Coarse-grained simulations of DNA-Polyethyleneimine complex formation

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The formation of DNA-polycation complexes, able to enter cells via endocytosis, is a topic of high current medical and fundamental interest, which requires advanced computational modeling. Due to its remarkable buffering capacity, polyethyleneimine (PEI) is a genetic vector widely in use to condense DNA into polyplexes. With a view to developing a high-quality coarse-grained (CG) force-field for modeling DNA-PEI complexes, we performed extensive atomistic (AA) simulations based on our recently developed AA FF for PEI [1,2] and applied Boltzmann inversion techniques to extract the detailed CG FF parameters (including bonds, angles, and dihedrals) [3]. Combining our FF with the Martini FF for DNA of Marrink et al. [4], we carried out CG molecular dynamics simulations of DNA-PEI polyplexes. In order to accurately account for the significant electrostatic interactions between the protonated PEI beads and the negative phosphate groups of DNA, we employed a polarizable water model [5]. To characterize the mainly electrostatic attachment of PEI to DNA, we studied the distance distributions between the mentioned DNA and PEI sites in dependence on the number of polymer chains, as well as on their length and protonation fractions. Besides providing essential insights into the formation of the DNA-PEI polyplexes, our simulations enable predictions for efficient practical realizations of DNA-PEI condensation.