STSM REPORT

STSM Application number: COST-STSM-ECOST-STSM-BM1205-190514-044689

STSM Grantee: Alexey Popov

STSM title: Nanoparticles for cancer treatment

Home Institution: University of Oulu

Host Institution: Aix-Marseille University

STSM period: 09 May 2015 to 16 May 2015

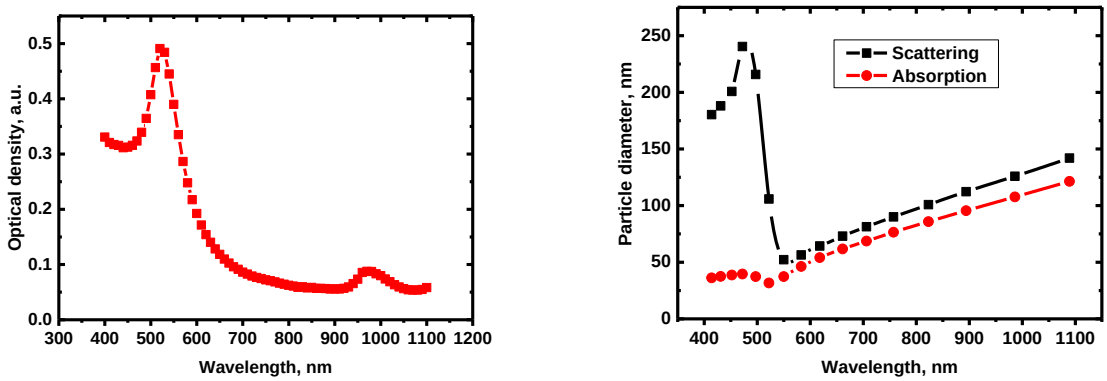
STSM purpose
Improving collaboration between the Finnish and French laboratories in the area of biophotonics in general and in applications of nanoparticle for cancer diagnostics and treatment in particular.

Description of the work carried out during the STSM
In frames of the above-mentioned STSM, gold and silicon nanoparticles for future experiments *in vitro* were fabricated by laser ablation. The utilized Yb: KGW laser emitted radiation with the following properties: wavelength - 1025 nm, pulse duration – 480 fs, pulse repetition rate – 1 kHz. The laser beam with an initial diameter of 2.3 mm was focused by a 75 mm lens onto the center of the cuvette, while the solution was stirred by a magnet to homogenize the ablation process. The duration of the laser fragmentation step was selected to provide a stabilized "quasi-equilibrium" size distribution of nanoparticles after the fragmentation of all microcolloids, as was determined from Transmission Electron Microscopy (TEM) images. The duration of this step depended on the concentration of the initial solution and varied from 45 minutes for 0.08 g L^{-1} to 5 hours for 1 g L^{-1} solutions. The experiments were carried out both in ambient conditions when water was saturated with air under atmospheric pressure and after bubbling of the solutions by nitrogen gas in order to deoxygenate them. The results of the laser-assisted nanoparticle fabrication are depicted in Fig. 1.

(a) (b)

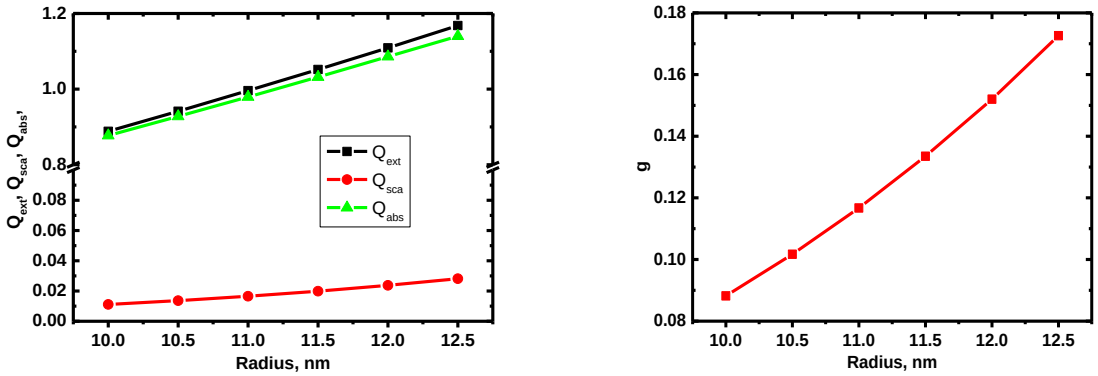
Fig. 1. Silicon (a) and gold (b) nanoparticles prepared by laser ablation.

The fabricated gold nanoparticles suspended in water were characterizes by their optical density spectrum (Fig. 2a). The pronounced peak localized in the green spectral range corresponds to the plasmon resonance of the particles. The other, much smaller peak in the near-infrared (NIR) spectral range is related to substantially larger particles with diameters of about 130 nm. Theoretical description of the optical properties of gold nanoparticles was performed by the Mie theory describing light interaction with spherical particles. Dependence of the most efficient particle sizes from the viewpoint of scattering and absorption, on the irradiated wavelength is depicted in Fig. 2b. The optical properties, such as extinction, scattering and absorption factors and a scattering anisotropy factor are illustrated by Fig. 3.



(a) (b)

Fig. 2. Optical density spectrum of the gold nanoparticles prepared by laser ablation (a) and theoretically calculated (Mie theory) dependence of the most efficient particle size from the wavelength.



(a) (b)

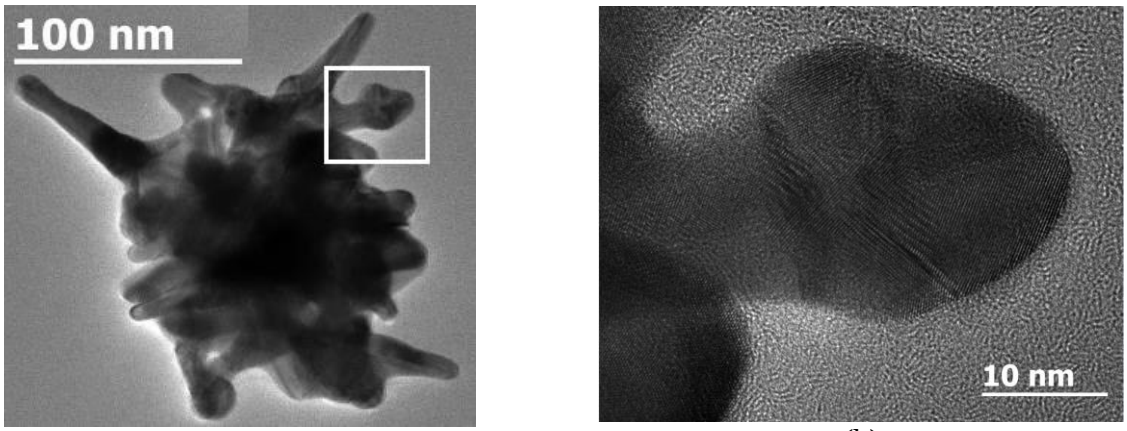
Fig. 3. Extinction, scattering and absorption factors (a) and scattering anisotropy factor (b) of gold nanoparticles in water for 532-nm irradiating wavelength calculated according to the Mie theory.

In addition to experimental and theoretical studies of the nanoparticles, discussions not only with the host, Dr Andrei Kabashin, Head of one of groups in the visited laboratory, but also with other group leaders (Dr Thierry Sarnet, Dr Olivier Uteza, Dr Jörg Hermann) were performed. Facilities of the Lasers, Plasma and Photonic Processes Laboratory (LP3) of Aix-Marseille University, such as laser systems for chemical-free fabrication of nanoparticles, an atomic force

microscope, and a unique powerful laser system for generation of X-rays were observed.

Several topics induced mutual interest, were discussed: nanoparticles for cancer diagnostics and treatment; optical techniques for food analysis and laser printing technology. We paid special attention to joint research in the field of COST action BM1205, involving utilization of nanoparticles fabricated in France for their applications in Finland. The application includes toxicity tests of gold, silicon and gold-silicon nanoparticles prepared by laser ablation; optical imaging of HeLa cancer cells labelled with nanoparticles; optoporation of HeLa cancer cells as model cells for cancer treatment using suitable lasers and relevant nanoparticles. We discussed collaboration in frames of Erasmus+ student and staff exchange program; invitation of Dr Kabashin to University of Oulu for teaching a short course later this year for doctoral students specializing in biophotonics, electrical engineering, materials physics and biology. Utilization of LP3 facilities for Finnish researchers was discussed.

High-resolution images of gold nanostars delivered from Finland were obtained in University of Caen, in collaboration with Dr Oleg Lebedev (Fig. 4). Further analysis of the images allows for refined synthesis. The images are of high importance for modelling of optical properties of such objects. The modelling is currently under way in Finland.



(a) (b)

Fig. 4. High-resolution TEM photographs of gold nanostars: whole object (a) and the enlarged fragment (b).

Description of the main results obtained

1) Silicon and gold nanoparticles for toxicity tests and cancer treatment were produced;
2) Optical properties of the gold nanoparticles were assessed experimentally and theoretically;
3) High-resolution images of gold nanostars and up-conversion nanoparticles were obtained;
4) Schedule for cancer diagnostics and treatment with nanoparticles was agreed;
5) Visits of Dr Kabashin and Dr Ryabchikov to Finland for lecturing and experiments were agreed.

The collaboration will result in innovative nanotechnological products for cancer treatment resulting in lower cost of diagnostics and treatment.

Mutual benefits for the Home and Host institutions

Complementarity of the collaborating teams in France and in Finland is a basis for mutual beneficial collaboration. The performed visit will result not only in research outcome in forms of new scientific publications, but also in joint projects (bilateral Finnish-French and multilateral, e.g. Horizon 2020). Student and staff exchange will also be a viable option, including joint Master's and Doctoral degrees. Master's program on Biophotonics being developed in the University of Oulu (Finland) will serve as a solid basis for this.

Future collaboration with the Host institution (if applicable)

In the future, the Host (Aix-Marseille University) will fabricate and delivery nanoparticles for the purpose of cancer diagnostics and treatment to Finland. Multiple meetings at International conferences will be held: in particular, a meeting in Jena (Germany) in frames of a big consortium is scheduled for June 1-3. Joint project applications are planned.

Foreseen journal publications or conference presentations expected to result from the STSM (if applicable)

Depending on the experimental results, we consider different options ranging from conference proceedings to journal articles in the area of biophotonics and nanotechnology (e.g. Journal of Biophotonics, Journal of Biomedical Optics, Small, Nano Letters etc.).

STSM outcome form

STSM application number	**Home institution & country**	**Host institution & country**	**BM1205 WG**	**Objective of the collaboration**	**Results of the collaboration**
COST-STSM-ECOST-STSM-BM1205-190514-044689	Optoelectronics and Measurement Techniques Laboratory, Department of Electrical Engineering, Faculty of Information Technology and Electrical Engineering, University of Oulu, 90014, Finland	Laboratory "Lasers, Plasmas et Procédés Photoniques" (LP3) UMR 7341, CNRS – Aix-Marseille University, Campus de Luminy Case 917, 163, Avenue de Luminy 13288 Marseille cedex 9, France	WG4	Utilization of chemical-free nanoparticles for cancer diagnostics and treatment	We were able to fabricate relevant nanoparticles suitable to cancer tests *in vitro*.

I acknowledge that the described short-term scientific mission has been successfully carried out in the conditions here specified, and prospects for future collaboration are clearly visible.

Marseille, France, 20 May 2015

Andrei V. Kabashin, PhD

Host

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