

Solvent effects on polymer conformation: Density-functional-theory approach

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Conformation properties of a polymer in a solvent are studied based on density-functional theory. Instead of integrating out the solvent density field in order to reduce the whole problem to that of one polymer with medium-induced effective interactions, we consider the solvent density profile and the polymer conformation self-consistently on equal footing. A two-dimensional model system is considered for which some numerical results are shown, with emphasis placed on solvents effects. [S1063-651X(97)09809-7]

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I. INTRODUCTION

The conformation of molecules or polymers in solutions has been one of the fundamental problems in physical chemistry and statistical mechanics [1]. It has gathered much attention, especially in connection with protein folding from the denatured to the nutured state [2]. Here the conformation with minimum (free) energy is searched numerically for various models, which can be roughly classified to a lattice and a continuous (off-lattice) ones.

Recently Iori, Marinari, and Parisi (IMP) proposed an off-lattice chain model for protein folding [3], whose energy E is given by the sum of the interaction between all the pairs of the different sites of the chain:

$$E = \sum_{i < j} \{ \delta_{i+1,j} r_{i,j}^2 + [R/r_{i,j}^{12} - A/r_{i,j}^6] + \eta_{i,j}/r_{i,j}^6 \}, \quad (1)$$

with $r_{i,j}$ the distance between sites i and j . The first term on the right-hand side (rhs) of Eq. (1) represents bonding of neighboring pairs, and the second one is the Lennard-Jones-type interaction. Reflecting a sequence of different amino acids, the intersite potential is assumed to have a quenched random part as represented by the third term on the rhs of Eq. (1). Here $\eta_{i,j}$ is the random number with zero average and finite standard deviation. Later a two-dimensional IMP model was studied in Ref. [4]. Extensive numerical calculations have revealed that the random part of the interaction plays an important role in the transition from a globular to a frozen (folded) state [3,4]. It is noted that the IMP model reduces to one for a homopolymer if the random part is neglected ($\eta_{i,j}=0$), and, second, that solvent effects are not explicitly taken into account in the IMP model.

In this paper we study solvent effects on polymer conformation with the aid of the density-functional theory (DFT) [5] and its dynamic extension [6]. Instead of integrating out over solvent density fluctuations to obtain an effective one-polymer problem, a strategy that is often employed in theoretical studies of conformation [7], we treat polymer conformation and the solvent density fluctuations on equal footing. This approach enables us to discuss density fluctuations induced by polymer conformation explicitly (see Sec. IV).

The remainder of this paper is outlined as follows. In Sec. II, within the framework of the DFT [5], we model our system, which consists of a (hetero)polymer and a solvent. In Sec. III, the dynamics of the system is formulated based on a dynamic DFT [6]. Section IV is devoted to numerical calculations for polymer conformation in a two-dimensional system. Here we integrate the Langevin equation for polymer sites and solve the hypernetted chain (HNC)-like integral equation for solvent density fluctuations iteratively. Section V contains some remarks.

II. DENSITY-FUNCTIONAL APPROACH TO POLYMER IN SOLVENT

We consider a system in which a polymer with P sites is put in a solvent, which we assume for simplicity to be a one-component simple liquid. Since the DFT for molecular systems is available [8,9], a solvent consisting of molecules gives rise to no essential difficulties. Within the framework of the DFT [5], the solvent is characterized by its free-energy functional

$$F_0[n_0] = (k_B T) \int d\mathbf{r} n_0(\mathbf{r}) \{ \ln[n_0(\mathbf{r}) \Lambda_0^3] - 1 \} + \frac{1}{2} \int d\mathbf{r} \int d\mathbf{r}' \delta n_0(\mathbf{r}) \phi_{0,0}^{\text{eff}}(|\mathbf{r}-\mathbf{r}'|) \delta n_0(\mathbf{r}'), \quad (2)$$

where $n_0(\mathbf{r})$ denotes the density field of the solvent, $k_B T$ the temperature in energy units, and Λ_0 the de Broglie thermal wavelength, and the effective potential $\phi_{0,0}^{\text{eff}}(r)$ between two solvent atoms is expressed in terms of the direct correlation function $c_{0,0}(r)$ of the pure solvent as [5]

$$\phi_{0,0}^{\text{eff}}(r) = -k_B T c_{0,0}(r). \quad (3)$$

We note that in Eq. (2) the excess part of F_0 is expanded up to second order in the density fluctuations $\delta n_0(\mathbf{r}) \equiv n_0(\mathbf{r}) - n_0$, with n_0 the equilibrium uniform density [5]. From the density functional (2) we can derive, with recourse to the Percus idea of regarding the one-body distribution around a fixed atom as the radial distribution function $g(r)$ [8,9], the HNC equation

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$$\ln g_{0,0}(r) = n_0 \int d\mathbf{r}' c_{0,0}(|\mathbf{r}-\mathbf{r}'|) [g_{0,0}(r') - 1] - \phi_{0,0}(r)/(k_B T), \quad (4)$$

where $\phi_{0,0}(r)$ is the (bare) interaction potential between two solvent atoms, and $c_{0,0}(r)$ is defined with the Ornstein-Zernike equation

$$g_{0,0}(r) - 1 = c_{0,0}(r) + n_0 \int d\mathbf{r}' c_{0,0}(|\mathbf{r}-\mathbf{r}'|) [g_{0,0}(r') - 1]. \quad (5)$$

Now we introduce a polymer to our model, whose free-energy functional is assumed to be of the form

$$F_P[\{n_i\}] = (k_B T) \sum_1^P \int d\mathbf{r} n_i(\mathbf{r}) \{ \ln [n_i(\mathbf{r}) \Lambda_i^3] - 1 \} + \frac{1}{2} \sum_{i,j(j \neq i)} \int d\mathbf{r} \int d\mathbf{r}' n_i(\mathbf{r}) \phi_{i,j}^{\text{eff}}(|\mathbf{r}-\mathbf{r}'|) n_j(\mathbf{r}'), \quad (6)$$

where $n_i(\mathbf{r})$ and Λ_i are the density and the de Broglie thermal wavelength for the site i . Finally the polymer-solvent interaction is represented by the free energy

$$F_{0,P} = \sum_1^P \int d\mathbf{r} \int d\mathbf{r}' n_i(\mathbf{r}') \phi_{0,i}^{\text{eff}}(|\mathbf{r}-\mathbf{r}'|) n_0(\mathbf{r}). \quad (7)$$

From the above we consider a polymer-solvent system with the total free energy

$$F = F_0 + F_{0,P} + F_P. \quad (8)$$

The details of the model are further specified when we perform numerical calculations in Sec. IV.

III. POLYMER-SOLVENT DYNAMICS

A. Formulation based on time-dependent DFT

From time-dependent DFT as developed in Ref. [6], the Langevin diffusion equation for the density field $n_i(\mathbf{r}, t)$ ($i=0, 1, \dots, P$) is

$$\partial n_i(\mathbf{r}, t) / \partial t = D_i \nabla \cdot [n_i(\mathbf{r}, t) \nabla \delta(F/k_B T) / \delta n_i(\mathbf{r}, t)] - \nabla \cdot \mathbf{J}_{R,i}, \quad (9)$$

where $\mathbf{J}_{R,i}$ and D_i denote the random current and the diffusion constant of the species i , respectively. The random current was shown to satisfy the fluctuation-dissipation relation

$$\langle \nabla \cdot \mathbf{J}_{R,i}(\mathbf{r}, t) \nabla \cdot \mathbf{J}_{R,j}(\mathbf{r}', t') \rangle = 2 \delta_{i,j} D_i (\nabla \cdot \nabla') n_i(\mathbf{r}, t) \delta(\mathbf{r}-\mathbf{r}') \delta(t-t'). \quad (10)$$

For later convenience, we explicitly write the Langevin diffusion equation for the solvent, Eq. (11), and the site i ($i=1, \dots, P$), Eq. (12), with use of Eq. (9) and the free-energy functional (8) for our model:

$$\begin{aligned} \partial n_0(\mathbf{r}, t) / \partial t = & D_0 \nabla \cdot \left[\nabla n_0(\mathbf{r}, t) - n_0(\mathbf{r}, t) \nabla \int d\mathbf{r}' \right. \\ & \times c_{0,0}(|\mathbf{r}-\mathbf{r}'|) \delta n_0(\mathbf{r}', t) + n_0(\mathbf{r}, t) \sum_{i=1}^P \nabla \int d\mathbf{r}' \\ & \left. \times \phi_{0,i}^{\text{eff}}(|\mathbf{r}-\mathbf{r}'|) n_i(\mathbf{r}', t) / (k_B T) \right] - \nabla \cdot \mathbf{J}_{R,0}, \end{aligned} \quad (11)$$

$$\begin{aligned} \partial n_i(\mathbf{r}, t) / \partial t = & D_i \nabla \cdot \left[\nabla n_i(\mathbf{r}, t) + n_i(\mathbf{r}, t) \nabla \int d\mathbf{r}' \right. \\ & \times \phi_{0,i}^{\text{eff}}(|\mathbf{r}-\mathbf{r}'|) \delta n_0(\mathbf{r}', t) / (k_B T) \\ & + n_i(\mathbf{r}, t) \sum_{j \neq i, 1}^P \nabla \int d\mathbf{r}' \\ & \left. \times \phi_{j,i}^{\text{eff}}(|\mathbf{r}-\mathbf{r}'|) n_j(\mathbf{r}', t) / (k_B T) \right] - \nabla \cdot \mathbf{J}_{R,i}. \end{aligned} \quad (12)$$

We note that the variational equation $\delta F / \delta n_i(\mathbf{r}) = \mu_i$ ($i=0, 1, \dots, P$) to determine the equilibrium density profile is equivalent to the stationary condition $\partial n_i(\mathbf{r}, t) / \partial t = 0$ in Eq. (9) without the random current. If we retain the random current however, the equilibrium distribution functional $P_{\text{eq}}[\{n_i(\mathbf{r})\}]$ can be shown to be proportional to $\exp[-F/(k_B T)]$ [6].

The set of equations (11) and (12) is rather complicated for studying polymer conformation, since one has to deal with the density fields $n_i(\mathbf{r}, t)$, $i=1, \dots, P$ instead of simple position variables of polymer sites [2,3,4]. To facilitate discussions on the conformation problem, we introduce the following localization approximation in which we assume that

$$n_i(\mathbf{r}, t) = \delta(\mathbf{r}-\mathbf{r}_i(t)), \quad (13)$$

where $\mathbf{r}_i(t)$, $i=1, \dots, P$ denotes position of the site i at time t . Under the approximation we have, immediately from Eq. (11),

$$\begin{aligned} \partial n_0(\mathbf{r}, t) / \partial t = & D_0 \nabla \cdot \left[\nabla n_0(\mathbf{r}, t) - n_0(\mathbf{r}, t) \nabla \int d\mathbf{r}' \right. \\ & \times c_{0,0}(|\mathbf{r}-\mathbf{r}'|) \delta n_0(\mathbf{r}', t) \\ & + n_0(\mathbf{r}, t) \sum_{i=1}^P \nabla \phi_{0,i}^{\text{eff}}(|\mathbf{r}-\mathbf{r}_i(t)|) / (k_B T) \left. \right] \\ & - \nabla \cdot \mathbf{J}_{R,0}. \end{aligned} \quad (14)$$

On the other hand, the equation of motion for $\mathbf{r}_i(t)$ is derived by first multiplying \mathbf{r} on both sides of Eq. (12) and integrating the resulting equation over \mathbf{r} . Thus we have

$$d\mathbf{r}_i(t) / dt = D_i \nabla_i \left[- \int d\mathbf{r} \phi_{0,i}^{\text{eff}}(|\mathbf{r}-\mathbf{r}_i(t)|) \delta n_0(\mathbf{r}, t) / (k_B T) \right]$$

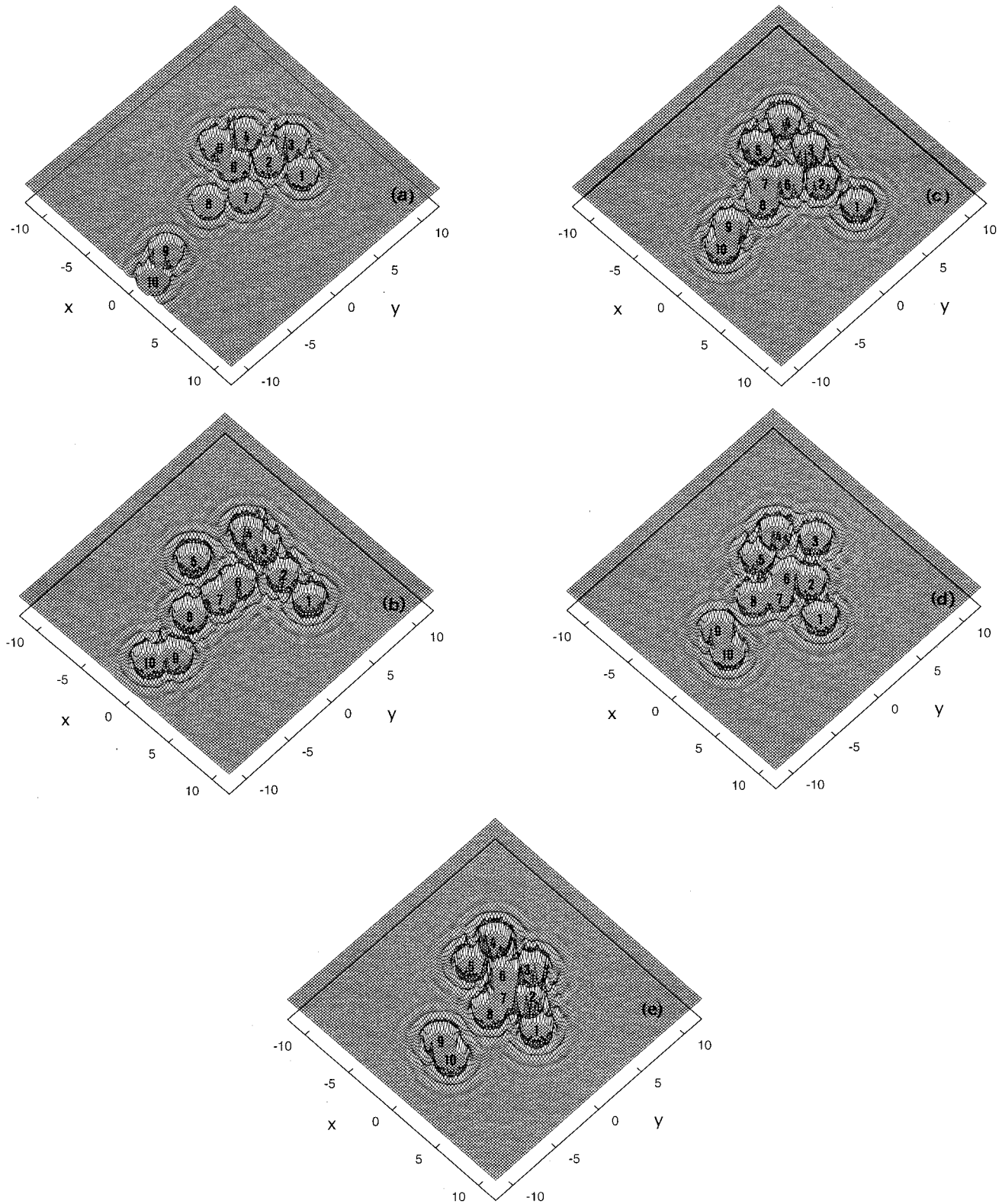


FIG. 1. Conformation $C(t)$ and the density profile $n_0(\mathbf{r}, t)$ for a heteropolymer with five hydrophilic ($i=1-5$) and five hydrophobic ($i=6-10$) sites at (a) $t=0$, (b) 1000, (c) 2000, (d) 3000, and (e) 4000. X and Y are in unit of σ_0 in Eq. (20).

$$-\sum_{j \neq i, 1}^P \phi_{j,i}^{\text{eff}}(|\mathbf{r}_i(t) - \mathbf{r}_j(t)|)/(k_B T) \Big] + \mathbf{f}_i(t). \quad (15)$$

$$\mathbf{f}_i(t) \equiv \int d\mathbf{r} \mathbf{J}_{R,i}(\mathbf{r}, t) \quad (16)$$

The random force defined by

is easily shown from Eq. (10) to satisfy the fluctuation-dissipation relation

$$\langle \mathbf{f}_i(t) \mathbf{f}_j(t') \rangle = 2D_i \delta_{i,j} \delta(t-t') I, \quad (17)$$

where I is the $d \times d$ unit matrix with d the dimension of the system.

Thus we describe the solvent in terms of the density field whose dynamics is governed by the Langevin-diffusion equation (14), while polymer conformation is characterized in terms of the site position, which evolves in time according to the Langevin equation (15). It is easily confirmed from the Fokker-Planck equation corresponding to Eqs. (14) and (15) that the equilibrium distribution is given by

$$P_{\text{eq}}[n_0(\mathbf{r}), \{\mathbf{r}_i\}] = C \exp \left[\left\{ -F_0 - \sum_{i < j}^P \phi_{i,j}^{\text{eff}}(|\mathbf{r}_i - \mathbf{r}_j|) - \sum_{i=1}^P \int d\mathbf{r} \phi_{0,i}^{\text{eff}}(|\mathbf{r}_i - \mathbf{r}|) n_0(\mathbf{r}) \right\} / \times (k_B T) \right], \quad (18)$$

with C a normalization constant. A simpler way to confirm Eq. (18) is to apply Eq. (13) to the equilibrium distribution functional $P_{\text{eq}}[\{n_i(\mathbf{r})\}] \propto \exp[-F/k_B T]$, which appeared under the line of Eq. (12).

We can sample the distribution (18) if we could solve the coupled equations (14) and (15) for long time. However it is noticed that to solve the Langevin diffusion equation is generally very difficult since the density field $n_0(\mathbf{r}, t)$ erroneously happens to take negative values at some place \mathbf{r} where the density itself can become physically very small [10]. In our problem at hand it occurs due to (strong) repulsion near each polymer site. So in Sec. III B we take another but closely related path to study the conformation problem.

B. Variational equation for solvent density and Brownian dynamics for polymer

To avoid explicitly solving the Langevin-diffusion equation (14), we consider the situation where the conformation $\{\mathbf{r}_i(t)\}$ is held fixed, and the solvent adjusts itself to the potential field produced by the polymer. The equilibrium density profile under the influence of the (fixed) solute polymer, to be denoted as $n_{\text{eq}}(\mathbf{r}|\{\mathbf{r}_i(t)\})$, is obtained from the variational principle $\delta \ln P_{\text{eq}} / \delta n_0(\mathbf{r}) = \mu$ (a constant), with P_{eq} given by Eq. (18). More explicitly we obtain

$$n_{\text{eq}}(\mathbf{r}|\{\mathbf{r}_i(t)\}) = n_0 \exp \left[\int d\mathbf{r}' c_{0,0}(|\mathbf{r} - \mathbf{r}'|) \delta n_{\text{eq}}(\mathbf{r}'|\{\mathbf{r}_i(t)\}) - \sum_1^P \phi_{0,i}^{\text{eff}}(|\mathbf{r} - \mathbf{r}_i(t)|) / (k_B T) \right]. \quad (19)$$

This integral equation is similar in structure to the HNC equation (4).

As for the dynamics of polymer sites, we employ Brownian dynamics [Eq. (15)], while the solvent density is determined from Eq. (19). What we have done *actually* in numerical calculations is an iteration (up to 4000 times) of the following, what we call the *hybrid*, step. That is, first to

integrate the Langevin equation (15) for some time τ_P with the (predetermined) solvent density field kept fixed (time-independent) and then to solve the HNC-like equation (19) to obtain the new solvent density with polymer sites held fixed at the final conformation of Brownian dynamics just mentioned above (for initial conditions, see Sec. IV).

IV. NUMERICAL RESULTS FOR CONFORMATION AND SOLVENT DENSITY PROFILE

To be concrete, our solvent is taken to be the soft-core liquid

$$\phi_{0,0}(r) = \epsilon_0 (\sigma_0/r)^{12}, \quad (20)$$

and after IMP [3], Eq. (1), $\phi_{i,j}^{\text{eff}}(r)$ is chosen to be

$$\phi_{i,j}^{\text{eff}}(r) = \epsilon_P [\delta_{i+1,j} (K/2) r^2 / \sigma_P^2 + \{(\sigma_P/r)^{12} - A(\sigma_P/r)^6\}]. \quad (21)$$

Interaction (21) consists of two parts, one for bonding and the other the Lennard-Jones-like potential. In the case $A=0$, we have no mutual long-range attraction between sites and, consequently, our polymer would not collapse to a globular state if put in vacuum (without the solvent) [1,11]. Since our main concern is around solvent effects on polymer conformation, we will consider only the case $A=0$ in this paper. The solvent-polymer interaction $\phi_{0,i}^{\text{eff}}(r)$ is assumed to be

$$\phi_{0,i}^{\text{eff}}(r) = \epsilon_{0,P} [(\sigma_{0,P}/r)^{12} - (\sigma_{0,P}/r)^6 B_i]. \quad (22)$$

We set ϵ_P and $\epsilon_{0,P}$ equal to ϵ_0 . As to the size of the polymer sites we take $\sigma_P = 2\sigma_0$ and $\sigma_{0,P} = (\sigma_0 + \sigma_P)/2 = 1.5\sigma_0$. K in Eq. (21) is set to be 1, after the choice in Ref. [4]. Heterogeneity in our model comes from the site-dependent constant B_i . When B_i is positive (negative), site i may be called hydrophilic (hydrophobic) [2]. Although B_i could be a random variable to express the quenched randomness, as for $\eta_{i,j}$ in Eq. (1), we consider a definite arrangement of ± 1 for B_i (see below).

In view of the heavy computational task due to the inclusion of the solvent density profile $n_0(\mathbf{r}, t)$, and for the sake of the simplicity with which one can analyze polymer conformations visually, we consider a two-dimensional (2D) system [4]. Thermodynamic state of a 2D soft-disk system is characterized by the nondimensional constant $\Gamma \equiv n_0 \sigma^2 (\epsilon_0/k_B T)^{1/6} \equiv \bar{n}_0 \bar{T}^{-1/6}$ and it freezes around $\Gamma = 0.96$ [12]. We take rather dense solvent with $\Gamma = 0.8$ for our experiments.

As units of length and energy we choose σ_0 and ϵ_0 [see Eq. (20)], respectively. Unit of time τ , which must be specified when one solves the Langevin equation (15), is taken to be $\tau = \sigma_0^2/D$, where the diffusion constant D_i is assumed to be site independent and equal to D . The time mesh Δt for the difference scheme to solve Eq. (15) is set to be $10^{-5}\tau$. The τ_P for one hybrid step is chosen to be $100\Delta t$ after some trial runs, which showed that the numerical results were not sensitive to τ_P of the order of a few tens to one hundred Δt .

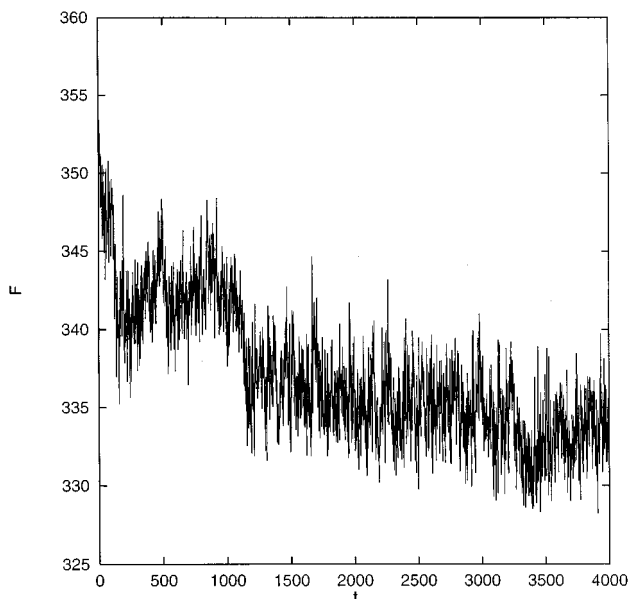


FIG. 2. The free energy $F(t)$ in unit of ϵ_0 in Eq. (20). The nondimensional time t denotes the number of hybrid steps.

Naturally if τ_p is chosen too small (of the order of a few Δt), the conformation hardly changes by one hybrid step, and it requires much more computation.

In numerically iterating the hybrid step, which is explained at the end of Sec. III, and is counted hereafter by t , we must first prepare the initial condition for polymer conformation $C(t=0) \equiv \{\mathbf{r}_i(t=0)\}$ and the density profile $n_0(\mathbf{r}, t=0)$. $C(t=0)$ is chosen to be the last conformation produced by simply solving Eq. (15) with no diffusion term (or, equivalently, for the uniform solvent density field) for some long time (e.g., for several τ) starting from a linear conformation. $n_0(\mathbf{r}, t=0)$ is obtained as the solution to Eq. (19) with $C(t=0)$ for $\mathbf{r}_i(t=0)$. Here in solving the integral equation (19) we employ the mesh $dx/\sigma_0=0.2$ with the cell size $25\sigma_0 \times 25\sigma_0$. In passing we note that we always put the center of gravitation of the polymer at the middle of the cell when we solve Eq. (19), and the cell turns out to be large enough so that the density field decays to its uniform value n_0 at the boundary of the cell (see Figs. 1 and 3 below).

In Fig. 1 we show a series of polymer conformation $C(t)$ and the density profile $n_0(\mathbf{r}, t)$ for $t =$ (a) 0, (b) 1000, (c) 2000, (d) 3000, and (e) 4000, at $\bar{T}=1.0$ and $\bar{n}_0=0.8$ starting from an arbitrarily produced (see above) initial condition $C(t=0)$. Sites 1–5 are hydrophilic ($B_i=1$) and the others hydrophobic ($B_i=-1$). In the first 1000 steps the group consisting of hydrophilic (hydrophobic) sites is seen to expand (contract), and in the remaining time the hydrophobic sites (6, 7, and 8) are gradually swallowed by the hydrophilic sites 1–5. This is one of the most important solvent effects, which contributes to the compaction of a heteropolymer, especially a protein [2]. Sites 9 and 10 are observed to form a cluster, which is expected to be a metastable state with long lifetime. The density profile is expressed here as the height in the direction perpendicular to the x - y plane. We note that detailed values $n_0(\mathbf{r}, t)$ taken by the density field are not

shown to avoid complications in the figures. We observe a shell structure around polymer sites, which is a characteristic of high-density liquids. If we look at, e.g., Fig. 1(e), we notice that the solvent exists or intrudes in between the hydrophilic sites 1–5 with the maximum density about $\bar{n}_0(\mathbf{r}, t) \approx 4$ around the middle of sites 3 and 4 (not readable from the figure) but for the clusters of sites 6, 7, or 8 or 9 or 10 the solvent is repelled by the clusters in conformity to the nature of the site-solvent interaction (22). In Fig. 2 is depicted the variation of the free energy of system (8) with time t , which is actually reduced to $-k_B T \ln P_{eq}$, Eq. (18), under the localization approximation (13). Although we observe overall decrease of the free energy in time, it does not monotonically decrease since we allow for the random force in Eq. (15) [6].

In Fig. 3 we show results for $C(t)$ and the density profile $n_0(\mathbf{r}, t)$ for (a) $t=1000$, (b) 2000, (c) 3000, and (d) 4000, in the case when sites 1–5 are hydrophobic ($B_i=-1$) and the others hydrophilic ($B_i=1$). The initial conformation $C(t=0)$ and T and n_0 are the same as the ones in Fig. 1(a), but the density profile is of course different from that in Fig. 1(a). We observe as before that the early response (up to $t=1000$) of the polymer to the solvent is characterized by the general tendency to shrinkage (swelling) of the group of hydrophobic (hydrophilic) sites. Site 7 is seen to move toward the cluster of the hydrophobic sites 1 and 2, and the cluster of sites 1, 2, and 7 seems to be rather stable in the presence of the solvent. Similarly two hydrophobic sites (4 and 5) and one hydrophilic site (6) are seen to form a rather stable cluster. From this observation together with the encircling by the hydrophilic sites of the hydrophobic sites as shown in Fig. 1, one may broadly note that the main effect of the solvent is to make polymer conformation compact by producing various kinds of clusters. However, a more elaborate numerical study seems necessary before we can draw conclusions definitely.

Before leaving this section we comment on our experiment in which we lower temperature from $\bar{T}=1.0$ to 0.5 to see possible temperature effects. Since the intersite potential (21) has no mutual attraction ($A=0$), we observed no conspicuous change, such as the rapid collapse phenomenon [11], compared with the results for $\bar{T}=1.0$.

V. SOME REMARKS

In this paper we proposed an (semidynamical) approach for studying solvent effects on polymer conformation based on a dynamic DFT [6], and applied it to a simple 2D heteropolymer problem. At present our program enables us to deal with a polymer with up to $P=15$ sites. Of course this depends on the density or more precisely Γ of the solvent. When Γ is large, the density profile $\delta n_0(\mathbf{r})$ does not decay to zero rapidly as \mathbf{r} moves off from the center of the polymer but oscillates, as is shown in Figs. 1 and 3. In this case we need a large solvent cell to immerse the polymer in. In case of a low- Γ solvent this does not happen, and we can deal with a polymer with more sites.

Although our approach based on either Eqs. (14) or (15) or (19) or (15) can give useful information on polymer-solvent dynamics and on solvent density fluctuations induced by polymer conformation, it mainly focuses on sampling polymer conformation according to the distribution function

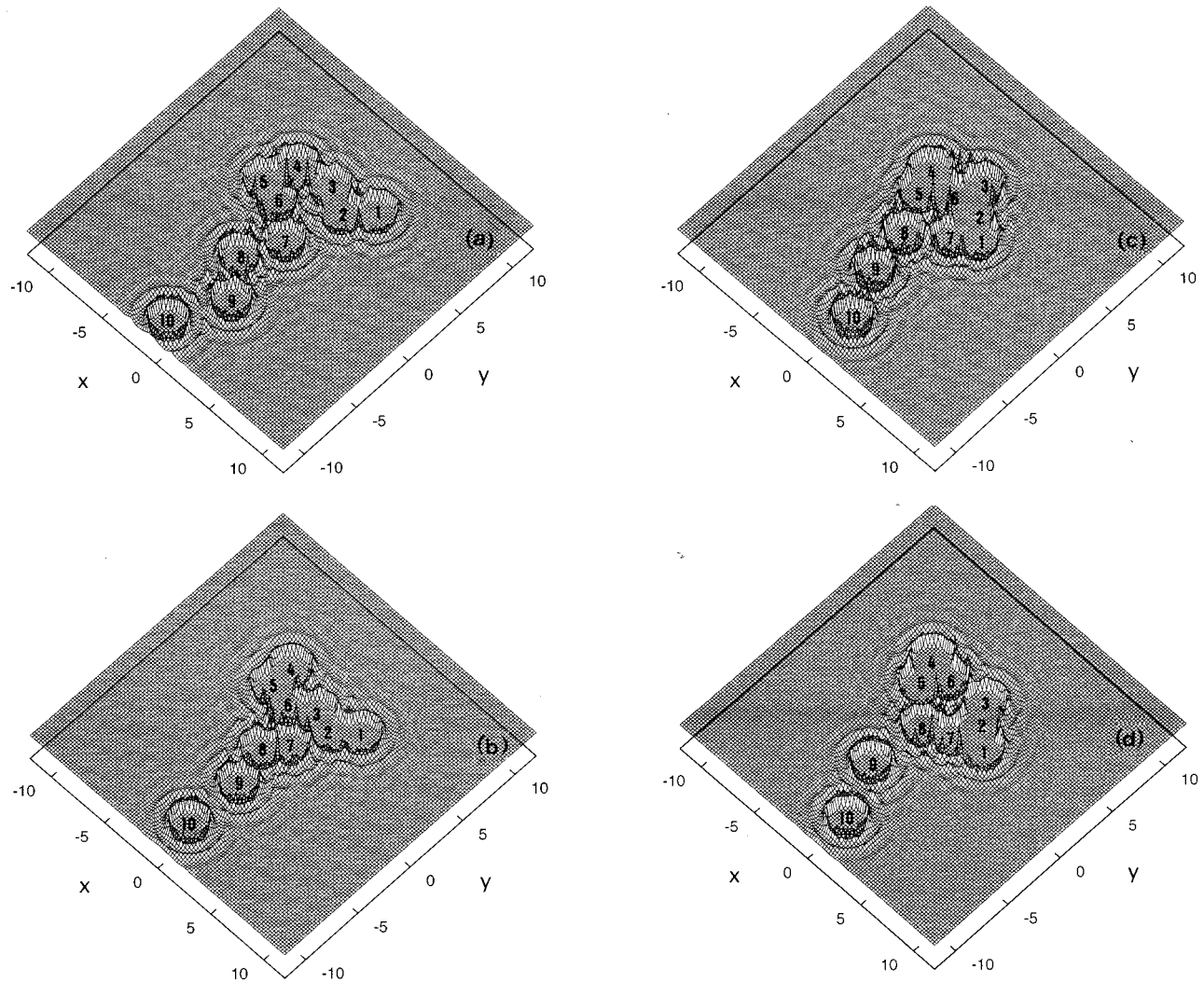


FIG. 3. Conformation $C(t)$ and the density profile $n_0(\mathbf{r},t)$ for a heteropolymer with five hydrophobic ($i=1-5$) and five hydrophilic ($i=6-10$) sites at (a) $t=1000$, (b) 2000, (c) 3000, and (d) 4000. X and Y are in units of σ_0 in Eq. (20). The conformation $C(t=0)$ is the same as the one shown by Fig. 1(a).

(18). So if one could functionally integrate Eq. (18) over solvent density fluctuations, the whole problem would be reduced to that of one polymer with extra medium-induced interaction. It is to be noted, however, that at present we have no systematic functional integration scheme for Eq. (18), which would be able to afford a sound starting point to investigate polymer conformation. This is due to the presence of the logarithmic term (free gas contribution) in the free energy F_0 , Eq. (2). If we employ the Gaussian approximation [7], the first term on the rhs of Eq. (2) becomes $(k_B T/2n_0) \int d\mathbf{r} [\delta n_0(\mathbf{r})]^2$, and after functional integration over $n_0(\mathbf{r})$ we have $P_{\text{eq}}(\{\mathbf{r}_i\}) = C \exp[-\sum_{i<j} \{\phi_{i,j}^{\text{eff}}(|\mathbf{r}_i - \mathbf{r}_j|) + \phi_{i,j}^{\text{solv}}(|\mathbf{r}_i - \mathbf{r}_j|)\} / (k_B T)]$, where the Fourier transform of the solvent-induced interaction $\phi_{i,j}^{\text{solv}}(r)$ is given by the product of the static structure factor $S(k)$ of the pure solvent and the effective potential $\phi_{0,i}^{\text{eff}}(k)$ and $\phi_{0,j}^{\text{eff}}(k)$ [7]. Under this approximation the interaction between, say, sites i and j is

independent of polymer conformation, which means that two sites located deep in the polymer and not exposed to solvent interact with each other in the same manner as the two sites on the surface of the polymer when it is folded. In contrast the Langevin equation (15) clearly shows that if a site is inside a polymer thus shielded from a solvent, it receives no direct effects from the solvent. However, by treating solvent and polymer on equal footing, we had the numerically heavy task of solving the HNC-like nonlinear integral equation (19). Of course it is possible to go beyond the Gaussian approximation by including more than two-body-induced interaction, and further theoretical and numerical studies seem to be necessary for a comparison of the two approaches, an effective medium one and ours, to solvent effects on polymer conformation.

Our final comments are concerned with possible extensions of our approach to more realistic situations. First the

solvent, which is usually composed of water, should be a molecular liquid with electrostatic and dynamic effects. Our DFT approach is expected to overcome this barrier, at least with respect to electrostatic effects, in view of the DFT available for molecular liquids [8,13]. If we want to deal with a polymer with large P (number of sites) in a 3D solvent, we must prepare a large cell (container) of solvent whose density is nearly constant ($=n_0$) around the edge thereof, and this of course requires considerable computer memories. However, in solving Eq. (19) to follow the time evolution of the density profile, we can change the size and shape of the

solvent cell according to the polymer conformation. This would contribute to a reduction of computer memories, and may be considered one merit of our semidynamic approach.

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