PHOTONICS RESEARCH GROUP

SILICON PHOTONICS AS AN ENABLER FOR HEALTH CARE APPLICATIONS

Roel Baets

Photonics Ireland June 2021

GHENT UNIVERSITY

imec embracing a better life

ePIXfab European Silicon Photonics Alliance

HEALTH CARE

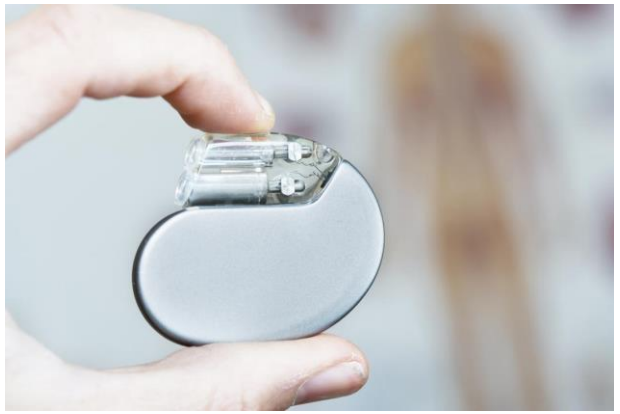
Enormous challenges:

- 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

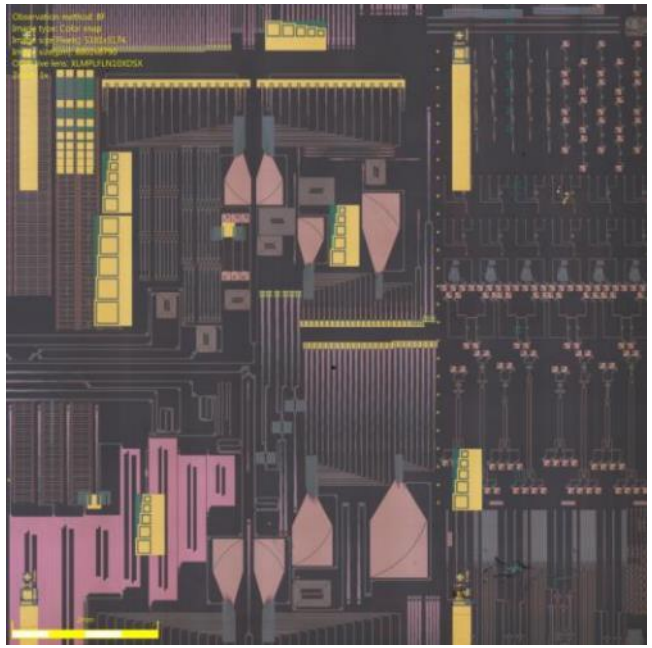
Mid-IR detector chip

Pulse Oximeter

Near IR LED and detector chips

WHAT IS SILICON PHOTONICS?

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



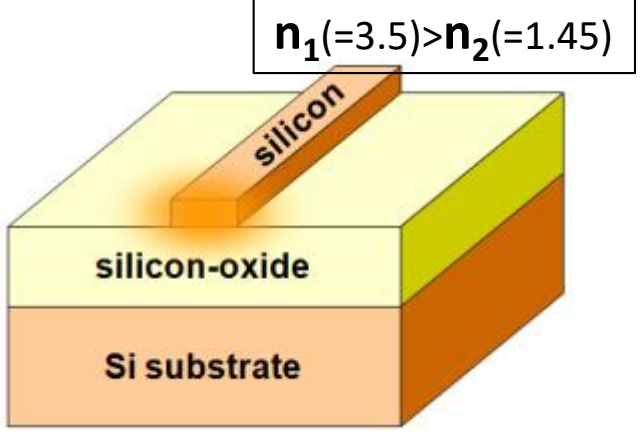
Pictures, courtesy of imec

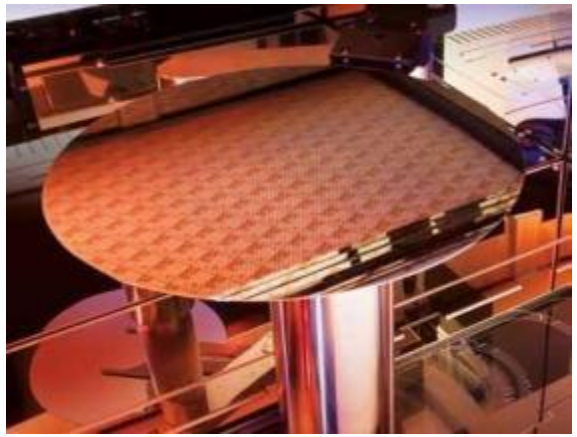
Enabling complex optical functionality on a compact chip at low cost

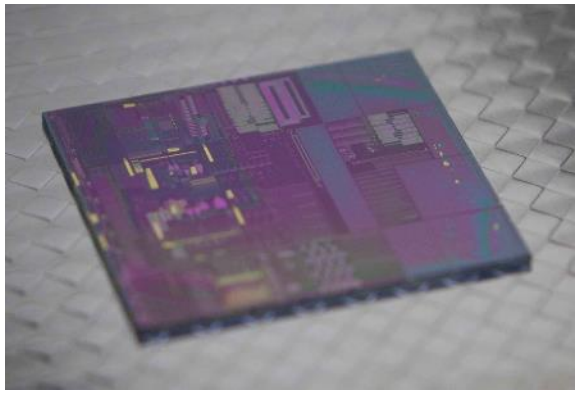
GHENT UNIVERSITY imec

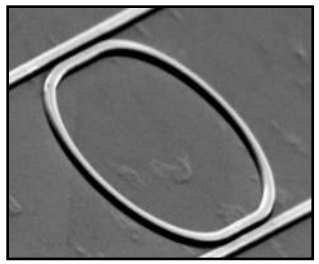
WHY SILICON PHOTONICS

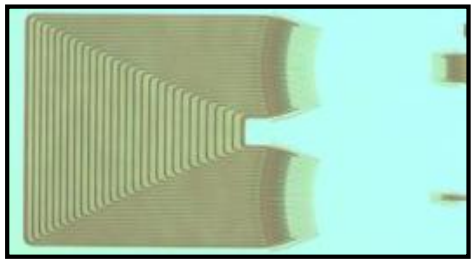
- High index contrast ⇒ **very compact PICs**
- CMOS technology ⇒ **nm-precision, high yield, existing fabs, low cost in volume**
- High performance passive devices
- High bitrate Ge photodetectors
- High bitrate modulators
- Wafer-level automated testing
- Hierarchical set of design tools
- Light source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

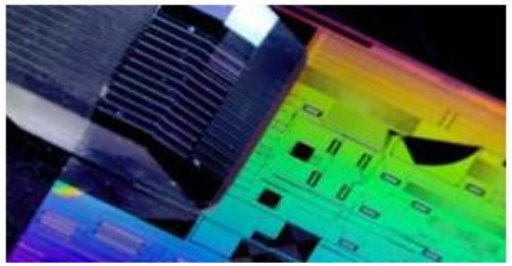












Transceivers for Data centers and for Telecom

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

KAIAM

ELENION TECHNOLOGIES

IBM

SKORPIOS TECHNOLOGIES

molex

GLOBAL FOUNDRIES

LUXTERA NANOPHOTONIC INTEGRATED CIRCUITS

cisco

Caliopa silicon photonics

HUAWEI

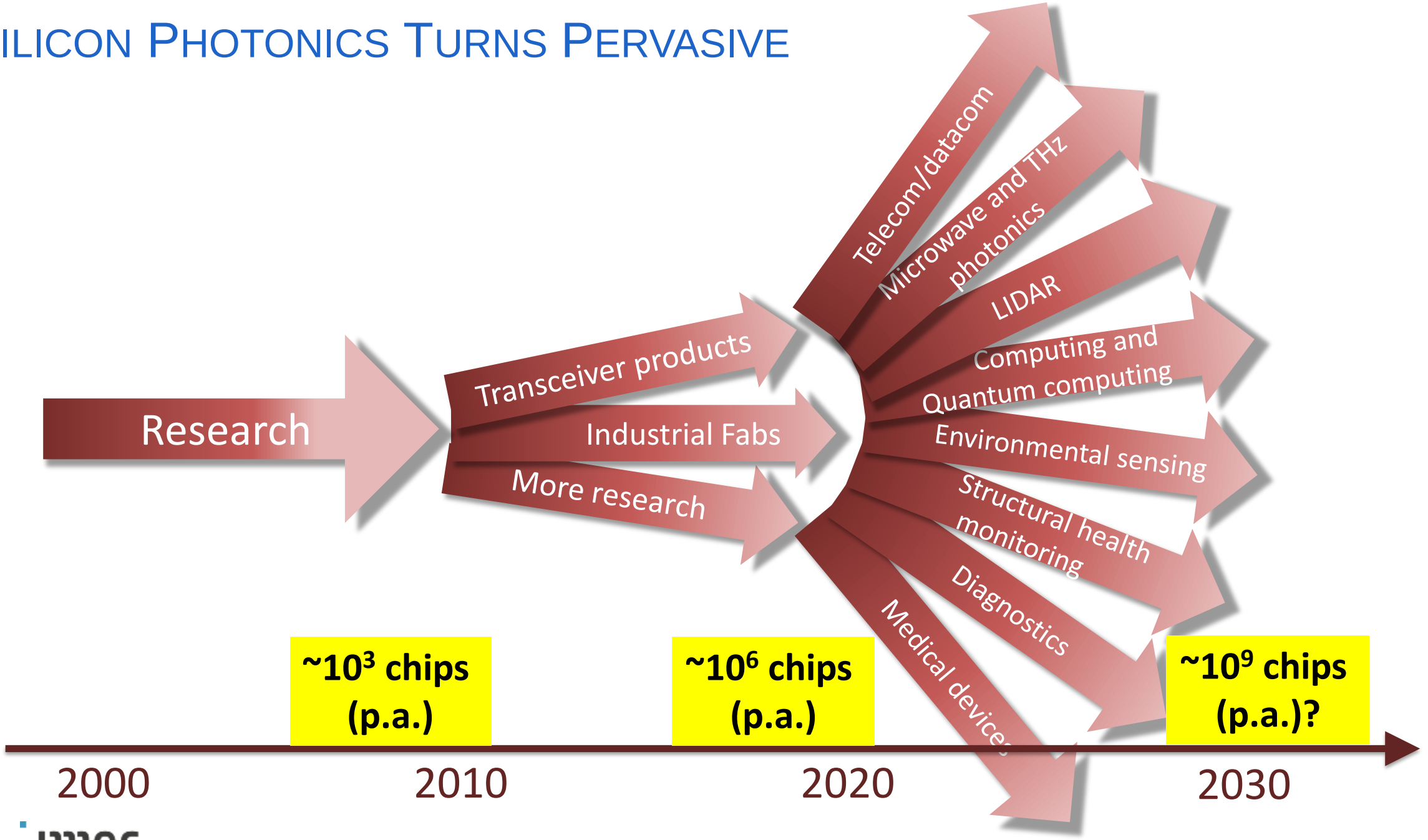
GHENT UNIVERSITY

imec

Mellanox TECHNOLOGIES

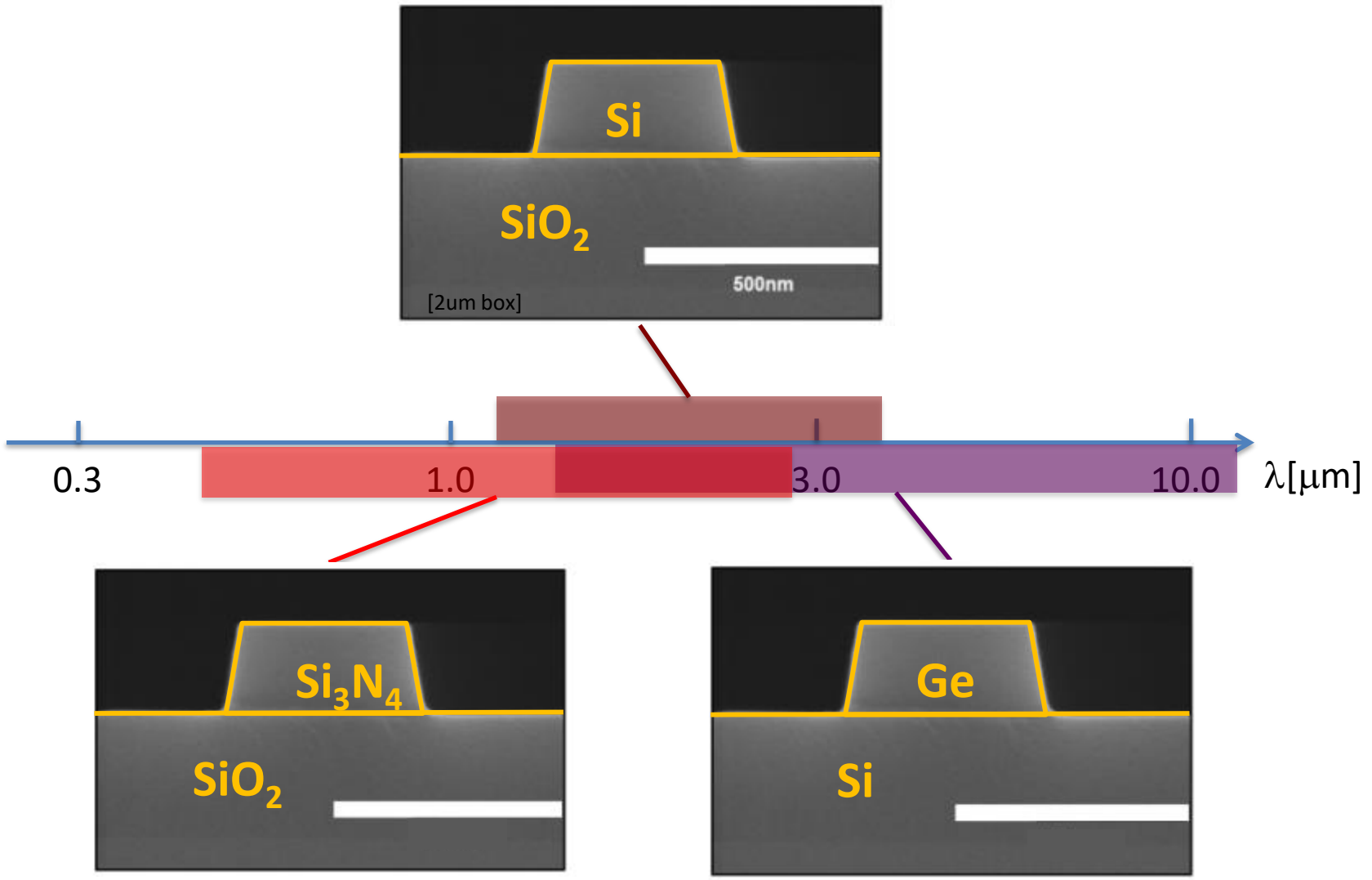
KOTURA

Silicon Photonics Turns Pervasive



SILICON PHOTONICS: EXTENDING THE WAVELENGTH RANGE

WITHOUT LEAVING THE CMOS FAB



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COMPLEMENTARITY OF SOI AND SIN AND GE-ON-SI (GOS)

	SOI	SiN	GOS
Compactness (high index contrast)			
High speed modulation			
Thermo-optic modulation			
High speed detection			
Optical loss (linear) (< 1.1 μm)			
Optical loss (linear) (1.1 – 4 μm)			(only above 2 μm)
Optical loss (linear) (> 4 μm)			
Optical loss (nonlinear)	(1-2 μm range)		
Sensitivity to fab error			
Temperature sensitivity			

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ASSETS OF SILICON PHOTONICS FOR MEDICINE AND HEALTH CARE

Rich set of sensing modalities

Sensing without physical contact

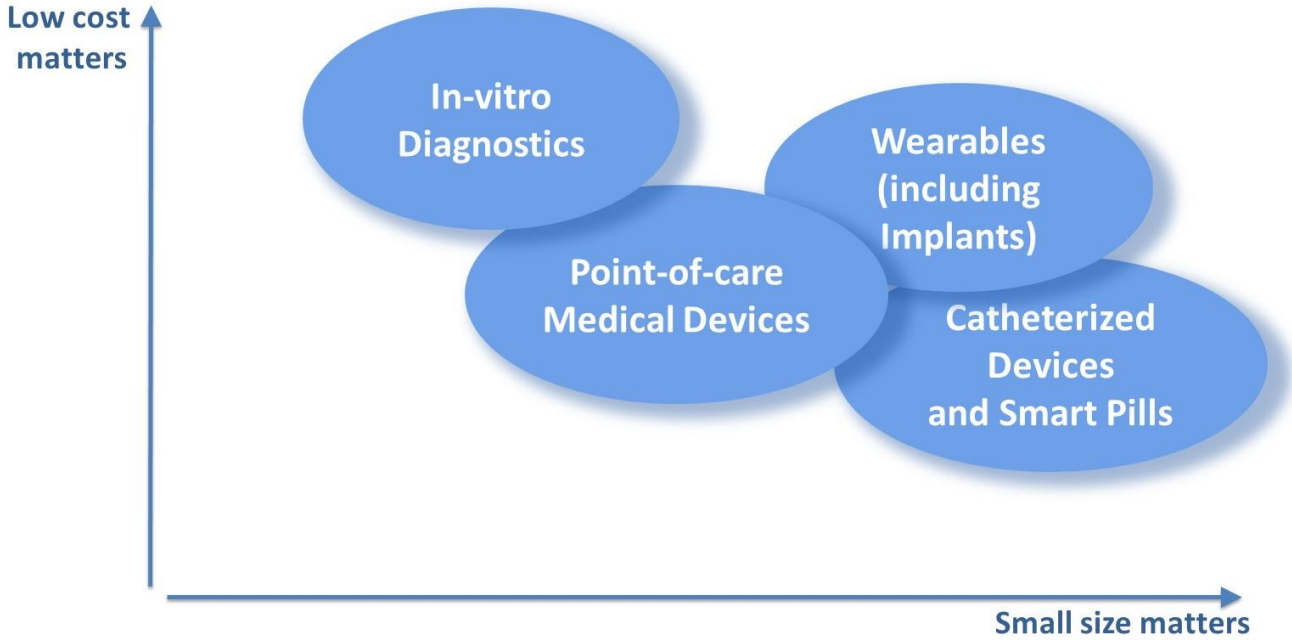
Low cost (even in moderate volume)

Disposable (use-once) devices

Very compact devices (even small enough for bodily implants)

Can address needs from visible to mid IR

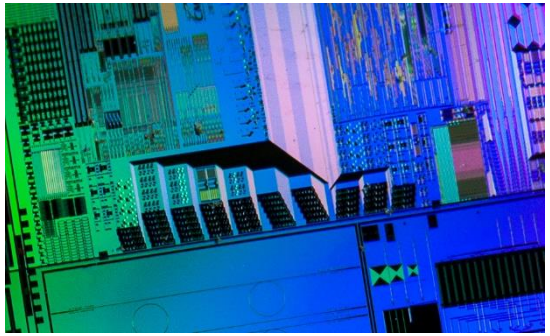
Mature supply chain



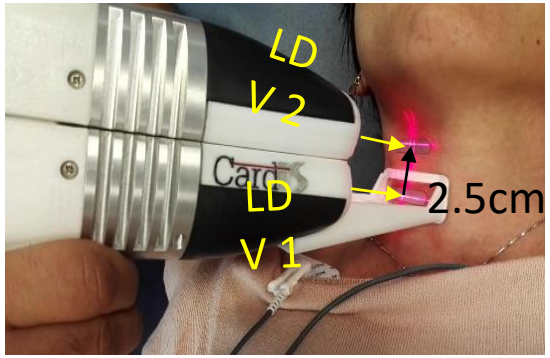
Three Application Cases

- In-vitro diagnostics

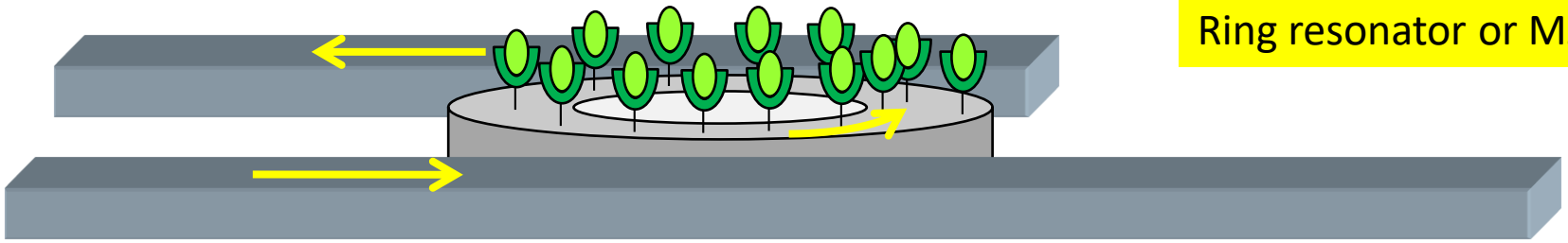
Continuous glucose monitoring



Cardiovascular monitoring

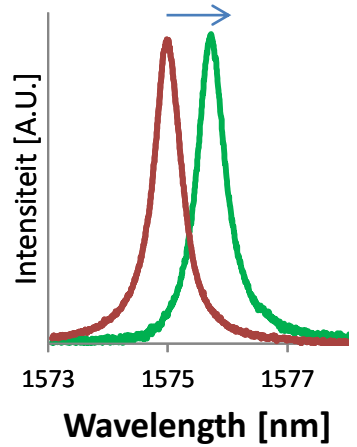


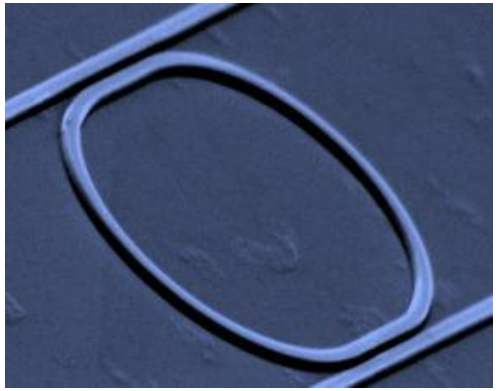
LABEL-FREE BIOSENSOR
THROUGH REFRACTIVE INDEX SENSING OF ANTIGEN-ANTIBODY BINDING



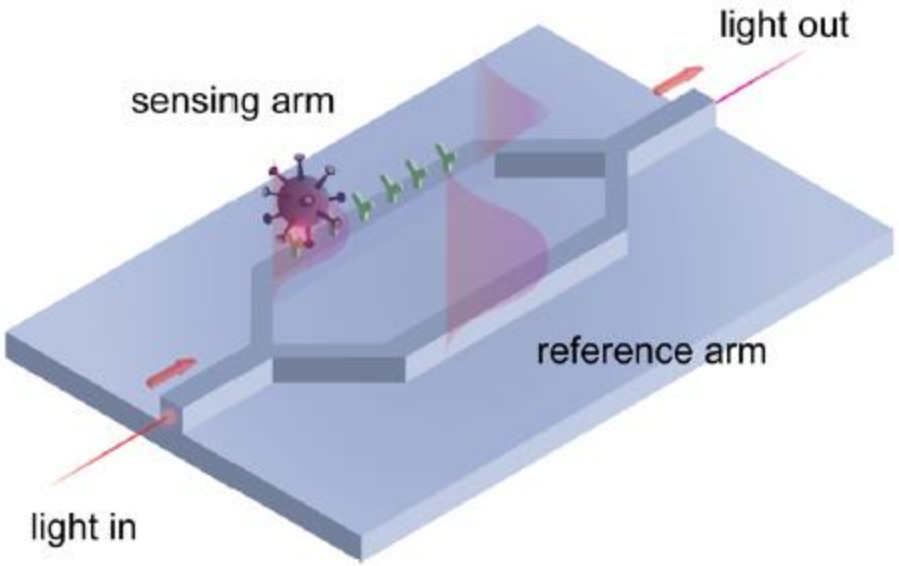
Ring resonator or MZI

Wavelength shift



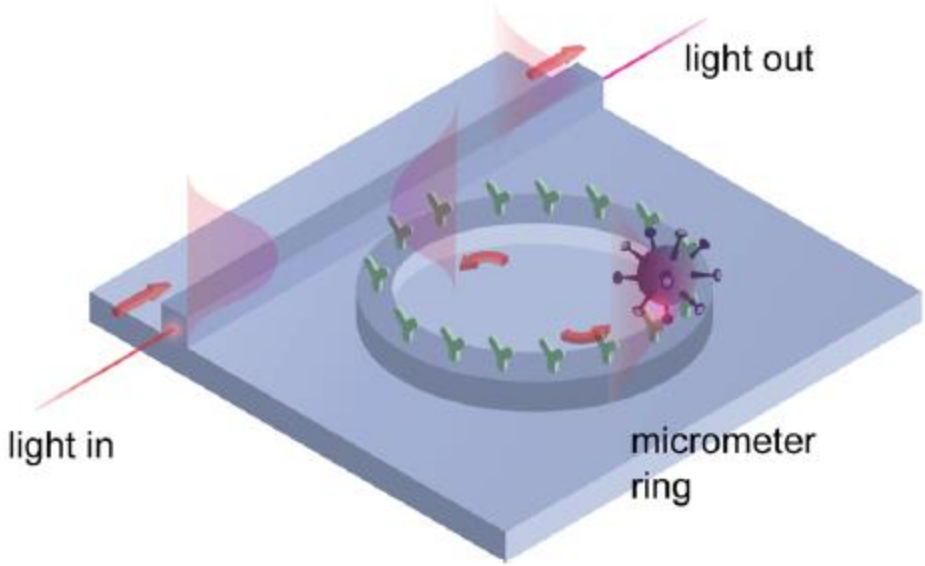


KEY PHOTONIC BIOSENSOR DEVICES



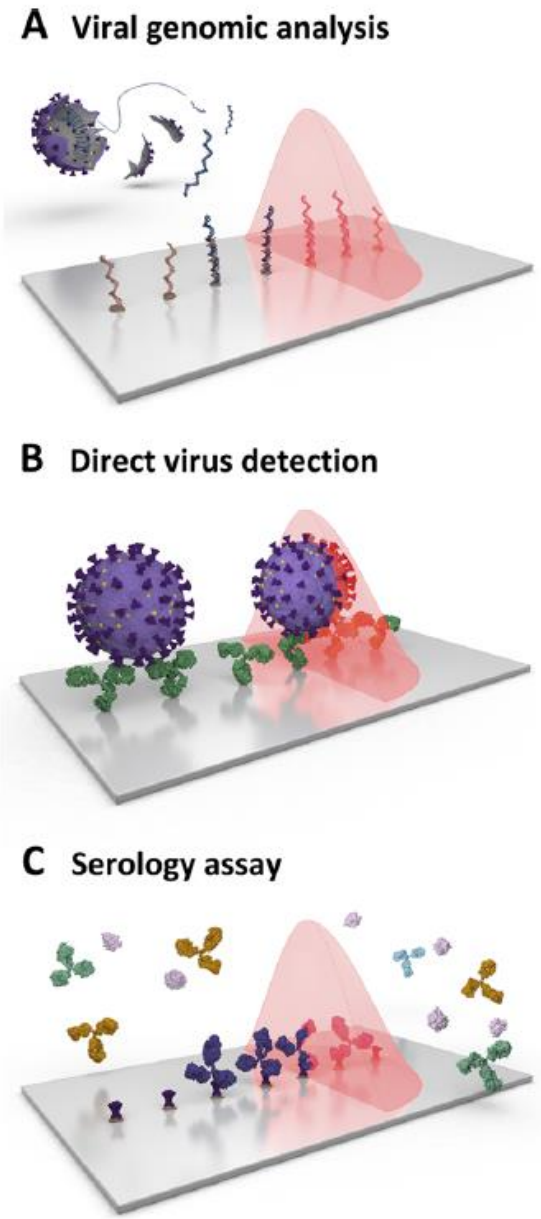
M. Soler et al,
ACS Sens. 2020

Mach-Zehnder Interferometer (MZI)



Micro-ring resonator (MRR)

BIOSENSING STRATEGIES FOR VIRAL INFECTION DIAGNOSIS



M. Soler et al,
ACS Sens. 2020

A. Genomic detection

Chip is functionalized with short stretches of nucleic acids, with complementary sequence to the viral target

B. Antigen-directed virus detection

Chip is functionalized with antibodies that bind to spike proteins at the surface of the virus

C. Serological test (blood)

Chip is functionalized with antigens that bind to antibodies that result from the body's immune response to the virus

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

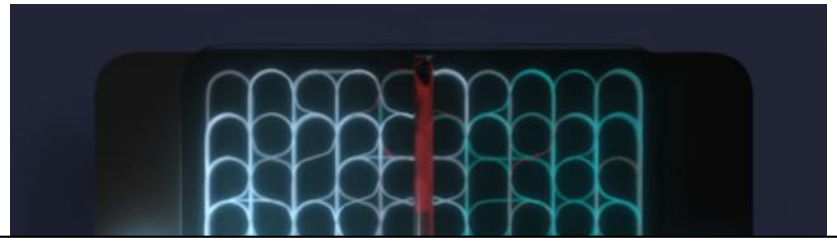
	PCR Result		
MAVERICK	Pos	Neg	
Pos	46	0	46
Neg	7	303	310
	53	303	

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



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

ANTELOPE DX

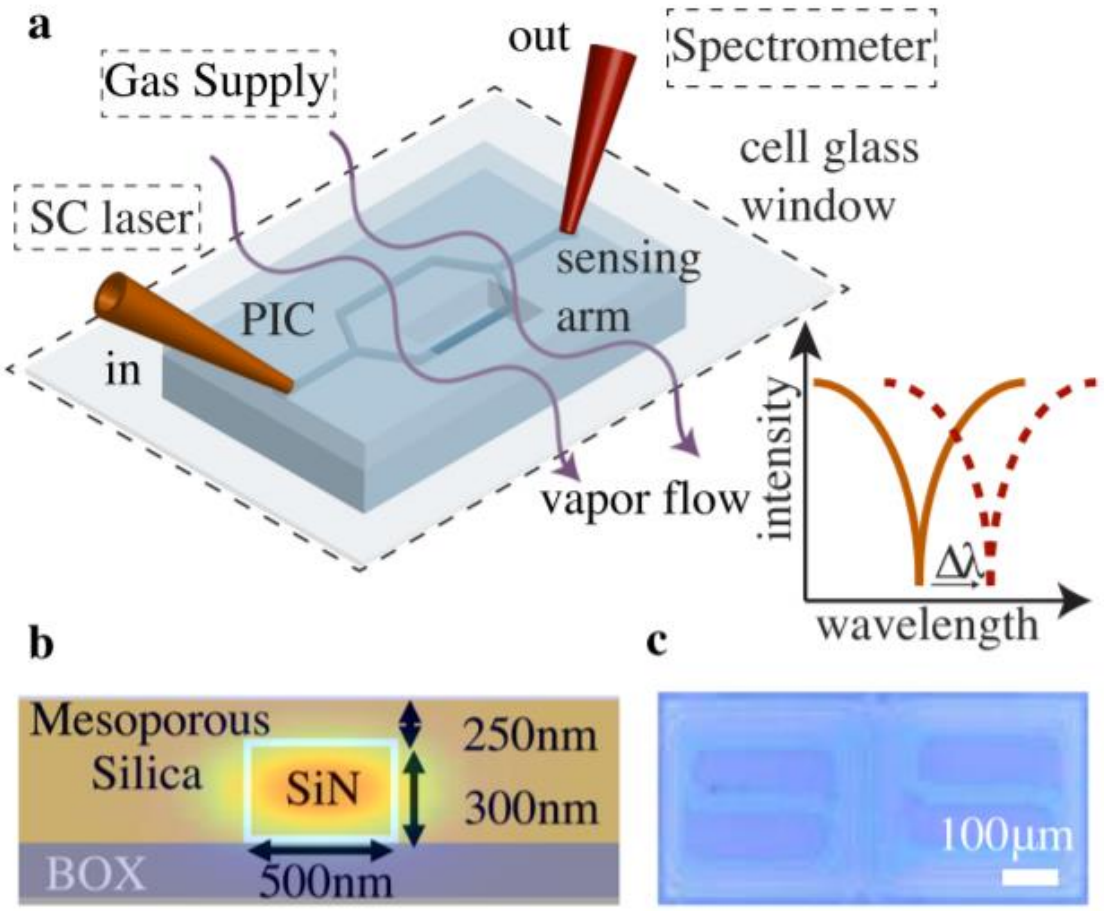
Antelope DX to join forces with In The Pocket and Extra Horizon for the development of its easy-to-use, high-quality home testing device.

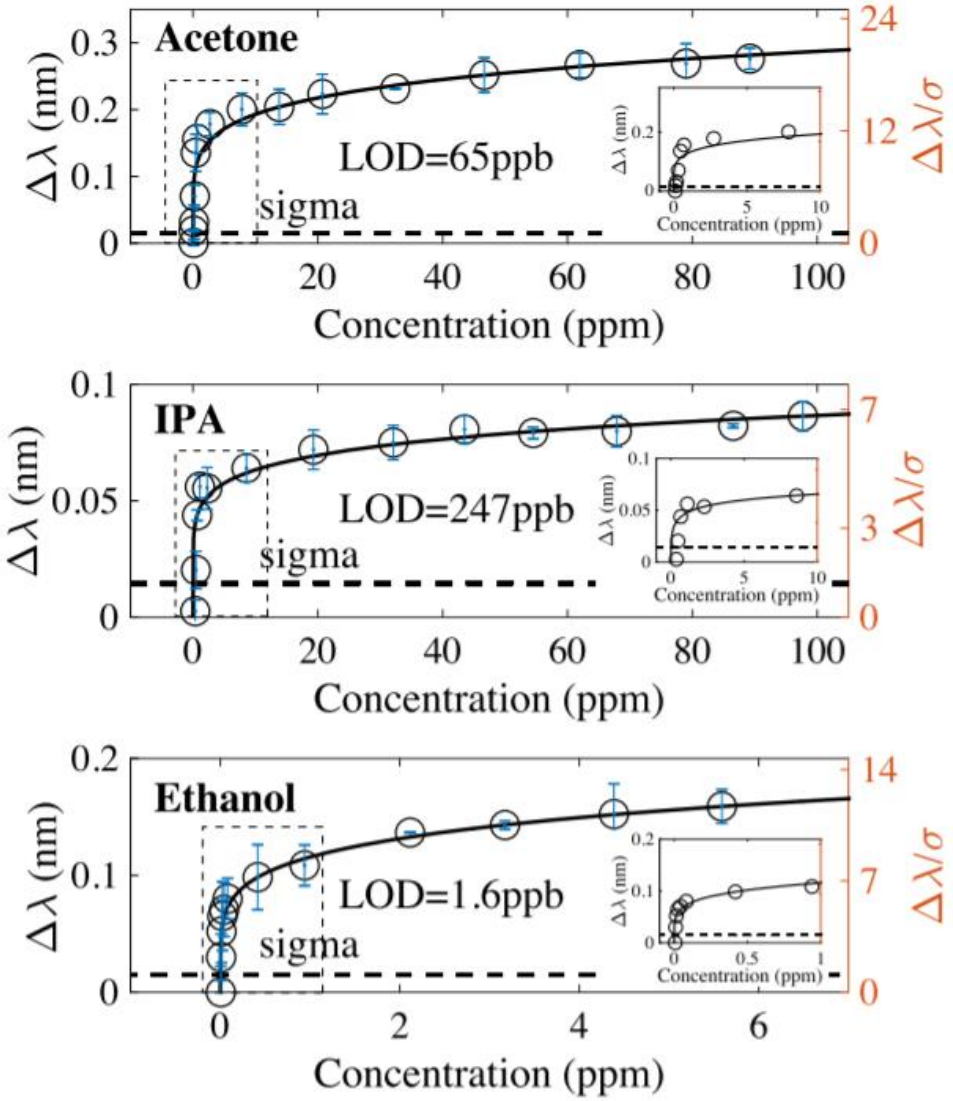
The first test on the market will be the Covid 19 & Flu self-test.

Ghent 15.04.2021. Antelope Dx, a Belgian based company that aims to bring high-quality health testing for the individual, announces the collaboration with In The Pocket and Extra Horizon for the development of an app and cloud-based services for its self-tests.

ULTRASENSITIVE GAS SENSING WITH REFRACTIVE INDEX SENSORS

Medical application: breath analysis



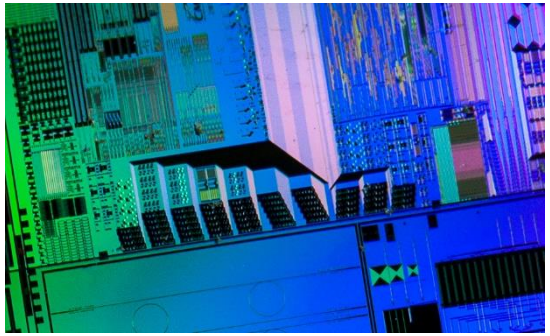


G. Antonacci et al, APL Photonics 2020

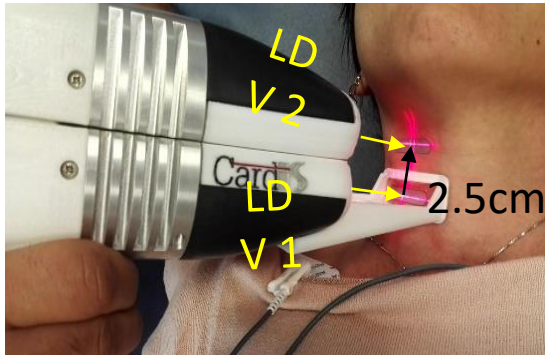
Three Application Cases

In-vitro diagnostics

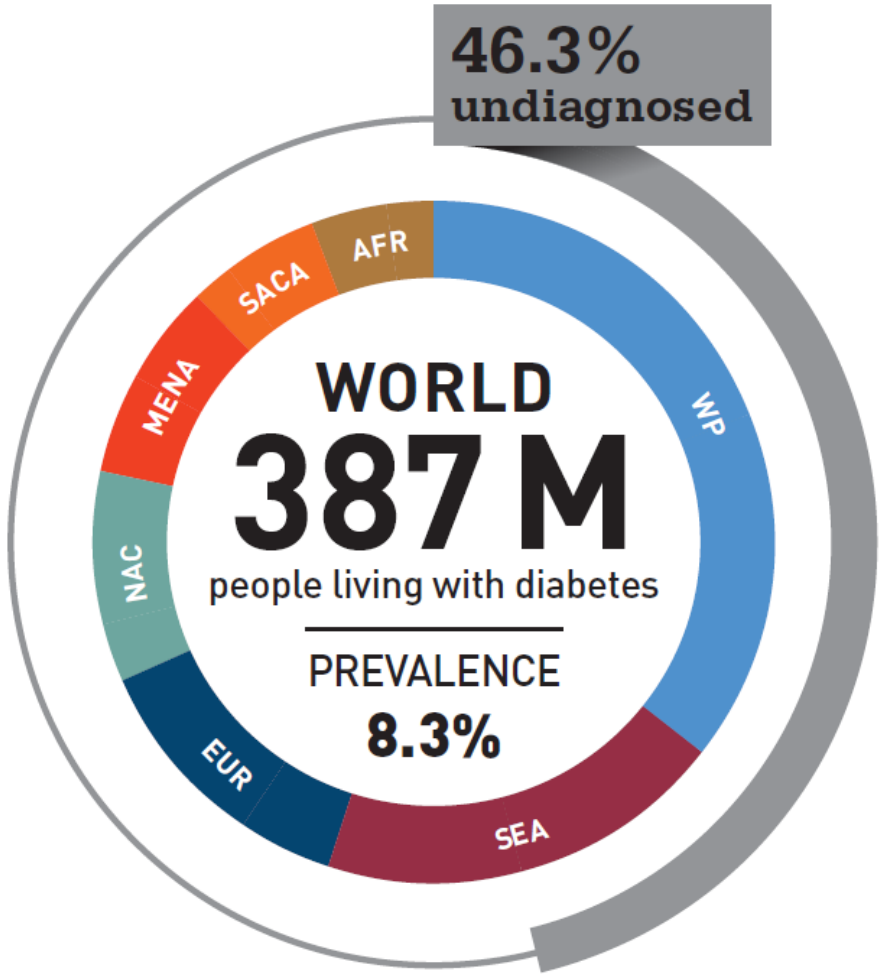
Continuous glucose monitoring

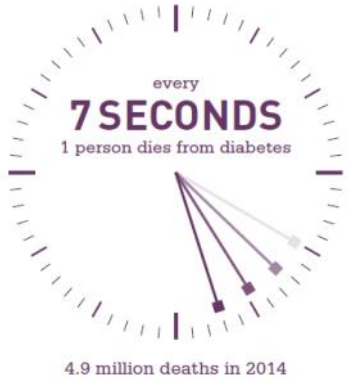


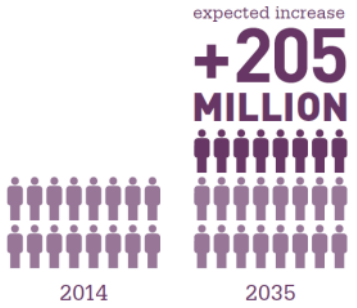
Cardiovascular monitoring



DIABETES IS THE 21ST CENTURY HEALTH CHALLENGE







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

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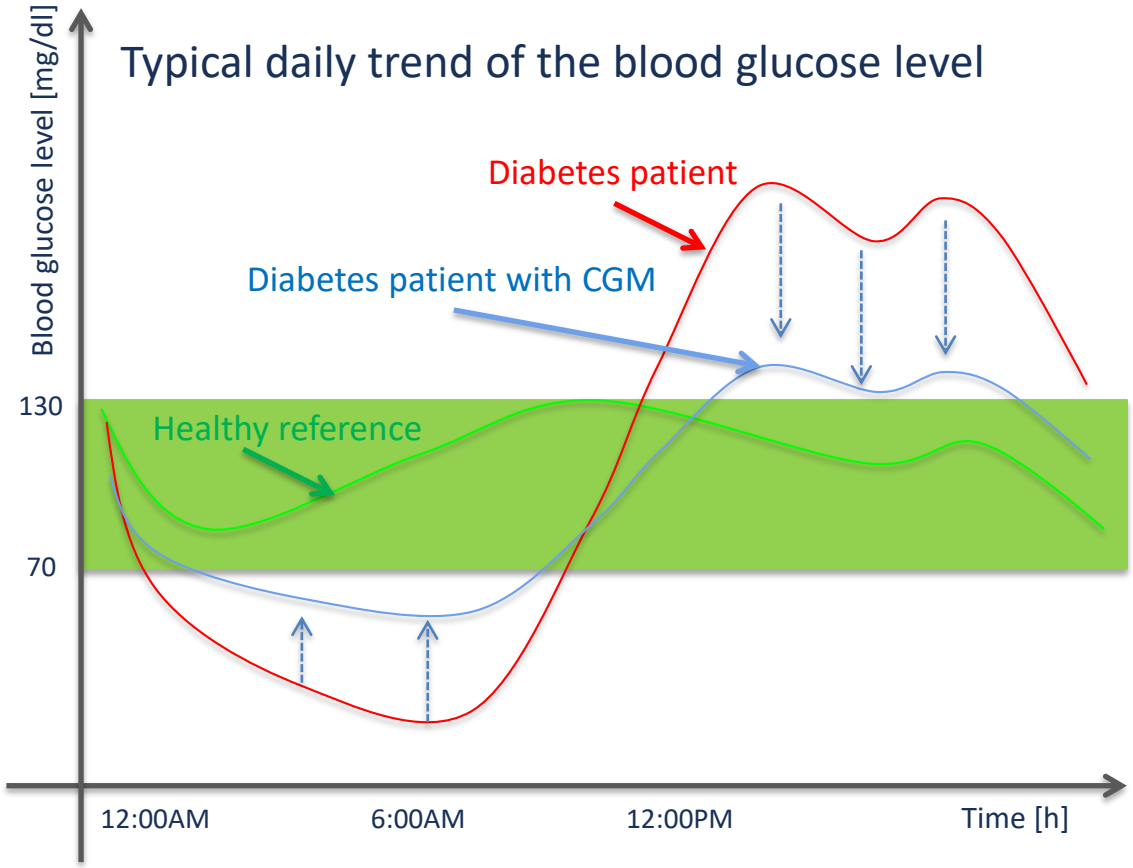
Continuous Glucose Monitoring (CGM) has proven to improve glycemic control of diabetes patients

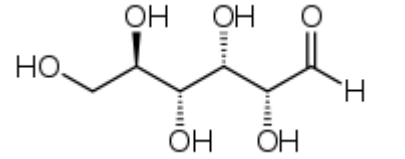
CGM systems show positive health impact *

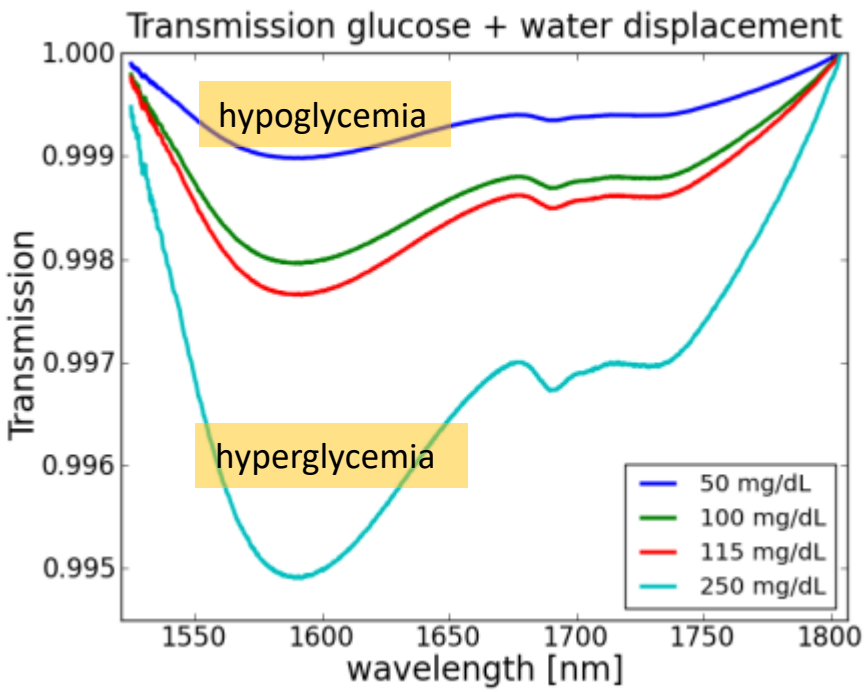
- lower average blood glucose levels
- decrease of hypoglycemic frequency



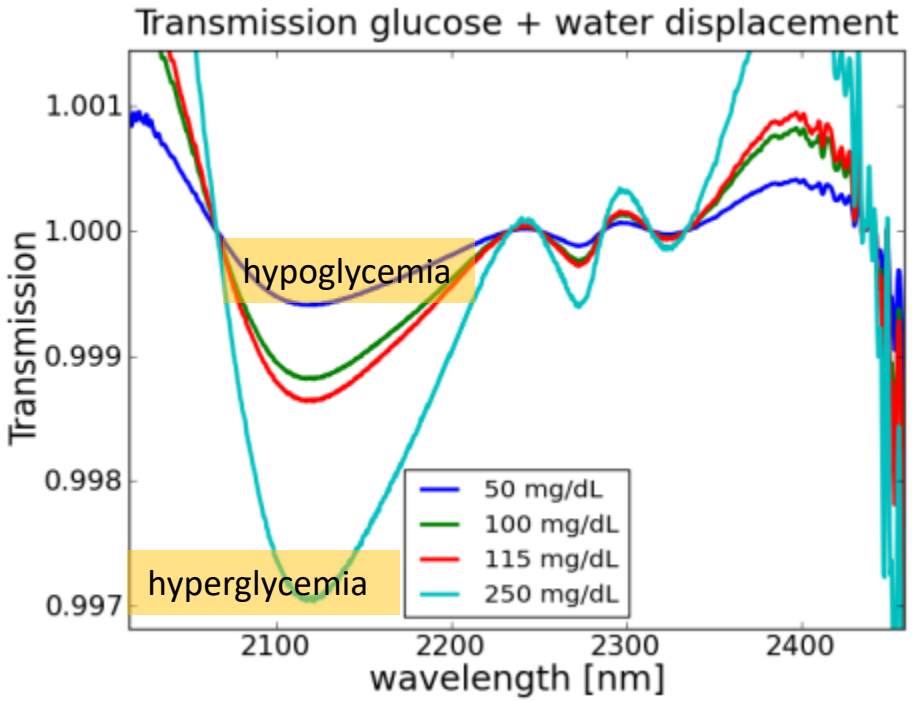
* Liebl A, Henrichs HR, Heinemann L, et al. Continuous glucose monitoring: evidence and consensus statement for clinical use. J Diabetes Sci Technol . 2013;7:500-519

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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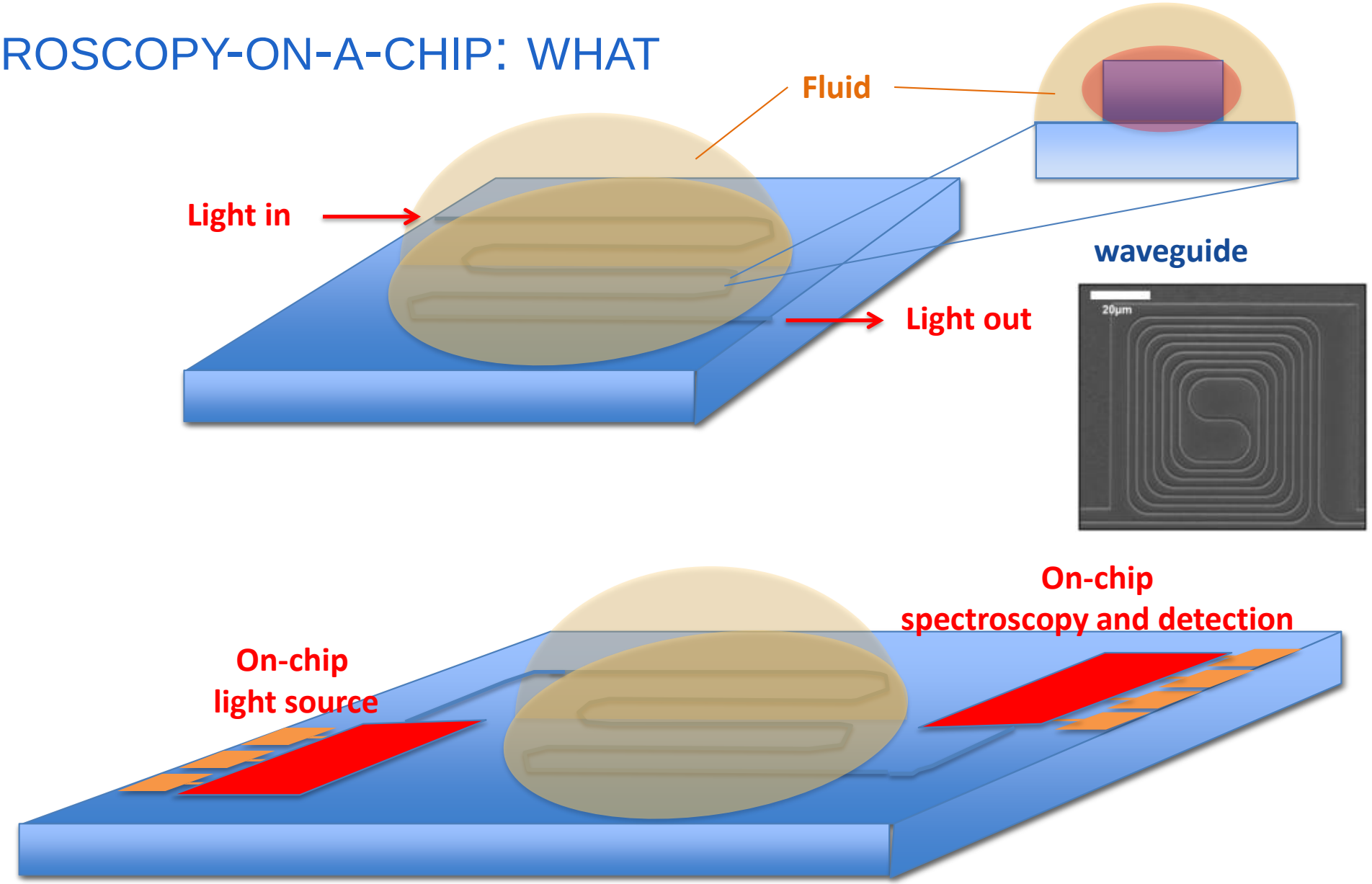
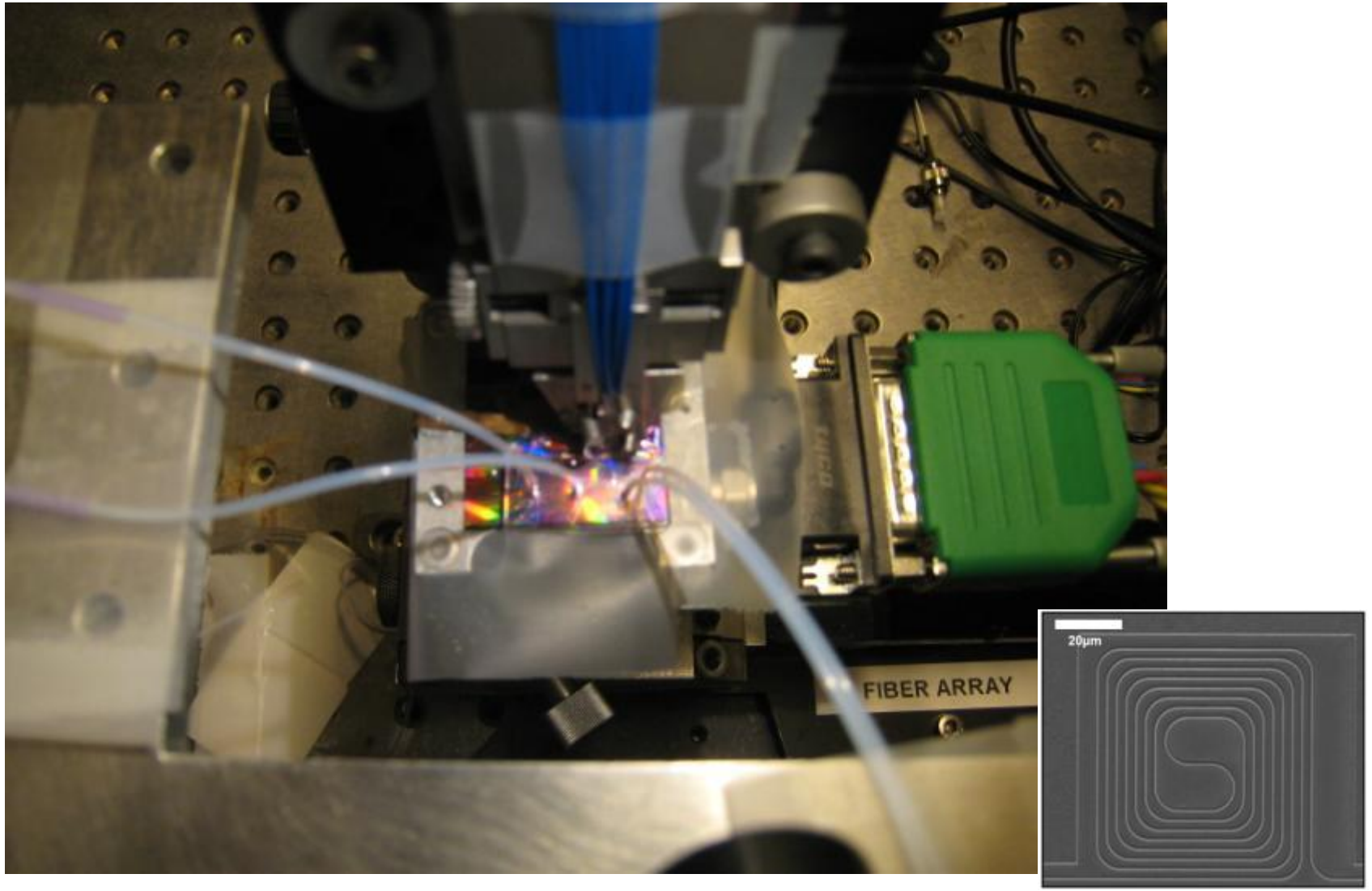
SPECTROSCOPY-ON-A-CHIP: WHAT



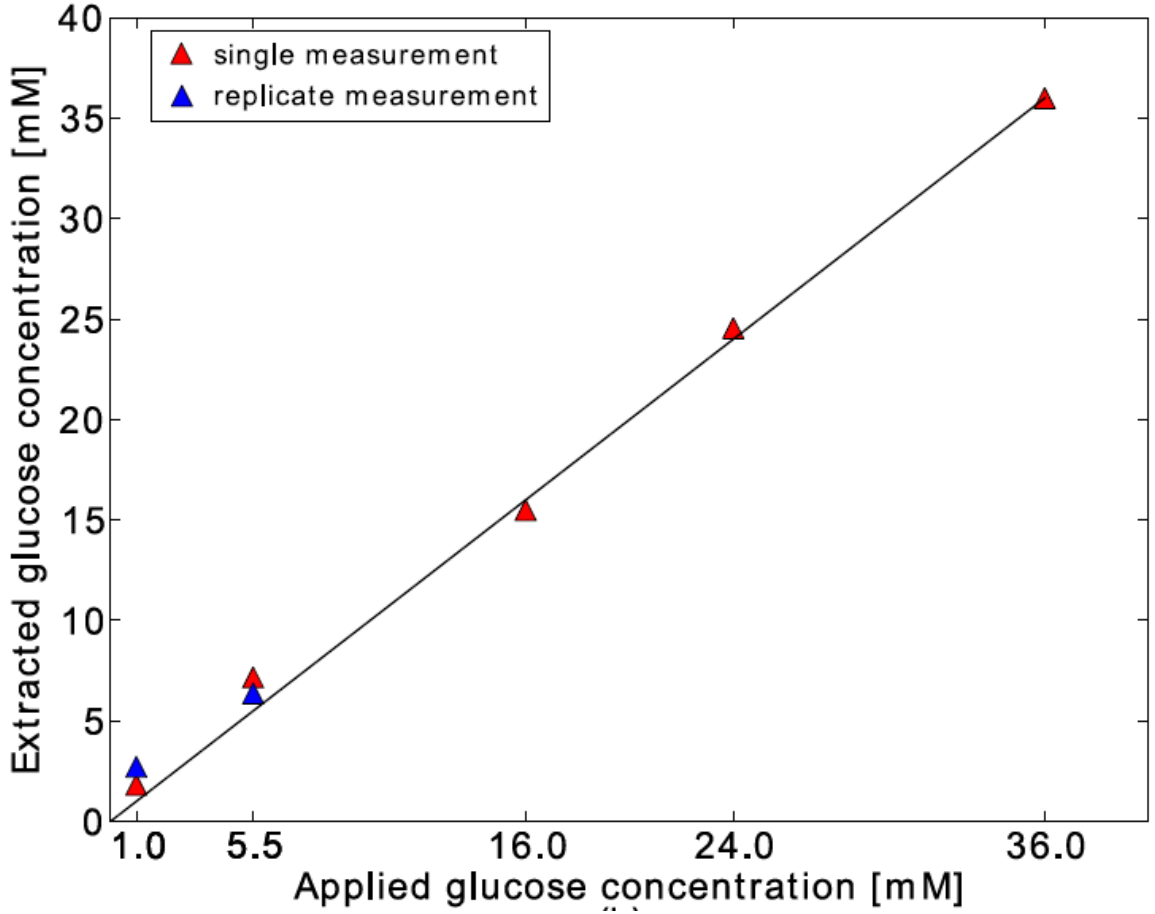
PROOF-OF-CONCEPT DEMO OF GLUCOSE SENSING IN THE LAB



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

GLUCOSE ABSORPTION SPECTROSCOPY: PROOF-OF-CONCEPT

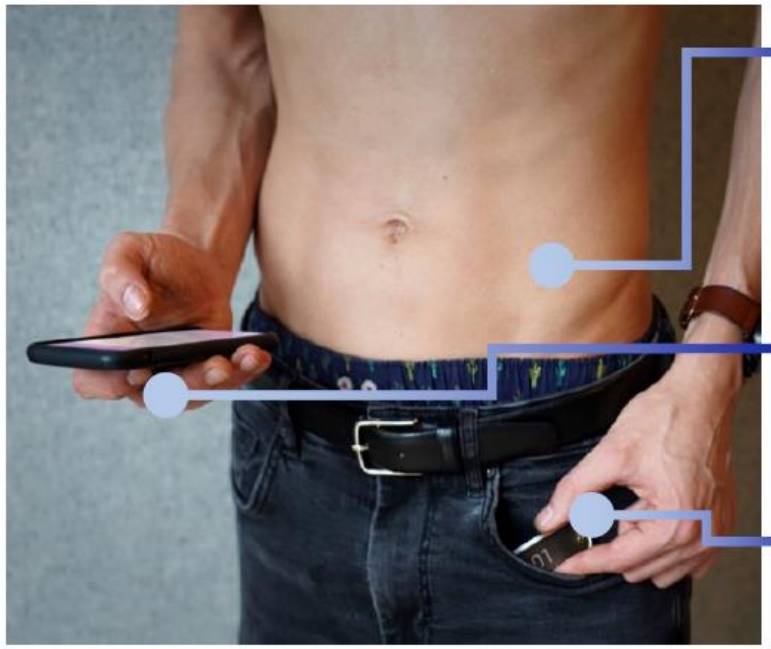
Use measured spectrum of 36 mM solution as the basic vector



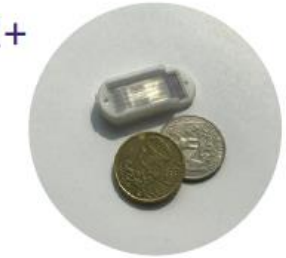
Demonstrated sensitivity of 1mM

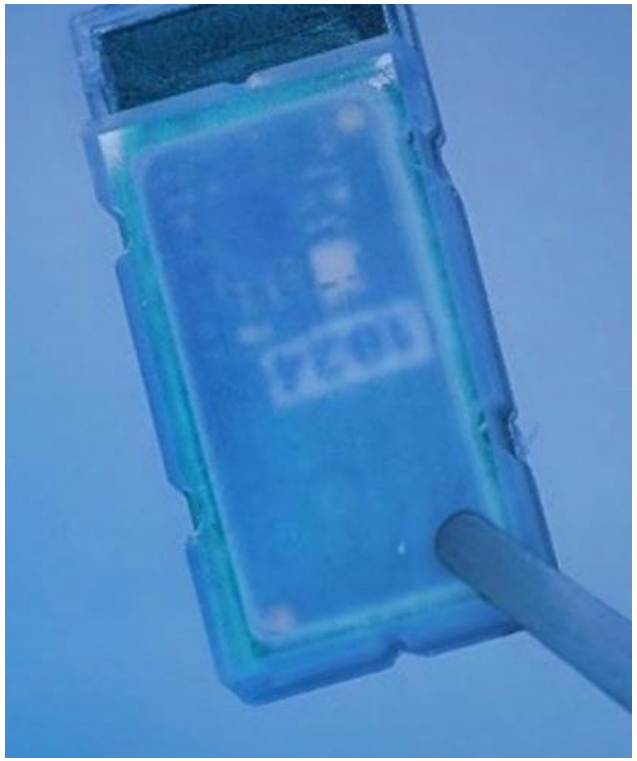
E. Ryckeboer et al, Biomedical Optics Express (2014)

Continuous Glucose Monitoring with Subcutaneous Implant

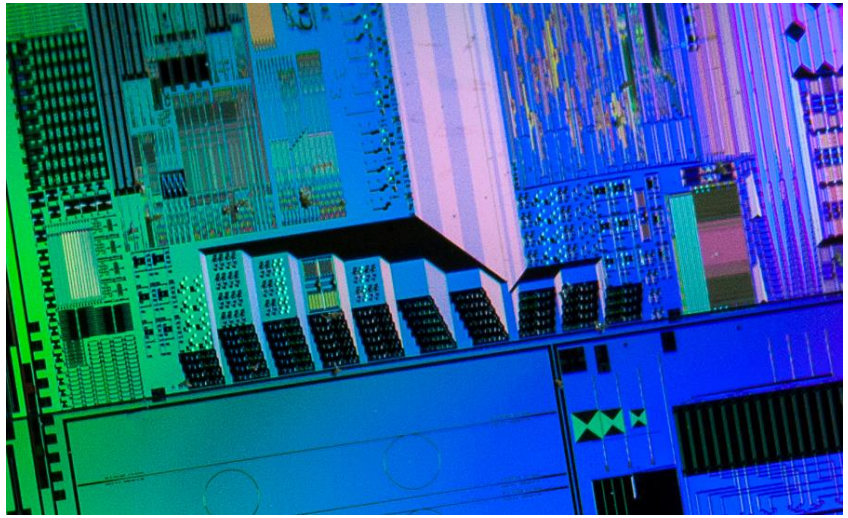


- Invisible, coin-sized 2+ years implant (rechargeable)
- Mobile app/cloud/connection to 3rd party iCGM devices
- Waterproof Bluetooth display unit





Implant

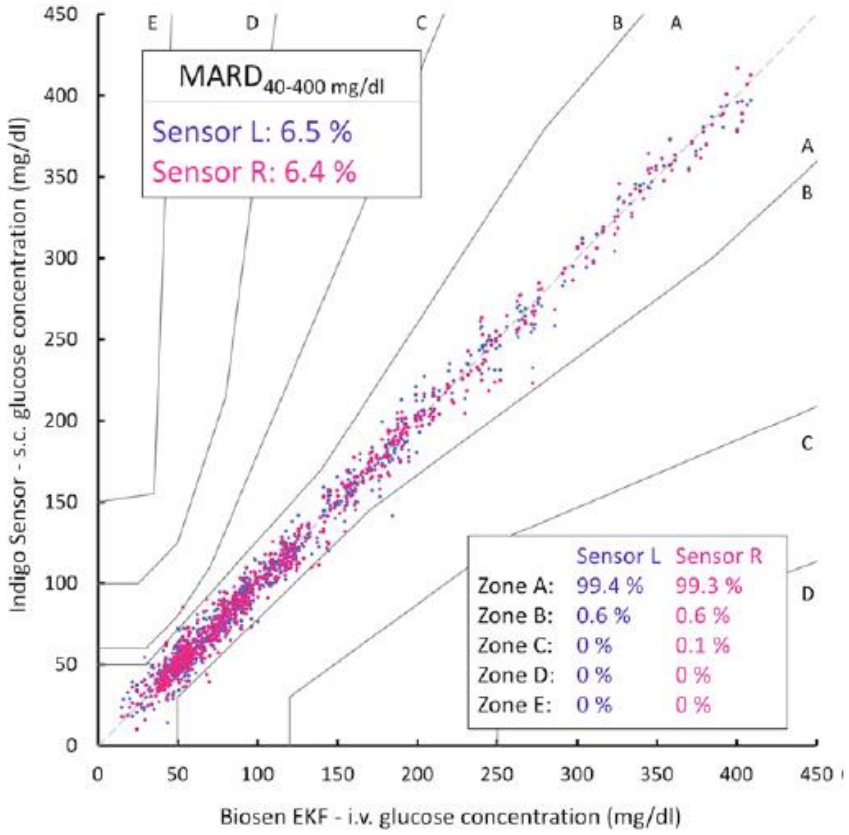


Microspectrometer chip

https://indigomed.com/

indigo

Continuous Glucose Monitoring with Subcutaneous Implant



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

Indigo Diabetes Initiates First Clinical Study of its Continuous Glucose Monitoring Sensor

BY INDIGO | MAR 18, 2021 | 2021, NEWS

March 18, 2021 – Ghent, Belgium

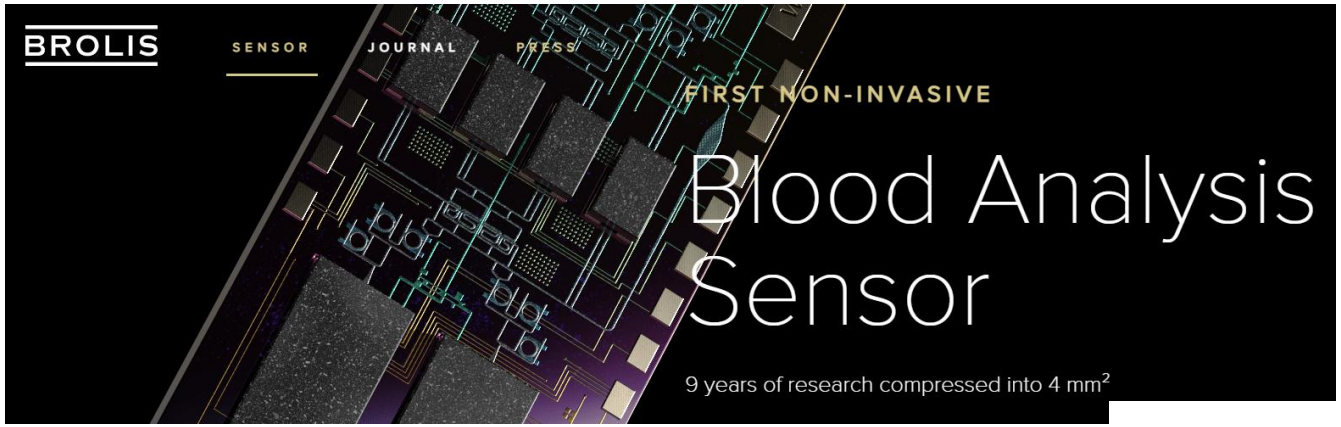
> ***Ground-breaking subcutaneous sensor aims to continuously monitor multiple metabolites including ketones in people living with diabetes***

BELGIUM – Ghent, March 18, 2021 – Indigo Diabetes N.V. ('Indigo' or the 'Company'), a pioneering developer of medical solutions using nanophotonics, announces that its continuous multi-metabolite ('CMM') sensor has been successfully implanted subcutaneously in the first three participants of its first clinical study, designed to evaluate the device. Indigo's CMM sensor is in development for the continuous measurement of glucose, ketone and lactate levels in people living with diabetes.

https://indigomed.com/

indigo

Non-invasive Glucose Monitoring based on silicon photonics



http://brolis.tech

DESIGNLINES | MEDICAL DESIGNLINE

Rockley Photonics to Deliver Glucose Monitoring for Apple Smartwatches

By Nitin Dahad 05.04.2021 0

Share Post Share on Facebook Share on Twitter

Rockley Photonics, which recently announced a $1.2 billion listing on the New York Stock Exchange via a special purpose acquisition company (SPAC), is thought to be developing advanced health monitoring features for smartwatches including for Apple.

Apple began purchasing products from Rockley in 2017; it is now Rockley's largest customer with $70 million of NRE commitment to date.

GHENT UNIVERSITY imec

BROLIS: GASB TUNABLE LASER TECHNOLOGY WITH SILICON PIC

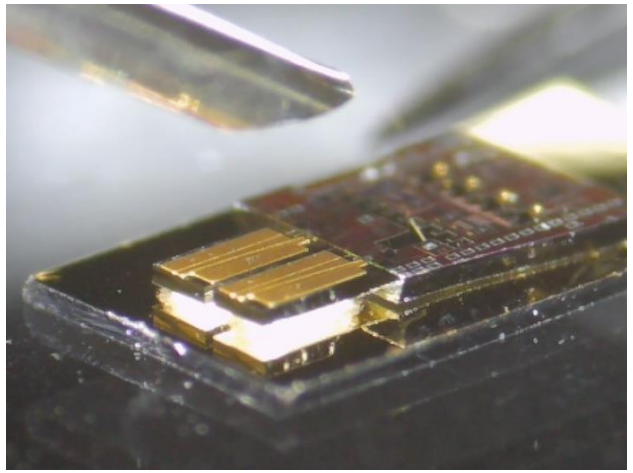
GaSb gain chips hybridly integrated with silicon PIC

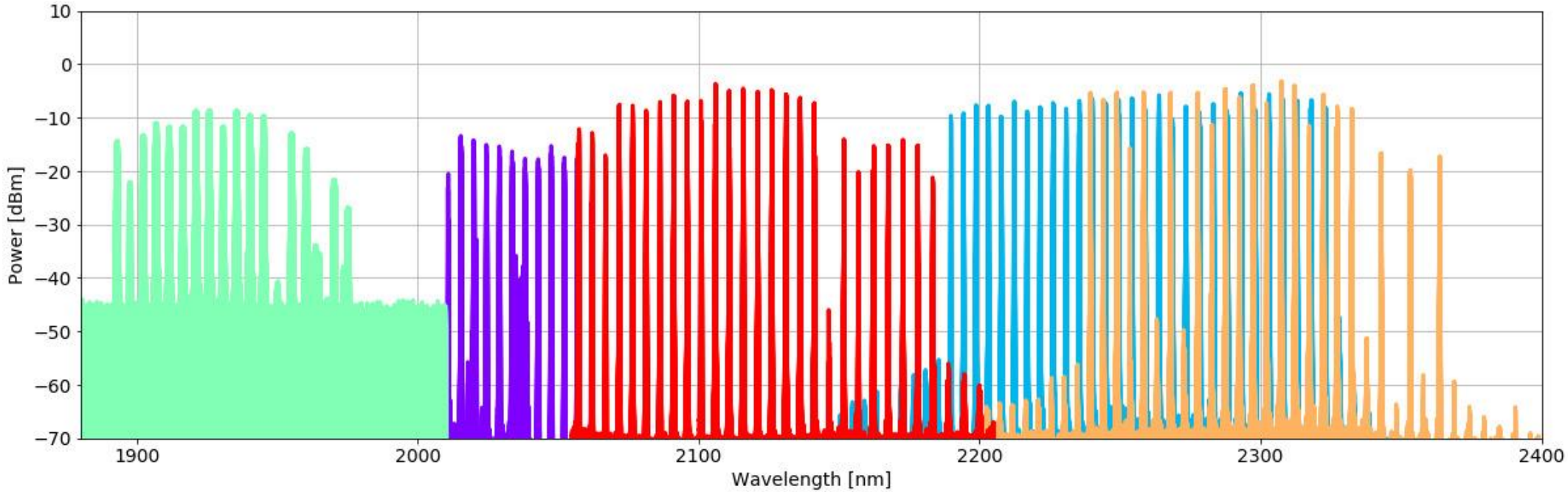
1880 – 2430 nm

0.1- 1 mW output power

Tuning speed up to 2 kHz

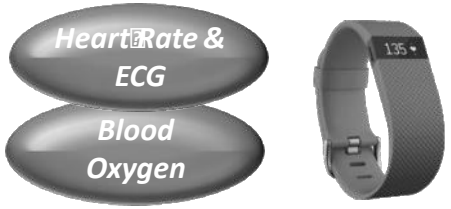
120 nm/gain-chip





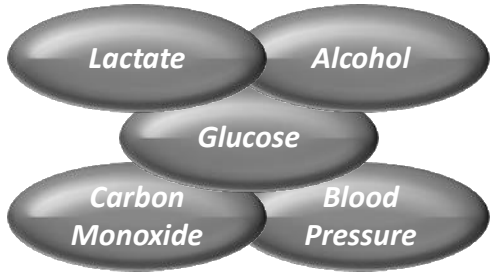
Current Smartwatch Technology

- ✗ Limited sensor capabilities
- ✗ Legacy LED technology
- ✗ Low resolution & accuracy



Current Medical Technology

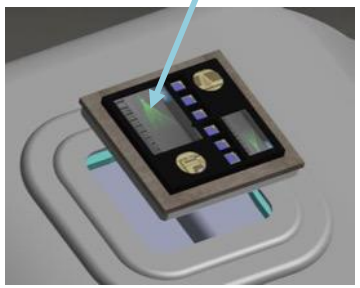
- ✗ In-clinic / in-hospital monitoring only
- ✗ Bulky, high-cost medical lab equipment not available to average consumer
- ✗ Different equipment for different tests



Rockley's Multi-Function Clinic-on-the-Wrist Capability

- ✓ **Single sensor for multi-modal biochemical / biophysical marker monitoring**
- ✓ **Functionality of numerous lasers on a single chip**
- ✓ **Unparalleled spectral resolution & accuracy**

Si Photonic PIC



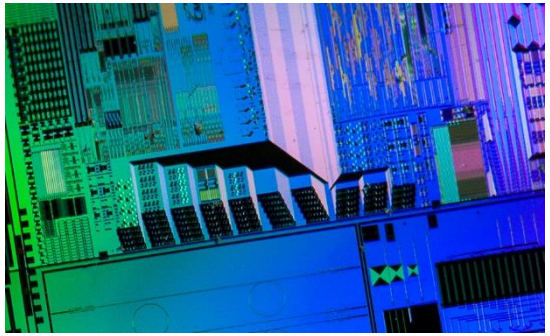
New sensing functions unlocked…

Rockley's integrated optical technology enables miniaturization of sensing devices necessary for the evolution of a wearable spectrometer

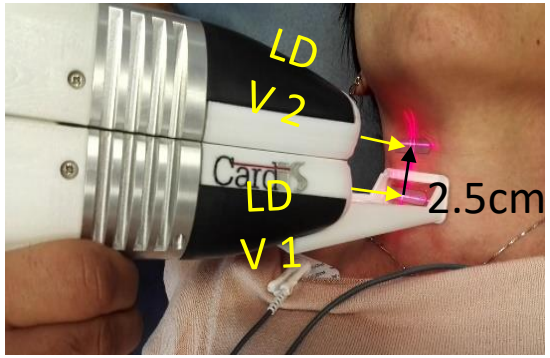
Three Application Cases

In-vitro diagnostics

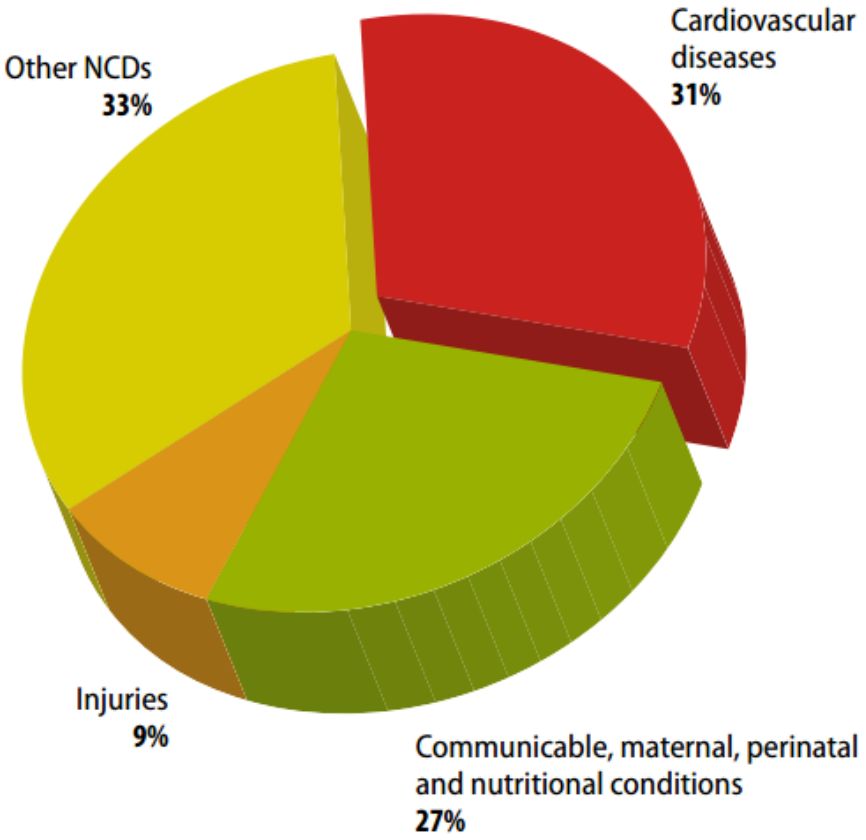
Continuous glucose monitoring



➡ Cardiovascular monitoring



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

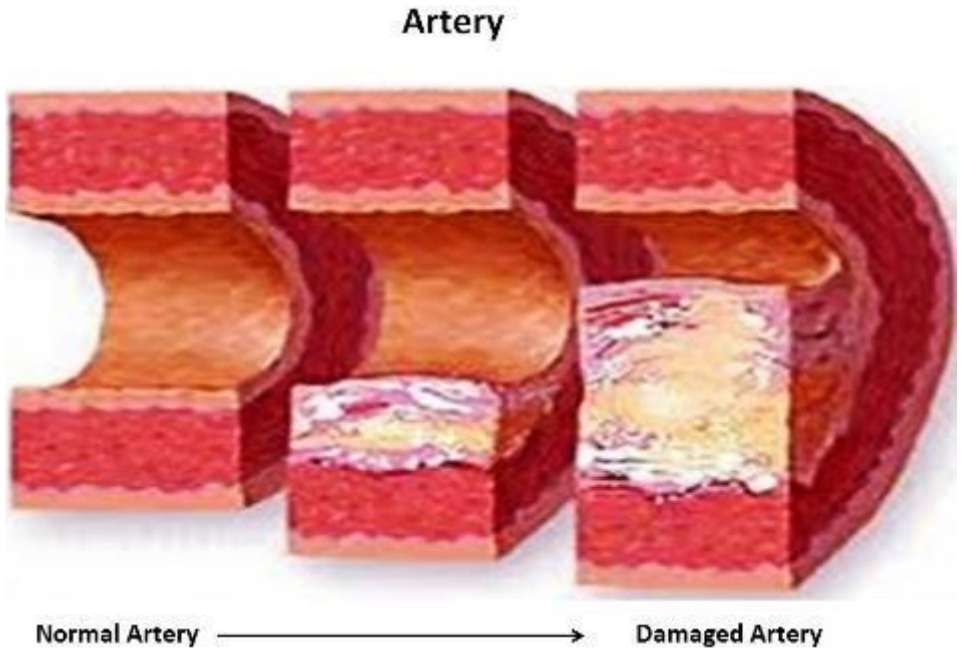
Atherosclerosis: deposition of plaque on the inner arterial walls (which can lead to stiffening)

Stenosis: abnormal narrowing in a blood vessel

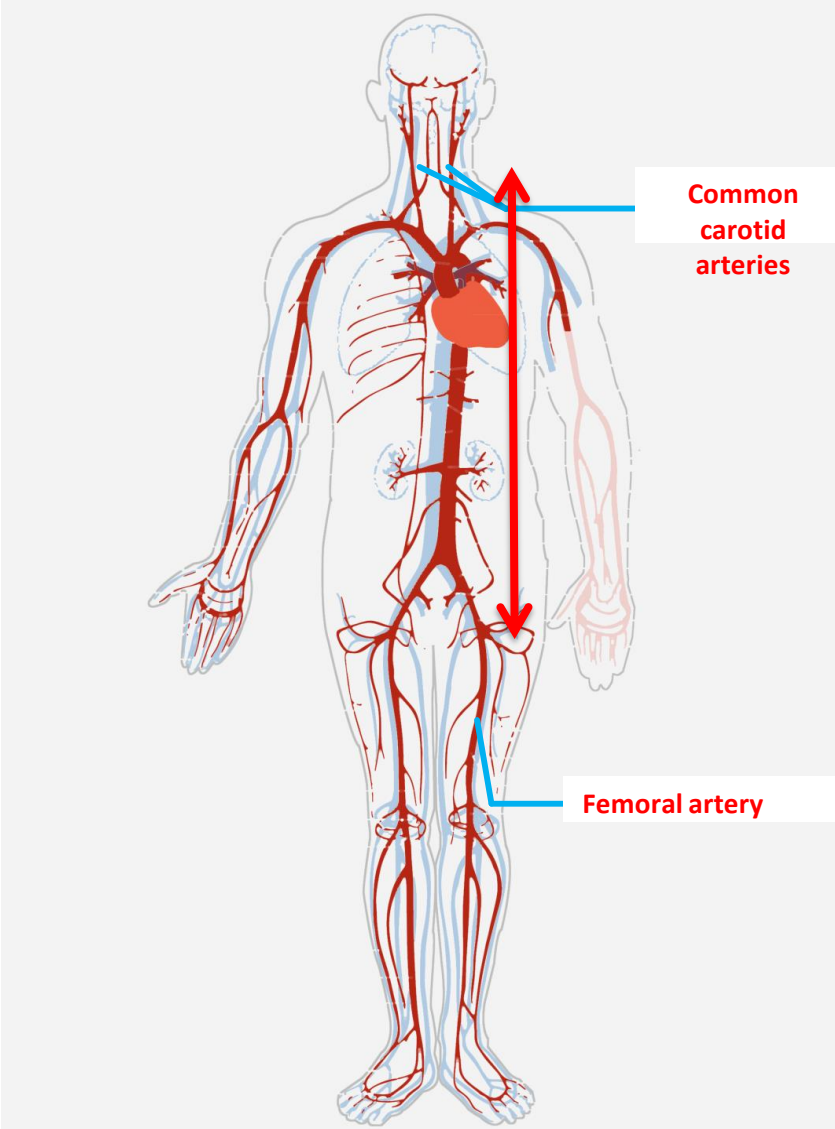
Heart Dyssynchrony: left and right part of the heart are not triggered synchronously

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

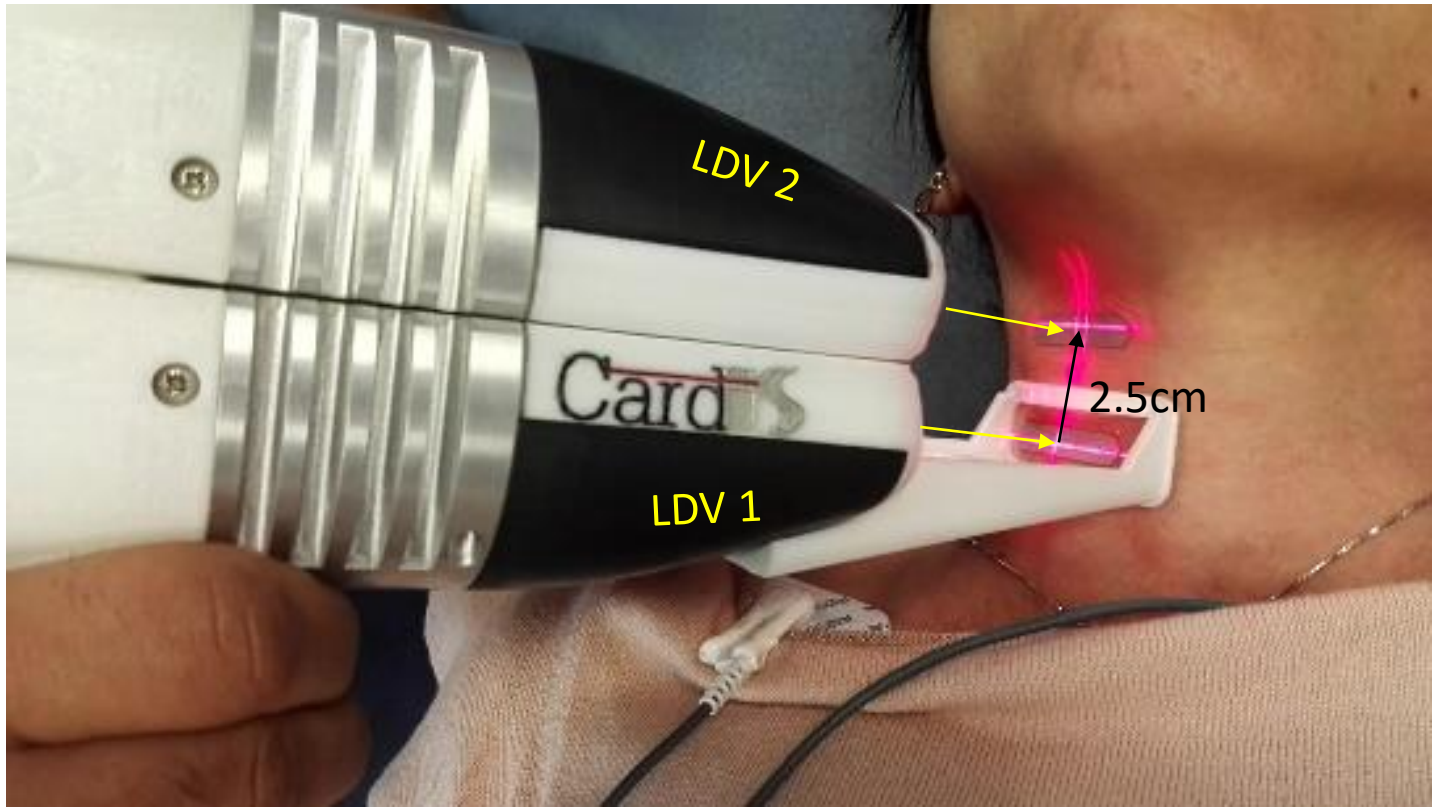


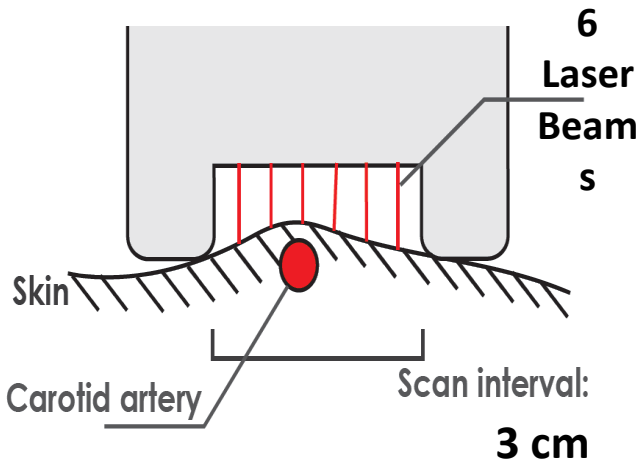
Pulse Wave Velocity: speed by which the pressure wave caused by a heart beat travels in the arteries

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

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

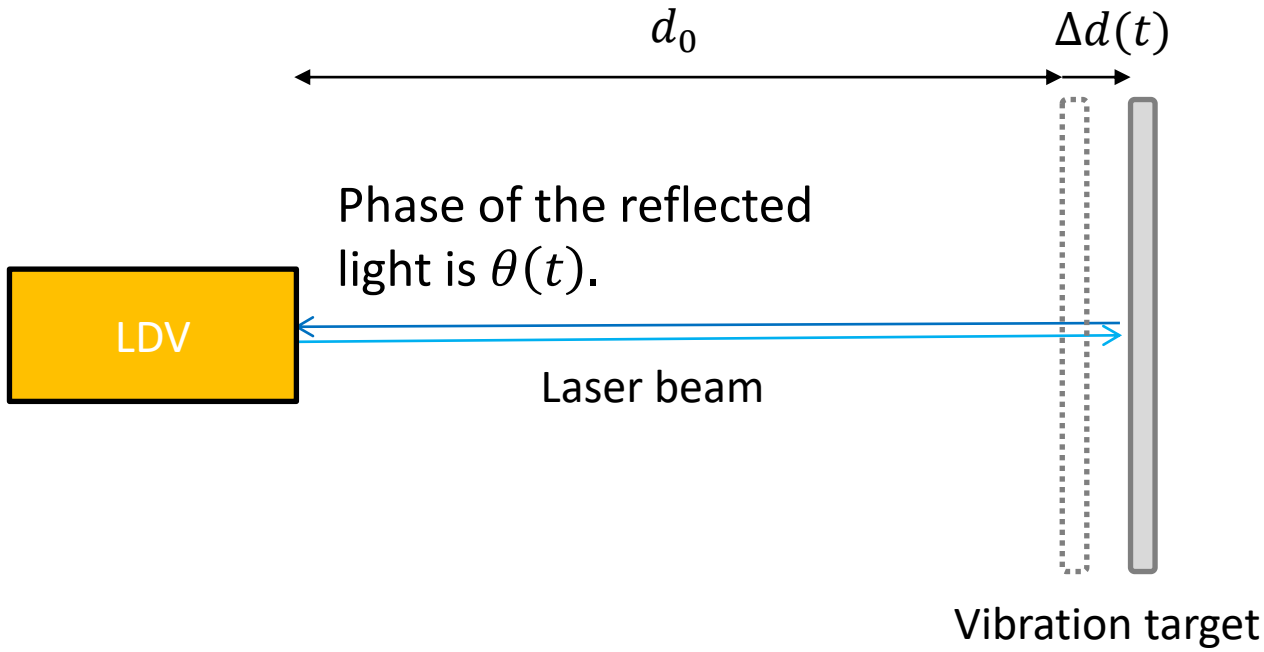
Approach: Measure PWV from local carotid Or carotid-femoral





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

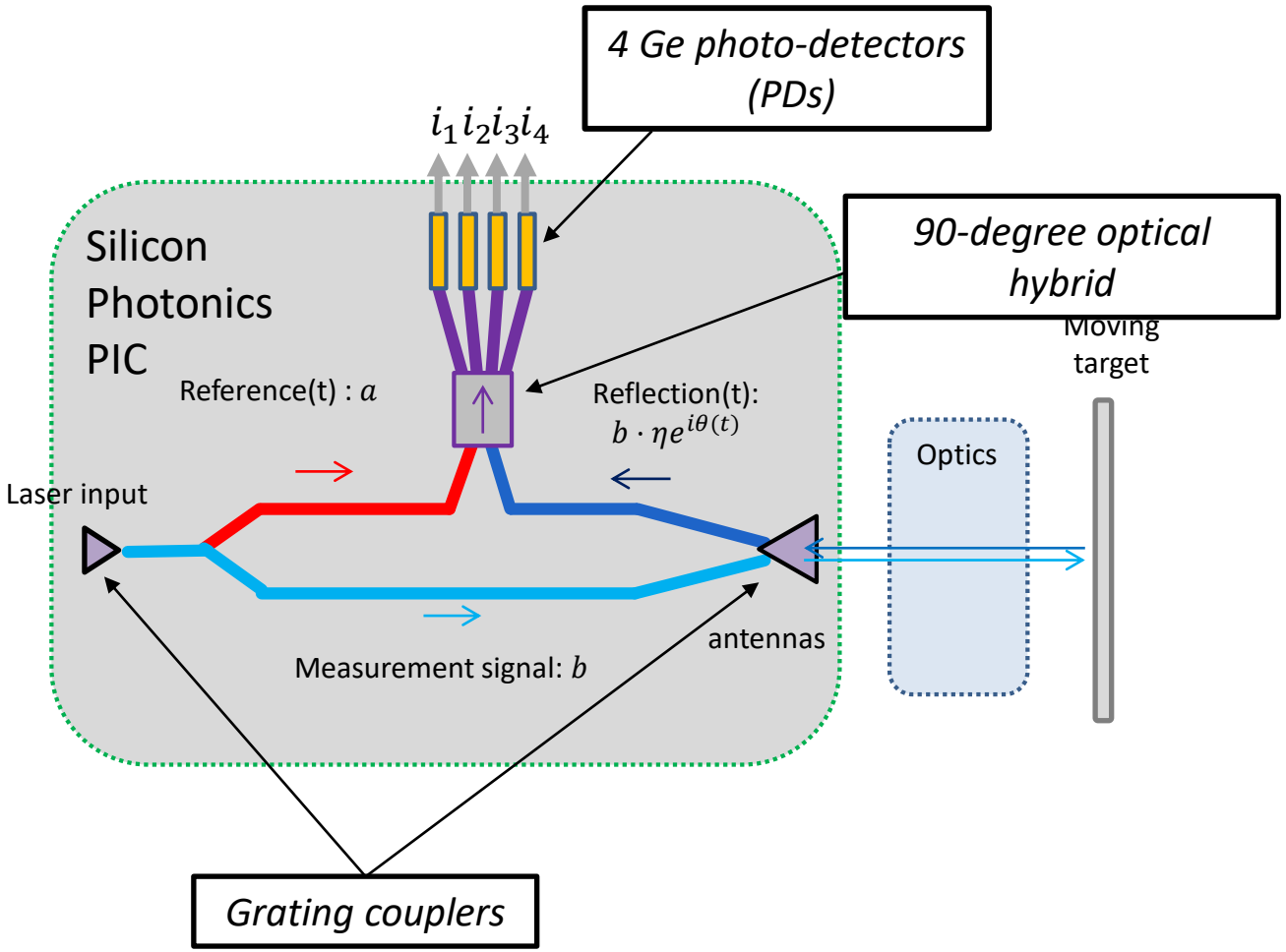
Working principle of LDV

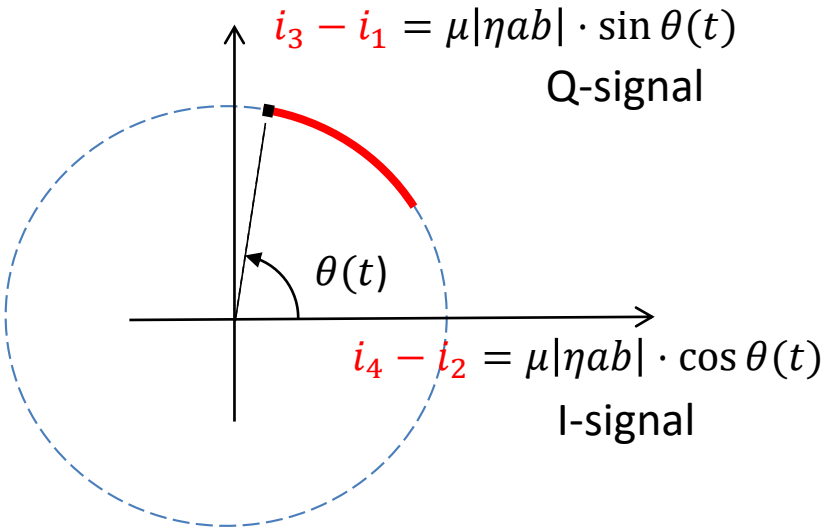


The displacement $\Delta d(t)$ can be retrieved by measuring $\theta(t)$, based on the relation

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

WORKING PRINCIPLE OF LDV: HOMODYNE DETECTION

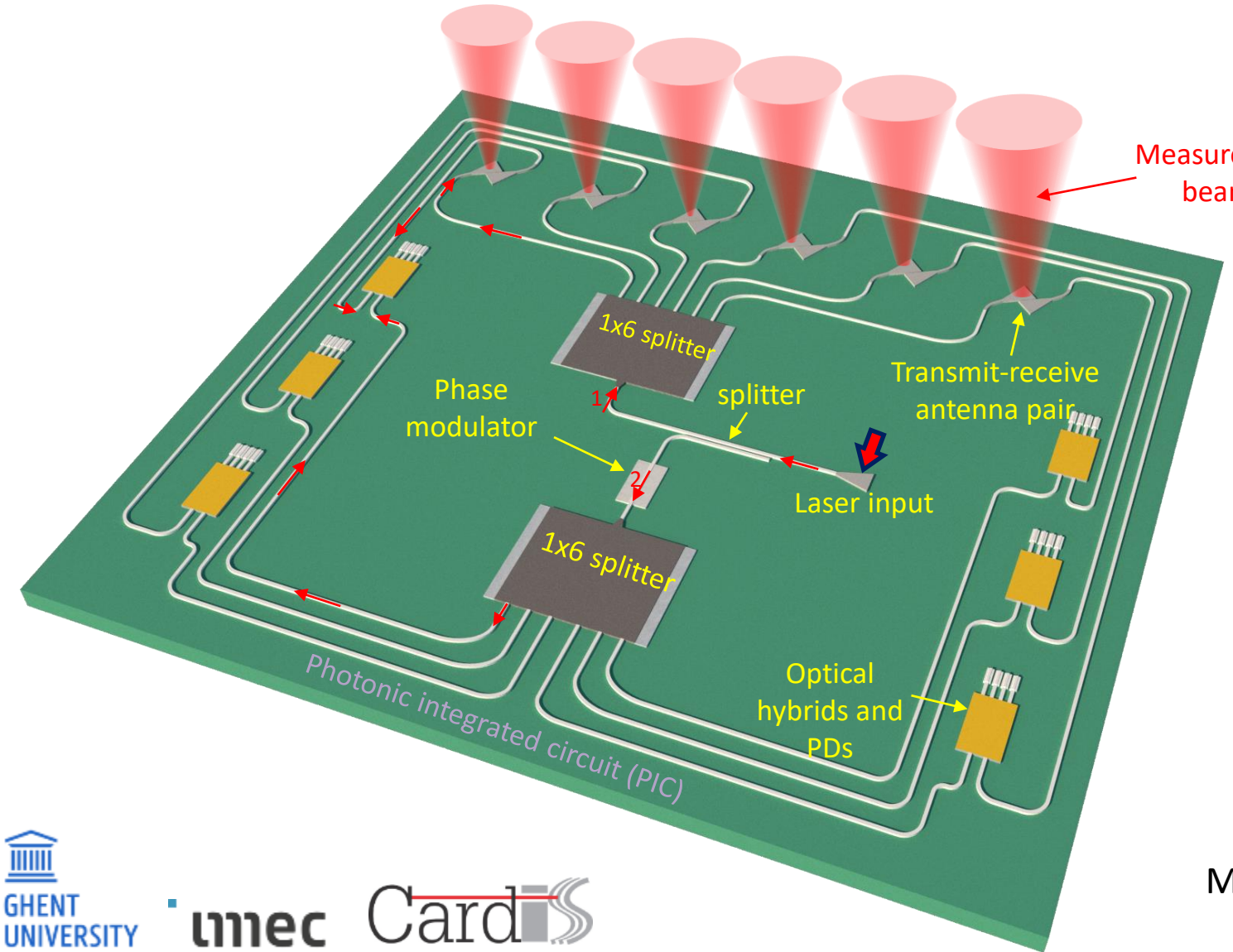


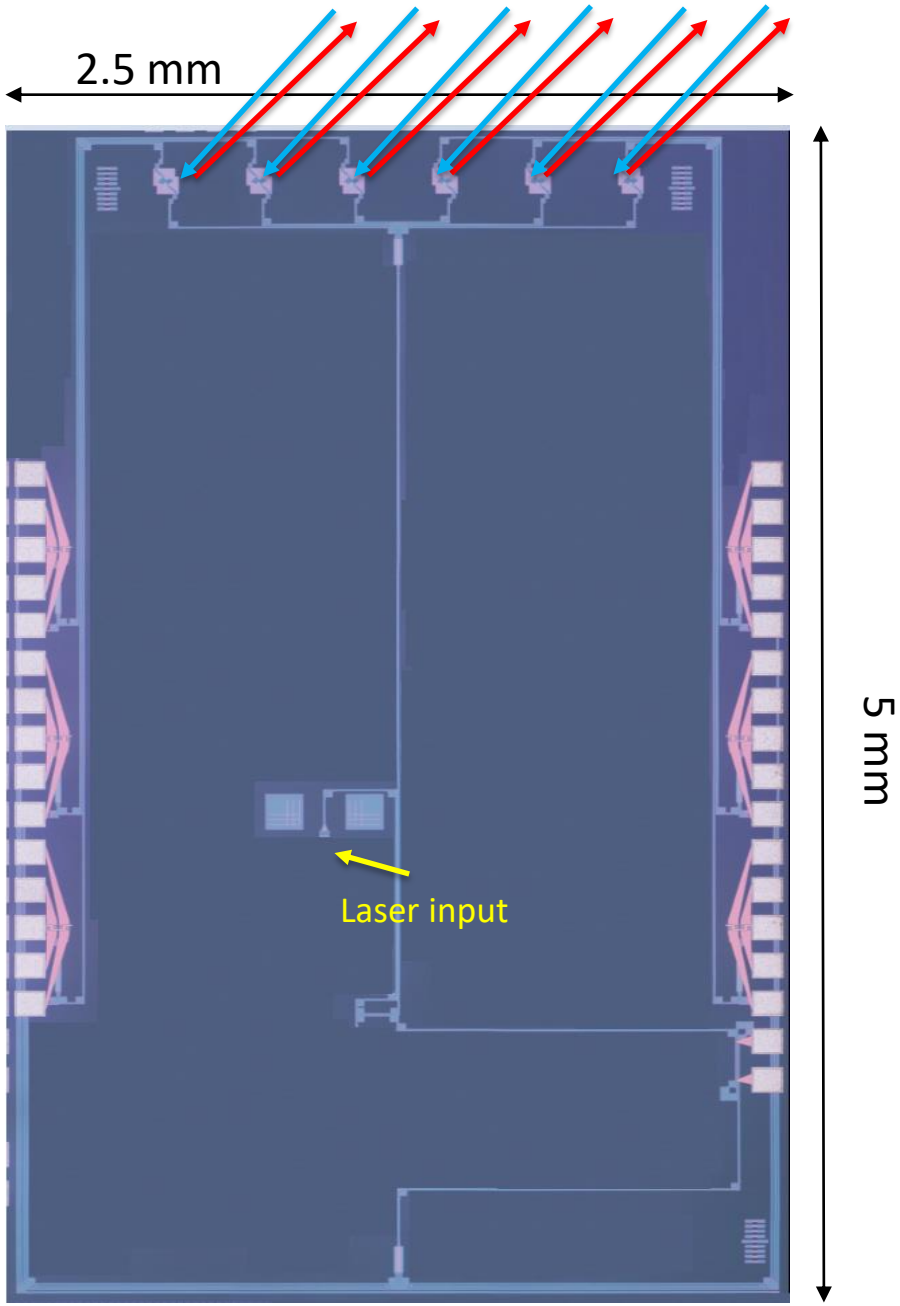


Demodulation method:

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

Realization of a six-beam LDV on silicon chip



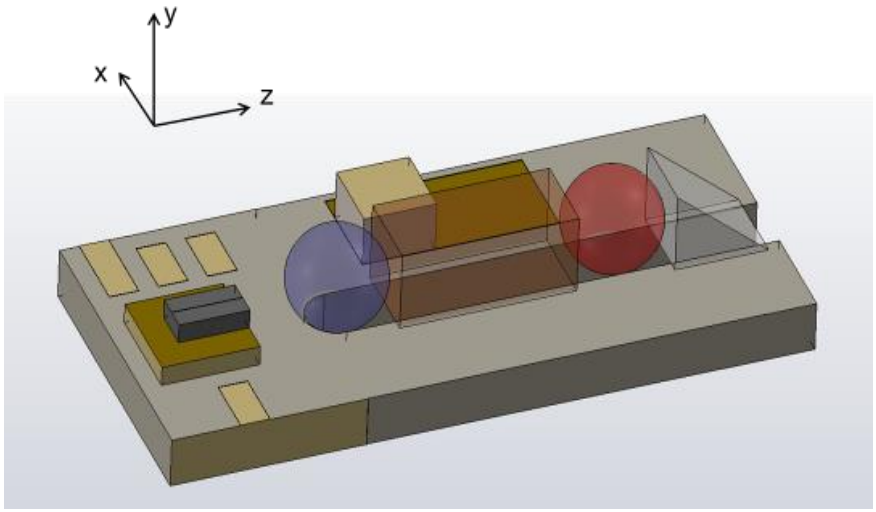


Microscope image of the photonic integrated circuit (PIC) in a silicon-on-insulator platform

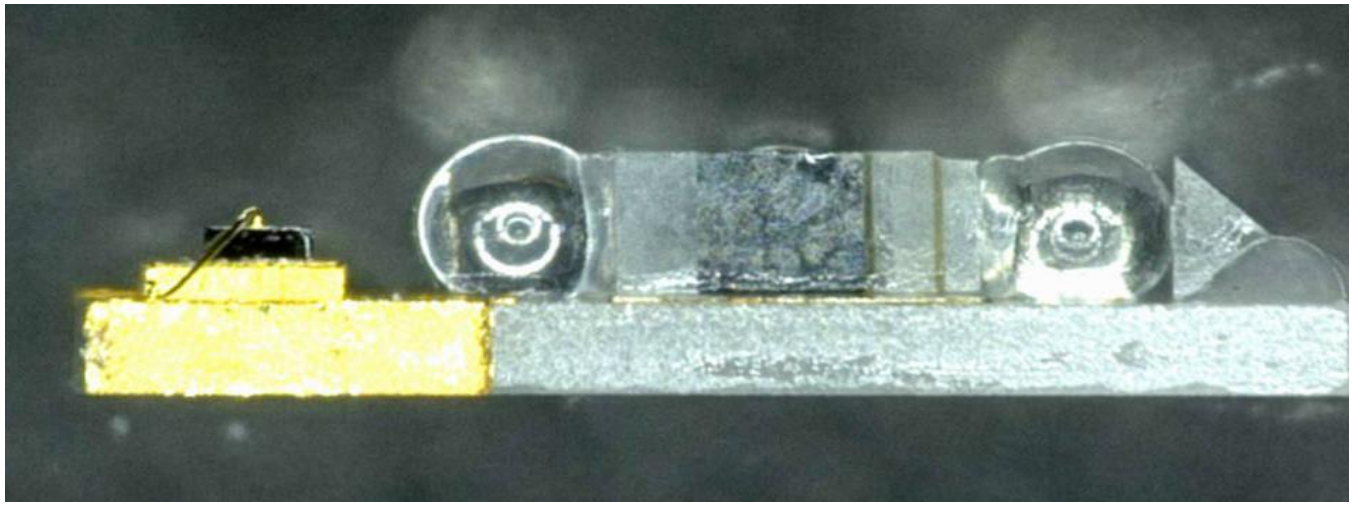
GHENT UNIVERSITY imec CardiS

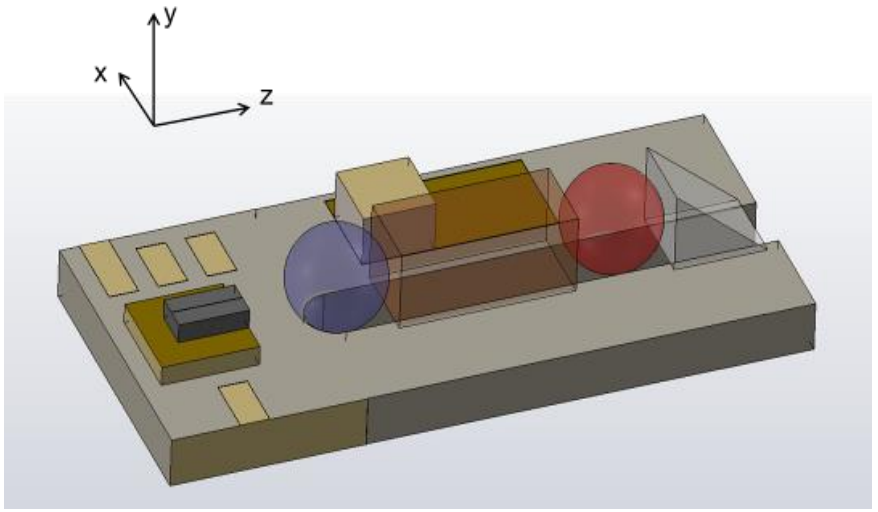
PHOTONIC INTEGRATED CIRCUITS (PICS)

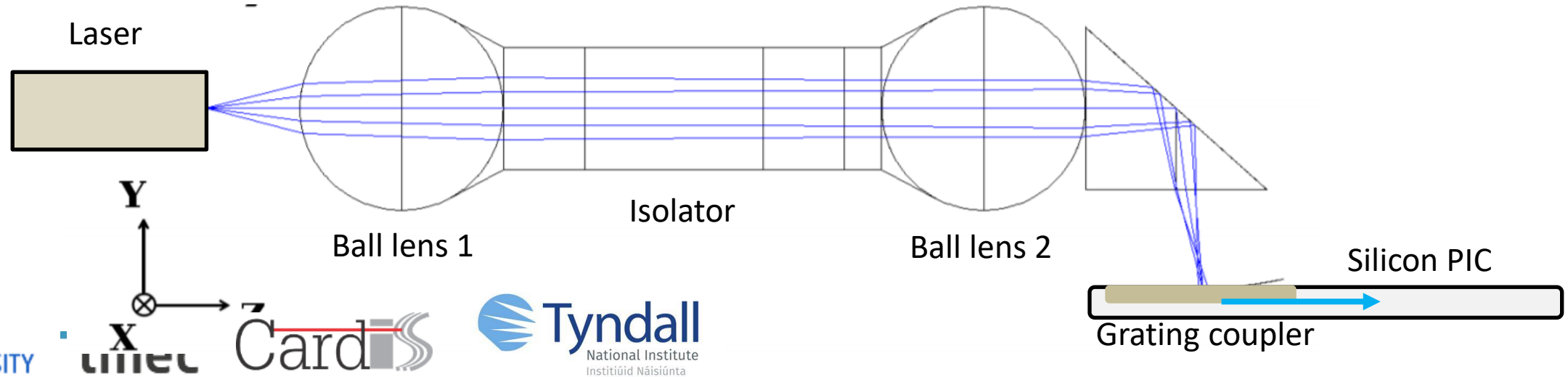
- PICs fabricated through Europractice MPW-service
- iSiPP50G SOI process at imec
- Laser diode is mounted on a Micro-Optic Bench (MOB) which is attached to the PIC



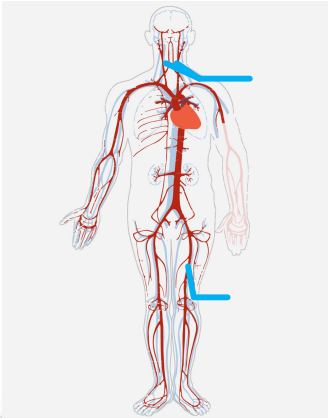
Hybrid laser integration: Micro-optic bench approach

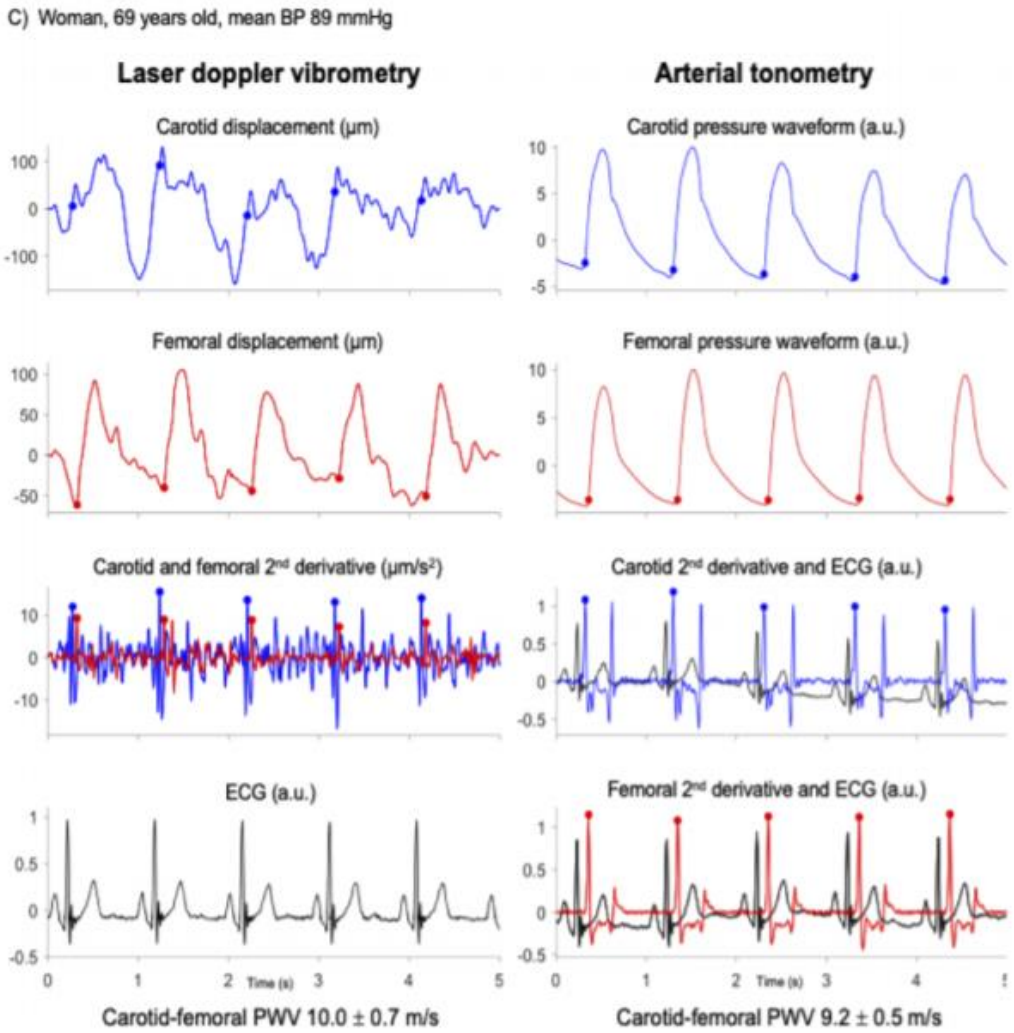


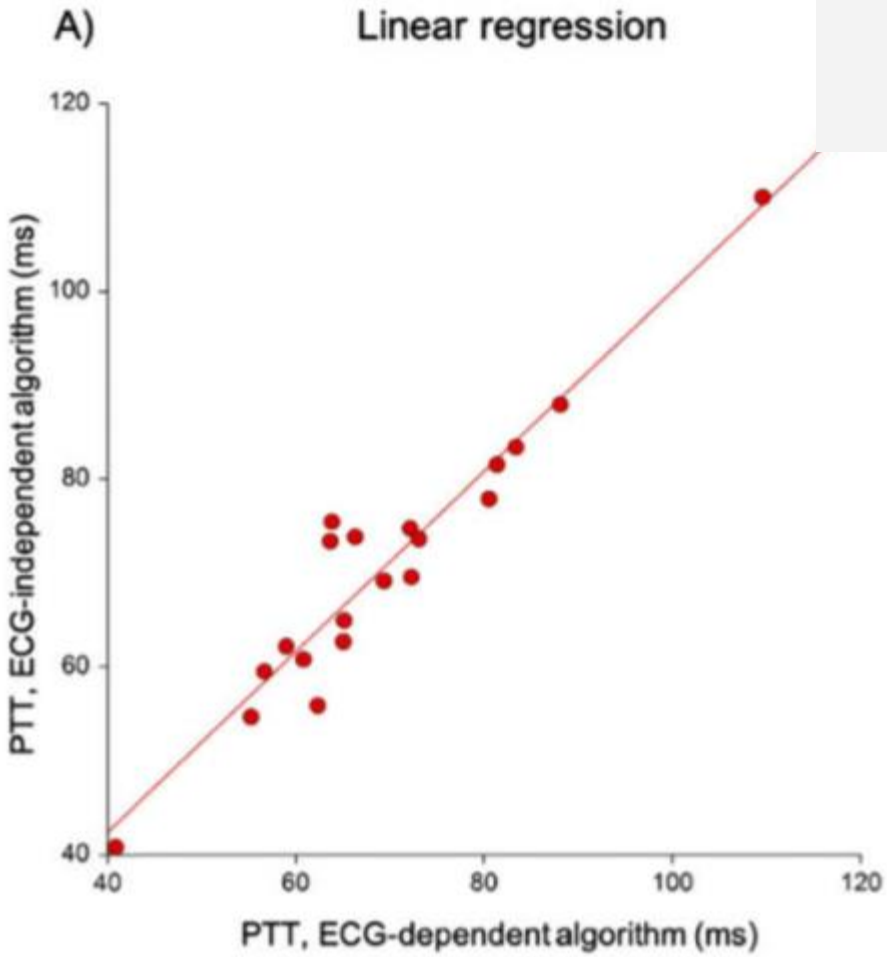




Carotid-femoral Pulse Wave Velocity Measurement







Y. Li 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 demonstration and product development for:

- Continuous Glucose Monitoring

  absorption spectroscopy on a silicon chip

- Pulse Wave Velocity (PWV) measurement

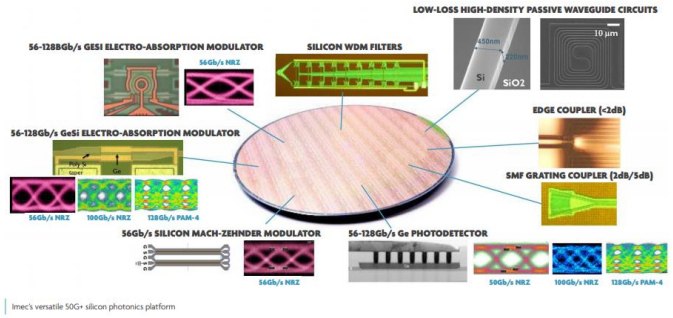
  multi-beam Laser Doppler Vibrometry enabled by a silicon chip

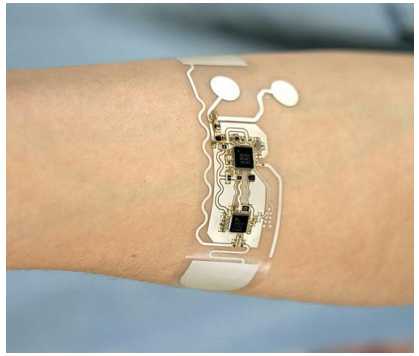
- Selective detection of medically relevant molecules

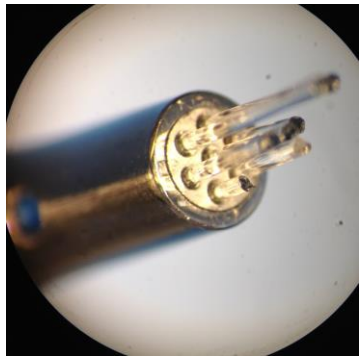
  Raman and absorption spectroscopy on a chip

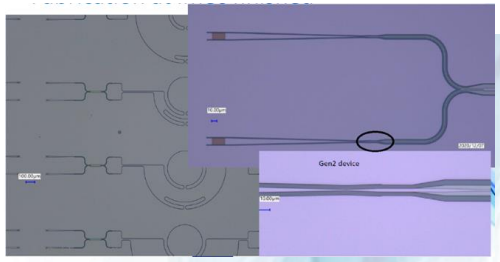
MedPhab: Pilot Line for Photonics-enabled Medical Devices

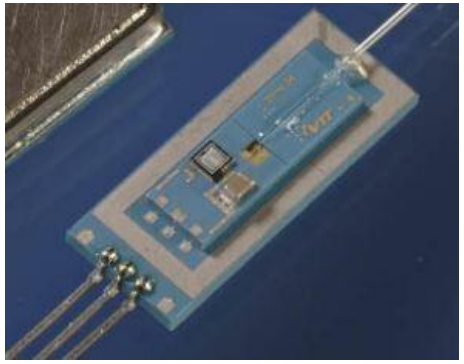
MedPhab
Photonic Medical Devices

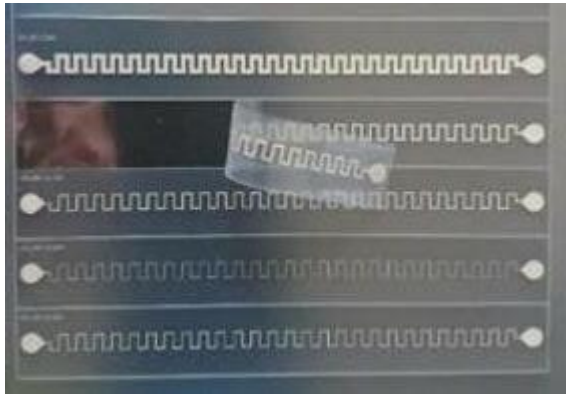


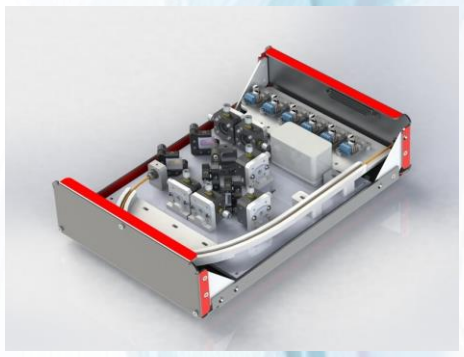












- MedPhab supports companies in medical device innovation
- with best-in-class advanced photonic technologies
- Call for **Demo-case project proposals call** is open
- Check out https://medphab.eu/open-call/

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