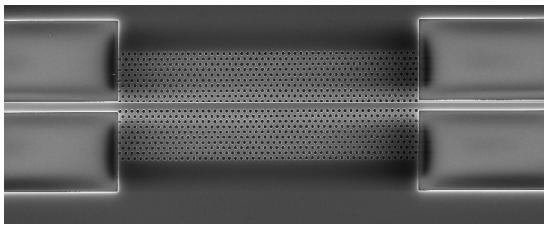
Development of high sensitivity biosensors using SOI photonic crystal waveguides



J. García-Rupérez[1], **V. Toccafondo[1]**, M. J. Bañuls[2], A. Griol[1], J. G. Castelló[1], S. Peransi-Llopis[2] and A. Maquieira[2]

1:Valencia Nanophotonics Technology Center, Universidad Politécnica de Valencia, Camino de Vera s/n, 46022 Valencia, Spain
2: Departamento de Química, Universidad Politécnica de Valencia, Camino de Vera s/n, 46022 Valencia, Spain

Outline

- Motivations
- High sensitivity Photonic Crystal waveguide based sensors
- Experimental results
  - Refractive index sensing
  - Protein sensing
  - DNA hybridization detection
- Conclusions

Introduction

- EU project **Intopsens** (A highly integrated optical sensor for rapid, point-of-care label-free detection of pathogenic bacteria causing sepsis and their antibiotic resistance profiles)
- Goal = **fast and reliable detection of sepsis** as first 48h are critical

Current diagnostic technology

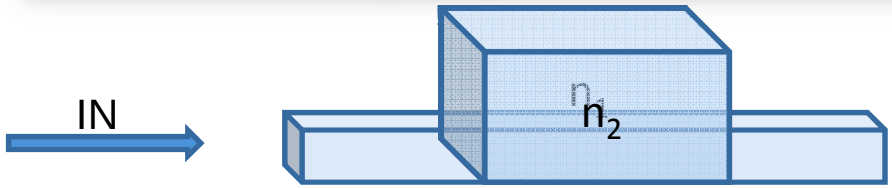
- Sample amplification through culture bottle
- Agar plate / antibiotic screening
- Taking up to **7 days**
- Lead to inappropriate antibiotic use and as such increased multidrug resistance & mortality

Intopsens Technology

- Microfluidic filtration and concentrating of existing bacteria + on-chip PCR
- Photonic sensors
- Disposable cartridges
- Result within **one hour**
- Correct medication

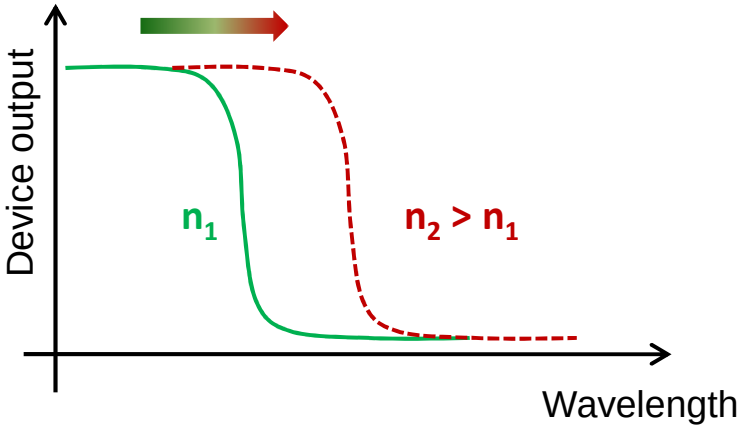
Optical sensor working principle

Ring resonators, corrugated wg, photonic crystal waveguides, MZI have a characteristic output spectrum with some resonance/peak/bandgap

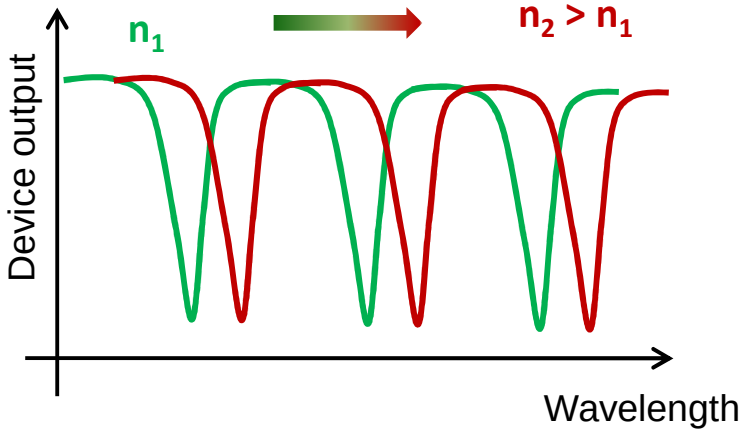


Optical waveguide

$\Delta n \rightarrow \Delta\lambda$



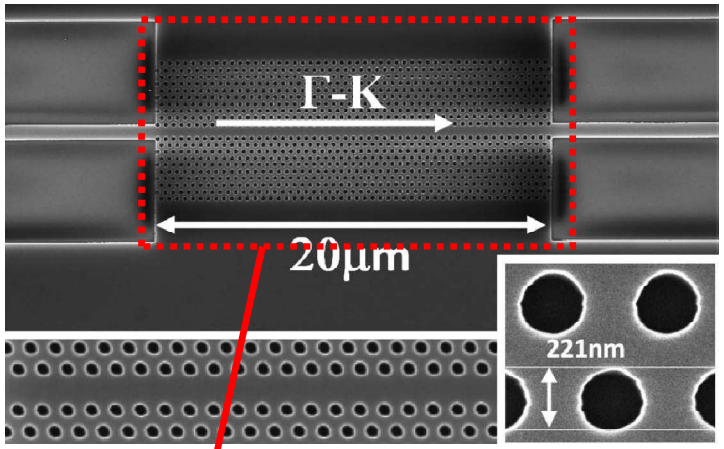
Photonic crystal wg



Ring resonator

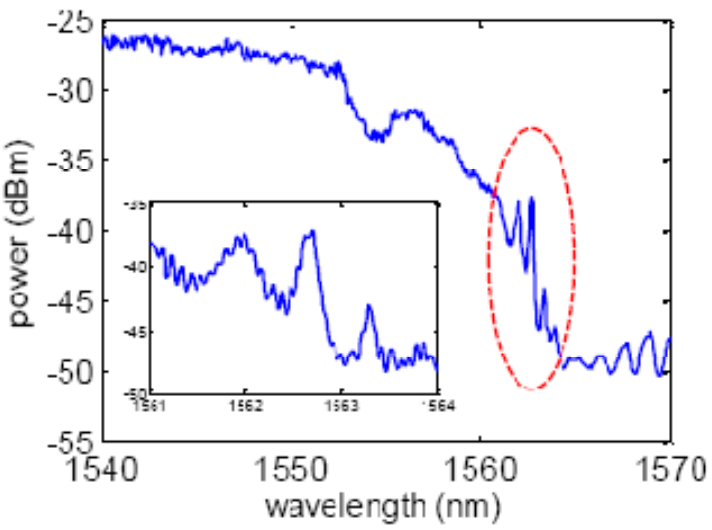
Photonic Crystal waveguide based sensors

- Why photonic crystals? Sharp fringes from cavity effect + slow light at band edge → stronger interaction with surrounding medium (around 1.5µm)



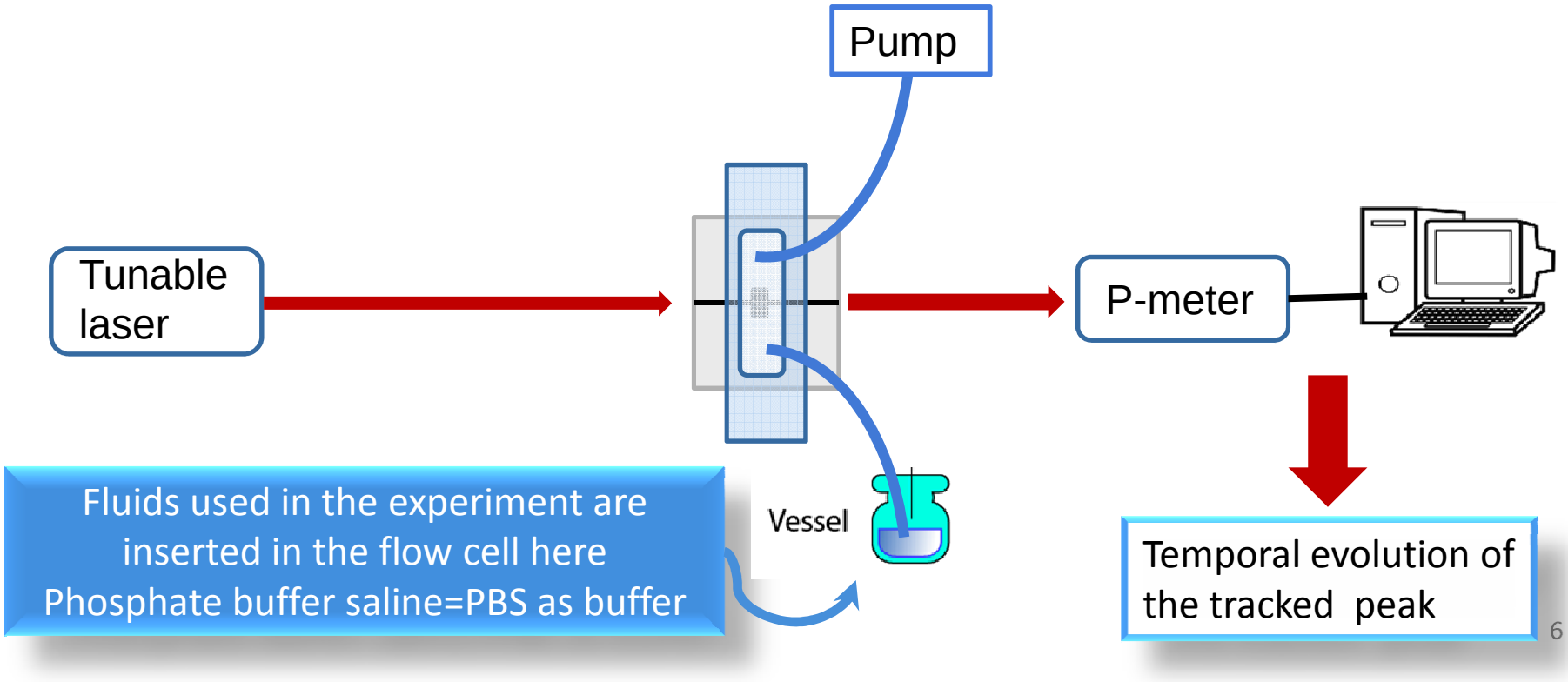
Sensor size ≈ 20µmx7µm
Potentially >7.000 sensing structures in a 1mm² area (limited by functionalization and fluidics)

Spectrum in air

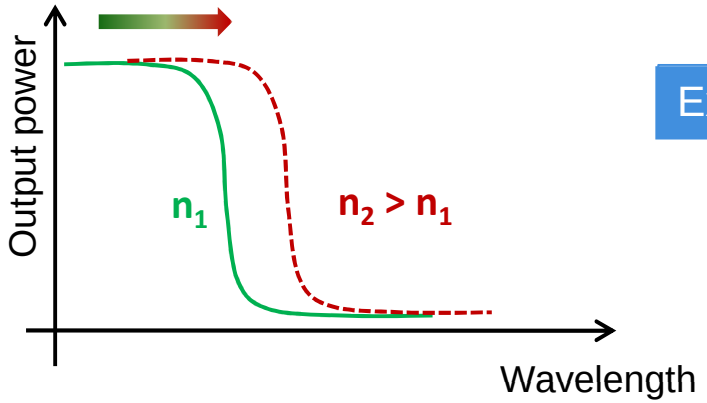


Measurement set-up and steps

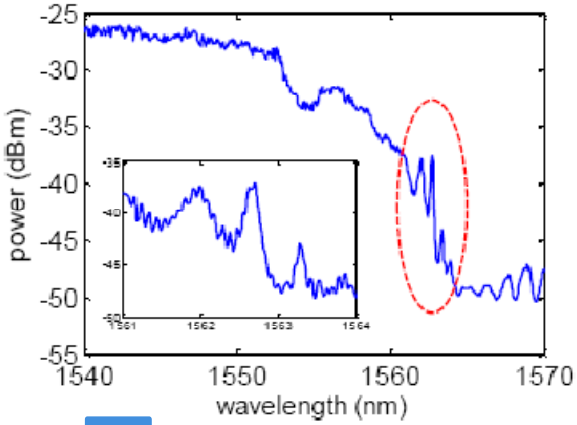
- Refractive index sensing → is the device sensitive enough?
- Protein detection → first "bio" assays
- DNA hybridization detection → the "ultimate" biosensor



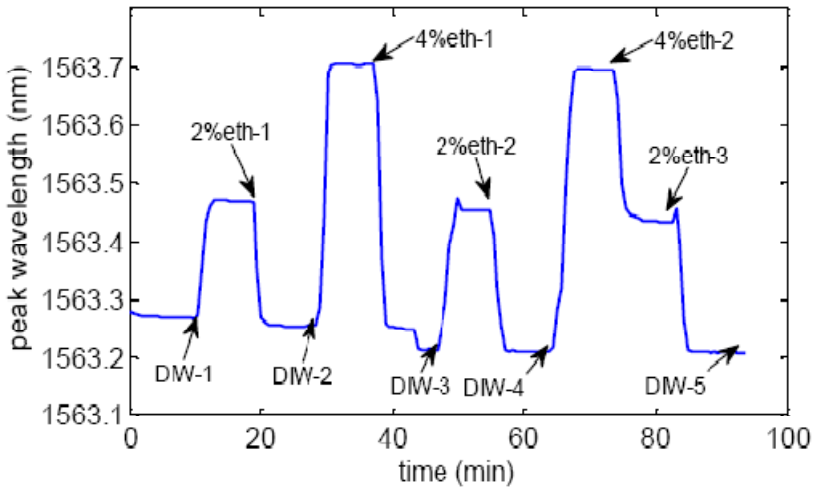
Refractive index sensing



Experimental



We follow the shift of the fringe during the whole experiment and plot its temporal evolution
For ethanol dilution in DI water

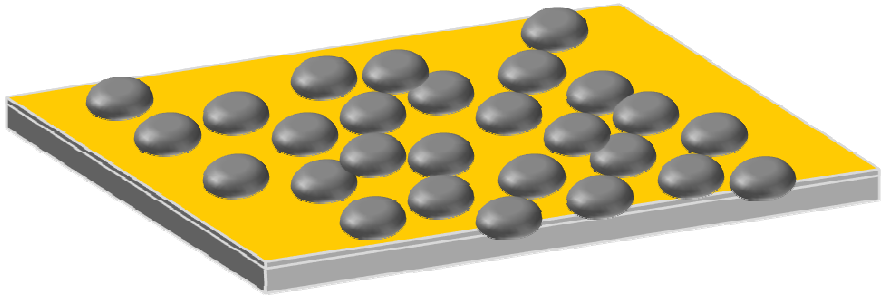


For RI sensing we achieve a sensitivity of 175 nm/RIU and an estimated detection limit of 3.5×10^{-6} RIU

Surface functionalization BSA/AntiBSA assay

- Chemical sample preparation (UPV-SYM)

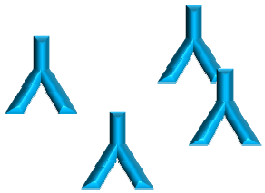
1. Surface activation (isocyanate layer)
2. Receptors (Bovine Serum Albumin BSA)
3. Ovoalbumin blocking

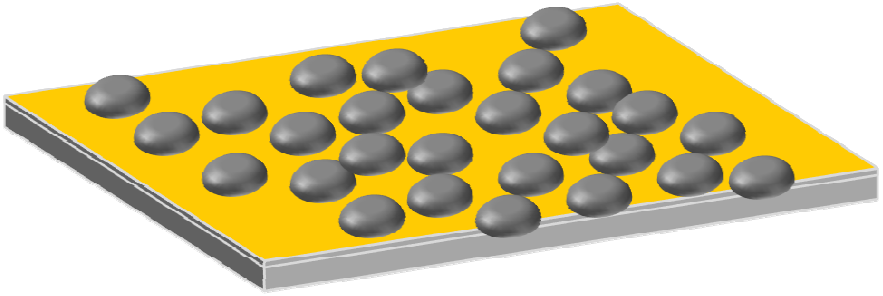


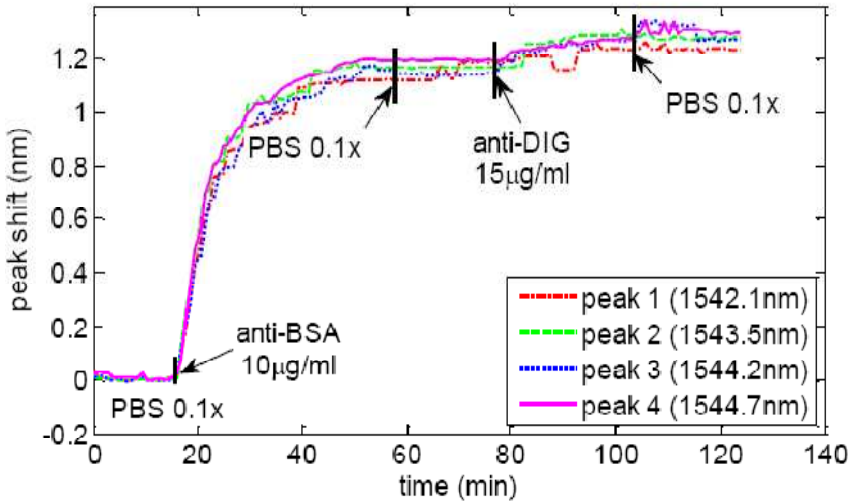
Result= BSA on surface ready to recognize antiBSA antibody

Protein sensing: BSA/AntiBSA

Anti-BSA







PBS=phosphate buffer saline
antiDIG= other antibody used for control

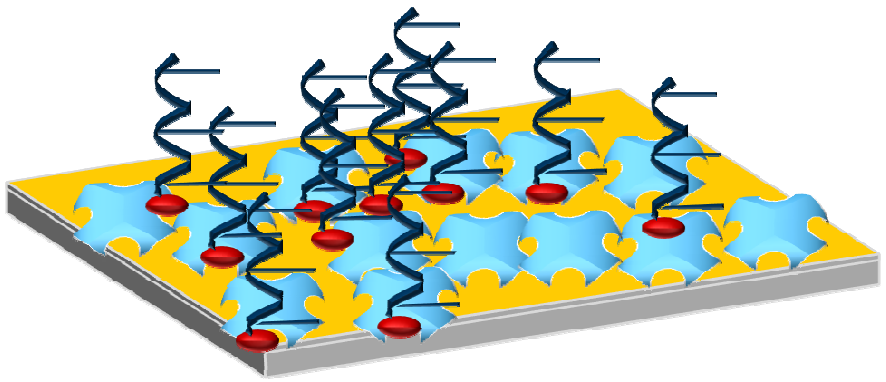
- Mass density detection limit below 2.1 pg/mm^2
- Specific detection achieved

J. García-Rupérez, V. Toccafondo, et al., Opt. Express, **18** (2010)

Surface functionalization for single strand DNA sensing

- Chemical sample preparation (UPV-SYM)

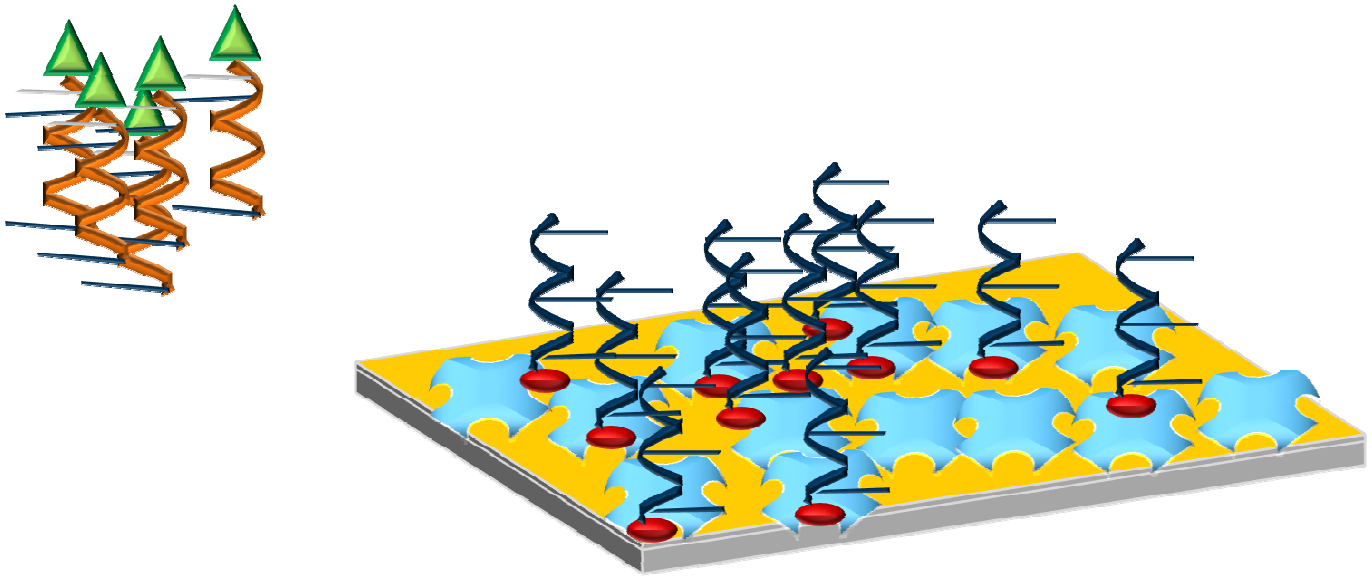
1. Surface activation (isocyanate layer)
2. Streptavidin incubation (receptors)
3. Ovoalbumin blocking
4. Biotinylated ssDNA probe incubation
   (biotin has high affinity with streptavidin)



Result = ssDNA probes are trapped on the chip's surface
↪ ready to bind with complementary strand

Sensing ssDNA with PhCr waveguide s

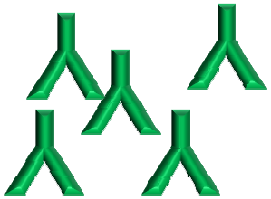
1. Flow of complementary ssDNA strand (labelled with digoxigenin)

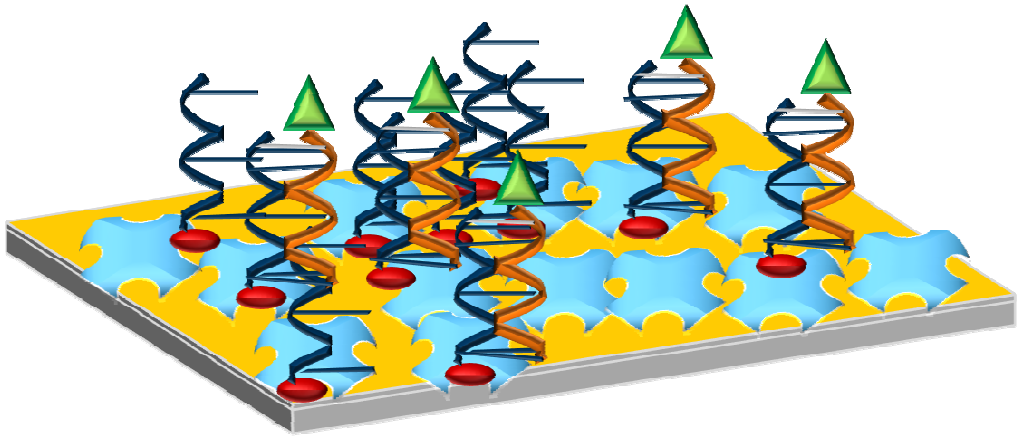


A small shift in the bandgap position is expected due to DNA hybridization on the sensor's surface

Sensing ssDNA with PhCr waveguide s

1. Flow of complementary ssDNA strand (labelled with digoxigenin)
2. Control measurement with antidigoxigenin (high affinity with DIG antigen → specific binding ONLY if complementary DNA on chip)



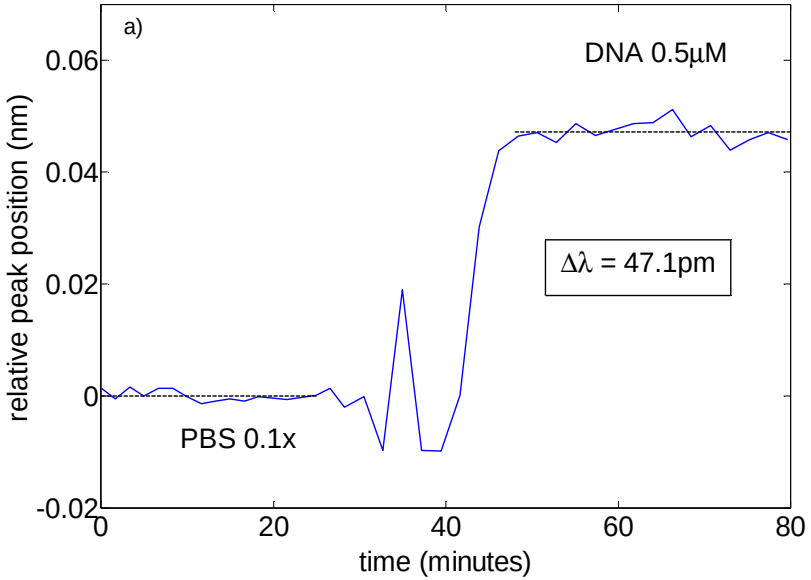


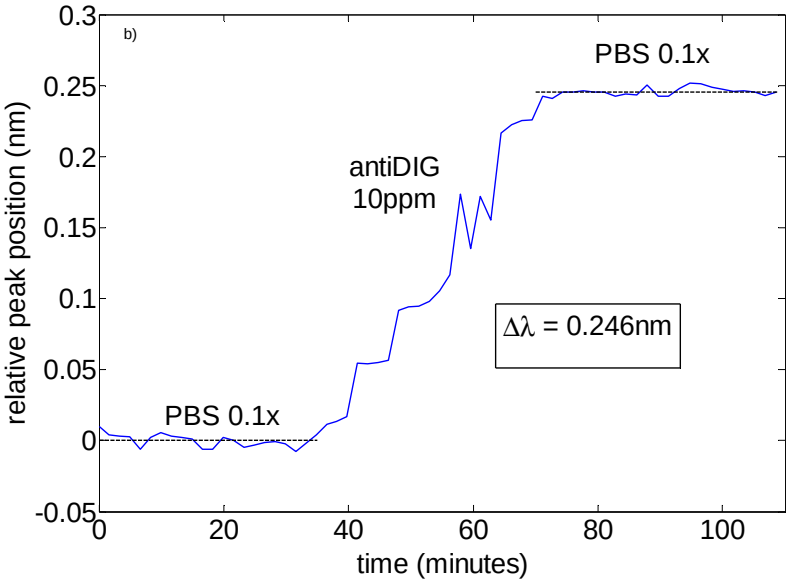
A larger shift in the bandgap position is expected due to the specific binding of antiDIG to the DIG on the DNA

Detecting DNA - Results

- Sensing experiment performed:

PBS → DNA 0.5µM → PBS → a-DIG → PBS





DL≃ 20nM

AntiDIG succesfully bound

V. Toccafondo et al. Optics Letters 2010

Conclusions

- ✓ Realization of Photonic Crystal waveguides for (bio)-sensing

- ✓ RI measurements and specific antibody/antigen recognition
  - S=175 nm/RIU, DL=3.5x10^{-6} RIU for ethanol
  - DL< 2.1pg/mm2 for AntiBSA (considering a monolayer)

- ✓ On chip DNA hybridization achieved with PhCr based photonic chip → Detection limit = 20nM for direct detection

- TO DO:

  → Integration with microfluidics and packaging

  → achieve better sensitivity…cavities, slots etc…

THANK YOU FOR YOUR ATTENTION!

Contact: Veronica Toccafondo
vertocca@ntc.upv.es

Acknowledgements to EU STREP

Spanish MICINN under contracts TEC2008-06333 and CTQ2007-64735/BQU
Universidad Politécnica de Valencia: PAID-06-09
Conselleria d'Educació through program GV-2010-031