Unified Thermodynamic Modeling of Polymer Solutions: Polyelectrolytes, Proteins, and Chain Molecules

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ABSTRACT: The thermodynamic description of the systems specified in the title requires in general dissimilar theories. This contribution presents an approach that is capable of modeling all of them with a maximum of three adjustable parameters. The Ansatz starts from the Flory−Huggins theory and extends it in a 2-fold manner: The number of segments assigned to the solvent is no longer one but treated as an adjustable parameter to account for the differences in the molecular geometries and in the free volumes of the components. Furthermore, the modeling allows for effects resulting from ternary contacts of the solvent/polymer/polymer type. Examination of the acquired thermodynamic expressions by means of literature data (composition-dependent chemical potentials of the solvents) demonstrates their validity. Solutions of proteins and of linear or branched chainlike macromolecules require two adjustable parameters for the quantitative thermodynamic modeling; polyelectrolyte solutions necessitate a third one.

■ INTRODUCTION

The straightforward thermodynamic description of polymer solutions starts in most cases from the well-known Flory−Huggins theory.[1,2] However, this approach was designed for solutions of linear chainlike macromolecules in low-molecular-weight solvents. In view of the underlying central assumption of combinatorial mixing as the reference behavior (placing the polymer segments on a lattice), this approach cannot be expected to hold true without fundamental changes for solutions of polyelectrolytes (because of their counterions), for globular proteins (because of their compact structure), or even for nonlinear-chain molecules (because of their molecular architecture). These particularities of different types of macromolecules constitute a considerable obstacle for the consistent modeling of ternary and multinary mixtures containing more than one type of polymer. In order to minimize artifacts due to systematic deviations of the individual approaches, it would be very helpful to dispose of a method that enables the modeling of all binary subsystems with one and the same expression.

The present contribution investigates the possibilities for a unified thermodynamic description encompassing solutions of all types of high-molecular-weight compounds. It attempts a common mathematical representation of the solution behavior of polyelectrolytes, proteins, and chain molecules differing in their molecular architecture. Published information on vapor pressures measured above the solutions of different types of macromolecules is used for that purpose on the experimental side. The theoretical treatment rests on the laws of phenomenological thermodynamics. More precisely, measured chemical potentials of the solvent are modeled quantitatively by means of a mathematical expression fulfilling all requirements of phenomenological thermodynamics.

■ THEORETICAL SECTION

The Flory−Huggins theory formulates the dependence of the reduced chemical potential of the solvent, $\Delta \overline{G}_1/RT$, i.e., the molar Gibbs energy of *dilution* normalized to thermal energy, on the volume fraction φ of the polymer as

$$\frac{\Delta \overline{G}_1}{RT} = \left(1 - \frac{1}{N}\right)\varphi + \chi\varphi^2 + (1 - \varphi)\ln(1 - \varphi) \tag{1}$$

where N is the number of polymer segments, defined in their size by the molar volume of the solvent. All system-specific contributions are lumped together in the Flory−Huggins interaction parameter χ. For the modeling of real systems, χ must be treated as a function of the composition, which normally requires two to three adjustable parameters. The integral form of the Flory−Huggins expression, the molar Gibbs energy of mixing, reads

$$\frac{\Delta \overline{G}}{RT} = (1 - \varphi)\ln(1 - \varphi) + \frac{\varphi}{N}\ln \varphi + g\varphi(1 - \varphi) \tag{2}$$

where the letter g was used for the interaction parameter to indicate that the numerical values of χ and g differ if they depend on the composition.

In an attempt to generalize and to extend the expression for the chemical potential of the solvent to cover different polymer architectures and to include charged macromolecules, eq 1 was rewritten as

$$\frac{\Delta \overline{G}_1}{RT} = a\varphi + b\varphi^2 + c\varphi^2(1 - 2\varphi) + z \ln(1 - \varphi) \tag{3}$$

(i) In view of the impracticality to use polymer segments defined in the usual manner for all types of polymers, the factor $1 - 1/N$ is replaced by the parameter a.

(ii) The second term of eq 1 is retained, but called b, to distinguish it from χ and g; all three parameters refer to the formation of binary contacts between the components established upon mixing of the pure substances (integral Gibbs energies).

(iii) A term, quantified by the parameter c, is introduced to account for extra effects (not covered by the parameter b) resulting from the formation of triple contacts polymer/polymer/solvent; allowance for the other possible types of ternary heterocontacts solvent/solvent/polymer turned out to be unnecessary for the present purposes.

(iv) Finally the logarithmic term of the Flory–Huggins expression is modified; the factor $1 - \varphi$ is replaced by the system-specific constant z. The physical implications of the changes formulated above will be discussed in more detail by means of eq 10 obtained from eq 3 for the Gibbs energy of mixing. Before that, however, we need to translate the parameters a and b into directly measurable quantities.

To that end, we make use of the fact that the chemical potential of the solvent and the osmotic pressure π are correlated by eq 4

$$\frac{\Delta \overline{G}_1}{RT} = -\frac{\pi \overline{V}_1}{RT} = -\frac{\overline{V}_1 c_p (1 + A_2 c_p M + \ldots)}{M} \quad (4)$$

where $\overline{V}_1$ is the molar volume of the solvent. For sufficiently dilute solutions, the dependence of the chemical potential on the polymer concentration c_p (mass/volume) can be approximated by the first two members of a series expansion in terms of the molar mass M of the solute and of the second osmotic virial coefficient A_2 as formulated above. The corresponding series expansion resulting from eq 3 reads

$$\frac{\Delta \overline{G}_1}{RT} = (a - z)\left(\frac{c_p}{\rho}\right) + (b - z)\left(\frac{c_p}{\rho}\right)^2 + \ldots \quad (5)$$

where the volume fractions φ were converted into c_p by dividing them by the density ρ of the polymer. Comparing eqs 4 and 5 yields

$$a - z = -\frac{\overline{V}_1 \rho}{M} = -k \quad (6)$$

and

$$b - z = -\overline{V}_1 A_2 \rho^2 = -l \quad (7)$$

The value of the parameter k, introduced in eq 6, is normally readily accessible from the known molar mass and density of the polymer plus the molar volume of the solvent (ignoring possible deviations from $\overline{V}_1$). In contrast to k, the value of l (eq 7) is normally not known experimentally because of the lack of information on A_2. Inserting a from eq 6 into eq 3 results in the following expression:

$$\frac{\Delta \overline{G}_1}{RT} = (z - k)\varphi + b\varphi^2 + c\varphi^2(1 - 2\varphi) + z \ln(1 - \varphi) \quad (8)$$

Integration according to

$$\Delta \overline{G} = -\frac{1}{1 - \varphi} \int_1^\varphi \Delta \overline{G}_1 \, d\varphi \quad (9)$$

yields the reduced Gibbs energy of mixing as

$$\frac{\Delta \overline{G}}{RT} = z(1 - \varphi) \ln(1 - \varphi) + k\varphi \ln \varphi + b\varphi(1 - \varphi)$$
$$- c(1 - \varphi)\varphi^2 \quad (10)$$

The present approach introduces two additional parameters compared with the Flory–Huggins theory, namely, z and c. The parameter z modifies the contribution of the solvent to the Flory–Huggins combinatorial entropy of mixing. By analogy to the meaning of k, it can be interpreted as the inverse of the *effective* number of solvent segments. The parameters z and k are, however, no longer based on the volumes of the components because this way of proceeding would ignore possible contributions of the differences in the free volumes of the pure components and in their molecular shape. The parameter c, on the other hand, was introduced to account for extra effects caused by the presence of a further *polymer* molecule in the vicinity of a given solvent/polymer pair. The analogous ternary interaction parameter for the presence of a further *solvent* molecule in the vicinity of a given solvent/polymer pair can be neglected in the present context but may become important in special cases.

Chemical potentials and integral Gibbs energies of mixing, discussed above, need to be complemented by the second derivative of the Gibbs energies for the straightforward assessment of the phase state of polymer solutions. Equation 10 yields the expression

$$\frac{\partial^2 (\Delta \overline{G}/RT)}{\partial \varphi^2} = -2(b + c) + \frac{k}{\varphi} + \frac{z}{1 - \varphi} + 6c\varphi \quad (11)$$

enabling determination of the spinodal conditions from the requirement that the second derivative be zero at the border between metastable and unstable mixtures. The mathematical form of the expression resulting from the Flory and Huggins theory is regained by setting $z = 1$ and $c = 0$.

The present approach was formulated in terms of the volume fractions. One could equally well use weight fractions w, instead of φ; in this case, it is, however, necessary to state to which composition variable the parameters refer.

■ RESULTS AND DISCUSSION

Composition-dependent vapor pressure data reported in the literature (cf. Table 1) are hereafter evaluated according to eq 12. This relation results from eq 10 upon substitution of the reduced Gibbs energy of dilution by the activity of the solvent, expressed in terms of the vapor pressure p above the solution normalized to p_0, the vapor pressure of the pure solvent, as

$$\frac{\Delta \overline{G}_1}{RT} = \ln \frac{p}{p_0}$$
$$= (z - k)\varphi + b\varphi^2 + c\varphi^2(1 - 2\varphi) + z \ln(1 - \varphi) \quad (12)$$

According to experience with similar systems, corrections for imperfections of the gas are not required so that we can directly employ the measured vapor pressures. Equation 12 was also used in case the vapor pressure data were reported in terms of weight fractions of the solute, simply replacing φ by w; to which composition variable the parameters refer is specified in Table 2, collecting the results. The thus-obtained system-specific parameters were used to calculate the reduced Gibbs energies of mixing for the different systems according to eq 10. Three

Table 1. Systems, Characterization of the Polymers, and Source of Information
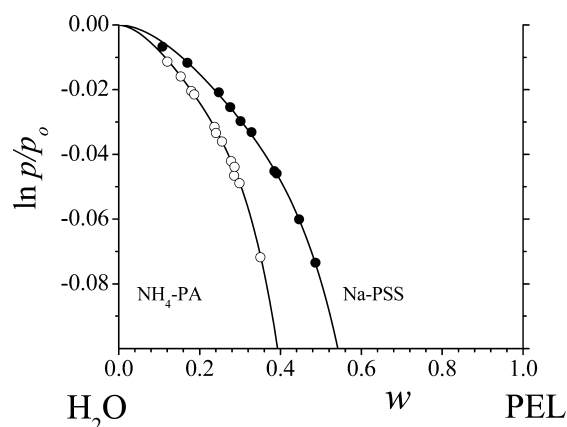
	abbrev	$M_n \times 10^{-3}$	M_w/M_n	T /°C	ref
Polyelectrolytes					
H$_2$O/ammonium poly acrylate	NH$_4$-PA	2.3	1.70	25.0	3, 8, 9
H$_2$O/sodium polyacrylate	Na-PA	6.9	2.51	25.0	3
H$_2$O/sodium poly(styrenesulfonate)	Na-PSS	127.0	1.17	25.0	3, 8, 9
H$_2$O/sodium poly(ethylenesulfonate)	Na-PES	6.9	1.71	25.0	3
H$_2$O/poly(dextryl chloride)	DEX-Cl	40.0	1.12	25.0	4
Proteins					
H$_2$O/lysozym	Lyso	14.4		25.0	5
H$_2$O/chymotrypsin	Chymo	21.6		25.0	6
Chain Molecules					
CH/polyisoprene branched	PI$_{bra}$	13.6	1.59	25.0	7
THF/poly(vinyl methyl ether)	PVME	50.5	2.60	20.0	4
THF/polystyrene	PS	29.8	1.10	20.0	4

Figure 1. Evaluation of the vapor pressures[3,8,9] of water as a function of the weight fraction of ammonium polyacrylate and of sodium poly(styrenesulfonate) according to eq 12. In this graph and in all of the following figures, the lines are calculated by means of the parameters collected in Table 2.

Figure 2. As in Figure 1 but for sodium poly(ethylenesulfate)[3] and for sodium polyacrylate.[3]

types of systems are studied: solutions of globular macro-molecules, of polyelectrolytes, and of chain polymers.
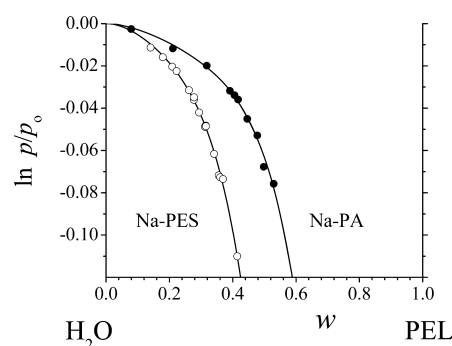
■ POLYELECTROLYTES

The number of reports concerning the vapor pressure of the solvent above solutions of charged or globular polymers in the absence of extra salt is expectedly much lower than that referring to chain molecules, where the situation for the polyelectrolytes is much better than that for the proteins. However, all but one publication concern polyanions. Figures 1 and 2 show the modeling of published vapor pressure data according to eq 12.

One remarkable conclusion that can be drawn from the above evaluation concerns the considerably dissimilar mixing tendencies of the polyelectrolytes with water, as expressed in terms of the reduced Gibbs energies of mixing shown in Figure 3. Surprisingly, the driving forces for mixing are in the present cases not correlated with the molar mass: Despite the 18 times larger M of Na-PSS, compared with that of Na-PES, the depth of the minimum in the Gibbs energy of mixing is almost identical. A further noteworthy finding concerns the fact that

these minima are, for all systems studied so far located at $w \approx 0.75$, practically independent of M.

The only set of vapor pressure data reported for polycation solutions[4] concerns derivatives of dextran (with a degree of polymerization of 247) with the formula

Table 2. System-Specific Parameters Resulting from Evaluation of the Vapor Pressure Data According to Equation 12[a]

|		b	error	c	error	z	error	$k \times 10^{-3}$
Polyelectrolytes								
H$_2$O/NH$_4$-PA	w	9.928	1.526	−3.835	0.561	14.161	2.063	8.32
H$_2$O/Na-PA	w	6.191	1.270	−2.248	0.512	9.174	1.690	3.18
H$_2$O/Na-PSS	w	1.540	0.306	−0.874	0.138	2.399	0.399	0.16
H$_2$O/Na-PES	w	1.680	0.702	−0.774	0.357	2.503	0.908	3.39
H$_2$O/DEX-Cl	φ	−0.238	0.040	(0.05)	(0.12)	0.159	0.028	0.64
Proteins								
H$_2$O/Lyso	w	3.395	0.263	3.756	0.431	0.733	0.058	1.63
		1.181	0.120			1.164	0.055	0.71
H$_2$O/Chymo	w	2.601	0.256			2.114	0.127	1.08
Chain Molecules								
CH/PI$_{bra}$	φ	0.144	0.037			0.600	0.032	1.21
THF/PVME	φ	0.203	0.020			1.080	0.012	0.37
THF/PS	φ	−0.085	0.027			1.092	0.022	0.60

[a]To which composition variable these data refer is indicated by either w (weight fractions) or φ (volume fractions).
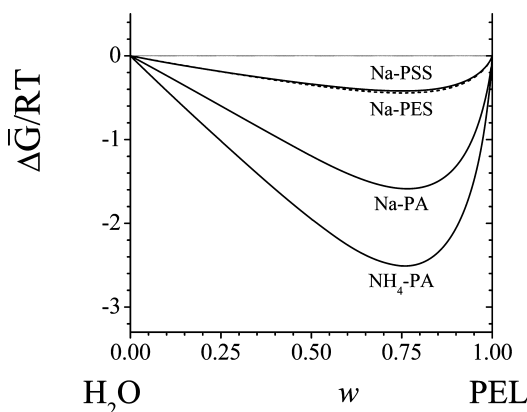
Figure 3. Comparison of the reduced Gibbs energies of mixing as a function of the composition for the different aqueous solutions of polyanions.
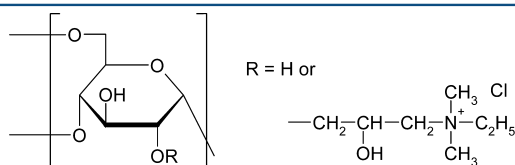

in which R stands either for H or for N-ethyl-N,N-dimethyl-N-(2-hydroxypropyl)ammonium chloride; these data refer to polymers containing different fractions f of charged monomer units. The evaluation of the vapor pressure data shown in Figure 4 was performed for the sample with the highest f value of 0.9.
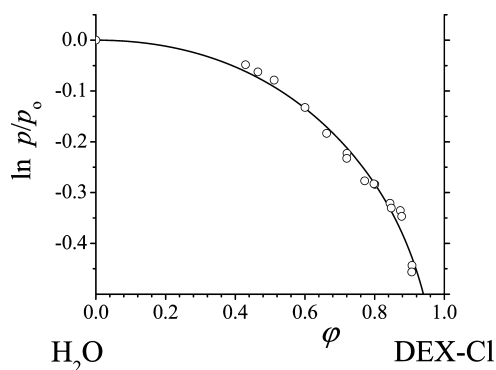
Figure 4. Evaluation of the vapor pressures of water as a function of the volume fraction of the polycation dextryl chloride[4] by means of eq 12.

According to the concentration dependence of the Gibbs energy of mixing, as calculated from eqs 10 and 11, and the parameters of Table 2, all polyelectrolytes are completely miscible with water in agreement with experience. Within the group of charged macromolecules, the polycation behaves in an exceptional manner: As demonstrated in Figure 5, the minimum in the Gibbs energy of mixing is only about one-fourth of the shallowest minimum for the polyanions (Na-PSS), despite the lower molar mass. For the time being, it is unclear whether this is a more general feature of polycations, a consequence of the incomplete substitution, i.e., $f < 1$, or a result of the bulky polymer backbone. Furthermore, the c parameter of the polycation is not, as for the polyanions, within the range of −0.8 to −3.8 but either 0 or, ignoring the large error, even positive.
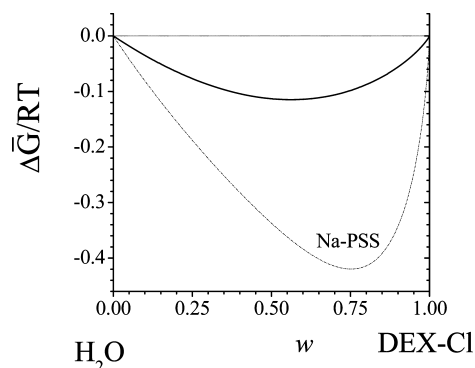
Figure 5. Gibbs energies of mixing as a function of the composition for the polycation dextryl chloride compared with that of Na-PSS, the polyanion with the shallowest minimum.

It is comparatively easy to rationalize the necessity of accounting for the ternary contacts of the form solvent/polymer/polymer in the case of polyelectrolytes: The presence of a further polyelectrolyte molecule in the vicinity of a given polymer/solvent contact must modify the binary interaction due to the charges that this additional partner carries with it. The negative sign of c observed for the polyanions implies a reduction in the mixing tendency of the components according to eq 10; this is probably a consequence of coil shrinkage resulting from the increased local ionic strength. Presently, one can only speculate why the c value of the polycation is either close to 0 or positive. It may be a consequence of the comparatively large distance of the charges from the polymer backbone, making the polyelectrolyte effect less efficient.

A further common feature of the modeling of the solution thermodynamics of charged macromolecules consists of the pronounced deviation of the parameter z from unity. This finding implies that the efficient number of solvent segments differs largely from unity. At least two possible explanations are conceivable: (i) Calculating the parameter k according to eq 6 from the molar mass of the polymer ignores the presence of counterions and thus establishes a misleading basis for its number of segments; to compensate for this deficiency, it may be necessary to redefine the number of segments of the solvent adequately. (ii) Modifying the structure of water by the presence of polyelectrolytes can also not be ruled out. However, thinking, for instance, in terms of a destruction of icebergs, this effect should result in z values of less than unity.

■ **PROTEINS**

In view of the great biological importance of this class of polymers, the information on their solution behavior is surprisingly scarce. This may have to do with the fact that many of them are not completely soluble in water. The only vapor pressure data that could be found concern highly concentrated solutions of lysozyme[5] and chymotropsin.[6] Figure 6 shows the result for the former system.

Because of the lack of data for sufficiently low polymer concentrations, the modeling remains comparatively imprecise. For instance, it is not clear whether it is justified to set the parameter c of eq 12 to 0, as demonstrated in Figure 6. Despite these uncertainties, the composition dependence of the Gibbs energy of mixing testifies the existence of a large miscibility gap beyond a doubt, as demonstrated in Figure 7, and explains the lack of vapor pressure data for dilute solutions.
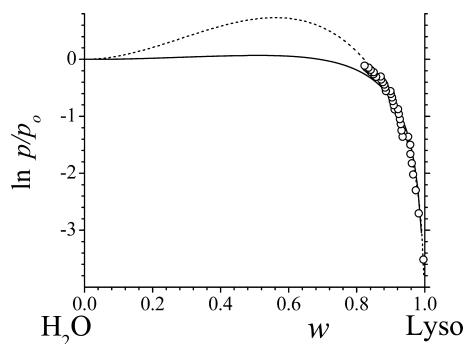
Figure 6. Evaluation of the vapor pressures[5] of water as a function of the weight fraction of lysozyme according to eq 12. Broken line: adjustment of all parameters. Full line: $c = 0$.
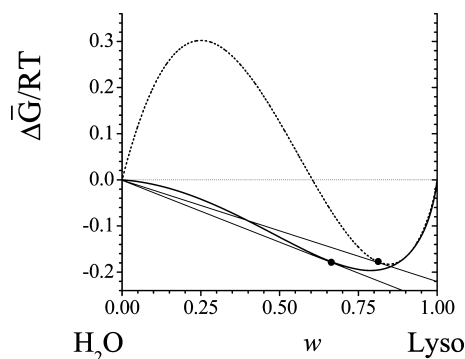
Figure 7. Reduced Gibbs energies of mixing as a function of the weight fraction of lysozyme. Dotted curve: adjustment of all parameters. Broken curve: $c = 0$. The calculated compositions of the coexisting phases are indicated by full circles.

The predictions concerning the phase behavior are at least in qualitative accord with literature reports.[10,11] Sorption calorimetric investigations[12] concerning the protein-rich side of the phase diagram state that flexible lysozyme coexists with free water. This finding can be interpreted in terms of the coexistence of two phases. Cloud-point measurements[11] reported for lysozyme solutions at different pH values cannot immediately be compared with the present results obtained without buffering.

Chymotrypsin is another representative of globular macromolecules. Figure 8 shows the modeling of the vapor pressure of water reported[6] for its solutions. Again the data are confined to high polymer concentrations, making the modeling difficult, however, not to the extent observed with lysozyme.
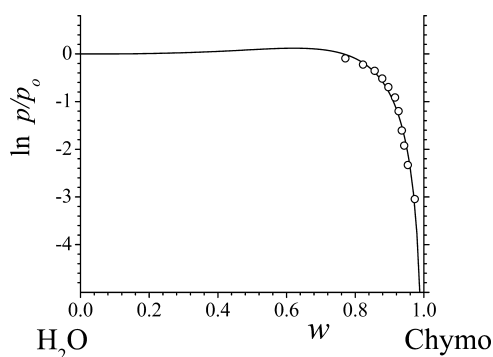
Figure 8. As in Figure 6 but for chymotrypsin,[6] setting $c = 0$.

The Gibbs energy as a function of the composition (cf. Figure. 9) predicts an extended two-phase region again.
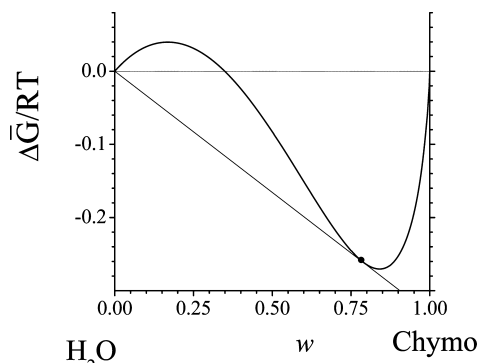

Figure 9. As in Figure 7 but for chymotrypsin,[6] setting $c = 0$.

Unfortunately, it turned out to be impossible to find literature data on the measured phase behavior; the only available information stems from the catalogues of chymotropsin suppliers. Merck[13] states that 10 g/L is soluble in the pH range from 3 to 5, and Byozym[14] writes that the protein is sparingly soluble in water. These data are in qualitative accord with the present findings.

Despite the limited experimental information concerning protein solutions, it appears improbable that the parameter c is required for the modeling of such systems. This tentative conclusion is backed by the observation for polyelectrolytes, according to which nonzero c values come along with pronounced deviations of z form unity.

Chain Molecules. The combinatorial reference behavior underlying the Flory−Huggins theory must necessarily also become obsolete for branched macromolecules. Again there is little information available on the solution thermodynamics of this class of polymers. The only available publication[7] concerns the system cyclohexane (CH)/branched polyisoprene (PI_{bra}). Figure 10 shows the modeling of the reported vapor pressure data.
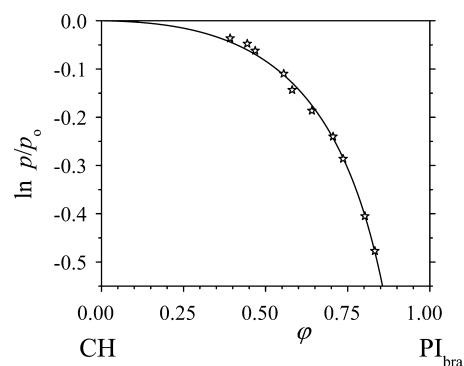
Figure 10. Evaluation of the vapor pressure data published[7] for the system CH plus PI_{bra} according to eq 12.

The reduced Gibbs energies of mixing as a function of the composition (cf. Figure 11) calculated from the resulting system-specific parameters (cf. Table 2) evince the absence of a miscibility gap in agreement with direct experimental observation. Despite the low molar mass (13.6 kg/mol), the minimum of this dependence is much shallower than that
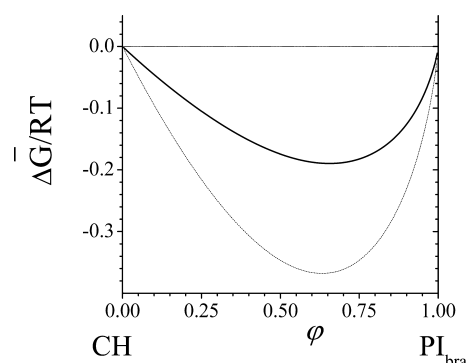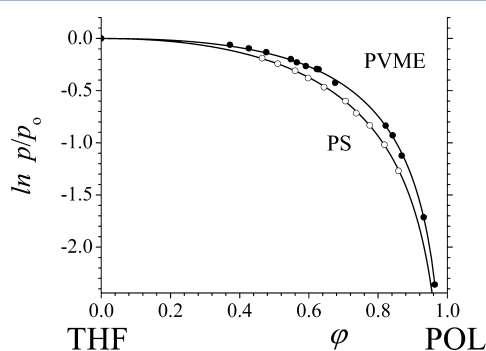
Figure 11. Reduced Gibbs energies of mixing as a function of the volume fraction of PI_{bra} (full line). The dotted line shows that the minimum of the combinatorial term is considerably deeper, even in the limit of infinitely long chains.

Figure 13. Gibbs energies of mixing for the systems of Figure 12. The dotted curve was calculated by means of eq 2, setting $g = 0$ and $N = 5000$.

calculated for combinatorial behavior in the limit of the least driving forces, i.e., for infinitely long polymer chains.

For the sake of completeness and in view of the objective to acquire a common description for all polymer solutions, irrespective of the particular architecture of the macromolecules, linear-chain molecules are also included in the present investigation. Figure 12 shows the modeling of vapor pressures reported[7] for the systems tetrahydrofuran (THF)/polystyrene and THF/poly(vinyl methyl ether).

Figure 12. Evaluation of vapor pressures for the systems THF/poly(vinyl methyl ether)[4] and for THF/polystyrene according to eq 12.
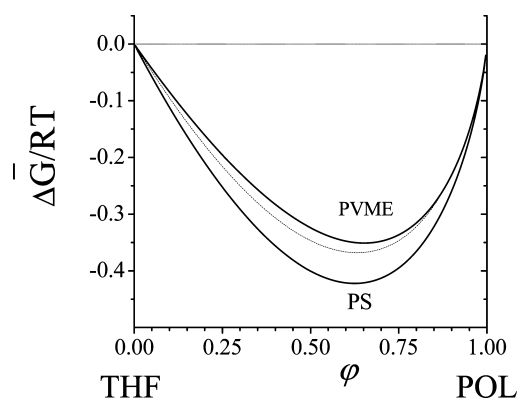
The composition dependence of the Gibbs energy calculated by means of parameters obtained from the above evaluation demonstrates (Figure 13) that the combinatorial behavior is indeed a reasonable choice for the solutions of linear polymers.

With respect to the desired modeling of multinary mixtures made up of different types of macromolecules, it turns out to be advantageous that the present approach also encompasses the classical thermodynamic cases.

For the sake of completeness, Table 2 also displays the parameters k (eq 6), despite the fact that these values are rather inaccurate in the case of polyelectrolytes and proteins because their densities in the pure liquid state can only be estimated. This situation does, however, not affect the present evaluation because k is typically on the order of one-tenth of a percent of z (eq 10), so that it can be neglected with respect to z.

CONCLUSIONS

The examination of eq 12 by means of solvent potentials published for the different types of polymer solutions

demonstrates its validity; according to the still limited experimental material, it correctly predicts the segregation of a second liquid phase from polymer solutions. This straightforward expression, requiring only two to three adjustable parameters, enables—to the best knowledge of the author—for the first time a consistent modeling of mixtures containing more than one type of polymer. This option appears particularly helpful to forecast the behavior of joint solutions of proteins and chain molecules or of charged and uncharged polymers.

It should go without saying that considerably more efforts are required to understand the different implications of the present approach in more detail. Above all, it is necessary to check to which extent the proposed correlation of the adjusted z parameters with molecular geometries and free volumes can be substantiated. Another interesting item concerns the influences of the polymer molecular weight on vapor pressures and, consequently, on liquid/liquid phase separation. It needs to be clarified whether the M value contained in the parameter k (eq 6) suffices or whether it is necessary to allow for M dependencies of z or c, as with the original Flory−Huggins interaction parameter. Last but not least, it is necessary to learn whether the sign of the c parameter is really different for polyanions and for polycations, as suggested by the still very limited experimental material.

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Notes
The authors declare no competing financial interest.

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