MS12. Crystallization and crystal treatment

Chairs: Terese Bergfors, Matthew Bowler

MS12-P1 Crowning proteins: modulating the protein properties using crown ethers

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Protein crystallization is a main bottleneck in protein X-ray crystallography analysis. Crystallization optimization is often achieved only on a case-by-case, trial-and-error basis. By first identifying a ring-shaped binding mode for low-molecular weight polyethylene glycol (lmwPEG) in a number of protein crystal structures, we established crown-ether (18-Crown-6; CR) as reliable crystallization additives as a powerful crystallization tool. Our studies showed that crown ethers can modify protein surface behavior dramatically by stabilizing either intra- or inter-molecular interactions. Crown ethers can also be used to modulate a wide variety of protein surface behaviors beyond crystallization, such as oligomerization, domain-domain interactions, or stabilization in organic solvents.By solving the structures of several crystals obtained in the presence of CRs, we observed direct interactions in crystals. In some cases, CR improved crystal quality and resolution, making it possible to solve the complex structure. CRs were found to modify protein surface properties by yielding complexes, which resulted in alternative tertiary and quaternary structures. There are three distinct CR interaction modes, namely the K-crown, the C-crown and the KC-crown modes (Figure). CRs also increased protein rigidity and, by CR–CR stacking, mediated direct interactions between hydrophobic patches and charged amino acids. We therefore propose that CRs, by their ability to modify protein surfaces, can be used as: 1) powerful additives in protein crystallography; 2) molecular probes to search for potential binding pockets; and 3) reporters of protein conformational changes.

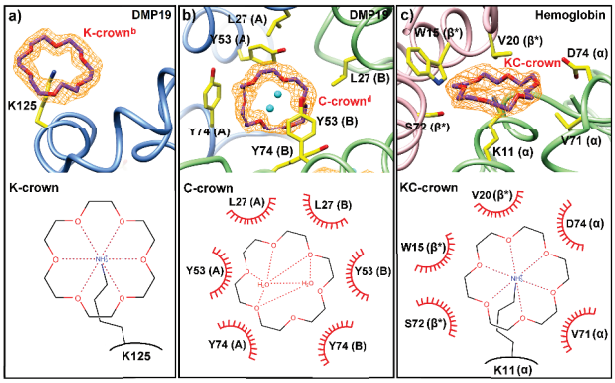

Figure 1. CR binding modes. a) K-crown, a single Lys binds the CR axially. b) C-crown, hydrophobic and p-orbital containing side-chains interact laterally with CR. c) KC-crown, the CR is coordinated axially by a Lys, while hydrophobic and p-orbital containing side-chains interact with it laterally.

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