INTERNATIONAL SUMMER SCHOOL ON
FLUORESCENT NANO-PARTICLES IN BIO-MEDICINE

Integration of nanoparticles into complex sensors for biodetection

Luis M. Liz-Marzán

Colloid Chemistry Group
Universidade de Vigo

http://webs.uvigo.es/coloides/nano

Nanoplasmonics

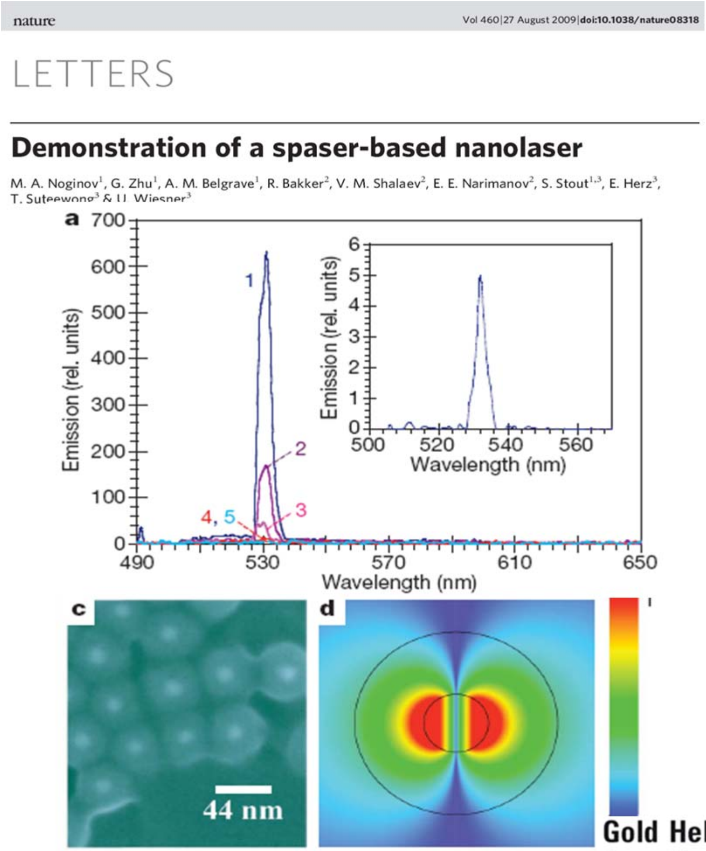
"control of the flow of light at the nanometer scale"

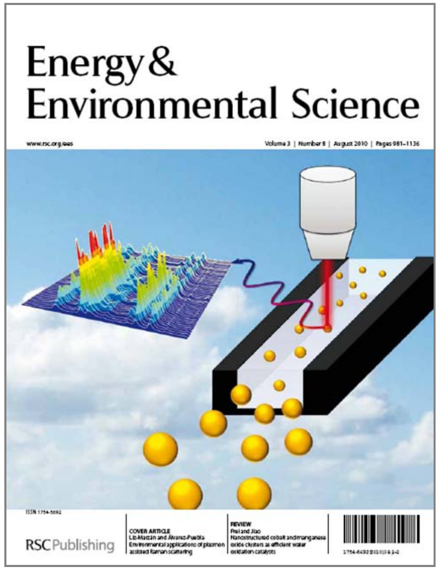
Colloids

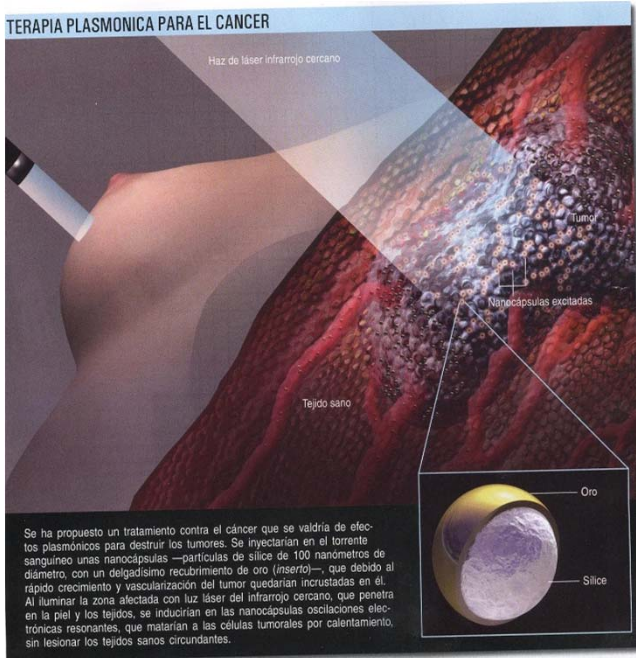
"..any substance consisting of particles substantially larger than atoms or ordinary molecules but too small to be visible to the unaided eye; more broadly, any substance, including thin films and fibres, having at least one dimension in this general size range, which encompasses about 1nm -1 micron…."

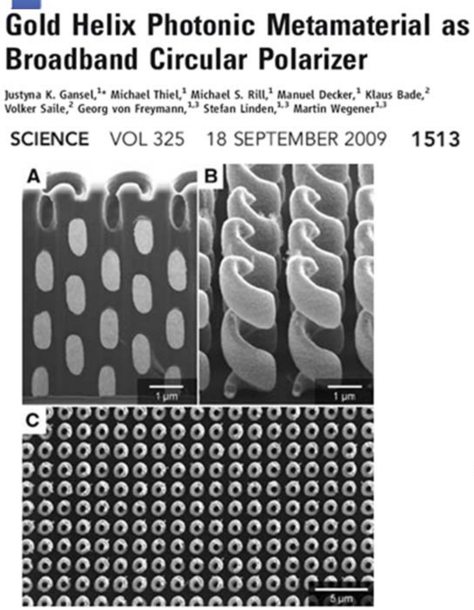
W. Ostwald, in "The World of Neglected Dimensions" (1927)

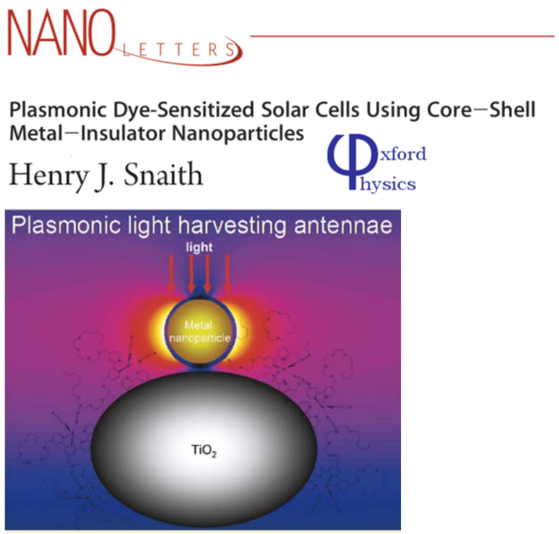
Some applications of nanoplasmonics

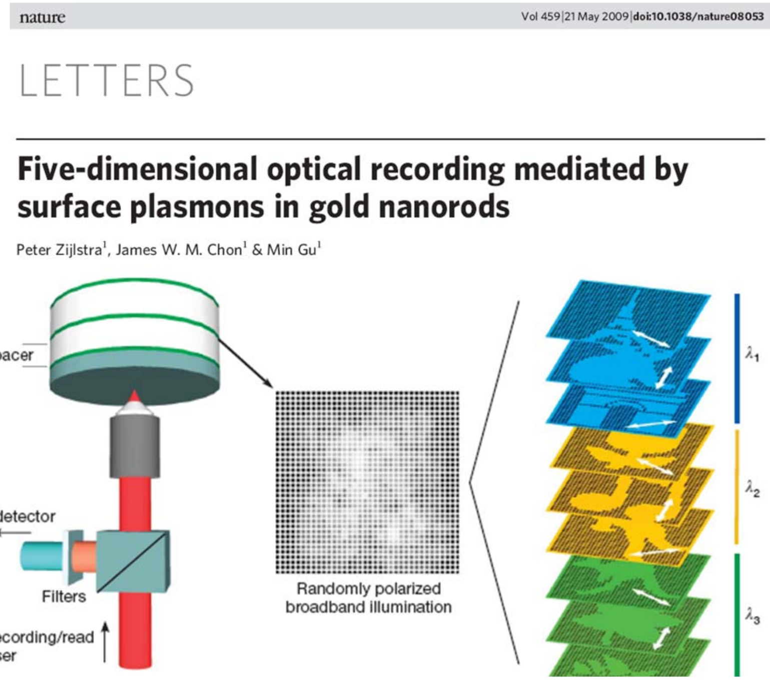




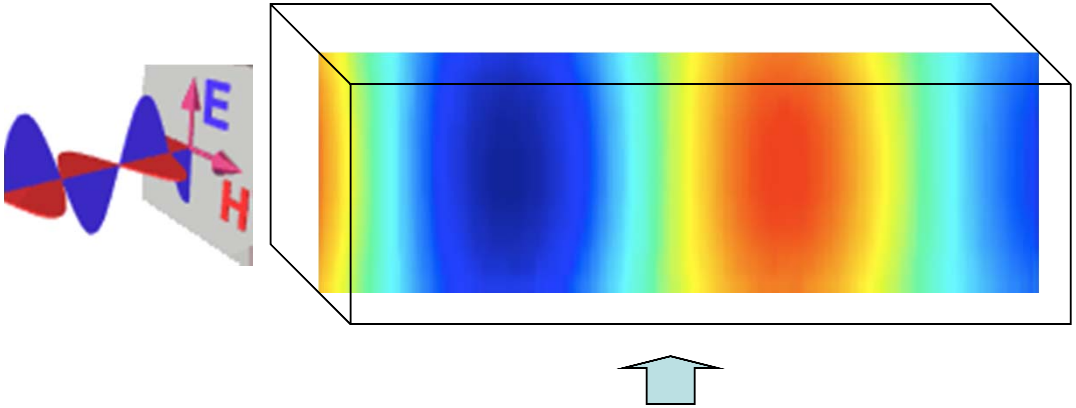








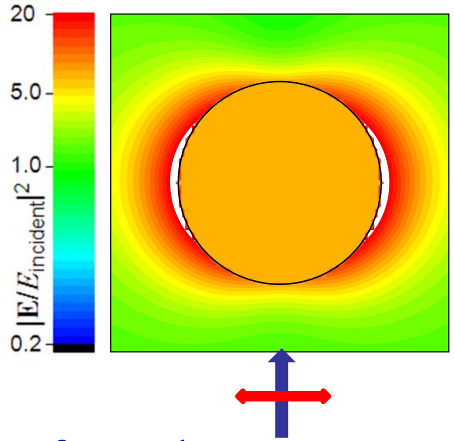
Interaction of light with metals: **Plasmons**
(charge density waves)

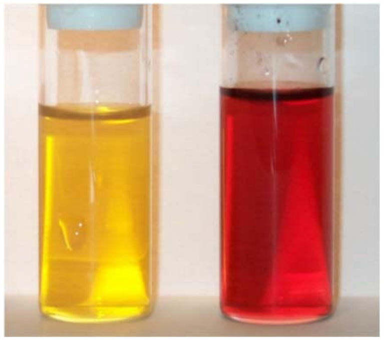


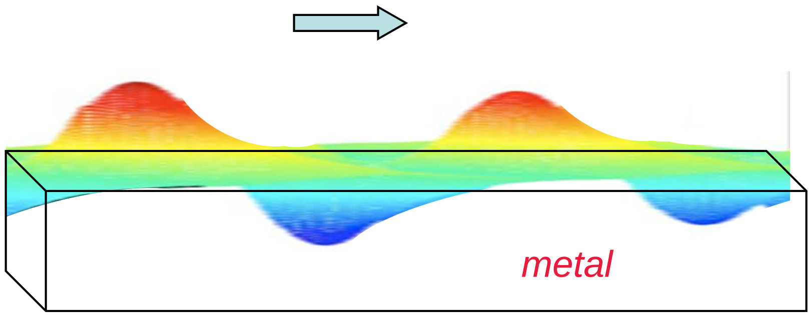
Purely longitudinal waves

Bulk plasmons

ω_p



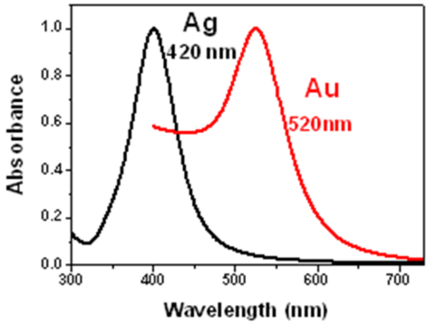




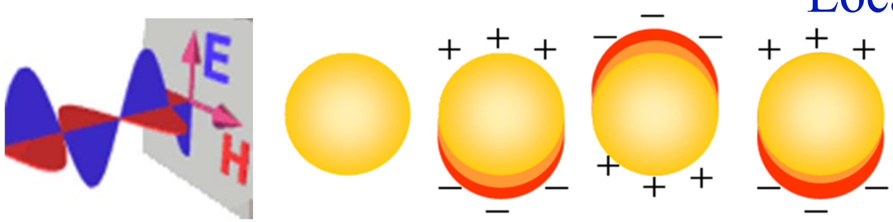
displacement

Surface plasmons

$\omega_p / \sqrt{2}$



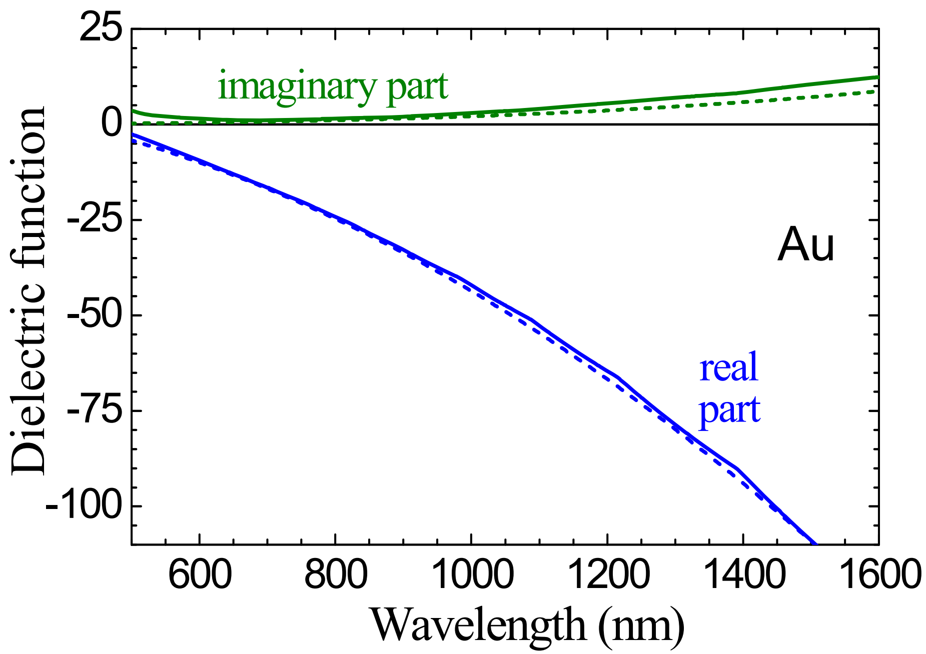
Localized Surface plasmons

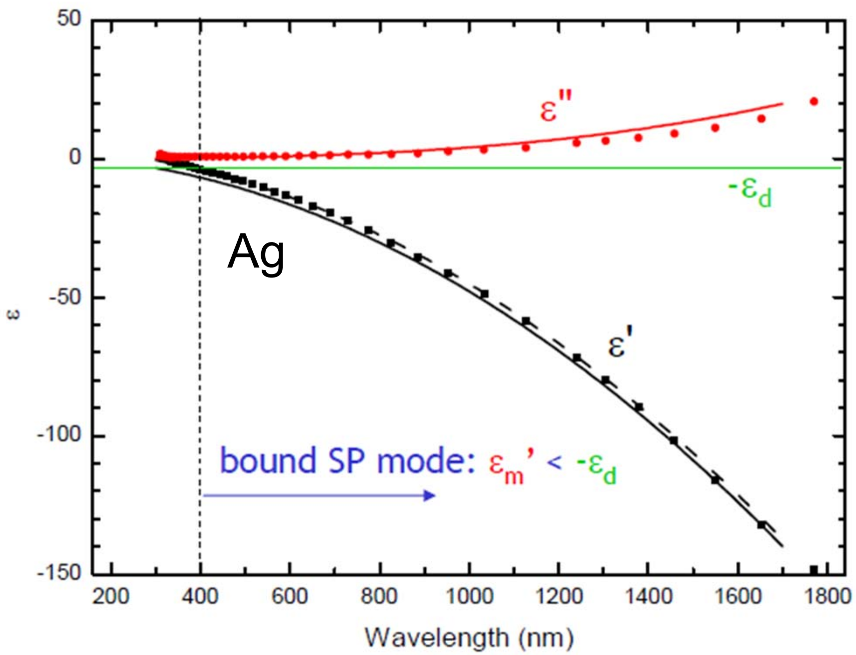


$$\omega = \omega_p / \sqrt{3}$$

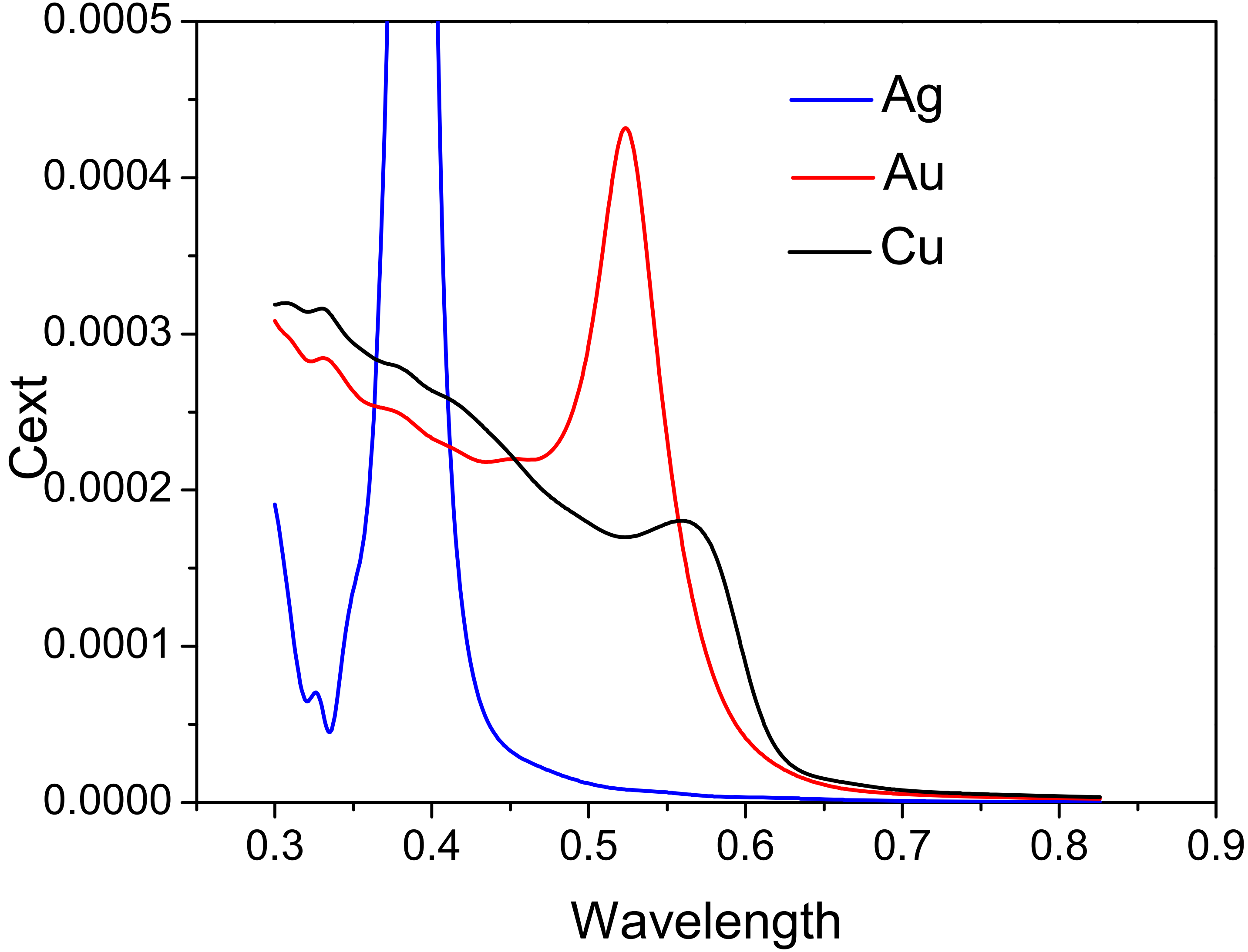
The dielectric function of Metals → Mie theory

$$C_{ext} = \frac{24\pi^2 R^3 \varepsilon_m^{3/2}}{\lambda} \frac{\varepsilon''}{(\varepsilon' + 2\varepsilon_m)^2 + \varepsilon''^2}$$

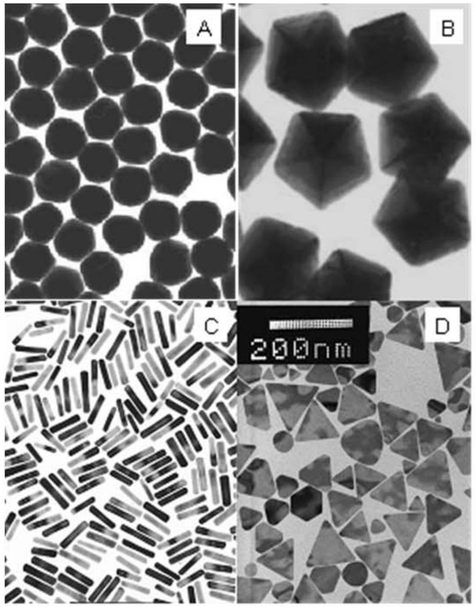


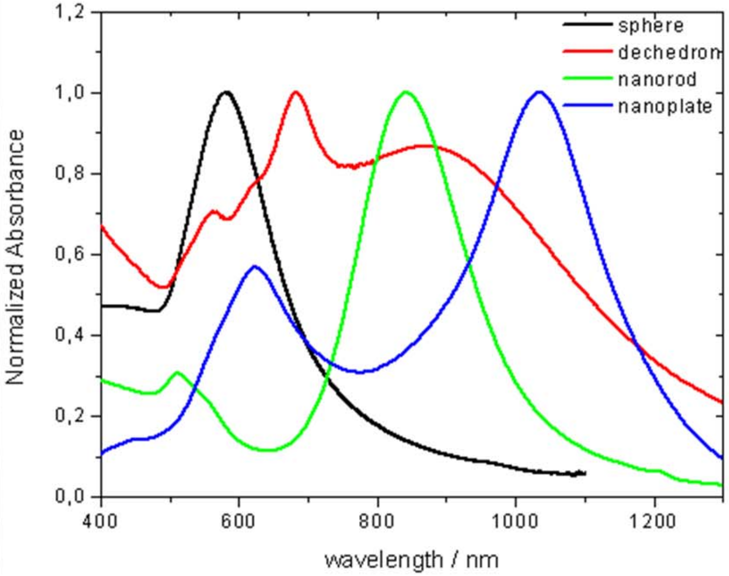


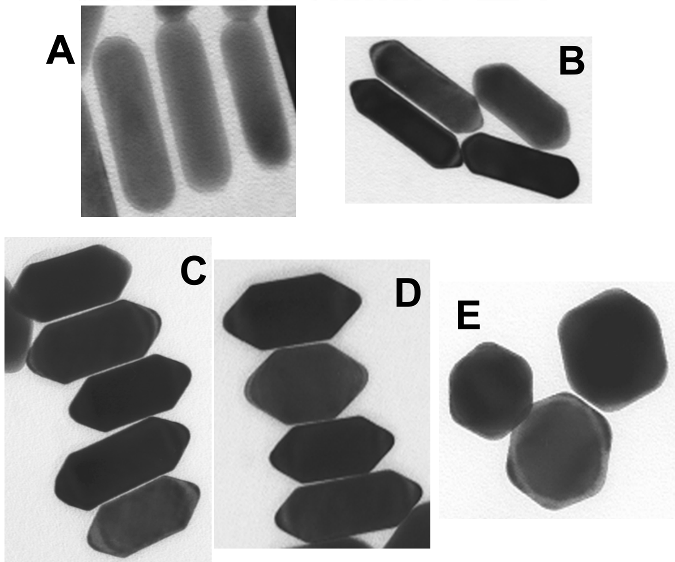
Calculated spectra for different metals (sphere, d=10 nm)

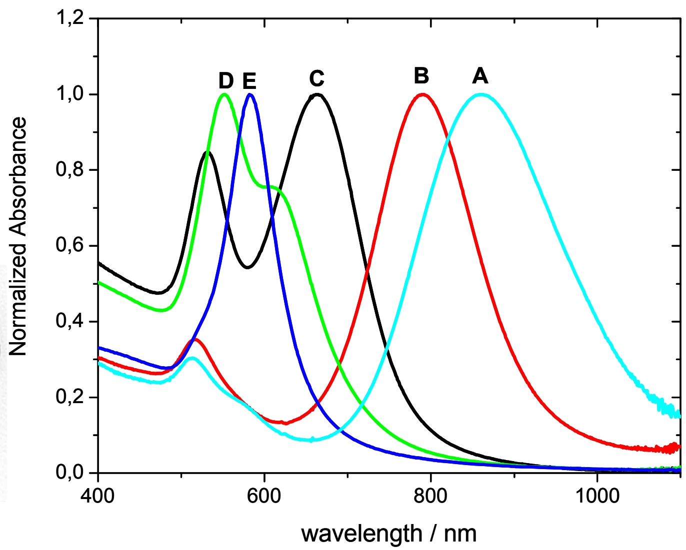


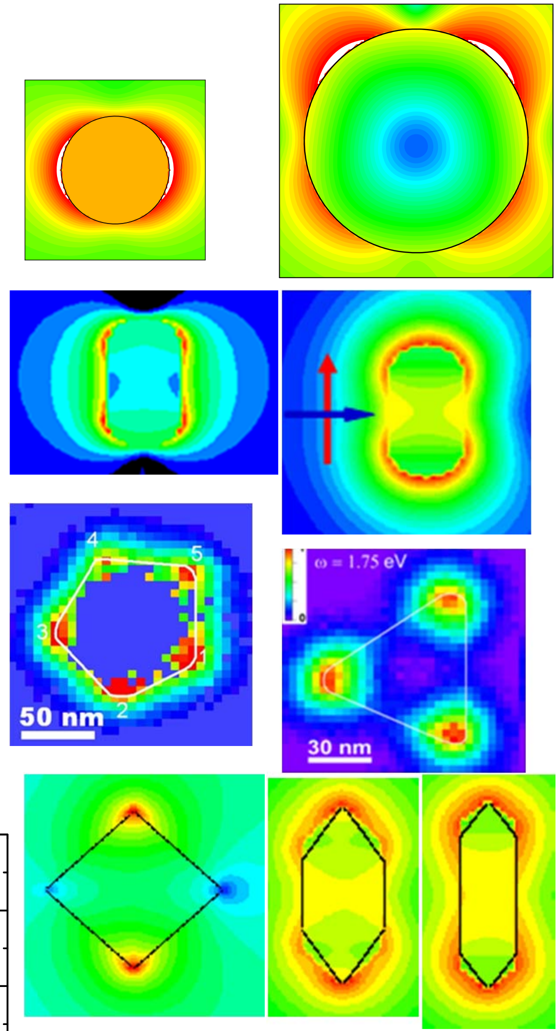
Tuning the plasmonic response from metal colloids











Coord. Chem. Rev. **2005**, *249*, 1870
Langmuir **2006**, *22*, 32
J. Mater. Chem. **2008**, *18*, 1724
Chem. Soc. Rev. **2008**, *37*, 1783
Adv. Funct. Mater. **2009**, *19*, 679
Adv. Mater. **2010**, *22*, 1182
ACS Nano **2010**, *4*, 3591
Curr.Op.Coll.Int.Sci. **2011**, 16, 118
ACS Nano **2012**, *6*, 3655

Numerical solutions for the 3D electromagnetic problem

Chem. Soc. Rev. **2008**, *37*, 1792

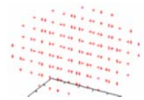
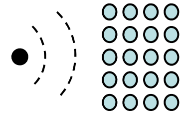
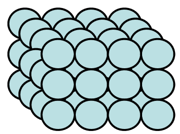
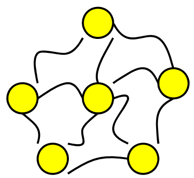
Maxwell's Equations:

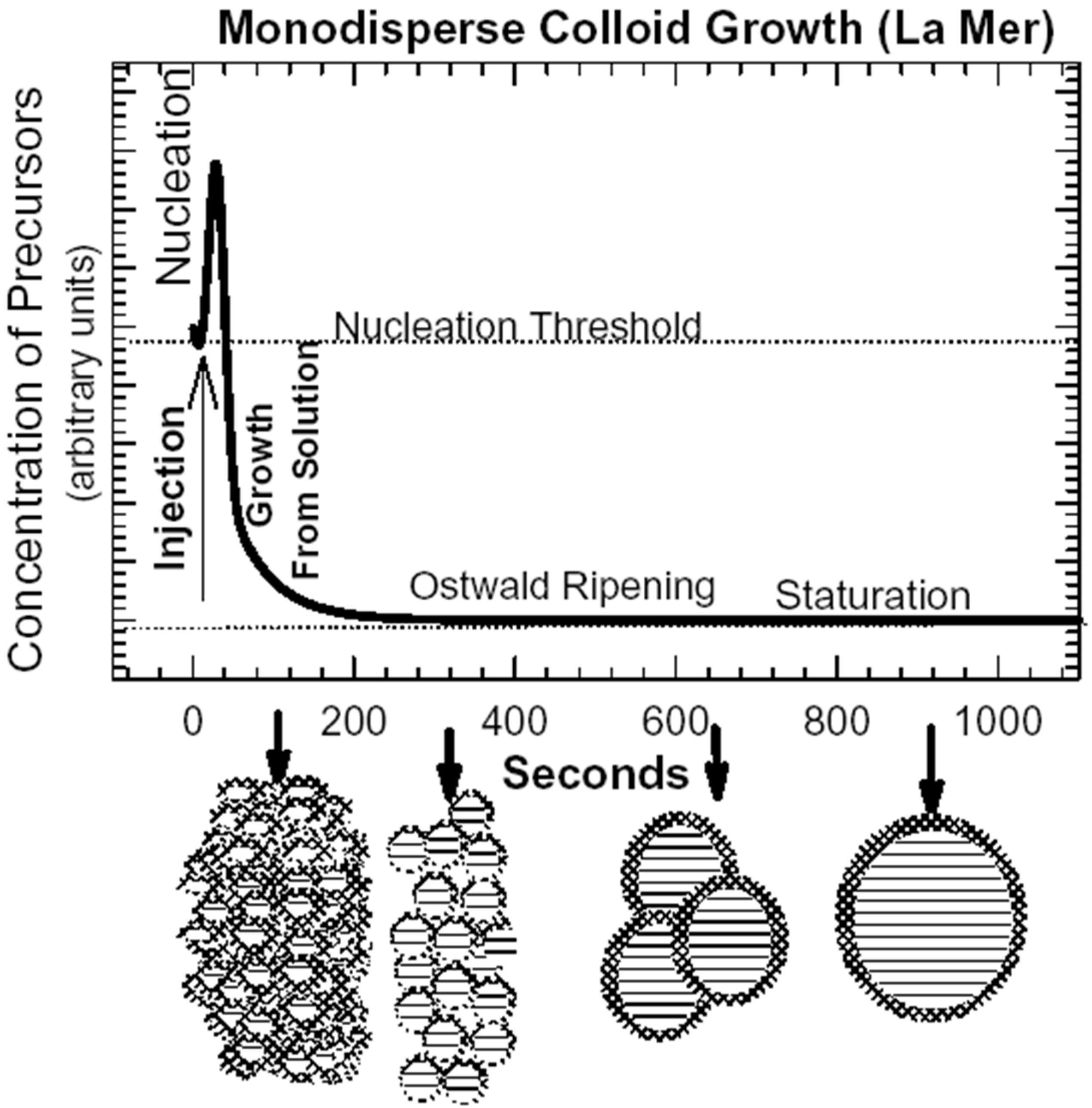
$$\nabla \bullet \mathbf{D} = \rho_f$$

$$\nabla \bullet \mathbf{B} = 0$$

$$\nabla \times \mathbf{E} = -\,\partial \mathbf{B}/\partial t$$

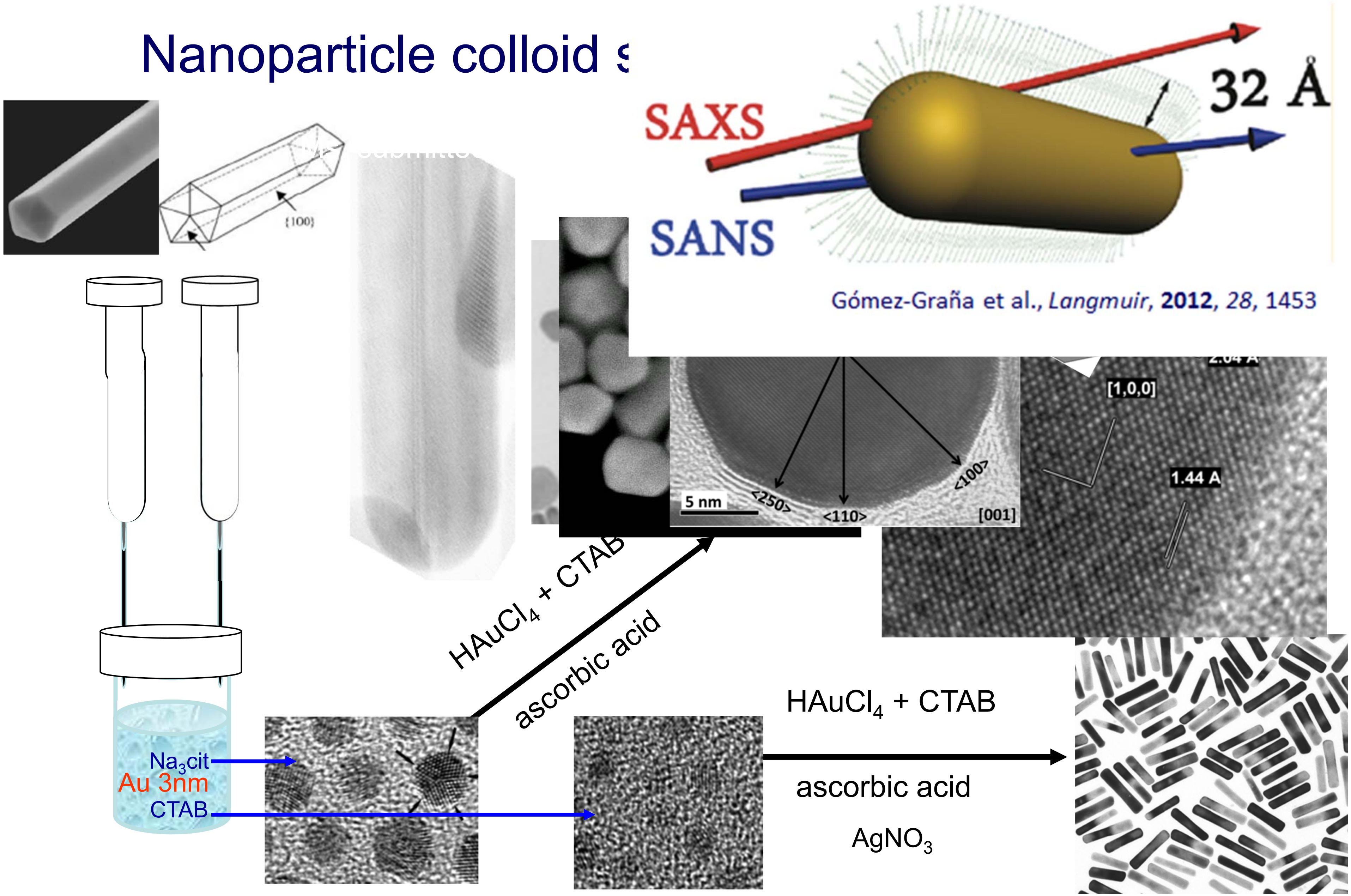
$$\nabla \times \mathbf{H} = \mathbf{J}_f + \partial \mathbf{D}/\partial t$$

	periodic systems	finite geometries	convergence with high ε (e.g. metals)	effective dimensionality	
discrete dipole approximation Purcell & Pennypacker Draine & Flateau	✓			3D	
boundary element method García de Abajo & Howie	✓			2D	
finite difference in the time domain Joannopoulos	✓			3D	
plane wave expansions Leung	✓		poor	3D	
transfer matrix approach Pendry	✓		poor	2D	
multiple scattering Ohtaka; Wang; García de Abajo	✓	✓			



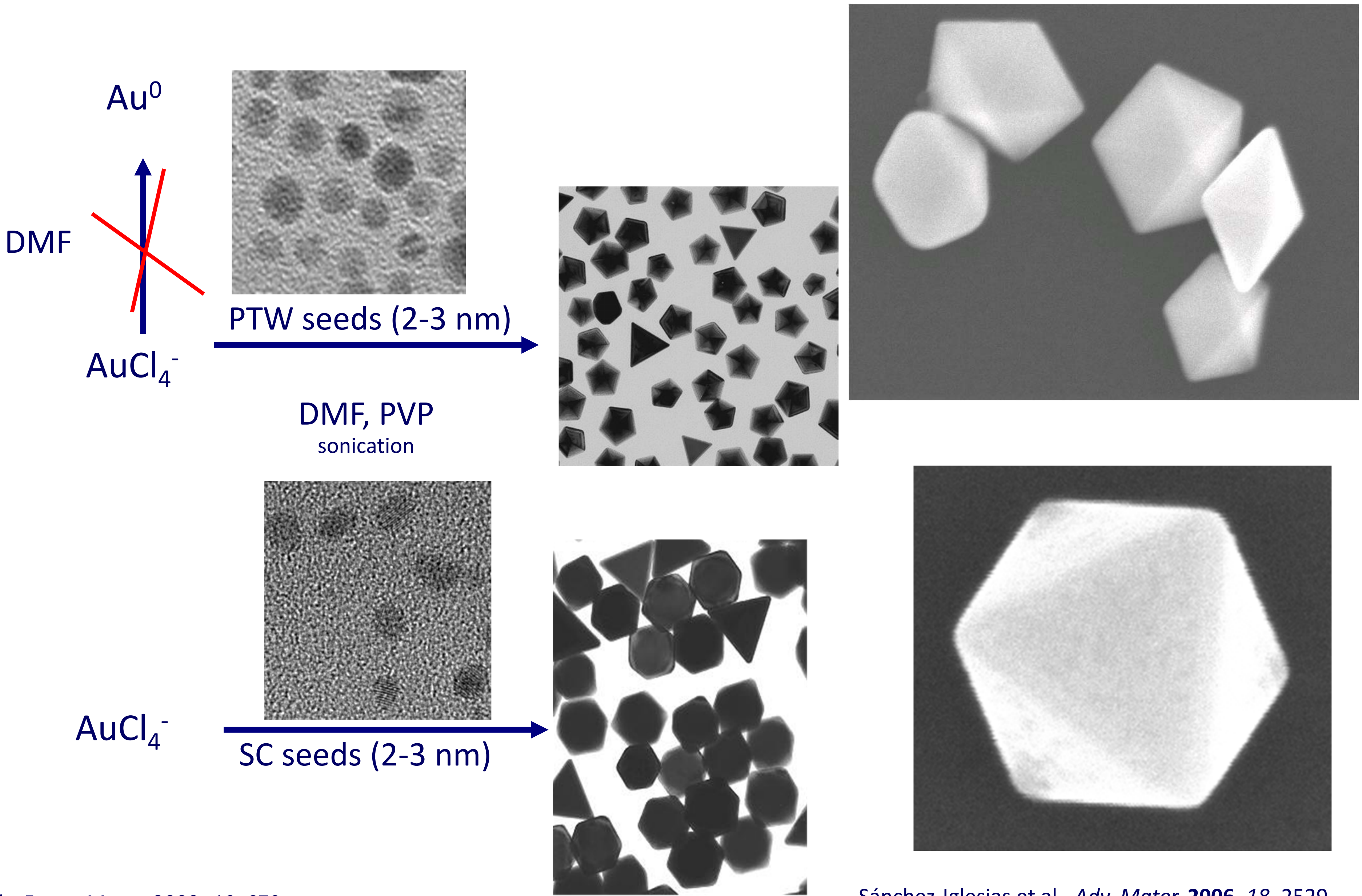
V.K. La Mer, R.H. Dinegar, *J. Am. Chem. Soc.* **1950**, *72*, 4847

Nanoparticle colloid s



Murphy, El-Sayed, others
Coord. Chem. Rev. **2005**, *249*, 1870
Chem. Soc. Rev. **2008**, *37*, 1783

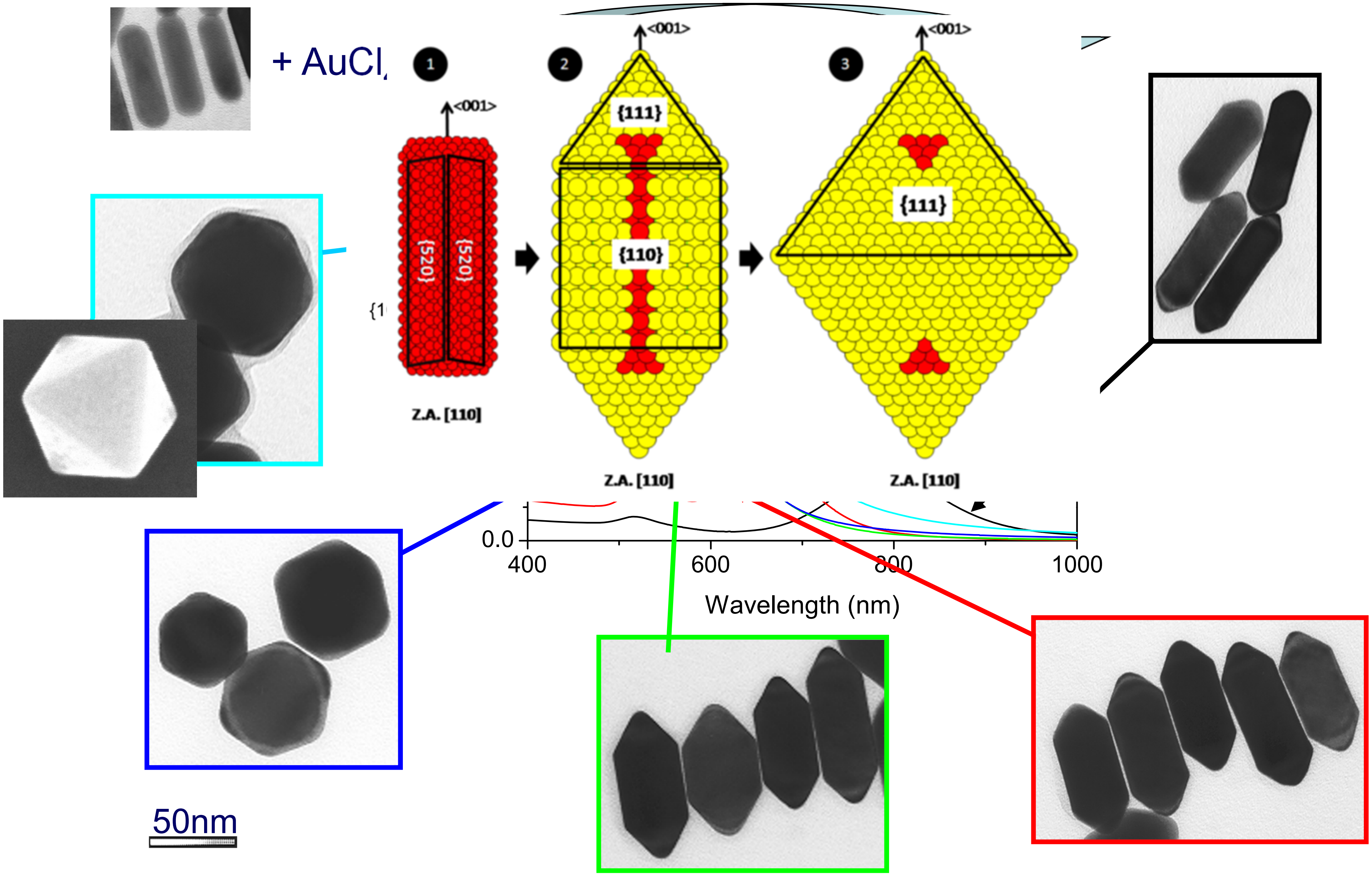
Seeded growth in DMF



Adv. Funct. Mater. **2009**, *19*, 679

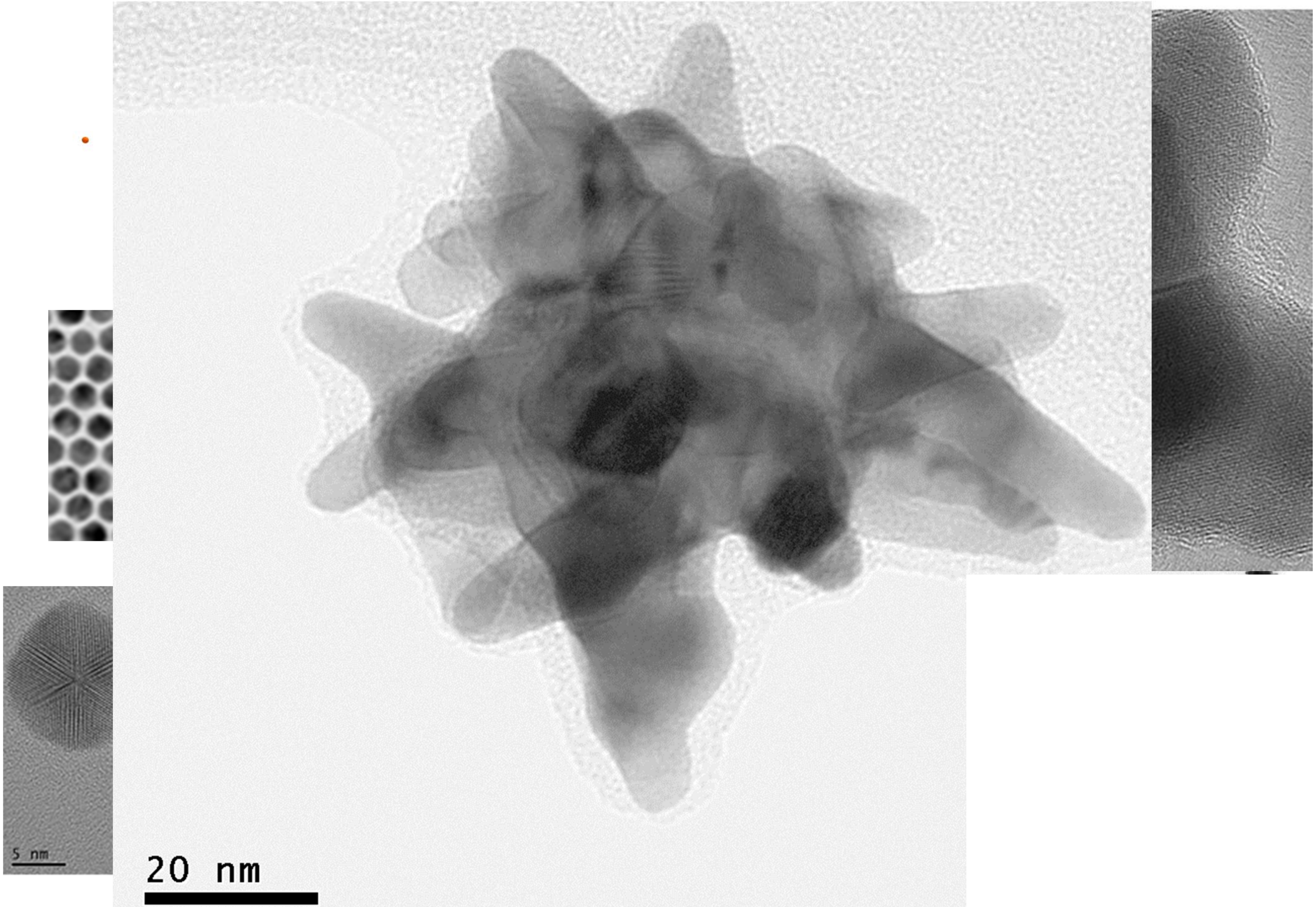
Sánchez-Iglesias et al., *Adv. Mater.* **2006**, *18*, 2529

Shaping Au nanorods with DMF



Carbó-Argibay et al., *Angew. Chem. Int. Ed.* **2007**, *46*, 8983

Growth and branching: Au nanostars



Kumar et al., *Nanotechnology* **2008**, *19*, 015606(1-6); Barbosa et al., *Langmuir* **2010**, *26*, 14943

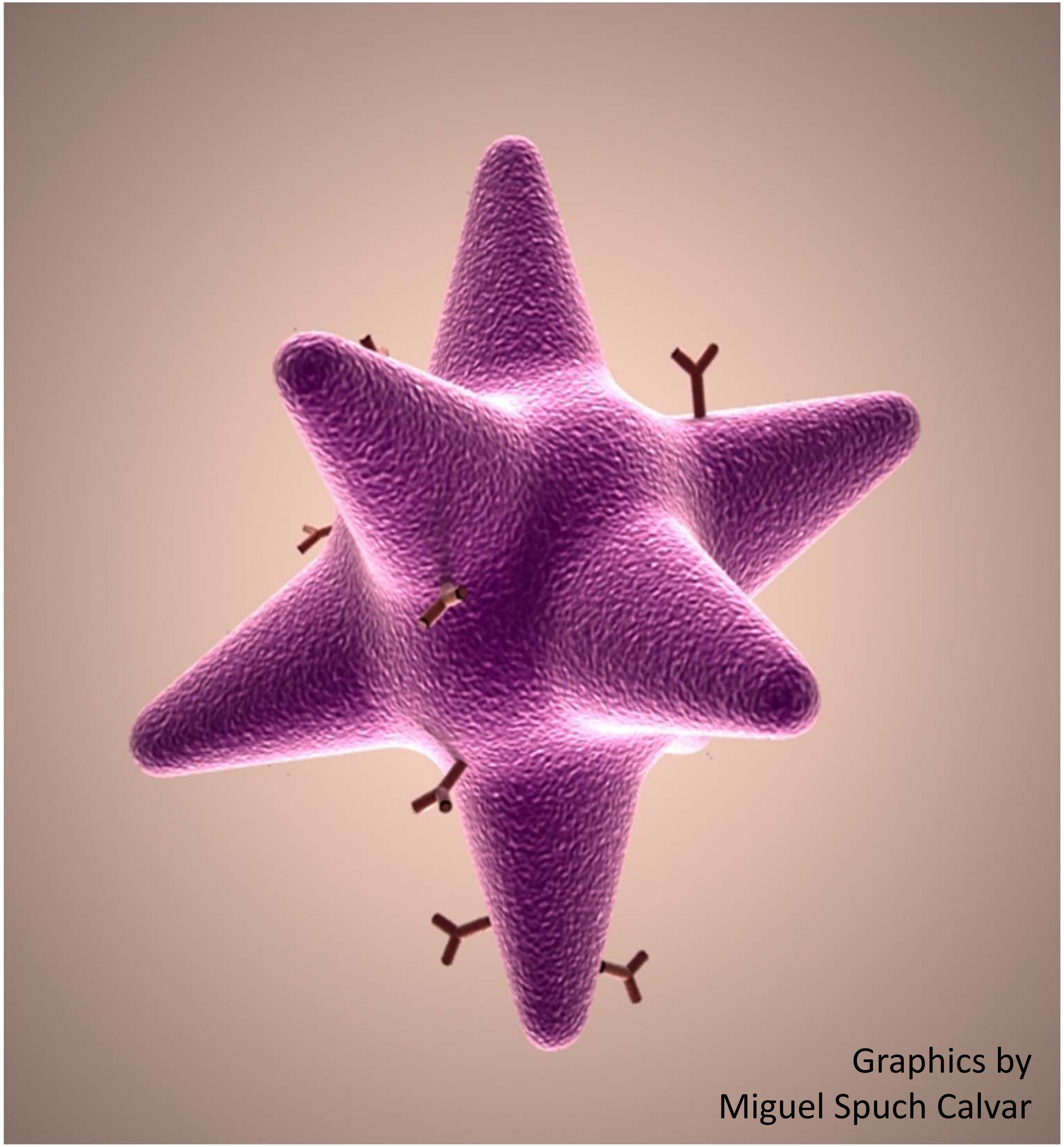
Designing biosensing that gets more sensitive as the concentration of analyte gets lower!

"Inverse sensitivity"

1. Binding of polyclonal antibody on Au nanostars

Rodríguez-Lorenzo et al., *Nature Mater.* **2012**, *11*, 604

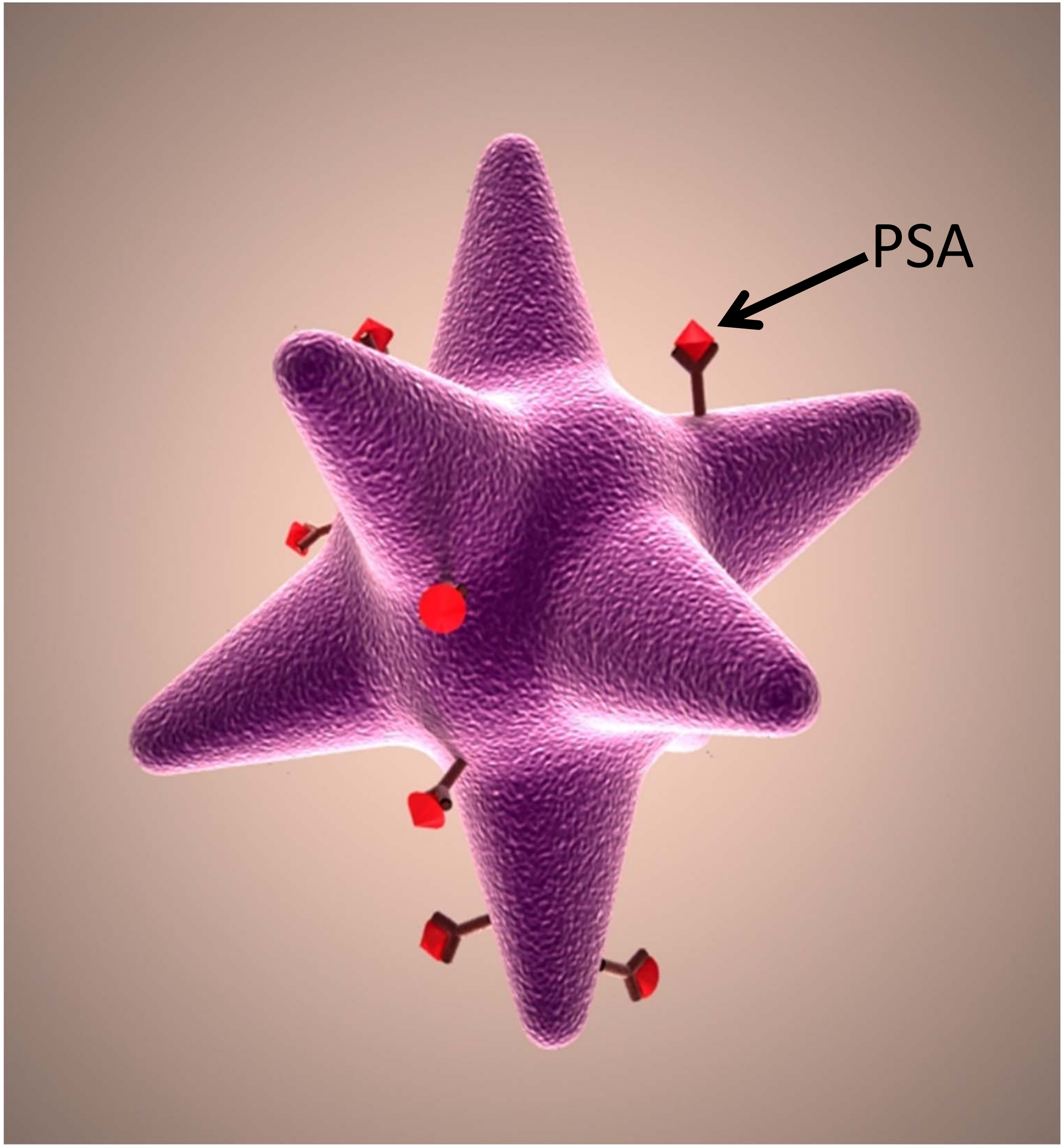
Col. **Molly Stevens** (Imperial College)



Designing biosensing that gets <u>more</u> sensitive as the concentration of analyte gets lower!

"Inverse sensitivity"

2. Selective recognition of prostate cancer antigen



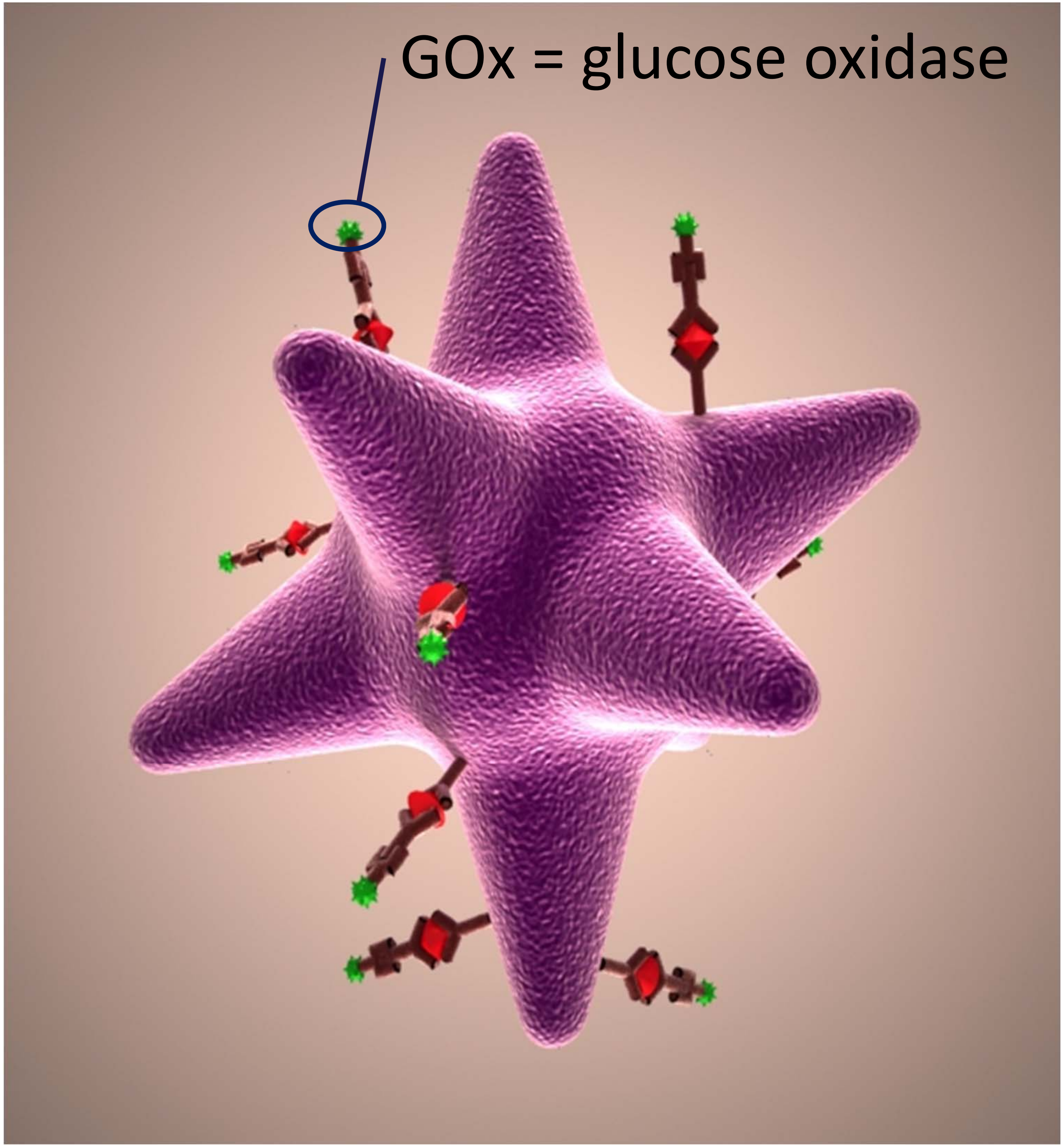
Rodríguez-Lorenzo et al., *Nature Mater.* **2012**, *11*, 604

Col. **Molly Stevens** (Imperial College)

Designing biosensing that gets more sensitive as the concentration of analyte gets lower!

“Inverse sensitivity”

3. Selective binding of monoclonal antibody containing glucose oxidase (GOx)



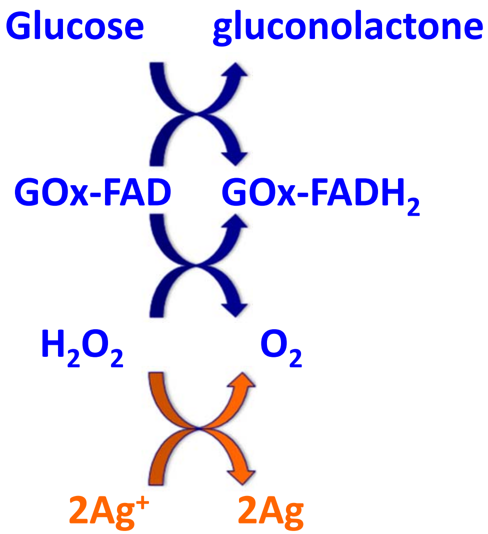
Rodríguez-Lorenzo et al., *Nature Mater.* **2012**, *11*, 604

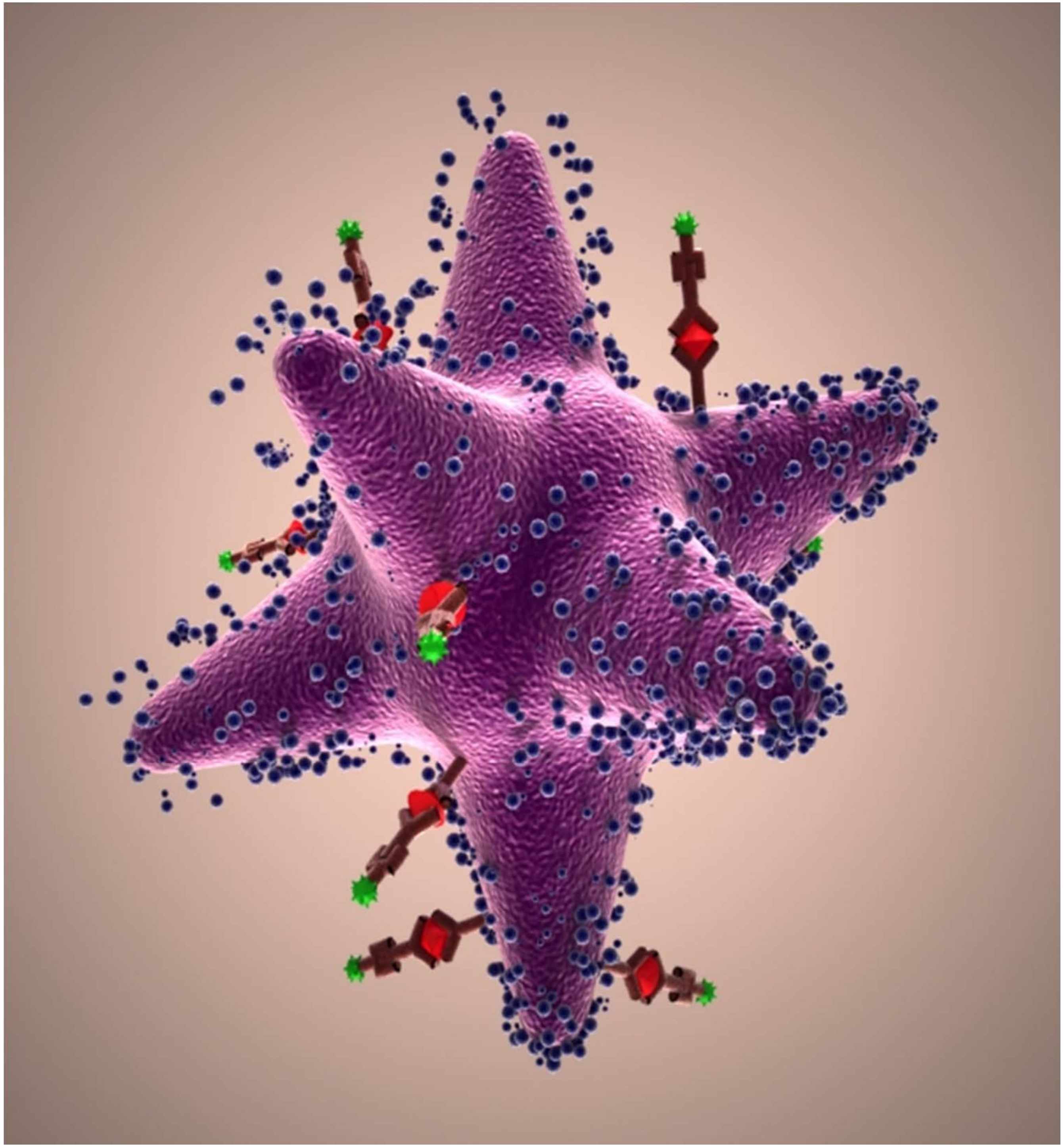
Col. **Molly Stevens** (Imperial College)

Designing biosensing that gets <u>more</u> sensitive as the concentration of analyte gets lower!

“Inverse sensitivity”

4. Reduction of Ag on Au nanostars by glucose oxidase

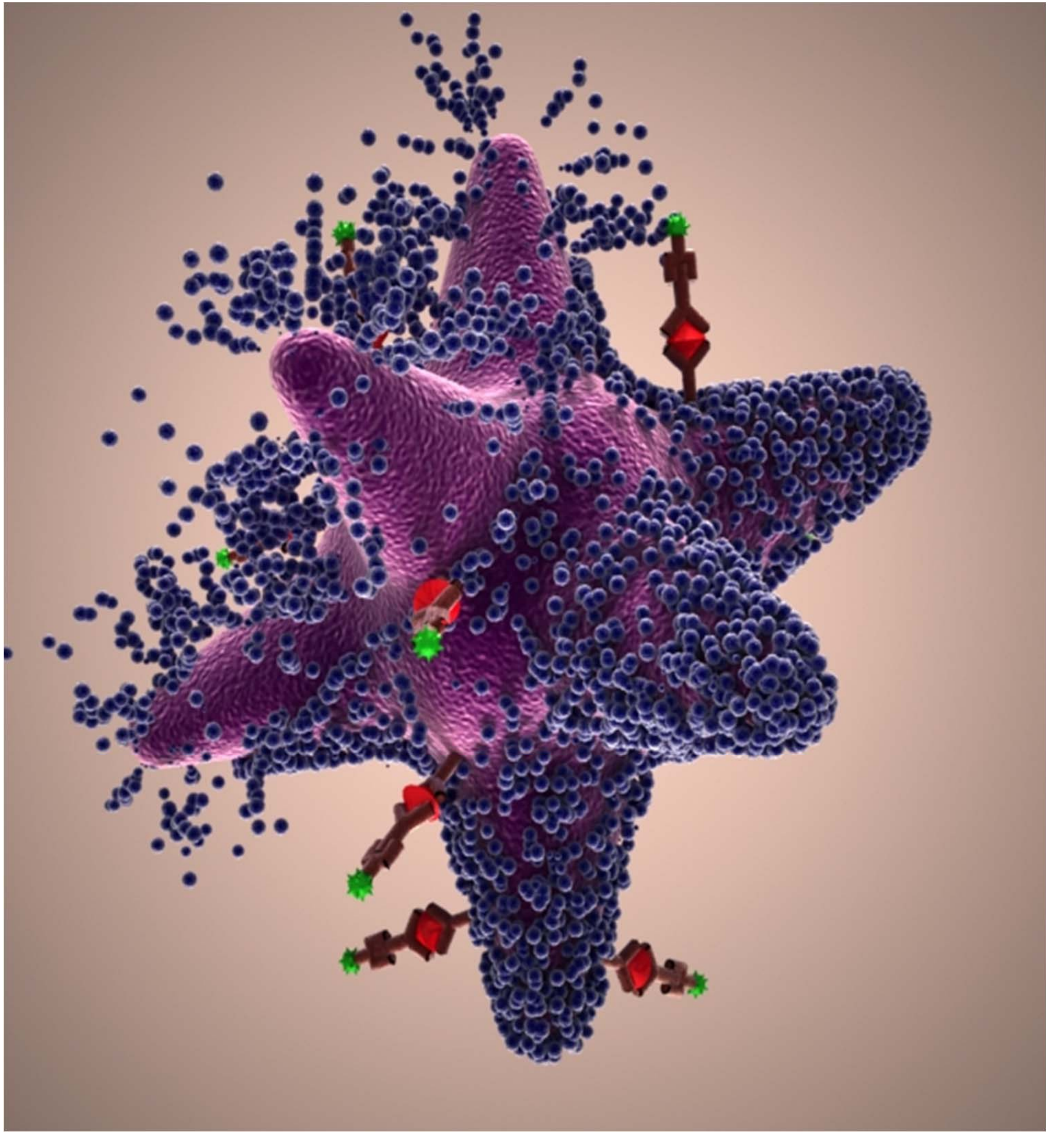




Designing biosensing that gets more sensitive as the concentration of analyte gets lower!

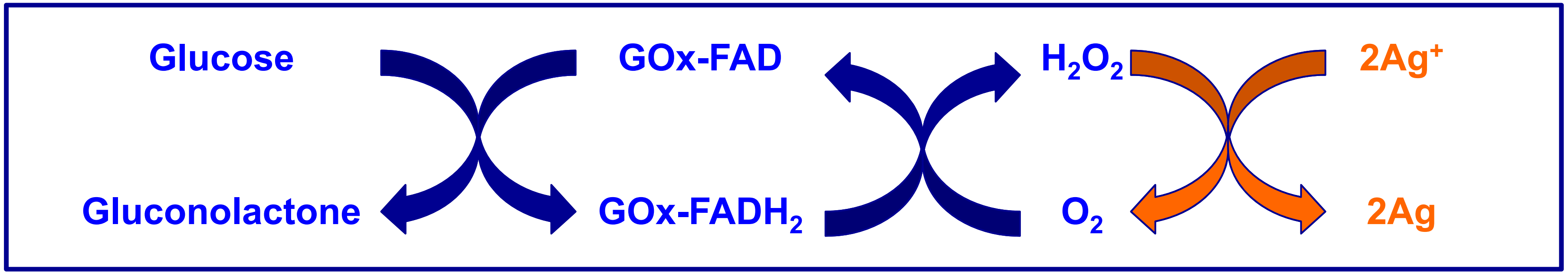
“Inverse sensitivity”

5. Homogeneous coating leads to strong surface plasmon shifts

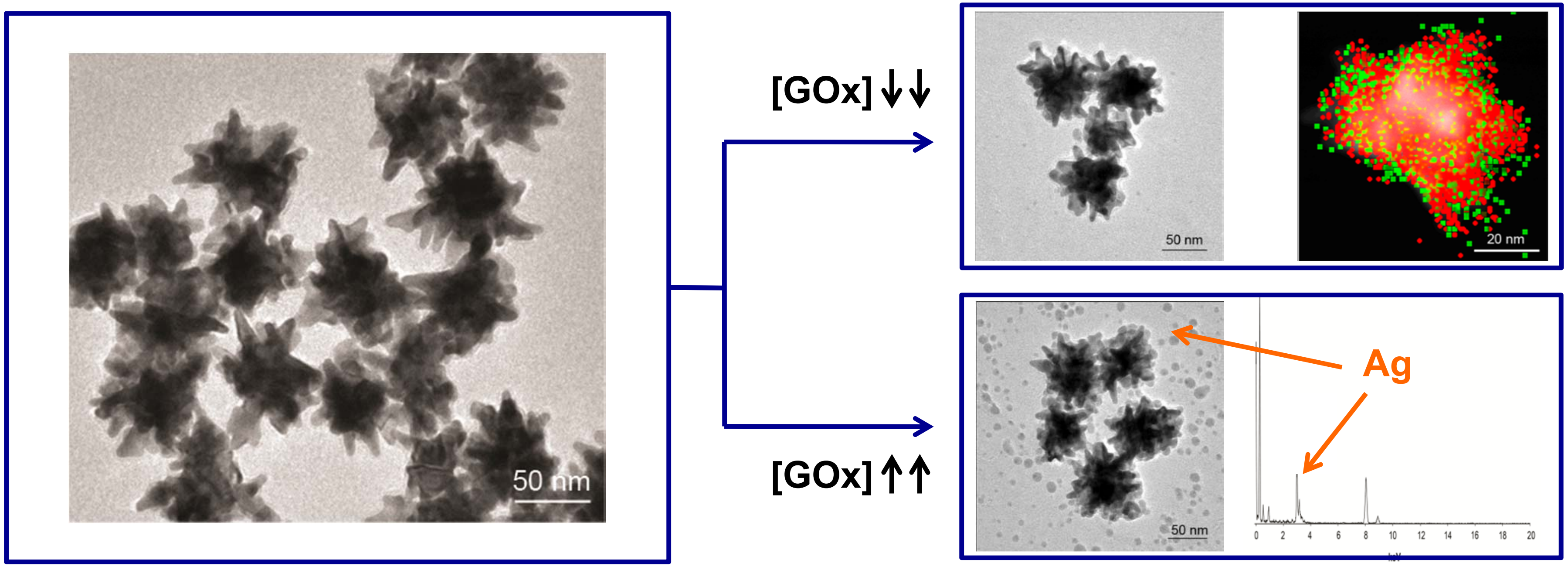


GOx-mediated silver reduction on Au nanostars

Biocatalytic cycle of glucose oxidase can be linked to silver reduction



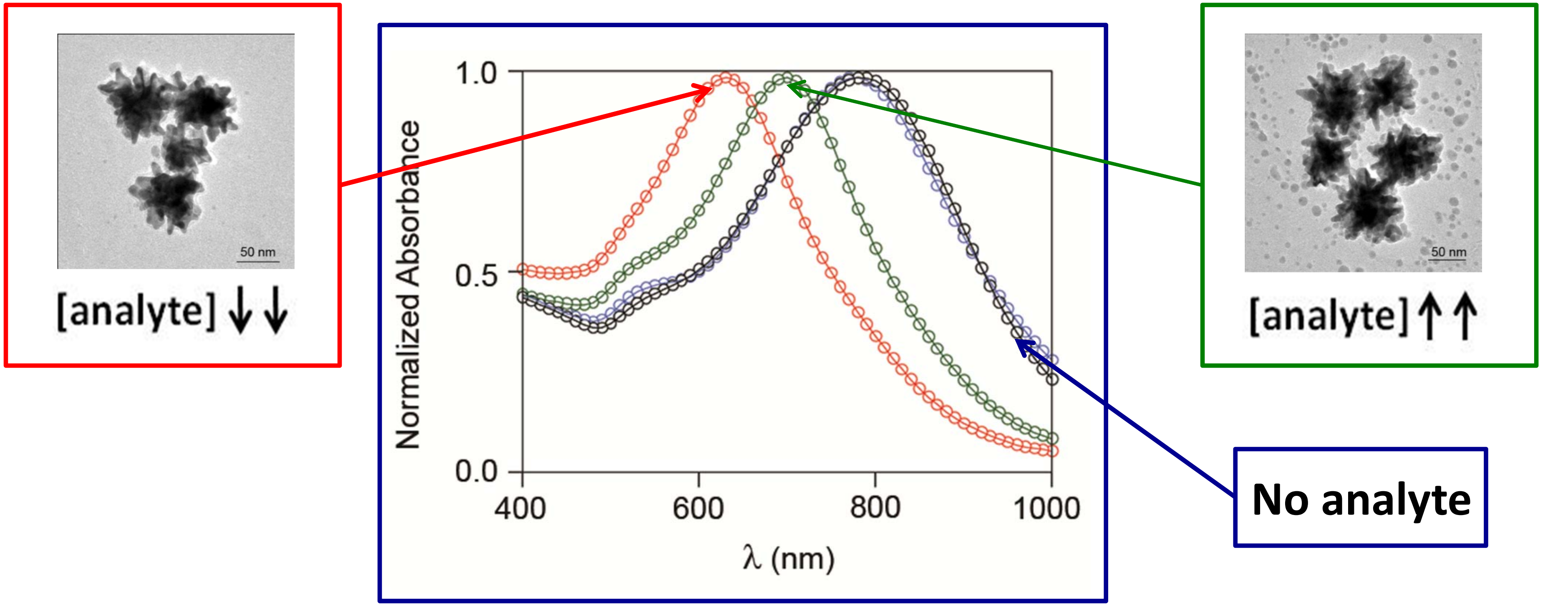
Nanosensors: Gold Nanostars



Redefining the limit of detection:
“Inverse sensitivity”

Silver coating around the transducer

Nucleation of silver nanocrystals in solution

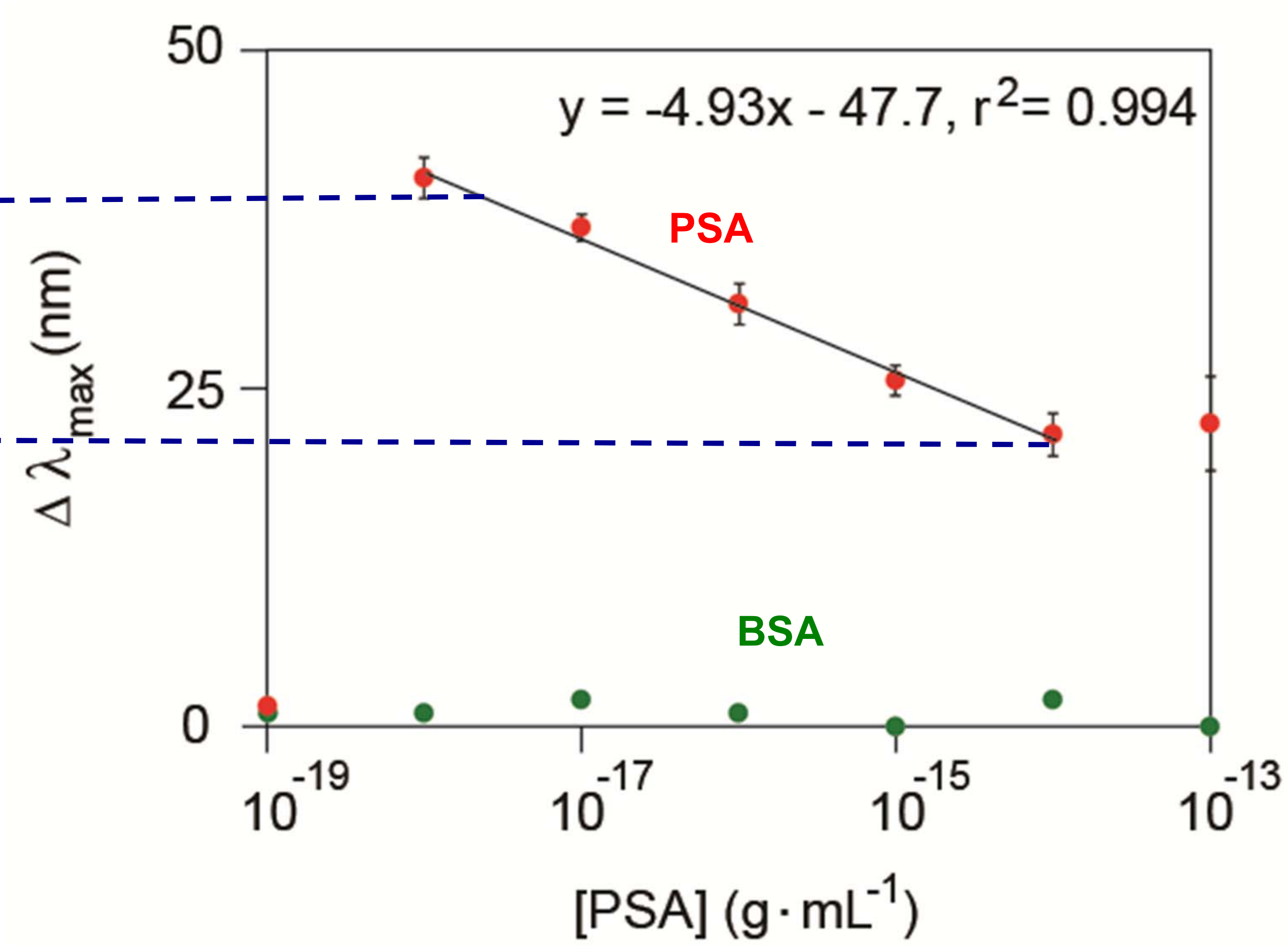


As the concentration of analyte decreases, the signal increases!

Rodríguez-Lorenzo *et al., Nature Mater.* **2012**, *11*, 604

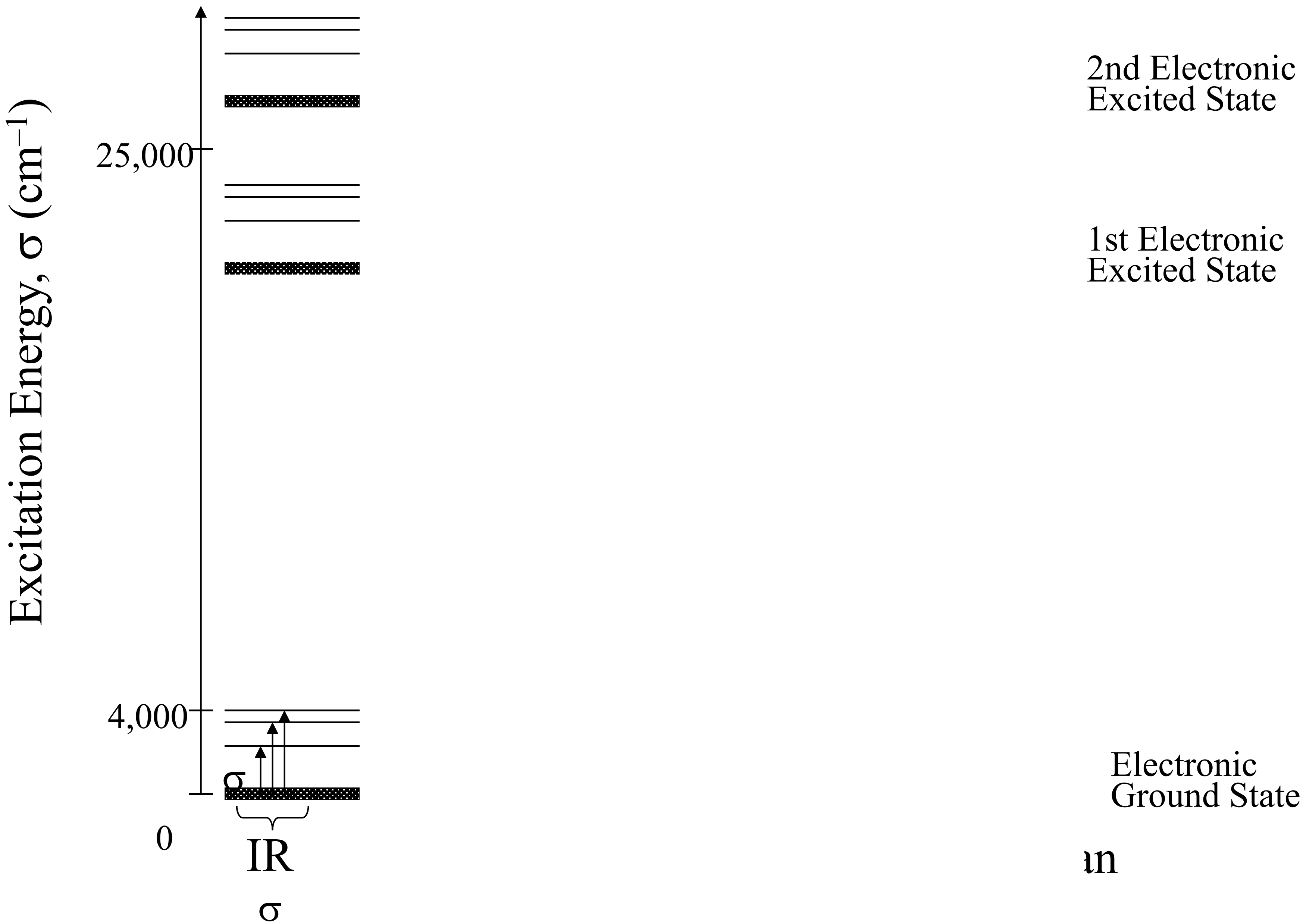
Ultrasensitive detection of PSA in serum

Negative slope:
<u>Inverse Sensitivity</u>

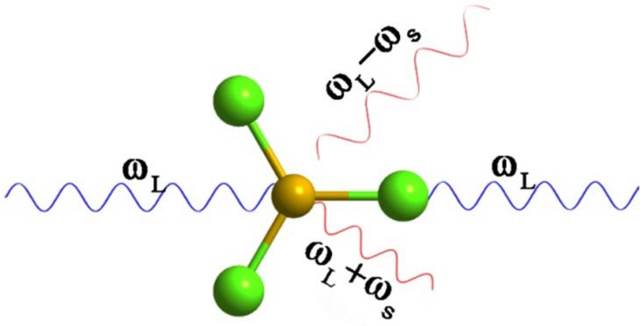


Rodríguez-Lorenzo *et al.*, *Nature Mater.* **2012**, *11*, 604 (col. **Molly Stevens**)

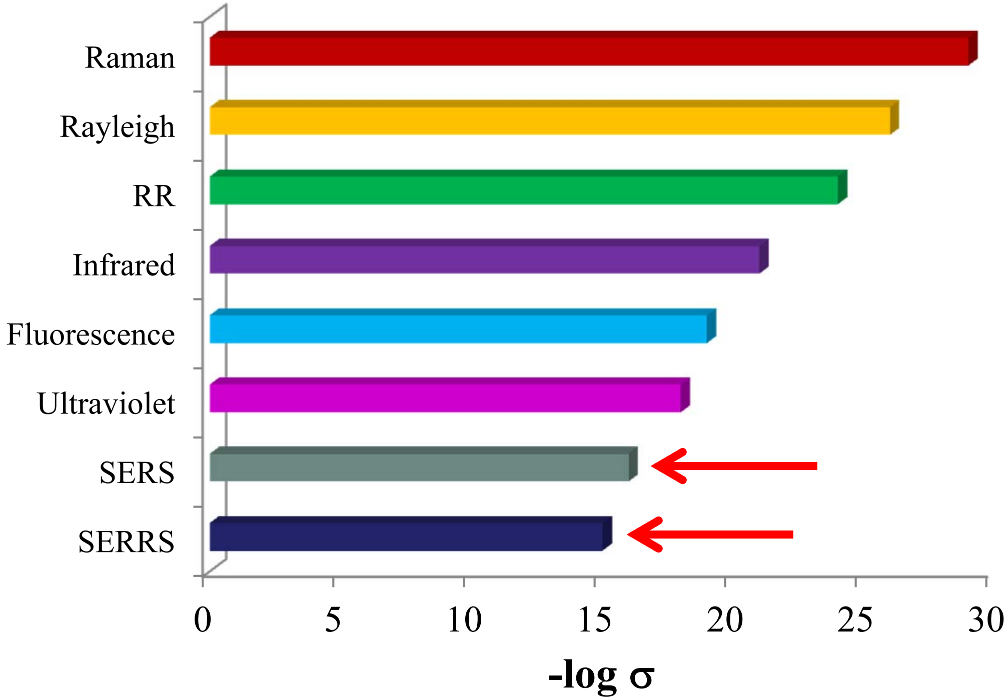
Raman scattering



Raman scattering



Extremely inefficient:
1 in 10^8 incident photons are scattered inelastically.



R. Aroca, *Surface-Enhanced Vibrational Spectroscopy* . Wiley **2006**

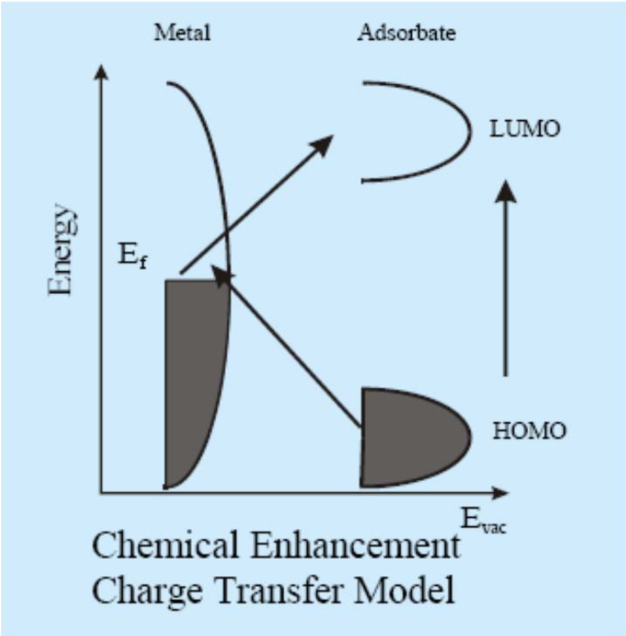
RAMAN SPECTRA OF PYRIDINE ADSORBED AT A SILVER ELECTRODE

M. FLEISCHMANN, P.J. HENDRA and A.J. McQUILLAN
Department of Chemistry, The University, Southampton SO9 5NH, UK

Received 27 February 1974

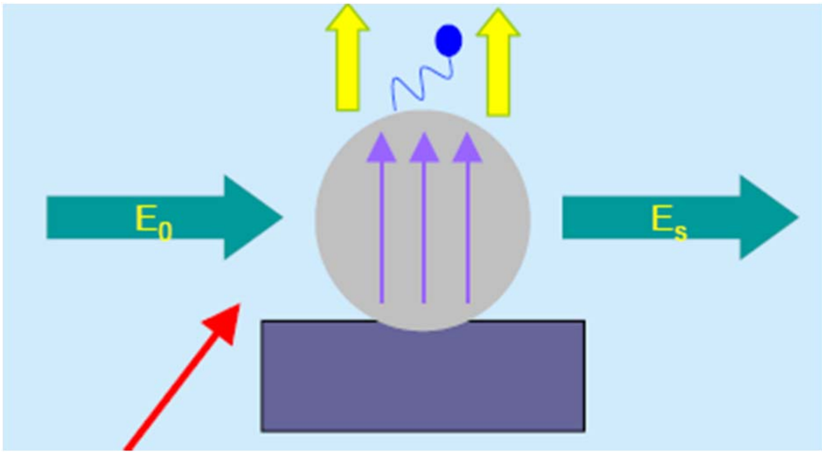
Raman spectroscopy has been employed for the first time to study the role of adsorption at electrodes. It has been possible to distinguish two types of pyridine adsorption at a silver electrode. The variation in intensity and frequency of some of the bands with potential in the region of the point of zero charge has given further evidence as to the structure of the electrical double layer; it is shown that the interaction of adsorbed pyridine and water must be taken into account.

The Chemical Effect



Otto et al., Surf. Sci. Lett., 1980, 92, A50

Electromagnetic Mechanism (EM)

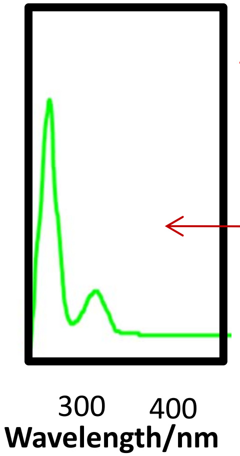


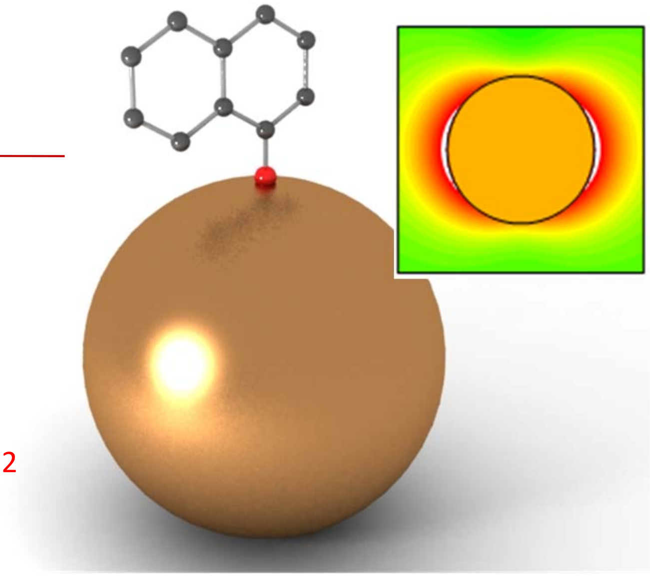
Jeanmarie & Van Duyne, J. Electroanal. Chem. 1977, 84, 1
Albrecht & Creighton, J. Am. Chem. Soc. 1977, 99, 5215
Moskovits, J. Chem. Phys. 1978, 69, 4159

Surface Enhanced Raman Scattering

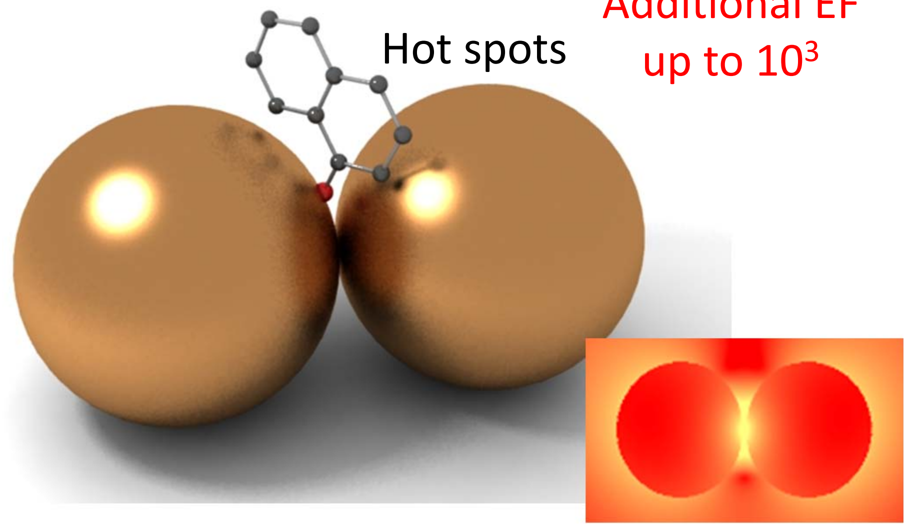
Bioapplications:
Alvarez-Puebla & L-M, *Small* **2010**, *6*, 604

Jeanmarie & Van Duyne, *J. Electroanal. Chem.* **1977**, *84*, 1
Albrecht & Creighton, *J. Am. Chem. Soc.* **1977**, *99*, 5215
Moskovits, *J. Chem. Phys.* **1978**, *69*, 4159



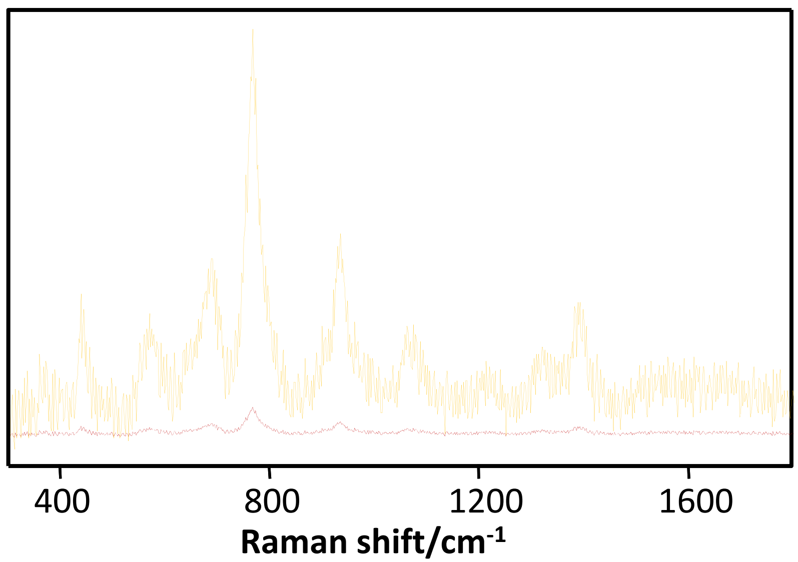


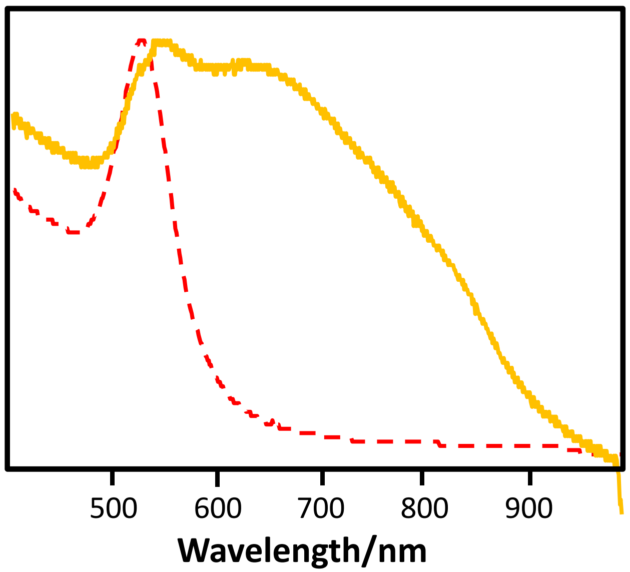
Additional EF up to 10^3



EF up to 10^{12}

Average SERS



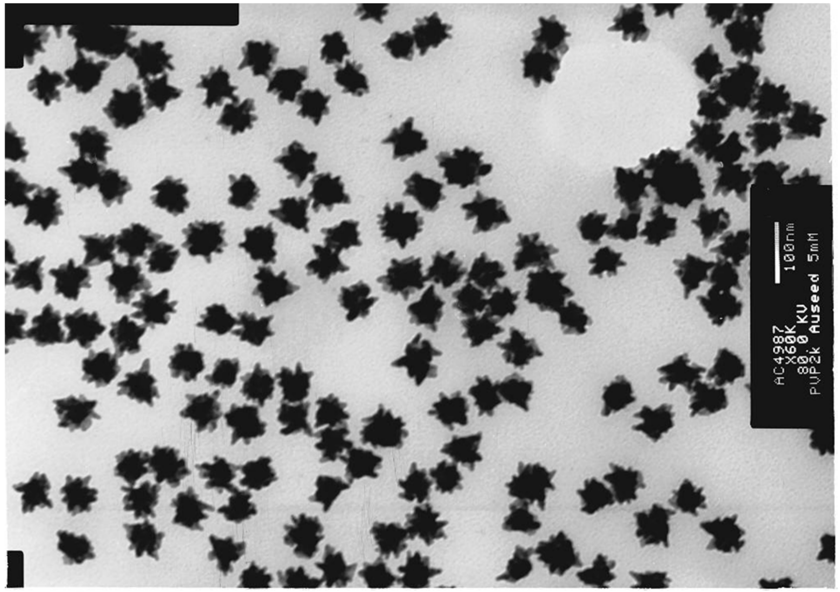


SERS as Analytical Tool

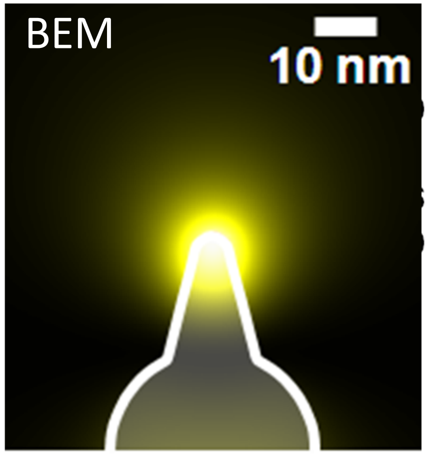
- Selective
  (spectroscopic fingerprint)
- Sensitive
  (single molecule detection)
- Fast (ms)
- Portable
  (no sample preparation)
- Encoding capability
  (spatial resolution)
- General application

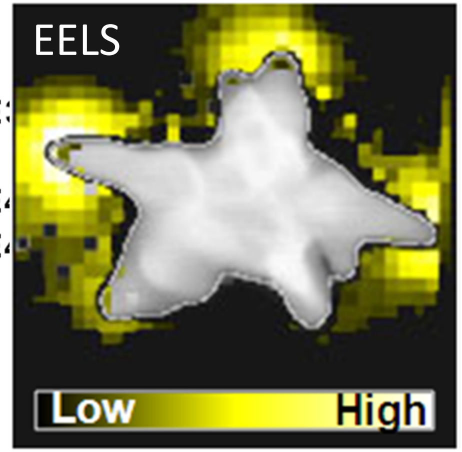
- Low reproducibility
- Low substrate uniformity
- Requires direct contact of analyte with metal surface

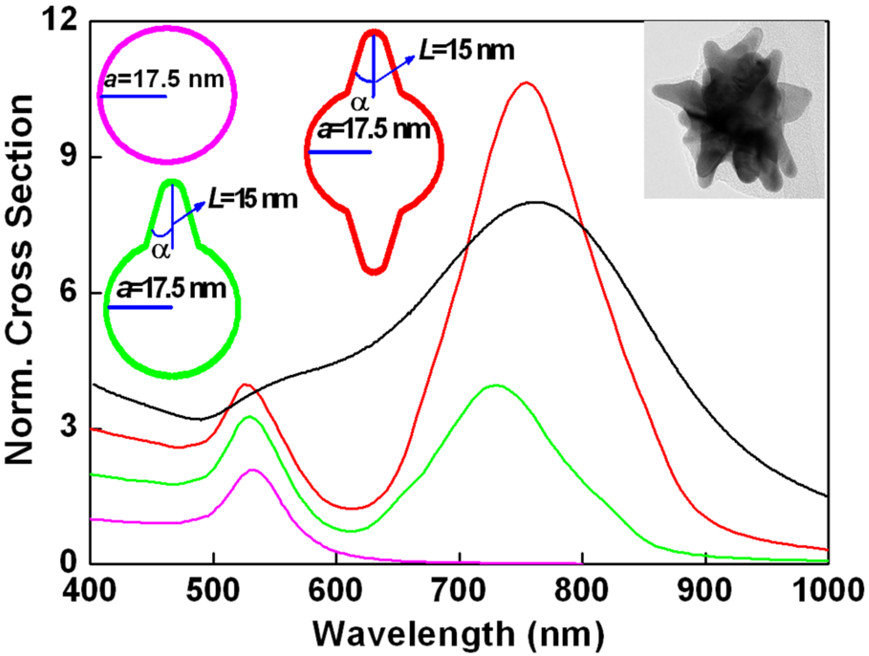
Au nanostars as SERS substrates

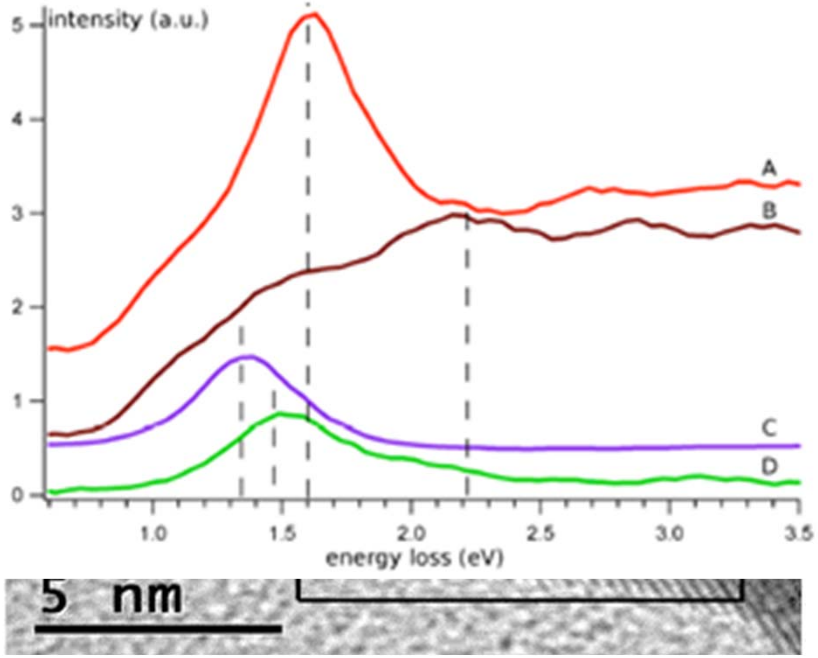


Nature Phys. **2007**, *3*, 348; Rodríguez-Lorenzo, *JACS* **2009**, *131*, 4616



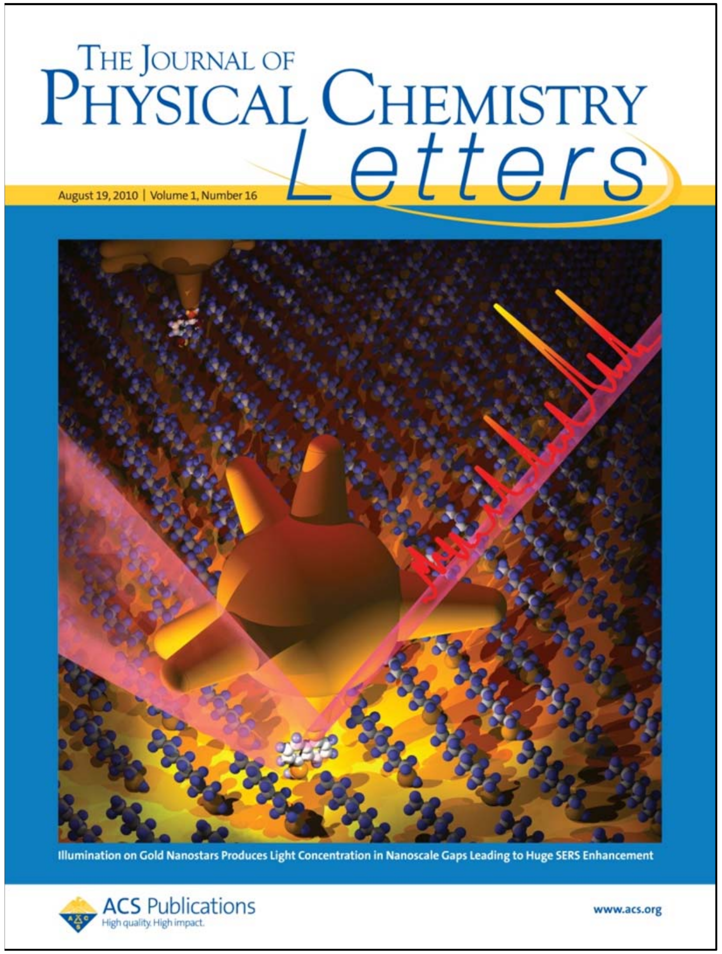


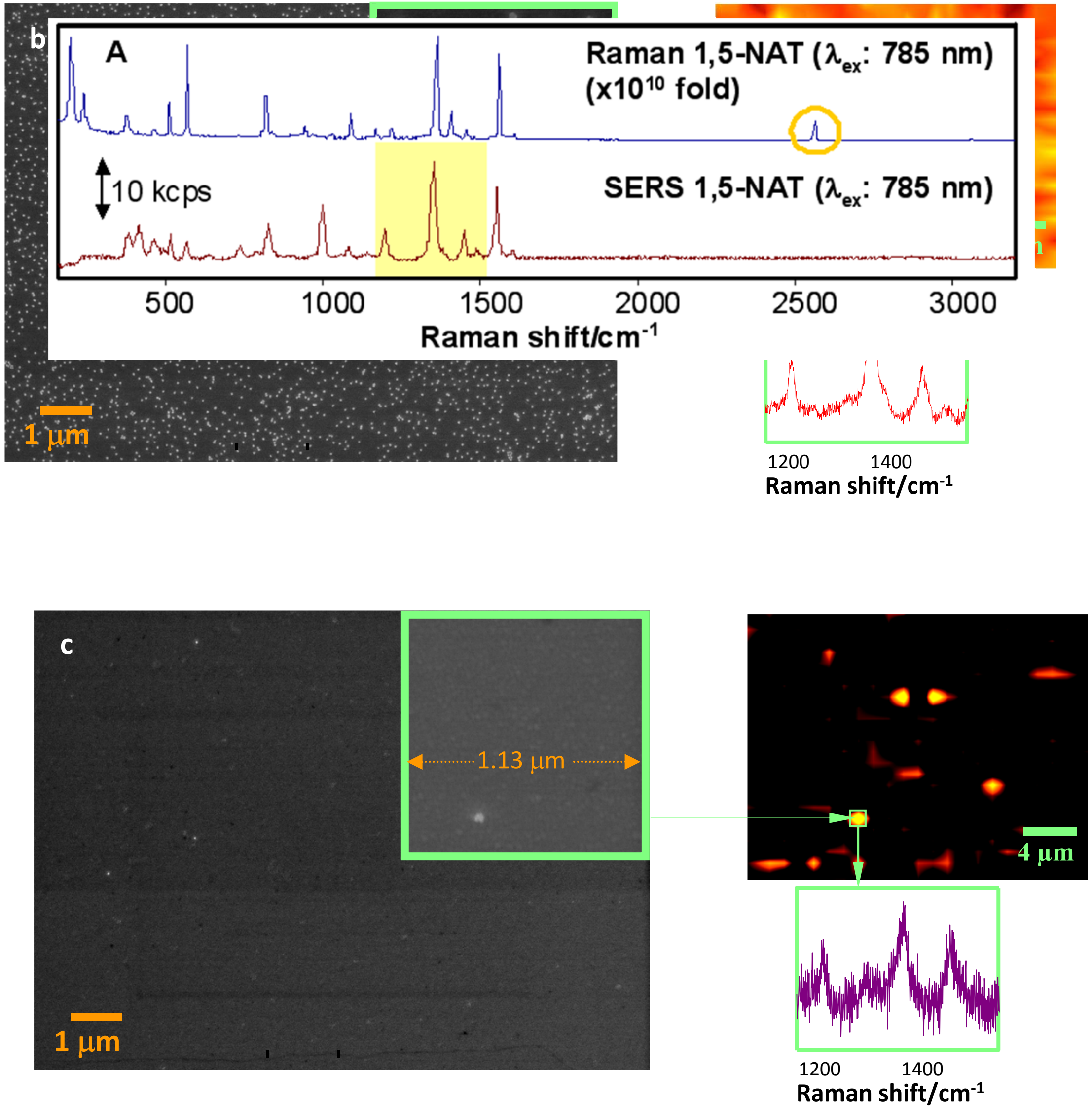




Kumar et al., *Nanotechnology* **2008**, *19*, 015606

Single molecule detection using nanostars



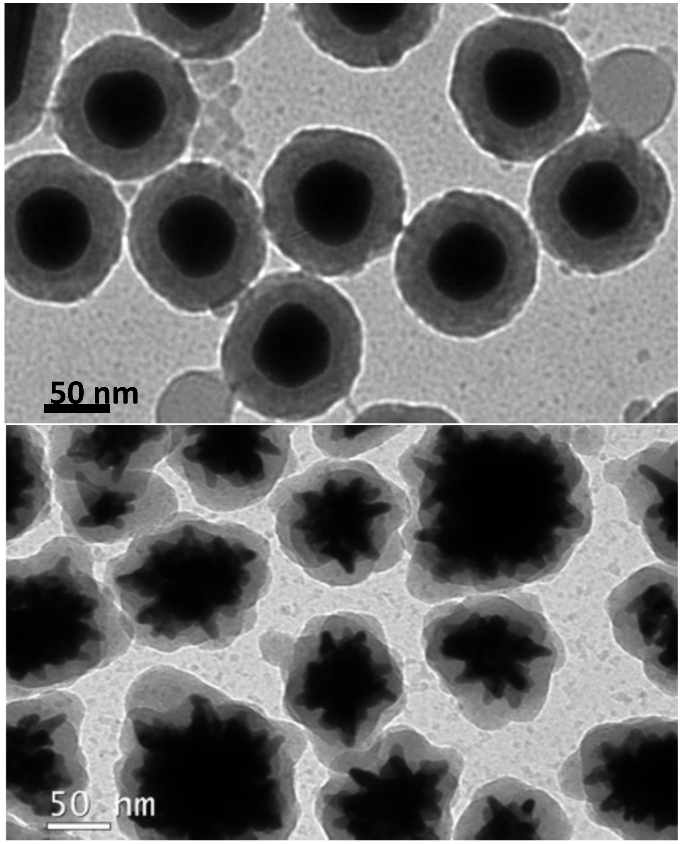


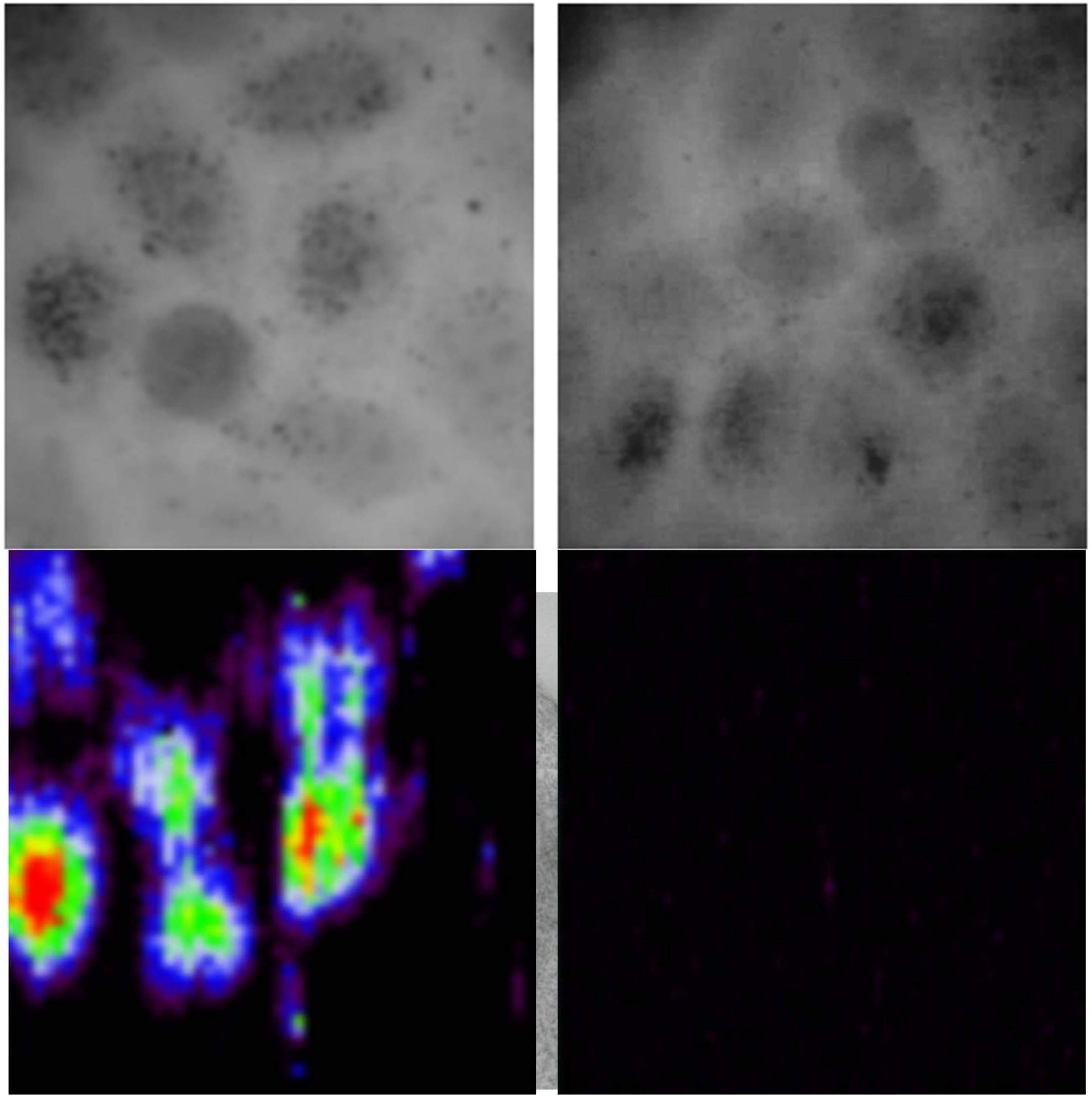
$$EF = \frac{I_{SERS} / N_{surf}}{I_{Raman} / N_{vol}} \approx 10^{10}$$

Alvarez-Puebla et al., *J. Phys. Chem. Lett.* **2010**, *1*, 2428

Rodríguez-Lorenzo et al., *J. Am. Chem. Soc.* **2009**, *131*, 4616

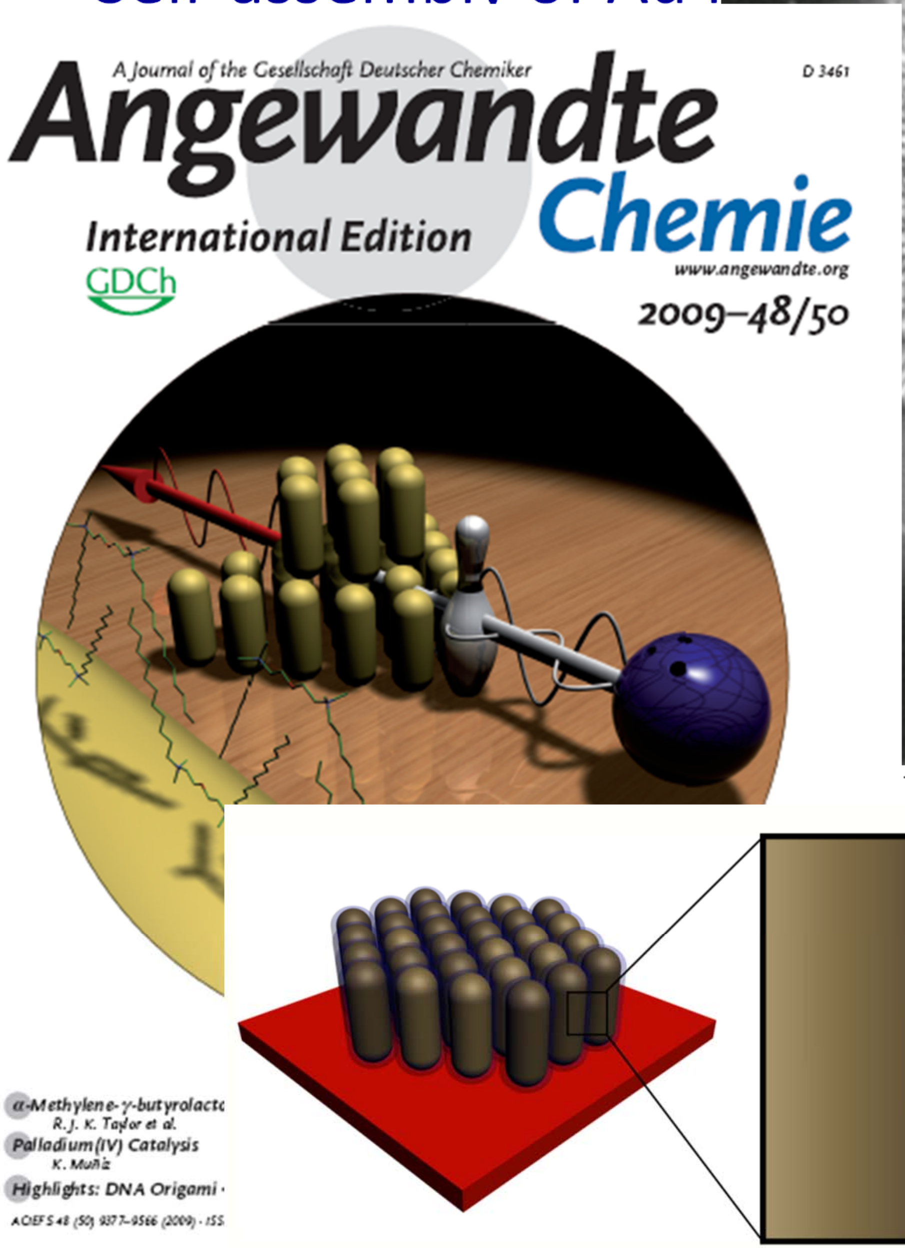
Enhanced SERS imaging using Au@SiO_2 nanostars

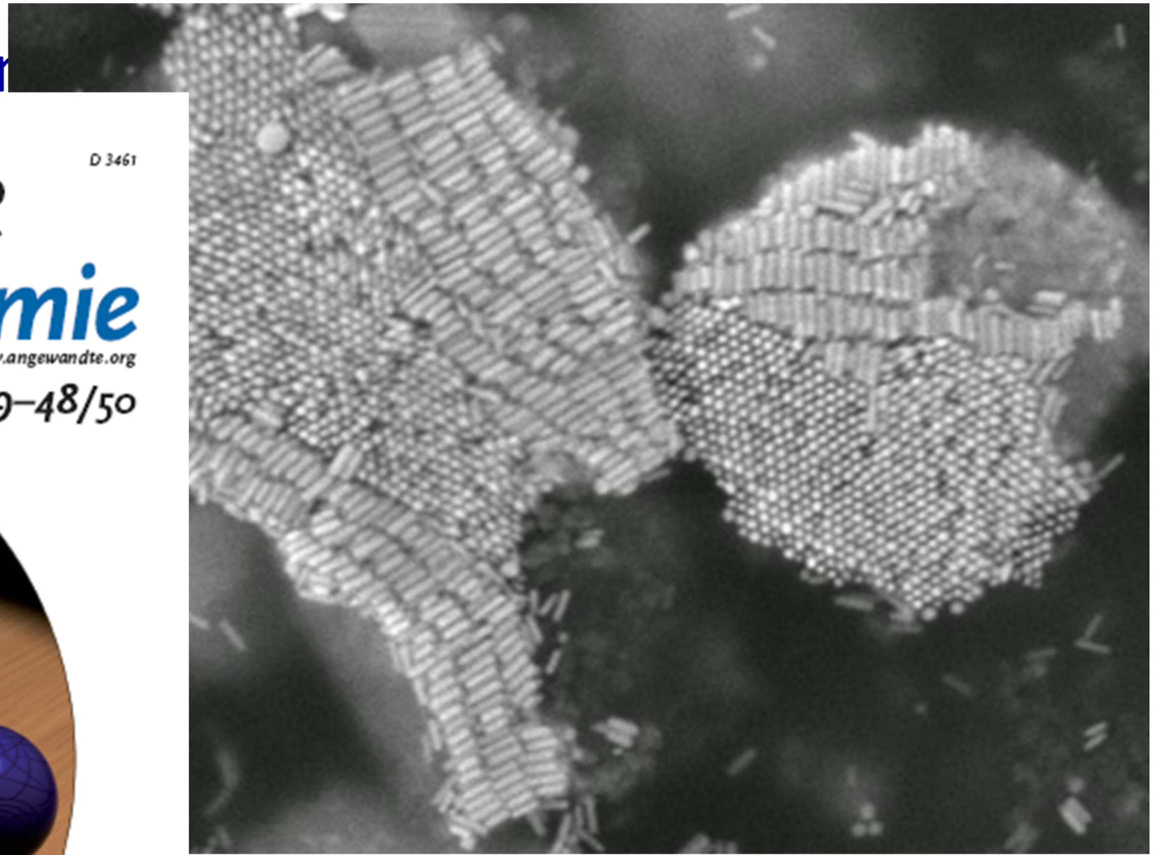


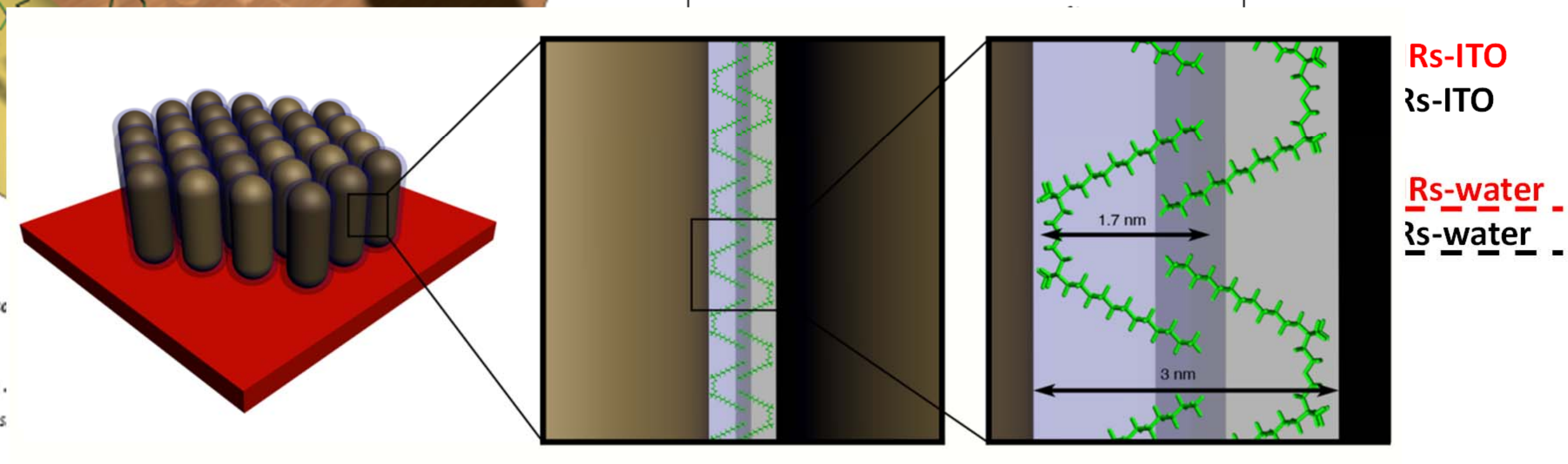


Rodríguez-Lorenzo et al., *Int. Biol.* **2011**, *9*, 922

Self-assembly of Au r

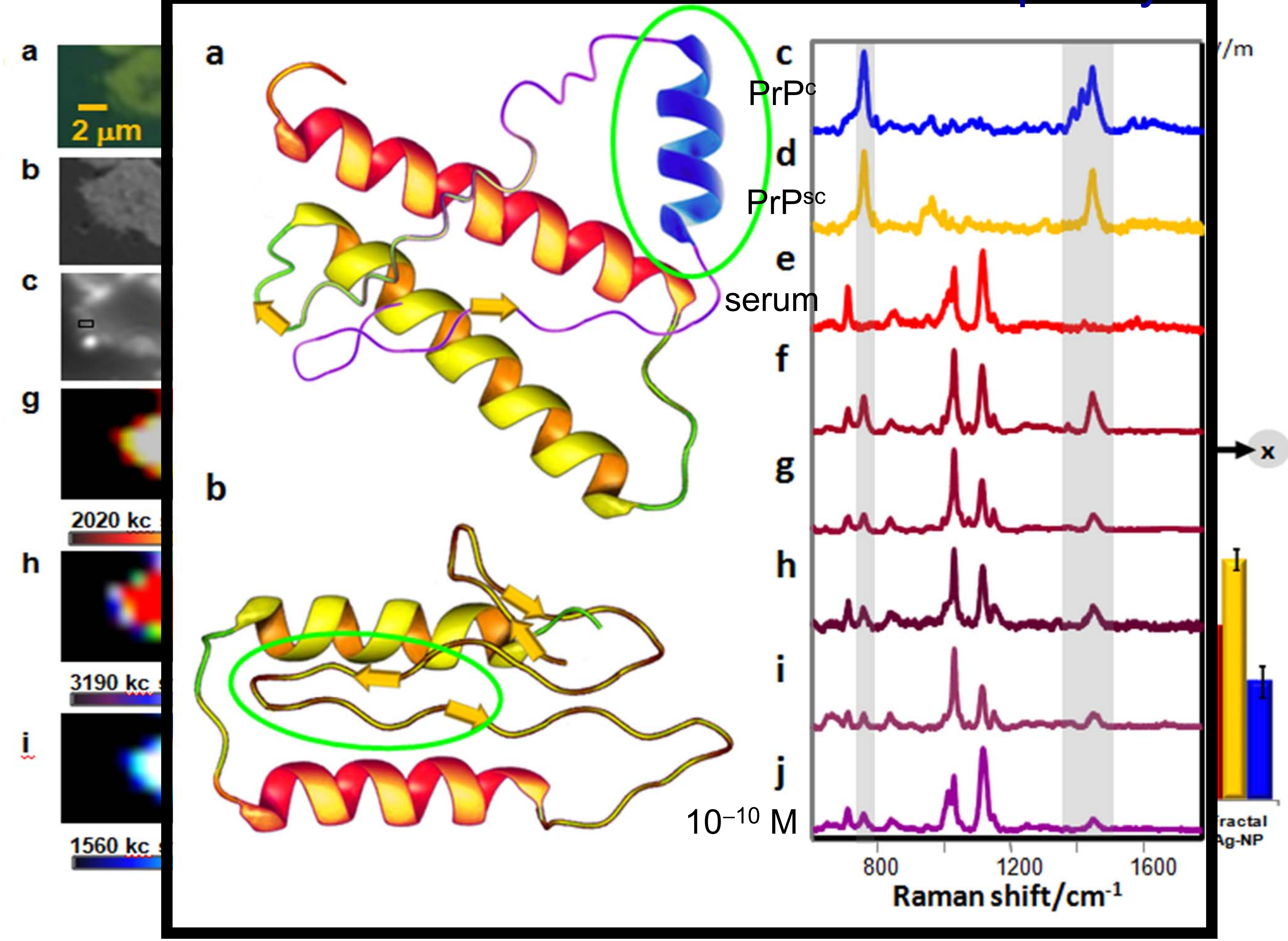






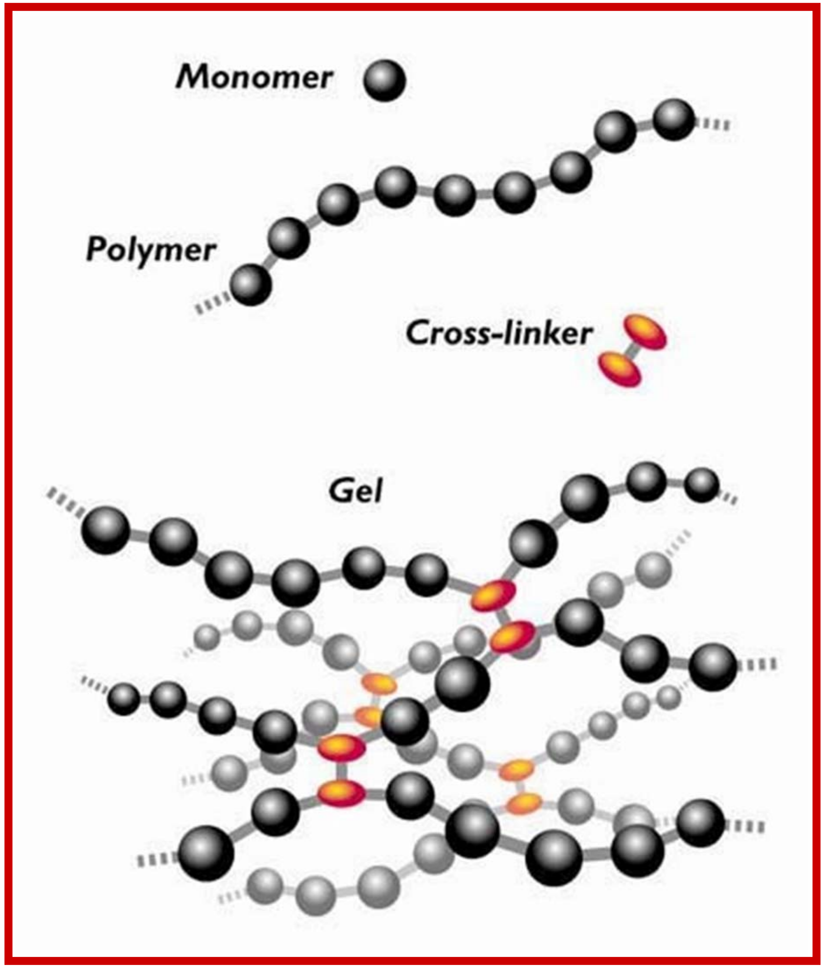
Guerrero-Martínez et al., *Angew. Chem. Int. Ed.* **2009**, 48, 9484

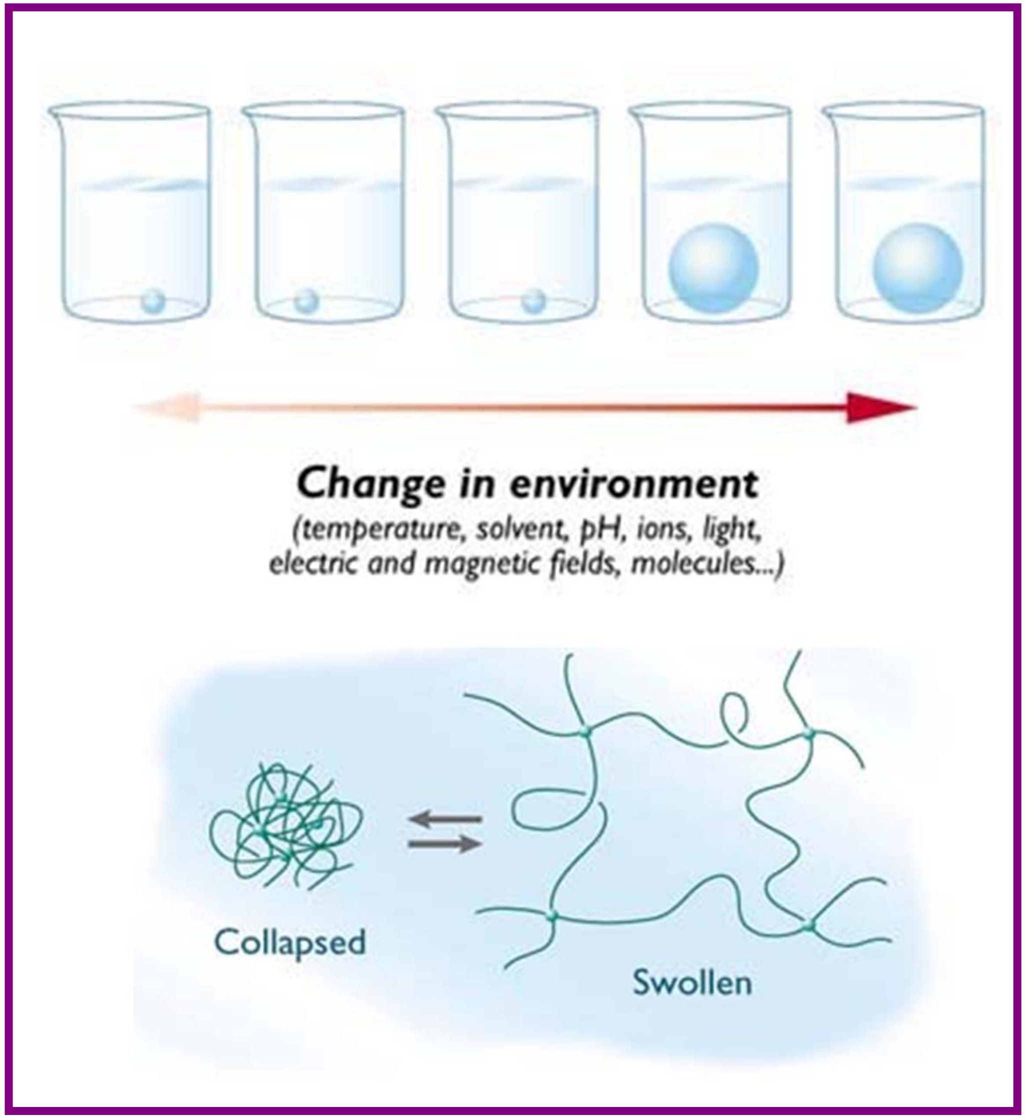
Extended Nanoantenna Efects in NR Supercrystals



Alvarez-Puebla et al., *PNAS* **2011**, *108*, 8157; *Nano Today* **2012**, *7*, 6

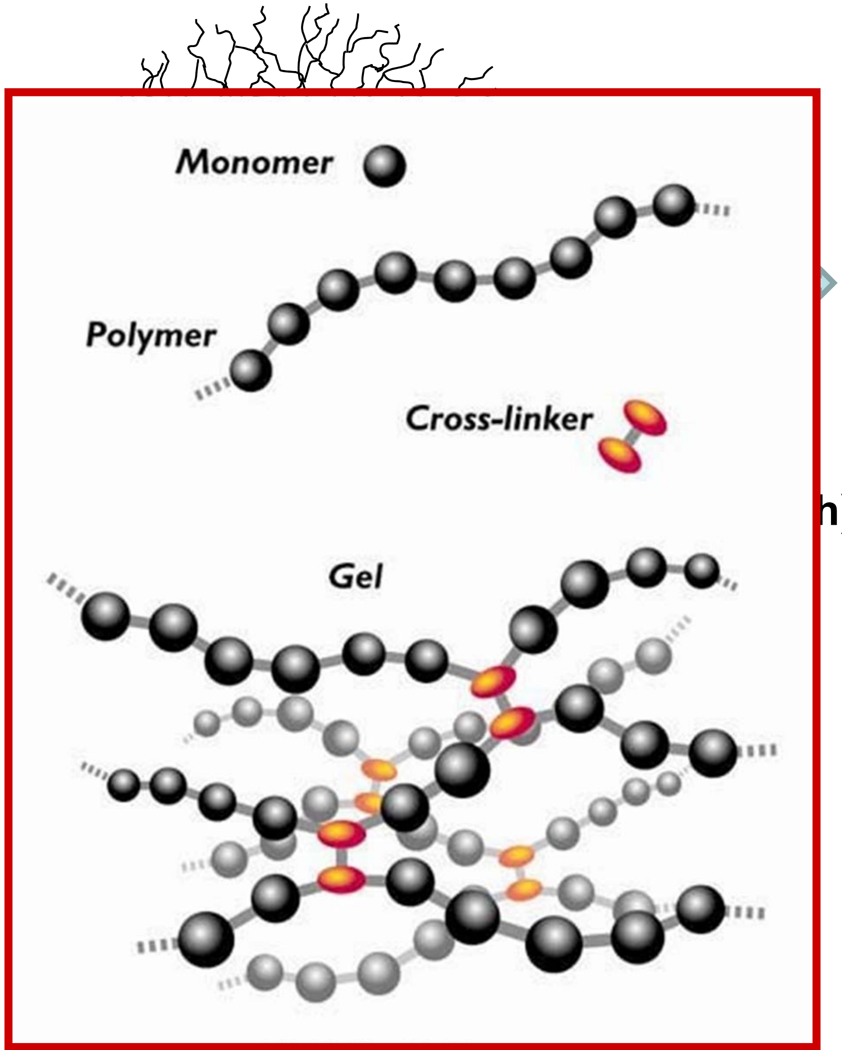
Smart hydrogels

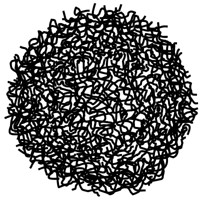


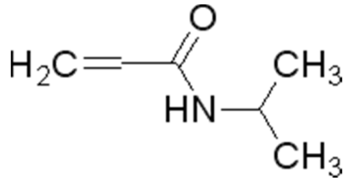


pNIPAM microgels: thermoresponsive colloids

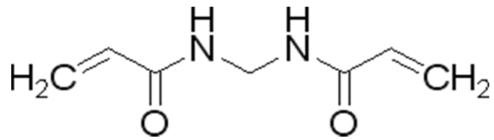
Karg & Hellweg, *Curr. Op. Colloid Interface Sci.* **2009**, *14*, 438-450

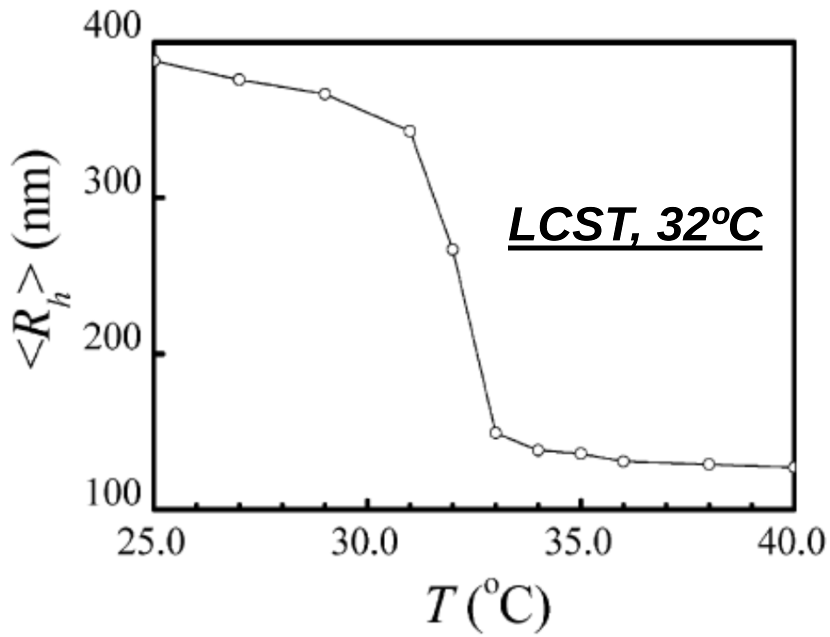






N-Isopropylacrylamide
(NIPAM monomer)



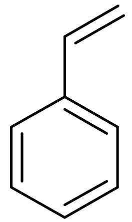


pH and temperature
responsive microgels

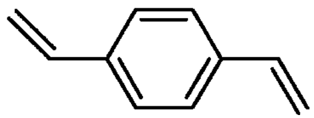
Karg et al. *Langmuir* **2009**, *25*, 3163

Core-Shell Systems. Synthesis of Au@pNIPAM microgels

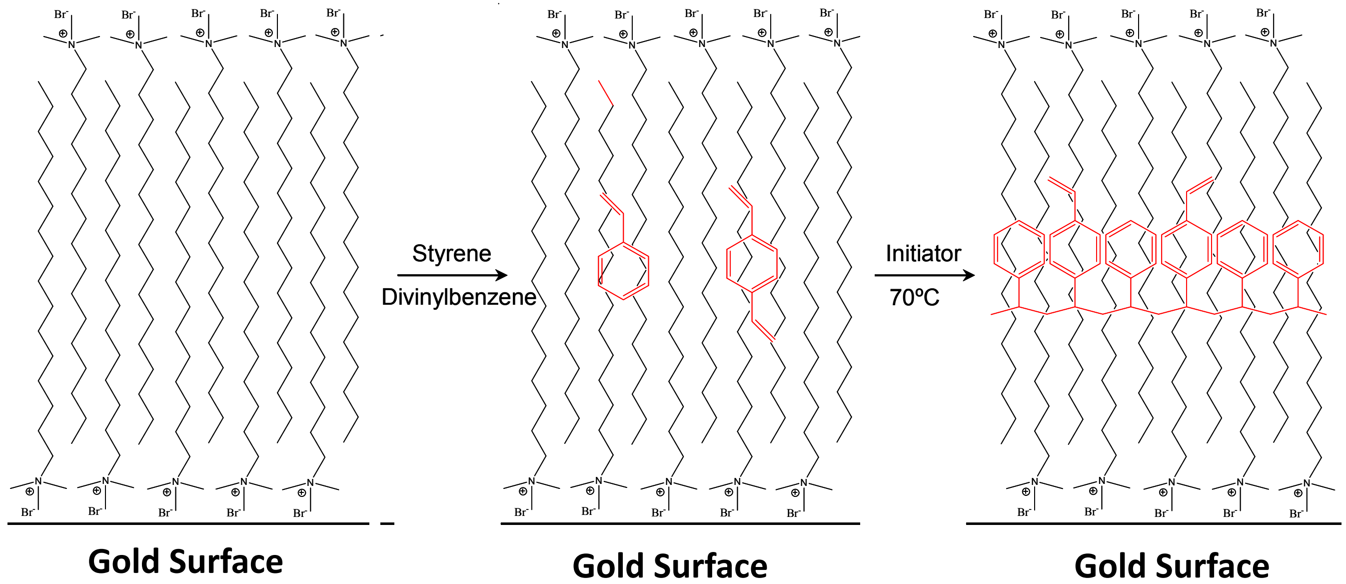
CTAB promoted polystyrene coating of the particles

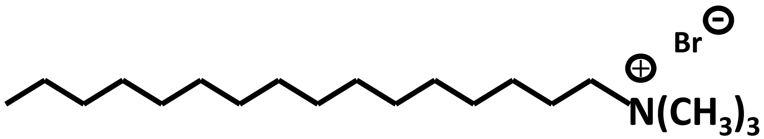


Styrene

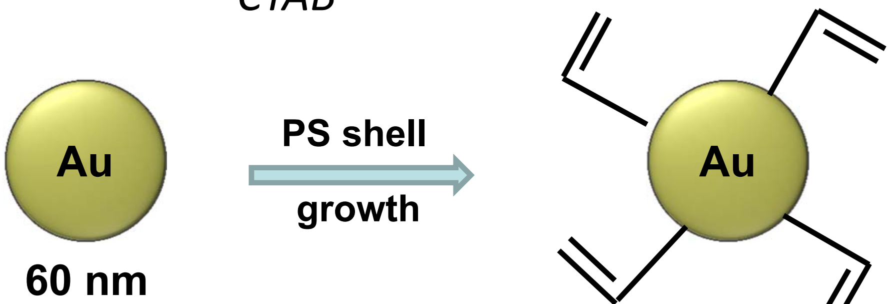


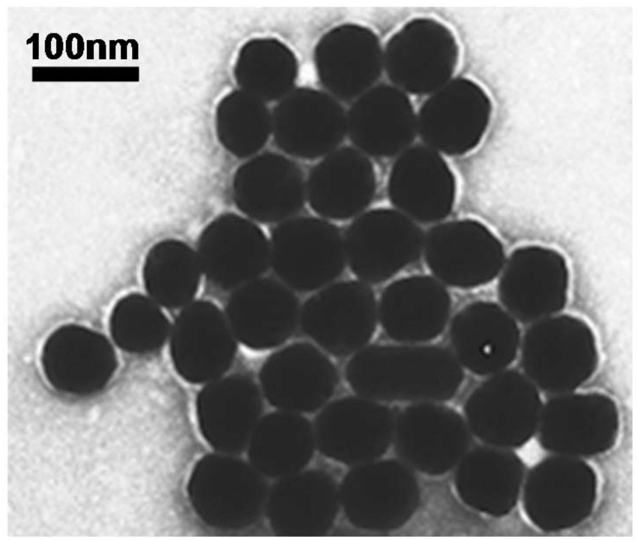
Divinylbenzene





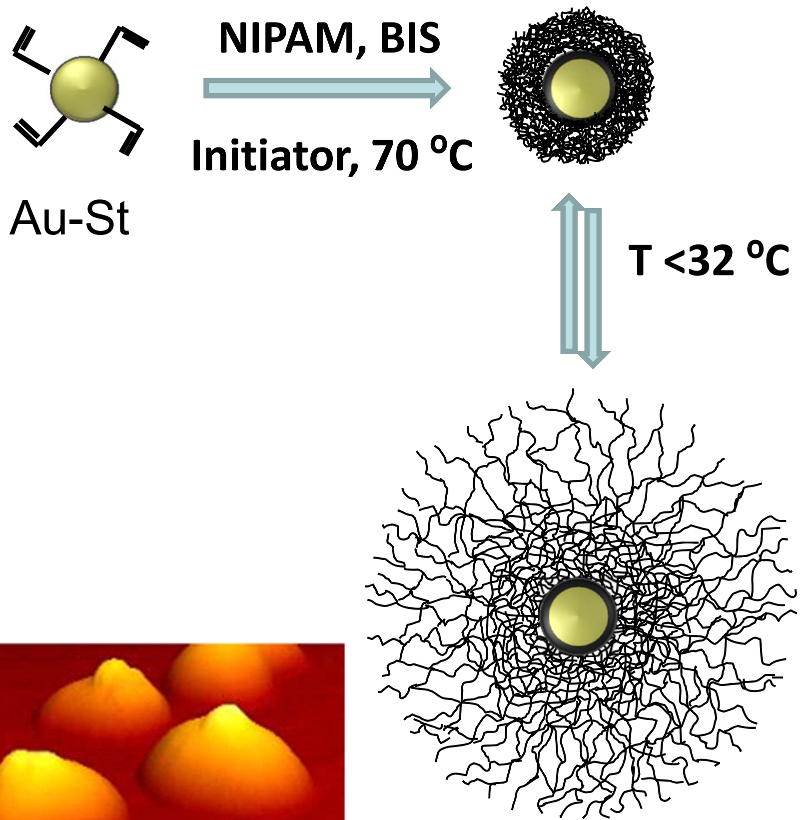
CTAB

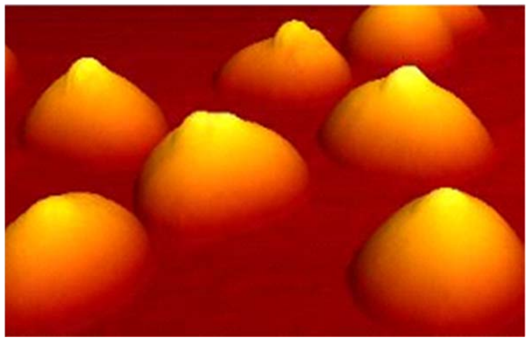


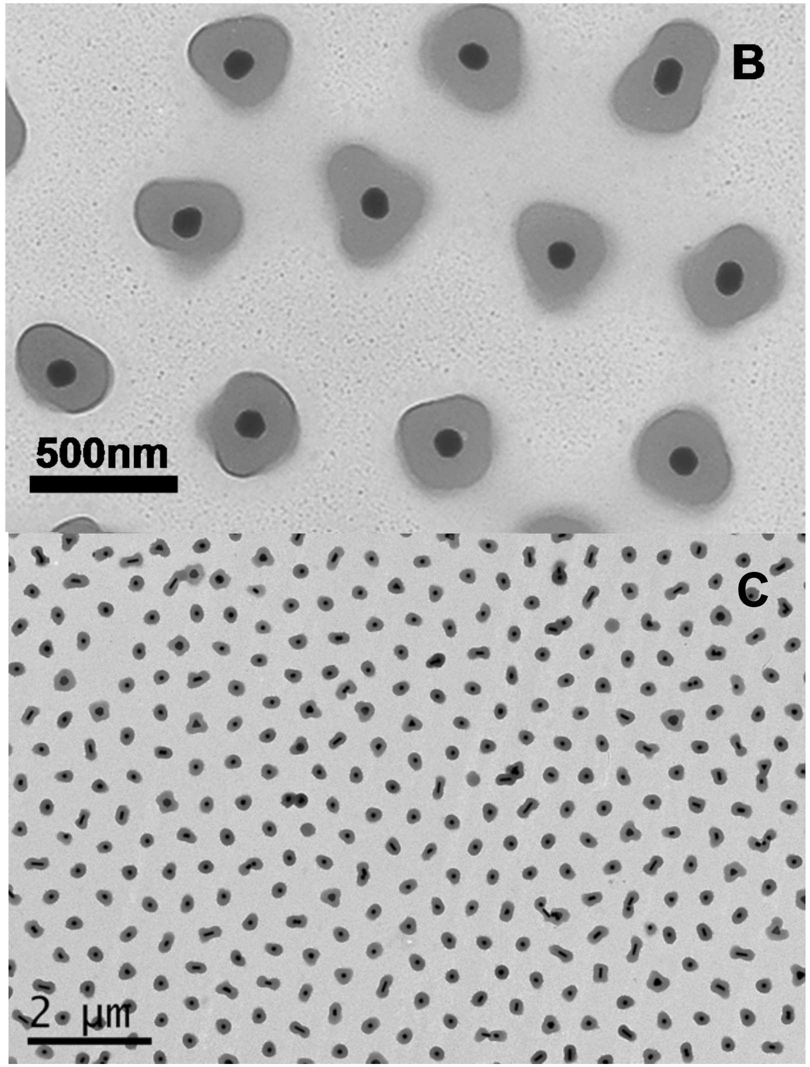


O'Haver et al. *Langmuir* **1994**, 10, 2588-2593

Au@PNIPAM core-shell particles

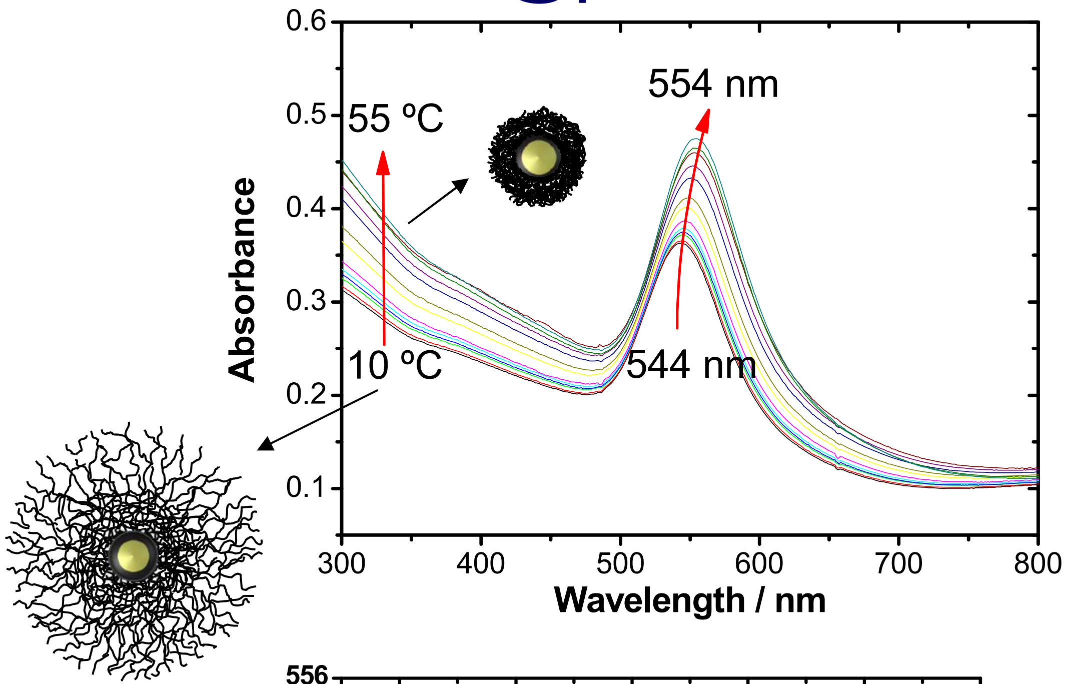


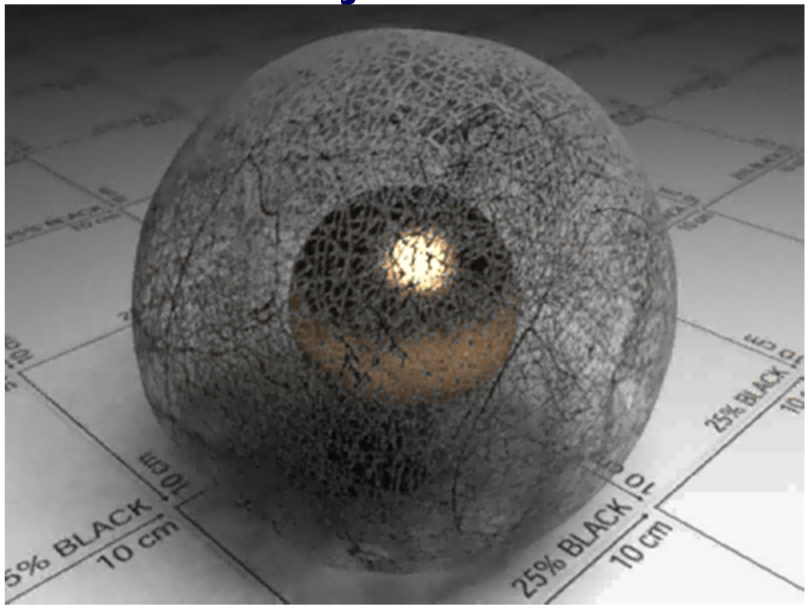


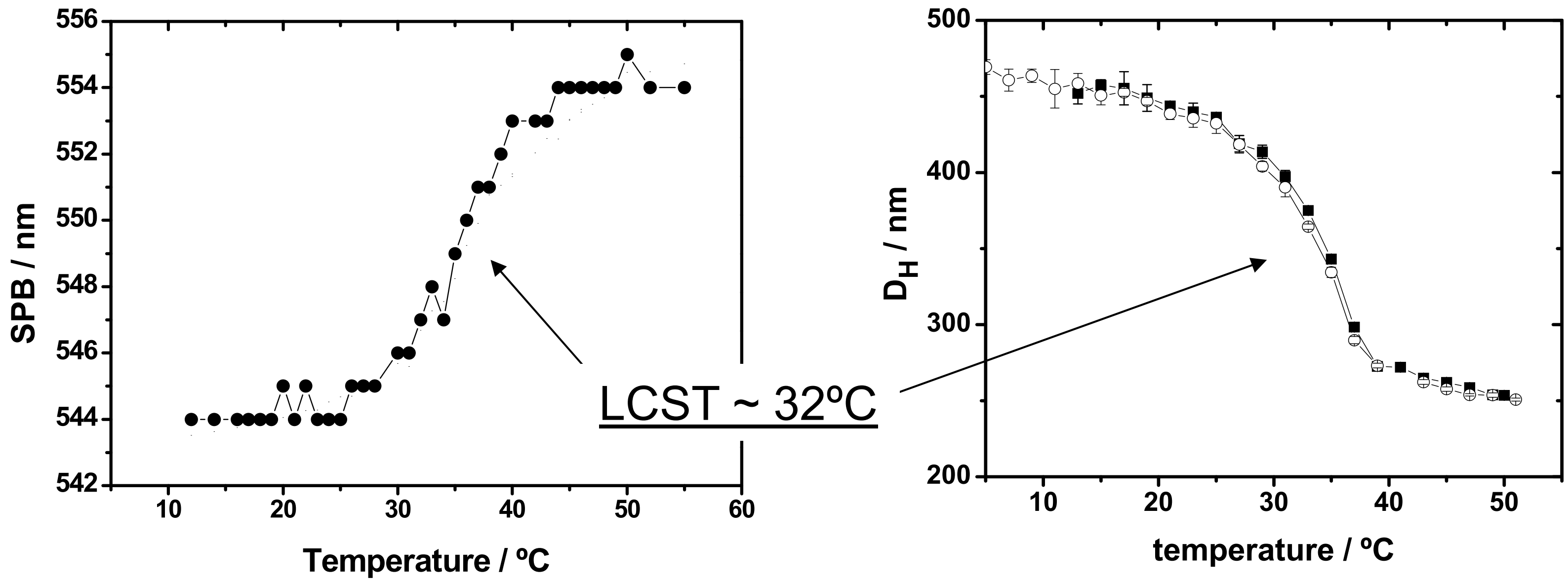


Contreras-Cáceres et al., *Adv. Mater.* **2008**, *20*, 1666

Au@pNIPAM: thermal sensitivity

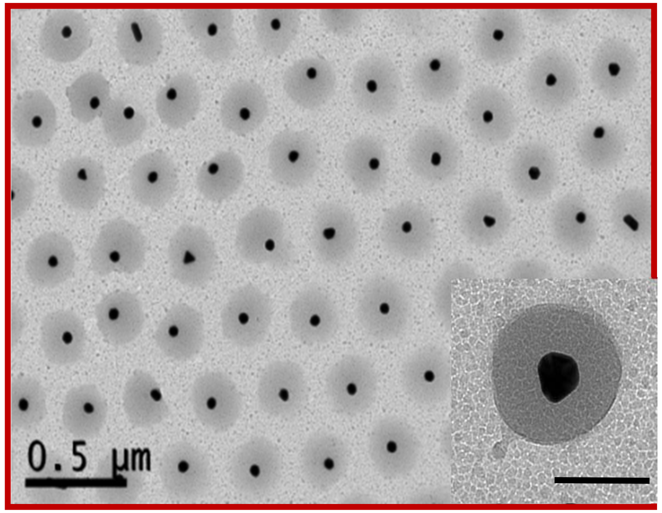


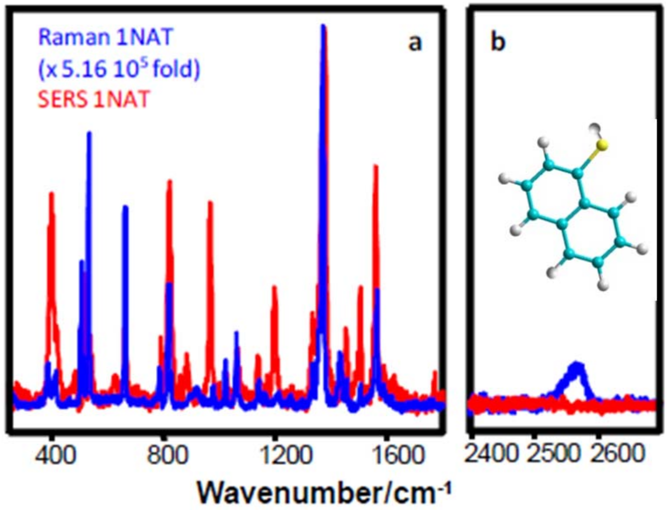


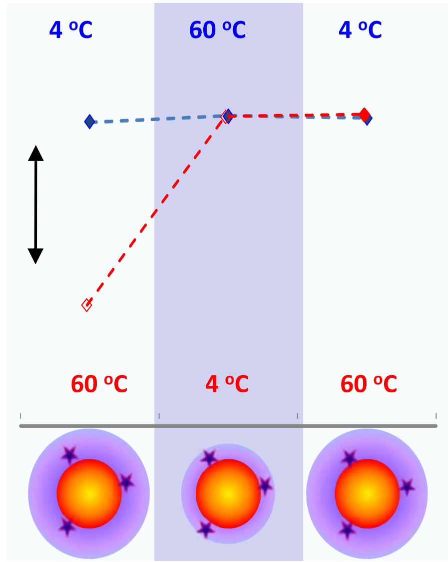


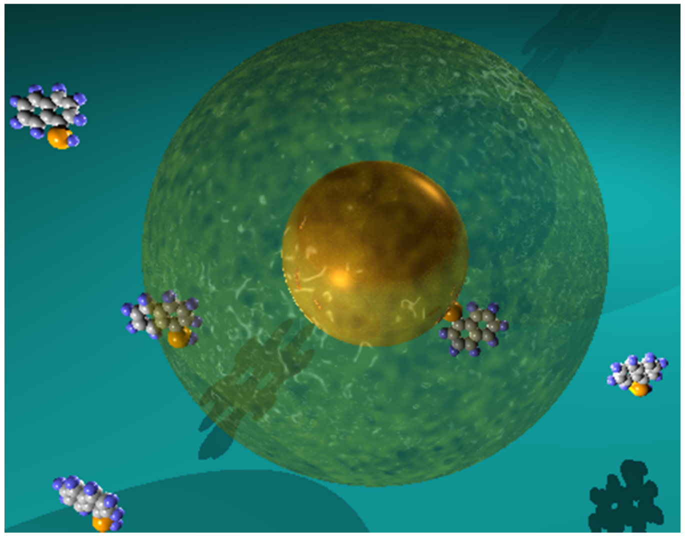
Contreras-Cáceres et al., *Adv. Mater.* **2008**, *20*, 1666

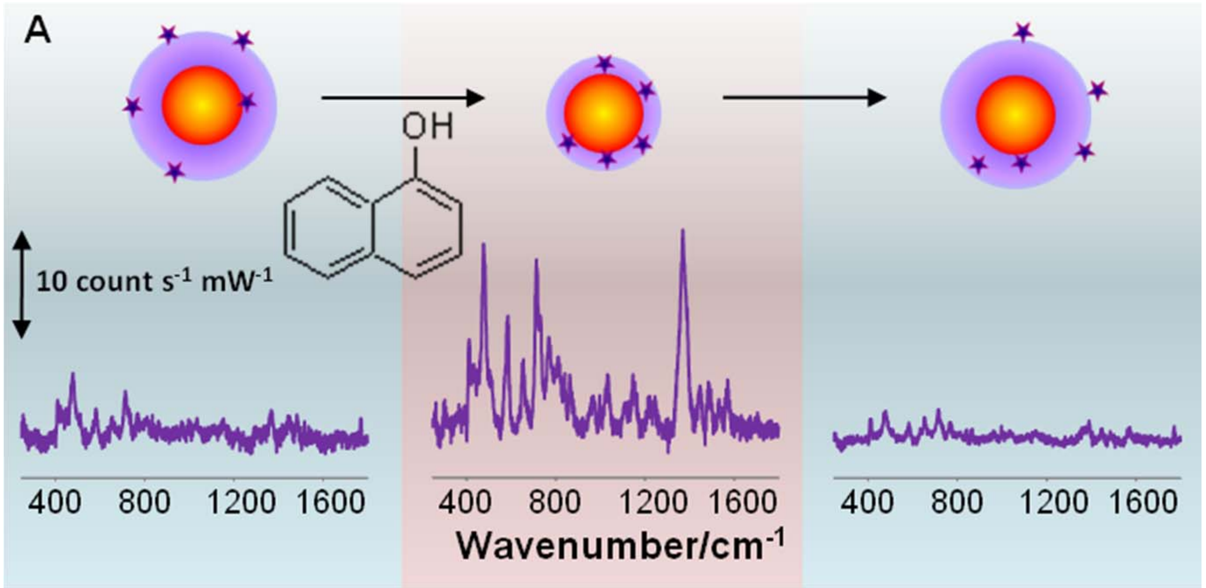
Au@PNIPAM traps for SERS detection





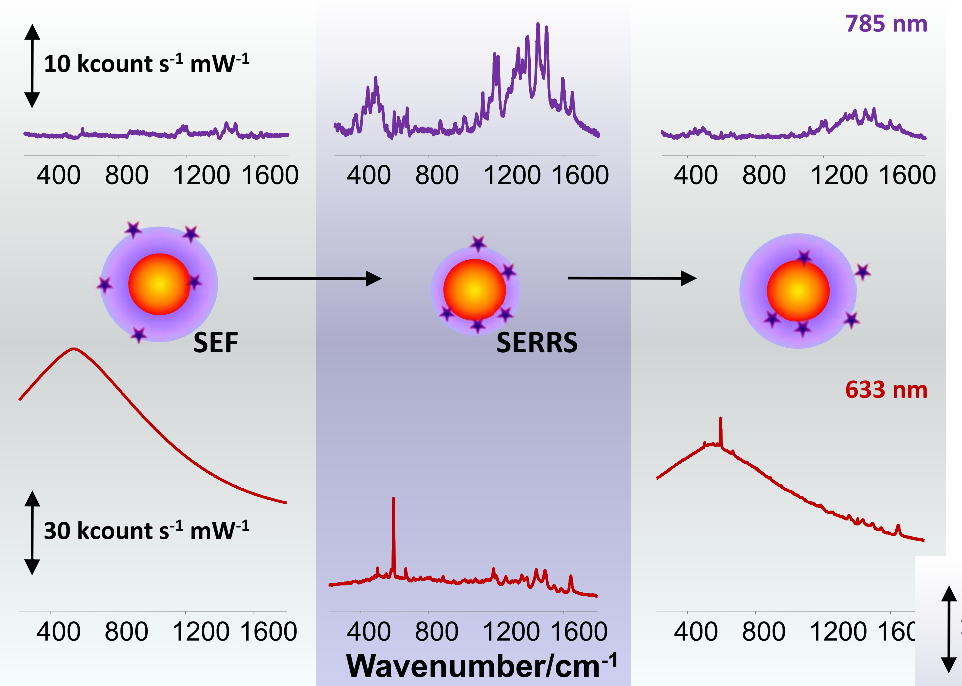


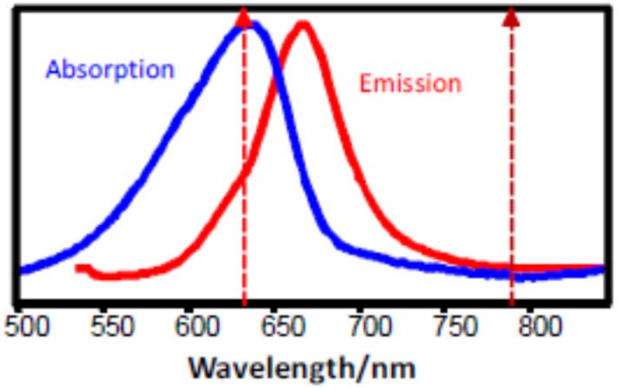


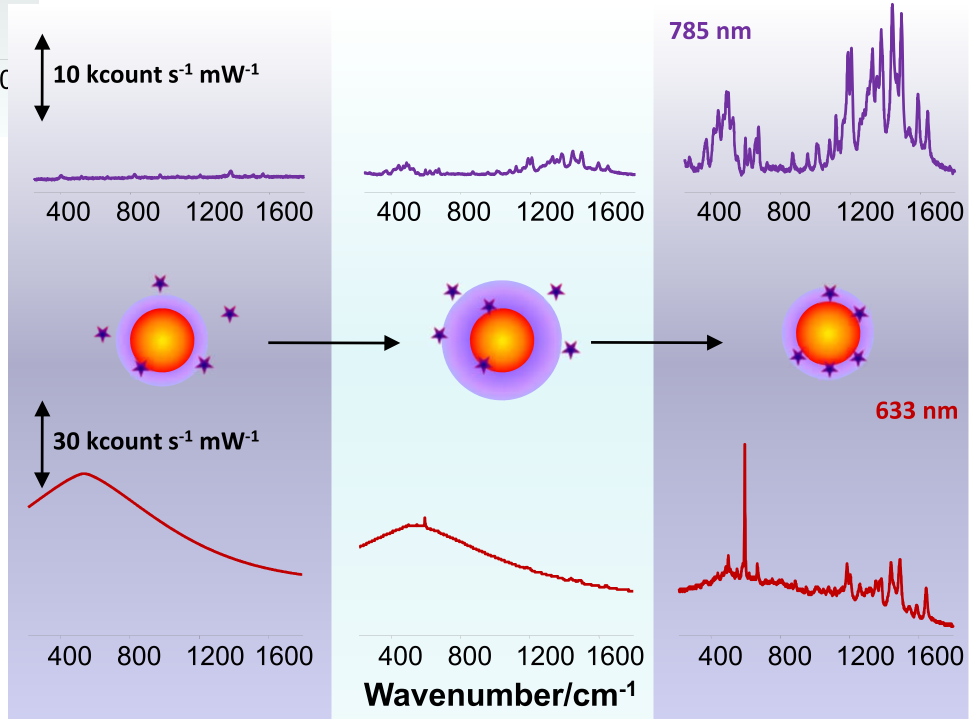


Alvarez-Puebla et al., *Angew. Chem. Int. Ed.* **2009**, *48*, 138

SEF/SERRS modulation







Alvarez-Puebla et al., *Angew. Chem. Int. Ed.* **2009**, *48*, 138

CONCLUSIONS

- Colloid Chemistry is a powerful tool for tailoring nanoparticle size and shape, allowing LSPR tuning
- Nanoplasmonics can be exploited in different ways for (bio)detection
- Functional SERS platforms can be conveniently designed through tailored synthesis and assembly

Colloid Chemistry Group

U. Melbourne
U.Michigan
Rice Univ.
U. Bayreuth
U. Münster
FU Berlin
Max-Planck Inst.
U. Hamburg
FZ Jülich
U. Marburg
U. Fribourg
U.Lyon
CNRS
UC London
U. Cambridge
U. Liverpool
Imperial College
U. Cardiff
U. Trieste
U. Antwerp
KU Leuven
U. Utrecht
U. Minho
U. Aveiro
FORTH
U. Buenos Aires
R.B.Inst.Zagreb
CSIC
U. Santiago
U. Almería
U. Valencia
U. Málaga
U. País Vasco
U. Barcelona

SEVENTH FRAMEWORK PROGRAMME

erc

MINISTERIO DE CIENCIA E INNOVACIÓN

XUNTA DE GALICIA

UniversidadeVigo