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Simulation of DNA in water/ethanol mixture

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HIGHLIGHTS

- The structure of DNA is easily affected by ethanol aqueous solutions.
- The structure changes depend on the concentration of ethanol in the solvent.
- Na^+ and ethanol molecules intrude into the first hydration shell.

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ABSTRACT

The study of B-DNA in mixed solvent comprised of water and ethanol with different concentrations at 298 K has been conducted by molecular dynamics simulation. We find that the structure of DNA is easily affected by the aqueous environment. Property and structure changes of the solvent will influence the local structure of DNA helix, induce the conformation transition between different forms, and even cause the degeneration of DNA. The addition of ethanol can reduce the activity of water, changes the solvent structure around DNA. DNA in the solvent with low concentration of ethanol changes little, when the ethanol increases in the solvent, large structure changes occur at the ends of the helix first, then show the characters of A-form, the minor groove becomes wider and shallower, and the length is shortened when in the solvent with the concentration of 0.88 g/cm^3. The mechanism behind is discussed, and we find the competition between the solvent molecules and counterions coupling to the free oxygen atoms of the phosphate groups, and the breaking of the spin of water both contribute to the structure changes of DNA in the simulation.

1. Introduction

The study of DNA in a mixed solvent comprised of water and ethanol at 298 K has been conducted with molecular dynamic (MD) simulation. As a macromolecule, DNA has conformational flexibility with a double helix, and it always adopts right-handed B-form at physiological conditions. Much of what we know about B-DNA comes from the studies of CGCGAATTCGCG, the so-called Dickerson–Drew dodecamer [1,2]. The helix of DNA also can adopt other forms, A-DNA, C-DNA and the left-handed Z-DNA. Comparing with B-DNA, the A-form has a wider and shorter helix with a shallower and wider minor groove, and a deeper and narrower major groove. The polymorphic structure and conformation flexibility of

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DNA make it possible to carry and express the genetic information. In addition to its physiological function, DNA also plays crucial roles in the process of forming drug-DNA and protein–DNA complex and is widely applied to nano-biotechnology and supermolecular chemistry [3–6]. These functions all depend on the structure of DNA, which can be influenced by the environment factors, including temperature [7,8], cations [9–17], the presence of ligand, and water activity [18]. Understanding DNA's structure changes in different environment is thus a necessary step in the function realization of DNA.

Water is very important for DNA double helix. In aqueous solution, DNA should be always hydrated, with hydration shells around the free negative oxygen atoms on phosphate along the DNA backbone. The hydration can screen the repulsion between the negatively charged oxygen atoms. Water molecules also form a network arching across the DNA grooves, just like a water spine, and connecting phosphates on opposite sides [19,20], which will change the size of the grooves. Both the screening of repulsion and spine of hydration may influence the conformation of DNA.

Because DNA is highly charged, the solvent counterions are required for its stabilization in the solution. The cation, for its positively charged, can reduce the electrostatic repulsion of the phosphate group, and bind to the atoms of base pairs, causing the local structural changes of DNA. The interaction between ions and DNA happens under the mechanism that the water structure is destroyed, the ions intrude into the shell of hydration, and reside there by direct or indirect contact with atoms on DNA, replacing the water molecules.

Therefore, it can be assumed that, the conformation translations of DNA widely depend on the structure or property of solvent around DNA. The factors destroying the structure and property of solvent may induce the structure changes of DNA. What we have studied about the temperature influence on DNA supported this topic [21]. As the temperature increases (under the melting temperature of DNA), the Hydrogen-bonds are broken, the hydration structure around DNA is destroyed, and the water molecule in the inner hydration shell is replaced by cations. The direct interaction between cations and DNA molecules largely screens the repulsions generated by the charged phosphate groups, leading to the conformation transition of DNA, and the intermediate states (mixed A–B structure) appear in the transition process.

The structure and property of solvent can be affected by many factors. In addition to the temperature effect, many works have been done to study the DNA conformation transition in mixed solutions, by adding aliphatic alcohols such as ethanol [22] or methanol [23]. For the CGCGAATTCGCG, it assumes B form in pure water, while the A form is an expected form in the water and ethanol mixed solvent at room temperature [24–27]. Ivanov and co-workers [28,29], showed that the ability of DNA to undergo A $\rightarrow$ B conversion is a function of water activity, with the study of calf thymus DNA in mixed solution. They derived that the B-form favored under conditions of high water activity, and A-form stabilized under low water activity.

The addition of a large proportion of ethanol can reduce the activity of water, and displace water molecules hydrating the helix. The water molecules prefer to form clusters [22], distribute less homogeneous in the solution, and most of them are found concentrated close to the DNA surface [24]. Many works have been done to study the conformation transition in the mixed solvent by adding ethanol [24–27,30]. However, most of the previous reports focused attention on the ratio of ethanol in the solvent for which the conformation transition occurs.

In this paper, we conducted the simulations of water and ethanol mixture with five different weight percent of ethanol to study the property of mixed solvent. After that, we put one B-DNA segment into the mixed solvent to study the structure changes of DNA influenced by the property of solvent.

2. Theoretical method and simulation details

The package we use to perform molecular dynamics simulation is M.DynaMix [31,32], it can be used for simulations of flexible molecules based on the double time step algorithm [33] and run in parallel execution. Amber94 force field [34] is implemented in our simulation, which is well suited for reflecting the effects of solvent activity on DNA structures. The intermolecular and intramolecular potential energy in the system can be described as: $U = U_{LJ} + U_{el} + U_{bond} + U_{ang} + U_{tors}$, where U_{LJ} is the sum of Lennard-Jones interactions taken over non-bonded atom pairs, U_{el} is the sum of electrostatic interactions, U_{bond} is the sum standard harmonic potential between the two bonded atoms, U_{ang} describes the sum harmonic potential of the covalent angles, and U_{tors} is the sum torsion potential for dihedral angles. They are expressed as

$$U_{LJ} = \sum_{non\text{-}bonded} 4\varepsilon_{ij}\left[\left(\frac{\sigma_{ij}}{r_{ij}}\right)^{12} - \left(\frac{\sigma_{ij}}{r_{ij}}\right)^{6}\right], \tag{1}$$

in which r_{ij} is the distance between atoms i and j, ε and σ determine the energy and distance scale of Lennard-Jones interaction, respectively.

$$U_{el} = \sum_{non\text{-}bonded} \frac{q_i q_j}{4\pi\varepsilon_0 r_{ij}}, \tag{2}$$

ε_0 is the vacuum permittivity, q is the charge of the atom.

$$U_{bond} = \sum_{covalent\ bonds} K_r(r_m - r_0)^2 \tag{3}$$