Periodicity-dependent stiffness of periodic hydrophilic-hydrophobic heteropolymers

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From extensive Monte Carlo simulations of a Larson model of perfectly periodic heteropolymers (PHP) in water, a striking stiffening is observed as the period of the alternating hydrophobic and hydrophilic blocks is shortened. At short period and low temperature needlelike conformations are the stable conformations. As temperature is increased thermal fluctuations induce kinks and bends. At large periods compact oligomeric globules are observed. From the generalized Larson prescription, originally developed for modeling surfactant molecules in aqueous solutions, we find that the shorter the period is the more stretched the PHP is. This novel effect is expected to stimulate polymer synthesis and trigger research on the rheology of aqueous periodic heteropolymer solutions. [S1063-651X(99)51508-0]

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Almost all the important "molecules of life," e.g., DNA, RNA, and proteins, are heteropolymers [1]. Therefore, in order to gain insight into the in vivo "structure" and "function" of these macromolecules, in recent years, physicists and chemists have been studying the in vitro structure and dynamics of simpler heteropolymers consisting of only two different types of monomers. The sequence distribution is totally random in what are known as random heteropolymers (RHP's) [2]. The RHP's are of special interest to theorists also because of their close relation to the random energy model [3] and spin glasses [4]; these similarities and the unusual properties of the RHP are consequences of the combination of quenched disorder and a special type of frustration arising from the competing interactions in the RHP [5,6]. Very recently, random heteropolymers with correlated sequence distribution, have also been considered theoretically [7]. On the other hand, perfectly periodic heteropolymers (PHP's) have begun to receive attention only very recently [8]. Orlandini and Garel [8] carried out what may be loosely called the first *in vacuo* [9] Monte Carlo (MC) simulations of PHP. The aim of this paper is to report the results of in vitro MC simulations of a very simple model of PHP in water to demonstrate a novel dependence of the stiffness of the PHP on the periodicity of the hydrophilic (or hydrophobic) segments.

We follow the recent reformulation [10] of the Larson model [11,12] of surfactants in water [13] to model the PHP in water. In the spirit of lattice gas models, the system is modeled as a simple cubic lattice of size $L_x \times L_y \times L_z$. Each of the molecules of water can occupy a single lattice site. A surfactant occupies several lattice sites, successive pairs of which are connected by a nearest-neighbor bond of fixed length. We shall refer to each site on the surfactants as a *monomer*. The *primary structure* of each PHP can be described by the symbol $I_p O_p I_p O_p \ldots I_p O_p$, where I and O refer to the hydrophilic and hydrophobic monomers, and the

basic building block $I_p O_p$, each of length L_p, is repeated n times such that $2 L_p n = L_a$ is the total length of the PHP. No monomer is allowed to occupy a site that is already occupied by a water molecule. Besides, no two monomers of the PHP are allowed to occupy the same site simultaneously.

If the chain consisted of only hydrophilic monomers, it would behave exactly as a self-avoiding walk *in vacuo* because of the complete identity between the hydrophilic monomers and the molecules of water. On the other hand, if it consisted of only hydrophobic monomers, it would collapse forming a compact globule. What makes the model PHP so interesting is the competition between these two conformations arising from the competing hydrophilic-hydrophobic effects.

For the convenience of computation, we have reformulated the model of PHP in terms of classical Ising-spin-like variables, generalizing the corresponding formulation for the single-chain surfactants [10]. In this reformulation, a classical Ising-spin-like variable S is assigned to each lattice site; $S_i = 1$ if the ith lattice site is occupied by a water molecule. If the jth site is occupied by a monomer belonging to a PHP, then $S_j = 1, -1$ depending on whether the monomer at the jth site is hydrophilic or hydrophobic, respectively. The temperature T of the system is measured in the units of J/k_B, where J denotes the strength of the interaction between a spin and its six nearest neighbors. This reformulation in terms of Ising-spin-like variables has been successfully used in studying a wide variety of phenomena exhibited by various types of surfactant molecules in aqueous media [14–18] and should not be confused with magnetic polymers [19]. Besides, molecular dynamics simulation of similar molecular models [20] have also been carried out to study the spontaneous formation of self-assemblies of surfactant molecules.

Both the position of the center of mass and the conformation of the PHP is random in the initial state of the system. The allowed moves of the PHP are the same as those of the small surfactants in the Larson model (see Ref. [12]), namely, reptation, buckling, and antibuckling (also called pull) and kink movement [18]. Starting from the initial state,

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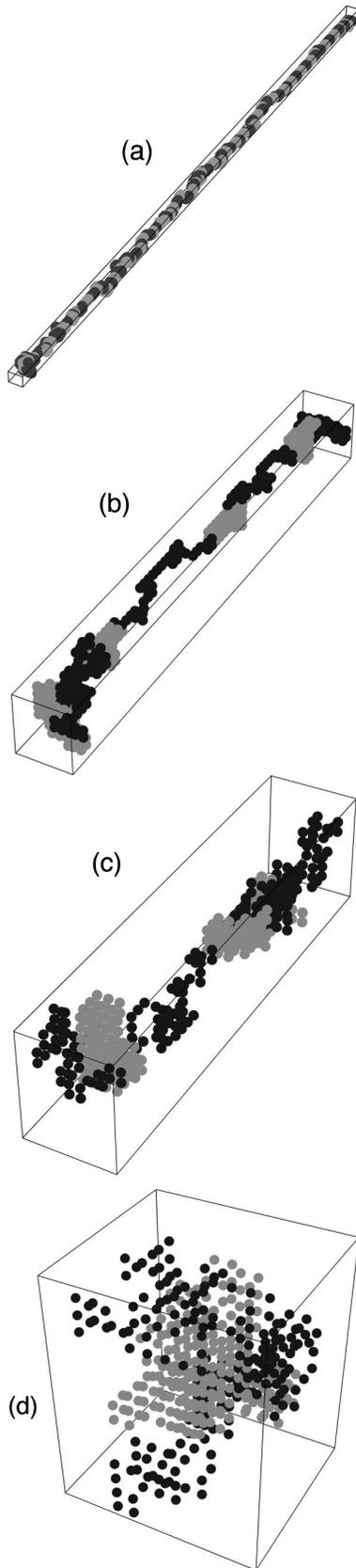*On leave from Physics Department, IIT, Kanpur 208016, India.

FIG. 1. Typical snapshots of a PHP with $L_a = 400$ for (a) $L_p 4$, (b) $L_p = 40$, (c) $L_p = 50$, and (d) $L_p = 100$. The hydrophilic and hydro-phobic monomers are denoted by the black and gray circles, respectively. The boxes are unavoidable artifacts of the graphics package used for plotting.
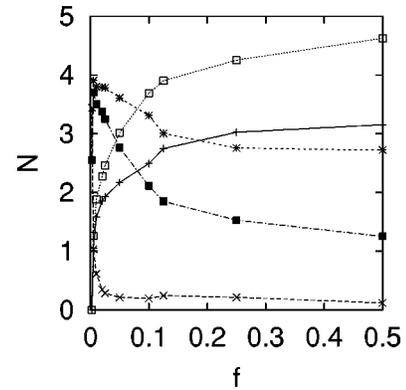

FIG. 2. Quantities N_{ii}, N_{io}, N_{iw}, N_{oo}, and N_{ow} (see text for definitions), which are represented collectively by the label N, are plotted against $f = L_p / L_a$ at a fixed temperature $T = 2.0$. The symbols $+, \times, *$, open square, and filled square correspond to N_{ii}, N_{io}, N_{iw}, N_{oo}, and N_{ow}, respectively.

the system is allowed to evolve following the standard Metropolis algorithm; each of the attempts to move the PHP takes place certainly if $\Delta E < 0$ and with a probability proportional to $\exp(-\Delta E / T)$ if $\Delta E \geq 0$, where ΔE is the change in energy that would be caused by the proposed move of the PHP.

In order to collect information on the qualitative features of the conformations of the PHP, we have directly looked at many snapshots of the PHP at various stages of MC updating of the state of the system. We have also computed several different quantities that provide important quantitative information on various aspects of the conformation of the PHP.

A gross measure of the ''size'' of the PHP in water is given by its radius of gyration,

$$R = \sum_{j=1}^{L_a} (\vec{r}_j - \vec{R}_{cm})^2, \qquad (1)$$

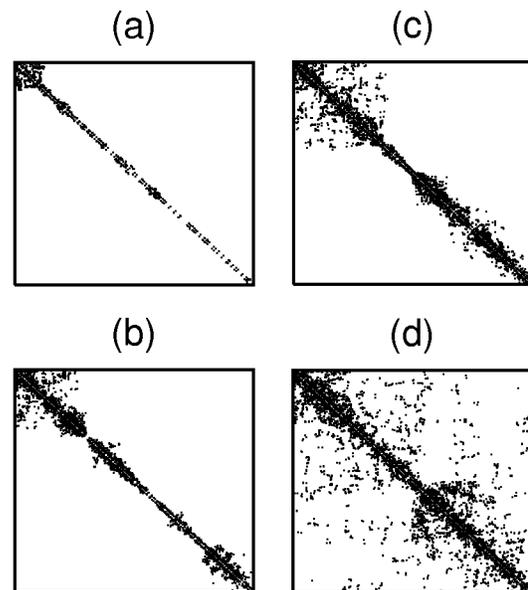FIG. 3. Nonzero elements of the contact maps of a PHP with $L_a = 400$ for (a) $L_p = 4$, (b) $L_p = 40$, (c) $L_p = 50$, and (d) $L_p = 100$, which are denoted by dots.
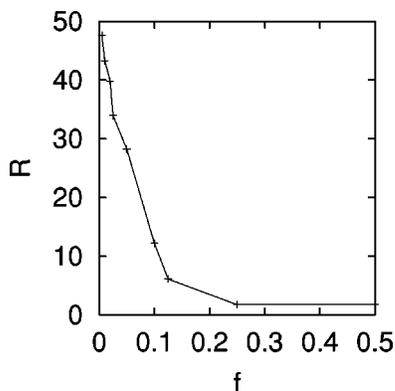
FIG. 4. Average radius of gyration R of a PHP plotted against $f = L_p/L_a$ at a fixed temperature $T = 2.0$.

FIG. 5. Radius of gyration R plotted against the temperature T at a fixed $f = 0.01$.

where $\vec{r}_j$ is the position vector of the jth monomer and $\vec{R}_{cm}$ is the position of the center of mass, which is defined as $R_{cm} = (1/L_a)\Sigma_{j=1}^{L_a}\vec{r}_j$.

Insight into the composition of the local neighborhood of an arbitrary hydrophilic monomer can be gained by computing the quantities N_{ii}, N_{io}, and N_{iw}, which are the average numbers of its nearest-neighbor sites that are occupied by a hydrophilic monomer, a hydrophobic monomer, and a water molecule, respectively. Similarly, the composition of the local neighborhood of an arbitrary hydrophobic monomer is reflected in the numbers N_{oi}, N_{oo}, and N_{ow}, which are the average numbers of its nearest-neighbor sites that are occupied by a hydrophilic monomer, a hydrophobic monomer, and a water molecule, respectively. Obviously, $N_{io} = N_{oi}$ since, throughout this paper, we consider PHP consisting of an equal number of hydrophilic and hydrophobic segments of the same length L_p.

Suppose an index j ($j = 1,2,\ldots,L_a$) labels the monomers sequentially along the primary structure of the PHP chain from one fixed end. The i,jth element, C_{ij}, of the contact map C, is defined to be nonzero if and only if in at least one of its equilibrium configurations, the ith and the jth monomers (irrespective of whether hydrophilic or hydrophobic), are not nearest neighbors along the chain but occupy two nearest-neighbor lattice sites [21]. The contact map has been used to reconstruct the three-dimensional conformation of biopolymers.

For a given L_a, L_p, and T, after equilibration, we have computed the above-mentioned quantities of our interest. Then we have repeated the calculations for several values of L_a, L_p, and T. All the data reported in this Rapid Communication, however, have been generated for $L_p = 400$, corresponding to the longest PHP, for which we could sample, after equilibration, the sufficiently large number of configurations required for averaging.

For a fixed $L_a = 400$, typical snapshots of the PHP for a few different L_p are shown in Figs. 1(a)–1(d). The PHP is very stiff for $L_p = 4$ [Fig. 1(a)]. For intermediate values of L_p, e.g., $L_p = 40$ [Fig. 1(b)] and $L_p = 50$ [Fig. 1(c)], it has a necklacelike conformation where ''beads'' of hydrophobic monomers are connected by hydrophilic chains. Finally, when L_p is of the same order as L_a, e.g., $L_p = 100$ [Fig. 1(d)], the hydrophic monomers form a large collapsed globule surrounded by hydrophobic monomers.
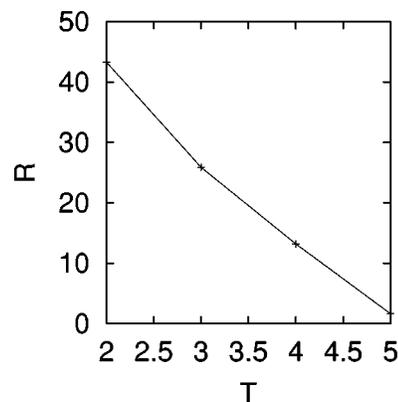
Each of the hydrophilic (hydrophobic) monomers has a tendency to have hydrophilic (hydrophobic) nearest neighbors and to avoid having hydrophobic (hydrophilic) nearest neighbors. The snapshots shown in Fig. 1 also indicate that a longer L_p enables the PHP to satisfy these tendencies. This can be shown more quantitatively (Fig. 2) by plotting N_{ii}, N_{io}, N_{iw}, N_{oo}, and N_{ow}, against $f = L_p/L_a$ at a fixed temperature $T = 2.0$.

One striking feature of the PHP is that the shorter the period is, the more stretched the PHP is, as shown by the snapshots in Fig. 1. This trend of variation is reflected in the structure of the contact maps, shown in Figs. 3(a)–3(d), corresponding to Figs. 1(a)–1(d), respectively. In the contact map for $f = L_p/L_a = 0.01$ there are very few nonzero elements outside the diagonal backbone of the map. With an increase in f, more and more nonzero elements far from the diagonal backbone appear to be signaling the folding or collapse of the PHP. This trend of variation in the ''size'' of the PHP can also be seen quantitatively in Fig. 4, where we plot the radius of gyration R of the PHP as a function of f. Finally, keeping f fixed at a small value, say $f = 0.01$, corresponding to when the PHP is very stiff, if we raise T, the R of the PHP falls monotonically with increasing T (Fig. 5), as expected, because of stronger thermal fluctuations.

In summary, in this Rapid Communication we have developed a Larson-type model of a periodic heteropolymer. By carrying out MC simulations of this model PHP, each consisting of equal numbers of hydrophilic and hydrophobic monomers, we have investigated the effects of varying the period on its conformations in equilibrium. We have observed that, at a given temperature, the smaller the ratio $f = L_p/L_a$ is, the stiffer the PHP is. We would like to emphasize that the stiffness of the PHP at a fixed temperature decreases with increasing $L_p = L_a/(2n)$, where n is the number of segments of each type, in spite of the fact that, nL_p, the total number of hydrophobic monomers remains fixed for the given L_a. This prediction, we believe, can be tested directly in laboratory experiments.

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