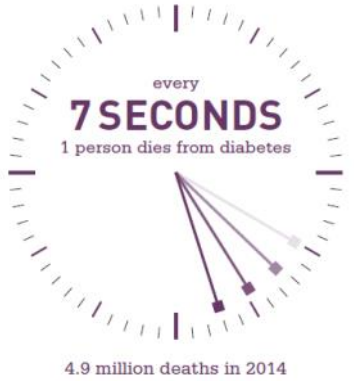
Cardiovascular monitoring

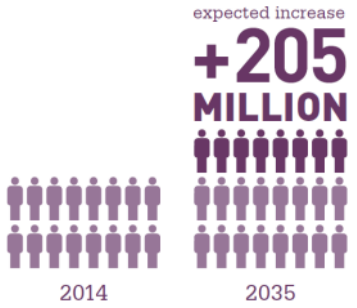
In-vitro diagnostics



DIABETES IS THE 21ST CENTURY HEALTH CHALLENGE







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

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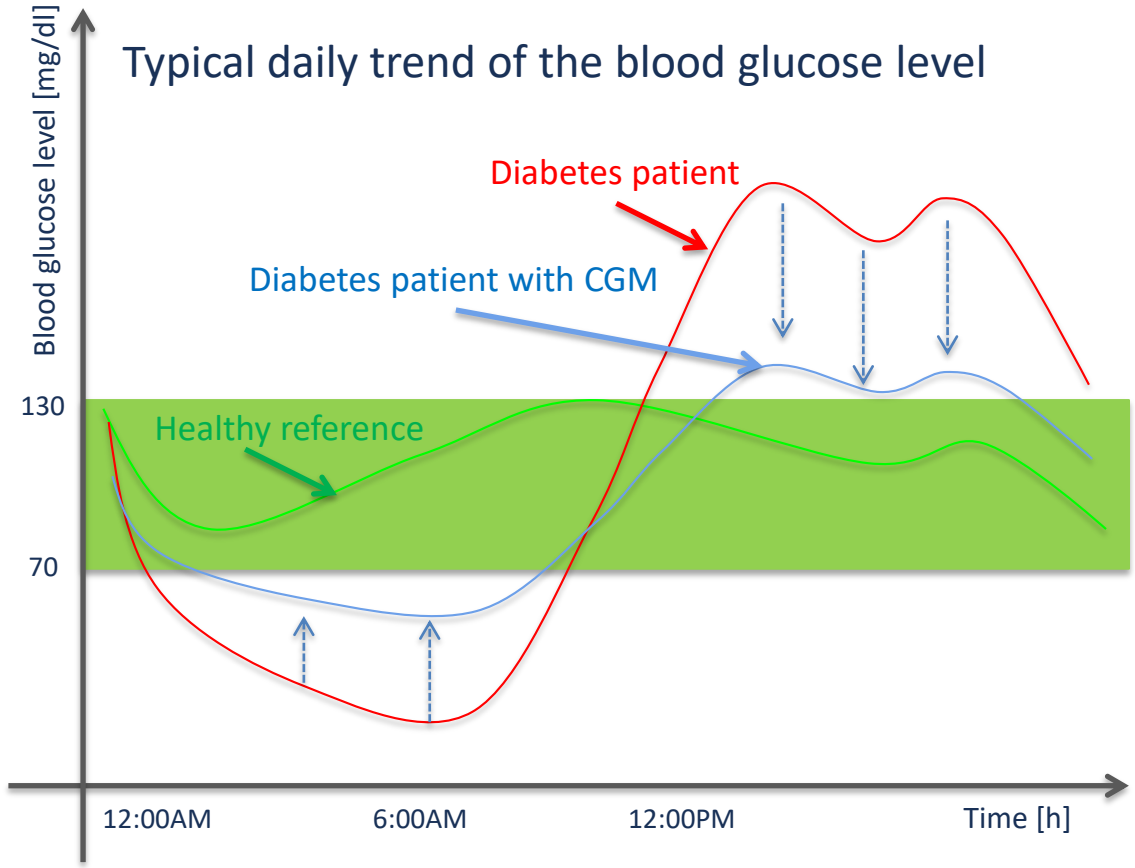
Continuous Glucose Monitoring (CGM) has proven to improve glycemic control of diabetes patients

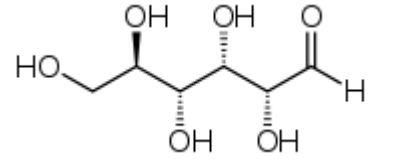
CGM systems show positive health impact *

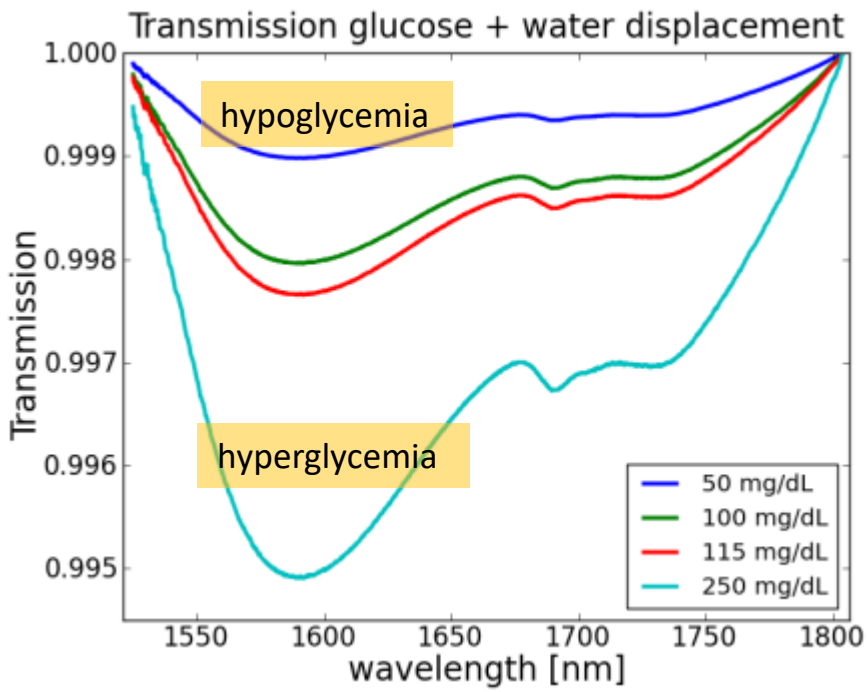
- lower average blood glucose levels
- decrease of hypoglycemic frequency



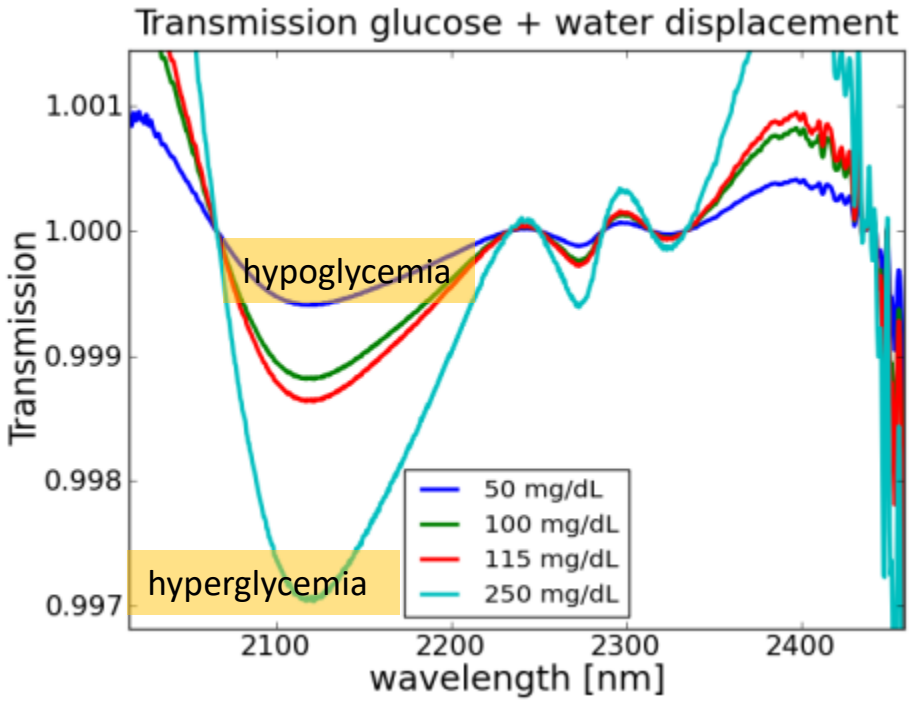
* Liebl A, Henrichs HR, Heinemann L, et al. Continuous glucose monitoring: evidence and consensus statement for clinical use. J Diabetes Sci Technol . 2013;7:500-519

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%

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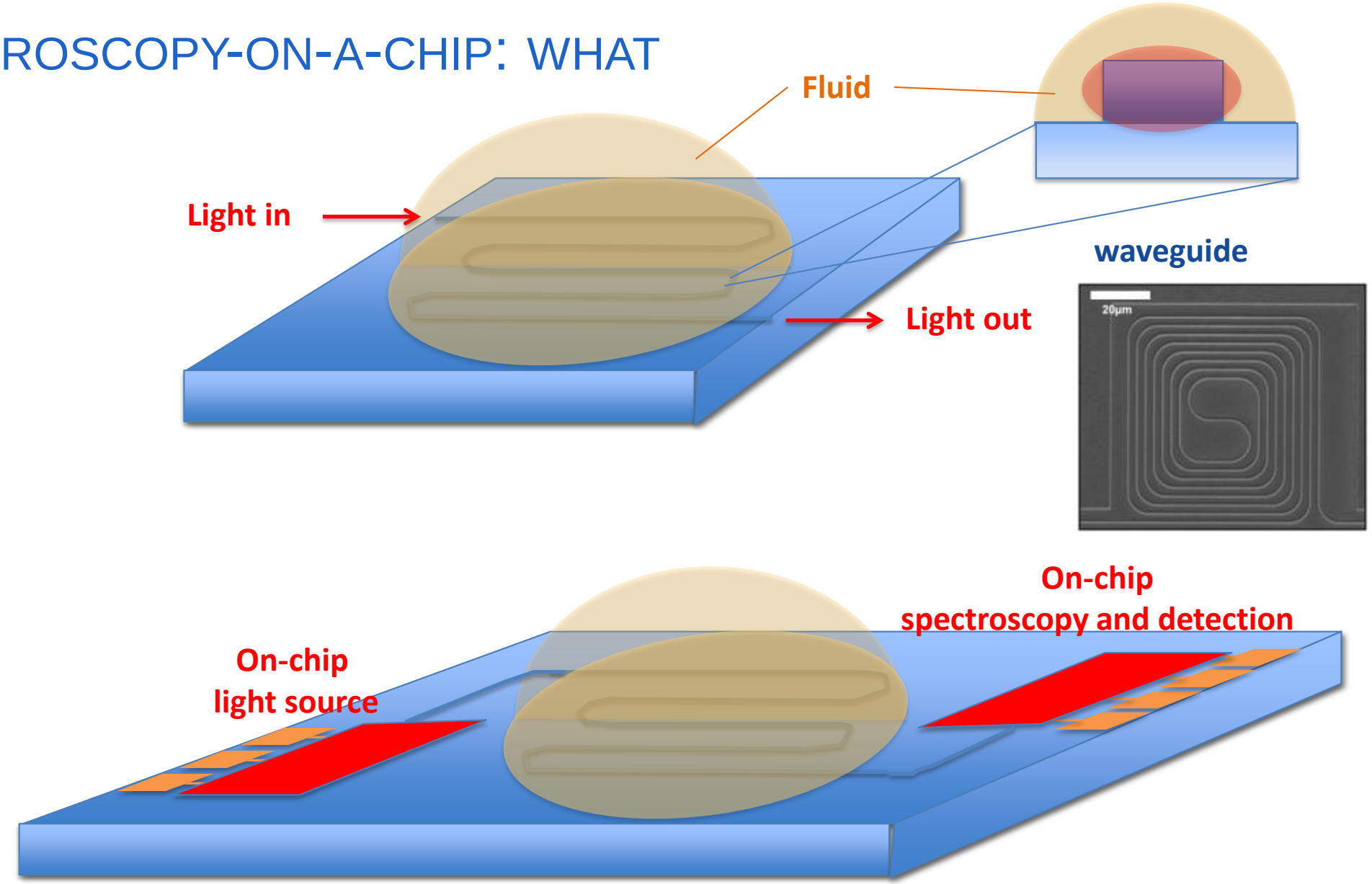
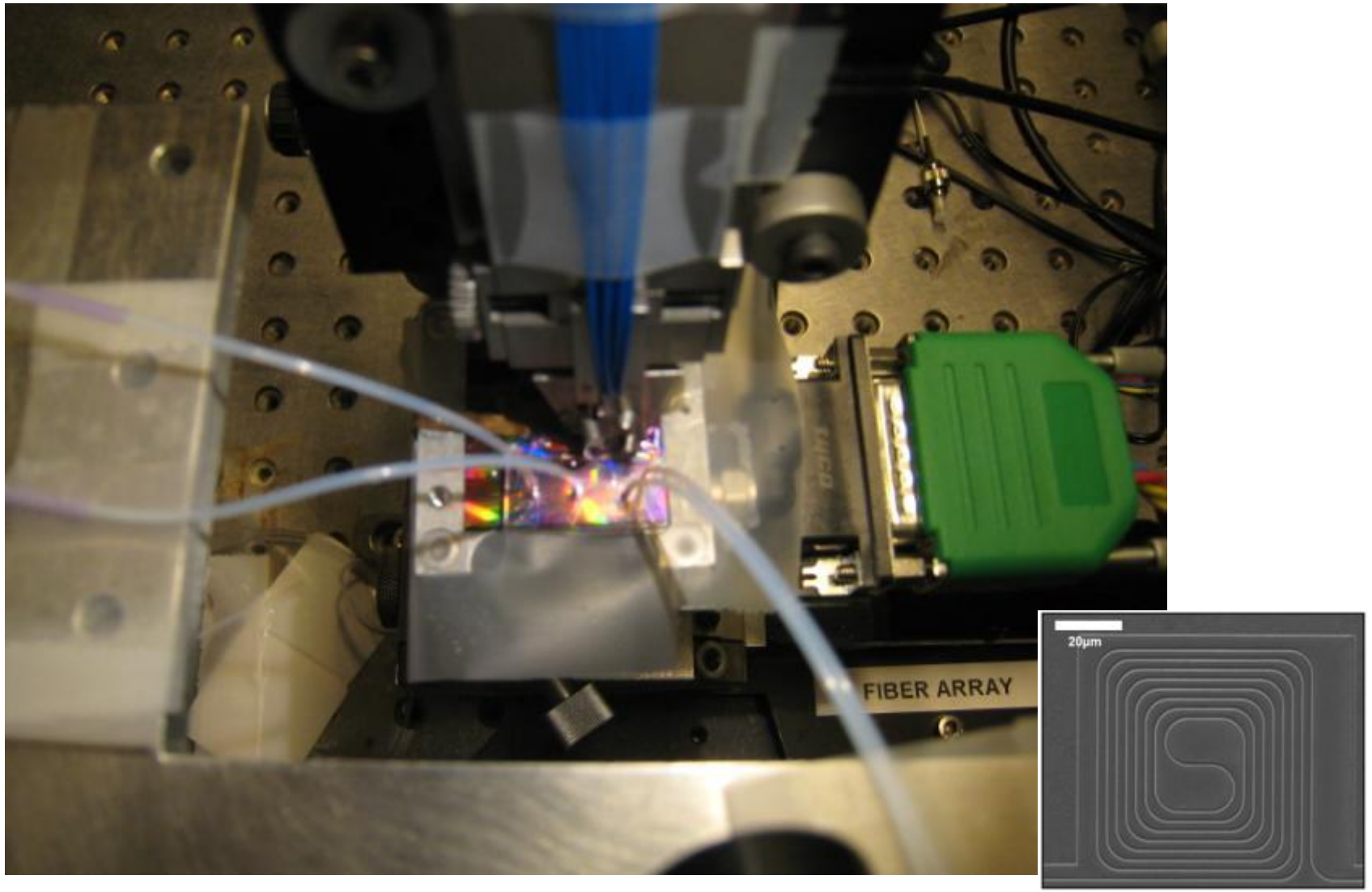
SPECTROSCOPY-ON-A-CHIP: WHAT



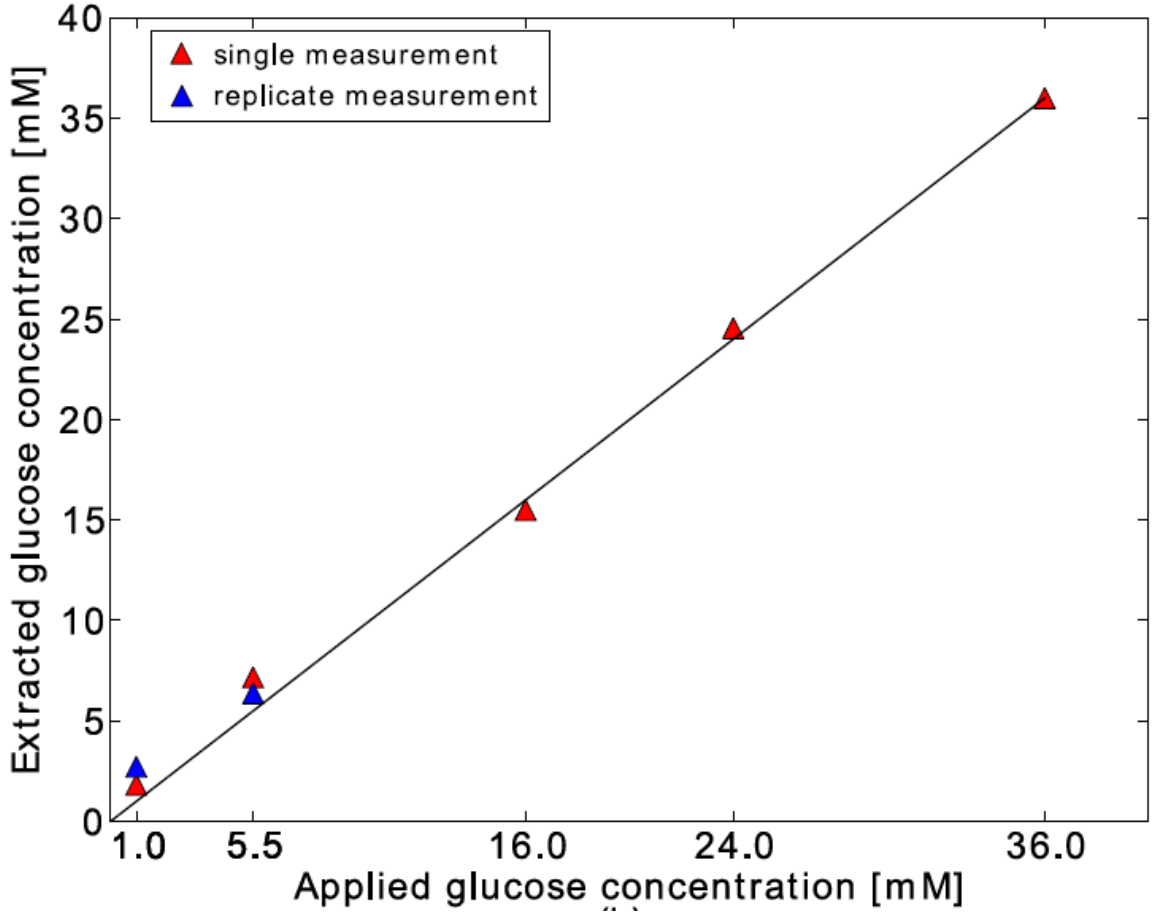
PROOF-OF-CONCEPT DEMO OF GLUCOSE SENSING IN THE LAB



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

GLUCOSE ABSORPTION SPECTROSCOPY: PROOF-OF-CONCEPT

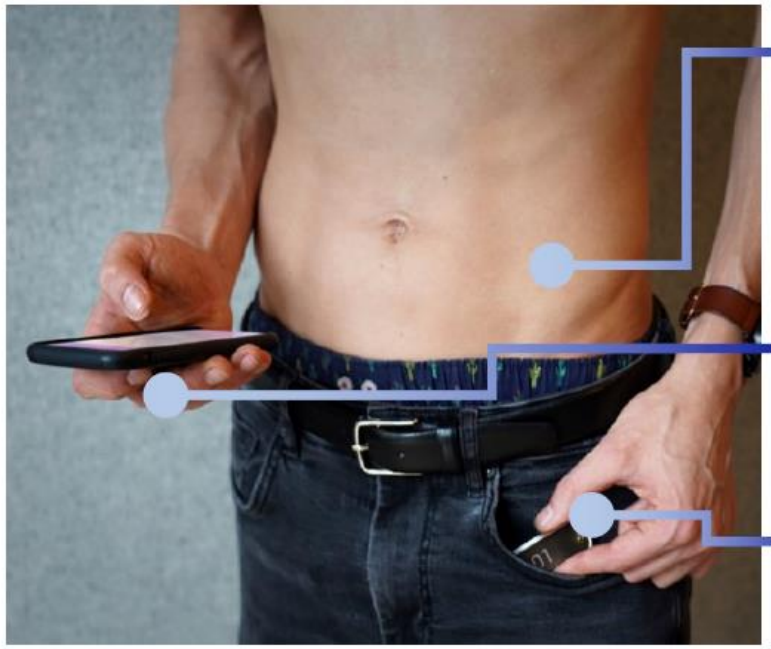
Use measured spectrum of 36 mM solution as the basic vector



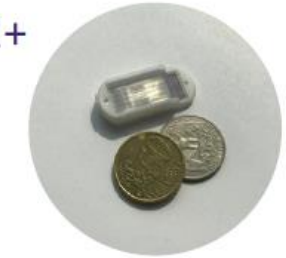
Demonstrated sensitivity of 1mM

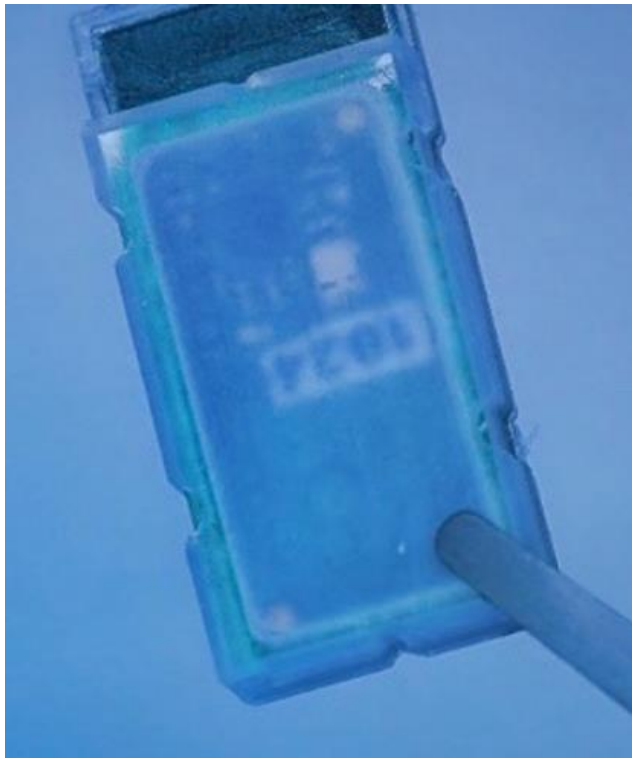
E. Ryckeboer et al, Biomedical Optics Express (2014)

Continuous Glucose Monitoring with Subcutaneous Implant

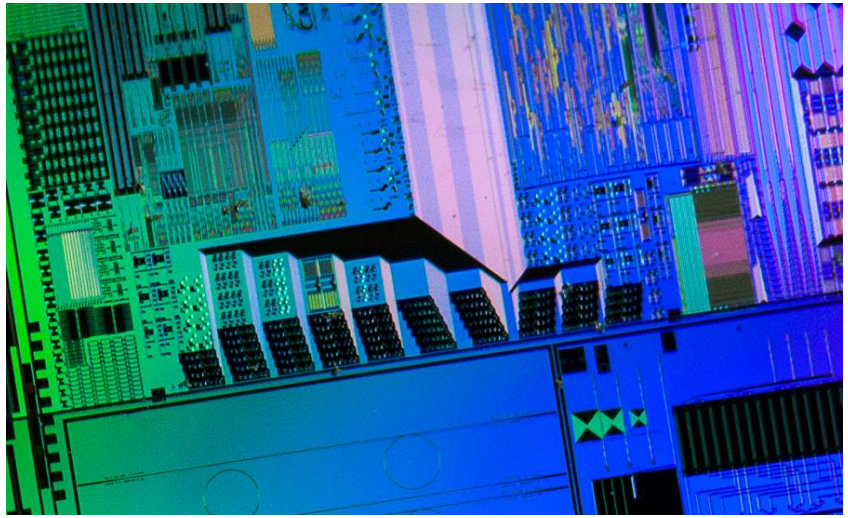


- Invisible, coin-sized 2+ years implant (rechargeable)
- Mobile app/cloud/connection to 3rd party iCGM devices
- Waterproof Bluetooth display unit





Implant

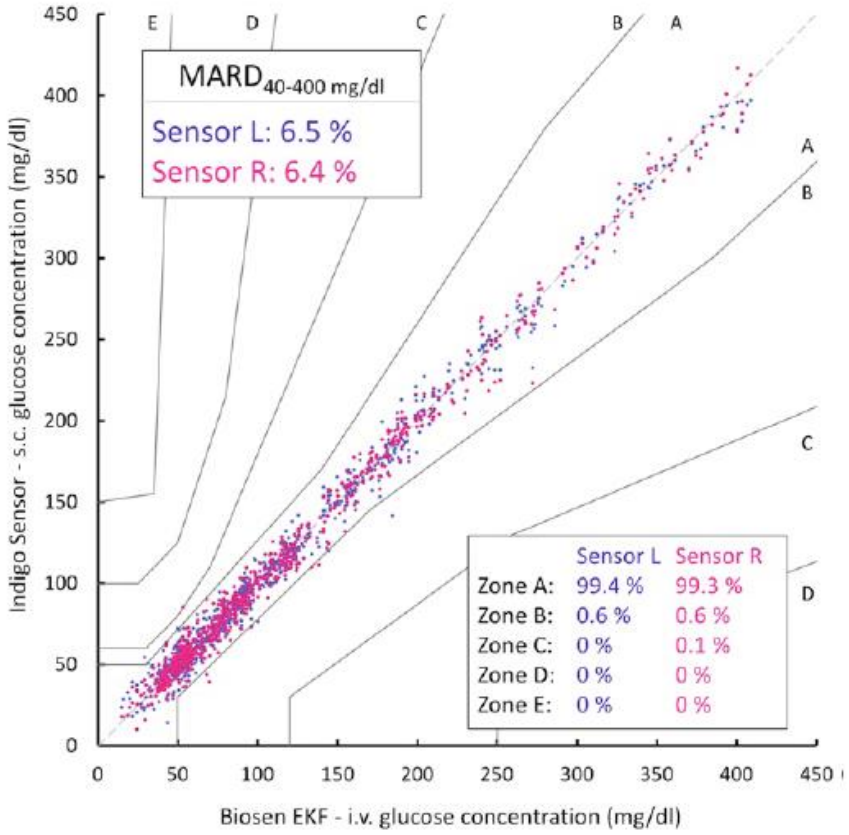


Microspectrometer chip

https://indigomed.com/

indigo

Continuous Glucose Monitoring with Subcutaneous Implant



Results on pig model (D. Stocker, EASD 2020)

- Proof-of-concept demonstration of glucose, lactate and ketone monitoring in pig model
- Future: human clinical trial

https://indigomed.com/

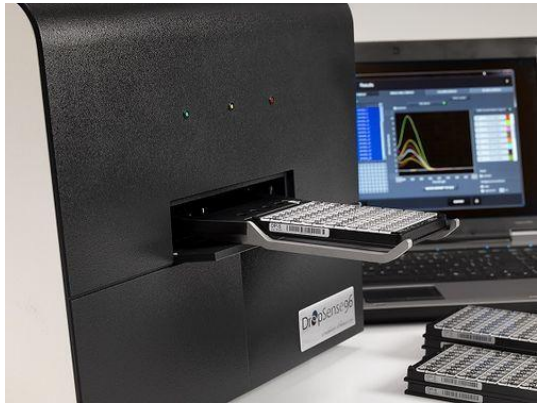
indigo

Three Application Cases

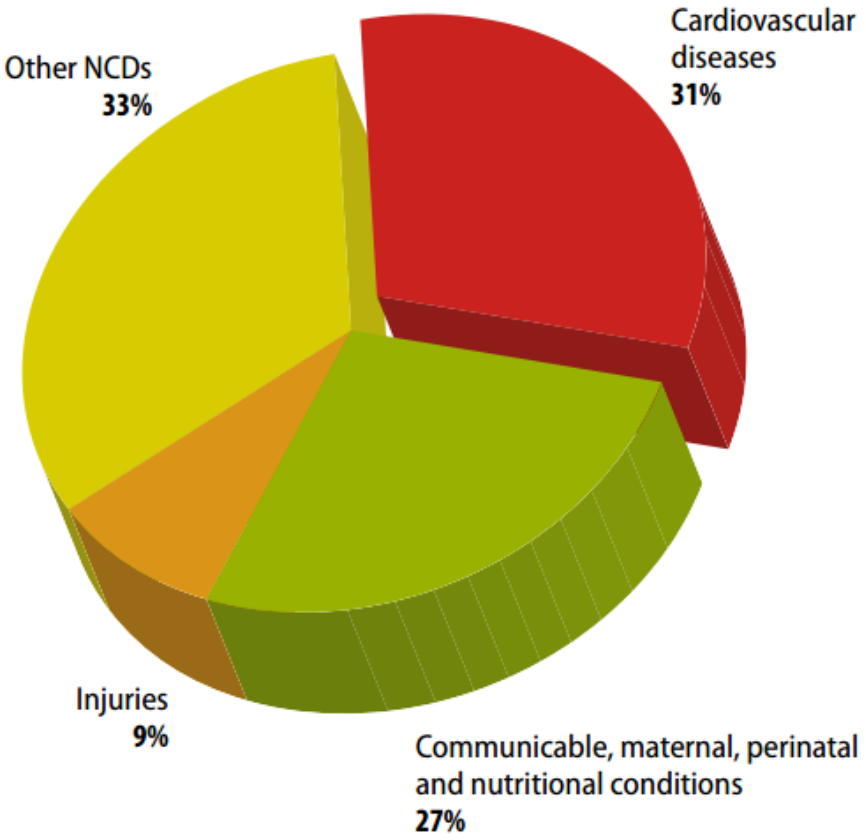
Continuous glucose monitoring

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

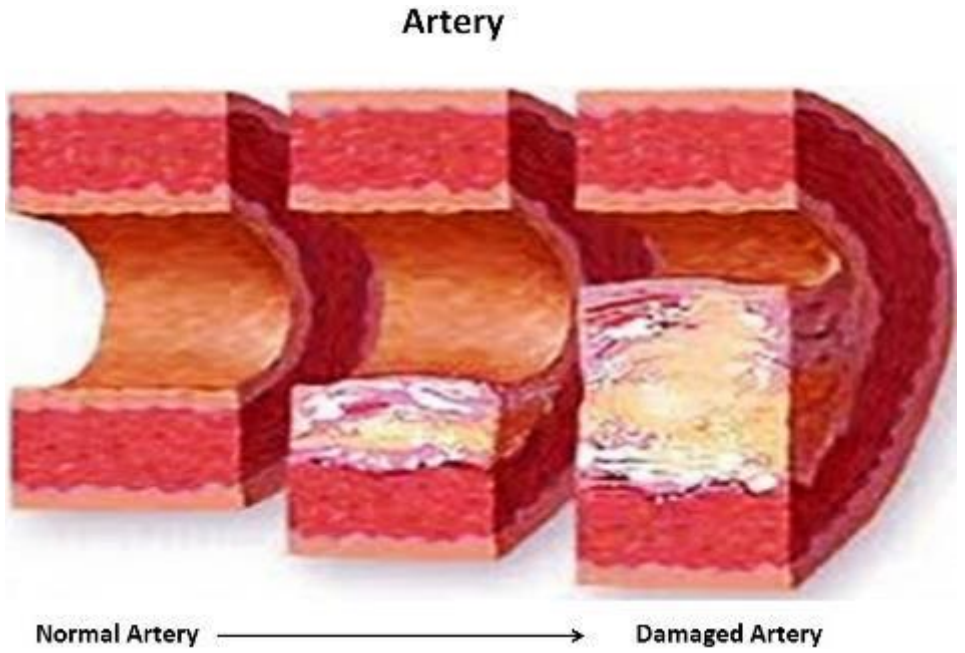
Atherosclerosis: deposition of plaque on the inner arterial walls (which can lead to stiffening)

Stenosis: abnormal narrowing in a blood vessel

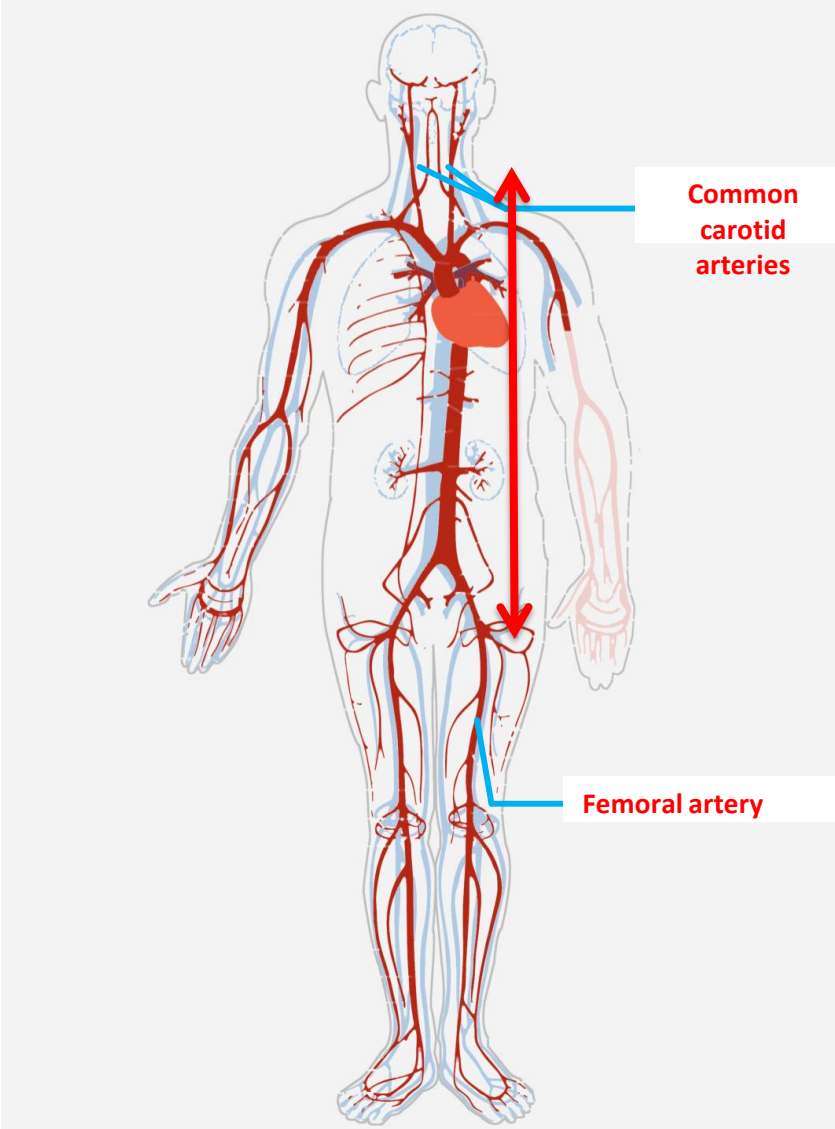
Heart Dyssynchrony: left and right part of the heart are not triggered synchronously

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

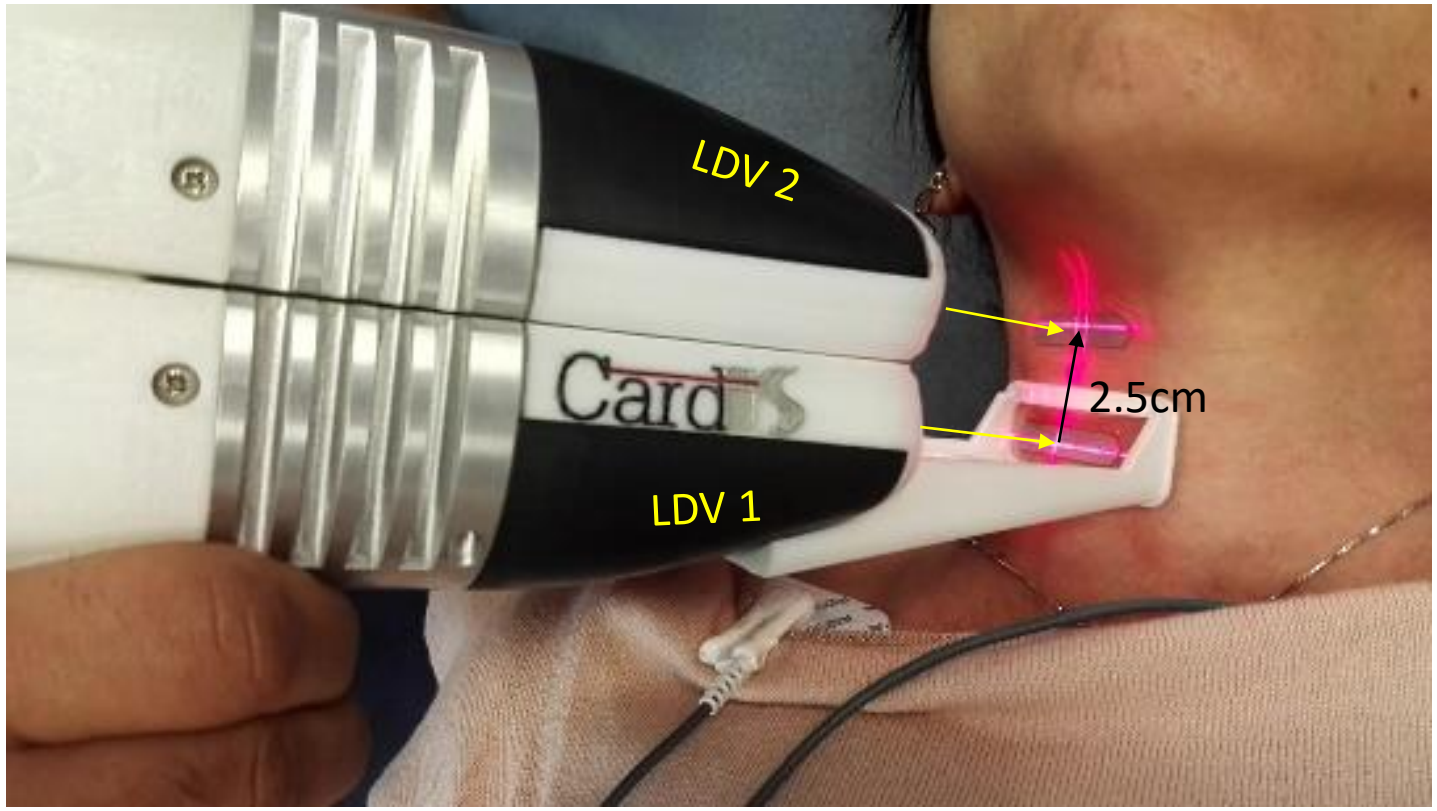


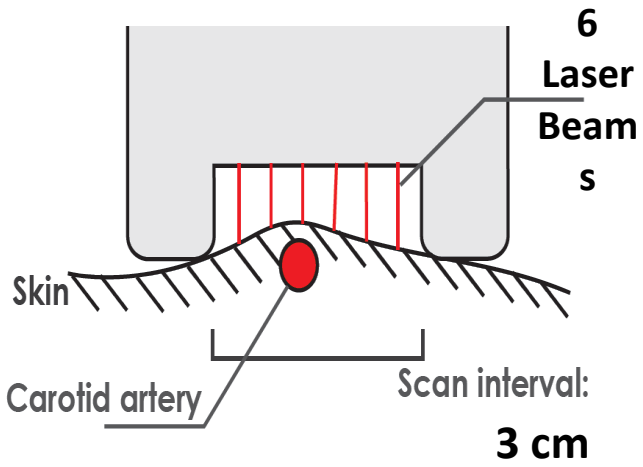
Pulse Wave Velocity: speed by which the pressure wave caused by a heart beat travels in the arteries

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

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

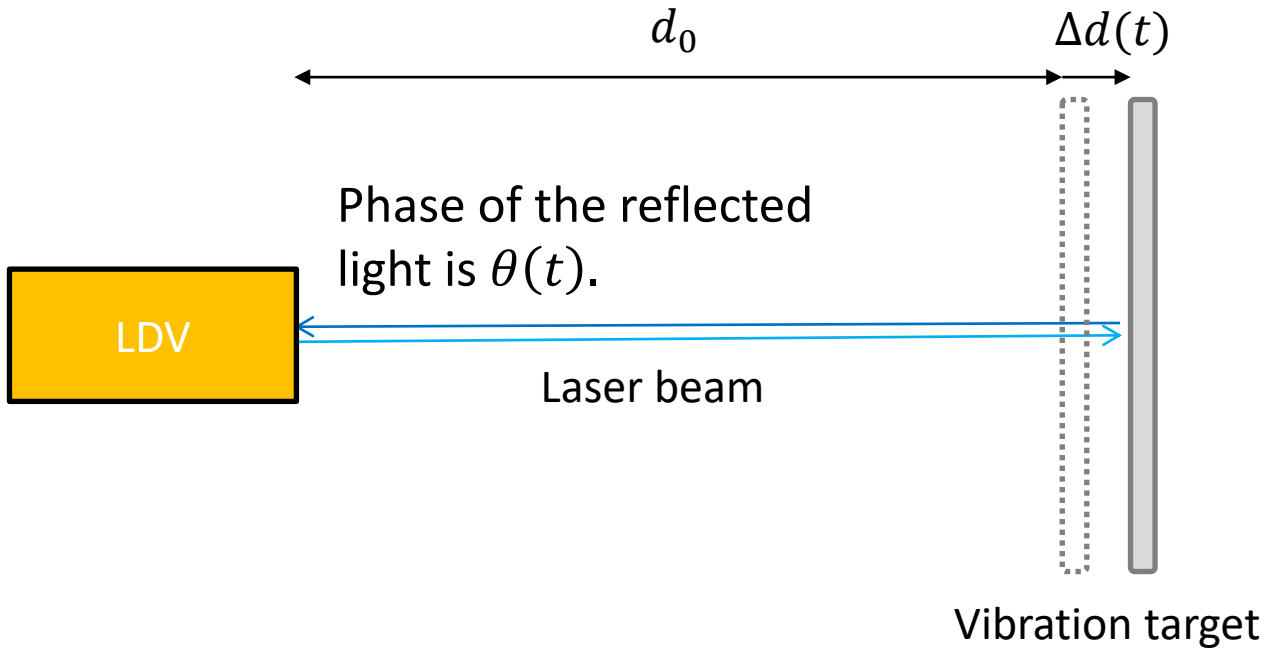
Approach: Measure local common-carotid PWV





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

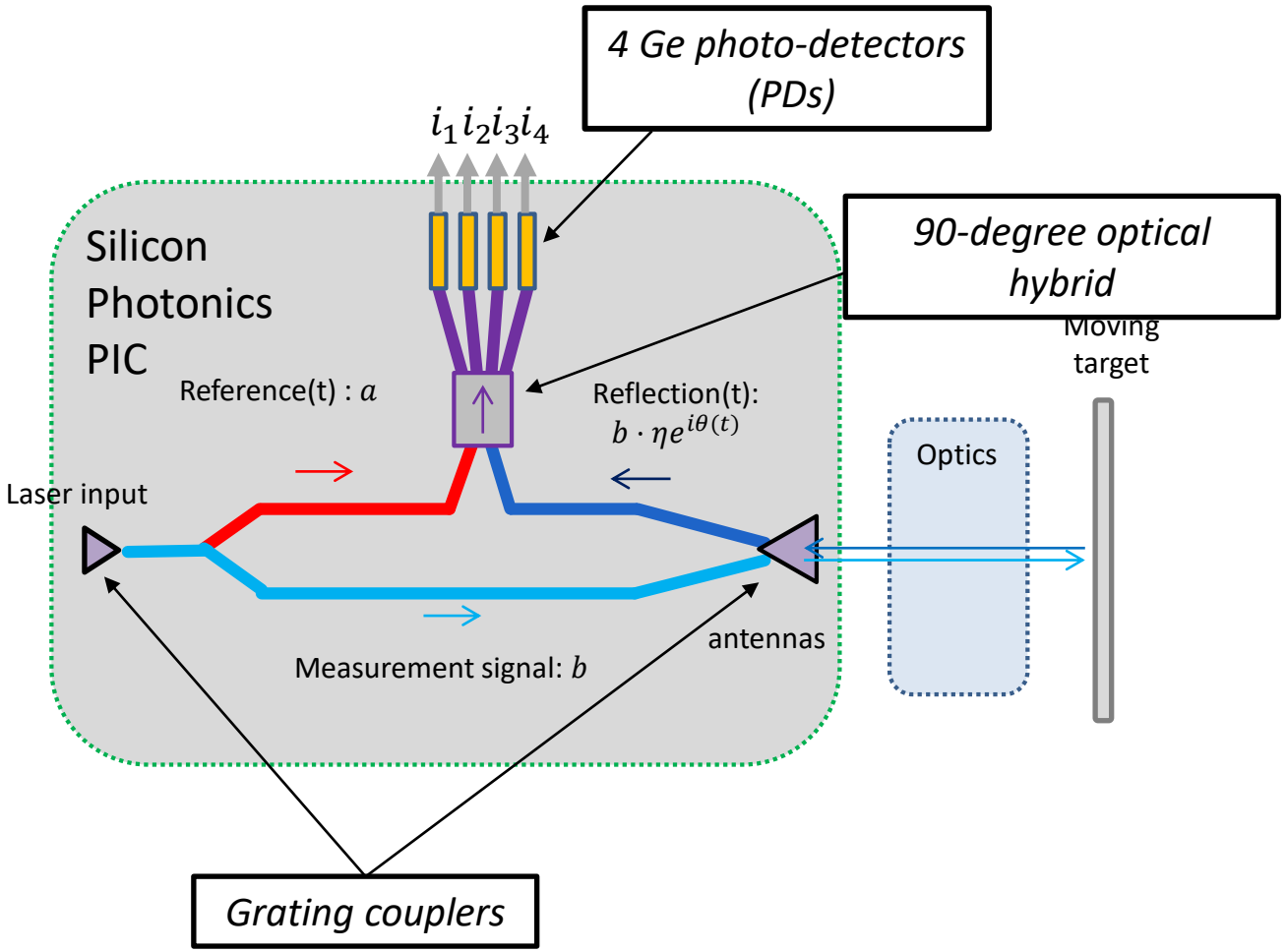
WORKING PRINCIPLE OF LDV

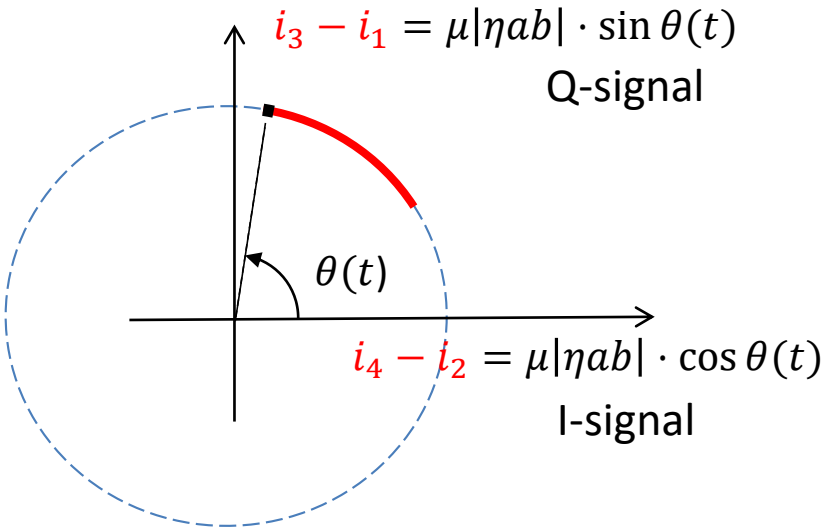


The displacement $\Delta d(t)$ can be retrieved by measuring $\theta(t)$, based on the relation

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

WORKING PRINCIPLE OF LDV: HOMODYNE DETECTION

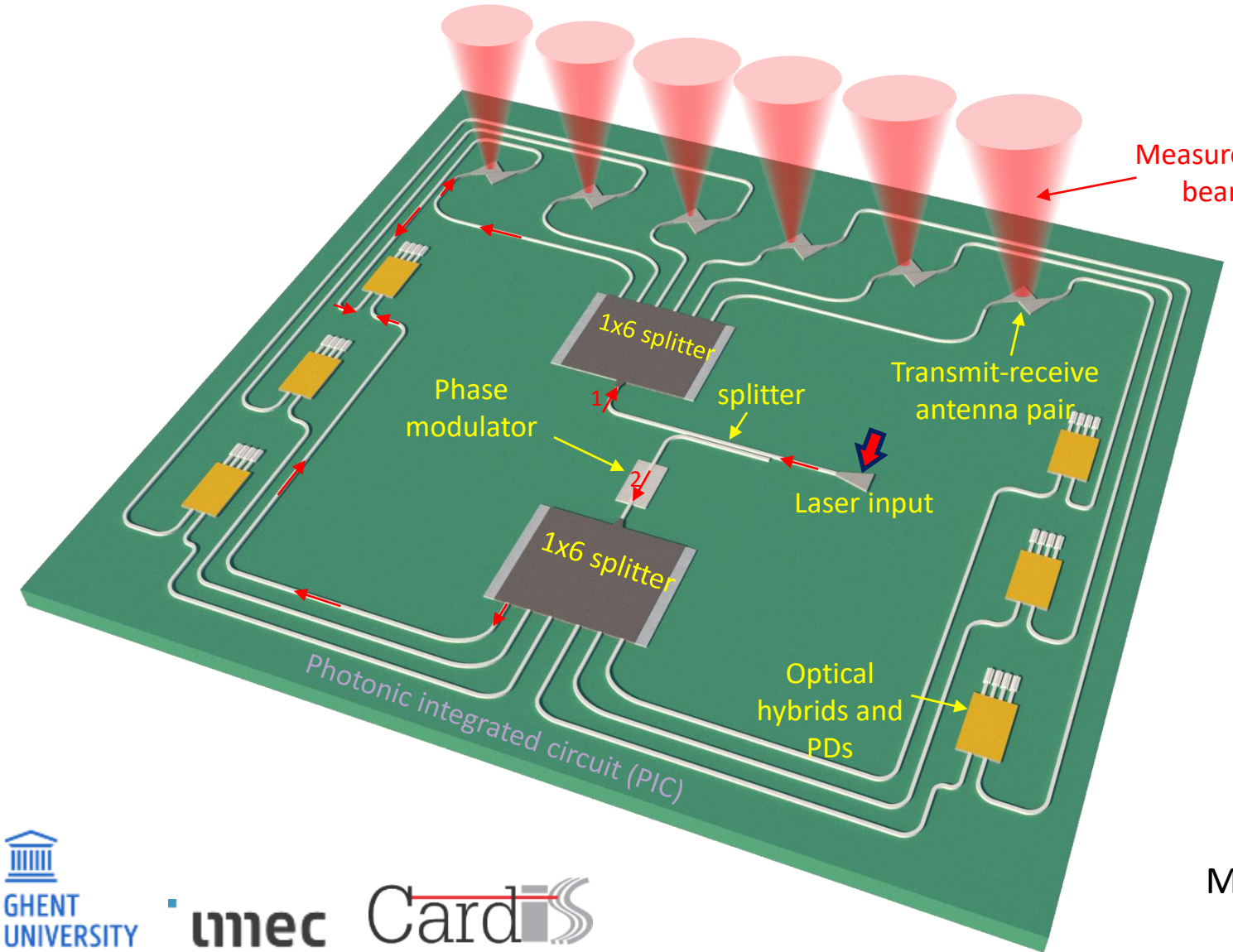


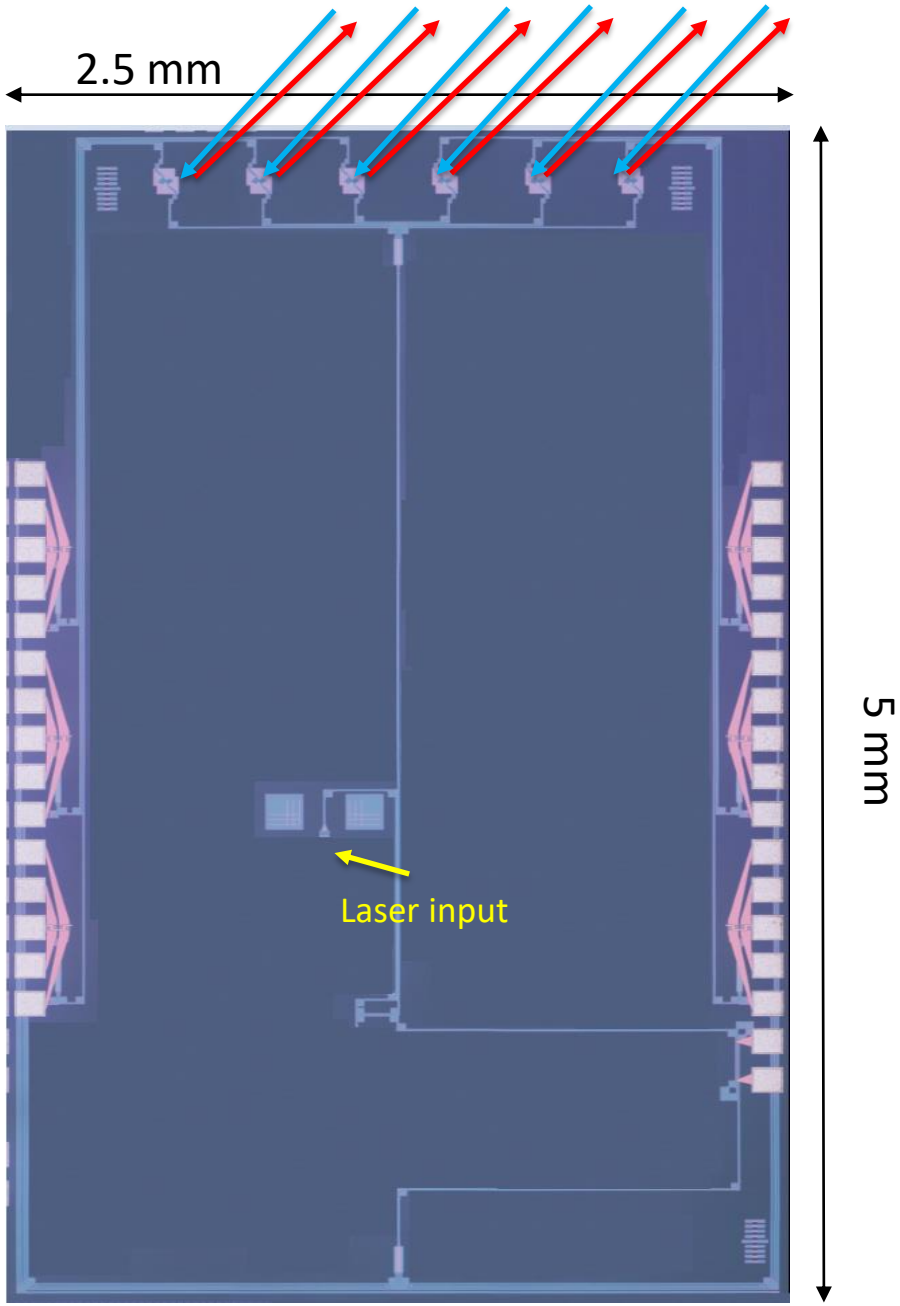


Demodulation method:

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

REALIZATION OF A SIX-BEAM LDV ON SILICON CHIP

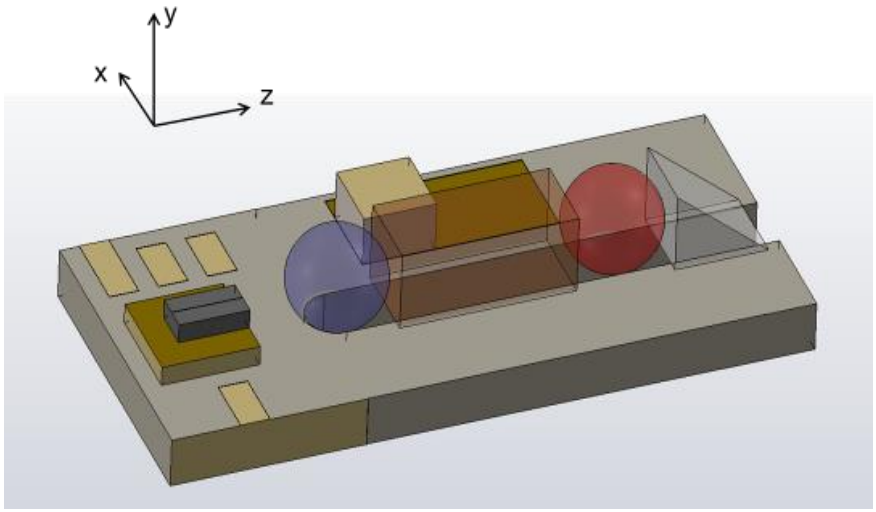




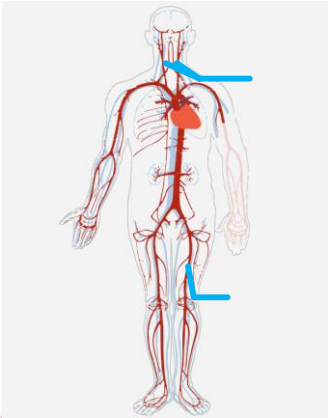
Microscope image of the photonic integrated circuit (PIC) in a silicon-on-insulator platform

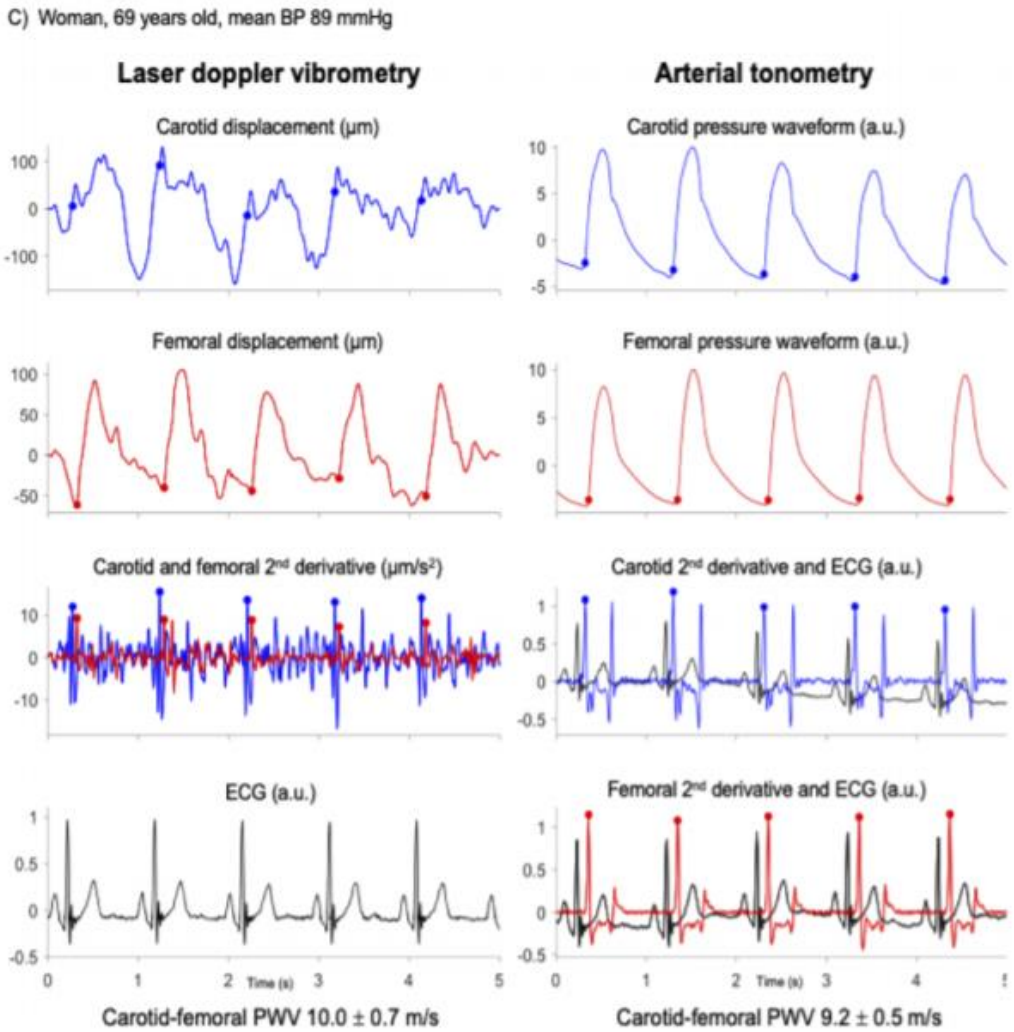
PHOTONIC INTEGRATED CIRCUITS (PICS)

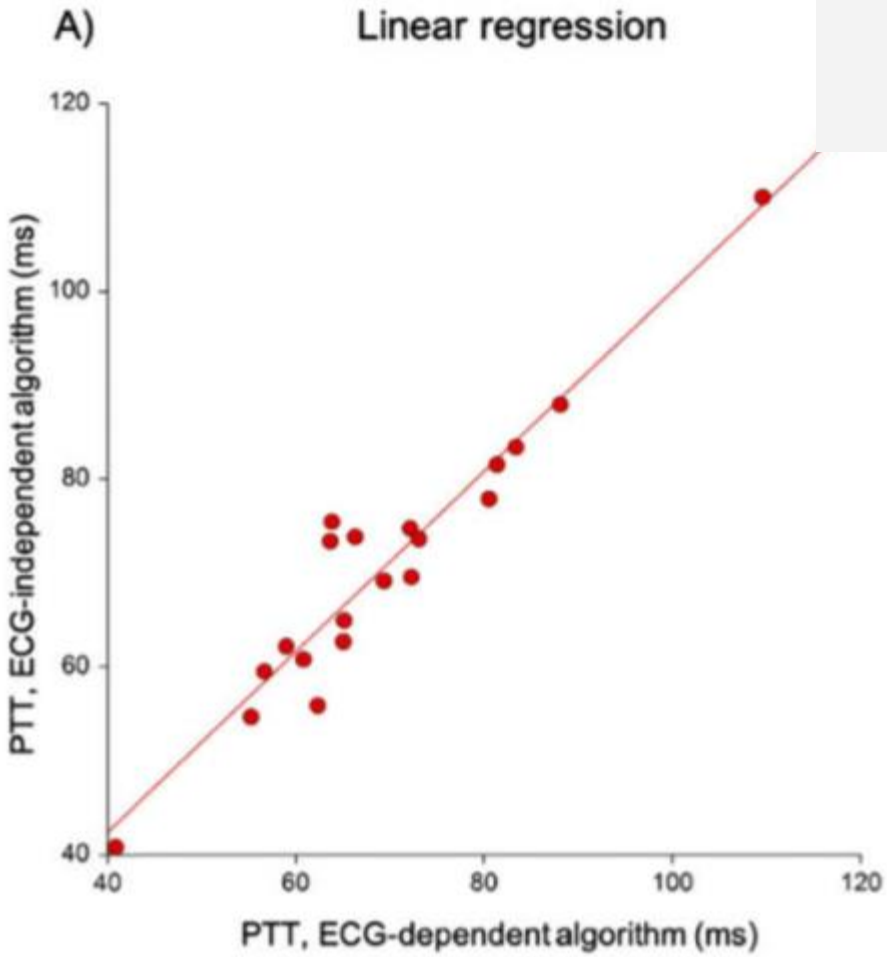
- PICs fabricated through Europractice MPW-service
- iSiPP50G SOI process at imec
- Laser diode is mounted on a Micro-Optic Bench (MOB) which is attached to the PIC



Carotid-femoral Pulse Wave Velocity Measurement







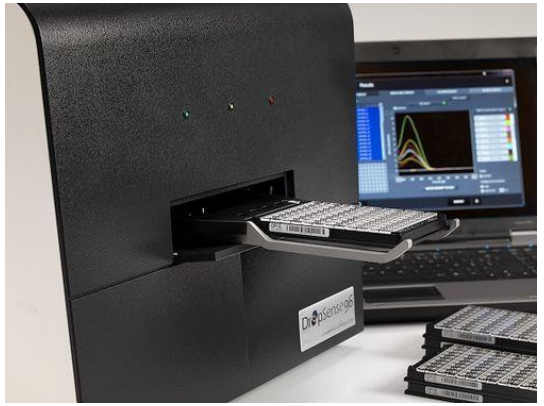
Y. Li et al, Biomedical Optics Express 2020

Three Application Cases

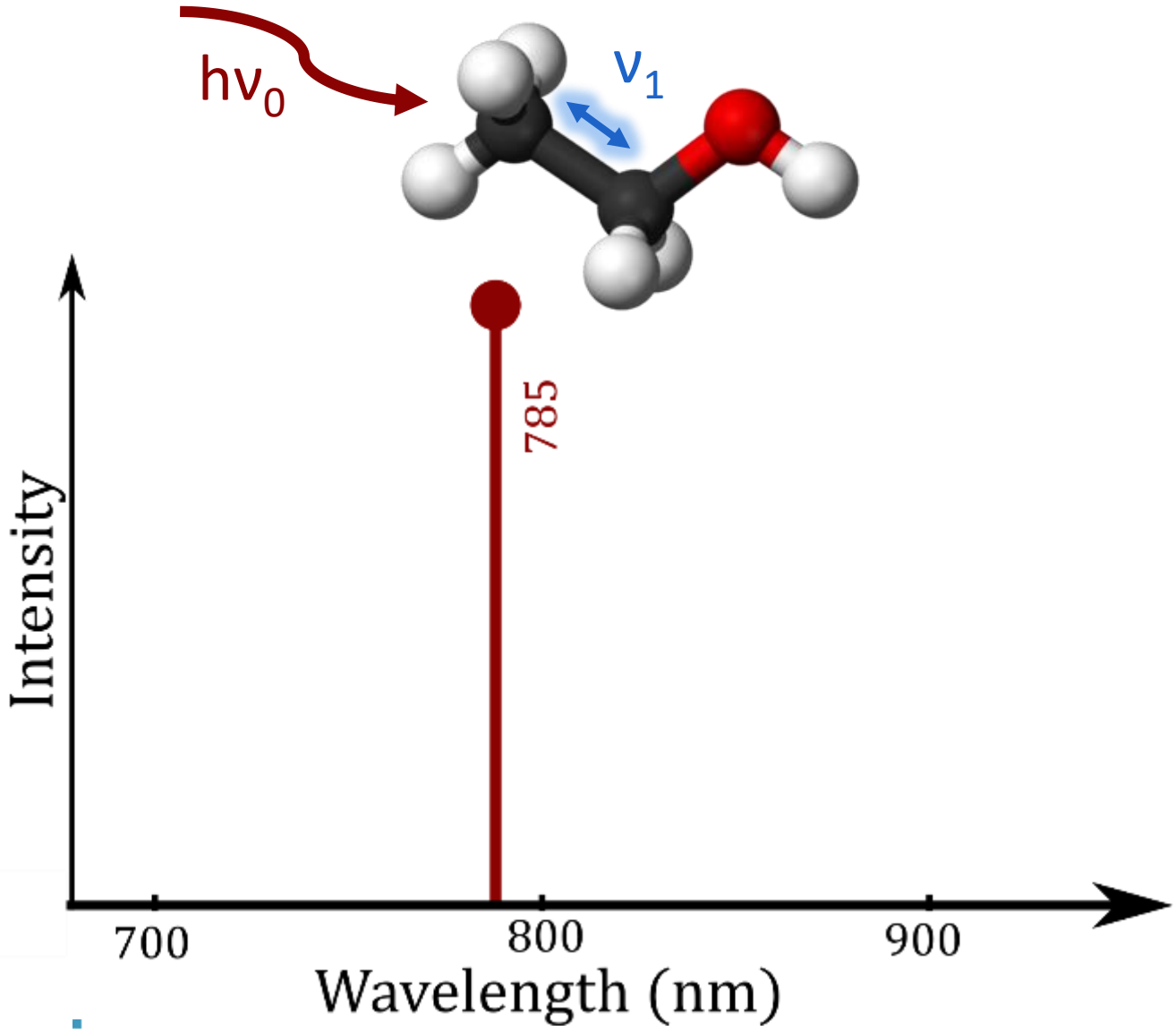
Continuous glucose monitoring

Cardiovascular monitoring

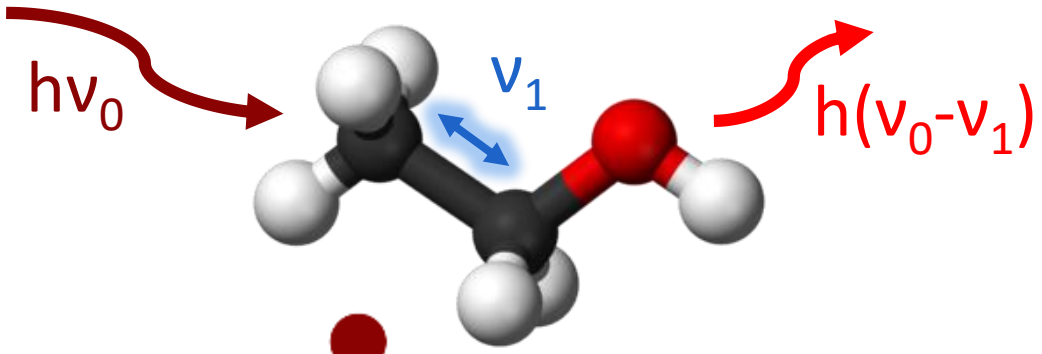
In-vitro diagnostics by on-chip Raman

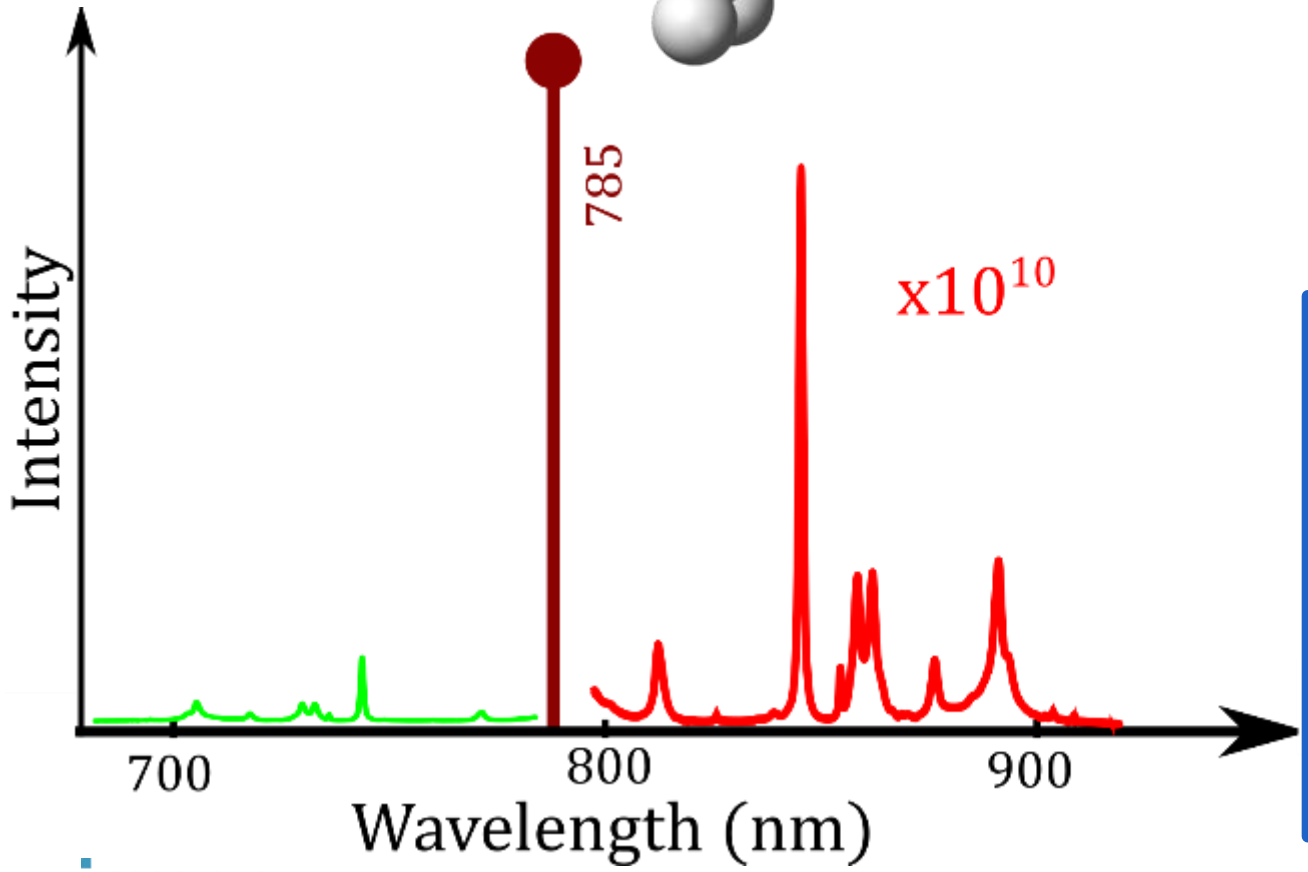


THE RAMAN SPECTRUM IS A FINGERPRINT OF A MOLECULE'S VIBRATION



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



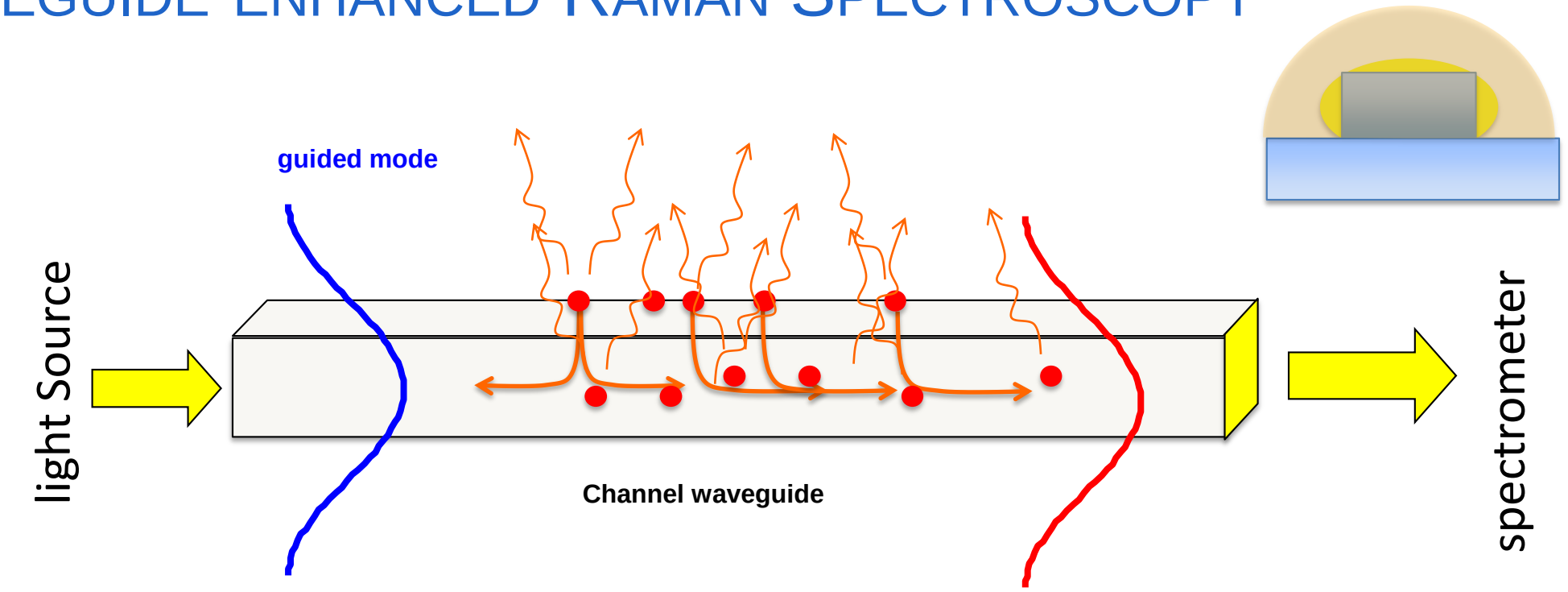


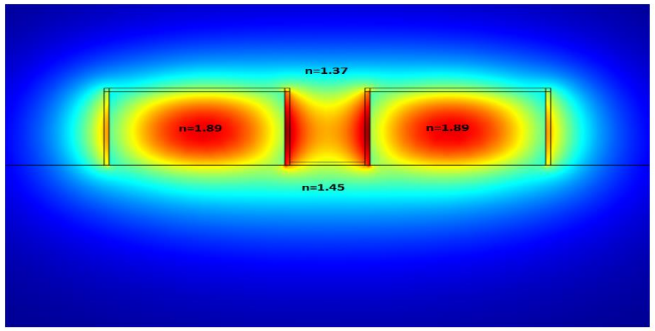
+ Specific chemical information without any labeling or contact

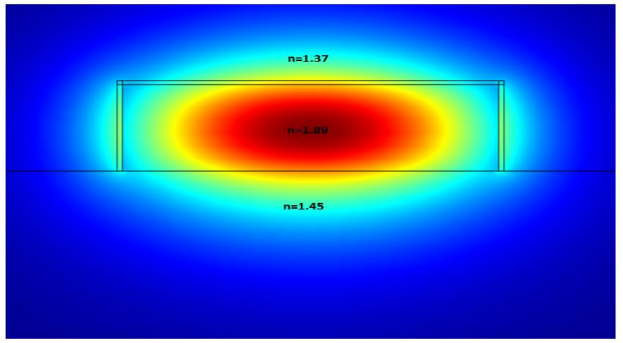
- Weak signals

GHENT UNIVERSITY imec

WAVEGUIDE-ENHANCED RAMAN SPECTROSCOPY

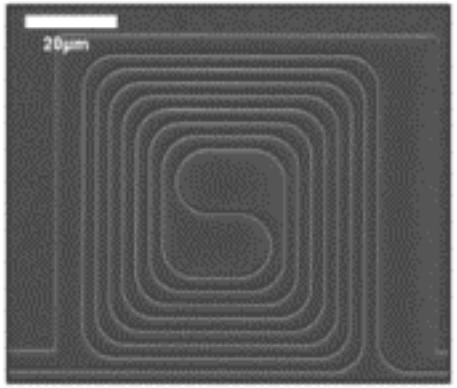


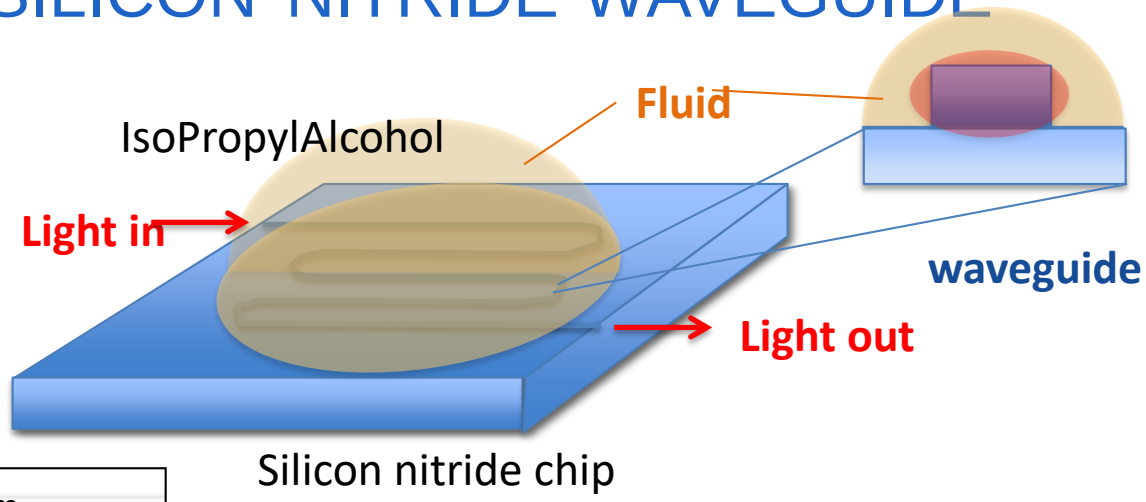


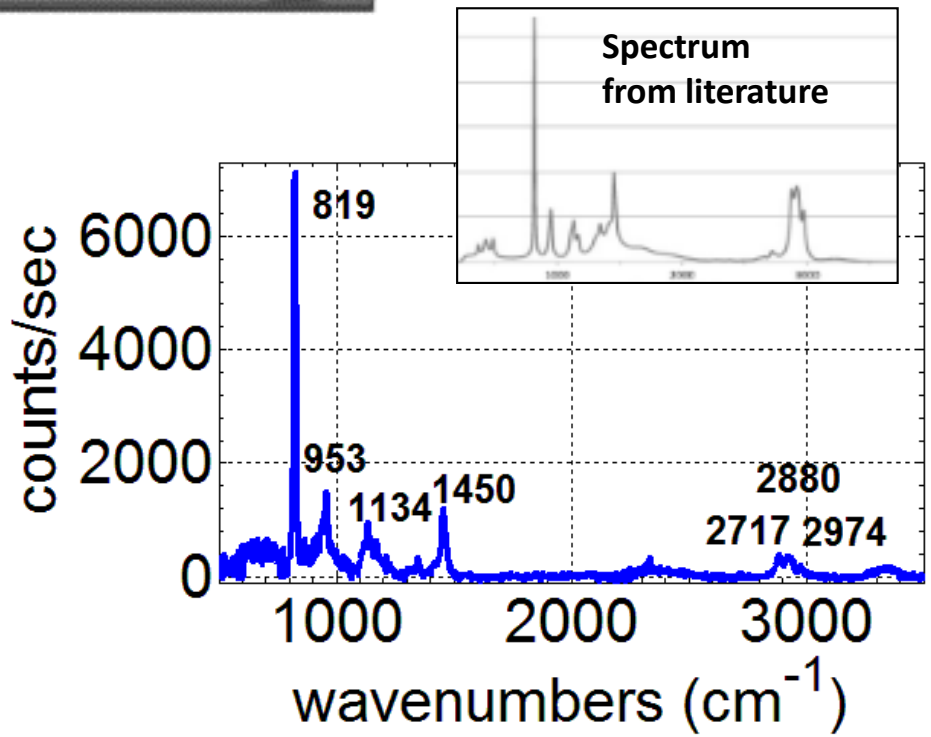


A. Dhakal *et al.*, ACS. Photonics. **3**, 2141-2149 (2016)
Z. Wang *et al.*, Opt. Letters. **41**, 4146-4149 (2016)
C. Evans et al., ACS Photonics 3, 1662-1669 (2016)

RAMAN SPECTRUM OF IPA ON SILICON-NITRIDE WAVEGUIDE



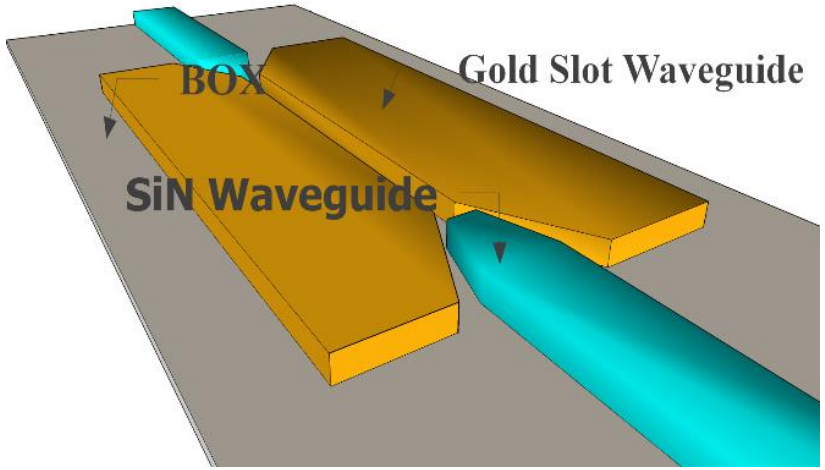


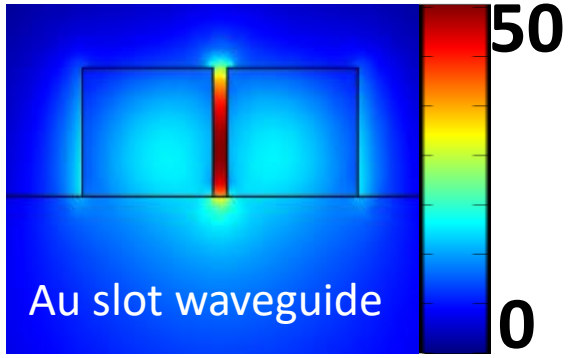


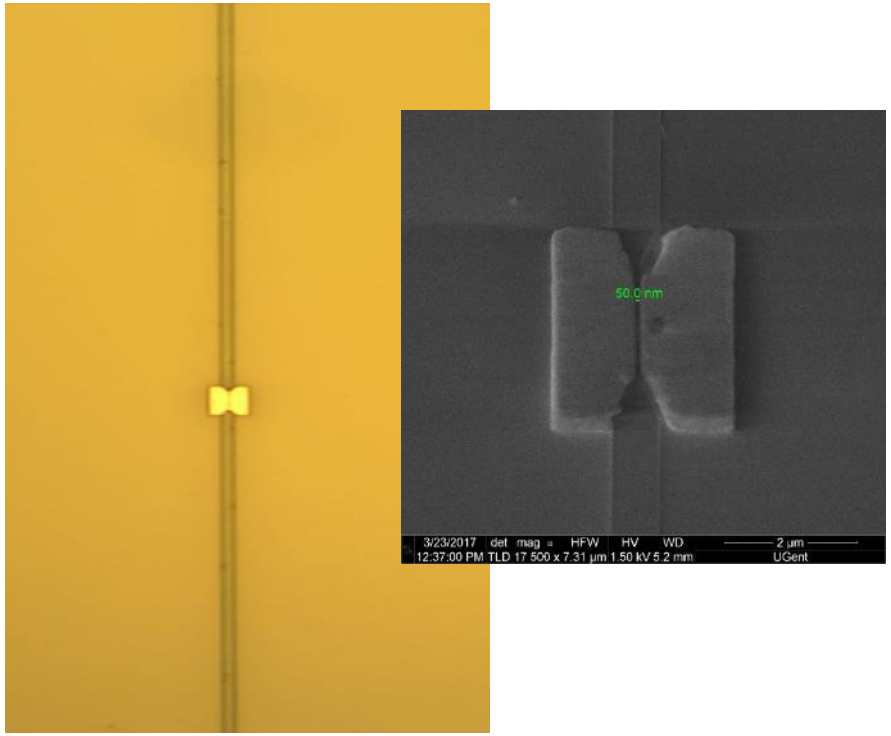
Efficiency of collection 10-100x better than in Raman microscope

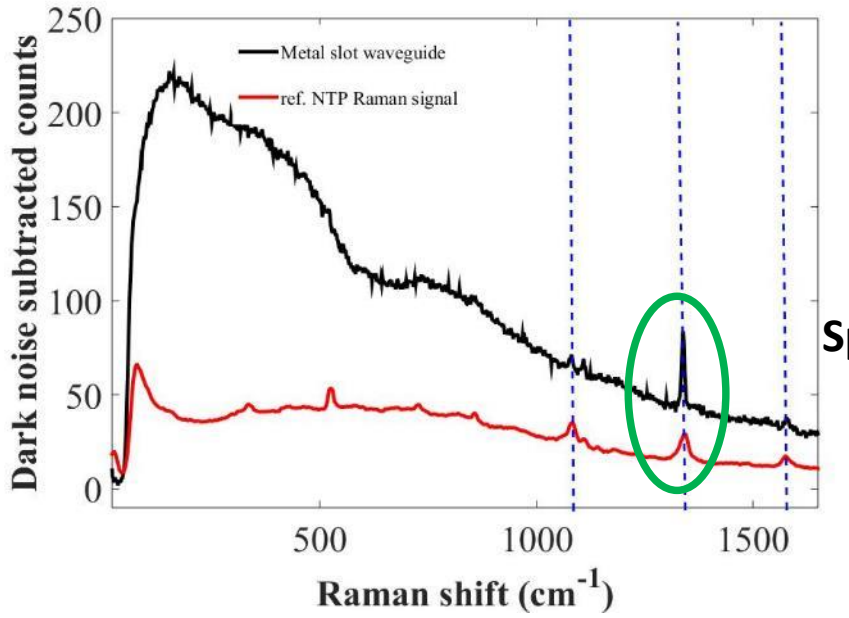
A. Dhakal et al, Opt. Lett. (2014)
A. Dhakal et al, Optics Express (2015)

USING METAL SLOT WAVEGUIDES TO ENHANCE THE RAMAN SCATTERING





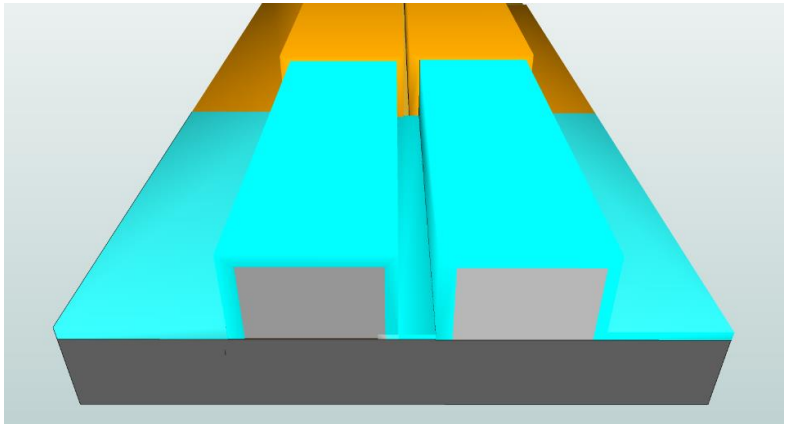


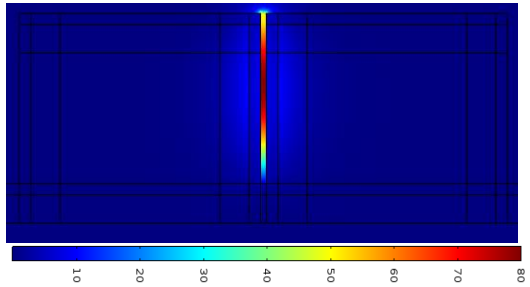


Spectrum of NTP (4-NitroThioPhenol) bound to gold

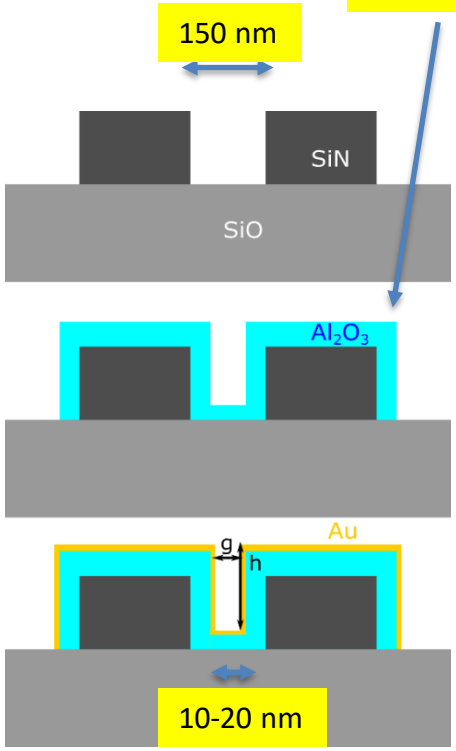
A. Raza et al, ECIO 2017

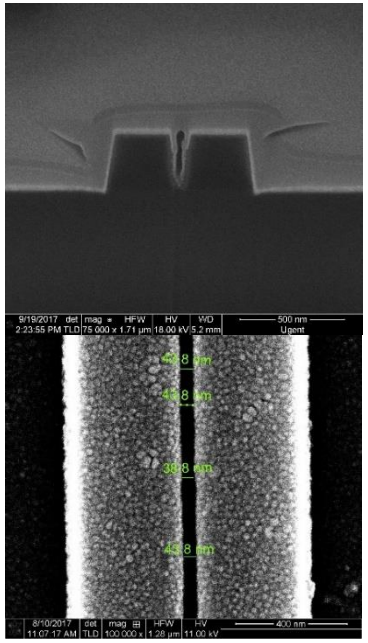
All Deep-UV fabricated Hybrid Photonics Plasmonics waveguide





Conformal ALD coating of Al_2O_3





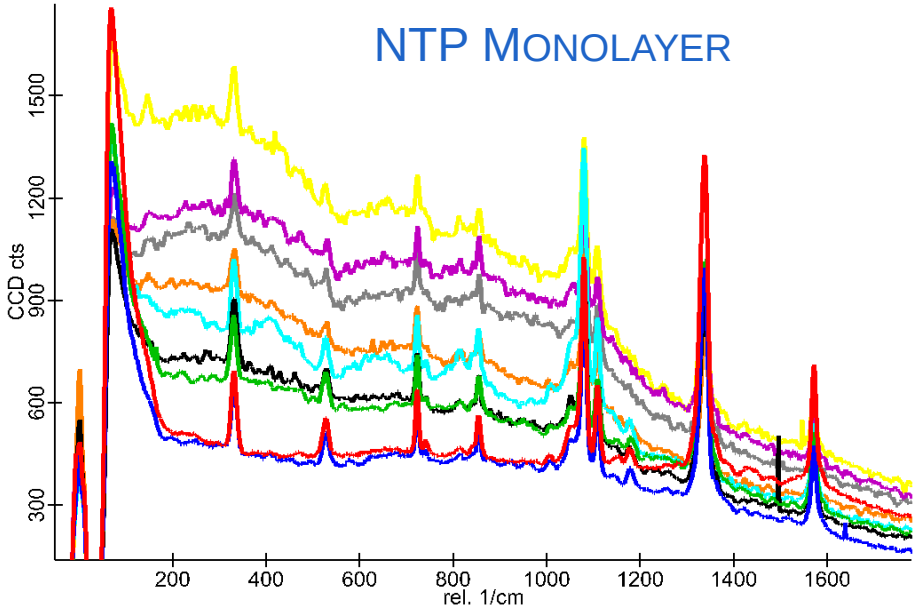
A. Raza et al, CLEO 2018

A. Raza et al, APL Photonics 2018

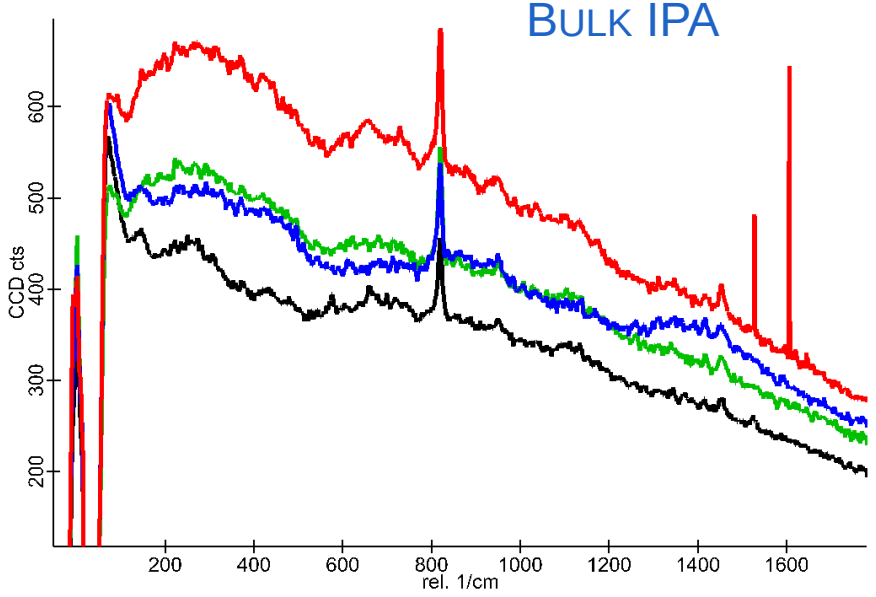
All Deep-UV fabricated Hybrid Photonics Plasmonics waveguide

Strong enhancement:

NTP Monolayer



Bulk IPA



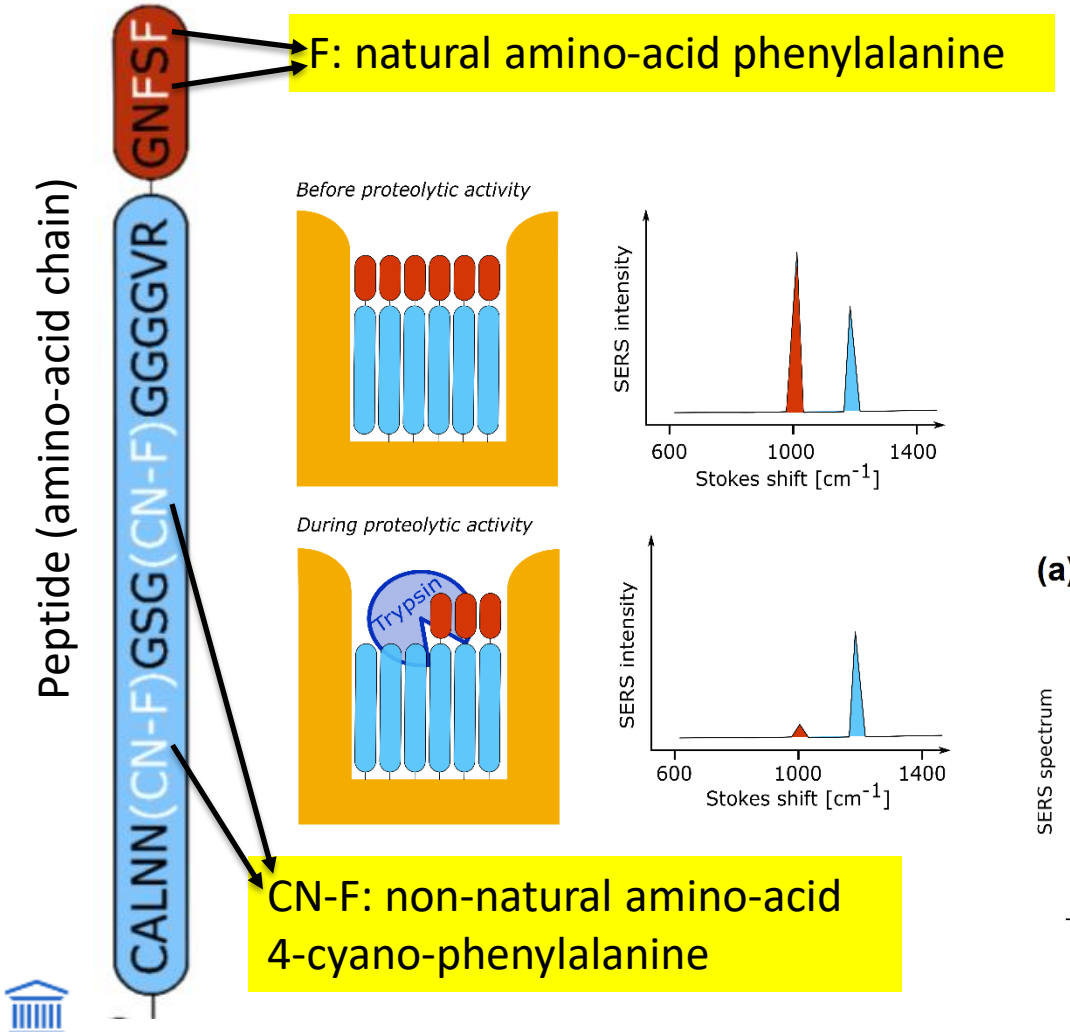
Variability of enhancement: 5%

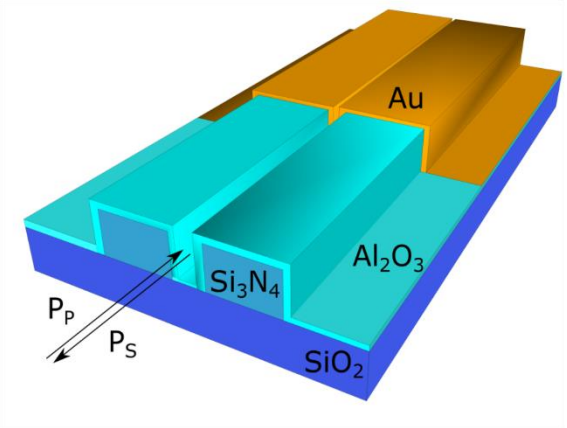
A. Raza et al, CLEO2018

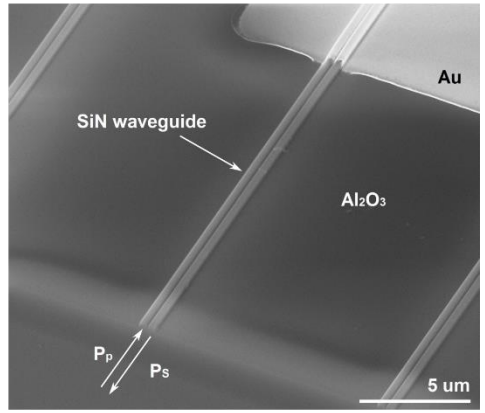
A. Raza et al, APL Photonics 2018

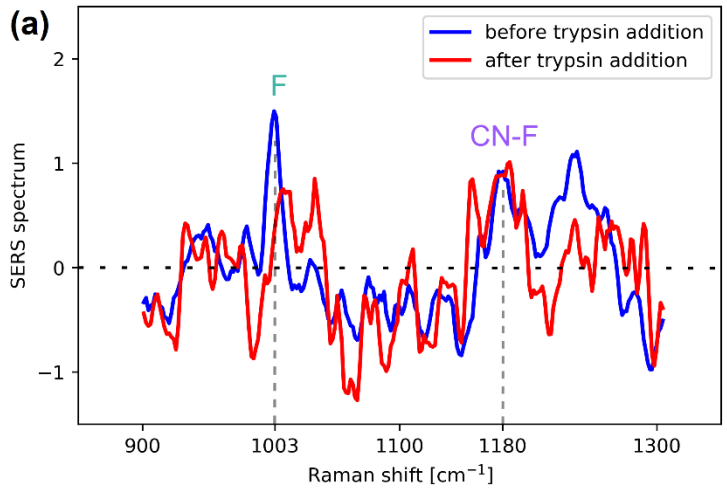
APPLICATION: MONITORING OF ENZYMATIC ACTIVITY BY PROTEASES

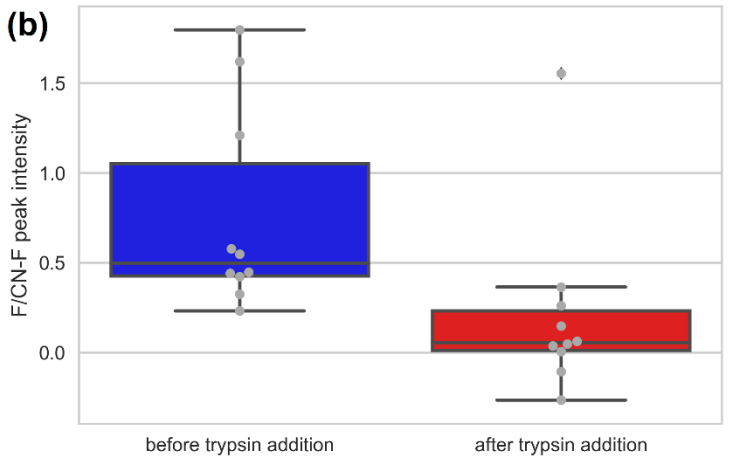
Proteases play an important role in signaling pathways in relation to various diseases











N. Turk et al, Biomedical Optics Express 2020

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

In the market:

- Biosensors for immuno-assays

  refractive index sensing

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

AGENTSCHAP INNOVEREN & ONDERNEMEN

erc

THE FRAMEWORK PROGRAMME FOR RESEARCH AND INNOVATION
HORIZON 2020

CardioS

InSiDe

Photonics Research Group of Ghent University – imec

imec Silicon Photonics platforms (SOI and SiN)

GHENT UNIVERSITY imec