

## Mutual Backbone Phosphate Group Interactions Promote DNA Double Helix Bending at High Salt Concentrations in Solution

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**Abstract.** Results of free energy calculations connected with the backbone phosphate group interactions upon local bending and helical twist modifications of A-, B- or Z-DNA at high salt concentrations have been reported recently (Jursa and Kypr 1990). Here we calculate energies necessary for DNA bending, using three models based on experimentally determined persistence length values. A comparison of energies following from the two quite different approaches suggests that high salt concentrations induce A- and mainly B-DNA bending into the double helix minor groove at least up to 10°.

**Key words:** DNA bending — High-salt — Theoretical calculations

### Introduction

DNA is heavily compacted in vivo (Kellenberger 1988). The compaction is accomplished by basic proteins which induce similar changes in the CD spectra of DNA as do high salt concentrations (Adler and Fasman 1971; De Murcia et al. 1978). In addition, high salt concentrations induce interesting conformational isomerizations in synthetic DNA molecules (Vorlíčková et al. 1983; Jovin et al. 1983; Vorlíčková et al. 1988). The above phenomena have been amply demonstrated but their mechanisms remain obscure owing to experimental troubles with high salt concentrations and the long time lasting non-existence of any acceptable theory describing DNA in high salt solutions. Soumpasis (1984) formulated the theory of DNA behaviour at high-salt solutions but the relative simplicity and approximate nature of the theory required first a demonstration of its correctness through a comparison with experimental data. The theory has gained credibility after a successful reproduction of the B-Z transition induced by an increasing NaCl concentration (Soumpasis 1984) and then of even its counterion dependence (Soumpasis et al. 1987a). The predictive force of the

theory has further been demonstrated by Soumpasis et al. (1987b) and Soumpasis (1988). We have used this theory previously (Jursa and Kypr 1990) to investigate DNA bending in the presence of high salt concentrations. The previous study is complemented here by a comparison with results considering not only the backbone phosphate interactions but also whole DNA molecules characterized by experimentally determined persistence length or values of the Young modulus.

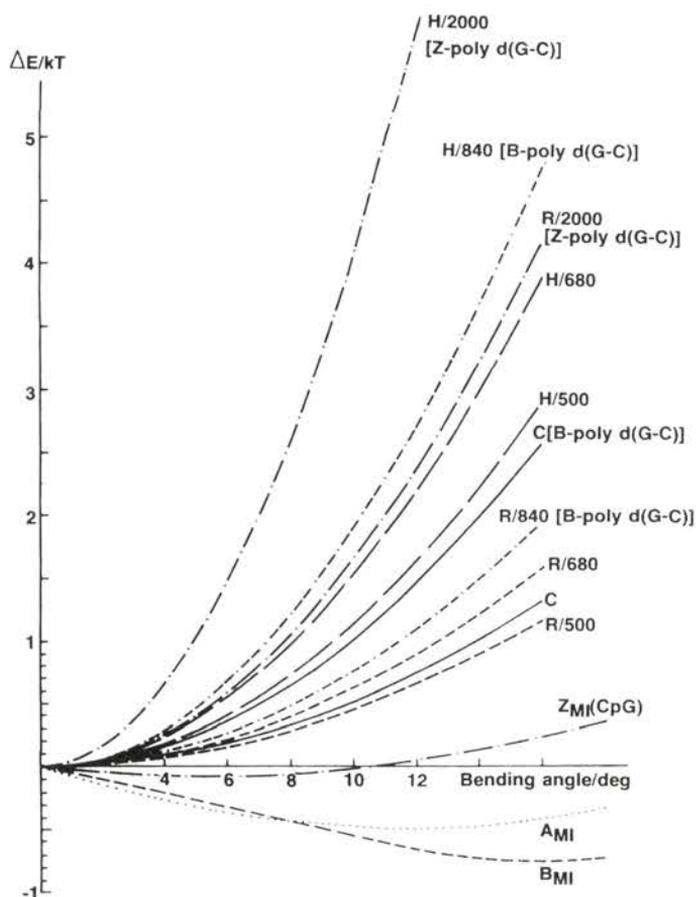
## Materials and Methods

The energies connected with DNA bending were calculated using three models of DNA bending: (i) Continuum elastic rod model (Hogan and Austin 1987), (ii) Schellman's Random  $\Phi$ , and (iii) Hinge models (Schellman 1974). The values of the Young modulus and persistence length were taken from Hogan and Austin (1987), Thomas and Bloomfield (1983), and Trifonov et al. (1987).

## Results and Discussion

Fig. 1 shows for illustration the dependences on the bending magnitude of the free energy gained upon backbone bending of the various double helix types into their minor grooves at 4.2 mol/l NaCl. The dependences were calculated as previously (Jursa and Kypr 1990). It can be seen that, for example, B-DNA gains 0.76 kT units of free energy under these conditions if it bends by about 15° into the double helix minor groove. It should, however, be mentioned that the energy gain is doubled if the bending is combined with local double helix unwinding by about 5° (Jursa and Kypr 1990). The same bending of A-DNA is slightly less favored while bending of Z-DNA larger than 10° is already disfavored. We demonstrate the rigidity of Z-DNA on only one example here but this is a general property of Z-DNA as indicated by our calculations (Jursa and Kypr 1990) but also by experimental data (Thomas and Bloomfield 1983). The main question we want to answer in this paper is whether the energy of interphosphate interactions gained upon B- or A-DNA backbone bending is sufficient to bend real DNA where also other than the interphosphate forces operate. For this purpose, the energy required to bend DNA was here calculated using a completely different approach based on DNA persistence length or Young's modulus measurements.

Experimental studies demonstrate that persistence length or Young's modulus depends on the base sequence and DNA conformation (Hogan and Austin 1987). All values reported for persistence length and Young's modulus in the



**Fig. 1.** Energy dependences on the bending angle evaluated using different models of DNA bending, different DNA conformations and nucleotide sequences.  $B_{MI}$ ,  $A_{MI}$  and  $Z_{MI}$  (CpG) stand for dependences calculated using the Soumpasis theory for bending into the minor grooves of B-, A- and Z-DNA (at the CpG step) at 4.2 mol/l NaCl. Note that in the former two cases the bending is connected with energy gains. The remaining dependences were calculated using the continuum (abbreviated C in the Figure), random  $\Phi$ (R) or hinge (H) models (for details see the Method section). The abbreviations of the models used for each calculation are followed by persistence length values (no values are given in cases when the dependences were calculated from the Young modulus), conformation (B or Z) and the polynucleotide (poly(dG-dC)) for which the persistence length or Young modulus have been experimentally determined. In cases when the conformation and polynucleotide are not specified, random sequence DNA in B conformation is considered. The Soumpasis and hinge models consider localized bends the magnitudes of which correspond to the bending angles used in the calculations. In the remaining two models the bending angle is evenly distributed among five consecutive bends (random  $\Phi$  model) or along the length of five base pairs (continuum bend model).

literature for various DNA molecules in various conformations have been considered in the present calculations to find the dependences of energy required to bend DNA on the magnitude of the bending angle. The results are summarized in Figure 1 where the dependences can directly be compared with the results of the Soumpasis theory discussed above. It can be concluded from a comparison of these two kinds of curves that the energy gains connected with salt-induced backbone deformations are sufficient to non-negligibly bend real DNA molecules. Naturally how much DNA is really bent in high-salt solutions depends on the base sequence the stacking properties of which certainly modulate the extent and the preferred direction of bending.

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