Determination of Structure of Nanoparticles by Small-Angle X-ray Scattering: Application to LDL Lipoproteins and to Refolding of SDS-Denatured Proteins

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Abstract: During the last two decades, there has been a tremendeous development of small-angle x-ray scattering (SAXS) instrumentation, at synchrotrons as well as at home sources. In particular the development of more powerful home sources and advanced optics means that even weakly scattering samples can be measured at home, and the commercialization of the instruments has led to a large increase in capacity, so that the use has become much more widespread. Simultaneous development of analysis and modelling methods means that more detailed structural information can be extraxted from the SAXS data. At Aarhus University we have in 2014 installed a SAXS instrument from Bruker AXS [1], which uses a powerful Ga metal jet X-ray source from Excillum, and which employs an optimized geometry with homebuilt scatterless slits [2]. In this contribution a recent application of this SAXS instrument for investigating the structure of low-density lipoprotein (LDL) particles [3] as a function of temperature will be presented. LDL is involved in atherosclerosis and the build-up of plaque inside the arteries, which is broadly involved in cardio-vascular deceases, the leading cause of death in the western hemisphere. In the work [3], a new model for determination of the structure of the LDL particles base on super ellipoids weas derived. The model allows fitting both size and shape, and also to determine the particular internal layering of the fats inside the LDL core. This gives in addition information on changes in the conformation of the protein component, which wraps the fatty core. The new approach allows a fast assessment of the structure which can be used routinely in research projects. This approach, now allows the monitoring of structural changes in the LDL upon different stresses from the environment, such as changes in temperature, oxidation, or external agents used or currently in development against atherosclerotic plaque build-up and which are targeting the LDL. In another project, protein-detergent interactions have been studied [4]. Globular proteins are usually unfolded and denatured by the anionic surfactant sodium dodecyl sulphate (SDS). This was also found for four investigated proteins, bovine serum albumin (BSA), α-lactalbumin, (αLA), lysozyme (LYZ), and β-lactoglobulin (βLG), which all form complexes, which are protein-decorated SDS micelles. Somewhat surprisingly, it was found that most of these proteins could be refolded by addition of the non-ionic surfactants (NIS), octaethylene glycol monododecyl ether (C12E8) and dodecyl maltoside (DDM). A relatively simple data analysis approach based on linear combination of SAXS data recorded for native protein, complexes, pure and mixed micelles, as well as mass conservation was employed. The addition of NIS to the protein-SDS samples resulted in extraction of the SDS from the protein-SDS complexes and refolding of βLG, BSA, and LYZ, while αLA changed to its NIS-bound state instead of the native state. It was conclude that NIS competes with globular proteins for association with SDS, making it possible to refold SDS-denatured proteins by adding sufficient amounts of NIS, unless the protein also has significant interactions with the NIS.

References

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