Aggregation of a Highly Charged Peptide in Monovalent Salt Solution

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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). Measurements at high NaCl and low peptide concentrations provide the form factors of the studied cationic homopolymers. Comparison of SAXS curves at low salt concentration with the form factors shows that R10 aggregates while interactions between K10 chains are purely repulsive. The aggregation of R10 occurs to a larger extent at low ionic strength indicating that the attraction between R10 molecules has a dominating electrostatic component. SAXS data is complemented by potentials of mean force between the peptides calculated by means of Umbrella Sampling Molecular Dynamics simulations. Atomistic Molecular Dynamics simulations elucidate the origin of the R10-R10 attraction by providing structural information on the dimeric state [1]. The propensity of R10 to aggregate may play a role in its mode of cellular uptake which is significantly more efficient than for K10 [2].

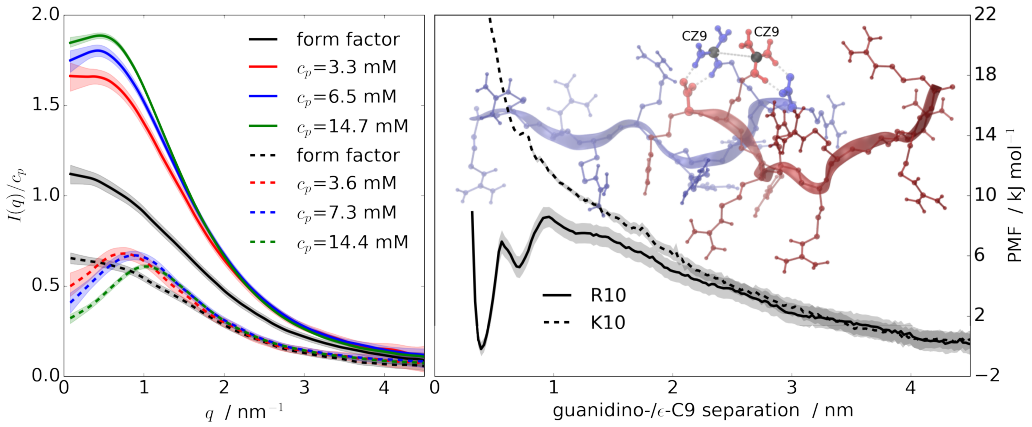

Figure 1: SAXS curves for deca-arginine (R10) (full lines) and deca-lysine (K10) (dashed lines) in NaCl solutions at various peptide concentrations, c_p; colored and black curves correspond to low (10 mM NaCl) and high (300 mM NaCl) ionic strength solutions, respectively (left panel). Potentials of mean force calculated from Umbrella Sampling Molecular Dynamics Simulations for pairs of R10 (full line) and K10 (dashed line) molecules as a function of the separation between the guanidino-C (CZ9) and the ϵ-C of the 9-th residues (right panel). Atomistic model of the R10 dimer characterized by salt bridges between the negatively charged carboxyl groups and the stacked positively charged guanidinium moieties of the 9-th residues (right panel).

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