SELF-ASSOCIATION OF A HIGHLY CHARGED, ARGININE-RICH CELL-PENETRATING PEPTIDE

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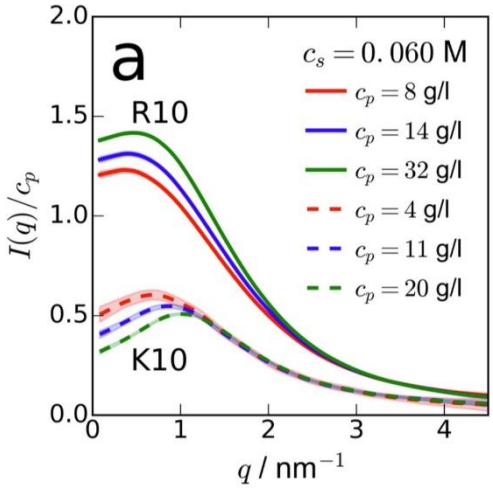
Small angle X-ray scattering (SAXS) measurements reveal a striking difference in intermolecular interactions between two short, highly charged peptides, namely deca-arginine (R10) and deca-lysine (K10). Comparison of SAXS curves at high and low salt concentration shows that R10 self-associates, while interactions between K10 chains are purely repulsive. The self-association of R10 occurs to a larger extent at low ionic strength indicating that the attraction between R10 molecules has an important electrostatic component.

SAXS data is complemented by potentials of mean force between the peptides calculated by means of umbrella sampling molecular dynamics (MD) simulations. Atomistic MD simulations elucidate the origin of the R10-R10 attraction by providing structural information on the dimeric state: the last two C-terminal residues of R10 constitute an adhesive patch achieved by stacking of the side chains of two arginine residues and by salt bridges formed between the like-charge ion-pair and C-terminal carboxyl groups. A statistical analysis of the protein data bank reveals that this mode of interaction commonly occurs in proteins.



Concentration normalized scattering intensities for deca-arginine (R10, full lines) and deca-lysine (K10, dashed lines) at various peptide concentrations, c_p. Attraction is observed between R10, while K10 repel each other. Molecular insight is given through atomistic Molecular Dynamics simulations