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Nanostructural characterisation of glycosylated protein biomarkers interaction with lipid bilayer membranes: basis for biosensor development

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Plasma proteins are often used as biomarkers for severe pathologies including cancers and autoimmune diseases since they provide a circulating representation of the body conditions. Nevertheless, their detection in blood samples is still challenging due to their low abundance (pico- and nano-grams level), but mostly due to their glycosylated state which is believed to favor protein-lipid complexes. In this context, the study and understanding of protein-lipid interactions is of great importance, especially to optimise the sensitivity and reliability of biosensing techniques to identify protein biomarkers, in particular when present in their glycosylated forms [1].
In the project we investigated at nanostructural level the interaction of glycosylated protein biomarkers with biologically relevant lipid bilayer membranes using neutron and x-ray reflectometry, to identify how different lipids and glycosylation can affect this interaction to build a potential biosensor that is aimed for early detection of scarce biomarkers in blood samples.
The glycosylated proteins of interest for the study are soluble vascular-endothelial cadherin (sVE) and alpha-fetoprotein, two clinical biomarkers found in the blood for the detection of vascular abnormalities and liver cancer respectively [2,3,4].
Neutron and x-ray reflectivity results, together with QCM-D complementary data, showed significant changes in the lipid bilayer after the injection of glycosylated proteins, while smaller changes were reported in presence of non-glycosylated protein. We highlighted that the kinetic has an important role for the interaction and we proved that the interaction behavior is influenced by the lipid composition of the system as well as the degree of glycosylation on the protein.
Thanks to the study and glycosylation chemistry, it was possible to set the basis for the development of a lipid-based protein-biosensor in collaboration with the industrial partner of the project.

References
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Biological membranes and interfaces

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