Comment on "Flexibility of short DNA helices with finite-length effect: From base pairs to tens of base pairs"

Midas Segers, Enrico Skoruppa, Jan A. Stevens, Merijn Vangilbergen, Aderik Voorspoels, and Enrico Carlon

Soft Matter and Biophysics, KU Leuven, Celestijnenlaan 200D, 3001 Leuven, Belgium

(Dated: October 26, 2021)

While analyzing the persistence length of DNA atomistic simulations Wu et al. [J. Chem. Phys. 142, 125103 (2015)] introduced an empirical formula to account for the observed length-dependence. In particular they found that the persistence length increases with the distance. Here, we derive the formula by Wu et al. using a non-local twistable wormlike chain which introduces couplings between distal sites. Finally, we show that the same formula can account for the length-scale dependence of the torsional persistence length and is, in fact, applicable to any kind of polymer model with non-local couplings.

In Ref. [1] Wu et al. analyzed the bending flexibility of short DNA segments (of up to 50 bps) by molecular dynamics and Monte Carlo simulations. They found that DNA is softer at short lengths, which they accounted for with the empirical formula

\[ l_B(m) = l_B^\infty - \frac{A}{B + m}, \quad (1) \]

where \( l_B(m) \) is the persistence length of a sequence of \( m \) base pair-steps, \( l_B^\infty \) the asymptotic persistence length and \( A, B \) some fitting parameters. In this comment we show that the above formula is consistent with the asymptotic expansion of the non-local Twistable Wormlike chain (nlTWLC)\(^a\) which gives

\[ l_B(m) = l_B^\infty \left(1 - \frac{B}{B + m}\right) + \ldots \quad (2) \]

with the dots indicating higher order corrections. Such expansion is valid both for (1) the local persistence length of a long DNA molecule measured from the tangent-tangent correlation of two base pairs separated by \( m \) steps and for (2) the persistence length obtained from the correlation of the endpoint tangent vectors for a DNA molecule of finite length \( m \).

The latter is the quantity analyzed by Wu et al.\(^a\) Furthermore, we will show, that an expansion of the type \( (2) \) is also valid for the torsional persistence length. Note, that expression \( (2) \) contains one parameter less than \( (1) \) implying that \( A = l_B^\infty B \). This relation holds approximately for the values reported by Wu et al.\(^a\) with \( l_B^\infty = 50 \) nm, \( A = 450 \) nm and \( B = 10 \).

Non-local couplings – The nlTWLC describes DNA configurations using the three rotational densities tilt, roll (the two bending modes), and twist indicated with \( \tau_n, \rho_n, \) and \( \Omega_n + \omega_0 \) respectively, with \( n = 1, 2, \ldots , N \) enumerating the base pair-steps along the chain. The twist is subdivided into a constant intrinsic twist density \( \omega_0 = 1.75 \) nm\(^{-1}\) corresponding to one turn of the helix every 10.5 base pairs, and a fluctuating excess twist \( \Omega_n \). While in the ordinary TWLC couplings are strictly local and the energy is quadratic in \( \tau_n, \rho_n, \) and \( \Omega_n \), the nlTWLC introduces couplings between distal sites, such as for instance \( \tau_n \tau_{n+m} \) with \( m > 0 \). Non-local couplings have been observed in several all-atom simulations\(^3\) and they typically extend to three flanking dinucleotide steps\(^3\).

Persistence lengths – The nlTWLC predicts similar length scale dependence of both the bending and the torsional persistence length, hence we discuss both. In the limit of an infinite long chain \( N \to \infty \) the correlation functions between two sites separated by \( m \) base pairs decay with \( m \)-dependent persistence lengths given by the following expressions\(^3\):

\[ \frac{1}{l_x} = \frac{1}{m \pi} \int_{-\pi/2}^{+\pi/2} \frac{\sin^2 (my)}{\sin^2 y} f_x(y) \, dy, \quad (3) \]

with \( x \in \{B, T\} \) labeling either the bending or the torsional persistence length. The variable \( y = \pi y / N \) is the rescaled momentum and \( f_x(y) \) are functions of the bending fields (tilt and roll) and the excess twist field for the \( l_B \) and \( l_T \) respectively. The full expressions are reported in Ref.\(^2\) We also note, that while the former expression contains certain approximations, the latter is exact. The functions \( f_x(y) \) are symmetric in \( y \), so for small \( y \) the following expansions hold

\[ f_x(y) \approx f_x(0) + \frac{1}{2} f''(0) y^2 + O(y^4). \quad (4) \]

To proceed further it is convenient to split \( f_x(y) \) in Eq. \( (3) \) into two terms, a constant \( f_x(0) \) and the increment \( f_x(y) - f_x(0) \) and integrate these two terms separately. That way, one obtains (to simplify the formula we omitted the integration boundaries)

\[ \frac{1}{l_x} = \frac{f_x(0)}{m \pi} \int_{-\pi/2}^{+\pi/2} \frac{\sin^2 (2my)}{\sin^2 y} \, dy + \frac{1}{2m \pi} \int_{-\pi/2}^{+\pi/2} \frac{\cos(2my) - f_x(y) - f_x(0)}{\sin^2 y} \, dy \]

\[ = f_x(0) \left(1 + \frac{B_x}{m}\right) + O\left(e^{-m/\lambda}\right), \quad (5) \]

where we have used

\[ \int_{-\pi/2}^{+\pi/2} \frac{\sin^2 (2my)}{\sin^2 y} \, dy = m \pi, \quad (6) \]

and the definition

\[ B_x = \frac{1}{2\pi f_x(0)} \int_{-\pi/2}^{+\pi/2} \frac{f_x(y) - f_x(0)}{\sin^2 y} \, dy. \quad (7) \]

The oscillatory term \( \cos(2my) \) in \( (5) \) yields an exponentially small factor proportional to \( e^{m/\lambda} \), where the characteristic decay length \( \lambda \) can be obtained from the poles of

\(^a\)Electronic mail: enrico.carlon@kuleuven.be
the integrand\textsuperscript{[2]}]. We note that the integral in (7) is convergent, in particular\textsuperscript{[1]} implies that the integrand does not diverge as \( y \to 0 \). Finally, inverting Eq. (5) one gets (3) with \( l_B^\infty = 1/f_B(0) \) and \( B = B_B \).

While so far we have considered the limit \( N \to \infty \) we can extend the analysis for a sequence of finite length. For brevity we limit the discussion to the bending persistence length. For finite \( N \) this is given by\textsuperscript{[3]}

\[
1/l_B = a/(2m) \left\{ \left( m-1 \right) \sum_{n=0}^{m-1} \tau_n^2 + \left( m-1 \right) \sum_{n=0}^{m-1} \rho_n^2 \right\}
\]

(8)

where \( \tau_n^* \) and \( \rho_n^* \) are related to the original variables tilt and roll by a linear transformation\textsuperscript{[2]}\textsuperscript{[3]}\textsuperscript{[4]}. In particular, as in Ref.\textsuperscript{[1]} we are interested, in the case \( m = N \), where \( l_B \) is obtained from the tangent-tangent correlation function between the two ends of the chain. On general grounds the averages in (8) will produce a bulk type term extensive in \( m \) and boundary corrections \( \langle X \rangle = m \Gamma_1 + \Gamma_2 + \ldots \), with \( X \) indicating the terms averaged in (8). Such expression produces again the expansion (2).

Monte Carlo simulations—Figure 1 shows an example of both torsional and bending persistence lengths obtained from Monte Carlo simulations of the nTWLC compared to fits with Eq. (4)\textsuperscript{[2]}\textsuperscript{[3]}\textsuperscript{[4]} (solid lines). Left plots are for \( N = 200 \) and finite \( m \), while the right plot for sequences of finite length \( m = N \). As expected the asymptotic persistence lengths are the same in these two cases, as both converge towards the same \( l_B^\infty \) for large \( m \). However, the \( B_T \) are determined by the boundary contributions of short segments (small \( m \)). These contributions are manifestly different when comparing a partial segments located within a larger chain (\( m \ll N \)) and segments spanning the entire chain (\( m = N \)), as the latter case lacks any couplings spanning beyond the considered range.

Static contributions—Thus far we have solely considered models in which the persistence length only depends on the thermal bending fluctuations of the molecule. However, it is well established, that the ground-state of a DNA molecule is not straight, but exhibits significant static bending. These bending components will further expedite the decorrelation of tangents. It has been shown\textsuperscript{[5]} that the bending persistence length can be decomposed into the dynamic component \( l_D \) determined by thermal fluctuations and the static component \( l_S \) as

\[
1/l_B = 1/l_D + 1/l_S.
\]

(9)

When considering a sufficiently large chain, one can define the average \( m \)-dependent static persistence length by considering a sequence ensemble. We assume that in this ensemble averaging produces uncorrelated static bends. Following this assumption \( l_S \) is taken \( m \)-independent, while for the dynamic component (which is of thermal origin) Eq. (5) still holds. Hence we find

\[
1/l_B = 1/l_D \left( 1 + B_D m \right) + 1/l_S,
\]

(10)

which ultimately gives Eq. (2)\textsuperscript{[2]}\textsuperscript{[3]}\textsuperscript{[4]} with

\[
1/l_B^\infty = 1/l_D^\infty + 1/l_S^\infty \quad \text{and} \quad B = B_B^\infty B_T^\infty.
\]

(11)

REFERENCES

1. Y.-Y. Wu, L. Bao, X. Zhang, and Z.-J. Tan, “Flexibility of short DNA helices with finite-length effect: from base pair to tens of base pairs,” J. Chem. Phys. \textbf{142}, 03B614_1 (2015).
2. E. Skoruppa, A. Voorspoels, J. Vree, e and E. Carlon, “Length-scale-dependent elasticity in DNA from coarse-grained and all-atom models,” Phys. Rev. E \textbf{103}, 042408 (2021).
3F. Lankaš, J. Šponer, J. Langowski, and T. E. Cheatham, “DNA basepair step deformability inferred from molecular dynamics simulations.” Biophys J. 85, 2872–2883 (2003).
4A. Noy and R. Golestanian, “Length scale dependence of DNA mechanical properties,” Phys. Rev. Lett. 109, 228101 (2012).
5E. N. Trifonov, R. K.-Z. Tan, and S. C. Harvey, “DNA Bending and Curvature,” in Structure and Expression, edited by W. K. Olson, M. H. Sarma, and M. Sundaralingam (1987) p. 243.