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Nanophotonic silicon-based biosensors and biochips

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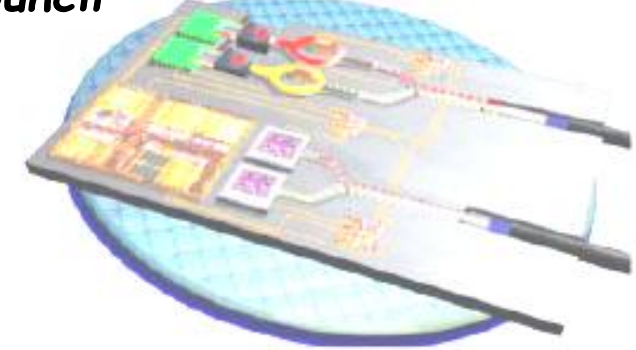
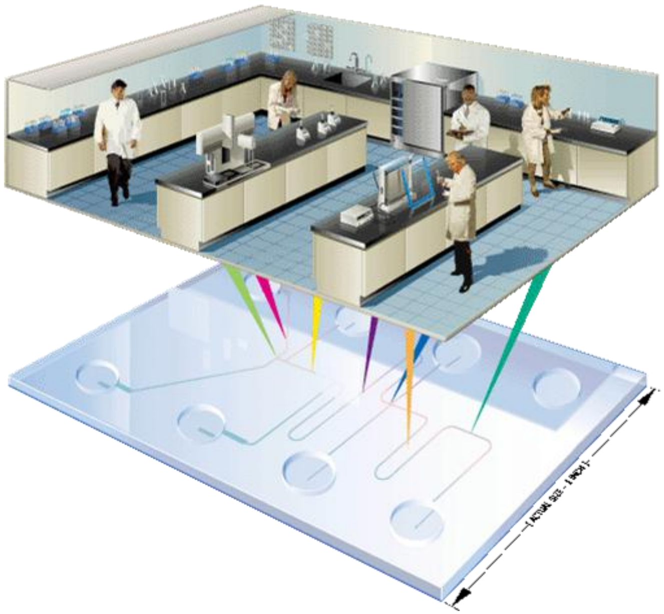


One of the new frontiers of the "information age", based on silicon technology, is the realization of photonics devices integrated on chip capable of manipulating light at the nanoscale

…and also the realization of new chips capable of performing complex functions:

- to sense and interact with the environment
- manipulate fluids
- to be remotely interrogated and powered



Health: a global challenge

tries[3,4]. For example, of the world's population of 6.1 billion people, 3 billion lack basic sanitation, 2 billion do not have access to electricity and more than 1 billion lack basic healthcare services and clean drinking water[5,6]. For every public health triumph such as the

- ***1 billion, or half of the world's children, live in poverty***

- ***more than half the deaths in the poorest countries are the result of infection diseases (compared to 5% in the reachest ones)***

[Source: P. Yager, et al., Nature, Vol. 442, 27 July 2006)]

NATURE|Vol 442|27 July 2006|doi:10.1038/nature05064

Microfluidic diagnostic technologies for global public health

Paul Yager[1], Thayne Edwards[1], Elain Fu[1], Kristen Helton[1], Kjell Nelson[1], Milton R. Tam[2] & Bernhard H. Weigl[3]

The developing world does not have access to many of the best medical diagnostic technologies; they were designed for air-conditioned laboratories, refrigerated storage of chemicals, a constant supply of calibrators and reagents, stable electrical power, highly trained personnel and rapid transportation of samples. Microfluidic systems allow miniaturization and integration of complex functions, which could move sophisticated diagnostic tools out of the developed-world laboratory. These systems must be inexpensive, but also accurate, reliable, rugged and well suited to the medical and social contexts of the developing world.

Challenges in biomedicine

- New technologies for small, cheap, reliable point-of-care testing (label free nanosensor arrays and lab-on-chips) for instant diagnostic, in any place at any time
- Very high sensitive biosensors, with extremely low detection limits for early stage disease detection
- Ultra-high resolution microscopy (below the diffraction limit) for real time sub-cellular imaging
- Micro and nano-systems for smart drug delivery (*i.e.*, in cancer therapy)

Negative photonic crystals to trap light at the nanoscale and excite optical resonances …useful in biosensing

Well known applications of plasmonic resonances in biosensing

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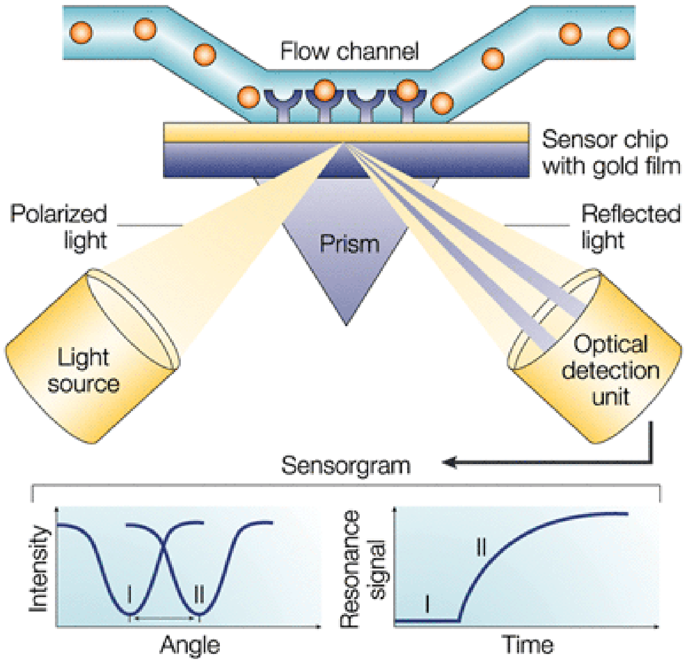
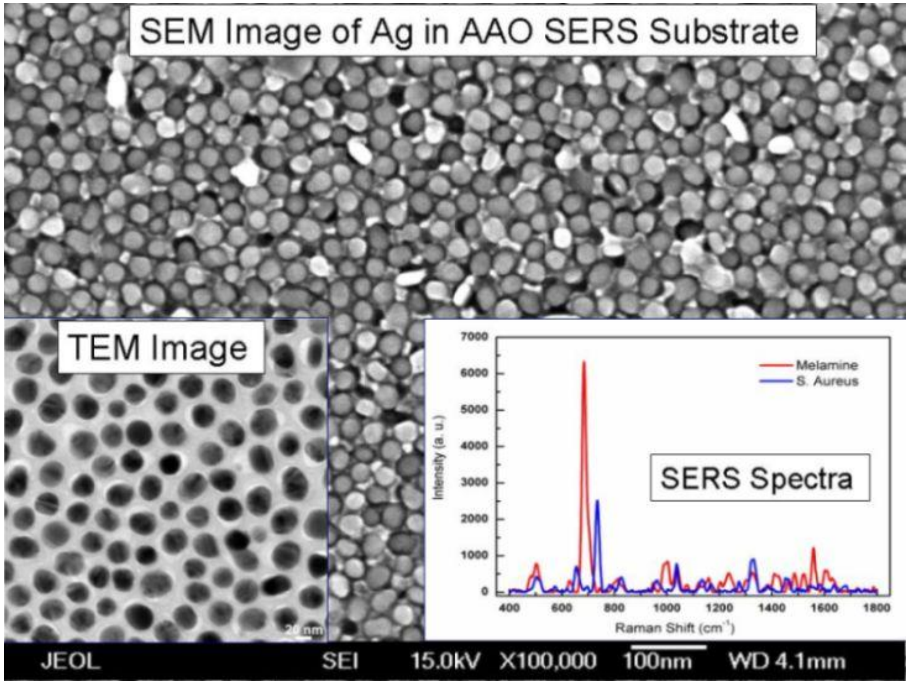
Surface plasmon resonance (SPR) sensors



Nature Reviews Drug Discovery 1, 515-528 (2002)

Surface enhanced raman spectroscopy based on localized-SPR effect



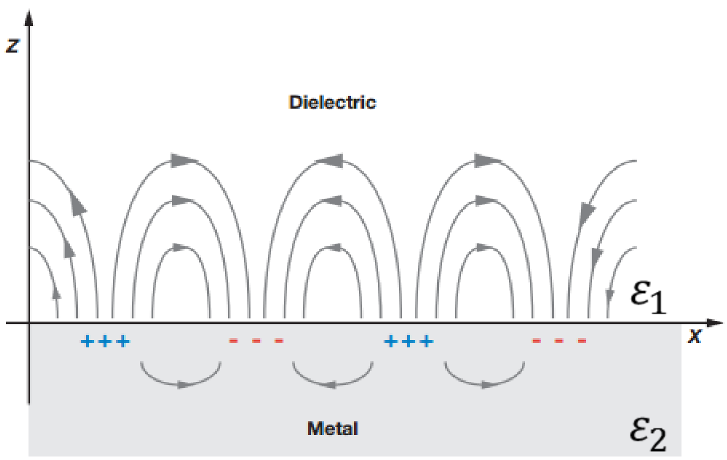
Advanced Materials 18, 491 (2006)

- **label free technique**
- **real-time detection**
- **high enhancement factors**

Analogy between…

…metal plasmonic structures

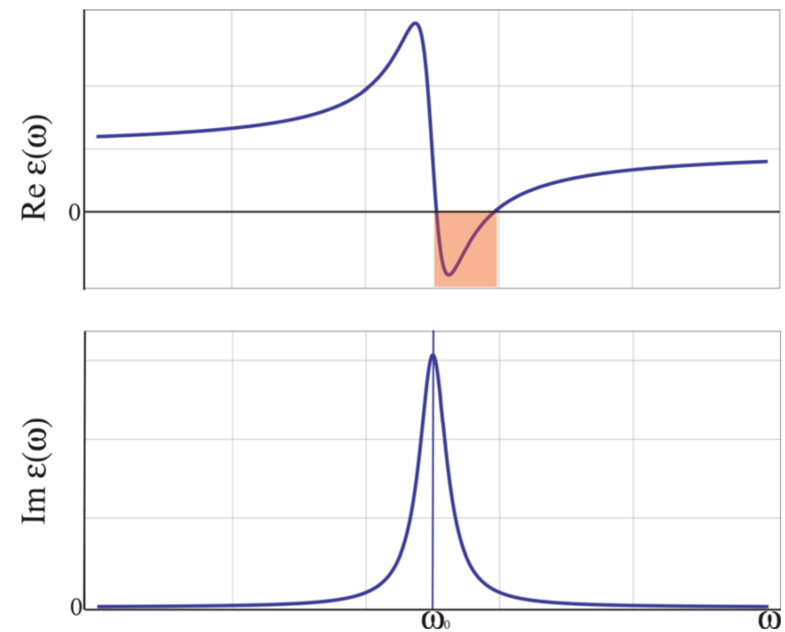
$$\varepsilon(\omega) < 0$$



Metals: Drude model

$$\epsilon = \epsilon_0 - \omega_p^2/(\omega^2 - i\gamma\omega)$$

… non-metal negative photonic crystals



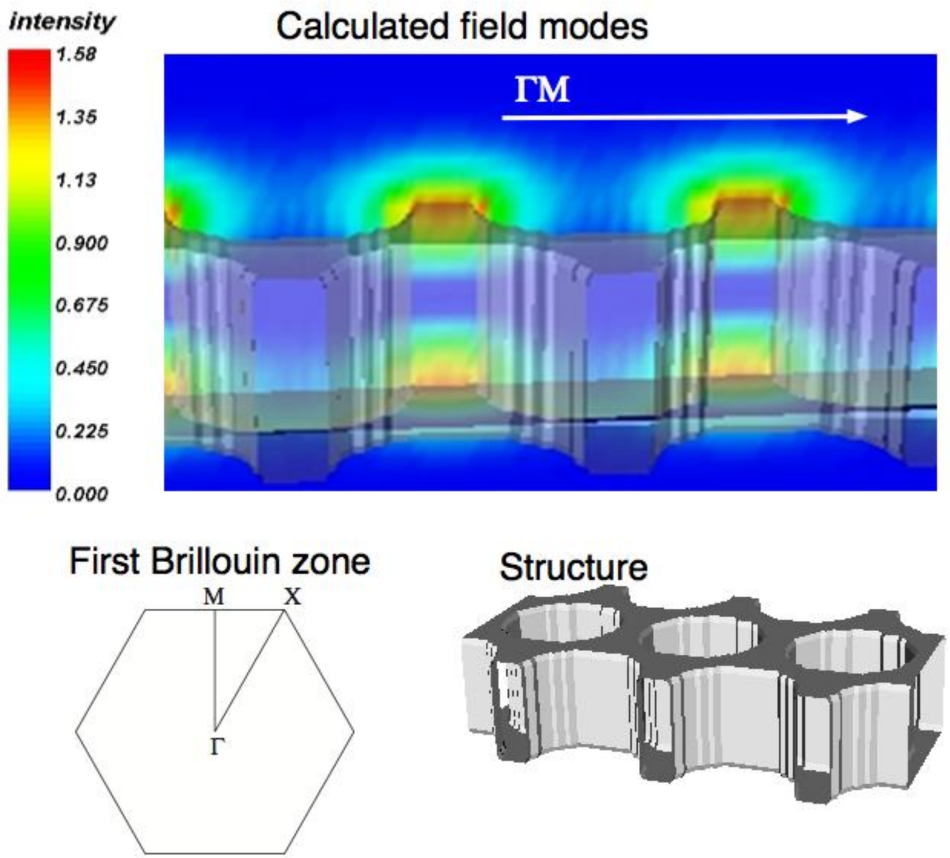
Non-metals: Lorentz model

$$\varepsilon = \varepsilon_\infty + f\ \omega_0^2/(\omega_0^2 - \omega^2 + j\gamma\omega)$$

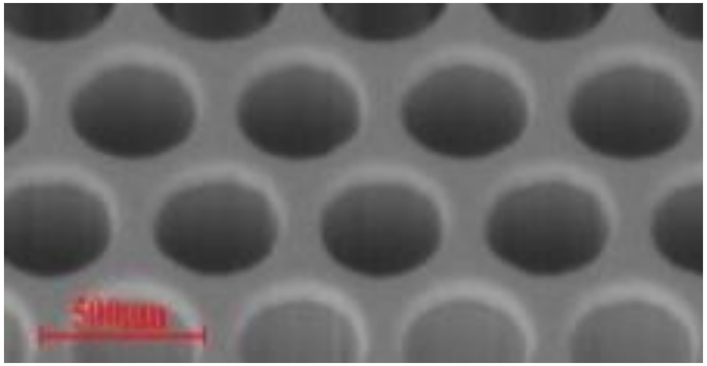
<u>Our idea</u>: to exite *plasmon-like* resonances at the interface with *negative* **dielectric** photonic crystals, so avoiding:

- optical absorption in metals
- resonance peak broadening
- local unwanted heating

Finite Difference Time Domain simulations in a 2D negative PhC



Device realization



2D PhC silicon slab on a SOI wafer

- Lattice constant *a*: 472 nm
- Hole radius *r*: 0.385*a*
- Thickness: 700 nm
- Effective negative refractive index around normalized frequency $a/\lambda=0.31$

Plasmon-like surface states: experimental characterization

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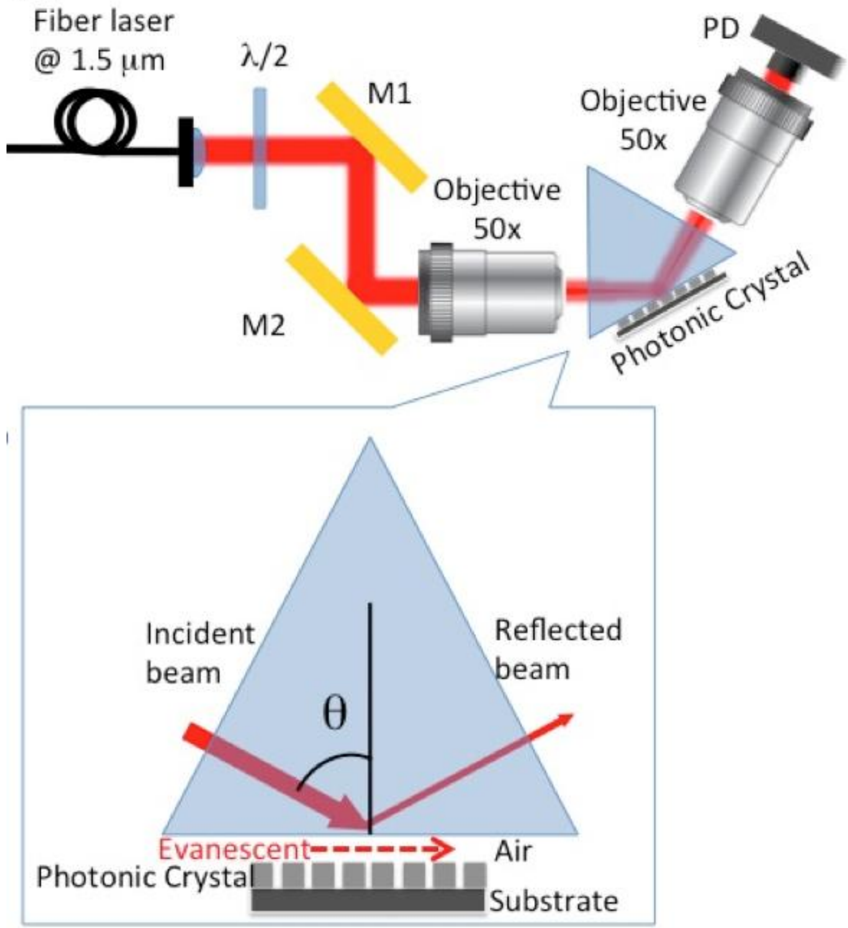
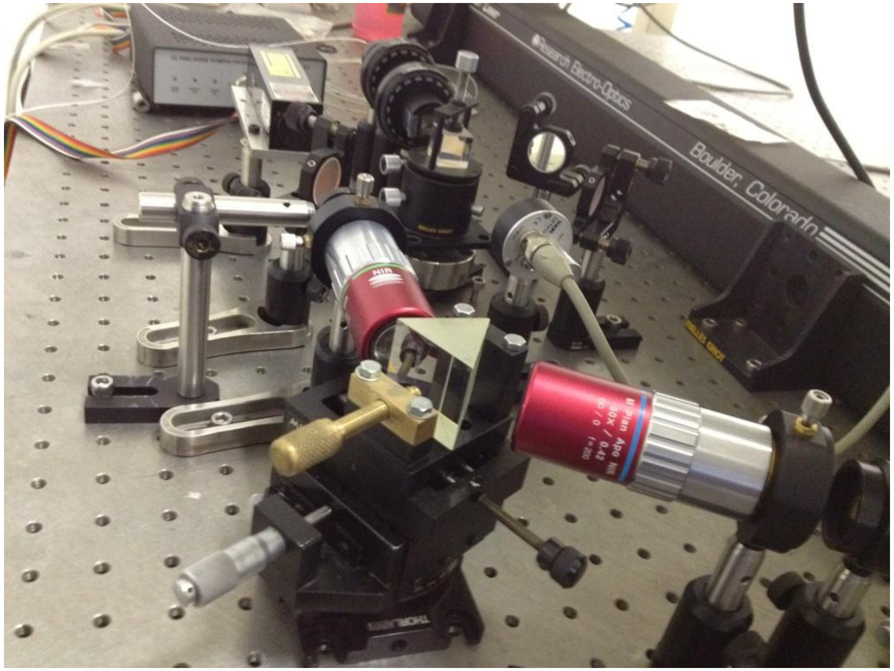
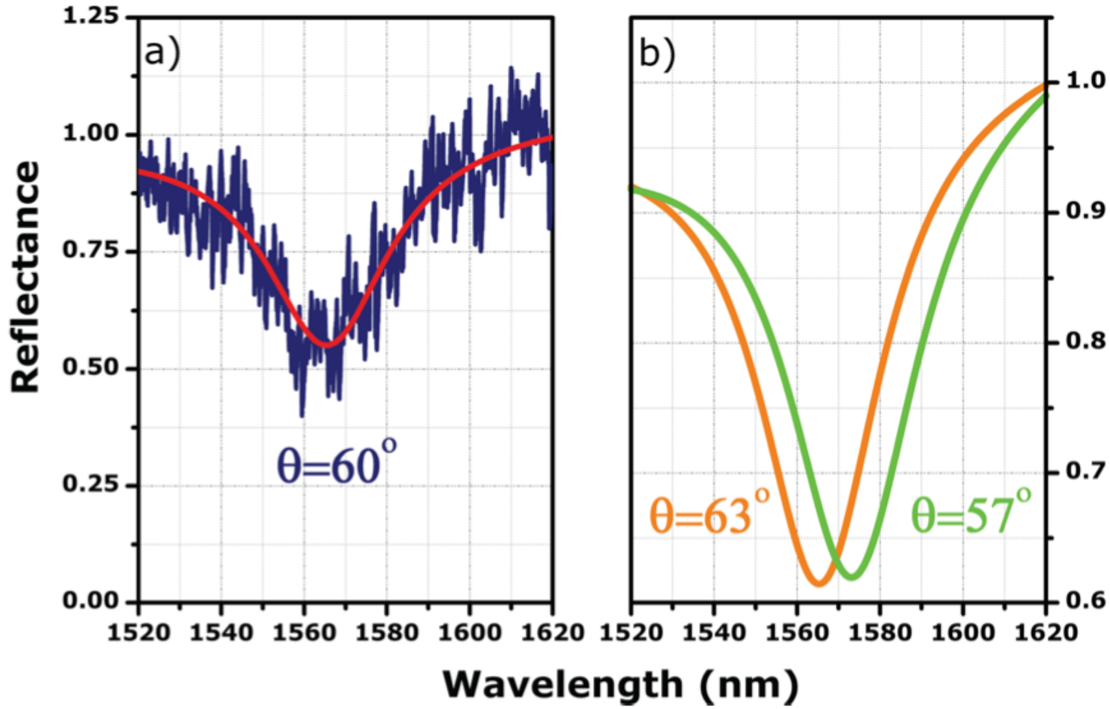
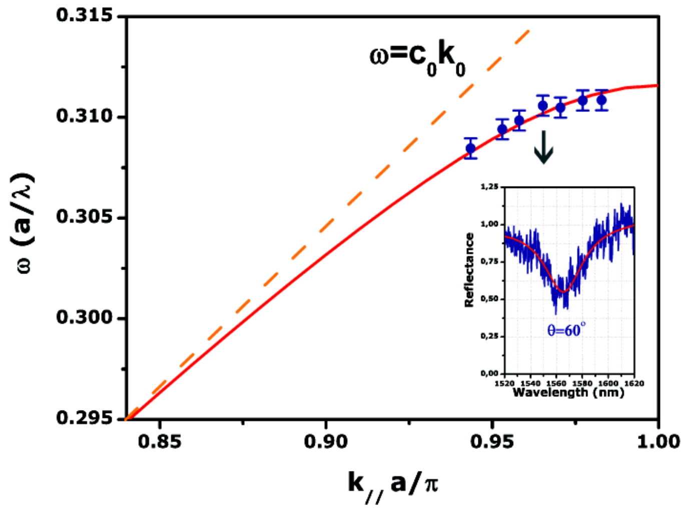


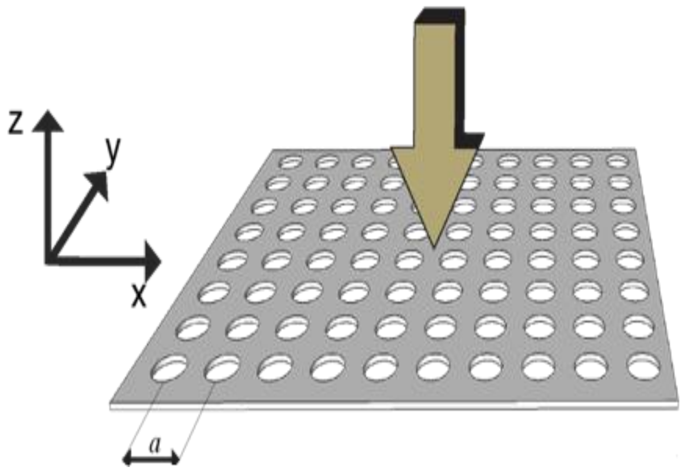


Experimental evidence of plasmon-like resonances



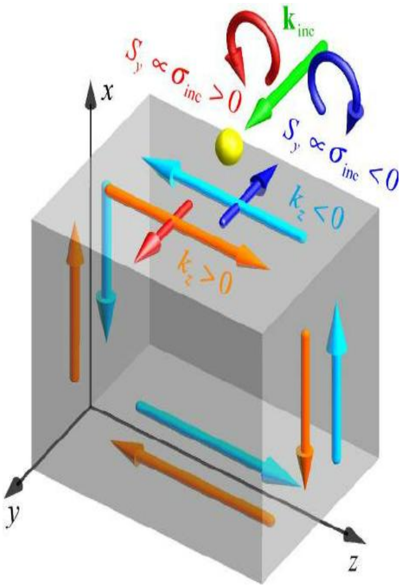


Sharp distributed resonances by exciting Bound States in Continuum (BICs) of radiation modes



- **Normal-to-the-surface configuration**
- **Distributed resonances**
- **Easy and reliable coupling of light to PhC**
- **High enhancement of the E-field at the PhC interface**
- **High-Q resonators**
- **Good tolerance to fabrication imperfections**

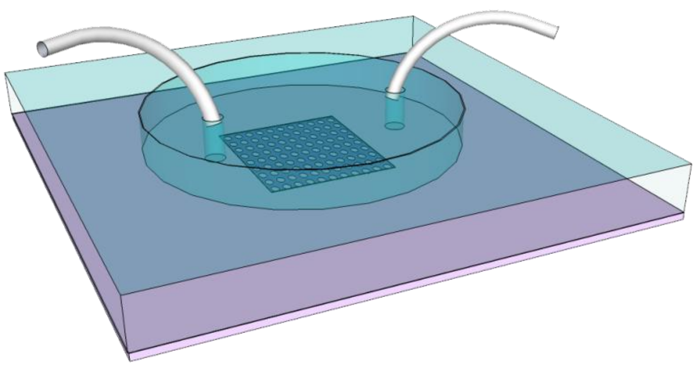
- Distributed resonances with predicted infinite lifetimes
- Fabrication imperfections and the finite extent of the structure partially break the crystal symmetry allowing the coupling of these resonances, and the excitation of evanescent surface waves



Qubit manipulation by optical Quantum Spin-Hall Effect

Design and realization of new sensors:

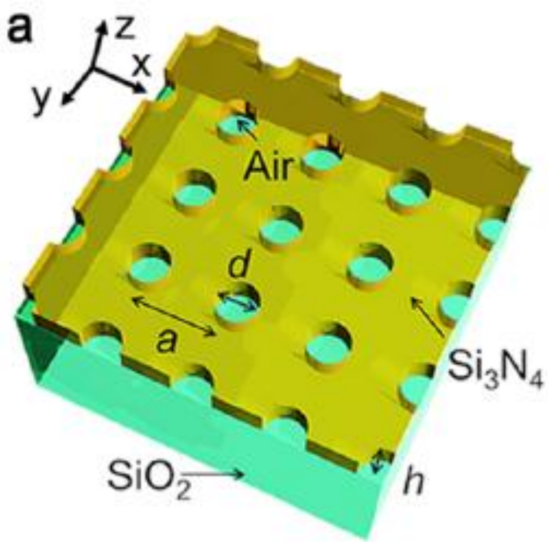
nanostructured surfaces where light is confined and enhanced, enabling very high sensitivities



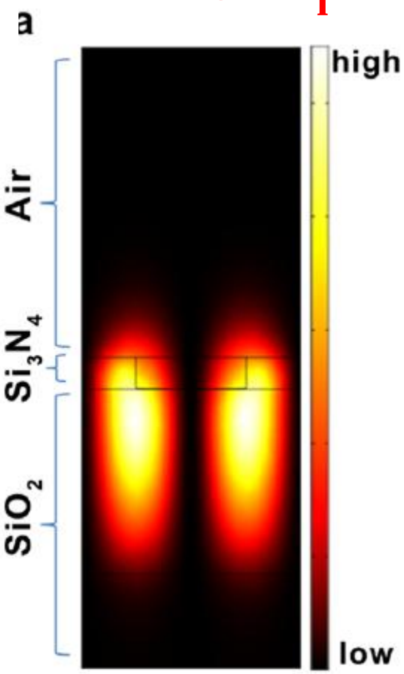
PhC sensing surface design

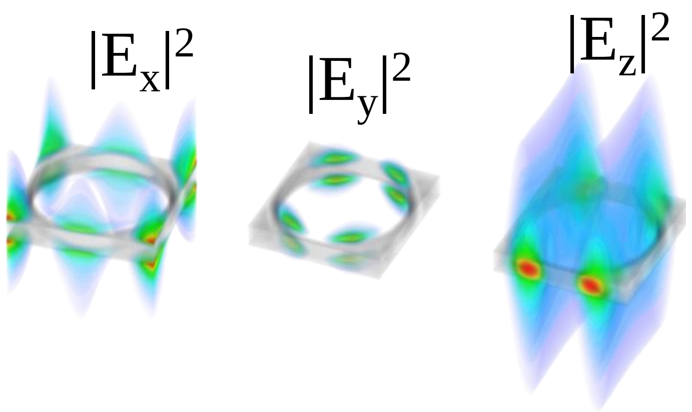
- 2D-PhC in Si_3N_4 (n~2; h~60 nm) on a SiO_2 substrate
- square lattice of cylindrical holes a~500 nm; d~130 nm

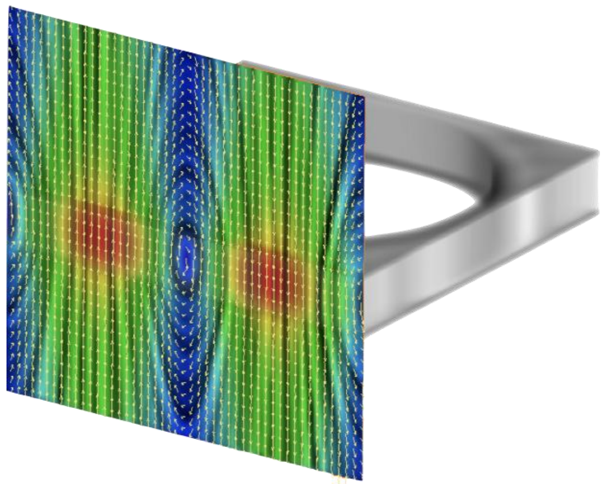
1) λ_{res} ~ 780 nm
2) λ_{res} ~ 545 nm



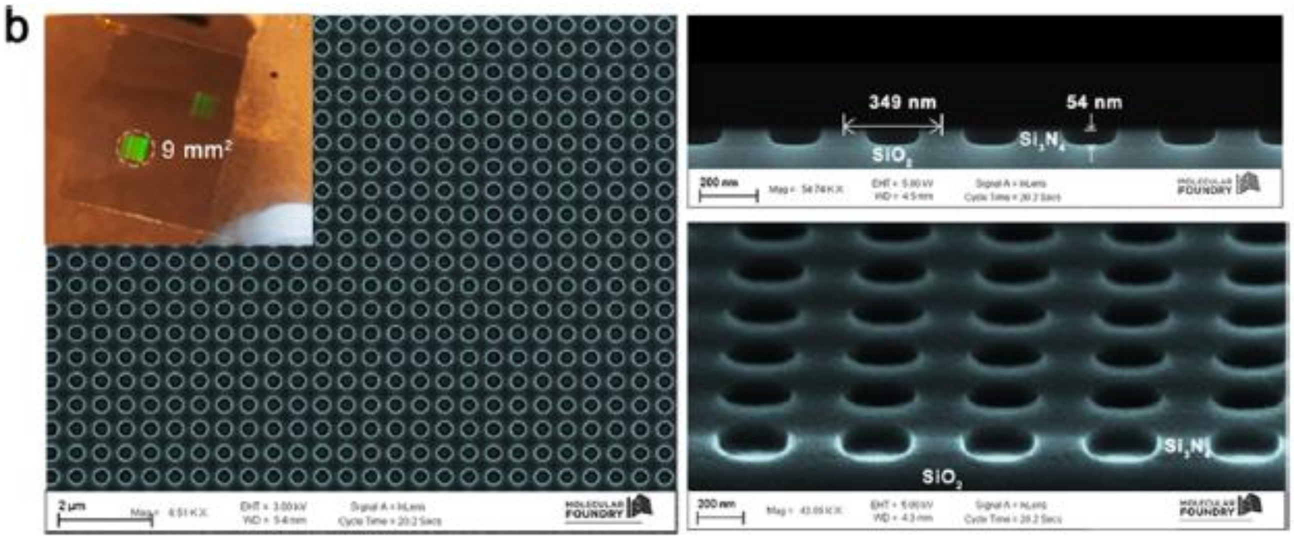
$E=10^8\ E_i$

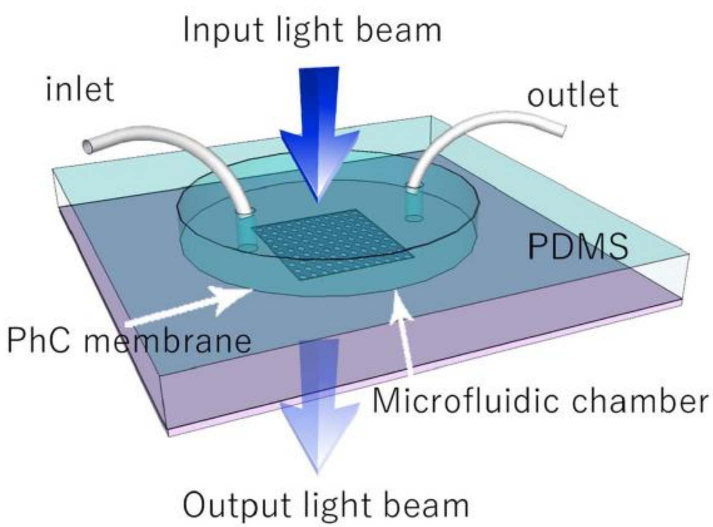


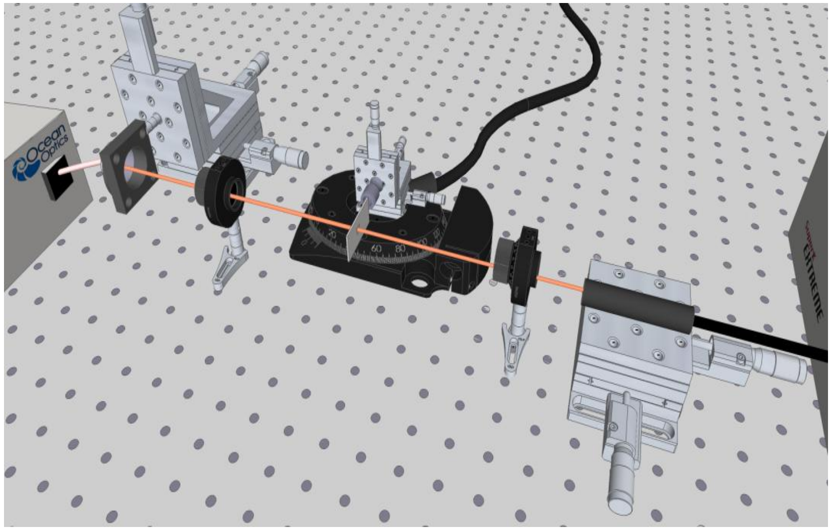




Device fabrication







Device characterization

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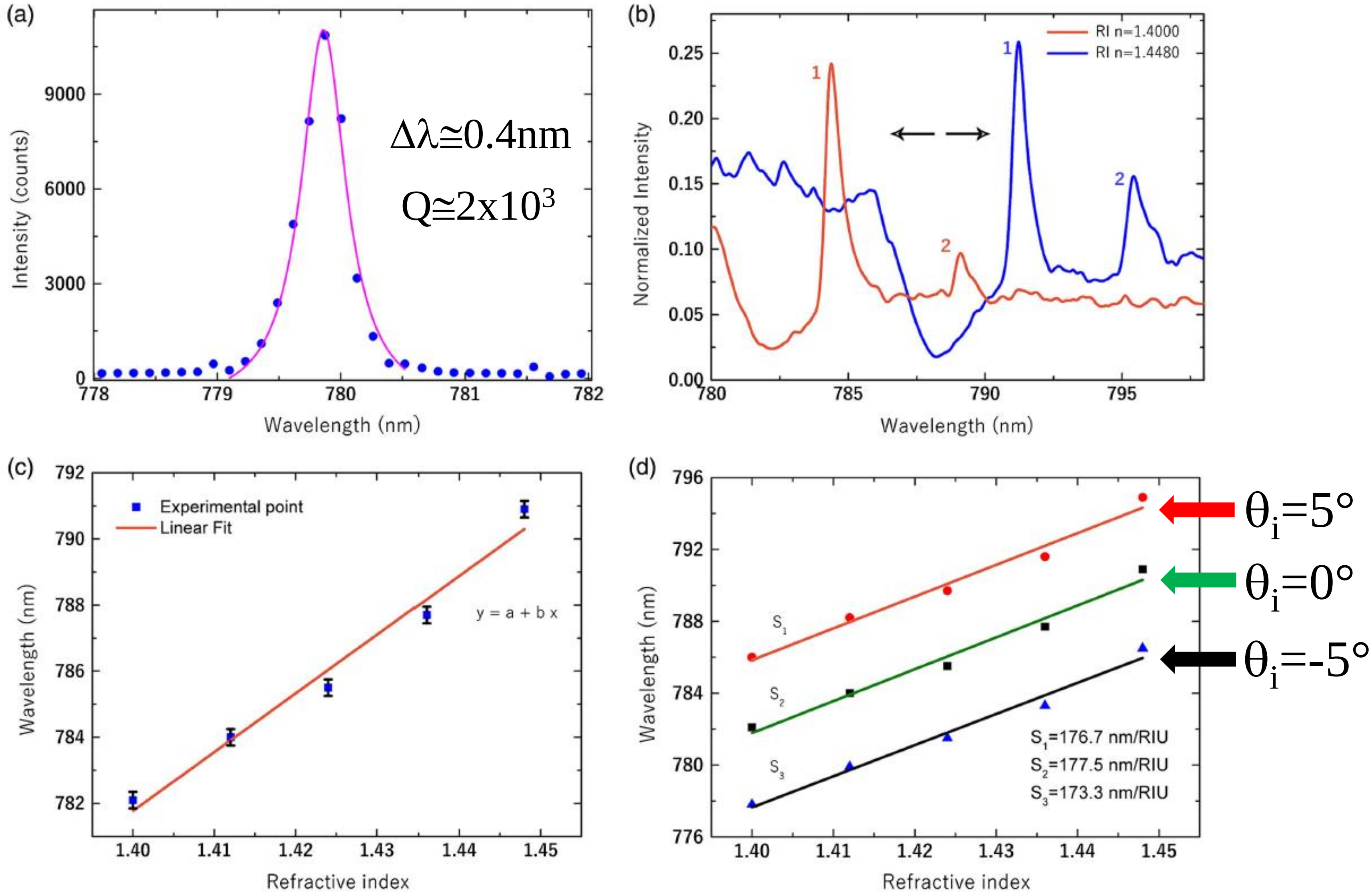
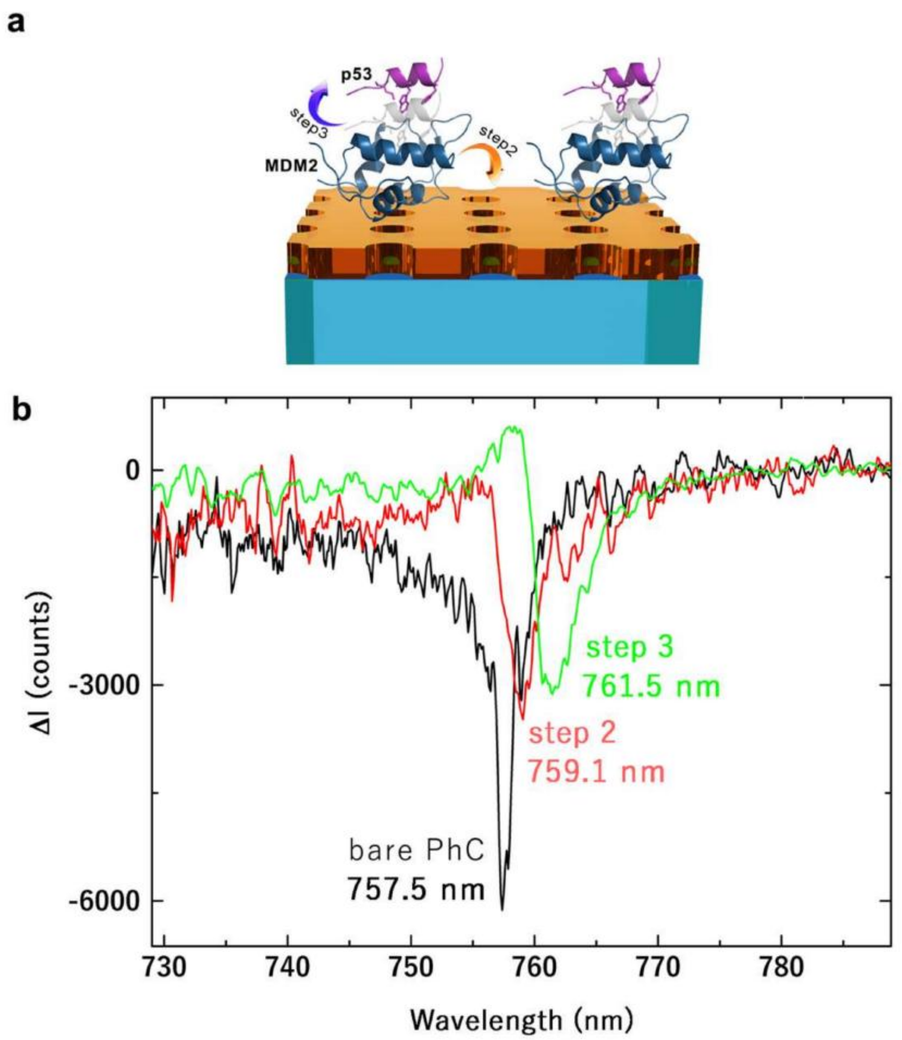
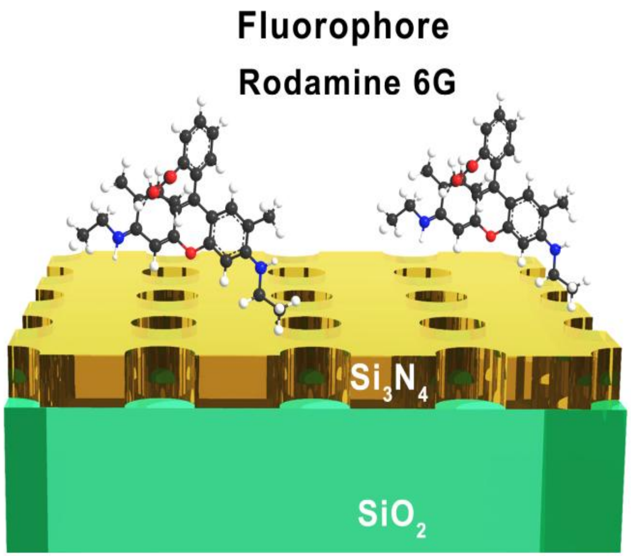


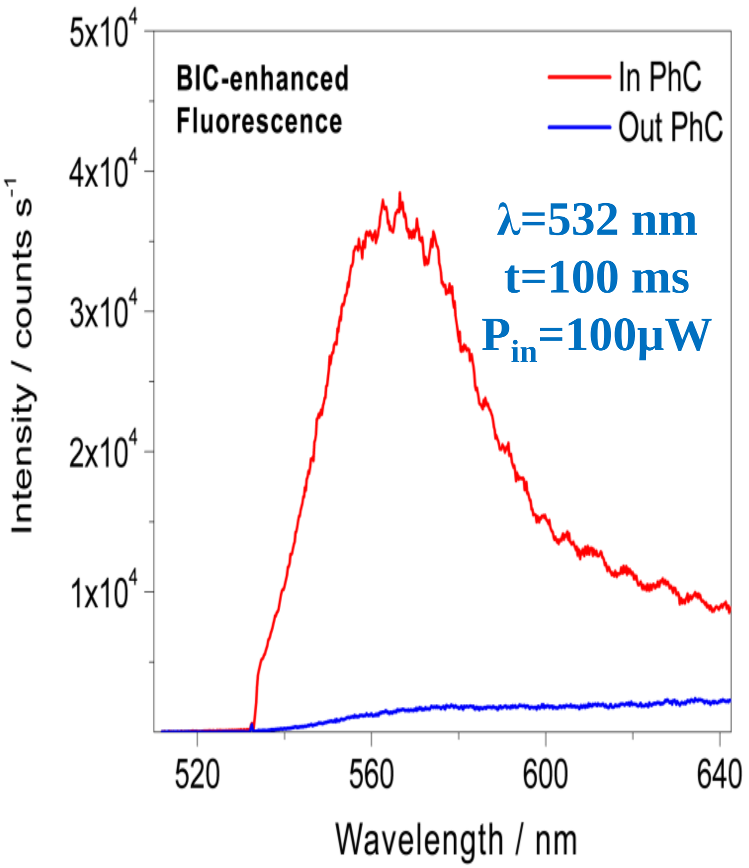
First study of MDM2-p53 protein-protein interaction



BIC-Enhanced Fluorescence

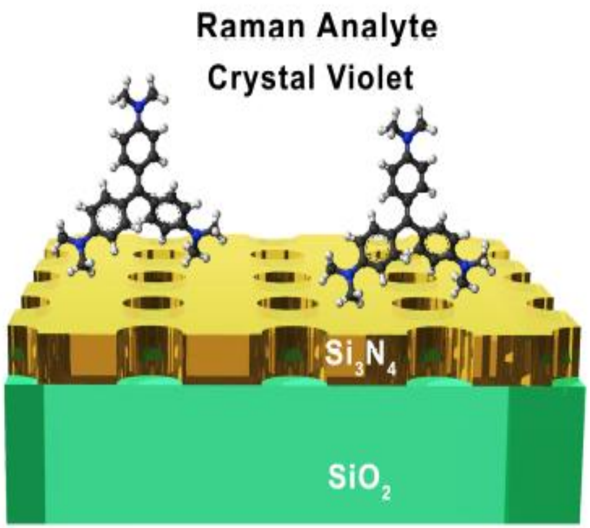


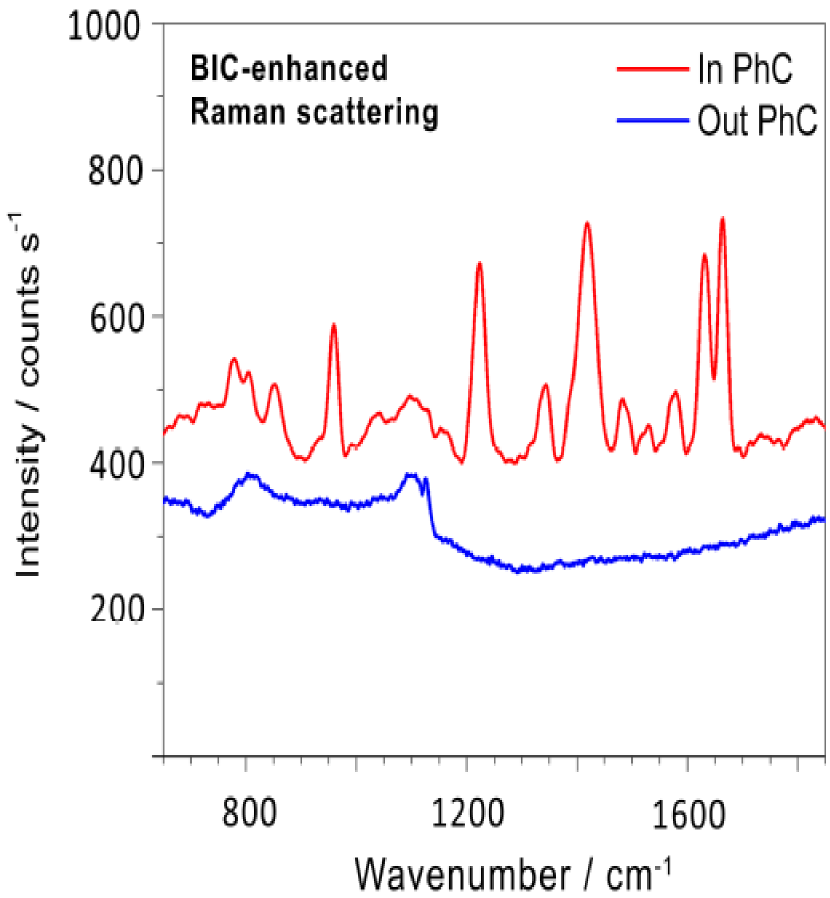
Rodamine 6G dispersed in PMMA
C=10 μM



SEF factor ~ 10^3

BIC-Enhanced Raman effect





- λ=532 nm
- Crystal Violet solution in ethanol

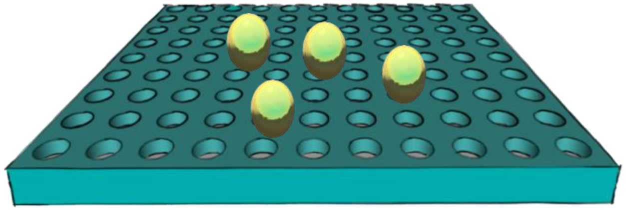
$F_{BIC-R} > 10^3$

BIC-LSPR hybrid effect

Randomly dispersed Au-Nanoparticles

+

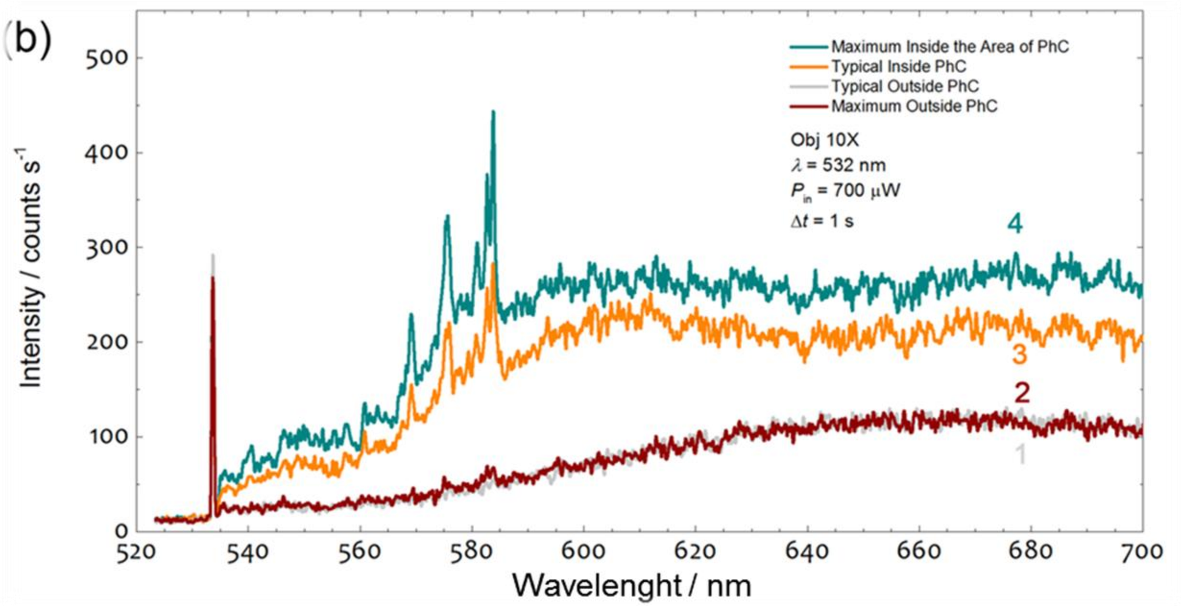
Crystal Violet molecules

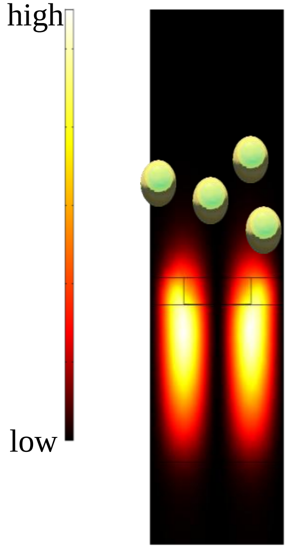


Au-NPs diameter ≅ 40 nm

$\lambda_{res} \sim 530$ nm

$F_{BIC\text{-}LSPR} \approx 13$

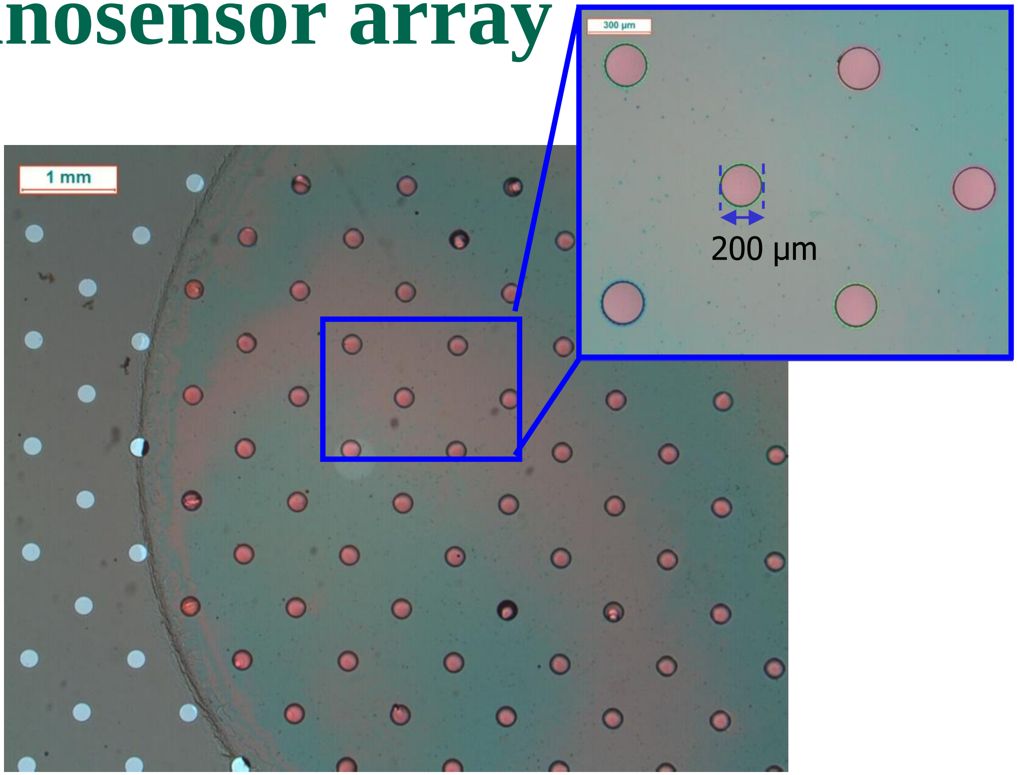


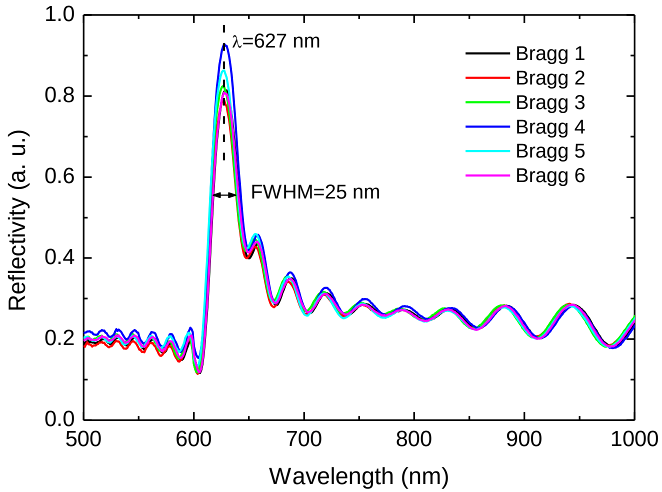


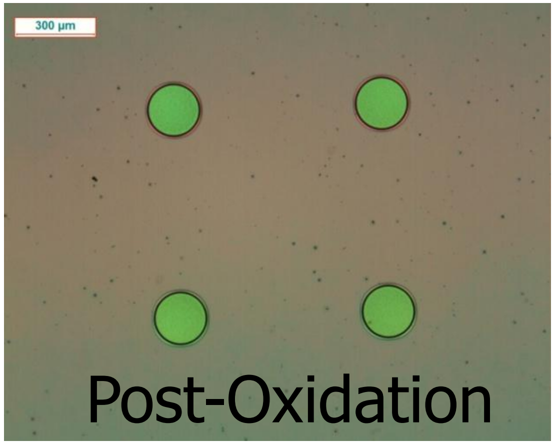
Next step:

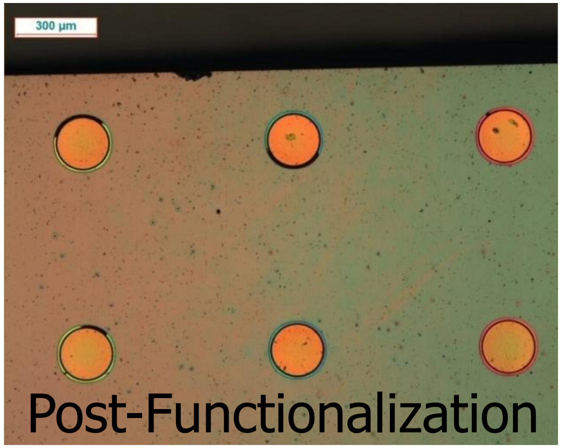
integration with microfluidics

Nanosensor array

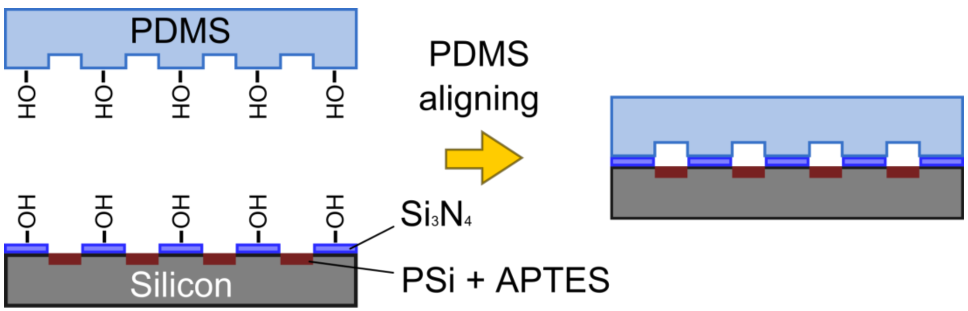




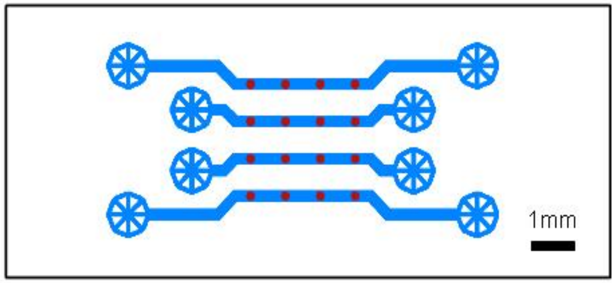


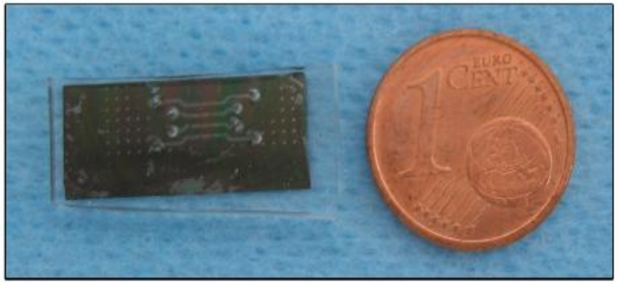


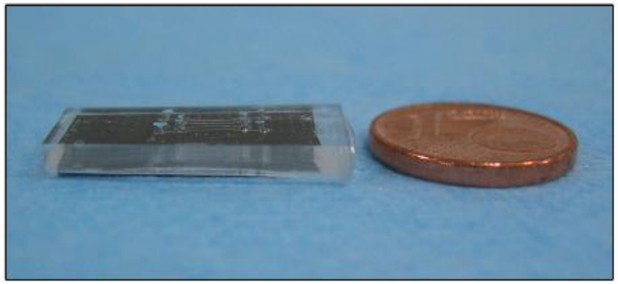
Integration with microfluidics

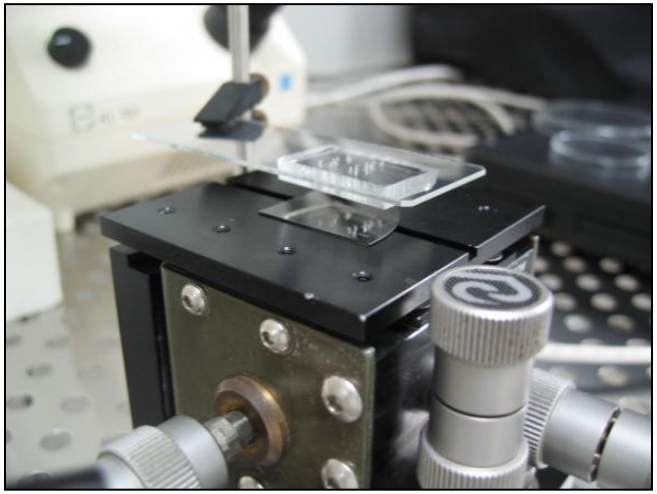


a) b)





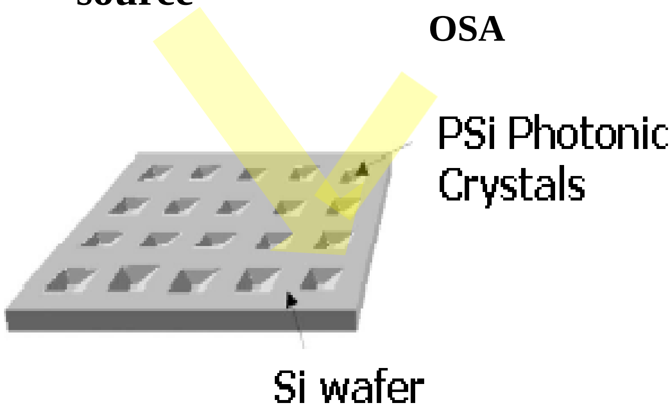




Alignment setup

Label-free DNA chip…

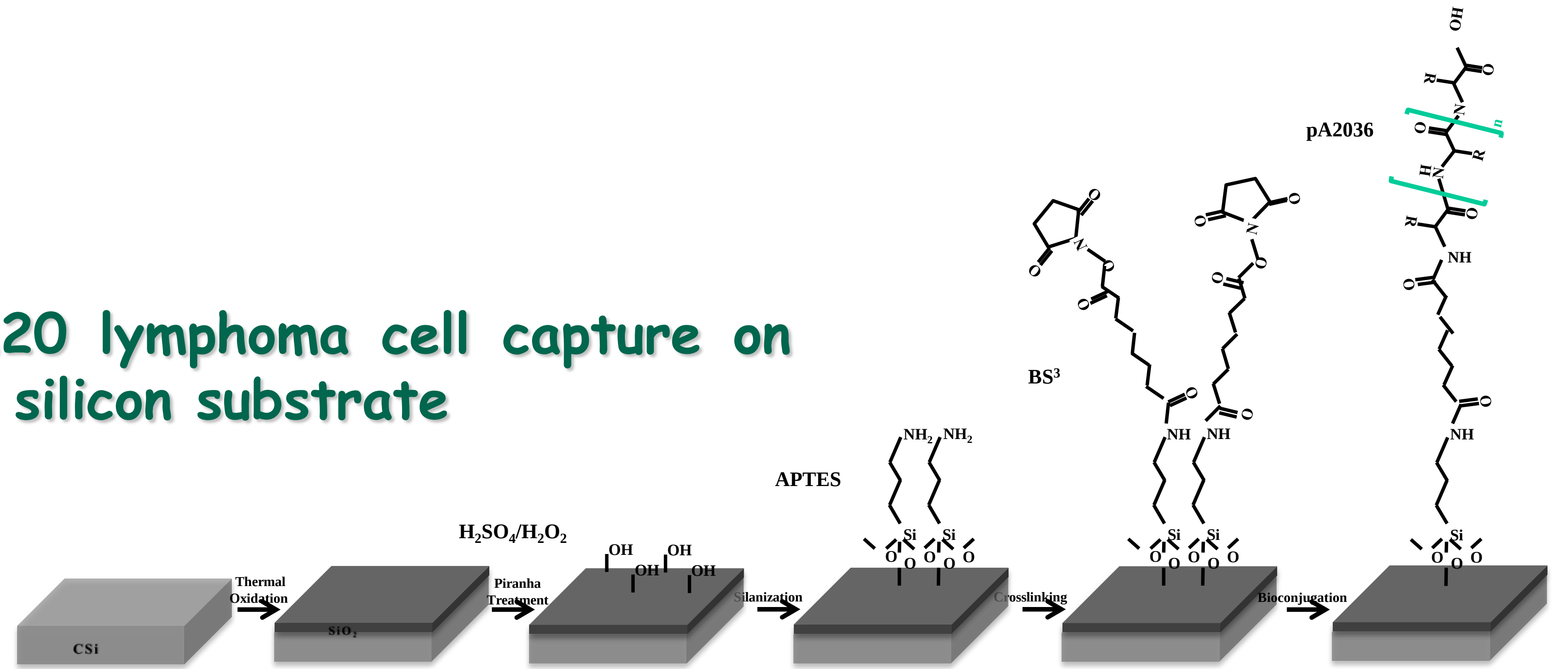
…based on a microarray of nanophotonic biosensors integrated with microfluidics



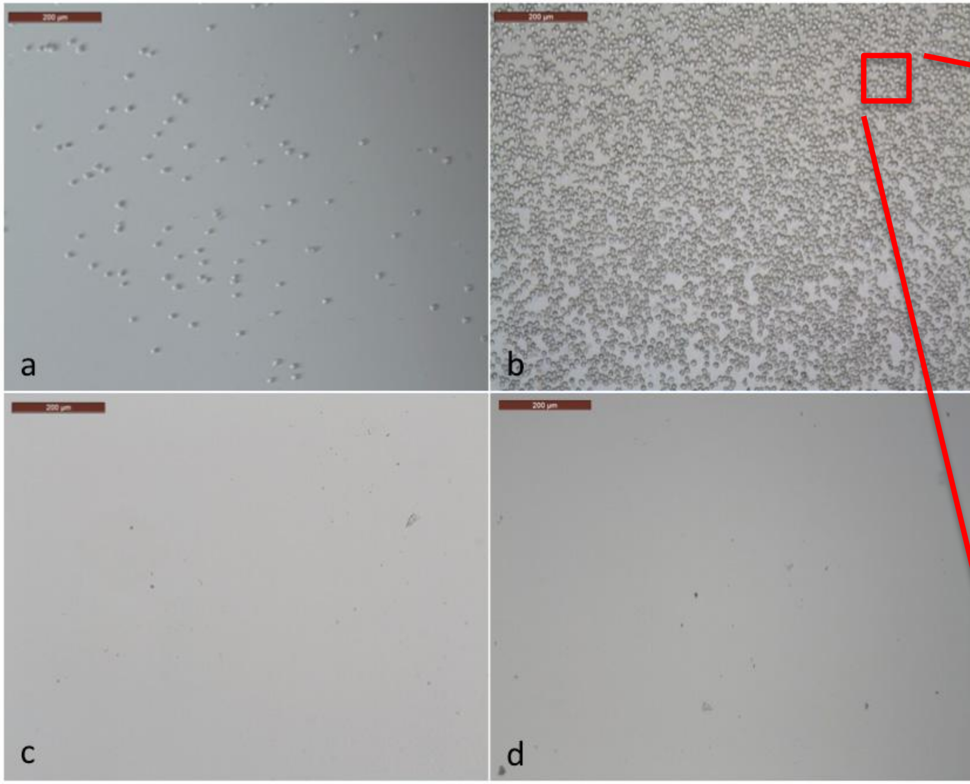
- No labeled samples
- Direct optical read-out
- Small liquid volume

Microfluidic chips for cancer cell detection:

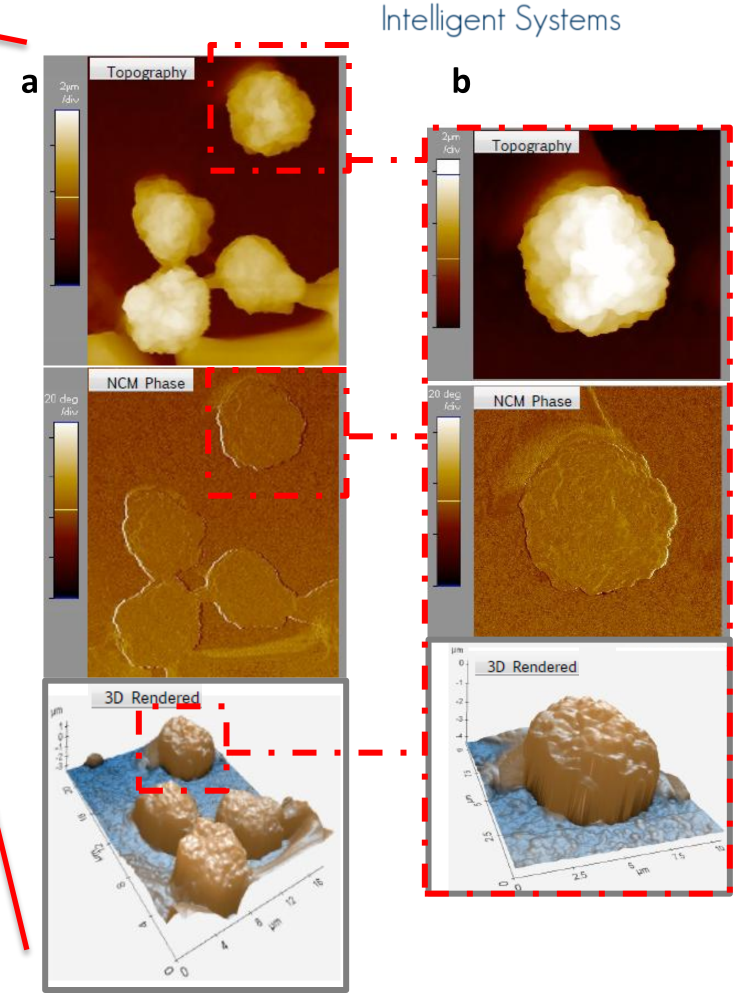
A20 lymphoma cell capture on a silicon substrate



Immobilization scheme of A2036 peptide on silicon surface to detect A20 B lymphoma cells (APTES 5% in absolute ethanol; BS^3 10mM; pA2036 150µM)



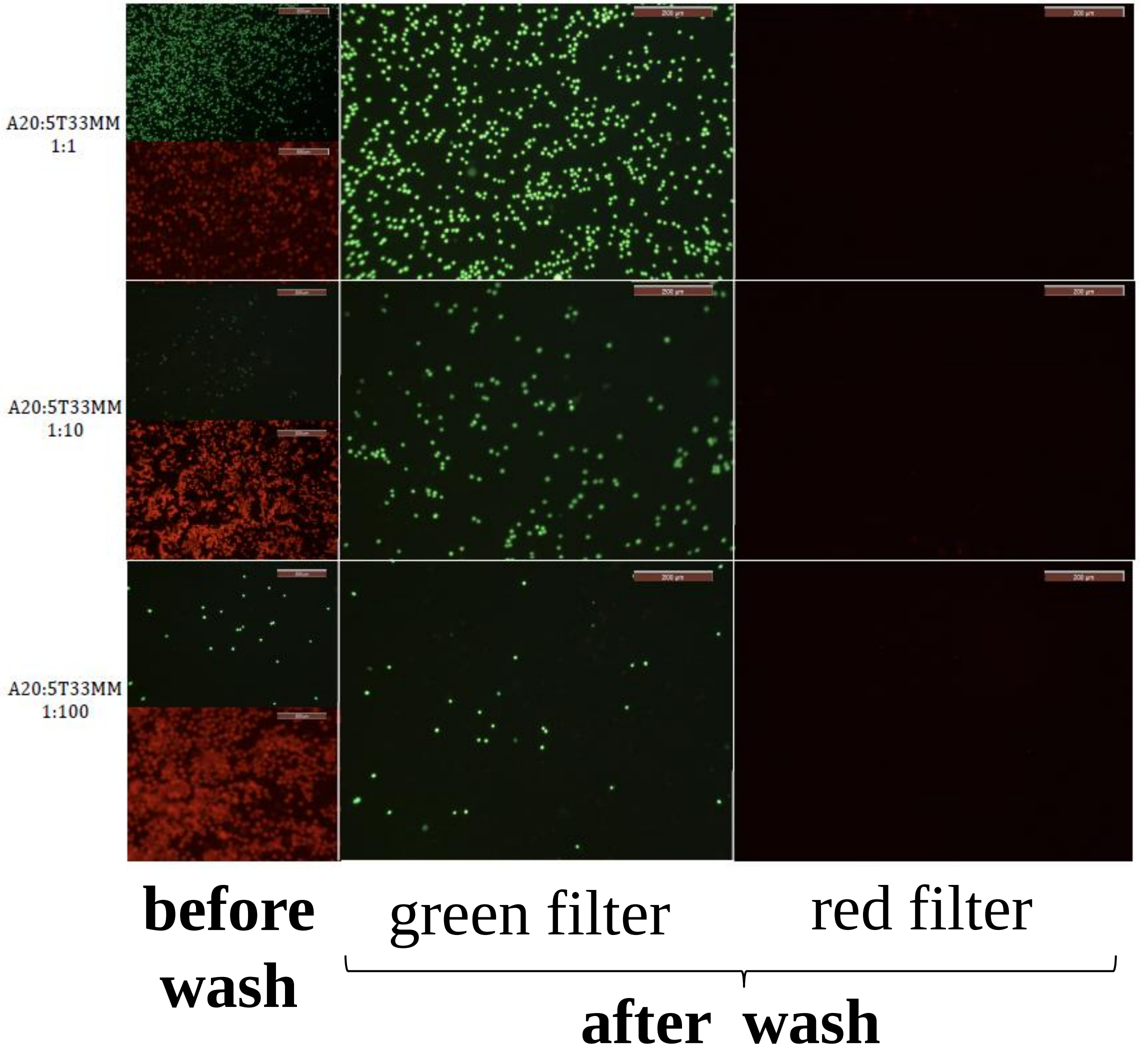
A20 cell detection on planar silicon pA2036 modified-sensor after incubation with 1×10^{4} cells/mL (a) and 5×10^{6} cells/mL (b).
(c) Optical image of random-peptide modified-sensor incubated with A20 cells. (d) Optical image of pA2036 modified-sensor incubated with 5T33MM cells.



AFM images of live A20 cells detected on silicon surface

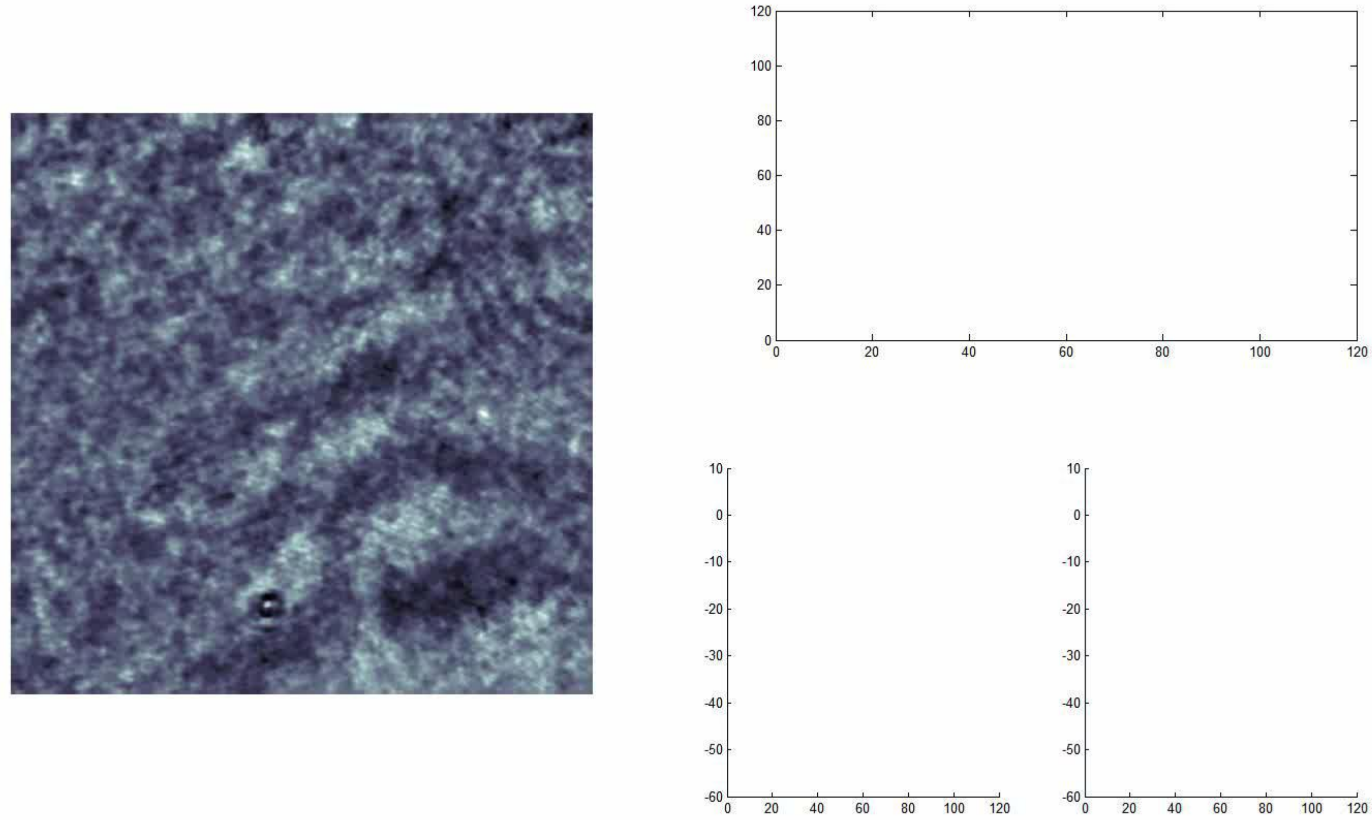
Coverage of 85% of silicon surface

A20 and 5T33MM mixed system



Fluorescence image of A20 cells (green) detection in system mixed with 5T33MM cells (red) on planar silicon pA2036 modified-chip after incubation at indicated ratios

3D tracking of live cells



A whole flow-cytometer in a microfluidic chip

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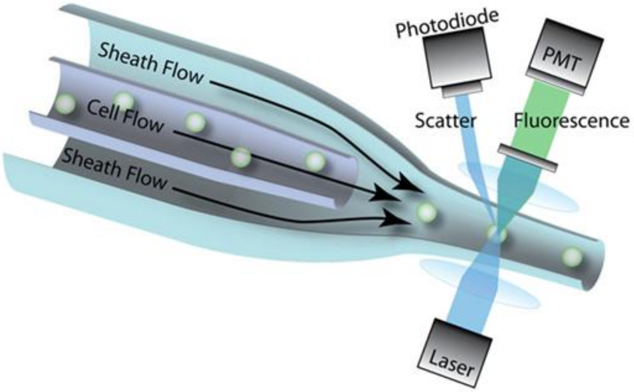

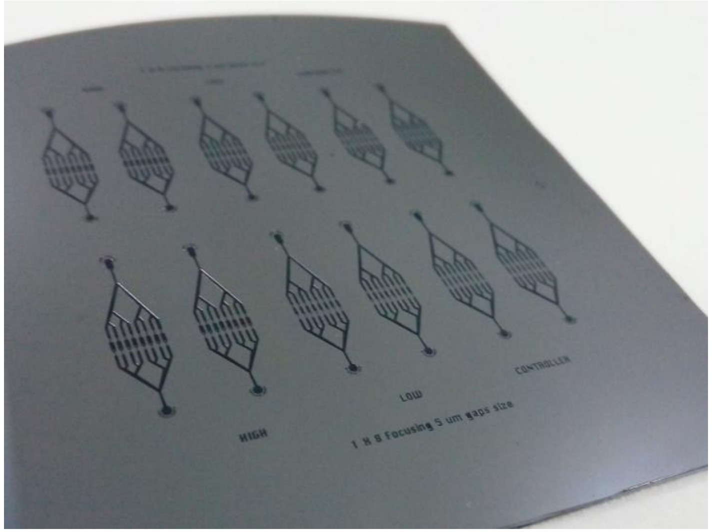

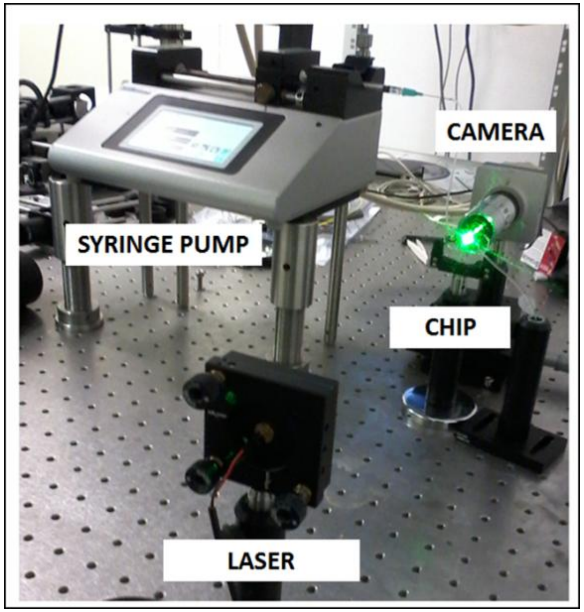

Hydrodynamic focusing of cancer cells on a silicon chip

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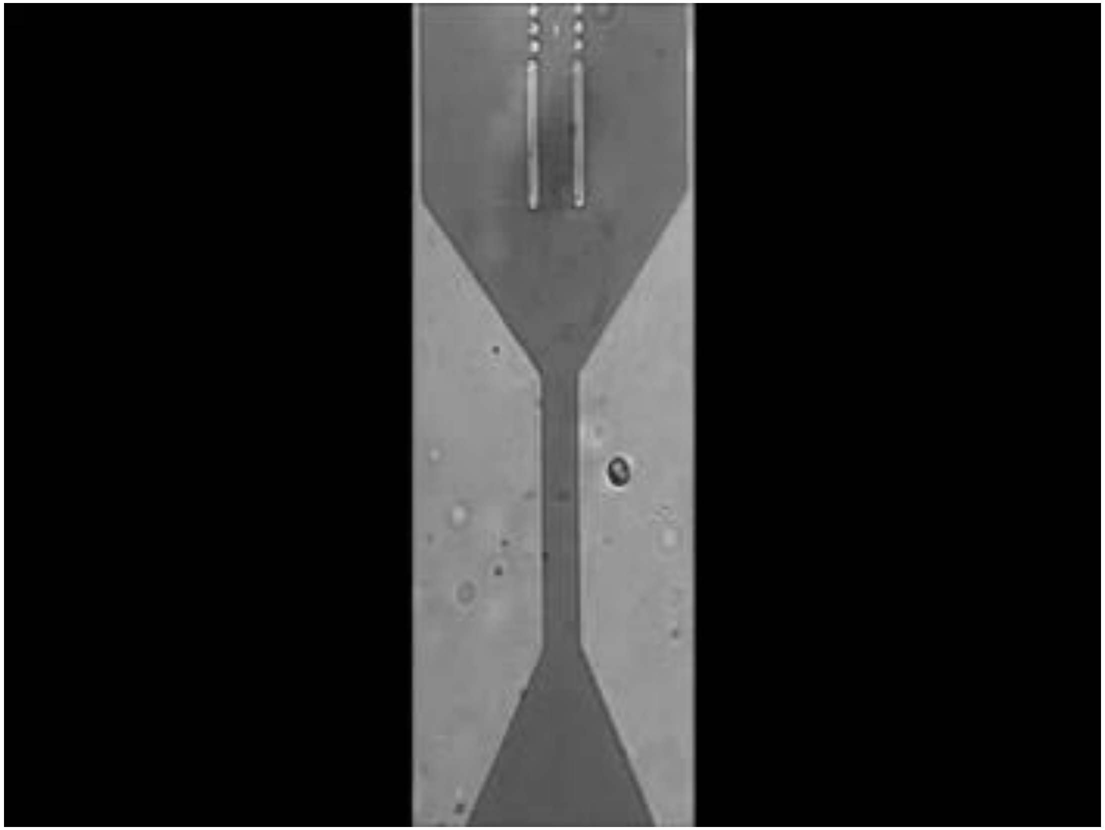

Cell manipulation (rotation) for better on-chip imaging

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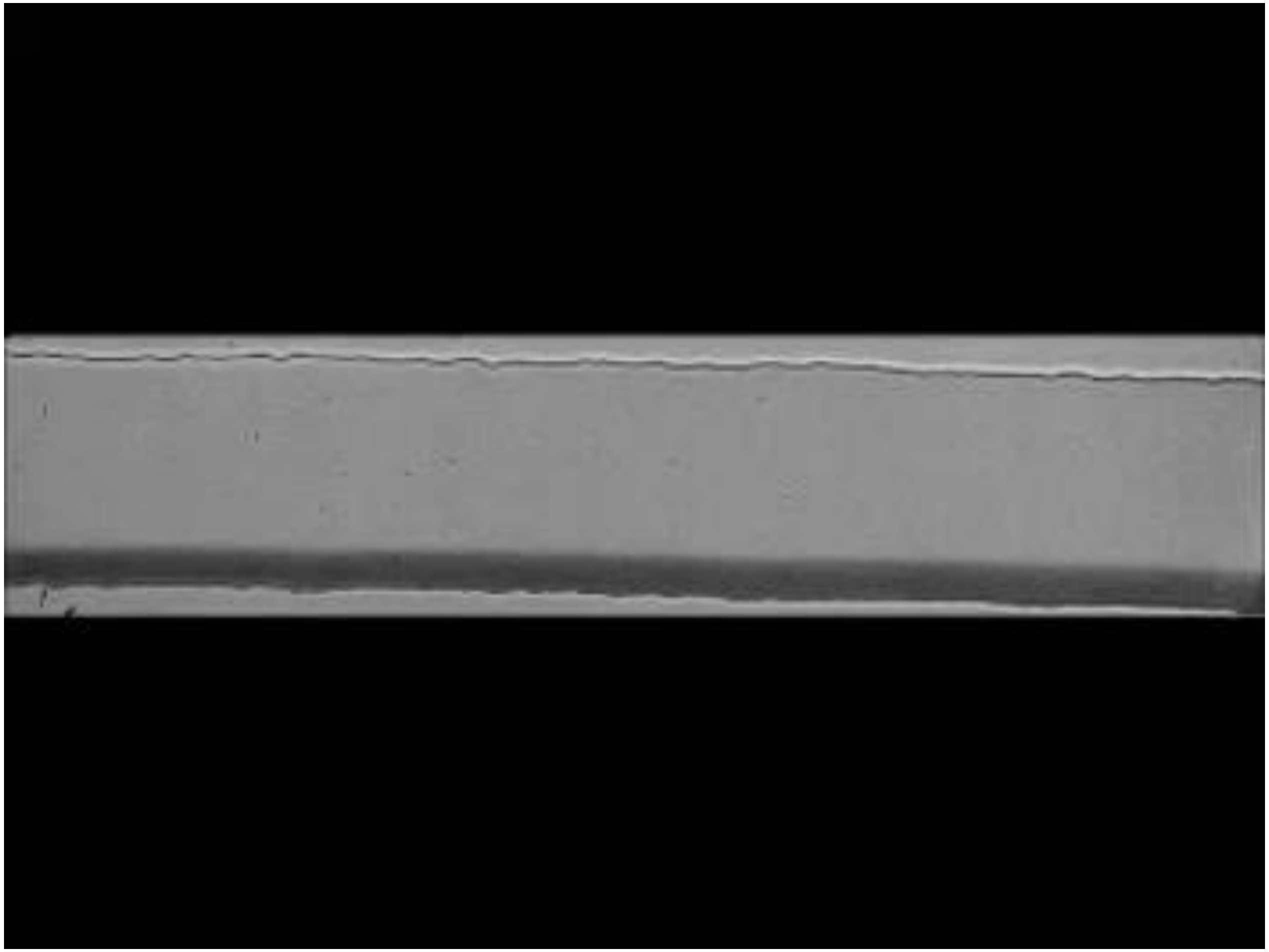

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Giuseppe Scala

Vito Mocella

Luca De Stefano

Mario Iodice

Giuseppe Coppola