

Computation of the Variance of Writhe for Nicked Circular DNA Molecules

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Our computational analysis of the variance of writhe is based on the Monte Carlo sampling of equilibrium conformational ensemble of DNA molecules. In these computations we model the double helix as the discrete wormlike chain (see ref. (1) for review). A double-stranded DNA molecule of N base pairs in length is modeled as a chain consisting of m rigid cylinders of equal length l . The value of l does not affect the simulation results if it is sufficiently small. Specific choice of l depends on the conformational properties of interest. We found that for the variance of writhe the model chains have to consist of at least 40 straight segments and should have at least 20 segments per DNA persistence length. The energy of the chain, E_b , is specified by the angles between the directions of adjacent segments i and $i+1$, θ_i :

$$E_b = g' \sum_{i=1}^m \theta_i^2 \quad (1)$$

where g' is the bending rigidity constant. The constant g' is proportional to the DNA persistence length, a : $g' = ak_B T / l$ (if $l \leq a/10$), where $k_B T$ is the Boltzmann temperature factor. The cylinders have a certain diameter, d , and are impenetrable one for another. The value of d accounts both for the geometrical diameter of the double helix and for electrostatic repulsion between negatively charged DNA segments. Thus, the value of d is larger than the geometric diameter. The concept of effective diameter is the simplest but sufficiently accurate way to account for the electrostatic interaction (2,3). Thus, g and d are the only two parameters in this model. The values of these parameters depend on ionic conditions we want to simulate. For near-physiological ionic conditions used in this study the value of a equals 48 nm at 22 °C (4-7). Correspondingly, for the majority of the calculations each segment of the model chain corresponded to 14 base pairs, although shorter segments were used in the simulation of very small DNA circles. The value of d equals 5 nm at these conditions (8). We assumed in this study that d does not depend on the temperature.

The Metropolis-Monte Carlo procedure is used for the statistical sampling of chain conformations. The procedure consists of consecutive displacements of the chain parts. At each step of the procedure a new trial conformation can be accepted or rejected (9). If the trial conformation is rejected, the current conformation must be added again to the constructed conformational set. The starting conformation is chosen arbitrarily. For circular chains used in the simulations the displacement represents a crankshaft rotation: a subchain is rotated by a randomly chosen angle, ϕ , around the straight line connecting two randomly chosen vertices of the chain (Fig. 1A). The values of ϕ are uniformly distributed over interval $(-\phi_0, \phi_0)$, chosen so

that about half of the trial conformations are accepted. Conformations with intersecting segments are considered as having infinite energy. According to the acceptance rules such conformations are rejected. Of course, there is a strong correlation between successive conformations constructed by the Metropolis procedure, so the constructed conformational sets should be sufficiently large to overcome this correlation. In this study the sets of up to 1 billion conformations were constructed to obtain sufficiently small statistical errors. The calculated variance of writhe corresponds to the subset of unknotted DNA molecules. We tested that all constructed conformations correspond to unknotted chains by calculating Alexander polynomial for each new conformation generated in the Metropolis procedure (see ref. (1) for details).

To estimate the variance of writhe we calculated its values for each of the simulated conformations. To do so we used the algorithm suggested in ref. ((10)). The results of these calculations are shown in Fig. 1 and expressed by the interpolating Eqs. (2-3) of the main text.

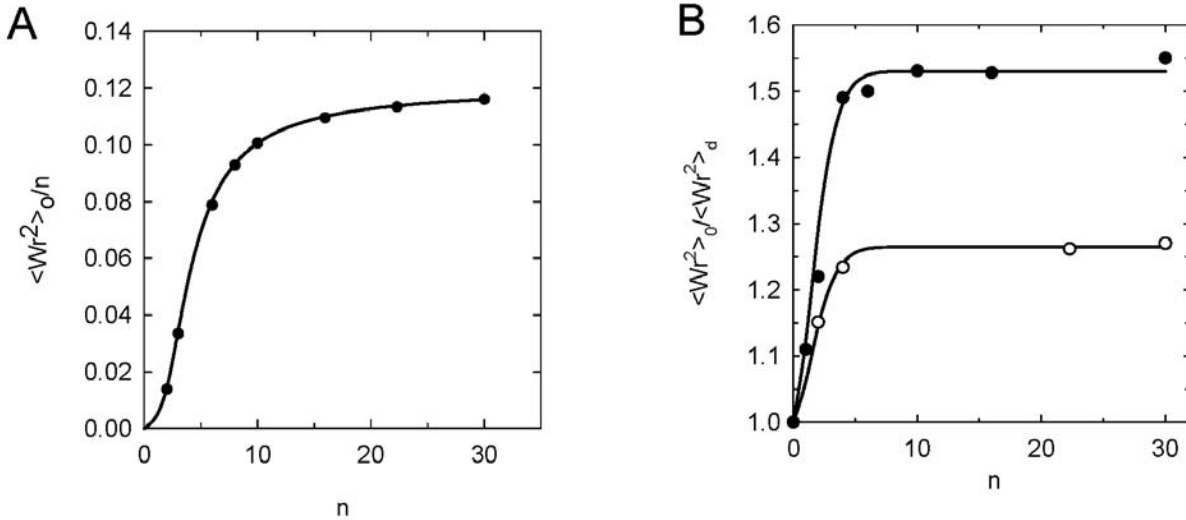


Figure S1. Computed dependence of the variance of writhe, $\langle (Wr)^2 \rangle$, on the number of Kuhn statistical segments, n . (A) The values $\langle (Wr)^2 \rangle_0$ obtained for the model chain with zero diameter, $\langle (Wr)^2 \rangle_0$. The simulation results are shown by filled circles; the line corresponds to Eq. (2) of the main text. (B) The effect of chain thickness on $\langle (Wr)^2 \rangle$. The simulation results were obtained for $d/a = 0.1$ (\circ) and $d/a = 0.2$ (\bullet); the lines correspond to Eq. (3) of the main text for the same values of d/a .

REFERENCES

1. Vologodskii, A. (2006) In Lankas, F. and Sponer, J. (eds.), *Computational studies of DNA and RNA*. Springer, Dordrecht, pp. 579-604.
2. Stigter, D. (1977) Interactions of highly charged colloidal cylinders with applications to double-stranded DNA. *Biopolymers*, **16**, 1435-1448.

3. Vologodskii, A.V. and Cozzarelli, N.R. (1995) Modeling of long-range electrostatic interactions in DNA. *Biopolymers*, **35**, 289-296.
4. Hagerman, P.J. (1988) Flexibility of DNA. *Ann. Rev. Biophys. Biophys. Chem.*, **17**, 265-286.
5. Taylor, W.H. and Hagerman, P.J. (1990) Application of the method of phage T4 DNA ligase-catalyzed ring-closure to the study of DNA structure. II. NaCl-dependence of DNA flexibility and helical repeat. *J. Mol. Biol.*, **212**, 363-376.
6. Vologodskaia, M. and Vologodskii, A. (2002) Contribution of the intrinsic curvature to measured DNA persistence length. *J. Mol. Biol.*, **317**, 205-213.
7. Geggier, S. and Vologodskii, A. (2010) Sequence dependence of DNA bending rigidity. *Proc. Nat. Acad. Sci. USA*, **107**, 15421-15426.
8. Rybenkov, V.V., Vologodskii, A.V. and Cozzarelli, N.R. (1997) The effect of ionic conditions on DNA helical repeat, effective diameter, and free energy of supercoiling. *Nucleic Acids Res.*, **25**, 1412-1418.
9. Metropolis, N., Rosenbluth, A.W., Rosenbluth, M.N., Teller, A.H. and Teller, E. (1953) Equation of state calculations by fast computing machines. *J. Chem. Phys.*, **21**, 1087-1092.
10. Le Bret, M. (1980) Monte Carlo computation of supercoiling energy, the sedimentation constant, and the radius of gyration of unknotted and knotted circular DNA. *Biopolymers*, **19**, 619-637.