Statistical mechanics of DNA-nanotube adsorption

Shushanik Tonoyan, Davit Khechoyan, and Yevgeni Mamasakhlisov
Department of Molecular Physics, Yerevan State University, A. Manougian Street 1, 375025, Yerevan, Armenia

Artem Badasyan*
Materials Research Laboratory, University of Nova Gorica, Vipavska 13, SI-5000 Nova Gorica, Slovenia

(Received 5 December 2019; accepted 15 June 2020; published 29 June 2020)

Attraction between the polycyclic aromatic surface elements of carbon nanotubes (CNTs) and the aromatic nucleotides of deoxyribonucleic acid (DNA) leads to reversible adsorption (physisorption) between the two, a phenomenon related to hybridization. We propose a Hamiltonian formulation for the zipper model that accounts for the DNA-CNT interactions and allows for the processing of experimental data, which has awaited an available theory for a decade.

DOI: 10.1103/PhysRevE.101.062422

Deoxyribonucleic acid (also known as DNA) is a biomolecule, composed of two polymer chains, stabilized by hydrogen bonds (H bonds) in the perpendicular direction to its axis. If the H bonds are broken, and the two strands are separated, each single strand DNA (ssDNA) will remain stabilized by the π stacking of neighbor nucleotides in the direction parallel to the axis. Polymer physics, as a rule, considers linear polymers as one-dimensional (1D) objects in the absence of any of long-range interactions (including loops) [1–3]. Another constituent of this complex under study, carbon nanotubes (CNTs), is a system with cylindrical symmetry that has unique electronic properties due to the relevant size-quantization effects as well as outstanding mechanical properties thanks to their amazing structures [4,5]. Not surprisingly, CNTs have found numerous applications in varied areas, such as nanoelectronics, medicine, environmental safety, and microbiology. Due to the large longitudinal to lateral dimension ratio, CNTs can be considered as one-dimensional objects as well. Attraction between these two rigid 1D objects results in the formation of a ssDNA-CNT complex, which, at a later stage of hybridization, serves as a landing site for free ssDNAs from solution. Once hybridized on the surface of the CNT, double-stranded (ds) DNA undergoes a *B* to *z* conformational transition that modulates the dielectric environment of the single-walled CNT and allows for the optical detection of such an event [6,7]. The presence of an attracting 1D surface significantly enriches the phase diagram of adsorbed dsDNA [8] and, thus, opens doors for numerous applications.

There are several reasons motivating the study the DNA-CNT complex. One is the insolubility or extremely poor solubility of CNTs, which imposes a considerable challenge when it comes to applications. Different techniques were developed to improve CNT dispersion including the use of surfactants, oligomers, biomolecules, polymer wrapping, and chemical functionalization. One of the most efficient dispersing agents for water solutions is ssDNA, which forms a (very) stable complex with CNTs [9]. Another line of reasoning originates from the wide range of existing applications for the DNA-CNT complexes in various nanotechnologies. Short single-stranded DNA oligomers composed of $\simeq 10$ nucleotides (nts) have been reported to be of exceptional relevance for many applications [10].

Despite the fact that there are several reviews on biological [11] or biosensing [12] applications for carbon nanomaterials, there is a negligibly small number of both theoretical and experimental studies devoted to the equilibrium picture of reversible adsorption (physisorption) of short single-stranded DNA oligomers on CNTs.

The standard approach in the field consists of the application of first principles calculations (mostly, using DFT software) to estimate the energies of interaction between the nucleotides and the carbon-based substrates with and without water (see, e.g., Ref. [13] and references therein). Another wide group of approaches is through the use of all-atom molecular dynamics simulations to reach conclusions about the thermodynamics of ssDNA-SWNT interactions (see, e.g., Refs. [14,15]).

Recently, several phenomenological models have been employed towards the problem, mainly through the modifications of adsorption theories known from the past. Thus, to process the experimental data, a recent experimental study [16] has treated the adsorption of ssDNA oligomers and dimers as a simple chemical reaction.

Kato *et al.* [17] have applied the Hill formula to estimate the adsorption free energy of single-stranded cytosine oligo-DNAs on single-wall nanotubes (SWNTs). In a recently published article [18], an extended version of Langmuir's approach is developed to describe the histidine and alanine adsorption on CNT. Although simple and seemingly effective, adsorption isotherm models adopted to the biopolymer-CNT story suffer from the apparent and long-known limitations of the Hill-Langmuir approach in describing the cooperative adsorption of polymers. In particular, the assumed presence

*Corresponding author: abadasyan@gmail.com

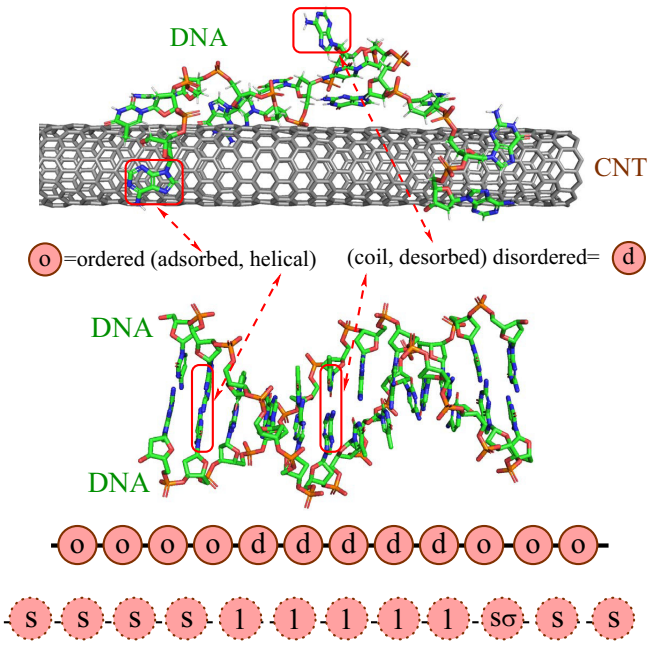

FIG. 1. Scheme illustrating the similarity between the mixtures of adsorbed and desorbed nucleotides of ssDNA on a CNT (above) and the helical and coil nucleotide pairs in dsDNA (below). Both systems can be reduced to the same sequence of ordered (o) and disordered (d) repeat units, giving rise to the sequence of statistical weights of Zimm-Bragg type.

of only two states (adsorbed and desorbed) is not justified. Instead, there are several minima present on the theoretical free energy landscape of the short ssDNA oligomer adsorbed on the CNT at room temperature [15], in agreement with experimental studies [19].

A general problem in the field is the absence of a statistical mechanical approach with a model Hamiltonian that would provide a thermodynamic picture of reversible adsorption of a short ssDNA oligomer on the CNT.

A recent experimental study serves as a bright example illustrating this apparent gap in knowledge. In 2009, Albertorio *et al.* reported an experiment on the association of ssDNA oligomers with CNTs [20]. The authors managed to process the results of kinetics experiments and to extract the association enthalpies with the help of the Eyring equation [20]. At the same time, they failed in extracting the data from the equilibrium measured curves of the temperature dependence of the DNA-CNT fraction because of the absence of a corresponding theory. The best they could do was to fit what they called a sigmoidal function to their measured points without providing any reasoning for the particular choice of function. Up to now, a theory that would provide a fit for experimental data, such as the one from Albertorio *et al.* [20] to a physical model with a well-defined microscopic Hamiltonian, has not been suggested.

In this paper, we describe the CNT-ssDNA physisorption phenomenon using the spin Hamiltonian formulation of a zipper model [21] and validate theoretical results against experimental data. The zipper model is the limiting case of the Zimm-Bragg (ZB) model where the length of the chain is so short that there can be no more than one ordered and no more than one disordered region and, consequently, will be no loops in the chain.

We start by invoking the conceptual similarity between ssDNA adsorption on the CNTs and the helix-to-coil transition or DNA melting (Fig. 1). Indeed: (i) Due to the correlation of nucleotide conformations, ssDNA adsorption is promoted on the scale of the persistence length, and DNA melting is correlated (cooperative) on some spatial scale as well. (ii) The entropy of the adsorbed conformation is substantially smaller as compared to the desorbed one because of the very different number of available conformations. In a similar way, helical repeat units are in a low-entropy conformation as opposed to molten DNA.

(iii) Short-range interactions (H bonding between the strands of DNA and stacking between DNA and a nanotube) stabilize the association between the two one-dimensional systems.

Using the above mentioned similarity, we make use of models suggested in the past [22–24] and describe the adsorption of DNA on the CNT with an energy function (Hamiltonian) that depends on the coarse-grained variables of the system. We do so by adopting the Potts-like spin model [24–26] to the problem of DNA-CNT association. Employing the nearest-neighbor approximation, we start with a spin Hamiltonian formulation, equivalent to the Zimm and Bragg model [26],

$$H_{\mathrm{ZB}}(\{\gamma_i\}) = -U\sum_{i=1}^{N}\delta(\gamma_i,1)\delta(\gamma_{i+1},1) \equiv -U\sum_{i=1}^{N}\delta_i^{(2)}, \tag{1}$$

where $\gamma_k = 1, 2, \ldots Q$ are spin variables describing the conformations of each of $i = 1, 2, \ldots N$ repeat units (nucleotides), spin value $\gamma = 1$ corresponds to the ordered (bound) conformation, other $Q-1$ values describe disordered (free) conformations; $U(>0)$ is the stacking energy per nucleotide. The Hamiltonian Eq. (1) leads (see Ref. [26]) to a transfer matrix with the characteristic equation,

$$\Lambda^2 - \Lambda(W-1+Q) + (W-1)(Q-1) = 0, \tag{2}$$

where $W = e^{U/T}$ and T is the temperature. Using mapping,

$$\frac{\Lambda}{Q} \to \lambda, \qquad \frac{W-1}{Q} \to s, \qquad \frac{1}{Q} \to \sigma \tag{3}$$

allows us to transform Eq. (2) into the original characteristic equation of ZB,

$$\lambda^2 - \lambda(s+1) + s(1-\sigma) = 0, \tag{4}$$

with obvious roots,

$$\lambda_{1,2}(\sigma,s) = \frac{1}{2}[1+s\pm\sqrt{(1-s)^2+4\sigma s}] = \frac{1}{2}\left[1+s\pm(1-s)\sqrt{1+\frac{4\sigma s}{(1-s)^2}}\right]. \tag{5}$$

Since the thermodynamics is fully determined by the characteristic equation of the model, Eq. (1) can be considered the

Hamiltonian of the ZB model [26]. The solutions of Eq. (4) are eigenvalues that provide the link between model parameters s, σ and the partition function,

$$Z(\sigma, s) = c_1\lambda_1^N + c_2\lambda_2^N = \lambda_1^N[c_1 + c_2 e^{-N/\xi}], \tag{6}$$

where N is the number of repeat units, $c_1 = \frac{1-\lambda_2}{\lambda_1-\lambda_2}$, $c_2 = \frac{\lambda_1-1}{\lambda_1-\lambda_2}$ ([27]) and

$$\xi(\sigma, s) = 1/\ln(\lambda_1/\lambda_2) \tag{7}$$

is the spatial correlation (or persistence) length, a curve with its maximum at the transition point. For finite correlation lengths ($\xi < \infty$), the effect of the second eigenvalue on the partition function decreases exponentially with the increase in N,

$$Z(\sigma, s) \xrightarrow[N\gg\xi]{} c_1\lambda_1^N \approx \lambda_1^N. \tag{8}$$

This is the regular large N limit of the Zimm-Bragg theory, meaningful for longer polymer chains but not applicable to our problem of interest: oligomer DNA adsorption on carbon nanotubes. In their experiment, Albertorio *et al.* used DNA oligomers of 12 nucleotide bases long, which is on the order of the Kuhn length of a ssDNA, i.e., $N \sim 2\xi$. Therefore, we need to return to Eq. (5) and apply the single-sequence approximation of the Zimm-Bragg model. At the heart of the single-sequence approximation is the impossibility of having more than one uninterrupted sequence of helical (ordered) repeat units due to small system sizes ($N < 2\xi$). For this regime, the role of the small parameter is played by

$$\frac{4\sigma s}{(1-s)^2} \ll 1. \tag{9}$$

After resolving Eq. (5) into the Taylor series by this small parameter and keeping the first terms, we obtain the eigenvalues,

$$\lambda_1(\sigma, s) = 1 + \frac{\sigma s}{1-s}, \quad \lambda_2(\sigma, s) = s - \frac{\sigma s}{1-s}. \tag{10}$$

When inserted into Eq. (6), we obtain

$$Z(\sigma, s) = \frac{\left(1 - s + \frac{\sigma s}{1-s}\right)\left(1 + \frac{\sigma s}{1-s}\right)^N + \frac{\sigma s}{1-s}s^N\left(1 - \frac{\sigma}{1-s}\right)^N}{1 - s + \frac{2\sigma s}{1-s}}. \tag{11}$$

After resolving the powers into series, rearranging the results and keeping only terms linear in σ, we obtain

$$Z(\sigma, s) = 1 + \frac{\sigma s}{(1-s)^2}(N - 1 - Ns + s^N) + O(\sigma^2). \tag{12}$$

The order parameter (helicity degree) is calculated from the partition function as

$$\begin{aligned}\theta(\sigma, s) &= \frac{1}{N}\frac{\partial \ln Z(\sigma, s)}{\partial \ln s} \\ &= \frac{s}{NZ(\sigma, s)}\frac{\partial Z(\sigma, s)}{\partial s} \\ &= \frac{\sigma s}{N(s-1)^3}\left[\frac{(N-1)(s^{N+1}-1) - s(N+1)(s^{N-1}-1)}{1 + \frac{\sigma s}{(s-1)^2}(N - 1 - Ns + s^N)}\right].\end{aligned} \tag{13}$$

Equation (13) is a well-known helicity degree formula for a zipper model, appearing in many papers and books [27,28]. Thus, using the analogy between the adsorption of one DNA strand onto another in double-stranded DNA and single-strand DNA adsorption onto a nanotube, we have derived Eq. (13) as a theoretical formula, describing the order parameter, the fraction of adsorbed nucleotides. The expression contains oligomer length (in nucleotides) as a parameter since we have explicitly taken into account finite-size effects that dominate the behavior of the zipper model. Before the application of Eq. (13) to data treatment, we need to translate the Zimm and Bragg parameters s and σ into experimental variables. There have been several definitions of these parameters in the past [27]. We stick to one of the most general definitions from Ref. [27] and following our previous publications [22,25,26] we consider the stability parameter s as a statistical weight in terms of a (Gibbs or Helmholtz) free energy change between the bound and the unbound states as

$$s = \exp\left(-\frac{\Delta G}{RT}\right) = \exp\left(-\frac{\Delta H - T\,\Delta S}{RT}\right), \tag{14}$$

where the enthalpy of binding per nucleotide and the entropic price of adsorption per nucleotide can be expressed through U and Q as

$$\Delta H = -U \quad \text{and} \quad \Delta S = -R\ln Q, \tag{15}$$

respectively [22,25,26]. The cooperativity parameter σ by its definition describes how much the original probability of bounded region growth s is hindered by the fact that there is no preceding bounded repeated unit. It can be estimated (see Refs. [22,25,26]) as

$$\sigma = Q^{1-l}, \tag{16}$$

where l (= 6 nucleotides) is the persistence length of ssDNA.[1] After inserting the definitions of s and σ into Eq. (13), we arrive at

$$\theta(s, \sigma) = \theta(T, U, Q, l = 6,\ N = 12) = \theta(T, U, Q), \tag{17}$$

a formula that contains only two free parameters: U and Q.

In order to check how adequately the proposed theory describes the phenomenon, we have chosen an experimental study which reports the measured fraction of adsorbed nucleotides, namely, the study by Albertorio *et al.* [20]. In their study, a solution of 12-base-long[2] single stranded DNA homopolymers consisting of poly $d(A)_{12}$, poly $d(T)_{12}$, poly $d(C)_{12}$, poly $d(G)_{12}$, as well as regular heteropolymers poly $d(AC)_6$ and poly $d(GT)_6$ was added to the SWNTs at a 1:1 DNA:SWNT mass ratio. The

[1]Persistence length depends on a sequence with a typical range of values between 3 and 10 nt. We chose the l = 6-nt value to simplify the expressions.

[2]Many authors have reported the same choice of oligomer lengths about 10–12 nt to be optimal for applications. This is the very scale of Kuhn length for ssDNA and can serve as a possible explanation of such a choice since sequence specificity, recognition, and sensing are optimal at exactly this scale. Yet another property of ssDNA oligomers is the absence of loops below 12 nt [15], which is logical: The system is too rigid to wrap around the CNT.

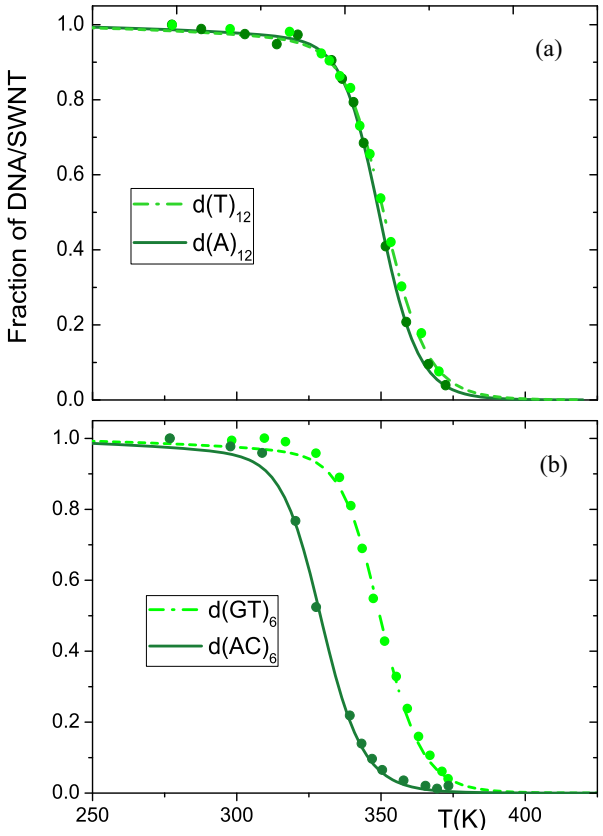

FIG. 2. The fraction of total initial DNA-SWNTs as a function of temperature for (a) poly $d(A)_{12}$, poly $d(T)_{12}$, and (b) poly $d(AC)_6$, poly $d(GT)_6$ fitted by the zipper model. The dots are experimental points from Ref. [20], and the lines correspond to fitted Eq. (17). Two curves [poly $d(C)_{12}$ and poly $d(G)_{12}$] are not shown due to the low quality of experimental data, which resulted in large fitting errors.

DNA-SWNT mixture was sonicated, and then, the bundles of nondispersed nanotubes and the remaining free DNA were removed. The thermal stability of the obtained hybrids was quantified indirectly by measuring the extent to which 12-base-long ssDNA polymers dissociated from the nanotubes after incubation in an aqueous buffer solution at different temperatures in the 4–99 °C range for 10 min by the detection of optical absorption at 815 nm.

We have digitized Figs. 2 and 3 of Ref. [20] reporting the temperature-dependent fractions remaining in solution and fit them with Eq. (17). Results of the fit are shown in Fig. 2 and in Table I. As one can see, the fit is close to perfect, which, considering that there are just two free parameters, ensures the validity of the statistical approach developed. The values of fitted energies (enthalpies) of adsorption (Table I) are all about -3 kcal/mol per nucleotide, in agreement with previously reported values [15,20]. The obtained adsorption parameters are lower than the same parameters for the dsDNA melting. For example, $\Delta H_{\rm ads} \approx -3.28$ kcal/mol against $\Delta H_{\rm melt} \approx -8$ kcal/mol and $\Delta S_{\rm ads}/R \approx -3.37$ against $\Delta S_{\rm melt}/R \approx -11$ for the AT base pair. The halved enthalpy can be explained by the fact that the ssDNA adsorbed on the surface of the CNT is not stabilized by H bonds, which are known to contribute

TABLE I. Parameter values resulting from fit. All quantities are per mole and per base of nt; U and ΔH are in the units of kcal $\times$ mole^{-1} $\times$ base^{-1}; the fit error is shown in brackets. The first two columns result from the fit of Eq. (17), and the other three columns recalculated with Eqs. (15) and (16). Heteropolymers have been fitted, assuming the length of 12 nucleotides, and, therefore, the fitted parameters correspond to averaged quantities.

	U	Q	ΔH	$\Delta S/R$	σ
$d(A)_{12}$	3.28(0.06)	29(1.7)	−3.28	−3.37	4.8×10^{-8}
$d(T)_{12}$	3.03(0.06)	22(1.3)	−3.03	−3.03	1.9×10^{-7}
$d(AC)_6$	2.77(0.10)	21(2.1)	−3.03	−3.05	2.5×10^{-7}
$d(GT)_6$	3.13(0.09)	25(2.4)	−3.13	−3.22	1.0×10^{-7}

roughly 50% to free energy [1]. The absence of H bonds has also entropic consequences: ssDNA adsorbed on the CNT has higher freedom (number of available conformations) as compared to ssDNA adsorbed on a complementary ssDNA and fixed by H bonds. Regarding the particular ordering of adsorption enthalpies by nucleotide type, there is a long history of contradictory reports as is nicely reviewed by Pramanik and Maiti [14]. Based on the data provided in Ref. [20], we cannot support a particular view on the adsorption strength ordering of nucleotides since the experimental curves for poly $d(C)_{12}$ and poly $d(G)_{12}$ span outside the experimentally accessible range of temperatures, and their desorption is incomplete (Fig. 2 of Ref. [20]), thus, essentially decreasing the quality of the fit (not shown). However, based on the available data on poly $d(A)_{12}$ and poly $d(T)_{12}$, our analysis confirms purines having larger enthalpy of adsorption as compared to pyrimidines (i.e., $A > T$ order), in agreement with many reported studies (see Ref. [14] and references therein). Since we are not aware of any other published data on the temperature dependence of the ratio of adsorbed nucleotides on the CNT, more experimental data are needed to make a conclusion about the order of adsorption strengths for different nucleotides.

However, not only are the fitted numbers relevant *per se*, but also the model itself since it provides a language for the treatment of the phenomenon. For instance, in the same paper, Albertorio *et al.* [20] also mentions problems with the stability of adsorbed DNA because of desorption. They have introduced extra stabilization by increasing the free DNA concentration in solution. This stabilizing effect is reported but not explained or modeled. Instead, a line of naive argumentation could lead to the opposite expectations that the presence of extra free ssDNAs in solution will result in the promotion of ssDNA-ssDNA interactions, which should introduce a destabilizing effect onto the ssDNA-CNT complex because of obvious competition between the two targets for adsorption. In view of our previous studies of the osmotic stress effects onto DNA conformations [23], the reported increase in stability of bound conformations finds its explanation as arising because of the increased osmotic stress due to the increased excluded volume effects (crowding) from the free DNA added. From the physical point of view, up to Eq. (8), the model allows for both cooperative (for small nontrivial σ at $s \approx 1$) and phase transition (at $\sigma = 0$ and $s = 1$) pictures. But after we assume that chain (oligomer) sizes are of the order of Kuhn length and accept the single-sequence approximation

through Eq. (9), the resulting zipper model describes the finite-size effects of the transition. Small but nonzero values of fitted σ in Table I reflect the deviation from the ideal phase transition picture. Thus, by providing a statistical mechanical Hamiltonian to describe the DNA-CNT interaction, which is at the heart of numerous nano(bio)technologies, we contribute towards a better understanding of the principles behind the relevant biotechnologies and suggest a route to the predictable design of nanodevices.

A.B. and D.K. acknowledge support from Erasmus+ Project No. (2018-1-SI01-KA107-046966); Y.M and S.T. acknowledge financial support from Enterprise Incubator Foundation (EIF) Research Faculty 2019 Award; S.T. and D.K. acknowledge financial support from the RA MES State Committee of Science through the Research Project No. (16YR-1F046). A.B. acknowledges financial support from the Javna Agencija za Raziskovalno Dejavnost RS through Project No. (J1-1705).

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