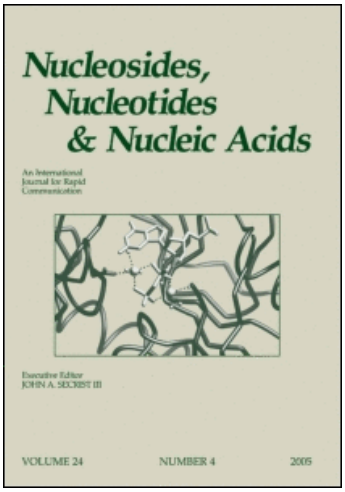

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THE COMPUTATIONAL STUDIES ON THE CONFORMATION-STABILIZING FACTORS OF THE LEFT-HANDED Z-DNA

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ABSTRACT: The conformation-stabilizing factors of the left-handed Z-DNA was estimated by the molecular dynamics calculations using the various metal cations and the polyamines. We concluded the conformation-stabilizing effect of metal cation for Z-DNA was more significant than that of the polyamine by theoretically.

In nature the double-stranded DNA molecule adopts normally the right-handed B-form. However, under high salt concentration, the right-handed B-DNA might be changed to the left-handed Z-DNA (1). On the other hand, the concentration of polyamine is essential for B-Z transition and the stabilization of the left-handed Z-DNA by polyamine is very important because polyamine might be one of the promoting factors for carcinogenesis. Furthermore, the metal cations (mono-and divalent cations) are also important stabilizing factors of the left-handed Z-DNA because the metal cations are used as counterions for neutralizing of negatively charged phosphate group (2). In general, polyamine and metal ion partipate in the cell proliferation, growth and differentiation. Using the molecular dynamics (MD), we have been investigating on the mutual interactions among the left-handed Z-DNA, metal cations (Mg^{2+}, Na^{+} and K+) and several polyamines (7). The starting model for the left-handed Z-DNA with cations or with the polyamine, $NH_2(CH_2)_2NH(CH_2)_2NH(CH_2)_2NH_2$ (PA(222)), was essentially based on the X-ray crystal structure (3-6). In the latter crystal structure, a polyamine molecule was found in the

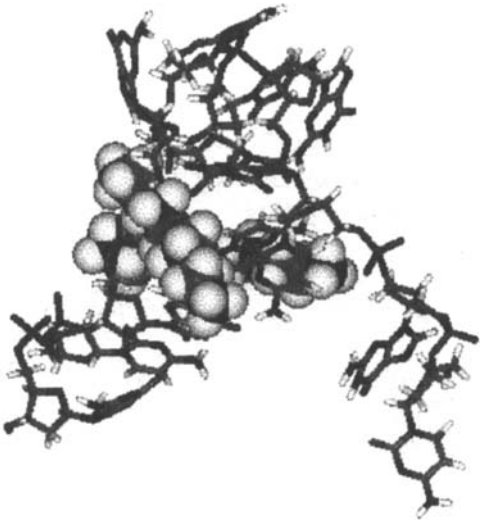

Fig. 1 The molecular structure of d(CG)3 + 2PA(222) complex after 30 ps MD calculation

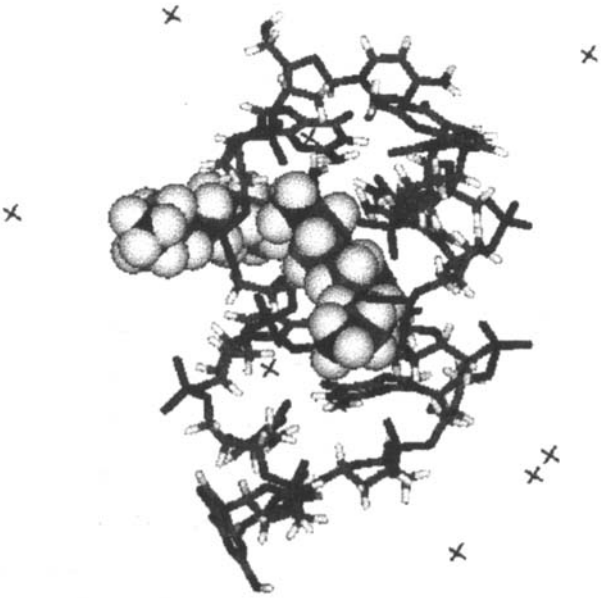

Fig. 2 The molecular structure of d(CG)3 + 10Na + 2PA(222) complex after 30 ps MD calculation

minor groove of the left-handed Z-DNA hexamer $d(CG)_3$ duplex. We used a new version of MD calculation program (Discover), in which we are able to vary the potential function for each atom, and the simulation time was 1.0 ns using amber force field. It has been postulated that several mono- and di-valent cations and polyamines are main enhancers for B-Z transition (right-handed B-DNA- left-handed Z-DNA transition). The MD result for Z-DNA with PA(222) indicated that after 30 ps the PA(222) molecule was separated from the minor groove of the left-handed Z-DNA and the double-stranded Z-DNA itself was partly unwinded (Fig. 1). On the other hand, the MD simulation for Z-DNA with metal cation (sodium or potassium cation) which has higher dielectric constant and ionic strength than the PA(222) molecule indicated that the conformation of Z-DNA was rather stable even after 30 ps simulation (Fig. 2). Therefore, the conformation-stabilizing effect of metal cation for Z-DNA is more significant than that of polyamine (PA(222)). It was considerable that after the B-Z transition occured, the PA(222) molecule probably bound to the minor groove of Z-DNA.

REFERENCES

1. Wang, A.H.J. et al. *Nature* **1979**, *282*, 680-686.
2. Gessner,R.V. et al. *J. Biol. Chem.* **1989**, *264*, 7921-7935.
3. Tomita, K. et al. J. *Mol. Graphics* **1989**, *7*, 71-75.
4. Ohishi, H. et al. *FEBS Letters* **1991**, *284*, 238-244.
5. Ohishi, H. et al. *FEBS Letters* **1996**, *391*, 153-156.
6. Ohishi, H. et al. *FEBS Letters* **1996**, *398*, 291-296.
7. Ohishi, H. et al. *Biochem. Biophys. Research Commun.* **1997**, *236*, 146-150.