Random hydrophilic-hydrophobic copolymers

by

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Abstract

We study a single statistical amphiphilic copolymer chain AB in a selective solvent (e.g. water). Two situations are considered. In the annealed case, hydrophilic (A) and hydrophobic (B) monomers are at local chemical equilibrium and both the fraction of A monomers and their location along the chain can vary, whereas in the quenched case (which is relevant to proteins), the chemical sequence along the chain is fixed by synthesis. In both cases, the physical behaviour depends on the average hydrophobicity of the polymer chain. For a strongly hydrophobic chain (large fraction of B), we find an ordinary continuous $\theta$ collapse, with a large conformational entropy in the collapsed phase. For a weakly hydrophobic, or a hydrophilic chain, there is an unusual first-order collapse transition. In particular, for the case of Gaussian disorder, this discontinuous transition is driven by a change of sign of the third virial coefficient. The entropy of this collapsed phase is strongly reduced with respect to the $\theta$ collapsed phase.
Copolymères aléatoires hydrophiles-hydrophobes

Résumé

Nous étudions un copolymère aléatoire amphiphile AB dans un solvant sélectif (par exemple, de l’eau). Nous considérons deux cas. Dans le cas du désordre mobile, les monomères hydrophiles (A) et hydrophobes (B) sont à l’équilibre chimique local, et la fraction de monomères A ainsi que leur position dans l’espace peuvent varier, alors que dans le cas du désordre gelé (qui est relié au problème des protéines), la séquence chimique est fixée par synthèse. Dans les deux cas, le comportement de la chaîne dépend de son hydrophobicité moyenne. Pour une chaîne fortement hydrophobe (grande fraction de B), on trouve un point d’effondrement $\theta$ continu ordinaire, avec une grande entropie conformationnelle. Pour une chaîne faiblement hydrophobe ou hydrophile, on trouve une transition inhabituelle du premier ordre. En particulier, dans le cas du désordre gaussien, cette transition discontinue est pilotée par un changement de signe du troisième coefficient du viriel. L’entropie de cette phase collapsée est fortement réduite par rapport à celle d’un point $\theta$ ordinaire.
I. Introduction

The study of random heteropolymers in solutions has been recently developed, the main reason being a plausible connection of this problem with the protein folding puzzle\(^{(1,2)}\). Various kinds of quenched randomness have been considered. Here, we wish to emphasize the role of the solvent (water) in the folding process. Indeed, it is widely believed that the hydrophobic effect\(^{(3,4)}\) is the main driving force for the folding transition: in a native protein, the hydrophobic residues are buried in an inner core, surrounded by hydrophilic (or less hydrophobic) residues. In this paper, we consider a simple model, where the monomers of a single chain are (quenched) randomly hydrophilic or hydrophobic. They interact with the solvent molecules through an effective short range interaction, which is attractive or repulsive, depending on their nature. A related model has been considered by Obukhov\(^{(5)}\), but he did not study its phase diagram. We first consider the corresponding annealed case, which is simpler and gives useful insights into the nature of the low temperature phase. It may well be of interest for hydrophilic polymers in the presence of complexing amphiphilic molecules. In section II, we describe the model. Section III deals with the annealed case, and section IV with the quenched case, both for Gaussian and binary distributions of hydrophilicities.

II. The model

We consider a chain of \(N\) monomers which can be either hydrophilic (L) or hydrophobic (P). The hydrophilicity degree of monomer \(i\) is measured by \(\lambda_i\), and the monomer-solvent interaction is assumed to be short-ranged (\(\delta\)-interaction). More precisely, we con-
sider a monomer-solvent interaction of the form:

$$H_{ms} = - \sum_{i=1}^{N+1} \sum_{\alpha=1}^{N} \lambda_i \delta(\vec{r}_i - \vec{R}_\alpha)$$

(1)

where the $\vec{r}_i$ are the positions of the $N$ monomers and the $\vec{R}_\alpha$ are the positions of the $N$ solvent molecules \(^1\). Here, the $\lambda_i$ are independent annealed or quenched random variables. A positive (resp. negative) $\lambda$ corresponds to a hydrophilic (resp. hydrophobic) monomer.

Using the incompressibility condition of the chain-solvent system \(^6\), i.e. the sum of the monomer and solvent concentration is constant: $\rho_m(\vec{r}) + \rho_s(\vec{r}) = \rho_0$, the solvent degrees of freedom can be eliminated, and the full Hamiltonian reads:

$$\beta H(\lambda_i) = \frac{1}{2} \sum_{i \neq j} [v_0 + \beta(\lambda_i + \lambda_j)] \delta(\vec{r}_i - \vec{r}_j)$$

$$+ \frac{1}{6} \sum_{i \neq j \neq k} w_3 \delta(\vec{r}_i - \vec{r}_j) \delta(\vec{r}_j - \vec{r}_k)$$

$$+ \frac{1}{24} \sum_{i \neq j \neq k \neq l} w_4 \delta(\vec{r}_i - \vec{r}_j) \delta(\vec{r}_j - \vec{r}_k) \delta(\vec{r}_k - \vec{r}_l)$$

(2)

In equation (2), the $v_0$ term accounts for entropic excluded volume interactions as well as effective AB interactions described by Flory parameter $\chi_{AB}$ \(^2\). Usually, when considering a polymer collapse transition, it is sufficient to include terms up to $w_3$. Here, we have included a repulsive four-body term $w_4$ which will play an essential role.

In the continuous limit \(^7\), the partition function reads:

$$Z(\lambda(s)) = \int \mathcal{D}\vec{r}(s) \exp \left( - \frac{d}{2a^2} \int_0^N ds \left( \frac{d\vec{r}(s)}{ds} \right)^2 - \beta H(\lambda(s)) \right)$$

(3a)

\(^1\) Note that $-\lambda/kT$ is identical to the standard Flory parameter $\chi$, often used in the polymer literature.

\(^2\) In the Flory-Huggins model of polymer solutions, $v_0 = a^3(1 - 2\chi_{AB})$, $w_3 = a^6$ and $w_4 = a^9$, where $a$ is the monomer size\(^6\).
\[ \beta H(\lambda(s)) = \frac{1}{2} \int_0^N ds \int_0^N ds' (v_0 + \beta(\lambda(s) + \lambda(s'))) \delta(\vec{r}(s) - \vec{r}(s')) + \frac{w_3}{6} \int_0^N ds \int_0^N ds' \delta(\vec{r}(s) - \vec{r}(s')) \delta(\vec{r}(s) - \vec{r}(s')) + \frac{w_4}{24} \int_0^N ds \int_0^N ds' \int_0^N ds'' \delta(\vec{r}(s) - \vec{r}(s')) \delta(\vec{r}(s) - \vec{r}(s')) \delta(\vec{r}(s) - \vec{r}(s')) \] (3b)

where we have implicitly assumed that the origin of the chain is pinned at \( \vec{0} \) and its extremity is free. The parameter \( a \) denotes the statistical segment (Kuhn) length, and \( d \) denotes the dimension of space. In the following, we shall study the case where the hydrophilicities \( \lambda(s) \) are random independent Gaussian variables, with average \( \lambda_0 \) and variance \( \Delta \):

\[ P(\lambda_i) = \frac{1}{\sqrt{2\pi\Delta^2}} \exp\left(-\frac{(\lambda_i - \lambda_0)^2}{\Delta^2}\right) \] (4)

We shall also discuss briefly the technically more complicated case where the \( \lambda_i \) are random independent binary variables, taking the value \( \lambda_A \) with probability \( p \) for a hydrophilic monomer and \( \lambda_B \) with probability \( q = 1 - p \) for a hydrophobic monomer. This case is more relevant to synthetic random copolymers.

The annealed case amounts to take the average of the partition function \( Z \) on the randomness, whereas the quenched case corresponds to taking the average of \( \log Z \). Since the quenched case is achieved by introducing replicas \(^{(8)}\) and using the identity \( \log Z = \lim_{n \to 0} \frac{Z^n}{n} \), we compute directly the average \( \overline{Z^n} \) for integer \( n \), and then treat separately the annealed \((n = 1)\) and quenched \((n = 0)\) cases. For Gaussian disorder and integer \( n \), the average yields:

\[ \overline{Z^n_G} = \int \prod_{a=1}^n D\vec{r}_a(s) \exp\left(-\frac{d}{2a^2} \int_0^N ds \sum_{a=1}^n \left( \frac{d\vec{r}_a(s)}{ds} \right)^2 - A_G \right) \]
\exp \left( \frac{\beta^2 \lambda^2}{2} \int_0^N ds \int_0^N ds' \int_0^N ds'' \sum_{a,b=1}^n \delta(\vec{r}_a(s) - \vec{r}_a(s')) \delta(\vec{r}_b(s) - \vec{r}_b(s'')) \right) \quad (5a)

\text{with}

\begin{align*}
A_G &= \frac{1}{2} (v_0 + 2 \beta \lambda_0) \int_0^N ds \int_0^N ds' \sum_{a=1}^n \delta(\vec{r}_a(s) - \vec{r}_a(s')) \\
+ \frac{w_3}{6} \int_0^N ds \int_0^N ds' \int_0^N ds'' \sum_{a=1}^n \delta(\vec{r}_a(s) - \vec{r}_a(s')) \delta(\vec{r}_a(s') - \vec{r}_a(s'')) \\
+ \frac{w_4}{24} \int_0^N ds \int_0^N ds' \int_0^N ds'' \int_0^N ds'''
\sum_{a=1}^n \delta(\vec{r}_a(s) - \vec{r}_a(s')) \delta(\vec{r}_a(s') - \vec{r}_a(s'')) \delta(\vec{r}_a(s'') - \vec{r}_a(s'''))
\end{align*}

(5b)

whereas for binary disorder:

\begin{align*}
\overline{Z}_B^n &= \int \prod_{a=1}^n D\vec{r}_a(s) \exp \left( -\frac{d}{2a^2} \int_0^N ds \sum_{a=1}^n \left( \frac{d\vec{r}_a(s)}{ds} \right)^2 - A_B \right) \quad (6a)
\end{align*}

\text{with}

\begin{align*}
A_B &= \frac{v_0}{2} \int_0^N ds \int_0^N ds' \sum_{a=1}^n \delta(\vec{r}_a(s) - \vec{r}_a(s')) \\
+ \frac{w_3}{6} \int_0^N ds \int_0^N ds' \int_0^N ds'' \sum_{a=1}^n \delta(\vec{r}_a(s) - \vec{r}_a(s')) \delta(\vec{r}_a(s') - \vec{r}_a(s'')) \\
+ \frac{w_4}{24} \int_0^N ds \int_0^N ds' \int_0^N ds'' \int_0^N ds'''
\sum_{a=1}^n \delta(\vec{r}_a(s) - \vec{r}_a(s')) \delta(\vec{r}_a(s') - \vec{r}_a(s'')) \delta(\vec{r}_a(s'') - \vec{r}_a(s''')) \\
- \int_0^N ds \ \log \left( p e^{\beta \lambda_1} \sum_{a=1}^n \int_0^N ds' \delta(\vec{r}_a(s) - \vec{r}_a(s')) + q e^{\beta \lambda_2} \sum_{a=1}^n \int_0^N ds' \delta(\vec{r}_a(s) - \vec{r}_a(s')) \right)
\end{align*}

(6b)

We now study separately the annealed and quenched cases.

**III. The annealed case**

We set \( n = 1 \) in equations (5) and (6). Denoting the monomer concentration by \( \rho(\vec{r}) \), we assume the validity of ground state dominance \((6,9)\). The ground state wave-function
\( \varphi(\vec{r}) \) is normalized, and we perform a saddle-point approximation of the partition function. We quote here only the results, leaving the details of the calculations for the quenched case (section IV). These approximations yield the following annealed free energy per monomer:

\( \text{a) Gaussian disorder} \)

\[
\beta f_G = \frac{a^2}{2d} \int d^d r \left( \nabla \varphi(\vec{r}) \right)^2 + \frac{\left( v_0 + 2 \beta \lambda_0 \right)}{2} N \int d^d r \varphi^4(\vec{r}) + N^2 \frac{w_3'}{6} \int d^d r \varphi^6(\vec{r}) + \frac{w_4}{24} N^3 \int d^d r \varphi^8(\vec{r}) - E_0 \int d^d r \varphi(\vec{r})^2 \quad (7a)
\]

where

\[
w_3' = w_3 - 3\beta^2 \lambda^2 \quad (7b)
\]

The energy \( E_0 \) appearing in (7a) is the Lagrange multiplier enforcing the normalisation of the wave-function \( \varphi \). The equation of state is obtained by minimizing the free energy (7a) with respect to the wave-function \( \varphi(\vec{r}) \). The monomer concentration is given by:

\[
\rho(\vec{r}) = N\varphi^2(\vec{r}) \quad (8)
\]

The phase diagram of the system can be easily discussed: for any non-zero concentration of hydrophobic monomers, there is a transition between a swollen phase (\( \rho = 0 \)) at high temperature, and a collapsed phase (finite \( \rho \)) at low temperature. The nature of the transition depends on the average hydrophobicity of the chain \( \lambda_0 \) and variance \( \lambda \).

For strong average hydrophobicity (\( \lambda_0 < 0 \)), there is a second order collapse transition, similar to an ordinary \( \theta \) point for polymers in a bad solvent \(^{10}\). This occurs when the coefficient of the \( \varphi^4 \) term in (7a) becomes negative while the coefficient of the \( \varphi^6 \) term is
still positive. This occurs if the average hydrophobicity $\lambda_0$ satisfies the condition:

$$\lambda_0 \geq \frac{v_0 \lambda}{2} \sqrt{\frac{3}{w_3}} \quad (9a)$$

and the transition temperature is given by:

$$T_0 = -\frac{2\lambda_0}{v_0} \quad (9b)$$

When condition (9a) is not satisfied, the collapse transition becomes first order, and is driven by the change of sign of $w_3'$, i.e. by a change of sign of the effective third virial coefficient. This is quite an unusual mechanism.

Such is the case if the system is weakly hydrophobic, or hydrophilic. The minimization of the free energy (7a) leads to a non-linear partial differential equation for $\varphi$ which cannot be solved analytically. It is possible to restrict the minimization to a subset of Gaussian wave-functions, and this will be discussed in the section on quenched systems (see eq.(20) below). Within this Gaussian approximation, the first order transition temperature $T^*$ is given by the equation:

$$3^{d+1} w_4 (v_0 + \frac{2\lambda_0}{T^*}) = 2^{3d/2} (w_3 - \frac{3\lambda^2}{T^*^2})^2 \quad (9c)$$

b) Binary disorder

In this case, the free energy per monomer reads:

$$\beta f_B = \int d\mathbf{r} \left( \frac{a^2}{2d} (\nabla \varphi)^2 + N \frac{v_0}{2} \varphi^4 + N^2 \frac{w_3}{6} \varphi^6 + N^3 \frac{w_4}{24} \varphi^8 - G \right) \quad (10a)$$

where

$$G = \varphi^2 \log \left( p e^{-N\beta\lambda\lambda \varphi^2} + q e^{N\beta\lambda_b \varphi^2} \right) + E_0 \varphi^2 \quad (10b)$$
By taking derivatives with respect to the chemical potentials \( \lambda_\pm \), it is easily seen that the concentrations of hydrophilic and hydrophobic monomers are given by:

\[
\rho_+(\vec{r}) = N\varphi^2(\vec{r}) \frac{p \, e^{-N\beta \lambda_a \varphi^2}}{p \, e^{-N\beta \lambda_a \varphi^2} + q \, e^{N\beta \lambda_B \varphi^2}}
\]
\[
\rho_-(\vec{r}) = N\varphi^2(\vec{r}) \frac{q \, e^{N\beta \lambda_B \varphi^2}}{p \, e^{-N\beta \lambda_a \varphi^2} + q \, e^{N\beta \lambda_B \varphi^2}}
\]

(11)

Note the Boltzmann weights in (11), which govern the chemical composition of the polymer. It clearly appears that the regions of high monomer concentration are hydrophobic, whereas those of low concentration are hydrophilic. The main conclusions of the Gaussian case above remain valid, except that the transition temperatures cannot be calculated explicitly. We find again an ordinary second order \( \theta \) point for strongly hydrophobic chains, and a first-order collapse for weakly hydrophobic or hydrophilic chains.

As can be seen by a numerical study of this case, the transition is strongly first-order, and this implies the existence of a large latent heat at the transition, and thus a sharp drop of the entropy. This drop in entropy can be interpreted as the formation of a hydrophobic core, surrounded by a hydrophilic coating, which is energetically favourable, but entropically unfavourable. This is confirmed by equations (11), which show that high concentration regions are hydrophobic, whereas low concentration regions are hydrophilic. Finally, we see from (11) that at low temperature, the total number of hydrophilic monomers goes to zero, whereas the number of hydrophobic monomers goes to \( N \).

IV. The quenched case

We have to take the \( n = 0 \) limit in (5) and (6). Introducing the parameters \( q_{ab}(\vec{r}, \vec{r}') \)
, with \( a < b \), and \( \rho_a(\vec{r}) \) by:

\[
q_{ab}(\vec{r}, \vec{r}') = \int_0^N ds \, \delta(\vec{r}_a(s) - \vec{r}) \delta(\vec{r}_b(s) - \vec{r}')
\]

\[
\rho_a(\vec{r}) = \int_0^N ds \, \delta(\vec{r}_a(s) - \vec{r})
\]

we may write equations (5) as:

a) Gaussian disorder

\[
\mathcal{Z}_G = \int \mathcal{D}q_{ab}(\vec{r}, \vec{r}') \mathcal{D}\hat{q}_{ab}(\vec{r}, \vec{r}') \mathcal{D}\rho_a(\vec{r}) \mathcal{D}\phi_a(\vec{r}) \exp \left( G(q_{ab}, \hat{q}_{ab}, \rho_a, \phi_a) + \log \zeta(\hat{q}_{ab}, \phi_a) \right)
\]

(13a)

where \( \hat{q}_{ab}(\vec{r}, \vec{r}') \) and \( \phi_a(\vec{r}) \) are the Lagrange multipliers associated with (12), and:

\[
\begin{align*}
G(q_{ab}, \hat{q}_{ab}, \rho_a, \phi_a) &= \int d\vec{r} \sum_a \left( i\rho_a(\vec{r})\phi_a(\vec{r}) - (v_0 + 2\beta\lambda_0) \frac{\rho_a^2(\vec{r})}{2} - \frac{w_3'}{6} \rho_a^3(\vec{r}) - \frac{w_4}{24} \rho_a^4(\vec{r}) \right) \\
&\quad + \int d\vec{r} \int d\vec{r}' \sum_{a < b} \left( iq_{ab}(\vec{r}, \vec{r}') \hat{q}_{ab}(\vec{r}, \vec{r}') + \beta^2 \chi^2 q_{ab}(\vec{r}, \vec{r}') \rho_a(\vec{r}) \rho_b(\vec{r}') \right)
\end{align*}
\]

(13b)

and

\[
\zeta(\hat{q}_{ab}, \phi_a) = \int \prod_a \mathcal{D}\vec{r}_a(s)
\]

\[
\times \exp \left( -\frac{d}{2a^2} \int_0^N ds \sum_a \left( \frac{d\vec{r}_a}{ds} \right)^2 - i \int_0^N ds \sum_a \phi_a(\vec{r}_a(s)) - i \int_0^N ds \sum_{a < b} \hat{q}_{ab}(\vec{r}_a(s), \vec{r}_b(s)) \right)
\]

(13c)

where \( w_3' \) is defined in equation (7b).

Using the identity of equation (13c) with a Feynman integral \(^{(9,11)}\), we can write:

\[
\zeta(\hat{q}_{ab}, \phi_a) = \int \prod_a d^d r_a < \vec{r}_1 \ldots \vec{r}_n | e^{-NH_n(\hat{q}_{ab}, \phi_a)} | \vec{0} \ldots \vec{0} >
\]

(14a)
where $H_n$ is a “quantum-like” $n \to 0$ Hamiltonian, given by:

$$H_n = -\frac{a^2}{2d} \sum_a \nabla_a^2 + \sum_a i\phi_a(\vec{r}_a) + \sum_{a<b} i\hat{q}_{ab}(\vec{r}_a, \vec{r}_b) \quad (14b)$$

Anticipating some kind of (hydrophobically-driven) collapse, we assume that we can use ground-state dominance to evaluate (14), and write, omitting some non-extensive prefactors:

$$\zeta(\hat{q}_{ab}, \phi_a) \simeq e^{-NE_0(\hat{q}_{ab}, \phi_a)}$$

$$= \exp \left( -N \min_{\{\Psi(\vec{r})\}} \{ <\Psi|H_n|\Psi> - E_0 ( <\Psi|\Psi> - 1) \} \right) \quad (15)$$

where $E_0$ is the ground state energy of $H_n$. At this point, the problem is still untractable, and we make the extra approximation of saddle-point method (SPM). The extremization with respect to $q_{ab}$ reads:

$$i\hat{q}_{ab}(\vec{r}, \vec{r}^\prime) = -\beta^2 \lambda^2 \rho_a(\vec{r}) \rho_b(\vec{r}^\prime) \quad (16)$$

This equation shows that replica symmetry is not broken, since $\hat{q}_{ab}$ is a product of two single-replica quantities $\rho_a$. To get more analytic information, we use the Rayleigh-Ritz variational principle to evaluate $E_0$. Due to the absence of replica symmetry breaking (RSB), we further restrict the variational wave-function space to Hartree-like replica-symmetric wave-functions, and write:

$$\Psi(\vec{r}_1, \ldots, \vec{r}_n) = \prod_{a=1}^{n} \varphi(\vec{r}_a) \quad (17)$$

Because of replica symmetry, we can omit replica indices and take easily the $n \to 0$ limit. The variational free energy now reads:

$$-\beta F_G(q, \hat{q}, \rho, \phi, \varphi) = \int d\vec{r} \left( i\rho(\vec{r})\phi(\vec{r}) - (v_0 + 2\beta\lambda_0) \frac{\rho^2(\vec{r})}{2} - \frac{w'_3}{6} \rho^3(\vec{r}) - \frac{w_4}{24} \rho^4(\vec{r}) \right)$$
\[
-\frac{1}{2} \int dr \int dr' \left( i q(\vec{r}, \vec{r}') \dot{q}(\vec{r}, \vec{r}') + \beta^2 \lambda^2 \ q(\vec{r}, \vec{r}') \rho(\vec{r}) \rho(\vec{r}') \right) \\
- N \left\{ \int d^d r \ \varphi(\vec{r}) \left( \frac{-\alpha^2}{2d} \nabla^2 + i \phi(\vec{r}) \right) \varphi(\vec{r}) - \frac{i}{2} \int d^d r' \int d^d r'' \dot{q}(\vec{r}, \vec{r}') \varphi^2(\vec{r}) \varphi^2(\vec{r}'') \right\} \\
+ NE_0 \left( \int d^d r \varphi^2(\vec{r}) - 1 \right) 
\]  

(18)

The SPM equations read:

\[
\rho(\vec{r}) = N \varphi^2(\vec{r}) \\
q(\vec{r}, \vec{r}') = N \varphi^2(\vec{r}) \varphi^2(\vec{r}') \\
i \phi(\vec{r}) = (v_0 + 2 \beta \lambda_0) \rho(\vec{r}) + \frac{w_2}{2} \rho^2(\vec{r}) + \frac{w_4}{6} \rho^3(\vec{r}) + \beta^2 \lambda^2 \int d^d r' q(\vec{r}, \vec{r}') \rho(\vec{r}') \\
i \dot{q}(\vec{r}, \vec{r}') = -\beta^2 \lambda^2 \rho(\vec{r}) \rho(\vec{r}') 
\]

(19)

We still have to minimize with respect to the normalized wave-function \( \varphi(\vec{r}) \). This leads to a very complicated non-linear Schrödinger equation, and we shall restrict ourselves to a one-parameter family of Gaussian wave-functions of the form:

\[
\varphi(\vec{r}) = \left( \frac{1}{2\pi R^2} \right)^{d/4} \exp\left( -\frac{\vec{r}^2}{4R^2} \right) 
\]

(20)

where \( R \) is the only variational parameter.

Using equations (18) and (19), the variational free energy per monomer (\( \overline{f_G} = \overline{F_G}/N \)) reads:

\[
\beta \overline{f_G} = \frac{a^2}{2d} \int d^d r \left( \nabla \varphi(\vec{r}) \right)^2 + \frac{(v_0 + 2 \beta \lambda_0)}{2} N \int d^d r \varphi^4(\vec{r}) \\
+ N^2 \left\{ \frac{w_2}{6} \int d^d r \varphi^6(\vec{r}) + \frac{\beta^2 \lambda^2}{2} \left( \int d^d r \varphi^4(\vec{r}) \right)^2 \right\} + \frac{w_4}{24} N^3 \int d^d r \varphi^8(\vec{r}) \\
- E_0 \int d^d r \varphi^2(\vec{r}) 
\]

(21)

Note that the only difference between this free energy and the annealed one of eq.(7a), is the presence, in the quenched case, of an additional disorder induced term, which we have
grouped together with the $\varphi^6$ term for reasons that will become clear below. Using the Gaussian wave function (20), and the value of $w'_3$ given in (7b), the free energy reads:

$$
\beta f_G = \frac{a^2}{8R^2} + \frac{1}{8(2\sqrt{\pi})^d} \frac{(v_0 + 2\beta \lambda_0) N}{R^d}
+ \left( \frac{1}{(2\pi \sqrt{3})^d} \frac{w_3}{6} - \frac{1}{(2\pi)^d} \frac{\beta^2 \lambda^2}{2} (3^{-d/2} - 2^{-d}) \right) \left( \frac{N}{R^d} \right)^2 + \left( \frac{1}{(32\pi^3)} \right)^{d/2} \frac{w_4}{24} \left( \frac{N}{R^d} \right)^3
$$

(22)

At low temperatures, one has to study the sign of the third term of eq(22). This sign indeed becomes negative at low temperature, due to disorder fluctuations, yielding the following results:

i) $\lambda_0 > 0$ : the hydrophilic case.

In our approximation, we find that there is a first order transition towards a collapsed phase ($R \sim N^{1/d}$) induced by a negative three-body term (and stabilized by a positive four-body term). This transition is neither an ordinary $\theta$ point (since the two-body term is positive), nor a freezing point (the replica-symmetry is not broken). Note that since our approach is variational, the true free energy of the system is lower than the variational one, and we thus expect the real transition to occur at an even higher temperature. Since the transition is first order, we expect metastability and retardation effects to be important near the transition; we also expect that (due to the latent heat), there will be a reduction of entropy in the low temperature phase, compared to an ordinary second order $\theta$ point.

ii) $\lambda_0 < 0$ : the hydrophobic case.

In this case, defining the two temperatures:

$$
T_0 = 2|\lambda_0|/v_0
$$

$$
T_1 = \lambda \frac{\sqrt{3}}{\sqrt{w_3(1-3^{d/2}/2^d)}}
$$

(23)
leads to two possible scenarii, in a very similar way as in the annealed case:

a) Weakly hydrophobic case: $T_1 > T_0$

The collapse transition is again driven by the disorder fluctuations of the three-body interactions. The resulting first-order transition is very similar to the hydrophilic case i).

b) Strongly hydrophobic case: $T_0 > T_1$

The collapse transition is now driven by the strong two-body $\lambda_0$ term. The resulting phase transition is very similar to an ordinary $\theta$ point, and is therefore second-order.

The phase diagram of the quenched case seems quite similar to the annealed case, but, as we shall see on the case of binary disorder, the physics is quite different. Note also that the transition temperature in the quenched case is lower than in the corresponding annealed case, as can be checked from (7a) and (21). This may be viewed as an effect of geometrical frustration induced by the chain constraint.

b) Binary disorder

Using the same approximations as in the previous case, namely ground state dominance, no replica symmetry breaking and Hartree variational wave-function, the free energy per monomer reads:

\[
\beta \overline{F_B} = \frac{a^2}{2d} \int d^d r \left( \nabla \varphi(\vec{r}) \right)^2 + \frac{v_0}{2} N \int d^d r \varphi^4(\vec{r}) + N^2 \frac{w_3}{6} \int d^d r \varphi^6(\vec{r}) + \frac{w_4}{24} N^3 \int d^d r \varphi^8(\vec{r}) - E_0 \int d^d r \varphi^2(\vec{r}) + N \beta \lambda_A \int d^d r \varphi^4(\vec{r}) - \sum_{l=1}^{\infty} \frac{(-1)^{l+1}}{l} \frac{a^l}{p^l} \log \left( \int d^d r \varphi^2(\vec{r}) e^{N \beta \lambda l \varphi^2(\vec{r})} \right)
\]

(24)

where $\lambda = \lambda_A + \lambda_B$.

In this case, we see that even the Gaussian variational form is not tractable, but a numerical study shows that the system has exactly the same phase diagram as for Gaussian
disorder. However, the interest of this model is that it allows to calculate the concentration of hydrophilic and hydrophobic monomers. We obtain:

\[
\rho_{+}(\vec{r}) = N\varphi^2(\vec{r}) \left[ 1 - \sum_{l=1}^{\infty} (-1)^{l+1} \left( \frac{q}{p} \right)^l \int d^d r \varphi^2 e^{\beta \lambda N \varphi^2} \right]
\]

\[
\rho_{-}(\vec{r}) = N\varphi^2(\vec{r}) \sum_{l=1}^{\infty} (-1)^{l+1} \left( \frac{q}{p} \right)^l \frac{e^{\beta \lambda N \varphi^2}}{\int d^d r \varphi^2 e^{\beta \lambda N \varphi^2}}
\]

(25)

It is easily seen on (25) that the two concentrations satisfy the sum rules:

\[
\int d^d r \rho_{+}(\vec{r}) = Np
\]

\[
\int d^d r \rho_{-}(\vec{r}) = Nq
\]

(26)

and thus (as expected for a quenched chain), the overall chemical composition of the chain remains unchanged.

V. Conclusion

We have studied a simple model of a randomly hydrophilic-hydrophobic chain in water. The randomness may be annealed or quenched. The low temperature phase is always collapsed; depending on the degree of hydrophobicity of the chain, this collapsed phase is reached either through an usual second order \( \theta \) point, or through a first order transition. In all cases (see eq.(11) and (25)), the interior of the compact globule is mainly hydrophobic, whereas its exterior is hydrophilic (as expected). In the case of a first order transition, the existence of a latent heat implies a decrease of the entropy of the collapsed chain, due to the burial of the hydrophobic monomers in the core. Studies of similar models for semi-dilute solutions and melts in random or block copolymers are currently under way.
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