Predicting DNA-mediated colloidal pair interactions

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Recently, Rogers *et al.* [1] proposed a method to predict the interaction between colloids coated with two kinds of single-stranded DNA (ssDNA), A and B. A key step in Ref. [1] was to estimate the average number of DNA bonds, $\langle N \rangle$, assuming Local Chemical Equilibrium (LCE) between hybridized and unhybridized sticky end concentrations:

$$\langle N \rangle = \int d\mathbf{r}\, C_A(\mathbf{r}) C_B(\mathbf{r}) \frac{\exp[-\beta \Delta G_0]}{\rho_0}$$
$$= \int d\mathbf{r}\, [C_A^0(\mathbf{r}) - C_{AB}(\mathbf{r})][C_B^0(\mathbf{r}) - C_{AB}(\mathbf{r})] \frac{\exp[-\beta \Delta G_0]}{\rho_0}. \tag{1}$$

$C_X(\mathbf{r})$ and $C_X^0(\mathbf{r})$ are the concentrations of X with or without hybridization, ΔG_0 is the solution hybridization free energy of A and B [2], and ρ_0 is $1\,\mathrm{M}$.

Here, we show that LCE predictions differ from simulation results obtained using standard statistical mechanics (SM). We consider the same model as Ref. [1]. Tethered ssDNAs are modeled as freely jointed chains of 8 segments with complementary reactive ends. Binding incurs an entropic cost $-\Delta G^{(\mathrm{cnf})}/T$ given by [3]

$$\exp[-\beta \Delta G^{(\mathrm{cnf})}(\mathbf{r}_1, \mathbf{r}_2)] = \frac{1}{\rho_0} \frac{Q_{\mathrm{HW}}(\mathbf{r}_1, \mathbf{r}_2)}{Q_{\mathrm{W}}(\mathbf{r}_1) Q_{\mathrm{W}}(\mathbf{r}_2)}. \tag{2}$$

$Q_{\mathrm{W}}(\mathbf{r})$ is the partition function of a chain tethered at $\mathbf{r}$, and $Q_{\mathrm{HW}}(\mathbf{r}_1, \mathbf{r}_2)$ is that of a hybridized chain tethered at $\mathbf{r}_1$ and $\mathbf{r}_2$. Using standard polymer simulation techniques [4], we sample DNA bindings using the weight $\exp[-\beta \Delta G^{(\mathrm{cnf})} - \beta \Delta G_0(T)]$ [3].

Fig. 1a compares $\langle N \rangle$ per unit area, as given by SM and LCE, for flat colloids covered by one type of ssDNA ($A+B$ system in [1]). LCE is quantitative only for weak binding. Larger discrepancies are expected for nonideal chains. When loops can form ($AB + AB$ system in [1]), LCE performs even worse, as evidenced by the ratio of bridges to loops (Fig. 1b).

Given $\langle N \rangle$, Ref. [1] estimated the interaction potential, V, as

$$V \approx V_{\mathrm{rep}} - k_B T \langle N \rangle, \tag{3}$$

where V_{rep} is the repulsive part of the potential. The rigorous relation between $\langle N \rangle$ and V is [3]

$$V = V_{\mathrm{rep}} + \int_{\infty}^{\Delta G_0(T)} \langle N \rangle_{\Delta G_0'}\, d\Delta G_0', \tag{4}$$

equal to Eq. 3 only if N is Poisson–distributed, which is only true at high coating densities. Fig. 1c shows that Eq. 3 and Eq. 4 differ by several $k_{\mathrm{B}}T$ at the lowest experimental temperatures.

Because LCE does not reproduce the results of a correct SM treatment of the same model system, the good agreement between the experiments and the predictions of Ref. [1] must be fortuitous. The key problems in Ref. [1] are the use of Eq. (3) and the LCE approximation. To obtain more reliable theoretical predictions of experimental results on DNA-coated colloids, we must go beyond the current level of description of DNA-mediated interactions.

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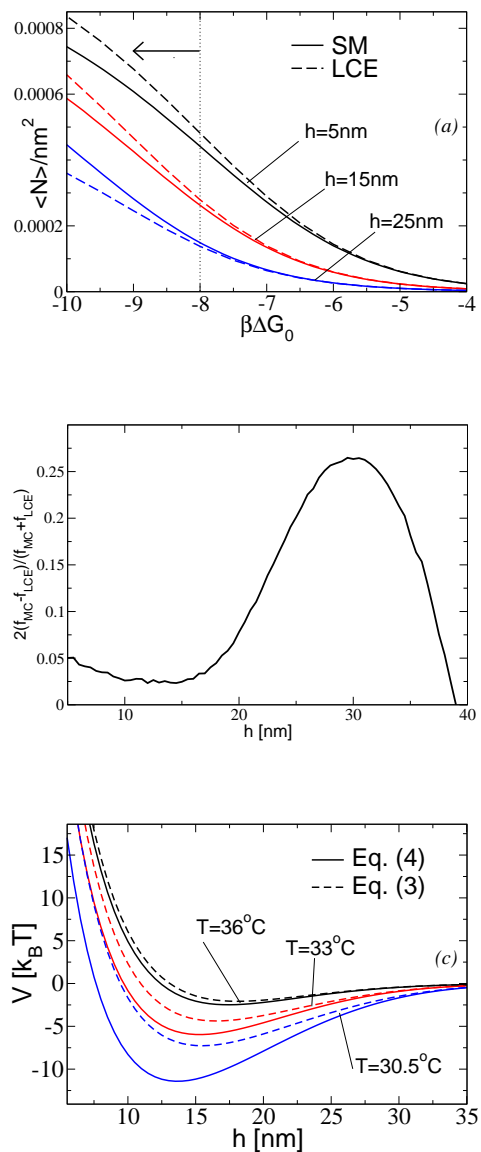
FIG. 1. *(a)* Average DNA bridges per unit area between two planes at separation h. The arrow points toward the values of ΔG_0 used in Ref. [1]. *(b)* Relative discrepancy between LCE and MC predictions of the bridges to loops ratio $f = \langle N \rangle / \langle N_{\mathrm{loop}} \rangle$, at $T = 24\,^{\circ}C$. *(c)* Colloid–colloid pair potentials for the $A + B$ system of Ref. [1] at temperature T.