Surface Enhanced Raman Scattering: Substrate Design and Fabrication

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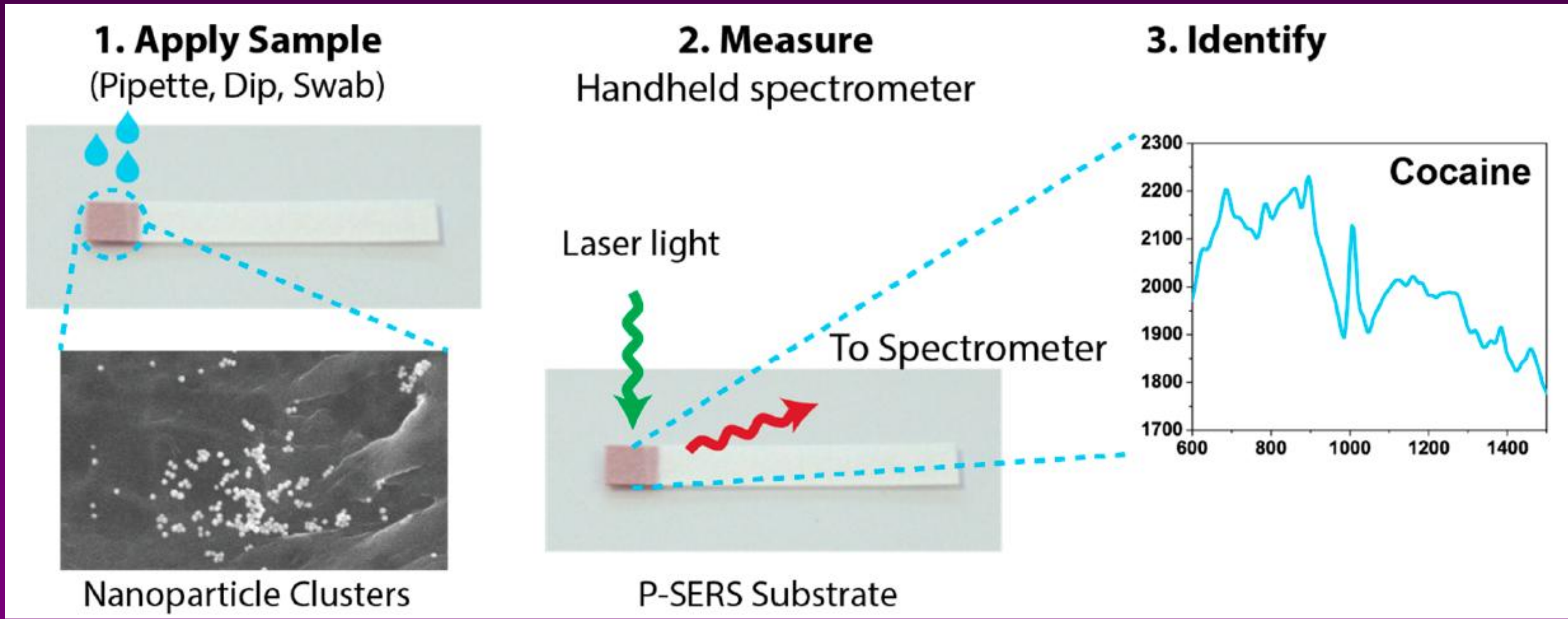
Outline

- SERS principles and applications
- SERS substrates
  - Design
  - Fabrication methods
- Commercial SERS substrates
  - Specification
  - Understanding substrate design and processing
  - Proper substrate choice

Trace detection technologies

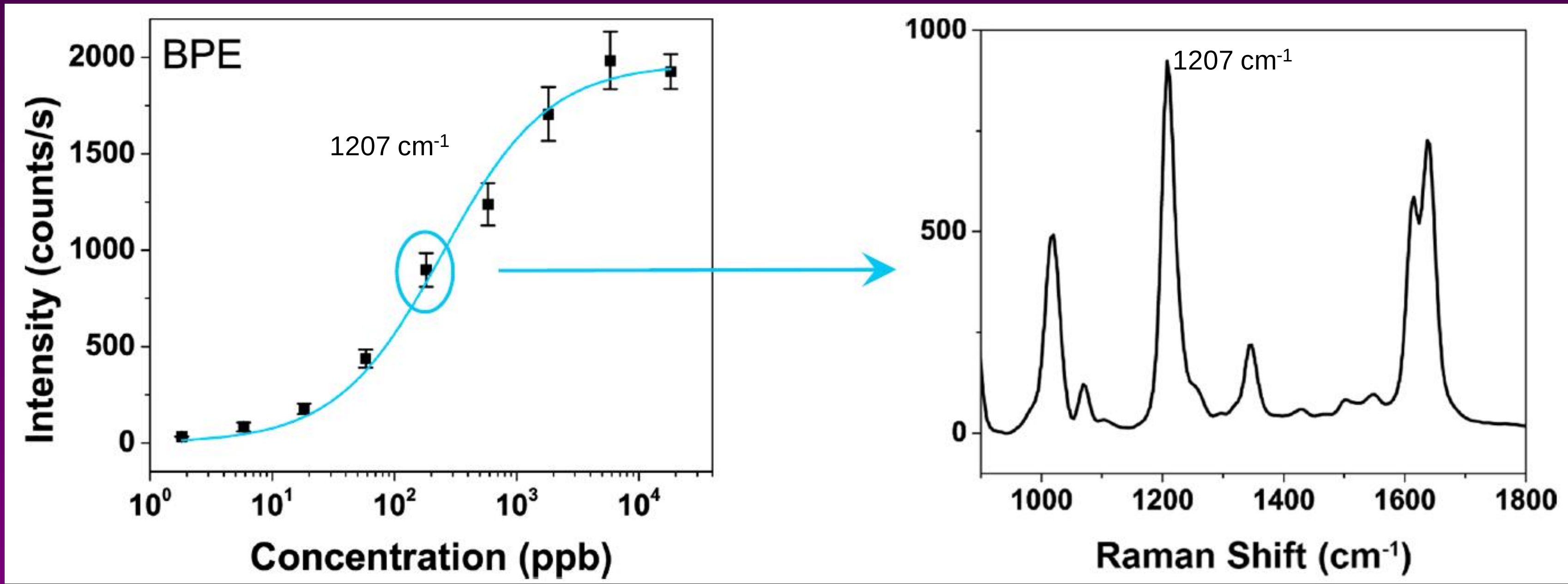
- Mass spectrometry and gas chromatography
  - Cost
  - Size
- Fluorescence spectroscopy
  - Excitation in visible range
  - Requires fluorophore
- SERS
  - Substrate price $10's-$100
  - Sensitivity and repeatability issues

SERS measurements using a substrate



P-SERS™ Technology Technical Paper
Diagnostic anSERS https://www.diagnosticansers.com/technical/

Trace chemical marker detection



BPE (1,2-Bis(4-pyridyl)ethylene)

Diagnostic anSERS https://www.diagnosticansers.com/technical/

SERS advantages

- Can be used with solids, liquids or gases
- No sample preparation needed (KBr, nujol)
- Non-destructive, non-invasive
- Works *in-situ* and *in-vitro* for biological samples
- No vacuum needed
- Works under a wide range of conditions (temperature, pressure)
- Short time scale
- Can work with aqueous solutions
- Glass vials can be used
- Can use down fiber optic cables for remote sampling
- Very small analyzing volume – till single molecule
- Extremely high spatial resolution
- Inexpensive, portable equipment
- Simultaneous detection of multiple sample constituents (multiplexing)

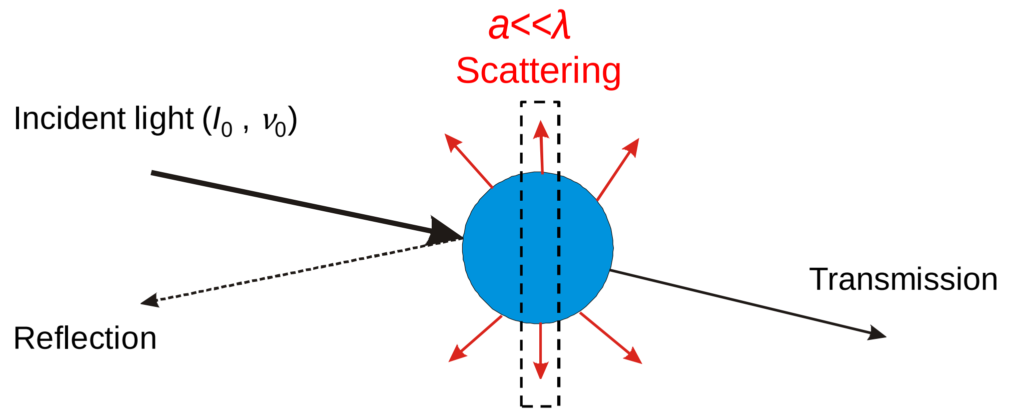
SERS disadvantages

- Cannot be used for metals or alloys
- Problems with quantitative analysis
- Can be swamped by fluorescence from some materials
- Stability and repeatability issues

SERS applications

- Pharmaceutical industry
- Biotech industry
  - Bacteria, DNA and protein detection
  - Intracellular measurements (glucose measurement *in vivo*)
- Food industry
  - Melamine detection in milk
  - Pesticide detection
- Law enforcement and homeland security
  - Explosives detection (DNT)
  - Trace detection of narcotics such as cocaine and heroin
- Anti-counterfeiting (tags)
  - Weakened/inactive counterfeit drugs
  - Counterfeit petrol, perfumes and liquors
- Nanosensors

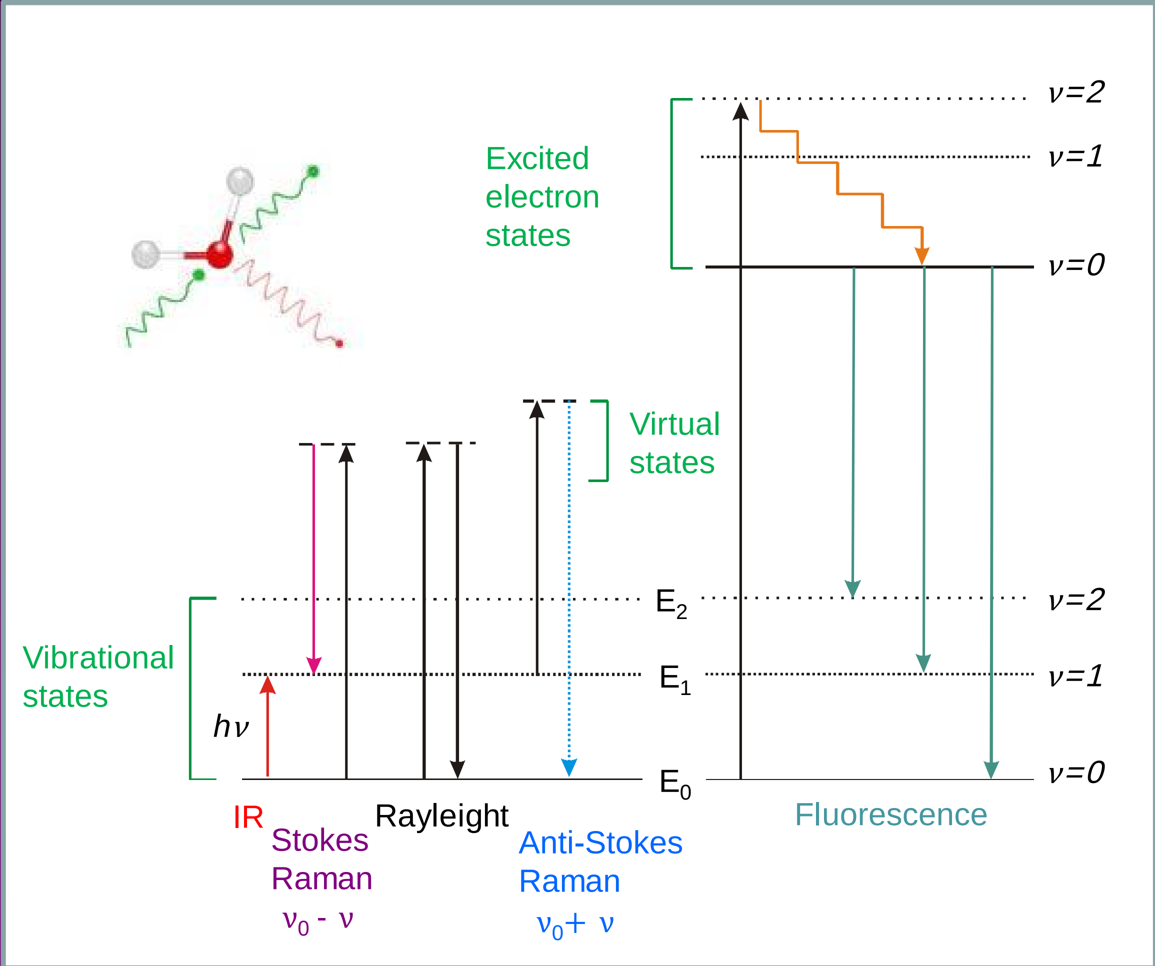
Scattered radiation



Scattering processes

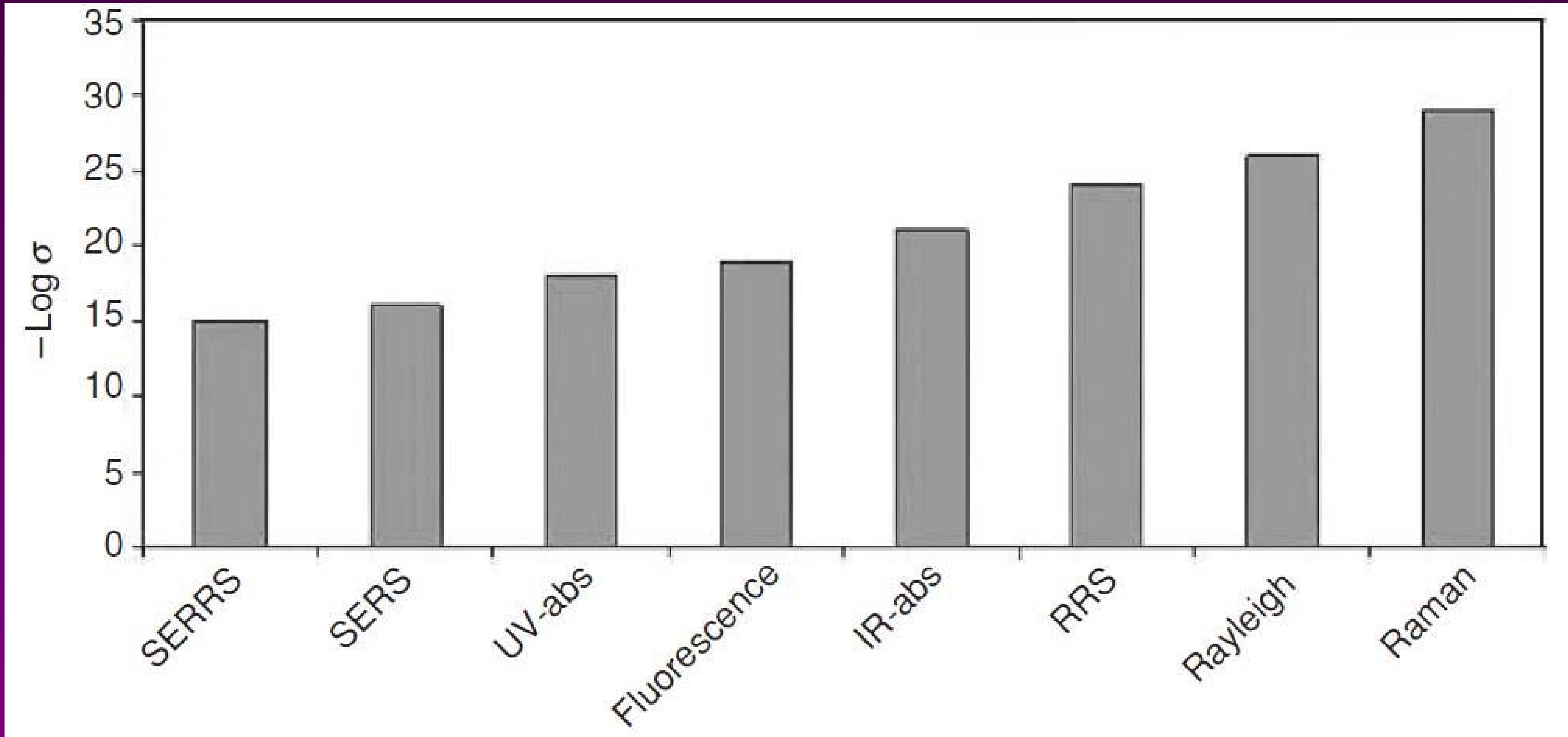
Rayleigh	Raman
ν_0	$\nu_0 \pm \nu$
particles	molecular vibrations, phonons
$I_s \sim 10^{-3} I_0$	$I_s \sim (10^{-6} – 10^{-9}) I_0$
	$\nu < 10^4$ cm^{-1}

Energy levels



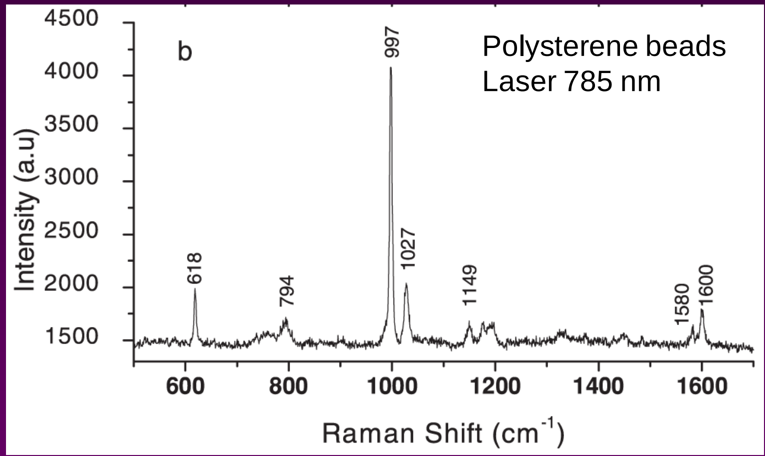
In Raman ν is invariant to ν_0

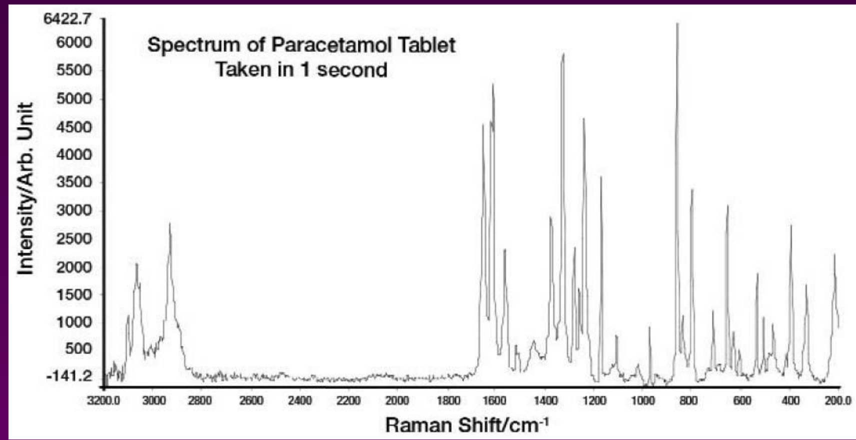
A! Cross-sections of the optical processes

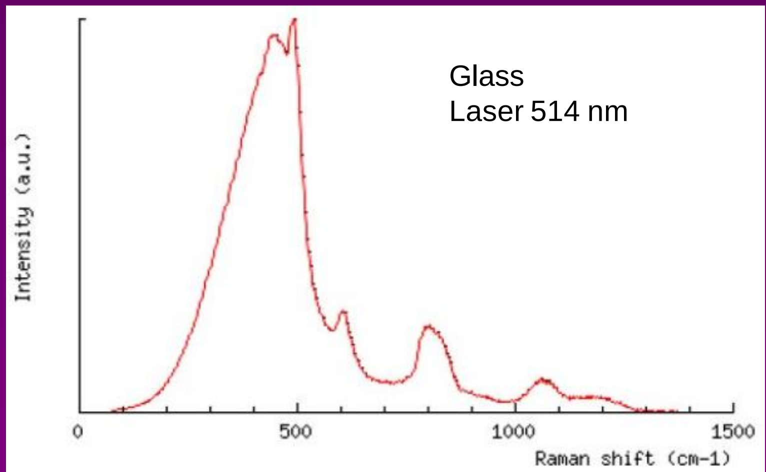


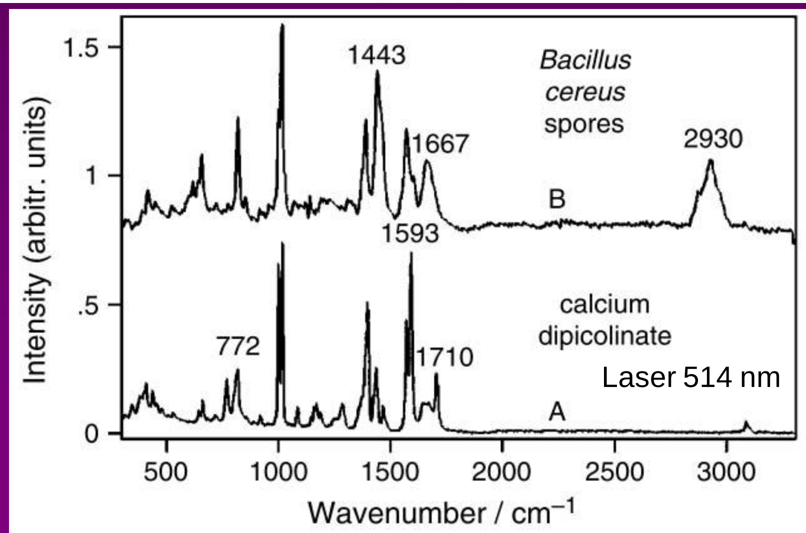
R. Aroca, Surface-Enhancend Vibrational Spectroscopy, J.Wiley & Sons Ltd, 2007

Raman spectrum examples









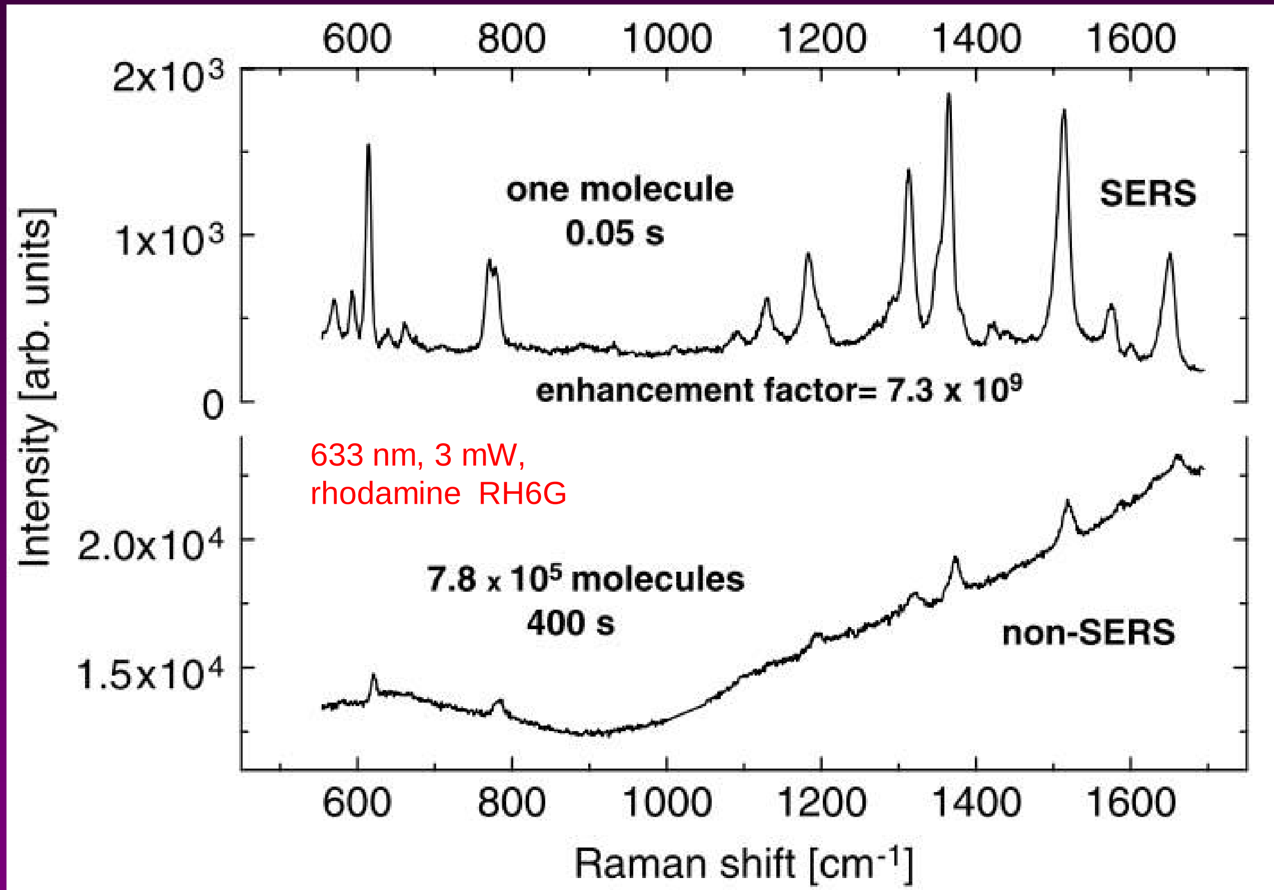
Bankapur A et all, (2010) .PLoS ONE 5(4): e10427. doi:10.1371/journal.pone.0010427.
Laboratoire de Sciences de la Terre ENS-Lyon

www.perkinelmer.com , Introduction to Raman Spectroscopy
J. Raman Spectrosc. 2004; 35: 82–86

Intermediate conclusion I

- Raman spectroscopy provides ‘fingerprint’ of molecular bonds and crystalline structure (phonons) in dependence on environment conditions (temperature, pressure …) through non-resonance excitation of any vibrational transitions
- At the same time method applications in real life are hindered by very low cross-section of Raman scattering

Bulk Raman versus SERS



Bulk: 100 µM solution in a 13 µm³ scattering volume, × 100 immersion objective with 400 s integration time.
SERS: signal from a single molecule under the same experimental conditions, but with 0.05 s integration time.

E. C. Le Ru et al., J. Phys. Chem. C, 111, 2007, p.13794–803

Steps of Raman development

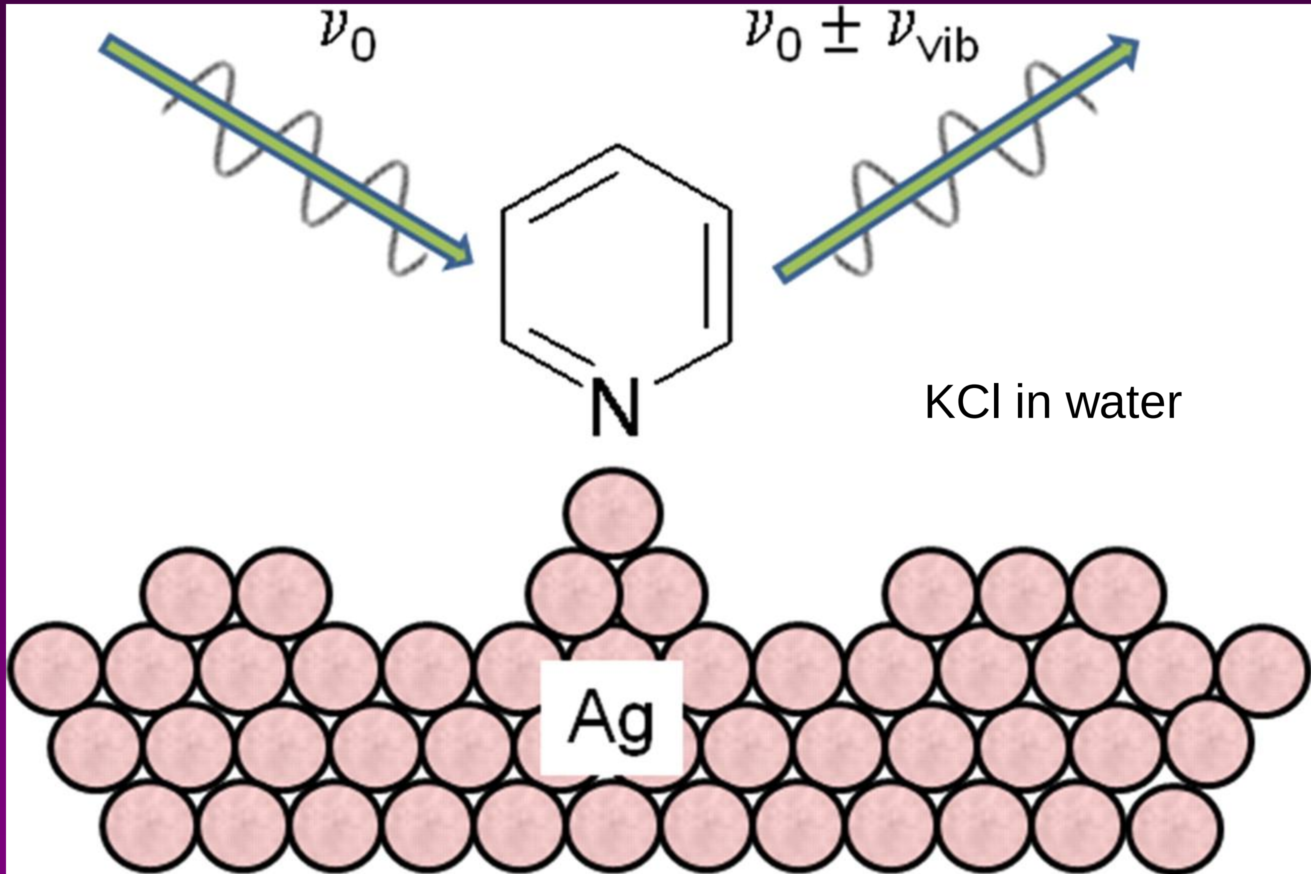
- Laser application
  - dramatically improved power of excitation and Raman signal
- SERS effect
  - Enhanced method sensitivity up to 10^{14}
- Raman microscope
  - Decreased probe volume (light spot diameter below 1 μm)
- Portable SERS
  - Mobility of analyses

C. Douketis et al., J. Chem. Phys. 2000, **113**, 11315-23

SERS discovery

- M. Fleischmann, P. J. Hendra, and A. J. McQuillan. "Raman spectra of pyridine adsorbed at a silver electrode."Chem. Phys. Lett., **26**, 1974, p.163–66
- Jeanmaire D.L. and Van Duyne R.P., "Surface Raman spectroelectrochemistry, part 1: heterocyclic, aromatic, and aliphatic amines adsorbed on the anodized silver electrode." *J. Electroanal. Chem*., **84**, 1977, p.120
- Albrecht and Creighton, "Anomalously intense Raman spectra of pyridine at a silver electrode." *J. Am. Chem. Soc*., **99**, 1977, p.5215-17

SERS experiment with pyridine adsorbed on silver



McQuillan A J Notes Rec. R. Soc. 2009;63:105-109

SERS definitions

- SERS is a phenomenon associated with the enhancement of the electromagnetic field surrounding small objects optically excited near an intense and sharp plasmon resonance. The enhanced fields excite the adsorbate (probe) and the scattered radiation will again be enhanced.

- *Surface-enhanced Raman scattering* (SERS) consists in using the large local field enhancements that can exist at metallic surfaces (under the right conditions, typically by profiting from localized surface plasmon resonances) to boost the Raman scattering signal of molecules at (or close to) the surface.

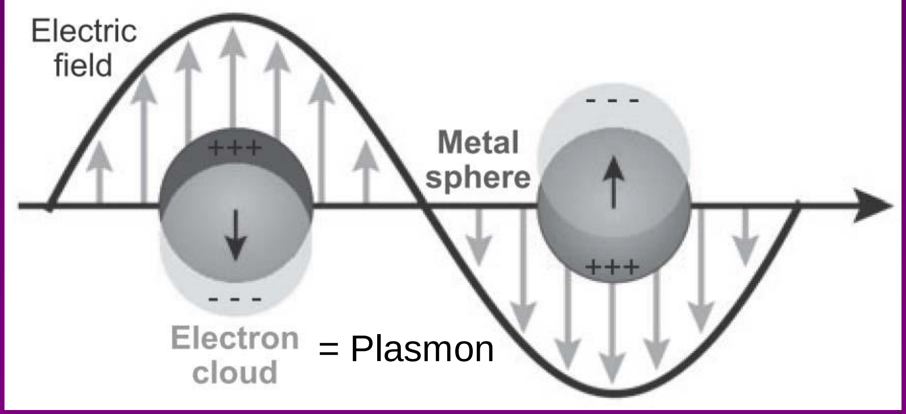
E.C. Le Ru and P. G. Etchegoin, Principles of Surface-Enhanced Raman Spectroscopy and related plasmonic effects, Elsevier , 2009

A! Lolcalized surface plazmon resonance (SPR) in metal sphere

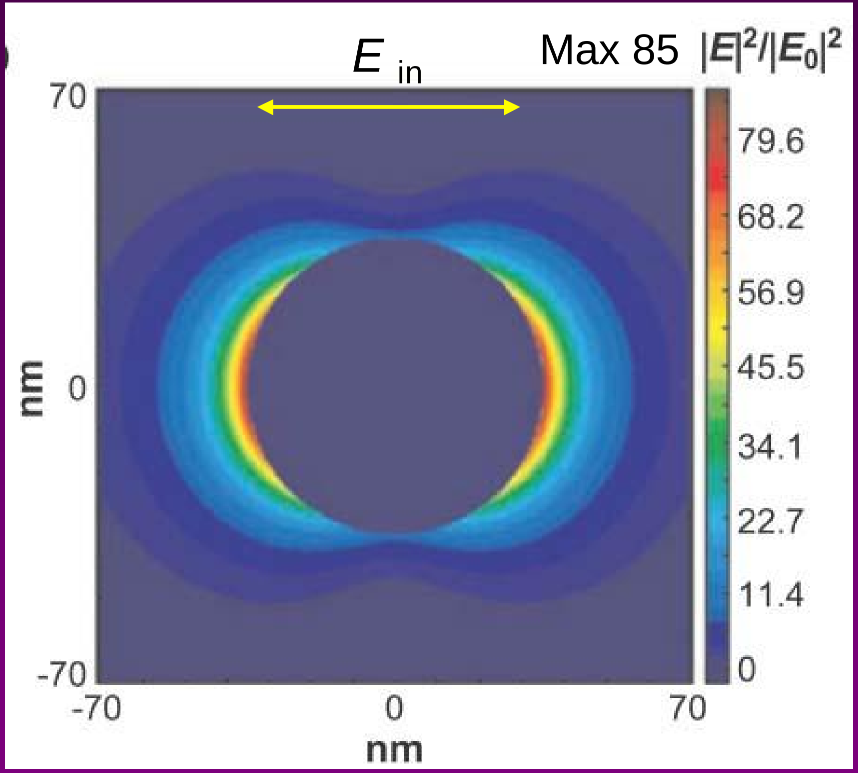
The (complex) electric field inside the sphere is constant

$$E_{in} = \frac{3\varepsilon_M}{\varepsilon(\omega) + 2\varepsilon_M} E_0$$

ε_M - relative dielectric constant of medium



Ag sphere (r = 35nm) in vacuum, at resonance wavelength 370 nm



E.C. Le Ru and P. G. Etchegoin, Principles of Surface-Enhanced Raman Spectroscopy and related plasmonic effects, Elsevier , 2009.
Stiles P.L. *et all*, Annual Review of Analytical Chemistry, 1, 2008, p.601-26

Electric field outside of metal sphere

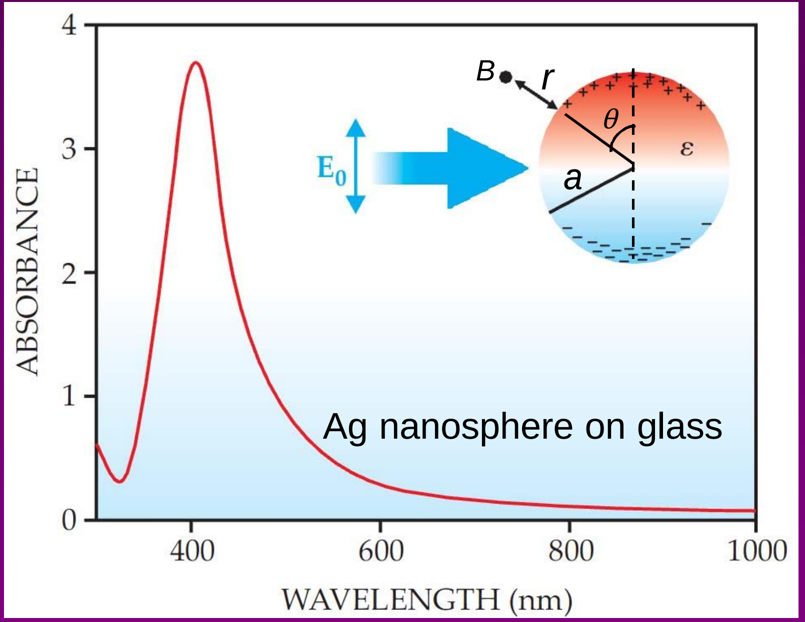
$$\mathbf{E}_{out}(x,y,z) = E_0\hat{\mathbf{z}} - \alpha E_0\left[\frac{\hat{\mathbf{z}}}{r^3} - \frac{3z}{r^5}(x\hat{\mathbf{x}} + y\hat{\mathbf{y}} + z\hat{\mathbf{z}})\right]$$

x, y, z – Cartesian coordinates,
r – radial distanse from sphere to the point $B(x, y, z)$
$\hat{\mathbf{x}}, \hat{\mathbf{y}}, \hat{\mathbf{z}}$ – Cartesian unit vectors

$$\alpha = ga^3$$

a– radius of the sphere

$$g = \frac{\varepsilon(\omega) - \varepsilon_M}{\varepsilon(\omega) + 2\varepsilon_M}$$



K. Kneipp, Physic Tody, **60**(11), 2007, p. 40-46
Stiles P.L. *et all*, Annual Review of Analytical Chemistry, 1, 2008, p.601-26

E^4 enchancement of outside field

Electric field at the surface of nanosphere

$$|\mathbf{E}_{out}|^2 = E_0{}^2[|1 - g|^2 + 3\cos^2\theta(2\mathrm{Re}(g) + |g|^2)]$$

Maximum $\mathbf{E}_{out}$ at θ=0°

$$|\mathbf{E}_{out}|^2 = 4E_0{}^2|g|^2$$

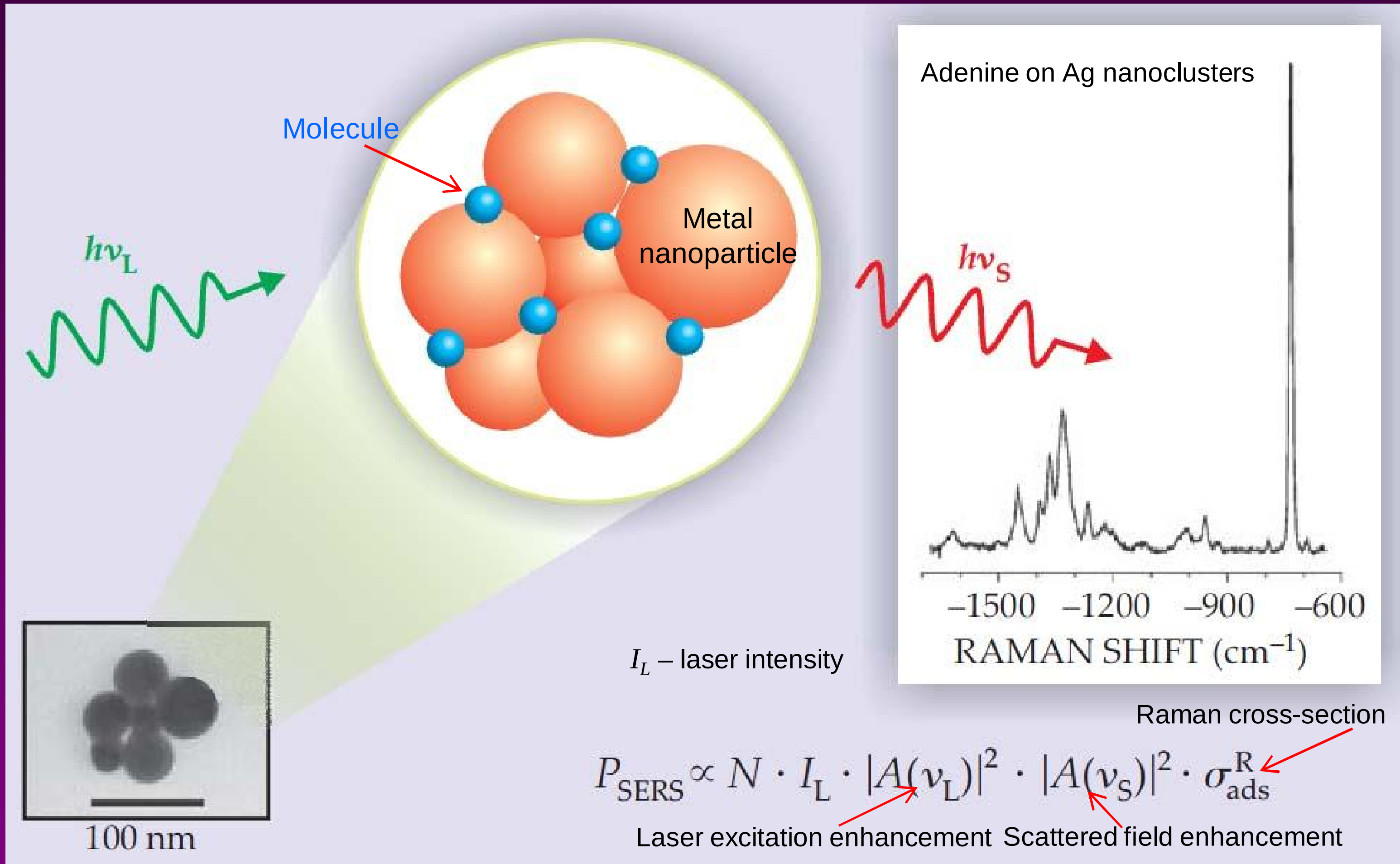
Enhancement factor:

$$EF = \frac{|\mathbf{E}_{out}|^2|\mathbf{E}'_{out}|^2}{|\mathbf{E}_0|^4} = 4|g|^2|g'|^2$$

(in theory 10^{11} and 10^3, for field and chemical, respectively)

Stiles P.L. *et all*, Annual Review of Analytical Chemistry, 1, 2008, p.601-26

A! Electromagnetic enhancement in near-field

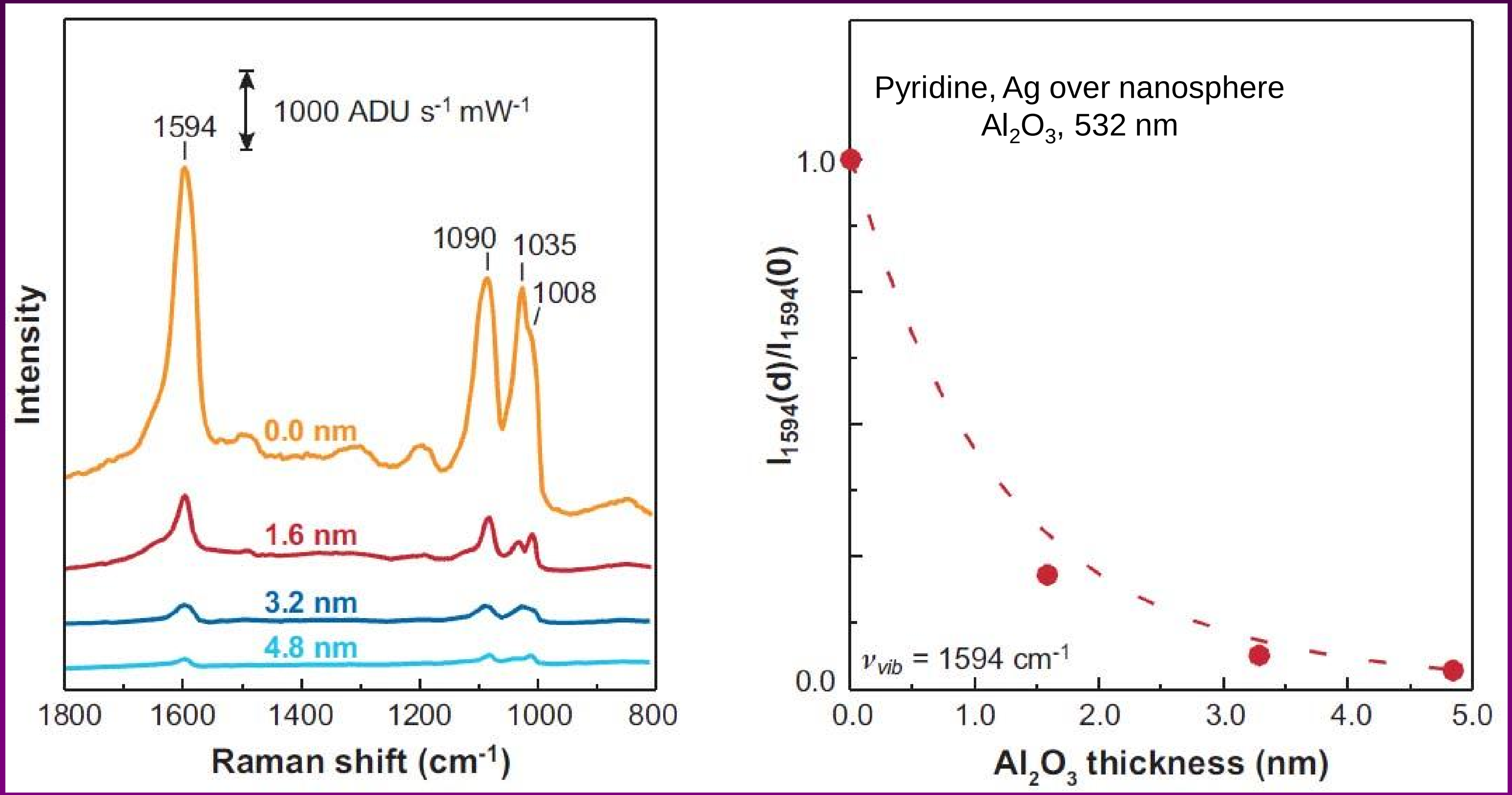


$$P_{SERS} \propto N \cdot I_L \cdot |A(\nu_L)|^2 \cdot |A(\nu_S)|^2 \cdot \sigma_{ads}^{R}$$

K. Kneipp, Physic Tody, **60**(11), 2007, p. 40-46

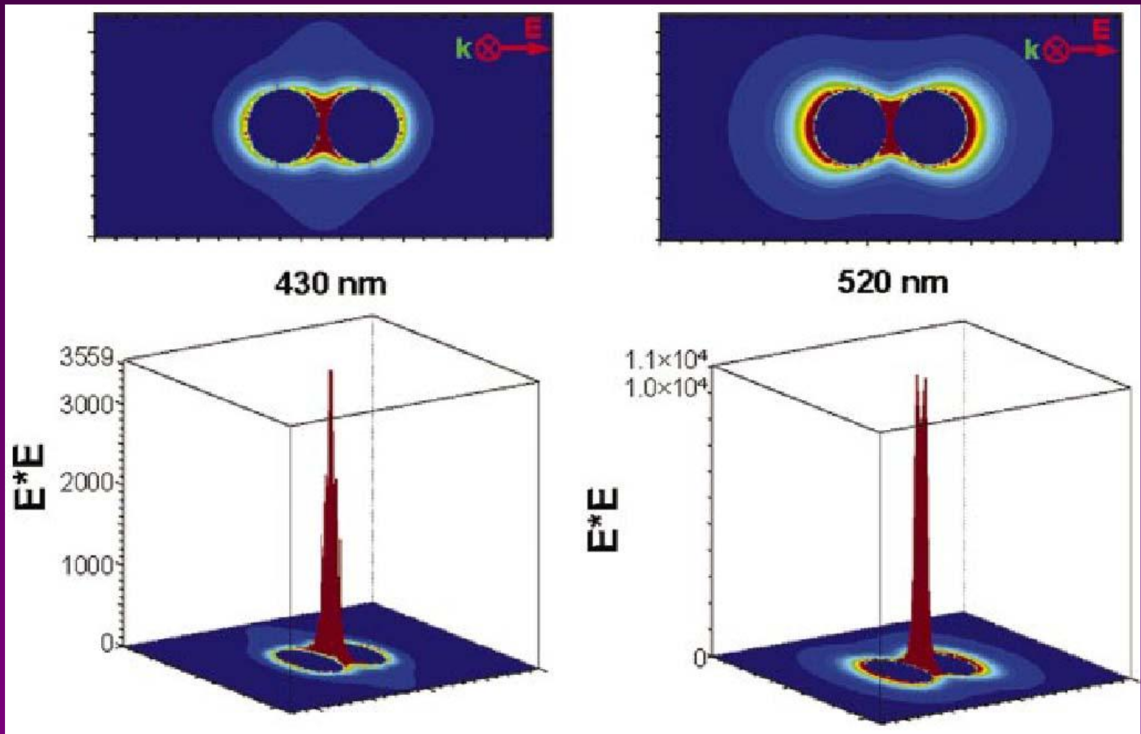
Distance dependence

$$I_{SERS} = \left(\frac{a + r}{a}\right)^{-10}$$



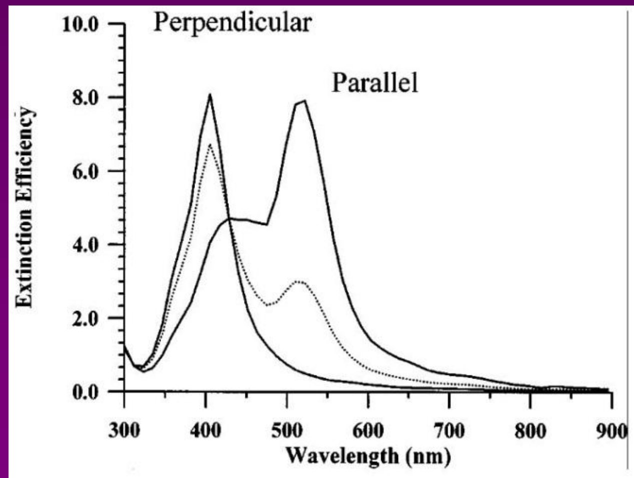
Stiles P.L. *et all*, Annual Review of Analytical Chemistry, 1, 2008, p.601-26

Ag dimer enhancement



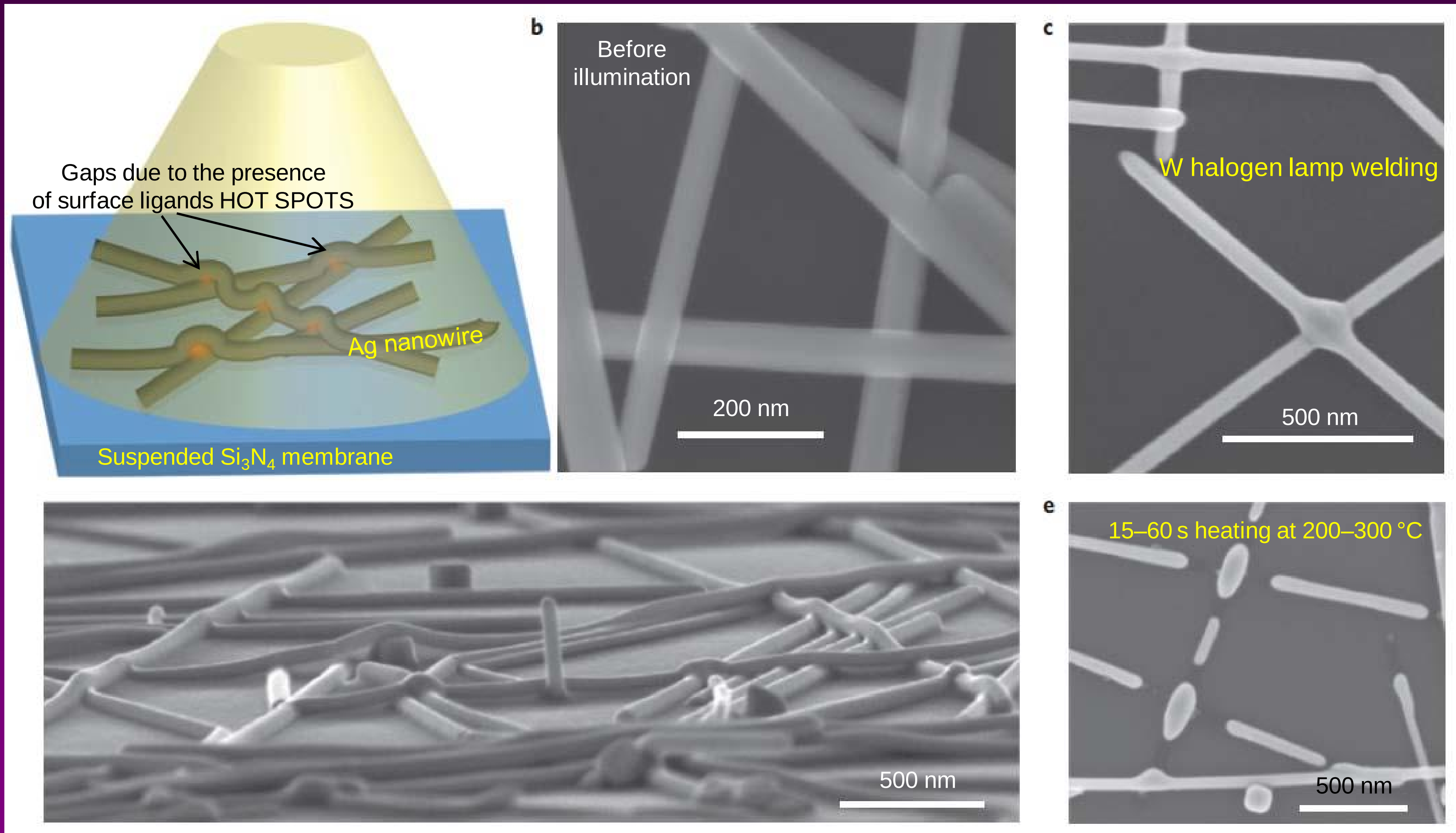
36 nm spheres separated by 2 nm gap.

For sphere enhancement is 85 (slide 19)



E. Hao and G. C. Schatz, J. Chem. Phys., Vol. 120, No. 1, 1 January 2004

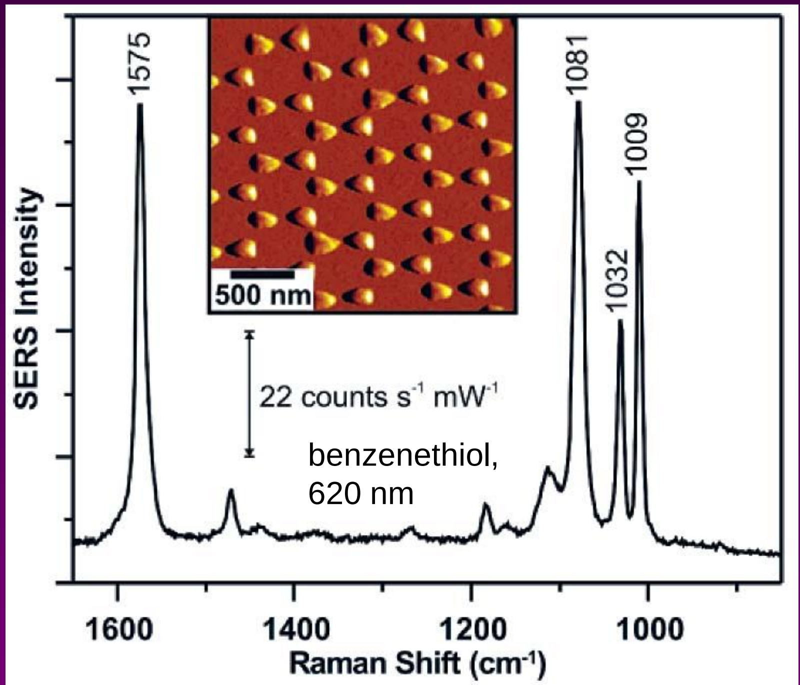
Plasmonic welding

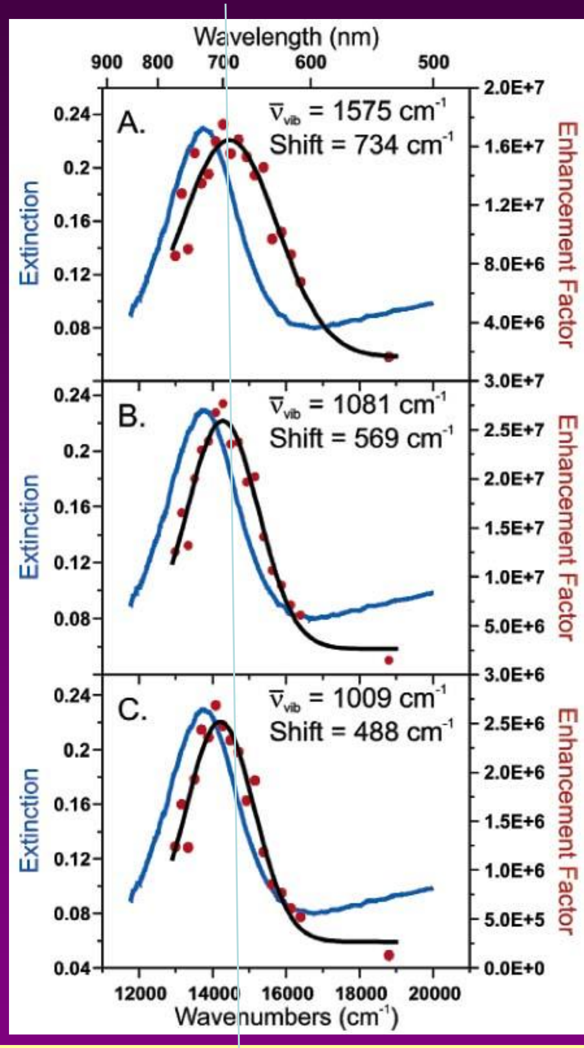


E. C. Garnett, Nature Materials 11, 241–249 (2012)

Wavelength dependence

$\lambda_{max}=(\lambda_{ex}+\lambda_{vib})/2$





NSL with 450nm spheres, 55 nm Ag on glass

SERES – suraface enhanced ecxitation spectroscopy

SERS is maximum when laser excitation is between SPR and the analized specturm line

J. Phys. Chem. B **2005,** *109,* 11279-11285

Inetrmediate conclusion II

- High local electromagnetic field near the plasmon nanostructures provides very high enhancement of Raman scattering (SERS)
- SERS effect depends on metal-molecule affinity and resonance conditions in molecule
- The highest *EF* is reached in random 'hot spots', if the probe molecule has got at this 'spot'

Main types of SERS substrates

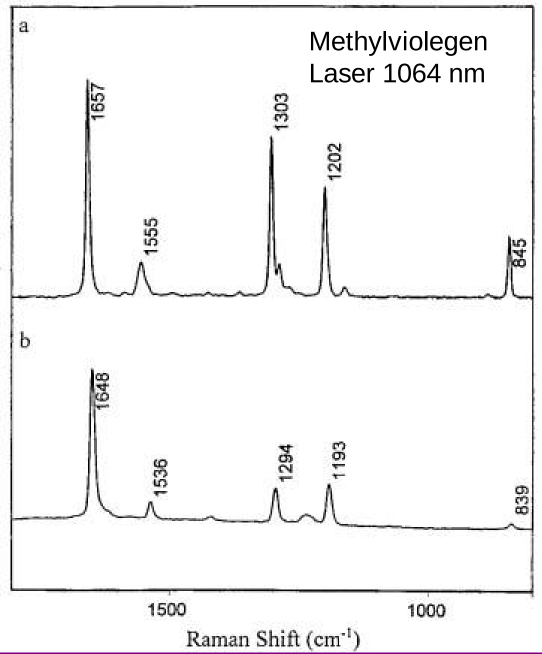
- A SERS substrate is any metallic(?) structure (nano-structure) that produces SERS enhancement:
  – Metal electrodes in electrochemistry (roughed electrodes)
  – Metal nano-particles in solution (colloids)
  – ‘Planar’ metal structures or arrays of metal nano-particles supported on a planar substrate (glass, silicon)

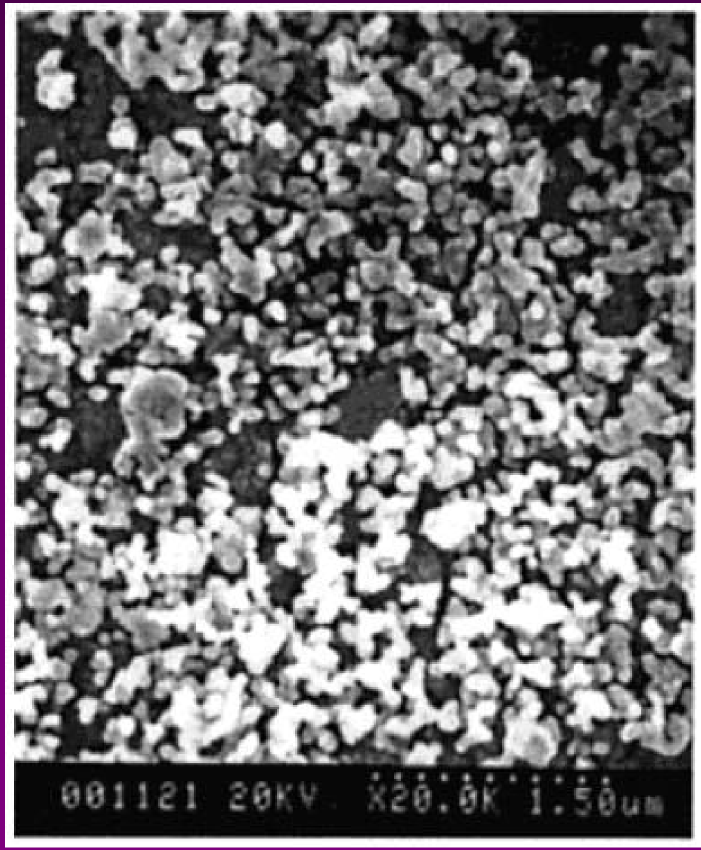
Metal electrodes

- Surface protrusions 25-500 nm
- Ag in KCl electrolyte
- Oxidation-reduction cycles

SERS

bulk Raman





Zheng et al., J. Phys. Chem. B, Vol. 106, No. 5, 2002, p.1019-23

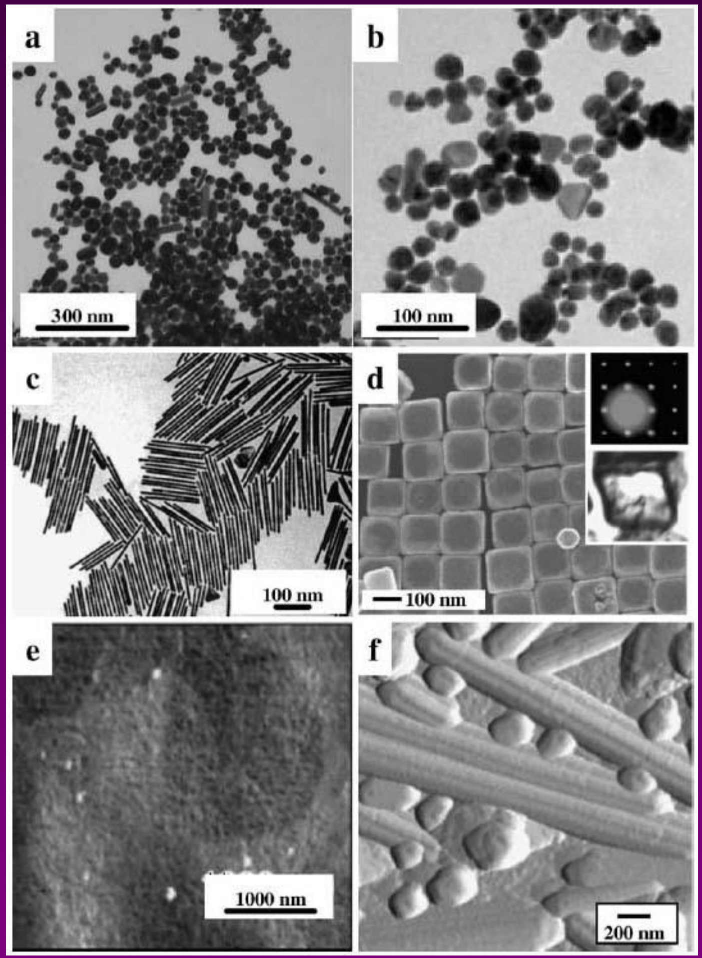
Metal colloids for plasmonics

- Mainly Au, Ag or Cu nanoparticles (diameter 10 – 80 nm) in water
- Produced by:
  - Chemical reduction (co-precipitation and reducing). Process depends on:
    - Kind of metal
    - Reducing reagent
      - $AgNO_3$ in sodium citrate (Lee and Meisel, 1982). Average 60 nm
      - $HAuCl_4$ (Frens, 1973 and Natan 1995). Range 16 – 150 nm
    - Temperature (boiling 1 h)
    - Stabilizing agents
    - Metal ion concentration
  - Laser ablation
  - Photoreduction
- The best SERS is provided by highly aggregated colloids (dimers etc.)
- Enhancement up to 10^{14} (SMD possible)

Images of metal colloids

TEM of Ag citrate colloid
λ_{max}= 406 nm

TEM of Au borohydride colloid,
Au particles 20-70 nm,
λ_{max}= 535 nm



TEM of Au nanorods,
λ_{max}= 525 nm and 885 nm

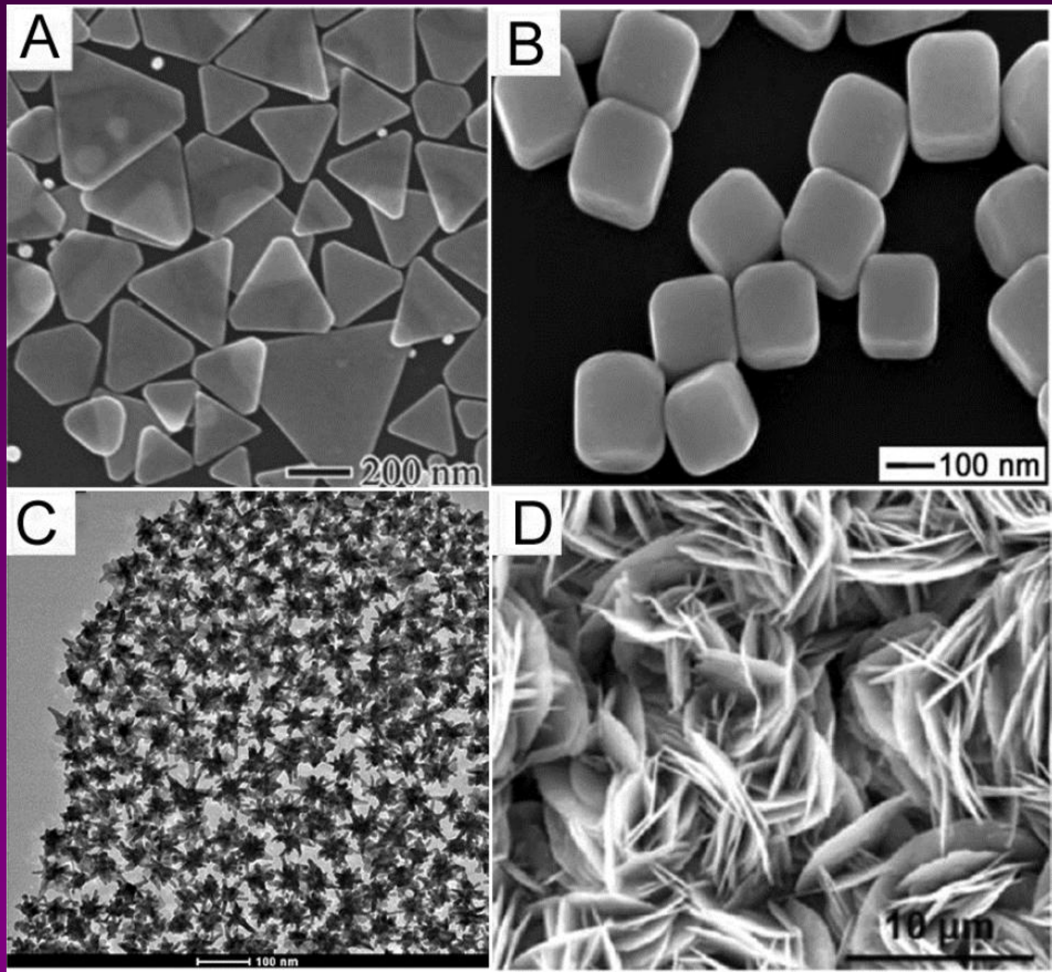
TEM of Au nanosquares

AFM of Au nanospheres embedded
in film of biopoymer chitosan
(inert organic matrix)

AFM of Ag nanowires
in dendrimer matrix

R.F. Aroca et al. / Advances in Colloid and Interface Science 116 (2005) 45–61

Variety of geometric morphologies



nanoprisms

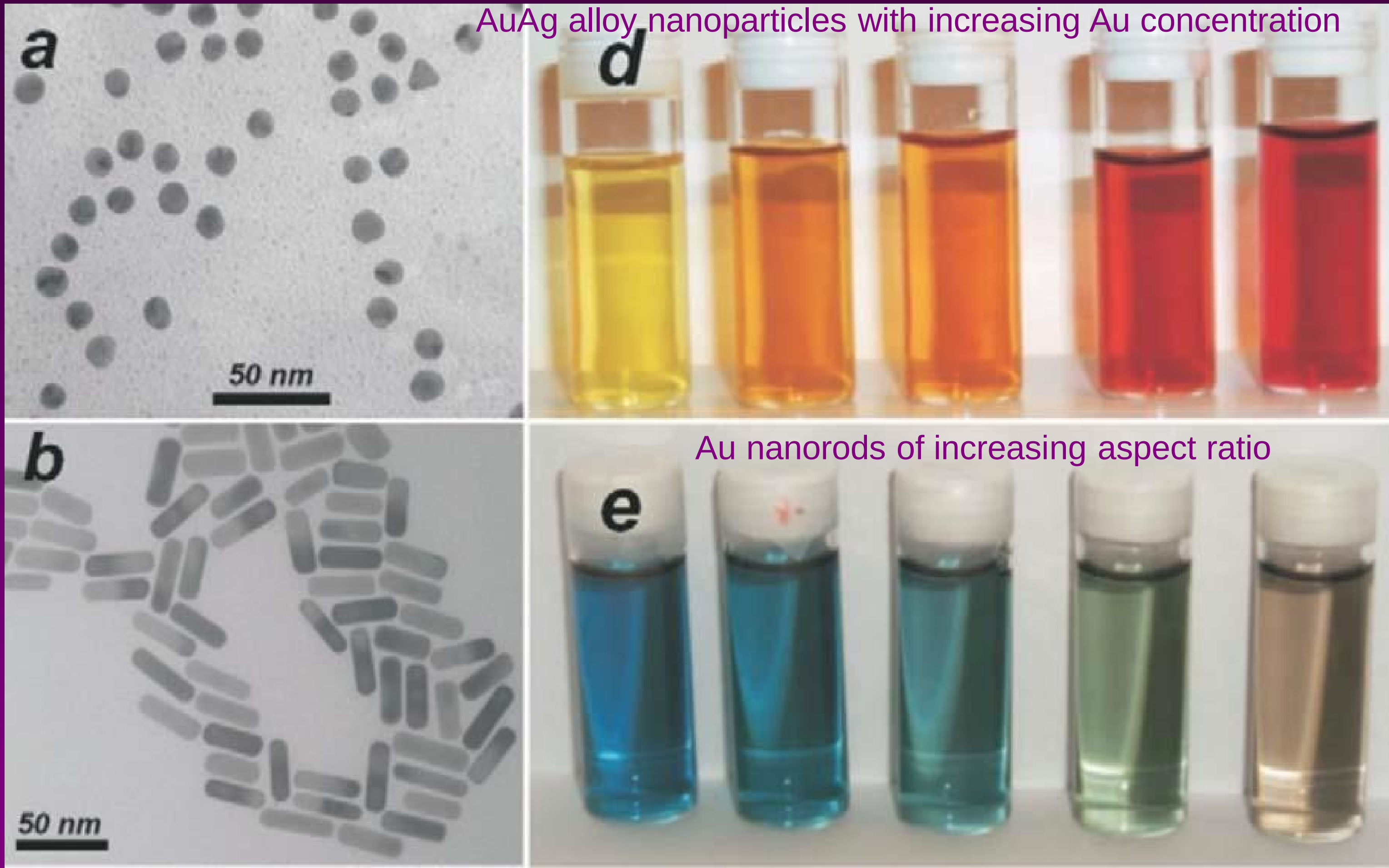
nanocubes

nanostars

nanosheets

A. X. Wang, and X. Kongl., *Materials* 2015, *8*, 3024-3052

Material and size effect in plasmon resonance

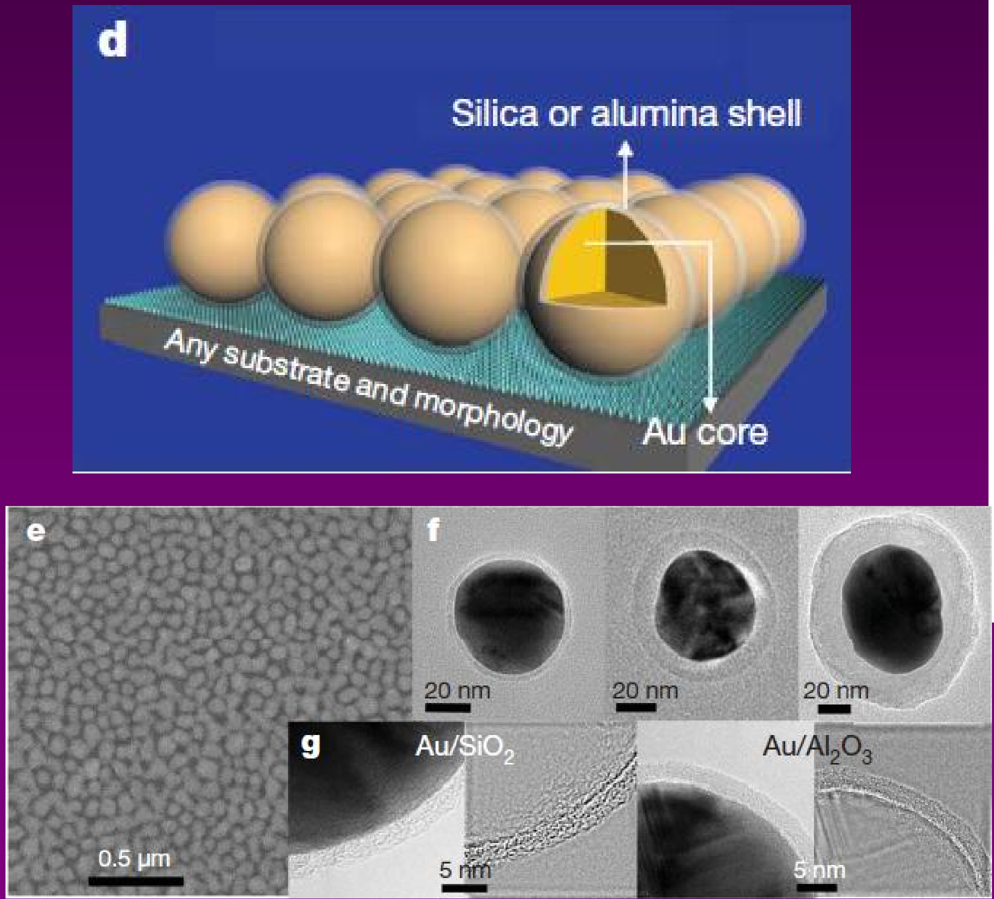


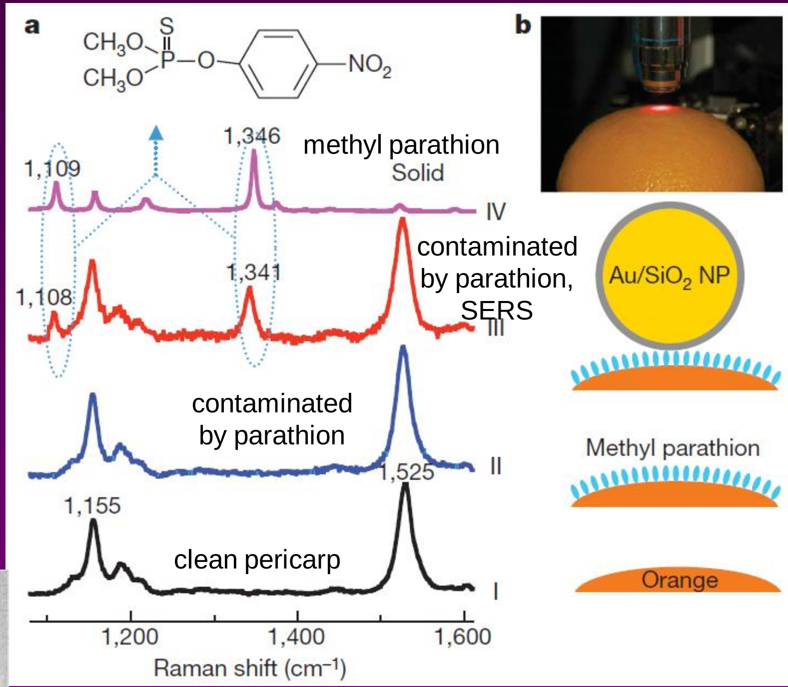
Materials Today, Feb 2004, p. 26-31

Material dependent features

- Ag – the highest EF, up to 10^{14}
- Au - bio-compatibility
- Mixture of Au and Ag nanoparticles – immuno-gold colloids
- Core-shell $Ag@SiO_2$, $Au@Al_2O_3$–
  - stability in all environments
  - better spreading on different surfaces
  - agglomeration protect
- Magnetic core for particle position controle

Detection of insecticide

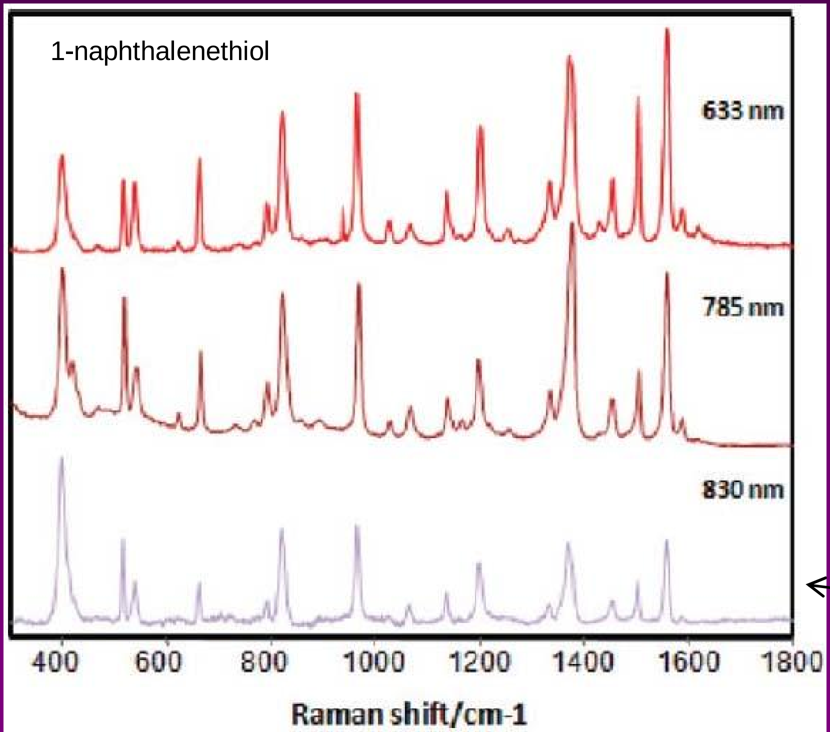


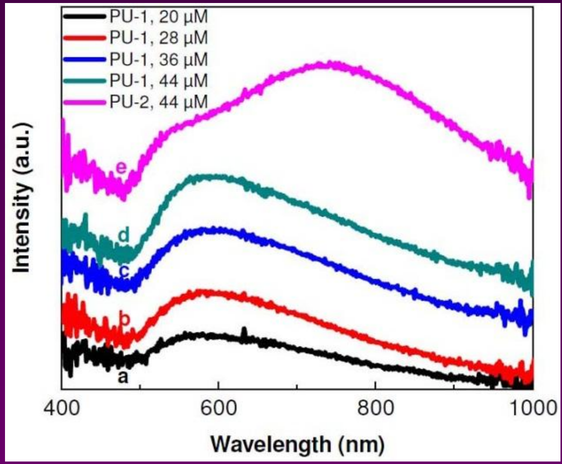


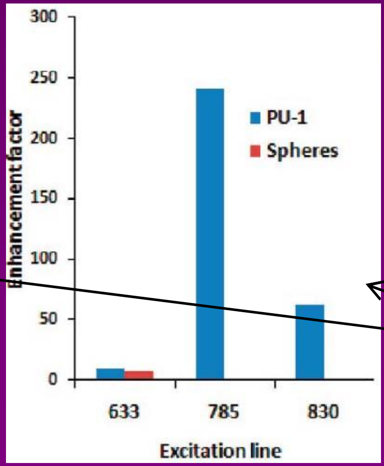
Li, J.F. Et al., Nature 2010, 464, pp.392–395

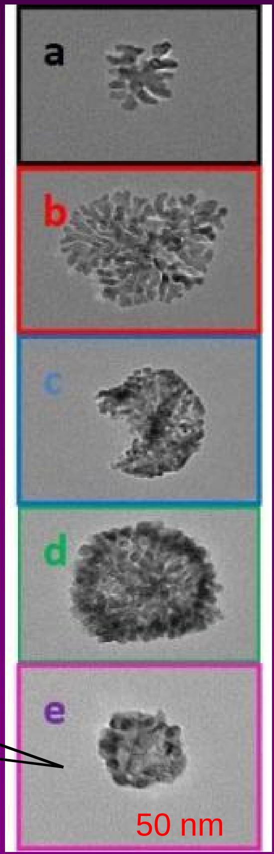
Gold lace nanoshells

PU means amphiphilic polyurethane template





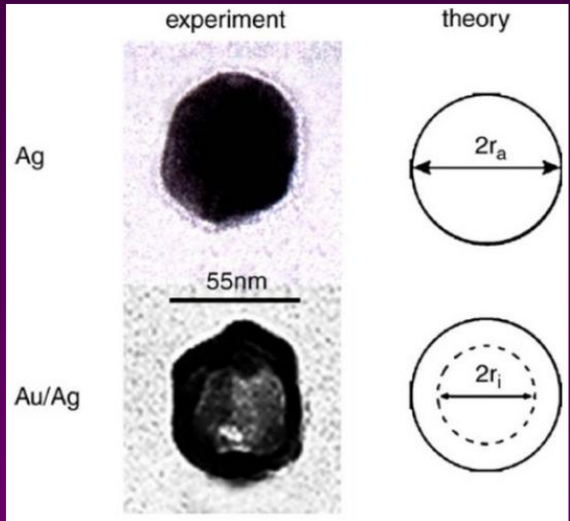


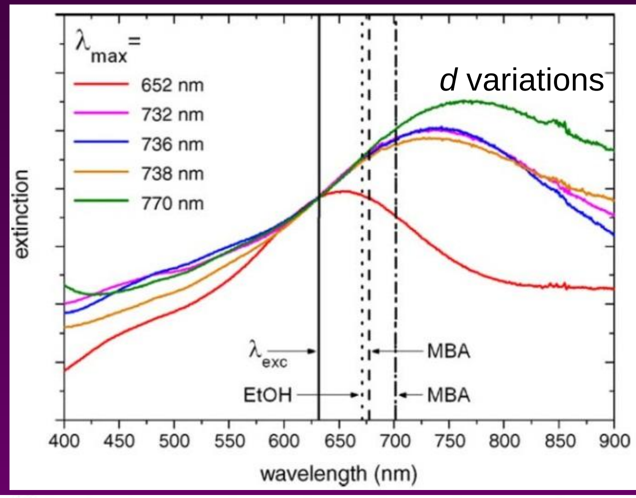


M. Yang et al., SERS-Active Gold Lace Nanoshells with Built-in Hotspots, *Nano Lett.* 2010, *10*, 4013-–4019

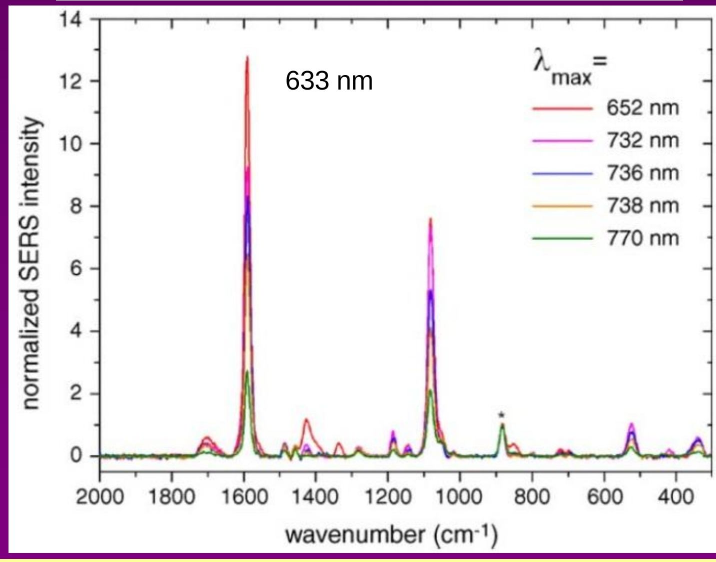
Nanoshell (core-shell)

4-mercaptobenzoic acid (MBA)





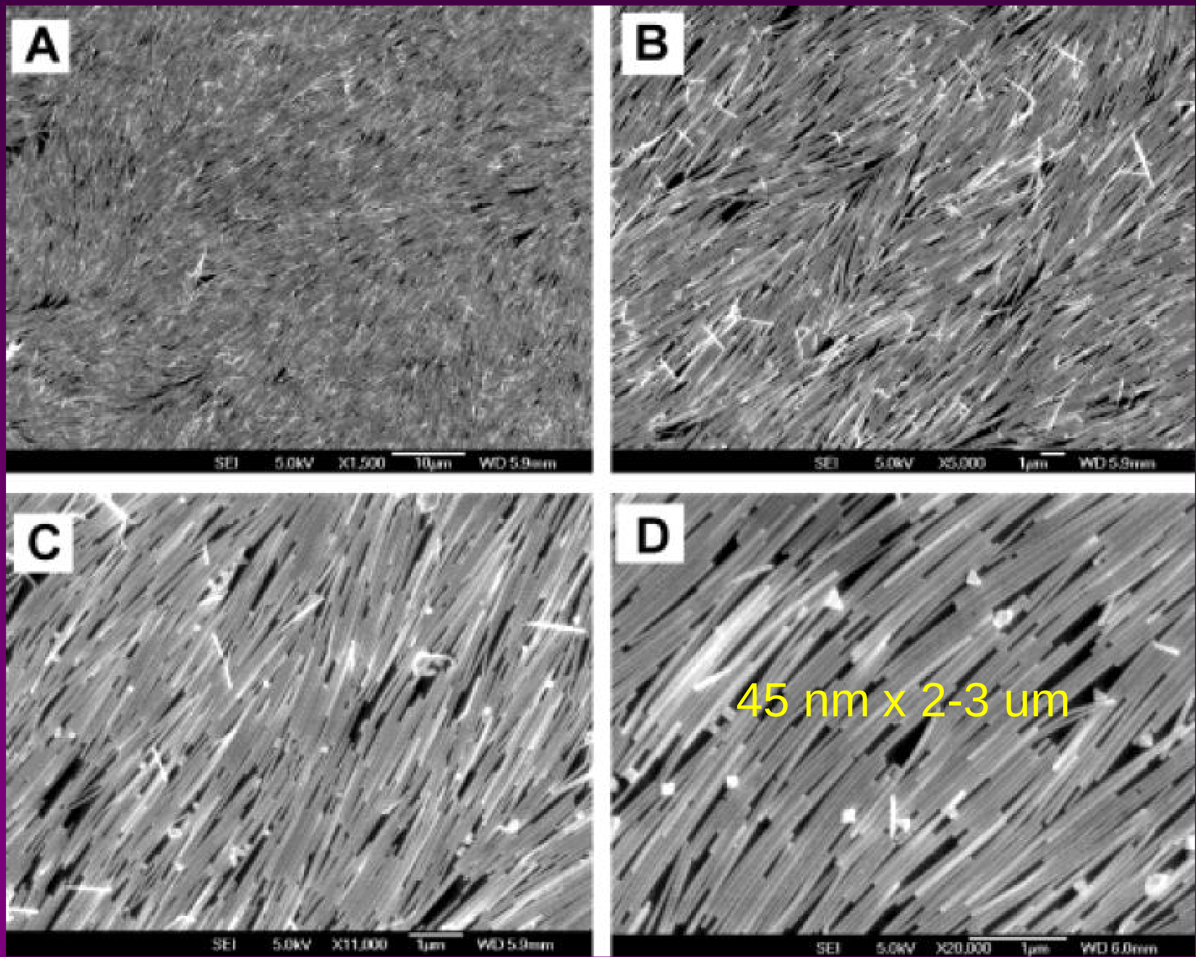
$d = (r_a - r_i)$



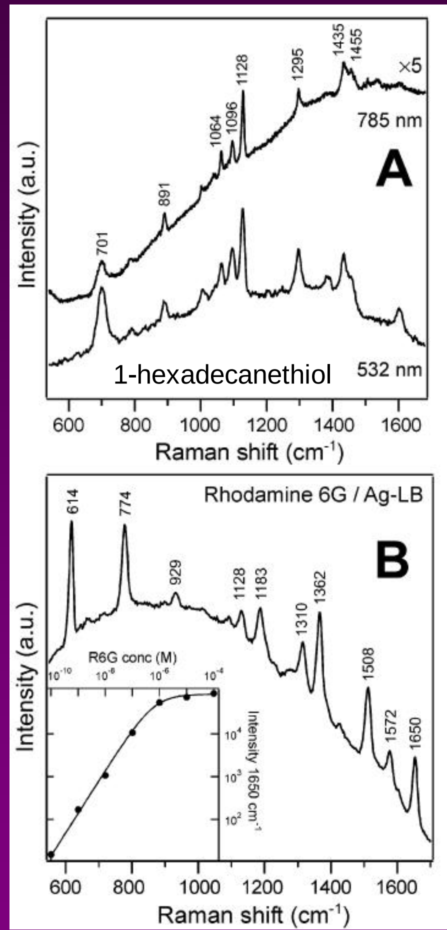
- additional degree of tunability of SPR by changing the thickness *d* of shells
- more uniform signal (less fluctuations)

M. Gellner et al. / Vibrational Spectroscopy 50 (2009) 43–47

Ag nanowires



EF 2x10^5



EF 2x10^9

Tao et al., *Nano Lett.* 2003, *3*, 1229–1233

Colloid disadvantages

- Storage – usually are used fresh prepared
- Using in portable spectrometers
- Reproducibility
- Cost
- Limited range of materials

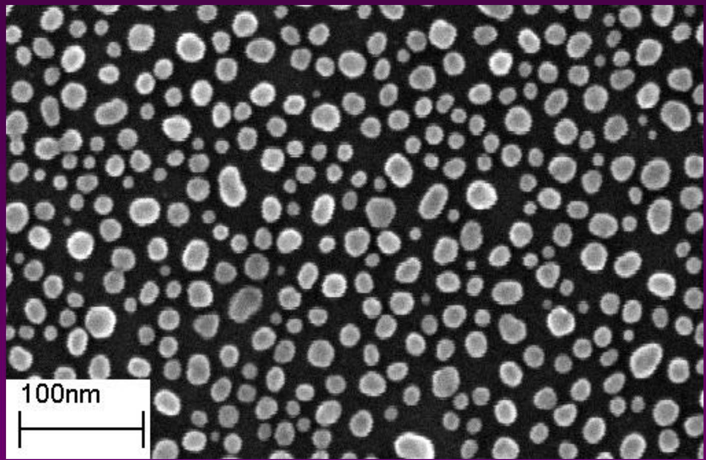
Fabrication of planar SERS substrates

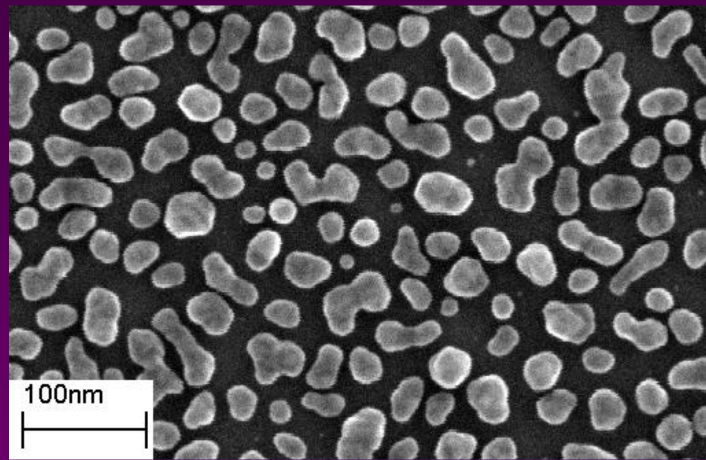
- Deposited films (self-organized metal islands)
- Beam lithography (ring, crescent, dimer...)
  - EBL
  - FIB
- Interference lithography
- Nanoimprint
- Template assisted lithography
  - Porous polymers (polycarbonate membranes)
  - Porous anodic alumina Al_2O_3
  - Nanosphere lithography (NSL)

As deposited silver films

Room temperature

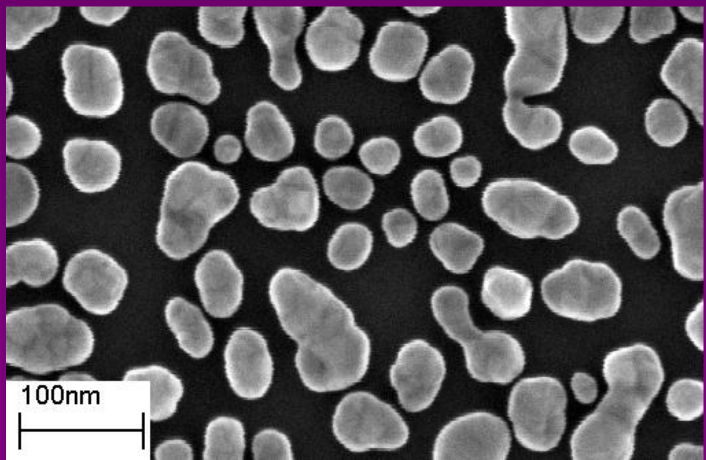
4 nm
0.2 Å/s

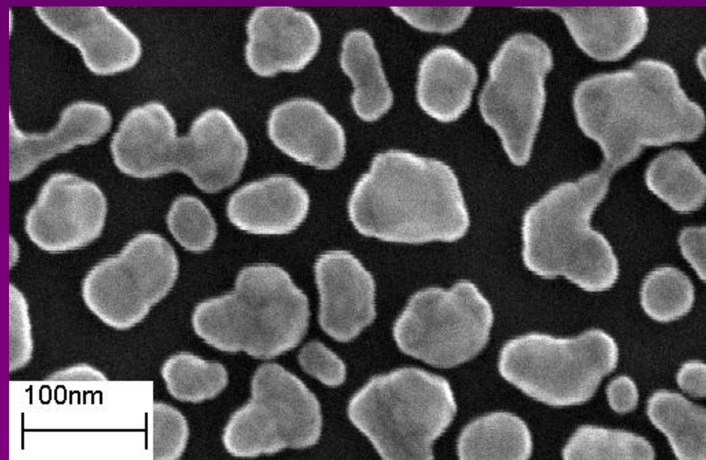




5.5 nm
0.5 Å/s

10 nm
2.0 Å/s



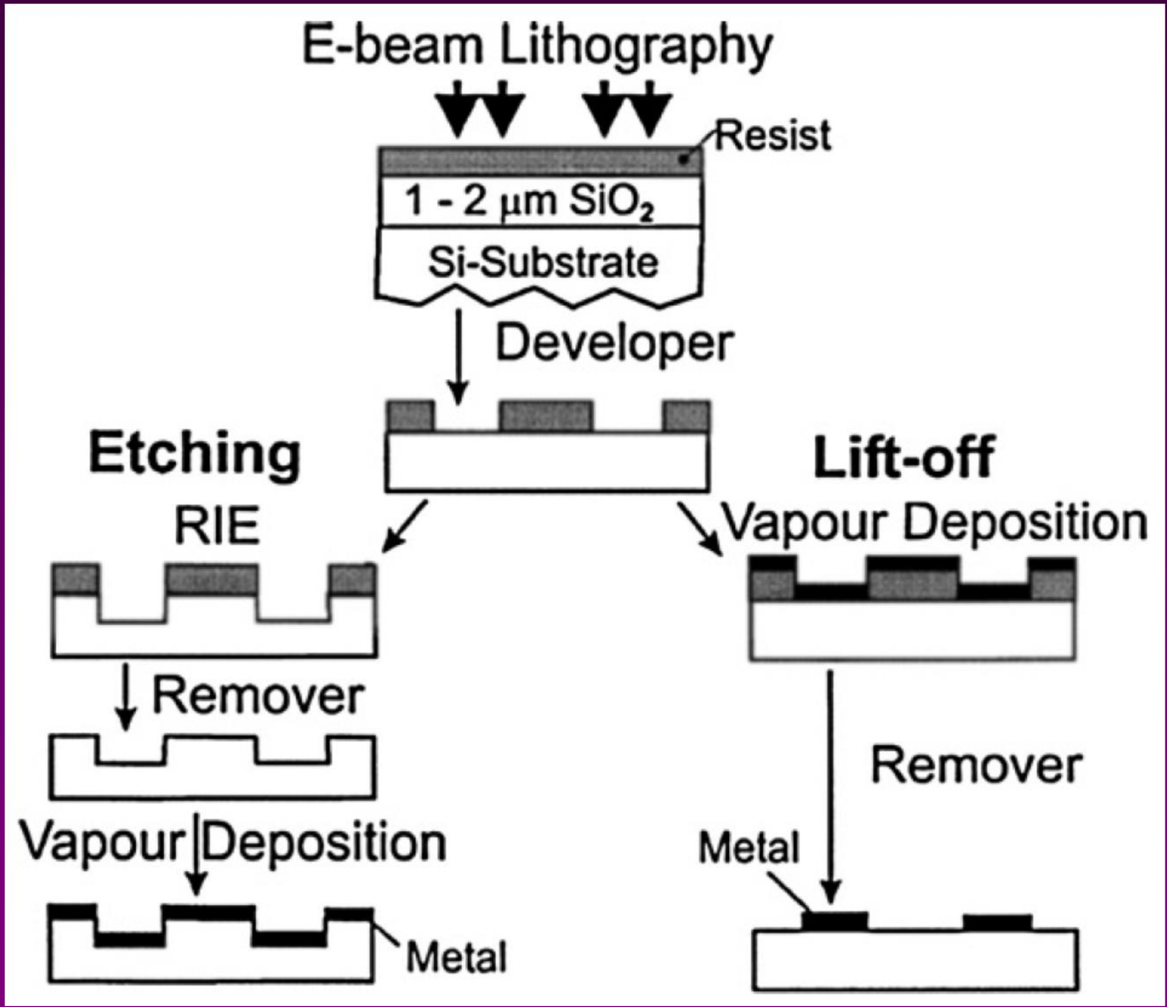


12 nm
0.2 Å/s

A! 'Planar' substrates - metal island films

- Prepared by PVD – physical vapor deposition
- Applicability to any substrate
- High purity
- Structure can be controlled by
  - deposition rate (0.1 – 10 Å/s)
  - substrate roughness and temperature
  - mass thickness (4 - 8 nm)
  - Annealing (200 – 400°C)

EBL



M. Kahl et al., Sensors and Actuators B-Chemical, 51 (1998), p. 285

Nanohole array by lift-off

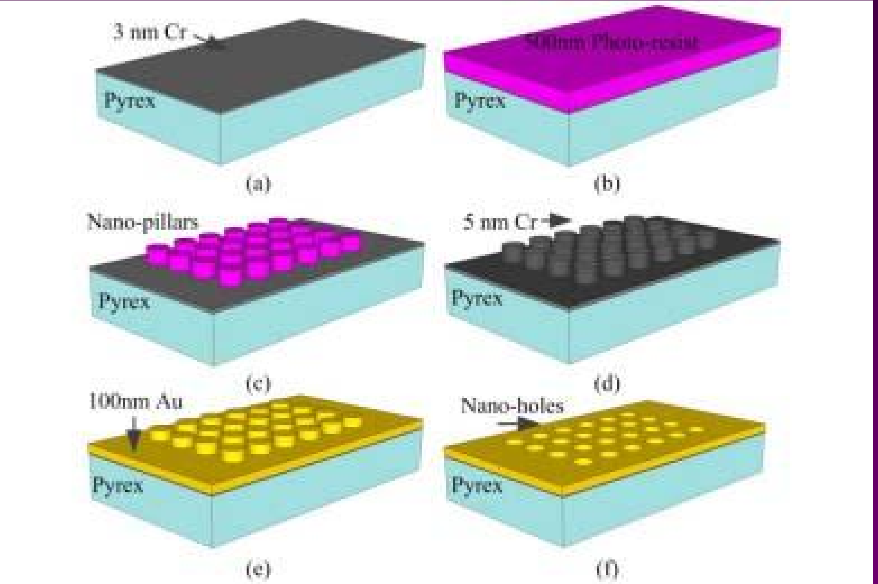
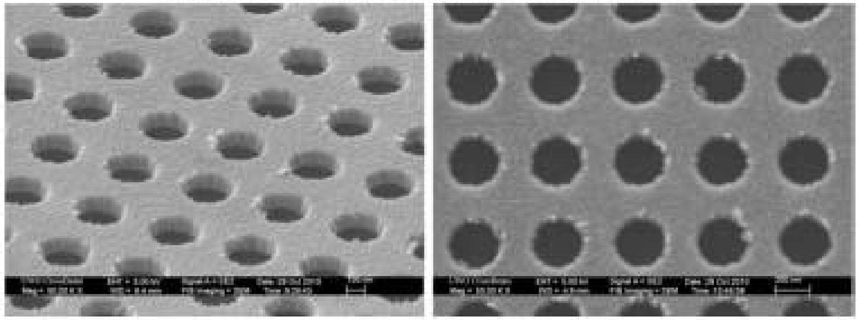


Fig. 1. Electron beam lithography (EBL) for fabrication of nano-hole arrays



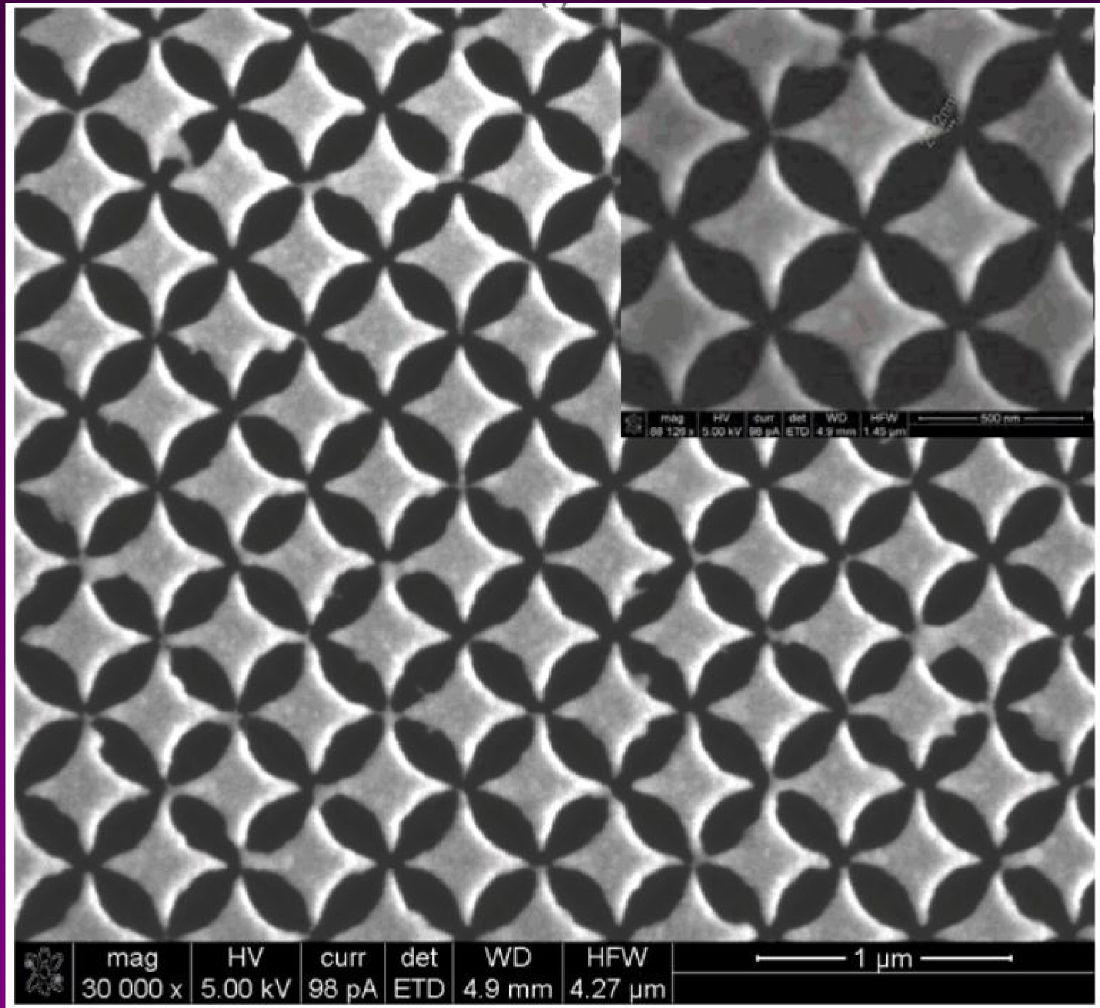
100 nm thick Au
200 nm holes

M. Najiminaini et al., Opt. Express 19, 26186-26197 (2011)

FIB

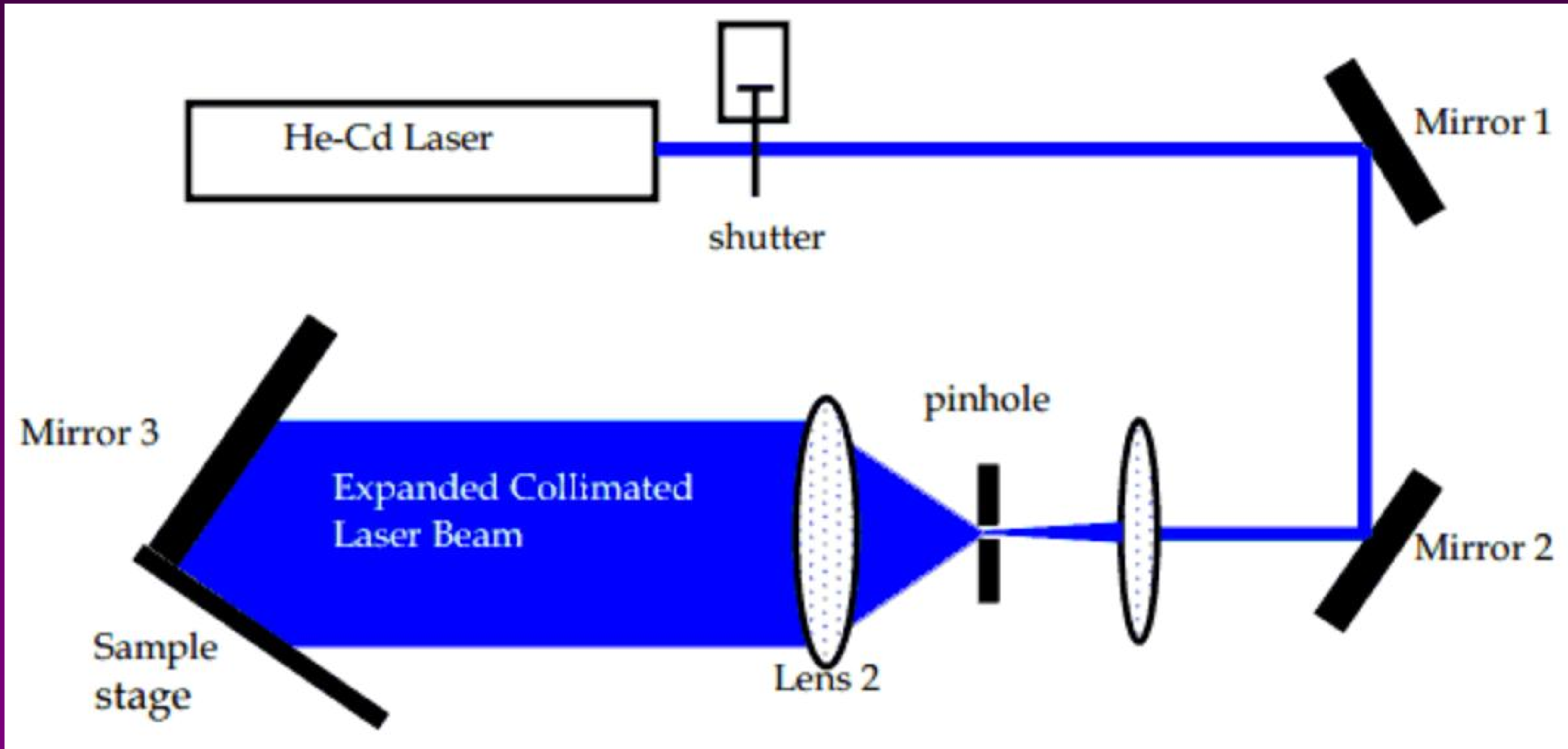
- FIB lithography is superior to EBL:
  - Higher resolution
  - Higher resist sensitivity
- Additionally to EBL:
  - Local ion beam etching (subtractive lithography)
    - 3D patterning
  - Local deposition of materials (additive lithography)
  - Direct patterning of hard mask layers
- Multi-beam systems

FIB, Au, thickness 60 nm



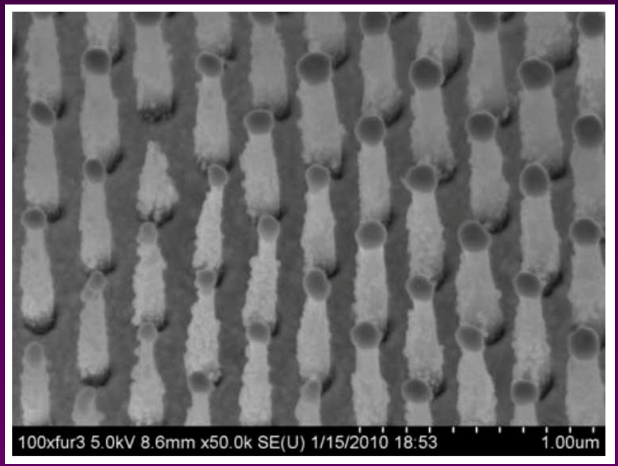
Nanofabrication, InTech, 2011, p. 247

Lloyd's mirror interference lithography

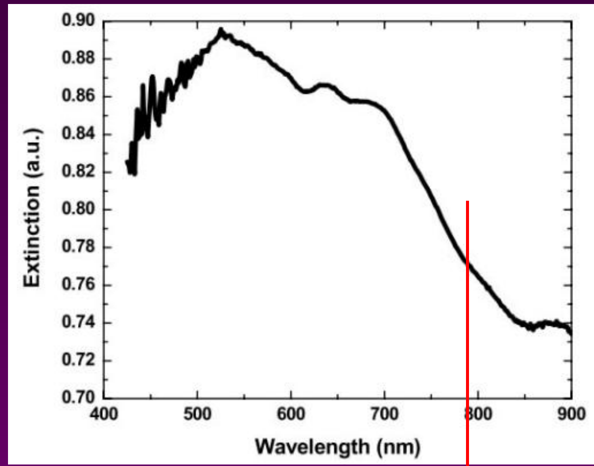


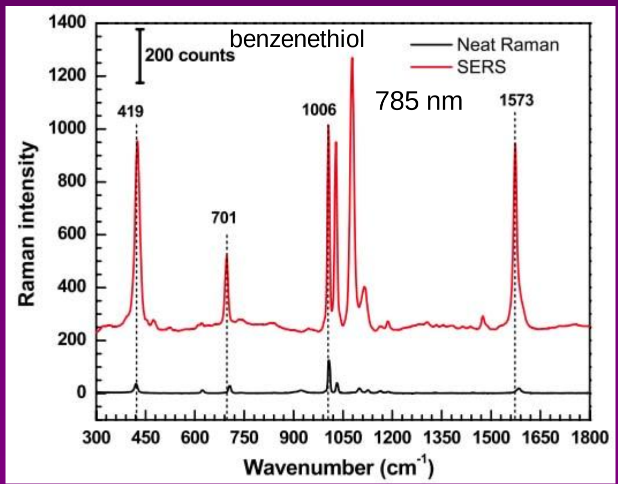
Nanofabrication, InTech, 2011, p. 256

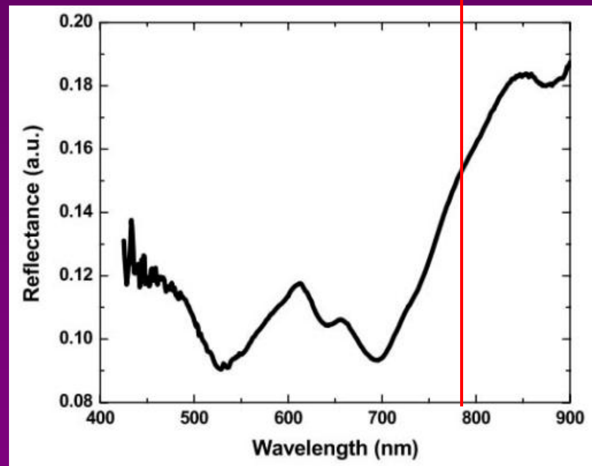
Pillar based substrate



SiO2
d=150nm
gap 350 nm
h=500nm
Ag 80nm
EF=5·10^7





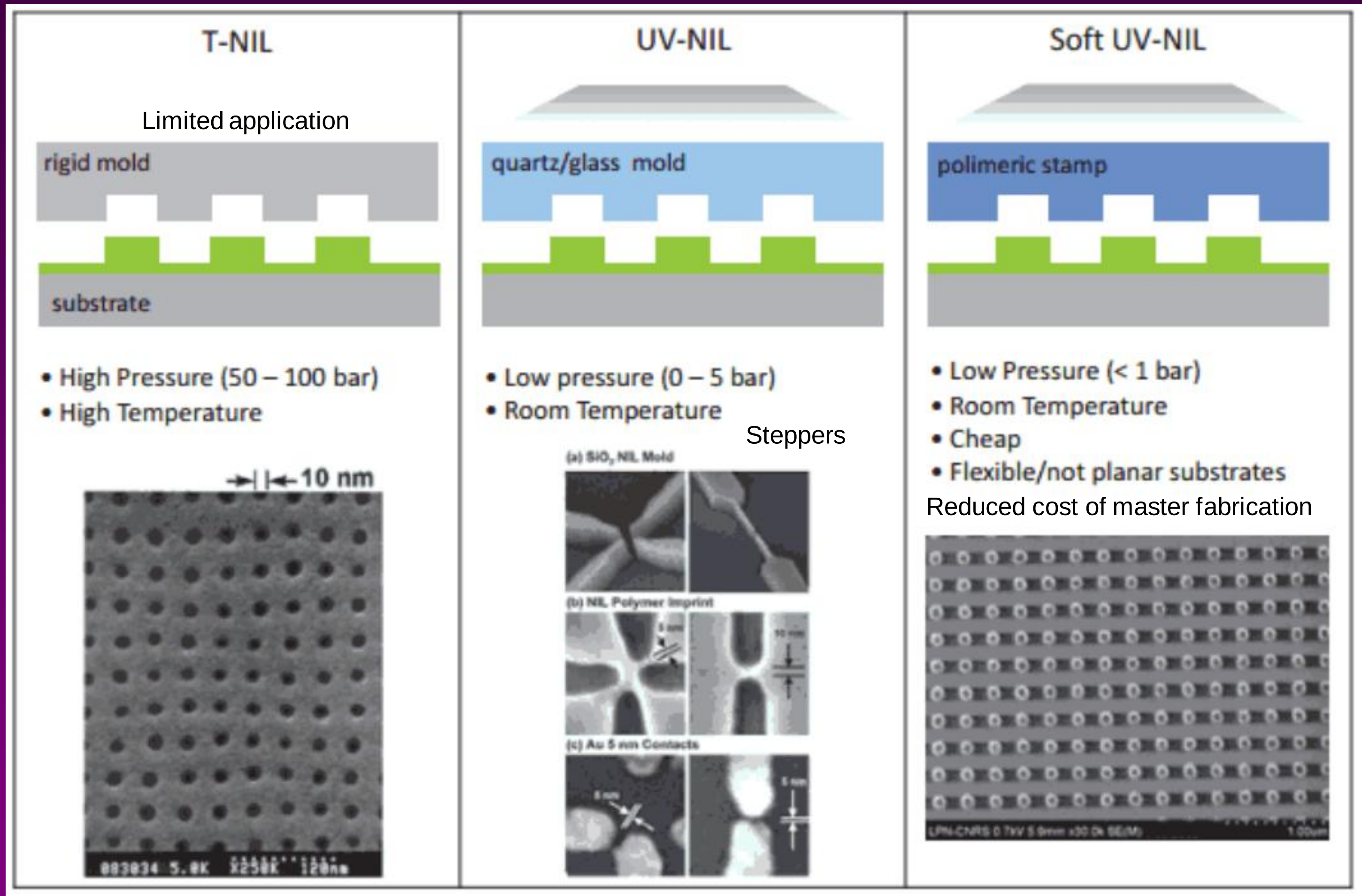


M. R Gartia et al., Rigorous surface enhanced Raman spectral characterization of large-area high-uniformity silver-coated tapered silica nanopillar arrays, Nanotechnology, 21(2010) 395701 (9pp)

Nanoimprint lithography (NIL)

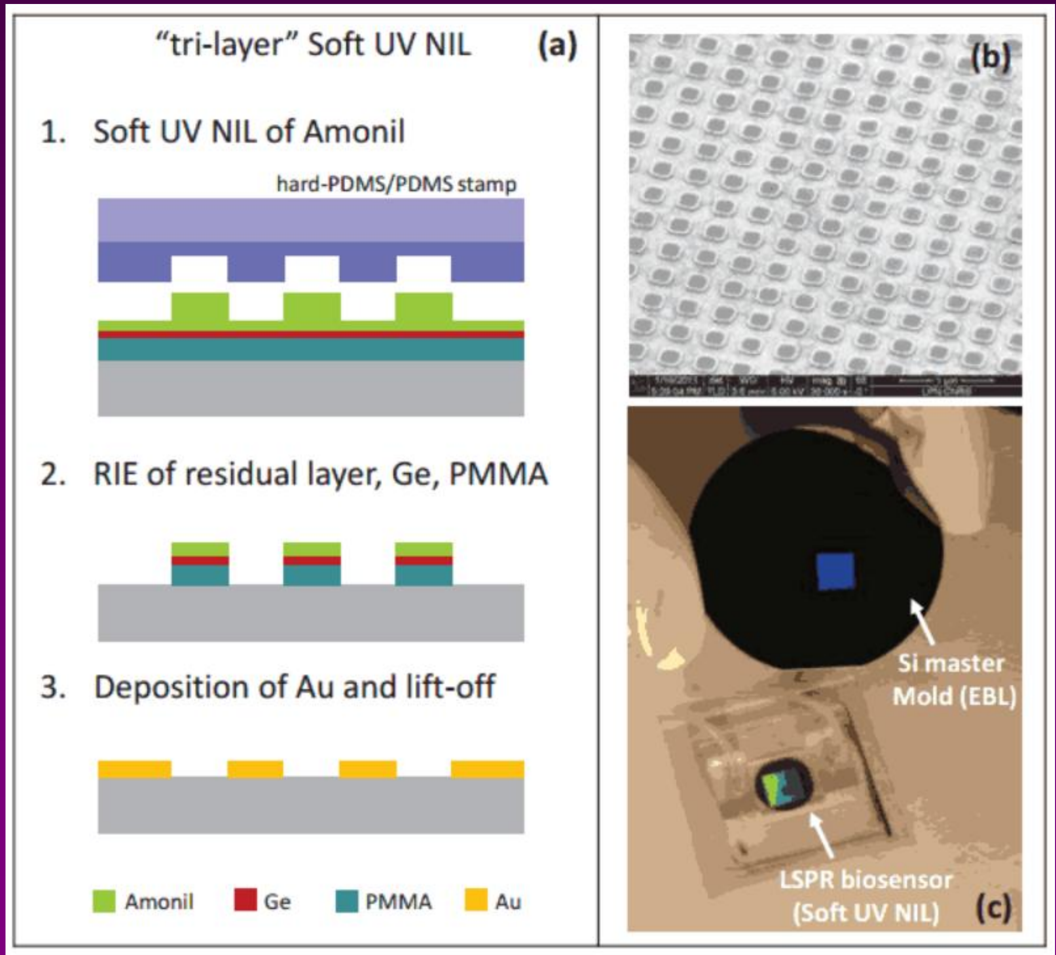
- Thermal assisted (T-NIL), 50 nm pitch, 100°C above T_g, 50-100 bar, 1995
- UV-NIL, 5 nm features, 0-5 bar
- Soft UV nanoimprint lithography (Soft UV-NIL), sub-50 nm range

Nanoimprint



Recent Advances in Nanofabrication Techniques and Applications, InTech, 2011, p. 140

Plasmonic nanocavities 200 nm, pitch 400 nm

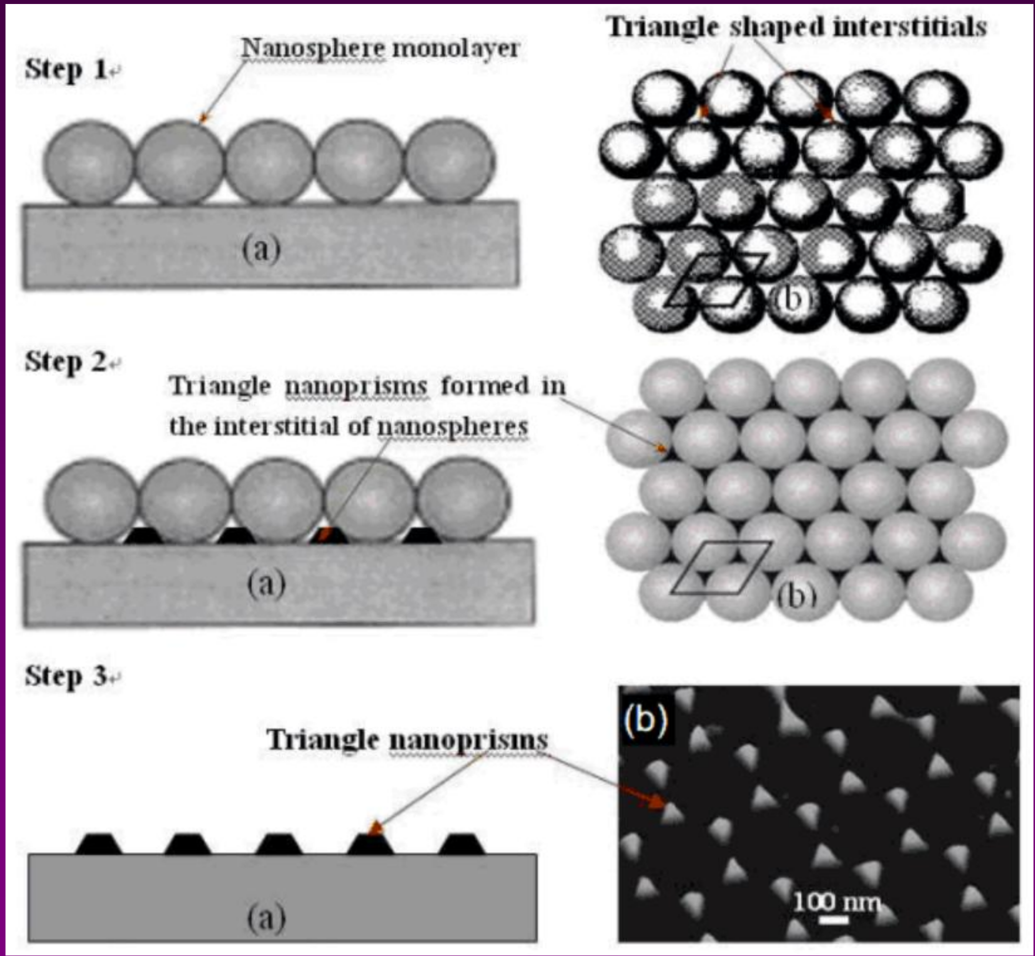


Glass substrate, large surface < 1cm^2,
Au/dielectric/Au islands
Ge -10 nm thick to improve the selectivity Amonil/PMMA
Amonil (NIL resist) is not soluble in solvents

A. Cattoni et al., Nanoletters, 2011, pp. 3557-3563

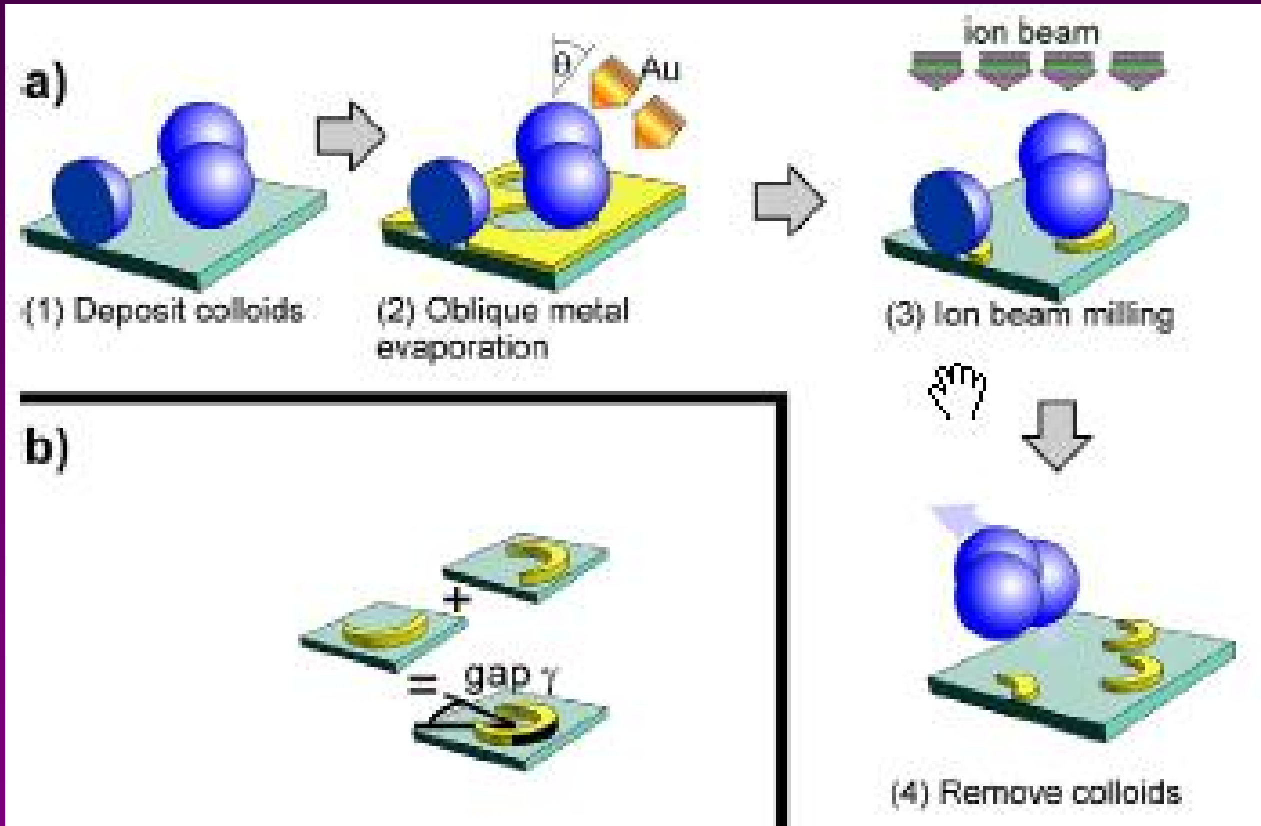
NSL

Dip-coating, drop-coatin, spin on.
Problems for < 100 nm spheres: surface roughness



Recent Advances in Nanofabrication Techniques and Applications, InTech, 2011, p. 508

Nanocrescents fabricated by nanosphere lithography



H. Rochholz *et al*., New Journal of Physics, **9** (2007) 53

Exotic SERS substrates

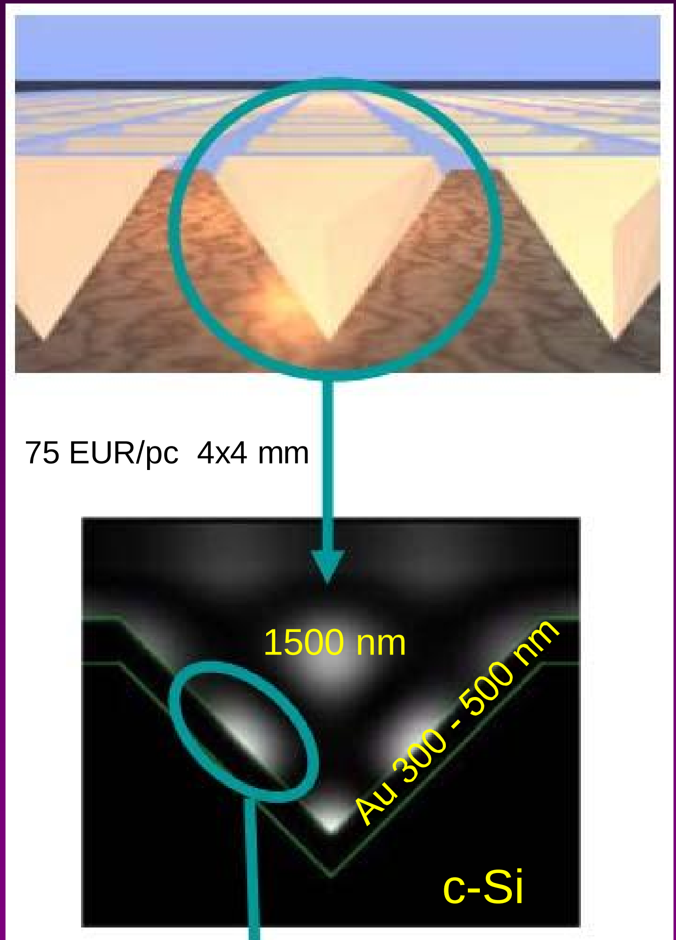
- On-wire lithography (segmented structures)
- Nano-capsules
- Nano-antennas (Bowtie, Yagi-Uda)
- Gratings and periodic structures (SPP)
  Nanoporous gold
- Hybrid SERS substrates (optical waveguide in leaky mode and nanoparticles
- Bio-enabled materials
- Optical fibers

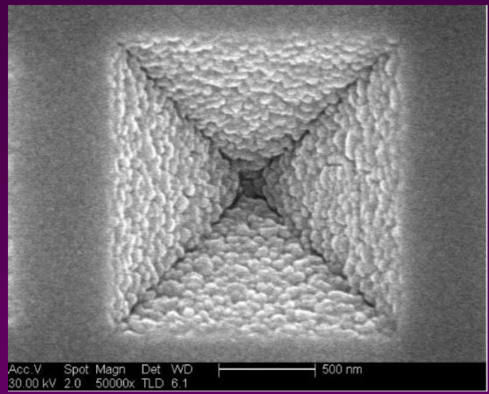
Ideal SERS substrate

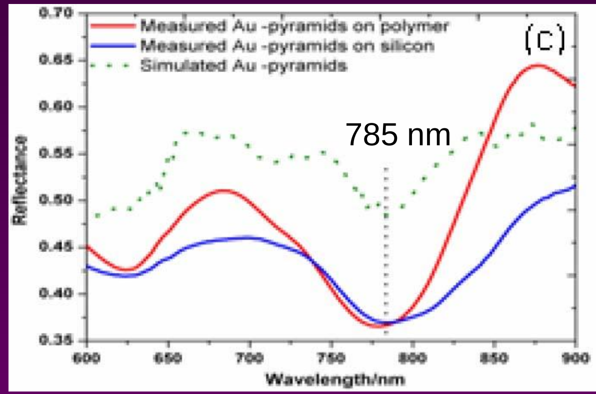
- High *EF*
- No fluorescence background
- Broad wavelength range
- Unlimited laser power
- Long shelf life
- Reproducibility
- Different environments
- Different available sizes
- Homogenity through the substrate area

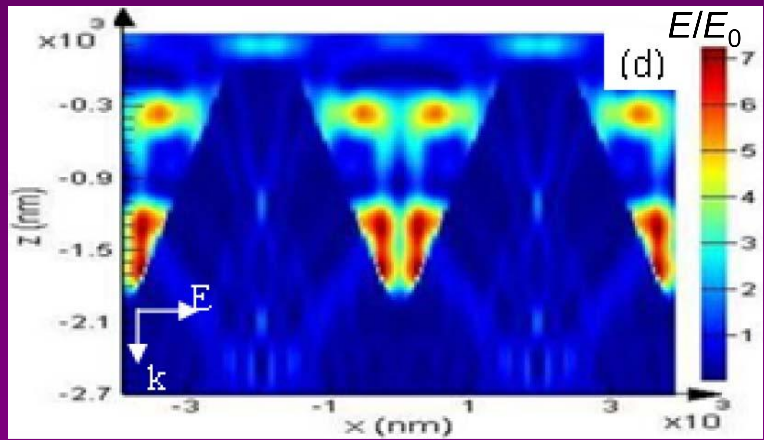
Saleable SERS substrate (Klarite)

Very high enhancement is ‘sacrificed’ in favor of homogeneity and reproducibility





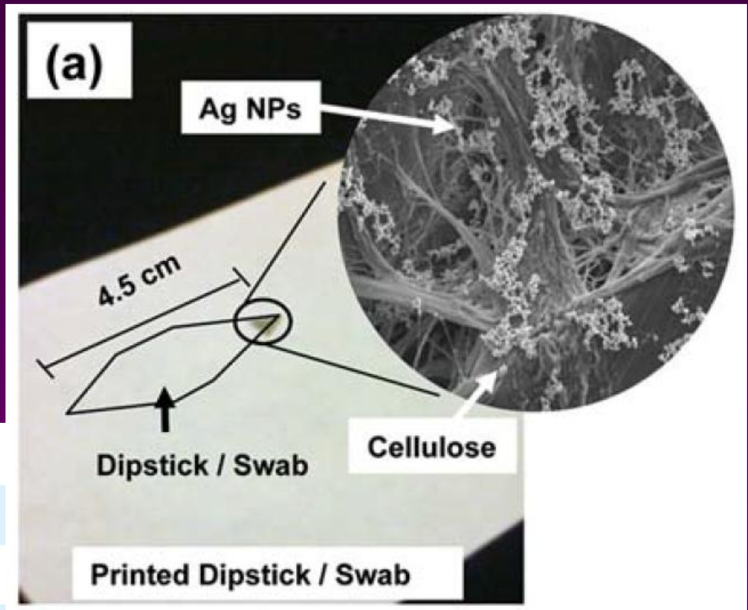




www.d3technologies.co.uk - www.renishawdiagnostics.com/en/klarite-sers-substrates
ZHIDA XU, Master Thesis, University of Illinois at Urbana-Champaign, 2011

Diagnostic anSERS Inc, USA

Metal purity
Temperature and humidity effect



Specifications	P-SERS™ 2.0
Physical	
Unmounted	~9 × 35 mm, ~9 × 5 mm sensing region
Slides	25 × 75 x 1 mm, 0.25 inch ø sensing region
SERS Sensor	
Enhancement	≈ 10^6, analyte dependent
Excitation	633 nm ≤ λ ≤ 1064 nm, 785 nm optimal
SERS material	Gold nanoparticles
Support	Cellulose (customizable)
Shelf life	3 months guaranteed, 6+ months typical

Ink jet printing

https://www.diagnosticansers.com/

Ocean Optics Inc, USA

Metal purity
Temperature and humidity effect

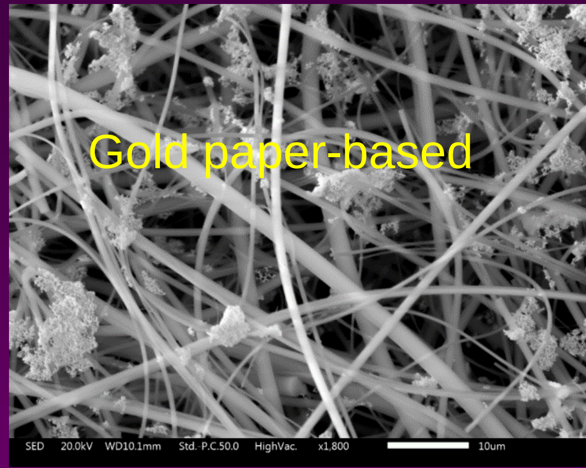
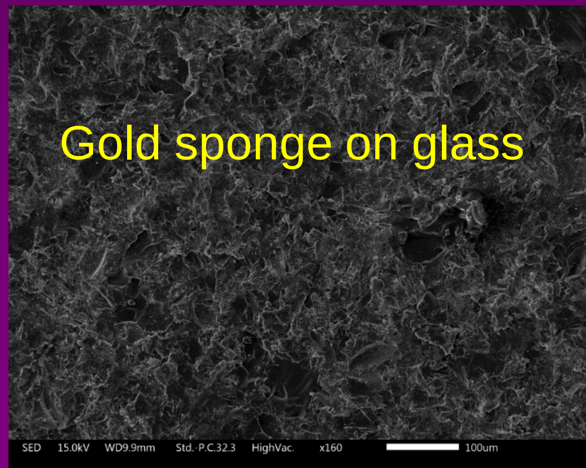


Table 1: SERS Substrate Product Details

Specification	**RAM-SERS-AU**	**RAM-SERS-AG**	**RAM-SERS-SP**
SERS Slide Dimensions	25.4 x 76.2 x 1 mm	25.4 x 76.2 x 1 mm	25.4 x 76.2 x 1 mm
SERS Active Area	5.5 mm diameter circle	5.5 mm diameter circle	4 x 4 mm square
SERS Active Chemistry	Gold (Au) Nanoparticles	Silver (Ag) Nanoparticles	Gold/Silver Film
Slide Material	Borosilicate Glass	Borosilicate Glass	Borosilicate Glass
Raman Excitation Wavelength	785 nm	532 nm	638 nm
Storage Lifetime	1.5 months	1 month	6 months
Reusable	No	No	Yes
Laser power	≤20 mW	≤20 mW	≤100 mW
Volume of analyte	15 µL	15 µL	10 µL



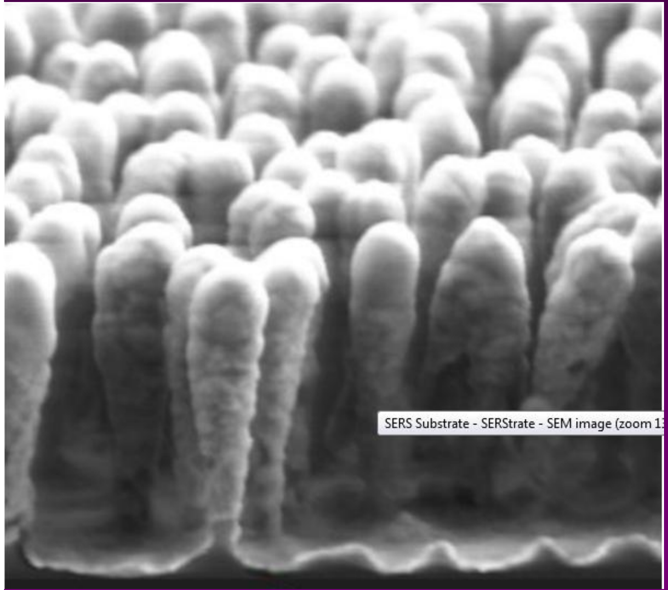
Special nanoparticle ink onto a flexible substrate

http://oceanoptics.com/product/sers/

Silmeco ApS, Denmark

SERStrate - Specifications

Dimensions	4x4 mm *(other dimensions are available on custom request)*
SERS active area	16 mm^2
Sensitivity	ppm to ppb
SERStrate surface metals	Gold or Silver, ***customization available***
Substrate material	Nanostructured Si
Measurement area	Arbitrary
Sampling methods*	Vapor deposition, drop deposition, substrate incubation (immersion)
Laser excitation wavelengths*	514 (silver), 532 (silver), 633 (silver), 780-785 (silver + gold) nm
Laser power density*	<10 W/cm^2

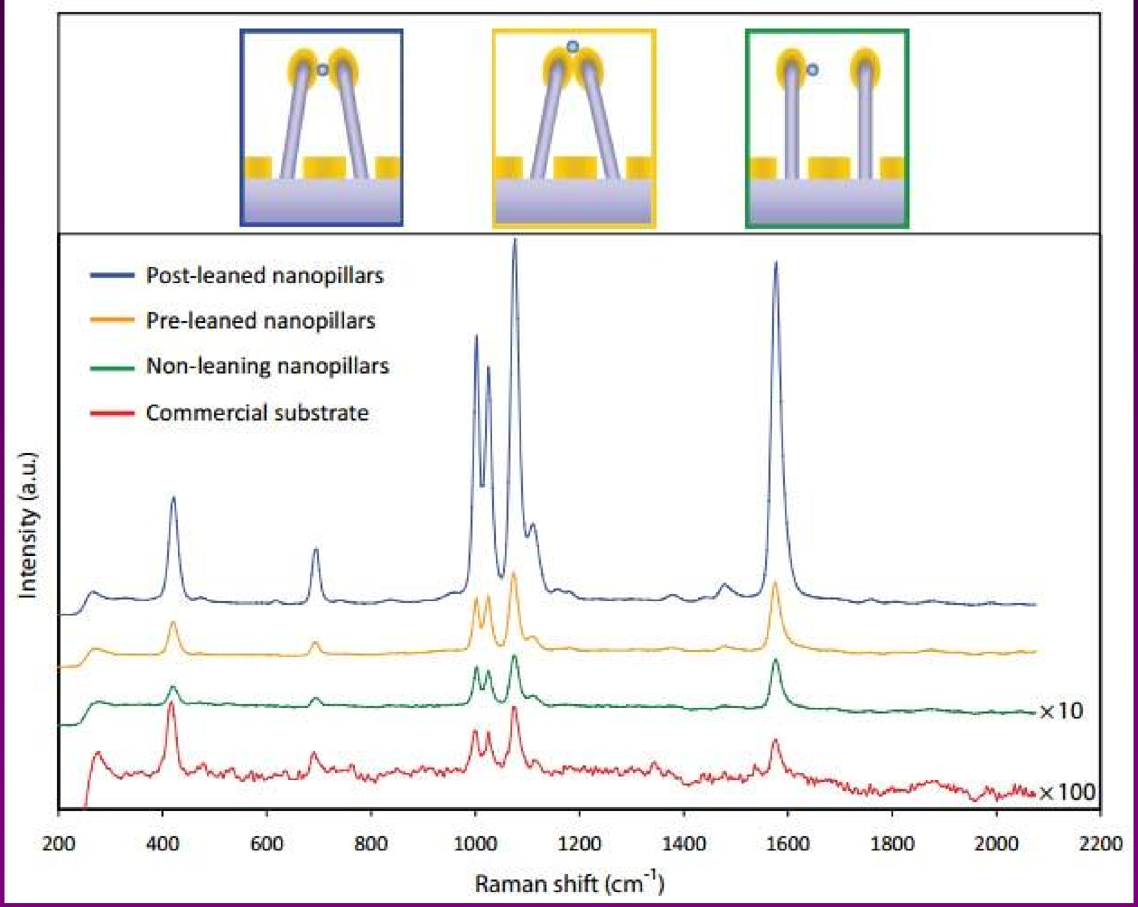


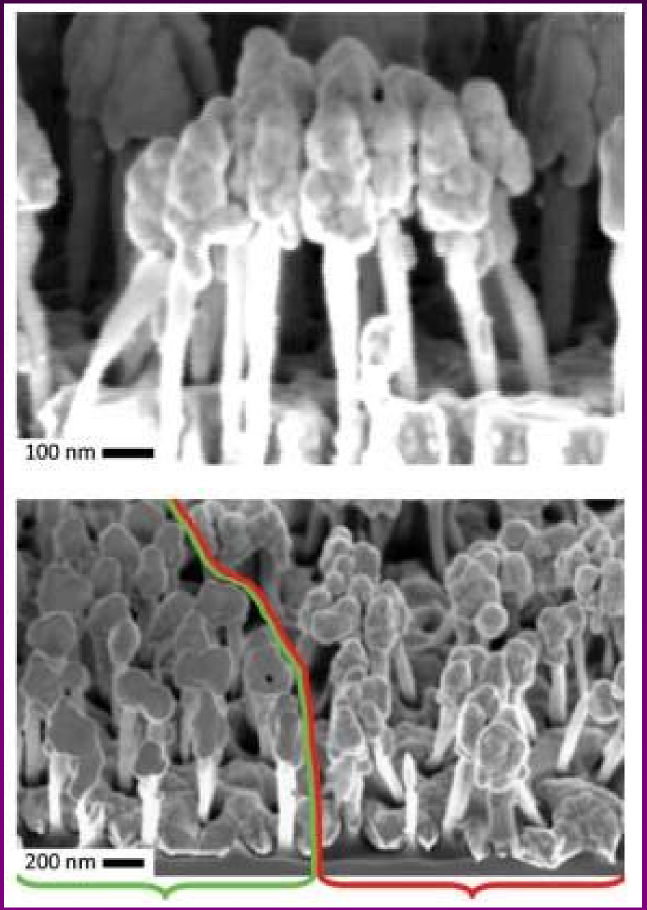
Self organized polymer mask and RIE

Cost

http://www.silmeco.com/

Leaning Si pillars





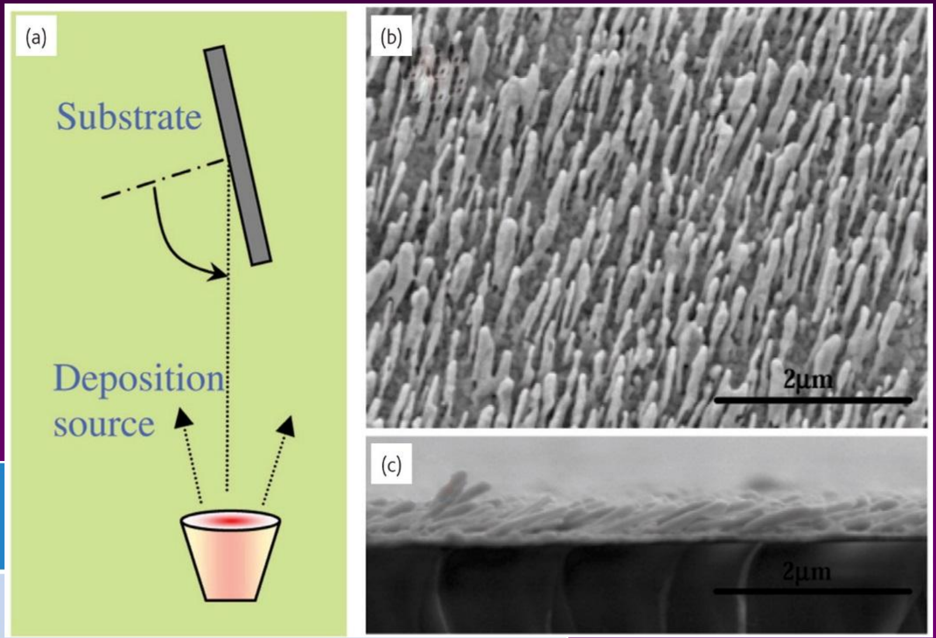
M.S. Schmidt et al., Adv. Mater. 2012, 24, OP11–OP18

no leaning leaning

HORIBA, Ltd., Japan

Dynamic oblique angle
vacuum evaporation

High cost



Specifications

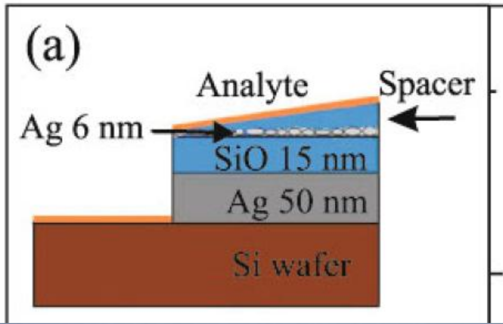
- **External dimension (slide glass type):** 76 mm x 26 mm
- **Active area dimensions (SERS chip dimensions):** 4 mm x 3 mm or 5 mm x 7 mm
  Recommended measurement field: 4 mm diameter area in the centre
- **Recommended excitation wavelength:** 633 nm, 785 nm, 830 nm
  Designed for enhancement around 800 nm
- The SERS chips are available separately in chip case or already mounted on the glass slide.

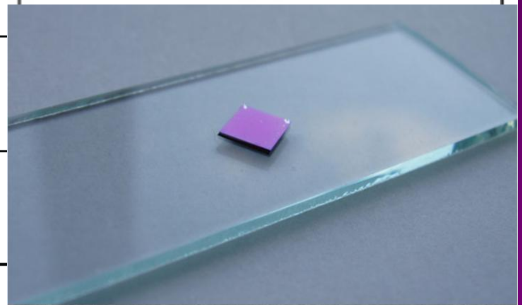
http://www.horiba.com

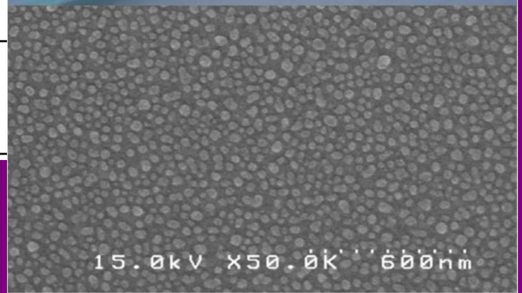
Enhanced Spectrometry, Inc., USA

Low EF
High cost
Only silver

EnSpectr substrate	Unmounted Chips
Size (mm)	6x6x0.5
Active area (mm)	ø 5
Sampling methods	Liquid drop deposition-evaporation Liquid drop spin coating Immersion Vapour phase deposition
Laser excitation parameters	λ 450 – 550 nm Spot size – arbitrary Power density < 5000 W/cm^2
Enhancement factor, relative to a non-enhancing surface	$>10^5$ - for neutral substances $>10^7$ – for resonant Raman analytes and substances exhibiting affinity to silver
Relative standard deviation in signal	<10%
Twofold reduction of the enhancement factor at open air	70 hours after opening the package



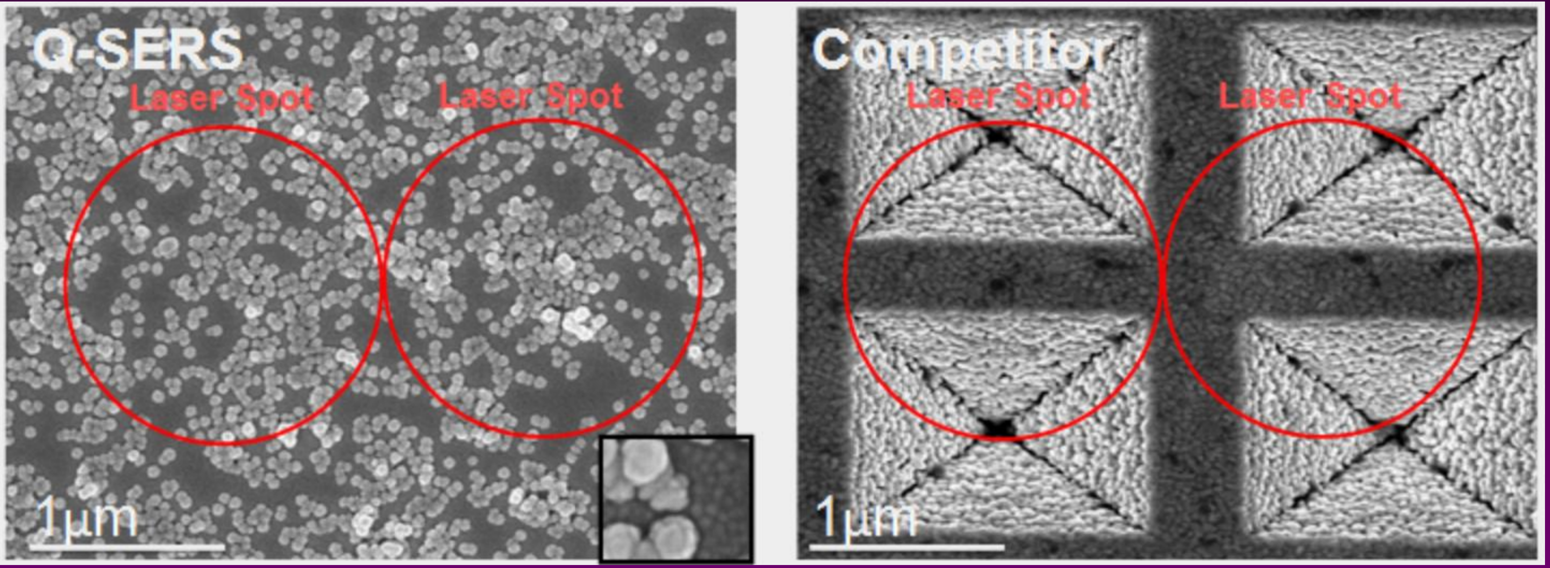




As deposited silver nanoparticles
Additional amplification due to Ag layer

http://enspectr.com/sers-substates/

Nanova Inc., USA



Bimodal gold particle distribution 60 nm and 15 nm
Excitation 785 nm

Large particles from colloid?
Small particles by evaporation

http://www.q-sers.com

Summary

- Metal nanostructures provide huge *EF* of the Raman scattering, making possible single molecule detection
- High informativity and sensitivity of SERS bursted multiple applications of the method in different areas
- SERS substrate fabrication, distribution and reproducibility are still main problems for SERS
- Desing and fabrication of SERS substrate provide additional information about substrate functionality

SERS future

- Commercial production of reproducible and cheap SERS substrate
- Cheap and functional portable Raman spectrometers
- Application of new plasmonic materials (graphene, semiconductors)
- Standartization and data bases for spectrum interpetation