Nanobiosensors based on optical platforms

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nanobiosensors and bioanalytical applications

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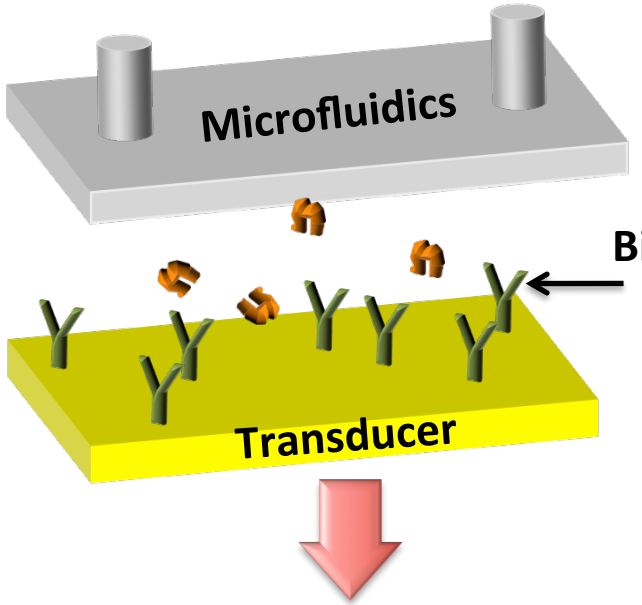
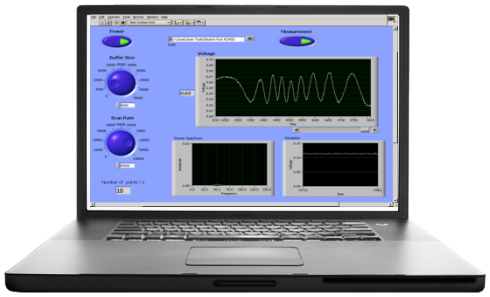
Outline

- What is a biosensor? Different types of biosensors
- **Optical biosensors** vs **Nano-optical biosensors** -> **Nanoplasmonic** biosensors
- Introduction to nanoplasmonics (refractive index and near field effects)
- Main steps to develop a nanoplasmonic biosensor
  - Nanofabrication of plasmonic nanostructures
  - Biofunctionalization
  - Microfluidic integration
  - Detection system
- Examples of nanoplasmonic biosensing applications
  - Aggregation colorimetric assays
  - Refractometric sensing
- New and additional functionalities of plasmonic nanostructures
- Conclusions

What is a biosensor?





Applications ↔ Specific Receptor

Molecular and cell biology

Biomolecular interactions and their affinity (DNA, RNA, proteins, lipids…,)

Biomedicine

Diagnostics

Detection of biomarkers, pathogens

Treatment

Discovery and validation of drugs

Environmental control, food industry…

Elimination of sample pretreatments

Direct detection in serum, urine, saliva

Types of transducers

Electrochemical, mechanical, photonic…

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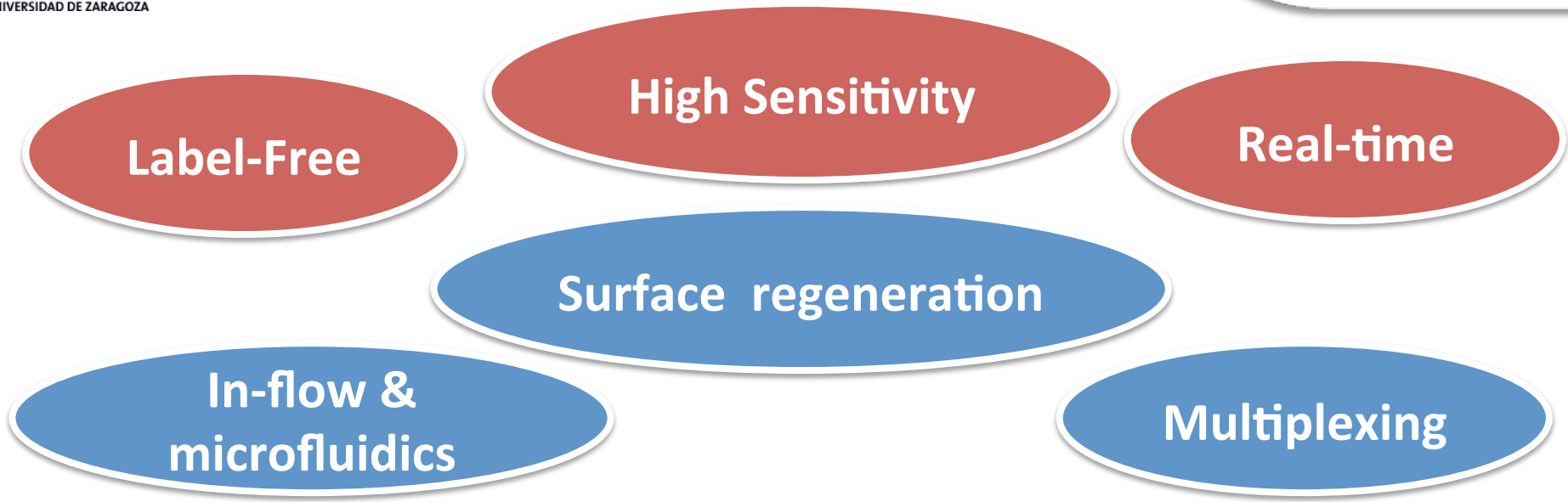
Biosensor Features



Transducer Requirements

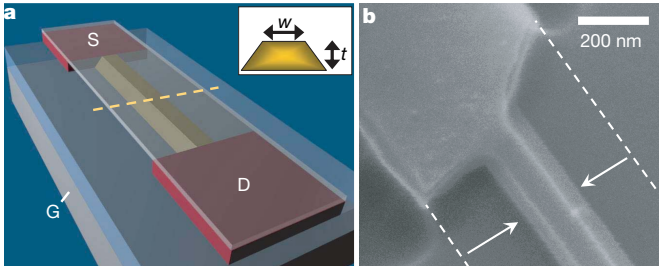
Transducers

Electrochemical

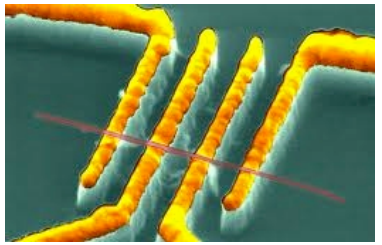
Amperometric
Potentiometric
Impedance
Field effect transistors

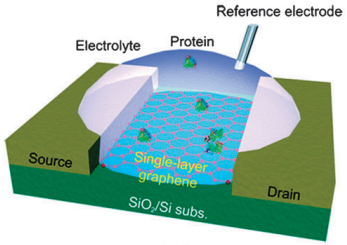
Glucose sensor

Silicon nanowires (FET)

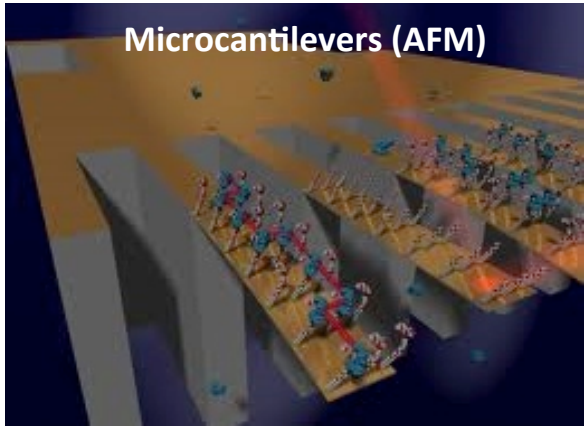


Carbon Nanotubes and Graphene

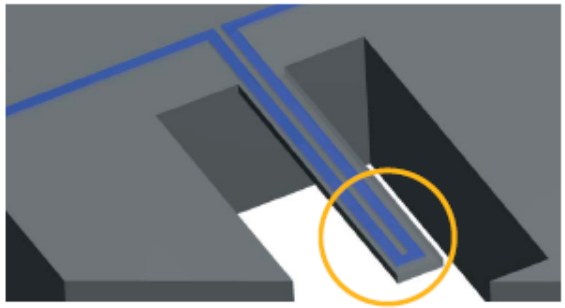


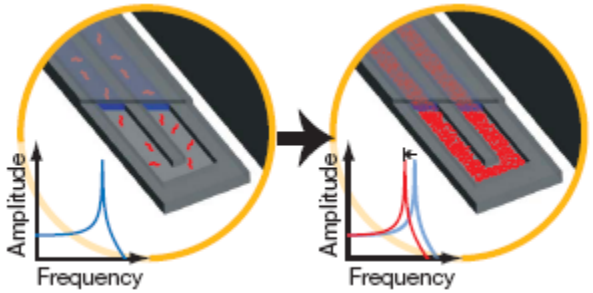


Nanomechanical



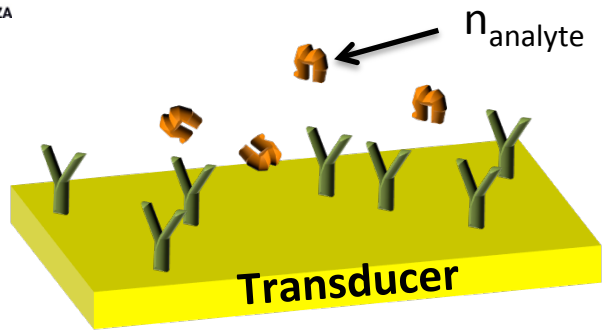
Cantilevers with embedded microfluidics





Magnetic, calorimetric…

Optical Biosensors



Advantages of optical sensing

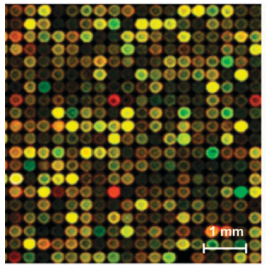
- ✓ Immunity to electromagnetic interferences
- ✓ High bandwidth
- ✓ Miniaturization
- ✓ Capacity of integration in lab-on-a-chip
- ✓ Multiplexing -> Imaging

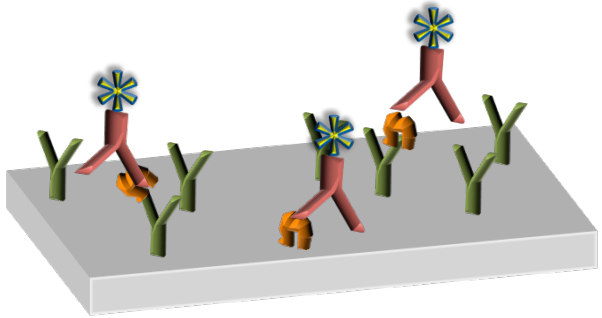
Detection principles

- **Refractive index changes** (real part)
  $Re[n_{analyte}] \neq Re[n_{liquid}]$
- **Absorption changes** (imaginary part)
  $Im[n_{analyte}] \neq 0$
- **Fluorescence**
  Analyte absorbs λ_1 and emits λ_2
  Labels -> microarrays
- **Raman scattering**
  Inelastic scattering from molecular
  mechanical vibrations -> analyte fingerprint
  Very low Raman cross-section

Optical transducing

Fluorescence labeling -> Microarrays (DNA, proteins) -> High-throughput Plate readers





Drawbacks

- Photo-bleaching
- Quenching
- Indirect, end point assay -> No access to interaction kinetics
- Difficult quantification (false positives)

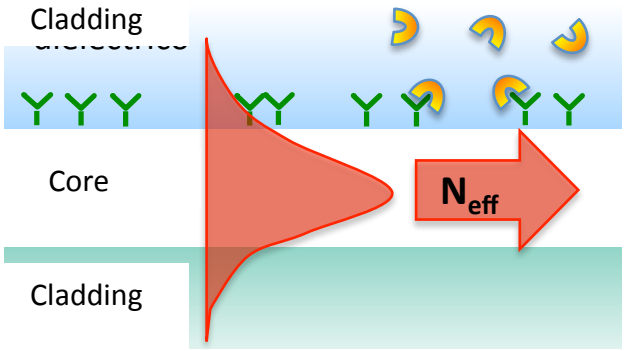
Label-free sensors

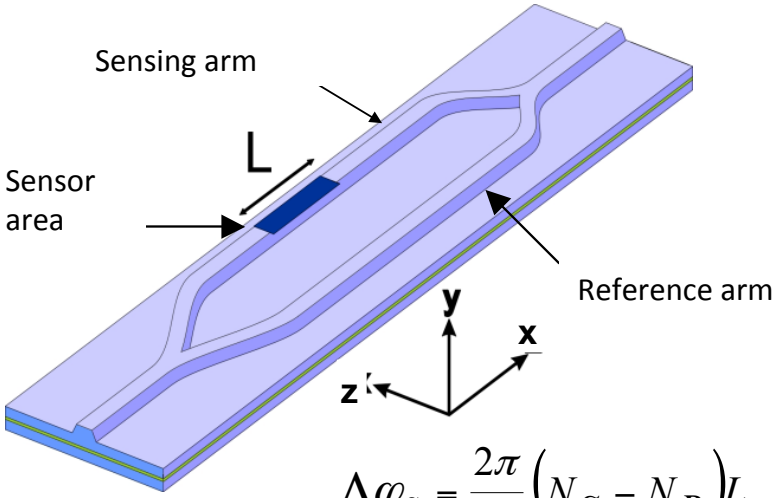
- ✓ Real-time
- ✓ Direct assay -> Access to interaction kinetics
- ✓ Minimum sample pre-treatments
- ✓ Accurate quantification

Examples: Integrated optical sensors, Plasmonic sensors…

Integrated optical sensors

Integrated optical waveguides -> Dielectric waveguides

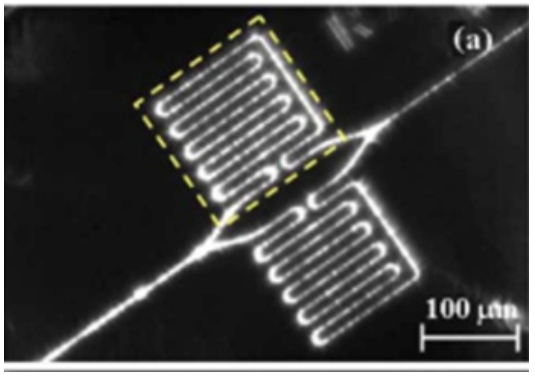




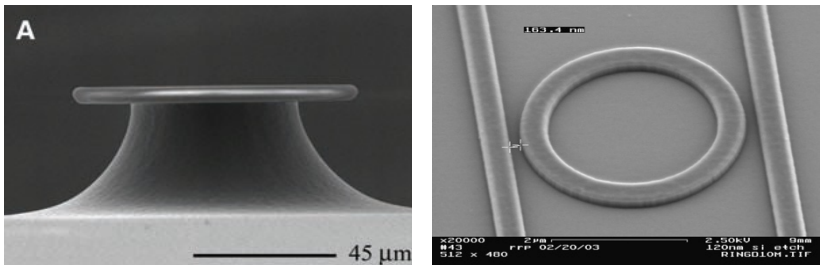
$$\Delta\varphi_S = \frac{2\pi}{\lambda}\left(N_S - N_R\right)L$$

$$I_T = I_S + I_R + 2\sqrt{I_S I_R}\cos\Delta\varphi_S$$

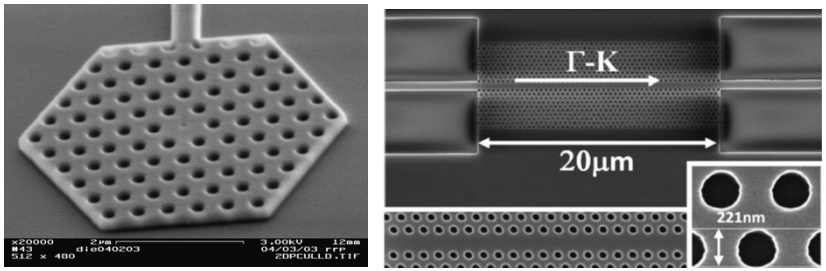
Silicon Nanowires



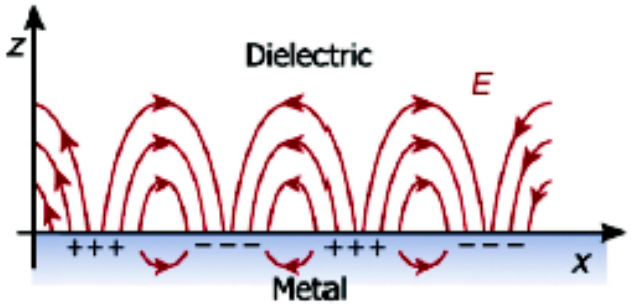
Ring resonators

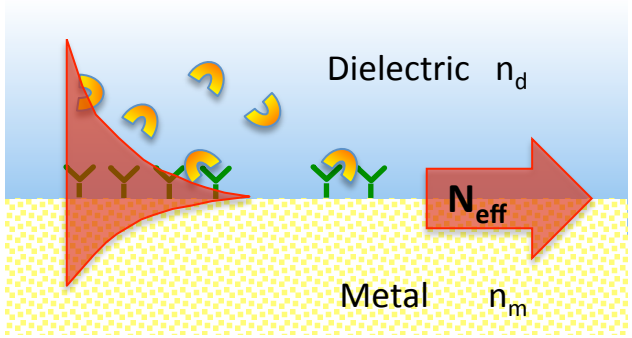


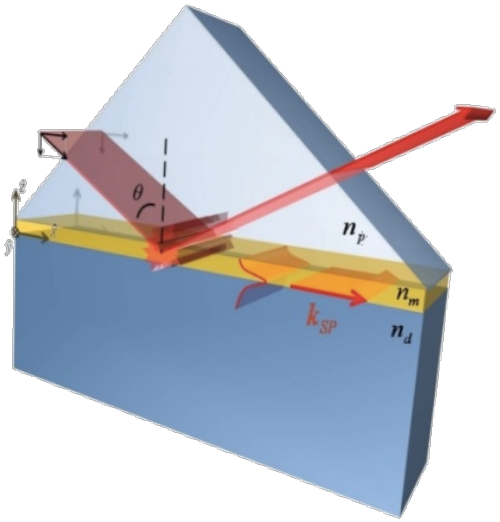
Photonic crystals



Surface Plasmon Resonance Sensor



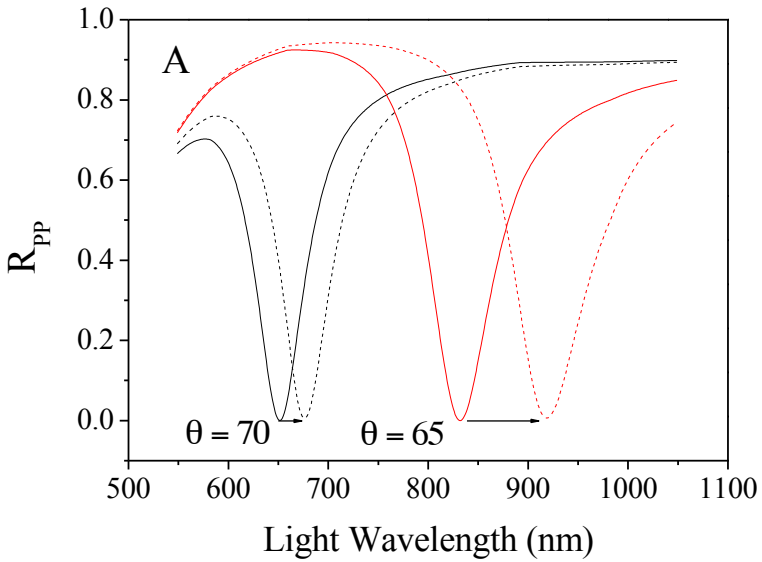




$$k_{SP} = k_0 \frac{n_m n_d}{\sqrt{n_d^2 + n_m^2}} = k_0 N_{eff}$$

Propagation distance (visible) ~ 10-100μm

Detection principle



Most developed and commercially available

More than 20 companies worldwide:
Biacore, Horiba, Biosensing Instruments, Sensia, Analytical systems, Reichert, Moritex…

Going nano, why?

- To improve sensitivity
- Miniaturization
  - Multiplexing
  - Minimize reactant consumption
  - Improve time response
- New functionalities
  - Electromagnetic field enhancement
    - SERS -> Molecular fingerprint
    - Surface enhanced fluorescence
    - Photo-thermal effects
  - Opto-fluidic systems

Going nano -> Nanoplasmonic structures

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Introduction to nanoplasmonics

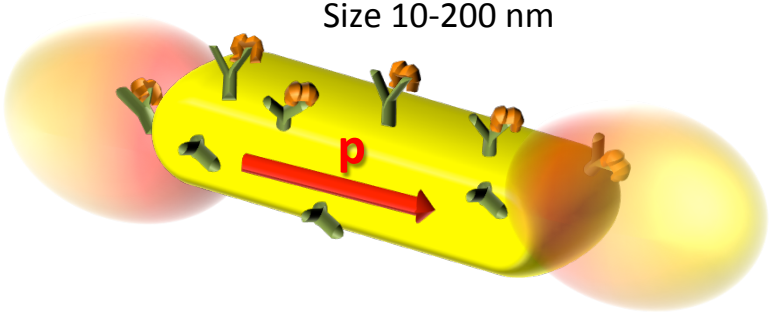
Near-field electromagnetic effects
Refractive index dependence

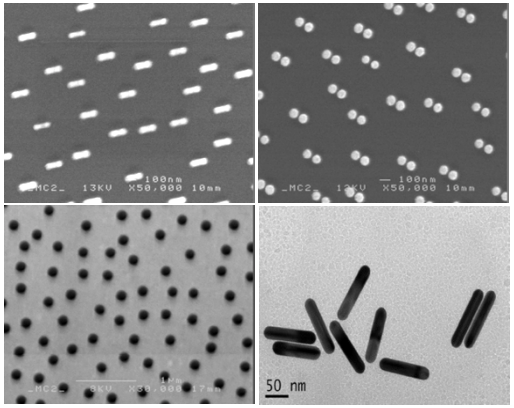
Opportunities for sensing

Nanoplasmonics

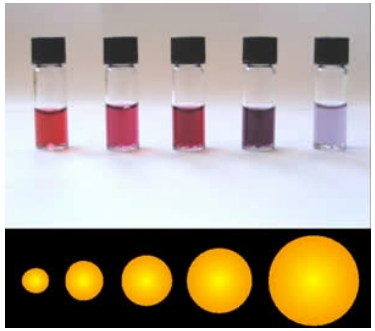
Interaction of metal nanostructures with light

Size 10-200 nm

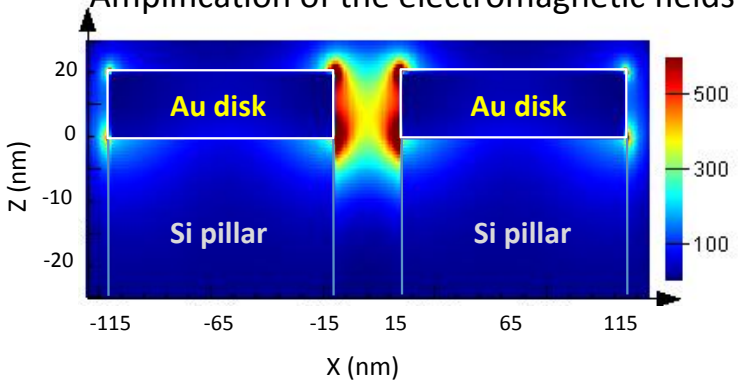




Resonance can be tuned



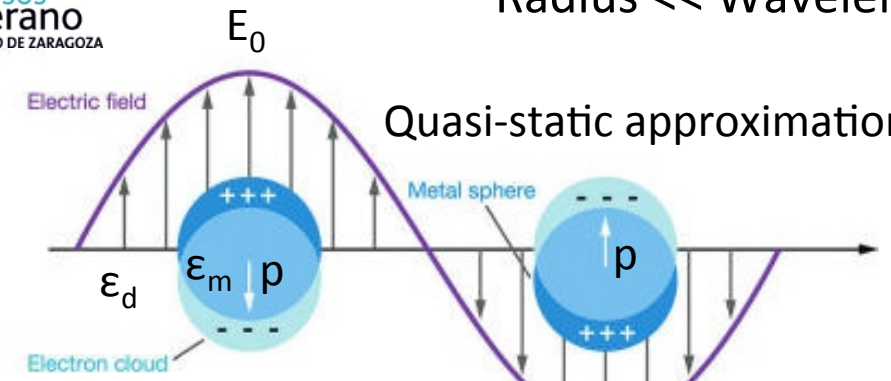
Amplification of the electromagnetic fields



- ❑ Localized optical resonances
- ❑ Surpass of diffraction limits
- ❑ Tunability (vis-IR)
- ❑ Amplification of electromagnetic fields
- ❑ Amplification of optical effects
  - ○ Non-linear optics
  - ○ Raman ➔ SERS
  - ○ Fluorescence ➔ SEF
  - ○ Infra-red Absorption ➔ SEIRA…

Metal sphere

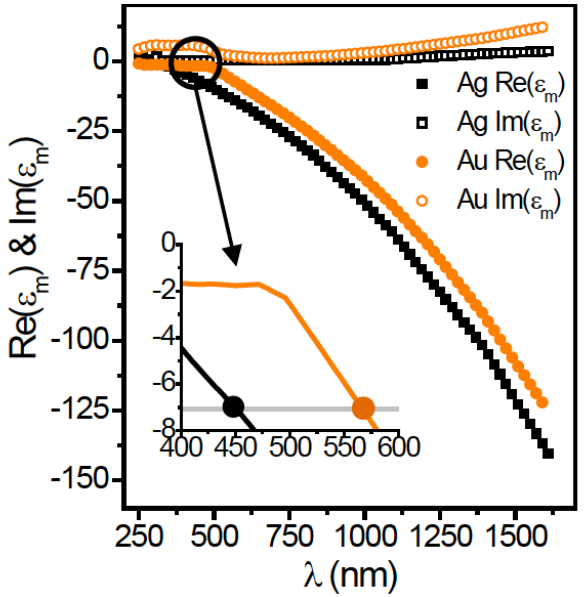
Radius << Wavelength



Quasi-static approximation

$$P = \epsilon_0 \epsilon_d \alpha_0 E_0$$

$$\alpha_0 = 4\pi a^3 \frac{\epsilon_m(\lambda) - \epsilon_d}{\epsilon_m(\lambda) + 2\epsilon_d}$$

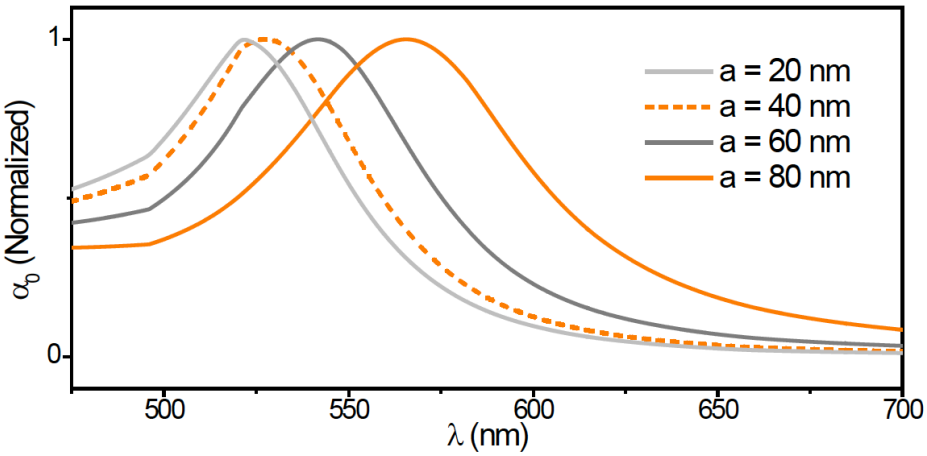


Localized surface plasmon resonance condition

$$\mathrm{Re}[\varepsilon_m] = -2\,\varepsilon_d$$

Size effect (a << λ)

$$\alpha_0 = 4\pi a^3 \cdot \frac{\epsilon_m(\lambda) - \epsilon_d}{\epsilon_m(\lambda) + 2\epsilon_d - \pi\,(\epsilon_m(\lambda) - \epsilon_d)\,(2ka)^2(1 + i\frac{2}{3}ka)}$$



Larger spheres: a ≥ λ

Multipolar contributions: dipole + quadrupole + … -> Mie Theory

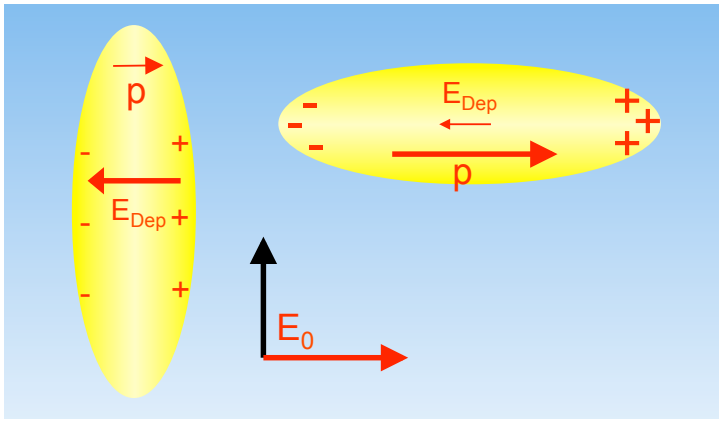
Metal ellipsoid

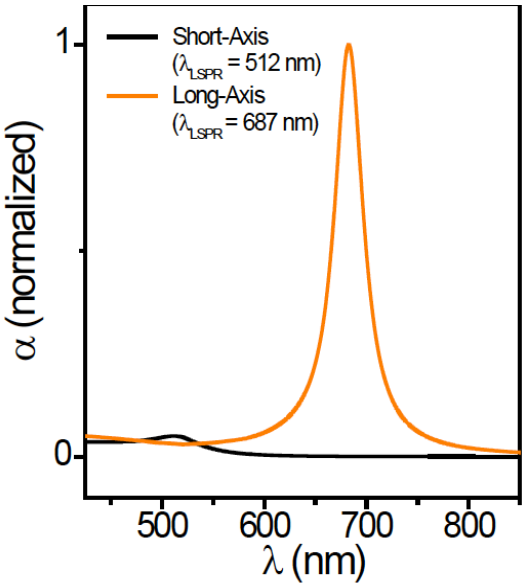
Size << Wavelength

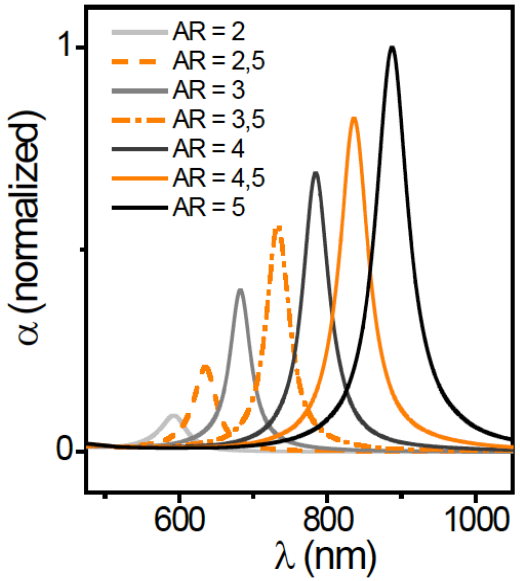
$$\alpha_i = \frac{4\pi}{3} abc \frac{\varepsilon_m - \varepsilon_d}{(1 - L_i)\varepsilon_d + L_i \varepsilon_m}$$

L_i shape factor

$L_i = [0,1]$







LSPR satisfied when

$$\mathrm{Re}\left[(1 - L_i)\varepsilon_d + L_i \varepsilon_m\right] = 0$$

Sphere $\Rightarrow L_i = 1/3$ $\quad \mathrm{Re}[\varepsilon_m] = -2\varepsilon_d$

Ellipsoid long axis $\Rightarrow L_i < 1/3$ $\quad \mathrm{Re}[\varepsilon_m] < -2\varepsilon_d$

$\Rightarrow$ **RED-SHIFTED RESONANCE**

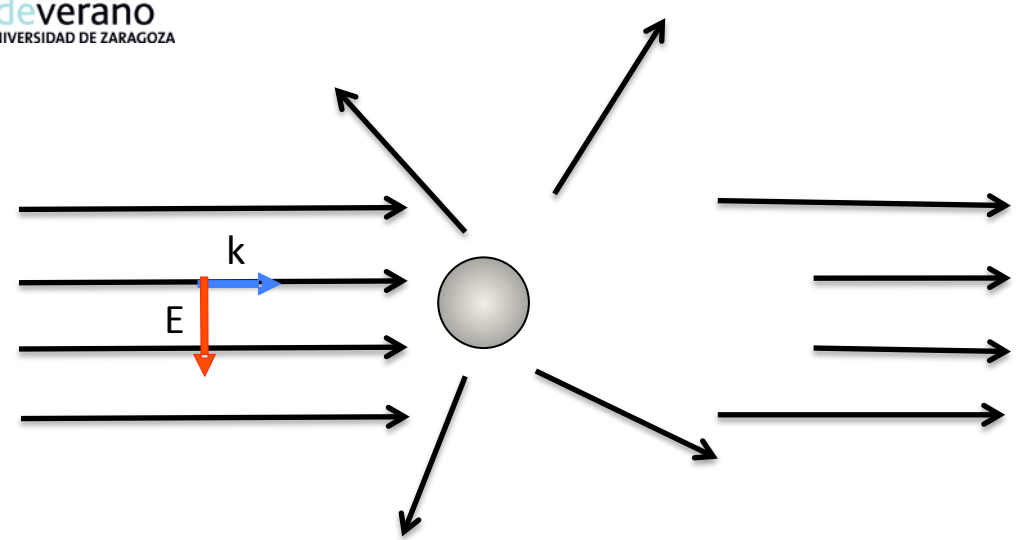
Ellipsoid short axis $\Rightarrow L_i > 1/3$ $\quad \mathrm{Re}[\varepsilon_m] > -2\varepsilon_d$

$\Rightarrow$ **BLUE-SHIFTED RESONANCE**

LARGE DIPOLE MOMENT IN LONG AXIS

WEAK DIPOLE MOMENT IN THE SHORT AXIS

Optical effects of the LSPR



Part of the light is absorbed -> heat

Part of the light is elastically scattered

Scattering cross section $C_{sca} = \frac{k^4}{6\pi} \cdot |\alpha|^2$

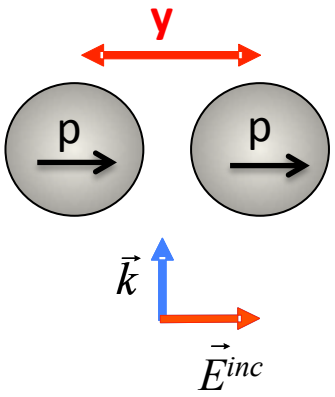
Absorption cross section $C_{abs} = k \cdot \mathrm{Im}(\alpha)$

Extinction cross section $C_{ext} = C_{sca} + C_{abs}$

High amplification of the scattering and absorption cross sections at the LSPR wavelength

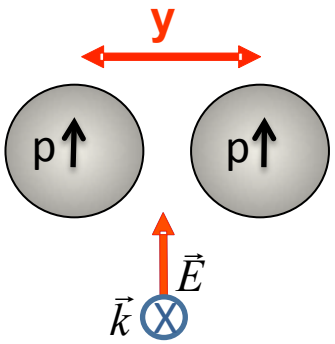
-> easy optical detection of the LSPR via absorbance or scattering measurments

Near-field interaction



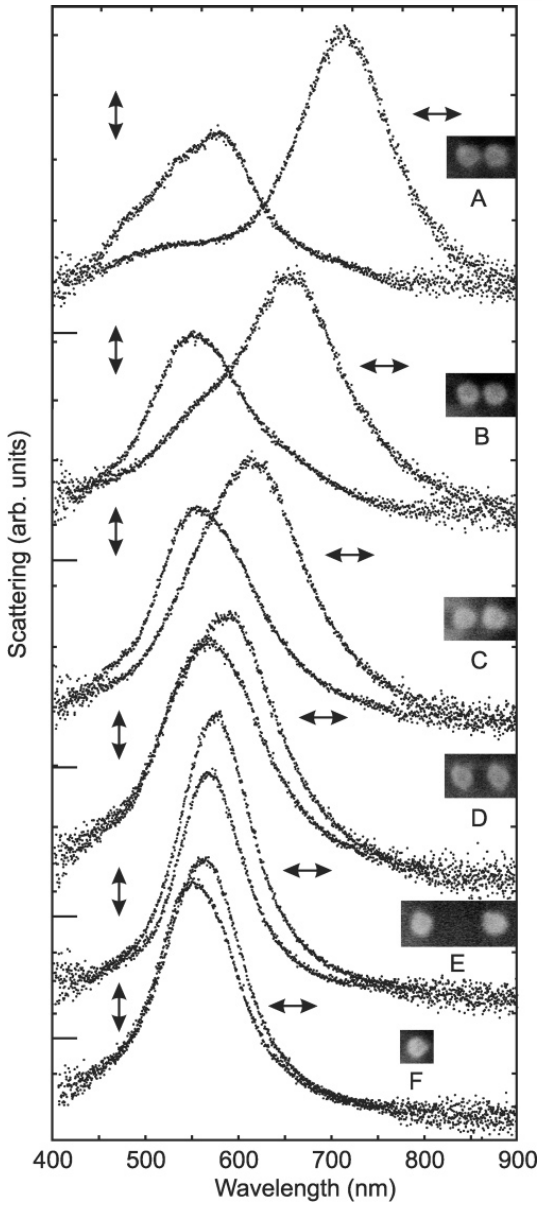
$$E_{1y} = E_y^{inc} + A_{yy} \cdot \alpha \cdot E_{2y}$$
$$E_{2y} = E_y^{inc} + A_{yy} \cdot \alpha \cdot E_{1y}$$
$$A_{yy} = \frac{2e^{iky}(-1+iky)}{y^3}$$

The dipoles cooperate → **RESONANCE RED-SHIFTS**



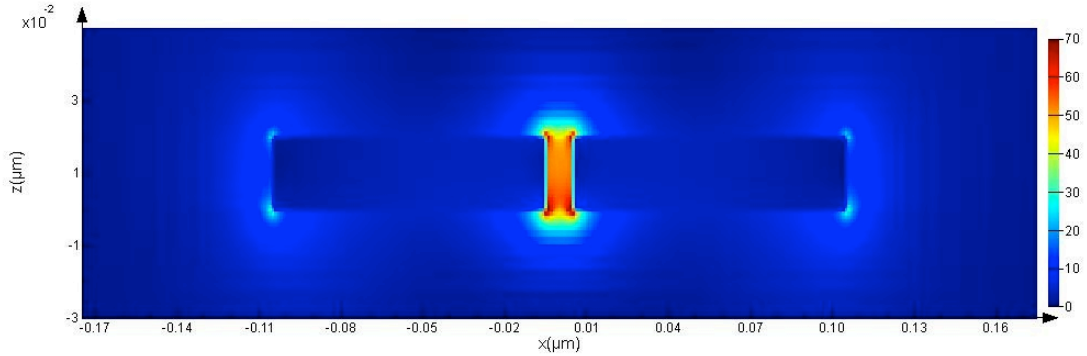
$$E_{1x} = E_x^{inc} + A_{xx} \cdot \alpha \cdot E_{2x}$$
$$E_{2x} = E_x^{inc} + A_{xx} \cdot \alpha \cdot E_{1x}$$
$$A_{xx} = \frac{e^{iky}(-1+iky+k^2y^2)}{y^3}$$

The dipoles counteract → **RESONANCE BLUE-SHIFTS**



Near-field interaction

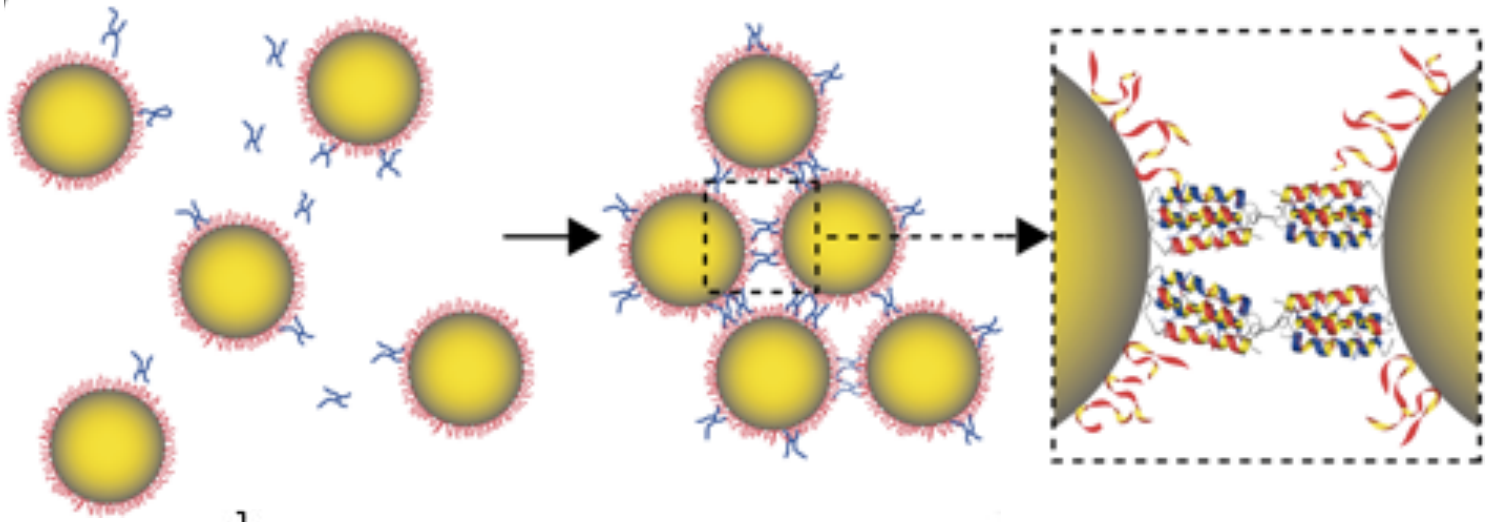
Amplification and confinement of electromagnetic fields

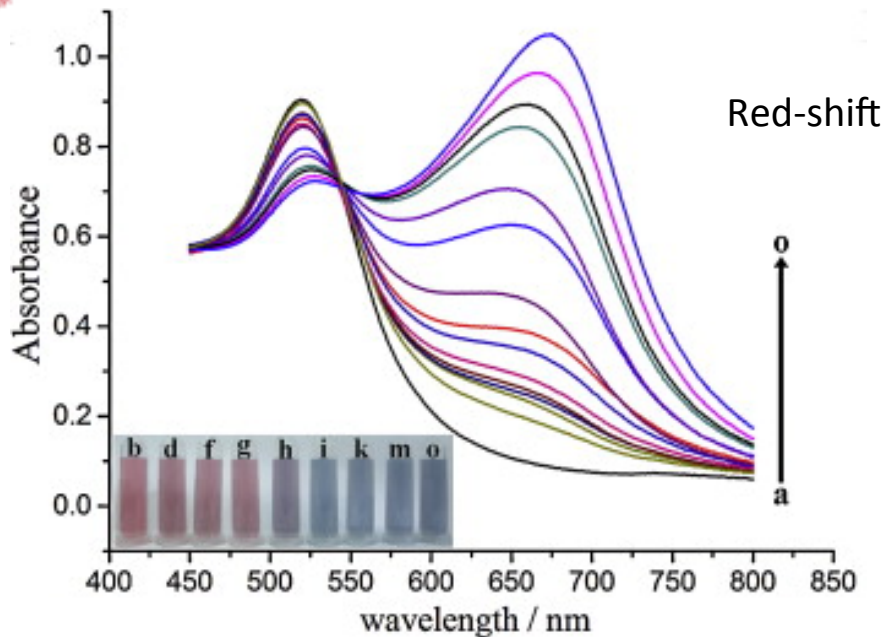


- ✓ **Colorimetric aggregation biosensing assays**
- ✓ **Sensitivity enhancement refractometric sensing**
- ✓ **Amplification of Raman Scattering (SERS)**
- ✓ **Amplification of fluorescence (SEF)**

Biosensing application
Near Field interaction

Colorimetric aggregation assays





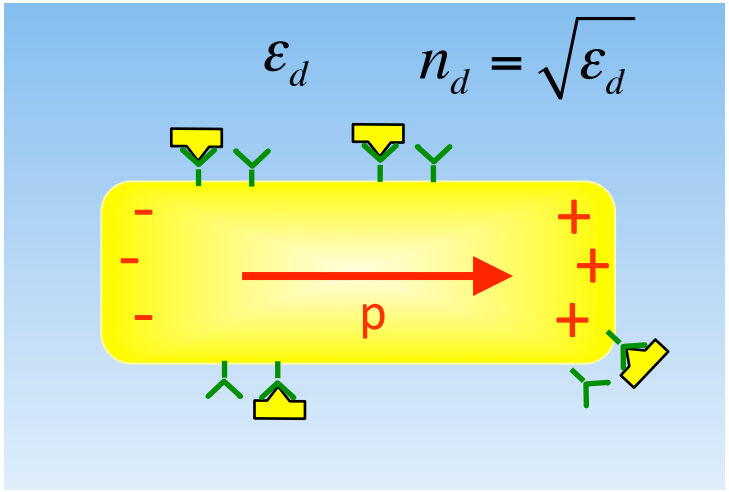
Red-shift + peak broadening

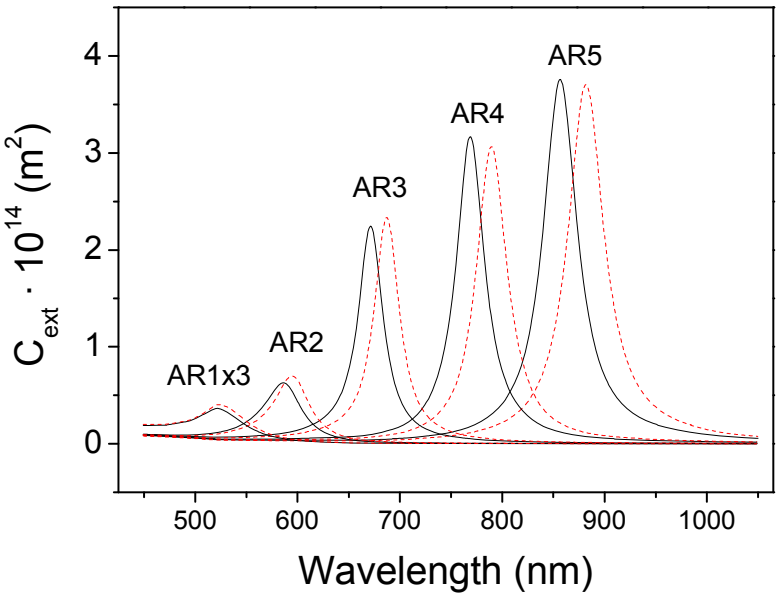
Colorimetric change visible with the naked eye

External refractive index dependence

$$p \propto \frac{\varepsilon_m - \varepsilon_d}{(1-L_1)\varepsilon_d + L_1\varepsilon_m} E_0$$

High sensitivity to refractive index (dielectric constant) changes



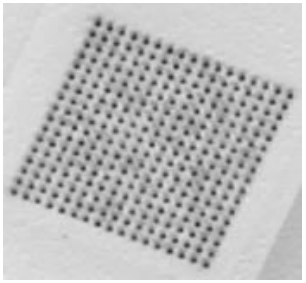
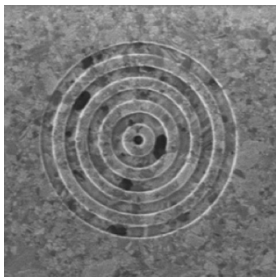
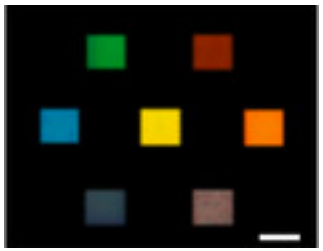


$$\mathrm{Re}[\varepsilon_m] = -\frac{L_i}{1-L_i}\varepsilon_d$$

Refractometric nanoplasmonic sensors -> Detection region ≈ 30 – 50 nm

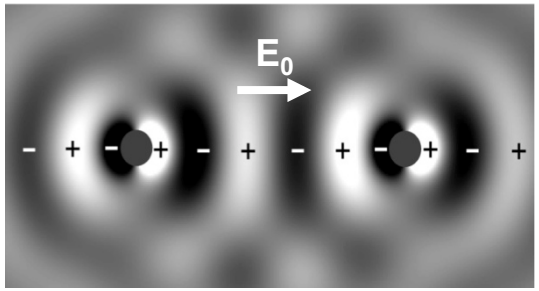
Other plasmonic nanostructures

Nanoholes in thick metal films (t > 100 nm): extraordinary transmission

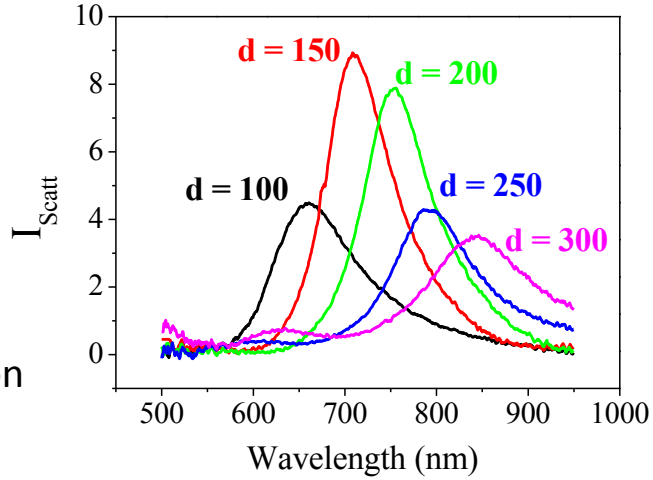




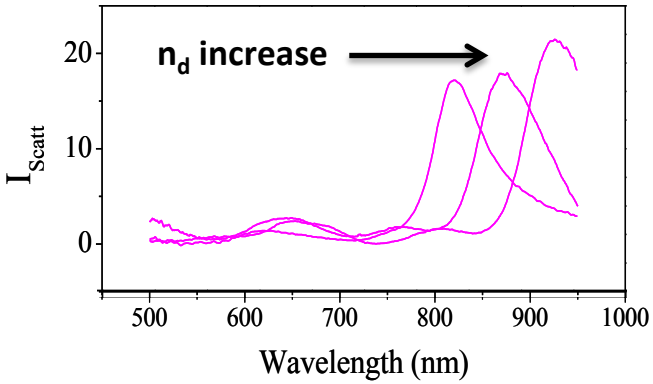
Combination of diffraction and surface plasmon excitation, plus electromagnetic tunnelling through the nanoholes

Nanoholes in thin metal films (t < 40 nm):



LSPR in the holes and interaction between surface plasmons

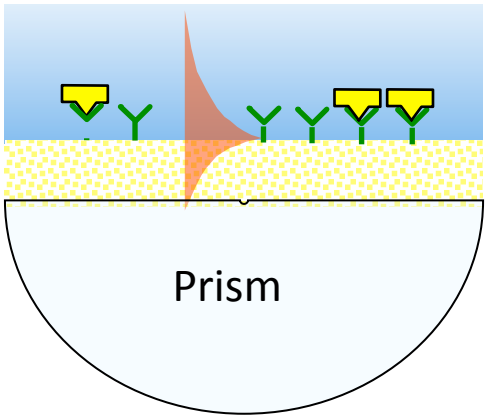




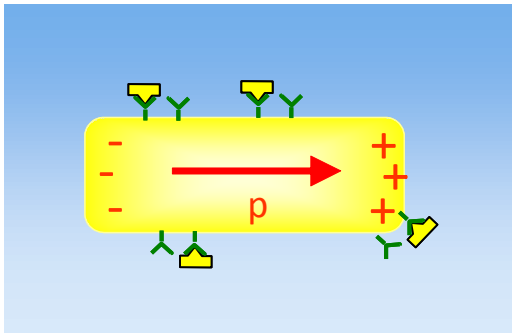
Resonances are also highly dependent on the external refractive index

Nature **391**, 667-669 (1997) *Nature Physics* **3**, 884 - 889 (2007) Optics Express 17(3): 2015-2023 (2009)

Propagating vs LSPR Refractometric Biosensing



- Simple
- Reliable
- Well-known immobilization techniques based on thiols
- Coupler required ($\lambda_{spp} < \lambda_0$)
- Bulky
- Minimum size of sensing area restricted by SP propagation (100x100µm)
- Penetration depth 200-500 nm
- Limited sensitivity
  not enough for direct detection of low molecular weight molecules



- Fabricated in self assembled processes in large scale
- Do NOT require coupler
- Penetration depth 30-50 nm
- Minimum sensing area given by particle size (50-100 nm)
- Huge multiplexing capabilities
- Sensitivity is in the same order of magnitude

Basic steps to fabricate and use a nanoplasmonic sensor

- What is a biosensor? Different types of biosensors
- **Optical biosensors** vs **Nano-optical biosensors** -> **Nanoplasmonic** biosensors
- Introduction to nanoplasmonics (refractive index and near field effects)
- **Main steps to develop a plasmonic biosensor**
  - **Nanofabrication of plasmonic nanostructures**
  - **Biofunctionalization**
  - **Microfluidic integration**
  - **Detection system**
- Examples of nanoplasmonic biosensing applications
  - Aggregation colorimetric assays
  - Refractometric sensing
- New and additional functionalities of plasmonic nanostructures
- Conclusions

Nanofabrication

Nanoplasmonic material

Selection of the plasmonic material for biosensing

- ✓ Real part of the dielectric constant is negative
- ✓ Small imaginary part of the dielectric constant -> Low absorption
- ✓ Chemical stability in liquid, especially in water
- ✓ Easy to functionalize

Silver: very low optical absorption, very good plasmonic properties, poor stability

Gold: low optical absorption, high chemical stability, functionalization via thiols

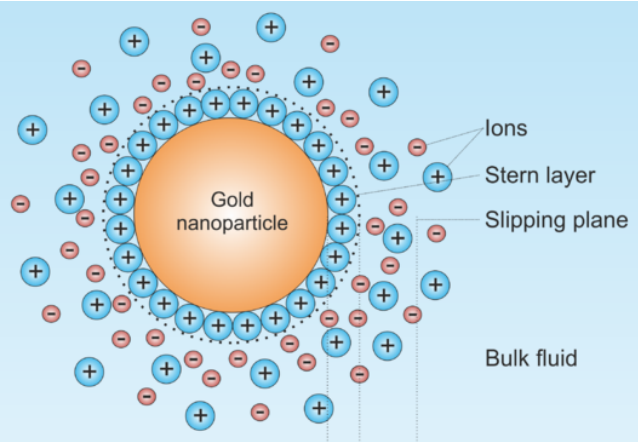
Copper, **Aluminum**: poor chemical stability

Nanofabrication

Bottom-Up: Chemical synthesis

Simplest method, not necessary expensive equipment

Reduction of chloroauric acid ($H[AuCl_4]$) solution (via p.e. sodium citrate)



Au^{3+} -> Au -> precipitation into nanoparticles

Stabilization of nanoparticles by repulsive surface charges or by stabilizing agents (surfactants)

- Colloidal structures for colorimetric aggregation assays, labels…
- Attachment (chemical, electrostatic) to a surface for refractometric sensing, SERS…

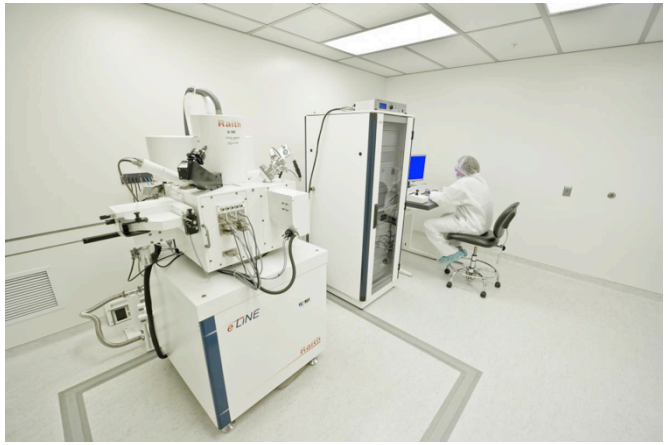
M.C Daniel and D. Astruc, Chem. Rev. 104, 293 (2004)
M.R Jones et al., Chem. Rev. 111, 3736 (2009)

Nanofabrication

Top-down

Plasmonic nanostructures 50-250 nm range -> Not accessible with Photolithography

Electron beam lithography



Focused ion beam

✓ **Very precise**

Very expensive
Slow
Limited to small areas
Low throughput

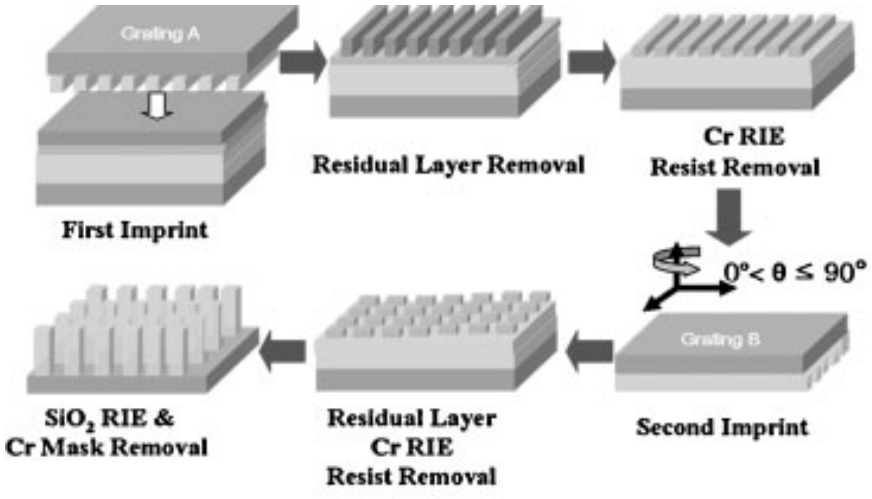
Not useful for biosensing

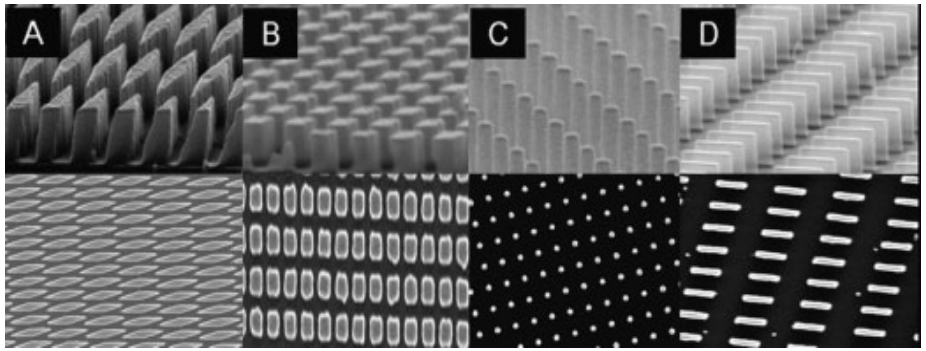
Nanofabrication

Top-down

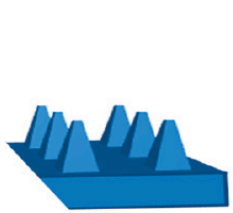
Nanoimprint lithography

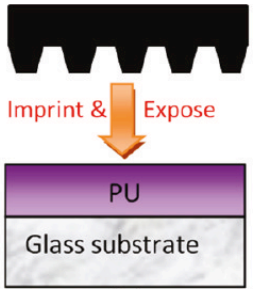
Hard masters

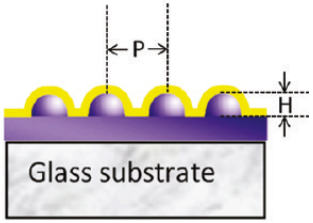


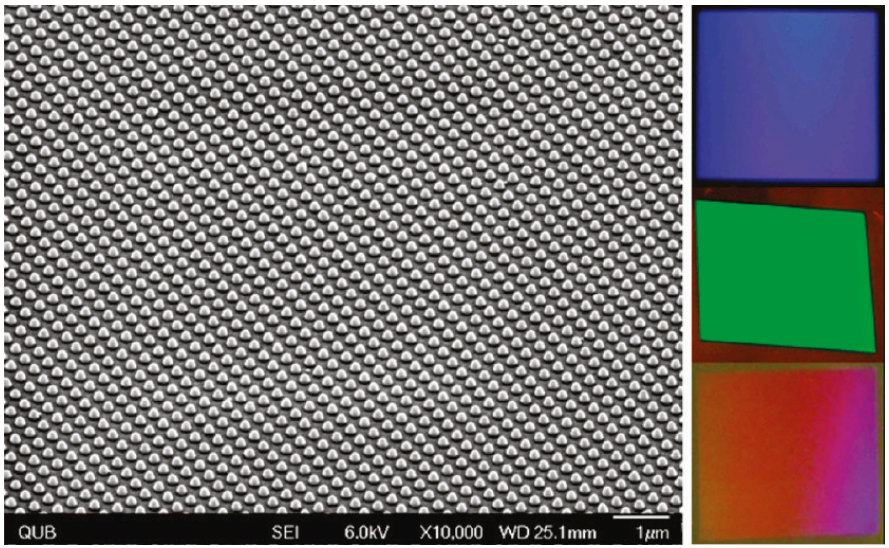


Soft molds







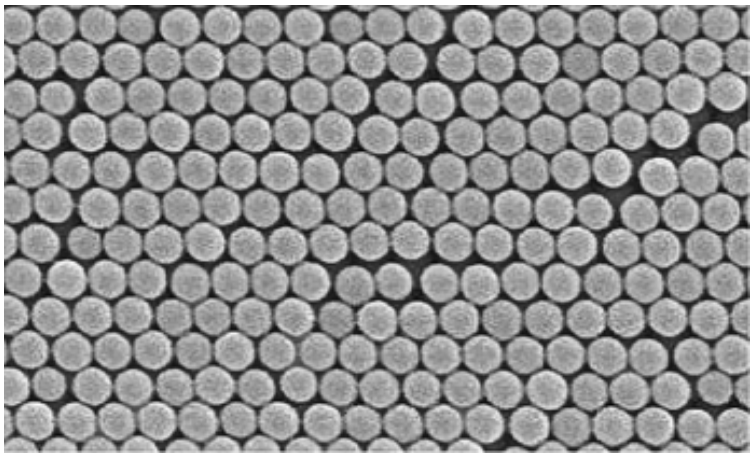


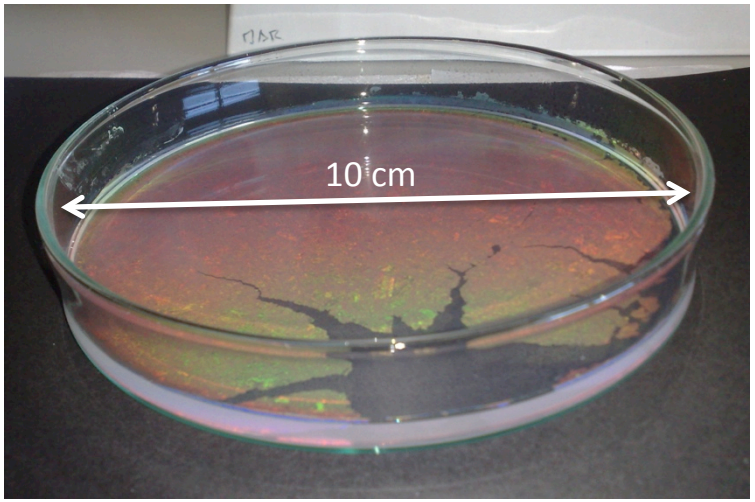
Drawback: a expensive nanopatterning tool is still needed for the hard mask

Nanofabrication

Top-down

Colloidal lithography

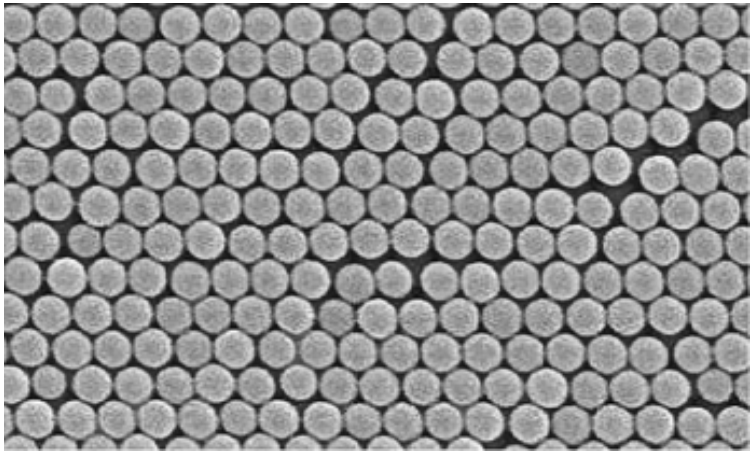




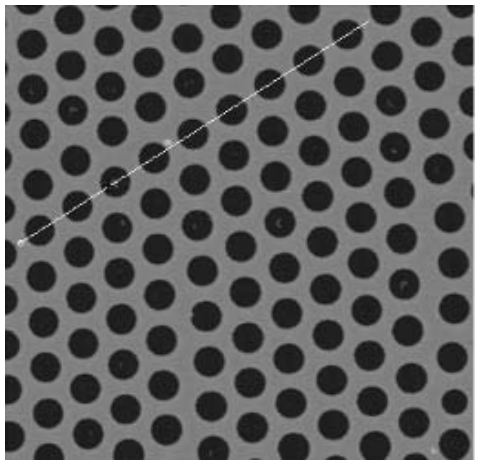
Nanofabrication

Top-down

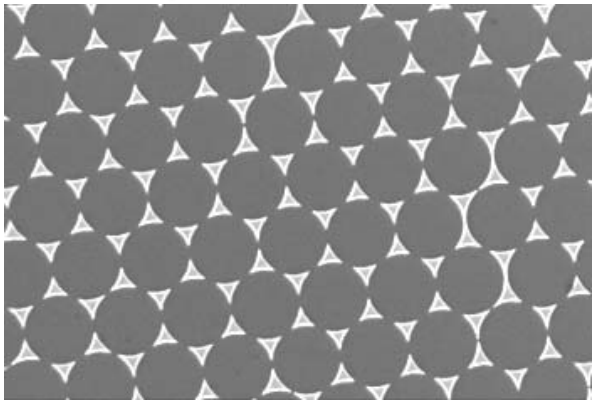
Colloidal lithography



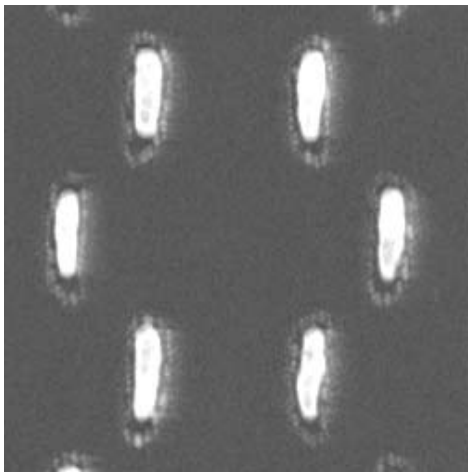
O2 RIE shrinking
Metal evaporation



Metal evaporation



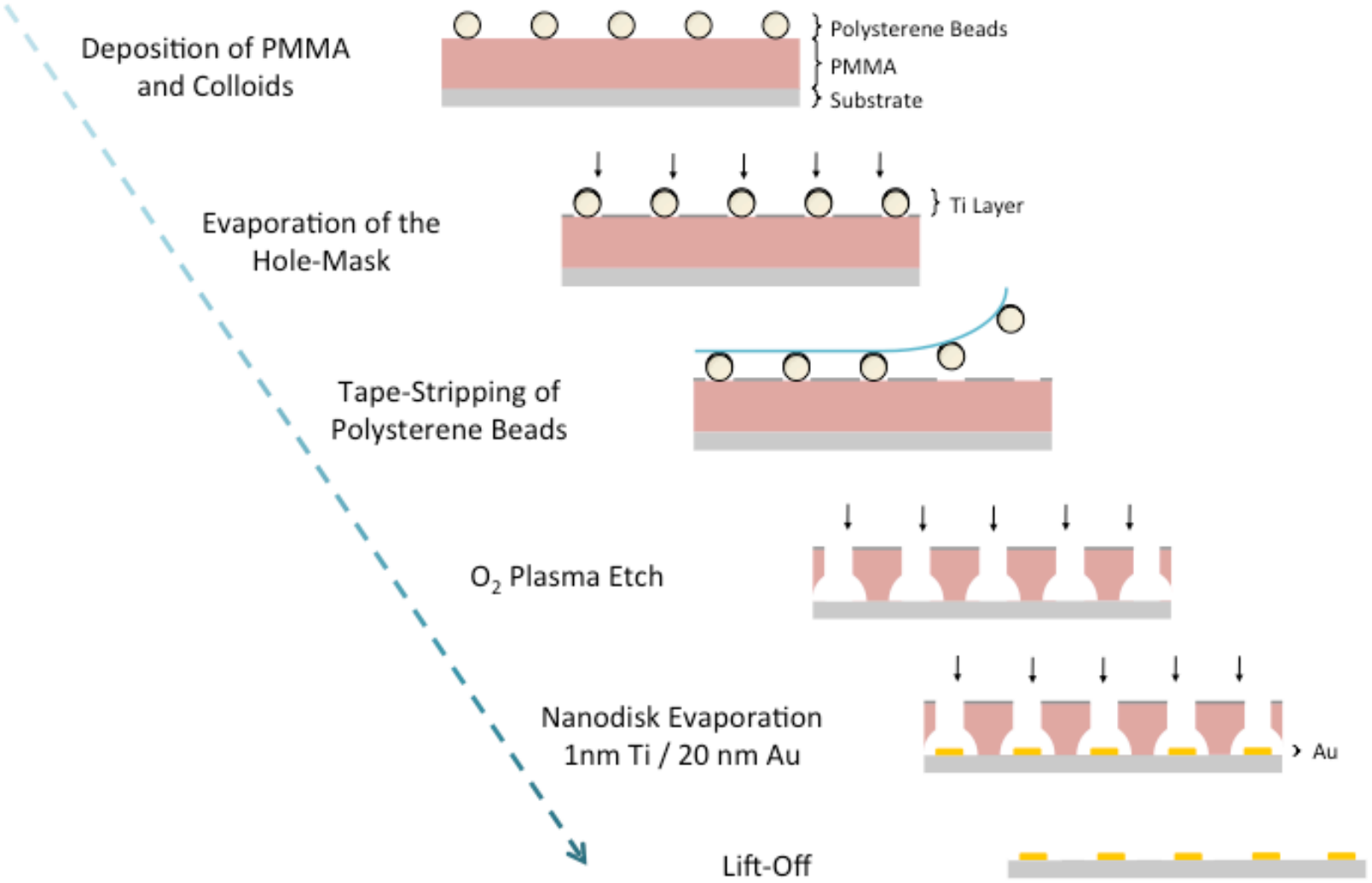
Melting and metal evaporation at an angle



Nanofabrication

Top-down

Hole-mask colloidal lithography

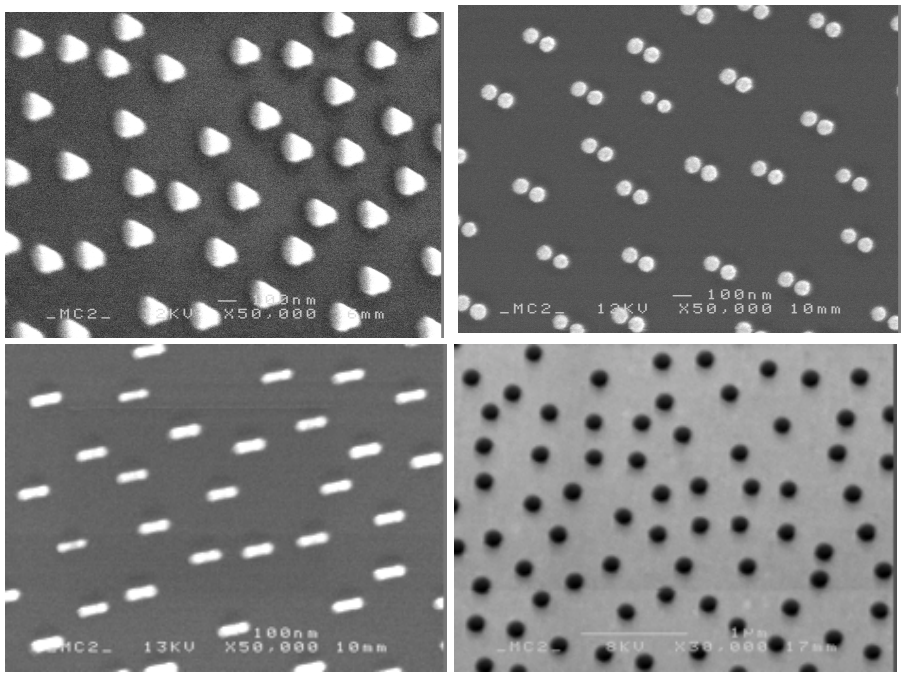


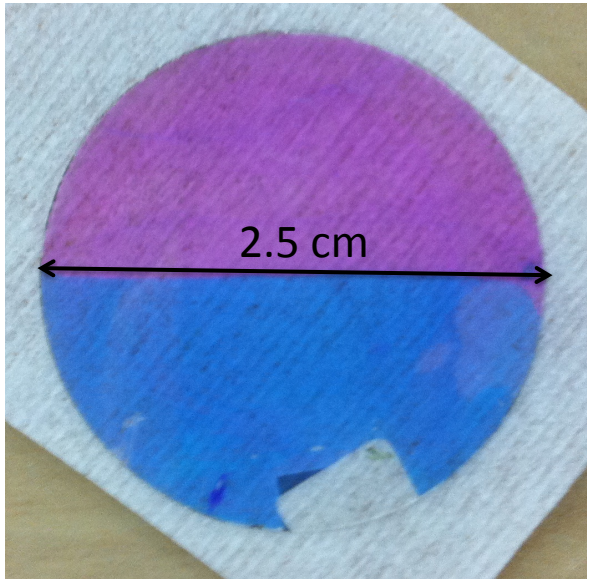
* H. Fredriksson et al., Adv. Mat. **2007**, 19, 4297

Nanofabrication

Top-down

Hole-mask colloidal lithography



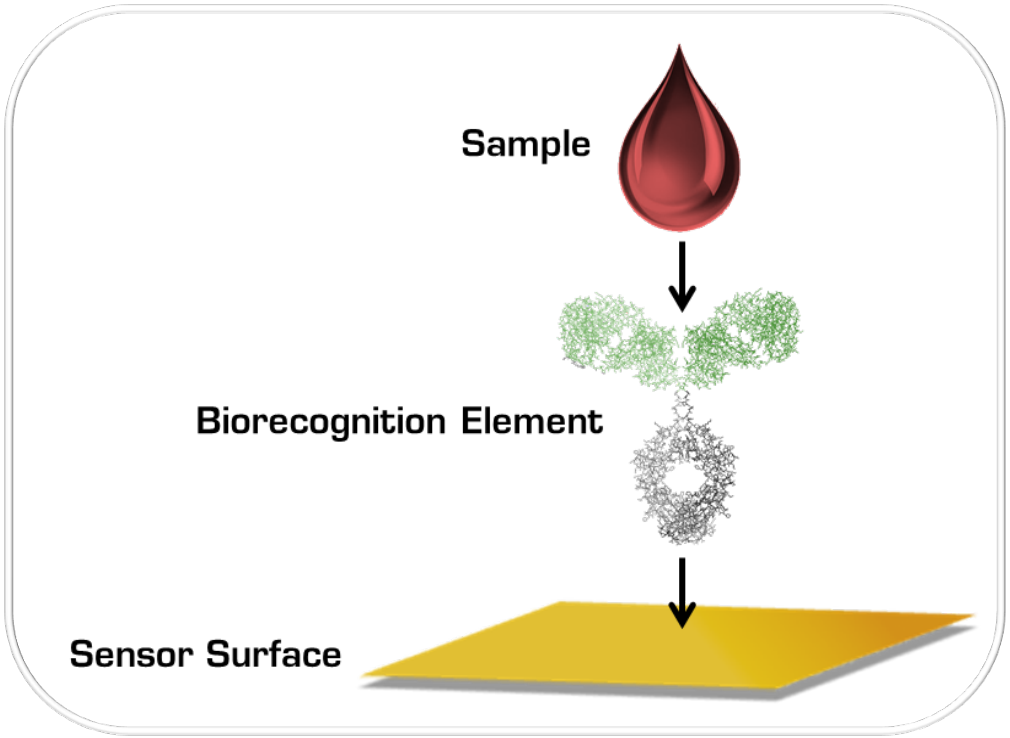


* H. Fredriksson et al., Adv. Mat. **2007**, 19, 4297

Biofunctionalization

General properties

Direct Detection



Main Goals

High Sensitivity

Oriented receptor immobilization

Stability

Minimization of receptor modification

Reproducibility

Efficient biosurface regeneration

Selectivity

Reduction of non-specific binding

Most common bioreceptors

- ❑ DNA (single strand, aptamers)
- ❑ Proteins (antibodies, enzymes…)

Biofunctionalization

DNA immobilization

DNA receptors -> Detection of DNA and RNA strands

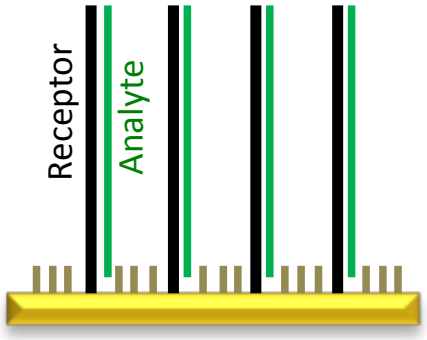
-> Detection of proteins or other molecules via aptamers

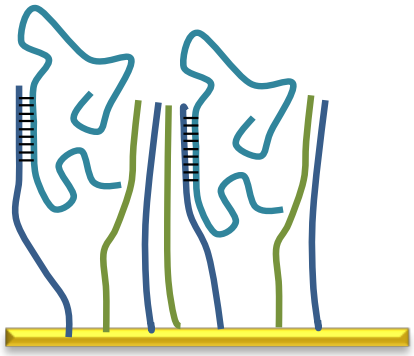
Receptor: single strand of nucleotides (A, C, T, G) complementary to the target DNA or RNA

Detection: hybridization (double-helix) (A/T, C/G)

Synthetic DNA with functional groups for attachment to the surface

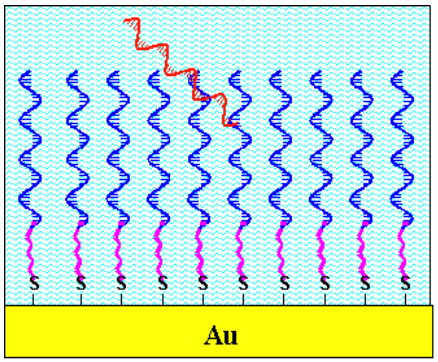
Gold -> thiolated (-SH) single-stranded DNA (high affinity Au <-> SH)





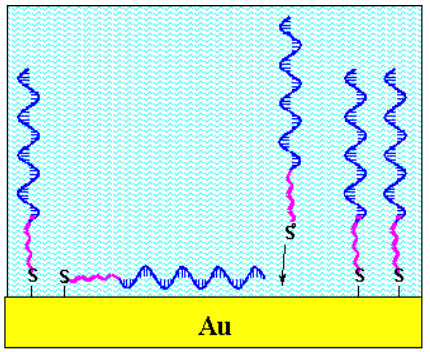
Importance of the DNA coverage on the surface

HIGH COVERAGE



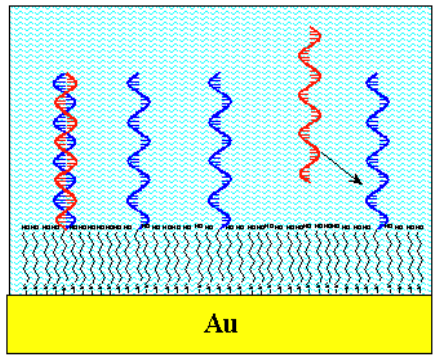
Steric hindrance

LOW COVERAGE



Non-specific adsorption

OPTIMUM COVERAGE

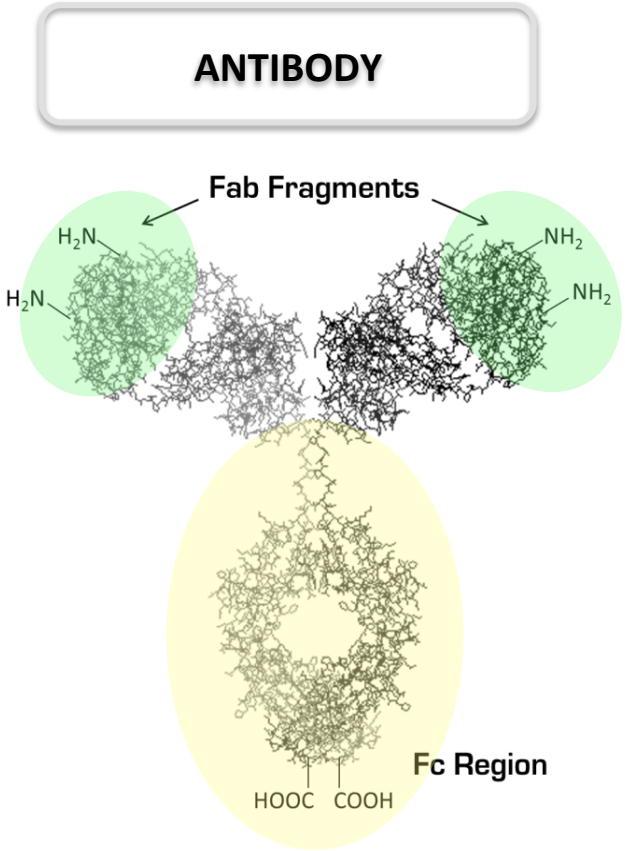


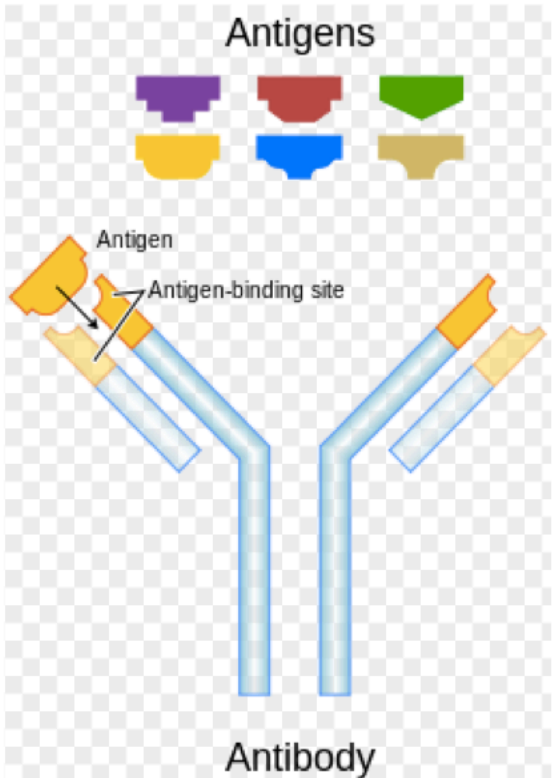
Lateral and vertical spacers to improve access of the analyte and prevent non specific adsorption

Biofunctionalization

Proteins (antibodies) immobilization

Proteins (chains of amino acids) cannot be chemically synthesized
-> chemical modification of the protein / use their chemical groups

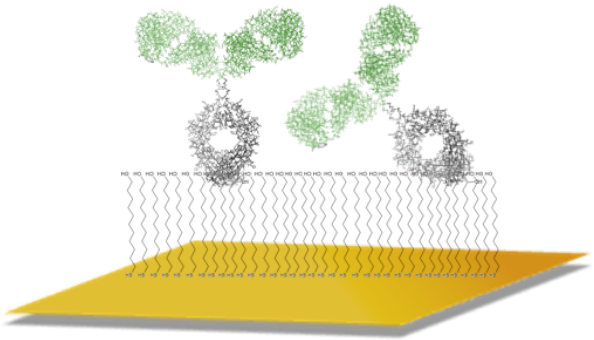




Biofunctionalization

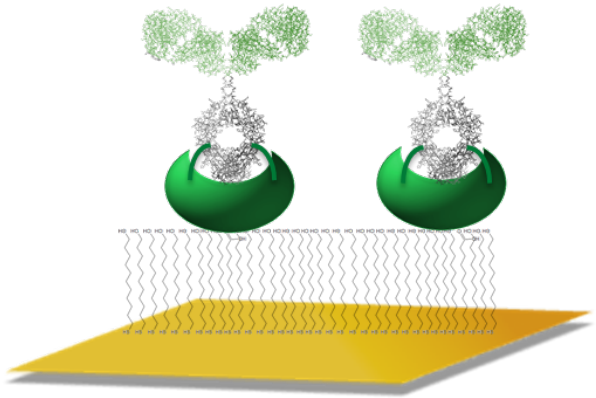
Proteins (antibodies) immobilization

Covalent Strategy
amine groups of proteins



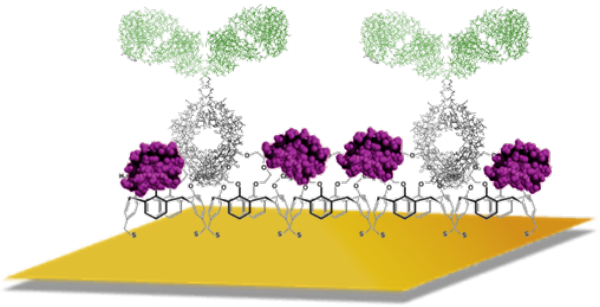
1) Alkanethiol SAM (SH-CH_2…-COOH)
2) Activation with EDC/NHS
3) Antibody covalent binding via NH_2 groups

Protein G Strategy



1) Alkanethiol SAM (SH-ROH:SH-RCO_2H)
2) Protein G covalent binding
3) Antibody (Fc region) affinity capture
4) Crosslinking ProteinG-mAb (BS^3)

Prolinker Strategy

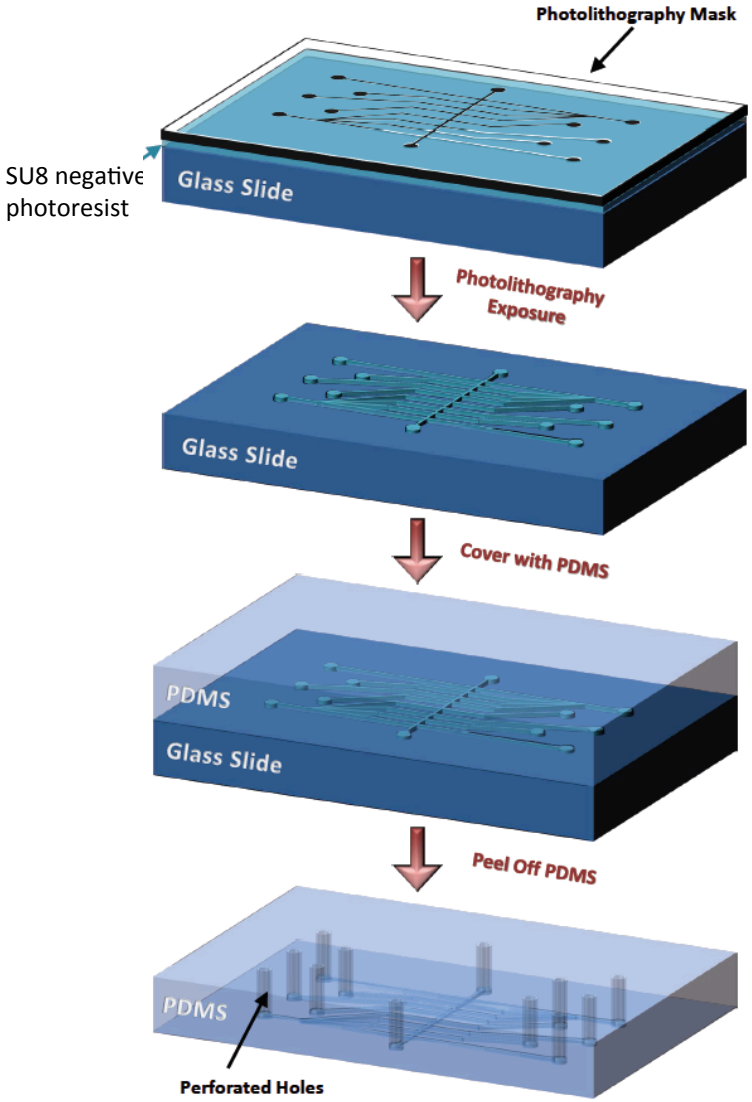


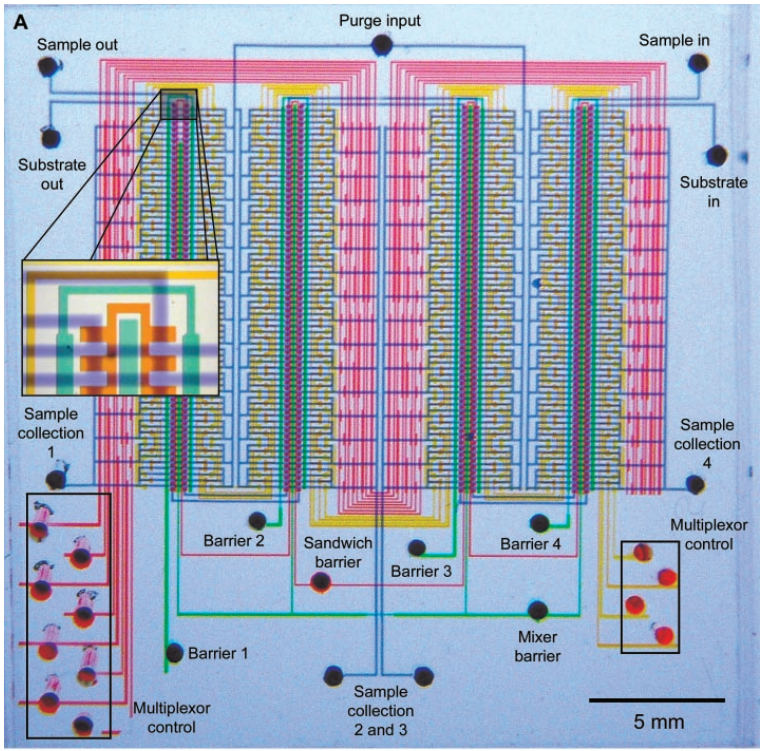
1) Prolinker™
2) Antibody affinity capture
3) BSA blocking

	Covalent	Protein G	Prolinker
Controlled Antibody Orientation	Low	High	High
Antibody Modification	High	Medium	Low
Efficiency on Biosurface Regeneration	High	High	Very High

Microfluidics Integration

Soft lithography fabrication



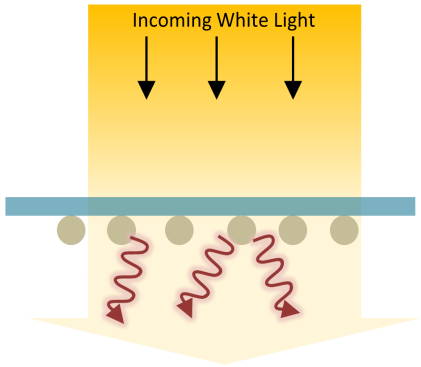


Science **298**, 580 (2002)

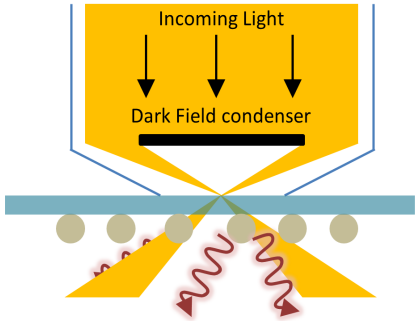
→ Reversible or irreversible binding to the transducer surface

Illumination & Detection

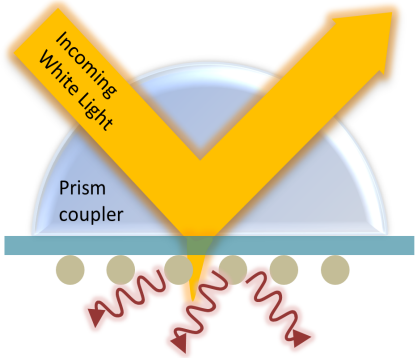
A Extinction Measurement



B Dark Field Microscopy

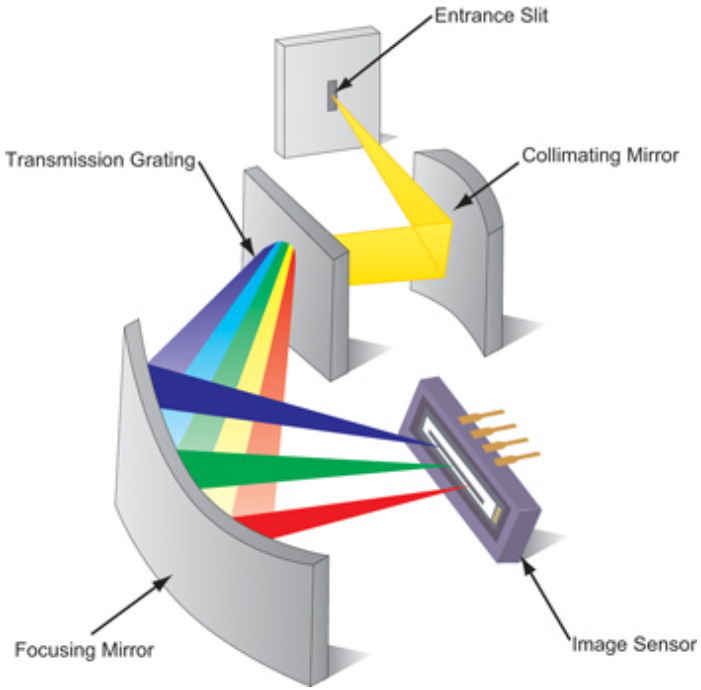


C TIR Microscopy

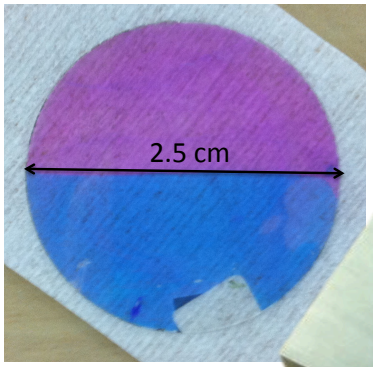


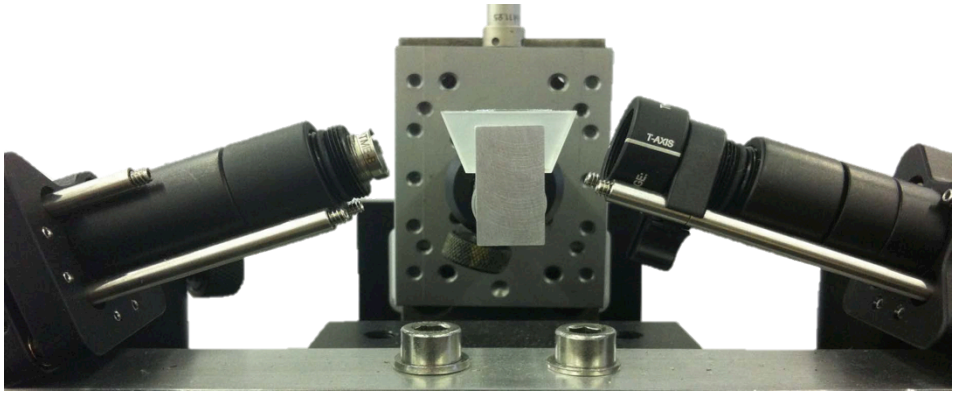
Spectrometer

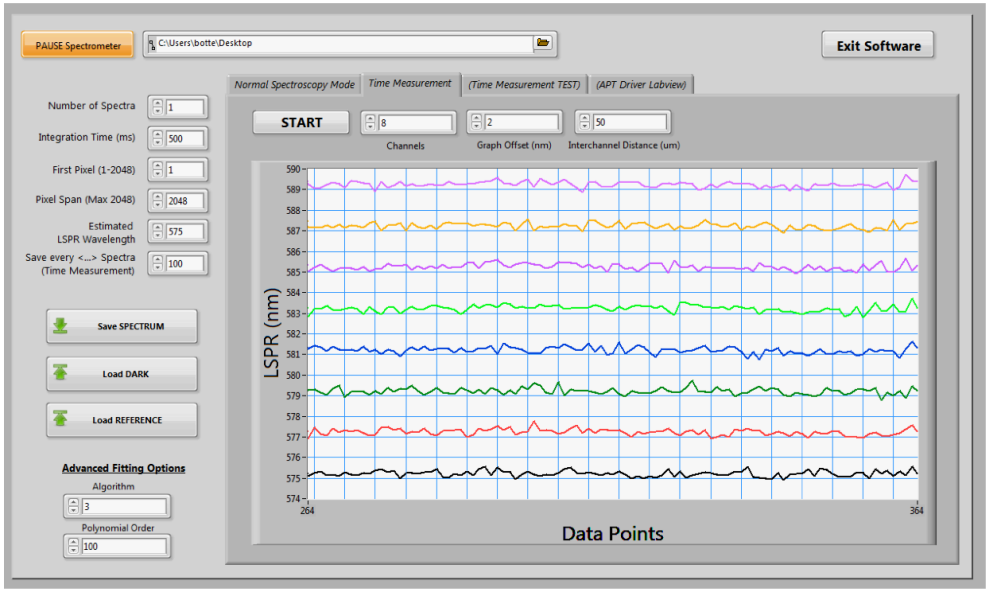
Microscope objective



Multiplexed biosensor device







Biosensing Applications

- What is a biosensor? Different types of biosensors
- **Optical biosensors** vs **Nano-optical biosensors** -> **Nanoplasmonic** biosensors
- Introduction to nanoplasmonics (refractive index and near field effects)
- Main steps to develop a plasmonic biosensor
  - Nanofabrication of plasmonic nanostructures
  - Biofunctionalization
  - Microfluidic integration
  - Detection system
- **Examples of nanoplasmonic biosensing applications**
  - **Aggregation colorimetric assays**
  - **Refractometric sensing**
- **New and additional functionalities of plasmonic nanostructures**
- Conclusions

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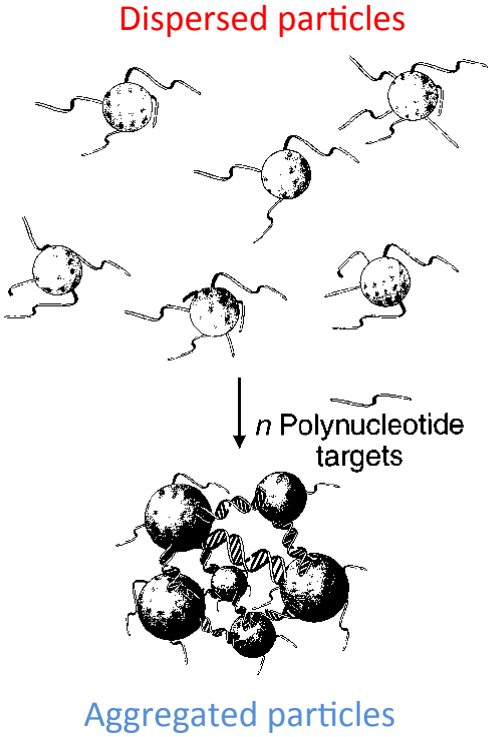
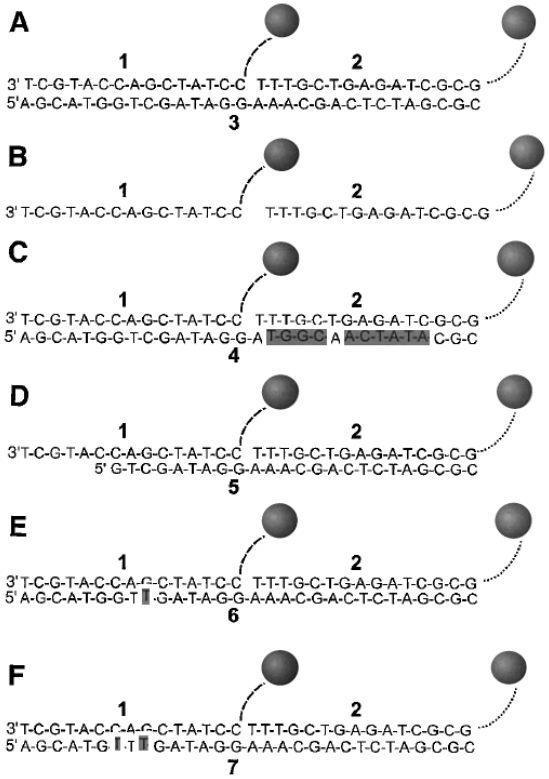
Colorimetric aggregation assays

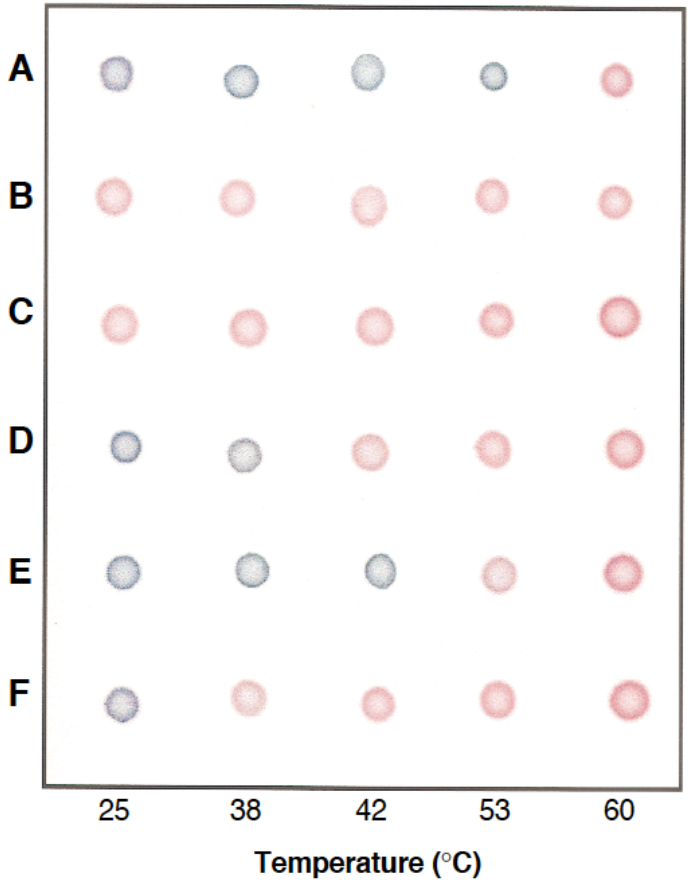
Biosensing Examples

Colorimetric aggregation assays

Detection of DNA targets







DNA functionalized nanoparticles are very stable due to the high negative charge of DNA

Robert Elghanian et al., Science 277, 1078 (1997)

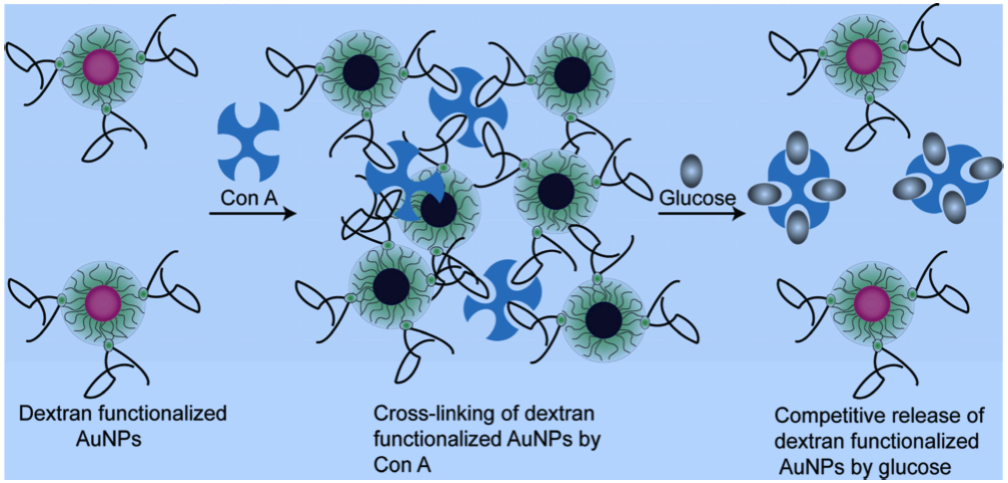
Colorimetric aggregation assays

Protein detection

Functionalization of colloidal particles with proteins (e.g. antibodies) is much more complex
(proteins have different isoelectric point and differen hidrophilicity)

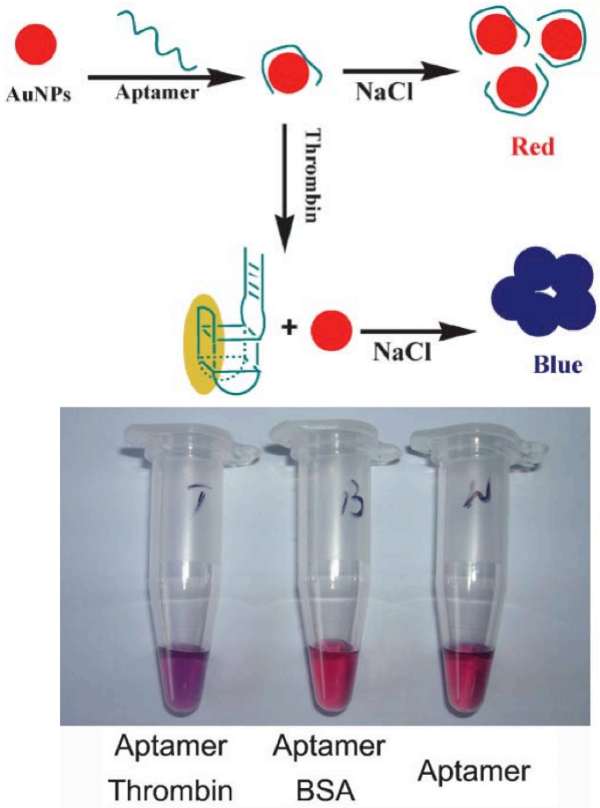
➡ There is not universal strategy -> every protein is a different world

Detection of Concanavalin A and glucose



K. Aslan et al., Anal. Biochem., 330, 145 (2004)

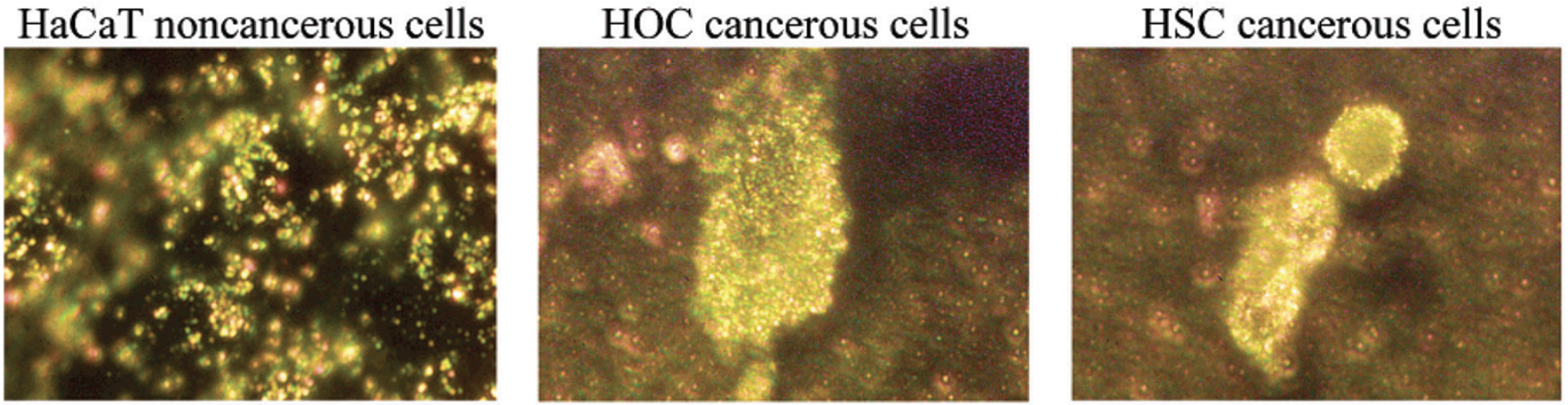
Detection of thrombin



Colloidal Nanoparticles as labels

	Fluorescence molecules / Qdots	Au nanoarticle
Chemical Stability	✗ Photobleaching	✔
Photonic stability	✗ Blinking	✔
Absorption cross section		**Higher**
Background Signal	✔	✗ High

Anti-EGFR functionalized AuNPs -> diagnosis of oral epithelial cancer cells

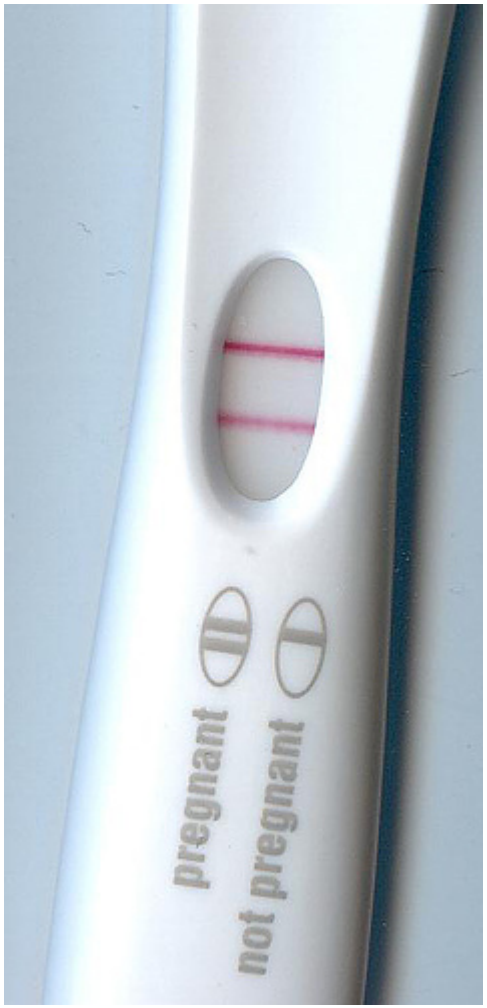


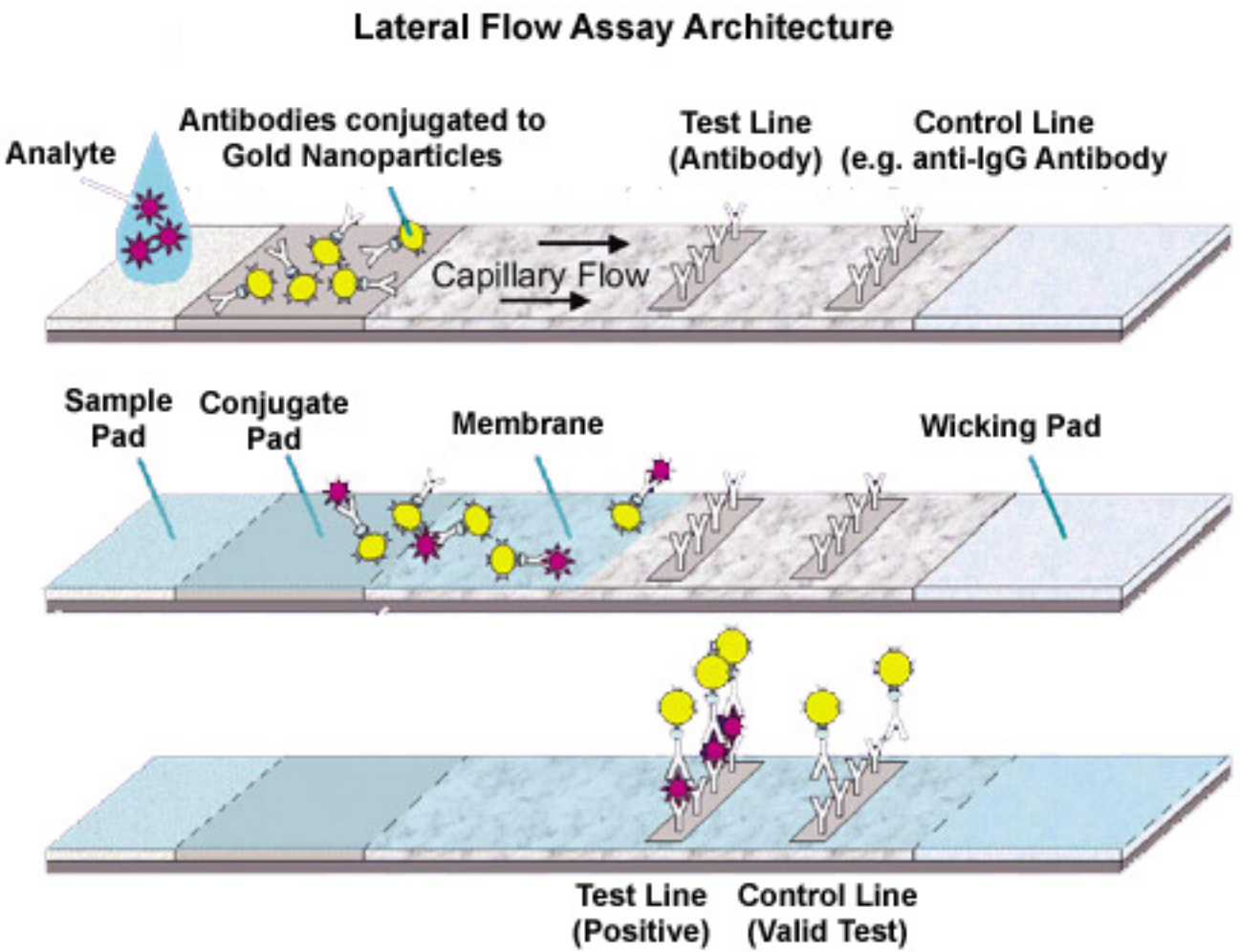
AuNPs bind 600% stronger to oral malignant cells
HOC 313 clone 8 and HSC 3

El-Sayed, et al., Nano Lett. 5, 829 (2005)

Colloidal Nanoparticles as labels

Pregnancy test





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Refractometric sensing

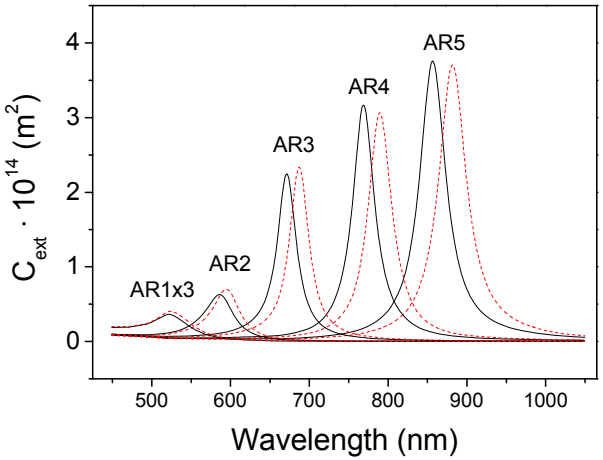
Sensitivity considerations

Biosensing examples

Refractometric assays

Important features to improve sensitivity

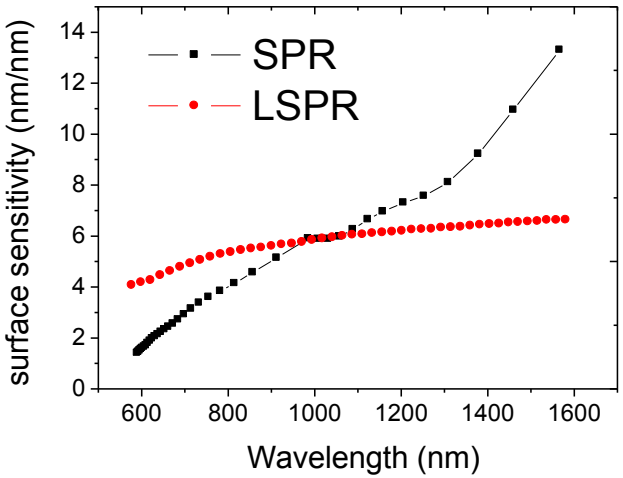
Importance of the resonance wavelength (size and shape of the nanoparticles)

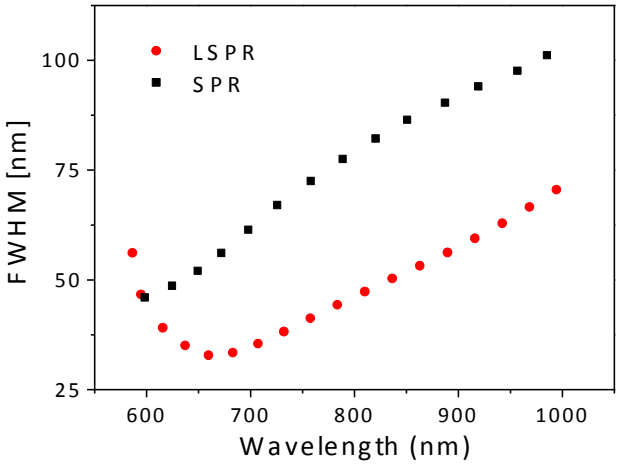


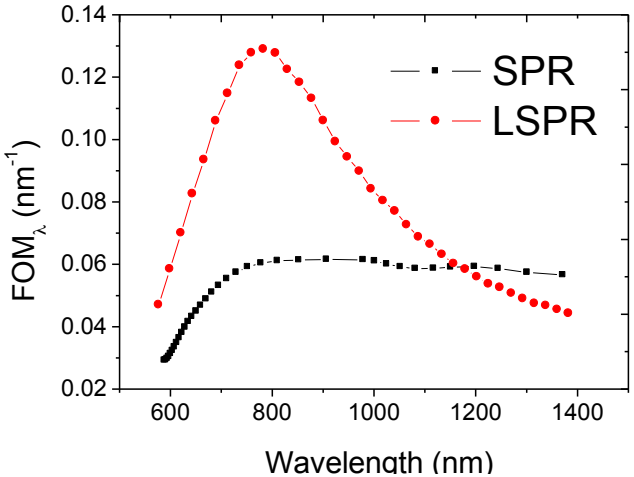
Surface sensitivity $\eta_\lambda = \frac{\partial \lambda_R}{\partial d_{bio}}$

Width of the resonance Full-width-half-maximum (FWHM)

Figure of Merit (FOM) $FOM = \frac{\eta_\lambda}{FWHM}$







M .A. Otte, ACS Nano 4, 349 (2010)

Refractometric assays

Important features to improve sensitivity

Nanostructures attached to a solid substrate

Colloidal nanoparticles – chemical bonding (thiols or EDC/NHS chemistries)

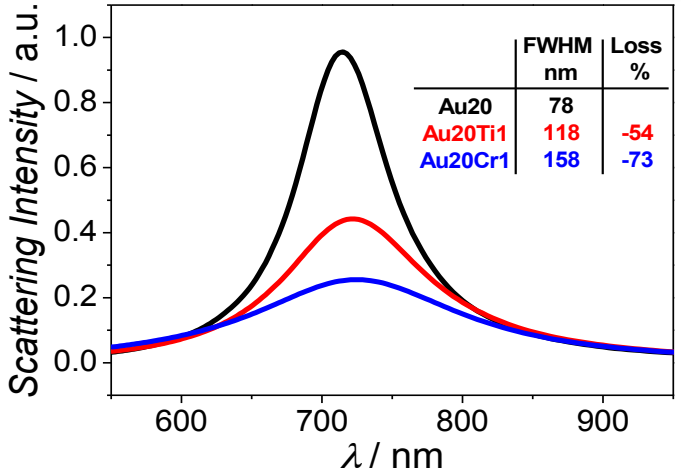
Nanolithography – Adhesion layers (Cr, Ti)

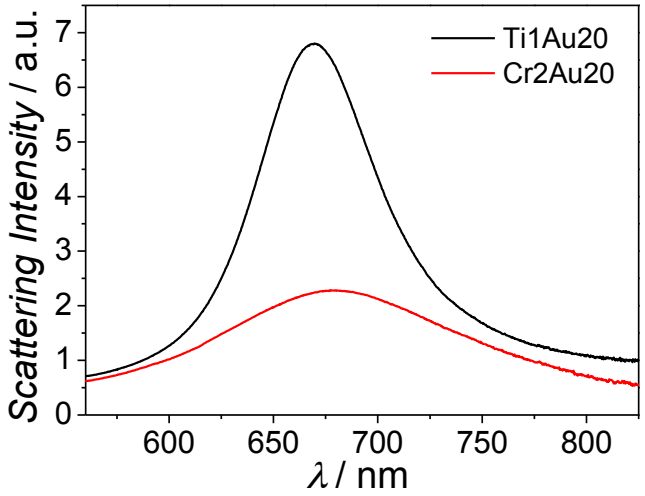
Refractometric assays

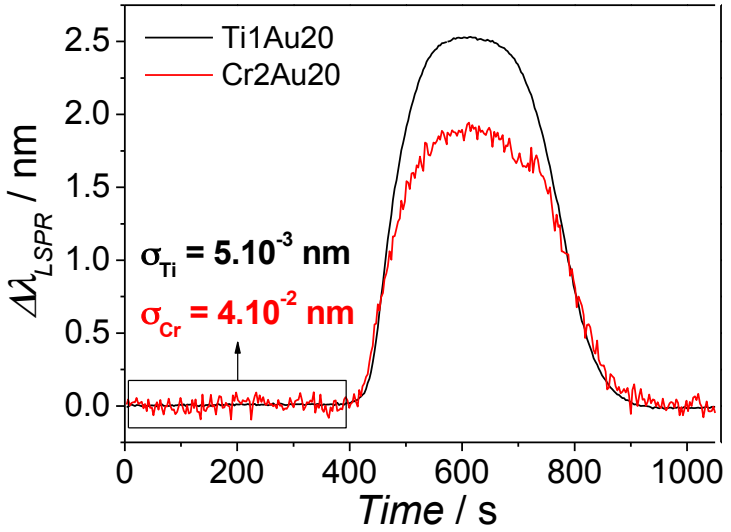
Important features to improve sensitivity – **Substrate effect**

Effect of the adhesion layers on the sensing performance

No adhesion layer
⇒ no mechanical stability







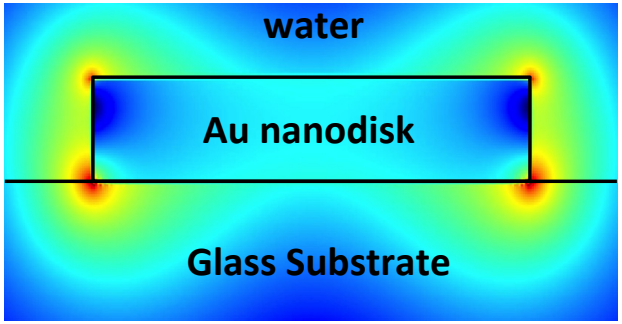
One order of magnitude decrease of the signal-to-noise ratio !!!

M .A. Otte, et al J Phys Chem C 13, 5344 (2011)

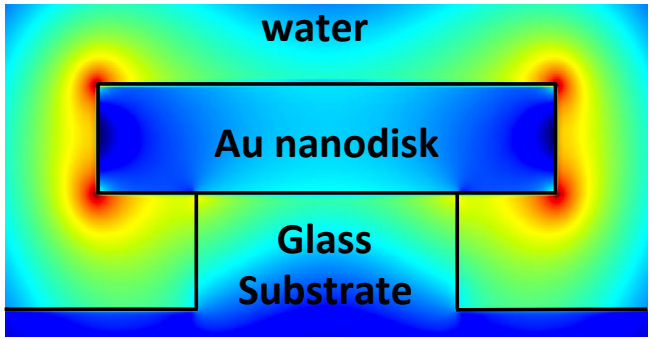
Refractometric assays

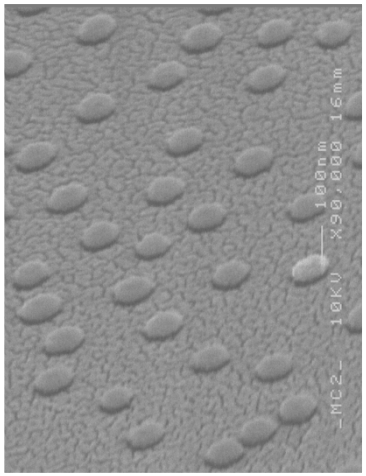
Important features to improve sensitivity – **Substrate effect**

Improving the access of analytes to the hot-spots

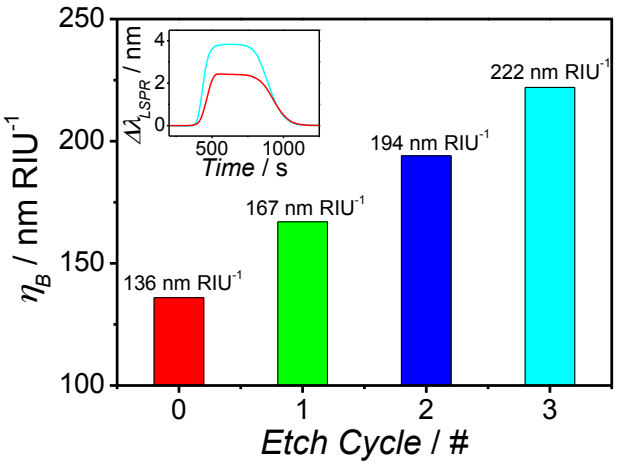


Sensitivity reduction

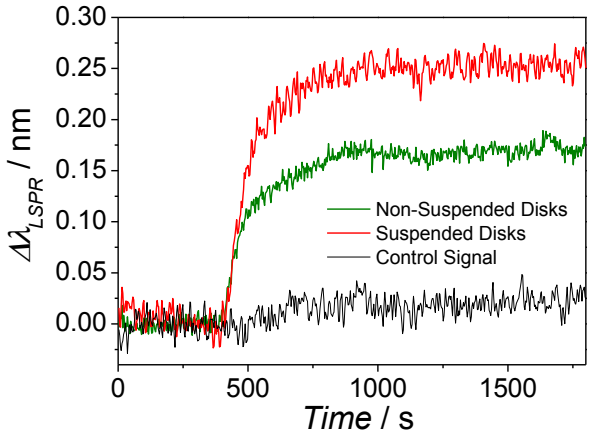




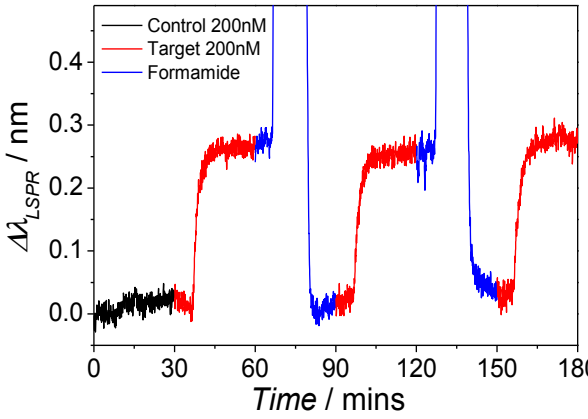
Bulk sensitivity



DNA detection



Surface regeneration

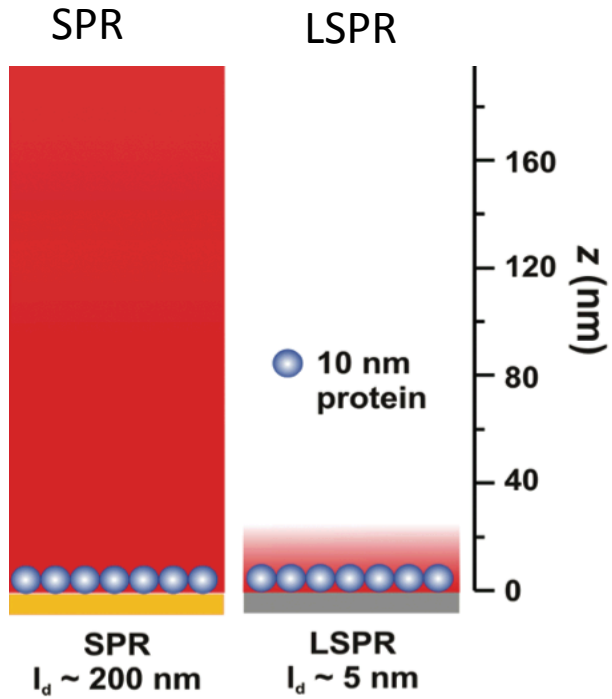


M .A. Otte, et al J Phys Chem C 13, 5344 (2011)

Refractometric assays

Example detection of protein conformational changes

Protein Calmodulin suffers conformational change in the presence of Ca^{2+}



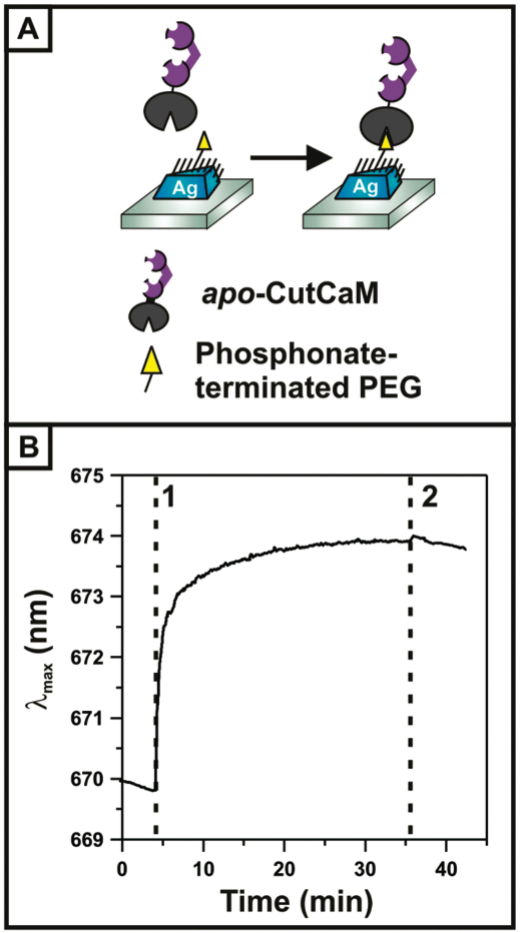
W. Page Hall, Nano Lett. 11, 1098 (2011)

Refractometric assays

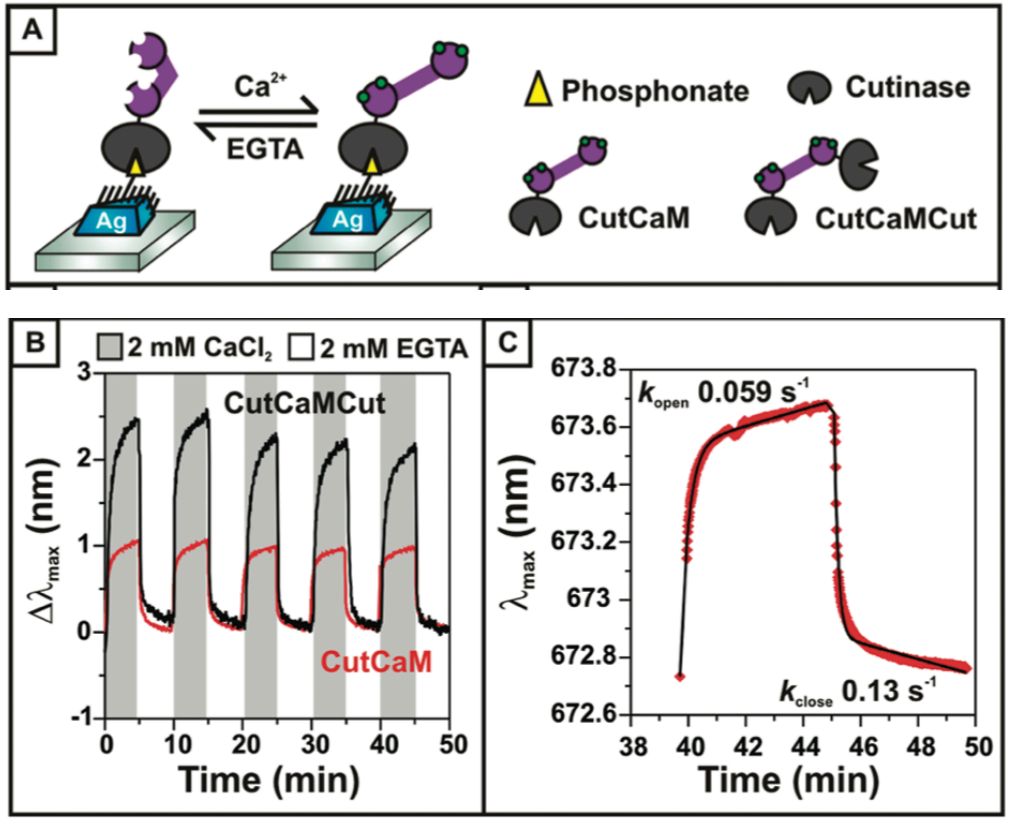
Example detection of protein conformational changes

Protein Calmodulin suffers conformational change in the presence of Ca^{2+}

Immobilization of Calmodulin
via linker protein cutinase



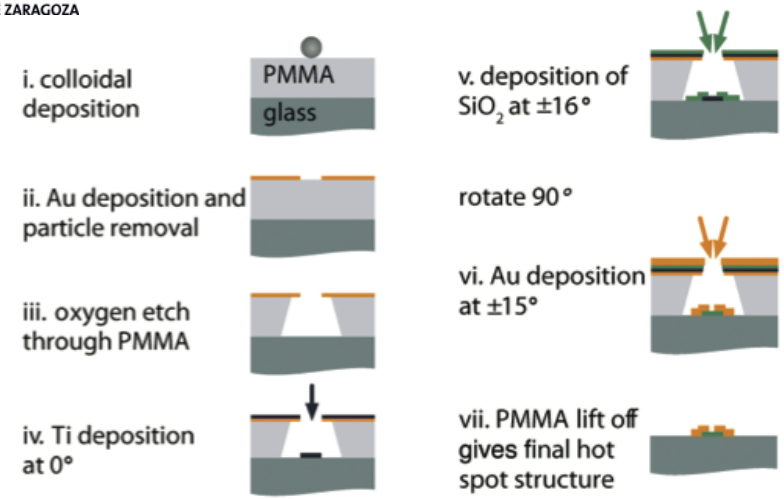
With out Ca^{2+} **folded state**
With Ca^{2+} **elongated state**
Ethylene glycol tetraacetic acid (EGTA) chelates Ca^{2+} -> **folded state**

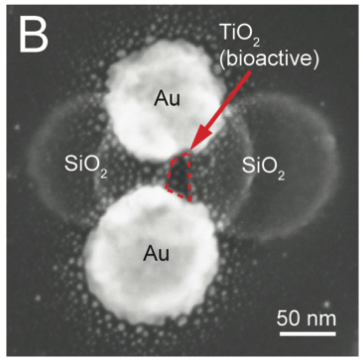


W. Page Hall, Nano Lett. 11, 1098 (2011)

Refractometric assays

Directed functionalization on hot spots

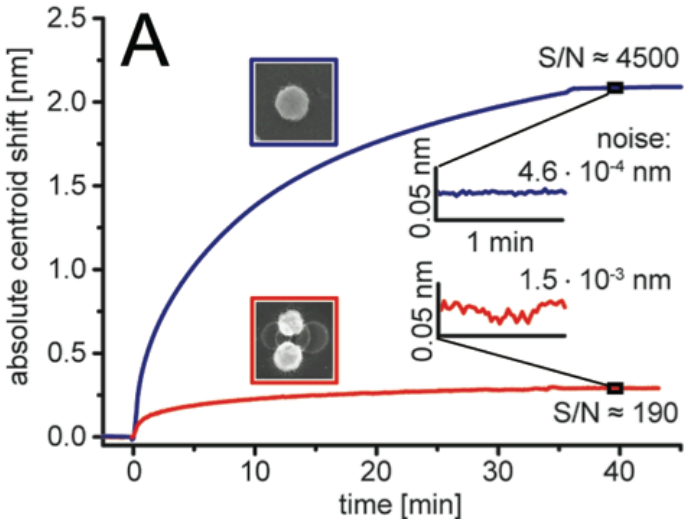


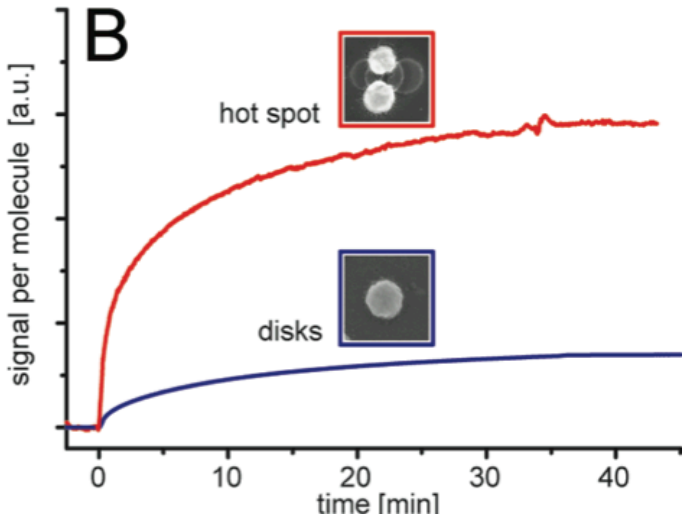


SH-PEG -> Gold

PLL-PEG -> SiO_2 (glass)

ND-PEG-Biotin -> TiO_2





L. Feuz et al., *Nano Lett. 12*, 873 (2012)

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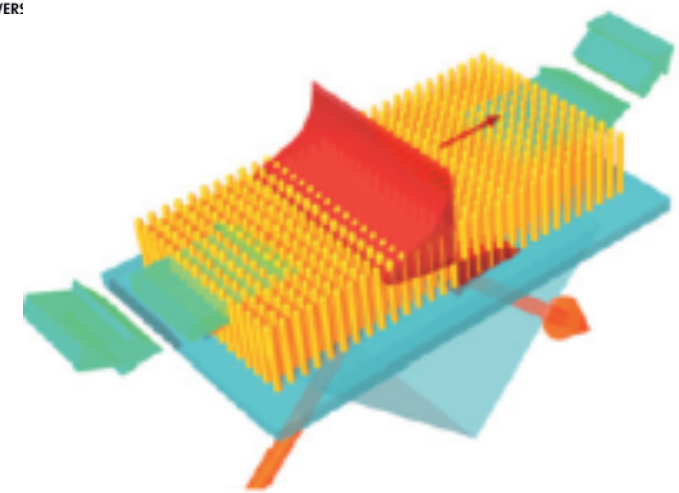
New functionalities

Metamaterials

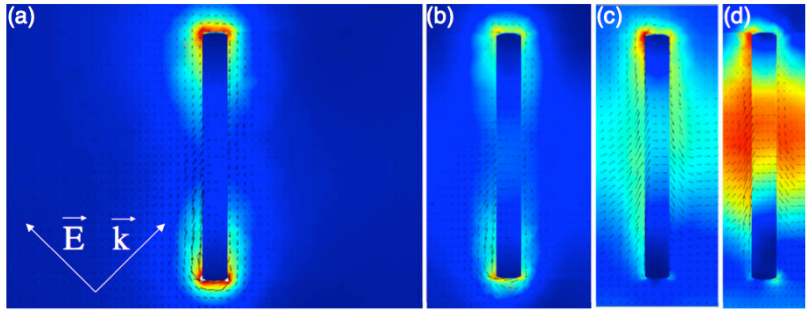
Flow-through sensors

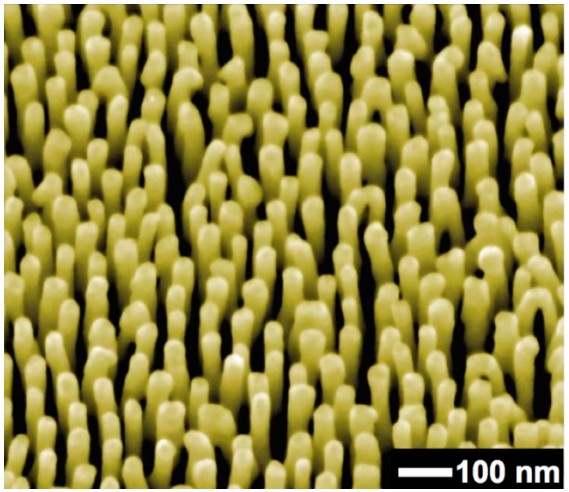
New functionalities

Metamaterials Near-Field interaction



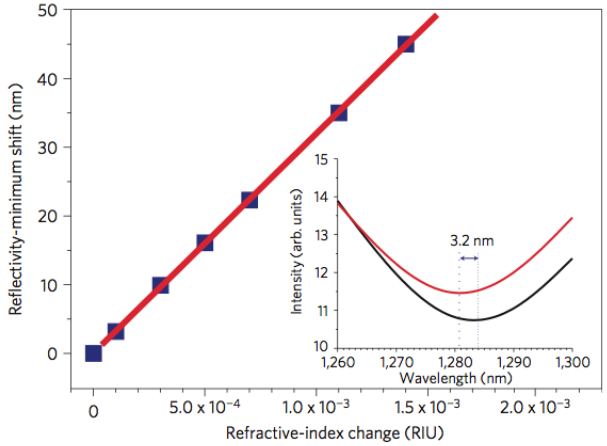
Large near-field interaction between nanopillars



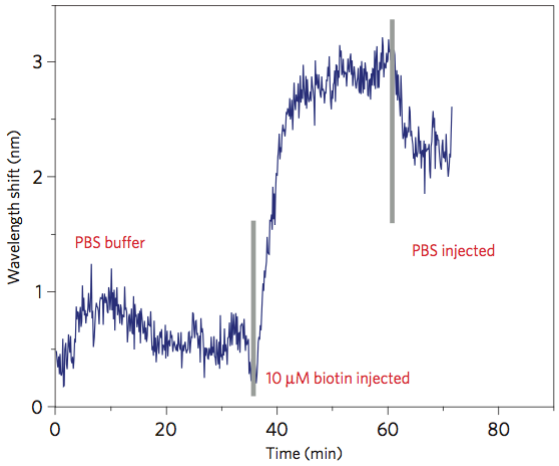


Au nanopillars -> electrolytic deposition on porous alumina substrates

Bulk refractometric sensitivity



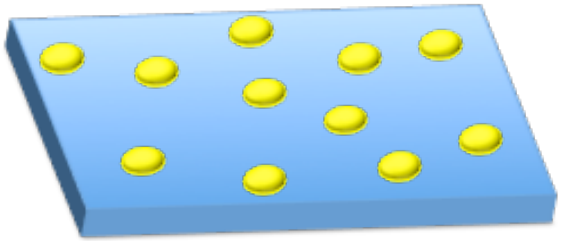
Biotin detection



A.V. Kabashin et al, Nat. Mater. 8, 867 (2009)

New functionalities

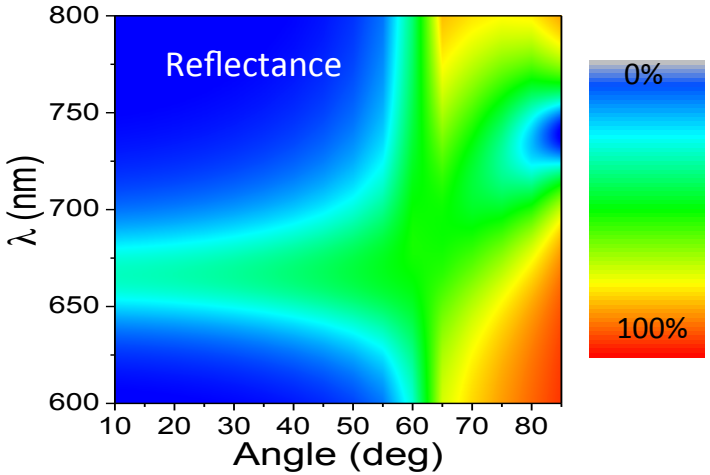
Metamaterials (Far field interaction)

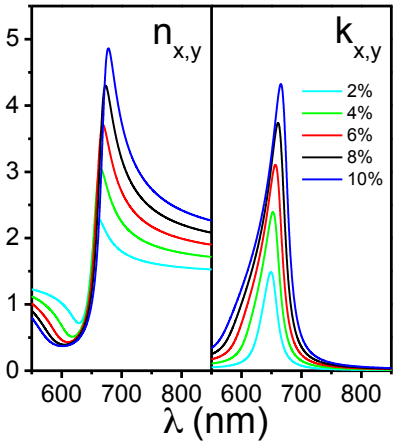


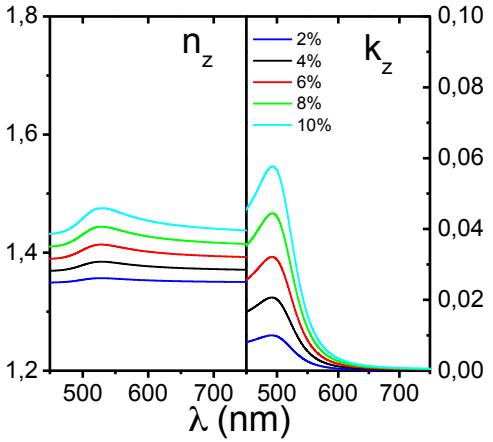
Random 2D array

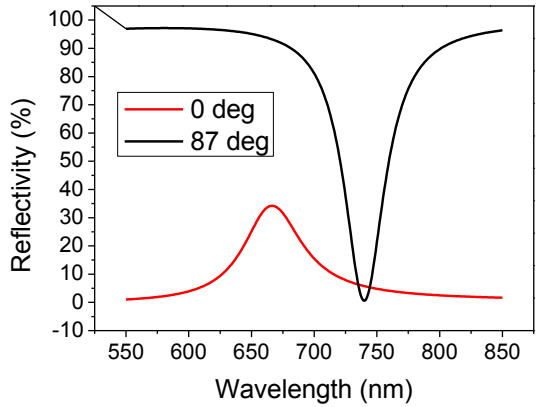
Maxwell Garnett effective medium with shape anisotropy

$$N_{eff} = n_{eff} + i\,k_{eff}$$



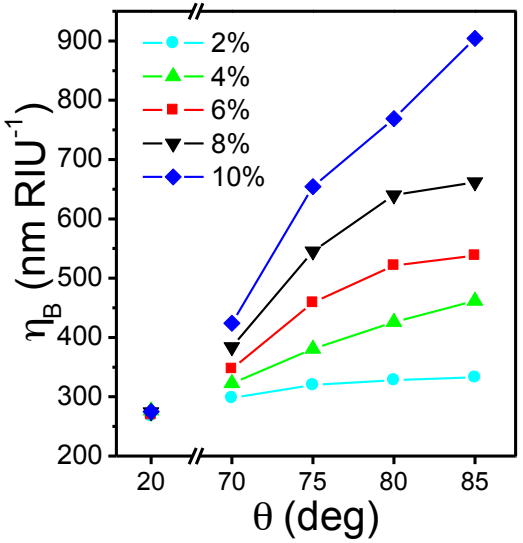






Bulk Sensitivity

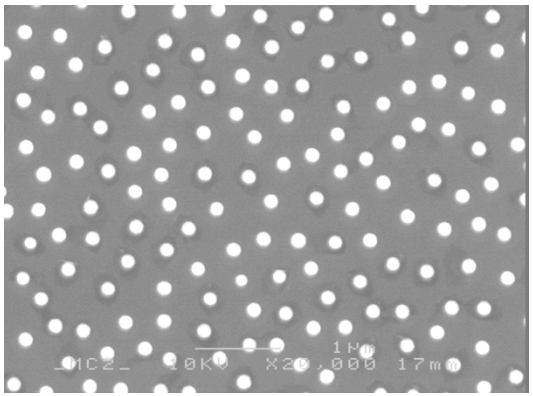
$$\eta_B = \frac{\partial \lambda_R}{\partial n_e}$$



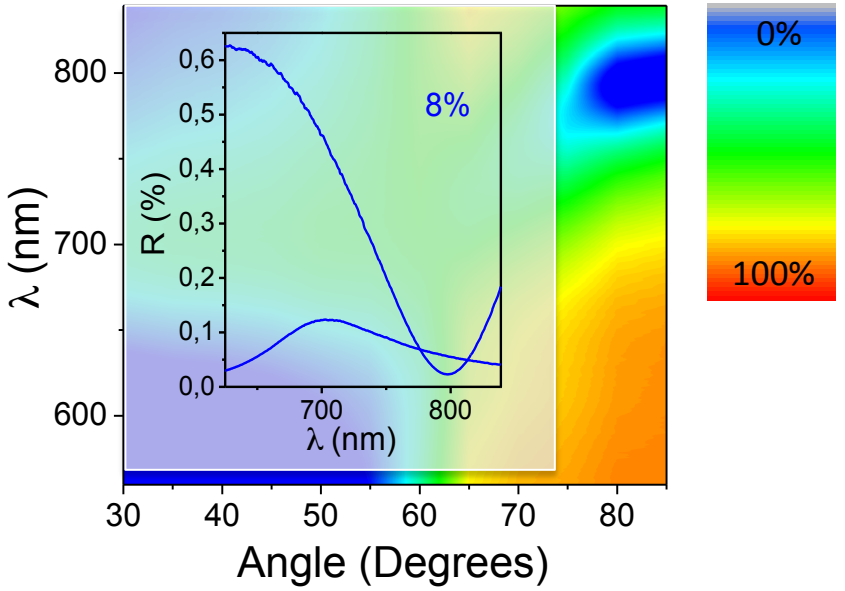
New functionalities

Metamaterials (Far field interaction)

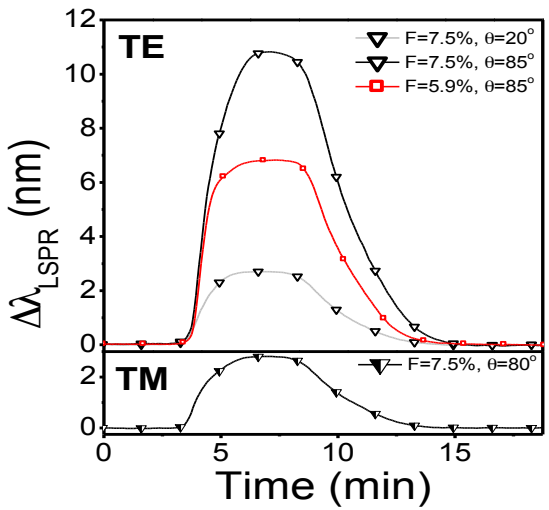
Hole mask colloidal lithography
(electrostatic self-assembly)
Tunable density
D = 100 nm, h =20 nm

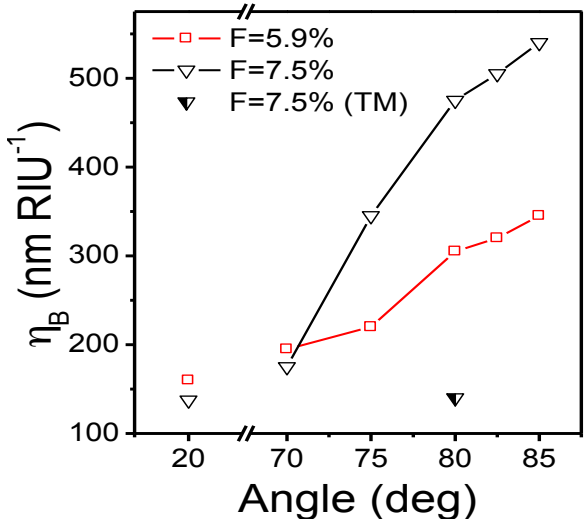


High density ~ 8 %



Experimental sensitivity enhancement

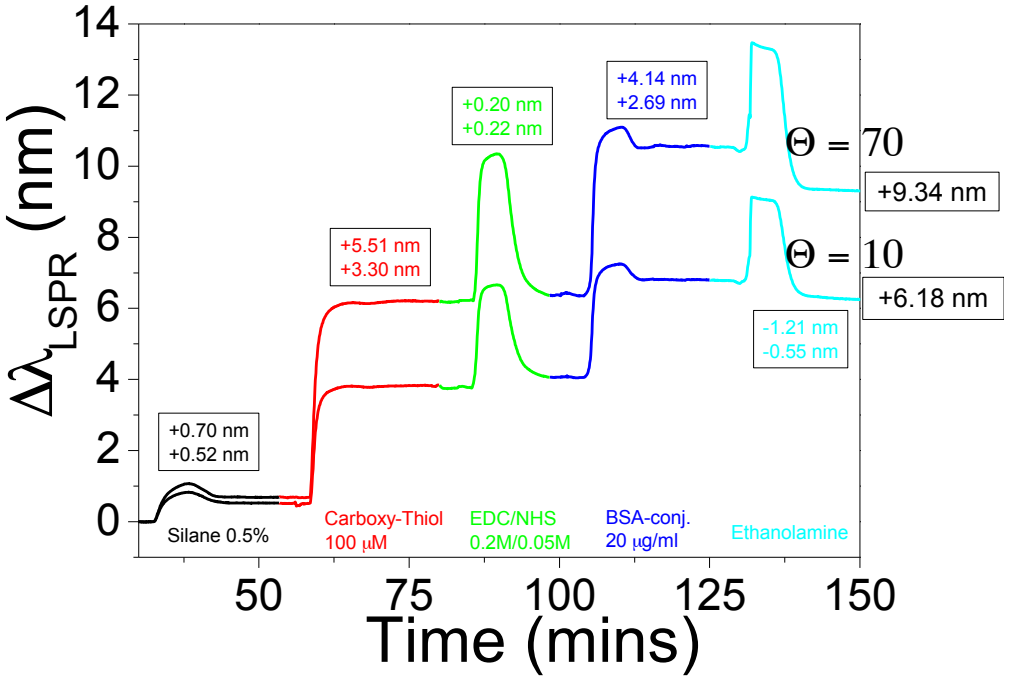


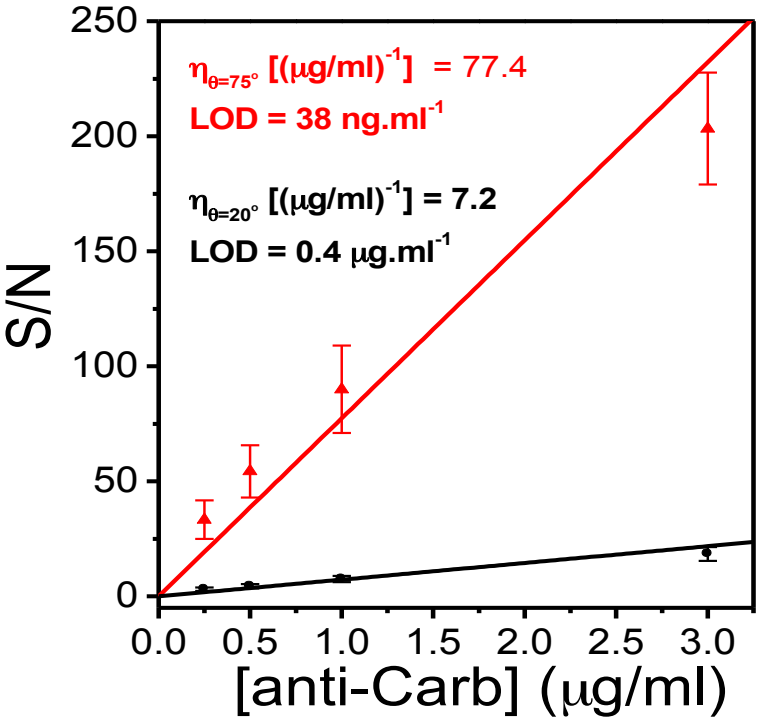


New functionalities

Metamaterials (Far field interaction)

Detection of monoclonal antibodies of carbaryl pestizide





One order of magnitude signal-to-noise ratio enhancement

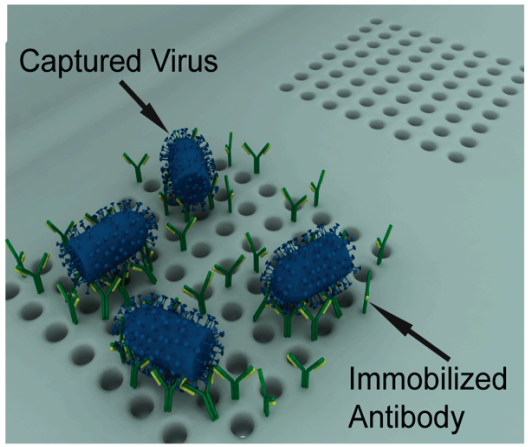
M.A. Otte, ACS Nano, 91 79 (2011)

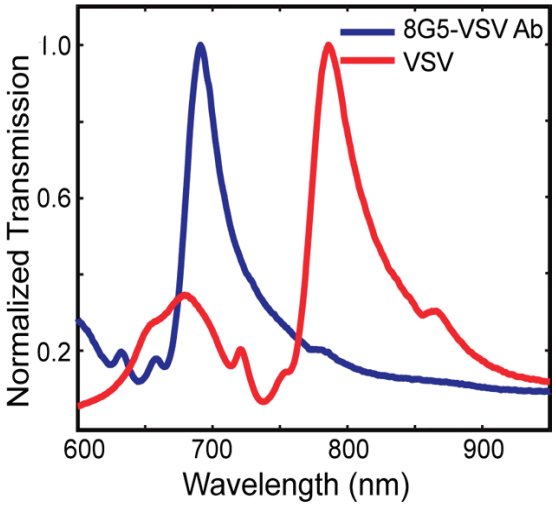
New functionalities

Flow-through sensors nanohole arrays

Bringing the analyte to the hot-spot

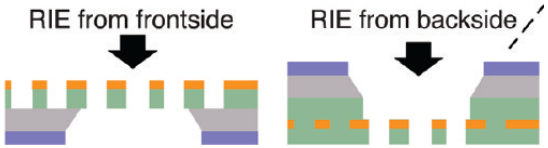
Virus detection -> no flow through

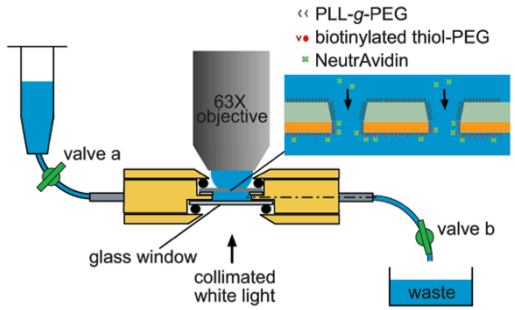


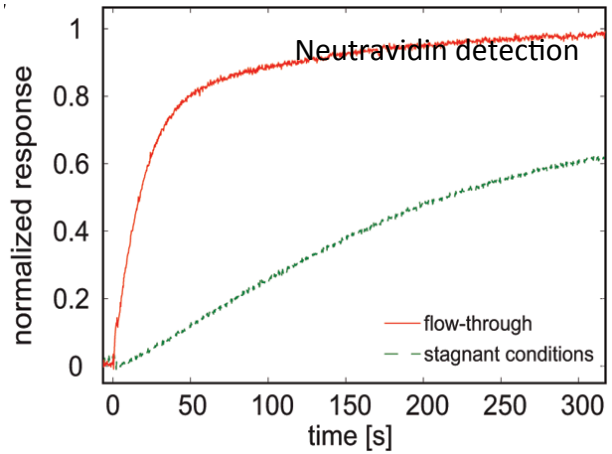


Nano Letters 10, 4962 (2010)

Flow through & passivation

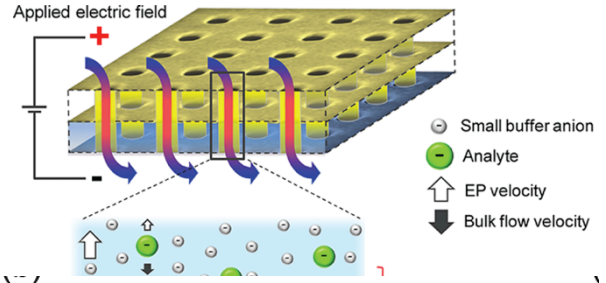


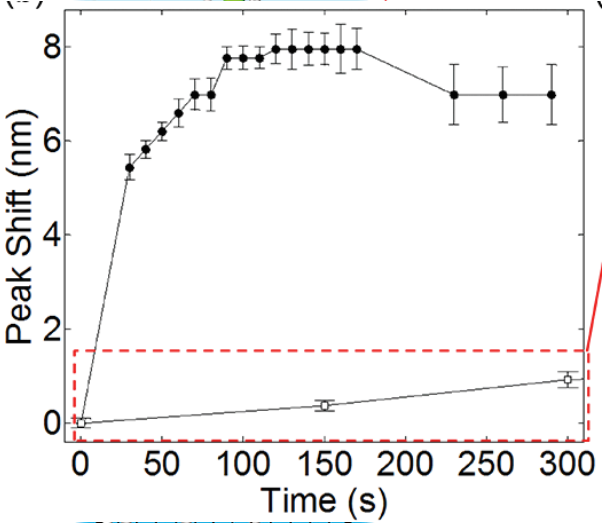


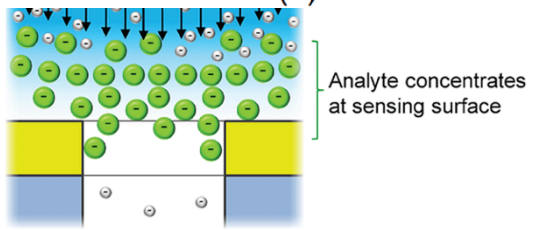


Anal. Chem. 82, 1 (2010)

Electrophoretic concentrator







Nano Letters 12, 1592 (2012)

cursos de verano
UNIVERSIDAD DE ZARAGOZA

ICN2
Institut Català de Nanociència i Nanotecnologia

Surface enhanced effects

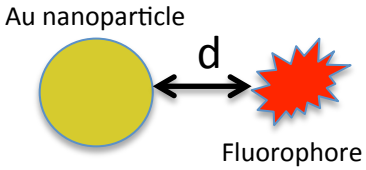
Fluorescence

Raman Scattering

Heating

Surface enhanced effects

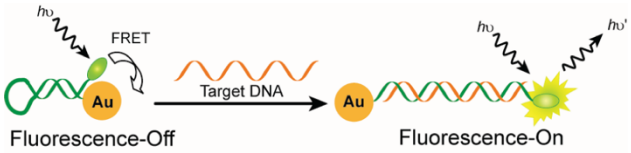
Surface enhanced fluorescence and quenching

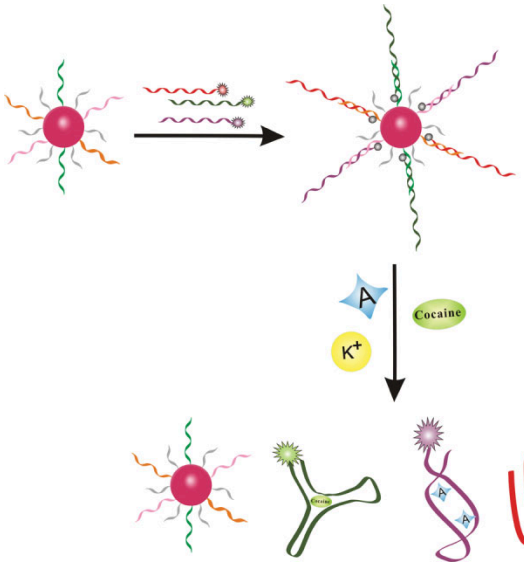


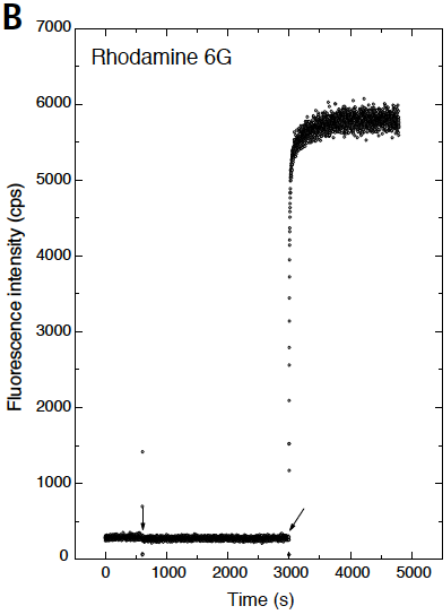
d < 5 nm -> Fluorescence quenching -> coupling to non-radiative metal modes

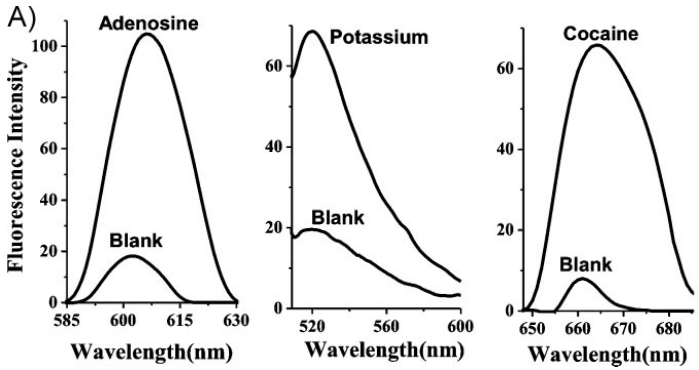
5 < d < 15 -> Fluorescence enhancement -> field enhancement

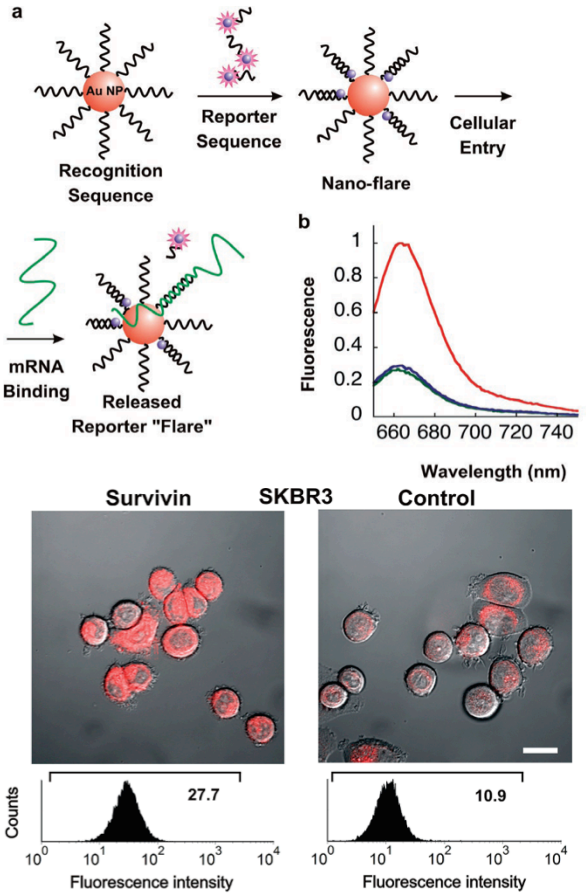
+ increase radiative decay rate











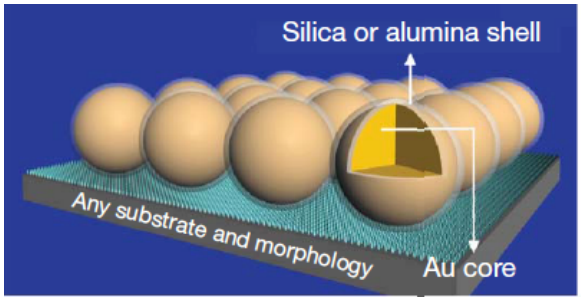
Nat. Biotech. 19, 366 (2001)

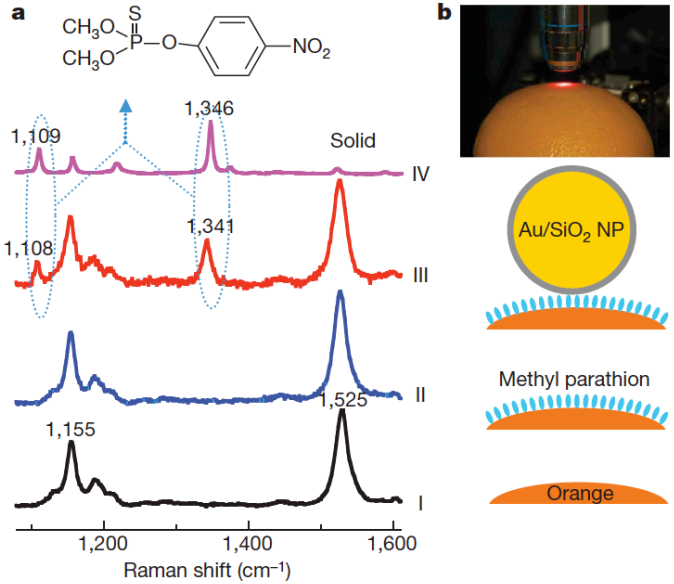
Small 6, 201–204 (2010)

J. Am. Chem. Soc. 129, 15477 (2007)

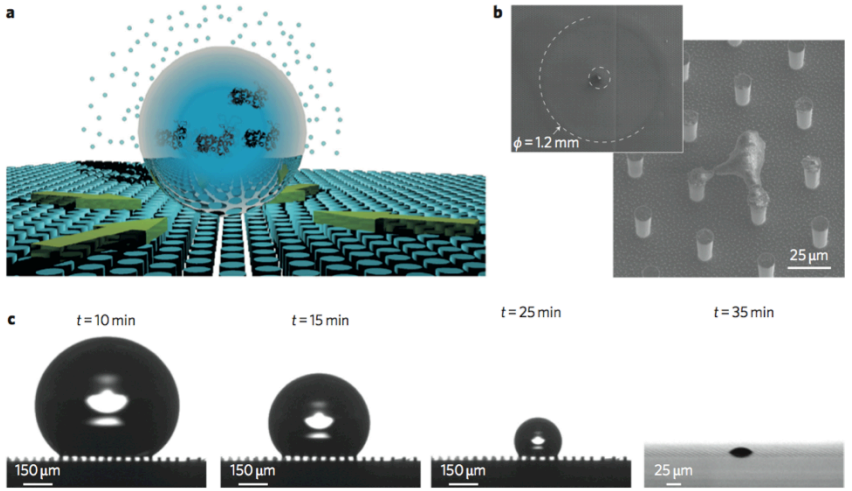
Surface enhanced effects

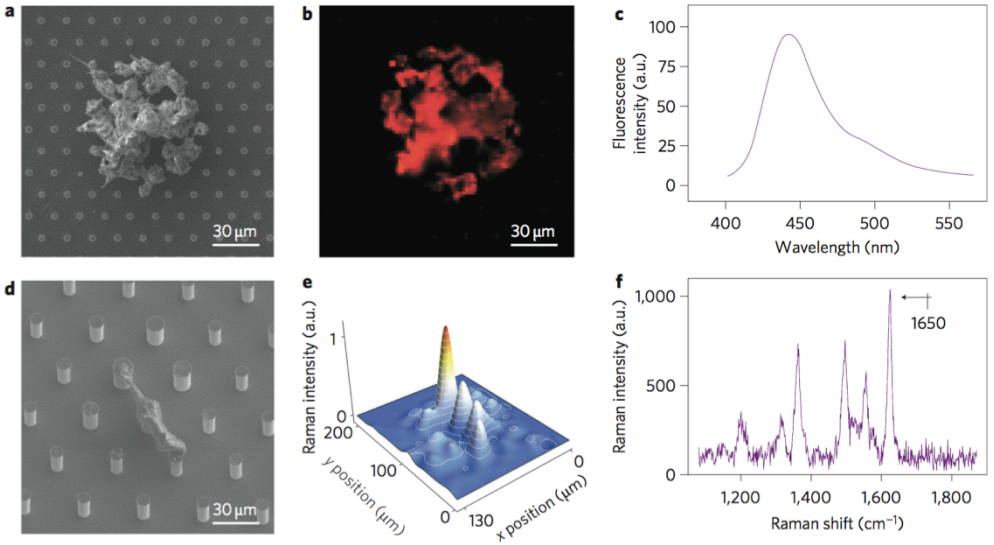
Surface enhanced Raman scattering (SERS)





Nature 464, 392 (2010)





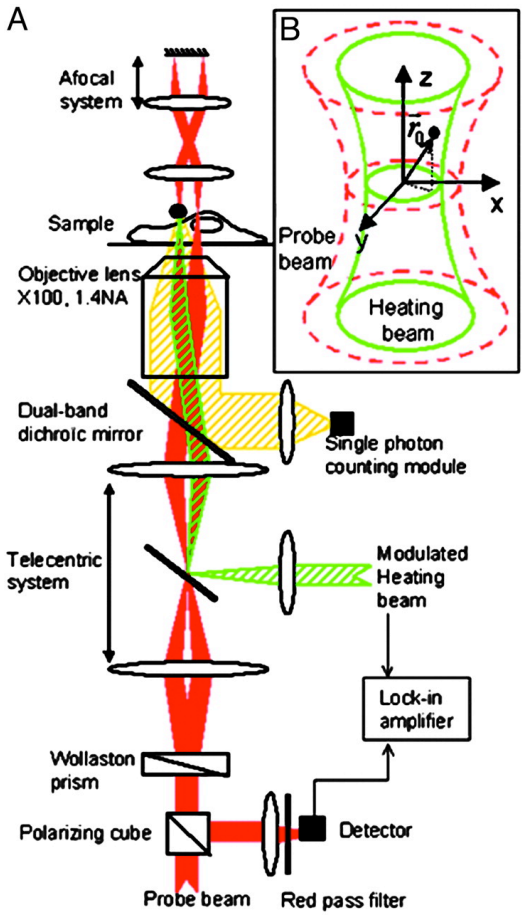
Nat. Photon. 5, 682 (2011)

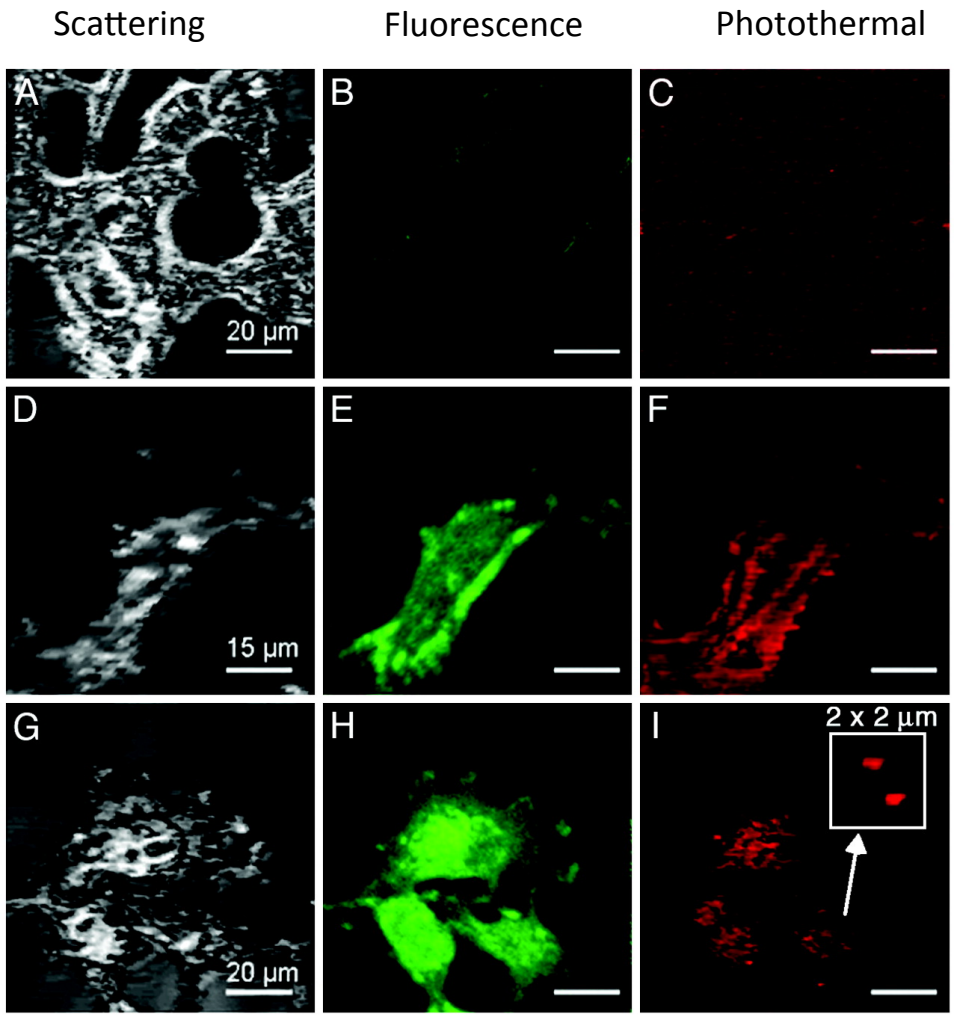
Photo-thermal effects

Heat generation

$$C_{abs} = k \cdot \mathrm{Im}(\alpha)$$

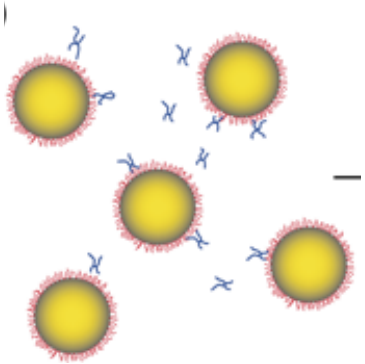
Detection of particles in complex media

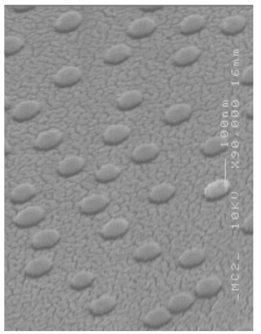


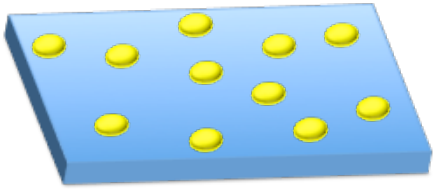


Cognet L et al. PNAS100, 11350 (2003)

Conclusions







Gold Colloidal particles in solution

Colorimetric aggregation assays -> near field intraction

- ✔ Very sensitive -> femto-molar range
- ✔ Inexpensive chemical synthesis
- ✗ Low stability -> small nanoparticles 2-30 nm
- ✔ No surface negative effects
- ✗ Complex biofunctionalization
- ✗ Challenging in complex buffers (serum)
- ✗ No regeneration
- ✗ Difficult lab-on-chip integration
- ✔ Large multiplexing capabilities

Gold Nanostructures in a surface

Refractometric assays

- ✔ ✗ Lower sensitivity-> pico/nano-molar range
- ✔ Inexpensive lithographic fabrication
- ✔ High stability
- ✗ Surface negative effects
- ✔ Easy biofunctionalization
- ✔ ✗ Complex buffers are possible (difficult)
- ✔ Regenerable
- ✔ Easy lab-on-chip integration
- ✔ Large multiplexing capabilities

Thanks for your attention

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B. Sepulveda et al., Nano Today 4, 244 (2009)
Nanoplasmonic Sensors, Springer ISBN 978-1-4614-3933-2 (2012)