FACULTY OF SCIENCE

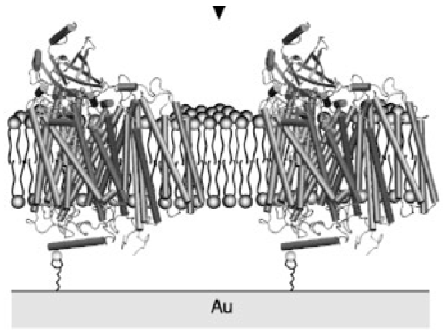
UNIVERSITY OF COPENHAGEN

**LOOKING FOR A MASTER PROJECT?**

**Designing of platforms for the reconstitution of membrane proteins on surfaces.**

New surface chemistry and reconstitution methods will be employed to improve the oriented immobilization and display of membrane proteins on surfaces in a biologically compatible environment. We will create a platform in such a way that 1) the membrane protein is not in direct contact with the underlying surface and therefore in a biologically friendly environment, and 2) we ensure the correct display of the membrane protein in the bilayer, exposing for instance the intracellular region towards the underlying surface, increasing the sensitivity of our structural techniques and controlling the functionality of the protein (due to all proteins being aligned accordingly to the ion-gradient).

***Objectives*** *First*, design a new molecule which has three parts (1) an ANTA head group for Ni(II) binding/chelation, (2) a biocompatible $OEG_4$ spacer, (3) *either* a thiol for immobilization to gold surfaces, *or* a silane for immobilization glass surfaces. *Secondly*, we will optimize surface modification for specific binding to a transmembrane protein in DDM by for instance dilution with a $OEG_4$-thiol or –silane molecule in order to decrease the non-specific binding and maximize the amount of protein bound and displayed correctly. The protein will be reconstituted into a lipid bilayer, using the mixed DDM-lipid micelle approach, allowing functionality studies (since an aqueous pocket and therefore an ion gradient can theoretically be established at the interface). This master project is a part of other projects that use chemistry for organization of proteins at interfaces and aim at the study of membrane protein function and structure (UNIK). This project requires organic chemistry knowledge for the synthesis of the lunker and then the use of several surface techniques for characterization and structural studies. The project will be under the supervision of Marité Cárdenas Gómez cardenas@nano.ku.dk in close collaboration with groups at LIFE and SUND. We have already a beam time assigned on the neutron reflectometer D17 at the ILL, Grenoble France.




dimyristoylphosphatidylcholine (DMPC)

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## Protein-Dendrimer interactions and their effect on interfacial properties of the dendrimer

Dendrimers are a unique class of nanostructured vehicles for drug and gene delivery into intracellular targets. They are unique given their monodispersity and multivalency, and can be used both by covalently attaching or encapsulating drugs. Dendrimers produce high intracellular drug release and target efficiently tumors for therapeutic and diagnostic applications. The surface chemistry of dendrimers influence their transport across epithelial and endothelial barriers. Dendrimer endocytocis via caveola/lipid rafts is markedly dependant on the dendrimer surface chemistry. For instance, dendrimers of a certain size and charge are able to dig holes in lipid membrane eventually leading to cell death. Nanotoxicity is thus a major challenge. However, the properties of the nanoparticles/dendrimers facing the cell membrane might not reflect the chemical and physical properties of the dendrimers on their own. This is due to the fact that, once dendrimers are exposed to a serum-like medium, they are prone to interact with all biomolecules present in such medium. Recently, the term nanoparticle-protein corona was introduced in the scientific community. Such term reflects the importance of the composition and structure of the proteins surrounding the dendrimer (see schematics below) for the final fate of nanoparticles in the body.

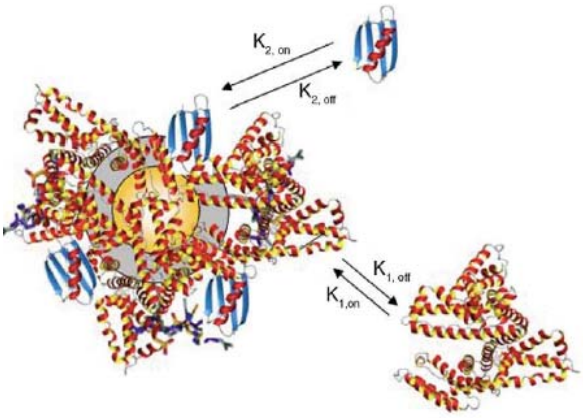


**Figure 1. Nanoparticle-protein corona illustrating that the properties of the nanoparticle might be dominated by those of the proteins it is associated with.**

We have developed several methods to study the molecular mechanisms of dendrimer interaction with lipid bilayers. We now propose to find out the relevance of such protein corona on the final fate of our dendrimers. Among the methods we will be using are Dynamic light scattering, Fluorescence Microscopy, Quartz Crystal Microbalance with Dissipation, Spectroscopic Ellipsometry, Neutron reflection, the atomic force microscope.

If this project rings your bells, contact Assoc. Prof. Marité Cárdenas Gómez by e-mailing cardenas@nano.ku.dk or skype MATIRE. You might be able to find me at D406 or around the lab DS09.

References of interest:

Lynch & Dawson. Nano (2008) 3: 40.

Åkesson et al. PCCP (2010) 38: 12267