

CATION–DNA OUTER SPHERE COORDINATION IN DNA POLYMORPHISM

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There are two approaches to describing the interaction of the DNA polyion with ions. The first, physical, approach is the analysis of electrostatic interactions between the ions and the charges on the DNA. Coordination chemistry approach looks, as a rule, for modes of direct binding of ions to DNA ionophores. We study [1] both the inner and outer sphere coordination of ions by the ionophores of A and C forms of DNA in molecular dynamics simulations. We calculate free energies of A- and C-complexes in two weakly polar solutions: in ethanol-water and methanol-water mixtures with 80 vol.% of alcohol. We show that one needs to take into consideration the ion-DNA outer sphere coordination to understand the experimentally observed conformational polymorphism of the DNA molecule: a transition to the A form in ethanol and to the C form in methanol. We identify the ionophores that are necessary for the existence of the A- and C-complexes. The C-complex is stabilized by ions in the minor groove ionophores, primarily by ions linking pairs of O4'-N3/O2 water bridges of opposing strands. Similarly, the A-complex is stabilized by ions in the major groove. The ions in the main ionophore of the A-complex are outer sphere coordinated to phosphates on both strands and, thus, narrow down the major groove. In both the A- and C-complexes, the ions' inner sphere ligands are in mostly water molecules; the ions reside in water clusters. In the ethanol-water mixture, the water clusters are large. When A-DNA is solvated by such a mixture, the major groove is filled with water, and all ionophores of the major groove are accessible to ions. In the methanol-water mixture, the water clusters are small. In the methanol-water solution, a large number of the small methanol clusters are present in the major groove of A-DNA. They interfere with the coordination of ions in one of the ionophores in the major groove and also in other ionophores near phosphates. Therefore, in methanol, the interaction energy of counterions with DNA cannot compensate for the repulsion between closely located phosphates in A-DNA. Consequently, the ions fill the more accessible ionophores of the C-complex, converting DNA into the C form. This work was supported by the Program of Fundamental Research of the Russian Academy of Sciences.

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