

Charge Density-modulated Nanostructure of DNA-Dendrimer Complex

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Cationic dendrimers are a potential nonviral vector for gene therapy because of their ability to form electrostatic complexes with DNA as well as their lack of immunogenicity. The structure of the complexes can influence their interactions with cells and hence the transfection efficiency; however, the supramolecular structure of DNA-dendrimer complexes (dendriplexes) formed under different conditions remain to be explored in detail. Using synchrotron small angle X-ray scattering, here we show that DNA in the complexes with poly(amidoamine) (PAMAM) G4 dendrimer exhibited three distinct packaging states modulated by the charge density of the dendrimer prescribed by its average degree of protonation (dp , the average number fraction of protonated amine groups in dendrimer). A new “hexagonally-packed DNA superhelices” structure was observed at $dp = 0.3$ as an intermediate state between square columnar phase (formed at $dp = 0.1$) and beads-on-string structure (formed at $dp \geq 0.9$). Our results revealed that the curvature of DNA in the complexes was progressively templated by the surface curvature of dendrimer with increasing macrocation charge density. This structural transformation was in accord with the increasing weighting of electrostatic attraction over DNA bending energy with increasing charge density.

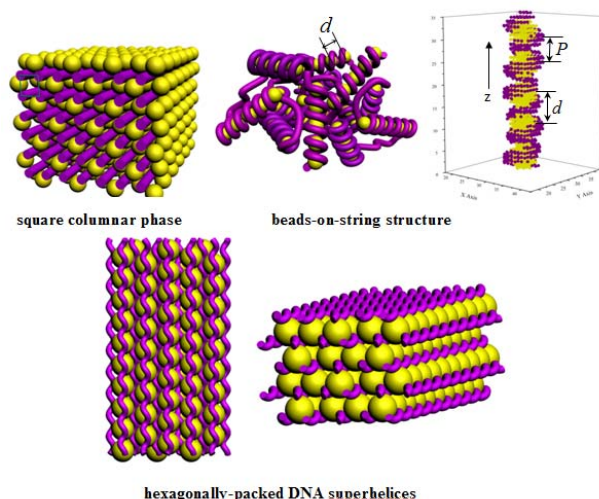


Fig. 2: Schematic illustrations of the three distinct structures of the dendriplexes formed at different dendrimer dp values. The rods/strings and the balls represent DNA and dendrimer, respectively. (a) Square columnar phase formed at $dp/0.1$. (b) Nucleosome-like beads-on-string structure formed at $dp/0.6$ and $dp/0.9$. (c) Hexagonally-packed DNA superhelices formed at $dp/0.3$.

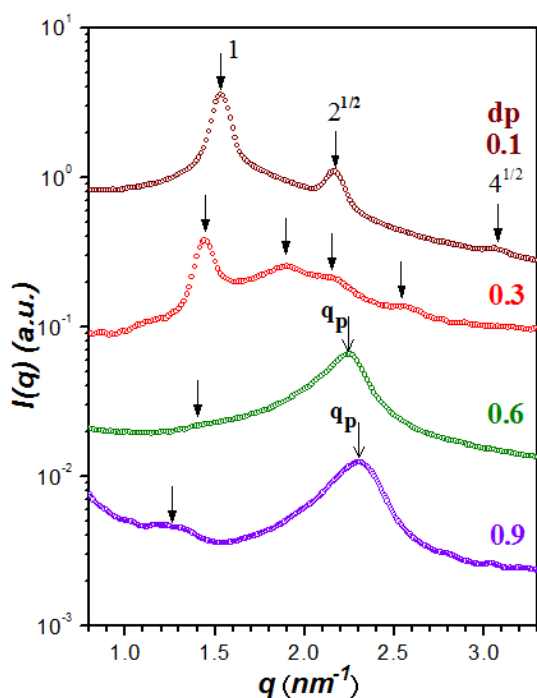


Fig. 1: SAXS profiles of the dendriplexes with the dp values of 0.1, 0.3, 0.6 and 0.9.

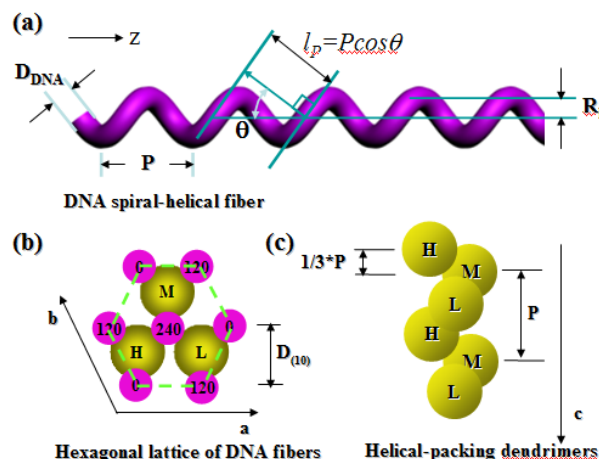


Fig. 3: (a) Definitions of the geometric parameters of a DNA superhelix used for model calculation. (b) Top view of the hexagonally-packed DNA superhelices. The purple balls represent the DNA cross section and the numbers within the balls are the phase angles of the superhelices. The dark yellow balls are dendrimers. (c) The spiral arrangement of dendrimer macrocations in the interstitial channels between the DNA superhelices in the hexagonal lattice.