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THERMODYNAMICS OF POLYMER-WATER SYSTEMS

BY

NAVEEN KOAK

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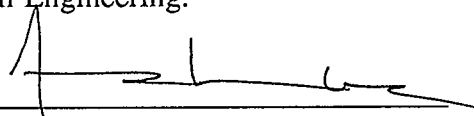
FACULTY OF GRADUATE STUDIES

The undersigned certify that they have read, and recommend to the Faculty of Graduate Studies for acceptance, a thesis entitled "Thermodynamics of Polymer-Water Systems" submitted by Naveen Koak in partial fulfillment of the requirements for the degree of Master of Science in Chemical Engineering.
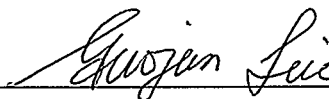
Dr R.A. Heidemann (supervisor)
Department of Chemical and
Petroleum engineering.

Dr A.K. Mehrotra
Department of Chemical and
Petroleum Engineering.

Dr A. Chakma
Department of Chemical and
Petroleum Engineering.

Dr G. Liu
Department of Chemistry.

1993-12-07

Date

ABSTRACT

Flory-Huggins theory has been employed to successfully correlate various types of data pertaining to polymer-water systems. The data include binary and ternary water activities, binary closed-loop phase diagrams, ternary constant temperature and pressure liquid-liquid equilibrium diagrams, and protein partition coefficients in aqueous two-phase systems. Correlation was done with the original Flory-Huggins theory and variations of it which included treating the Flory-Huggins interaction parameter as a function of composition or temperature and treating the polymer chain length "r" as a parameter to fit the data or as a function of temperature. Preliminary results of correlation of protein partitioning in aqueous two-phase systems are encouraging.

A scheme to characterise polymers using a pseudocomponent approach is demonstrated. This scheme is based on the log-normal distribution in the polymer molar mass.

Owing to the nature of the model, computational difficulties were encountered with the conventional successive substitution flash calculation procedure. This work describes the use of two algorithms (i) damped successive substitution and (ii) Heidemann's algorithm (1974) for performing equilibrium calculations. Calculations were initiated with these algorithms and then switched to the Newton-Raphson procedure for faster convergence.

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Dedicated to my family

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Nomenclature

a	:	activity; constant.
A	:	virial coefficient.
b	:	polydispersivity parameter; constant.
c	:	concentration; constant.
d	:	constant.
DF	:	damping factor.
e	:	constant.
$\bar{f}$	:	error vector.
f	:	constant.
$F(M)$	:	molecular weight distributuion.
H	:	enthalpy.
J	:	jacobian.
k	:	ratio of weight fractions.
K	:	equilibrium constant.
K_P	:	protein partition coefficient.
L	:	phase fraction.
$\bar{M}$	:	average molecular weight or molar mass.
M	:	molecular weight or molar mass.
M_N	:	molecular weight or molar mass.
M_o	:	constant of logarithmic-normal distribution.

M_W	:	molecular weight or molar mass.
n	:	number of moles.
p	:	phase mole number.
$\boldsymbol{p}$	:	vector containing parameters.
P	:	pressure.
q	:	phase mole number.
r	:	ratio of molar volumes; chain length.
R	:	gas constant.
rn	:	total number of moles.
S	:	entropy.
t	:	dummy variable; node.
T	:	temperature.
tol	:	tolerance.
V	:	partial specific volume.
w	:	interaction energy; weight fraction.
x	:	weight fraction; mole fraction.
y	:	weight fraction; vector containing OF values.
z	:	coordination number.

Superscripts

I	:	denotes phase.
II	:	denotes phase.
j	:	iteration count.

new   :   refers to current value.

o   :   refers to standard state.

old   :   refers to the value in the previous iteration step.

p   :   exponent to modify combinatorial entropy of mixing.

Subscripts

c   :   value at the critical point.

calc   :   calculated value.

exp   :   experimental value.

hi   :   maximum value.

i   :   component index.

L   :   refers to the lower critical solution temperature.

lo   :   minimum value.

old   :   value in the previous iteration step.

p   :   polymer.

s   :   solvent.

U   :   refers to the upper critical solution temperature.

Greek symbols

α :   constant; element of covariance matrix.

β :   constant.

γ :   constant

δ :   constant.

ΔH_M : enthalpy of mixing.

ΔS_C : combinatorial entropy of mixing.

Δt : increment in t.

Δw_{12} : change in interaction energy.

θ : transformed variable.

μ : chemical potential.

σ : constant in logarithmic normal distribution.

ϕ : volume fraction.

χ : Flory-Huggins interaction parameter.

CHAPTER 1

INTRODUCTION

This thesis is concerned with the correlation and/or prediction of the phase behaviour of aqueous solutions of certain water-soluble polymers. Water-soluble polymers have diverse applications. Molyneux (1991) points out that they are used in water treatment in oil recovery processes. They are also finding increasing use in paints and coatings (Klientjens, 1993). The two-phase aqueous systems obtained from different mixtures with two different water-soluble polymers have been used as an extraction medium for bioseparations (Albertsson, 1971) and are the main area of interest in this research. The focus is on mixtures involving polyethylene glycol and dextran, since these are the water soluble polymers that have received the most attention in the chemical engineering literature on aqueous two-phase systems.

The polyethylene glycols, PEG, have a structural unit $-[OCH_2CH_2]-$. Molyneux (1991) refers to these polymers as poly(ethylene oxide) but PEG is the name used most commonly. Dextran is a polysaccharide (polyglucose) that results from certain natural processes with the apparent formula $[C_6H_{10}O_5]_x$.

Chapter 2 contains a literature review. The PEG and Dextran used in producing the data described in Chapter 2 came from various suppliers and had a range of molar masses. Table 1.1 presents the molar masses of some typical polymers.

The data arise from several different kinds of phenomena. Some experimenters report the activity of water above solutions involving either PEG or Dextran (or both).

Table 1.1. Sources and molecular weights of some water-soluble polymers

POLYMER	SUPPLIER	SOURCE	M_N
PEG 3350	Union Carbide Carbowax	Haymes et al. (1989)	3790
PEG 8000	-do-	-do-	9037
DX T-70	Pharmacia	-do-	29630
DX T-500	-do-	-do-	167000
PEG 200	Hulls AG, Marl	Gaube et al. (1993)	201
PEG 600	-do-	-do-	582
PEG 1550	-do-	-do-	1440
PEG 3000	-do-	-do-	2840
PEG 6000	-do-	-do-	7750
DX 40000	Fluka Chemie AG, Buchs	-do-	23600
DX 70000	Pfeifer Langen, Dormagen	-do-	46300
DX 110000	-do-	-do-	64800
DX 500000	-do-	-do-	101000

Some researchers have measured the mutual solubility of PEG and water over a temperature range. The PEGs with lower average molar mass have closed solubility curves and exhibit complete miscibility at low and high temperatures but separate into two liquid phases at intermediate temperatures. A third kind of data relate to the phase separations that occur when a Dextran and a PEG are both dissolved in water in amounts greater than 5 to 10 mass percent.

Chapter 3 presents a description of the Flory-Huggins model. This excess free energy expression was derived from a model of the fluid as a lattice (Flory, 1953) with a monomer of a size sufficient to occupy a lattice site and with the polymer pictured as connected monomer groups that therefore must lie at adjacent lattice positions. This is the principal model used for solvent-polymer systems and it has been used in this research to correlate the data of several kinds that were available for the water-soluble polymer mixtures. Molyneux (1991) has raised the question whether it is appropriate to regard water in the same way as the monomer in the monomer/polymer solutions that were the basis for the original derivation of the Flory model. He points out that hydrogen bonding between water and the certain sites on the PEG may be an important consideration. However, the results reported in Chapter 5 demonstrate that the flory model can be used with some success to describe water activity, liquid-liquid coexistence curves, closed-loop binary phase diagrams and protein partitioning in aqueous two-phase systems.

In Chapter 4 are presented the numerical techniques used to correlate the parameters in the Flory-Huggins model and to perform the equilibrium calculations. Chapter 4 also contains a description of a new method for accounting for the fact that

each of the polymers is a mixture with molecules of many different chain lengths. The so-called polydispersivity of the polymers is potentially important in determining phase separations.

The conclusions reached through this research are summarized in Chapter 6.

CHAPTER 2

LITERATURE REVIEW

This chapter contains a review of the literature on polymer-water systems. It is divided into two sections. The first section covers the synthetic polymer(s)-water systems. The second section briefly covers some of the prominent studies of bioparticle or biopolymer partitioning in aqueous two phase systems.

In the two sections, first the papers containing experimental data are dealt with in a chronological manner and then the modeling efforts are covered in a similar way. Whenever a paper contains both experimental data and theoretical modeling of data a joint survey of the two aspects is presented.

The modeling efforts have primarily revolved around two models. These are

(a) the virial equation and,

(b) the Flory-Huggins lattice theory or some variation of it.

The point to be noted about the majority of modeling efforts is that predictions of thermodynamic behaviour employing the two models have not been made from first principles, i.e. from the chemical structure of the components. Rather, the models involve empirical parameters that have been correlated to fit measured thermodynamic properties (Walter et al, 1991).

The aqueous two polymer systems have application in bioseparations. As the name suggests, these are three-component solutions consisting of two polymers and water. Above critical concentrations of the polymers, an aqueous two-phase system separates into

two phases. One phase is rich in the first polymer and the other is rich in the second polymer. Biomolecules like proteins have a tendency to partition between the two phases and hence separation can be achieved. The phases are essentially aqueous, therefore, provide a mild environment for the labile biomaterials.

2.1 Synthetic polymer(s)-water systems

Malcolm and Rowlinson (1957) reported vapor pressure measurements over aqueous solutions of polyethylene glycols (PEG 300,3000 and 5000) and polypropylene glycol 400. The heats of mixing and densities were also reported. The temperature ranges from 30°C to 65°C. They have also presented mutual solubility curves for polyethylene glycols 3000 and 5000 and polypropylene glycol 400 in water.

Albertsson (1971) reported phase equilibrium data for many polymer-polymer-water and salt-polymer(s)-water systems at various temperatures. The two-phase systems studied by him were:

dextran/polyethylene glycol (PEG)/water

dextran/ucon/water

dextran/pluronic/water

dextran/tergitol/water

dextran/ficoll/water

ficoll/PEG/water

dextran/hydroxypropyldextran/water

hydroxypropyldextran/hydroxypropyldextran/water

hydroxypropyldextran/PEG/water

dextran/methylcellulose/water

dextran/polyvinylalcohol/water

DEAE/dextran/PEG/lithium sulfate/water

Na dextran sulfate/PEG/sodium chloride/water

Na dextran sulfate/methylcellulose/sodium chloride/water

Na dextran sulfate/polyvinylalcohol/water

Na carboxymethyldextran/PEG/sodium chloride/water

potassium phosphate/PEG/water

potassium phosphate/methoxypolyethylene glycol/water

potassium phosphate/polypropylene glycol/water

ammonium sulfate/PEG/water

magnesium sulfate/PEG/water

Saeki et al. (1976) have reported the upper and lower critical solution temperatures for solutions of polyethylene glycol in t-butyl acetate and water over the molar mass range 2180 to 1020000. Temperature/weight fraction phase diagrams for polyethylene glycols 719000, 21200, 14400 and 8000 in t-butyl acetate are reported. The paper also contains temperature/weight fraction phase diagrams for polyethylene glycols 1020000, 21200, 14400, 8000, 2290, 2270, 2180 in water.

King et al. (1988) reported experimental ternary phase diagrams for polyethylene glycol (PEG)/dextran/water systems at 25 °C. The polymers studied were PEG 3350 and 8000 and dextran T-70 and T-500. Size-Exclusion-High-Performance-

Chromatography (SEC) was employed for measuring phase compositions in ternary polymer/polymer/water systems. Low-angle-laser-light-scattering (LALLS) measurements were made to determine osmotic virial coefficients. Second virial coefficients, A_{ii}, were determined from LALLS measurements on binary polymer/water systems. Second cross virial coefficients, A_{ij}, were determined from LALLS measurements on three component (polymer/polymer/water) systems. These coefficients are reported. The osmotic virial equation was employed for phase equilibrium calculations involving PEG 8000/dextran T-500/water and PEG 3350/dextran T-70/water systems at 25 °C. The agreement between experimental and calculated two-phase curves is good. However, a comparison of tie-lines is not shown.

Haynes et al. (1989) reported vapor pressures for binary aqueous solutions containing 5-40% polyethylene glycol (PEG) or dextran. The polymers used were PEG 3350 and 8000 and dextran T-70 and T-500. The measurements were made with a differential-vapor-pressure apparatus. The activity of water is related to the vapor pressure difference by

$$a_1 = (P_1^{\,o} - \Delta P)/P_1^{\,o} \qquad\qquad (2.1)$$

where, a_1 is the activity of water and ΔP is the vapor pressure difference between pure water and polymer solution. $P_i^{\,o}$ is the vapor pressure of pure water at 25 °C and its value is 23.758 mm Hg. Their data show that ΔP is the greatest for the lowest molar mass polymer, PEG 3350. The vapor pressure lowering decreases with an increase in the molar mass of the polymer. This implies that the effect of the polymer on solvent activity

decreases with an increase in the polymer molar mass.

Haynes et al. (1989) have used a virial expansion for expressing the chemical potential of the solvent (1), in this case water, given by

$$\mu_1 - \mu_1^o = \frac{R\ T\ M_1 C_2}{1000}\ (\frac{1000}{M_{n2}}+A_{22}C_2+A_{222}C_2^2+...)$$ (2.2)

The second virial coefficients A_{22} were calculated from experimental water activity data using the expression for the chemical potential of the solvent. The second virial coefficients and number-average molar masses are reported for the four polymers. The osmotic second virial coefficients from this work are compared with those obtained from low-angle-laser-light-scattering (LALLS) data in an earlier work (King et al., 1988). The coefficients from vapor pressure data are consistently higher than those from LALLS data. The authors speculate that the difference could be because of errors induced in extrapolating semi-dilute (5-15%) solvent activity data to infinite dilution. They regard the osmotic coefficients from the vapor pressure data as "effective" second virial coefficients which may contain contributions from higher order interactions in addition to the two-body interactions.

Haynes et al. (1989) compared experimental vapor pressure data with predictions from the osmotic virial expansion truncated after the second virial coefficient term for PEG 3350 in aqueous solution at 25 °C. The second virial coefficient from LALLS data were used. The comparison shows that higher order terms (third order or more) are necessary for accurate representation of experimental data at higher concentrations of the

polymer. In order to match the experimental data better, "effective" third virial coefficients were calculated using experimental vapor pressure data and second virial coefficients from LALLS data in the virial expression for the chemical potential of the solvent. These coefficients for the four polymers are reported. The match between experimental and predicted differential vapor pressure for PEG 3350/water system at 25 °C was found to be very good with the inclusion of third order term in the virial expansion.

Haynes et al. (1989) also reported results of ternary liquid-liquid equilibria (LLE) calculations for the PEG 3350/dextran T-70/water system at 25 °C with the osmotic virial equation (OVE) truncated after second order terms and after third order terms. The match between experimental data and the results of calculations is satisfactory for the former case and very good for the latter. The cross second virial coefficients (A_{ij}) were obtained from LALLS measurements on three component (polymer/polymer/water) systems by King et al. (1988). The cross third virial coefficients (A_{ijj}) for the latter set of phase equilibrium calculations were obtained from the third order virial coefficients (A_{iii}) assuming a geometric-mean combining rule. The authors recommend accounting for the polydispersivity of dextran in calculations for more accurate results.

In a later section of the Haynes et al. (1989) paper, Flory-Huggins (F-H) interaction parameters for aqueous binary solutions of PEG 3350 and 8000 determined from differential vapor pressure data at 25 °C are reported. The parameters are shown to vary with the concentration of the polymer. The authors suggest that F-H theory is not applicable to PEG/water systems.

Diamond and Hsu (1989) reported phase diagram data at 4 °C for aqueous two phase systems composed of polyethylene glycol (PEG)/dextran/water. The systems studied were PEG 3400/dextran T-40, PEG 3400/dextran T-70, PEG 3400/dextran T-500, PEG 8000/dextran T-40, PEG 8000/dextran T-70, PEG 8000/dextran T-500, PEG 20000/dextran T-40, PEG 20000/dextran T-70, and PEG 20000/dextran T-500 in water. The experimental phase compositions of the phases were determined through a combination of polarimetric and refractive index analyses. The dextran concentration was measured by polarimetry as it possesses optical activity. The PEG concentration was determined by refractive index measurements.

Rathbone et al. (1990) reported weight-average molar masses and osmotic second virial coefficients obtained from LALLS measurements on binary aqueous solutions of eight nonionic polymers at 25 °C. The polymers studied were poly(vinylpyrrolidone) (PVP-10,PVP-24,PVP-40,PVP-360), poly(vinyl alcohol) (PVA-14, PVA-78, PVA-108), methylcellulose (MC-41,MC-63,MC-86), methoxypoly(ethylene glycol) (MOPEG-0.5, MOPEG-2000, MOPEG-5000), dextran (T-10, T-40, T-70, T-500), aquaphase PPT, bermocoll E, Ficoll. In binary aqueous solutions the concentrations of optically active polymers were determined with polarimetry and those of nonoptically active polymers through size-exclusion-high-performance-liquid-chromatography (SE-HPLC).

The following expression (osmotic virial expansion) was used for the chemical potential, μ_0, of the solvent for dilute binary aqueous solutions

The second osmotic virial coefficients and weight-average molar masses of the polymers

$$\mu_0 - \mu_0^o = R\ T\ V_0^o c_i\ (\frac{1}{M_{w_i}} + A_{ii}c_i + A_{iii}c_i^2)$$
(2.3)

were calculated from LALLS data in combination with equation 2.3. The authors also report cross second osmotic virial coefficients for several ternary systems at 25 °C. LALLS measurements on ternary (polymer/polymer/water) aqueous systems were made for this purpose.

Rathbone et al. (1990) have compared the accuracy of their LALLS data with that reported by Edsman et al. (1987) for dextran T-40 and T-70. Weight-average molar masses agree to within 13% and osmotic second virial coefficients to within 1%. They have also compared the measured solvent (water) vapor pressures for the dextran T-70/water system at 25 °C with values calculated using the osmotic virial expansion truncated after second order terms. The deviations between calculated and experimental values are significant for higher polymer concentrations (approximately > 10 weight% polymer). The authors conclude that higher order terms are required for accurate representation of data at higher polymer concentrations. They also recommend the use of LALLS experiments for determining the weight-average molar mass and osmotic second virial coefficient of a nonionic water soluble polymer.

Connemann et al. (1991) report tie-lines in the system poly(ethylene glycol)/dextran 500000/water at 0, 20 and 40 °C. The concentrations of the polymers were measured by size exclusion chromatography (SEC). The weight-average and the number-average molar masses of the polymers are also reported. The average molar masses of

dextran in the phases (corresponding to tie-line length and temperature) are reported. Tables of the complete data set, including the molar mass distributions of dextran, are available in supplementary material.

Großmann et al. (1993) have reported ternary phase equilibrium data for poly(ethylene glycol) (PEG)/dextran/water systems. The experimental water activities for binary aqueous solutions of PEG and dextran are also reported. The experimental data are presented in the form of graphs. The polymers studied were PEG 6000 and 35000 and dextran T-500 at 20 °C. Vapor pressures for determining experimental water activities were measured by an isotonic method. Phase equilibrium measurements involved polarimetry for dextran and UV/VIS spectroscopy analysis for PEG. A virial equation like expression for the Gibbs free energy similar to Pitzer's equation for electrolyte solutions (Pitzer,1973) was utilised to correlate and predict the vapor pressure data and ternary liquid-liquid equilibria (LLE). The expression is given by

$$\frac{G^E}{n_w R\, T} = \sum \sum A_{ij}\, N_i\, m_i\, N_j\, m_j + \sum \sum B_{ijk}\, N_i\, m_i\, N_j\, m_j\, N_k\, m_k \qquad (2.4)$$

where, N_i is the degree of polymerisation of component i, m_i is the molality of component i and n_w is the number of moles of water. The coefficients A_{ii} and B_{ii} were fitted to the binary vapor pressure data of PEG 6000 and dextran T-500 aqueous solutions. The model was able to correlate the experimental water activity data very well for these systems. It was also able to predict the activity of water for the system PEG 35000/water. The cross coefficients A_{ij}, B_{iij} and B_{ijj} were fitted to LLE data. The calculated phase diagrams for the

aqueous polymer systems PEG/dextran/water match the experimental phase diagrams well.

Gaube et al. (1993) reported measurements of water activity above various binary and ternary aqueous solutions of poly(ethylene glycol) (PEG) and dextran. The polymers used were PEG 200,600,1550,3000 and 6000 and dextran 40000, 70000, 110000 and 500000. The water activity above the binary solutions was measured at 20, 40 and 60 °C by vapor pressure osmometry in all cases and by membrane osmometry for certain dilute dextran solutions. The data for the binary mixtures were correlated with high precision by equations of the form

$$\ln a_1 = -V_1 M_1 \left(\frac{c_i}{M_{n,i}} + A_{ii} \, c_i^2 + A_{iii} \, c_i^3 \right) \tag{2.5}$$

where the subscript (1) refers to water and (i) refers to the polymer. $M_{n,i}$ is the number average molar mass and c_i is the concentration of component i. The original data are not presented in the paper but the coefficients A_{ii} and A_{iii} and the number average molar masses of the polymers, $M_{n,i}$, were fitted to the activity data and are tabulated at each of the three temperatures studied. Gaube et al. also presented values for the specific volumes of PEG and dextran (in units of cm^3/g) that were used in calculating the mixture volumes that enter the concentration terms. The paper also reports that the measurements of water activity were made for the ternary system PEG 3000, dextran 110000 and water over the homogeneous liquid range up to a polymer weight fraction of 30 mass percent and at 20, 40 and 60 °C. The water activity data were correlated with a ternary version of the osmotic virial equation with parameters A_{23}, A_{223} and A_{233} being fitted to the ternary data.

The coefficients are given in the paper and the original data are available in supplementary material.

The authors compared their water activity data for the system dextran 500000/water at 20 °C with the data reported by Haynes et al. (1989) and by Zhu et al. (1992). The latter set of data covers a wider range of polymer concentration but within the range of overlap compares very well with the data of Gaube et al. However, the data of Haynes et al. show a significantly lower water activity than was measured by Gaube et al.

Bae et al. (1993) reported LLE and VLE data for polystyrene (molar mass 100,000)/cyclohexane and polyethylene glycol (molar mass 8000)/water systems. They have applied an extended version of the Flory-Huggins equation to both VLE and LLE calculations involving several polymer/solvent systems. In their work, the Flory-Huggins interaction parameter was given an empirical temperature and composition dependence in order to fit the experimental data. The parameters of the model are reported. The calculated results show very good agreement with the experimental data in most cases.

As mentioned above, the modelling efforts in this area have primarily revolved around two approaches. The first approach has been the application of Flory-Huggins (F-H) lattice theory [Flory (1953)] to polymer-water systems. The latter approach has utilized the osmotic virial equation (OVE) some examples of which have been discussed above.

The original F-H theory is a classical statistical mechanical theory and accounts for the macroscopic behaviour of a solvent-polymer water system through interactions between solvent molecules and polymer segments and polymer-polymer segments. An

excellent qualitative analysis of the theory for polymer1-polymer2-water systems is available in the literature [Scott (1949)]. Scott has demonstrated the ability of the F-H theory to describe many qualitative features of polymer/polymer/solvent systems. In recent years the quantitative reliability of the theory for describing the thermodynamic behaviour of polymer-water has been tested by Gustafsson and Wennerstrom (1986) and by Kang and Sandler (1987).

Gustafsson and Wennerstrom (1986) have investigated the molecular mechanism leading to phase separation in aqueous two-polymer systems. They have analyzed two explanations for describing the phase separation phenomenon in these systems- (i) from virial expansion and, (ii) from the Flory-Huggins (F-H) theory.

The first explanation is due to Edmond and Ogston (1968). They employed a virial expansion (up to and including second order terms) for a thermodynamic description of phase separation. In their work the chemical potential of the solvent, in this case water, is given by the expression

$$\mu_1 - \mu_1^o = \frac{R\,T\,M_1}{1000} \left(m_2 + m_3 + \frac{c}{2}\, m_2^2 + \frac{d}{2}\, m_3^2 + a\, m_2\, m_3 \right) \qquad (2.6)$$

where, 2 and 3 refer to the two polymers and c and d are the second virial coefficients of binary systems and a is the interaction coefficient for the two polymers. m_i is the molal concentration. Gustafsson and Wennerstrom pointed out that though the approach is justified for dilute polymer solutions, its use is not appropriate at semi-dilute concentrations (5-15% (w/w) polymer) when the phase separation occurs. The "virial

coefficients" are properly viewed as empirical parameters fitted to experimental data. In their interpretation, Edmond and Ogston (1968) treated the phase separation phenomenon as a consequence of the size and shape of the polymer molecules by considering only the excluded volume contribution to virial coefficients. This interpretation is also questioned by Gustafsson and Wennerstrom (1986).

The second explanation for the phase separation phenomenon (Flory-Huggins theory) describes the phenomenon in terms of interaction parameters χ_{ij}. These can be related to enthalpic molecular interactions (segment-segment, solvent-segment interactions). The derivation of F-H theory takes into account the flexibility of polymers in the entropy of mixing term. Gustafsson and Wennerstrom (1986) used the F-H theory for correlating the phase equilibrium data of the PEG 6000/D17/water system at 20 °C and obtained a reasonable quantitative fit. The experimental data of Albertsson (1971) was used. Gustafsson and Wennerstrom point out that although the F-H theory gives a good qualitative description of polymer water systems and a satisfactory quantitative description of phase equilibrium of the system mentioned above there are problems associated with its application to these systems. The first one stems from the assumption of equality of volume of the water and a segment (monomer) of the polymer. The second problem is a consequence of the structural nature of water. The interaction parameter χ would have to be interpreted differently for polymer-water systems. Its nature would be free energy type rather than enthalpic only because solvation of a monomer unit involves many solvent molecules with the accompanying changes in the degrees of freedom.

At the end of their paper, Gustafsson and Wennerstrom (1986) conclude that

interactions between polymer units are more important than the excluded volume concept for a description of phase separation phenomenon.

Kang and Sandler (1987) have employed the Flory-Huggins lattice theory for calculating phase diagrams involving PEG/dextran/water systems at 273 K and 293 K. The systems studied by them were PEG 6000/dextran(17,24,37)/water. The experimental data of Albertsson (1971) was used. The F-H interaction parameters for these systems are presented. Parameter estimation was done by two approaches (i) by treating all parameters as adjustable and fitting them to ternary equilibrium data and, (ii) by fixing one *a priori* and estimating others. Calculated phase diagrams with parameters obtained using the first approach for PEG 6000/dextran (17,24,37)/water systems at 293 K are shown. The match between experimental and calculated values is satisfactory.

Although Flory-Huggins theory has been successful at describing thermodynamic properties of polymer-water systems, adaptations have been necessary to enable the description of lower critical solution temperature (LCST) behaviour of polymer solutions. There have been attempts at modifying the theory to overcome such limitations and there are successful efforts in literature. Two of the recent successful efforts are described briefly below. Yu et al. (1992) have presented a thermodynamic model to account for phase separation in binary aqueous solutions of polymers. Their model consists of two contributions - (i) a chemical contribution and, (ii) a physical contribution. The chemical contribution accounts for hydrogen bonding (orientation dependent effects) as well as the entropy of mixing. They assume a cross association or solvation reaction (through hydrogen bonds) between solvent and solute. It is further assumed that only one

polymer molecule associates with several solvent molecules. The equilibrium constant for the cross association reaction is related to standard enthalpy (ΔH°) and entropy of association (ΔS°). The excess entropy of mixing is accounted for by a modified F-H theory. The modification involves raising n (the ratio of the molecular volume of the solute to the solvent) to the power 0.75. This would give a lower entropy of mixing as effectively the chain length of the polymer is reduced. The physical contribution accounts for intermolecular interactions and for this purpose the NRTL equation (Renon et al., 1968) was used. The parameters in the NRTL equation were given inverse temperature dependence.

For each binary pair the model used by Yu et al. (1992) has six parameters, i.e.,ΔH°, ΔS°, two average association numbers (numbers of molecules involved in the cross association reaction), and two NRTL parameters. As mentioned above the association number for the polymer was fixed at one for this work. The remaining five parameters were estimated by fitting the model to the experimental data. The experimental data of Saeki et al. (1976) and Malcolm and Rowlinson (1957) were used. The agreement between calculated and experimental mutual solubility curves for binary aqueous solutions of polypropylene glycol and polyethylene glycol was found to be good.

Cheluget et al. (1993) have modified the Flory-Huggins-Goldstein model to describe closed loop phase diagrams of fourteen binary aqueous systems (hydrogen bonded) containing solutes ranging from high molar mass polymers such as PEG to those having a moderate molar mass such as nicotine. The hydrogen bonding aspect has been incorporated into the model through the interaction parameter χ. Following the work of

Goldstein (1984,1985) the interaction parameter has been assumed to have a free energy type nature and is taken to be temperature dependent. Cheluget at al. have employed three approaches to making χ temperature dependent.

The first approach (I) involves a single energetic level of hydrogen (H) bonding, the second (II) involves two energetically different levels of H-bonding in the solution. The third (III) employs a polynomial function for the temperature dependence of χ. (I) requires determination of four parameters and the other two an additional two parameters i.e., six in all. An interesting feature of the work Cheluget et al. is the use of an effective r (ratio of molar volume of the polymer to the solvent) for accurate representation of experimental data. They have demonstrated two ways of calculating r - (i) from critical compositions and, (ii) from two points on the experimental coexistence curve. The appendix to the paper of Cheluget et al. (1993) contains a method for estimating temperature independent parameters. The parameters and effective r's for fourteen binary systems are contained in the paper. Comparisons between experimental and calculated phase diagrams and experimental and calculated values of $\chi(T)$ are shown for various systems. Model III (a fifth order polynomial function) was found to be superior in fitting $\chi(T)$ to temperature. For calculating saturation curves, models II and III are only marginally better than model I. An important conclusion of their work is the adequacy of the effective value of r over the whole temperature range between lower and upper critical consolute temperatures in view of the polydispersivity of polymers. There are, however, up to five parameters used to fit the mutual solubility data for a binary pair. The experimental data of Saeki et al. (1976) and Sorensen et al. (1980) were used in this

work. The osmotic virial equation (OVE) is also derived from statistical mechanical considerations. It was first employed by Edmond and Ogston (1968). Their approach has been discussed above. At this point, only their computational scheme will be highlighted. The condition of phase equilibrium is the equality of chemical potentials of components in the two phases and is given by

$$\mu_i^I = \mu_i^{II} \qquad :i=1,2,...,n. \qquad (2.7)$$

where n refers to the number of components and I and II to the phases in equilibrium. For a three component two-polymer aqueous system there are three equations and four unknown quantities (molalities of the two polymers in the two equilibrium phases). By choosing a suitable value of, say, m_2^I the other three molalities can be calculated from the three equations.

In recent years OVE has been used by King et al. (1988), Cabezas et al. (1989, 1990), Haynes et al. (1989) and Gaube et al. (1992). The first three groups have used a virial expansion truncated after the second order terms while the last group has taken the virial expansion up to the third order terms. The work of King et al. has been discussed above.

Cabezas et al. (1989, 1990) have developed a model for calculating the phase diagrams of two-polymer aqueous two-phase systems from the solution theory of Hill (1957,1959). The model gives chemical potentials in terms of isobaric isothermal osmotic virial coefficients. The authors present predictive expressions for the dependence of these coefficients on molar mass and polydispersivity based on Renormalization Group theory.

For a two-polymer system their model contains three monomer interaction coefficients and two scaling exponents. The experimental data used was mainly taken from the works of Albertsson (1986) and King et al. (1988). The computation scheme employed was similar to that of Edmond and Ogston (1968). They report good results for calculated phase diagrams of four polymer/polymer/water systems. A statistical mechanical analysis was also offered by Forciniti and Hall (1990).

Haynes et al. (1989) rationalize their model on the basis of McMillan-Mayer solution theory. They report good results for phase equilibrium calculations involving PEG 8000/Dextran T-500/water system containing 50 mM KH_2PO_4 at 25 °C. Osmotic second virial coefficients used in their model were determined according to the protocol of King et al. (1988).

Gaube et al. (1992) have employed their version of OVE for phase equilibrium calculations. They have presented results for PEG 3000/dextran 110000/water system at 293.15 K with and without accounting for polydispersivity in their calculations. The match between experimental data and calculated values is good for the monodisperse case. The match is further improved on inclusion of the polydispersivity of dextran in calculations. This suggests that polydispersivity of polymers may be an important factor in treatments intended to be quantitative. The parameters of the model were determined from VLE measurements of Gaube et al. (1993).

It is unquestionable that OVE has had significant success in predicting phase diagrams for ATPS. However, the claim of supporters of OVE as to the correct description of the mechanism of phase separation has to be treated with caution as the

virial coefficients may be no more than empirical parameters [Albertsson (1971), Gustafsson et al. (1986) and Baskir et al. (1987)].

Kang and Sandler (1987,1988) have employed the UNIQUAC equation for phase equilibrium calculations involving two-polymer aqueous two-phase systems. They report good results for the PEG/dextran/water systems studied. They have also incorporated polydispersivity into phase equilibrium calculations (1988). Their approach for incorporating polydispersivity would be useful for other models as well. The experimental data of Albertsson (1971) was used in their work.

2.2 Bioparticle partitioning in polymer1-polymer2-water systems

King et al. (1988) reported experimental protein partition coefficients for albumin, lysozyme and α-chymotrypsin in aqueous two phase systems (ATPS) containing dextran (T-70,T-500)/PEG (3350,8000)/water at 25 °C. Osmotic second virial coefficients for aqueous mixtures containing proteins, salts (KCl, KH_2PO_4 and K_2SO_4 at concentrations 50 and 100 mM) and several combinations of polymer-protein pairs are also reported. In addition to these data the paper contains data on the measured electrochemical potential difference between the two phases. LALLS measurements were made on binary and ternary aqueous systems to determine virial coefficients. Experimental protein partition coefficients were determined from ultraviolet spectrophotometry. Liquid scintillation and voltametry were employed to determine salt partition coefficients and the electric-potential difference between the phases respectively. The authors used the following expression for

the chemical potential of the protein (p)

$$\Delta\mu_p = R\ T\ (\ \ln\ m_p\ +\ a_{pp}\ m_p\ +\ a_{2p}\ m_2\ +\ a_{3p}\ m_3\ )\ +\ z_p\ F\ \phi \qquad (2.8)$$

The last term represents the experimentally measured electric-potential difference between the two phases. The authors report that inclusion of this term was necessary for accurate representation of experimental protein partitioning data. Salt and water have been treated as a pseudosolvent in their development. They point out that this is not theoretically correct as salts partition between the phases and therefore the standard state is not the same between both the phases. The match between calculated and experimental protein partition coefficients is very good with their approach.

Diamond and Hsu (1989) report experimental partition coefficients for several dipeptides and proteins in PEG/dextran/water systems at 4 °C. The dipeptides studied by them were gly-gly, gly-ala, gly-α and gly-Nval which differ from one another by the addition of a CH_2 group on the c-terminal amino acid residue. Nine different proteins with a range of molar masses from 13000 to 145,000 were studied by them. These were cytochrome, lysozyme, ribonuclease, trypsin, α-amylase, BSA, transferrin, ovalbumin and alcohol dehydrogenase. The Flory-Huggins theory was used to correlate the partitioning of biomolecules in ATPS. The proteins and dipeptides were treated as linear polymers. The following expression for the natural logarithm of partition coefficient of the biomolecule (from F-H theory after certain simplifying assumptions) was used by them

where 0,1,2 and 3 refer to water, PEG, dextran and biomolecule respectively. K_3 is the

$$\ln(K_3) = m_3[\frac{\alpha_1}{m_1} + \frac{\alpha_2\phi}{m_2} + (\alpha_1 + \alpha_2\phi)(\chi_{03} - 1)$$
$$- \alpha_1\chi_{13} - \alpha_2\phi\chi_{23}]$$
$$* (w_1^I - w_1^{II})$$

(2.9)

protein partition coefficient. m_i is the molar volume ratio of species i to that of water. w is the weight fraction. I and II refer to the two phases. α is the product ρV. ρ is the density and V is the partial molar volume. ϕ is given by $(w_2^{II}-w_2^I)/(w_1^{II}-w_1^I)$. For a biomolecule partitioned in the tie-line compositions of a particular phase diagram the preceding expression can be written as

$$\ln(K_3) = A(w_1^I - w_1^{II})$$

(2.10)

since the term in the square brackets is constant.

The authors report an interesting trend for dipeptide partitioning. The natural logarithm of the partition coefficient [$\ln(K_3)$ vs $(w_1^{II} - w_1^I)$ plot] for a particular dipeptide converged on a single line regardless of the PEG/dextran/water system used. This combined with the fact that the line passes through the origin (corresponding to partitioning at the plait point) suggests that only one experimental data point is required to obtain the slope A. However, the author of this review is of the opinion that it is not advisable to rely on a single experimental measurement. Diamond et al. have utilised the results of dipeptide partitioning to present a hydrophobicity profile for PEG/dextran/water systems. The partitioning of low-molecular-weight proteins in a particular PEG/dextran/water system was observed to follow a linear relationship with the tie-line

compositions. However, the partitioning of high-molecular-weight proteins exhibited non-linearities.

Großmann et al. (1993) report partition coefficients of three amino acids (glycine (Gly), L-glutamic acid (Glu) and L-phenyl alanine (Phe)) and some of their peptides in PEG/dextran/water systems at 20 °C. The partition coefficients were measured by coupling derivative spectroscopy and HPLC. The experimental data were correlated with an empirical excess Gibbs energy model similar to Pitzer's equation for electrolyte solutions (Pitzer 1973) and similar to the similar to the osmotic virial equation. The partition coefficient calculations were done by assuming that all ternary interaction parameters involving amino acids and peptides as well as binary interactions between those compounds were negligible. Electrostatic interactions were neglected and the remaining binary parameters were fitted to experimental data. The authors also studied the effect of pH on the partitioning of Gly. For this purpose the glycine parameters were treated as pH dependent. Großmann et al. report very good correlation of partition coefficients with their model.

CHAPTER 3

MODELLING

Flory-Huggins lattice theory for polymer solutions forms the basis for all modelling effort in this work. The theory was applied in the original form along with variations of it to the systems of interest. The chapter begins with a section describing the Flory-Huggins lattice theory. Subsequent sections deal with variations of the theory that were employed to correlate and/or predict experimental data.

3.1 Flory-Huggins Lattice Theory

The Flory-Huggins (F-H) Lattice theory for polymer solutions was proposed independently by Flory and Huggins in 1942. They visualised a polymer solution as being approximately represented by a lattice as shown in Figure 3.1. In this scheme a cell of the lattice can be occupied by either a solvent molecule or a polymer segment. The different ways of arranging the polymer and solvent molecules on the lattice give rise to the combinatorial or configurational entropy of the system. The total number of arrangements is determined from statistics. The polymer is assumed to be a randomly coiling molecule. The expression for the combinatorial entropy of mixing (ΔS_C) for a binary solution (solvent {1}, solute {2}) is given by

$$\Delta S_C = -R \ (n_1 \ \ln \phi_1 \ + \ n_2 \ \ln \phi_2) \qquad (3.1)$$

where,

Figure 3.1

Representation of polymer and solvent molecules on the lattice

R   =   gas constant

n_i =   number of moles of component i

ϕ_i =   volume fraction of component i

    = $n_i \, r_i \, / \, \Sigma \, n_j \, r_j$

r_i =   number of segments on a molecule of component i. r has a value

of unity for the solvent monomer. r_i can be taken as the ratio of the

molar volume of the solute to that of the monomer solvent.

It is to be noted that ΔS_C represents the entropy change on mixing because of the

different ways available for arranging the molecules comprising the solution on the lattice.

The interactions between neighbouring segments or molecules are not included in the

expression.

The intermolecular interactions in the solution are represented by the heat of

mixing ΔH_M. ΔH_M is a consequence of replacing some like contacts (i.e., contacts between

like molecules or segments) by an equal number of unlike contacts (i.e., contacts between

solvent molecules and polymer segments). In the development of the theory only the first

or nearest neighbour contacts are assumed to be of importance. The expression for ΔH_M

of a binary polymer solution is

$$\Delta H_M = R \, T \, \chi \, n_1 \, \phi_2 \qquad\qquad (3.2)$$

where,

T   =   temperature

χ =   Flory-Huggins interaction parameter

The F-H parameter is given by the expression

$$\chi \quad = \quad (z\ \Delta w_{12})/(RT)$$

$$\Delta w_{12} \quad = \quad w_{12} - (w_{11}+w_{22})/2$$

$$z \quad = \quad \text{coordination number or the number of nearest neighbours}$$

w_{ij} is the interaction energy associated with an i-j contact.

The free energy of mixing (ΔG_M) for a binary polymer solution is obtained by combining equations 3.1.1 and 3.1.2 and is given by

$$\frac{\Delta G_M}{RT} = n_1 \ln \phi_1 + n_2 \ln \phi_2 + \chi\ n_1\ \phi_2 \qquad (3.3)$$

The free energy of mixing for a multicomponent solution from F-H theory is given by

$$\frac{\Delta G_M}{RT} = (\sum n_i \ln \phi_i + \frac{1}{2} \sum\sum \chi_{ij}\ \phi_i\ \phi_j)\ \sum n_i\ r_i \qquad (3.4)$$

where χ_{ij} is the F-H interaction parameter for the ith and j[th] components. χ_{ij} is equal to χ_{ji} i.e., the interaction parameters are symmetric.

3.2 Donohue's modification of ΔS_C expression from Flory-Huggins lattice theory

One of the assumptions of F-H theory is that the solute molecule is a random coiling molecule. Therefore the theory, in the strictest physical sense, is only appropriate for long chain molecules with very few constraints on the degrees of freedom. A segment

of the solute molecule when placed on the lattice can have at most one connection with already placed segments as shown in Figure 3.2. The development of the theory precludes the type of situation depicted schematically in the Figure 3.3. As a consequence, in physical terms, the theory is not applicable to rigid or bulky molecules which have constraints on degrees of freedom because of internal bonds. Also, the arrangement of segments is random. At lower concentrations of polymer it seems more probable that new segments of a polymer molecule added to the lattice would be found in the vicinity of the segments already present i.e., the polymer molecule would have a tendency to curl up to some extent. One is inclined to believe that in such a situation the F-H theory would overpredict the number of configurations or in other words the ΔS_C obtained would be higher than what may actually be the case.

Lichtenthaler et al. (1973) proposed an expression for the combinatorial entropy of mixing for molecules differing in size and shape with the purpose of overcoming the limitation mentioned above. Their work was based on lattice solution theory. However, their expression cannot be generalised to multicomponent mixtures (Lichtenthaler et al., 1973; Donohue and Prausnitz, 1975). Donohue and Prausnitz (1975) suggested a simple modification of $(\Delta S_C)_{F-H}$ by inclusion of an exponent p_i for obtaining the combinatorial entropy of mixing molecules that differ in size and shape. The exponent p_i in their work was based on the work of Lichtenthaler et al. This approach is valid for both binary and multicomponent mixtures. The modified expression for the combinatorial entropy of mixing (ΔS_C) is given by

Existing segments

Addition of a segment

Figure 3.2

Addition of a polymer segment to the lattice

Figure 3.3

Representation of a polymer molecule with internal bonding

$$\frac{\Delta S_C}{R} = -\sum_{i=1}^{nc} n_i \ln \left(\frac{n_i \, r_i^{p_i}}{\sum_{j=1}^{nc} n_i \, r_i^{p_i}} \right) \tag{3.5}$$

Note that the quantity in the parenthesis of equation 3.5 is the modified volume fraction of component i. An upper limit of unity and a lower limit of zero for the value of p_i was suggested by them. With these limits, the expression for the combinatorial entropy of mixing interpolates between that for the ideal solution with

$$\frac{\Delta S_C}{R} = -[\, n_1 \ln \left(\frac{n_1}{n_1 + n_2} \right) + n_2 \ln \left(\frac{n_2}{n_1 + n_2} \right)] \tag{3.6}$$

and the Flory-Huggins lattice solution with

$$\frac{\Delta S_C}{R} = -[\, n_1 \ln \phi_1 + n_2 \ln \phi_2 \,] \tag{3.7}$$

This is in accordance with the observation of Hildebrand (1947) that equation 3.6 gives a lower limit and equation 3.7 gives an upper limit for the combinatorial entropy of mixing.

The modification essentially involves altering the value of r_i. The dependence of ΔS_C on r can be looked at in purely mathematical terms. The combinatorial entropy of mixing expression for a binary (solvent-polymer) system is

$$\frac{\Delta S_C}{R} = -\left[n_1 \ln \left(\frac{n_1}{n_1 + n_2 \, r_2} \right) + n_2 \ln \left(\frac{n_2 \, r_2}{n_1 + n_2 \, r_2} \right) \right] \tag{3.8}$$

Note that r_1(solvent) is unity.

At a particular composition we can treat ΔS_C as a function of r_2 only. The derivative of ΔS_C with respect to r_2 is given by

$$\frac{d}{dr_2} \frac{\Delta S_C}{R} = \frac{n_1 n_2 \, (\, r_2 - 1 \,)}{r_2 \, (n_1 + r_2 \, n_2)} \tag{3.9}$$

The derivative is always greater than zero for r_2 greater than or equal to 2. Therefore, ΔS_C is a monotonically increasing function of r_2. In other words the combinatorial entropy of mixing for a binary solution increases with an increase in r_2 and vice versa.

3.3 Composition dependent interaction parameter

As can be seen from the discussion in Chapter 2, most of the data on polymer-water phase behaviour is limited to relatively low concentrations of polymer. This is particularly true of the data taken on water activity in the solutions. However, the data of Malcolm and Rowlinson (1957) for PEG 5000 in water at 65°C, includes measurement of the water activity in solutions up to 99% polymer by weight.

The Malcolm and Rowlinson data have been correlated in the past by Chen (1993) employing a model that combines Flory-Huggins model with the NRTL model [Renon

and Prausnitz (1968)]. The Flory-Huggins theory represents the configurational entropy of mixing in this model and the NRTL equation accounts for the local composition contribution from mixing solvents and polymer segments. Difficulties with matching these data and the observation of Flory (1953) regarding the compositional dependence of the interaction parameter have led to suggestions that the interaction parameter may be given a compositional dependence to match experimental data. Tompa (1956) has suggested a polynomial functional dependence of χ on composition given by

$$\chi = a + b\ \phi_2 + c\ \phi_2^2 + ... \tag{3.10}$$

where, $a,b,c,....$ are constants and ϕ_2 is the polymer volume fraction in the binary polymer/water mixture.

For a linear composition dependence of χ (retaining only the first two terms in equation 3.10) the expression for the activity of water is given by (after differentiating the Gibbs free energy of mixing expression with respect to the number of moles of water)

$$\ln\ (water\ activity) = \ln\ (1 - \phi_2) + (1 - \frac{1}{r})\ \phi_2$$
$$+ \phi_2^2\ \chi - \phi_1\ \phi_2^2\ b \tag{3.11}$$

Here 2 refers to the polymer.

3.4 Modelling of closed-loop phase diagrams

A limitation of the Flory-Huggins lattice theory with the enthalpic term given by equation 3.2 is its inability to describe closed loop phase diagrams or in other words the inability of the theory to describe the phase behaviour of systems showing both lower critical solution temperature (LCST) and upper critical solution temperature (UCST). Earlier studies [Hirschfelder et al. (1937); Barker and Fock (1953)] suggest that this kind of behaviour is because of the presence of strong orientation dependent effects such as hydrogen bonding in aqueous solutions. Qian and co-workers (1991) have made χ an empirical function of temperature and composition to fit closed-loop solubility curves. Bae et al. (1993) have simplified Qian's model by using a different composition functionality. Cheluget et al. (1993) have employed a temperature dependent χ to describe behaviour of systems showing simultaneous LCST and UCST.

In this section an alternative approach is presented to model the phenomenon mentioned in the preceding paragraph. It is proposed that r (chain length) be made an empirical function of temperature given by

$$r(T) = d + e\ T + f\ T^2 \qquad (3.12)$$

and, following Qian et al., χ be given the following temperature functionality

$$\chi(T) = a + \frac{b}{T} + c\ \ln T \qquad (3.13)$$

This method requires a knowledge of six parameters (a,b,c,d,e and f) for a binary

system consisting of a long-chain solute and a monomer solvent. At least three of these can be determined from critical conditions. The other three can be treated as adjustable parameters for a binary system. Details of parameter estimation are contained in a later Section (4.2).

3.5 Correlation of protein partitioning

Protein partitioning in aqueous two phase systems (polymer1-polymer2-water) can be correlated with Flory-Huggins lattice theory. However, one objection to its use for this purpose is that proteins are globular molecules rather than random coiling polymers to which F-H theory is applicable. An approximate method for overcoming this objection to some extent is described in Section (3.2) where the use of an r (chain length) other than the ratio of the molar volume of the solute to the solvent is suggested. The details concerning the parameter estimation are contained in Section (4.3). Results of correlation for the partitioning of two proteins are contained in Section (5.4).

CHAPTER 4

PARAMETER ESTIMATION AND COMPUTATIONAL TECHNIQUES

This chapter contains details of techniques of parameter estimation employed for fitting various sets of experimental data. Section 4.5 of this chapter deals with the computational techniques employed for liquid-liquid equilibrium calculations. Section 4.6 describes a method for characterising polydisperse polymers.

The types of experimental data involved in parameter estimation were:

(a) Water activities for binary polymer water systems. These could be experimental values or those from the virial equation. The virial coefficients were obtained from experimental measurements such as LALLS and osmometric methods.

(b) LLE data for binary (polymer-water) and ternary (polymer-polymer-water) systems.

(c) Protein partition coefficients in aqueous two-phase systems.

The parameter estimation techniques corresponding to the various types of data are covered in separate sections. The results of calculations with the estimated parameters are presented in chapter 5.

4.1 Fitting water activity data

When the data were measurements of the water activity in single-phase polymer-water solutions, the objective function used was

$$O.F. = \sum^{ndata} (\ln a_{exp} - \ln a_{calc})^2 \qquad (4.1)$$

where, a is the solvent (water) activity, *exp* refers to the experimental value and *calc* refers to the value calculated from the Flory-Huggins equation. The number of data points is *ndata.*

4.1.1 Solutions with one polymer

The activity in a solution with a single polymer is given by (assuming constant χ)

$$\ln a = \ln (1 - \phi_2) + (1 - \frac{1}{r})\phi_2 + \chi \, \phi_2^2 \qquad (4.2)$$

where, r is the ratio of the molar volumes of the solute to that of the solvent and ϕ_2 is the polymer volume fraction. The value of r could be obtained from an apparent specific volume of the polymer as it exists in solution (V_P, cm^3/g) and its number average molar mass (M_P, g/mol)

$$r = \frac{V_p \, M_p}{V_s \, M_s} \qquad (4.3)$$

where, V_S is the water specific volume (1.00 cm^3/g) and M_S is the water molar mass (M_S = 18.0 g/mol).

In the original Flory-Huggins theory, the solvent was expected to be the monomer from which the polymer was composed. Then r was the "degree of polymerisation", i.e.,

the number of monomers per polymer molecule.

. As was discussed in Chapter 3, in some cases r was treated as a fitting parameter available, along with χ, to minimize the objective function in (4.1).

In the attempt to fit the data of Malcolm and Rowlinson (1957), the interaction parameter was treated as linear in the polymer volume fraction

$$\chi = a + b \, \phi_2 \tag{4.4}$$

Then equation (4.2) has to be modified to give

$$\ln a_1 = \ln (1 - \phi_2) + (1 - \frac{1}{r}) \, \phi_2 + \phi_2^2 \, \chi - \phi_1 \, \phi_2^2 \, b \tag{4.5}$$

4.1.2 Water activity in polymer-polymer-water solutions

The data of Gaube et al. (1993) include measurements of water activity in polymer-polymer-water systems. In fitting these data the objective function (4.1) was also used.

The equation for calculating the activity of a component (including the solvent) in a solution with several polymers in the same solvent is given in Appendix A3.

4.2 Fitting liquid-liquid equilibrium data

Liquid-liquid equilibrium (LLE) data are available for binary-polymer systems. Some of these systems show closed-loop phase diagrams with a lower critical solubility temperature and an upper critical solubility temperature bounding the interval where two

liquid phases can exist. A number of ternary polymer-polymer-water binodal curves have also been reported.

Two objective functions (OF) were used for parameter estimation involving LLE data. These were

$$OF(I) = \sum \sum \sum \ (\frac{X_{calc} - X_{exp}}{X_{calc} + X_{exp}})^2 \qquad (4.6)$$

and

$$OF(II) = \sum \sum \sum \ \frac{(X_{calc} - X_{exp})^2}{ndata} \qquad (4.7)$$

ndata refers to the number of points. The summation is for all the components and phases over all the data points. OF(I) has been recommended by Kang and Sandler (1987) who estimated parameters for some ternary polymer-polymer-water systems. OF(II) was found to fit the experimental data better for systems containing higher molar mass dextrans such as dextrans 110000 and 500000.

4.2.1 Binary systems with closed-loop phase diagrams

Recall that in section 3.4 it was proposed that r be given the following temperature dependence

$$r(T) = d + e \ T + f \ T^2 \qquad (4.8)$$

and χ be given by

$$\chi(T) = a + \frac{b}{T} + c \ln T \qquad (4.9)$$

Two features of the Flory-Huggins theory reduce the number of adjustable parameters to three. The critical χ is given by

$$\chi_c = \frac{1}{2} \left(1 + r^{-\frac{1}{2}} \right) \qquad (4.10)$$

where c refers to the critical state. The critical r is given by

$$r_c^{\frac{3}{2}} = \frac{(w_1 / w_2)_c}{(M_1 / M_2)} \qquad (4.11)$$

where w_i and M_i are the weight fraction and the molar mass respectively [Cheluget et al. (1993)]. In equation (4.11) 1 refers to the solvent and 2 to the polymer or the long-chain molecule. Assuming that the LCST (T_L), the UCST (T_U) and the two critical compositions are known, χ_c and r_c can be calculated.

Let,

$$\chi_c = a + \frac{b}{T_L} + c \ln T_L \qquad (4.12)$$

and

$$\chi_c = a + \frac{b}{T_U} + c \ln T_U \qquad (4.13)$$

Using a guess for "a" the previous two equations can be solved to give

$$c = \frac{(\chi_c - a) (T_L - T_U)}{T_L \ln T_L - T_U \ln T_U} \qquad (4.14)$$

and

$$b = (\chi_c - a) T_L - T_L \ln T_L \qquad (4.15)$$

Treating e and f as adjustable parameters we get

$$d = r_c - e \, T_L + f \, T_L^2 \qquad (4.16)$$

Three parameters (a,e and f) are available to match compositions in coexisting phases. The others (c,b and d) are found from equations (4.14)-(4.16).

A disadvantage of this approach is that the mutual solubility curve is very flat in the critical region and the critical compositions are known only approximately. Objective function I (equation 4.6) was employed for parameter estimation.

4.2.2 Ternary systems (polymer1-polymer2-water) at constant T and P

The LLE (liquid-liquid equilibrium) data of King et al. (1988), Connemann et al. (1991) and Gaube et al. (1993) have been correlated in this study.

Correlation and/or prediction of ternary LLE data requires estimation of at least three parameters; i.e., two water-polymer interaction parameters and one polymer1-polymer2 interaction parameter. All three parameters can be fitted to ternary LLE data. Alternatively, the polymer-water parameters can be obtained from binary data e.g., binary water activity data (refer section 4.1) and then the polymer1-polymer2 interaction parameter (χ_{P1P2}) can be obtained from ternary LLE data. The ratios of polymer molar volumes to the water molar volume (r_1 and r_2) can be assumed known from the number average molar mass and the apparent liquid molar volumes of the polymers. In later discussions, correlations obtained by taking r_1 and r_2 as known are referred to as 1FHP theory (one Flory-Huggins parameter).

An alternative is to treat r_1 and r_2 as free parameters, as well as the three χ values. There are, in the procedure, two parameters (r and χ) per binary pair. This approach is referred to, in what follows, as 2FHP theory.

Both objective functions, (4.6) and (4.7) have been used in correlating data.

4.3 Protein partitioning

The efficacy of Flory-Huggins theory in correlating the partitioning of proteins in aqueous two-phase systems was tested. The experimental data of King et al. (1988) was used for this purpose.

Neglecting electrostatic forces (note that the experimental data involved the presence of small concentrations of salts in the solution) and using molar volume ratios as $r's$ for the two polymers values of the following parameters are required to calculate

protein partition coefficients:

(i) Three interaction parameters corresponding to the two polymers and water. These were obtained by fitting the F-H theory to ternary (polymer1-polymer2-water) two-phase data.

(ii) Interaction parameters to represent interactions between ions and molecular species. These were set equal to zero.

(iii) r parameter for the protein and three interaction parameters to represent the interaction between proteins and water and the two polymers.

King et al. (1988) did not present data for the water-protein equilibria but rather correlated data with a virial type equation. For water with one dissolved polymer (protein) the solvent (water) activity is given by

$$\ln a_s = -V_s \, c_i \left(\frac{1}{M_{Ni}} + A_{ii} \, c_i \right) \qquad (4.17)$$

where i refers to the solute. M_{Ni} is the molar mass of the solute. c_i is the concentration of the solute. V refers to the molar volume. A_{ii} is the virial coefficient.

The values of $\ln a_s$ were obtained from the previous equation (4.17) using the virial coefficient (A_{ii}) presented by King et al. Equation 4.2 for water activity (Flory-Huggins theory) in a polymer-solvent system was then fitted to $\ln a_s$ treating both r and χ (protein-water) as parameters. The objective function given by equation 4.1 was employed for parameter estimation. V_s was fixed at 18 cm³/mol. The partial specific volume of water was assumed to be unity and that of the proteins was assumed to be 0.7 cm³/g (since the

partial specific volumes of proteins are in the vicinity of 0.7 cm³/g). The partial specific

volumes are required for the conversion of c_i to weight fraction and vice versa.

The remaining two interaction parameters (corresponding to the interactions of the

proteins with the two polymers) were obtained from experimental protein partition

coefficient data. The parameter estimation procedure is described below.

Experimental data were available for polymer1-polymer2-water-protein-salt

systems for the estimation of protein-polymer interaction parameters. The amounts of

protein and salts in the system were very small (0.5-2.5 mg/ml for the protein and 50 mM

for the salt). The experimental data were in terms of tie-line lengths and corresponding

protein partition coefficients. The equilibrium phase compositions of polymers and water

can be obtained from tie-line lengths as the compositions are not significantly different

from those in ternary polymer1-polymer2-water systems because of the low concentrations

of other solutes. The equilibrium phase compositions of polymers and water are required

for the estimation of protein-polymer interaction parameters.

The following objective function was employed for parameter estimation

$$OF = \sum^{ndata} (\ \ln K_{P\,calc} - \ln K_{P\,exp}\ )^2 \qquad (4.18)$$

where K_P is the protein partition coefficient. In order to obtain K_{Pcalc} a feed corresponding

to the experimental tie-line was flashed. Instead of using the feed compositions provided

by King et al., feed compositions lying on a line passing through the origin and the

calculated plait point and cutting across the experimental tie-lines was chosen. This is

illustrated in figure 4.1.

Figure 4.1

Calculation of feed compositions

Let the desired line be

$$\frac{w_2}{w_1} = k \qquad (4.19)$$

where,

$$k = \frac{w_2^c}{w_1^c} \qquad (4.20)$$

and where c refers to the calculated plait point. w is the weight fraction.

Now for a particular tie-line

$$w_1 = L\, x_1 + (1 - L)\, y_1 \qquad (4.21)$$

and

$$w_2 = L\, x_2 + (1 - L)\, y_2 \qquad (4.22)$$

where the x_i and the y_i are experimental equilibrium phase compositions (weight fractions) and the w_i are the feed compositions. L is the phase fraction. Subscripts 1 and 2 refer to the phase forming polymers.

Equations 4.19, 4.20, 4.21 and 4.22 can be solved to give the phase fraction L which is given by

$$L = \frac{y_2 - k \, y_1}{k \, (\, x_1 - y_1 \,) + (\, y_2 - x_2 \,)} \tag{4.23}$$

The w_i's can now be calculated from equations 4.21 and 4.22. The feed compositions so calculated along with the small amounts of other solutes were flashed to estimate protein-polymer interaction parameters.

Note that this does not alter the computational results in any way as any feed on a tie-line will give two phases whose compositions are given by the ends of the tie-line. The partition of the protein is governed by the composition of equilibrium phases. This also facilitates the comparison of calculated and experimental protein partition coefficients based on the total amount of polymers in the feed in a consistent way.

4.4 Minimization algorithm

4.4.1 Method of Nelder and Mead (1965)

The minimization algorithm of Nelder and Mead (1965) was employed for parameter estimation. This "downhill simplex method" requires function evaluations only. This method is slower as compared to some other minimization algorithms. However, this was not a drawback for this research effort as the computational load was not very large and the algorithm was found to be robust and reliable. The subroutine given in Numerical Recipes (pages 292-293, 1990) was used as is except when single parameter estimation was done. For the latter purpose it had to be modified.

A simplex is geometrical figure the dimension of which is equal to the number of

parameters to be estimated. When there is a two parameter search the operating simplex is a triangle. The objective function is evaluated at the vertices of the simplex. The tolerance for estimation is given by

$$tol = \frac{2(|y_{hi}| - |y_{lo}|)}{|(y_{hi} + y_{lo})|}$$

(4.24)

where y_{hi} is the highest value of the objective function and y_{lo} is the lowest value of the function. For correlating binary water activities $tol=10^{-12}$ was used. For estimation involving flash calculations tol$=10^{-6}$ was used.

4.4.2 Confidence limits

Confidence ellipses were calculated according to the scheme outlined in Numerical Recipes (page 537, 1990).

The objective function employed is given by

$$OF = \sum^{ndata} [\frac{\ln a_{i\,exp} - \ln a_{i\,calc}}{\sigma_i}]^2$$

(4.25)

σ_i was fixed at 0.02. Variance-covariance matrix had elements

$$\alpha_{k\,l} = \frac{1}{2}\frac{\partial^2(OF)}{\partial p_k \partial p_l}$$

(4.26)

The parameters (for two parameter estimation) are $p_1=\chi$ and $p_2=r$. The derivatives of $\ln a_{i\,calc}$ were found analytically.

The equation for the confidence ellipse is

$$\Delta = p^{T}[\alpha]p \qquad (4.27)$$

where p is the vector containing the parameters and $\Delta=6.17$ for the 95.4% confidence ellipse.

4.5 Liquid-Liquid equilibrium calculations

The liquid phase compositions in the objective functions of (4.6) and (4.7) had to be computed repeatedly during the parameter estimation process. For each trial set of parameters "flash" calculations had to be performed at each of the compositions where data were to be fitted.

The flash calculations proved to be difficult for several reasons. Care had to be taken at every step with machine precision and round off error since mole fractions of the polymers were always very small (since the molar masses are very large) and the activities and activity coefficients were extremely large or small. The equilibrium ratio of mole fractions of a component in the two phases is given by

$$x_i^{II}/x_i^{I} = K_i = \gamma_i^{I} / \gamma_i^{II} \qquad (4.28)$$

where the subscripts I and II refer to the phase and γ_i is the activity coefficient of component i. These K_i equilibrium ratios also ranged over many orders of magnitude.

In addition to these precision problems, problems arose with use of conventional

flash calculation procedures.

4.5.1 Damped successive substitution

In flash calculations a mixture with known mole fractions, z_i, is assumed to separate into two equilibrium phases with mole fractions x_i' and x_i''. The fraction of moles in phase II is β.

At equilibrium, the ratio of the mole fractions in the two phases must be given by equation (4.28), which requires

$$a_i' = x_i'\gamma_i' = a_i'' = x_i''\gamma_i'' \qquad (4.29)$$

The "successive substitution" procedure for solving the combined mass balance and equilibrium equations has been shown to converge to a minimum in the Gibbs free energy (when it converges) and generally only suffers from slow convergence near the critical points in calculations on hydrocarbon mixtures where it is most widely used (see Heidemann, 1983).

The procedure involves estimating the K_i equilibrium ratios. From the estimated values, the mole fractions in the phases can be calculated in terms of the phase amounts. The fraction in phase II is found as the solution to the equation

$$\sum_i (x_i'' - x_i') = 0 = \sum_i \frac{z_i(K_i - 1)}{(1 - \beta) + K_i\beta} \qquad (4.30)$$

which is solved assuming constant K_i.

The mole fractions are given by

$$x_i^{\,\prime} = \frac{z_i}{(1-\beta) + K_i\beta} \qquad (4.31)$$

and

$$x_i^{\,\prime\prime} = K_i\, x_i^{\,\prime} \qquad (4.32)$$

where the K_i are the estimated values.

Given the mole fractions, the activity coefficients in the phases can be found and new values of the K_i equilibrium ratios can be calculated from equation (4.28). With new K_i values equations (4.30)-(4.32) can be solved again for updated phase amounts and mole fractions.

The iterative procedure is equivalent to taking

$$K_i = \frac{a_i^{\,\prime}}{a_i^{\,\prime\prime}}\, K_{i(old)} \qquad (4.33)$$

where *old* refers to the value of K_i in the previous iteration.

Surprisingly, this procedure simply did not work when the activity coefficients were obtained from the Flory-Huggins model. No matter how close to the converged solution the K_i values are initiated, the successive iterations tend towards an oscillatory state where first the whole mixture is in phase I and then, in the next iteration, in phase II.

An analysis of the equations by Michelsen (1993) demonstrates that successive substitution simply cannot work for the Flory-Huggins model with the parameters needed to describe the aqueous two-phase polymer systems. No matter what initiation strategy is used, the procedure will show oscillatory divergence.

On Michelsen's (1993) suggestion a "damped" version of the procedure was implemented and was made to work. The working equation employed is

$$K_i = (\frac{a_i^{\prime}}{a_i^{\prime\prime}})^{DF} \ K_{i(old)} \tag{4.34}$$

where DF is the damping factor with a value less than unity. A DF=0.07 was used as the damping factor. This value is quite arbitrary. It was observed that with an increase in the molar mass of the polymer the value of the damping factor decreased for carrying out equilibrium calculations successfully. This modification enabled successful convergence of successive substitution by stabilising the flash calculations. The modified procedure can be and was used with the incorporation of an acceleration technique (Crowe and Nishio, 1975) to give faster convergence. However, convergence was sometimes very slow and unpredictable. Convergence was taken to be

$$\sum \ (\ln \ a_i^{\prime\prime} - \ln \ a_i^{\prime} \ )^2 \leq \varepsilon \tag{4.35}$$

where ε was 10^{-12}.

4.5.2 Free energy minimization (Heidemann, 1974)

An alternative to the successive substitution flash calculation procedure is the flash calculation procedure of Heidemann (1974). Heidemann's algorithm can be used for multi-phase flash calculations also. This algorithm was also employed to perform equilibrium calculations with Flory-Huggins theory. The scheme was robust, since for any initial guess it always moved towards a Gibbs free energy minimum. However, the convergence became extremely slow as the equilibrium compositions were approached. The mode of implementation of Heidemann's algorithm is described below.

Let the two phases be represented by I and II. Let p_i's and q_i's be the corresponding mole numbers. Let rn_i's be the total mole numbers of component i. The Gibbs free energy of mixing of the systems was calculated as

$$\frac{\Delta G}{RT} = \sum_i (p_i \, \ln a_i^I + q_i \, \ln a_i^{II})$$

(4.36)

The calculation of new mole numbers depended on the values of the activities (a). If a_i^I was greater than a_i^{II}, p_i's were treated as independent variables and were updated as

$$p_i^{j+1} = p_i^j \left(\frac{a_i^{II}}{a_i^I} \right)^{\Delta t}$$

(4.37)

where j refers to the iteration count and Δt is the dummy variable in the algorithm.

In this case the new q_i's were calculated as

$$q_i^{j+1} = rn_i - p_i^{j+1}$$ (4.38)

However, if a_i^{II} was grater than a_i^{I}, the q_i's were treated as independent variables and the new q_i's were calculated as

$$q_i^{j+1} = q_i^{j} \left(\frac{a_i^{I}}{a_i^{II}} \right)^{\Delta t}$$ (4.39)

and the new p_i's were calculated as

$$p_i^{j+1} = rn_i - q_i^{j}$$ (4.40)

The value of Δt was varied as suggested by Heidemann and was permitted to increase so long as G decreased. For each iteration step, the calculated value ΔG was stored for the calculation of change in ΔG only if the current value was less than the previous value. This insured that the calculations moved towards a minimum of the Gibbs free energy. The calculations were begun with a small value of Δt, it being 0.002 or smaller. The value of Δt was never allowed to increase beyond 0.2.

In some cases, the mole numbers were found to change extremely little between iterations and very many iterations were required to reach convergence. This procedure, however, was very useful early in the research before the difficulties with successive substitution were resolved.

4.5.3 Newton iteration

Both the damped successive substitution method and Heidemann's method showed unpredictable or extremely slow convergence. Ultimately, convergence was obtainable by switching to the Newton-Raphson procedure when the convergence criterion of (4.35) was less than 10^{-7}.

Let I and II represent the two equilibrium phases. Let p_i and q_i be the corresponding mole numbers in the two phases. The total number of moles of the ith component are given by rn_i.

Conservation of mass gives for each component i,

$$p_i + q_i = rn_i = constant \qquad (4.41)$$

Therefore,

$$dp_i = - dq_i \qquad (4.42)$$

Let p the independent mole numbers.

At equilibrium,

$$\vec{f} = \nabla_p(\frac{\Delta G^{I}}{RT}) - \nabla_q(\frac{\Delta G^{II}}{RT}) = 0 \qquad (4.43)$$

$\vec{f}$ is the error vector. ΔG is the Gibbs free energy of mixing. ∇ is the gradient vector. We solve for p_i's in order to reduce the error vector to zero.

The Jacobian is given by

$$[J_{ij}]_{nc \times nc} = \nabla_p^2 (\frac{\Delta G'}{RT}) + \nabla_p^2 (\frac{\Delta G''}{RT}) \qquad (4.44)$$

The alterations in p_i given by Δp_i can be found by solving the following set of equations

$$[J_{ij}]_{nc \times nc} [\Delta p_i]_{nc \times 1} = - [f_i]_{nc \times 1} = - \bar{f} \qquad (4.45)$$

The updated p_i's are

$$p_i^{new} = p_i^{old} + \Delta p_i \qquad (4.46)$$

The updated q_i's are

$$q_i^{new} = rn_i - p_i^{new} \qquad (4.47)$$

The iterative procedure is continued until the elements of the error vector approach a preset tolerance.

The Jacobian elements involve derivatives of $\ln a_i$ with respect to the mole numbers. The required expressions are given in appendix A3.

4.6 Characterising polydisperse polymers

So far in all calculations involving polymers the polymers were treated as

monodisperse i.e., having a single molar mass. Number average molar masses of the polymers were used whenever available. Polydispersivity of polymers and its effect on phase equilibrium calculations has been the subject of some previous studies. Two recent works are those of Kang et al. (1988) and Gaube et al. (1992). Kang et al. represented polymer molar mass distribution through psuedocomponents and showed the effect of polydispersivity of polymers on the two phase equilibrium curve qualitatively. They employed the UNIQUAC equation for phase equilibrium calculations. Gaube et al. also used psuedocomponents to represent polydispersivity of polymers in phase equilibrium calculations with the virial equation. Their results show a quantitative improvement in the two phase equilibrium curve. The objective of the work pertaining to this section was to study the effect of polydispersivity of polymers on phase equilibrium calculations with Flory-Huggins theory using a pseudocomponent approach. The scheme for determining psuedocomponents is outlined below.

4.6.1 Log-Normal distribution

Logarithmic-normal (L-N) distribution is employed to represent the molar mass distribution of the polymer. L-N distribution is given by

$$F(M) = \frac{1}{(2\pi)^{0.5}\sigma} \exp(-\frac{1}{2\sigma^2}\ln^2 \frac{M}{M_o}) \qquad (4.48)$$

where, $(F(M)/M)dM$ is the fraction with molar mass between M and $M+dM$, and M_o and σ are the parameters of the distribution. Sometimes in the subsequent discussion $2^{0.5}\sigma$ will

be referred to as β.

The number average molar mass (M_N) and the weight average molar mass (M_W) are given by the following equations (after integration)

$$\frac{1}{M_N} = \frac{\int_0^\infty \frac{1}{M}F(M)dM}{\int_0^\infty F(M)dM} = \frac{1}{M_o \exp(\frac{\beta^2}{4})} \qquad (4.49)$$

and,

$$M_W = \frac{\int_0^\infty MF(M)dM}{\int_0^\infty F(M)dM} = M_o \exp(\frac{3}{4}\beta^2) \qquad (4.50)$$

From equations 4.49 and 4.50 the so called "polydispersivity parameter" b can be obtained as

$$b = \frac{M_W}{M_N} = \exp(\frac{\beta^2}{2}) \qquad (4.51)$$

4.6.2 Determination of pseudocomponents

Frequently experimental values of M_N and M_W are given, then the two parameters M_o and σ or β can be found.

Now $F(M)$ has been used in this research to find pseudocomponents as follows: $F(M)$ can be expressed as

$$F(M) = \frac{1}{(2\pi)^{0.5}}\exp(-\frac{\theta^2}{2}) \tag{4.52}$$

where,

$$\theta = \frac{\ln(M/M_o)}{\sigma} \tag{4.53}$$

Note that equation (4.52) is the normal distribution for θ. $F(M)d\ln(M)$ represents the mole fraction of the polymer between $\ln(M)$ and $\ln(M)+d\ln(M)$. The mole fraction x_i between $\ln(M_i)$ and $\ln(M_{i+1})$ is given by

$$x_i = \int_{M_i}^{M_{i+1}} F(M)d\ln(M) \tag{4.54}$$

On a plot of $F(M)$ vs $d\ln(M)$ x_i is the area between $\ln(M_i)$ and $\ln(M_{i+1})$.

The variable in equation 4.54 can be transformed to give

$$x_i = \int_{\theta_i}^{\theta_{i+1}} F(M)\sigma d\theta \tag{4.55}$$

The x_i's or areas for intervals on θ can be found from the tables of the normal distribution. The average molar mass $\bar{M}_i$ for the interval $\ln(M_i)$ to $\ln(M_{i+1})$ can be calculated as

$$\ln \overline{M}_i = \frac{\ln M_i + \ln M_{i+1}}{2} \qquad (4.56)$$

or,

$$\overline{M}_i = (M_i M_{i+1})^{0.5} \qquad (4.57)$$

$\overline{M}_i$ corresponds to x_i.

EXAMPLE 4.5.1

Consider dextran 110000 with M_N and M_W equal to 64800 and 110000 respectively [Gaube et al. (1993)]. M_N and M_W along with equations 4.49 and 4.50 give M_o and σ as 49737 and 1.0288 respectively. Let us take θ to extend from -3 to 3 i.e., from -3σ to +3σ. Also, let the desired number of psuedocomponents be six.

Now,

$$M_i = M_o \exp(-t_i \sigma) \qquad (4.58)$$

where, t_i = -3, -2, -1, 0, 1, 2, 3. t_i represents to θ.

The six x_i's read from the tables of normal distribution (Handbook of tables for Mathematics, fourth edition, The Chemical Rubber Co., 1970) are (after normalising) 0.0214, 0.136, 0.3413, 0.3413, 0.136, 0.0214. The corresponding average molar masses ($\overline{M}_i$) are 8069, 16702, 34571, 71556, 148110, 306564. The number average molar mass

for the polymer is given by

$$M_N = \sum_i^n x_i \overline{M_i}$$
(4.59)

where n is the number of pseudocomponents. The calculated number average molar mass is 65539. The error in calculated M_N is 1.14%. Hence, the number of pseudocomponents is sufficient. Also, the success of the proposed scheme in representing M_N with a reasonable number of pseudocomponents is demonstrated. The weight fractions w_i are given by

$$w_i = \frac{x_i \overline{M_i}}{\sum x_i \overline{M_i}}$$
(4.60)

The w_i's are 0.0026, 0.0347, 0.1805, 0.3736, 0.3081 and 0.1004. The calculated weight average molar mass is 109886 which is in excellent agreement with the experimental value of 110000.

Once the pseudocomponents are determined the phase equilibrium calculations can be performed. To simplify the calculation procedure it can be assumed that for all pseudocomponents corresponding to a particular polymer same values of interaction parameters can be used or in other words the interaction parameters are assumed to be independent of chain length.

CHAPTER 5

RESULTS AND DISCUSSION

The Flory-Huggins model has been used to correlate polymer-water phase equilibrium data of the several different kinds that were discussed in the previous Chapters. Following the pattern of Chapter 4, the results corresponding to different types of data are presented in separate sections.

5.1 Fitting water activity data

Water activity data of Gaube et al. (1993), Grossmann et al. (1993), Haynes et al. (1989) and Malcolm and Rowlinson (1957) have been correlated. The data are mainly for binary mixtures of one polymer (either PEG or dextran) in water but Gaube et al. also report water activity data for one ternary mixture. The data generally cover a limited range of polymer weight fraction in the solution with the exception of the Malcolm and Rowlinson (1957) data, which are is discussed in a separate section.

5.1.1 Solutions with one polymer

Gaube et al. (1993) studied solutions of several PEG and dextran polymers over a range of temperatures. The data they produced were obtained as "supplementary material" to their paper and have been reproduced in Tables A.1 and A.2 in the Appendix. Gaube et al. (1993) correlated their own data with a version of the "osmotic virial equation" as was discussed in Chapter 2. (Their two virial coefficients are given in Table 5.1 and 5.2). The data have been recorrelated with the Flory-Huggins model in two

Table 5.1. Interaction parameters of PEG-water systems (Gaube et al.,1993).

polymer	T (°C)	Mn	Mn(eff)	Aii* 10^3	Aiii* 10^2	χ(1FHP)	χ(2FHP)	err (1FHP) * 10^7	err (2FHP) *10^8
PEG200	20	201	214.0	7.16	1.78	0.2752	0.3066	1.38	12.90
	40		174.0	5.64	1.61	0.3563	0.2938	0.707	0.944
	60		176.0	4.89	1.59	0.3816	0.3319	0.387	0.858
PEG600	20	582	584.0	4.26	1.62	0.3747	0.3761	0.0201	0.207
	40		512.0	2.99	1.55	0.4375	0.3860	1.25	0.927
	60		440.0	2.92	0.88	0.4821	0.4073	0.676	0.152
PEG1550	20	1440	1480.0	3.10	1.54	0.4034	0.4133	0.0214	0.113
	40		1195.0	2.42	1.16	0.4568	0.4026	0.346	0.0706
	60		1038.0	1.46	0.91	0.5060	0.4250	1.037	0.9550
PEG3000	20	2840	3238.0	2.72	1.63	0.4135	0.4438	0.0088	0.0378
	40		2307.0	2.37	1.00	0.4606	0.4053	0.101	0.0072
	60		1885.0	1.20	0.81	0.5172	0.4167	1.306	0.109
PEG6000	20	7750	6957.0	2.60	1.26	0.4361	0.3974	0.137	0.207
	40		5534.0	2.25	0.97	0.4828	0.3688	1.18	0.024
	60		4081.0	1.53	0.54	0.5142	0.3533	0.661	0.043

χ = F-H interaction parameter : M_n = number average molecular weight.

eff = estimated value. : A's = virial coefficients of Gaube et al. (1993).

(1FHP) = estimation of χ with M_n fixed at author's value. : (2FHP) = estimation of both χ and M_n.

err = value of the objective function at the minima.

Table 5.2. Interaction parameters of dextran-water systems (Gaube et al., 1993)

polymer	T (°C)	Mn	Mn(eff)	Aii* 10^{-3}	Aiii* 10^{-2}	χ(1FHP)	χ(2FHP)	err (1FHP) *10^8	err (2FHP) *10^9
Dx40000	20	23600	30039	1.31	0.81	0.3918	0.4573	0.2887	0.6190
	40		26593	1.24	0.69	0.4235	0.4519	0.235	0.0019
	60		25547	0.93	0.67	0.4449	0.4618	0.036	0.1950
Dx70000	20	46300	42434	0.99	0.40	0.4550	0.4346	0.0683	0.3960
	40		33408	0.94	0.30	0.4852	0.4042	1.029	0.2540
	60		33122	0.72	0.28	0.4945	0.4297	0.795	3.720
Dx110000	20	64800	46410	0.65	0.26	0.4969	0.4246	1.62	0.8560
	40		39667	0.76	0.24	0.5088	0.3863	6.430	0.3410
	60		46261	0.45	0.24	0.5188	0.4618	1.951	0.6880
Dx500000	20	101000	74035	0.64	0.25	0.4994	0.4328	1.33	0.2840
	40		66922	0.57	0.23	0.5136	0.4316	1.882	0.1720
	60		58935	0.39	0.18	0.5197	0.4411	0.631	0.0107

χ = Flory-Huggins interaction parameter.

M_n = number average molecular weight.

err = value of the objective function at the minima

eff = estimated value.

A's = virial coefficients of Gaube et al. (1993).

(1FHP) = estimation of χ with M_n fixed at author's value.

(2FHP) = estimation of both χ and M_n.

different ways, as was discussed in Chapter 4.

In the first instance, the r parameter in the Flory-Huggins equation was taken as given by the apparent number average molar mass reported by Gaube et al. (1993) for the given polymer and by the polymer apparent liquid volume. The r parameter, in this case, is calculated from

$$r = M_N \ V_P/(18.01 \ cm^3/mol) \tag{5.1}$$

Gaube et al. (1993) give polymer liquid volumes as 0.8302, 0.8573 and 0.8711 cm^3/g for PEG and 0.5959, 0.6203, 0.6322 cm^3/g for dextran at temperature of 20, 40 and 60 °C, respectively. The number average molar masses used by Gaube et al. are in Tables 5.1 and 5.2. With the r parameter fixed, only the Flory-Huggins χ parameter was available to fit the data. The objective function employed is given in equation 4.1. The results of the one parameter Flory-Huggins theory (1FHP) are tabulated in Tables 5.1 and 5.2.

The second approach treated r as a free parameter available to fit the data in addition to χ. These two parameter Flory-Huggins theory results (2FHP) are also tabulated in Tables 5.1 and 5.2. (The numerical procedure for performing the minimization was discussed in Chapter 4.) Instead of reporting the r value in the Table, an effective number average molar mass has been presented. The number is calculated from

$$M_{Neff} = r \ (18.01 \ cm^3/mol)/ \ V_P \tag{5.2}$$

Figures 5.1-5.3 compare the experimental PEG activities with those calculated
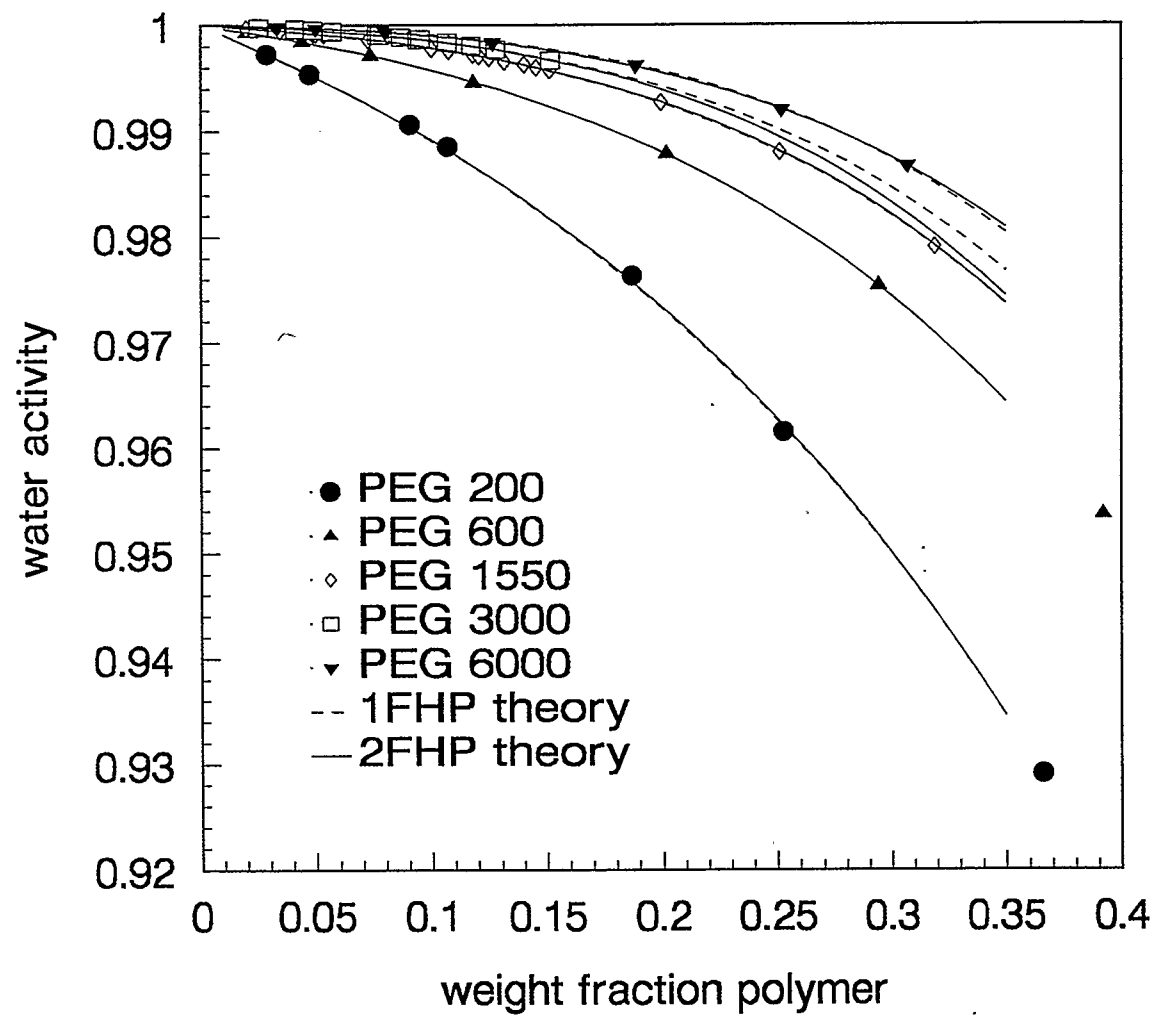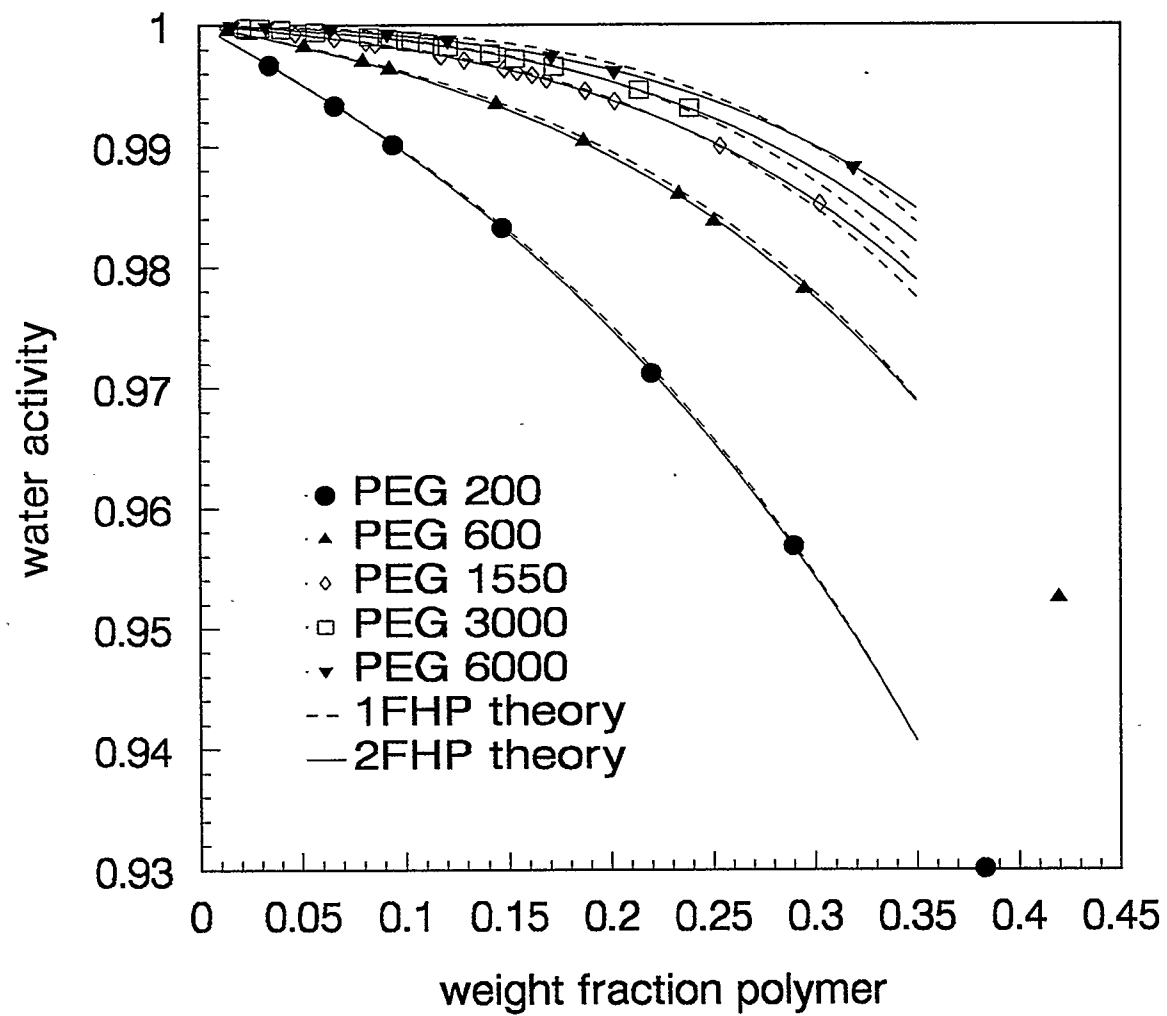
Figure 5.1. PEG/water solutions at 20 C.

Figure 5.2. PEG/water solutions at 40 C.

Figure 5.3. PEG/water solutions at 60 C.

from 1FHP and 2FHP models. The Figures show the water activity in the 5 different PEG solutions at temperatures of 20, 40 and 60 °C, respectively. In each Figure, the water activity is lowest at a given polymer weight fraction when the polymer has the lowest molar mass. (This follows from the fact that the mole fraction of water is lower at a given weight fraction of polymer if the molar mass of the polymer is lower.)

Figures 5.4-5.6 contain the comparison between experiments and models for the dextran solutions.

Figures 5.7-5.14 repeat some of the curves that appear in the first six Figures but for one polymer at one temperature in each. These are presented so that some of the details can be seen more clearly.

The correlations obtained using χ as the single correlating parameter (1FHP) gave excellent results in some instances, particularly for the PEG polymers at 20°C (as can be seen in Figure 5.1). The correlations with the PEG polymers at the two higher temperatures and with the dextran polymers at all three temperatures are satisfactory but do show errors increasing with polymer molar mass and with temperature.

When r was treated as a correlating parameter in addition to χ (2FHP theory), the results are excellent for all polymers at all temperatures. In many cases, there is a reduction of an order of magnitude in the minimum value of the objective function used in correlating data. These values are shown in the last two columns of Tables 5.1 and 5.2. It is interesting to note that the optimal values of r parameter correspond to effective molar masses that are reasonable when compared to the number average molar masses that Gaube et al. report for the polymers.

Figure 5.4. Dextran/water solutions at 20 C.

Legend within figure:
- Dx 40000
- Dx 70000
- Dx 110000
- Dx 500000
- -- 1FHP theory
- — 2FHP theory

Axes: water activity (y-axis), weight fraction polymer (x-axis)

Figure 5.5. Dextran/water solutions at 40 C.

Figure 5.6. Dextran/water solutions at 60 C.

Figure 5.7. PEG 600/water solution at 60 C.

Figure 5.8. PEG 3000/water solution at 60 C.

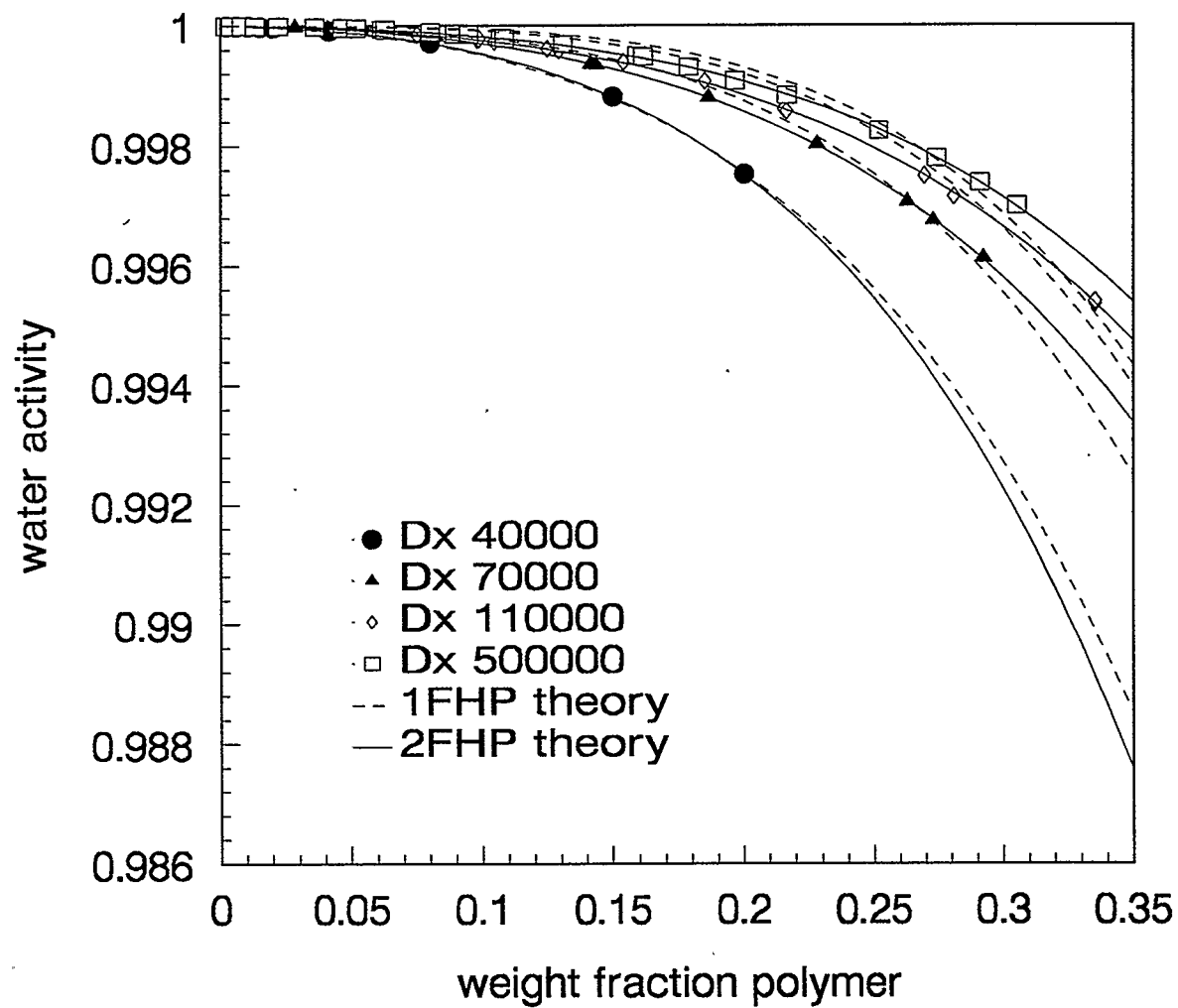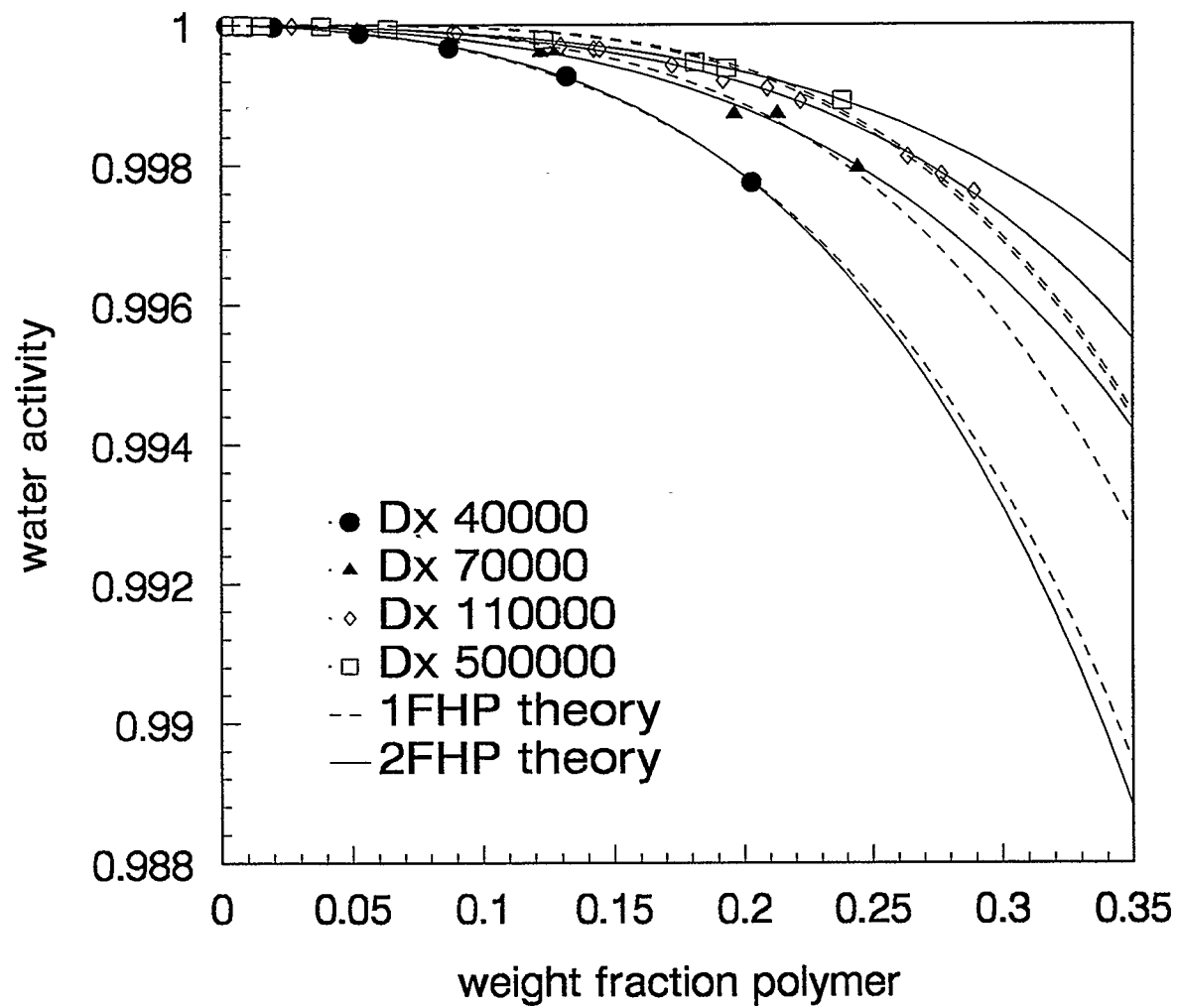Figure 5.9. PEG 6000/water solution at 40 C.

Figure 5.10. PEG 6000/water solution at 60 C.

Figure 5.11. Dextran 70000/water solution at 40 C.

Figure 5.12. Dextran 110000/water solution at 40 C.

Figure 5.13. Dextran 500000/water solution at 20 C.

Figure 5.14. Dextran 500000/water solution at 60 C.

The publication of Großmann et al. (1993) contains a figure showing water activities in two PEG and one dextran polymer systems. The data points were digitised and the resulting numbers are presented in table A.4. The publication of Haynes et al. (1989) contains tables of differential vapor pressure measurements in binary polymer-water solutions for two PEG and two dextran polymers. These data have also been correlated with the 1FHP approach and the 2FHP approach with results that are presented in Table 5.3. The results for the three systems measured by Großmann et al. (1993) are shown in Figure 5.15 for 2FHP theory.

Großmann et al. did not measure the number average molar mass of their polymer samples and the r value based on the nominal molar mass of the polymer as indicated by the supplier is uncertain. The effective molar mass that is obtained when both the r parameter and χ are used in correlating the data (the 2FHP) approach is somewhat different from the nominal value but is still reasonable. The fit of the data with the 2FHP approach is excellent, as is shown in Figure 5.15.

The Haynes et al. (1989) data are rather scattered and proved to be very difficult to correlate. When r was left free to vary, it tended to zero as is shown in Table 5.3. This signifies the absence of enthalpic interactions between the polymer and the solvent which does not seem a correct representation. The correlation obtained was, in general, unsatisfactory. Gaube et al. (1993) commented on the differences between their measurements and those of Haynes et al. (1989) on similar systems.

The correlation between the estimated r and χ was also studied for the data of Gaube et al. (1993). The correlation matrix for the dextran 500000/water system at 20°C

Table 5.3. Interaction parameters of PEG or dextran-water systems.

polymer	T(°C)	M_n(au.)	M_n(eff)	χ (1FHP)	χ (2FHP)
PEG 6000[1]	20	6000	8629.2	0.3693	0.5014
PEG 35000[1]	20	35000	46355	0.36	0.4726
PEG 3350[2]	25	3790	1583	0.4613	0
PEG 8000[2]	25	9037	4380	0.4995	0.1859
Dx 500000[1]	20	174000	95428	0.5432	0.2937
Dx T-70[2]	25	29630	9394	0.571	0
Dx T-500[2]	25	167000	43678	0.5498	0

1	= data of Großmann et al. (1993)
2	= data of Haynes et al. (1989).
M_n	= number average molecular weight.
au.	= author's value.
eff	= estimated value.
χ	= F-H interaction parameter.
(1FHP)	= only χ estimated.
(2FHP)	= both χ and r or M_n estimated.

Figure 5.15. PEG/Dextran - Water solutions at 20 C.

is shown below.

$$\begin{vmatrix} 1 & 0.99 \\ 0.99 & 1 \end{vmatrix}$$

The off-diagonal terms are very close to unity and hence r and χ are very strongly positively correlated. This fact is also evident from figure 5.16. To generate this Figure, r was fixed at the values shown and corresponding χ's were estimated. The values of the objective function at the minima varied only between 0.28×10^{-9} and $0.49 \times^{-9}$. The sets of parameters fall almost along a straight line. Similar results show high correlation between the parameters that were obtained for PEG 3000/water system at $20^\circ C$.

The equation of 95% confidence ellipse for r and χ corresponding to PEG 3000/water system at $20^\circ C$ is

$$2.9586 \; \chi^2 - 8.372*10^{-3} \; \chi \; r + 0.5988*10^{-5} \; r^2 = 6.17 \qquad (5.3)$$

The ellipse covers a large r and χ space and the estimated parameters fall within the ellipse. Although calculations are for only one system, similar results are expected for all others.

The pattern involving effective M_Ns reported in table 5.1 raises an important point regarding the nature of PEG-water solutions. For all PEGs, the effective M_N or the related quantity r (chain length) decreases with an increase in temperature (only a few exceptions appear in the table). This might be interpreted as "curling up" of the polymer chain. This

Figure 5.16. Correlation of F-H interaction parameter and r for the system Dx 500000/water at 20 C.

kind of behaviour could be attributed to breaking of hydrogen bonds with an increase in temperature. There is evidence that PEG forms hydrogen bonds in aqueous solutions (Molyneux, 1991). This curling up of the polymer is possibly the reason for the inability of the 1FHP theory to correlate binary water activities as well as the 2FHP theory at higher temperatures.

5.1.2 Data of Malcolm and Rowlinson

The data of Malcolm and Rowlinson (1957) for the PEG 5000/water system at 65°C was difficult to correlate because of the range of polymer concentrations involved. The concentration range of the polymer was very wide for this set of data, extending from 0.5 to nearly 0.99 weight fraction polymer. In the objective function that was minimised in the parameter estimation, the low values of water activity are given more weight. Hence, sometimes it would be expedient to use some carefully chosen data points rather than the whole set of data points, particularly if higher accuracy for the middle range of concentrations is required.

Several different fitting procedures were attempted.

<u>Procedure 1</u>: The value of r was fixed at $r=114$. Chen (1993) used this value in his correlation of the Malcolm and Rowlinson data with a modified NRTL equation. The value is obtained as the "degree of polymerisation" by dividing the nominal number average molar mass of 5000 by the molar mass of the PEG unit element (44 g/mol) and rounding to the nearest integer. With the value of r fixed a $priori$ in this manner the χ parameter was obtained by minimizing the objective function in equation (4.1). The minimum of the objective function was obtained with $\chi=8.154$.

The results of the fitting are shown in Figure 5.17, along with similar results to be described shortly. With the parameters obtained in this procedure, the activity of water shows inflection points and a positive slope in an interval of the polymer weight fraction. These features indicate a thermodynamically unstable liquid phase and a phase separation that is not supported experimentally. As a result, the data fit is unsatisfactory.

The quality of the fit could be measured by an "average deviation" defined as

$$\frac{\sum |a_{exp} - a_{calc}|}{N_{data}} \times 100$$

Using procedure 1, the average deviation for the fit is 8.154.

<u>Procedure 2</u>: As discussed in Chapters 3 and 4, the r parameter in the Flory-Huggins model has been considered by others to be an empirical parameter available for fitting. When the objective function is minimized with respect to both r and χ simultaneously, the optimal parameters found are $r=37.828$ and χ very small, essentially zero. The average deviation for this fit is 4.432 and should be compared with the value 8.152 obtained when r was held constant at 114. However, the zero value for χ is unexpected and the curve of activity against polymer mole fraction, which can be seen in Figure 5.17 is not satisfactory.

<u>Procedure 3</u>: In this procedure, the Flory-Huggins interaction parameter was assumed to have a linear dependence on the polymer volume fraction; i.e.,

Figure 5.17. PEG 5000/water system at 65 C.

$$\chi = a + b \, \phi_2 \qquad\qquad (5.4)$$

where a and b are constants. The activity of the water in the solution is given by;

$$\ln a_1 = \ln (1 - \phi_2) + (1 - \frac{1}{r}) \, \phi_2 + \phi_2^2 \, \chi - \phi_1 \phi_2^2 \, b \qquad (5.5)$$

The three parameters (r,a and b) were fitted to the data by minimizing the objective function of equation 4.1. The values obtained were r=61.8, a=0.015 and b=0.628. The average deviation using these parameters was reduced to 0.296. The corresponding curve in Figure 5.17 shows an excellent fit of the data.

Procedure 4: The liquid instability that resulted in Procedure 1 can be eliminated if the χ parameter is kept small enough. If χ<0.5 liquid instability is impossible for any value of r (Scott, 1949). In this case χ was fixed at 0.4 and the optimal r was found to be 106. Only five data points corresponding to the lower concentrations of the polymer were used for parameter estimation. The resulting curve of activity versus polymer weight fraction, shown in Figure 5.17, is not acceptable although the liquid-liquid separation is not found. The average deviation calculated using all the data points was 7.283.

Procedure 5: Cheluget et al. (1993) fitted the liquid-liquid equilibrium data for PEG-water systems and reported temperature dependent χ values. Their correlation for PEG 2290-water at 65°C gives χ=0.235. This value has been used for PEG 5000-water. Three different approaches were used to examine the effect of the data correlated on the quality of the results obtained.

(a) When all the data points were used, the optimal r was 48.66 with an average deviation of 4.66.

(b) When six points at the lowest polymer concentrations were used, the optimal r was 83.88 and the average deviation was 4.7 (based on the whole data set).

(c) When the five data points at the lowest polymer concentrations were used, the optimal r was 83.88 and the average deviation was 4.83 (based on the whole data set).

The water activity versus polymer weight fraction curves for these cases are shown in Figure 5.18.

Procedure 5 is preferable to Procedure 2 in spite of a slightly higher average deviation as an extremely small value of χ was produced in Procedure 2, implying the absence of enthalpic interaction between water and the PEG. However, only by using Procedure 3, in which the interaction parameter was taken as composition dependent, was it possible to get a good quantitative match of the data over the whole composition range.

5.1.3 polymer-polymer-water systems

The supplementary material accompanying the Gaube et al. (1993) manuscript contains very extensive data for water activity above water-PEG 3000-dextran 110000 solutions at 20,40 and 60°C. These tables have been reproduced in the Appendix A1.

The data at 20°C have been correlated by taking the water-polymer parameters for the two binary mixtures, as given. The values are shown in Tables 5.1 and 5.2. There was then a single parameter available to correlate the ternary data; i.e., χ_{12} where the subscripts refer to the two polymers.

The fit of the data had a minimum value of the objective function as 1.01×10^{-8} and

Figure 5.18. PEG 5000/water system at 65 C.
Procedure 5.

with the optimized χ_{12} as 0.0787.

5.2 Closed-loop phase diagrams

Saeki et al. (1976) published curves showing closed-loop phase diagrams for several PEG-water binary systems. These polymers, above a minimum molar mass, show a lower critical solubility temperature and an upper critical solubility temperature with liquid-liquid phase separations at intermediate temperatures. The curves in the Saeki et al. (1976) paper show the data points. These points for the system PEG 2290-water have been digitized and the resulting values are shown in Table A.6.a in the Appendix. The points do not in general correspond to compositions in coexisting phases. In order to expedite parameter estimation, the smooth curves drawn by Saeki et al. through their data were used to estimate compositions of coexisting phases at several temperatures. These digitised coexisting weight fractions are given in Table A.6.b.

The lowest data point and the highest temperature data point were taken as the two critical points that were needed in the model.

The model employed in correlating the data assumes that both r and χ are temperature dependent with three empirical constants in each expression. Three of the constants were eliminated using the two critical points, leaving only three parameters available for fitting the coexisting phase compositions. The expressions for χ and r are:

$$\chi = a + b/T + c \ln T \tag{5.6}$$

and

$$r = d + e\,T + f\,T^2 \qquad\qquad (5.7)$$

The discussion and the equations that apply at the critical points were given in Section 4.2.1. The objective function minimized was given in equation 4.6. Flash calculations were necessary at each of the pairs of coexisting compositions. The composition of the feed material in the flash calculation was obtained by mixing together equal amounts of the two experimental (i.e, digitized) coexisting phases. The value of the coefficients in the equations for the parameters are

a   =   97.313,   b   =   -6348.7398,   c   = -13.5118,

d   =   1691.5618,   e   =   -6.9859,   f   = 0.7471e-2.

Figure 5.19 contains the experimental and calculated mutual solubility curves for the system PEG 2290/water. The success of the model in correlating experimental data is evident from Figure 5.19. Cheluget et al. (1993) had a similar (but not superior) success in correlating these same data. The number of adjustable parameters in their work varied from two to four (their paper contains three temperature dependent χ expressions). The proposed approach offers a semi-empirical alternative for correlating closed-loop phase diagrams for binary systems.

5.3 Ternary liquid-liquid equilibrium

Four systems showing ternary liquid-liquid separations were correlated. PEG 3350/dextran T-70/water and PEG 8000/dextran T-500/water were studied by King et al. (1988). PEG 3000/dextran 500000/water was studied by Connemann et al. (1991). Data

Figure 5.19.   PEG 2290/water system

for the compositions of the two coexisting phases and of the overall mixture were given in the two papers. PEG 3000/dextran 110000/water data are presented in a figure in the manuscript by Gaube et al. (1993). The data points in the figure have been digitized and are tabulated in Appendix A2, Table A.5.

5.3.1 Coefficients from water activity

The paper by Gaube et al. (1993) also contained the extensive water activity data that were correlated as described in Section 5.1. The parameters obtained from the 1FHP approach were used to produce Figure 5.20.

5.3.2 Direct correlation of data

Figures 5.21 to 5.24 contain results of ternary LLE calculations with 1FHP and 2FHP theories. Parameter estimation procedures were described in section 4.2. Tables 5.1, 5.2 and 5.4 contain the values of parameters employed for equilibrium calculations.

Figures 5.21 and 5.22 show the results of ternary LLE calculations with 1FHP theory for systems PEG 3350/dextran T-70/water at 25°C and PEG 8000/dextran T-500/water at 25°C. The experimental data were taken from the paper of King et al. (1988). All three interaction parameters were treated as adjustable parameters or in this context were fitted to ternary LLE data. OF(I) (equation 4.6) was employed for parameter estimation and the parameters are given in the Table 5.4. The fit is satisfactory for the two systems studied.

Figures 5.23 and 5.24 contain results of ternary LLE calculations with 1FHP and 2FHP theories. The experimental data was taken from the papers of Connemann et al. (1991) and Gaube et al. (1993). The polymer-water parameters (χ in the case of 1FHP

Figure 5.20. DX 110000/PEG 3000/Water System at 293 K.

Figure 5.21. Dx T-70/PEG 3350/Water System
Temperature = 25 C

Figure 5.22. Dx T-500/PEG 8000/Water System
Temperature = 25 C

Figure 5.23. DX 500000/PEG 3000/Water System at 313 K.

Figure 5.24. DX 110000/PEG 3000/Water System at 293 K.

Table 5.4. Interaction parameters of PEG-dextran-water systems.

System	T($^\circ$C)	χ_{13} (1FHP)	χ_{23} (1FHP)	χ_{12} (1FHP)	χ_{12} (2FHP)
Dx T-70(1)/PEG 3350(2)/H$_2$O(3)[1]	25	0.5171	0.4714	0.04238	-
Dx T-500(1)/PEG 8000(2)/H$_2$O(3)[1]	25	0.4713	0.3886	0.0135	-
Dx 110000(1)/PEG 3000(2)/H$_2$O(3)[2]	20	*	*	0.05073	0.0738
Dx 500000(1)/PEG 3000(2)/H$_2$O(3)[3]	40	*	*	0.04155	0.0895

1	=	data of King et al. (1988).
2	=	data of Gaube et al. (1993).
3	=	data of Connemann et al. (1991).
χ	=	F-H interaction parameter.
*	=	polymer water parameters for these systems are contained in tables 5.1.1 and 5.1.2.

theory and, r and χ in the case of 2FHP theory) were obtained from the binary water activity data of Gaube et al. (1993), given in Tables 5.1 and 5.2. The polymer1-polymer2 interaction parameters were obtained from ternary LLE data. OF(I)I (equation 4.7) was employed for parameter estimation and the parameters are given in the Table 5.4. A comparison of the slopes of the tie-lines for the 1FHP theory and 2FHP theory shows that for the latter the match with the experimental tie-lines is better. Also, the two phase envelope is better represented. This is not surprising as the 2FHP theory was able to fit water activities for binary systems (polymer-water) better.

Figure 5.25 provides the rationale for the choice of objective function OF(II) for estimation of the polymer1-polymer2 interaction parameter (χ_{P1P2}) for systems containing higher molar mass dextrans (dextrans 110000 and 500000). The system studied was dextran 110000/PEG 3000/water at 293 K (Gaube et al., 1993). 1FHP theory was employed for phase equilibrium calculations. The polymer-water interaction parameters were determined from binary water activity data. χ_{12} was determined using OF(I) and OF(II) from LLE data. A comparison of the two sets of results shows that although OF(I) related calculations match the two phase envelope better on the PEG rich phase side and the slopes of the tie-lines are comparable, the two phase envelope is better represented on the dextran rich side for OF(II) related calculations. The overall picture is better for the OF(II) related calculations.

5.3.3 Effect of polydispersivity

The system studied was dextran 110000/PEG 3000/water at 293 K [Gaube et al. (1993)]. A pseudocomponent approach was employed for representing the polydispersivity

Figure 5.25. DX 110000/PEG 3000/Water System at 293 K.

of dextran. Six pseudocomponents were chosen for dextran. PEG was treated as monodisperse as PEG 3000 molar mass distribution has a sharp peak [Gaube et al. (1992)]. The details regarding the determination of pseudocomponents are covered in Section 4.6. As was shown in Section 4.6, the dextran 110000 used by Gaube et al. (1993) with M_N=64,800 and M_W=110000 can be represented by six components with mole fractions 0.0214, 0.136, 0.3413, 0.3413, 0.1360 and 0.0214 and molar masses 8069, 16702, 34571,71556, 148110 and 306564 respectively. For the sake of simplicity, for all pseudocomponents corresponding to dextran, the same values of interaction parameters were used in phase equilibrium calculations. The PEG 3000/water and dextran 110000/water parameters in Tables 5.1 and 5.2 were used. The PEG/dextran parameter was regressed to be 0.04998.

Figure 5.26 contains a comparison of phase equilibrium calculations for the monodisperse and polydisperse cases. As can be seen from the Figure, the tie-lines in the two cases are not significantly different. However, for the PEG rich phase, there is a slight shift in the two-phase equilibrium curve towards the right. This is probably due to the fractionation of dextran i.e., the lower molar mass pseudocomponents have a tendency to go into the PEG rich or lighter phase and the heavier molar mass components have a tendency to stay in the heavier (dextran rich) phase.

5.4 Correlation of protein partitioning

The reader is referred to Sections 3.5 and 4.3 for details regarding the model and parameter estimation procedures, respectively. Gupta (1991) presented tables of protein

Figure 5.26. Dx 110000/PEG 3000/water system at 293 K.
6 components for dextran

partition coefficients obtained by digitizing data points on figures in the paper by King et al. (1988).

Figures 5.27 and 5.28 contain the results of calculations for partitioning of lysozyme and albumin in PEG 3350/Dextran T-70/water/KCl system, respectively. The three polymer-water parameters were estimated from ternary LLE data and are given in Table 5.4. The protein water parameters (r and χ) were obtained from second order virial equation using virial coefficients estimated by King et al. as discussed in Section 4.3. The values of lysozyme-water and albumin-water parameters (r and χ) were 0.6488 and 212, and 0.0843 and 407, respectively. The two protein-polymer interaction parameters were fitted to the protein partition coefficient data of King et al. The values of lysozyme-PEG 3350/dextran T-70 and albumin-PEG 3350/dextran T-70 were 0.1647 and 0.1521, and -0.3061 and -0.1363, respectively. Figures 5.27 and 5.28 demonstrate the success of the model in correlating protein partition coefficient data in terms of the total feed concentration.

The protein interaction parameters are empirical as for the sake of simplicity, electrostatic effects due to the presence of low concentration of salts (50mM) were neglected. This was necessary as otherwise the model would have had an inordinate number of parameters with respect to the number of data points available for parameter estimation.

Figure 5.27. Lysozyme/PEG 3350/Dextran T-70/water/KCl system at 25 C.

Figure 5.28.　Albumin/PEG 3350/Dextran T-70/water/KCl system at 25 C.

CHAPTER 6

CONCLUSIONS AND RECOMMENDATIONS

6.1 Conclusions

The conclusions of this research effort are as follows:

1)   The binary water activities for polymer-water systems have been correlated with a fair measure of accuracy with one parameter Flory-Huggins (1FHP) theory. The correlation results are excellent with two parameter Flory-Huggins (2FHP) theory. This applies for approximately up to forty weight percent polymer. If correlation for the entire concentration range (up to and above 90 wt % polymer) is required, it was found that the interaction parameter has to be made concentration dependent.

2)   Binary closed-loop phase diagrams can be successfully correlated by a variation of Flory-Huggins theory. The variation involved making r and χ temperature dependent. Parameter r has been treated as a constant in related correlation efforts. This new semi-empirical approach (with three adjustable parameters) proposed in this work offers an alternative to those reported in the literature.

3)   The ternary (polymer1-polymer2-water) phase equilibria at constant T and P can be satisfactorily correlated with 1FHP theory i.e., the approach involving three χ

parameters with the $r's$ determined from molar volumes. The correlation is improved by the use of 2FHP theory i.e., by letting the two $r's$ to be fitting parameters in addition to the three χ parameters. However, it is to be noted that in both cases one parameter, polymer-polymer interaction parameter, needs to be fitted to the LLE data. The others can be determined from binary VLE data.

4)   Preliminary results of the correlation of protein partitioning in aqueous two-phase systems are encouraging. However, the approach followed in this work was not theoretically rigorous. As a consequence, the protein interaction parameters were treated as empirical parameters.

5)   The number average and weight average molecular weights of polymers can be accurately represented using the new pseudocomponent approach proposed in this work. This approach is based on the log-normal distribution.

6)   Contrary to the results reported in the literature for other thermodynamic models, there was not a significant difference in the two-phase equilibrium curves, calculated from Flory-Huggins theory, for monodisperse and polydisperse systems using the pseudocomponent approach proposed in this work.

7)   The successive substitution algorithm incorporating Rachford-Rice scheme was unsuccessful in performing phase equilibrium calculations with Flory-Huggins theory. The

algorithm had to be damped for these calculations. The rate of convergence of flash calculations was improved by switching to a Newton scheme after a sufficient degree of convergence was achieved.

The flash calculation algorithm of Heidemann (1974) in conjunction with Newton scheme offers an alternative to the modified successive substitution algorithm.

8)   The Flory-Huggins lattice theory, although simplistic, provides a theoretical basis for modelling the thermodynamic behaviour of polymer-water systems. In the course of this work, the theory along with its modifications was remarkably successful at correlating the various types of thermodynamic behaviour of polymer-water systems. Flory-Huggins theory should provide a basis for more elaborate models in future.

6.2 Recommendations

The author makes the following recommendations regarding the thermodynamic modelling of polymer water systems:

1)   A generalised model is needed for at least correlating the various types of thermodynamic behaviour exhibited by polymer-water systems. The author is of the opinion that this would require a complete experimental data set (covering various types of thermodynamic behaviour) from one source. Possibly a modified Flory-Huggins theory can be used as a generalised model.

2)   This work along with related efforts in this area raises an important issue regarding the role of hydrogen-bonding in aqueous solutions containing polymers. Water is capable of forming hydrogen bonds with the solutes. The hydrogen bonding aspect of modelling has been treated through empirical models. It would be desirable to have a model that treats hydrogen bonding in aqueous solutions in a fundamental way.

3)   The modelling of protein partitioning in this work leaves a lot to be desired in terms of theoretical satisfaction. The salt interactions ought to be treated in a more elaborate way. One way of doing this is by the incorporation of electrolyte models. Also, the model would have to take into account the rigid structure of many biopolymers. An approximate way of dealing with this issue is described in this work as far as Flory-Huggins theory is concerned. However, it would be more satisfactory to employ a sophisticated approach which entails modifications in the derivation of the Flory-Huggins theory. In any case, prgress will also depend on the availability of more and better data.

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APPENDIX A1.

Experimental data of Gaube et al. (1993).

Table A.1.a

Water Activity a_1 in Water (1) - PEG 200 (2) Solutions

293.15 K		313.15 K		333.15 K	
w_2	a_1	w_2	a_1	w_2	a_1
0.0289	0.997267	0.0344	0.996725	0.0229	0.997897
0.0473	0.995385	0.0664	0.993370	0.0352	0.996748
0.0908	0.990597	0.0944	0.990140	0.0564	0.994590
0.1071	0.988566	0.1473	0.983229	0.0927	0.990686
0.1871	0.976320	0.2200	0.971211	0.1418	0.984503
0.2529	0.961546	0.2900	0.956826	0.2001	0.975630
0.3659	0.929081	0.3833	0.930084	0.2723	0.961875
				0.3457	0.944029

Table A.1.b

Water Activity a_1 in Water (1) - PEG 600 (2) Solutions

293.15 K		313.15 K		333.15 K	
w_2	a_1	w_2	a_1	w_2	a_1
0.0202	0.999355	0.0138	0.999591	0.0282	0.999105
0.0442	0.998495	0.0223	0.999309	0.0507	0.998308
0.0737	0.997139	0.0244	0.999256	0.0769	0.997274
0.1183	0.994568	0.0516	0.998229	0.1001	0.996323
0.2021	0.987853	0.0517	0.998243	0.1514	0.993670
0.2945	0.975367	0.0800	0.997032	0.2234	0.988642
0.3920	0.953604	0.0928	0.996368	0.3000	0.981109
		0.1446	0.993482		
		0.1873	0.990407		
		0.2337	0.986034		
		0.2509	0.983766		
		0.2952	0.978133		
		0.4196	0.952463		

Table A.1.c

Water Activity a_1 in Water (1) - PEG 1550 (2) Solutions

293.15 K		313.15 K		333.15 K	
w_2	a_1	w_2	a_1	w_2	a_1
0.0200	0.999721	0.0182	0.999770	0.0420	0.999443
0.0248	0.999650	0.0268	0.999643	0.0594	0.999133
0.0347	0.999471	0.0473	0.999280	0.0736	0.998814
0.0490	0.999192	0.0665	0.998900	0.0888	0.998574
0.0501	0.999181	0.0815	0.998563	0.0890	0.998576
0.0536	0.999119	0.0861	0.998410	0.1332	0.997469
0.0729	0.998636	0.0861	0.998443	0.1428	0.997289
0.0999	0.997861	0.1170	0.997511	0.1502	0.996988
0.1003	0.997782	0.1179	0.997480	0.2225	0.993681
0.1077	0.997573	0.1292	0.997116	0.2987	0.988857
0.1183	0.997191	0.1484	0.996371		
0.1208	0.997112	0.1484	0.996350		
0.1251	0.996895	0.1484	0.996382		
0.1318	0.996573	0.1548	0.996110		
0.1405	0.996296	0.1622	0.995846		
0.1458	0.996003	0.1692	0.995485		
0.1518	0.995778	0.1881	0.994578		
0.1997	0.992701	0.1881	0.994553		
0.2516	0.988018	0.1881	0.994530		
0.3191	0.979046	0.1881	0.994520		
		0.1881	0.994563		
		0.2025	0.993694		
		0.2540	0.989977		
		0.3029	0.985199		

Table A.1.d

Water Activity a_1 in Water (1) - PEG 3000 (2) Solutions

293.15 K		313.15 K		333.15 K	
w_2	a_1	w_2	a_1	w_2	a_1
0.0253	0.999784	0.0231	0.999822	0.0463	0.999650
0.0413	0.999629	0.0299	0.999760	0.0489	0.999654
0.0490	0.999536	0.0402	0.999654	0.0788	0.999300
0.0571	0.999409	0.0571	0.999447	0.0801	0.999280
0.0767	0.999081	0.0830	0.999047	0.0998	0.998991
0.0780	0.999043	0.0935	0.998864	0.1144	0.998741
0.0871	0.998858	0.1010	0.998709	0.1472	0.998074
0.0944	0.998647	0.1037	0.998659	0.1748	0.997332
0.0953	0.998650	0.1117	0.998480	0.2257	0.995517
0.1070	0.998372	0.1189	0.998300	0.2993	0.991573
0.1174	0.998075	0.1213	0.998213		
0.1280	0.997709	0.1417	0.997664		
0.1521	0.996684	0.1537	0.997263		
		0.1728	0.996574		
		0.2145	0.994607		
		0.2389	0.993113		

Table A.1.e

Water Activity a_1 in Water (1) - PEG 6000 (2) Solutions

293.15 K		313.15 K		333.15 K	
w_2	a_1	w_2	a_1	w_2	a_1
0.0335	0.999835	0.0159	0.999949	0.0155	0.999950
0.0502	0.999702	0.0328	0.999880	0.0399	0.999845
0.0804	0.999344	0.0644	0.999625	0.0727	0.999615
0.1267	0.998325	0.0920	0.999277	0.1224	0.999076
0.1888	0.996181	0.1212	0.998764	0.1690	0.998321
0.2523	0.992024	0.1715	0.997408	0.2044	0.997388
0.3072	0.986702	0.2022	0.996205	0.2522	0.995809
		0.3192	0.988253		

Table A.2.a
Water Activity a_1 in Water (1) - Dextran 40000 (3) Solutions

293.15 K		313.15 K		333.15 K	
w_3	a_1	w_3	a_1	w_3	a_1
0 0023	0.99999751	0.0023	0.99999784	0.0021	0.99999801
0.0061	0.99999298	0.0061	0.99999363	0.0064	0.99999307
0.0108	0.99998644	0.0108	0.99998813	0.0103	0.99998797
0.0153	0.99997934	0.0153	0.99998188	0.0196	0.99997411
0.0201	0.99997104	0.0201	0.99997345	0.0528	0.999889
0.0443	0.999887	0.0417	0.999921	0.0872	0.999675
0.0974	0.999494	0.0804	0.999711	0.1322	0.999275
0.1456	0.998764	0.1503	0.998814	0.2033	0.997755
0.1923	0.997561	0.2006	0.997522		
0.2212	0.996311				

Table A.2.b
Water Activity a_1 in Water (1) - Dextran 70000 (3) Solutions

293.15 K		313.15 K		333.15 K	
w_2	a_1	w_2	a_1	w_2	a_1
0.0015	0.99999919	0.0021	0.99999907	0.0030	0.99999831
0.0048	0.99999726	0.0117	0.99999362	0.0060	0.99999641
0.0112	0.99999258	0.0199	0.99998699	0.0099	0.99999302
0.0189	0.99998497	0.0287	0.99997751	0.0522	0.999929
0.0579	0.999901	0.0412	0.999955	0.0884	0.999812
0.0923	0.999734	0.0540	0.999931	0.1225	0.999615
0.1616	0.999064	0.0826	0.999814	0.1284	0.999632
0.2029	0.998227	0.0890	0.999790	0.1966	0.998729
0.2441	0.997175	0.1419	0.999359	0.2131	0.998729
		0.1442	0.999343	0.2444	0.997958
		0.1866	0.998808		
		0.2283	0.998024		
		0.2632	0.997062		
		0.2732	0.996750		
		0.2925	0.996127		

Table A.2.c

Water Activity a_1 in Water (1) - Dextran 110000 (3) Solutions

293.15 K		313.15 K		333.15 K	
w_3	a_1	w_3	a_1	w_3	a_1
0.0022	0.99999920	0.0020	0.99999923	0.0050	0.99999854
0.0046	0.99999835	0.0052	0.99999787	0.0073	0.99999720
0.0083	0.99999627	0.0099	0.99999517	0.0129	0.99999466
0.0181	0.99999026	0.0204	0.99998766	0.0269	0.99998594
0.0392	0.99996944	0.0441	0.999942	0.0886	0.999898
0.0453	0.999941	0.0504	0.99994009	0.0903	0.999895
0.0967	0.999791	0.0755	0.999858	0.1301	0.999706
0.0982	0.999791	0.0983	0.999775	0.1426	0.999656
0.1049	0.999731	0.0990	0.999786	0.1449	0.999653
0.1204	0.999663	0.1049	0.999740	0.1728	0.999429
0.1242	0.999642	0.1249	0.999619	0.1922	0.999204
0.1332	0.999608	0.1295	0.999589	0.2092	0.999095
0.1676	0.999333	0.1545	0.999394	0.2221	0.998917
0.1697	0.999296	0.1853	0.999077	0.2636	0.998116
0.1760	0.999230	0.2158	0.998624	0.2768	0.997858
0.1959	0.998963	0.2158	0.998629	0.2893	0.997613
0.2219	0.998567	0.2158	0.998609		
0.2250	0.998541	0.2168	0.998575		
0.2299	0.998508	0.2697	0.997499		
0.2577	0.997818	0.2811	0.997152		
0.2596	0.997783	0.3356	0.995361		
0.2799	0.997238	0.3355	0.995403		
0.2992	0.996772				
0.3003	0.996729				

Table A.2.d

Water Activity a_1 in Water (1) - Dextran 500000 (3) Solutions

293.15 K		313.15 K		333.15 K	
w_3	a_1	w_3	a_1	w_3	a_1
0.0028	0.99999957	0.0019	0.99999967	0.0041	0.99999934
0.0068	0.99999887	0.0021	0.99999961	0.0078	0.99999862
0.0096	0.99999800	0.0034	0.99999942	0.0153	0.99999691
0.0136	0.99999671	0.0041	0.99999918	0.0382	0.99998542
0.0221	0.99999419	0.0082	0.99999843	0.0638	0.999948
0.0555	0.999949	0.0132	0.99999716	0.1237	0.999795
0.0971	0.999811	0.0222	0.99999380	0.1814	0.999469
0.1201	0.999694	0.0363	0.99998397	0.1936	0.999380
0.1532	0.999487	0.0468	0.999966	0.2385	0.998918
0.2251	0.998533	0.0522	0.99996238		
0.2333	0.998434	0.0622	0.999936		
0.2373	0.998389	0.0634	0.999936		
0.2566	0.997983	0.0634	0.99993487		
0.2830	0.997310	0.0806	0.999897		
0.3101	0.996437	0.0901	0.999864		
		0.0952	0.999851		
		0.1074	0.999810		
		0.1087	0.999787		
		0.1311	0.999691		
		0.1596	0.999501		
		0.1618	0.999483		
		0.1791	0.999307		
		0.1970	0.999079		
		0.2169	0.998837		
		0.2521	0.998254		
		0.2745	0.997791		
		0.2912	0.997385		
		0.3055	0.997003		

Table A.3

Water Activity a_1 in Water (1) - PEG 3000 (2) - Dextran 110000 (3) Solutions

293.15 K			313.15 K			333.15 K		
w_2	w_3	a_1	w_2	w_3	a_1	w_2	w_3	a_1
0.0490	0.0000	0.999536	0.0935	0.0000	0.998864	0.0489	0.0000	0.999654
0.0323	0.0411	0.999552	0.0742	0.0205	0.998999	0.0389	0.0184	0.999670
0.0237	0.0620	0.999574	0.0637	0.0316	0.999100	0.0294	0.0359	0.999675
0.0147	0.0840	0.999593	0.0544	0.0414	0.999191	0.0190	0.0552	0.999731
0.0078	0.1010	0.999620	0.0381	0.0586	0.999337	0.0087	0.0743	0.999808
0.0000	0.1204	0.999663	0.0299	0.0673	0.999418	0.0000	0.0903	0.999895
			0.0185	0.0794	0.999549			
			0.0000	0.0990	0.999786			
0.0767	0.0000	0.999081	0.1037	0.0000	0.998659	0.0801	0.0000	0.999280
0.0624	0.0312	0.999095	0.0865	0.0307	0.998659	0.0640	0.0286	0.999290
0.0474	0.0639	0.999114	0.0713	0.0579	0.998681	0.0537	0.0470	0.999336
0.0332	0.0949	0.999142	0.0575	0.0825	0.998701	0.0337	0.0826	0.999396
0.0197	0.1245	0.999198	0.0368	0.1195	0.998770	0.0177	0.1112	0.999493
0.0097	0.1463	0.999268	0.0284	0.1345	0.998808	0.0000	0.1426	0.999656
0.0000	0.1676	0.999333	0.0196	0.1502	0.998875			
			0.0085	0.1702	0.998949			
			0.0000	0.1853	0.999077			
0.0871	0.0000	0.998858	0.1189	0.0000	0.998300	0.1144	0.0000	0.998741
0.0725	0.0294	0.998864	0.1175	0.0025	0.998280	0.0460	0.1252	0.998745
0.0571	0.0606	0.998872	0.1161	0.0050	0.998260	0.0452	0.1266	0.998753
0.0430	0.0892	0.998897	0.0353	0.1524	0.998352	0.0345	0.1462	0.998778
0.0292	0.1 70	0.998964	0.0296	0.1628	0.998376	0.0276	0.1588	0.998794
0.0145	0.1467	0.999076	0.0247	0.1718	0.998391	0.0229	0.1673	0.998850
0.0000	0.1760	0.999230	0.0169	0.1859	0.998444	0.0158	0.1802	0.998916
			0.0127	0.1936	0.998483	0.0000	0.2092	0.999095
			0.0064	0.2052	0.998523			
			0.0000	0.2168	0.998575			

(continued)

293.15 K			313.15 K			333.15 K		
a_1	w_2	w_3	a_1	w_2	w_3	a_1	w_2	w_3
0.0953	0.0000	0.998650	0.1537	0.0000	0.997263	0.1748	0.0000	0.997332
0.0808	0.0298	0.998660	0.1520	0.0029	0.997245	0.0227	0.2408	0.997530
0.0662	0.0598	0.998636	0.1511	0.0045	0.997227	0.0177	0.2488	0.997573
0.0522	0.0887	0.998650	0.0502	0.1817	0.997136	0.0131	0.2560	0.997653
0.0434	0.1068	0.998681	0.0436	0.1931	0.997166	0.0078	0.2644	0.997744
0.0192	0.1564	0.998797	0.0381	0.2029	0.997201	0.0033	0.2715	0.997799
0.0000	0.1959	0.998963	0.0363	0.2060	0.997210	0.0000	0.2768	0.997858
			0.0264	0.2233	0.997274			
			0.0144	0.2445	0.997360			
			0.0097	0.2527	0.997416			
			0.0000	0.2697	0.997499			
0.1070	0.0000	0.998372						
0.0261	0.1702	0.998329						
0.0170	0.1892	0.998387						
0.0105	0.2030	0.998420						
0.0000	0.2250	0.998541						
0.1280	0.0000	0.997709						
0.0174	0.2218	0.997737						
0.0139	0.2290	0.997748						
0.0070	0.2433	0.997772						
0.0000	0.2577	0.997818						
0.1521	0.0000	0.996684						
0.0086	0.2820	0.996693						
0.0056	0.2883	0.996710						
0.0031	0.2929	0.996733						
0.0000	0.2992	0.996772						

APPENDIX A2.

Digitised sets of data.

Table A.4

System	:	PEG/water solutions at 20°C.
Data type	:	Weight fraction polymer vs activity of water.
Source	:	Großmann et al. (1993).

Table A.4.a

wt frn (PEG 6000)	acty (water)
0.117	0.9988
0.136	0.9980
0.164	0.9972
0.173	0.9967
0.175	0.9957
0.194	0.9956
0.195	0.9951
0.199	0.9940
0.222	0.9933
0.228	0.9918
0.251	0.9890
0.273	0.9865
0.282	0.9850
0.291	0.9836
0.300	0.9821
0.308	0.9802
0.318	0.9786

Table A.4.b

wt frn (PEG 35000)	acty (water)
0.115	0.9987
0.136	0.9980
0.155	0.9971
0.193	0.9955
0.216	0.9932
0.258	0.9889
0.279	0.9863
0.284	0.9848
0.298	0.9834
0.304	0.9819
0.314	0.9801
0.322	0.9784

System   :   Dextran (Dx) 500000/water at 20 °C.
Data type   :   Weight fraction polymer vs activity of water.
Source   :   Großmann et al. (1993).

Table A.4.c

wt frn (Dx 500000)	acty (water)
0.197	0.9983
0.249	0.9977
0.285	0.9968
0.307	0.9961
0.320	0.9953
0.338	0.9947
0.351	0.9935
0.369	0.9930
0.388	0.9917
0.437	0.9888
0.465	0.9863
0.474	0.9847
0.487	0.9833
0.499	0.9819
0.504	0.9800
0.515	0.9791
0.520	0.9785
0.539	0.9753
0.553	0.9746
0.571	0.9685

Table A.5

System	:	Dextran (Dx) 110000/PEG 3000/ Water at 293 K.
Data type	:	Binodal.
Source	:	Gaube et al. (1993).

Phase I (wt frn)		Phase II (wt frn)	
Dx	PEG	Dx	PEG
0.16236	0.03250	0.01440	0.1053
0.18976	0.02734	0.00977	0.11273
0.21970	0.02183	0.00408	0.12844
0.23574	0.01879	0.00263	0.13633
0.25430	0.01639	0.00167	0.14410
0.28194	0.01236	0.00106	0.15834

Table A.6

System	:	PEG 2290/water
Data type	:	Temperature-concentration two-phase curve.
Source	:	Saeki et al. (1976).

Table A.6.a

wt frn(PEG)	T (K)
0.19034	436.4
0.23593	436.5
0.29492	437.9
0.37682	444.8
0.39902	451.3
0.39763	489.9
0.37508	496.7
0.29679	506.1
0.23868	508.2
0.19197	508.6
0.11200	505.9
0.07113	495.6
0.07068	488.4
0.07135	454.7
0.07242	447.6
0.11662	438.2

Table A.6.b

wt frn^I	wt frn^{II}	T(K)
0.11732	0.29585	437.8
0.0810	0.37516	444.0
0.07234	0.40025	450.0
0.06789	0.41172	457.4
0.06645	0.42181	470.0
0.06757	0.41263	483.6
0.07431	0.37825	496.7
0.08912	0.32578	503.3
0.11252	0.28432	506.4

APPENDIX A3.

Derivatives of Flory-Huggins model.

Derivatives of Flory-Huggins model:

The first partial derivative of Gibbs free energy of mixing with respect to the number of moles of a component is given by

$$\frac{\Delta\mu_i}{RT} = \ln \phi_i + 1 - r_i\sum_j \frac{\phi_j}{m_j}$$
$$+ r_i\sum_j \chi_{ij} \phi_j - \frac{1}{2}r_i\sum_k \sum_j \chi_{jk} \phi_i \phi_j \qquad (A.1)$$

where,

$$\phi_j = \frac{n_j r_j}{D} \quad , \quad D = \sum_i n_i r_i \qquad (A.2)$$

The first partial derivative of the chemical potential of a component with respect to the number of moles of a component is given by

$$\frac{\partial(\Delta\mu_i/RT)}{\partial n_j} = \frac{1}{n_t}[\frac{\delta_{ij}}{x_i} - \frac{(r_i + r_j)}{D} + \frac{r_i r_j}{D^2}$$
$$+ \frac{r_i r_j}{D}(\chi_{ij} - \sum_l (\chi_{il} + \chi_{jl})$$
$$+ \sum_l \sum_s \chi_{ls} \phi_l \phi_s)] \qquad (A.3)$$

The second partial derivative of the chemical potential with respect to the number of moles is given by

$$\frac{\partial^2(\Delta\mu_i/RT)}{\partial n_k\,\partial n_j} = \frac{1}{n_t^2}\Big[-\frac{\delta_{ijk}}{x_i^2} + \frac{(r_i\,r_j + r_i\,r_k + r_j\,r_k)}{D^2}$$

$$-\frac{2\,r_i\,r_j\,r_k}{D^3} + \frac{r_i\,r_j\,r_k}{D^2}(-(\chi_{ij} + \chi_{ik} + \chi_{jk})$$

$$+ 2\sum_l (\chi_{il} + \chi_{jl} + \chi_{kl})\,\phi_l - 3\sum_s\sum_l \chi_{sl}\,\phi_s\,\phi_l)\Big] \qquad (A.4)$$