

PHOTONICS RESEARCH GROUP

TUTORIAL

SILICON-PHOTONICS-BASED SPECTROSCOPIC SENSING
FOR ENVIRONMENTAL MONITORING AND HEALTH CARERoel Baets
Ghent University and imec

Optical Fiber Conference (OFC) 2021

Online presentation

Paper control number: 3469069



1

ABSTRACT

Spectroscopic sensing is a powerful modality for numerous applications in medicine, biotechnology and structural health monitoring. Often the implementation is bulky or costly, which is a barrier for high volume markets. Integrated photonics - in particular silicon and silicon nitride photonics - is changing this and will boost spectroscopic sensing to such markets, for example in personalized medicine. This tutorial will discuss underlying principles, technologies and application cases.

Acknowledgements:

Photonics Research Group, Ghent University – imec

imec: SOI and SiN PIC manufacturing platforms

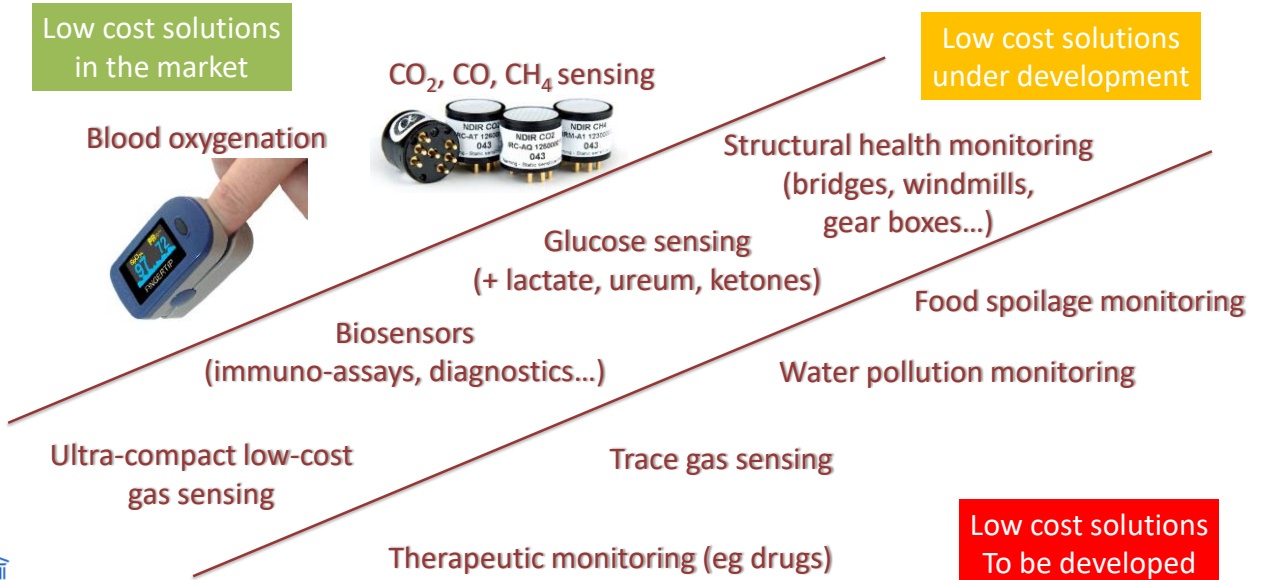
ePIXfab, European Silicon Photonics Alliance

Funding by European Commission (H2020 and ERC), FWO, Methusalem-program



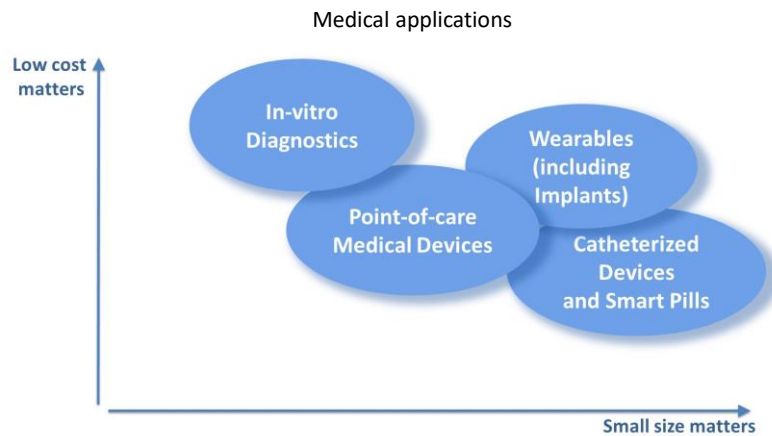
2

SPECTROSCOPIC SENSING: VAST APPLICATION SPACE



WHY MOVE TO MORE INTEGRATED SOLUTIONS USING SILICON PHOTONICS?

- Low cost in volume
- Mature technology and supply chain
- Extreme miniaturization



OUTLINE

- ➔ Brief introduction to silicon and silicon nitride PICs
 - Spectroscopic sensing modalities
 - On-chip spectrometers
 - On-chip tunable lasers
 - On-chip Raman spectroscopy
 - Application cases

WHAT IS SILICON PHOTONICS?

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

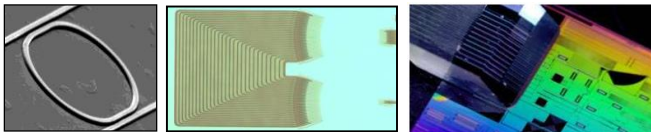
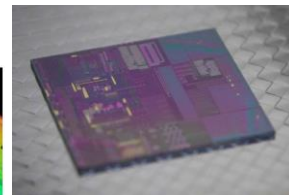
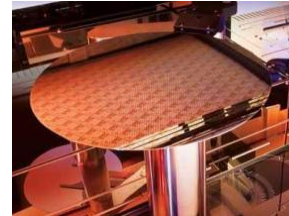
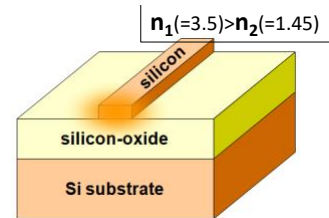


Pictures, courtesy of imec

Enabling complex optical functionality on a compact chip at low cost

WHY SILICON PHOTONICS

- High index contrast \Rightarrow **very compact PICs**
- CMOS technology \Rightarrow **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?)



CHIP COST IN A CMOS FAB (ORDER OF MAGNITUDE)

	Simple/small chip	Complex/large chip
Very low volume (MPW) (~ 100-1000 chips per year)	100€	1000€
Low volume (<10K chips per year)	10€	100€
Moderate volume (10K – 1M chips per year)	3€	30€
High volume (>1M chips per year)	1€	10€

In high volume, the chip is “for free”

Even in moderate volume the cost per chip is low

Even in low volume the chip has a high value for money

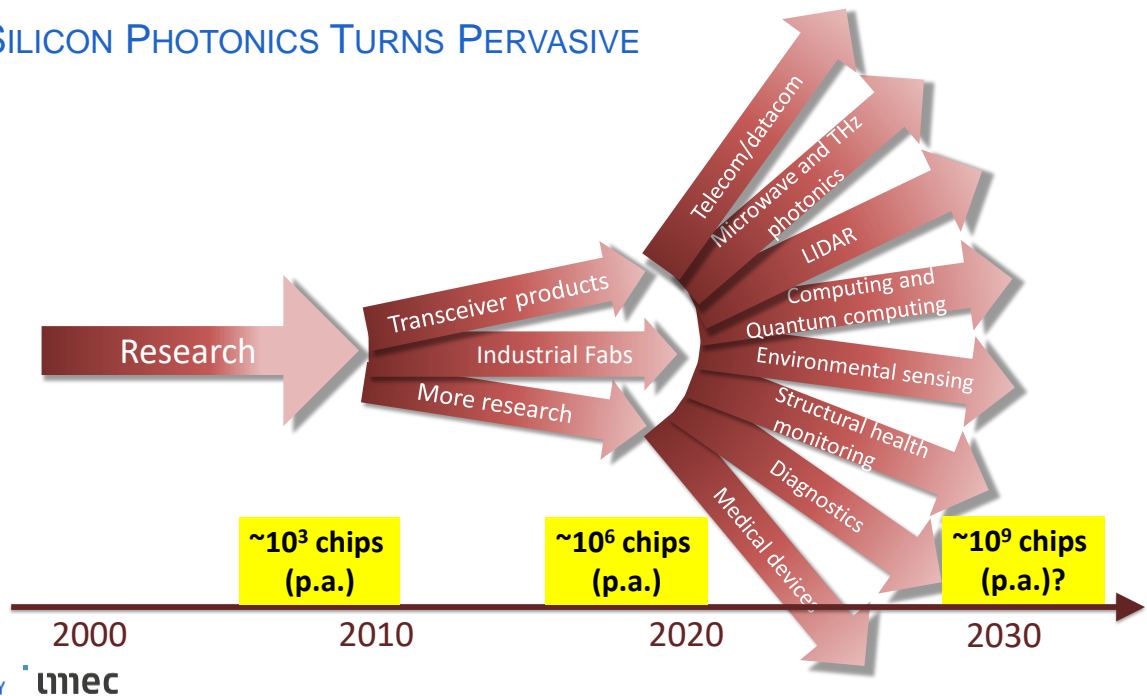
TRANSCEIVERS FOR DATA CENTERS AND FOR TELECOM



Under development:
Data rate: 800 Gb/s
Symbol rate: 100 Gbaud

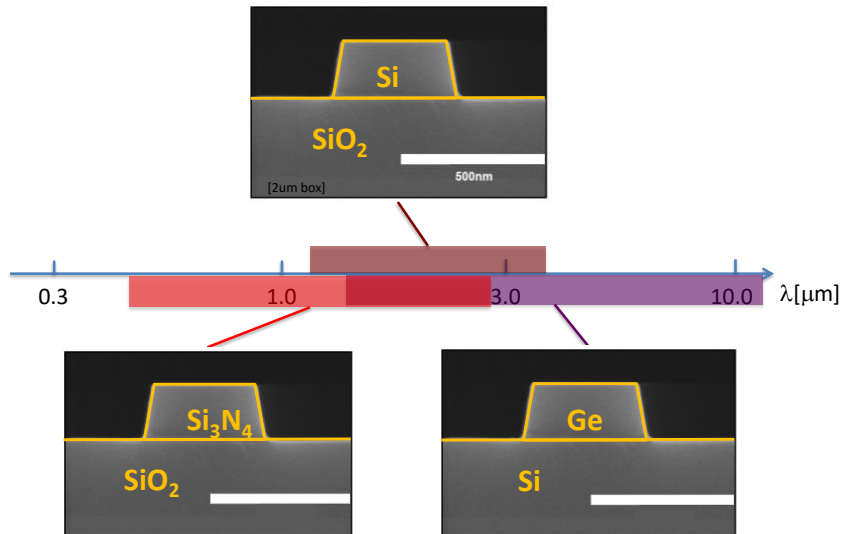
- Typical data rate: 100-400 Gb/s**
Typical symbol rate: 25-50 GBaud
- PSM4 (4 parallel fibers)
 - WDM (4 wavelengths)
 - PAM4
 - Coherent (2 polarisations + QPSK)
 - Coherent (16-QAM)

SILICON PHOTONICS TURNS PERVASIVE



SILICON PHOTONICS: EXTENDING THE WAVELENGTH RANGE

WITHOUT LEAVING THE CMOS FAB



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

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

OUTLINE

Brief introduction to silicon and silicon nitride PICs

➡ Spectroscopic sensing modalities

On-chip spectrometers

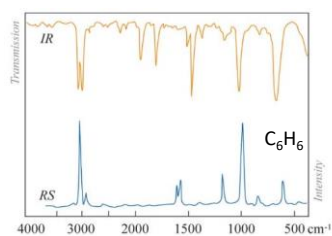
On-chip tunable lasers

On-chip Raman spectroscopy

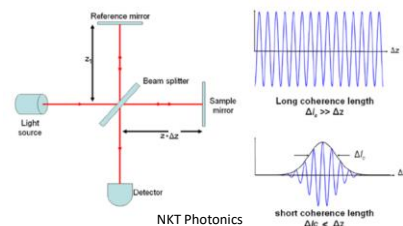
Application cases

SENSING MODALITIES

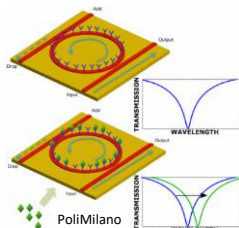
Vibrational spectroscopy (absorption, Raman)



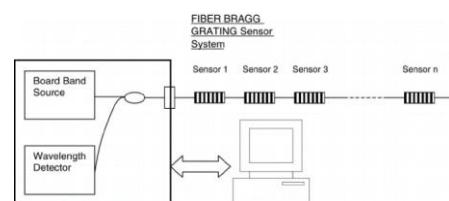
3D imaging (Lidar, OCT, LDV)



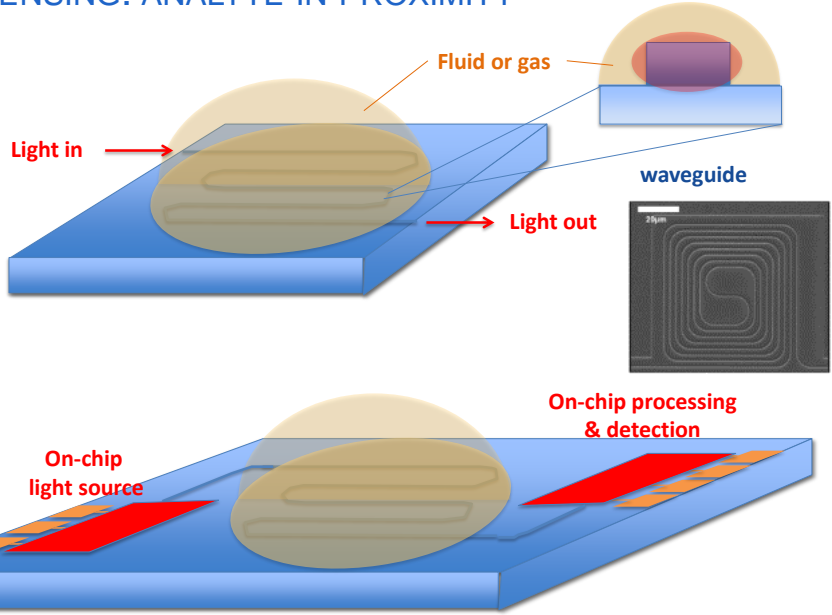
Refractive index sensing (biosensing, gas sensing)



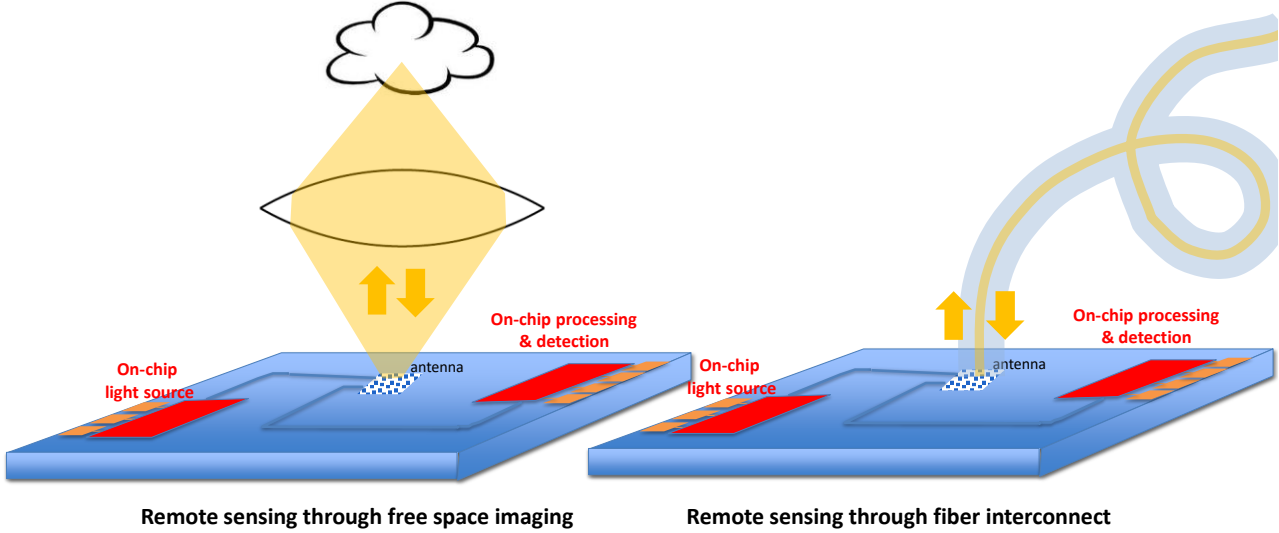
Fiber sensor readout (FBG, Brillouin, Raman)



NEAR FIELD SENSING: ANALYTE IN PROXIMITY

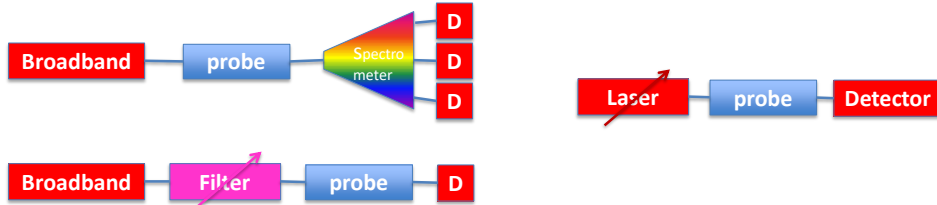


FAR-FIELD SENSING: SENSED AREA IS REMOTE

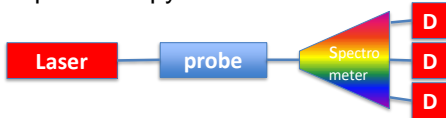


SPECTROSCOPY-ON-CHIP: APPROACHES

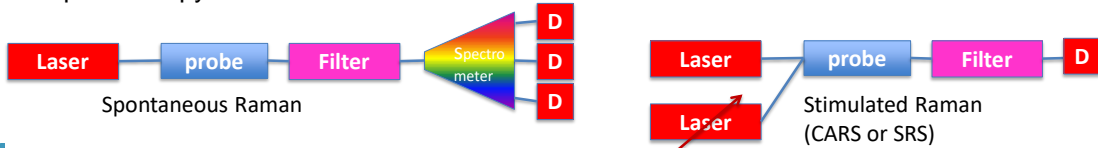
Absorption spectroscopy



Fluorescence spectroscopy



Raman spectroscopy



SPECTROSCOPY-ON-CHIP: APPROACHES

Absorption spectroscopy (eg Tunable Diode Laser Absorption Spectroscopy = TDLAS)



$$T(\lambda) = e^{-(\alpha(\lambda) + \alpha_s)L}$$

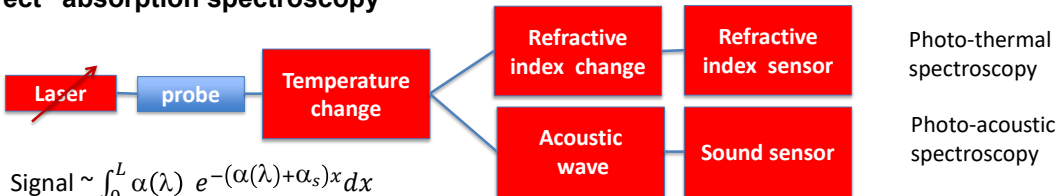
$$dT/d\alpha \text{ max when } (\alpha(\lambda) + \alpha_s)L = 1$$



Optimal (total) loss: 4.3 dB

When $\alpha_{tot}L \ll 1$: signal $\sim 1 - \alpha_{tot}L$

“Indirect” absorption spectroscopy



$$\text{Signal} \sim \int_0^L \alpha(\lambda) e^{-(\alpha(\lambda) + \alpha_s)x} dx$$



No optical detector

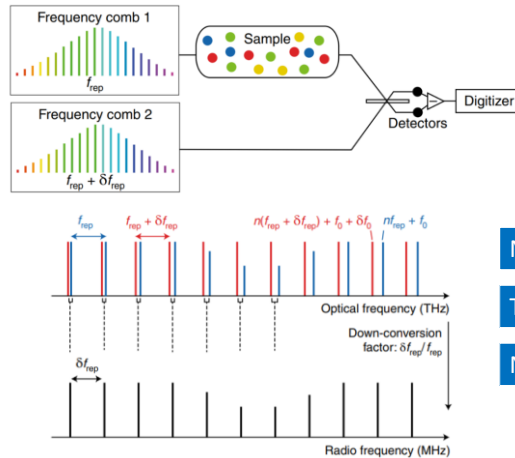
When $\alpha_{tot}L \ll 1$: signal $\sim \alpha(\lambda)L$

DUAL COMB ABSORPTION SPECTROSCOPY

REVIEW ARTICLE | FOCUS nature
photonics
<https://doi.org/10.1038/s41966-018-0347-5>

Frequency comb spectroscopy

Nathalie Picqué^{1*} and Theodor W. Hänsch^{1,2}



No need for laser tuning

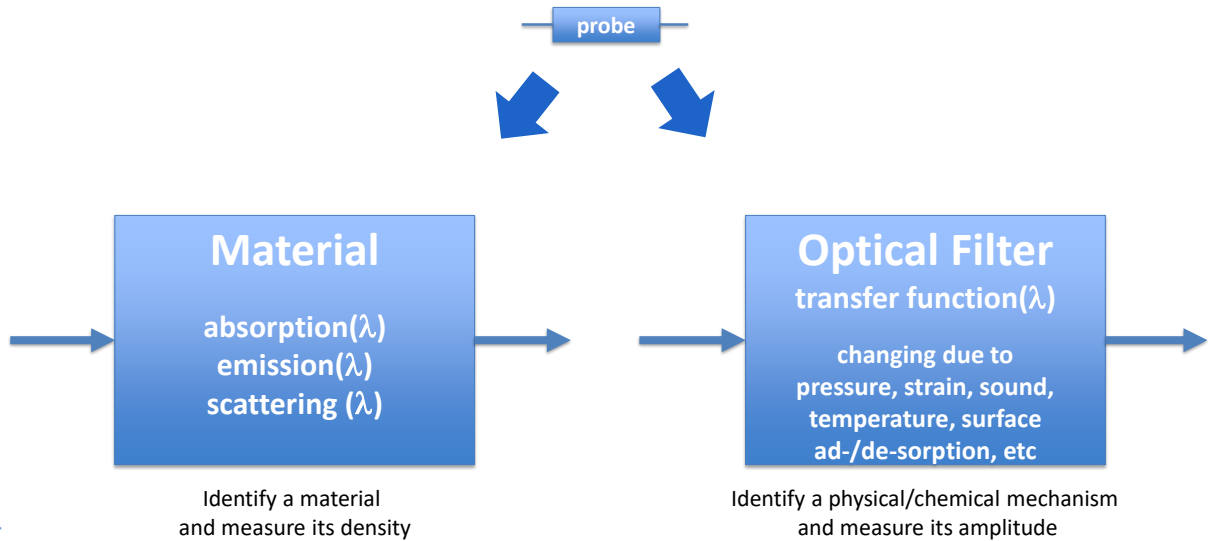
Translation of optical spectrum to RF spectrum

Need for high speed detectors


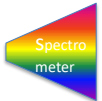




WHAT IF ABSORPTION IS WEAK?

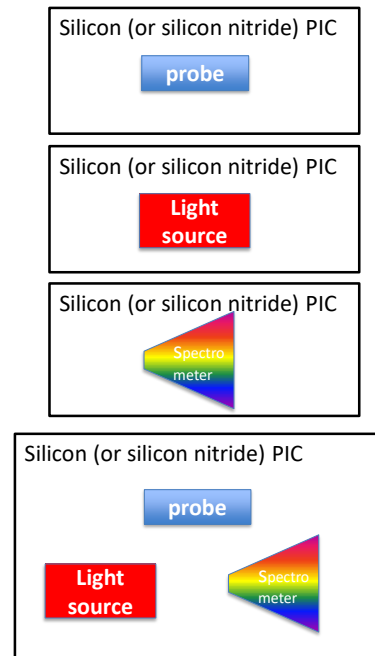
- increase path length
 - spirals on chip
 - on-chip integrating sphere
 - resonant optical device
- (non-optical) resonant signal enhancement of modulated signals
- densification of analyte
 - adsorption to waveguide surface
 - adsorption in a mesoporous coating covering waveguide

PROBE



KEY COMPONENTS NEEDED

-  Probe on-chip
-  Integrated spectrometer
-  Integrated broadband source
-  Integrated laser
-  Integrated tunable laser
-  Integrated comb source



OUTLINE

Brief introduction to silicon and silicon nitride PICs

Spectroscopic sensing modalities

➔ On-chip spectrometers

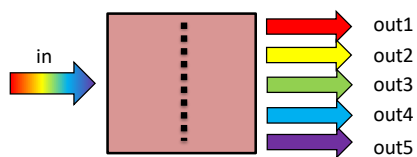
On-chip tunable lasers

On-chip Raman spectroscopy

Application cases

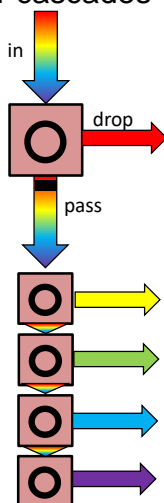
SPECTROMETERS

Dispersive devices



Mechanism used: grating diffraction
(multi-beam interference)

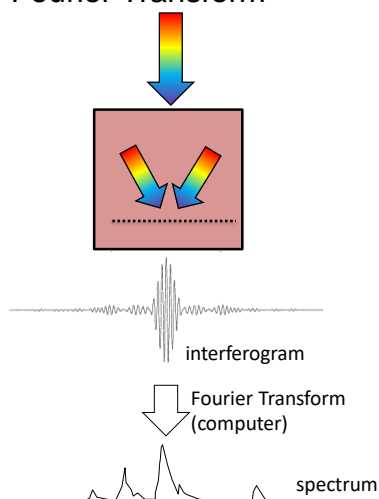
Filter cascades



Mechanism used: resonance
or interference or Bragg reflection

And Combinations!

Fourier Transform



Mechanism used: two-beam interference

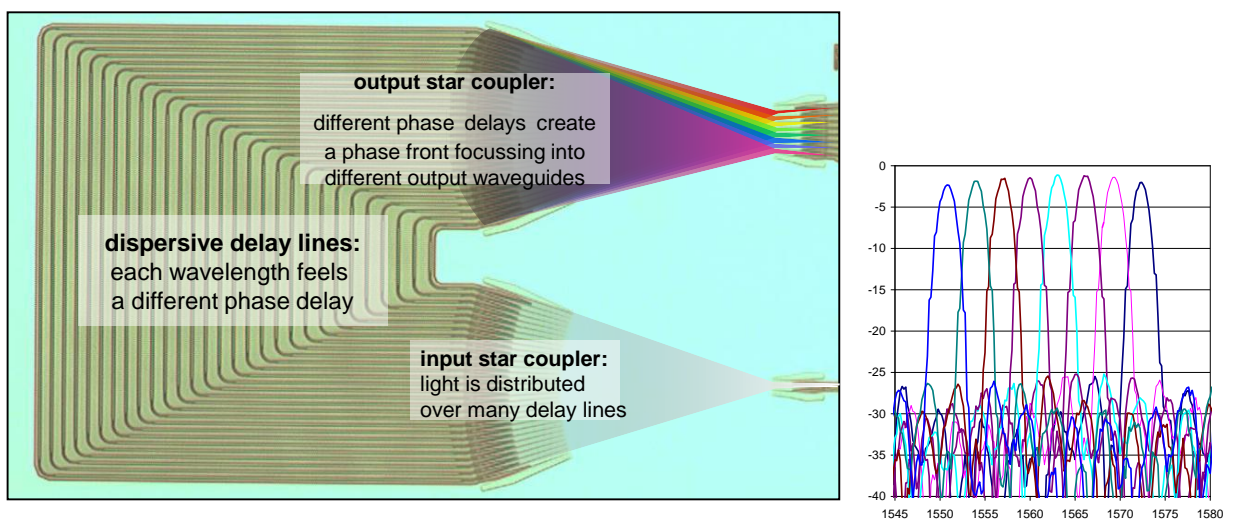
FIGURES OF MERIT

- Spectral resolution (channel spacing)
- Overall bandwidth (Free Spectral Range)
- Crosstalk and dynamic range
- Absolute wavelength accuracy
- Polarisation sensitivity
- Chip area needed
- Sensitivity to fabrication error
- Sensitivity to temperature
- Complexity of design



Many solutions
depending on
application
context

ARRAYED WAVEGUIDE GRATING (AWG) SPECTROMETER (200 x 350 μm^2)



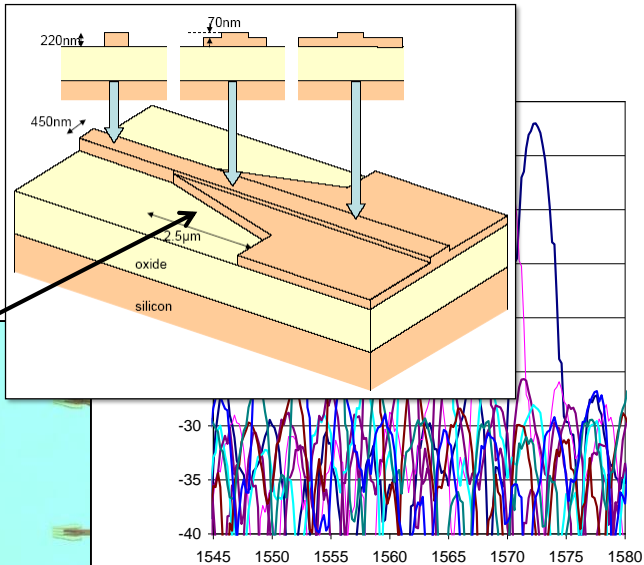
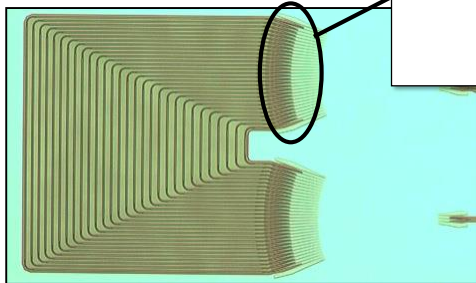
ARRAYED WAVEGUIDE GRATING

8-channel, 400GHz

FSR = 30nm

footprint = 200 x 350 μm^2

- -25 dB crosstalk level
- -1 dB insertion loss (center channel)
- 1.5 dB non-uniformity



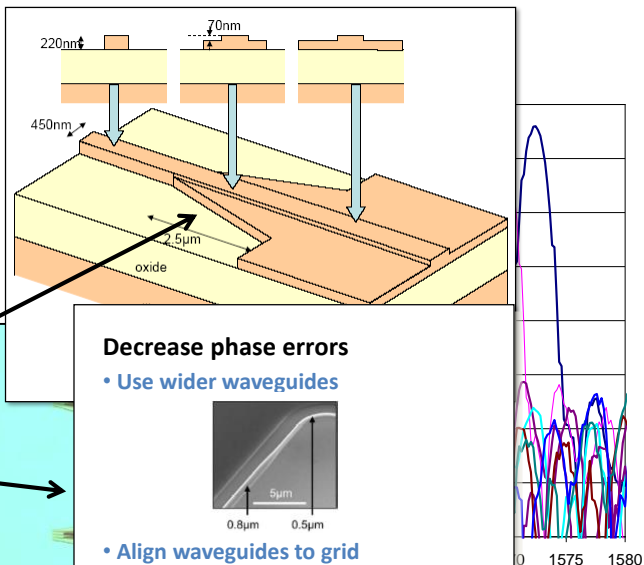
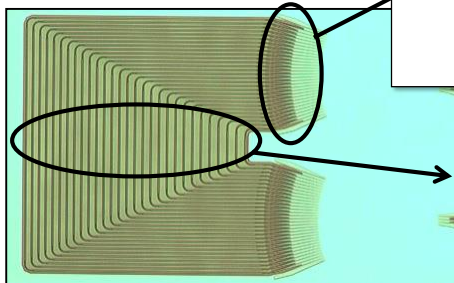
ARRAYED WAVEGUIDE GRATING DESIGN

8-channel, 400GHz

FSR = 30nm

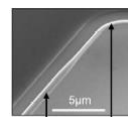
footprint = 200 x 350 μm^2

- -25 dB crosstalk level
- -1 dB insertion loss (center channel)
- 1.5 dB non-uniformity



Decrease phase errors

- Use wider waveguides



- Align waveguides to grid

• See also: *P. Dumon, PhD thesis UGent 2007*
S. Selvaraja, PhD thesis UGent 2014
<http://photonics.intec.ugent.be>

S-shaped AWG for IEEE 400GBase-LR8



AWG Generation

Simulation & Analysis

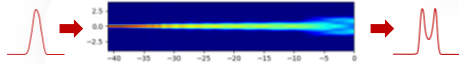
Finalization

Specifications

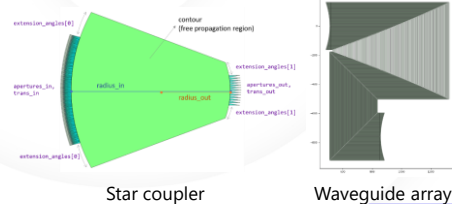


Subcomponents & Synthesis

MMI aperture



Assembly

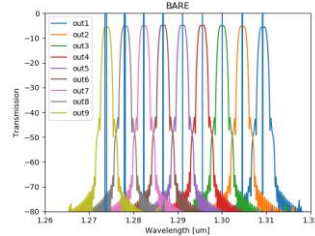


Star coupler

Waveguide array



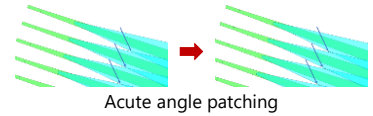
Simulation



Analysis

- Peaks
- Crosstalk
- Insertion loss
- Nearest-neighbour crosstalk

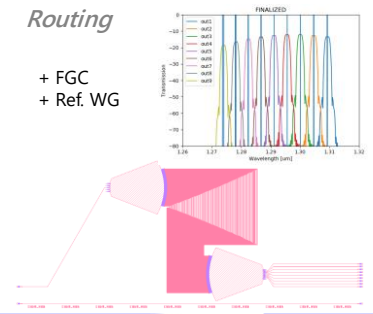
Tape-out prep



Acute angle patching

Routing

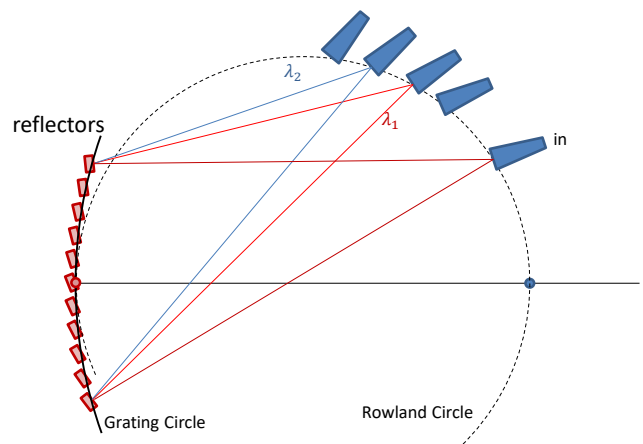
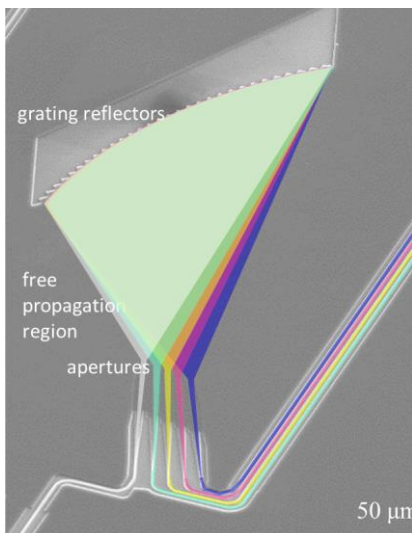
- + FGC
- + Ref. WG



Take control of your photonics design flow

31

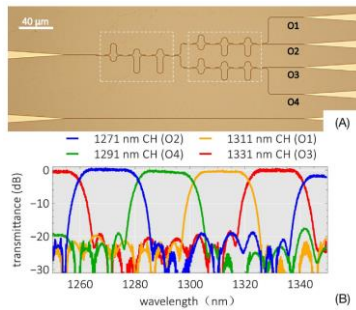
ECHELLE DIFFRACTION GRATINGS (EDG) AKA PLANAR CONCAVE GRATING (PCG)



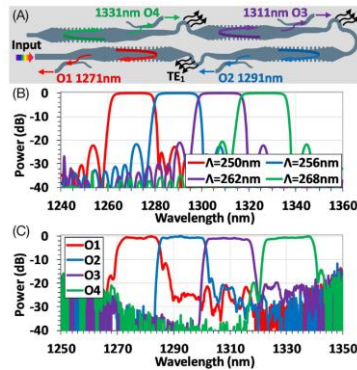
32

FILTER CASCADES

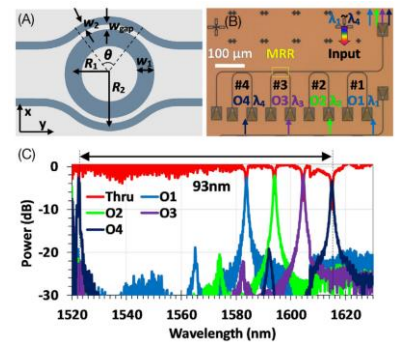
Mach-Zehnder Interferometers (MZI)



Distributed Bragg Reflectors (DBR)



Micro Ring Resonators (MRR)



REVIEWS OF SILICON MICRO RING RESONATORS

Laser Photonics Rev. 6, No. 1, 47–73 (2012) / DOI 10.1002/lpor.201100017

Silicon microring resonators

Wim Bogaerts*, Peter De Heyn, Thomas Van Vaerenbergh, Katrien De Vos, Shankar Kumar Selvaraja, Tom Claes, Pieter Dumon, Peter Bienstman, Dries Van Thourhout, and Roel Baets

IEEE JOURNAL OF SELECTED TOPICS IN QUANTUM ELECTRONICS, VOL. 24, NO. 6, NOVEMBER/DECEMBER 2018

5900324

Integrated Silicon Photonic Microresonators: Emerging Technologies

Zhanshi Yao, Kaiyi Wu, Bo Xue Tan, Jiawei Wang, Yu Li, Yu Zhang, and Andrew W. Poon, Member, IEEE

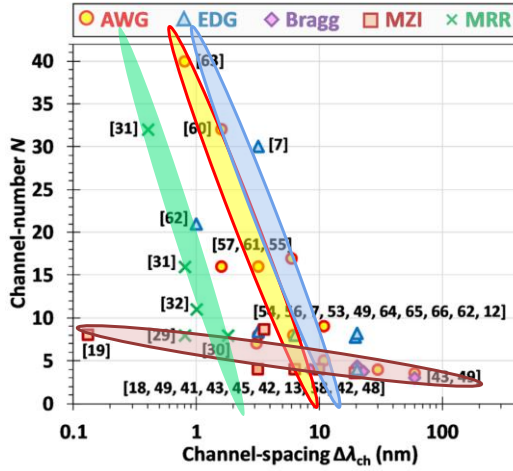
IEEE JOURNAL OF SELECTED TOPICS IN QUANTUM ELECTRONICS, VOL. 26, NO. 2, MARCH/APRIL 2020

8200810

Statistical Behavioral Models of Silicon Ring Resonators at a Commercial CMOS Foundry

Peng Sun, Jared Hulme, Thomas Van Vaerenbergh, Jinsoo Rhim, Charles Baudot, Frederic Boeuf, Nathalie Vulliet, Ashkan Seyedi, Marco Fiorentino, and Raymond G. Beausoleil

COMPARISONS: CHANNEL # AND SPACING IN SOI-BASED SPECTROMETERS



Received: 5 January 2020
DOI: 10.1002/mop.32509

REVIEW

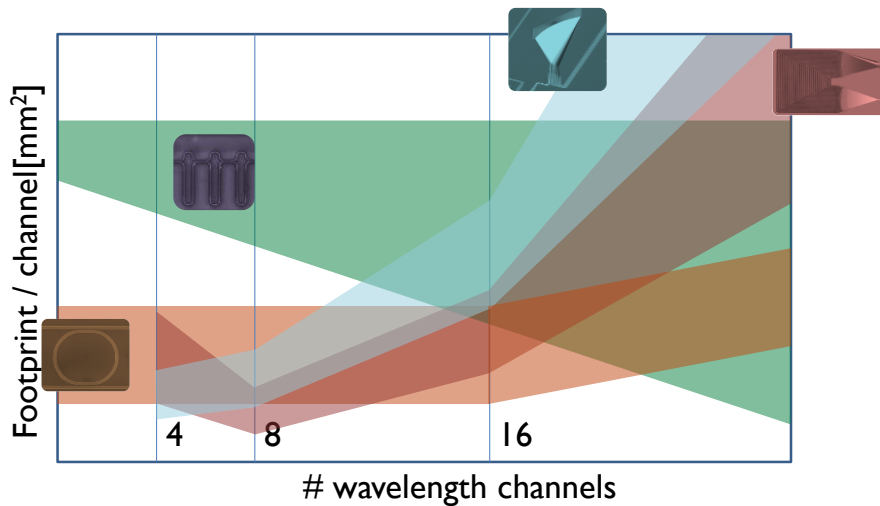
Silicon photonic filters

Dajian Liu^{1,2} | Hongnan Xu^{1,2} |
Ying Tan^{1,2} | Yaocheng Shi^{1,2} |
Daoxin Dai^{1,2}

¹Center for Optical and Electromagnetic Research, State Key Laboratory for Modern Optical Instrumentation, International Research Center for Advanced Photonics (Haining), Zhejiang University, Hangzhou, China
²Ningbo Research Institute, Zhejiang University, Ningbo, China

D. Liu et al, Microw. Opt. Techn. Lett. 2020
<https://doi.org/10.1002/mop.32509>

COMPARISONS: FOOTPRINT OF SOI-BASED SPECTROMETERS



W. Bogaerts et al, Proc. SPIE 9365 (2015) doi:10.1117/12.2082785

COMPARISONS: AWGs AND EDG (PCG) ACROSS PLATFORMS

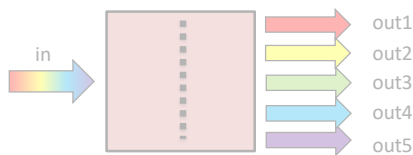
Table 1. Performance Comparison between AWGs and PCGs Across Different Platforms

Device/Technology	Central Wavelength (μm)	Footprint (μm^2)	No. of Channels/Channel Spacing (nm)	FSR (nm)	Insertion Loss (dB)	Crosstalk (dB)
AWG/SOI [38]	1.55	530×435	16/3.2	57.6	<3.0	>25.0
AWG/ Si_3N_4 [41]	0.89	450×750	12/2.0	30	<1.5	20.0
AWG/Ge-on-Si [42]	5.3	1000×1000	5/19.0	148	2.5	20
S-AWG/SOI [36]	1.55	305×260	4/30	144	<2	19
PCG/SOI [36]	1.55	700×385	8/6.5	100	<1.5	<20
PCG/SOI [44]	3.8	1800×1700	8/10	105	<2	<20
PCG/Ge-on-Si [45]	5.0	1500×1200	6/25	170	<5	22

A. Subramanian et al, *Photonics Research* (2015) [doi:10.1364/PRJ.3.000B47](https://doi.org/10.1364/PRJ.3.000B47)

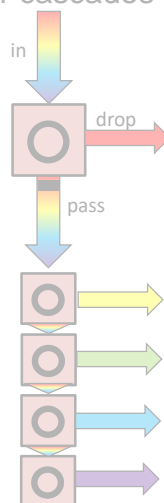
SPECTROMETERS

Dispersive devices



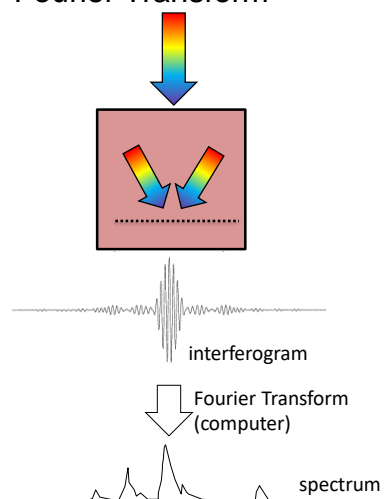
Mechanism used: grating diffraction (multi-beam interference)

Filter cascades



Mechanism used: resonance or interference or Bragg reflection

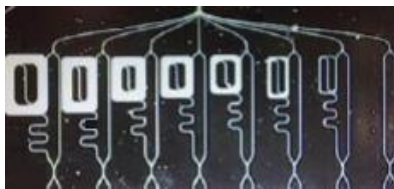
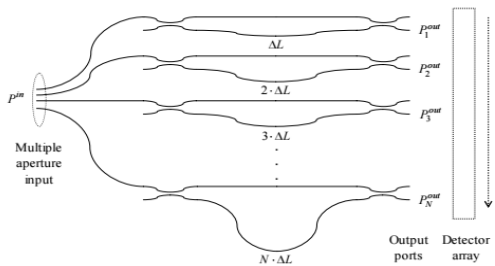
Fourier Transform



Mechanism used: two-beam interference

SPATIAL HETERODYNE SPECTROMETERS (SHS)

Set of parallel MZIs with increasing pathlength difference



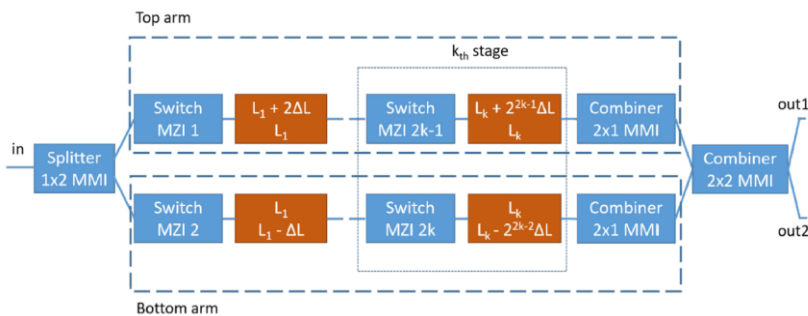
Bandwidth: 0.184 nm
Resolution: 0.023 nm

SHS:

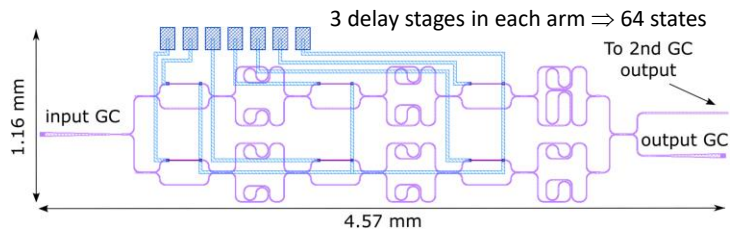
- Interferogram is created by an array of waveguide MZI with increasing OPD, recorded by a detector array.
- Bandwidth limited by FSR of MZI
- Number of MZI channels: $N = \frac{2\Delta\lambda}{\delta\lambda}$
- Recent work:
 - SHS on CMOS compatible SiN platform (TriPlex™)
 - Resolution of 0.023nm, bandwidth 0.184nm at 1550nm requires area of 4mm × 8mm.

DIGITAL FOURIER TRANSFORM SPECTROMETER

Temporal switching of MZI pathlength difference

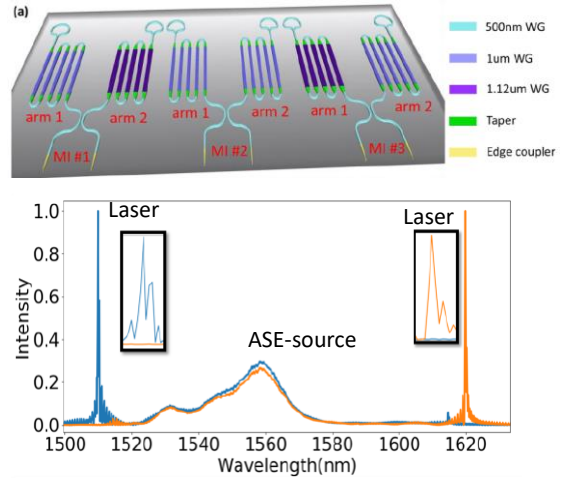
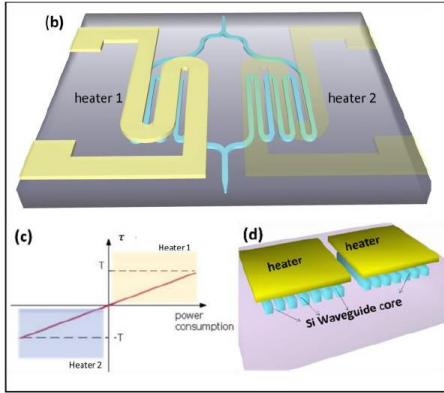


Bandwidth: 130 nm (around 2300 nm)
Resolution: 1.5 nm



TEMPORAL FOURIER-TRANSFORM SPECTROMETER

Temporal tuning of MZI pathlength difference



Bandwidth: > 130 nm
Resolution: 0.16 nm

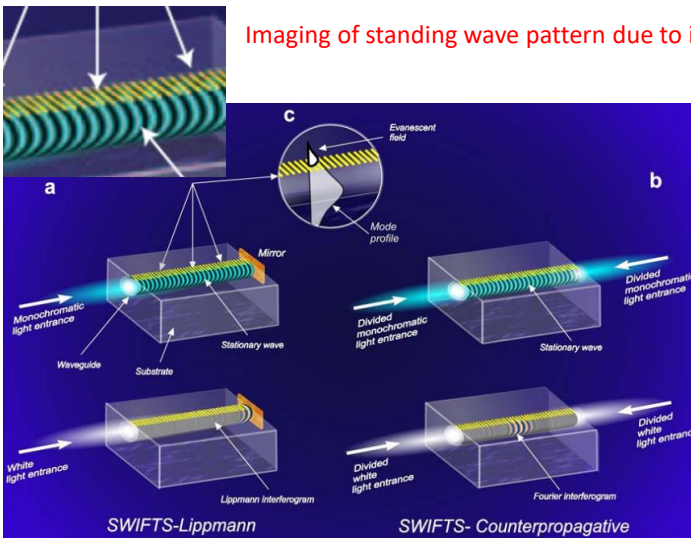
A. Li et al, *Lasers and Phot. Rev.* (2021) doi.org/10.1002/lpor.202000358

41



STATIONARY WAVE INTEGRATED FTS (SWIFTS)

Imaging of standing wave pattern due to interference of counterpropagating waves



SWIFTS:

- Interferogram created as an **optical standing wave**, is scattered by Nano-dots loaded on waveguide and recorded by a detector array.

- Increasing waveguide length (L) gives higher resolution: $\delta\lambda = \frac{\lambda^2}{n_{eff}L}$ [1]

- Operational bandwidth is limited by **subsampling**:

- Period of the interferogram = $\frac{\lambda}{2n_{eff}}$ \ll pixel pitch of commercially available detector array

Bandwidth: ~ 100 nm
Resolution: 4 nm

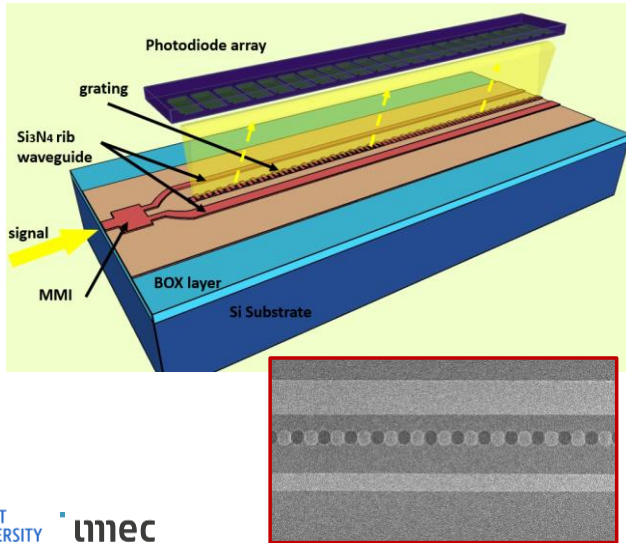
E. Le Coarer, et al. *Nature Photonics* (2007) [doi:10.1038/nphoton.2007.138](https://doi.org/10.1038/nphoton.2007.138)

42



CO-PROPAGATIVE STATIONARY FOURIER TRANSFORM SPECTROMETER

Imaging of standing wave pattern due to interference of co-propagating waves



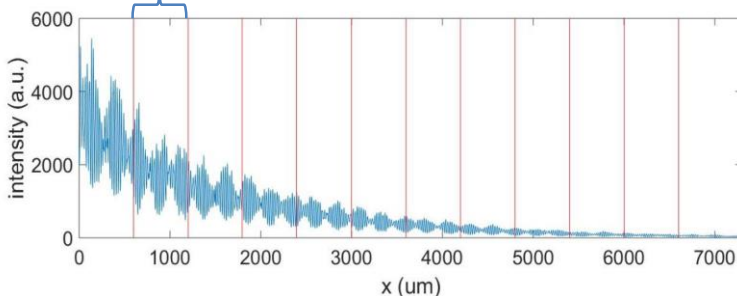
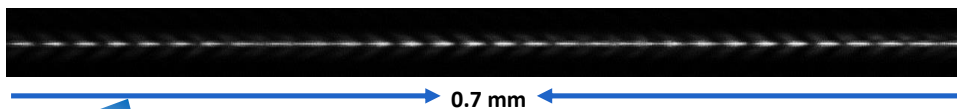
- Interferogram is created by the interference between the **evanescent fields of two waveguide modes propagating at different phase velocity** (due to waveguides with different width)
- Interferogram is diffracted by a grating towards a detector array .
- Subsampling is avoided → broadband operation:
 - Interferogram period = $\frac{\lambda}{\Delta n_{eff}}$
 - Increased by a factor $\frac{2n_{eff}}{\Delta n_{eff}}$ comparing with SWIFTS
- Still allows for moderately high resolution $\frac{\lambda^2}{\Delta n_{eff}L}$

X. Nie et al, Optics Express (2017) doi:10.1364/OE.25.00A409 43

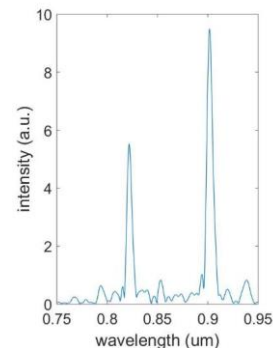


CO-PROPAGATIVE STATIONARY FOURIER TRANSFORM SPECTROMETER

Dual-wavelength injection:



Intensity of the complete interferogram (11 images stitched)



Fourier transform mapped to wavelength axis

Bandwidth: ~ 100 nm
Resolution: 6 nm

X. Nie et al, Optics Express (2017) doi:10.1364/OE.25.00A409 44



OUTLINE

Brief introduction to silicon and silicon nitride PICs

Spectroscopic sensing modalities

On-chip spectrometers

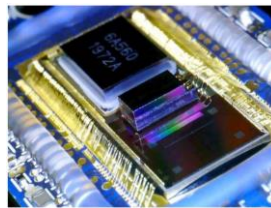
➔ On-chip tunable lasers

On-chip Raman spectroscopy

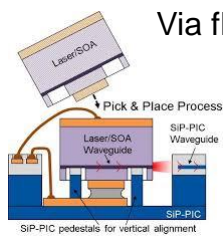
Application cases

HYBRID INTEGRATION OF III-V LIGHT SOURCES IN SILICON PIC

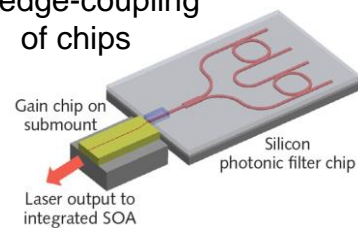
Via a micro-optic bench



Via flip-chip



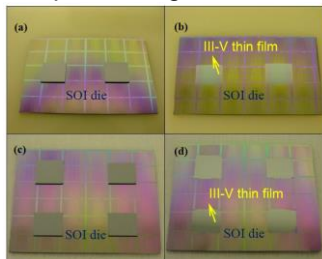
Via edge-coupling of chips



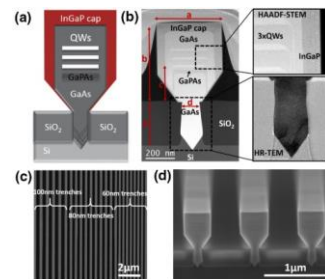
WAFER-LEVEL HETEROGENEOUS INTEGRATION OF III-V LIGHT SOURCES ON SILICON PIC

die-to-wafer bonding

(III-V processing after bonding)

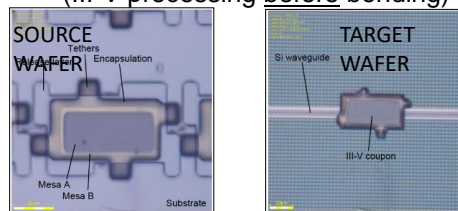


III-V epitaxy on silicon

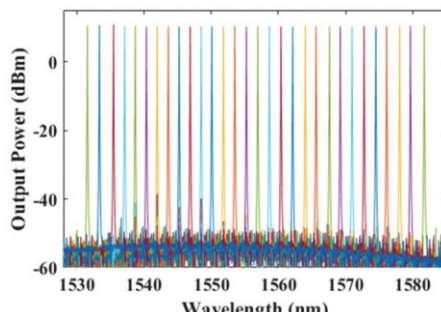
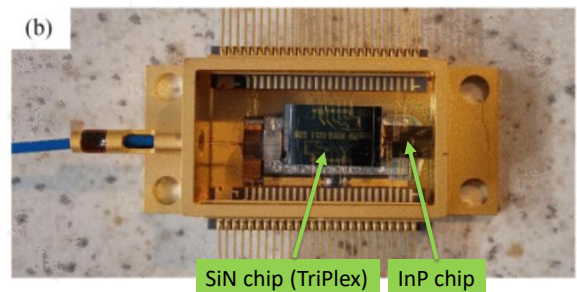
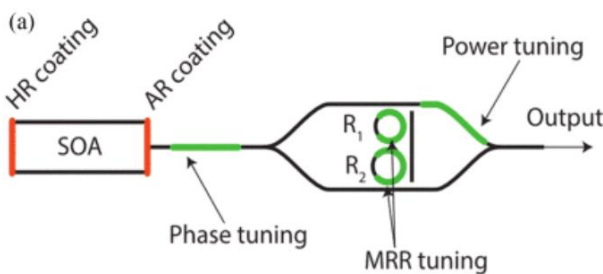


micro transfer printing

(III-V processing before bonding)

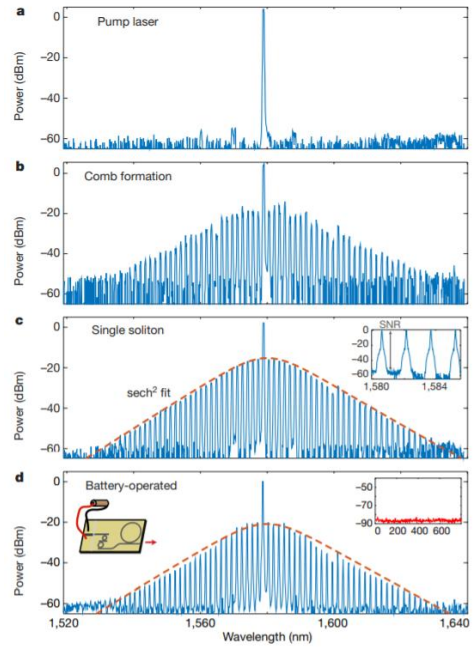
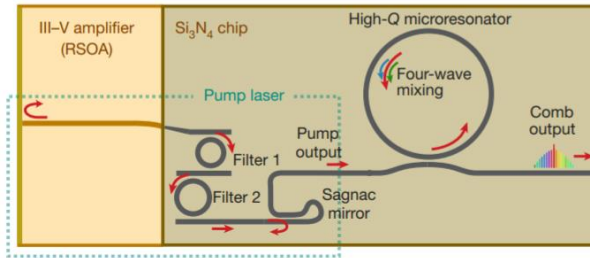


HYBRID INTEGRATION OF INP RSOA AND SIN PIC FOR WIDELY TUNABLE C-BAND LASER



Y. Lin et al, IEEE Phot. Journ. (2018)
[10.1109/JPHOT.2018.2842026](https://doi.org/10.1109/JPHOT.2018.2842026)

HYBRID INTEGRATION OF INP RSOA AND SIN PIC FOR C-BAND KERR COMB SOURCE

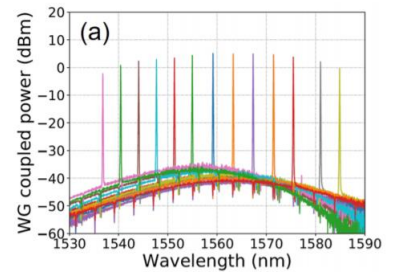
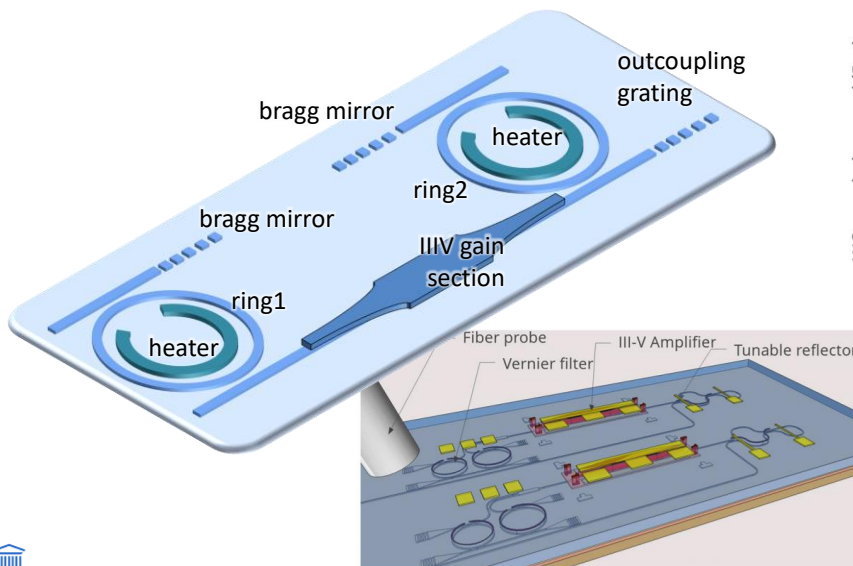


B. Stern et al., *Nature* (2018)
<https://doi.org/10.1038/s41586-018-0598-9>



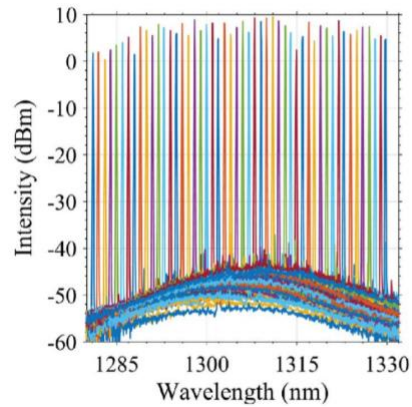
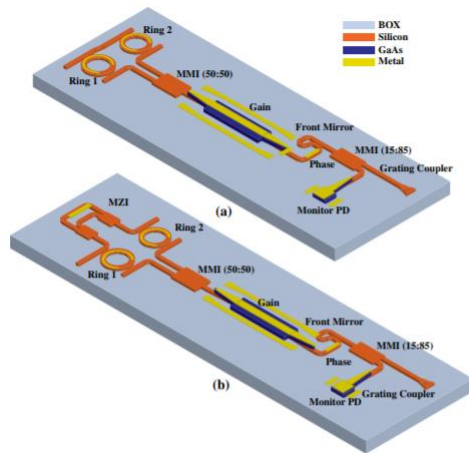
49

MICRO-TRANSFER-PRINTED WIDELY TUNABLE C-BAND LASER ON SILICON



Jing Zhang et al, *APL Photonics* (2019) [doi:10.1063/1.5120004](https://doi.org/10.1063/1.5120004)

EPI-BONDED WIDELY TUNABLE O-BAND LASER ON SILICON



OUTLINE

Brief introduction to silicon and silicon nitride PICs

Spectroscopic sensing modalities

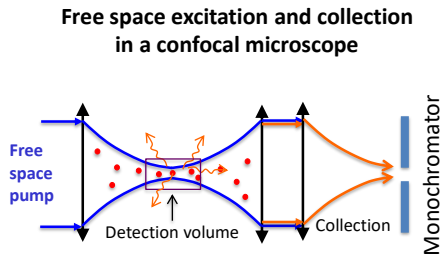
On-chip spectrometers

On-chip tunable lasers

➡ On-chip Raman spectroscopy

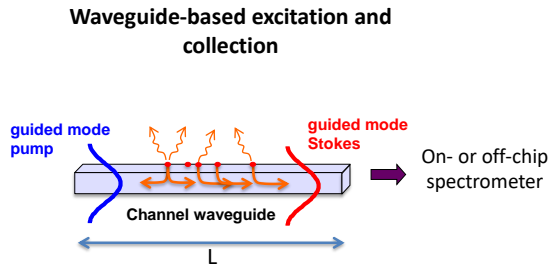
Application cases

WAVEGUIDE-ENHANCED RAMAN SPECTROSCOPY



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

density
scattering cross-section

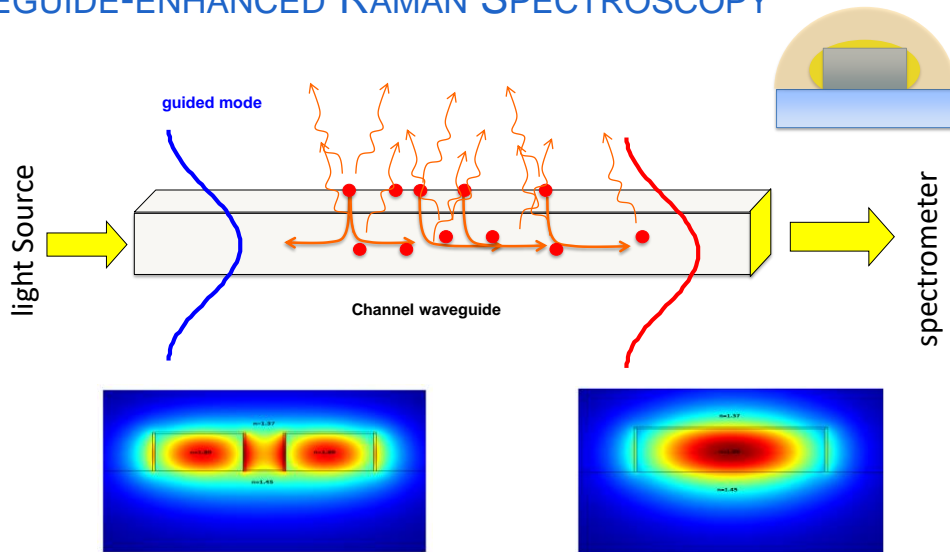


$$\frac{P_{coll}}{P_{pump}} = L \eta_0 \rho \sigma_{scat}$$

$$\eta_0 \equiv \frac{1}{n(\vec{r})k_v} \left(\frac{\pi n_g \lambda_0}{\epsilon_0} \right)^2 \left(\frac{\iint_{Clad} |\vec{e}_m(\vec{r})|^2 d\vec{r}}{\iint_{\infty} \epsilon(\vec{r}) |\vec{e}_m(\vec{r})|^2 d\vec{r}} \right)^2$$

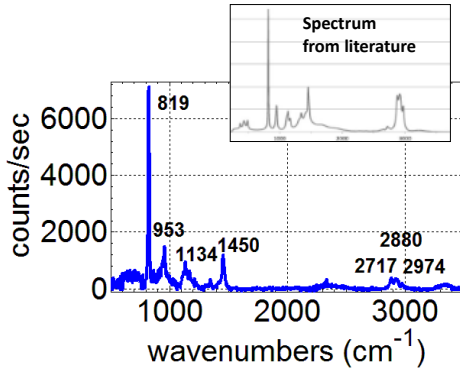
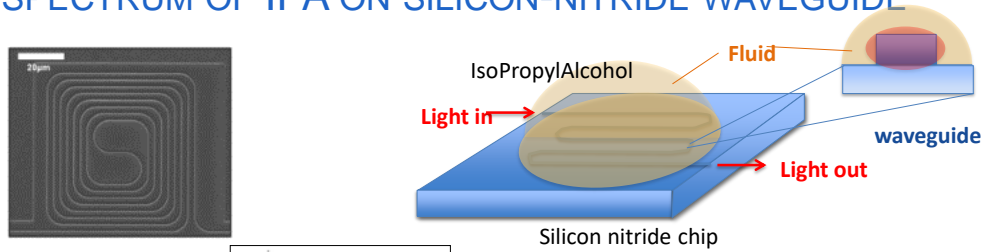
High index contrast matters

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

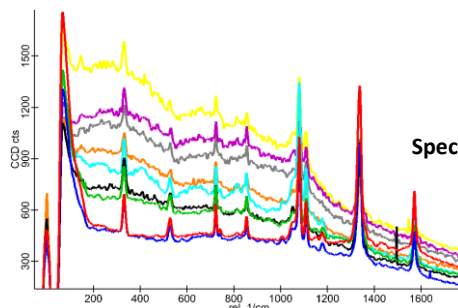
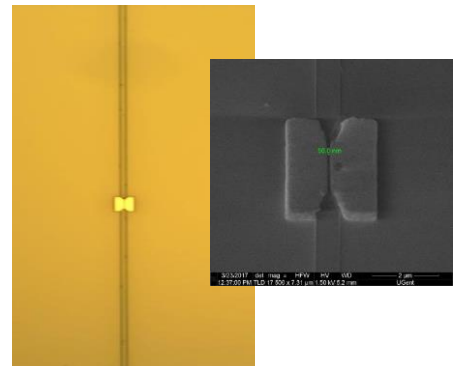
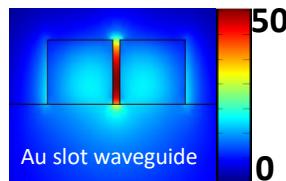
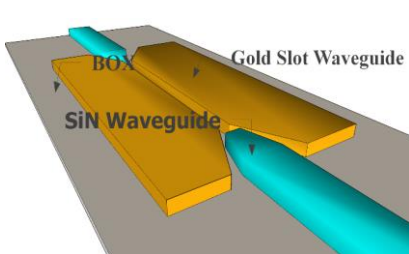


Efficiency of collection 10-100x better than in Raman microscope

A. Dhakal et al, *Opt. Lett.* (2014) [doi:10.1364/ol.39.004025](https://doi.org/10.1364/ol.39.004025)

A. Dhakal et al, *Optics Express* (2015) [doi:10.1364/OE.23.027391](https://doi.org/10.1364/OE.23.027391) 55

USING METAL SLOT WAVEGUIDES TO ENHANCE THE RAMAN SCATTERING



Spectrum of NTP (4-NitroThioPhenol) bound to gold

A. Raza et al, *ECIO* 2017

A. Raza et al, *CLEO2018* [doi:10.1364/CLEO_SI.2018.SW3L.6](https://doi.org/10.1364/CLEO_SI.2018.SW3L.6)

A. Raza et al, *APL Photonics* 2018 [doi:10.1063/1.5048266](https://doi.org/10.1063/1.5048266)

OUTLINE

Brief introduction to silicon and silicon nitride PICs

Spectroscopic sensing modalities

On-chip spectrometers

On-chip tunable lasers

On-chip Raman spectroscopy

➡ Application cases

OUTLINE

Brief introduction to silicon and silicon nitride PICs

Spectroscopic sensing modalities

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On-chip tunable lasers

On-chip Raman spectroscopy

Application cases

➡ Glucose monitoring

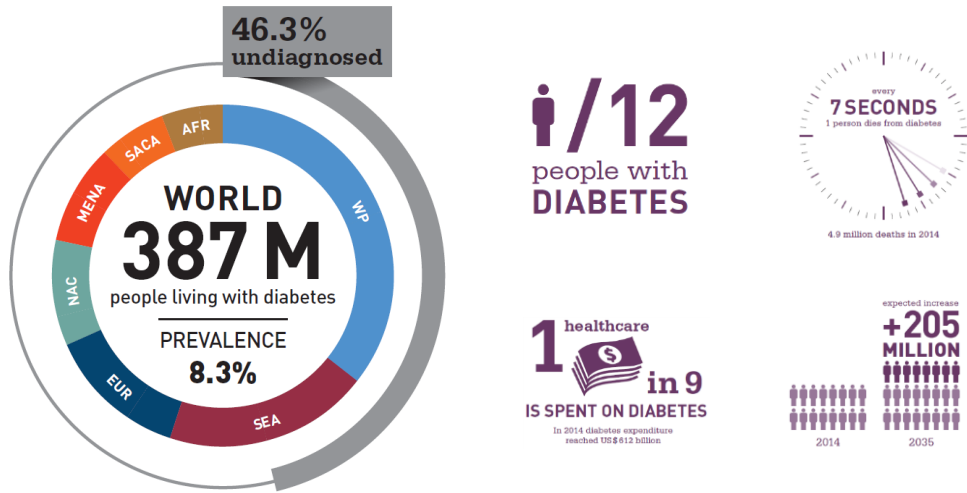
Biosensing

Gas sensing

Fiber Bragg Grating readout

Water pollutant monitoring

DIABETES IS A MAJOR 21ST CENTURY HEALTH CHALLENGE

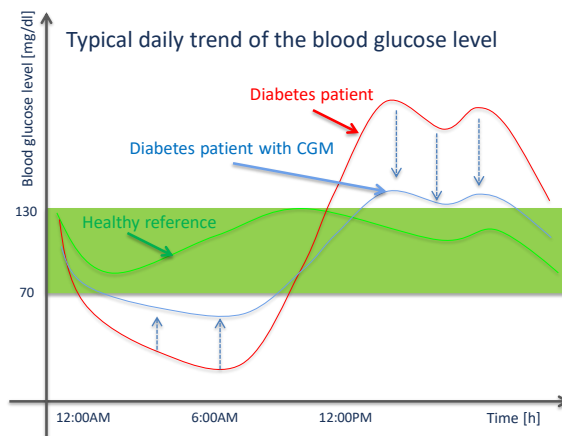


<http://www.idf.org/diabetesatlas/update-2014>

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

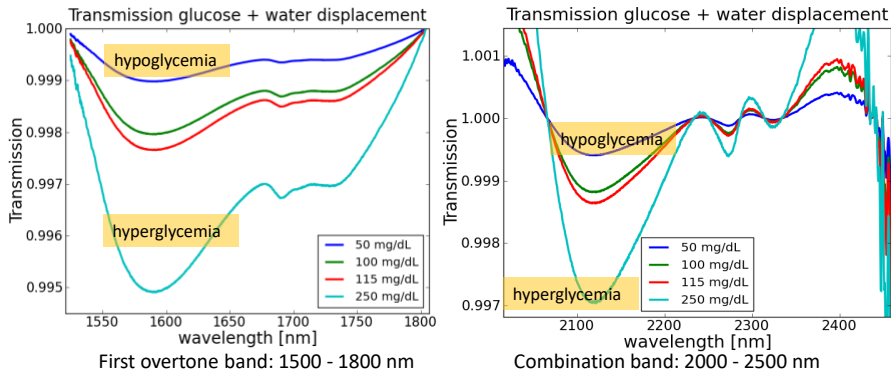
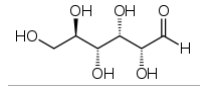
CGM systems show positive health impact *

- lower average blood glucose levels
- decrease of hypoglycemic frequency



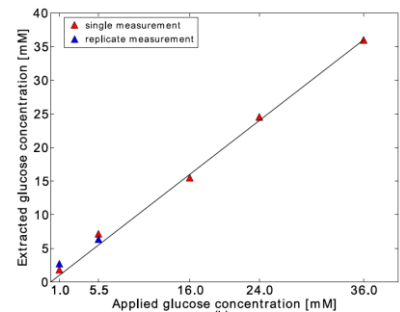
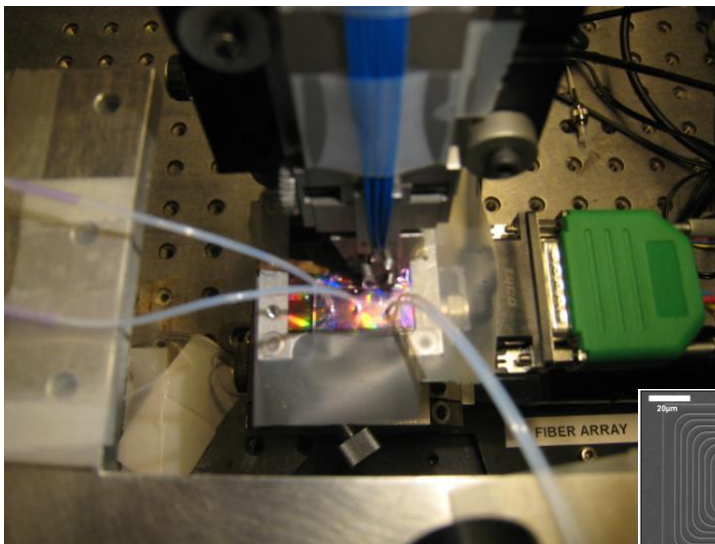
* Liebl A, Henrichs HR, Heinemann L, et al. Continuous glucose monitoring: evidence and consensus statement for clinical use. J Diabetes Sci Technol. 2013;7:500-519

GLUCOSE ABSORPTION SPECTROSCOPY

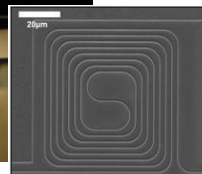


For glucose sensing in humans (3-15 mM): Largest change in transmission is 0.5 %
Required sensitivity : 0.02%

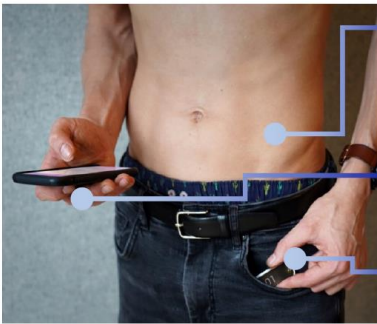
PROOF-OF-CONCEPT DEMO OF GLUCOSE SENSING IN THE LAB



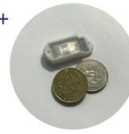
Demonstrated sensitivity of 1mM



CONTINUOUS GLUCOSE MONITORING WITH SUBCUTANEOUS IMPLANT

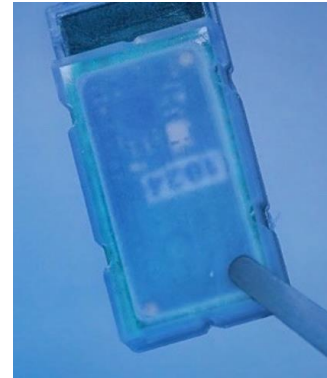


• Invisible, coin-sized 2+ years implant (rechargeable)

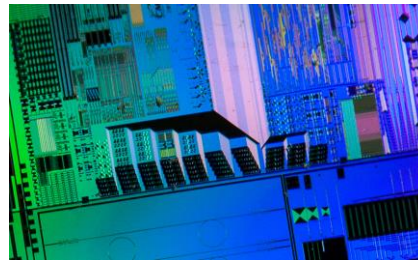


• Mobile app/cloud/connection to 3rd party iCGM devices

• Waterproof Bluetooth display unit



Implant

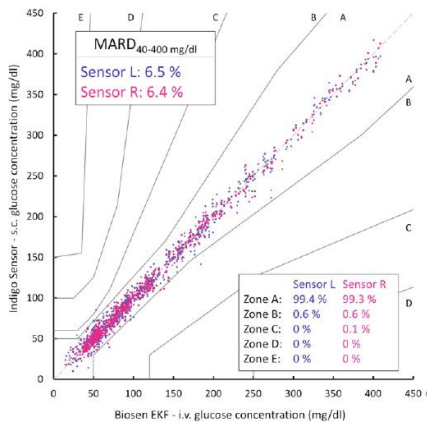


Microspectrometer chip

<https://indigomed.com/>



CONTINUOUS GLUCOSE MONITORING WITH SUBCUTANEOUS IMPLANT



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

<https://indigomed.com/>



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

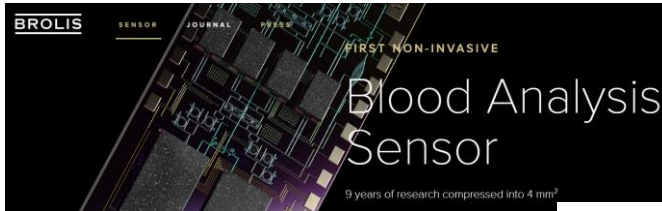
BY INDIGO | MAR 18, 2021 | 2021, NEWS

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.

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

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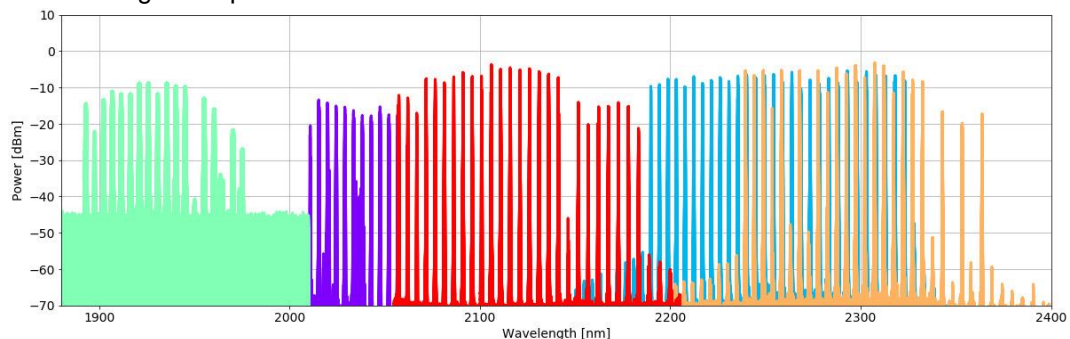
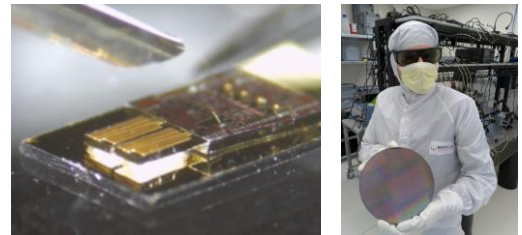
Rockley Photonics, which recently announced a \$1.2 billion listing on the New York Stock Exchange via a special purpose acquisition company (SPAC), is thought to be developing advanced health monitoring features for smartwatches including for Apple.

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



Brolis: GaSb tunable laser technology with silicon PIC

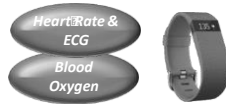
- GaSb gain chips hybridly integrated with silicon PIC
- 1880 – 2430 nm
- 0.1- 1 mW output power
- Tuning speed up to 2 kHz
- 120 nm/gain-chip



BROLIS

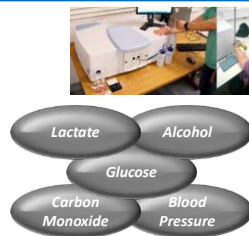
Current Smartwatch Technology

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



Current Medical Technology

- X In-clinic / in-hospital monitoring only
- X Bulky, high-cost medical lab equipment not available to average consumer
- X 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

©2021 Rockley Photonics Ltd.

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On-chip Raman spectroscopy

Application cases

Glucose monitoring

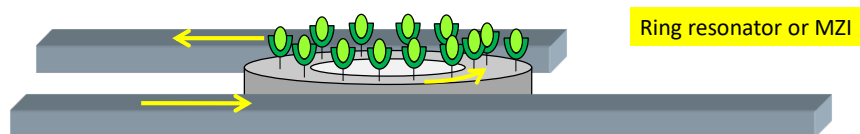
➡ Biosensing

Gas sensing

Fiber Bragg Grating readout

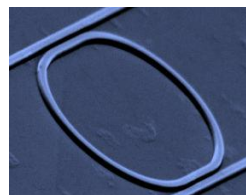
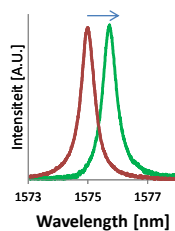
Water pollutant monitoring

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

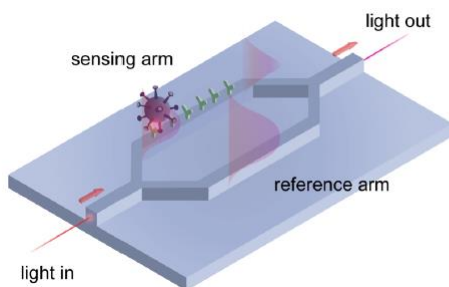


Ring resonator or MZI

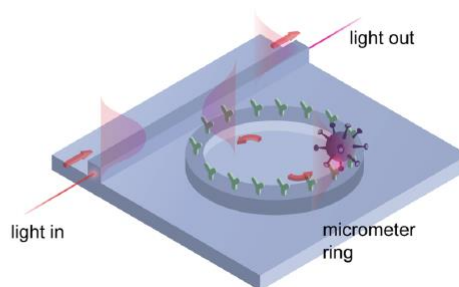
Wavelength shift



KEY PHOTONIC BIOSENSOR DEVICES



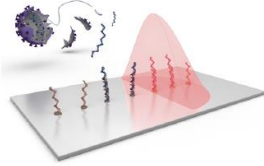
Mach-Zehnder Interferometer (MZI)



Micro-ring resonator (MRR)

BIOSENSING STRATEGIES FOR VIRAL INFECTION DIAGNOSIS

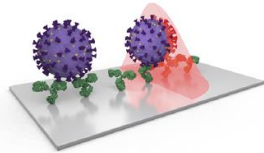
A Viral genomic analysis



A. Genomic detection

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

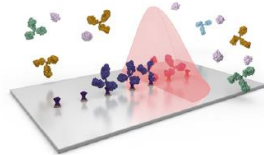
B Direct virus detection



B. Antigen-directed virus detection

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

C Serology assay



C. Serological test (blood)

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

M. Soler et al, ACS Sens. (2020) doi.org/10.1021/acssensors.0c01180 71



<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

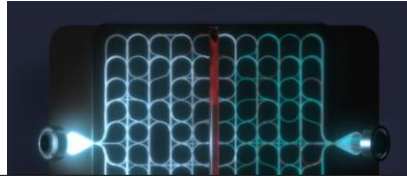
MAVERICK	PCR Result		
	Pos	Neg	
Pos	46	0	46
Neg	7	303	310
	53	303	




Post Seroconversion: > 14 days

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

BIOSENSORS FOR HOME AND POC USE

- Consumer price
- Rapid self-test for STDs, Covid-19, flu



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.

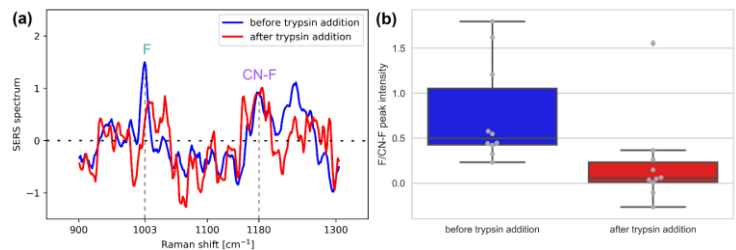
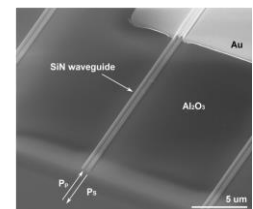
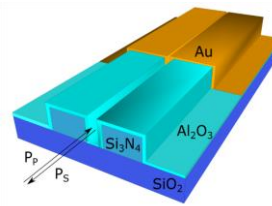
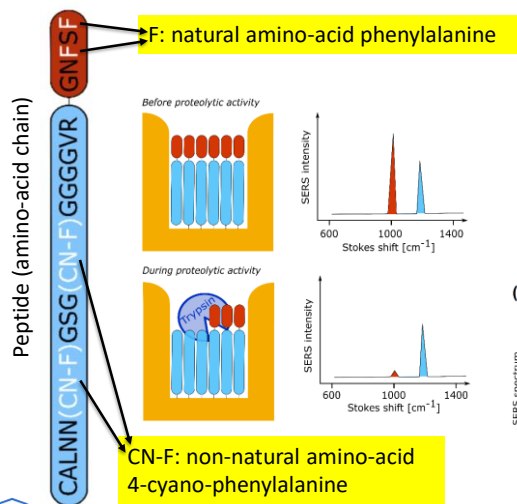
<https://www.antelope-dx.com/>



73

ON-CHIP RAMAN SPECTROSCOPY FOR MONITORING OF ENZYMATIC ACTIVITY

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



OUTLINE

Brief introduction to silicon and silicon nitride PICs

Spectroscopic sensing modalities

On-chip spectrometers

On-chip tunable lasers

On-chip Raman spectroscopy

Application cases

Glucose monitoring

Biosensing

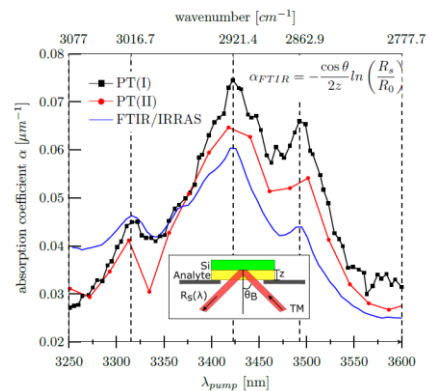
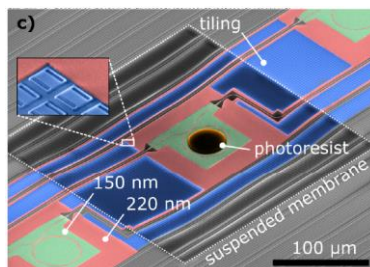
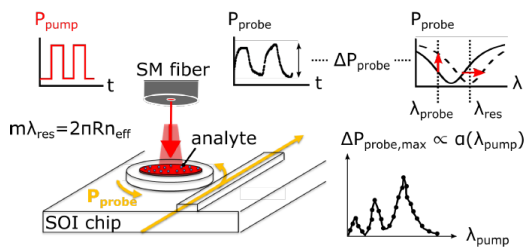
➔ Gas sensing

Fiber Bragg Grating readout

Water pollutant monitoring

MID-IR PHOTOTHERMAL ABSORPTION SPECTROSCOPY WITH SOI RING

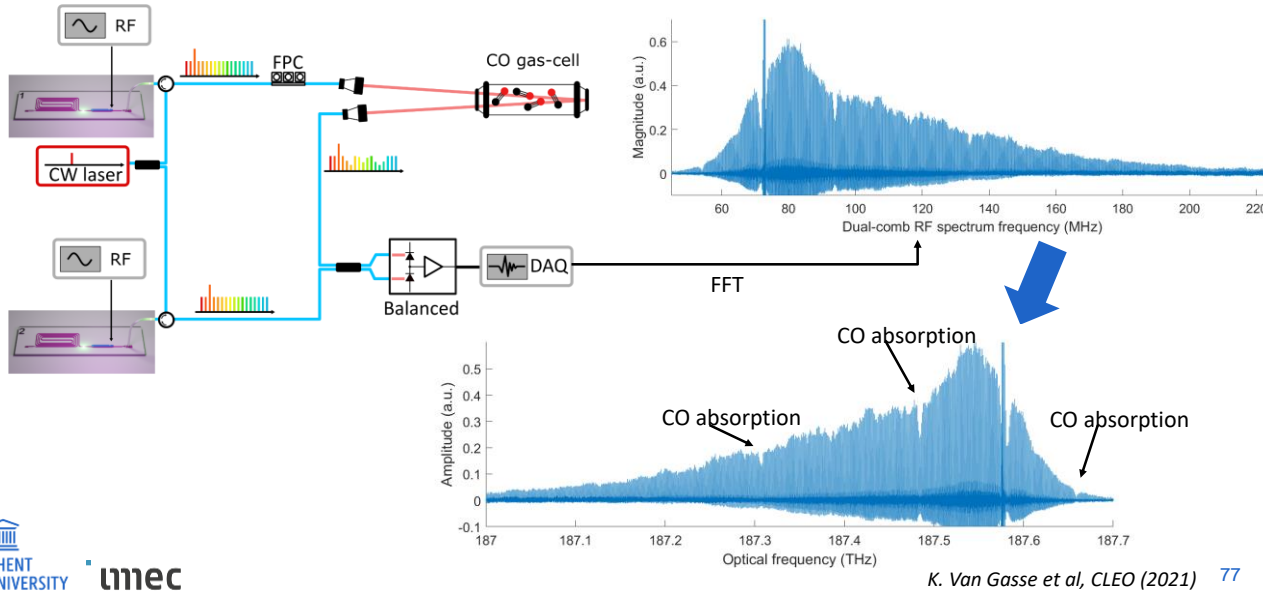
absorption $\alpha(\lambda_{\text{pump}}) \rightarrow \Delta T \rightarrow \Delta n_{\text{eff}} \rightarrow \Delta \lambda_{\text{probe, res}} \rightarrow \Delta P_{\text{probe}}$



Proof-of-concept demonstration using photoresist as analyte

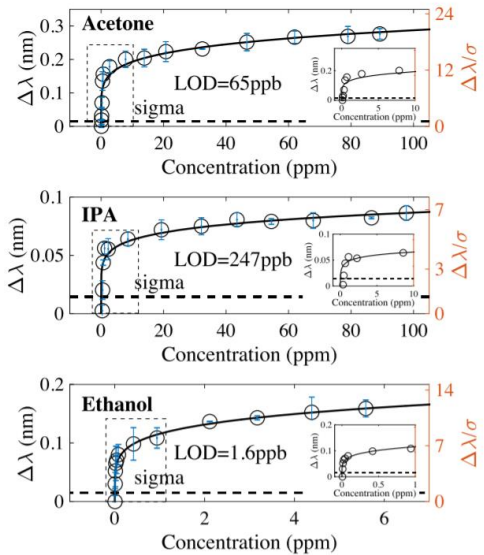
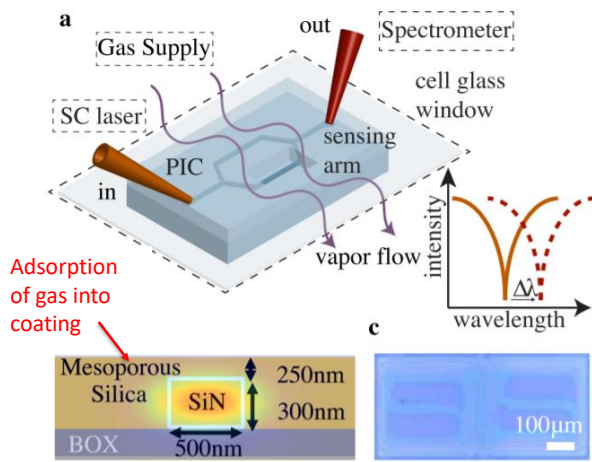
Vasiliev et al, ACS-Sensors (2017) [10.1021/acssensors.6b00428](https://doi.org/10.1021/acssensors.6b00428)

DUAL-COMB SPECTROSCOPY OF CO WITH TWO INP-ON-SOI COMB LASERS

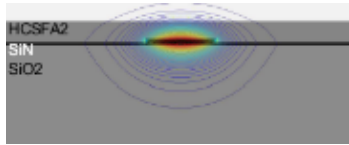


ULTRASENSITIVE GAS SENSING WITH REFRACTIVE INDEX SENSORS

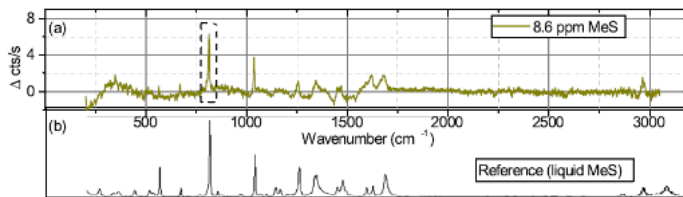
Medical application: breath analysis



TRACE GAS SENSING WITH ON-CHIP RAMAN SPECTROSCOPY



Hypersorbent polymer (HCSFA2)
coating on SiN waveguides.
Partition coefficient $\sim 10^8$



Detection limit ~ 100 ppb
Densification $\sim 10^8$

Raman spectrum of gaseous MeS
(methyl salicylate, a hydrogen-bond basic organic ester)

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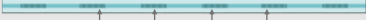
Gas sensing

➡ Fiber Bragg Grating readout


Water pollutant monitoring

SENTEA FBG INTERROGATOR


FIBER SENSOR




Multiple distributed sensing points




Resistant to harsh environments



Strain




Temperature

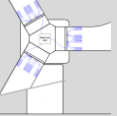


Vibration


**EASY INSTALL
PACKAGED OR EMBEDDED SENSORS**



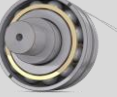
Fiber sensors mounted on bridges



Fiber sensors embedded in wind turbine blades




Fiber sensors for Industrial temperature sensing

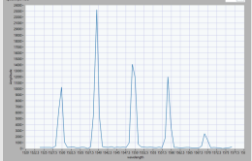


Fiber sensors embedded in bearings & gearboxes

**COST-EFFECTIVE FIBER SENSING
THROUGH SILICON PHOTONICS**



[On-chip polarization independent spectrometer with sub-pm resolution](#)





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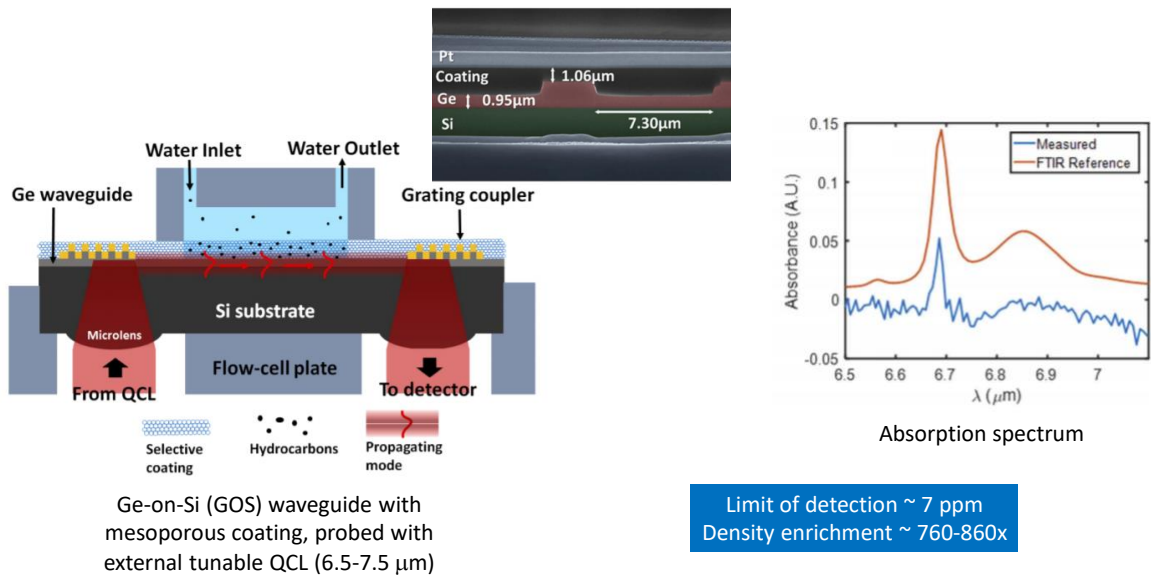
- Biosensing

- Gas sensing

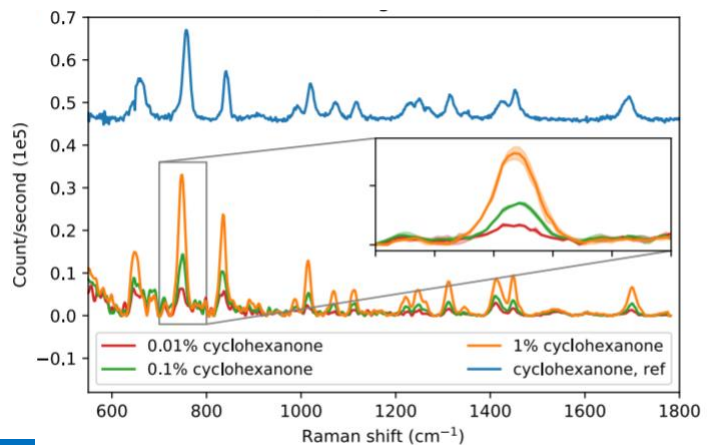
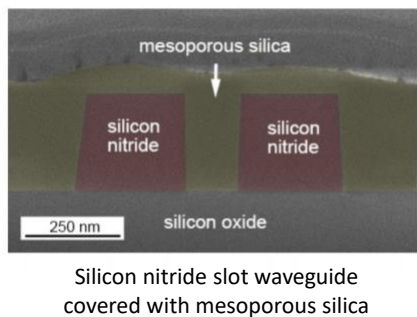
- Fiber Bragg Grating readout

- ➡ Water pollutant monitoring

MID-IR ABSORPTION SPECTROSCOPY OF TOLUENE IN WATER



ON-CHIP RAMAN SPECTROSCOPY OF CYCLOHEXANONE IN WATER



Detection down to 100 ppm demonstrated
Density enrichment by mesoporous coating ~ 600x

Detection of Cyclohexanone in water
(pump wavelength: 785 nm)

SUMMARY

Silicon PICs (SOI, SiN, GOS)

- compact
- low cost

Enabling many spectroscopic sensing modalities

- absorption spectroscopy
- Raman spectroscopy
- readout of spectral filters (RI-sensing, FBG...)

Emerging industrial take-up

- personal health care
- monitoring of critical functions (infrastructure, water quality, safety, industrial sensing...)