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Morphological diagram of amphiphilic *H-graft-P* macromolecules: Theory and computer experiment

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ABSTRACT

The morphological diagrams of *H-graft-P* macromolecules in poor solvent were evaluated by means of molecular dynamics simulations and analytical theory. The Diagrams contain regions of spherical solid, onion-like and vesicle particles, domains of elongated (disc-like, torus, and worm-like) structures, and the area with necklace and coil conformations. The diversity of different morphologies is a result of surface activity of monomer units leading to formation of surface-rich structures and outward orientation of polar groups at the surface. The shape depends on the macromolecule length, solvent quality and monomer unit characteristics. The Diagrams were constructed basing on the visual analysis and on the calculations of shape factors and aggregation numbers, and evaluated by the original analytical theory, where the interplay of bulk and surface effects determines the globule shape.

1. Introduction

Monomer units of many biological and water soluble artificial polymers comprise both hydrophobic and hydrophilic groups and have, in fact, an amphiphilic nature, being simultaneously affined and incompatible with polar as well as organic solvents [1–3]. The two-dimensional classification of amphiphilic monomers with respect to their partition between different solvents and accumulation at the interface was proposed in Refs. [2,3]. It reveals that many of amphiphilic repeat units have tendency toward interface concentration and could bear substantial surface activity. It was accounted for by simplest model of amphiphilic monomer units [4], which involves two different beads *H* (hydrophobic, insoluble) and *P* (polar, hydrophilic) linked by a fixed-length bond. The chain of amphiphilic *H-graft-P* units, connected with each other, is referred to as an amphiphilic homopolymer [4], in sense that the macromolecule is composed of the only type of repeat units and it is amphiphilic on the level of an individual monomer.

The conformational properties of amphiphilic homopolymers are significantly different from those of classical homopolymer chains of identical single-bead monomers [5]. It was shown that depending on the solvent quality and selectivity, individual amphiphilic homopolymers could self-assembly into different structures such as soluble core-shell globules, necklace conformations, cylindrical (worm-like), toroidal and vesicle-like particles [4,6–16]. Formation of these structures is triggered by the tendency of monomer units to be located in the way that the hydrophobic groups interact mainly with each other, while hydrophilic groups are immersed into the solvent and avoid contacts both with each other and hydrophobic groups. This leads to intramolecular segregation and formation of above-mentioned structures with enlarged, in comparison with a spherical shape, surface area (for sure, such structures emerge only at sufficiently high degree of polymerization).

Some of these structures are similar to multimolecular aggregates self-assembling in solutions of surfactants [17–20], lipids [21–27] and amphiphilic diblock-copolymers [28,29] and proteins [30,31] and relevant for many practical applications based on encapsulation and target delivery of hydrophobic or hydrophilic substances [21–26,29–31]. The multimolecular aggregates are built up by a huge number of molecules above critical micelle concentration [32]. In many cases, the formation of aggregates with a desired shape and size requires the complex techniques allowing condensation of appropriate quantity of amphiphilic molecules within proper volume [33–36]. The creation of those structures, especially hollow vesicles, demands careful selection of methods

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and precise control at each stage of preparation, including the choice of solvent and co-solvent, mixing order and mixing rate, amphiphile concentration, etc.

In amphiphilic homopolymers, the amphiphiles are connected into a chain by chemical bonds. That allows concentrating the amphiphiles just by solvent quality worsening and conformational transitions caused by it. As a result, the aggregates are formed by a single macromolecule and can be created at extremely low polymer concentration. One could expect that the shape and size of structure could be designed by an appropriate choice of amphiphilic macromolecule degree of polymerization. Other important factors governing self-organization are solvent selectivity and surface activity of monomer units.

The aim of the present study is to investigate the influence of macromolecular degree of polymerization on the self-organization of single amphiphilic homopolymers, to obtain a morphological diagram in coordinates of the contour chain length and surface activity (*H-P* incompatibility) of monomer units and, in particular, to find the areas of vesicle-like particle stability. For this purpose, we perform computer modelling and develop analytical theory.

2. Computer modelling

2.1. Model and technique of experiment

A macromolecule consists of N repeat units, each unit represented by *H-P* “dumbbell” of hydrophobic *H* and hydrophilic *P* beads. Beads *H* form a backbone of the macromolecule, and beads *P* are side pendants (Fig. 1). The macromolecule is immersed in excess of solvent being poor for main chain *H* beads and good for side *P* groups.

Computer simulations are carried out in a continuum space, time evolution of the system is determined by solving the Newton equations of motion using molecular dynamics technique. LAMMPS software package is applied [37].

The excluded volume between any two non-connected beads is considered via the repulsive part of Lennard-Jones potential:

$$E_{LJ}(r_{ij}) = \begin{cases} 4\varepsilon\left[\left(\dfrac{\sigma}{r_{ij}}\right)^{12} - \left(\dfrac{\sigma}{r_{ij}}\right)^{6} + \dfrac{1}{4}\right], & r_{ij} \le r_c \\ 0, & r_{ij} > r_c \end{cases}, \qquad (1)$$

where r_{ij} is the distance between i-th and j-th groups, $r_c = {}^{1/6}\sqrt[6]{2}\sigma$ is a cutoff distance of the potential; ε is a parameter controlling the energy scale, σ determines a length scale. We put $\varepsilon = \sigma = 1$, so that all of the results are presented in terms of parameters ε and σ.

Hydrophobic-hydrophilic intrachain interactions, induced by the solvent, are implicitly accounted for by the Yukawa-type potential:

$$E_{Y(\alpha\beta)}(r_{ij}) = \begin{cases} \varepsilon_{\alpha\beta}\left(\dfrac{\exp(-\kappa r_{ij})}{r_{ij}} - \dfrac{\exp(-\kappa r_{cY})}{r_{cY}}\right), & r_{ij} \le r_{cY} \\ 0, & r_{ij} > r_{cY} \end{cases}, \qquad (2)$$

where $r_{cY} = 4\sigma$ is a cutoff distance, $\kappa = 0.1$ is an inverse screening length, $\varepsilon_{\alpha\beta} = (\varepsilon_{HH}, \varepsilon_{PP}, \varepsilon_{HP})$ is an energetic parameter of pair *H-H*, *P-P* and *H-P* interactions. In accordance with the main aim of paper, we assume that (*i*) there are no additional interactions between side hydrophilic groups except the excluded volume interaction and set $\varepsilon_{PP} = 0$; (*ii*) the hydrophobic groups strongly attract each other and characteristic energy of *H-H* interactions is set to be negative: $\varepsilon_{HH} < 0$; (*iii*) the energy implicitly responsible for surface activity of monomer units is positive ($\varepsilon_{HP} > 0$) and is varied in the wide region: $0 \le \varepsilon_{HP} \le 2$.

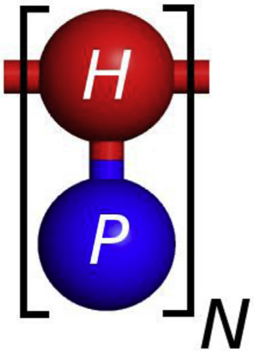

Fig. 1. Schematic representation of amphiphilic monomer unit.

An increase in repulsive interactions between *H* and *P* groups leads to growth of effective υ_{HP} second virial coefficient

$$\upsilon_{HP}(\varepsilon_{HP}) = \frac{1}{2}\int_0^{r_{cY}}\left[1 - \exp\left(-\frac{E_{LJ}(r) + E_{Y(HP)}(r)}{k_B T}\right)\right]d^3r$$

where T is temperature, k_B is the Boltzmann constant ($T = \frac{\varepsilon}{k_B}$), and its normalized value

$$B_{HP} = \frac{\upsilon_{HP}(\varepsilon_{HP})}{\upsilon_{HP}(0)} \qquad (3)$$

Neighboring *H* groups in the backbone and groups *H* and *P* in one “dumbbell” are connected via the rigid spring potential:

$$E_{bond} = K(r_{ij} - b)^2 \qquad (4)$$

here r_{ij} is the distance between i-th and j-th beads; $b = 1$ is the length of the bond; $K = 10000$ is a coefficient, which numerical value is sufficiently large to provide that bond length varies no more than by 1%.

The temperature T is kept constant by the Langevin thermostat. Also the equations of motion are supplemented by the drag force term $F_f = -\frac{m_b}{D}v$ (here, m_b is the mass of a bead, v is its velocity, $D = 100$ is a damping factor showing that temperature is relaxed within 100 time steps) and Langevin uncorrelated noise term $F_r \sim \sqrt{2k_B T m_b / Ddt}$, where $dt = 0.005\sigma\sqrt{\frac{m_b}{\varepsilon}}$ is the integration step. For integration of the equations of motion, the velocity Verlet algorithm is applied.

The simulation proceeds in a cubic cell with periodic boundary conditions, the length of the cell edge is varied from $L = 400$ to $L = 600$ depending on the polymerization degree N: $128 \le N \le 4096$. First relaxation was carried out for 2×10^7 time steps at $\varepsilon_{HH} = \varepsilon_{HP} = 0$. Then we use different procedures to reach target values of ε_{HP} and ε_{HH}. One scenario, during next 2×10^7 time steps, the calculation proceeds at $\varepsilon_{HH} = 0$ and $\varepsilon_{HP} > 0$ (ε_{HP} is chosen within the interval $0 \le \varepsilon_{HP} \le 2$ with the step $\Delta\varepsilon_{HP} = 0.1$). After that, ε_{HH} is smoothly changed from $\varepsilon_{HH} = 0$ to $\varepsilon_{HH} = -3.0$ with the step $\Delta\varepsilon_{HH} = -0.2$ and prolonged relaxation, 2×10^7 time steps at each stage, allowing to avoid quenching and to achieve equilibrium structure. Another scenario, vise versa, parameter ε_{HH} is changed stepwise from $\varepsilon_{HH} = 0$ to $\varepsilon_{HH} = -3.0$ with the step $\Delta\varepsilon_{HH} = -0.2$ and for each fixed ε_{HH} the value of ε_{HP} is increased smoothly from 0 till 2.0 with 2×10^7 time steps relaxation at each point. For the last