

Liquid–Liquid Equilibrium of Aqueous Polymer Two-Phase Systems Using the Modified Wilson Equation

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The modified Wilson equation, developed in a previous publication, for the excess Gibbs energy of aqueous polymer solutions, is extended to multicomponent mixtures. The model provides a flexible framework to correlate and predict phase equilibria of aqueous polymer two-phase systems. The results obtained with the model are in fair agreement with the experimental data.

Introduction

Beijerink¹ was the first to report on aqueous two-phase systems (ATPS). It took around 50 years before these systems became popular, with the efforts of Albertsson,² who applied them for separation processes. In recent years, the aqueous two-phase extraction has gained increased attention for purification and separation purposes particularly in the biotechnology field.³ A large number of publications have been reported concerning a wide range of applications of this method, including the separation of macromolecules, cell organelles, and viruses.^{3–5}

The most widely studied systems are those composed of poly(ethylene glycol) (PEG) and dextran (Dex), or by PEG and potassium phosphate.⁶ Regardless of the potential, the ATPS application is limited by the high cost of the polymers commonly used in phase separation. The chemical costs can be as high as 74% of the total production price.⁷ There are in the literature several alternative systems in order to overcome this drawback.^{8–10} Among these, the use of thermoseparating polymers seems to be one of the most promising approaches.^{11–13}

For the industrial success of a separation technique, it is advantageous to have mathematical tools accurately describing the thermodynamic properties of the process-associated systems. Their predictive ability is fundamental where experimental data is not available. There are in the literature principally two kinds of models describing ATPS: the osmotic virial-expansion models and those that lay on the lattice theory.^{14–18} Despite the relative practical success obtained with some of the foregoing models, they sometimes exhibit low accuracy in simultaneously predicting the phase diagrams of homologous ATPS (that differ only in the polymer molecular weight), and in some cases, they utilize different sets of model parameters to predict homologous ATPS. There is no such general solutions theory, and the development of new models may assist in understanding the experimental results observed in these complex systems. In a previous paper Xu et al.¹⁹ presented a new modified Wilson equation, to represent the vapor–liquid equilibrium (VLE) behavior of homologous aqueous polymer solutions, that incorporates

some ideas from previous models, but in which the heat capacity is taken into account. Here we extended it to multicomponent systems to test its ability in correlating and predicting the LLE of polymer–polymer–water aqueous two-phase systems.

Model Development

As usual the model development starts with the excess Gibbs energy G^E (eq 1). In this new modified Wilson equation the excess heat capacity, c_P^E , that provides an important link between the excess enthalpy and the excess entropy (eqs 2 and 3) is used:

$$G^E = H^E - TS^E \quad (1)$$

$$c_P^E = \left(\frac{\partial H^E}{\partial T} \right)_{P,x} \quad (2)$$

$$c_P^E = T \left(\frac{\partial S^E}{\partial T} \right)_{P,x} \quad (3)$$

The expression for the excess Gibbs energy can be easily obtained (Xu et al.):¹⁹

$$\frac{G^E}{RT} = -\frac{S_C^E}{R} + \frac{H^E}{RT} - \frac{1}{R} \int_{\infty}^T \frac{1}{T} \left(\frac{\partial H^E}{\partial T} \right)_{P,x} dT \quad (4)$$

The first term is called the combinatorial contribution: it is independent of temperature and accounts for the size/shape of the molecules; the last terms both depend on temperature and are called the residual contribution and reflect the interactions between segments of molecules. Therefore, the model consists of a combinatorial term G_c^E and a residual term G_R^E :

$$\frac{G_R^E}{RT} = \frac{H^E}{RT} - \frac{1}{R} \int_{\infty}^T \frac{1}{T} \left(\frac{\partial H^E}{\partial T} \right)_{P,x} dT \quad (5)$$

$$\frac{G_c^E}{RT} = -\frac{S_C^E}{R} \quad (5a)$$

The excess is defined on an asymmetric normalization: for water the reference state is the pure liquid and for the solutes it is a hypothetical liquid (one mole of solution in pure water, with interactions such as in an infinite diluted aqueous solution). The principles and methodologies adopted for the model development are

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given in the previous paper for binary mixtures (Xu et al.)¹⁹ The extension to multicomponent mixtures is straightforward, the expressions for the combinatorial and residual contributions for the excess Gibbs energy being as follows:

$$\frac{G_C^E}{RT} = \sum_{i=1}^m n_i \ln \frac{X_i}{x_i} + \frac{1}{\alpha} \sum_{i=1}^m q_i n_i \ln \frac{X_i}{\Phi_i} \quad (6)$$

$$\frac{G_R^E}{RT} = -\frac{n_q}{\alpha} \left[\sum_{i=1}^m X_i \ln \left(\sum_{j=1}^m X_j G_{ji} \right) \right] \quad (7)$$

where $X_i = \theta_i$, i.e., the effective mole fraction of a segment is equal to the surface/area fraction:

$$N_r = \sum_{i=1}^m N_i r_i, \quad \Phi_i = N_i r_i / N_r \quad (8)$$

$$N_q = \sum_{i=1}^m N_i q_i, \quad X_i = N_i q_i / N_q \quad (9)$$

n_i and N_i are the mole numbers and molecule numbers of species i , respectively; r_i are the numbers of segments per molecule. The Φ_i are volume fractions; q_i means effective segment number of species i and is correlated in the usual way,

$$q_i = [r_i(z-2) + 2]/z = r_i[1 - 2(1 - 1/r_i)/z] \quad (10)$$

The structural factor of the solution $2/z$ is defined as the nonrandom factor α . The typical value is 0.3.²⁰ Thus,

$$G_{ij} = \exp(-\alpha \tau_{ij}) \quad (11)$$

where τ_{ij} are the interaction parameters:

$$\tau_{ij} = \frac{1}{\alpha} \frac{\epsilon_{ij} - \epsilon_{jj}}{RT} \quad (12)$$

and q_i is rewritten as

$$q_i = r_i[1 - \alpha(1 - 1/r_i)] \quad (10a)$$

Using standard thermodynamics, the activity coefficients can be easily obtained:

$$\ln \gamma_i = \ln \gamma_i^C + \ln \gamma_i^R \quad (13a)$$

$$\ln \gamma_i^C = \ln \frac{X_i}{x_i} + \sum_{j=1}^m X_j \left(1 - \frac{q_i}{q_j} \right) + \frac{q_i}{\alpha} \left[\ln \frac{X_i}{\Phi_i} + \sum_{j=1}^m \Phi_j \left(\frac{q_j r_j}{q_i r_j} - 1 \right) \right] \quad (13b)$$

$$\ln \gamma_i^R = -\frac{q_i}{\alpha} \left[\ln \left(\sum_{j=1}^m X_j G_{ji} \right) + \sum_{k=1}^m \frac{X_k G_{ik}}{\sum_{j=1}^m X_j G_{jk}} - 1 \right] \quad (13c)$$

The activity coefficients are calculated, according to eqs 13a–c, in the mole fraction scale, and the variables have the meanings already presented. The activity coefficients of the polymers were normalized to the

reference state in ATPS. Thus, according to the non-symmetric convention,

$$\ln \gamma_i^* = \ln \gamma_i - \ln \gamma_i^{ref} \quad (14)$$

where $\ln \gamma_i^{ref}$ is the activity coefficient in the reference state and is calculated from eq 13, in which $x_1 = 1$ and $x_i = 0$ ($i \neq 1$), (1 stands for solvent and $i \neq 1$ for solutes).

The dependence of the interaction parameters, between water and segment of polymer and between the segments of polymers with the temperature, are, according to the suggestion of Wu,¹⁷ as follows:

$$\tau_{ji} = a_{ji}^{(1)}(T_0/T) + a_{ji}^{(2)}(T_0/T)^2 \quad (15a)$$

$$\tau_{ij} = a_{ij}^{(1)}(T_0/T) + a_{ij}^{(2)}(T_0/T)^2 \quad (15b)$$

$$a_{ji}^{(1)} = \frac{z}{2} \left[\frac{\epsilon_{ji} - \epsilon_{ii}}{kT_0} + \left(\frac{\delta_{ji}}{1 + q_{ji}} - \frac{\delta_{ii}}{1 + q_{ii}} \right) / T_0 \right] \quad (15c)$$

$$a_{ji}^{(2)} = -\frac{z}{2} \left[\frac{q_{ji}}{2(1 + q_{ji})^2} \left(\frac{\delta_{ji}}{kT_0} \right)^2 - \frac{q_{ii}}{2(1 + q_{ii})^2} \left(\frac{\delta_{ii}}{kT_0} \right)^2 \right] \quad (15d)$$

where ϵ is the interaction energy between segment–segment pairs; δ is the oriented interaction parameter between segment–segment pairs and q is the ratio of statistical degeneracy of two states. $a_{ij}^{(1)}$ and $a_{ji}^{(2)}$ can be expressed in a similar way to $a_{ji}^{(1)}$ and $a_{ij}^{(2)}$ replacing the underscripts i by j , and j by i . T_0 is the reference temperature, $T_0 = 298.15$ K. According to Xu et al.¹⁹ it is assumed that $a^{(1)}$ and $a^{(2)}$ are temperature and composition independent, and if the range of temperature is not too wide, the oriented interactions between the i – i and j – j pairs can be neglected ($\delta_{ii} = 0$). Thus, $a_{ji}^{(2)} = a_{ij}^{(2)}$.

Results and Discussion

To calculate the polymer–polymer interaction parameters, the component isoactivity criterion between the two-liquid phases is used:

$$(x_i \gamma_i)^I = (x_i \gamma_i)^{II} \quad (16)$$

where I and II represent both liquid phases. Therefore, the liquid–liquid data from the ternary systems water/polymer/polymer is needed to estimate the parameters. For this purpose, LLE data measured in our laboratory⁹ as well as data collected from literature were used to test the new model. The phase forming polymers studied in this work can be divided in two categories: the classical polymers, like poly(ethylene glycol) (PEG) and dextran (Dex) and the polymers that have been recently used in ATPS and which exhibit thermoseparating properties, like PES (a water soluble starch polymer) and random copolymers of ethylene oxide (EO) and propylene oxide (PO) (symbolized as EOPO and Ucon). The working equations are eqs 13a–c. For the calculations, pure substance properties are necessary, such as the molecular weight (M_j), the segment number (r_j) and the molar volume (V_j). The M_j was set equal to the polymer number average molecular weight (M_n). Since the van der Waals volume of a repeated unit in PEG molecule is very close to the double of a water molecule, V_{peg} is approximated as $(2n_{peg} + 1)V_w$, where n_{peg} is the polymerization degree of a PEG molecule and can be

Table 1. Modified Wilson Parameters for PEG-Dex and EOPO-PES ATPS

system	T(K)	α_{23}^a	τ_{32}	τ_{23}	ref
PEG6000-Dex40	298.15	0.3	-1.104	1.557	5
PES100-EOPO(1:1)	298.15	0.3	-3.282	46.42	16

^a Fixed at 0.30.

calculated from M_{peg}^{18} . Similarly, for EOPO, V_{eopo} is approximated as $(5n_{eopo} + 1)V_w$. For Dex, V_{dex} is calculated from its specific volume (v_{dex}), $v_{dex} = 5.96 \times 10^{-4} m^3 kg^{-1}$ at 293.15 K.¹⁸ For water, $r_w = 1$, $V_w = 18.05 \times 10^{-6} m^3 mol^{-1}$ at 298.15 K.¹⁸ The same value is used at other temperatures. Thus, $r_2 = V_2/V_1$. For PES r_{pes} was set equal to the polymerization degree of a PES molecule, n_{pes} .

Since the model describes satisfactorily the VLE using only two parameters, i.e., $a_{ji}^{(2)} = a_{ij}^{(2)} = 0$,¹⁹ in the LLE data treatment the oriented interactions were not accounted. Thus, it is only necessary to estimate the parameters τ_{ij} and τ_{ji} , which reflect the interactions between the polymers segments. For its calculation, the LLE data were adjusted using the following objective function, F, based on the isoactivity criteria, and used by other authors for the treatment of this kind of systems:²¹⁻²³

$$F = \sum_j \left[\frac{(x_1 \gamma_1^*)^I_j - (x_1 \gamma_1^*)^{II}_j}{(x_1 \gamma_1^*)^{II}_j} \right] + \sum_j \left[\frac{(x_2 \gamma_2^*)^I_j - (x_2 \gamma_2^*)^{II}_j}{(x_2 \gamma_2^*)^{II}_j} \right] + \sum_j \left[\frac{(x_3 \gamma_3^*)^I_j - (x_3 \gamma_3^*)^{II}_j}{(x_3 \gamma_3^*)^{II}_j} \right] \quad (17)$$

where I and II refer to both phases, and j is the number of tie-lines.

The modified Wilson model parameters, that reflect the interactions between the polymer-polymer segments, were obtained using the simplex method of Nelder and Mead.²⁴ Only two tie-lines were used to estimate the parameters. The other tie-lines for the same system, as well for other systems with different polymer molecular weight, were predicted using the same parameters, according to the equality of the activities of the components in both phases. This methodology has already been successfully used in our group to correlate and predict the LLE of polymer-salt/water aqueous two-phase systems.²⁵

Table 1 presents the polymer-polymer interaction parameters for the PEG-Dex and EOPO-PES ATPS. Table 2 summarizes the absolute deviations for the

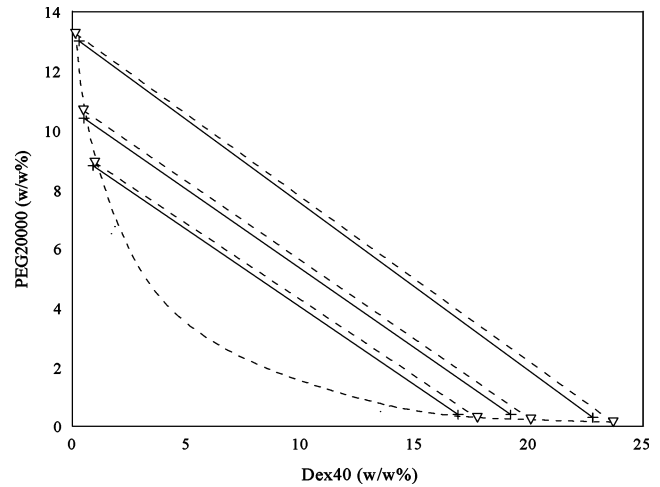


Figure 1. Phase diagram of PEG20000-Dex40 ATPS at 298.15 K. (+--+ experimental data and tie-lines; (∇--∇) predicted tie-lines; (---) predicted binodal. (Predictions with the PEG-Dex interaction parameters presented in Table 1).

ATPS studied, as well as the source of the experimental data used. Figures 1 to 5 show some comparisons between experimental and predicted phase diagrams.

The expressions for the calculation of δW_i^α , δW and δW_{max} are as follows:

$$\delta W_i^\alpha = \frac{\sum_{j=1}^N |W_{j,i}^\alpha(\text{calc.}) - W_{j,i}^\alpha(\text{exp.})|}{N} \quad (18)$$

$$\delta W = \frac{\sum_{\alpha} \sum_i \delta W_i^\alpha}{2N_1} \quad (19)$$

$$\delta W_{max} = \max\{|W_{j,i}^\alpha(\text{calc.}) - W_{j,i}^\alpha(\text{exp.})|\} \quad (20)$$

where δW_i^α , δW and δW_{max} mean the average absolute deviation in weight percentage of component i in phase α , the overall average absolute deviation and the maximum absolute deviation, respectively. N is the number of experimental data points and N_1 the number of components in the system.

From Table 2 it is possible to conclude that the predicted results are in fair agreement with the experimental data. In fact, all δW and almost all δW_i^α values

Table 2. Comparison of Predicted Results and Experimental Data for PEG-Dex and EOPO-PES ATPS

system	T(K)	$\delta W_2^{T(e)}$	$\delta W_3^{T(e)}$	$\delta W_2^{B(e)}$	$\delta W_3^{B(e)}$	δW	δW_{max}	STL ^(f)	
								exp.	pred.
PEG6000-Dex40 ^(a)	298.15	0.58	0.42	0.24	1.81	0.97	2.28	-0.50	-0.50
PEG8000-Dex40 ^(a)	295.15	0.18	0.13	0.13	0.34	0.22	0.66	-0.53	-0.49
PEG10000-Dex40 ^(a)	298.15	0.09	0.18	0.29	1.50	0.58	1.74	-0.51	-0.50
PEG20000-Dex40 ^(a)	298.15	0.07	0.06	0.35	1.89	0.67	2.05	-0.53	-0.50
PEG10000-Dex110 ^(a)	313.15	0.51	0.03	0.16	0.92	0.53	1.19	-0.55	-0.49
PEG6000-Dex70 ^(a)	296.15	0.45	0.06	0.22	0.64	0.46	0.95	-0.55	-0.50
PEG6000-Dex110 ^(a)	298.15	0.04	0.12	0.26	0.37	0.23	1.24	-0.48	-0.47
PEG6000-Dex500 ^(a)	298.15	0.08	0.20	0.28	1.47	0.38	2.18	-0.46	-0.44
EOPO(1:1)-PES100 ^(b)	298.15	0.61	0.47	0.63	0.62	0.61	1.94	-0.54	-0.60
EOPO(1:1)-PES200 ^(b)	298.15	0.14	0.19	0.45	0.60	0.29	2.13	-0.48	-0.48
Ucon-PES100 ^(c)	295.15	1.57	0.98	0.71	0.66	0.93	2.08	-0.46	-0.57

Data from: ^(a)(5); ^(b)(16); ^(c)(9); ^(d)(4). ^(e)The 2 component is predominant in the top phase, i.e., PEG and EOPO, and the 3 predominates in the bottom phase, i.e., Dex and PES. T and B mean top and bottom phase, respectively. ^(f)Slope of Tie Line.

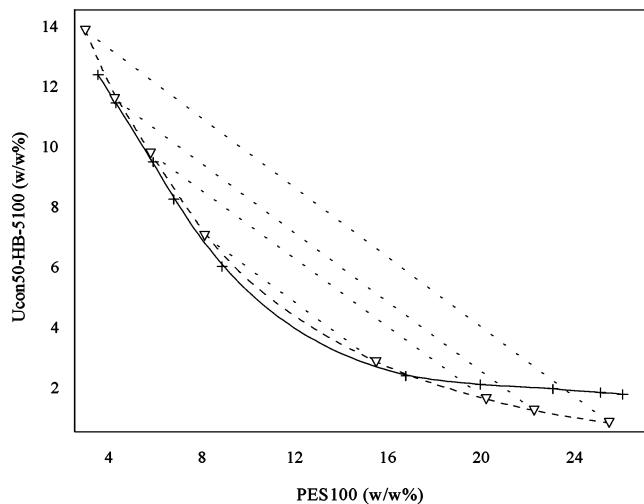


Figure 2. Phase diagram of Ucon-PES100 ATPS at 295.15 K. (+) experimental data and binodal; (∇) predicted tie-lines; (---) predicted binodal.

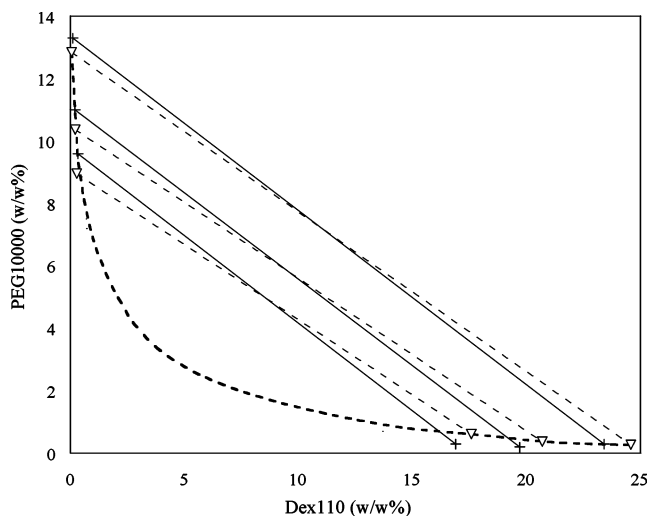


Figure 3. Phase diagram of PEG10000-Dex110 ATPS at 313.15 K. (+) experimental data and tie-lines; (∇) predicted tie-lines; (---) predicted binodal. (Predictions with the PEG-Dex interaction parameters presented in Table 1).

are smaller, in weight percentage, than 1.0 and δW_{max} assume values lower than 2.3. Thus, the model can predict accurately several phase diagrams in which the polymers differ only in the molecular weight, as can also be observed from Figure 1.

Although the Ucon and EOPO (1:1) polymers are slightly different, (the molar ratio in EO:PO is 1:1 in the polymer used in the correlation of the parameters, and approximately 1.3:1 in the Ucon), the prediction results are very satisfactory. Such fact explains the difference between the slope of the tie line (STL) and between the polymer concentrations experimentally obtained and calculated with the model (Figure 2 and Table 2).

The modified Wilson equation proves to be a powerful tool to correlate and predict homologous ATPS, even for systems at relatively high temperatures (Figure 3).

Regarding Figures 4 and 5, it is possible to see that the model also predicts accurately the influence of the molecular weight of the polymers on the phase diagram: increasing the polymer molecular weight the binodal moves towards the lower concentrations.

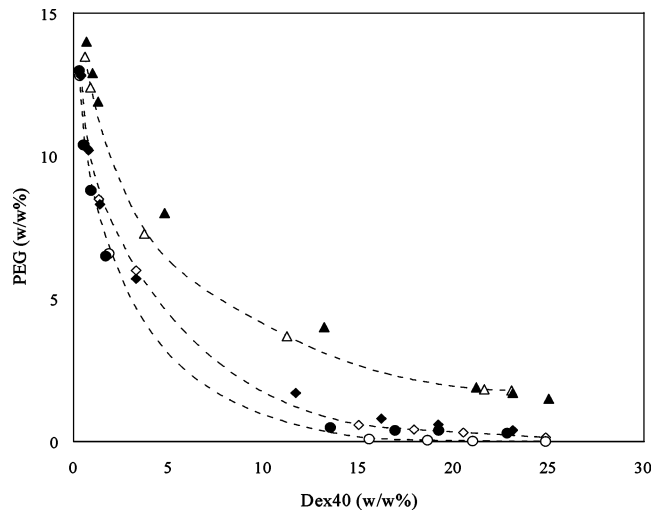


Figure 4. Influence of PEG's molecular weight in the PEG-Dex40 ATPS diagram at 298.15 K. Experimental data for (\blacktriangle) PEG6000, (\blacklozenge) PEG10000, and (\bullet) PEG20000. Predicted binodals for (\triangle) PEG6000, (\diamond) PEG10000, and (\circ) PEG20000.

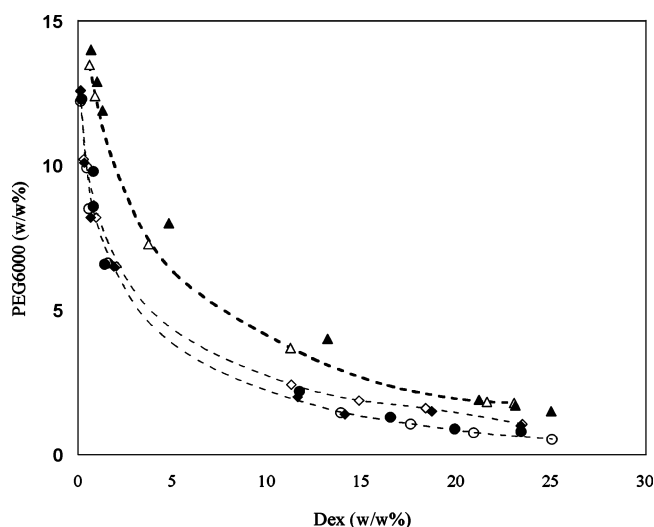


Figure 5. Influence of Dex's molecular weight in the PEG6000-Dex ATPS diagram at 298.15 K. Experimental data for (\blacktriangle) Dex40, (\blacklozenge) Dex110, and (\bullet) Dex500. Predicted binodals for (\triangle) Dex40, (\diamond) Dex110, and (\circ) Dex500.

Conclusions

The modified Wilson equation was extended to describe the LLE in polymer/polymer/water ATPS in multicomponent systems. The results obtained show that the model is a powerful framework, both for correlation and for prediction of phase diagrams of homologous ATPS, even at relatively high temperatures. Moreover, the data indicate that only one set of parameters is enough to predict homologous ATPS.

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List of Symbols

a = interaction parameter defined in eq 15, or activity
 $cal.$ = calculated

c_p^E = excess heat capacity/heat capacity change of mixing
exp. = experimental
 F = objective function
 G, G^E = binary parameter, excess Gibbs energy
 H^E = excess enthalpy
 K = Boltzmann constant
 M, M_n = molecular weight, number-average molecular weight
 n = mole number of segment–segment pairs, or polymerization degree
 N = number of molecules (segment–segment pairs), or experimental data points
 N_I = number of experimental data points
 P = pressure
Pred. = prediction
 q = effective segment number of polymer or ratio of statistical degeneracy of two states
 r = number of segments per molecule
 R = gas constant
 S^E = excess entropy
 SSQ = sum of squares
 STL = slope of tie line
 T = absolute temperature
 T_0 = reference temperature, 298.15 K
 V = molar volume
 W = weight fraction
 x = mole fraction of polymer solutions
 X = effective mole fraction of segments
 z = coordination number in the lattice theory

Greek Letters

α = nonrandom factor in the Wilson model
 δ = deviation or oriented interaction parameter between segment–segment pairs
 ϵ = interaction energy between segment–segment pairs
 Φ = volume fraction
 γ = activity coefficient
 θ = surface/area fraction
 τ = binary interaction parameter
 ν = specific volume
 ∂ = partial derivative
 ∞ = infinity

Subscripts

C = combinatorial factor
 i, j = any species or segments
 ii, ij, jj = segment–segment pairs
 R = residual contribution
 $I, 2$ = solvent and polymer, respectively

Superscripts

C = combinatorial factor
 E = notation of excess quality
 R = residual factor
 ref = reference state
 $(1), (2)$ = notation for distinction
 I, II = any aqueous phase

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