SAXS from protein solutions on ID02 – experiences with large multidomain proteins and their ligand interactions

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Complement factor H (CFH) is one of the most topical proteins in the human immune system. In the last few years, defective functioning in CFH has been shown to affect the regulation of the complement system of innate immunity, leading to disorders such as age-related macular degeneration (the most common cause of blindness in the elderly) and atypical haemolytic uraemic syndrome (a common cause of renal failure in the young). CFH interacts with five different ligands, namely (1) self-association with itself; (2) zinc; (3) complement C3b; (4) heparin; (5) C-reactive protein. Major experimental difficulties with CFH include the weak interactions it makes with its ligands and the multivalency of these CFH interactions. The presentation will show how the high flux available at ID02 facilitated the unravelling of several new major solution and biological properties of CFH. In this, the constrained scattering modelling of the ID02 data to yield structures that are deposited in the Protein Data Bank was a crucial part of the CFH solution studies. In addition, ID02 became an essential tool alongside analytical ultracentrifugation and surface plasmon resonance methods to decipher weak protein-ligand interactions. These three methods will be compared with one another.

References:

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