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Potentials of mean force between rigid solvated polymers

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Abstract

In this letter we discusses the first application of 3-dimensional nonlocal density functional calculations to the interactions of solvated rigid polymers. The three cases considered are cylindrical polymers, bead-chain polymers, and periodic polymers. We calculate potentials of mean force, and show that polymer surface structure plays a critical role in determining the solvation energy landscape which in turn controls routes to assembly of the macromolecules.

Polymer solutions are critical to the processing of a wide range of materials (from thin films for optical applications [1] to paper [2]). They are also critical to biological function as proteins are nearly always solvated in physiological conditions [3]. Theories for polymer solutions usually begin from a solution point of view, and focus on capturing polymer physics (polymer configurations, radius of gyration, etc.) while treating the solvent of the system with a single parameter that defines the strength of polymer-solvent interactions [4].

In this letter we follow an alternate approach that treats the polymers as surfaces that generate an external field in which the fluid molecules equilibrate. Potentials of mean force between three model polymers are calculated with a novel 3-dimensional (3D) nonlocal density functional theory code. This approach is complementary to molecular simulation, and allows for detailed free energy calculations of the solvated interactions of locally rigid interacting polymers. The calculations presented here show how polymer geometry can affect the solvation energy landscape, and more specifically how assembly of polymer bundles can occur via minor adjustments in the alignment of two polymer strands with respect to one another.

The statistical mechanics behind our approach has been detailed elsewhere [6]. Briefly, the semi-grand ensemble for a solution of N macromolecules in a solvent with known chemical potential, μ at a temperature, T and volume, V is

$$Z_{NV\mu T} = \int_V d\mathrm{R}^N e^{-\beta U_N(\mathrm{R}^N)} \times \left\{ \sum_{n=0}^{\infty} \frac{z^n}{n!} \int_V d\mathrm{r}^n e^{-\beta U_n(\mathrm{R}^N,\mathrm{r}^n)} \right\} \tag{1}$$

where $z = e^{\beta\mu}/\Lambda^3$ is the solvent activity, $\beta = 1/k_B T$, k_B is the Boltzmann constant, and Λ is the DeBroglie wavelength. Integrals are taken over all possible configurations of the N surfaces (denoted R^N) and the n solvent molecules (denoted r^n).

The potential energy of direct surface-surface interactions is given by U_N while the energy of both solvent-solvent and solvent-surface interactions are summed in U_n. Identifying the inner integral in Eq.1 as the grand partition function, $\Xi_{\mu VT}$ of a fluid in an external field of N fixed surfaces, the mixture partition function may then be written in terms of the grand

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potential,

$$\Omega(\mathrm{R}^N;\mu,T) = -\beta^{-1}\ln\Xi_{\mu VT}. \tag{2}$$

Substituting for $\Xi_{\mu VT}$, Eq.1 becomes

$$Z_{NV\mu T} = \int_V d\mathrm{R}^N e^{-\beta U_N(\mathrm{R}^N)} e^{-\beta\Omega(\mathrm{R}^N;\mu,T)}. \tag{3}$$

Taking two hard rigid macromolecules ($U_N = \infty$ if overlapping, otherwise, $U_N = 0$), potential of mean force (PMF) acting between the macromolecules is

$$W(\mathrm{R}) = \Omega(R;\mu,T) - \Omega(\infty;\mu,T) \tag{4}$$

in the limit of two surfaces separated by R in an otherwise infinitely dilute solution of the macromolecules (ie. $\rho_M \to 0$).

Providing that the Gibbs dividing surface is chosen to be identical at all surface separations, the PMF may also be written in terms of the surface free energy, $W(\mathrm{R}) = \Omega^s(R;\mu,T) - \Omega^s(\infty;\mu,T)$ where $\Omega^s = \Omega(R;\{\rho(\mathbf{r})\},T) - \Omega(R;\{\rho_b\},T)$, ρ_b is the bulk fluid density associated with the known μ, and $\rho(\mathbf{r})$ is the equilibrium nonuniform density distribution of fluid particles in the external field of the N macromolecules.

The surface free energy is directly related to the solvent mediated (or solvation) force acting on the polymer strands. This solvation force may be calculated from the sum rule [7]

$$f = -\frac{\partial\Omega^s}{\partial R} = \int \rho(\mathbf{r_s}) n_x d\mathbf{r_s} \tag{5}$$

where $\int d\mathbf{r_s}$ indicates a integral over the surface of the macromolecule, and $\mathbf{n}$ is the unit normal to the surface.

Surface free energies can be calculated with molecular simulation or nonlocal density functional theory (DFT). DFT is based on the functional minimization of the grand free energy, $\Omega[\rho(\mathbf{r})]$ with respect to the density distributions, $\rho(\mathbf{r})$ at constant temperature, T, and fluid chemical potential, μ.

$$\left(\frac{\delta\Omega}{\delta\rho(\mathbf{r})}\right)_{T,\mu} = 0. \tag{6}$$

The particular free energy functional, $\Omega[\rho(\mathbf{r})]$ we use was developed by Rosenfeld [8]. While most DFT calculations have considered geometries with considerable symmetry (slit-pores, cylindrical pores, spherical cavities etc); the polymer calculations here will require a full 3D DFT solution. Götzelmann et.al. have shown that when an accurate equation of state is known for the macromolecule-solvent mixture PMFs can be found by taking the explicit limit of $\rho_M \rightarrow 0$ [9]. While their approach shows great promise for certain geometries (e.g. spherical macromolecules near flat surfaces), it cannot be easily extended to the polymer-solvent mixtures considered here.

Our 3-dimensional numerical implementation is based on a Newton's method solve of the system of equations, and convergence is usually obtained in less than 20 Newton iterations. Each of the 3D polymer solutions presented here was obtained in approximately 3 minutes of CPU time on 50 processors of the ASCI-Red (Intel pentium 333 MHz chips) computer at Sandia National Laboratories. To the best of our knowledge, these are the first results from 3D nonlocal DFT calculations to be discussed in the literature. The algorithms behind our computational approach are detailed elsewhere [13] and have been applied to the wetting of chemically heterogeneous surfaces [14].

We restrict the current discussion to hard sphere fluids in contact with hard rigid polymers. Other physical effects (e.g. van der Waals, polarization, or Coulomb, forces) may be critical in many systems; however, our calculations demonstrate the expected magnitude of solvent packing effects in forces between solvated polymers.

While the stiffness of the polymer models discussed here is not a realistic representation of all polymers, there are some important exceptions. One example is deoxyribonucleic acid (DNA). The double helix of the DNA causes this important polymer to be quite rigid, and so DNA is often treated as a rigid polymer in molecular investigations [10–12]. In addition, on a small enough length scale, all polymers are rigid [4]. The question then becomes whether solvation forces in question are large for the appropriate length-scale of a particular polymer.

The polymer models discussed here include cylindrical, bead-chain, and periodic polymers. Taking the z-axis down the long axis of a polymer chain, the cylindrical polymer is described by $R_p(z) = 1.5\sigma$ where R_p is the radius of the polymer chain and σ is the diameter of the solvent particle. The bead chain polymer is composed of spheres with radius $R_p = 1.5\sigma$ where the centers of the spheres along the z-axis are separated by 3σ. The periodic polymer has a radius, $R_p(z) = r_o + Acos(2\pi z/\lambda)$ where the reference radius, $r_o = 0.75\sigma$, the amplitude, $A = 0.75\sigma$, and the period, $\lambda = 3\sigma$.

While all three polymer models exhibit surface curvature perpendicular to the long axis of the polymer, the bead-chain and periodic polymers also exhibit structure parallel to the polymer axes. Thus, we have calculated potentials of mean force as a function of both relative alignment and surface separation for these two cases.

Potentials of mean force for the three solvated polymer models are shown in Fig.1. In all cases, solvent packing leads to oscillatory potentials as a function of center-center separation. The magnitude of the oscillations is largest for the parallel cylinders in Fig.1A where densities are uniform along the long axis of the polymer strands. However, in all cases, the free energy peaks are substantial in comparison with kT. Consider the peak at $R/\sigma = 3.6$ in the case of the aligned bead-chain polymer. It's magnitude per unit length (in σ units) is $\approx 0.25kT$. One bead of the polymer chain has a length (diameter) of 3σ, and so, even 5 interacting segments will experience an energy of $\approx 3.75kT$.

The bead-chain case in Fig.1B demonstrates that the details of the surface structure of the polymer play an important role in assembly of the strands. Consider the energy barriers experienced by two polymer strands as they come together from infinite separation. If the strands remain in a perfectly aligned state, they will need to overcome the substantial solvation barriers mentioned above. However by shifting their orientations to 180° out of phase at the appropriate separations, the solvation barriers can be avoided altogether since the maxima in the aligned state very nearly correspond to the minima for the unaligned state. As a corallary, the forces experienced by the bead-chain polymers will be always attractive from infinite separation to contact provided that the polymers can freely change their relative orientation. The only way for the cylindrical polymers to avoid the large solvation barriers would be for the cylinders to rotate away from the parallel position. Such a rotation would be kinetically unfavorable in comparison with the small adjustments needed when surface structure is present.

While the surface structure on the bead-chain polymers provides a low-energy route to assembly by avoiding solvation energy barriers, this is not the case for the periodic polymer as shown in Fig.1C. Here, the unaligned and aligned cases have minima and maxima at similar separations. Nevertheless, the solvation energy landscape is significantly affected by the surface structure on the periodic polymers. Specifically, the period of solvation oscillations increases from 1σ (Fig.1A,B) to approximately 1.5σ (Fig.1C). In addition, the global free energy minimum is now found at $R/\sigma = 2.75$ where there is a layer of fluid between the polymer strands.

The solvated assembly of the periodic polymers is in contrast to both cylindrical and bead-chain cases (Fig.1A,B) where the global free energy minimum is found at contact. In these two cases, osmotic exclusion of the hard-sphere solvent results in the strong attractive depletion forces [9]. Thus while solutions composed of any of the three polymers would self-assemble in to tightly ordered arrays, the periodic polymer assembly will be the most highly solvated. Predicting solvated assembly is critical to studying protein crystals where the crystals may contain 50% solvent by volume [15,16].

For all of the cases in Fig.1 except the unaligned bead-chain polymer, the potential curves are drawn to the point of closest approach of the polymer strands. However, it was not possible to obtain solutions for the case of the unaligned bead-chain polymer when $R/\sigma \leq 3.5$. The numerical difficulty is due to the interaction of multiple steep density peaks that arise in the annuli around the points where two beads on one chain meet. An example of the density distribution in one slice of the 3D domain at $R/\sigma = 3.75$ is shown in Fig.2. The steepness of these peaks indicate that the fluid particles in these regions are effectively *bound* to the polymer strands although there are no chemical bonds present.

In this letter we have presented the first results from 3D-DFT calculations of interacting solvated polymers. We have shown how surface structure is linked to molecular recognition via the solvation energy landscape, and how both bound fluid molecules and solvated assemblies of macromolecules can arise in solvated polymer systems. This approach may be used to investigate complex phenomena such as molecular recognition, protein interactions, and physically bound solvent molecules on macromolecules.

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FIGURES

FIG. 1. The potential of mean force as a function of the center-center separation, R of two cylindrical (A), bead-chain (B), and periodic polymers (C). In B and C, the solid lines show the cases where the centers of the polymers are perfectly aligned while the dashed lines show cases where the polymers are 180^o out of phase as shown in the sketches. The bulk density for all cases was $\rho_b\sigma^3 = 0.63$.

FIG. 2. The density distribution as a function of position (x, y in units of σ) in a slice of constant z where two beads on the left chain come together. The white regions include both the polymer volume and solvent exclusion zones due to the hard interactions between the polymer and solvent particles. The two chains are unaligned (see the sketch corresponding to dashed lines in Fig.1B). The maximum densities in the figure are $\rho\sigma^3 = 10.7$ found at $x/\sigma = 6.375$, $y/\sigma = 4.5, 6.5$. The density maxima at the center between the surfaces is, $\rho\sigma^3 = 3.7$ and is located at $x/\sigma = 7.375$,$y/\sigma = 5.5$,$z/\sigma = 0.5$.

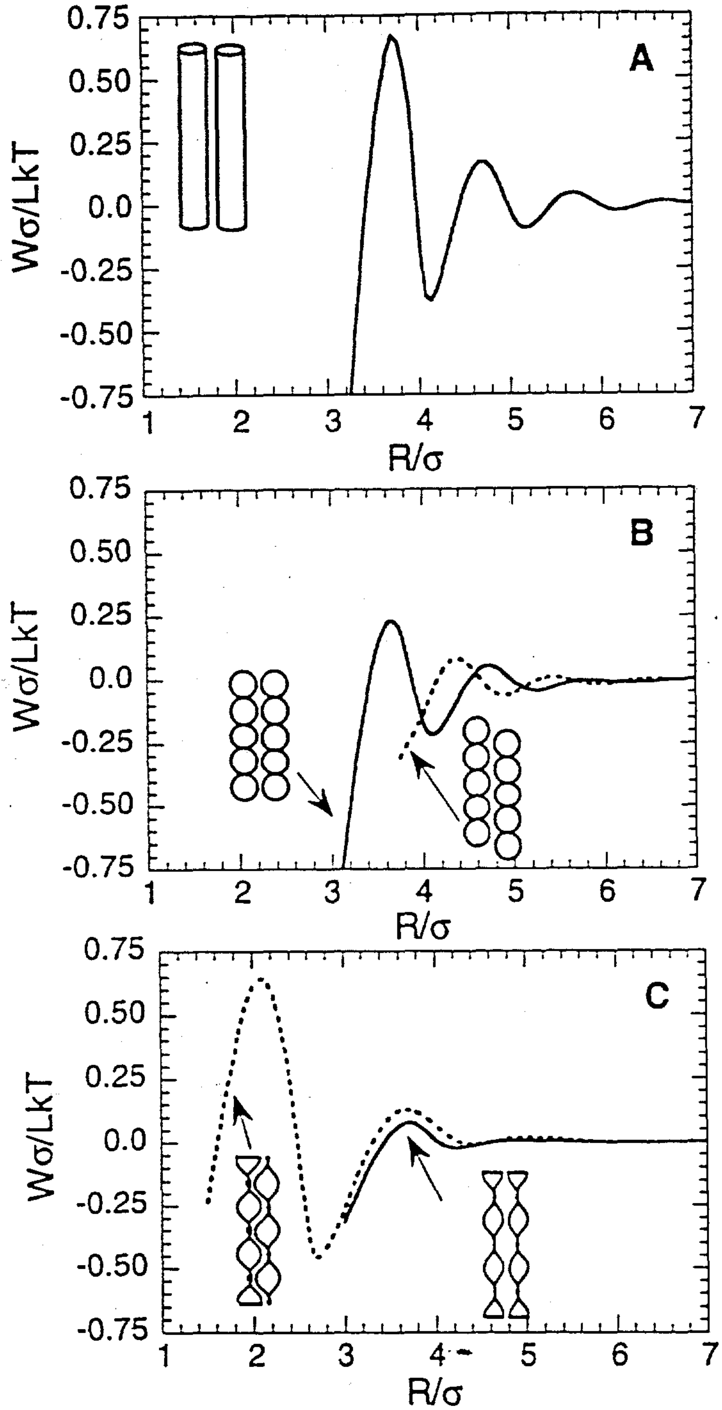

FIG.1

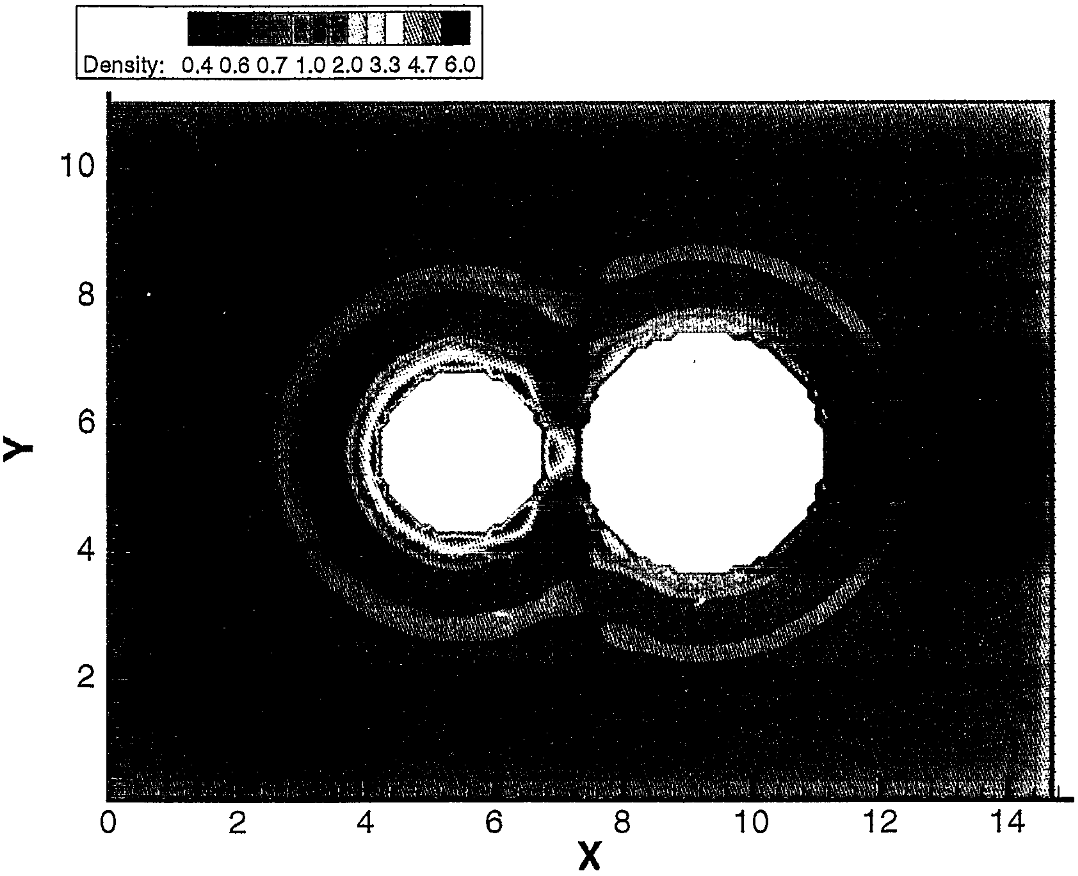

FIG.2