UNIVERSITY OF Southampton
Optoelectronics Research Centre

Integrated Photonics for Mid-IR Biochemical Spectroscopy

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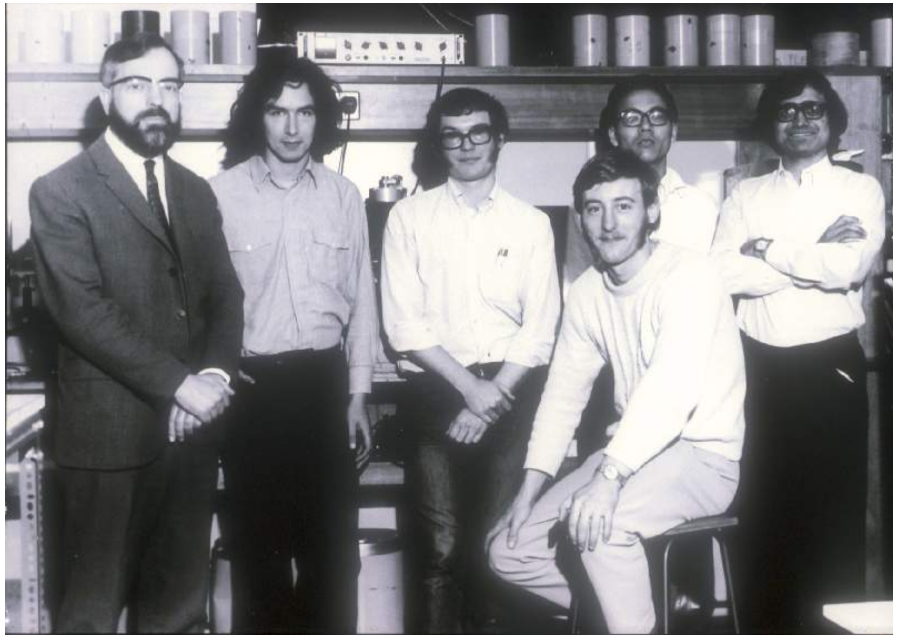
Motivation

- Biochemical spectroscopy on a photonic chip
- Label-free direct analysis
- “Point-of-care” detection and quantification
- Mid-IR molecular “fingerprint” region of spectrum
- Waveguides optimised for surface sensitivity
- New materials needed as platform for wideband spectroscopy
- Future applications in other fields
  - MIR supercontinuum
  - Lasers
  - Nonlinear optics

Optoelectronics Research Centre

Formed in 1989 as UK National Centre from

- Optical Fibre Group (Electronics Dept) &
- Laser Physics Group (Physics Dept)



Optical Fibre Group in ~1978

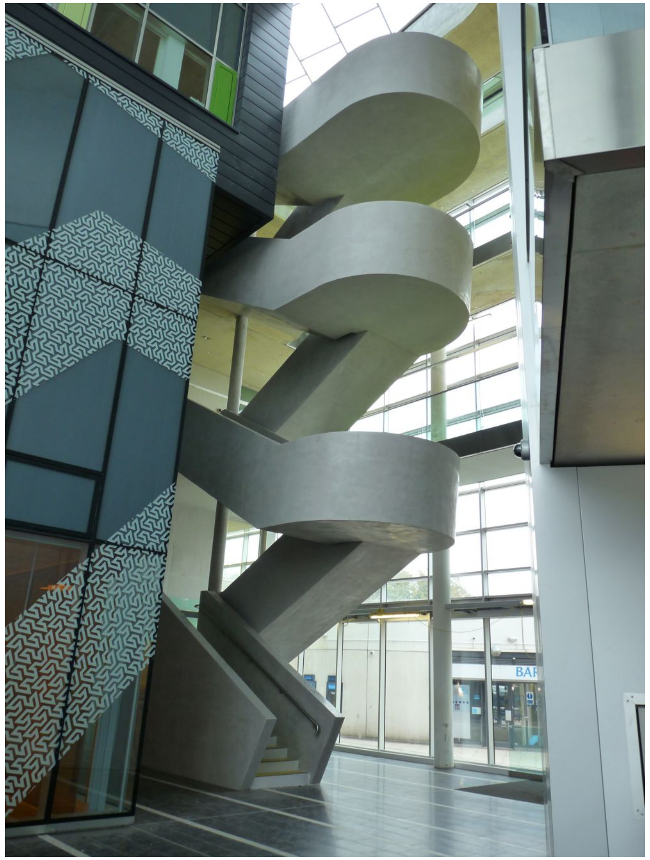
Optoelectronics Research Centre

- Largest photonics group in the UK (~250 staff / PhD students)
- Low loss optical fibres, EDFA, novel glasses, fibre lasers, crystalline lasers, integrated photonics, metamaterials, biophotonics …

- Joined by the Silicon Photonics Group from Surrey University in 2012.

- Formed the Zepler Institute in 2013, taking over management of Southampton Nanofabrication Centre from the School of Electronics & Computer Science in 2018.

- Prof Eric Zepler established the Electronics Dept at Southampton in 1947.



Beginnings of waveguide evanescent spectroscopy

IEEE JOURNAL OF QUANTUM ELECTRONICS, VOL. QE-7, NO. 7, JULY 1971

On the Use of Optical Waveguide Techniques for Internal Reflection Spectroscopy

J. E. MIDWINTER, MEMBER, IEEE

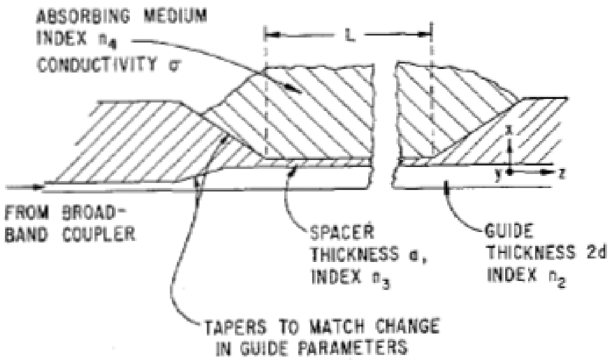


Fig. 1. Guide, cladding, and absorbing medium layout.

IEEE JOURNAL OF QUANTUM ELECTRONICS, VOL. QE-13, NO. 4, APRIL 1977 173

Absorption Spectroscopy in Scattering Samples Using Integrated Optics

GORDON L. MITCHELL, SENIOR MEMBER, IEEE

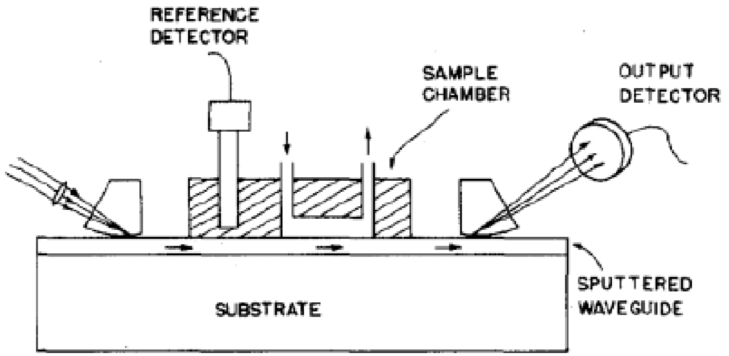
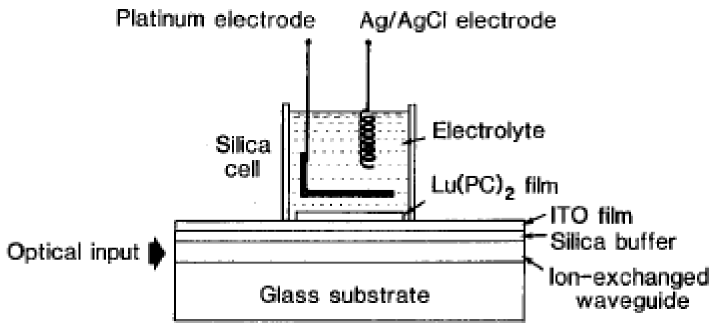
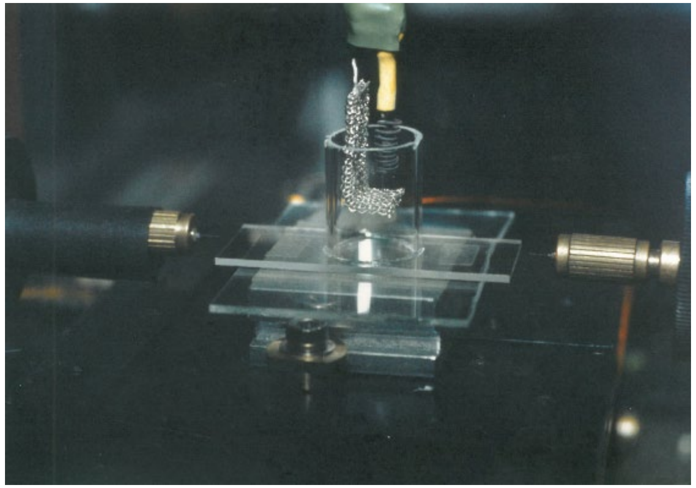
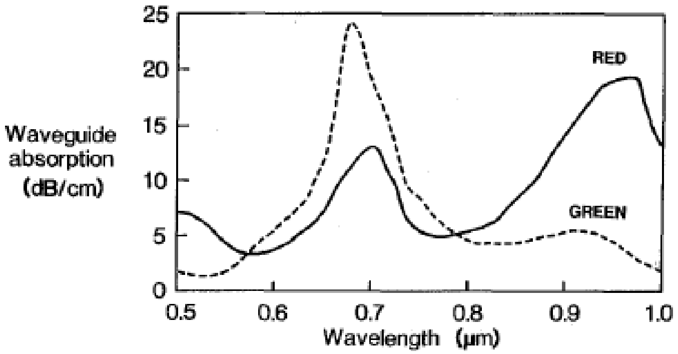


Fig. 4. Experimental integrated optic device used for absoprtion measurements. The reference detector measures light radiated from the waveguide to compensate for variations in input coupling efficiency and laser power.

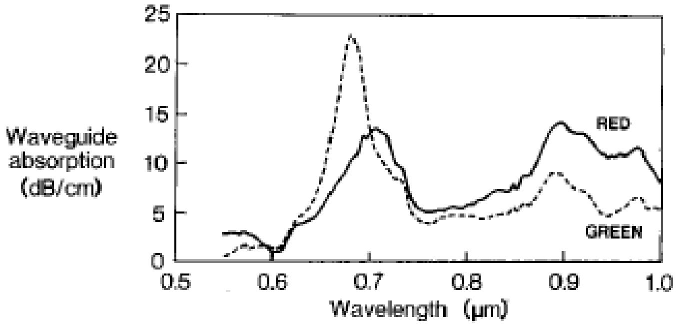
Ultrathin film absorption and electrochemical control







Theory from $Lu(PC)_2$ spectrum (TE)

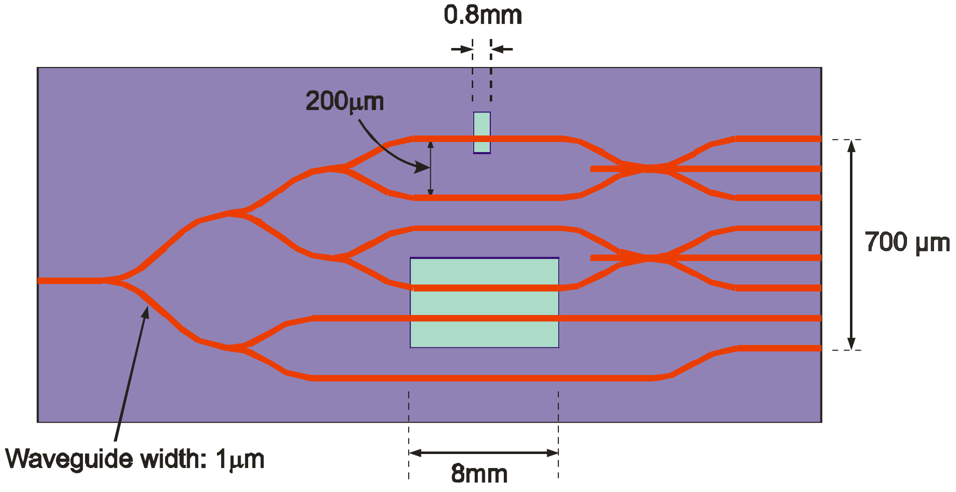


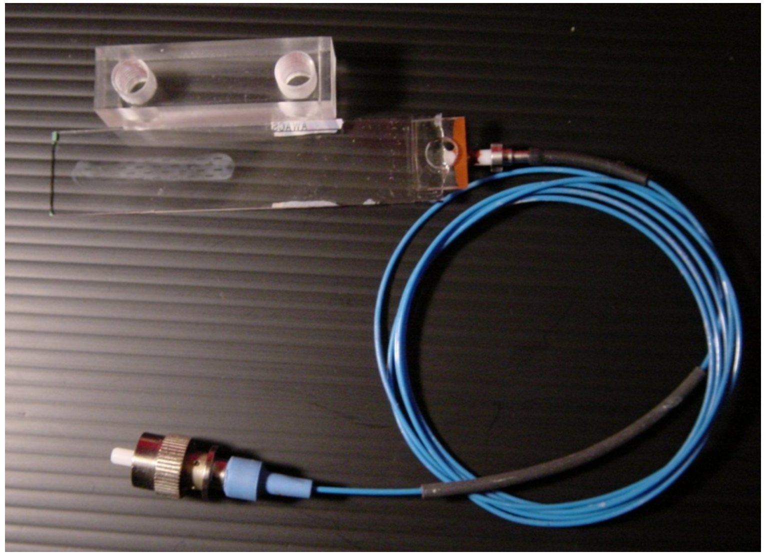
Waveguide experiment (TE)

Electrochemically-oxidised 10nm Lutetium Biphthalocyanine film on 10nm ITO film

C.Piraud, J.Yao, E.K.Mwarania, K.O'Dwyer, D.J.Schiffrin, & J.S.Wilkinson, “Optoelectrochemical Transduction on Planar Optical Waveguides”, J. Lightwave Technol. **10** 693-699 (1992) & C.Piraud, E.K.Mwarania, G.Wylangowski, K.O'Dwyer, D.J.Schiffrin, & J.S.Wilkinson, “Optoelectrochemical Thin-Film Chlorine Sensor Employing Evanescent Fields on Planar Optical Waveguides", Anal. Chem. **64**,651-655 (1992)

Approaches to NIR/Vis waveguide evanescent sensing





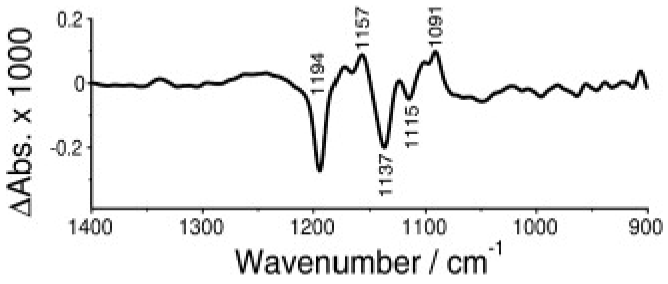
- Controllable evanescent interaction
- Surface sensitive
- Multisensor integration possible
- Compact, robust & mass-produced
- Very small sample volume

P.Hua, G.R.Quigley, B.J.Luff, K.Kawaguchi & J.S.Wilkinson, Integrated optical dual Mach-Zehnder interferometer sensor, Sensors & Actuators B **87** 250-257 (2002).

- Compatible with microfluidics
- "Solid-state" connection to instrument
- Patterning electrodes straightforward
- ☑ Absorption, index, Raman, fluorescence …

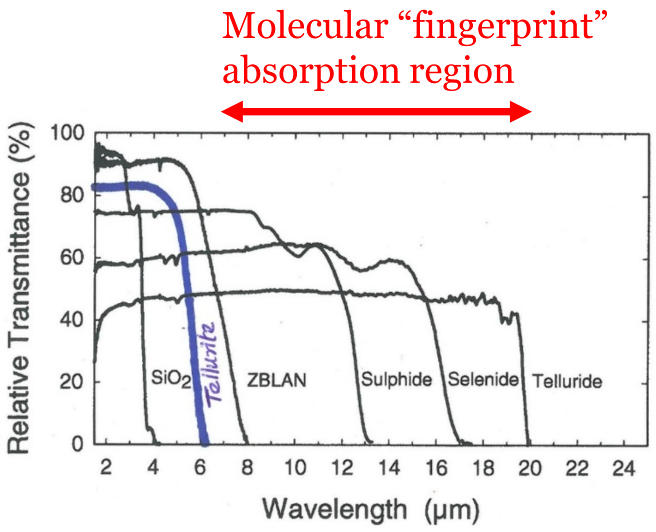
P.Hua et al., "Integrated optical fluorescence multisensor for water pollution", Optics Express **13** 1124-1130 (2005).

Mid-IR waveguide materials for evanescent spectroscopy



Difference spectrum for changes in P-O bond in protein
Scale corresponds to approx 7µm - 11µm wavelength

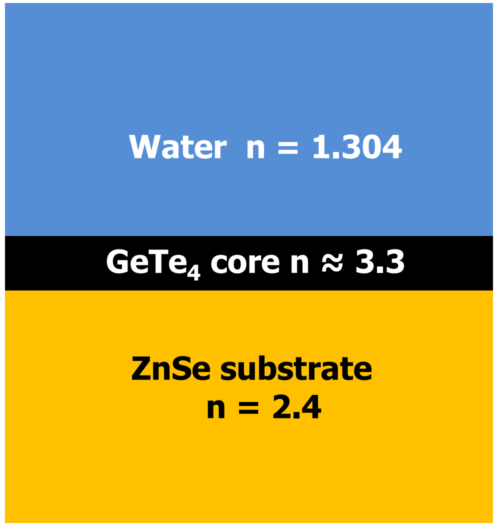
A. Barth, N. Bezlyepkina
PO bond destabilization accelerates phosphoenzyme hydrolysis of sarcoplasmic reticulum Ca^{2+} -ATPase
J. Biol. Chem., 279 (2004), pp. 51888–51896



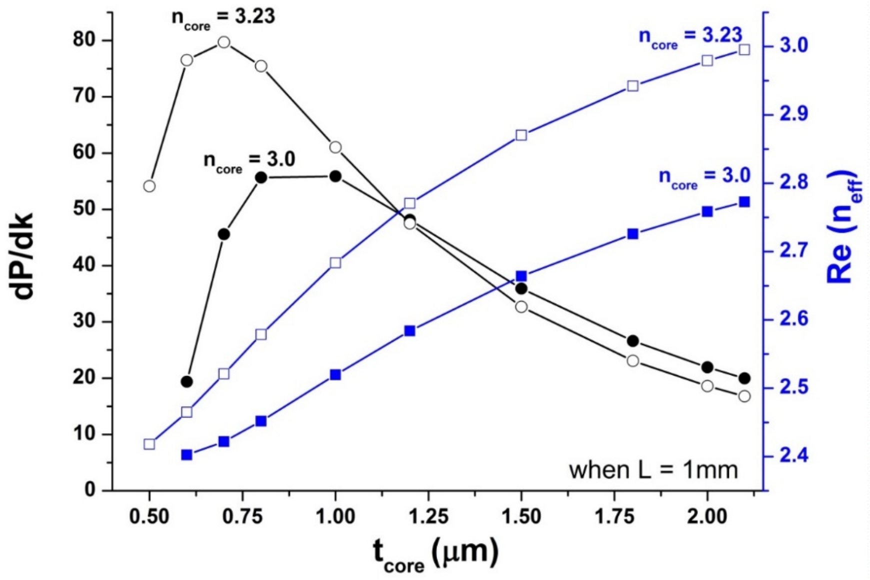
Sanghera, J.S. et al.,
Development and infrared applications of chalcogenide glass optical fibers.
Fiber and Integrated Optics, 2000. ***19****:*
p. 251-274.

- Fundamental vibrations of biomolecules are in the range from 2.5-20µm
- Absorption spectroscopy allows identification and quantification
- Waveguide approaches allow high sensitivity to surface-attached molecules

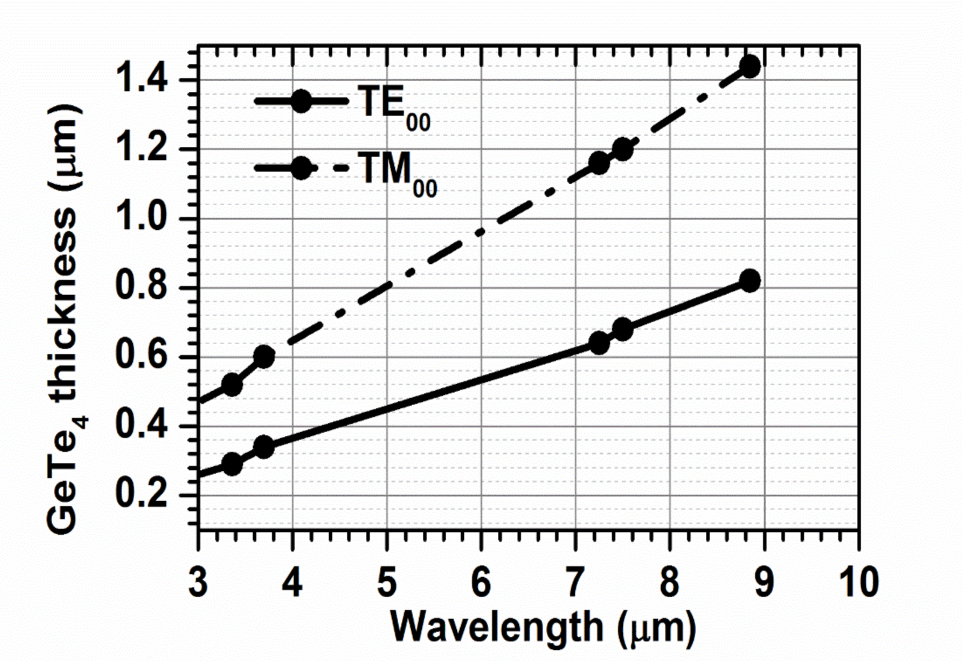
$GeTe_4$ / ZnSe waveguide sensitivity



Waveguide structure



Effective index and sensitivity vs thickness



Optimum thickness vs wavelength

COMSOL waveguide model

Solves for modal effective refractive index $n_{eff;}$ adds ultrasmall Δk (absorption) to water
Calculates the difference in transmission, ΔP; yields curves for sensitivity and optimum thickness

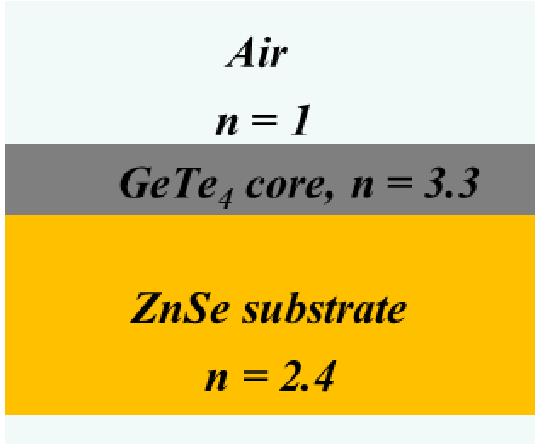
V. Mittal, "Mid-infrared Integrated Photonic Devices for Biosensing", PhD Thesis, University of Southampton, UK, *(2017)*

$GeTe_4$ waveguide films on ZnSe

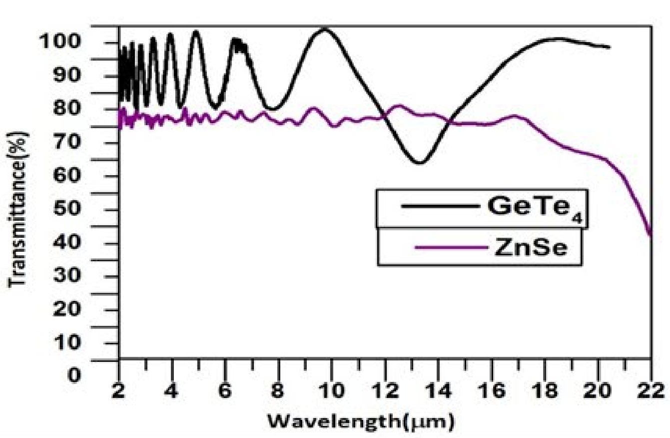
RF sputtered $GeTe_4$ film of 4.6 µm thickness

Sputter from $GeTe_4$ target in Ar at 10 mTorr
Deposition rate ~0.5 µm/h at 50W magnetron power

Film and substrate transparent to λ > 16 µm by FTIR
Amorphous by XRD
Surface roughness R_{rms} ≈ 1.7nm by AFM



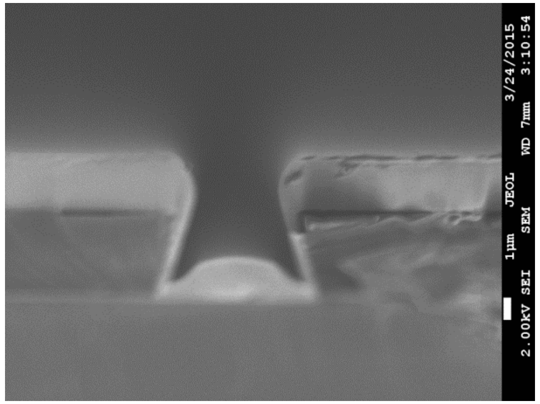
(c)

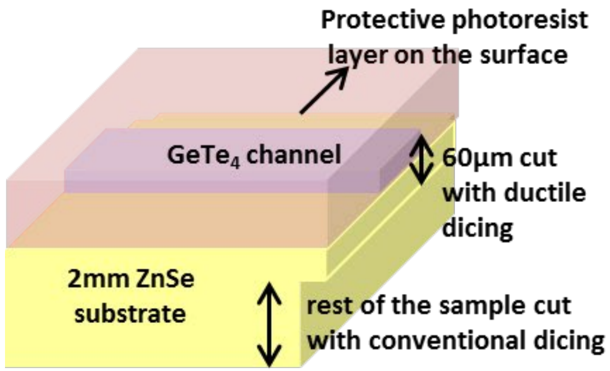


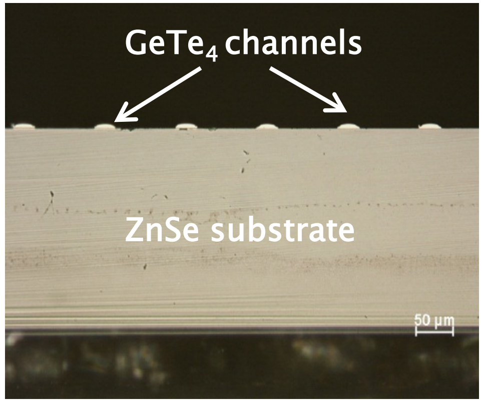
V. Mittal, "Mid-infrared Integrated Photonic Devices for Biosensing", PhD Thesis, University of Southampton, UK, *(2017)*

$GeTe_4$ channel waveguides on ZnSe

Pattern channel waveguides by photolithographic lift-off
8 µm thick lift-off resist LOR 30B
Waveguide widths from 15 µm - 30 µm

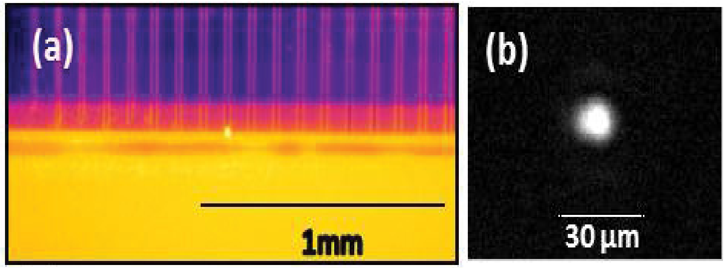






Guidance over 2.5 µm < λ < 7.5 µm

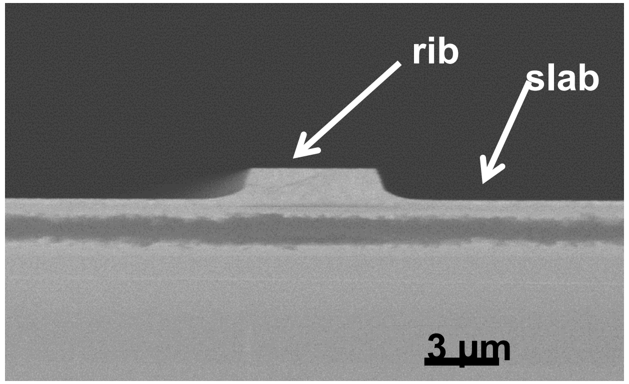
At λ = 3.5 µm:
Losses ≈ 1dB/cm
Mode spotsize ≈ 10µm x 8µm



V. Mittal, A. Aghajani, L. G. Carpenter, J. C. Gates, J. Butement, P.G.R. Smith, J. S. Wilkinson and G. S. Murugan
"Fabrication and characterization of high-contrast mid-infrared $GeTe_4$ channel waveguides" *Optics Letters* ***40*** *2016-2019 (2015)*

Evaluation of ZnSe waveguides on oxidised silicon

- Sputtered or e-beam evaporated from pressed ZnSe powder
- Patterned by photolithography and Ar ion beam etching
- Etch rate ~ 0.83 nm/s
- Etch depth 1.6 µm, slab 0.3 µm



RF sputtered $ZnSe/SiO_2/Si$ ribs

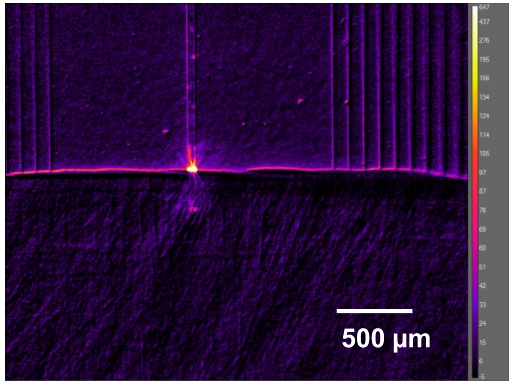
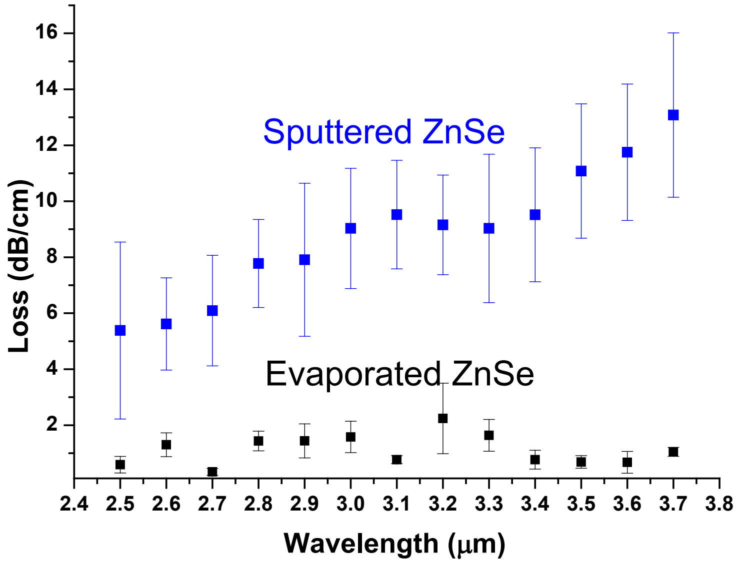


Image of guiding

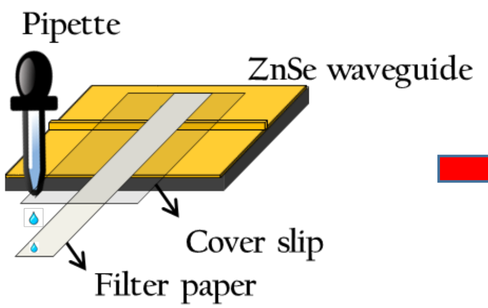


$ZnSe/SiO_2/Si$ waveguide losses

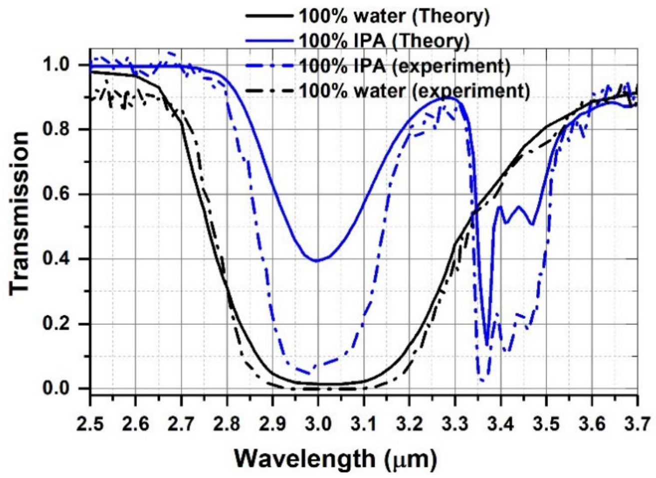
➡ E-beam evaporated films are of high optical quality
Appropriate as isolation layer in $GeTe_4/ZnSe/Si$ system
Potential for short wavelength MIR devices

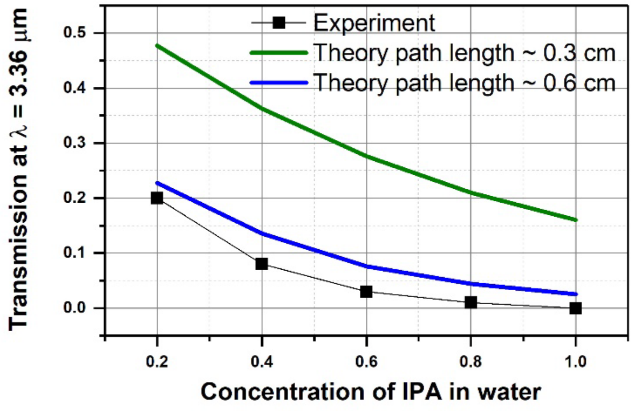
V. Mittal et al. "Optical quality ZnSe films and low loss waveguides on Si substrates for mid-infrared applications" Optical Materials Express **7** 712 (2017).

Analyte delivery by paper-based fluidics



- Low-cost method of sample delivery
- Paper does not interfere with evanescent field
- Potential for "wax-jet" printed fluidic circuitry
- Well-developed lateral flow assays
- Potential to incorporate dried reagents within paper

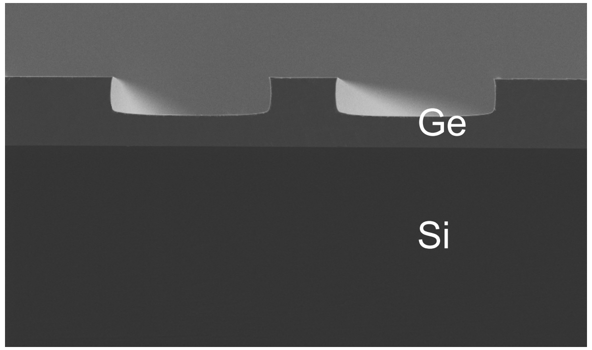




MIR absorption spectroscopy demonstrated on ZnSe waveguides

V. Mittal et al "Chalcogenide glass waveguides with paper-based fluidics for mid-infrared absorption spectroscopy", *Optics Letters* ***43*** *2913 (2018)*

Germanium on silicon (GOS) devices at λ = 2.0 - 3.8 μm

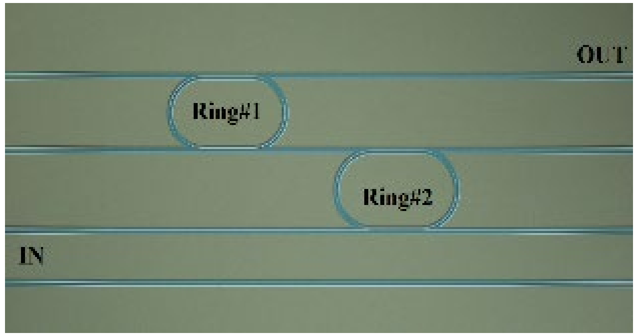


Ge-on-Si rib waveguides (0.6dB/cm)
H=3μm, W=2.7μm, D=1.7μm
MMIs: 0.2 dB/MMI
MZIs: 20 dB extinction ratio
5-channel AMMI

[M. Nedeljkovic et al., *IEEE PTL* 2015]

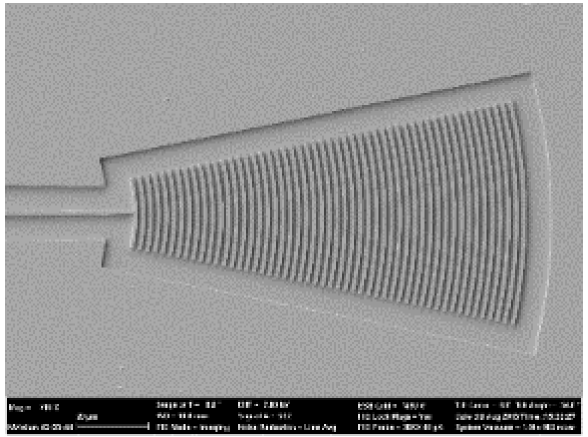
Silicon Photonics Group:

Goran Mashanovich,
Milos Nedeljkovic
and collaborators



Cascaded ring/racetrack resonators
[B. Troia et al., *Opt. Lett.* 2016]

University of Southampton
Politecnico di Bari



Grating couplers for Ge waveguides
[C. Alonso-Ramos, et al. *Opt. Lett.* 2016.]

University of Southampton
Université Paris Sud
Université Paris-Saclay

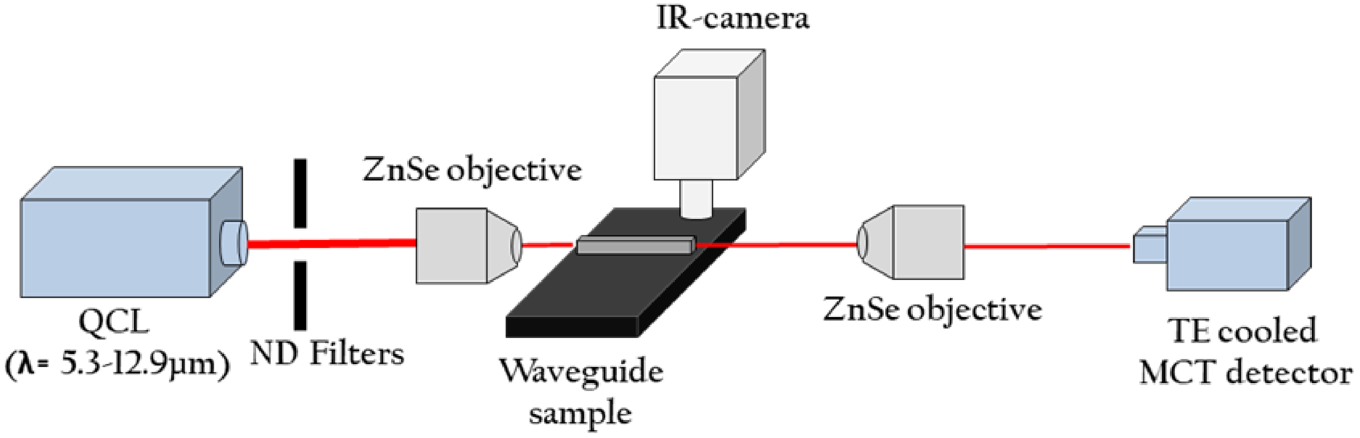
GOS waveguides at wavelengths up to 12.9 μm

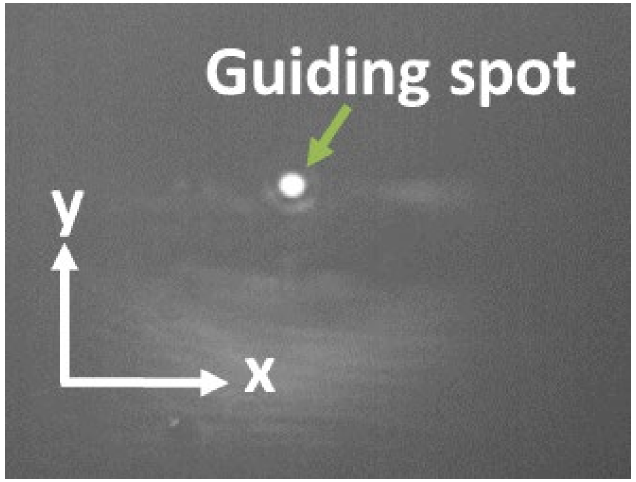
6” GOS wafers with 3 μm thick Ge films sourced commercially

20 micron wide waveguides formed by ICP etching using fluorine chemistry

End-facets prepared by ductile dicing

Fundamental mode spotsize 2.7μm × 12.6 μm at λ = 12.9 μm





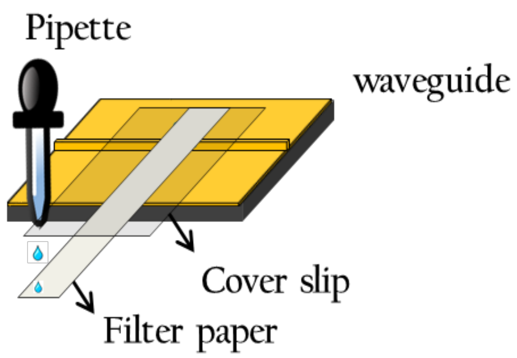
➡ Guidance demonstrated up to 12.9 μm (775 cm^{-1}); losses under evaluation

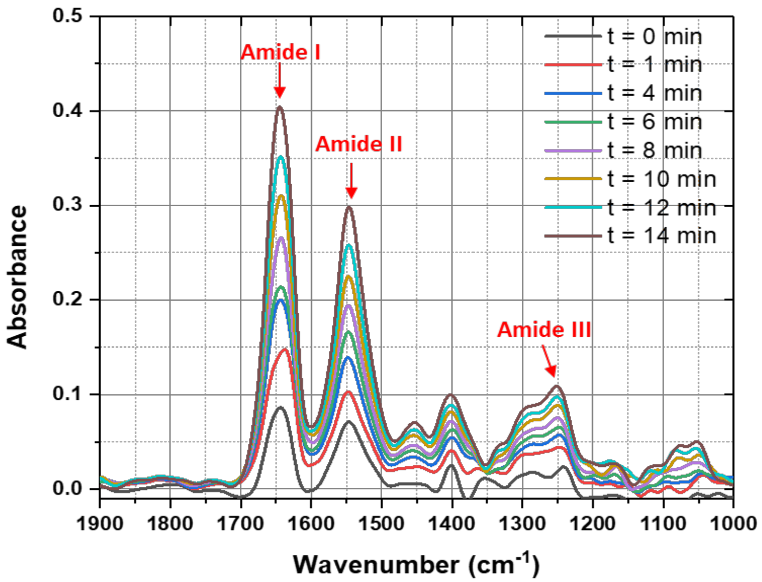
Ge on Si waveguide spectroscopy of BSA in buffer

3 μm × 20 μm GOS waveguide

M. Nedeljkovic et al., IEEE PTL **27**, 1040 (2015).

Liquids delivered to waveguide in water using 1mm wide paper fluidic strip





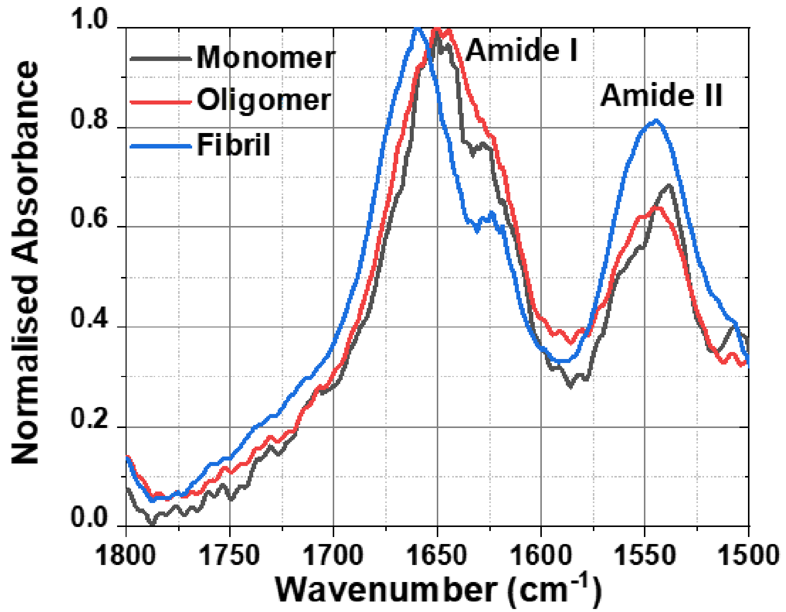
Three amide peaks clearly resolved – secondary structure under investigation

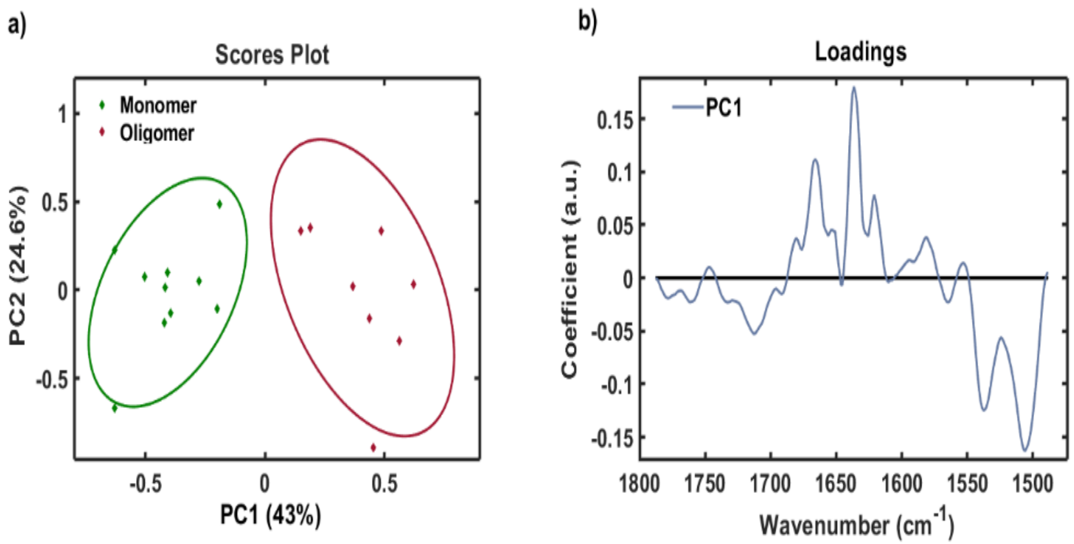
V. Mittal, M. Nedeljkovic, A. Z. Khokhar, L. G. Carpenter, G.S. Murugan, H. M. H. Chong, P.N. Bartlett, G. Z. Mashanovich & J.S. Wilkinson "Waveguide absorption spectroscopy of bovine serum albumin in the mid-infrared fingerprint region" ACS Sensors, 4, 1749-1753 (2019)

Ge on Si waveguide spectroscopy of BSA aggregates

3 µm × 20 µm GOS waveguide M. Nedeljkovic et al., IEEE PTL **27**, 1040 (2015).

Liquids delivered to waveguide using 1mm wide paper fluidic strip



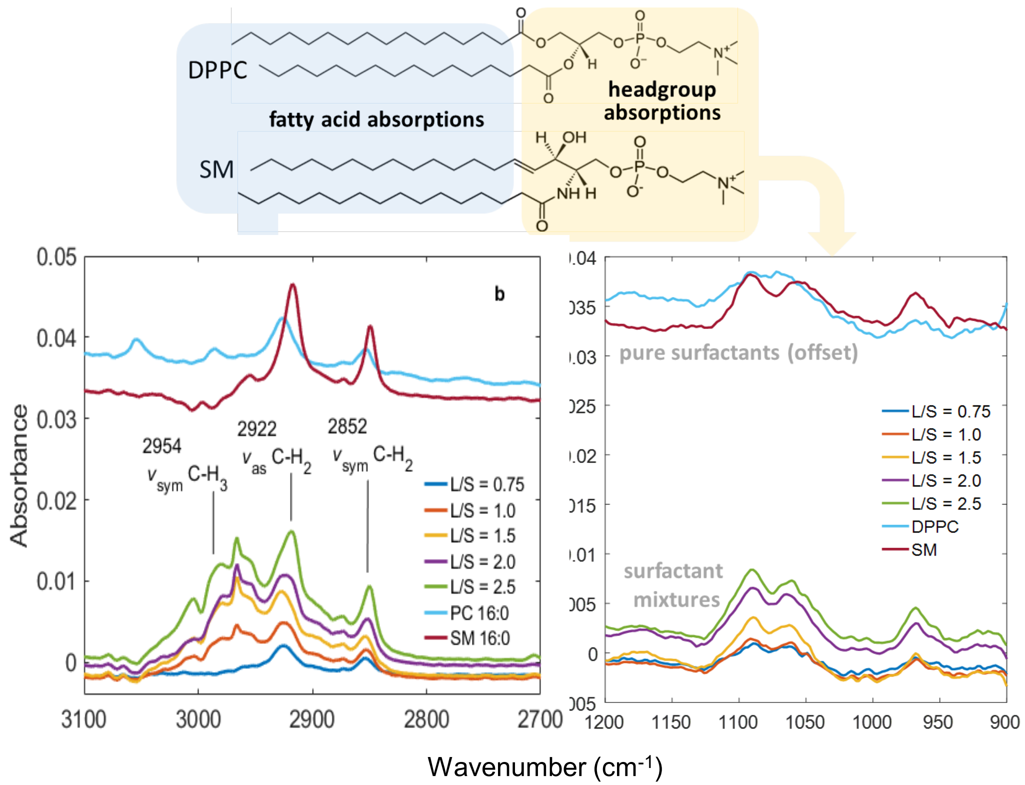


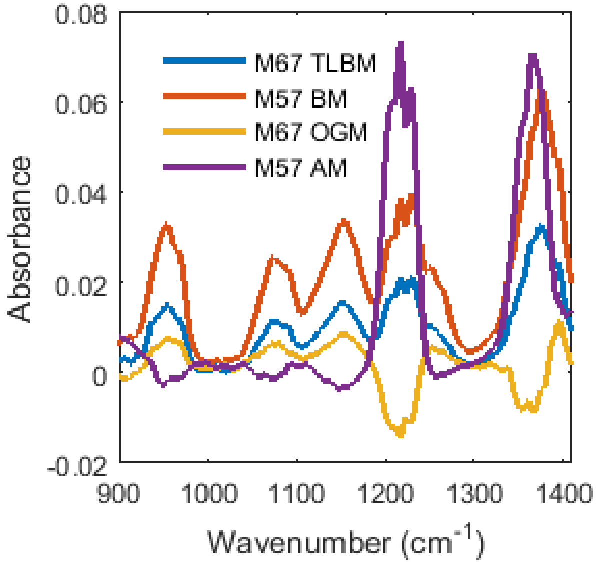
Principal component analysis of BSA monomer and oligomer amide I spectra.

V. Mittal, G. Devitt, M. Nedeljkovic, L.G.Carpenter, H. M. H. Chong, H.M.H. Chong, J.S. Wilkinson, S. Mahajan & G.Z. Mashanovich
Ge on Si waveguide mid-infrared absorption spectroscopy of proteins and their aggregates” Biomedical Optics Express , 11, 4714-4722 (2020)

Future applications: lung surfactants and stem cells

measurements by conventional ATR/FTIR





MIR-ATR absorption spectra for lung surfactant mixtures of varying lecithin/sphingomyelin ratio

diagnose Neonatal Respiratory Distress Syndrome

Blue ⇨ Yellow: differentiation to bone cells

Red ⇨ Purple: differentiation to fatty cells

In-situ real-time monitoring of differentiation

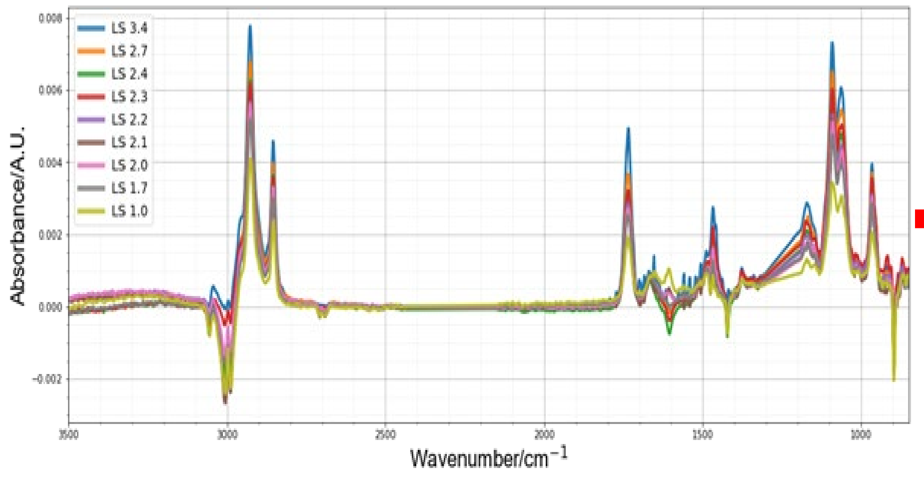
D.J.Rowe & J. S. Wilkinson, Biosensors 2016, Gothenburg, Sweden, 25-27 May 2016.
D.J. Rowe, N.D. Evans, G.S. Murugan, S.J. Pearce, J.S. Wilkinson “Mid-infrared Ta_2O_5 Waveguides for Evanescent Sensing of Stem Cell Differentiation” ECIO, Nice Jun 2014.

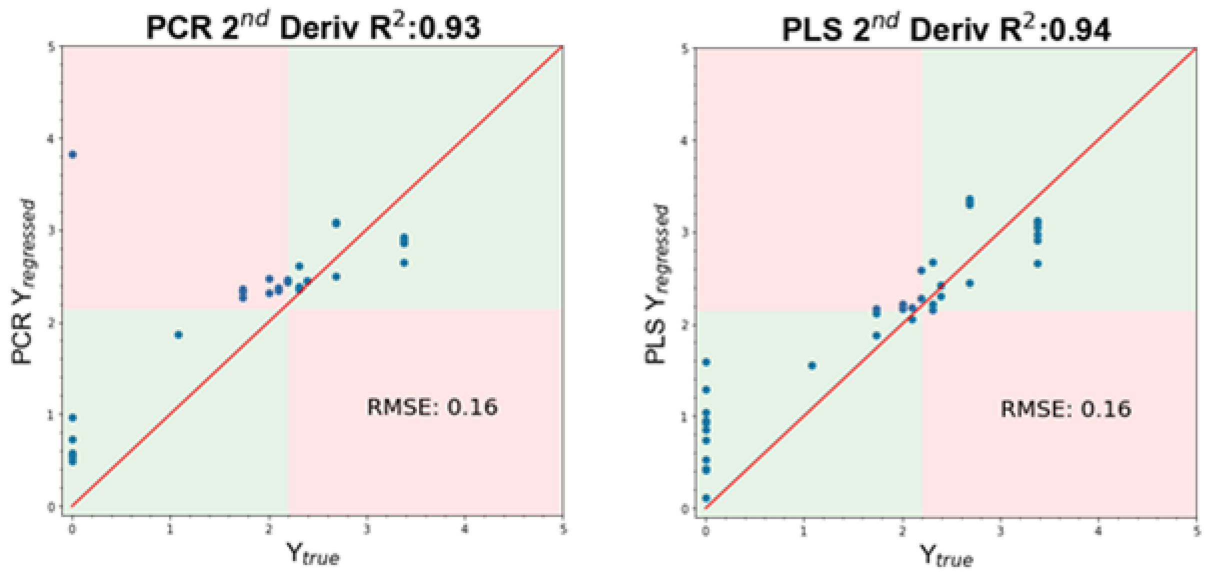
ATR Infrared Spectroscopy for the Diagnosis of Neonatal Respiratory Distress Syndrome

Lecithin/Sphyngomyelin (LS) ratio for lung surfactant analysis

Presently done by GC/MS

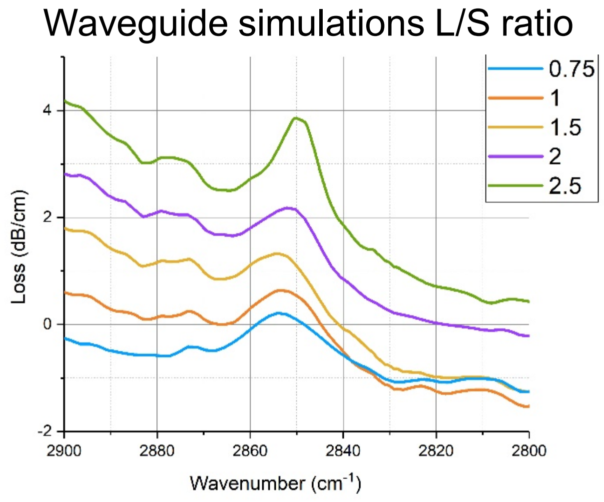
ATR/FTIR MIR spectra (in dichloromethane) combined with machine-learning



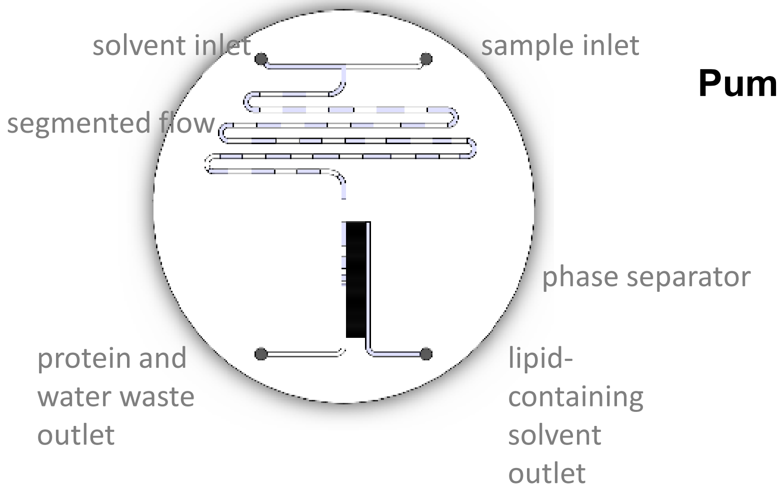


Waseem Ahmed, Aneesh Vincent Veluthandath, Jens Madsen, Howard W Clark, Antony D Postle, James S Wilkinson and Ganapathy S Murugan
Photonics West 2021 - Optical Diagnostics and Sensing XXI: Toward Point-of-Care Diagnostics; 1165104 (2021)

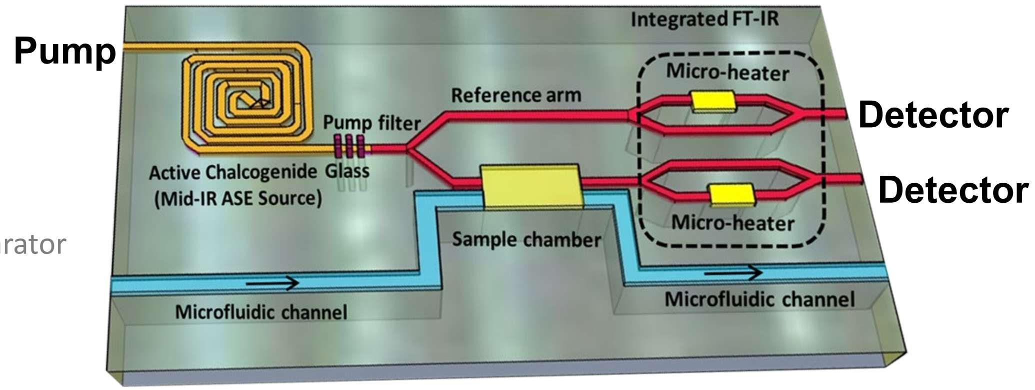
Ongoing work



Lung surfactants on waveguides



Liquid Phase Extraction



Mid-IR FTIR spectrometer on a chip

Requires improved waveguide processing for low loss and repeatability

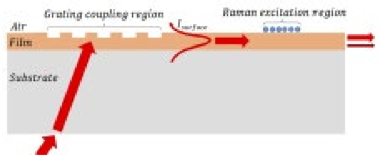
Improved instrumentation – low noise is as important as high sensitivity for LoD

Sample preparation and presentation – paper fluidics, monolithically-integrated, or hybrid

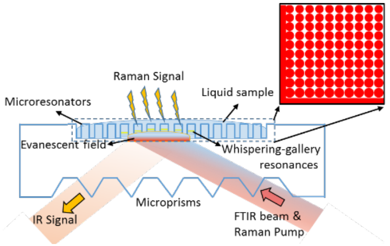
Compromise between sensitivity and fibre input/output coupling

Complementary work

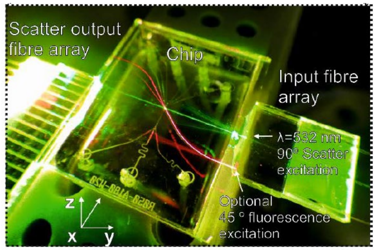
Southampton antimicrobial resistance clinical research facility
Robert Read, Saul Faust, James Wilkinson, Hywel Morgan, Jeremy Webb & Tristan Clark
UK National Institute for Health Research Capital Grant



Flexible Raman biosensing platform for low-cost health diagnostics
James Wilkinson, Philip Bartlett, Michalis Zervas & Robert Read
UK EPSRC Healthcare Technologies Grant



Combining the strengths of mid-IR and Raman spectroscopies on a single chip for rapid bedside biomarker diagnostics
Senthil Murugan Ganapathy, James Wilkinson, Antony Postle, Jens Madsen and Howard Clark;
UK EPSRC Healthcare Technologies Grant



Monolithically-integrated cytometer for measuring particle diameter in the extracellular vesicle size range using multi-angle scattering
Jonathan T. Butement, Paul M. Holloway, Joshua A. Welsh, Judith A. Holloway, Nicola A. Englyst, Peter Horak, Jonathan West and James S. Wilkinson, Lab Chip

MISSION A new UK EPSRC Programme Grant

Mid-Infrared Silicon Photonic Sensors for Healthcare and Environmental Monitoring

University of Southampton — Graham Reed (PI), Goran Mashanovich & James Wilkinson

University Hospital Southampton NHS Foundation Trust — Saul Faust

National Oceanography Centre — Matthew Mowlem

University of York — Thomas Krauss & Yue (Christina) Wang

The University Of Sheffield. — Jon Heffernan

- Therapeutic drug measurement (TDM)on patient blood samples
- Cancer diagnostics using stored patient serum samples
- Oceanic gas detection with climate relevant performance

Conclusion

- Integrated optical waveguides offer stable, high sensitivity optical detection using a range of basic optical tranduction phenomena
- Mass-manufacture should allow production of low-cost chips with high sensitivity and advanced functionality
- Present NIR/Vis approaches use labels and/or surface receptors
- Label-free waveguide Raman and mid-IR approaches under investigation
- Chalcogenide and GOS wavegides promising for direct vibrational spectroscopy
- Moving to integrating optical functions in microfluidic systems for low-cost water quality, health and personal safety systems
- Lung surfactants (IRDS), TDM, cancer, whooping cough, ebola, stem cells ....

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