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Globules of amphiphilic macromolecules

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Abstract

We consider the theoretical model of an amphiphilic macromolecule with a complex structure of hydrophobic/hydrophilic monomer units. Each unit consists of a hydrophobic group (H) in the backbone and a side hydrophilic group (P). The units are able to orient in the density gradient at the surface layer of a globule. First, we use the density functional method to obtain the surface tension at a flat surface. We obtain that the effect of orientation decreases the surface tension of an amphiphilic globule in comparison with the surface tension of a homopolymer globule of the same density. Therefore, the amphiphilic globule is more stable with respect to the transition to a coil conformation. Then, macromolecules with strong orientational ability of amphiphilic units are considered. The free energy of spherical, bead-like, disc-like and torus-like globules is analysed for flexible and rigid macromolecules. For very long macromolecules in poor solvent, it is predicted that a disc-like globule for flexible chains should be formed. It is shown that the coil–globule transition in amphiphilic macromolecules is in most cases accompanied by a disintegration of the initially formed globule into several 'bead globules'. Upon further increase of the attraction of hydrophobic units, these beads merge with each other with the formation of a disc-like or torus-like globule, depending on the chain stiffness.

1. Introduction

Macromolecules of amphiphilic polymers contain both hydrophobic and hydrophilic groups possessing different affinity to water and polar solvents. Many synthetic and biological polymers like proteins, phospholipids, and polysaccharides are referred to as polyamphiphiles.

Studying theoretical models of amphiphilic polymers leads to a better understanding of important protein and enzyme properties, for example, the regular transition phenomena in proteins [1–6]. Water solubility is a characteristic feature of protein globules provided by

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polar groups surrounding a dense core. The special three-dimensional structure (unique native conformation) of proteins [1, 2] is stabilized by the surface tension. Investigation of this important factor can help to explain a variety of amphiphilic globule shapes realized in nature. A large number of synthetic polymers can take spherical, rod-like, and disc shapes [7–11]. The DNA macromolecules often have a torus-like structure [1, 2, 12]. The complex structure of mixtures containing surfactants, as well as the shape transformations in such systems, are also controlled by the interfacial energy [13–15].

For amphiphilic globules the surface tension depends on types of polymer units at a globule surface. The simplest models of amphiphilic polymers involve two types of monomer units: H (hydrophobic) and P (hydrophilic or polar). Hydrophobicity can be described as a tendency of hydrophobic groups to reduce their surface of contact with a polar solvent: two hydrophobic groups try to stick together in order to hide their mutual surface of contact. On the other hand, the hydrophilic groups tend to be surrounded by solvent molecules. Therefore, the hydrophobic–polar interactions give rise to the formation of a compact structure with mostly hydrophobic core and polar shell [16].

The coil–globule transition for random HP copolymers was investigated for the annealed and quenched disorder in HP sequences [17–19]. The sequences of H and P units in polymer chains determine the interaction energy of globular macromolecules [4–6, 20, 21]. The type of sequences which model the protein property to have a dense core and to be soluble in water was called in [22–24] protein-like sequences. Normally, such sequences are obtained by transforming the surface monomer units of a ‘parental’ spherical globule to a polar type and the monomer units in the core to a hydrophobic type [22–24].

The stability of globules formed by regular, random, protein-like chains was analysed numerically using the self-consistent field approach and computer simulations [25]. The protein-like copolymers were predicted to be the most stable ones with respect to a coil–globule transition. All sequences mentioned above and HP–H sequences (formed by one long and many short H blocks) were considered theoretically for macromolecules with a small fraction of polar units located at the globule surface [26]. It was obtained that the HP–H copolymers have the lowest free energy. Protein-like copolymers were found to be very stable as well. Molecular architectures of HP–H copolymer chains and their aggregates were considered theoretically; different types of macromolecule structures were predicted to be thermodynamically stable depending on the sequence characteristics of such copolymers [27]. For HP multi-block-copolymers, it was shown that the shape transitions are accompanied by the formation of a surface pattern of fingers of different morphologies [28]. For amphiphilic comb-like copolymers, the formation of spherical, necklace-like, cylindrical, and lamellar structures was predicted [29].

A further development of the HP-copolymer model is the side-chain model introduced recently by Vasilevskaya *et al* [30]. The model mimics the dualistic character of each monomer unit containing both hydrophobic and polar groups. The backbone of the macromolecule is considered as a flexible chain consisting of H groups; one side P group is attached to each H group. The results of molecular dynamics simulations demonstrate that, as the solvent becomes poorer, chain conformations smoothly change from a swollen coil to a necklace-like conformation, then to a sausage-like conformation, and then to a cylinder.

Besides, the conformations of hydrophobic–amphiphilic copolymers were studied in molecular dynamics simulations, for both single-chain and multichain systems [31]. Random protein-like copolymers and regular copolymers with alternating hydrophobic H and amphiphilic HP units and with alternating blocks of these units were considered. It was found that regular copolymers tend to form compact conformations elongated in one direction, whereas protein-like copolymers readily adopt core–shell spherical conformations. Besides,

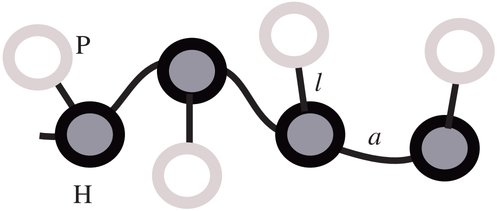

Figure 1. Structure of an amphiphilic macromolecule.

no large-scale aggregation for protein-like copolymers was observed due to the stabilizing hydrophilic envelope of their compact structures.

In the present work the side-chain model of amphiphilic macromolecules in the globular state is considered. We use the results for the surface tension for a flat surface of homopolymer globules obtained in the classical work [32] and extend them to the case of amphiphilic macromolecules with the composed (dimer) units. The dimer units are able to orient at a globule surface: H groups tend to get inside the globule because of the attraction to each other and P groups tend to locate at the globule surface because of the attraction to solvent molecules. The orientational contribution in the interaction energy and the orientational entropy of dimer units should be taken into account in the free energy. The orientation entropy is taken in the same form as in the liquid crystal theory [33].

Further, we consider amphiphilic globules with different shapes: a spherical globule, beads, disc, cylinder, and torus-like conformations. We write the expression for the free energy as a function of the globule density, shape, and surface area. The chain conformation is less perturbed for a spherical form of the globule than for a narrow disc or thin cylinder (for globules of the constant volume). At the same time the surface interaction energy of amphiphilic globules is negative and proportional to the surface area, this fact giving rise to a non-spherical shape. The equilibrium size and shape of amphiphilic macromolecules are determined by the balance between the surface free energy and other contributions (volume, conformation) to the free energy. We find the minimum of the free energy and obtain the shape diagram for amphiphilic macromolecules depending on solvent quality, chain length, and stiffness.

2. The model

Let us consider the model of a globule formed by an amphiphilic macromolecule in polar solvent. Every polymer unit has a hydrophobic group (H) in the backbone and a polar group (P) attached to the H group (figure 1). Let the macromolecule consist of N monomer units; v is the volume of a dimer monomer unit; v_{s} is the volume of a solvent molecule. Volumes of the hydrophilic and hydrophobic parts of a unit are supposed to be equal. The two parameters of unit interactions control the formation of a globule: $\varepsilon_{\mathrm{HH}}$ is the interaction energy for the H-group surrounded by H-groups, $\varepsilon_{\mathrm{Ps}}$ is the interaction energy for the polar group with solvent ($\varepsilon_{\mathrm{HH}} < 0$, $\varepsilon_{\mathrm{Ps}} < 0$). The conformation of the backbone chain is described by a Gaussian model [32] with the mean square distance between units a, this parameter corresponding to a persistent length of a macromolecule. The length of the H–P bond is denoted by l.

In this section let us assume that the amphiphilic molecule with the dimer hydrophilic–hydrophobic units forms a globule similar to a homopolymer one with nearly homogeneous dense core and loops at the edge. The polar groups of dimer units at the surface are oriented outwards due to the attraction of the polar groups to the solvent. We will investigate the stability of the amphiphilic globule related to the transition to a coil conformation and find the optimum form of such globules.

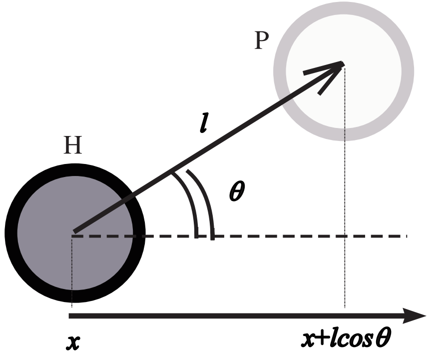

Figure 2. Orientation of a dimer unit.

Let us consider a large homogeneous globule. Let ϕ be the monomer volume fraction, then $\phi_\mathrm{H} = \phi_\mathrm{P} = \phi/2$ are the volume fractions of hydrophobic and polar groups respectively; $\phi_\mathrm{s} = 1 - \phi$ is the solvent volume fraction.

The interaction energy of a homogeneous globule consists of the energy of pair contacts and of the term related to the entropy of solvent molecules:

$$\frac{E_0}{k_\mathrm{B}T} = N\left(\frac{\varepsilon_\mathrm{HH}}{2}\phi_\mathrm{H} + \varepsilon_\mathrm{Ps}\phi_\mathrm{s}\right) + M_\mathrm{s}\ln\phi_\mathrm{s}, \tag{1}$$

where $M_\mathrm{s} = N\frac{v}{v_\mathrm{s}}\frac{\phi_\mathrm{s}}{\phi}$ is the number of solvent molecules within the globule.

In the volume approximation the free energy of a globule F_0 is equal to the interaction energy:

$$\frac{F_0(\phi)}{Nk_\mathrm{B}T} = \frac{\varepsilon}{2}\phi + \frac{v}{v_\mathrm{s}}\left(\frac{1-\phi}{\phi}\ln(1-\phi) + 1\right), \tag{2}$$

where a coil state of the macromolecule is taken as a reference state; $\varepsilon = \varepsilon_\mathrm{HH}/2 - 2\varepsilon_\mathrm{Ps}$ is the effective interaction energy. All interaction energy parameters are expressed in the units of $k_\mathrm{B}T$.

Within a mean-field approximation, the equilibrium volume fraction ϕ_0 corresponds to the minimum of the free energy (2): $\partial F_0/\partial\phi|_{\phi=\phi_0} = 0$. The minimum value F_0 is determined by the relations

$$\frac{F_0}{Nk_\mathrm{B}T} = \frac{3}{2}\varepsilon\phi_0 - \varepsilon\phi_0^2 + \frac{v}{v_\mathrm{s}}, \qquad \frac{\ln(1-\phi_0)}{\phi_0^2} + \frac{1}{\phi_0} = \varepsilon\frac{v_\mathrm{s}}{v}. \tag{3}$$

The whole free energy of a globule includes the bulk contribution (3) and the surface free energy, which will be calculated in the next sections taking into account the possibility of dimer unit orientation.

3. Surface free energy for spherical globules

We calculate the surface free energy for a large spherical globule, which depends on the density profile of units in the surface layer and on the dimer unit orientation. We introduce the unit volume fractions $\phi(\boldsymbol{r})$ depending on the radial coordinate and the function of unit orientation distribution $f(\theta, \boldsymbol{r})$, where θ is the angle between the H–P bond vector $\boldsymbol{l}$ and the radial direction (figure 2). The volume fraction profile $\phi(\boldsymbol{r})$ is assumed to be smooth ($a|\nabla\phi|/\phi_0 \ll 1$), and the normalization conditions for the functions $\phi(\boldsymbol{r})$ and $f(\theta, \boldsymbol{r})$ are $Nv = \int\phi(\boldsymbol{r})\,\mathrm{d}^3r$, $\int\mathrm{d}\Omega_l\, f(\theta, \boldsymbol{r}) = 1$.

The whole free energy of a globule can be written in the form

$$F(\phi, f) = E(\phi, f) - TS_{\mathrm{conf}}(\phi) - TS_{\mathrm{orient}}(\phi, f), \tag{4}$$

where E is the interaction free energy, S_{conf} is the conformational entropy of the backbone chain, and S_{orient} is the orientational entropy of dimer units.

Considering a coil conformation as a reference state, the interaction energy can be written in the form

$$\frac{Ev}{k_{\mathrm{B}}T} = \int \mathrm{d}^3r \int \bigg\{ \mathrm{d}\Omega_l\, \phi(\boldsymbol{r}) f(\theta, \boldsymbol{r}) \left(\frac{\varepsilon_{\mathrm{HH}}}{2} \phi_{\mathrm{H}}(\boldsymbol{r}) + \varepsilon_{\mathrm{Ps}} \phi_{\mathrm{s}}(\boldsymbol{r} + \boldsymbol{l}) - \varepsilon_{\mathrm{Ps}} \right) \\ + \frac{v}{v_{\mathrm{s}}} (\phi_{\mathrm{s}}(\boldsymbol{r}) \ln \phi_{\mathrm{s}}(\boldsymbol{r}) + \phi(\boldsymbol{r})) \bigg\}, \tag{5}$$

where $\phi_{\mathrm{s}}(\boldsymbol{r} + \boldsymbol{l}) = 1 - \phi(\boldsymbol{r} + \boldsymbol{l}) \approx 1 - \phi(\boldsymbol{r}) - (\boldsymbol{l} \boldsymbol{\nabla} \phi)$. Then, expression (5) can be written as

$$\frac{Ev}{k_{\mathrm{B}}T} = \int \mathrm{d}^3r \bigg\{ \varepsilon \frac{\phi^2(r)}{2} - \varepsilon_{\mathrm{Ps}} \phi(\boldsymbol{r}) \int \mathrm{d}\Omega_l\, f(\theta, \boldsymbol{r}) (\boldsymbol{l}\, \boldsymbol{\nabla} \phi) \\ + \frac{v}{v_{\mathrm{s}}} [(1 - \phi(\boldsymbol{r})) \ln(1 - \phi(\boldsymbol{r})) + \phi(\boldsymbol{r})] \bigg\}. \tag{6}$$

The second term in relation (6) corresponds to the decrease of the free energy ($\varepsilon_{\mathrm{Ps}} < 0$) due to the unit orientation in the region where the density gradient is not zero.

The conformational entropy at a small density gradient is given by the Lifshitz formula,

$$S_{\mathrm{conf}}(\phi)/k_{\mathrm{B}} = \frac{a^2}{6v} \int \mathrm{d}^3r\, \sqrt{\phi(\boldsymbol{r})} \Delta(\sqrt{\phi(\boldsymbol{r})}), \tag{7}$$

and the orientational entropy is taken in the same form as in the liquid crystal theory [33]:

$$S_{\mathrm{orient}}(\phi)/k_{\mathrm{B}} = -\frac{1}{v} \int \mathrm{d}^3r\, \phi(\boldsymbol{r}) \int \mathrm{d}\Omega_l\, f(\theta, \boldsymbol{r}) \ln(4\pi f(\theta, \boldsymbol{r})). \tag{8}$$

The equilibrium volume function profile $\phi(\boldsymbol{r})$ and the equilibrium function of orientation distribution $f(\theta, \boldsymbol{r})$ should correspond to the minimum of the free energy (4). The minimization of the free energy with respect to the function $f(\theta, \boldsymbol{r})$ gives

$$f(\theta, \boldsymbol{r}) = \frac{1}{4\pi} \frac{\varepsilon_{\mathrm{Ps}}(\boldsymbol{l} \boldsymbol{\nabla} \phi(\boldsymbol{r}))}{\sinh\{\varepsilon_{\mathrm{Ps}}(l \boldsymbol{\nabla} \phi(\boldsymbol{r}))\}} \exp(-\varepsilon_{\mathrm{Ps}}(\boldsymbol{l} \boldsymbol{\nabla} \phi(\boldsymbol{r}))). \tag{9}$$

The distribution function of unit orientation $f(\theta, \boldsymbol{r})$ over the angle θ calculated from expression (9) is represented in the figure 3 for different values of the volume fraction gradient. The orientation of units is more pronounced in the region with the larger value of the density gradient. The units are completely disordered ($f(\theta, \boldsymbol{r}) = 1/(4\pi)$) in the core of a globule, where $\phi(\boldsymbol{r}) = \phi_0$.

The free energy of a globule can be represented as a sum of the bulk free energy (3) and the surface free energy:

$$F = F_0 + \sigma S_{\mathrm{surf}}, \tag{10}$$

where σ is the surface tension and S_{surf} is the surface area of the globule. Further, we neglect the surface curvature and describe a flat surface. Then, the surface tension can be written as a unidimensional integral along the coordinate axis x in the radial direction:

$$\frac{\sigma v}{k_{\mathrm{B}}T} = \int \mathrm{d}x \left(\varepsilon \frac{\phi^2}{2} + \frac{v}{v_{\mathrm{s}}} [(1 - \phi) \ln(1 - \phi) + \phi] + \frac{a^2}{6} \frac{\phi'^2}{4\phi} \right) \\ - \int \mathrm{d}x\, \phi \left(\varepsilon \frac{\phi_0}{2} + \frac{v}{v_{\mathrm{s}}} \left[\frac{1 - \phi_0}{\phi_0} \ln(1 - \phi_0) + 1 \right] + \ln \frac{\sinh(ba\phi'/2)}{ba\phi'/2} \right), \tag{11}$$

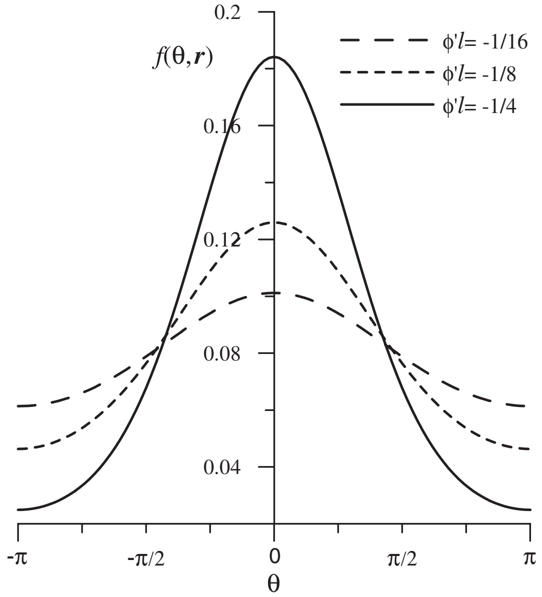

Figure 3. The distribution function of unit orientation over the angle θ between the H–P bond and the radial direction $f(\theta, \boldsymbol{r})$ for the different volume fraction gradients. The interaction energy $\varepsilon_{\mathrm{Ps}} = -4$.

where $b = 2l\varepsilon_{\mathrm{Ps}}/a$ is the orientational parameter. The orientation contribution is given by the last term in equation (11) and it is negative. Expression (11) can be rewritten using the virial expansion for $\phi \ll 1$ and the expansion of the last term for $\varepsilon_{\mathrm{Ps}} l \phi' \ll 1$ (for a smooth enough interface):

$$\frac{\sigma v}{k_{\mathrm{B}}T} = \int \mathrm{d}x \left(\frac{B}{2}\phi(\phi - \phi_0) + \frac{C}{6}\phi(\phi^2 - \phi_0^2) + \frac{a^2}{24}\frac{\phi'^2}{\phi}(1 - b^2\phi^2) \right), \tag{12}$$

where the second and the third virial coefficients $B = \varepsilon + v/v_{\mathrm{s}}$ and $C = v/v_{\mathrm{s}}$, and then $\phi_0 = -3B/(2C)$. The minimization leads to the differential equation for the volume fraction:

$$\phi' = \frac{2}{a}\frac{\sqrt{C}}{\sqrt{1 - b^2\phi^2}}(\phi - \phi_0)\phi. \tag{13}$$

Equation (13) can be solved analytically. It is convenient to take $x = 0$ at the point where $\phi = \phi_0/2$, and the boundary conditions $\phi(+\infty) = 0$, $\phi(-\infty) = \phi_0$.

A homopolymer globule is described by zero orientational parameter: $b = 0$. The well known result for a homopolymer globule (with the bulk density ϕ_0) [32]

$$\phi(x) = \frac{\phi_0}{2}\left(1 - \tanh\frac{x\phi_0\sqrt{C}}{a}\right) \tag{14}$$

can be easily obtained from equation (13).

Taking into account the orientation term leads to a non-symmetrical profile. The exact solution $\phi(x)$ of expression (13) for $b \neq 0$ can be written in the implicit form

$$x = \frac{a}{2\phi_0\sqrt{C}}\left(W\left(\frac{\phi_0}{2}\right) - W(\phi)\right), \tag{15}$$

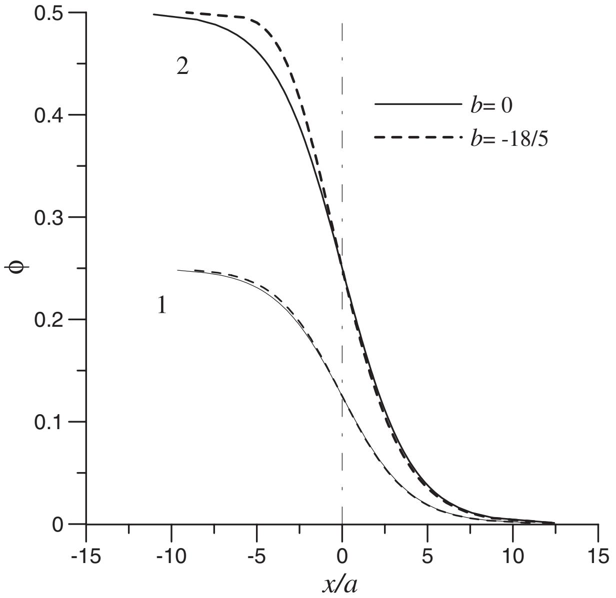

Figure 4. The volume fraction profiles for a homopolymer globule (solid line) and for an amphiphilic globule (dashed lines) corresponding to the different values of the bulk volume fraction ϕ_0: $\phi_0 = 0.25$ (1) and $\phi_0 = 0.5$ (2). The third virial coefficient $C = 2$.

where

$$W(\phi) = b\phi_0 \arcsin(b\phi) + \frac{1}{2}\ln\left|\frac{1-\sqrt{1-b^2\phi^2}}{1+\sqrt{1-b^2\phi^2}}\right| + \sqrt{1-b^2\phi_0^2}\ln\left|\frac{2\sqrt{1-b^2\phi^2}\sqrt{1-b^2\phi_0^2}}{\phi-\phi_0} + 2\frac{1-b^2\phi_0\phi}{\phi-\phi_0}\right|.$$

The volume fraction profiles for an amphiphilic macromolecule and for a homopolymer globule of the same density are presented in figure 4. As can be seen from the figure, the possibility of unit orientation leads to the steeper profile in comparison with a homopolymer globule, and the effect of orientation is more remarkable for a denser globule. Besides, the profile is non-symmetric and the larger fraction of units of an amphiphilic molecule is located in the region with $\phi > \phi_0/2$, this fact being related to the decrease of the interaction energy from the unit orientation, which is proportional to the concentration gradient (see equation (4)).

It should be noted that the allowable value of the orientational parameter b is limited by the condition that the concentration profile should be smooth enough. Then, it follows from equation (13) that the product $|b|\phi_0$ should not be close to unity: $|b| < 1/\phi_0$.

Now the surface tension can be found from expressions (12) and (13):

$$\sigma = \sigma_0\left\{\sqrt{1-b^2\phi_0^2} + \frac{1}{b\phi_0}\arcsin(b\phi_0) + \frac{2}{3b^2\phi_0^2}[(1-b^2\phi_0^2)^{3/2}-1]\right\}. \quad (16)$$

The well known result for the surface tension of a homopolymer globule corresponds to $b = 0$: $\sigma_0 = \frac{k_B T a}{v}\frac{\sqrt{C}\phi_0^2}{12}$. In figure 5 the surface tension calculated according to expression (16) is plotted as a function of the orientation parameter. For small value of the orientation parameter, expression (16) can be approximated by $\sigma = \sigma_0(1 + b\phi_0/4)$ ($|b|\phi_0 \ll 1$). The surface tension

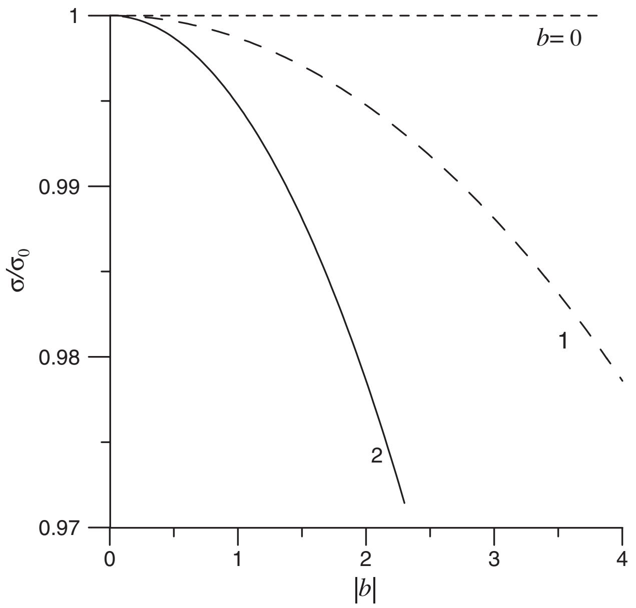

Figure 5. The dependence of the reduced surface tension σ/σ_0 on the orientation parameter b for different values of the bulk volume fraction ϕ_0: $\phi_0 = 0.25$ (1) and $\phi_0 = 0.5$ (2). The surface tension for a homopolymer globule corresponds to $b = 0$.

decreases with increasing the absolute value of the orientational parameter due to the increase of the benefit from the orientation of monomer units in the surface layer. The influence of the orientation is stronger for denser globules, since their density profiles are characterized by the larger gradients (see figure 4).

Now consider an amphiphilic globule near a coil–globule transition. The expression for the free energy F (4) is written relative to the free energy of a coil state, therefore the coil–globule transition temperature T_a corresponds to zero free energy $F = 0$. Let T_{hom} be the transition temperature for a homopolymer globule of the same density and size as an amphiphilic one. Then

$$F_0(T_{\mathrm{hom}}) + \sigma_0 S_{\mathrm{surf}} = F_0(T_a) + \sigma S_{\mathrm{surf}} = 0. \tag{17}$$

For the transition temperatures T_{hom} and T_a close to the so-called θ-temperature, we find the difference between the transition temperatures $\Delta T = T_a - T_{\mathrm{hom}}$ from equation (17): $\Delta T \approx (\sigma_0 - \sigma) S_{\mathrm{surf}} / (\partial F_0 / \partial T)$. Since the θ-temperature corresponds to the zero second virial coefficient $B = 0$, the transition temperature is equal to the θ-temperature in the limit $N \to \infty$.

Assuming that $B \approx (T - \theta)/\theta$ and using expressions (3) and (16), we obtain that the transition temperature increases at $\Delta T \approx |b| a^3/(C^{1/2} v N)$ ($|b|\phi_0 \ll 1$). Therefore, we can conclude that an amphiphilic globule is more stable related to a coil–globule transition, and that the shift of the transition temperature is proportional to the orientational parameter.

4. Shape diagram of amphiphilic globules

The surface free energy of the amphiphilic globule with oriented units is less than that of a homopolymer globule of the same density. In the previous section we considered the spherical

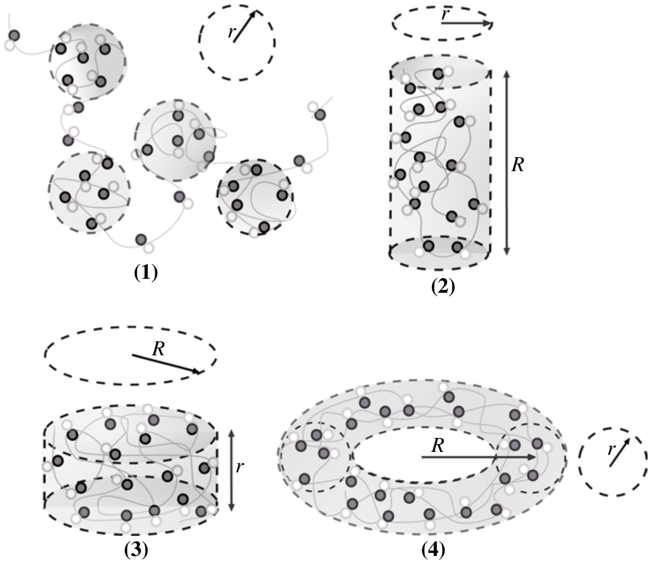

Figure 6. The possible globule shapes for an amphiphilic molecule: beads (1), cylindrical (2), disc-shaped (3), and torus-shaped (4) globules.

globule with smooth concentration profile at the interface and with positive surface tension. We obtained that for the very high value of the orientation parameter the thickness of the surface layer is of the order of the monomer unit size and all dimer units at the surface are oriented outward with respect to the globule. If the attraction of the polar groups to the solvent is very strong, then the surface free energy should become negative. The spherical form is not the most favourable for such globules, and the globule shape should be determined by the competition between the bulk free energy, the conformational free energy, and the surface interactions. In this section we will consider different possible shapes of the globule: the spherical globule and beads and the cylindrical, disc-shaped, and toroidal globules (figure 6).

The free energy of the globule F is taken as the sum of the bulk free energy F_{int}, the conformational free energy F_{conf}, and the interaction free energy corresponding to the unit orientation F_{orient}:

$$F = F_{\text{int}} + F_{\text{conf}} + F_{\text{orient}}. \tag{18}$$

We assume that the globule is almost homogeneous in the bulk: $\phi = Nv/V$, where V is the globule volume. We neglect the possible microsegregation in the globule and we will use, for the sake of simplicity, the virial expansion. Then, the interaction free energy has the usual form for all the globular shapes ($\phi \ll 1$):

$$F_{\text{int}} = k_{\text{B}}TN\left(\frac{B}{2}\phi + \frac{C}{6}\phi^2\right). \tag{19}$$

The minimum of expression (19) corresponds to the volume fraction $\phi_0 = -3B/(2C)$.

The last two terms in the free energy (19) depend not only on the globule density but on the globule shape as well. The surface interaction free energy F_{orient} is determined by the benefit from the orientation of monomer units at the surface. We assume that all monomer units at a thin globule surface are strongly oriented towards the solvent due to the strong attraction of polar groups to solvent molecules ($|\varepsilon_{\text{Ps}}|$ is of the order of unity or more). The interaction energy of a polar group and solvent in the bulk $\varepsilon_{\text{Ps}}(1 - \phi)$ is included in the free energy

F_{int} (19). The interaction energy of a polar group and solvent at a surface is approximately equal to $\varepsilon_{\text{Ps}}(1/2 + (1-\phi)/2)$. The difference yields the surface interaction free energy

$$F_{\text{orient}} = k_{\text{B}} T M_{\text{surf}} \varepsilon_{\text{Ps}}(\phi/2), \tag{20}$$

where $M_{\text{surf}} = \phi S_{\text{surf}}/v^{2/3}$ is the number of monomer units at the surface of the one-unit size thickness.

The chain conformation should adjust the effective walls formed by the layer of oriented dimer units at the surface. We assume that, for example, the chain in a narrow slit of size r has similar conformational constraints as the chain forming a narrow disc. We take the conformational free energy to be proportional to Na^2/r^2, where the size r is still greater than the monomer unit size a [34]. In a more general form, we introduce the characteristic sizes of the region in three dimensions (r_1, r_2, r_3) and take the conformational free energy in the form

$$F_{\text{conf}} = k_{\text{B}} T N a^2 \left(\frac{1}{r_1^2} + \frac{1}{r_2^2} + \frac{1}{r_3^2} \right). \tag{21}$$

For a spherical globule and beads $r_1 = r_2 = r_3 = r$, where r is the radius of a globule or one bead; $r_1 = r_2 = R$ and $r_3 = r$ for disc and torus; $r_1 = R$ and $r_2 = r_3 = r$ for cylinder (figure 6). The conformational free energy (21) plays an essential role only if any size r_i $(i = 1, 2, 3)$ is much less than the size of an unperturbed ideal chain in coil conformation $\sqrt{N}a$.

Taking into account different geometries, we find the free energy F for each conformation as a function of the volume fraction and linear dimensions. The macromolecule in a bead-like conformation consists of one or several spherical globules connected by linear parts of the chain. We assume that almost all units are included in beads, and the number of units in the linear part of the chain is negligible. Besides, the bead size should be large enough so that equation (21) is valid and the bead interactions may be neglected.

If m is the number of beads, then the total surface area and the total volume of the beads are equal to $S_{\text{surf}} = m4\pi r^2$ and $V = m4\pi r^3/3$. The surface area and the globule volume for the torus $S_{\text{surf}} = 4\pi^2 r(R - r)$, $V = 2\pi^2 r^2 (R - r)$; for the disc-like conformation $S_{\text{surf}} = 2\pi R^2 + 2\pi r R$, $V = \pi R^2 r$; and for the conformation of a cylinder $S_{\text{surf}} = 2\pi r R + 2\pi r^2$, $V = \pi r^2 R$.

Let us first consider the limit of very long chains and write out the N-independent terms from expressions (19)–(21) for the free energy per dimer unit $F/N (N \to \infty)$:

$$\frac{F}{N k_{\text{B}} T} = \frac{B}{2}\phi + \frac{C}{6}\phi^2 + \alpha_{\text{conf}} \frac{a^2}{r^2} + \alpha_{\text{orient}} \frac{\varepsilon_{\text{Ps}} \phi v^{1/3}}{r}. \tag{22}$$

The size r in expression (22) corresponds to the minimum characteristic size of the globule. Different shapes of globules correspond to different values of the factors α_{conf} and α_{orient}: $\alpha_{\text{conf}} = 1$ for the disc and torus-like conformations; $\alpha_{\text{conf}} = 2$ for the conformation of a cylinder; $\alpha_{\text{conf}} = 3$ for the bead-like conformation; $\alpha_{\text{orient}} = 1$ for the disc, cylinder, and torus-like conformations; $\alpha_{\text{orient}} = 3/2$ for the bead-like conformation.

Minimizing the free energy F (22) with respect to the size r and to the volume fraction ϕ, we obtain the minimum value of the free energy:

$$\frac{F_0}{N k_{\text{B}} T} = -\frac{C \phi_0^2}{6(1 - \alpha_0 \beta)}, \tag{23}$$

where $\beta = 3\varepsilon_{\text{Ps}}^2 / 8Cg^2$ is the parameter characterizing the orientational ability of dimer units and determined by the relation between ε_{Ps} and the flexibility parameter $g = a/v^{1/3}$. The coefficient α_0 is determined by globule shape: $\alpha_0 = 4$ for the disc and torus-like conformations; $\alpha_0 = 3$ for the bead-like conformation, $\alpha_0 = 2$ for the conformations of a cylinder.

The equilibrium values of the volume fraction and globule size are

$$\phi = \frac{\phi_0}{(1-\alpha_0\beta)}, \qquad r = \frac{\alpha_{\mathrm{conf}}}{\alpha_{\mathrm{orient}}}\frac{(1-\alpha_0\beta)g^2}{|\varepsilon_{\mathrm{Ps}}|\phi_0}v^{1/3}. \tag{24}$$

As can be seen from expression (24), the equilibrium volume fraction of monomer units in amphiphilic globules is larger than the volume fraction ϕ_0, and it increases with increasing $|\varepsilon_{\mathrm{Ps}}|$. The increase of the globule density is due to the tendency of dimer units to locate at the surface, the fraction of monomer units at the surface is inversely proportional to the globule size $M_{\mathrm{surf}}/N = S_{\mathrm{surf}}v^{1/3}/V \sim 1/r$ (r is the radius of the sphere or cylinder, the width of the disc etc), and therefore the smaller globule with the larger density is more favourable for surface contacts of polar groups with solvent. At the same time, this tendency should lead to inhomogeneous globule density: a denser shell and rarefied core. However, the consideration of this effect demands rather more cumbersome calculations and we neglect it, assuming that the character of shape transitions for amphiphilic globules remains unchanged.

The maximum value of α_0 in the expression (23) corresponds to the minimum value of the free energy F; therefore, the most favourable conformations of the amphiphilic globule are disc and torus-like ones. To distinguish between these shapes, we extend the expression for the free energy (18)–(21) for the disc and torus-like conformations in powers over $1/N$:

$$\frac{F_{\mathrm{dt}}}{Nk_{\mathrm{B}}T} = \frac{F_0}{Nk_{\mathrm{B}}T} + 2\gamma\left(\frac{8\pi g^5(1-4\beta)}{N\varepsilon_{\mathrm{Ps}}^2\phi_0}\right)^2\left[1-\left(\frac{2g^6(1-4\beta)^2}{N\varepsilon_{\mathrm{Ps}}^3\phi_0^2}\right)^2\right], \tag{25}$$

where $\gamma = 1$ for a disc-like and $\gamma = \pi^2$ for a torus-like conformation. Since the correction to F_0 is larger for the torus-like conformation, then the disc-like globule should be observed for large but finite values of the chain length N. The appearance of the torus-like structure can be expected for not very large N, when the second correction to the free energy F_0 in expression (25) is essential: $N < N_{\mathrm{cr}} \approx g^6/(\phi_0^2|\varepsilon_{\mathrm{Ps}}^3|)$. The bead-like structure can be formed if the first correction to the free energy is comparable with F_0: $N < N_{\mathrm{cr}} \approx g^5/(\sqrt{C}\phi_0^2\varepsilon_{\mathrm{Ps}}^2)$.

To obtain the complete shape diagrams, we calculate the free energy F (18)–(21) numerically, besides, the free energy for the bead-like conformation was analysed directly for $m = 1, 2, 3$ beads. The most favourable conformations for the amphiphilic molecule are presented at the shape diagrams depending on the parameters ($\varepsilon_{\mathrm{HH}}$, $\varepsilon_{\mathrm{Ps}}$) for different chain lengths and flexibilities (figure 7). The solvent quality is determined by the second virial coefficient and depends on both interaction energies $\varepsilon_{\mathrm{HH}}$ and $\varepsilon_{\mathrm{Ps}}$: $B = \varepsilon_{\mathrm{HH}}/2 - 2\varepsilon_{\mathrm{Ps}} + v/v_{\mathrm{s}}$. The straight line in the figure is the boundary between the coil and globular state corresponding to the zero second virial coefficient $B = 0$. With the change of the solvent quality the macromolecule coil transforms to the system of beads and, then, into the disc conformation for flexible chains or into the torus-like conformation for rigid chains. For the small values of $|\varepsilon_{\mathrm{Ps}}|$ the macromolecule forms only one bead (spherical globule), which turns to the disc or torus. The chain flexibility and the value of the interaction energy $\varepsilon_{\mathrm{Ps}}$ determine the equilibrium number of beads: the dashed curve with the number i separates the bead-like conformations with i and $i+1$ beads. The number of beads at the transition to disc or torus conformation can be predicted from figure 7 as well.

The structural transitions for flexible amphiphilic macromolecules were earlier investigated in computer experiments [30]. The transitions with decreasing second virial coefficient were the following: from a coil to a necklace-like conformation, then to sausage-like, and then to a cylindrical form. In our consideration the decrease of the second virial coefficient corresponds to the motion along the arrows in figure 7. Flexible macromolecules also transform from coil into beads, and then beads diminish in size and merge, forming a sausage-like conformation near the boundary between the necklace-like and disc-like

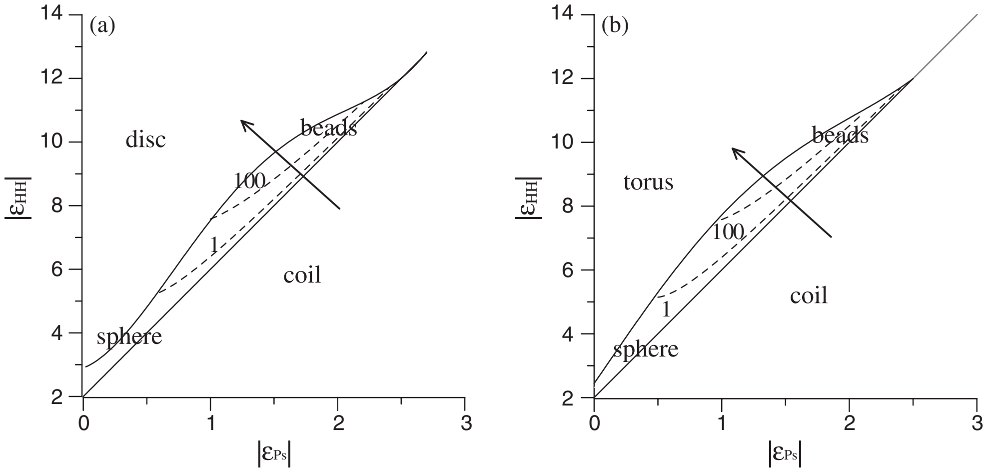

Figure 7. The shape diagram for amphiphilic globules depending on the interaction energy of polar groups and solvent ε_{Ps} and on the H–H group interaction energy ε_{HH}. The chain length $N = 10\,000$, the flexibility parameter $g = 1$ (a), $g = 5$ (b), the second and third virial coefficients $B = \varepsilon_{HH}/2 - 2\varepsilon_{Ps} + v/v_s$ and $C = v/v_s = 2$.

conformations. Therefore, the formation of sausage-like globules in computer simulations is in agreement with our consideration.

In a very poor solvent the amphiphilic macromolecules should form a disc-like conformation (the upper left corners at the diagrams 7(a), (b)). However, the disc-shaped globules were not obtained in computer experiments [30]. As we can assume, the sausage-like rather than disc-like globules were formed for kinetic reasons: a high threshold exists between these two conformations in poor solvent. We predict that a disc-like conformation can be obtained in a poor solvent for not very high values of the interaction energies ε_{HH}, ε_{Ps} via the deformation of a single globule rather than the transformation of a necklace-like structure.

Our consideration does not predict the formation of cylinder-shaped globules. This fact relates to the assumption of the high conformational free energy (20) of a chain confined in a narrow region in two dimensions for a cylinder. However, the present approach does not forbid the formation of a cylinder or other conformations, since very approximate expressions are used and the energetic benefit from the microsegregation in the globule is not taken into account.

The shape diagrams in the variables (ε_{Ps},g) are presented for loose globules (figure 8(a)) and for dense globules with $\phi = 1$ (figure 8(b)). With the increase of the interaction energy $|\varepsilon_{Ps}|$, the role of the orientational free energy F_{orient} increases ((18), (21)) and the larger surface area is more favourable. At the same time, the conformational free energy F_{conf} ((18), (20)) has the minimum over globules of the same volume for the spherical shape. For small values of $|\varepsilon_{Ps}|$ a single spherical globule is formed; the increase of the value $|\varepsilon_{Ps}|$ leads to the transition to several beads. The bead radius remarkably depends on the chain flexibility and ε_{Ps}, as can be obtained from the expressions (24): $r/v^{1/3} \approx 4(1 - 3\beta)g^2/(\phi_0|\varepsilon_{Ps}|)$. The equilibrium number of beads is approximately proportional to the length of the macromolecule.

When the size of the beads becomes quite small, the macromolecule becomes strongly deformed, this fact giving rise to further conformational transitions. At some critical size of beads the globule transforms into a disc or torus depending on the chain flexibility. The surface area of the disc and torus at the transition curve is somewhat less than that for the beads, whereas the deformation of the chain considerably decreases. For the more rigid macromolecules all transitions take place for the larger globule sizes for both conformations.

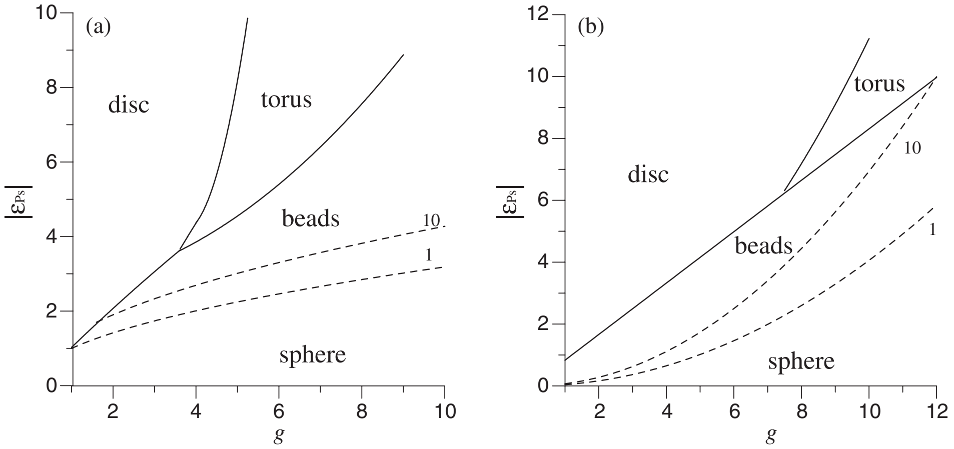

Figure 8. The shape diagram for amphiphilic globules depending on the interaction energy of polar groups and solvent $\varepsilon_{\mathrm{Ps}}$ and on the flexibility parameter g. The chain length $N = 1000$, the virial coefficients $B = -1/3$, $C = 2$ (a), and the volume fraction $\phi = 1$ (b).

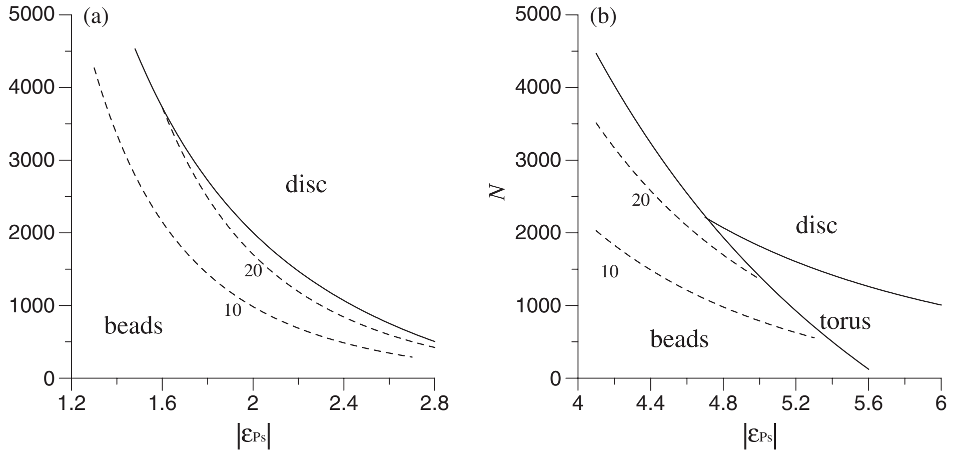

Figure 9. The shape diagram for amphiphilic globules depending on the interaction energy of polar groups and solvent $\varepsilon_{\mathrm{Ps}}$ and on the chain length N. The flexibility parameter $g = 3$ (a), $g = 5$ (b), the virial coefficients $B = -1/3$, $C = 2$.

The shape diagram for dense globules (figure 8(b)) slightly differs from that for loose globules mainly in the number of beads: the chain with dense structure does not form many beads. The size of beads is considerably smaller for the chain with $\phi = 1$, since the high conformational free energy of chain segments in such beads prevents their splitting.

It is worthwhile to note that a torus-like structure was considered earlier for a persistent homopolymer macromolecule in poor solvent, where the transitions from a coil to torus-like, and then to spherical conformation were predicted with increasing effective interaction energy of monomer units [12]. Such a sequence of conformational transitions differs from that in our consideration, since we take into account the negative interaction energy of dimer units at the surface oppositely to the positive surface energy of homopolymer globules.

To reveal the behaviour of an amphiphilic macromolecule with increasing chain length, the shape diagrams in the variables (N, $|\varepsilon_{\mathrm{Ps}}|$) are presented in figure 9. The existence of the

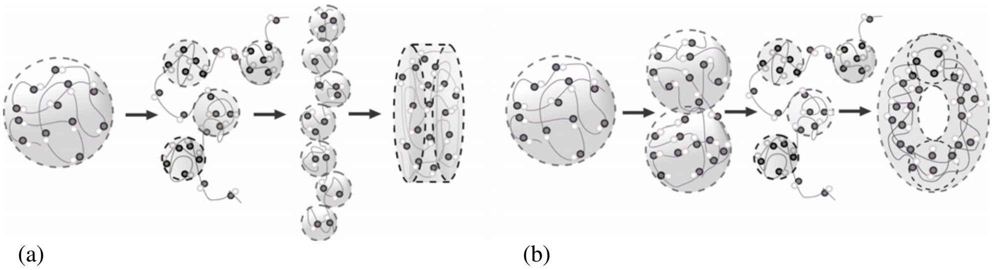

Figure 10. The transformations of a flexible (a) and rigid (b) amphiphilic macromolecule with increasing interaction energy of polar groups and solvent $|\varepsilon_{\mathrm{Ps}}|$.

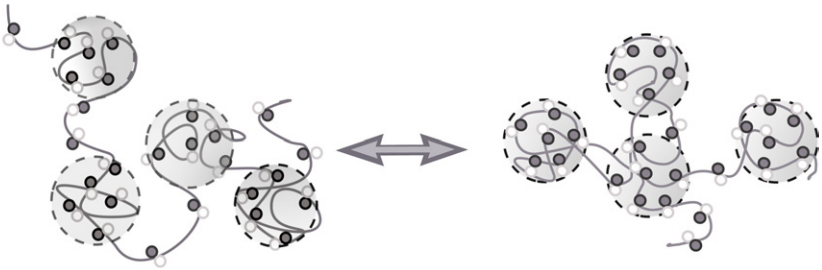

Figure 11. The types of bead-like conformation.

torus-like conformation is expected for not very long chains with high stiffness (figure 9(b)). For longer chains the transition from beads to disc-like conformation takes place for smaller values of the interaction energy $|\varepsilon_{\mathrm{Ps}}|$ in accordance with expression (25).

The sequence of shape transformations for flexible and rigid chains of the same length is illustrated in figure 10. Note that the bead size at the transition from beads to torus-like conformation (b) is larger than that for the transition from beads to disc-like conformation (a).

Besides, it is worth noting that for a bead-like structure the present approach does not predict the type of bead connection by linear parts of the chain. A necklace-like linear structure and any branched more compact structures of a macromolecule are possible as illustrated in figure 11. Only the number of beads which can be considered as structural subunits of a globule is predicted depending on the unit interaction energies, chain length, and flexibility.

5. Conclusions

In the present paper we investigated the globular state of amphiphilic macromolecules with hydrophobic–polar units. Such units orient at the globule surface, decreasing their interaction energy with solvent. We first considered large spherical globules formed by macromolecules with low orientation ability of the units. The competition between the interaction and the entropy contributions of oriented dimer units determines the distribution function of unit orientation, which depends on the concentration gradient and on the unit orientation ability: for the higher gradient the units are more strongly oriented towards the globule surface. The concentration profile at the surface layer and the surface tension are obtained from minimization of the free energy of the macromolecules. The orientation of monomer units diminishes the surface tension and makes the volume fraction profile steeper and non-symmetrical in comparison with homopolymer globules of the same density.

The shift of the coil–globule transition temperature is proportional to the change of the surface free energy. Thus, the decrease of the surface tension gives rise to more stable (with respect to a coil–globule transition) amphiphilic globules in comparison with homopolymer globules.

With further increase of orientational ability of monomer units the surface layer becomes very narrow (with the size comparable with one monomer unit). Therefore, the density gradient becomes very large and the method of the density functional cannot be used directly. In this case we proposed to write the expression for the free energy of the whole globule including the surface interaction and volume interaction contributions, and the conformational free energy. Then, we considered several globule shapes in order to select the equilibrium one and to find the equilibrium size of the globule depending on the solvent quality and chain length. We obtained the shape diagrams and the sequence of structural transitions for amphiphilic globules. The transitions with decreasing second virial coefficient are the following: from a coil to a bead-like conformation, and then to a disc-like form for flexible chains or to torus-like shape for stiff chains.

It is worth noting that the aggregation of the amphiphilic globules can be prevented by the oriented dimer units at the surface and, then, single macromolecular structures can be stable.

Our shape diagrams mainly agree with the results of molecular dynamics simulations for the same model of flexible amphiphilic macromolecules except for the possibility of formation of a disc-like structure in very poor solvent [30]. In the computer experiments the sausage-like and cylinder globules were obtained for the flexible chains at the conditions of poor solvent. The formation of cylinder globules is not predicted in our model, possibly because of neglecting the energy benefit from the microsegregation in the globules. Besides, we assume that the cylinder conformation is easier to obtain than the disc-like globules for kinetic reasons, and that further transformation to a disc can be hindered because of the high energy threshold. At the same time, the existence of disc-shaped biomacromolecules and synthetic amphiphilic polymers is well established [1, 2, 8].

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