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To cite this version:

Laurent Marichal, Fabrice Cousin, Gaël Giraudon–Colas, Serge Pin, Jean Philippe Renault. Assessing the in situ protein corona structure. JDN 2021 - Journées de la Diffusion Neutronique, Sep 2021, E-Conference, France. cea-03356089

HAL Id: cea-03356089

https://cea.hal.science/cea-03356089v1

Submitted on 27 Sep 2021

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Assessing the in situ protein corona structure

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As soon as nanoparticles are placed in a biological medium, dynamic interactions happen between their surfaces and neighbouring biomolecules. Proteins are particularly prone to interactions and can form the so-called protein corona around these particles. This gives a biological identity to nanoparticles that will condition their biodistribution and potential toxicity.

We thoroughly studied the interactions happening between model proteins (myoglobin and hemoglobin) and nanoparticles (silica). We combined a series of physico-chemical techniques such as oxygenation studies, isothermal titration calorimetry, circular dichroism, and small-angle neutron scattering (SANS). First, we found out that hemoglobin have a stronger affinity to silica surface compared to myoglobin, partly because of its larger size [1]. Secondly, adsorbed and free hemoglobin have different oxygenation properties, especially in terms of oxygen affinity (increase of oxygen affinity for adsorbed hemoglobin) [2]. The structure of adsorbed proteins was then assessed by circular dichroism and SANS. Very subtle secondary and tertiary structure changes could be found while the quaternary structure was totally preserved. This indicates that even without altering their structure, proteins adsorbed on nanoparticles can have their function drastically altered.

Finally, SANS studies allowed us to probe the complex structures of the protein corona (Fig.1) [2]. Myoglobin and hemoglobin form a monolayer of proteins around nanoparticle. We could also determine that, in every system studied, protein/nanoparticle interactions lead to a reaction-limited aggregation process. Besides, it was found that even incomplete coronas were organized by short-distance repulsive interactions between adsorbed proteins. For standard proteins such as the ones studied here the term “protein corona” is particularly well-suited even though, this is not a universal phenomenon since very large proteins tend to form open lattices when interacting with nanoparticles [1].

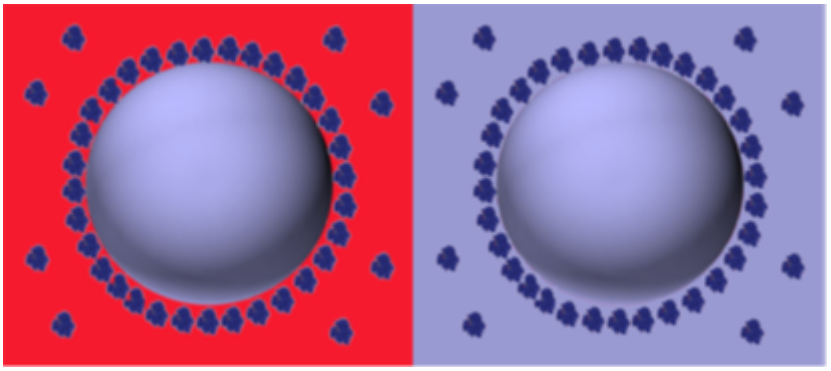

Figure 1. Schematic representation of the protein/nanoparticle system studied by small-angle neutron scattering. Solutions can be in H_2O (left) or D_2O (right) in order to contrast match the nanoparticles to the solvent.

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[2] Marichal L., Giraudon--Colas G., Cousin F., Thill A., Boulard Y., Aude J-C, Labarre J., Pin S., and Renault J.-P. Langmuir. 35 (2019) 10831-1083.