Real-time *in situ* analysis of Nanoparticle Surface Interactions

Nanoplasmonic sensing (NPS) enables real-time *in situ* analysis of biomolecular films on surface-associated metal core - dielectric shell nanostructures. Both initial adsorption and subsequent exchange can be followed. The surface chemistry and particle size can be freely tailored, making this platform very versatile and capable of mimicing the behaviour of free particles in suspension.

Introduction

When nanoparticles are exposed to a biological environment they are quickly covered with adsorbed biomacromolecules. The adsorption process is governed by parameters like the composition of biological environment, and the nanoparticle shape, size, and faceting. Formation of a biomolecular film (biocorona) alters the biological activity, cellular response and toxicity, of the nanoparticle. Therefore, *in situ* characterization of nanomaterials is crucial in order to understand their properties in a biological environment.

With nanoplasmonic sensing it is possible to track the biocorona formation in real time in a relevant ambient. To this end, Insplorion offers sensors with surface bound nanostructures that mimics dielectric nanoparticles in solution. These sensors enables real-time *in situ* analysis of biocorona formation and evolution without the risk of sample aggregation or the need for purification.

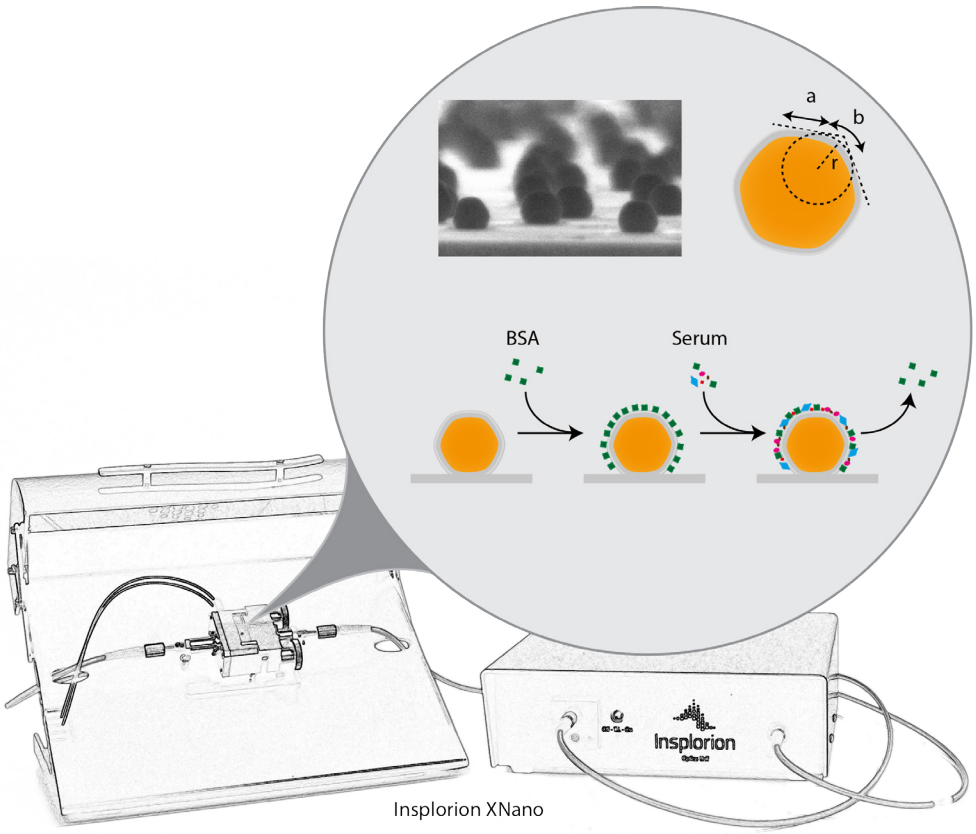

Figure 1: Insplorion XNano system. The ratio a/b varies with particle size while the curvature, r, remains largely constant. Biacorona formation and evolution can be followed in situ and in real-time.

SiO_2-coated nanoparticle sensors

The nanostructured sensors consists of silica covered gold nanoparticles on a glass support. The nanoparticles are facetted and by varying the particle diameter the ratio of flat facet vs. curved edge area can be controlled while the curvature remain constant. By comparing the results from sensors with different flat/curved ratios the influence of curvature can be quantitavely analyzed.

Experimental procedure

The facetted nanoparticle sensors are docked into the Insplorion XNano instrument and all sample solutions are introduced via the integrated microfluidic system.

All responses are normalized to account for the variation in sensitivity with the nanoparticle diameter. To investigate the influence of nanoparticle shape, sensors with different nanoparticle diameter (different flat/curved ratios) are compared.

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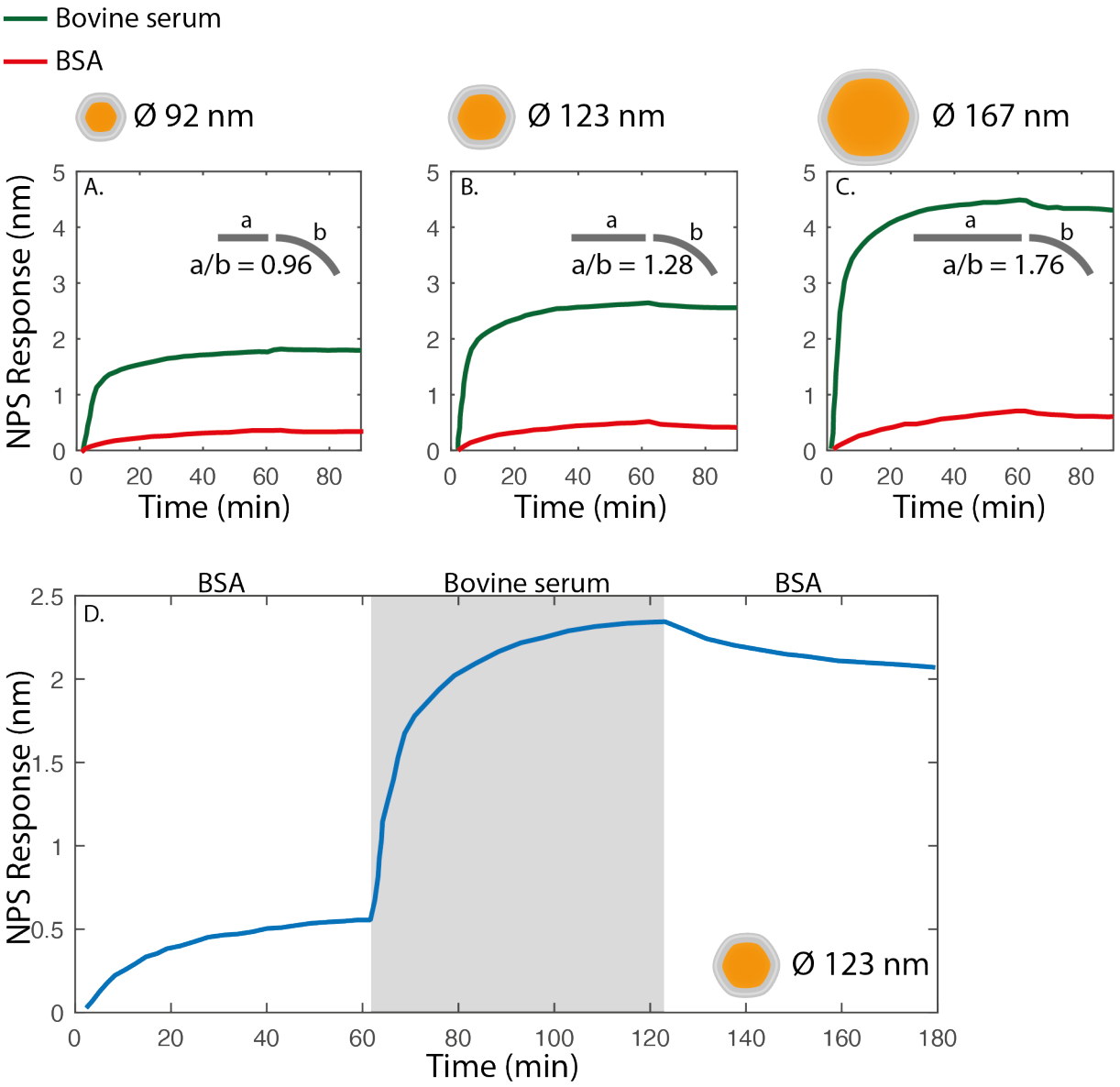

Figure 2: NPS data for adsorption of BSA and Bovine Serum. A-C) Adsorption to different sized nanoparticles with different flat/curved ratios showing the influence of particle shape on biocorona formation. D) Evolution of biocorona through completion or replacement of a preadsorbed BSA film upon introduction of serum.

Results and Conclusion

The responses upon introduction of BSA to the differently sized nanoparticle sensors are presented in Figure 2A-C. Quantitatively, the response is higher for the large diameter particles, suggesting the formation of a denser protein layer on flat over curved regions. This is apparent for both BSA and bovine serum samples and suggests that the biocorona formation is different for the different size particles. As can be seen in Figure 2D, after formation of a BSA film, subsequent adsorption of protein occurs when the sample is exposed to serum. This either suggests that the preformed BSA film constitutes an incomplete monolayer and/or is loosely bound allowing additional protein adsorption and exchange by the abundance of serum proteins.

NPS allows time resolved systematic analysis of biocorona formation in complex samples. The surface bound core-shell nanoparticle sensor presented here furthermore allows analysis under conditions that would otherwise promote aggregation if the particles had been free in suspension.

References

[1] R.Frost et.al. "Core-Shell Nanoplasmonic Sensing for Characterization of Biocorona Formation and other Nanoparticle Surface Interactions.", ACS Sens., **2016**, *DOI: 10.1021/acssensors.6b00156*.

[2] R.Frost et.al. "Real-time in situ analysis of biocorona formation and evolution on silica nanoparticles in defined and complex biological environments.", Nanoscale, **2017**, *DOI: 10.1039/C6NR06399C.*

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