Academia Romana

Plasmonic-Based Platforms to Provide Multiple Functionalities from Molecular Sensing to Imaging Diagnosis and Cancer Therapy

Simion Astilean,

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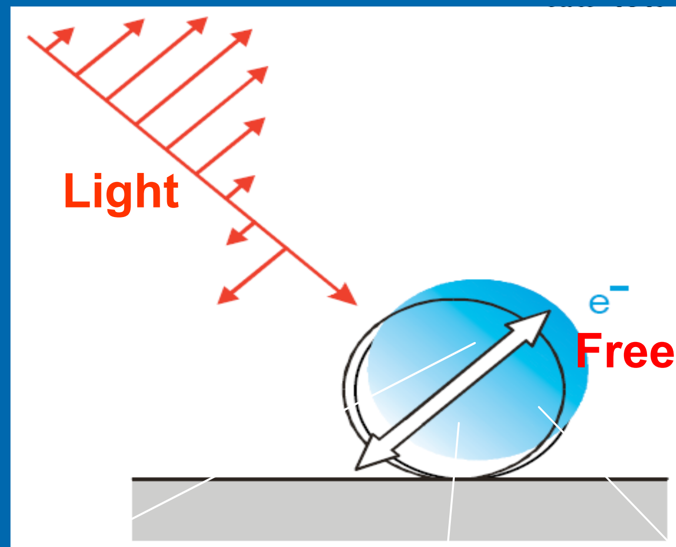
Babes-Bolyai University, Cluj-Napoca

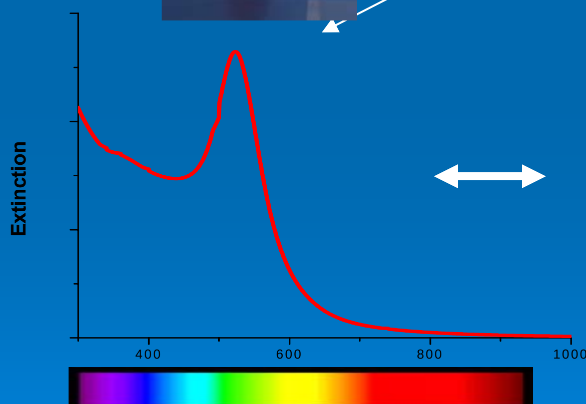
Seminarul National de Nanostiinta si Nanotehnologie, Editia a 14-a, 26 martie 2015

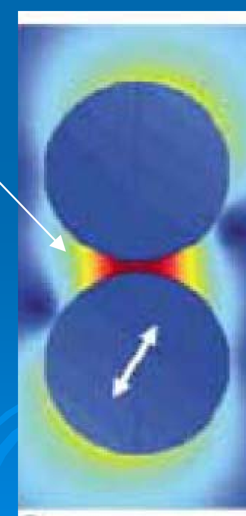
Outline

- **1**. Surface plasmon resoanance
- 2. Fabrication and functionalization of plasmonic and plasmonic-based hybrid nanostructures using inexpensive, flexible and massively parallel methods.
- 4. Applications in sensing via plasmon-enhanced spectroscopies: SERS & MEF, SERS & LSPR; SERS & SEIRA
- 3.Proof of concept for performing cell imaging / targeting / cancer therapy by combined photo-thermal / photo-dynamic effects
- 4. Conclusions

Surface Plasmon Resonances





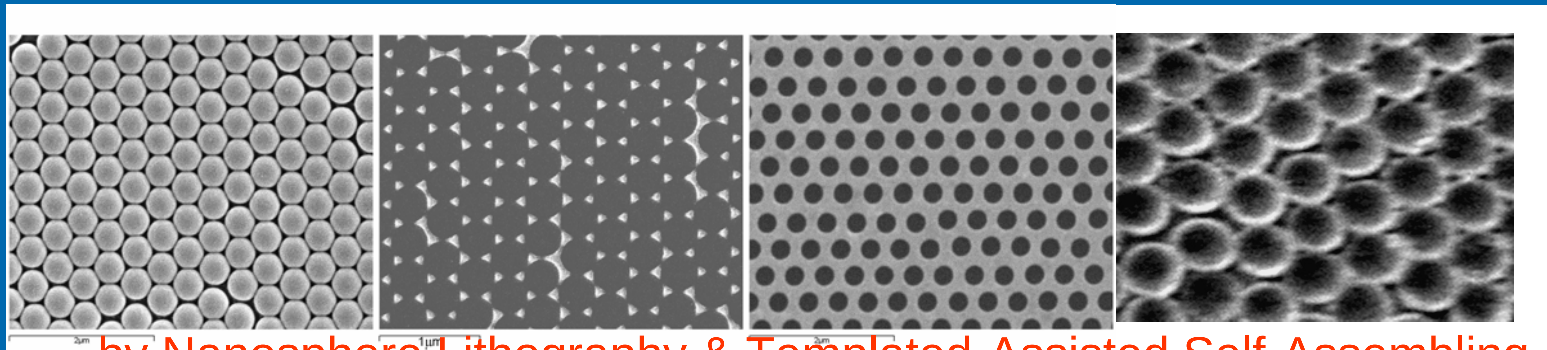


Resoanant Light Absorption
extinction coefficient of ~ 10^{11} M-1 cm-1

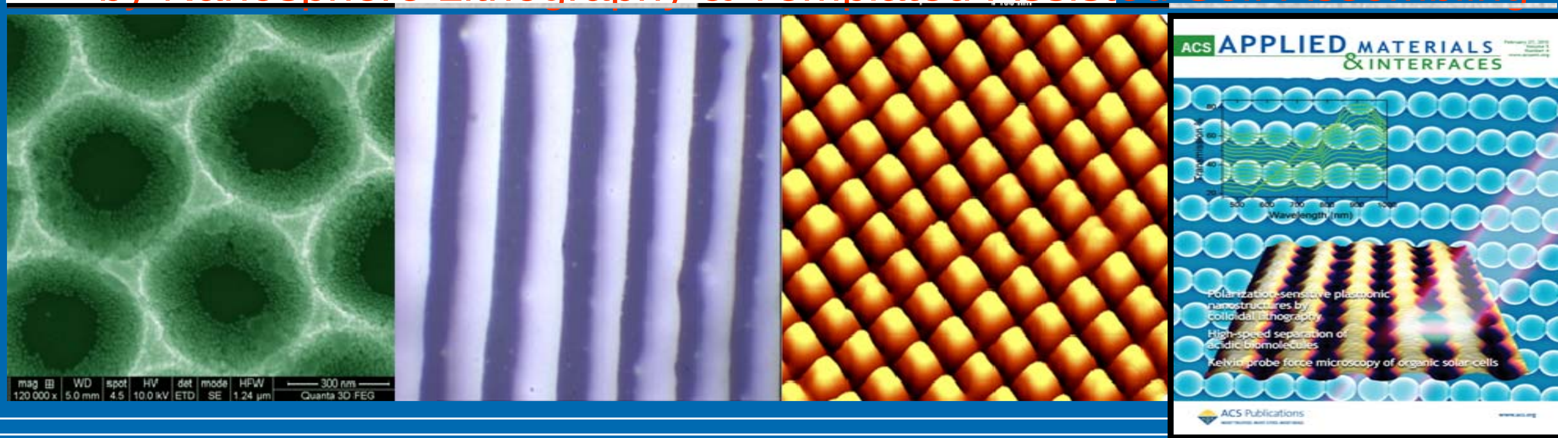
Resonant Light Scattering
~ 10^{6} dye fluorophores

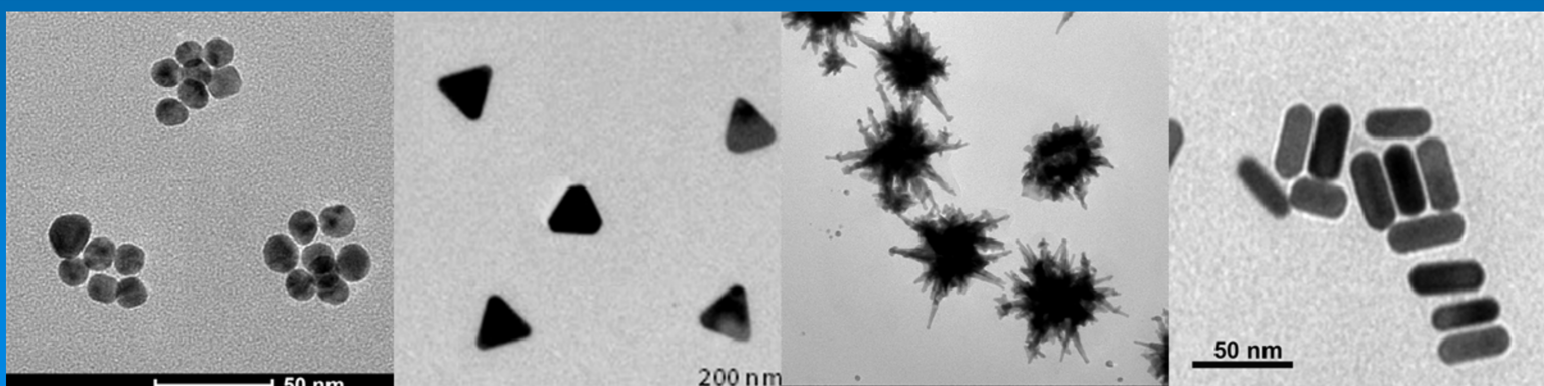
Enhanced Optical Field
~$10^{3\text{-}5}$ times

Plasmonic nanostructures fabricated in our laboratory



by Nanosphere Lithography & Templated-Assisted Self-Assembling

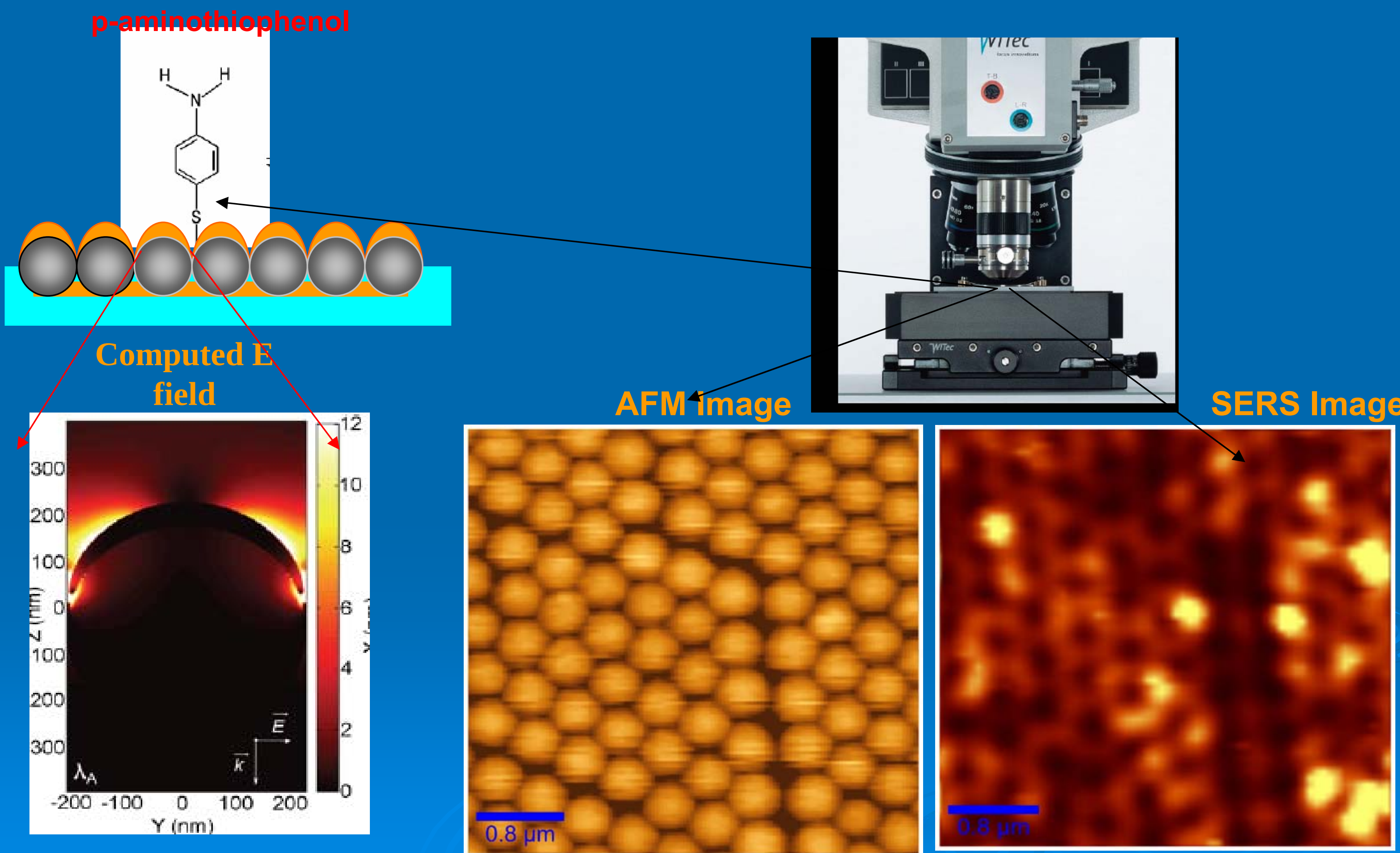




by Chemical Routes

Selected applications

Mapping the "electromagnetic enhancement" of SERS signal on metal-coated colloidal crystal

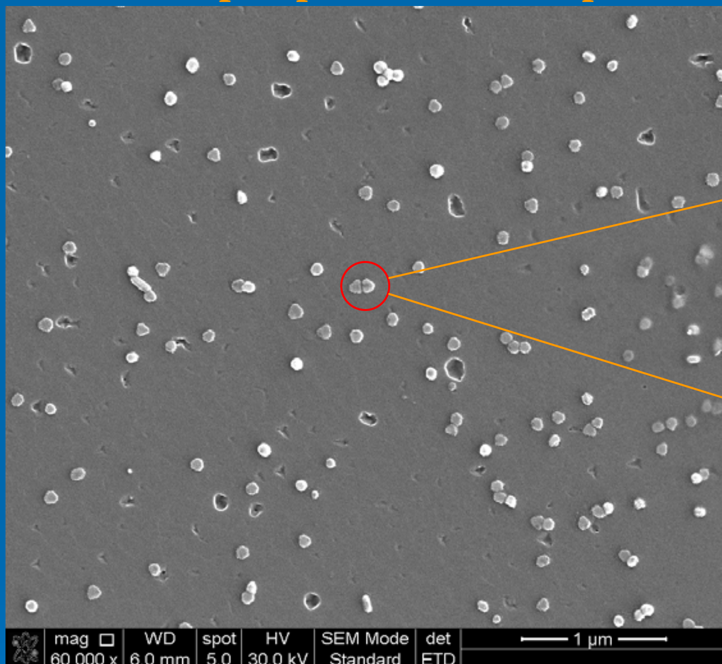


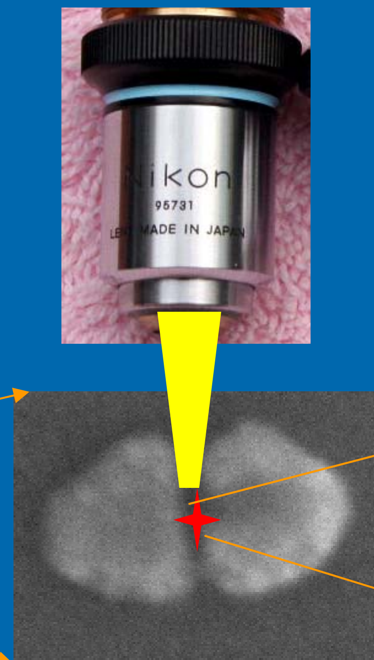
C Farcau and S Astilean, J. Phys. Chem. C, 114, 11717–11722 (2010)

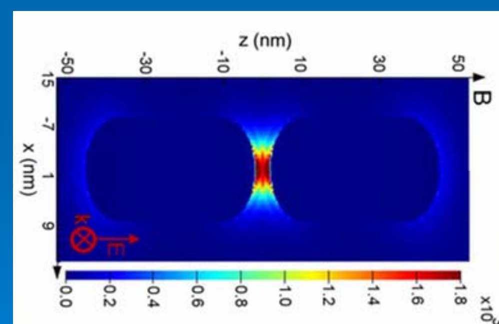
C. Farcau, M. Giloan, E. Vinteler, and S. Astilean, Appl. Phys. B 106:849–856 (2012)

Single-molecule detection *via* SERS

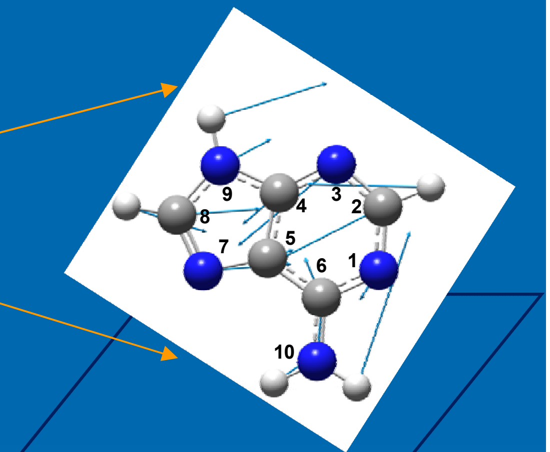
Chitosan-entraped plasmonic nanoparticles







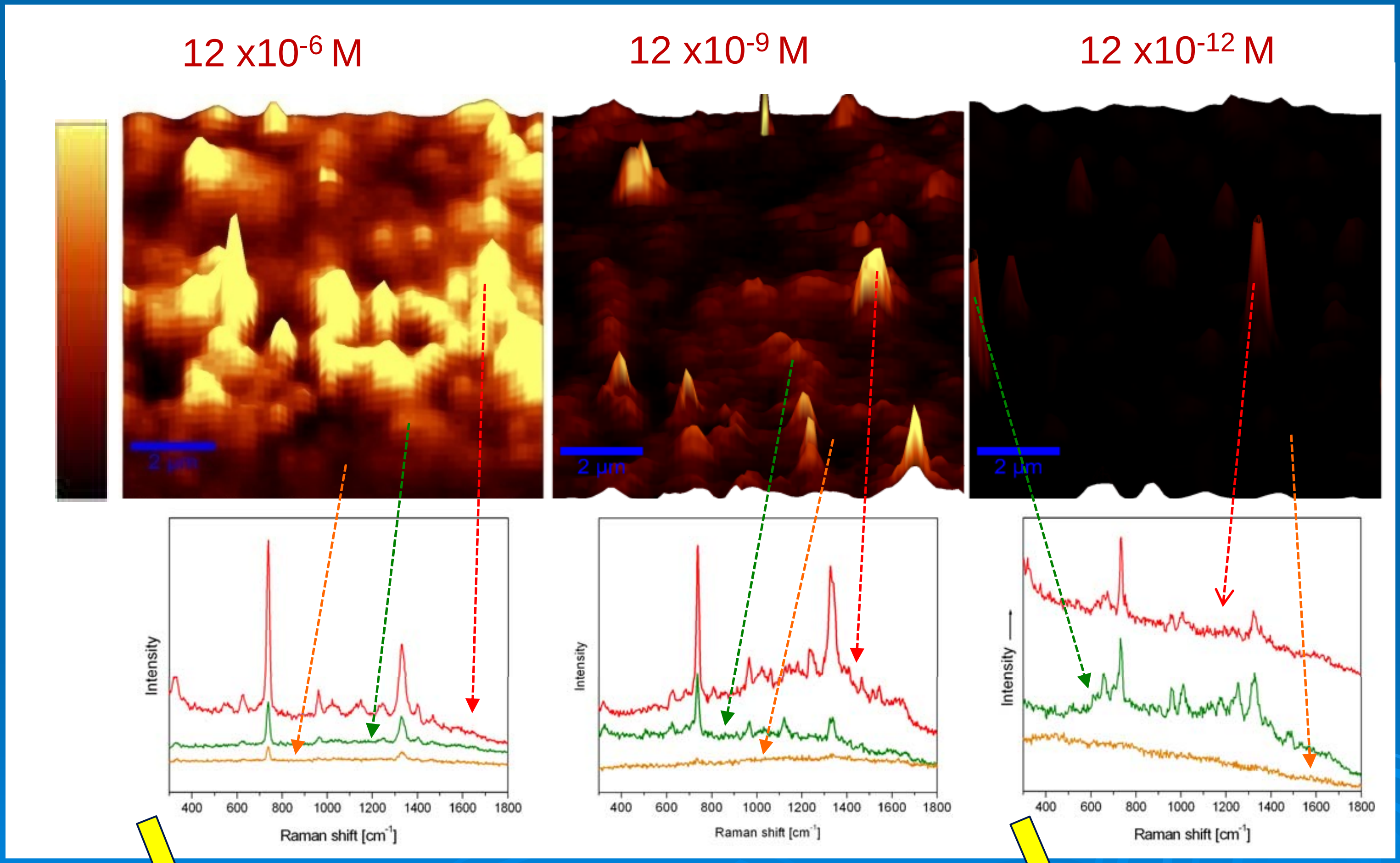
SERS spectrum of analyte molecule



Potara Monica, Baia Monica, Farcau Cosmin, Simion Astilean, Nanotechnology, Vol: 23 (5) Paper no 055501 (2012)

(highlighted at http://iopscience.iop.org/0957-4484/labtalk-article/48366)

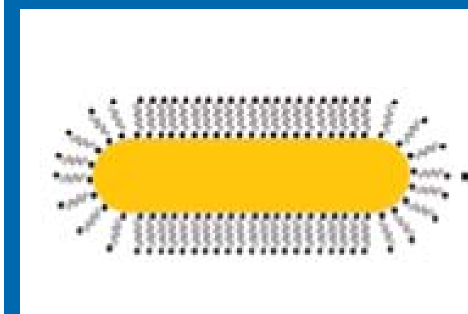
Single-molecule (adenine) SERS Imaging



SERS signal over the whole film surface

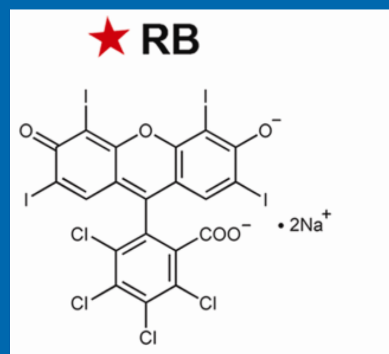
The SERS signal is highly localized

Gold Nanorods Performing as Multi-Modal Enhancers *via* MEF, SERS / SERRS

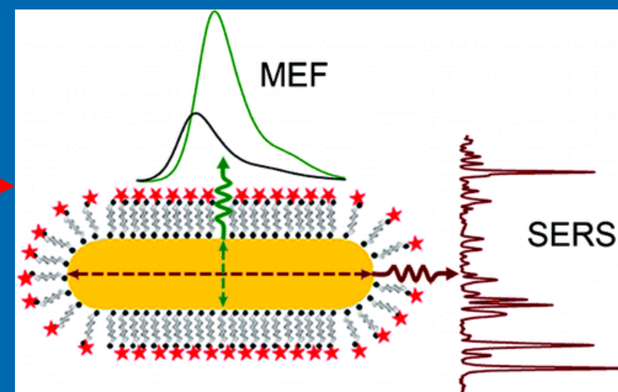


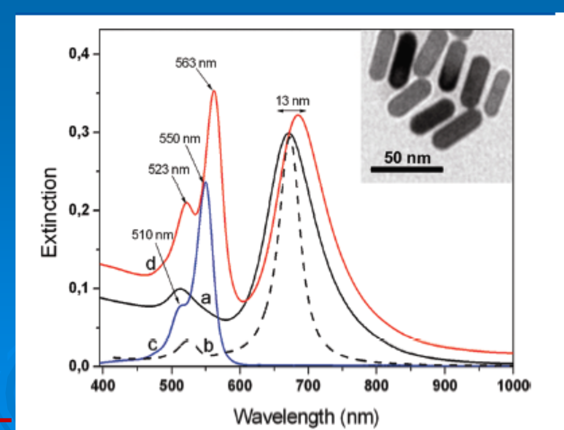
Gold nanorod

+



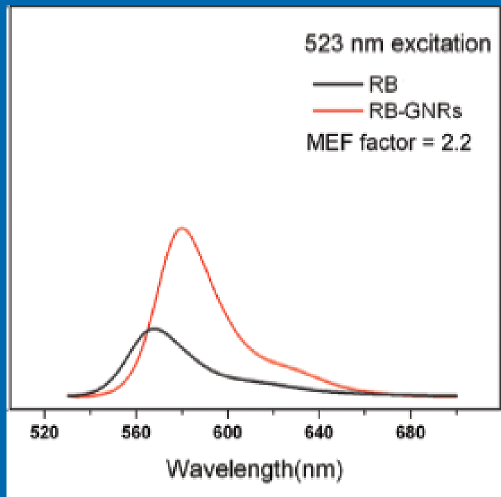
Rose Bengal
(Photosensitizer with low fluorescence quatum yield of 0.02)





A. M. Gabudean, M. Focsan and S. Astilean, J. Phys. Chem. C. 2012, 116, 12240−12249.

Metal-Enhanced Fluorescence



Steady-state fluorescence

The Journal of Physical Chemistry C

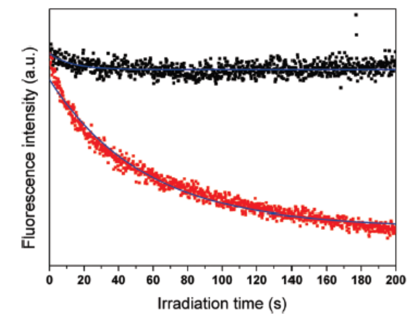


Figure 3. Photobleaching rate of RB−GNRs conjugates (black dots) as compared to that of free RB (red dots) upon high-intensity irradiation at 532 nm.

Photobleaching

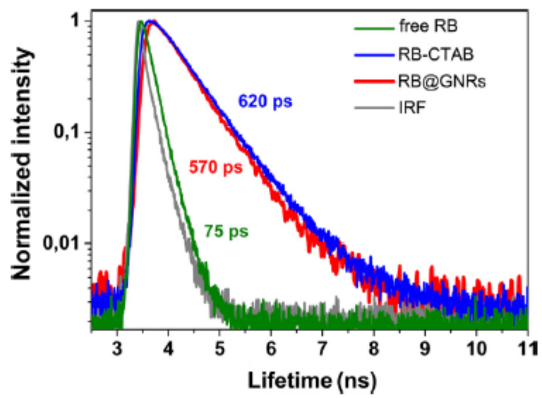
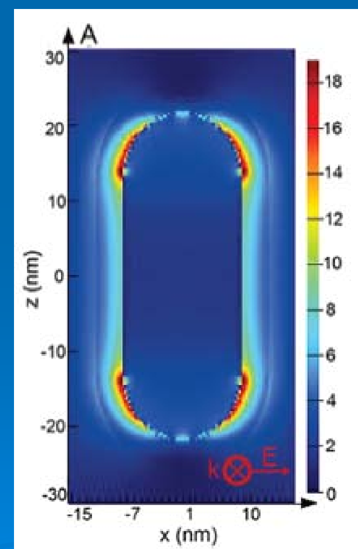


Fig. 3. Normalized fluorescence lifetime decays of free RB, RB–CTAB and RB@GNRs conjugates in solution. Final concentration of RB in the samples: 10^{-6} M. IRF represents the instrument response function. Excitation: 510 nm. Laser power: 0.36 μW.

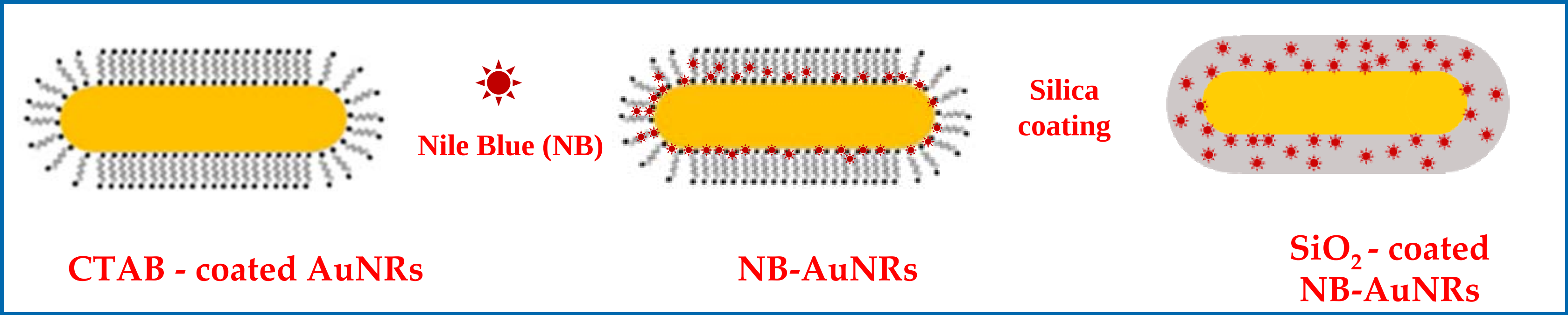
Fluorescence lifetime

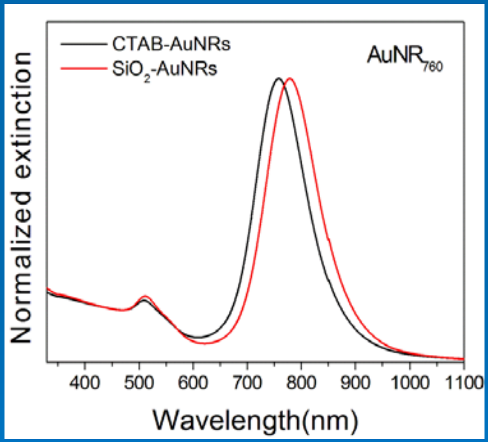


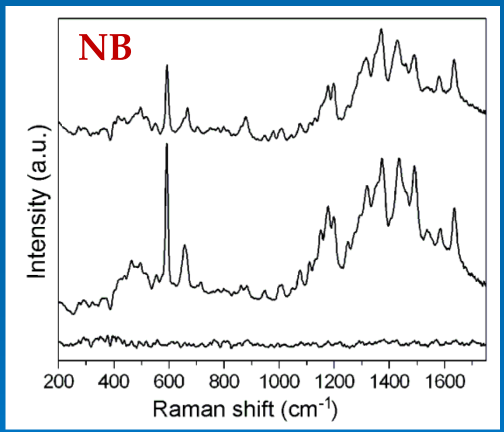
FDTD simulation

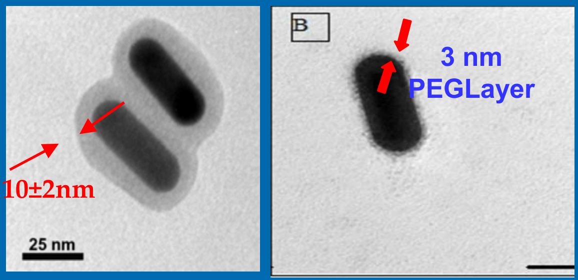
A. M. Gabudean, M. Focsan and S. Astilean, J. Phys. Chem. C. 2012, 116, 12240−12249.
A.-M. Gabudean et al. / Journal of Molecular Structure 1073 (2014) 97–101

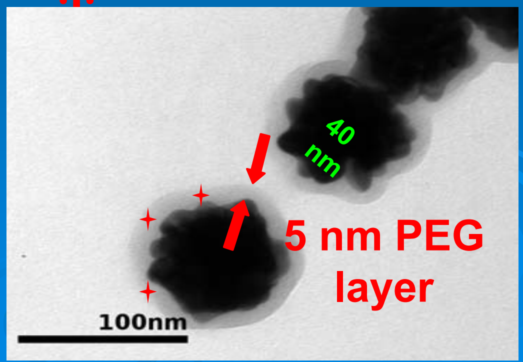
Detoxification of gold nanorods and SERS tagging





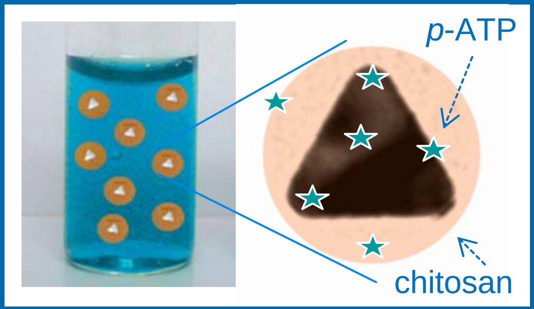




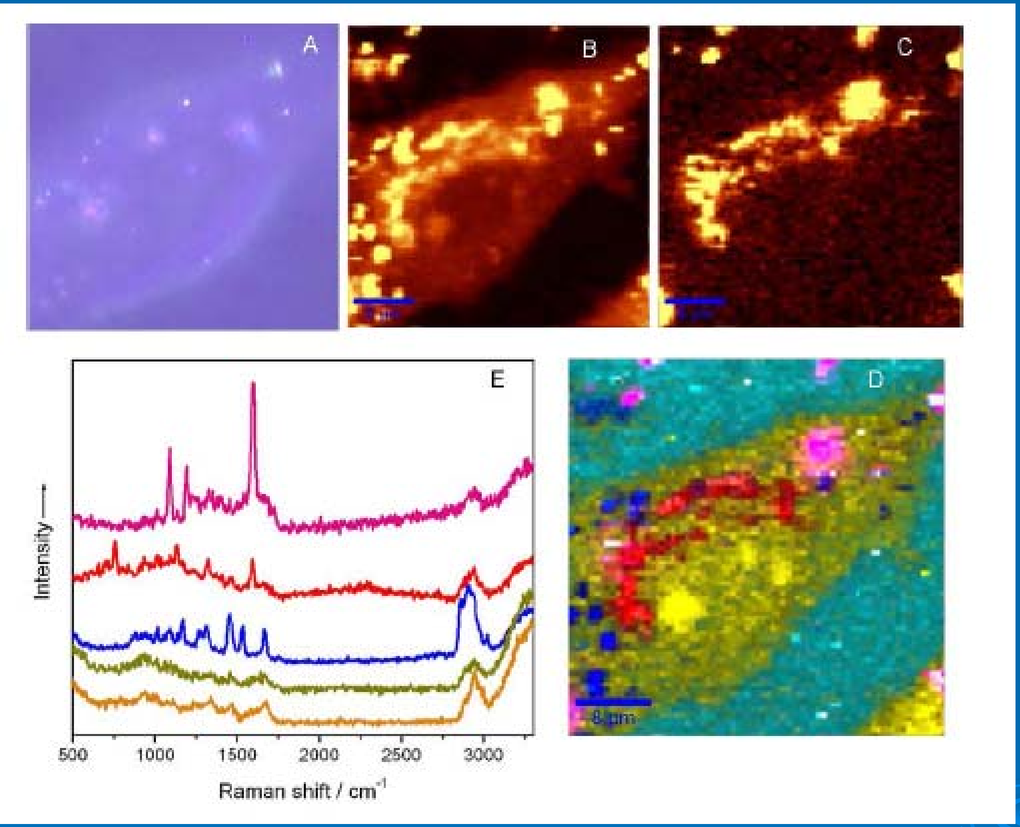


1. S. C. Boca, S. Astilean, Nanotechnology 21, 235601 (2010)
2. A. Gabudean, S. Astilean, Nanotechnology 23 (2012) 485706

Raman and SERS imaging of human lung carcinoma cell A549



p-ATP labeled chitosan-coated triangular silver nanoparticles



Mitochondria –blue

Cell body –dark yellow

SERS nanotags– red and pink

Nucleoli –yellow

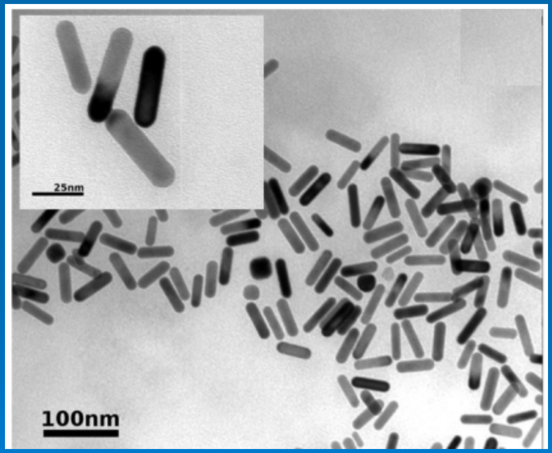
M. Potara, S. Boca, E. Licarete, A. Damert, M. C. Alupei, M. T. Chiriac, O. Popescu, U. Schmidt, S. Astilean, *Nanoscale* 5, 6013–6022, 2013

Plasmon mediated photothermal therapy

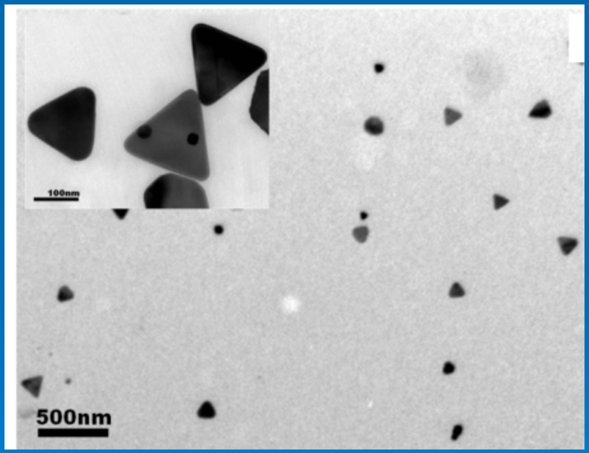
Cell types used in our experiments:

- **Human Embryonic Kidney (healthy)**
- **Human Lung Cancer Cells (tumoral)**

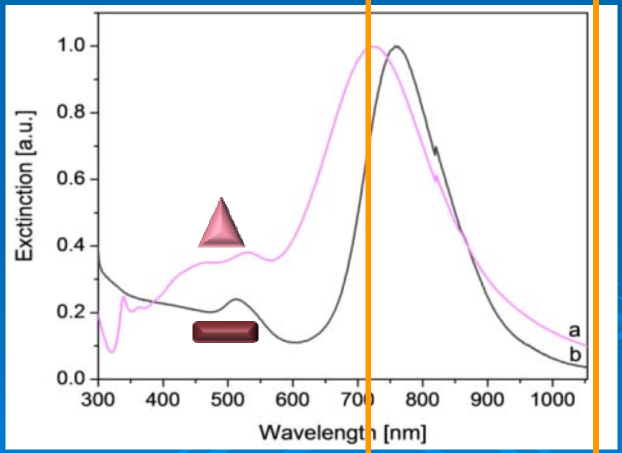
Nanoparticles used in our experiments



length: 50 nm
diameter:14 nm



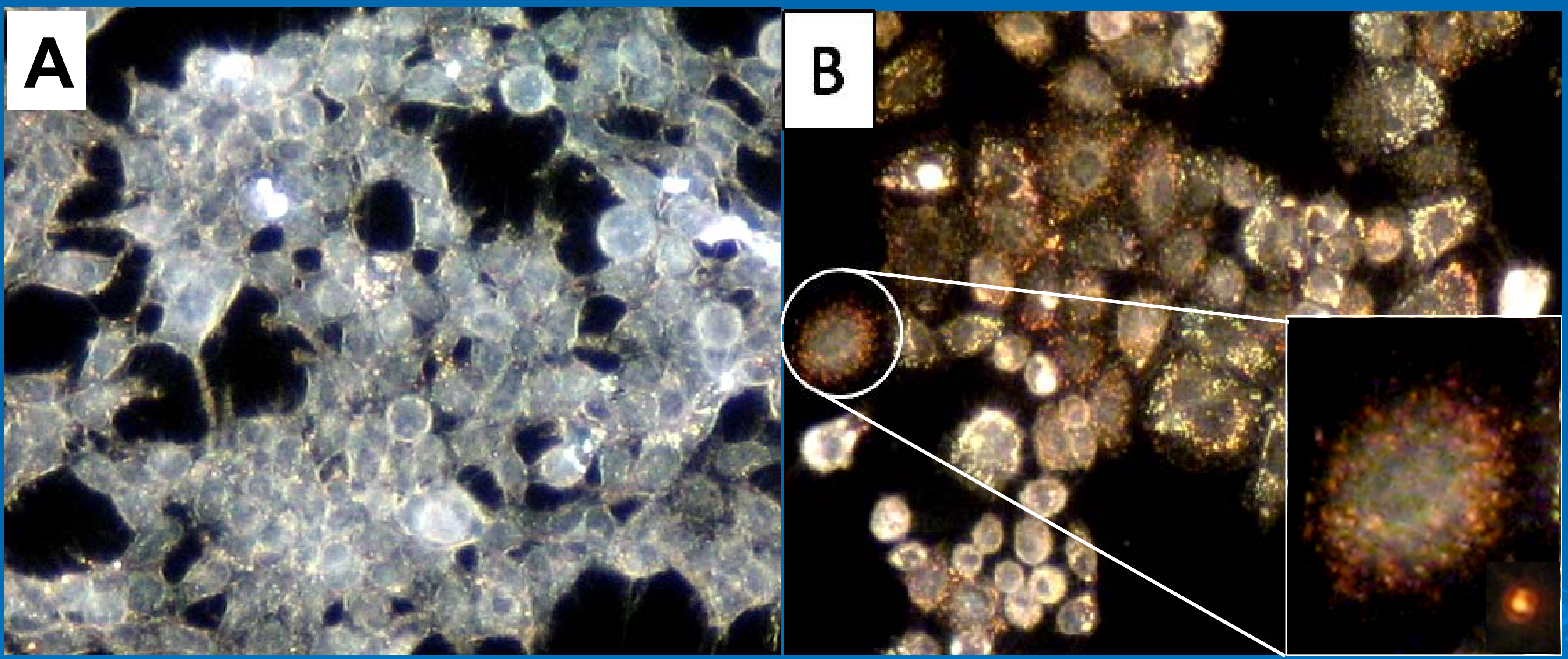
edge length: 120 nm
height: 11 nm



Biomedical spectral window

S. C. Boca, S. Astilean **Nanotechnology** 2010, *21*, 235601.
M. Potara, A. M. Gabudean, S. Astilean, J. Mater. Chem. 2011, *21*, 3625.

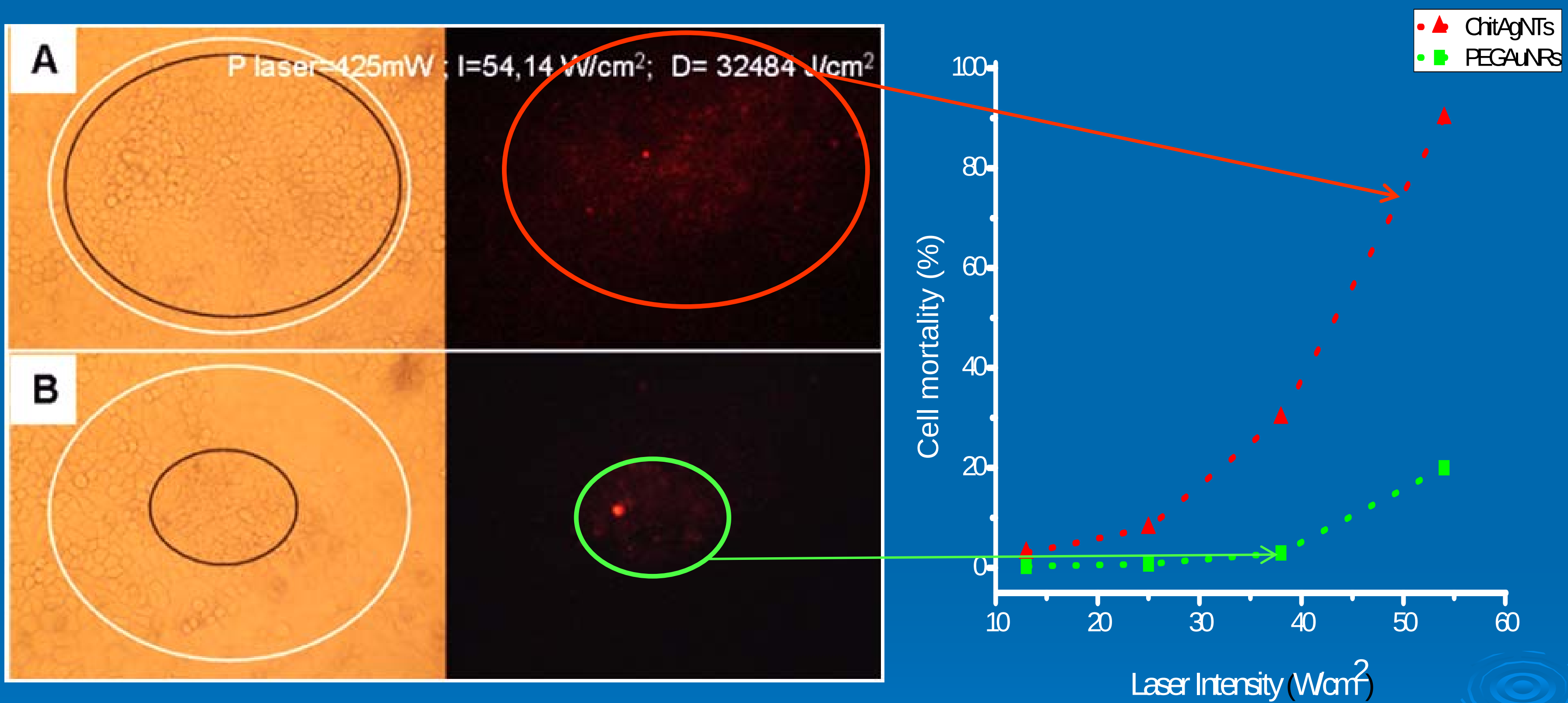
Assesment of nanoparticles uptake by cells
(dark field microscopy imaging)



Cells without nanoparticles

Rod shaped gold nanoparticles inside cells scatter red light

Plasmon mediated photothermal therapy of cancer cells



⇒ Cell mortality dependence on laser intensity

⇒ higher efficiency of **Chit-AgNTs** than PEG-AuNRs:
- -Density
- -Morphology
- -Silver thermal conductivity

S. C. Boca, M. Potara, A.-M. Gabudean, A. Juhem, P. L. Baldeck, S. Astilean, ***Cancer Letters*** **. Vol. 311(2):131-40, (2011 Dec. 8)**.

Perspective

molecular pharmaceutics

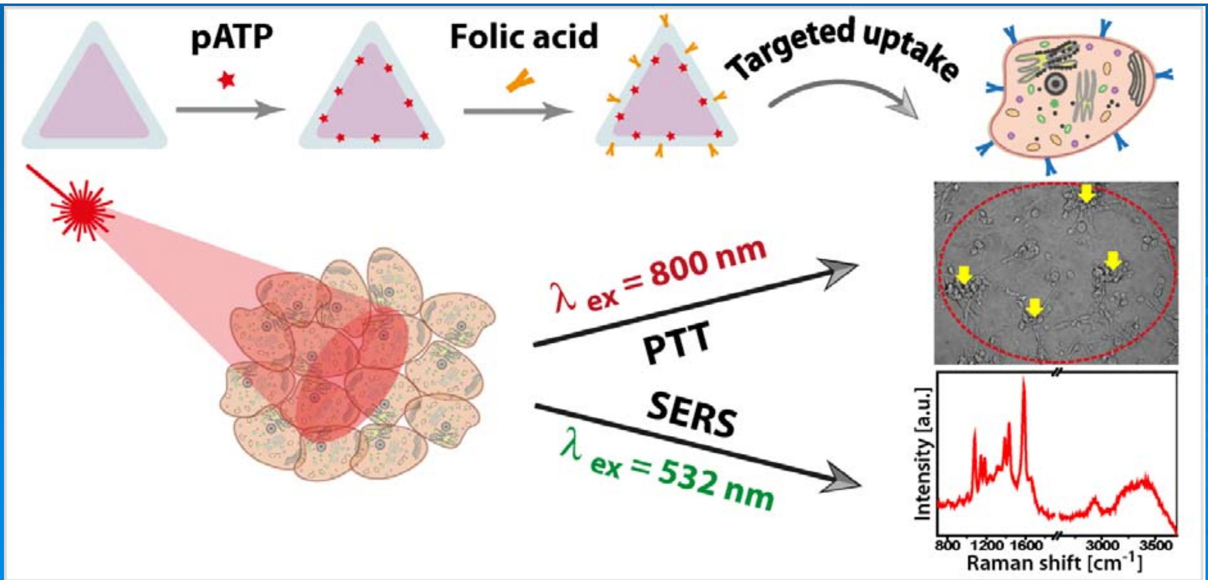
Article

Folic Acid-Conjugated, SERS-Labeled Silver Nanotriangles for Multimodal Detection and Targeted Photothermal Treatment on Human Ovarian Cancer Cells

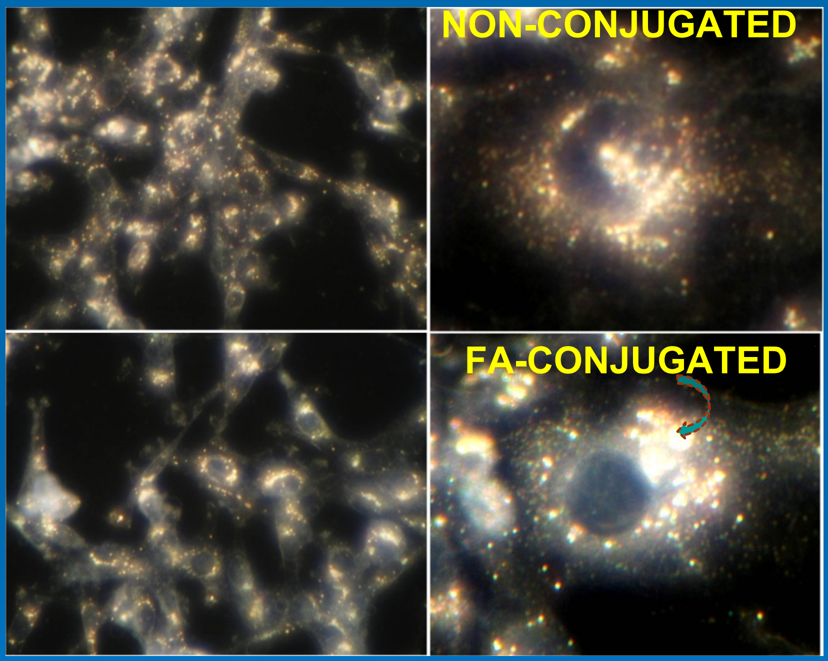
Sanda Boca-Farcau, Monica Potara, Timea Simon, Aurelie Juhem, Patrice Baldeck, and Simion Astilean

Mol. Pharmaceutics, **Just Accepted Manuscript** • Publication Date (Web): 04 Dec 2013

Just Accepted

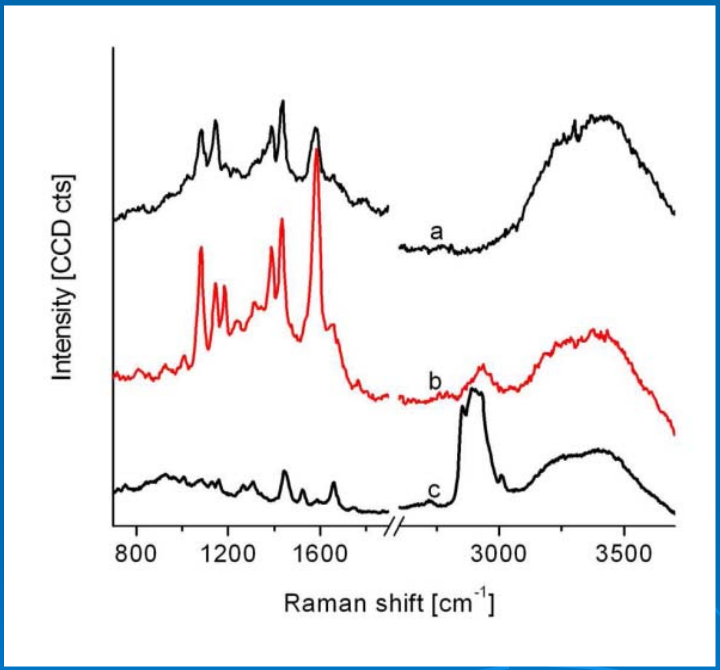


Nanopaticles can be detected inside cells by Dark field microscopy imaging



=> folic acid-pATP-Chit-AgNTs nanoparticles are **better internalized** and **specifically localized** inside cells than non-conjugated nanoparticles.

Nanopaticles can be detected inside cells by SERS spectroscopy



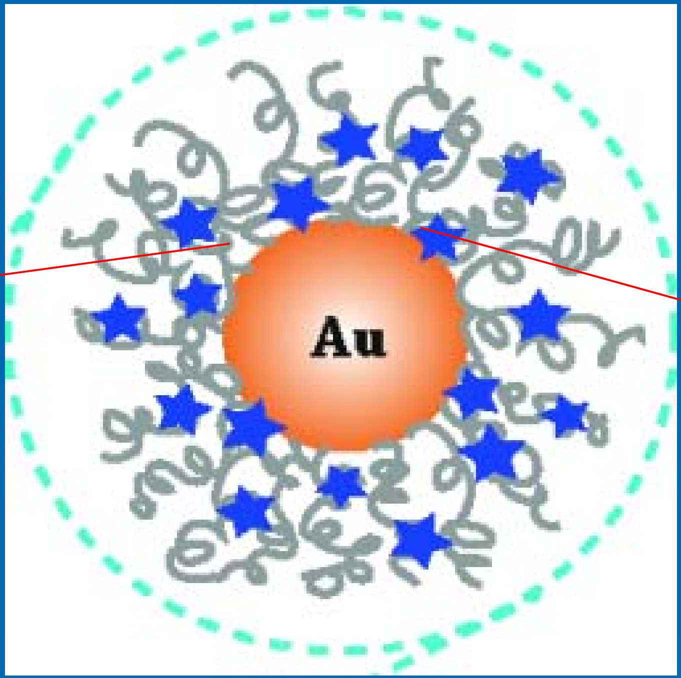
=> SERS spectrum of Raman-labeled, folic acid-conjugated chit-AgNTs inside living cells (red) presents the characteristic peaks of pATP reporter molecule

S. Boca-Farcau, M. Potara, T. Simon, A. Juhem, P. Baldeck, S. Astilean, **Molecular Pharmaceutics 2013**, **11 (2), 391-399**

Plasmon-assisted photodynamic therapy (PDT)

Polymer shell

(amphiphilic block co-polymer Pluronic)



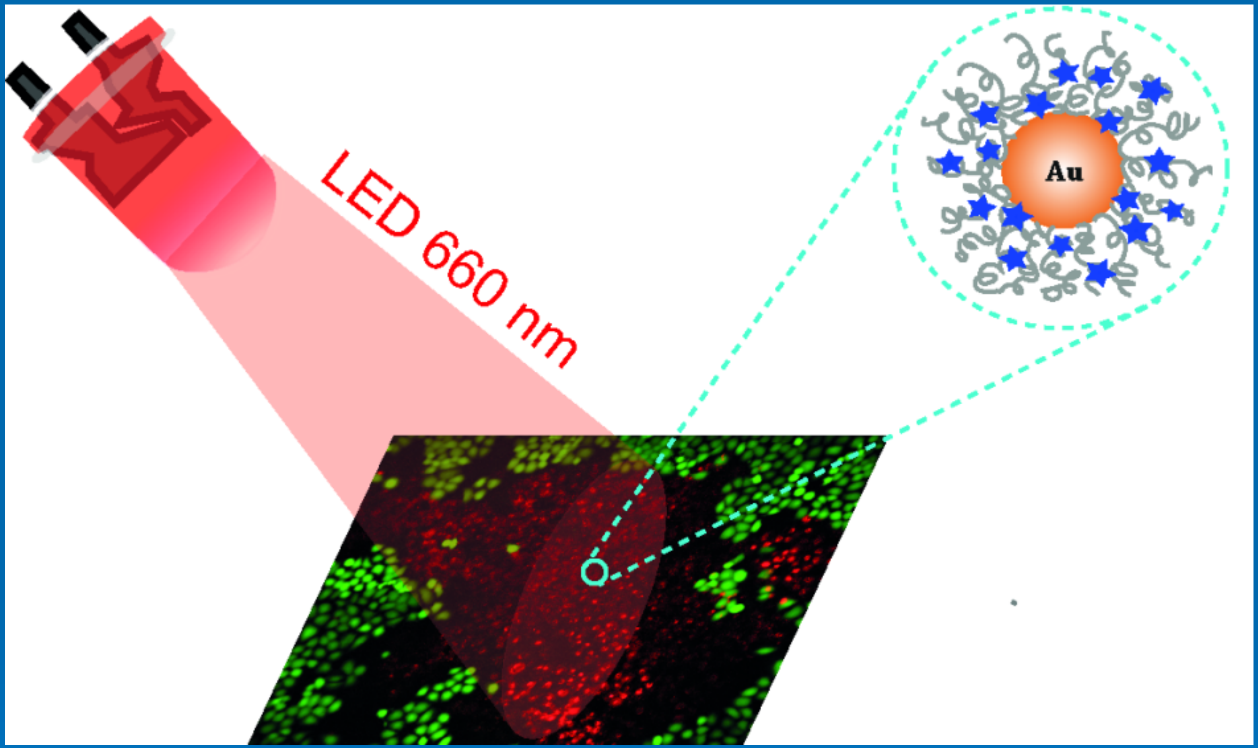
Photosensitezer

(methylene blue)

- synergistic treatment by ***combination plasmonic hyperthermia with PDT***
- plasmonic nanoparticles *reduce the photobleaching rate of photosensitizer*
- increase the triplet yield of photosensitizer, *enhancing singlet oxygen generation*
- polymer shell protects the photosensitizer from *enzymatic reduction*

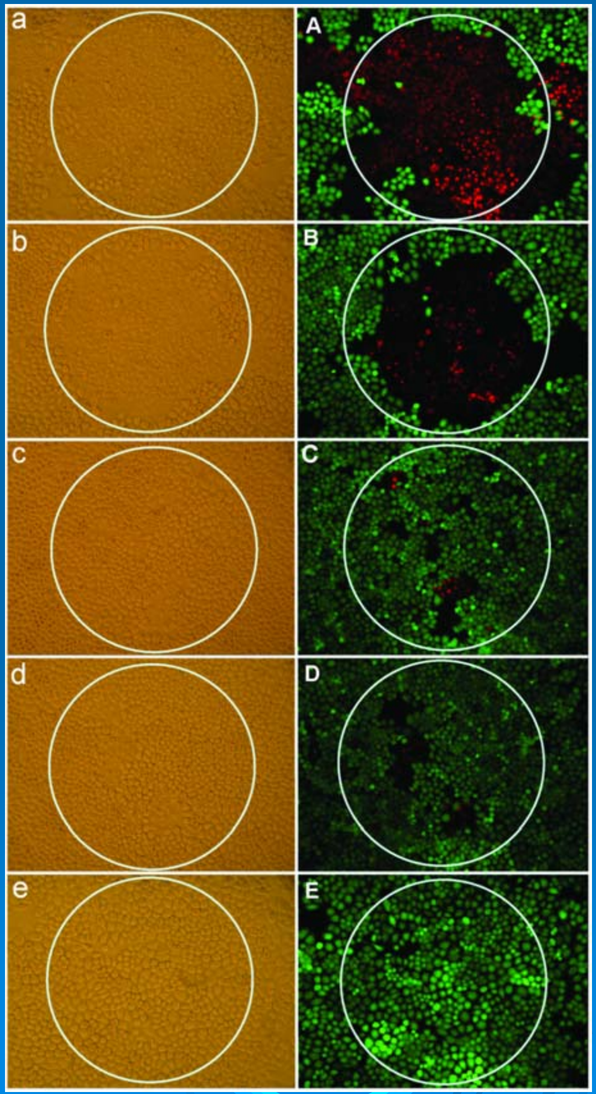
T. Simon, S. Boca-Farcau, A-M Gabudean, P. Baldeck, and S. Astilean, J. Biophotonics 1–10 (2013) 6 (11-12), 950-959

LED-activated methylene blue-loaded Pluronic-nanogold hybrids
(Au-PF127-MB)



T. Simon, S. Boca-Farcau, A-M Gabudean, P. Baldeck, and S. Astilean, J. Biophotonics 1–10 (2013) 6 (11-12), 950-959

Fluorescence microscopy illustrating the destruction of human lung carcinoma cells (HTB 177) loaded with Au-PF127-MB upon irradiation with LED.



780 mW/cm2

640 mW/cm2

520 mW/cm2

425 mW/cm2

780 mW/cm2
(control sample)

Acknowledgement

Financial support:

1. **Babes-Bolyai University**
2. **Project CEEX 71 /2006 (ANCS)**
3. **Project IDEI 407 / 2007 (CNCSIS)**
4. **Project IDEI COMPLEXE 129/ 2008 (CNCSIS)**
5. **Project IDEI COMPLEXE 312 / 2008 (CNCSIS)**

Collaboration:

Prof Octavian Popescu and collab**.,** Molecular Biology Center, Cluj-Napoca, Romania

Dr Patrice L. Baldeck and collab., Laboratoire de Spectrométrie Physique, Grenoble

Prof **Marc Lamy de la Chapelle** and collab., CSPBAT, Université Paris 13, France

Nanobiophotonics Group

(http://nano.uphero.com)

Mai multe informatii : http://nano.uphero.com

CENTER FOR NANOBIOPHOTONICS AND LASER MICROSPECTROSCOPY

User: Username Pass: ●●●●●●●●● Login

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Interdisciplinary Research Institute in Bio-Nano-Sciences
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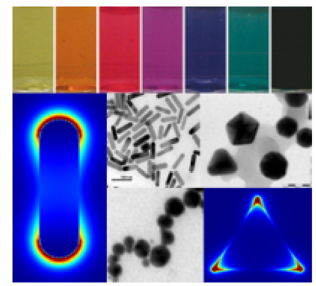
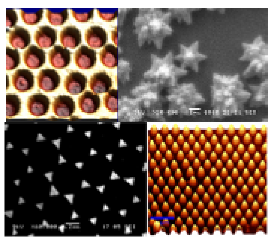
Tel.: 0040 (264) 405300
0040 (264) 454554
Fax: 0040 (264) 591906

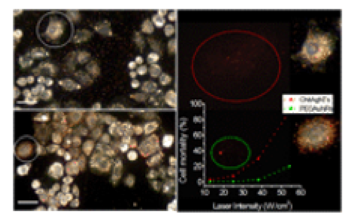
Welcome.



The *Center for Nanobiophotonics And Laser Microspectroscopy* develops an interdisciplinary research focused on the fabrication and biofunctionalization of noble metal, semiconductor and polymer nanoparticles and hybrid nanostructures that perform novel function in nanophotonics and plasmonics with the aim of enabling novel spectroscopic and plasmonic-oriented applications. Noble-metal nanostructures (Ag, Au) exhibit strong interaction with the visible light due to the excitation of collective electron oscillations (localized surface plasmons) and, on the other hand, can bind specifically to many biological entities (biomolecules, proteins, cells, bacteria).



Currently, we study the interactions between nanostructures and biological entities with standard optical spectroscopy (uv-visible, Raman, fluorescence) and advanced methods based on scanning confocal Raman microscopy, surface-enhanced Raman spectroscopy (SERS), surface-enhanced IR absorption (SEIRA), confocal reflectivity and fluorescence, localized surface plasmon resonances (LSPR), dark-field microscopy in combination with Atomic Force Microscoopy AFM.



We offer technical characterization of materials by Raman, fluorescence, and reflectivity with high performance instrumentation based on confocal Raman microscope (Alpha 300, three excitation wavelengths at 532 nm, 633 nm and 785 nm, detection between 100 - 3500 wavenumbers and lateral resolution better than ~ 250 nm) which is integrated with an atomic force microscope (AFM) of high spatial resolution and different operation modes. For more details concerning our infrastructure visit our Laboratory section. We are able to characterize, identify and image non-destructively chemical components and their molecular structure existing in heterogeneous materials, thin inorganic films, polymers, semiconductors, glasses, etc. in nanotechnology, life science, geology, pharmaceutical and food industry.

Additionally, we provide a large variety of nanostructured substrates (highly organized, regular arrays of noble-metal nanoparticles and films) with distinct optical properties and bio-chemical functionalities to operate as optical probe in bio- and chemical- sensing platform in the field of molecular biology, medicine and environment monitoring.