ORIGINAL CONTRIBUTION

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Two-dimensional classification of amphiphilic monomers based on interfacial and partitioning properties. 1. Monomers of synthetic water-soluble polymers

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Abstract A classification of amphiphilic monomers based on the interfacial and partitioning properties has been proposed. Monomers partitioned at equilibrium between two immiscible phases were ascribed with a pair of parameters: standard free energy of adsorption at the interface and standard free energy of partition between the two phases. These two parameters are represented in a form of two-dimensional diagram (both of them being normalized by kT factor). Comparison of the parameters in question gives information on energetic preferences of the molecules to be located at the interface or in the bulk phases. Four monomers of synthetic water-soluble polymers, namely, N-isopropyl-acrylamide, 1-vinylimidazole, N-vinylpyrrolidone and N-vinylcaprolactam have been classified according to the above method at various temperatures. The possibility to extend the classification to arbitrary chemicals is discussed.

Introduction

Description of water-soluble polymers is one of the main research tasks of polymer chemistry and physics, since for natural macromolecules, such as proteins and DNA, water is the basic good solvent. Moreover, in last decades, synthetic water-soluble polymers found wide use in various biomedical applications [1–3]. Understanding of solution behavior of water-soluble polymers (both synthetic and natural ones) is often important for knowing their biological role. The properties of such macromolecules in solutions depend on complicated interplay between hydrophobic, dipole–dipole, electrostatic interactions and hydrogen bonding. Therefore, it is a topical problem to propose some models that could describe the complicated ensemble of forces in a simplistic, yet correct, way. One of the initial attempts to do that was undertaken by Lau and Dill [4, 5], who proposed the subdivision of monomer units into two classes: hydrophobic units (H) and polar units (P) (HP model). The chains of amphiphilic polymers are modeled as consisting of hydrophilic (polar) or hydrophobic point sites (beads) distributed along the backbone in a linear fashion (Fig. 1a). For aqueous systems, it is assumed that the hydrophilic beads are in good solvent, while hydrophobic beads are in poor solvent, so that H-units attract each other, whereas, the interaction between P-units is repulsive.

Biological proteins are widely considered as HP copolymers and it is believed that the spatial structure of globular proteins is of the core-shell type: the core is mainly formed by H-units, whereas, the shell of a globule consists of P-units interacting with the solvent molecules and preventing them from contact with the H-core. Thus, HP-model is widely used in protein-folding concepts.
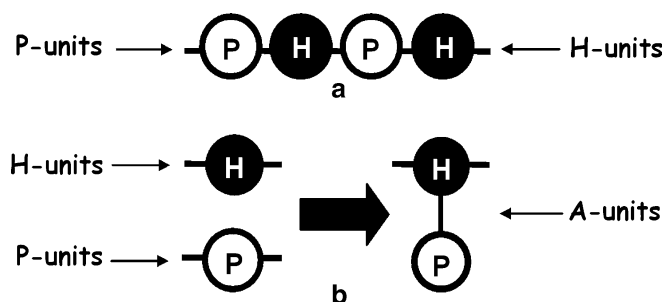
Fig. 1 Schematic representation of the HP-model (a) and the dumbbell HA-model (b) of a copolymer chain. H-units are hydrophobic, P-units are hydrophilic (polar) and A-units are amphiphilic

N-vinylpyrrolidone unit

ethylene oxide unit
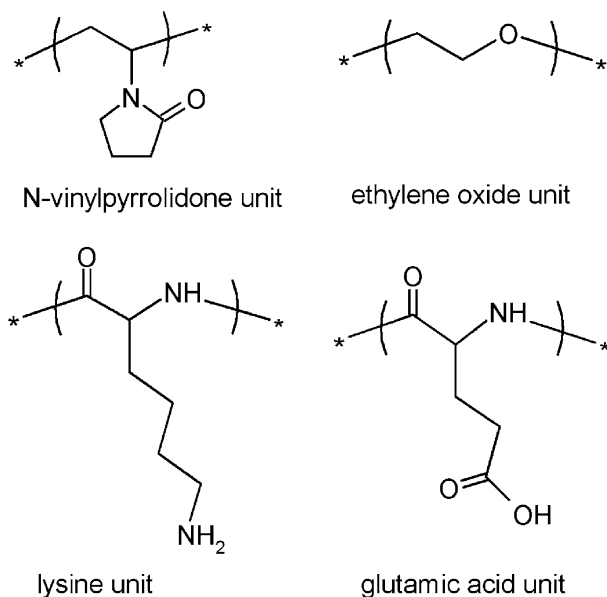
lysine unit

glutamic acid unit

Fig. 2 Amphiphilic monomer units of synthetic and natural polymers

However, looking at the chemical structures of both natural (e.g. amino acid units in polypeptides) and synthetic monomer units of water-soluble polymers (Fig. 2), it is easy to come to a conclusion, that they are neither hydrophilic nor hydrophobic, but rather amphiphilic, i.e. containing groups of both types (hydrophobic and polar). It appeared challenging to understand how the amphiphilic character of monomer units can affect the predicted properties of the water-soluble polymers and in references [6, 7], a new dumbbell model (HA-model) for copolymers in aqueous medium was introduced. In this model, amphiphilic monomer units (A-units) consist of two point sites (beads) each: hydrophobic beads represent nodes of a backbone, while polar (hydrophilic) beads represent side polar groups attached to the backbone nodes (Fig. 1b).

It was shown that in such model conformational properties of polymers, especially in the globular state, might be drastically different from those predicted by the model of H and P beads. In particular, it turned out that globules, formed by polymers containing amphiphilic (dumbbell) monomer units are not spherical.

While for purely hydrophobic or hydrophilic monomer units, the location only in hydrophobic or hydrophilic media should be suggested, for amphiphilic dumbbells the location at interfaces is most probable. In references [6, 7], it was found that this fact is indeed the main reason behind unusual conformational properties of polymers with amphiphilic monomer units. In that context, it was logical to estimate and compare the preferences of several widely used amphiphilic monomers to interface and bulk phases.

In the present study, we propose a thermodynamic classification of monomers according to a pair of properties: interfacial activity and affinity to hydrophobic or hydrophilic phase (partitioning properties). It is no news that each substance can be ascribed with the parameters characterizing its behavior at interfaces and partitioning between immiscible phases. Each parameter represents a quantitative tool for "one-dimensional" classification of a series of compounds according to the corresponding property. Indeed, a scale of n-octanol/water partition coefficient ($P_{o/w}$) [8] and reverse-phase chromatographic retention parameter [9] are widely used to characterize hydrophobicity of compounds; HLB (hydrophobic–lipophilic balance) scale [10] was introduced to classify surfactants according their emulsifying properties; solubility of compounds, which is a related property was characterized by Hildebrand solubility parameter (contribution of dispersion interactions) [11] and recently by solute–water association constants (contribution of hydrogen bonding) [12].

The parameters characterizing adsorption and partition properties are normally used independently of each other, even if measured or calculated together for certain compounds (e.g. [13–15]), and the attempts to trace correlations between thermodynamic parameters of adsorption and partition are scarce [16]. Hence, it appears a challenging task to unite in a systematic way the two one-dimensional classifications in question (i.e., classification by affinity to polar and non-polar phases and by interfacial activity) in a two-dimensional classification diagram.

For the illustration of the proposed diagram, four monomers of synthetic water-soluble polymers were classified according to the above principle. The experiments on interfacial and partitioning properties were carried out for N-isopropylacrylamide (NIPA), 1-vinylimidazole (Vim), N-vinylpyrrolidone (VP) and N-vinylcaprolactam (VC) (Fig. 3). Water was chosen as the hydrophilic phase, while hexane represented the hydrophobic one.
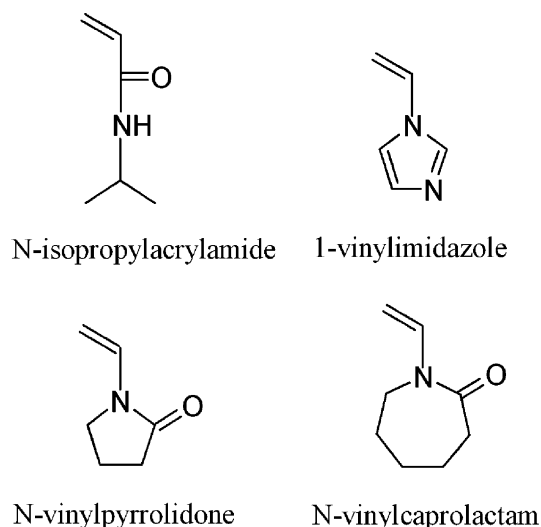
Fig. 3 Chemical structures of the monomers studied in the present paper

Table 1 Characteristics of light absorption by the monomers

	ε hexane (L/mol cm)	ε water (L/mol cm)	λ hexane (nm)	λ water (nm)
NIPA	3,400	7,200	221	221
Vim	10,500	9,300	234	226
VP	15,200	15,200	233	234
VC	10,000	11,400	236	237

Experimental section

Materials

VC and NIPA (Polysciences) were used as received. Vim (Aldrich) and VP (Merck) were distilled under reduced pressure and run through alumina column. Hexane (p.a. grade, Merck) was distilled at normal pressure and run through alumina column. Purity of hexane was checked by interfacial tension measurements: at 25 °C the interfacial tension at hexane/water boundary was found to be 50.4 mN/m, which is by 0.1 mN/m close to the literature data [17, 18].

Partition coefficient measurements

Equal-volume samples of hexane and water solution of the surfactant at known concentration c_w^0 were kept in contact at constant temperature long enough to obtain the partition equilibrium. The time for equilibration depended on experimental temperature and varied from 24 h to 72 h.

Partition coefficients were calculated using the well-known expression:

$$P = \frac{c_w^0 - c_h}{c_h}, \qquad (1)$$

where c_h is the equilibrium hexane concentration. The equilibrium concentrations of the substances studied were recorded spectrophotometrically, as they had UV-absorbing vinyl groups. Maximum absorption wavelengths and extinction coefficients both in water and hexane are presented in Table 1.

Interfacial tension measurements

The interfacial tension measurements were performed using drop-weight method [19, 20]. The experimental equipment was of the following type. A glass tube of the outer diameter $d = 0.675$ cm was attached to a burette with a point distance of 0.01 mL. Hereafter, the water phase was placed in the burette. The tip of the tube was placed in a thermostated vial containing the hexane phase. The drops were squeezed from the tube into hexane under the gravity force. The time of drop formation was always larger than 7 min, which allowed formation of equilibrium-size drops. In each experiment, 12–15 drops were collected. In most experiments, the total volume of drops was determined using reading of start- and end points of the liquid in the burette. To obtain a single drop size, the total volume was divided by the number of collected drops. The accuracy of this method of drop size measuring was 0.0003 mL, which was confirmed by weighting the collected drops in testing experiments.

The solutions for interfacial tension measurements were prepared using the same method as in partition coefficient measurements. After equilibration, the hexane and water phases were promptly separated from each other, the water phase being located in the burette, the hexane phase in the thermostated vial.

Results and discussion

As it was mentioned above, in this study, we propose the "two-dimensional" thermodynamic classification for amphiphilic monomers, which incorporates classifications by affinity to polar and non-polar phases and by interfacial activity (Fig. 4). Each substance can be ascribed with a two-dimensional coordinate, the abscissa and ordinate of which represent numeric characteristics for the above-stated properties. The abscissa dimension corresponds to the affinity to polar (water) or non-polar phase (hexane). The ordinate dimension corresponds to the interfacial activity. Standard free energy of partition between two phases is used as a quantitative parameter for the abscissa axis (ΔF_{part}), whereas, standard free energy of adsorption at interface defines the position along the ordinate axis (ΔF_{ads}).
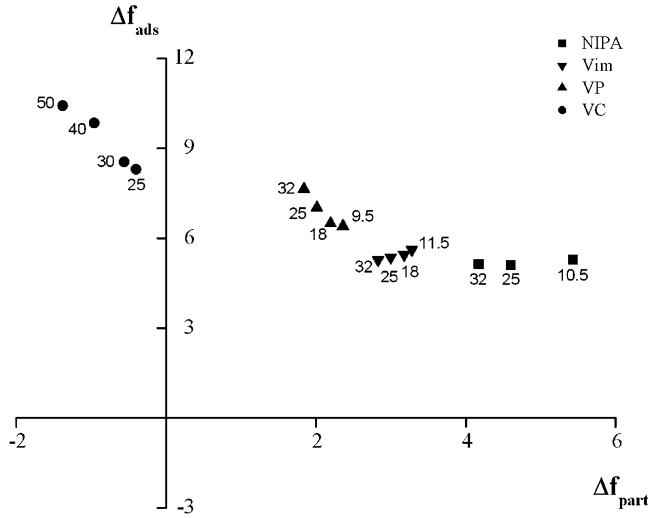
Fig. 4 Two-dimensional diagram of interfacial activity and phase affinity, general view

$$\Delta f_{\mathrm{ads}} = \ln\left[\alpha \cdot \frac{c_0}{\pi_0}\right] \tag{3}$$

$$\alpha = \left(\frac{\gamma^0 - \gamma}{c}\bigg|_{c\to 0}\right), \tag{4}$$

where c_0 is the standard state for the bulk solution, π_0 is the standard state for the interfacial monolayer, α is the derivative of interfacial pressure $\gamma^0 - \gamma$ with respect to concentration c, $c \to 0$.

It is evident that having chosen the standard state for the monolayer as a certain value of interfacial pressure, achieved by a hypothetic surfactant at a bulk concentration of 1 mol/L, we divide all the substances into two groups: those which give larger pressure at the same concentration represent interfacially active compounds, those which give the lower one are interfacially inactive compounds. This division is not applicable for the compounds, which tend to desorb from the interface, i.e. inorganic salts, some amino acids and carbohydrates. Indeed, if a substance desorbs from the interface, the resulting interfacial pressure would be negative, and in that case Eq. 3 has no sense. In reality, the described choice of the standard state can be successfully used only for compounds having high interfacial activity, where the total interfacial concentration of the surfactant is virtually equal to the excess interfacial concentration. If one is going to include into consideration the substances with low interfacial activity or those, which tend to desorb from the interface, it is worth-while to choose another standard state, the zero activity (no adsorption or desorption) being the most logical variant. However, it is well known that there is a problem of definition of interfacial layer associated to such a choice. As is known, there is no way to determine its thickness properly [21]. As a result, the concentration in the interfacial layer cannot be calculated precisely. However, in some cases a somewhat arbitrary value of 0.6 nm is postulated to be the average of the interfacial film thickness on condition that the film represents a monolayer [24–26]. If such assumption is made, the equation for standard free energy of adsorption can be written in the following form, first proposed by Langmuir [24]:

$$\Delta f_{\mathrm{ads}} = \ln\left[1 + \frac{\alpha}{RT\tau}\right], \tag{5}$$

where τ is the film thickness. Both for interface and bulk phases, standard concentrations are chosen as 1 mol/L (the corresponding factors are omitted in Eq. 5).

The Eqs. 2, 3 and 5 are based on the approximation that concentration is used instead of activity. This approximation is certainly valid for the case of relatively dilute solutions. In the present paper, partition coefficients for the use in Eq. 2 were determined for small

Both parameters are normalized by kT factor. The normalized values are denoted as Δf_{part} and Δf_{ads}, respectively. We define the sign of these parameters in such a way that the affinity to the water phase increases from the left to the right and the interfacial activity increases from the bottom to the top. Thus, we get a diagram with four quadrants: for hydrophobic interfacially active, hydrophobic interfacially inactive, hydrophilic interfacially inactive and hydrophilic interfacially active substances. For hydrophilic substances, Δf_{part} is postulated to be positive, while for hydrophobic ones it is negative. For interfacially active substances, Δf_{ads} is taken to be positive, while for interfacially inactive ones it is negative. From the above considerations, it is obvious that the proposed classification can be applied to compounds of any nature, not only to amphiphilic monomers, such as shown in Fig. 4.

The calculation of Δf_{part} was performed via partition coefficients,

$$\Delta f_{\mathrm{part}} = \ln P = \ln\frac{c_{\mathrm{w}}^0 - c_{\mathrm{h}}}{c_{\mathrm{h}}}. \tag{2}$$

Usually, for the calculation of free energy of adsorption, standard states are introduced, the definitions for which vary [21–23]. The value of standard free energy depends on the choice of the standard state. In fact, a standard concentration for the bulk solution is introduced, which is usually taken as 1 mol/L and a standard surface pressure is chosen for the interfacial monolayer, e.g. 1 mN/m [23]. However, this is not appropriate in our case, since such a choice will limit our classification. Indeed, for the standard free energy of adsorption the final expression is as follows:

concentrations of solute in both phases; α value in Eqs. 3 and 5 is, by definition, calculated for dilute solutions.

In our experiments, α was found via the Szyszkowsky equation [27]:

$$\frac{\gamma^0 - \gamma}{\gamma^0} = B\ln(\frac{c}{A} + 1),$$ (6)

where B and A are empirical constants. As the Szyszkowsky equation is empirical, it employs concentration, not activity, scale. It is valid for solutions of non-ionic surfactants at concentrations up to 1 mol/L [21]. To calculate α from the Szyszkowsky equation, interfacial tension measurements at several concentrations of solute were performed. The data obtained were fitted with the Eq. 6. When extrapolated to small concentration values, Eq. 6 can be approximated with a linear $\gamma-c$ dependency giving an expression for α [21]:

$$\frac{\gamma^0 - \gamma}{\gamma^0} = \frac{B}{A}c$$ (7)

$$\alpha = \frac{-\gamma^0 B}{A}.$$ (8)

For two contacting liquid phases in equilibrium, the adsorption of surfactant to the interface can take place from each of the phases. Accordingly, the standard Gibbs energies of adsorption can be calculated for both phases using the following equations:

$$\Delta f_{ads}^h = \ln\left[1 + \frac{\alpha_h}{RT\tau}\right]$$ (9)

$$\Delta f_{ads}^w = \ln\left[1 + \frac{\alpha_w}{RT\tau}\right],$$ (10)

where Δf_{ads}^h and Δf_{ads}^w are the standard free energies of adsorption from hexane and water, respectively; α_h and α_w are the derivatives of interfacial pressure with respect to concentration in hexane (c_h) and water (c_w), respectively, c_h, $c_w \rightarrow 0$.

It is logical to place the substances in the diagram in such a way that the ordinate axis represents standard free energy of adsorption from the bulk phase to which a substance's affinity is maximal (below we will refer to this choice as to the maximal affinity phase rule). In other words, for hydrophobic substances $\Delta f_{ads} = \Delta f_{ads}^h$, while for hydrophilic ones $\Delta f_{ads} = \Delta f_{ads}^w$.

As was said above, the behavior of four monomers of synthetic water-soluble polymers was analyzed with the help of the proposed two-dimensional diagram. For each monomer, a series of measurements was performed, in which the temperature effect on the position of experimental points in the diagram was studied. The results are given in Fig. 5.

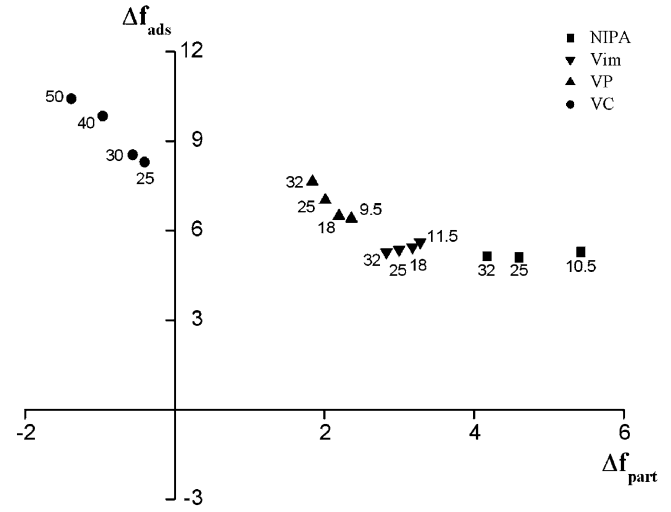Three of the four monomers (NIPA, Vim, VP) fall into the quadrant for hydrophilic interfacially active

Fig. 5 Two-dimensional diagram for monomers of synthetic water-soluble polymers. The numbers next to the points indicate measurement temperature in °C

compounds, whereas, VC finds itself in that for hydrophobic interfacially active compounds showing highest interfacial activity among the four. According to the maximum affinity phase rule formulated above, for VC $\Delta f_{ads} = \Delta f_{ads}^h$, while for VP, NIPA and Vim $\Delta f_{ads} = \Delta f_{ads}^w$.

The temperature behavior of the studied monomers is not the same. For all the four compounds, a decrease of the standard free energy of partition upon temperature increase is typical. Accordingly, they become more hydrophobic. This is logical since hydrophobic interactions have a tendency to increase with temperature [28]. The changes of the standard free energy of adsorption are different. When temperature is raised, both for VC and VP the increase of hydrophobicity is accompanied by the increase of interfacial activity. Vim shows the reverse tendency: its interfacial activity decreases with temperature, i.e., with hydrophobicity increase. As for NIPA, it shows almost no changes of interfacial activity with temperature.

If one compares Δf_{part} and Δf_{ads} of each monomer at a given temperature, it is clear that in most cases $|\Delta f_{part}| < |\Delta f_{ads}|$ (except NIPA at 10.5 °C), showing that the monomers have higher affinity to hexane/water interface than to the bulk phases. The behavior of the monomers is therefore amphiphilic, as they have both hydrophobic and hydrophilic groups in composition imparting them a tendency to have energetic preferences to interface rather than to hydrophobic or hydrophilic bulk phases.

Figure 6 shows the dependences of interfacial tension on concentration for NIPA, Vim, VP and VC. For each monomer, several isotherms measured at different temperatures are presented. For all the monomers studied, it is characteristic that at given equal concentrations of the
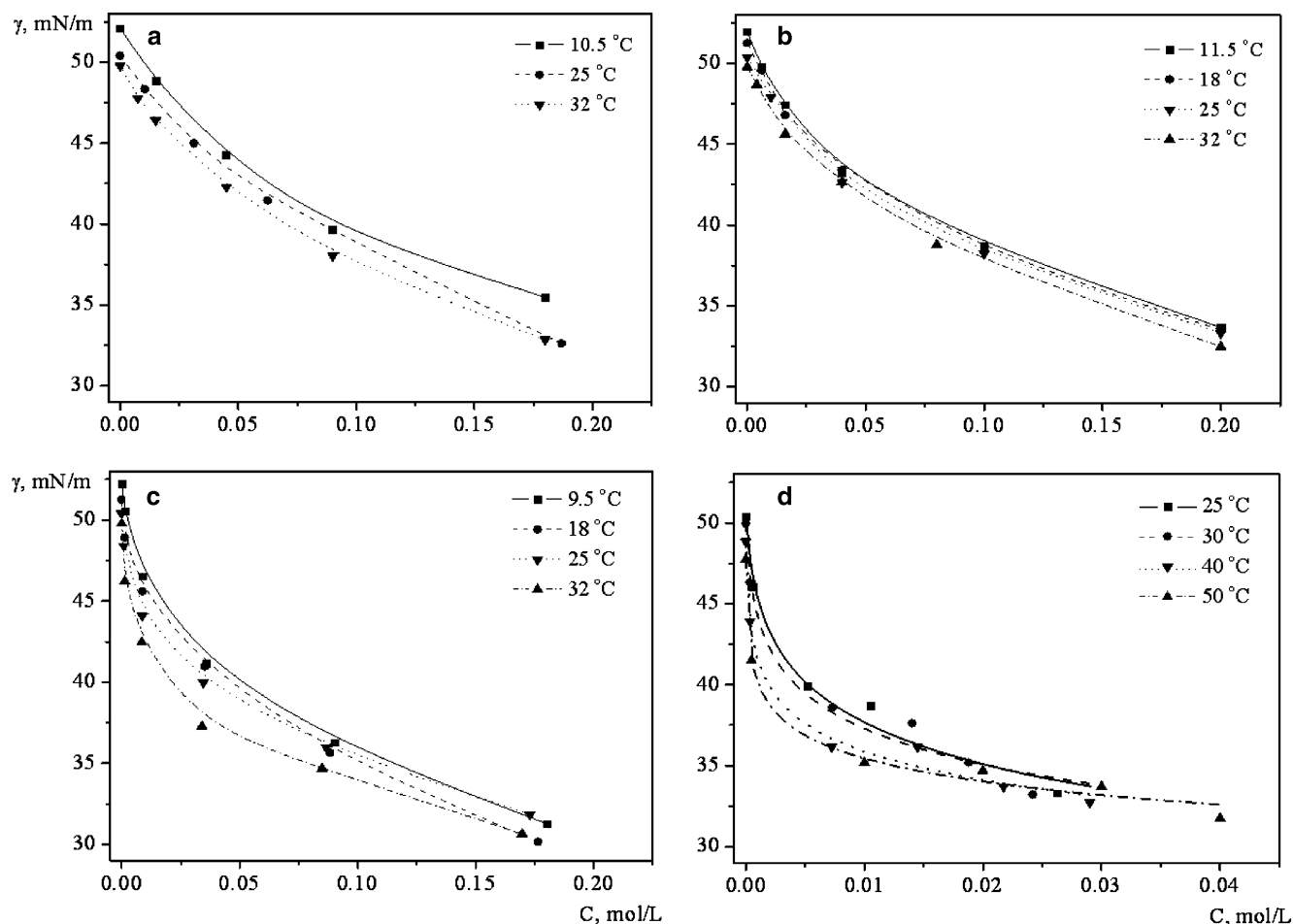
Fig. 6 Isotherms of interfacial tension at hexane/water interface for NIPA (**a**), Vim (**b**), VP (**c**), VC (**d**). Concentration scale refers to the water phase (**a–c**) and the hexane phase (**d**)

surfactant interfacial tension is smaller at higher temperatures than at lower temperatures. Despite the fact that the temperature dependences of the standard free energy of adsorption are not uniform for the monomers, the interfacial tension versus concentration dependences show similar behavior: raising temperature produces a shift of the isotherms down the ordinate, to the smaller interfacial tension values. It should be mentioned that the reverse regularities are also observed, where interfacial tension increases with temperature in the presence of oil-soluble tetradecanol [29]. On the other hand, in reference [30], where octaethylene glycol *n*-decyl ether was studied as a surfactant at hexane/water interface, the interfacial tension changes upon temperature variation were similar to those observed in this study.

We believe that the proposed diagram should be useful in predicting properties of the polymer systems with developed interfaces, (i.e., polymer globules, fine dispersions of polymer aggregates, micelles etc). Indeed,

normalized standard free energies of adsorption and partition (Δf_{part}, Δf_{ads}) are the factors, which quantify the affinity of molecules to bulk or interface. In case $\Delta f_{\mathrm{ads}} < \Delta f_{\mathrm{part}}$, the monomers are located mainly in the bulk phases (hydrophobic or polar), while if $\Delta f_{\mathrm{ads}} > \Delta f_{\mathrm{part}}$, the monomers are located primarily at the interfaces. Thus, the relation between Δf_{ads} and Δf_{part}, makes it possible to estimate semi-quantitatively the preferential distribution of monomers, monomer units or some other compounds in complex polymer systems. Furthermore, another way to use the diagram may be proposed. For a group of related compounds, one may get a special distribution of the datapoints after having put them in the diagram. In this distribution, it is possible to select subgroups of compounds with close values of Δf_{part} and Δf_{ads}. The hypothesis is that inside each subgroup some other properties might be quite similar. As an example, one may suggest a new classification of amino acid residues as protein monomers. Twenty amino acid residues may be split into several groups with similar Δf_{part} and Δf_{ads} values. Such classification will promote the search of correlations in protein sequences taking into account that it can be

assumed that basic properties of amino acid residues are connected with both their relative hydrophobicity/polarity and interfacial activity.

Conclusion

Two-dimensional diagram for classification of amphiphilic monomers on the basis of interfacial and partitioning properties have been proposed. As illustration, interfacial activity and partition between hexane and water phases were investigated for NIPA, Vim, VP and VC. Standard free energy of partition (Δf_{part}) and standard free energy of adsorption (Δf_{ads}) were taken as criteria for partition behavior and interfacial activity.

Variations of Δf_{part} and Δf_{ads} with temperature were studied. All the monomers considered become less hydrophilic upon temperature increase as indicated by the decrease of Δf_{part}. VC and VP become more interfacially active (Δf_{ads} grows) at the elevated temperatures, while Vim shows the reverse behavior. Δf_{ads} of NIPA is almost insensitive to the temperature regime. The isotherms of interfacial tension for all the monomers shift to the smaller values of interfacial tension with the increase of temperature, which correlates with the literature data.

Relative to the partition of the monomers between the bulk phases, it should be mentioned that VC has weak hydrophobic properties, while the other monomers are hydrophilic. VC was found to be most interfacially active of the four, which corresponds to the fact that hydrophilic and hydrophobic properties of this monomer are most balanced. However, for all the monomers $|\Delta f_{part}| < |\Delta f_{ads}|$ (except NIPA at 10.5 °C) and it may be stated that higher affinity to interface than to bulk phases is the key factor for those compounds.

Normalized standard free energies of adsorption and partition (Δf_{part}, Δf_{ads}) are the factors, which quantify the affinity of molecules to bulk or interface. In case $\Delta f_{ads} < \Delta f_{part}$, the overall bulk hydrophobicity/polarity is the key factor, while if $\Delta f_{ads} > \Delta f_{part}$, it is necessary to take into account primarily the ability of the molecules of the compound to adsorb at the interfaces. If the total interface area is small, the main part of the compound will be surely located in the bulk phases disregarding Δf_{ads} to Δf_{part} ratio. However, when the total interface area is large enough (e.g., in miniemulsions and biological tissues), the fraction of molecules adsorbing to the interfaces can be considerable. Thus, the proposed two-dimensional diagram method, which describes both bulk phases and interfaces as sites for the location of molecules of various compounds is promising from the viewpoint of predicting possible allocation of chemicals in the systems with developed interfaces.

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