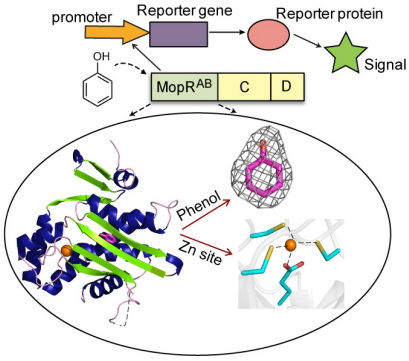

Figure 1. Crystal Structure of MopR^{AB} in complex with phenol

Keywords: MopR , aromatic biosensor , phenol , XylR , DmpR , NtrC

MS13-P7 Structures of amyloid a-synuclein and impact on our understanding of Parkinson's disease

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Protein amyloid fibrillation is associated with a number of grave diseases, most notably the neurodegenerative Alzheimer's and Parkinson's diseases (1). Structural investigation of protein fibrillation is however inherently challenging. A number of spatially and temporally diverse structural species co-exist during the fibrillation reaction, in an equilibrium that is highly sensitive to experimental conditions. Isolation of individual species is thus not possible. At the same time understanding of the structural species formed during the fibrillation pathway are key to understanding the molecular principles behind the process, and accumulating evidence links such intermediate species to cytotoxic activity, central to the progressive, degenerative diseases. We use small angle X-ray scattering (SAXS) to investigate the fibrillation reaction. Formation of a-synuclein (aSN) fibrils is associated with Parkinson's disease. We have previously characterized the low-resolution structure of intermediately formed aSN oligomers (2) and reveal that these oligomers are building blocks of the fibril structure (3). We have recently demonstrated, that early amyloidogenic aSN species can disrupt lipid model systems, and that lipid:protein co-aggregates in a non-amyloid state are formed in this context (4) while the effect on lipid membranes varies depending on the lipid composition (5). While the methodology behind the data analysis has been well elaborated both by us (6), and others (e.g. 7), the need for a robust, objective and (semi-)automated analysis system is evident, and our latest efforts in this direction will be presented. We apply the newly developed software to the analysis of a familial mutant of aSN, revealing the occurrence of intermediate species, which have a radically different nature than those previously characterized (manuscript submitted). Although the software has been developed aiming for the analysis of fibrillating systems, it is generally applicable to any developing, heterogeneous macromolecular system.

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Keywords: Parkinson's disease, amyloid, heterogeneous systems, data decomposition