Poster Presentation

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Combining SAXS with Rosetta for Identification of Native-like Protein Complexes

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It is well-known that recombinant human serum albumin (rHSA) has the ability to stabilize proteins in solution preventing protein adsorption, aggregation and oxidation. For this reason, rHSA is used as an excipient in the formulation of protein pharmaceuticals. To shed light on the molecular interactions, we have studied a variety of protein drugs that are known to bind to rHSA and thereby being stabilized. We observe that the interactions depend on protein concentrations and differ significantly between protein drugs. One approach to study these systems on a molecular level is the combination of small angle X-ray scattering (SAXS) and in-silico modelling. SAXS can be used to identify the overall shape of proteins and protein complexes and ab initio models can be derived from the scattering profile using programs such as Dammif [1]. These programs allow us to assess the overall conformation of the macromolecular structures, but cannot provide detailed information on the molecular level regarding protein-protein interfaces of the complexes. Here, the Rosetta modelling suite, a multipurpose software suite, can be utilized to perform protein-protein docking and to study the complexes. The challenge in using the Rosetta docking tool [2] is the difficulties in efficiently identifying the native-like structure. For better identification we apply SAXS constrains during the docking procedure. Although the method has been applied previously [3], no benchmarking has been published regarding the relative success of using SAXS constrains. We therefore have conducted an elaborate benchmarking, where we have used SAXS constrains for determination of complexes of non-identical components using the Rosetta docking protocol. A pool of complex structures has been chosen to evaluate the difference between conventional docking and docking performed using SAXS constrains. This allows us to optimize the parameters in the protocol and pave the way to study unknown complex structures.

[1] *D. Franke, D. I. Svergun, Journal of Applied Crystallography, 2009, 42, 342–346,* ***[2]*** *S. Chaudhury, M. Berrondo, B. D. Weitzner et al., PLoS One, 2011, 6, e22477,* ***[3]*** *N. G. Sgourakis, O. F. Lange, F. DiMaio et al., J. Am. Chem. Soc., 2011, 133, 6288–6298*

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