Photonic Crystal Microarray Nanoplatform for High-Throughput Detection of Biomolecules

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Motivation

Microarrays are omnipresent in the field of medical diagnostics

- Protein Microarray, DNA Microarray, RNA Microarray, etc…

Desired Microarray Characteristics

- No background noise from non-specific binding
- Multiple probe-target conjugates
- Real Time Detection: Binding or non-binding of all probe-target conjugates studied simultaneously
- Label Free platform to reduce complexities of binding chemistry as well as cost.

Label-Free Microarrays

- Surface Plasmon Resonance (SPR) commercialized by Biacore
- All other label-free techniques still in research or prototype development phase.

On-Chip Label-Free Biomolecule Microarray Platforms

Ring Resonator Array

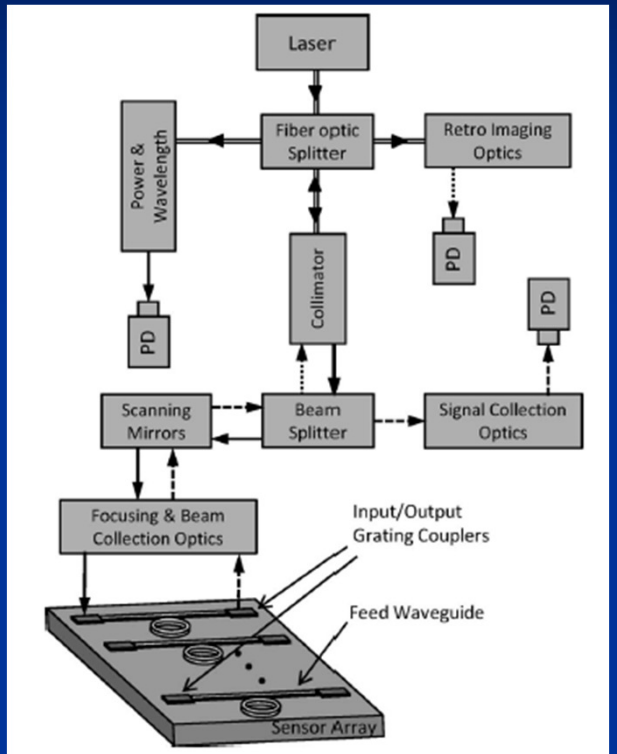
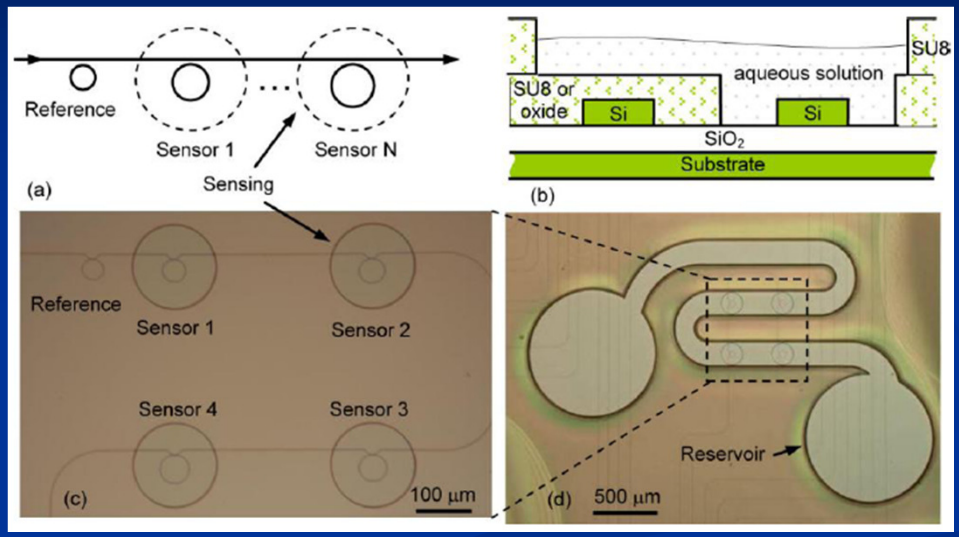


Fig. 2. High-level architecture of the biosensing platform.

Iqbal et al, IEEE JSTQE **16** (3), 654 (2010)

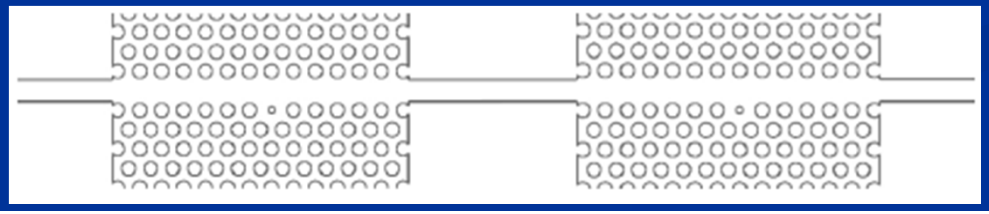
Interferometer Array with Wire Waveguides



Densmore et al, Optics Lett. **34** (23), 3598 (2009)

1D Photonic Crystal Array

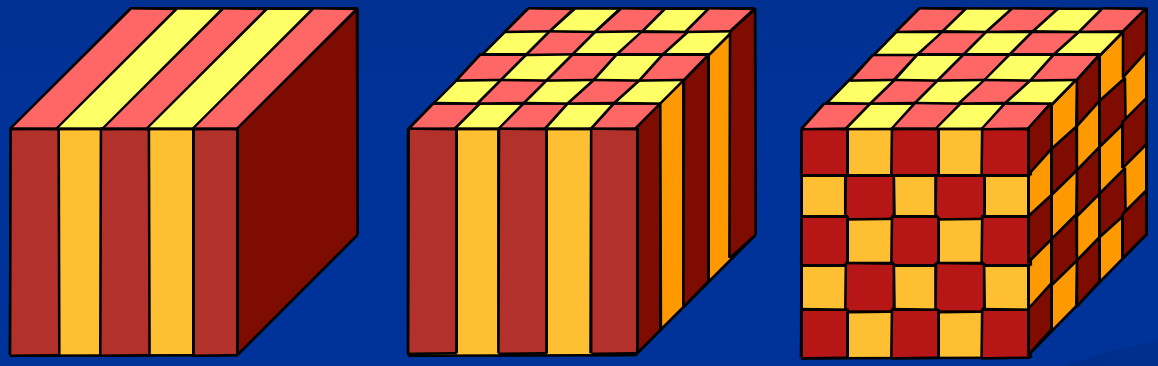
Mandal et al, Optics Exp. **16** , 1623 (2008)



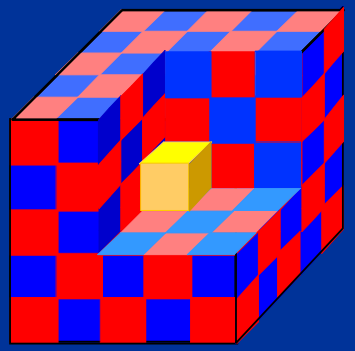
Guillermain et al, Mater. Res. Soc. Symp. 1191, 1191-OO-06 (2009)

➢What is Photonic Crystal?

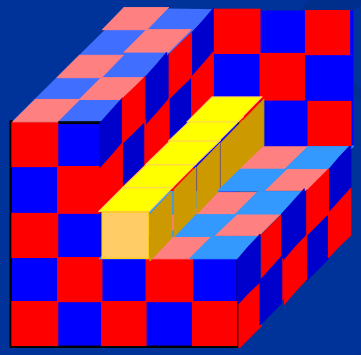
- **Periodic** electromagnetic media comparable to wavelength
- With **photonic band gaps**: "optical insulators"



1-D grating =1-D PhC
2-D PhC =2-D grating
3-D PhC =3-D grating
Similar to:
Semiconductors



can trap light in cavities



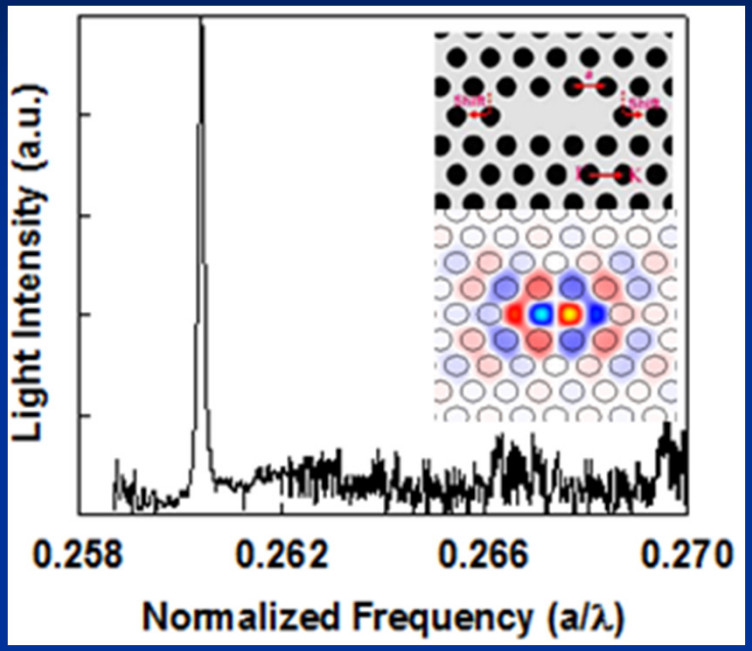
and waveguides ("wires")

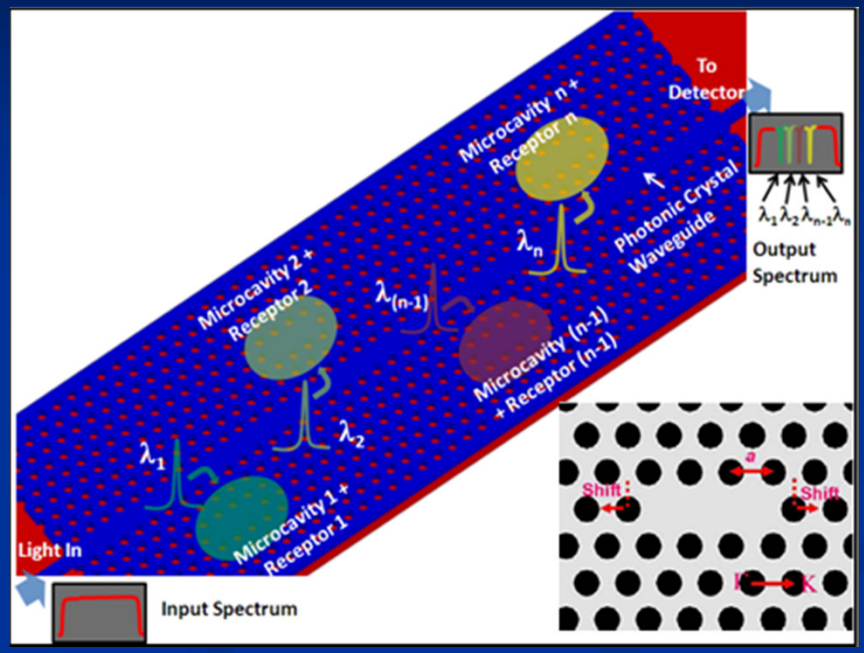
Defect structures can introduce defect mode inside the photonic bandgap
Similar to: Doping of Semiconductor

Comparison of Existing Bio-sensing Technologies on Photonic Crystal Platform

Research Group	**Mandal et al. (Optics Express 16(3), 1623 (2008))**	**Guillermain et al. (Mater. Res. Proc. Symposium 1191-OO11-06 (2009))**	**Zlatanovic et al. (Sensors and Actuators B 141, 13 (2009)**	**Omega Optics Photonic Crystal MicroArray**
Technology	1D photonic crystal sensor array	2D photonic crystal with 2 microcavities	2D photonic crystal with single microcavity	2D photonic crystal with multiple microcavities
Microcavity Q in bio-ambient	~3000 in water (no biomolecules)	400-500	425	~3430 (demonstrated)
Sensitivity			20pM	
# parallel measurements demonstrated (high throughput related)	1	2* (same bio-molecule coated)	1	Theoretically unlimited, Target: 96 spots.

Photonic Crystal Microarray Based Nanoplatform for High Throughput Detection

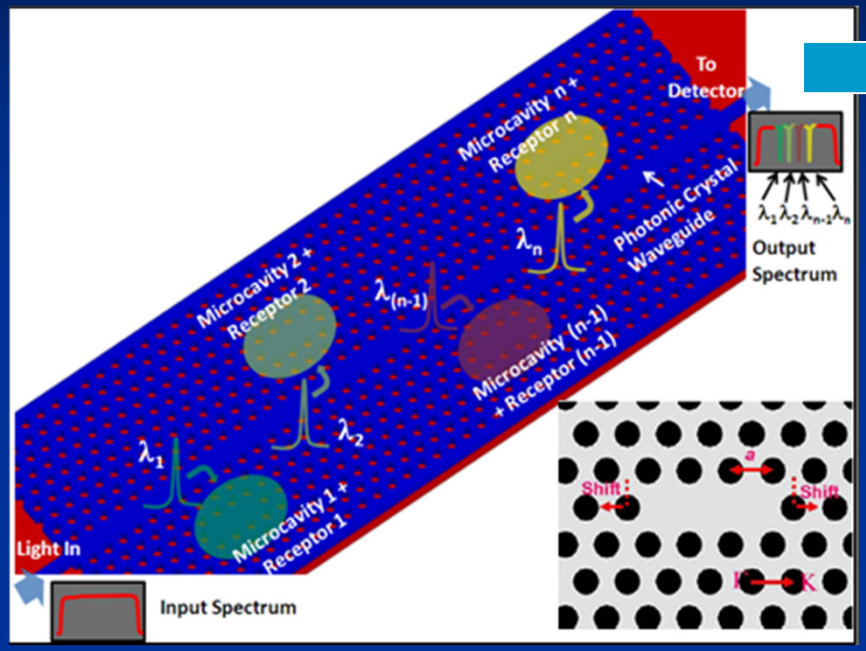


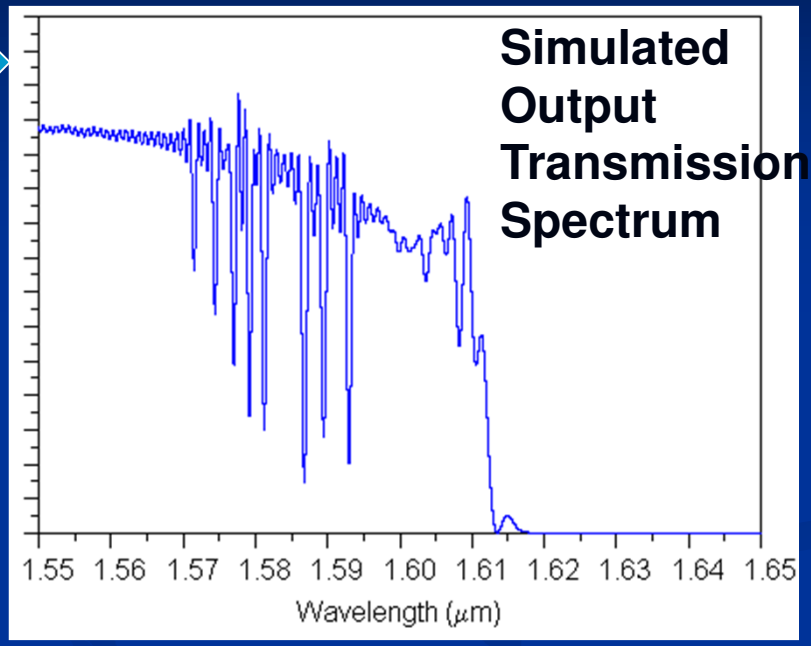


Principle of Operation:

- **Multiple photonic crystal microcavities are patterned along length of photonic crystal waveguide**
- **Each photonic crystal microcavity has unique resonance wavelength**
- **Resonance wavelength is a strong function of refractive index**
- **A photonic crystal microcavity adjacent to a photonic crystal waveguide traps its corresponding resonance wavelength; the wavelength is thus dropped from output transmission of waveguide**
- **Refractive index changes in the vicinity of an individual photonic crystal microcavity shifts the resonance wavelength**

Photonic Crystal Microarray Based Nanoplatform for High Throughput Detection of Cancers

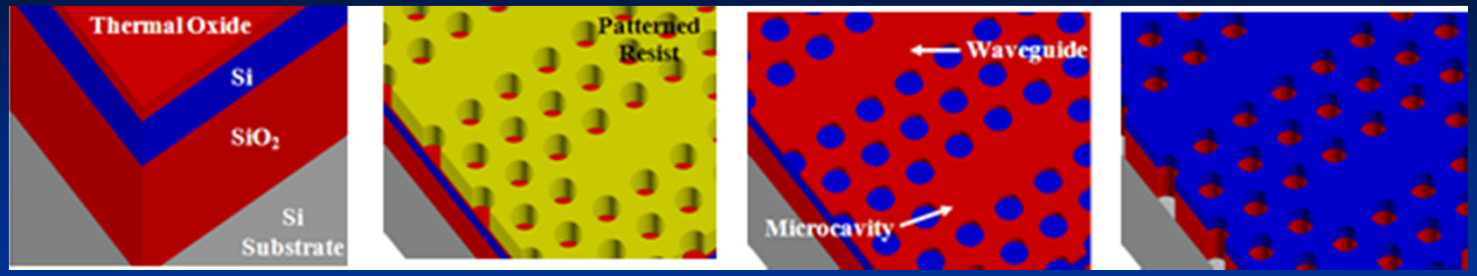




Principle of Operation:

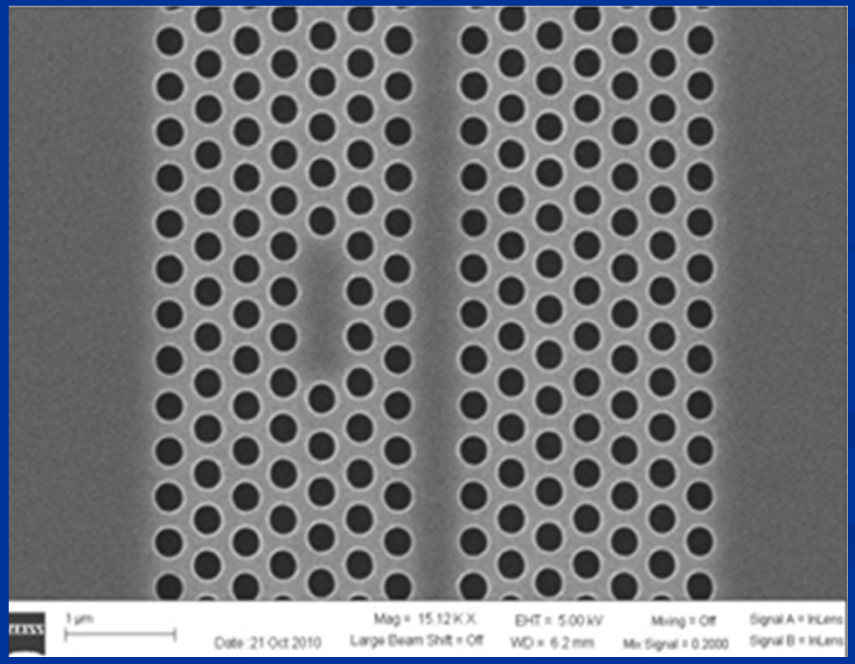
- Multiple photonic crystal microcavities are patterned
- Each photonic crystal microcavity has unique resonance wavelength
- Multiple dropped wavelengths in output transmission spectrum
- Each photonic crystal microcavity is coated with a unique receptor biomolecule
- Target biomolecule binds specifically to unique receptor on unique microcavity, which shifts the unique dropped wavelength, hence the biomolecule is detected.

Photonic Crystal Fabrication

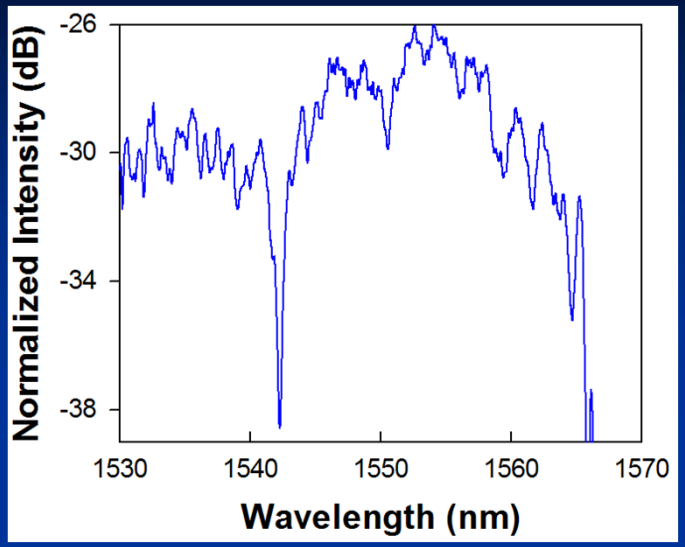


Thermal Oxide Growth | **Resist Pattern E-beam** | **Thermal Oxide Etch** | **Silicon Etch**

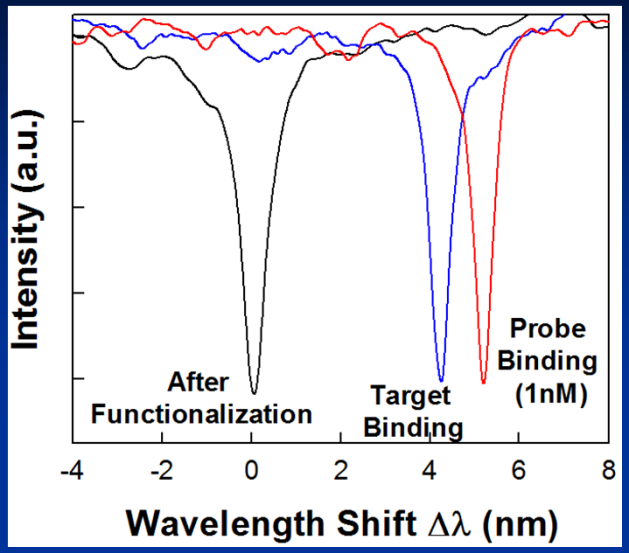
SEM Images



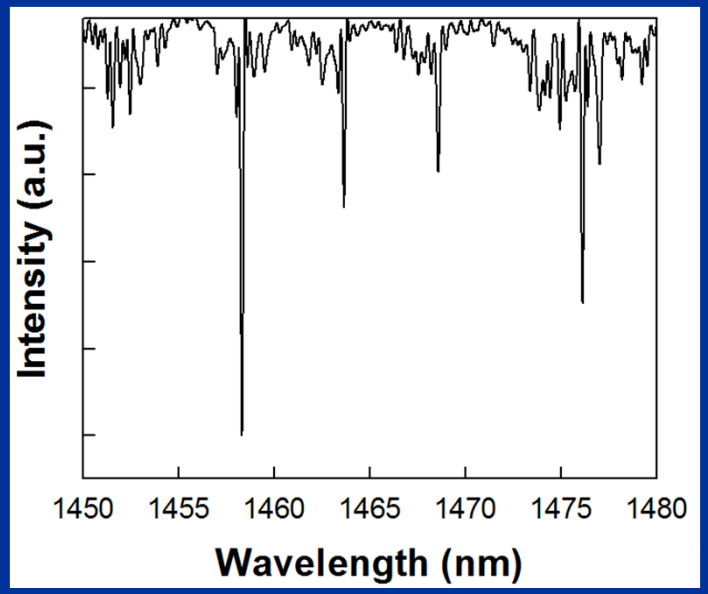
Transmission Measurements



Single Microcavity Transmission



1nm shift for 1nM binding

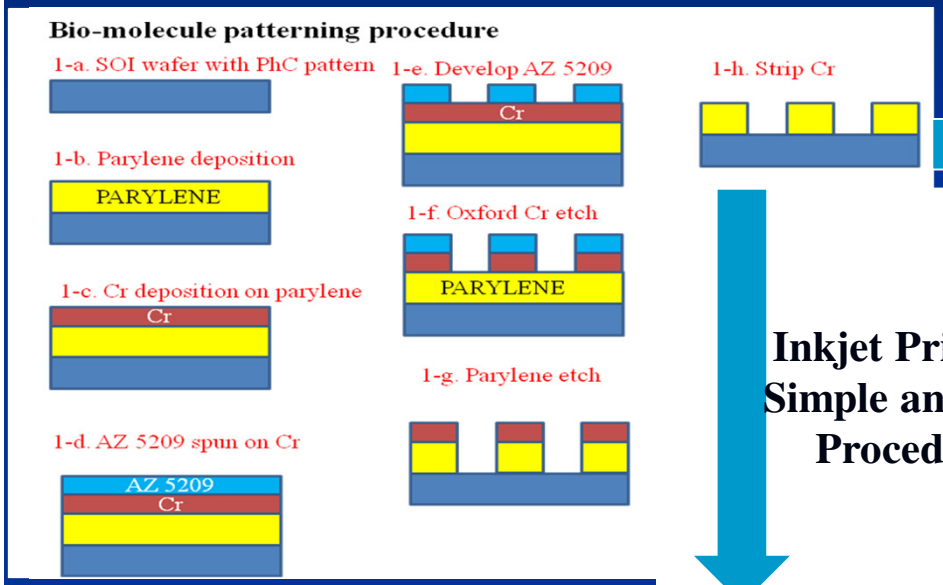


Multiple Microcavity Transmission

In contrast, over 25 mins,
~0.1nm shift observed for 1.2nM binding

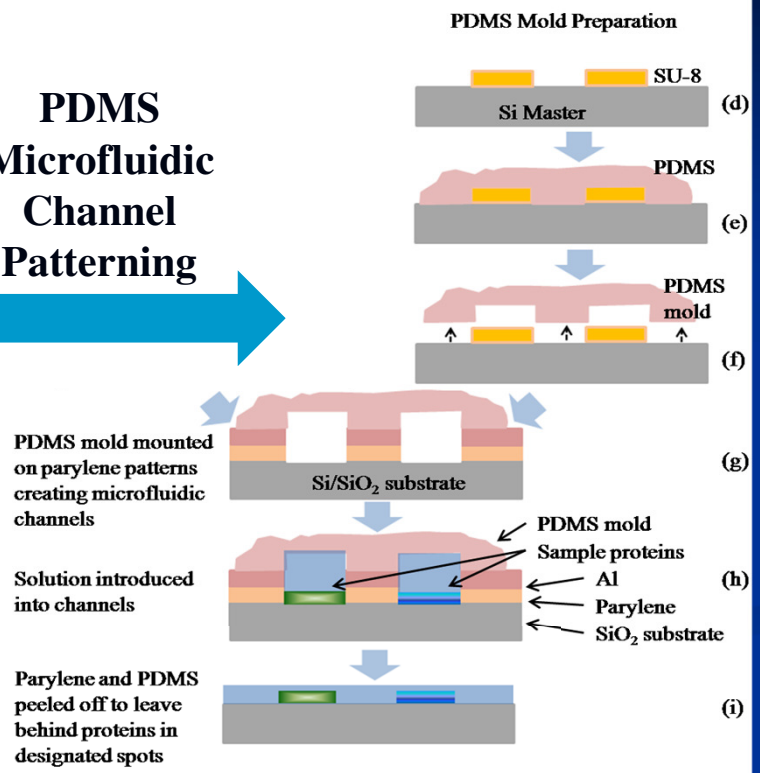
[1] Zlatanovic et al, Sens. & Actuators B-Chem 141, 13 (2009)

Biomolecule Patterning Procedure

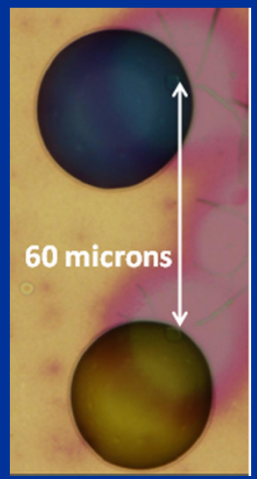


Inkjet Printing Simple and Fast Procedure

PDMS Microfluidic Channel Patterning



Spotting Size Calibration



Target and Probe Protein conjugates are chosen with high binding affinity (low Kd), not based upon molecular weight.

Target: BioRad HRP-conjugated goat-anti-rabbit antibody

Invitrogen Rabbit anti-goat Alexa Fluor 532 - MW ~ 153 Kilodaltons

Summary

2D Photonic Crystal Single Waveguide Coupled Multiple Microcavity based Microarray enables:

- **Simultaneous / parallel measurement of multiple mutually unique binding spots, simultaneously on-chip**
- **Biomolecule functionality preserved in aqueous phase**
- **Fast analysis and response time**
- **Miniaturization**
- **Feature dimensions achievable by 193nm photolithography, nano-imprint lithography**
- **CMOS platform--- low cost during high volume manufacturing**

Comparison of Existing Microarrays

Company	**Biacore Life Sciences (Surface Plasmon Resonance) Biacore 4000**	**NEB (ELISA) Pathscan Phospho-Ret Sandwich ELISA Kit**	**Photonic Crystal MicroArray**
Label-Free	Yes	No	Yes
Target protein Requirement	3-10 micro-gram/ spot	100 micro-gram - 1mg/spot	4.5 fg/spot [1]
Principle of Interaction	Dynamic	Thermodynamic	Dynamic
Sensitivity	100pM	1micro-molar	< 20pM [2]
Sample Solution Requirement	60 micro-liters	250 micro-liters	Nano-liters
# of Spots	384 different spots	96 different spots	Theoretically unlimited, different spots
Cost	$80K / unit	$35K /unit	~$40K
# Spots /Measurement	1	1	>96
Time to measure /spot	18 seconds per spot	Minimum 2 hrs for incubation	10 seconds per 96 spots

[1] Zlatanovic et al, Sens. & Actuators B-Chem 141, 13 (2009)