Optothermal and photoacoustic characterization of protein corona and blood using plasmonic nanoparticles: pharmaceutical aspects

Khosroshahi ME[(1,2)*], Woll-Morison V[(1)], Kim K[(1,3)], Lashkari B[(4)], Mandelis A[(2,4)*]

(1) Nanobiophotonics & Biomedical Research Laboratory, M.I.S. Electronics Inc., Richmond Hill, L4B 1B4, Canada

(2) Institute for Advanced Non-Destructive & Diagnostic Technologies (IANDIT), University of Toronto, Toronto M5S 3G8, Canada

(3) University of Waterloo, Department of Biochemistry, Waterloo, Canada

(4) Center for Advanced Diffusion-Wave and Photoacoustic Technologies, Department of Mechanical and Industrial Engineering, University of Toronto, M5S 3G8, Canada

*Corresponding authors' email: m.khosro@miselectronics.com; mandelis@mie.utoronto.ca

Introduction – Plasmonic nanoparticles such as gold nanoparticles (GNP) exhibit unique physical properties compared to bulk counterparts due to their aspect ratio, high surface free energy, and localized surface plasmon resonance (LSPR) [1]. When NPs are administrated into biological fluids, an interaction occurs between the biomolecules and blood plasma resulting in the formation of a layer of adsorbed biomolecules on the surface of NP known as 'protein corona' [2]. Therefore, the adsorption of proteins can modify the physicochemical properties such as size, shape, surface charge, surface composition, biocompatibility, biodistribution, and functionality, which effectively gives a new identity to NP compared to its original condition [3]. This is a critical factor in nanomedicine such as drug delivery in pharmaceutical industry. In this research, citrate-capped gold nanourchins (GNU) were conjugated to the model protein bovine serum albumin (BSA) via passive adsorption. GNU have unique optical properties compared to spherical gold nanoparticles of the same core diameter where the spiky uneven surface causes a redshift in the SPR peak and a larger enhancement of the electromagnetic field at the GNU spike tips in smaller and more localized volume [4]. A non-invasive technique that can used to study the corona is photoacoustic (PA) imaging. However, considering that the drug carriers are normally stabilized by BSA, its interaction will be at tissue or cellular levels. This implies an optimization of laser power interaction with cells to avoid possible damage particularly if it is in blood-containing environment. For this purpose an experiment was performed to assess an *in-vitro* PA effect on GNP-blood combination.

Experimental and results – Fig. 1(a) shows the experimental setup, and the Wavefront Sensor (WFS) results are seen in Fig.1(b). The WFS demonstrated an oscillatory response at given concentrations of GNU with a non-linear intensity distribution, Fig. 2(a). The CdS results showed a gradual transmission decrease followed by an increase after a short time but a faster rate at higher GNU concentrations. Thermal effects on bioplasmonic solution induced by a 800-nm diode laser were investigated using probe beam monitoring and a mid-infrared (MIR) camera, Fig. 2(b). The temperature variation due to protein unfolding and denaturation exhibited a similar non-linear pattern at different GNU volumes.

However, the temperature was lower at higher GNU concentrations indicating a higher rate of protein adsorption,

which effectively mitigates the LSPR heating. An 800-nm diode laser was used for photoacoustic radar imaging (PARI) with linear chirp laser modulation to provide visualization of blood with and without the use of GNPs. The PA signal amplitudes in different samples increased linearly up to 2.5 W in the order of S5>S2>S1 where S1 is blood only, S2 blood+10% (3.8 µg/mL) GNPs, and S5 S5 (de-oxygenated blood); from there onwards the signals decreased sharply. The cellular deformation time of S1 was found to be faster than S2 and S5 but from 2.5 W afterwards S1 and S2 showed the same rate of decrease.

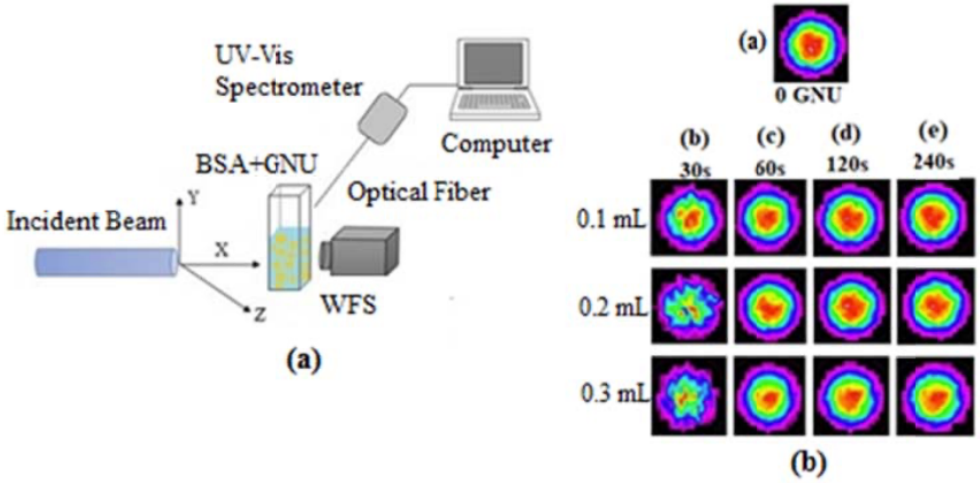

Fig. 1. (a) Experimental setup, **(b)** WFS oscillatory pattern of corona variation

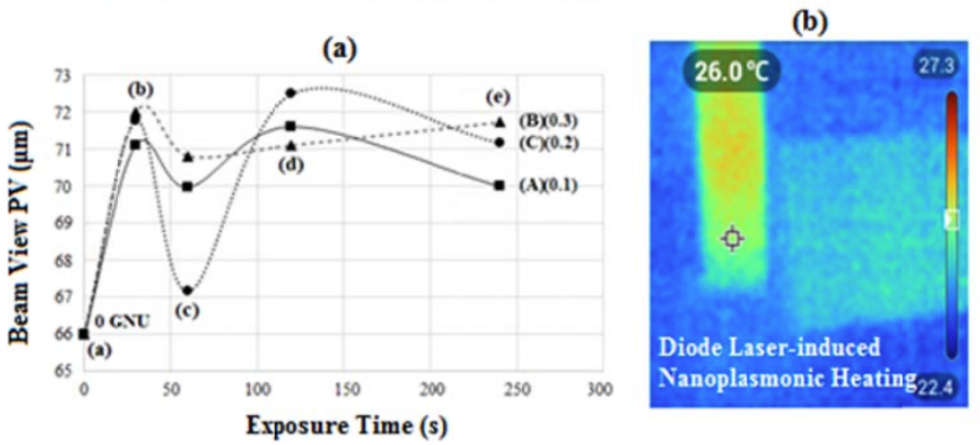

Fig. 2. (a) WFS beam view displacement versus laser exposure time, **b)** An example of nonbioplasmonic solution heated by a 2W diode laser

Conclusions – Optical and thermal characterization of protein and corona behavior is not only important in understanding the underlying principles, but will also assist in development of more smart drug delivery systems where the integrity of drug is preserved during the delivery process. Further research is needed to explore the short- (ms) and long-time (hours) effects of optical and thermal parameters on corona and its interaction with biofluid in regard to drug delivery system.

References

[1] M.E. Khosroshahi, A. Mandelis, B. Lashkari, J. Biomed. Opt. 20 (2015) 076009.

[2] M. Lundqvist, J. Stigler, L. Lynch, Proc. Natl. Acad. Sci. 105 (2008)14265-14270.

[3] P. Roach, D. Farrar, C. Perry, J. Am. Chem. Soc. 127 (2005) 8168-8173.

[4] R. Rodríguez-Oliveros R, J.A. Sánchez-Gill, Opt. Express 20 (2012) 621-626.