NUCLEIC ACID - POLYCATION COMPLEX FORMATION: A MOLECULAR DYNAMICS STUDY

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Charge bearing polymers, polyelectrolytes (PEs), are versatile synthetic materials with applications ranging from drug delivery and tissue engineering to sensing elements and solid electrolytes in fuel cells [1]. In this work, we study PE materials as carrier vectors in gene therapy. Successful gene therapy requires target recognition, safe and efficient delivery of the DNA into the cell, and a controlled release mechanism. Polyelectrolytes are widely pursued as non-viral delivery vectors as they are easily complexed with nucleic acids to form packages suitable for cellular uptake and lack the risk of mutation and immune system response observed with traditional viral carriers [2]. However, there are still open questions related to strength of the complex formation, targeting, controlled release, as well as complexation and release dynamics.

We target the molecular mechanism of nucleic acid-polycation complexation by means of all-atom molecular dynamics (MD) simulations with explicit solvent and ion description. This provides us an otherwise unattainable, microscopically detailed view on the structure and dynamics of the polyelectrolyte-DNA complexation. Such understanding of the molecular mechanism of complex formation is important for optimal design of nucleic acid delivery carriers. MD shows rapid complexation of the DNA with Poly-L-Lysine, a commonly used carrier. The role of charge compensation by the PE vs ions, as well as, water structuring and organization in the complex formation and dynamics is probed.

Figure 1: DNA double helix complexed with 2 Poly-L-Lysines.