INTRODUCTION

Amphiphilic polymers are of great interest because of their ability to self-assemble in selective solvents and to form stable aggregates (globules, mesoglobules, spherical micelles, threads, vesicles, etc.) with a few nanometers to micrometers in size or above as well as complex bicontinuous structures [1–9]. These objects can serve as a basis for the design of new functional and composite materials and as models of proteins and other biopolymers.

Amphiphilic chains comprise two types of units, i.e., soluble (polar P) and insoluble (hydrophobic H) units [5–9]. In some cases, the units can dissociate into ions and thus change solubility. This circumstance makes it possible to flexibly control the structure of solutions, for example, via addition of a salt. The mechanism of structure formation in solutions of amphiphilic chains is associated with two competing processes: On the one hand, the insoluble units have a tendency to aggregate and precipitate; on the other hand, the polar units tend to contact with the solvent, emerge on the surface of the aggregate, and hinder the aggregation process. Thus, there is formation of hydrophobic regions separated from the solvent by a shell of polar units [10–13]. This behavior of amphiphilic polymers is qualitatively different from the behavior of purely hydrophobic chains, which form separate globules at low concentrations of chains and precipitate with an increase in concentration [2, 3]. The presence of soluble units in the chain significantly increases the region of stability of the globules and contributes to the formation of mesoglobules and micelles that comprise a few chains. The hydrophilic units localized on the surface of these particles serve as a barrier to their further growth. In this case, the arrangement of the polar and hydrophobic units along the chain, i.e., the architecture of the chain, plays an important role [5, 7, 8, 10]. Stabilization of the aggregates can occur at both the thermodynamic level and the kinetic level.

To date, the most extensively studied systems are solutions of diblock copolymers containing hydrophobic and hydrophilic blocks [14–19]. The micelles resulting from the aggregation of these chains comprise a core formed by hydrophobic blocks and a shell built up of the polar blocks. Depending on the block length ratio, we can single out two limiting cases: (i) starlike micelles whose soluble corona exceeds the size of the insoluble core and (ii) crew-cut micelles whose corona is much smaller than the core. These micelles are the main subject of theoretical studies [20–23]. In real experiments, the size of the corona is usually comparable with the size of the core. A theoretical analysis of this general case is fairly complicated; it is the subject of forthcoming research.

The aggregation processes occurring in solutions of amphiphilic macromolecules of a more complex architecture have been studied to a lesser extent. These systems can form complex-shaped aggregates with a
core—shell structure [7, 8, 24–29]. Below, we focus on two examples that not only are of practical interest but also are important for the development of the theory. These examples are solutions of model oligopeptides that contain hydrophobic alanine (Ala) and charged aspartic acid (Asp) [30] and solutions of HP copolymers in which polar side P groups have a rigid bond to the hydrophobic backbone [6, 29, 31]. The study of these systems has recently made some progress. The choice of alanine and aspartic acid as subjects of research is, in a sense, a coincidence. The approach proposed in this paper can be used to study also other oligopeptides that contain both neutral and charged amino acid residues.

AGGREGATION IN SOLUTIONS OF MODEL OLIGOPEPTIDES

We begin our discussion with aqueous solutions of model oligopeptides that comprise amino acids of two types, i.e., hydrophobic alanine and polar aspartic acid. Aspartic acid that has undergone dissociation of the carboxyl group, $-\text{COOH} \rightarrow -\text{COO}^- + \text{H}^+$, becomes negatively charged. The general formula of the studied oligopeptide chains has the form $\text{Ala}_n\text{Asp}_m$. Consider four types of chains for which $n_p = 2$ and $n_H = 24$.

![Diagram of chains]

The total number of units in the chain is $n = n_H + n_p = 26$, and its contour length is $L = nl$ ($l \approx 0.4$ nm and $L \approx 10$ nm). It is obvious that these systems are difficult to analyze; therefore, we will further restrict ourselves to simple and fairly general model representations. Consider first the free chains. We denote the concentration of $\text{H}^+$ protons in solution through $cp$. It is related to pH through the formula $cp = 10^{-\text{pH}} [\text{M}]$, where $[\text{M}] = N_A \times 10^{-3}$ cm$^{-3}$. The constant of the proton addition to the carboxyl group (the protonation reaction), $k_1$, is written as $k_1 = 10^{pK}$. The fraction of charged Ala units in the solution is $\alpha = \frac{1}{1 + kcp} = \frac{1}{1 + kcp}$, where the parameter $\lambda = 10^{-\text{pH} + pK}$ defines the ratio of neutral Ala units to the fraction of charged Ala units. If we assume that the statistical weight of the dissociated Ala units is unity, the statistical weight of neutral Ala units can be represented as $w = cpv_{\text{bond}}E_1$, where $v_{\text{bond}}$ is the bond volume and $E_1$ and $E_2$ are the energies of the dissociated and neutral Ala units, respectively. In this case, $\alpha = \frac{1}{1 + w} = \frac{1}{1 + \lambda}$ and $\lambda = w = cpv_{\text{bond}}E_1-E_2$.

There are several modes of behavior of a solution of oligopeptide chains. If the concentration of chains is fairly low, they are free and do not aggregate. As the concentration increases above a critical value (the critical concentration of micelle formation), the chains begin to form stable micelles. An alternative is the formation of a precipitate.

For further analysis, we need to estimate the value of $pK$ for the Asp units in water, in the surroundings of alanine, and at the interface. In water with a permeability of $\varepsilon \approx 80$, $pK$ is estimated as $\approx 4$. In the surroundings of alanine, a nonpolar substance with a permeability of $\varepsilon \approx 4$, $pK \geq 10$ [30]. This means that the dissociation of Asp units in a nonpolar environment barely occurs. If aspartic acid is localized at the interface, $pK = pK_\text{int} \approx 4.2$ [30]. Thus, the dissociation of Asp units mainly occurs in the solution and on the surface of the aggregate.

**Free Energy of a Micelle**

Suppose that we are dealing with the range of stability of the micelles. The interior of a micelle is formed by hydrophobic alanine, and the shell is stabilized by Asp units. The free energy of this micelle per chain can be represented as the sum of the energy of the hydrophobic core and the energy of the shell:

$$F_{\text{mic}} = F_{\text{core}} + F_{\text{shell}} \quad (1)$$

The energy of the core comprises two main contributions, i.e., the interaction energy of the units, $F_{\text{int}}$, and the elastic energy of stretching of alanine blocks, $F_{\text{elast}}$:

$$F_{\text{core}} = F_{\text{int}} + F_{\text{elast}} \quad (2a)$$

The energy of the shell is comprises the localization energy of Asp units on the surface of the micelle, $F_{\text{loc}}$, surface-tension energy $F_{\text{surf}}$, which includes the Coulomb interaction energy; and surface-bending energy $F_{\text{bend}}$:

$$F_{\text{shell}} = F_{\text{loc}} + F_{\text{surf}} + F_{\text{bend}} \quad (2b)$$

Energy $F_{\text{int}}$ can be written as

$$F_{\text{int}} = -n_{\text{H}}\varepsilon_{\text{H}} \quad (3)$$

where $\varepsilon_{\text{H}}$ is the gain in the energy of the alanine residue during its transition from the solvent to the core. Elastic energy $F_{\text{elast}}$ is associated with the tension of the alanine blocks in the core. Its calculation is a fairly intricate problem; therefore, the estimation of $F_{\text{elast}}$ is based on the results of numerical simulation of the behavior of free alanine chains via the Monte Carlo method [32]. An analysis of distribution function $f(r)$ of the distance between the ends of the alanine chain, $r$, which was derived in the above study, shows that, if the number of units is small ($\leq 20$), the distribution

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