SMART LIGHTING

SMART LIGHTING ENGINEERING RESEARCH CENTER

Lighting Innovation for a Smarter Tomorrow

NSF

Point of Care Biosensors

ERC Biosensors Application Area

Michael Ruane, Professor, ECE, BU

Rensselaer · Boston University · UNM · Howard University · Rose-Hulman Institute of Technology · Morgan State University

SPA 2.1 Biosensors Application Area

SPA2.1: *Spectral Reflectance Imaging Biosensors (SRIB) (Ruane, Unlu, BU)

SPA2.2: *High Throughput Biosensors Using Plasmonic Nanostructures (Altug, BU)

SPA2.3: *Water Contamination Detection and Measurement using UV Intrinsic Fluorescence (Sawyer, RPI)

Spectral Reflectance Imaging Biosensors (SRIB)

Selim Ünlü, Michael Ruane, PI

Professors, ECE

Boston University

Graduate Students: Margo Monroe, Alexander Reddington

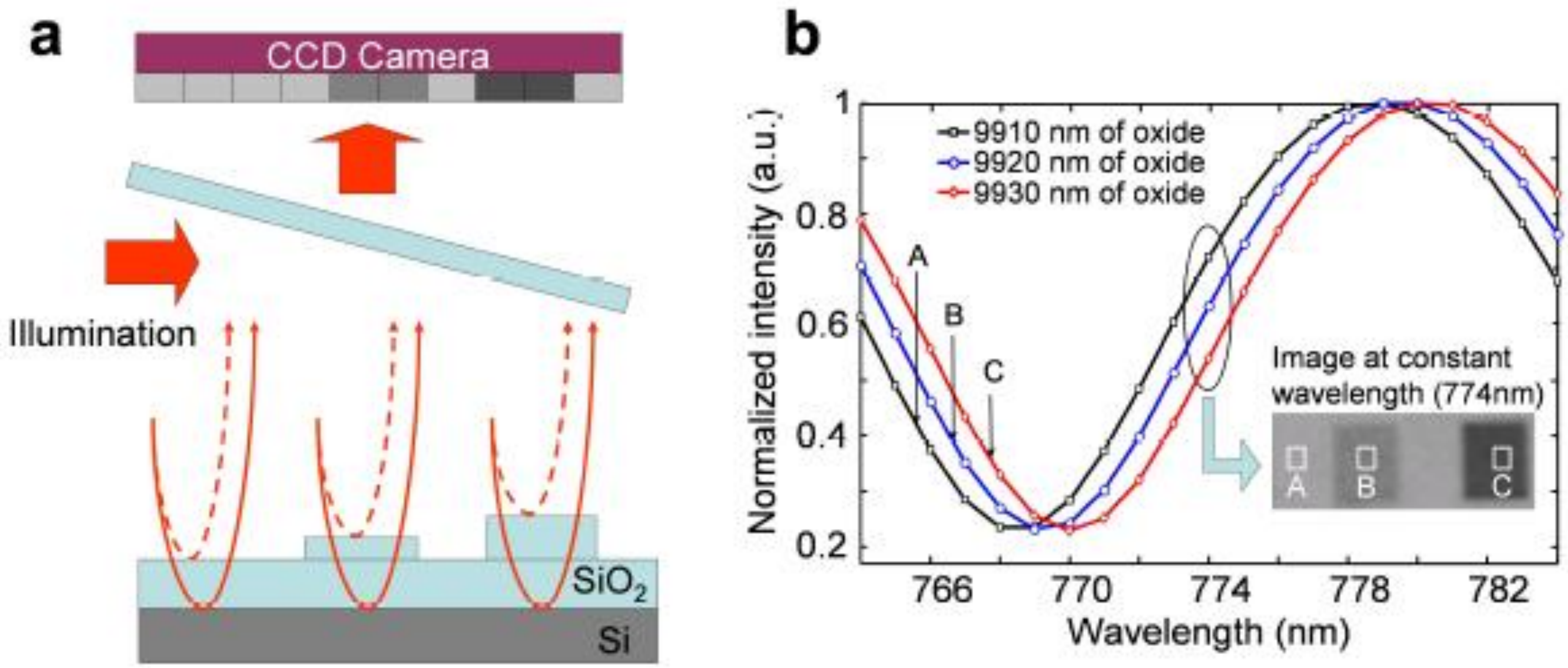
Biological Sensing and Imaging Laboratory

Spectral Reflectance Imaging Biosensors (SRIB)

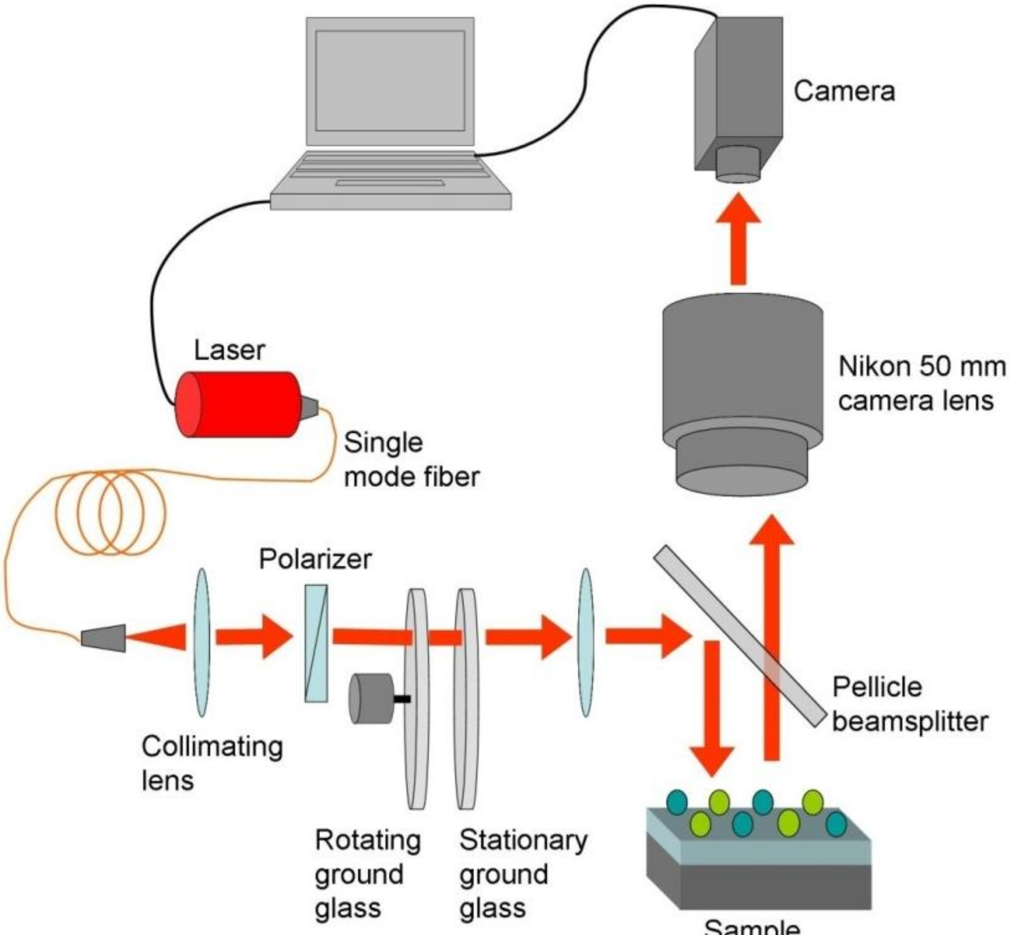
- ***Point-of-care medicine and public health***
- ***325 million DALYs per year*** (disability-adjusted life years) from the six highest infectious diseases
- More appropriate diagnostic tools for global health applications, especially point-of-care, developing world
  - **ELISA** (Enzyme-linked Immunosorbent Assay) – labeled, lab, skill
  - **SPR** (surface plasmon resonance) label free, temperature sensitive, laboratory
  - **Microarray** – label efficiency, quenching, bleaching, probe affinity

Spectral Reflectance Imaging Biosensors (SRIB)

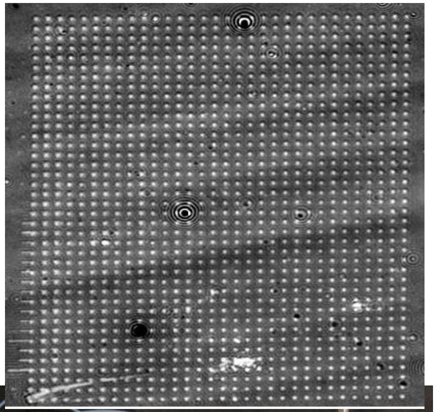
SRIB Principles

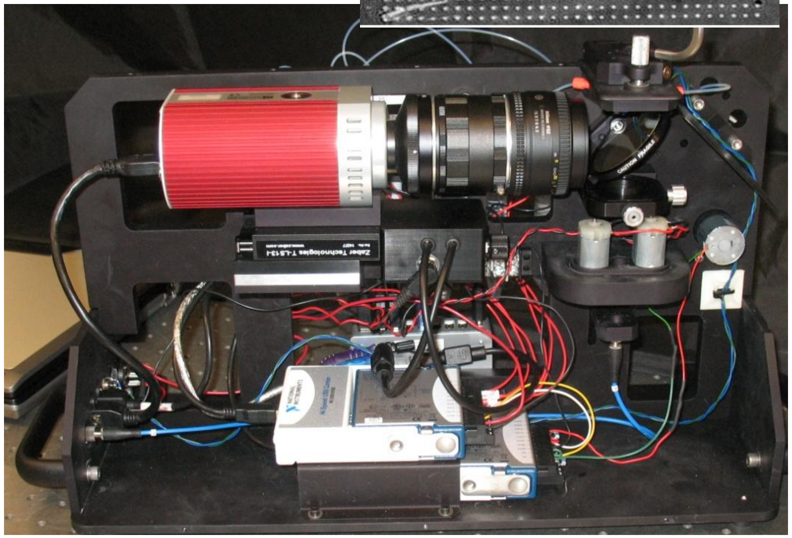


Spectral Reflectance Imaging Biosensors (SRIB)



1000-spot array

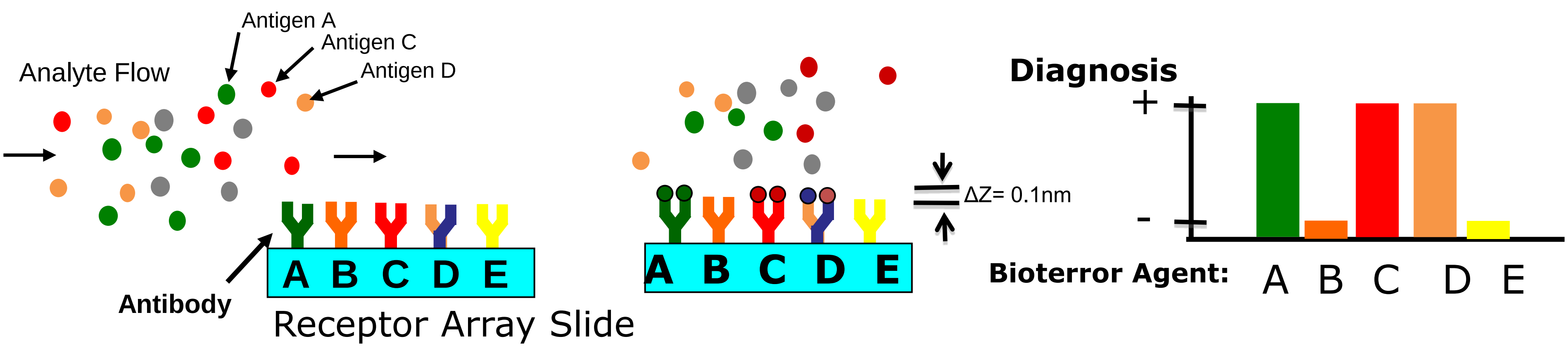




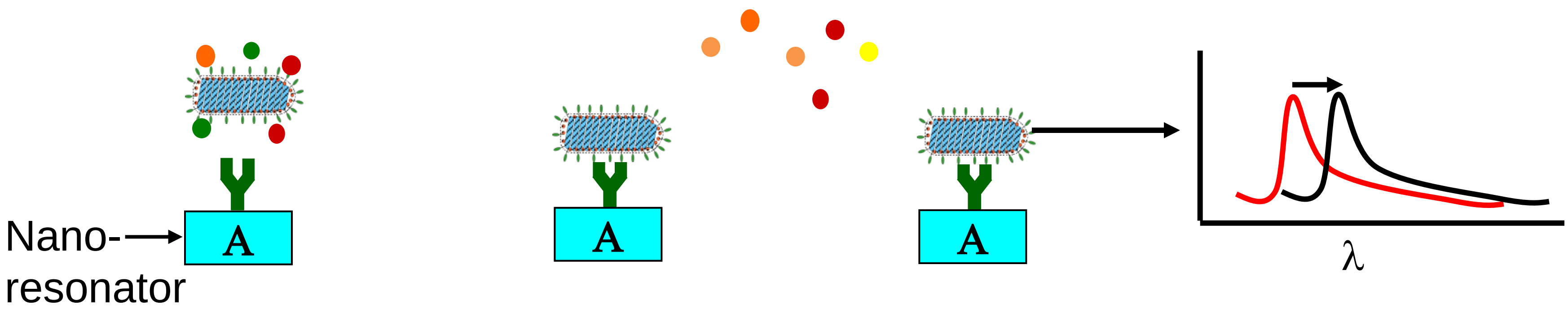
Zoiray, Inc., David Bergstein

Pathogen Detection Approaches

Antigen Detection



Whole virus detection



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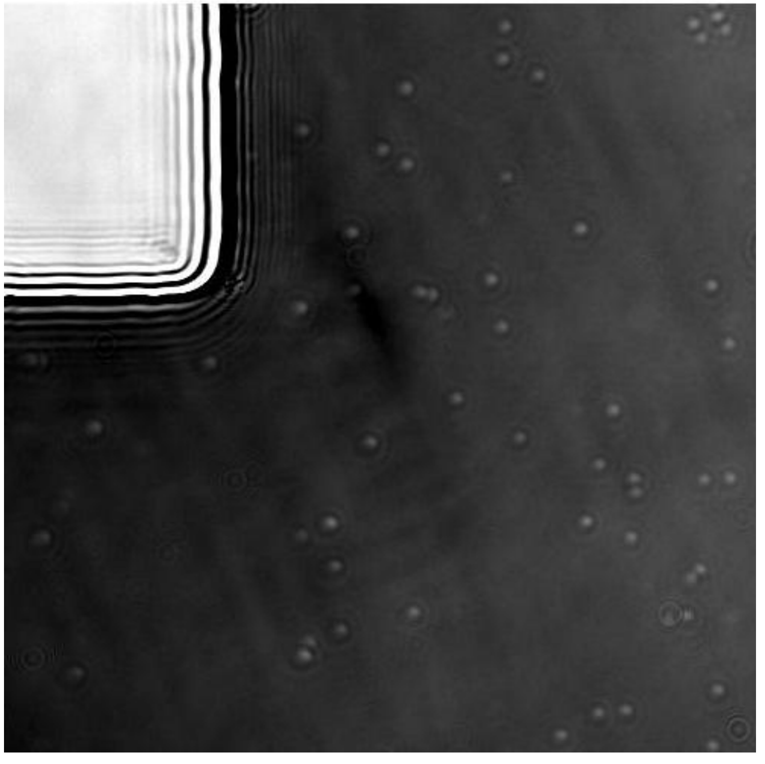
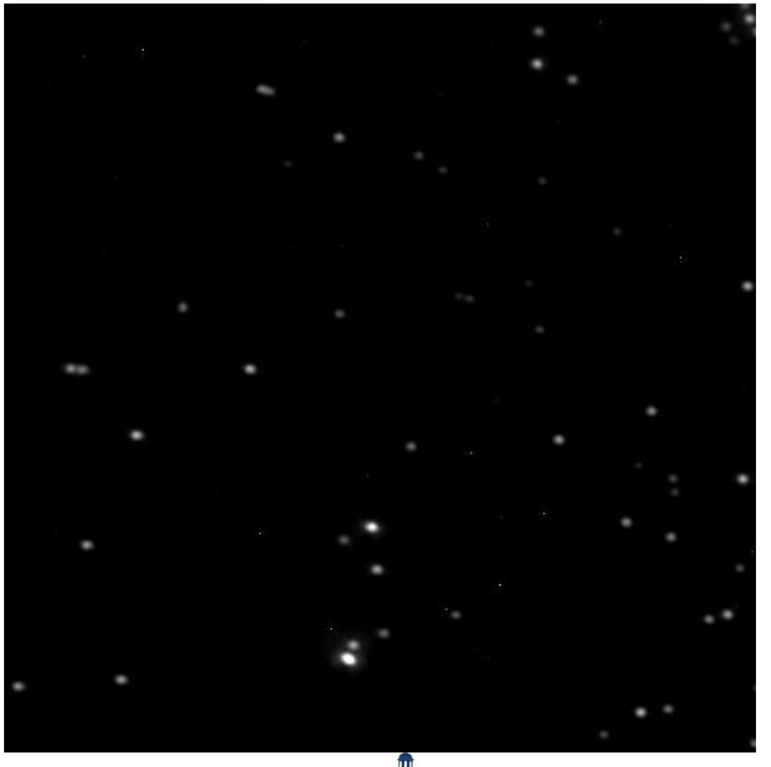
Spectral Reflectance Imaging Biosensors (SRIB) - Single Particle Detection

Fluorescent 100nm Carboxyl modified beads immobilized on Lysine surface. Incubation time 15min, 10^8 particles/ml

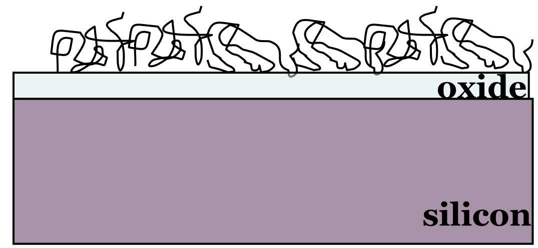




Surface Protocols

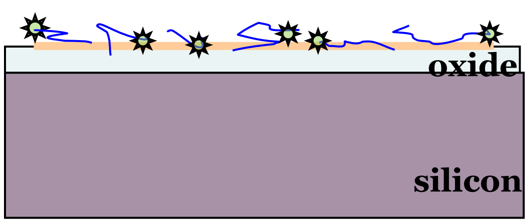
- Epoxysilanization (Control)
  - ▫ 0.1M NaOH
  - ▫ 4hr γ-GPS(glycidil propyl silane) (5% in dry toluene) at 37 C
  - ▫ toluene/methanol wash
  - ▫ overnight at 100 C

- Polymer Coating
  - – 0.1M NaOH
  - – 30min polymer
  - – extensive wash
  - – Vacuum dry at 80 C

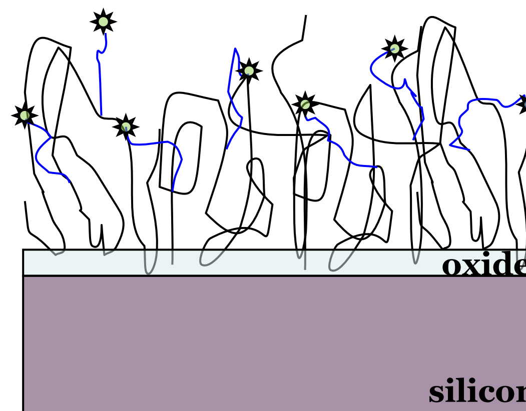


Spotting of Oligonucleotides

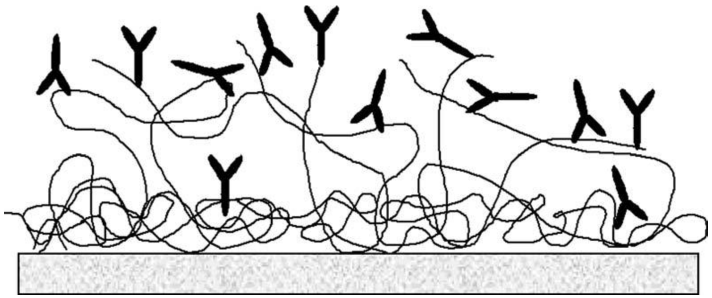
▫5′-amine-modified and 3’-Cy5-modified oligos in sodium phosphate buffer, non-contact microarray spotter.



Spotting

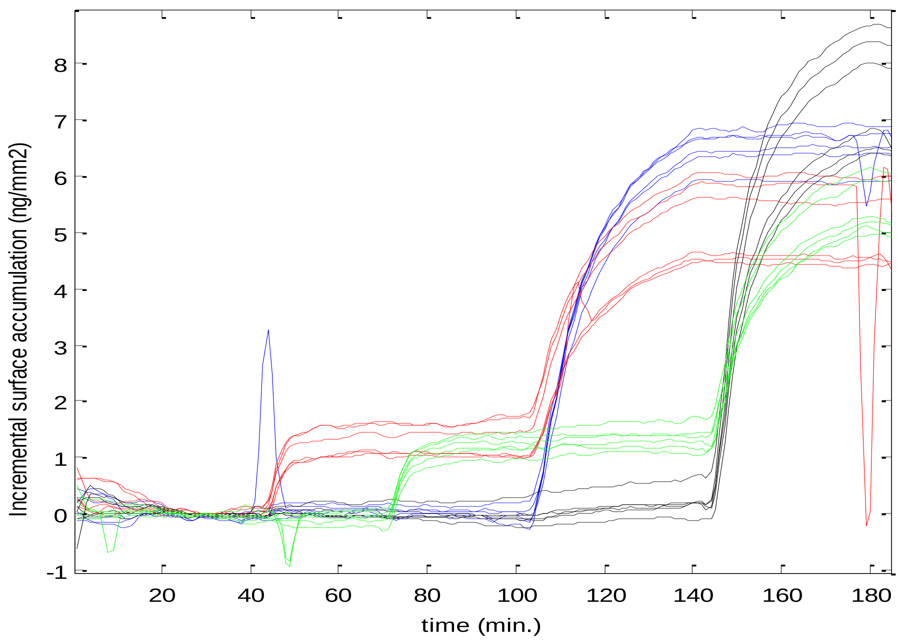


Functional antibodies on the surface

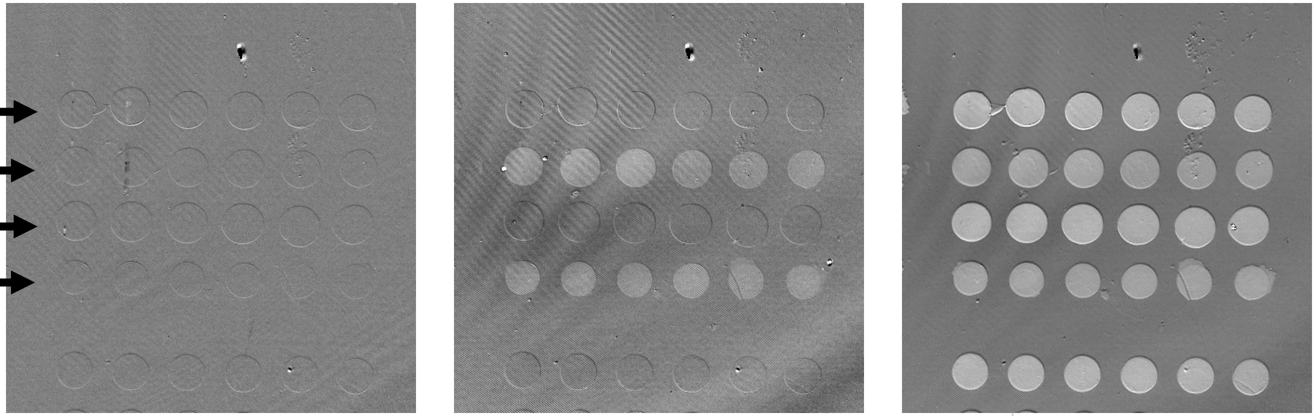


G. Pirri et al., Anal. Chem. 76, 1352-1358 (2004)

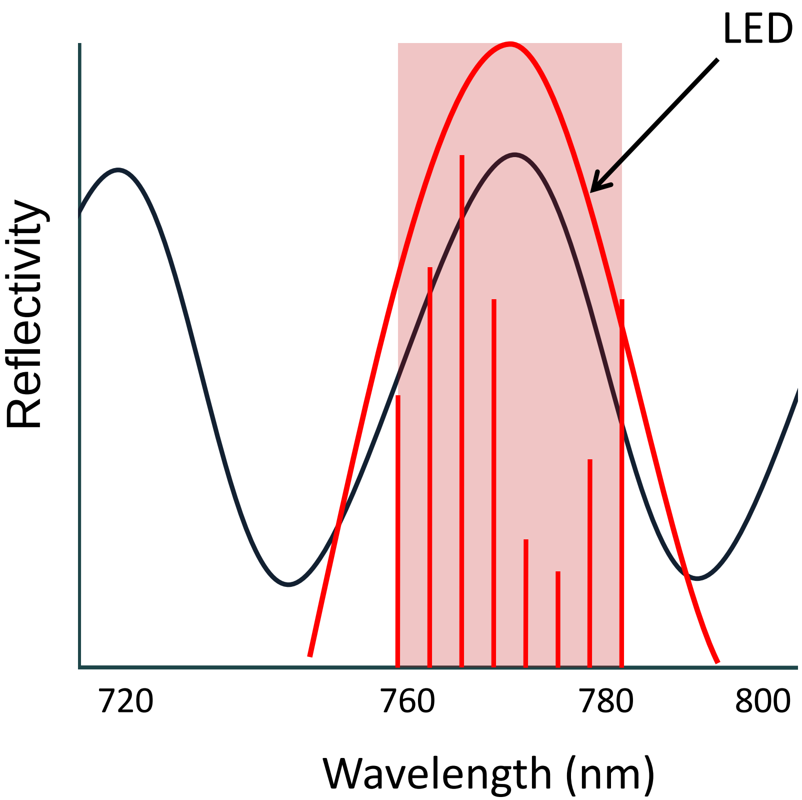
A. Yalcin et al., Anal. Chem. 81, 625-630 (2009)



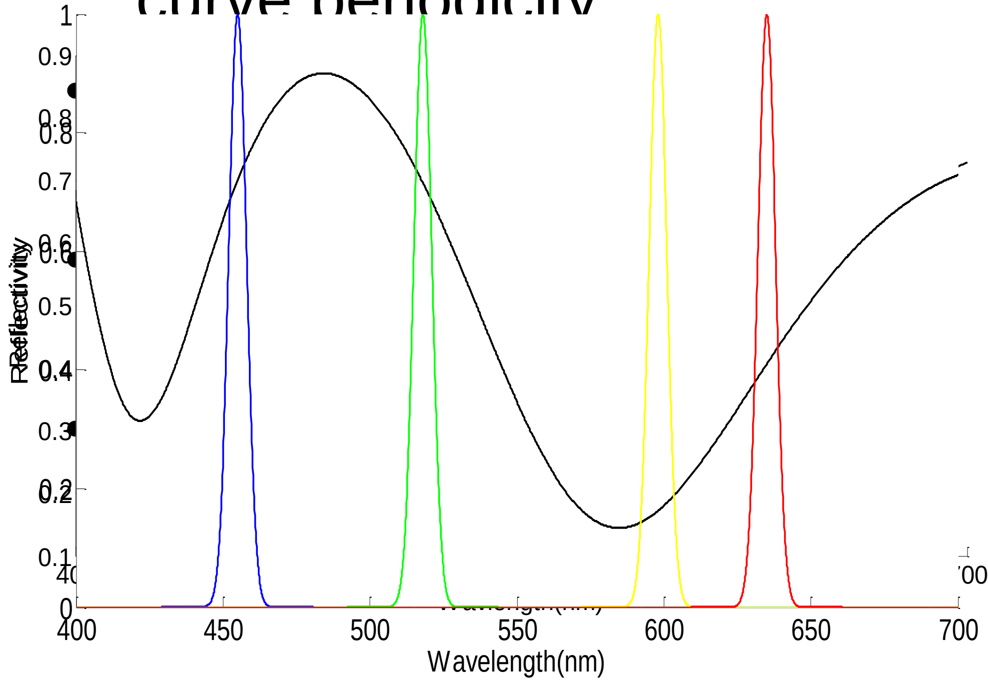
mouse IgG
anti-mouse IgG
rabbit IgG
anti-rabbit IgG

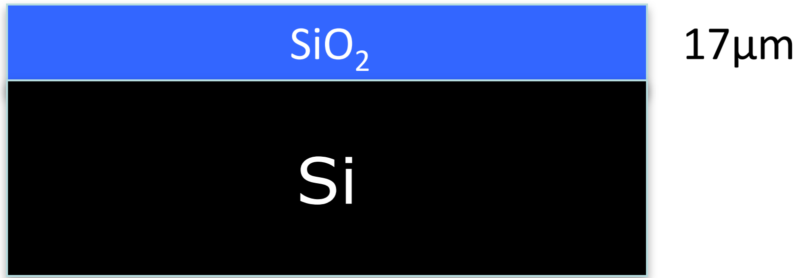


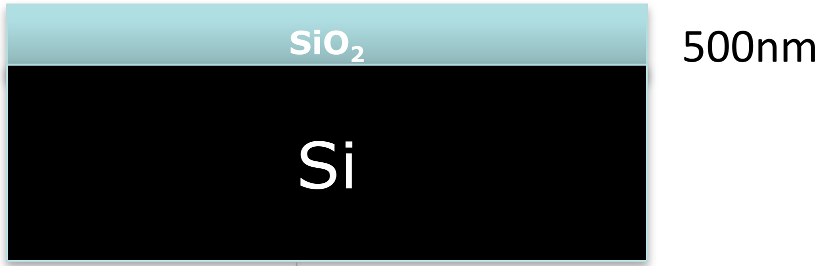
Interferometry with LEDs vs. Laser



- Oxide thickness affects curve periodicity







High Throughput Biosensors Using Plasmonic Nanostructures

Hatice Altug, PI

Assistant Professor, ECE

Boston University

Graduate Students: Ahmet Ali Yanik, Alp Artar, Min Huang, Ronen Adato

Integrated Nanophotonics and Biosensing Systems Lab

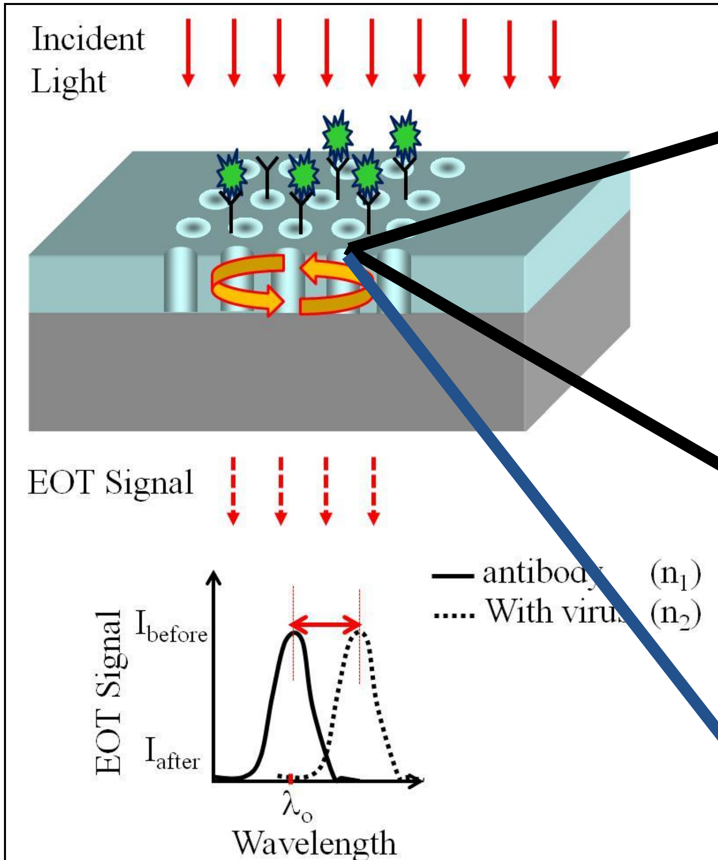
Nano-Photonics: Manipulating Light On-Chip

Applications:

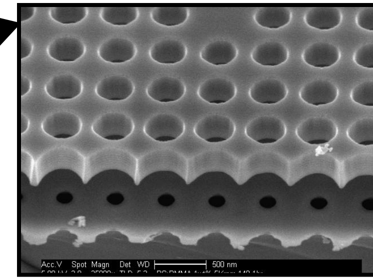
I- Life-Science
- ➔ Proteomics
- ➔ Cancer, Alzheimer's

II- Bio-defense
- ➔ Infectious Diseases
- ➔ Viral Out-breaks

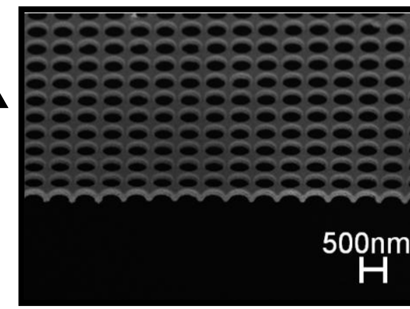
III-Pharmacology
- ➔ Drug/Vaccine Discovery



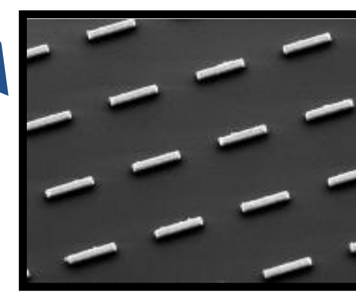
Photonic Crystals



Plasmonic Nanoholes

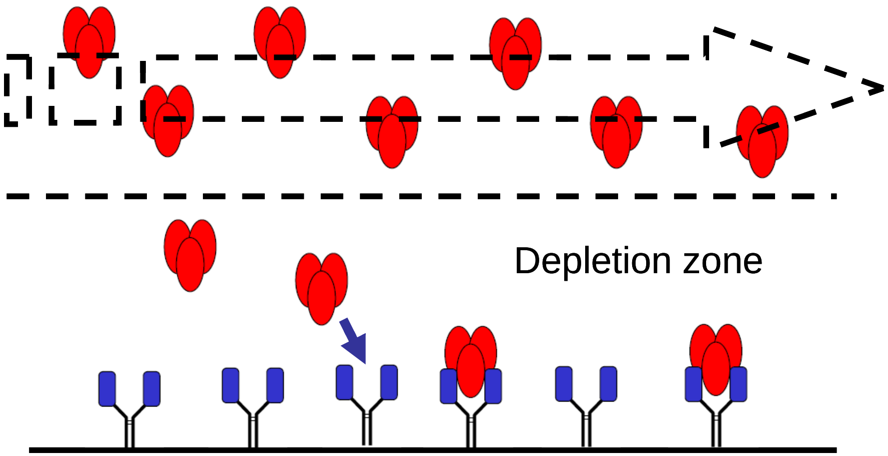


NanoAntennas



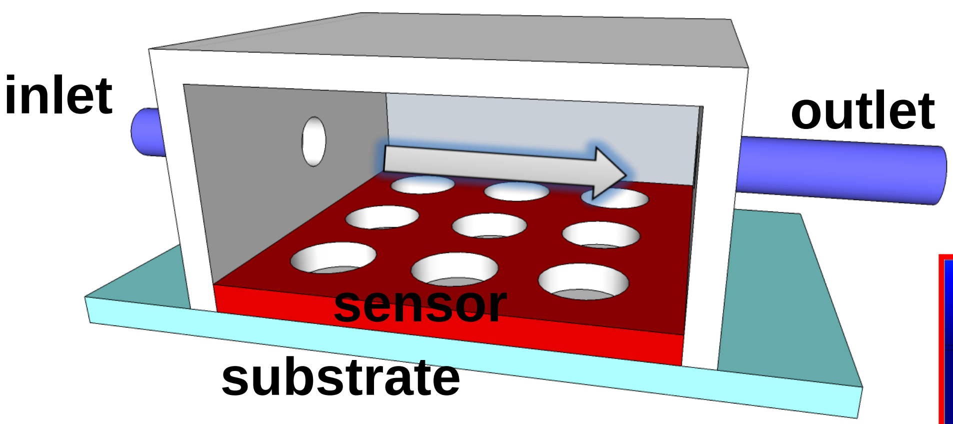
Photonic nano-resonators can enable:
- ➔ Localize light below sub-diffraction limit & enhance the field
- ➔ Increase light-molecule interaction
- ➔ Compact & Portable
- ➔ On-chip platform: Integration

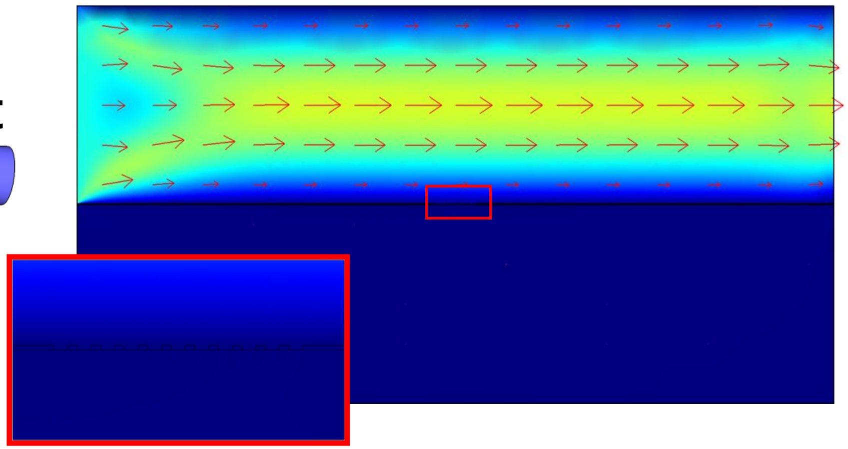
Mass Transport Limitation Problem



Nano scaled surface biosensors offers
1)Femto-molar sensitivity label-free detection
2)<u>On-chip integration</u> with microfluidics for point of care applications

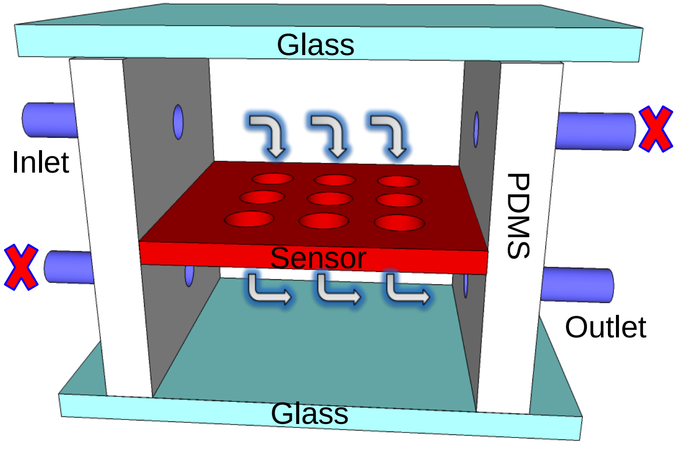
BUT…
Conventional fluidic channels leads
1) Passive delivery
2) Formation of depletion zones
<u>3) Mass transport limitation</u>

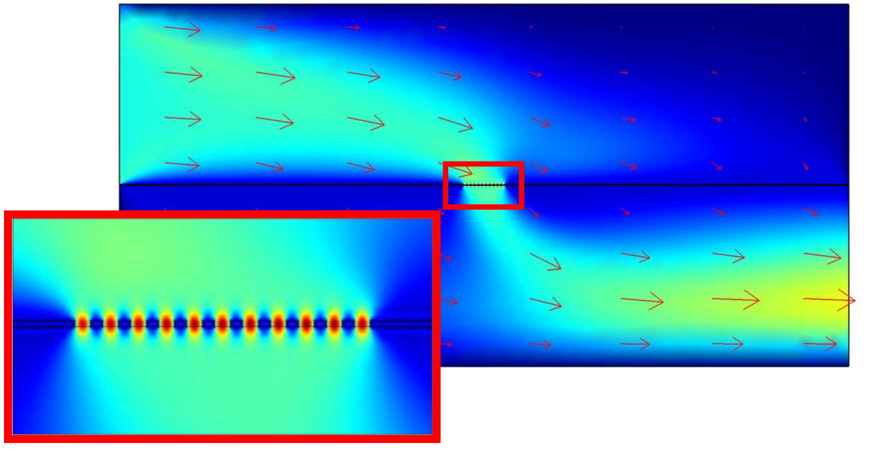




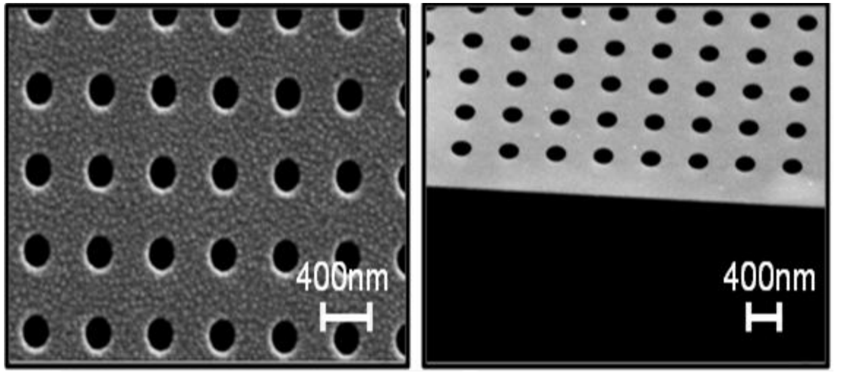
Direct Targeting Flow Scheme

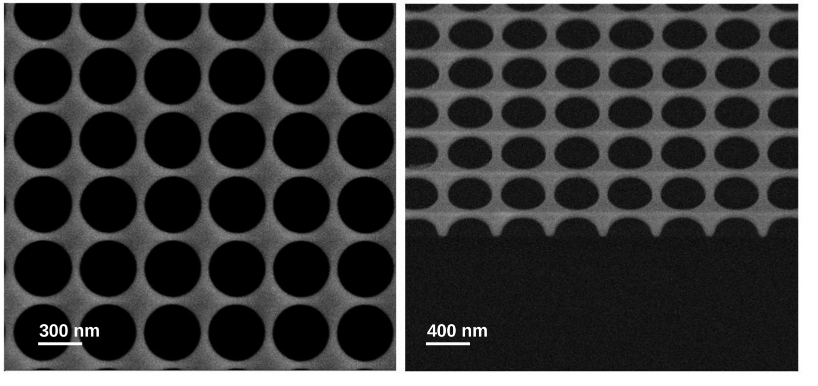
Proposed flow scheme
- Transport solutions at nano-scales
- Overcome mass transport limitations
- Actively control the fluidic flow
- Apply to highly viscosity solutions





This scheme can be employed at any nano-hole openings based sensors





Plasmonic structure

Photonic crystal structure

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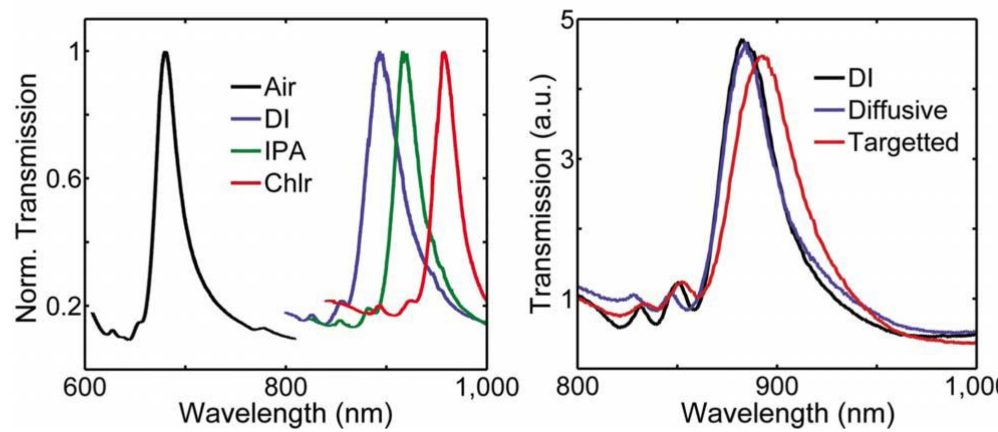
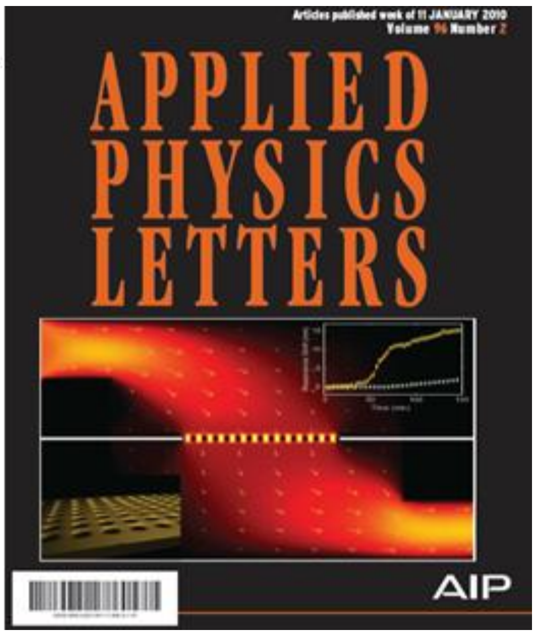
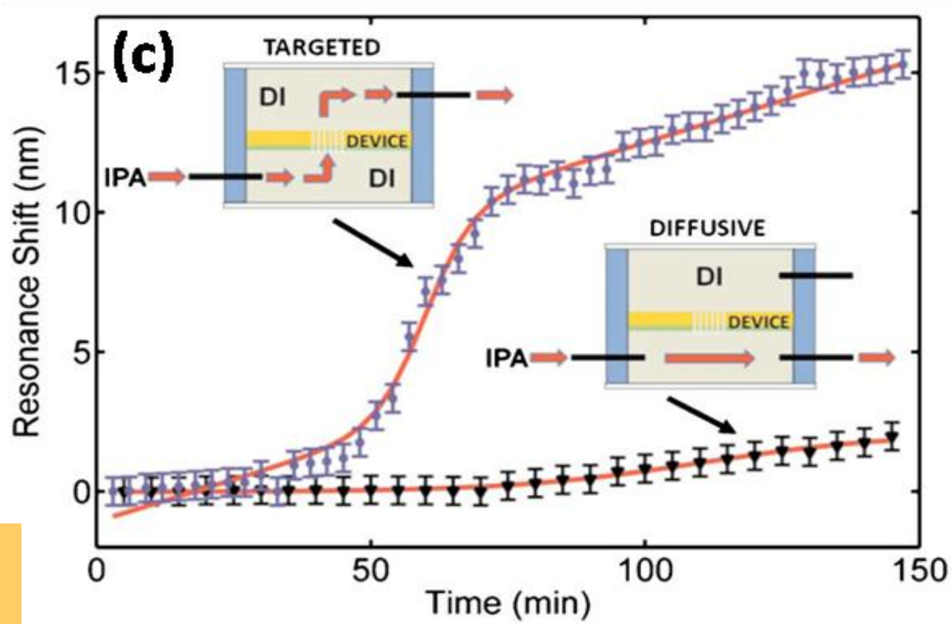
Experimental Results

Active delivery in plasmonic sensors
-Sensitivity reaches 610 nm/RIU !
-14-fold improvement in analyte delivery kinetics







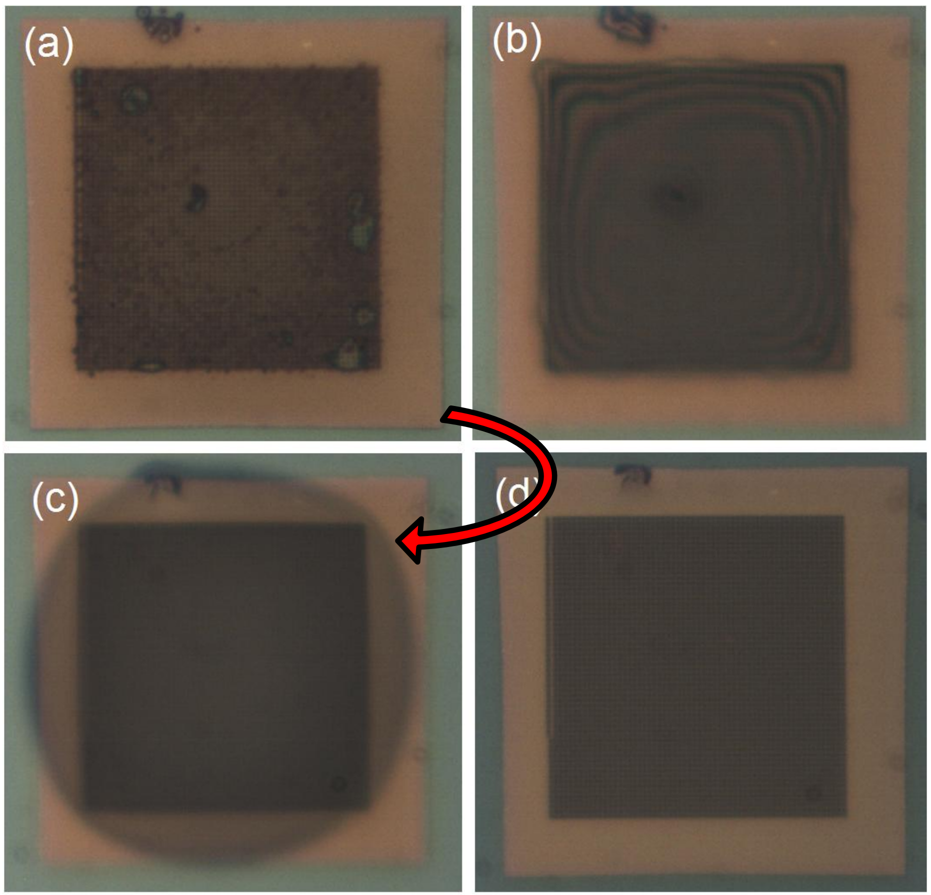
Yanik et. al, Appl. Phys. Lett . 2010

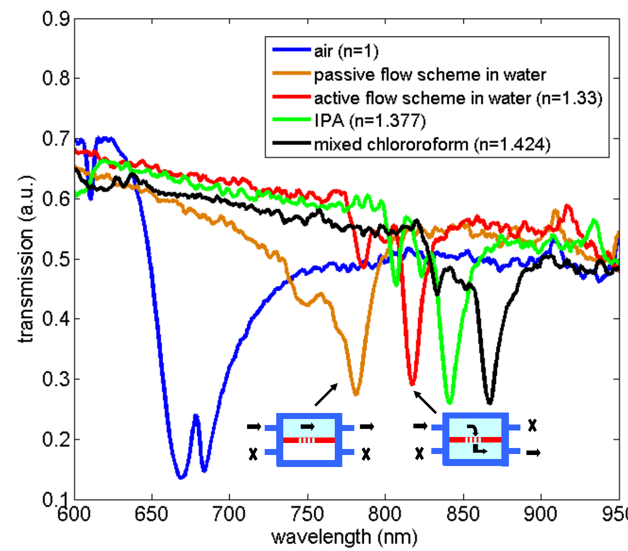
(cover of 11 January 2010)

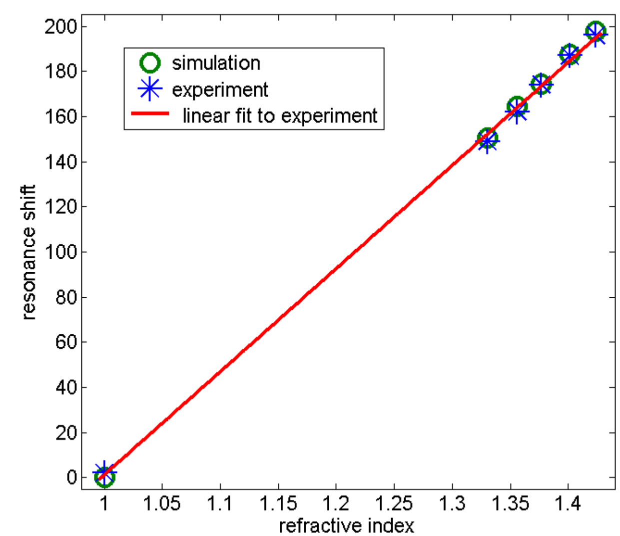
Experimental Results

Bulk measurement with photonic crystal

- Sensitivity reaches 510 nm/RIU



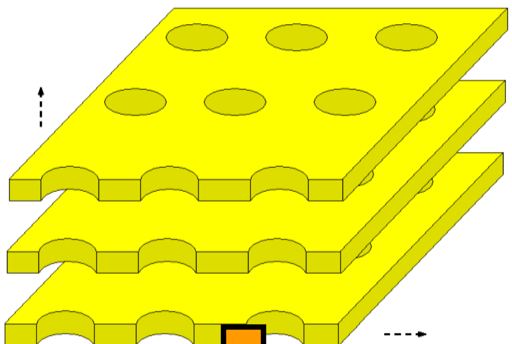




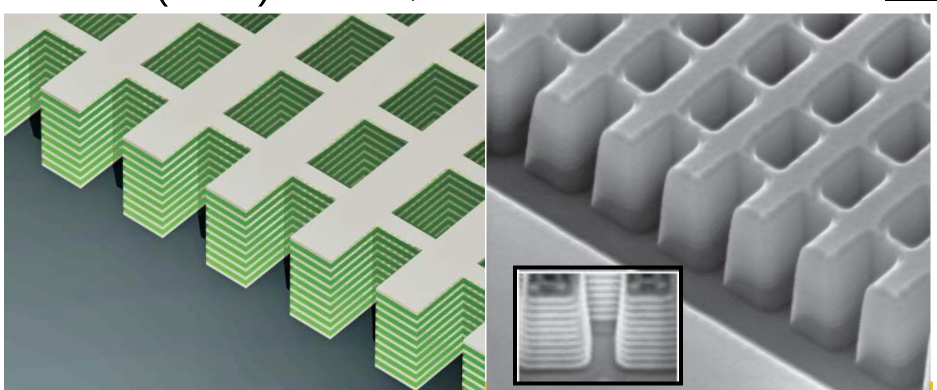
Huang et. al, Optics Express 2009

Multi-Layered Plasmonic Structures

1. Multi-Layered nanohole arrays

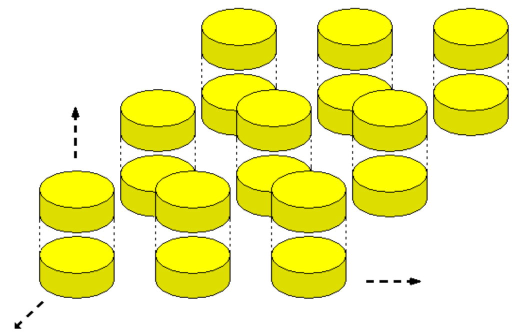


Valentiné *et. al.*
Nature (2008)

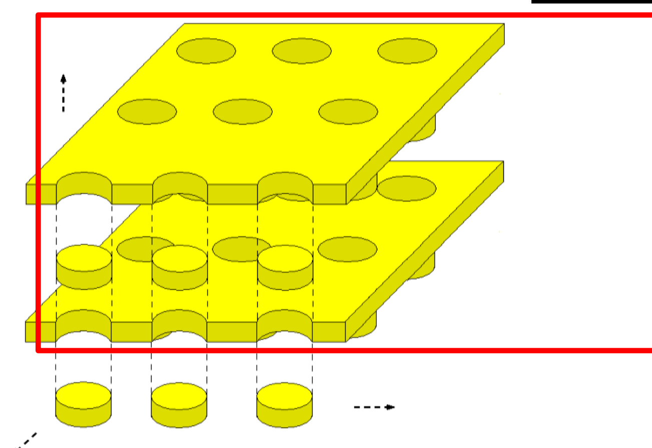


Resulting in metamaterials

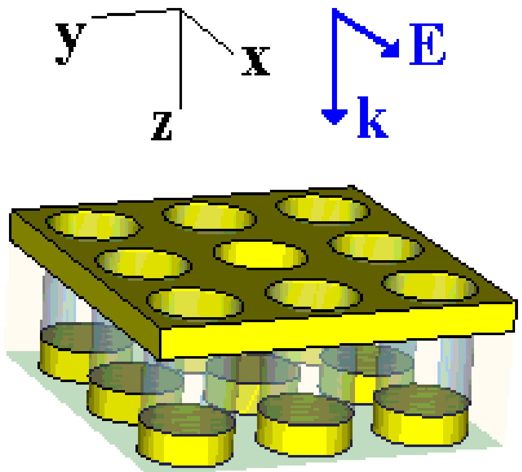
2. Multi-Layered nanoparticle arrays

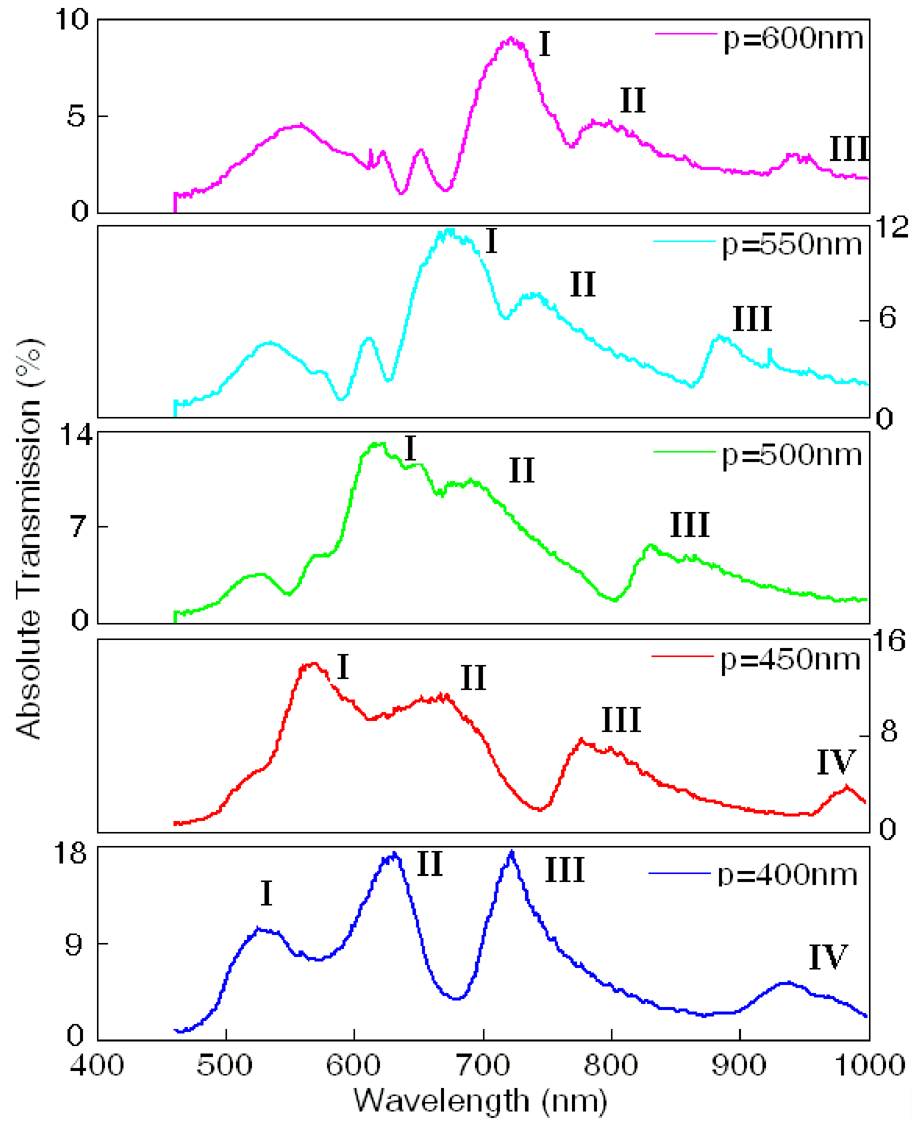


3. Multi-Layered hybrid structures



Multi-layered Plasmonic Nano-Structures





- ➔Studied multi-layered structures
- ➔Demonstrated for the first time

EOT in multi-layer structures

i) Through Fabry-Perot Resonances

ii) Through grating based SPP resonance

Artar et. al, Appl. Phys. Lett. 2009

(top 10 downloaded APL paper in August 2009)

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Enhancing Sensitivity

→ We show Fabry-Perot resonances offer superior field-media Resulting in much higher sensitivity to refractive index changes

→ Introduced a simple cavity model to account the behavior of the resonances

$\lambda_{FP} = 2hn_{eff}$

h: spacing between layers

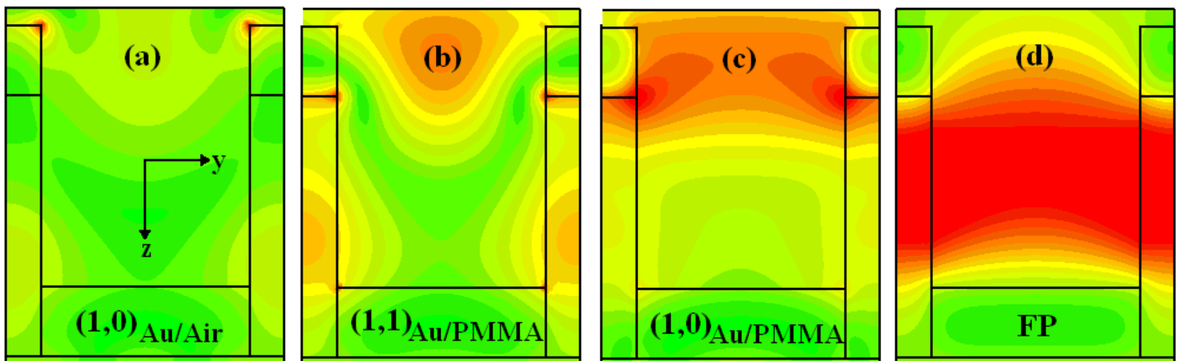
n_{eff} : effective index

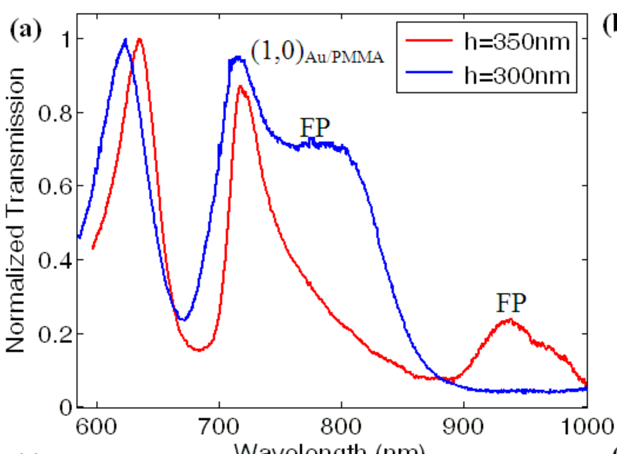
As predicted:

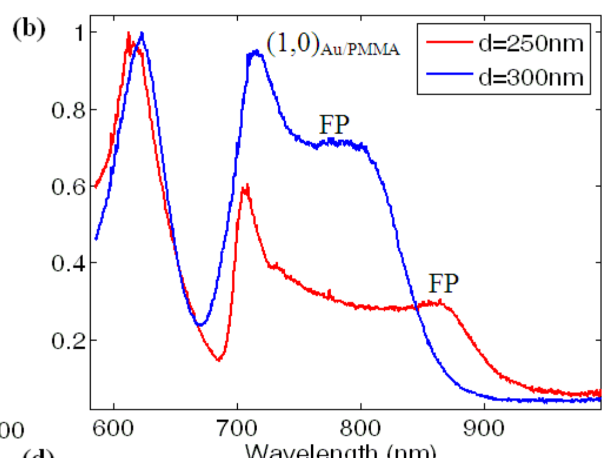
i) Increasing **spacing** red-shifts FP mode

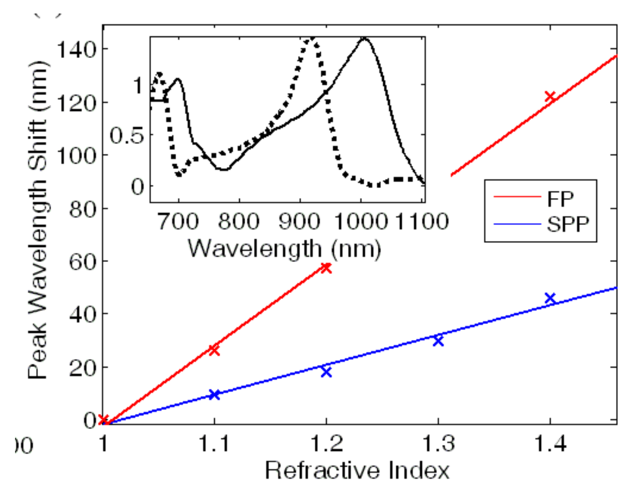
ii) Decreasing **diameter** increases effective index, thus red-shifts FP mode

→ while none effects SPPs



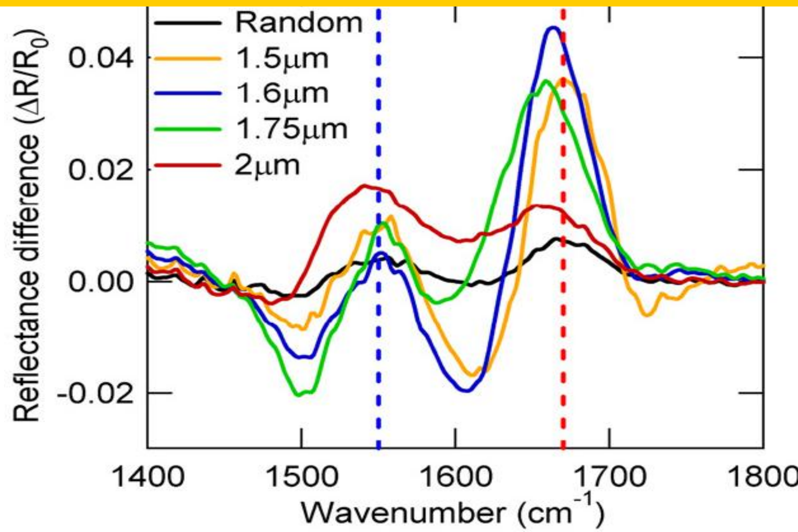


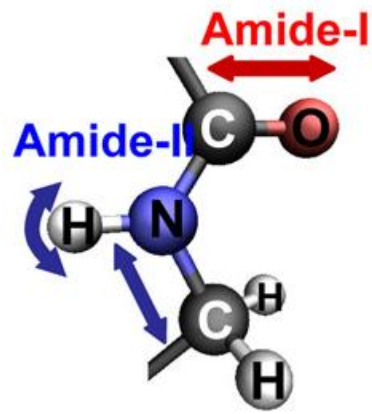


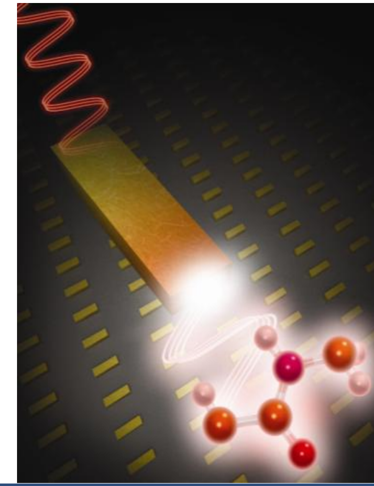


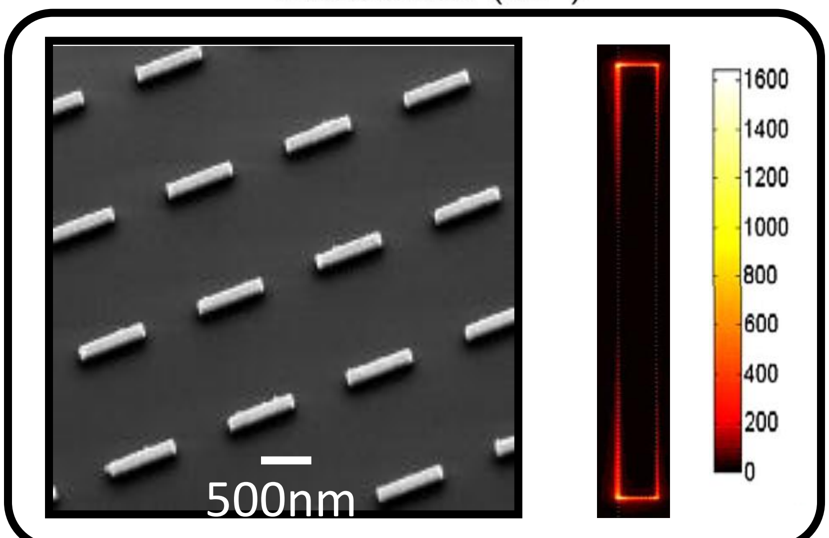
Ultra-sensitive Vibration Spectroscopy

Vibrational *Fingerprint* Signatures of Proteins









Adato and Yanik et. al, PNAS 2009

(highlighted on the cover of NSF)

Water Contamination Detection and Identification using UV Intrinsic Fluorescence

Shayla Sawyer, PI

Assistant Professor, ECSE

Rensselaer Polytechnic Institute

Main Project: Undergraduate Students: Renato Li, Nikhil Rao

Microbiologist: Irina Barash

Subproject: Graduate Student Liqiao Qin

Undergraduate Student: Chris Shing

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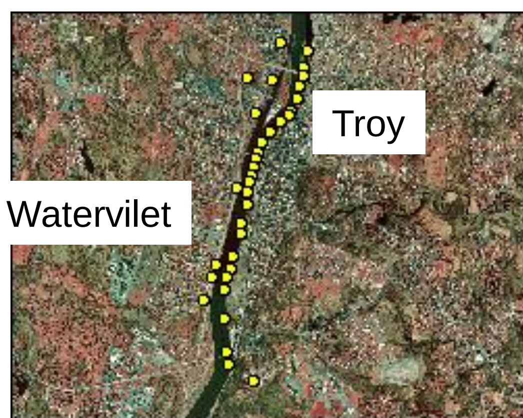
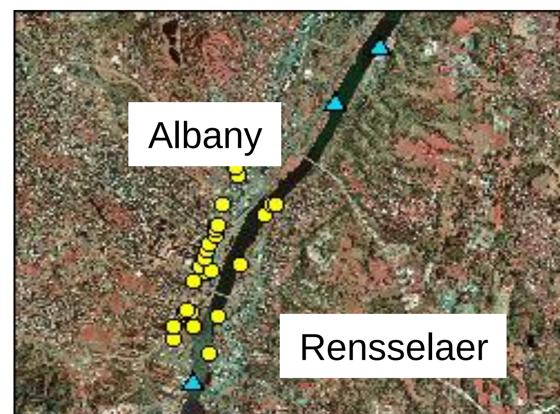
UV LED based Microbial Contamination Detection and Identification

NSF

- *Contamination in waterways* **is becoming increasingly significant around the world as populations grow rapidly**
- **~** ***20 million people become ill*** **yearly from drinking water containing bacteria and other pathogens often spread by untreated waste**
- **Example Hudson River, during wet weather, six communities** ***discharge raw sewage and bacteria*** **from almost** ***100 individual Combined Sewer Overflows (CSO)***
- ***Need to quantify large areas***





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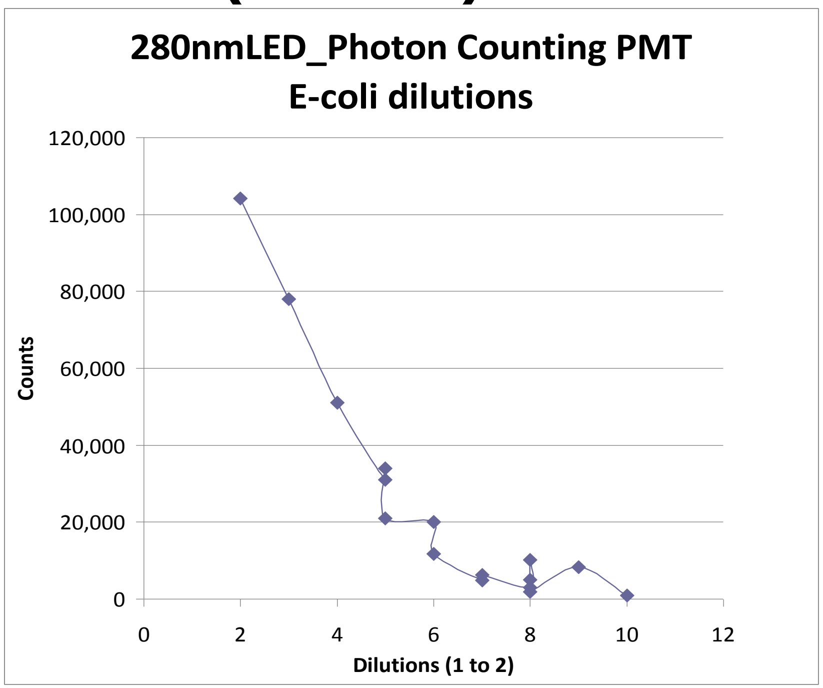
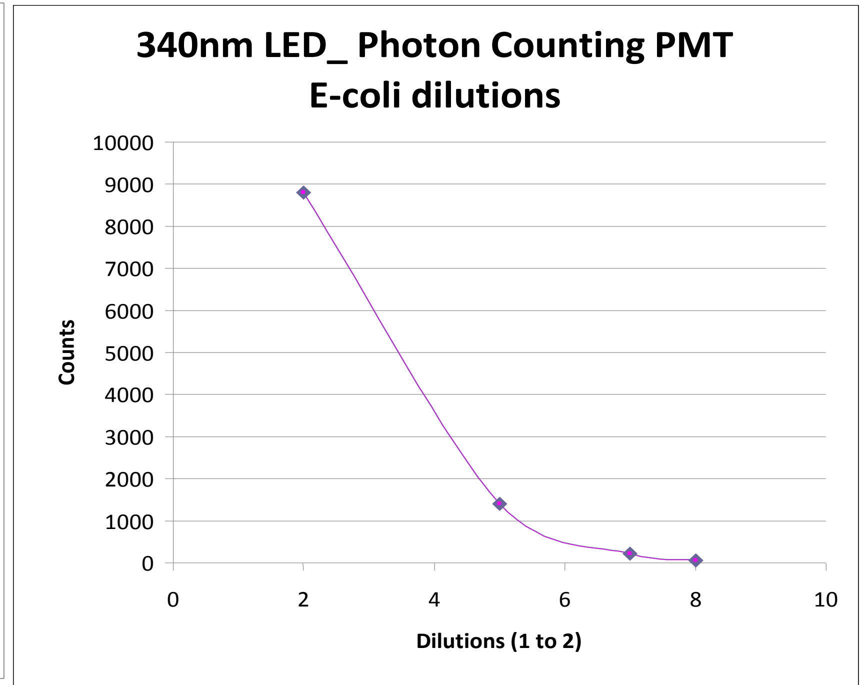
UV LED based Microbial Contamination Detection and Identification

- **UV LEDs provide compact field deployment monitoring systems using *intrinsic fluorescence* within the cell for identification and quantification**
- **Fluorescence advantages**
  - **High sensitivity**
  - **Short collection time**
  - **In situ measurement (no sample contact)**
  - **Reagentless (no consumables)**
  - **Monitoring of large areas/volumes continuously**
- **Solid state light source enables *switch between modes of quantification (alarm system) and identification***

UV LED based Microbial Contamination Detection and Identification

- **Quantification: Concentration of bacteria vs. Fluorescence Intensity for Tryptophan (280 nm) and NADH (340 nm) native fluorophores**

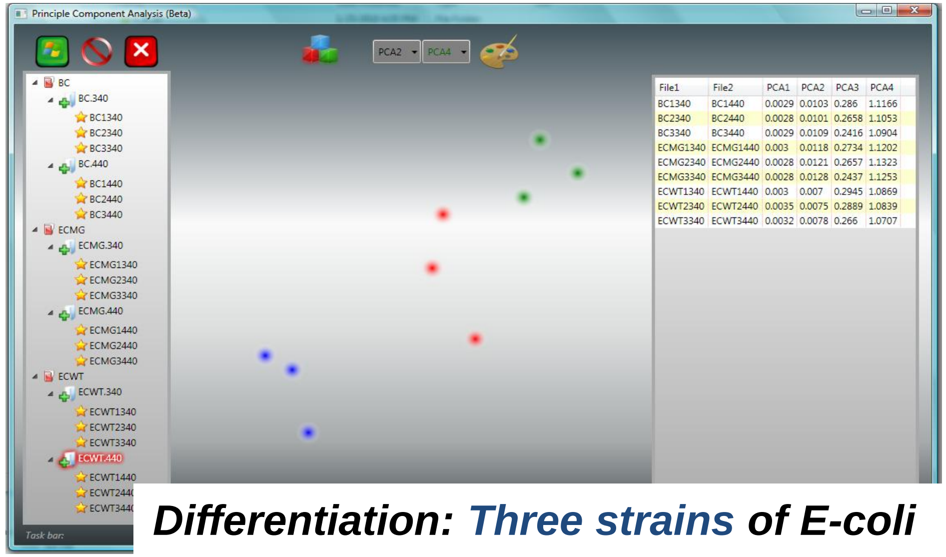




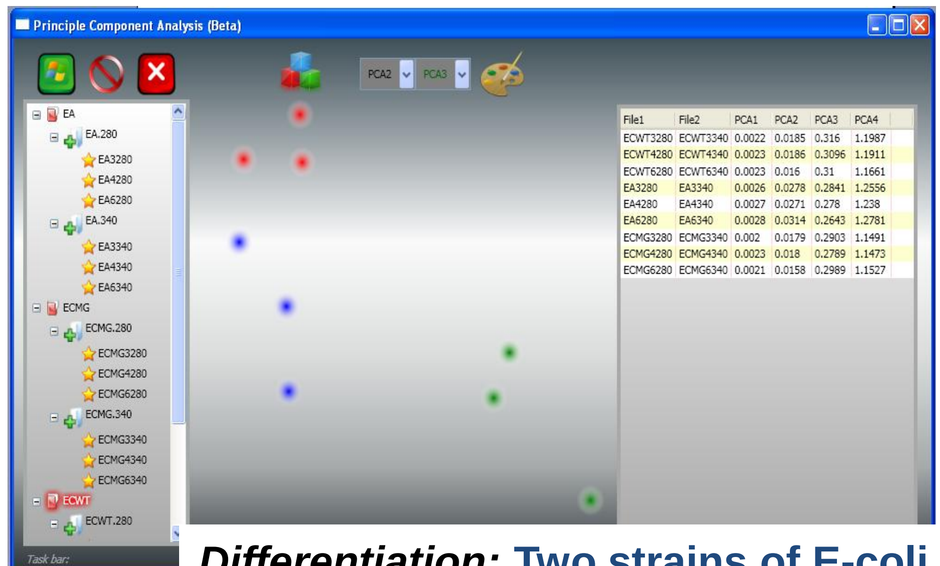
E-coli diluted samples measured in a quartz cuvette with path length of 3 mm by 280 and 340 nm UV LEDs and PMT photon counting module. A 340 nm band pass and 400 nm long pass emission filter was placed in front of the PMT for the 280 nm and 340 nm excitation repectively.

UV LED based Microbial Contamination Detection and Identification

- **Proof of concept: Identification on traditional system**
- **Differentiate *both species and strain* of bacteria using PCA**
- **Preliminary Computer program based on PCA**
  - **Fluorescence spectra from 280, 340, and 440 nm excitation**
  - **Small differences in spectra for each bacteria are amplified**



Differentiation:* Three strains *of E-coli



***Differentiation:* Two strains of E-coli and Enterobacter aerogenes**

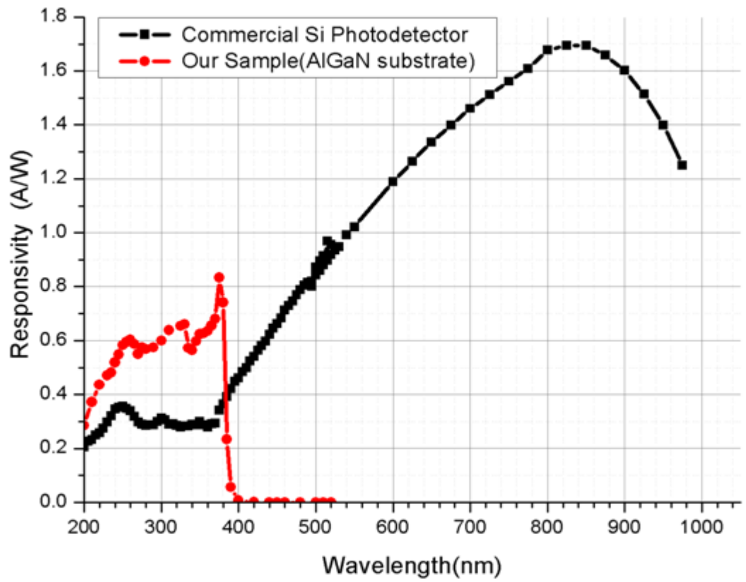
Biological Detection with Nanoparticle Based Detectors

- **Intrinsic fluorescence for identification and quantification requires high UV wavelength response (responsivity)**
- **Traditional detectors such as PMTs and Silicon Photodiodes are limited by:**
  - **Broad spectrum of detection (requires filters)**
  - **Low UV responsivity**
  - ***Non-ideal for field deployment of small sensors***
- **Demonstrate *a large area, wavelength selective UV photodetector* for intrinsic fluorescence biological system**
- **Bandpass response can be *tuned by the substrate and nanoparticle* material properties**

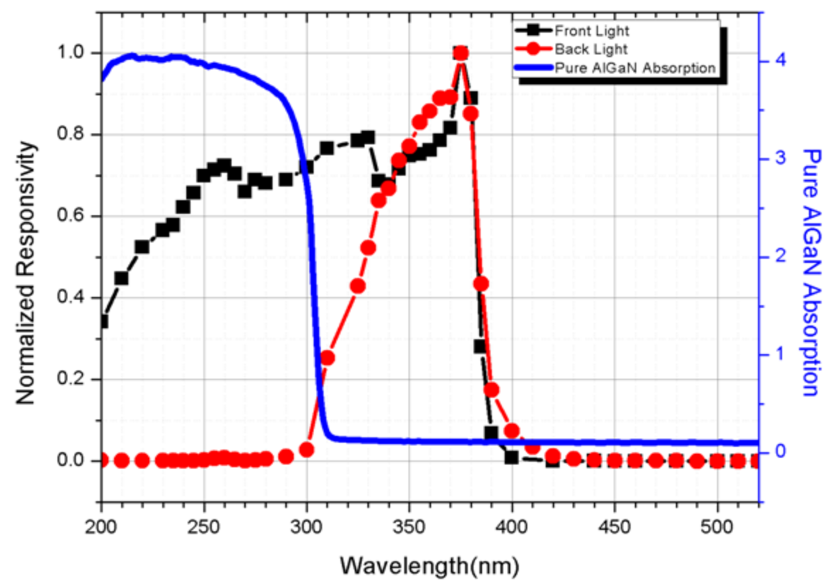
Biological Detection with Nanoparticle Based Detectors

Spectral Responsivity

a)

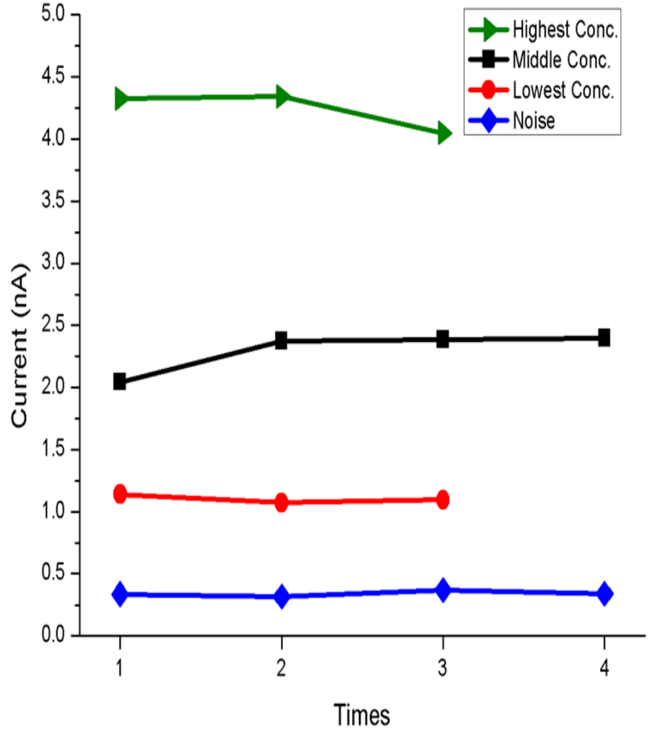


b)



Spectral response of ZnO nanoparticles-AlGaN substrate detector a) Front lighting compared with commercial UV enhanced Si based photodiode and b) Front and back lighting compared with absorption spectrum of AlGaN substrate

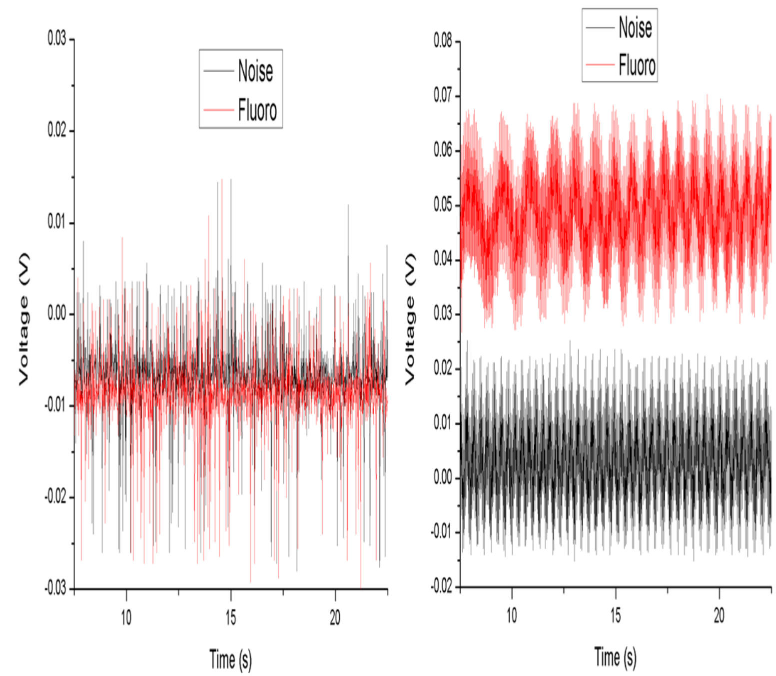
Biological Detection with Nanoparticle Based Detectors



Detection of tryptophan enzyme in E-coli (ATCC # 25922) in different concentration by ZnO nanoparticles-AlGaN substrate detector (back lighting) when the cells is excited by a 280nm LED.

Comparison of Tryptophan Detection in E-coli

a) UV Enhanced Si-PD b) ZnO NP on AlGaN



Photovoltage generated by a) commercial UV enhanced Si-PD and b) ZnO nanoparticles-AlGaN substrate detector (back lighting) when the tryptophan enzyme in E-coli(ATCC # 25922) excited by a 280nm LED.