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# Direct analysis of experimental tie line data (two polymer–one solvent systems) using Flory–Huggins theory

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**Abstract**

A computational method is described which allows experimental tie line data for two polymer–one solvent mixtures to be analysed directly in terms of Flory–Huggins theory. Three Flory–Huggins parameters and their uncertainties are calculated. These are, one polymer molecular weight and two $\chi$ values (one polymer segment–solvent $\chi$, i.e. $\chi 12$ or $\chi 13$, and $\chi 23$ the polymer–polymer segment interaction coefficient). Due to irreducible parameter correlation, the remaining two Flory–Huggins parameters, i.e. one polymer molecular weight and one polymer–solvent $\chi$, must be fixed at experimentally determined values. The paper also describes application of the method to experimental (literature) tie line data for some typical ternary systems based on uncharged polymers (synthetic polymers and biopolymers). While the description of phase diagrams was generally good, discrepancies between calculated and experimental polymer molecular weights and second virial coefficients, together with a significant dependence of the $\chi$ values on molecular weight, warn that the Flory–Huggins approach is unlikely to be an accurate quantitative predictor of phase behaviour for systems of the type discussed. The results were encouraging enough, however, to suggest that semi-quantitative conclusions about the influence of molecular factors on the positions of binodals, tie lines and critical points, and on the slopes of tie lines, were likely to be valid for mixed uncharged ternary systems. 

*Keywords*: Ternary phase diagrams; Tie line analysis; Flory–Huggins theory; Dextran; Agarose; Polyethylene glycol; Polystyrene; Polyisoprene; Edmond–Ogston theory

## 1. Introduction

Pseudo-ternary systems involving two polymer species and a solvent are of considerable practical importance both in the case where synthetic polymers are present in an organic solvent, and where biopolymers are dissolved in water. In the former situation, the synthetic polymer systems can be used in the fabrication of membranes and filters, whilst in the latter, mixed aqueous biopolymer solutions can give rise to multiphasic gels of value to the Food Industry. In all such ternary solution situations, a common factor of importance, is the phase behaviour of the system prior to gelation and/or removal of solvent, since microstructures ultimately formed are likely to be crucially dependent on this. Thus, substantial experimental effort is usually expended in determining such phase behaviour through determination of phase diagrams including binodals, tie lines and critical points (sometimes as a function of temperature and of the molecular weights of the polymers involved). Although the events subsequent to initial solution preparation are largely under kinetic control, characterisation of the starting state, in the manner just indicated, is important, as the course of such kinetics is usually strongly dependent on the nature of the starting condition, i.e. one phase, or two phase, solution state, etc.

Although much of the subject of ternary solution behaviour of polymers is experimental, and to some extent empirical, it is important to have available some kind of theoretical framework to help rationalise trends in phase behaviour in relation to component polymer structures, molecular weights, solvent quality, temperature, etc. Where extended linear polymers are concerned, the simplest available approach is that of Flory and Huggins (Flory, 1953), the application of which to ternary systems has been described in some detail by Hsu and Prausnitz (1974). These last authors discussed the method in computational terms, and examined the main features of the phase separation phenomenon in relation to the variables mentioned. Their treatment involves calculating the phase behaviour of hypothetical systems whose molecular weights and polymer–solvent and polymer–polymer interaction parameters can be changed at will.

In addition to examining the implications of the Flory–Huggins approach by what can be described as calculations

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conducted in a 'forward direction', i.e. by calculating hypothetical phase diagrams using selected molecular weight and solvent quality ($\chi$ value) parameters, it is tempting to fit real experimental data, to see just how well the model describes real systems. If successful, this would offer reassurance that the qualitative trends obtained by forward calculation are likely to be relevant in practice. Also, if the model does work well for biopolymer–water systems, and $\chi$ parameters show little variation with molecular weight and, together with the calculated molecular weights, agree well with experiment, some predictive element of more than a purely qualitative kind might be feasible. The present analysis of published phase diagram data for ternary biopolymer mixtures was undertaken with these aims in mind.

Given a set of measured tie lines of limited accuracy, the fitting procedure using the Flory–Huggins model is far from trivial. The obvious approach would be one of least-squares fitting of the model to the tie lines, perhaps constraining each theoretical tie line to pass through the points of initial solution concentration chosen experimentally. The object of the least-squares exercise would then be to find values for the five model parameters (two molecular weights and three $\chi$ values) in terms of least-squares optimisation of the ends of calculated tie lines in relation to corresponding experimental results. The present author has attempted this approach but the difficulty of obtaining reliable and rapid convergence of calculated tie lines in terms of the variable parameters, made fits to more than one tie line impractical. There were also problems associated with parameter correlation which made unique fitting impossible if all model parameters were varied simultaneously. It seemed necessary to fix at least one polymer–solvent $\chi$ value and one molecular weight at independently determined values, to achieve a definite (converged) answer. Even then, the calculations involved were very slow and convergence was rarely achieved.

The least-squares approach remains an attractive one, especially if fits based on a sizeable set of tie lines (rather than just one) could be achieved, but until this is accomplished computationally, it appears necessary to consider a second and somewhat simpler approach to data analysis which is computationally more stable and rapid, and which offers a straightforward explanation of, and solution to, the parameter correlation problems experienced. This procedure, which differs somewhat from the least-squares treatment in the way it handles experimental uncertainties and arrives at average results, is what can be called a 'direct data analysis' approach. It takes each tie line in turn, and directly outputs values for the Flory–Huggins parameters consistent with a perfect (i.e. exact) fit to the tie line involved. This procedure is carried out for all experimental tie lines in a set, quickly and reliably, and average parameters can be evaluated. The success of the Flory–Huggins model in describing the data is then measured by the spread (particularly the systematic spread) of the calculated parameter values over the experimental tie line range, and of course the quality of description of the experimental phase diagram indicated by forward calculations based on the overall average parameters obtained. A further indicator of success is obtained by fitting other sets of tie lines for the same polymer–solvent system, but involving different molecular weight fractions. The simple Flory–Huggins model implies that solvent quality $\chi$ parameters should be independent of molecular weight, hence similar values should be obtained for a series of systems as the molecular weight of at least one of the components is varied. Another obvious checking procedure is comparison of calculated molecular weights and $\chi$ values with corresponding experimental results where available.

The direct method of analysis is described in some detail in the present paper, particularly in relation to literature data where molecular weight variations have been examined. Both synthetic polymer mixtures and biopolymer mixtures containing polysaccharides are considered. The theory underlying the direct analysis approach is considered first, then results are discussed for cases where it has been applied to polystyrene–polyisoprene–toluene, and aqueous mixtures of polyethylene glycol (PEG)–agarose, PEG–dextran and dextran–agarose.

## 2. Theory

The basic Flory–Huggins polymer solution theory (Flory, 1953) is expressed in terms of molecular weight parameters for the two polymers and solvent, and energy parameters describing polymer–solvent and polymer–polymer segment interactions. In terms of this model theoretical phase diagrams are normally expressed in volume fraction concentration units, but these can easily be related to weight fraction results through appropriate conversion using partial specific volumes for the components. Polymer molecular weights are treated as ratios of polymer to solvent molar volumes this making the solvent molecular weight unity. Where the polymer segments and solvent have closely similar volumes then the molecular weight descriptors become equivalent to segment (or repeat unit) numbers, but this is not generally true. In the present work, the symbols $P2$ and $P3$ will denote the polymer molecular weight parameters defined in this way, with $P1 = 1$ referring to the solvent. The symbols $\chi 12$, $\chi 13$ and $\chi 23$, also used, denote the segment–solvent interaction parameters for polymer components 2 and 3 with solvent 1, and the parameter describing interaction between unlike polymer segments. Generally, values for $\chi 12$ and $\chi 13$ are numbers between zero and 0.5 (or a value slightly greater than 0.5) while the polymer–polymer interaction parameter is much smaller and can be negative. Here it is assumed that mixtures of the individual polymers with the solvent are miscible in all proportions (note that for polymer–solvent parameters significantly greater than 0.5 this will not be

true). No miscibility restriction is placed on the behaviour of undiluted mixtures of the two polymers, however.

In terms of these parameters the chemical potentials of components 1–3 can be written in the forms:

$$\Delta\mu 1/RT = \ln\{\Phi 1\} + (1 - 1/P2)\Phi 2 + (1 - 1/P3)\Phi 3 + (1 - \Phi 1)(\chi 12\Phi 2 + \chi 13\Phi 3) - \chi 23\Phi 2\Phi 3 \quad (1)$$

$$\Delta\mu 2/RT = \ln\{\Phi 2\} + (1 - P2)\Phi 1 + (1 - P2/P3)\Phi 3 + P2(1 - \Phi 2)(\chi 12\Phi 1 + \chi 23\Phi 3) - P2\chi 13\Phi 1\Phi 3 \quad (2)$$

$$\Delta\mu 3/RT = \ln\{\Phi 3\} + (1 - P3)\Phi 1 + (1 - P3/P2)\Phi 2 + P3(1 - \Phi 3)(\chi 13\Phi 1 + \chi 23\Phi 2) - P3\chi 12\Phi 1\Phi 2 \quad (3)$$

where the $\Delta\mu$ symbols indicate differences in chemical potentials for the components in relation to standard states at absolute temperature $T$, R is the gas constant, $\Phi$ symbolises volume fraction, and the other symbols have the meanings already described. For any solution composition, where phase separation occurs into two conjugate phases, the compositions of these phases can be represented by the volume fractions of two points, i.e. $\Phi 1', \Phi 2', \Phi 3'$ and $\Phi 1'', \Phi 2'', \Phi 3''$ connected by a tie line which also contains the original solution point. The condition for equilibrium is then that the chemical potential of each component is equal in the two phases (i.e. $\Delta\mu 1' = \Delta\mu 1''$, etc.).

If Eqs. (1)–(3) are rearranged into forms linear in $\chi 12$, $\chi 13$, and $\chi 23$ and then the equality condition for chemical potentials is assumed, linear equations of the following form are obtained, for the equilibrium condition:

$$\chi 12\{(1 - \Phi 1')\Phi 2' - (1 - \Phi 1'')\Phi 2''\} + \chi 13\{(1 - \Phi 1')\Phi 3' - (1 - \Phi 1'')\Phi 3''\} + \chi 23\{\Phi 2''\Phi 3'' - \Phi 2'\Phi 3'\} = \ln\{\Phi 1''/\Phi 1'\} + (1 - 1/P2)(\Phi 2'' - \Phi 2') + (1 - 1/P3) \times (\Phi 3'' - \Phi 3') \quad (4)$$

$$\chi 12\{(1 - \Phi 2')\Phi 1' - (1 - \Phi 2'')\Phi 1''\} + \chi 13\{\Phi 1''\Phi 3'' - \Phi 1'\Phi 3'\} + \chi 23\{(1 - \Phi 2')\Phi 3' - (1 - \Phi 2'')\Phi 3''\} = (1/P2)\ln\{\Phi 2''/\Phi 2'\} + (1/P2 - 1)(\Phi 1'' - \Phi 1') + (1/P2 - 1/P3)(\Phi 3'' - \Phi 3') \quad (5)$$

$$\chi 12\{\Phi 1''\Phi 2'' - \Phi 1'\Phi 2'\} + \chi 13\{(1 - \Phi 3')\Phi 1' - (1 - \Phi 3'')\Phi 1''\} + \chi 23\{(1 - \Phi 3')\Phi 2' - (1 - \Phi 3'')\Phi 2''\} = (1/P3)\ln\{\Phi 3''/\Phi 3'\} + (1/P3 - 1)(\Phi 1'' - \Phi 1') + (1/P3 - 1/P2)(\Phi 2'' - \Phi 2') \quad (6)$$

This transformation has already been described in the literature (Narasimhan, Huang & Burns, 1983; Tseng & Lloyd, 1987), and suggested as a basis for direct tie line analysis, but as will emerge in what follows, the previous publications were not entirely rigorous in the mathematical steps subsequently employed to solve Eqs. (4)–(6). To do this, it might seem obvious that all that is required is to take a tie line measured experimentally as a set of $\Phi i'$ and $\Phi i''$ values, assume experimental values for molecular weights to evaluate $P2$ and $P3$, and then solve the three linear equations above for the energy parameters $\chi 12$, $\chi 13$ and $\chi 23$. It turns out, however, that the equations are always severely ill-conditioned (i.e. determinant of coefficient matrix close to zero) and that there is no unique solution calculable. This underlines an important feature of the Flory–Huggins theory, namely that the tie line is determined essentially by the difference between $\chi 12$ and $\chi 13$, rather than the absolute values of these parameters. In consequence, a more realistic and mathematically tractable strategy, is to fix $\chi 12$ at some value determined by another type of experiment (e.g. light scattering, osmotic pressure), and to consider the properties of the three equations in the two unknown energy parameters which remain.

In relation to this problem, the suggestion in the literature cited above was to take any two of these equations, assume values for $P2$ and $P3$, and solve for $\chi 13$ and $\chi 23$, it being taken for granted that the particular choice of a pair of equations did not matter. However, it is readily shown that, if solutions are obtained for the two other pairs of equations, and compared, significant discrepancies occur, i.e. three linear equations in two unknowns have a unique and common solution only if the lines represented by the equations intersect at a common point, a condition not generally met. Investigation shows that $P2$ and $P3$ cannot be assigned arbitrary values. Once $P2$, for example, is fixed, only one value of $P3$ gives linear equations with a unique common solution (or one value for $P2$, if $P3$ is fixed). This shows that within the Flory–Huggins theory, there is also a certain indeterminacy in the molecular weight parameters which amounts to the fact that a single tie line, apart from its sensitivity to the difference between two polymer–solvent $\chi$ values, is also mainly determined by the ratio of the polymer molecular weight parameters. In practice, the only correct way to directly analyse data for a single tie line, in terms of the model, is to fix one polymer–solvent $\chi$ value, and one molecular weight $P$ parameter (not necessarily both for the same polymer component), and then vary the remaining polymer molecular weight until the three linear equations in the remaining two $\chi$ values have a unique and common solution for these. The output of the calculation is then a molecular weight, and two energy parameters, determined in terms of assumed (experimental) results for one molecular weight and one polymer–solvent interaction parameter.

Actually, as will be noticed from Eqs. (4)–(6), it is possible to solve for all three of the accessible parameters directly, by constructing three linear equations in the three unknowns,

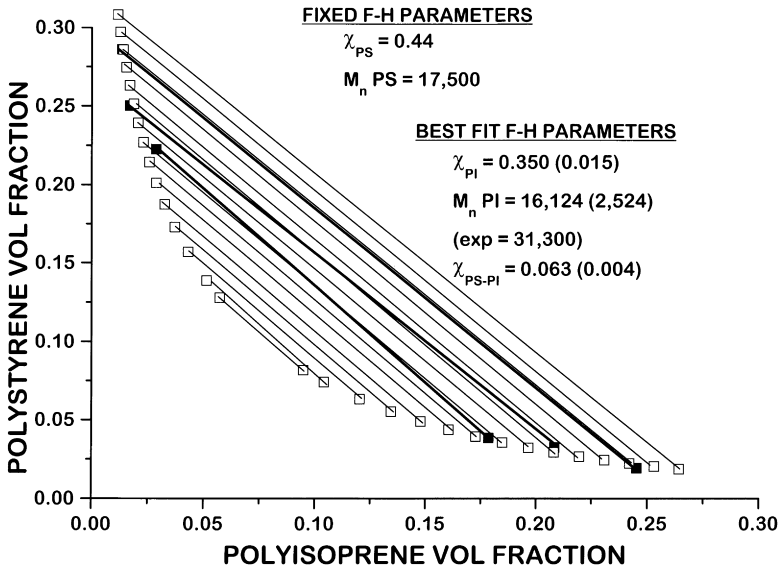


Fig. 1. Flory–Huggins direct analysis of polystyrene–polyisoprene tie line data (Tseng & Lloyd, 1987) for polystyrene, $M_n = 17,500$.

i.e. by transferring a linear reciprocal molecular weight term to the left-hand side, but this was not done in the present work, as the method is not generally applicable, i.e. in more complex circumstances, where ion effects become involved, non-linear molecular weight terms emerge. Here, a more general computational approach was adopted, which was to systematically vary one molecular weight (the variable one to be determined) until a common solution was found for the two energy parameters accurate to some preset tolerance. The fact that one molecular weight can be determined from tie line data as well as two $\chi$ values, is important, as this property allows a more critical test of the theory against experiment, where experimental values for this determined molecular weight are available.

## 3. The computer program

Fortran programs DIRCH2 and DIRCH3 were written to directly analyse a series of experimental tie lines defined in weight fraction terms. Partial specific volume data, also input, allowed the necessary conversion to volume fractions $\Phi$. DIRCH2 read in fixed values for $\chi 12$ and $P2$, and evaluated $\chi 13$, $\chi 23$ and $P3$ as described above, while DIRCH3 was based on fixed $\chi 12$ and $P3$ ($\chi 13$, $\chi 23$ and $P2$ being evaluated). Molecular weights were input/output in Daltons, but converted within the program to volume ratios in relation to solvent. The parameter results obtained for each tie line, by the direct analysis approach, were printed out and averaged, and the final averages output with standard deviations based on the spread of results over individual tie lines.

A facility was also included in both programs to allow the fixed parameters ($\chi 12$ and $P2$ or $\chi 12$ and $P3$) to be varied systematically, to obtain that final average result over a collection of tie lines which showed maximum consistency (lowest estimated standard deviations). However, while analysis of perfect data computed using Flory–Huggins theory, and known starting parameters (five in all), showed that for three or more tie lines, all five (molecular weight and energy) parameters could be recovered exactly using the minimisation facility, application to the same data with even small amounts of random error added, clearly demonstrated likely failure of the procedure in cases of real data. This means that, even where a considerable number of experimental tie lines have been determined to normal accuracy, parameter correlation is still important, making the only safe analysis procedure that of fixing two of the five variables at experimental values, and directly calculating the remaining three.

Clearly, however, having extra tie lines available is advantageous, as the spread of parameter values over a range of tie lines provides valuable information about how appropriate the Flory–Huggins model is for the system concerned, e.g. a systematic and large variation in parameter values over the range of tie lines available indicates a level of inappropriateness in the model. In work to be described below, such consistency was studied for both ternary synthetic (uncharged) polymer systems, and some similar systems based on uncharged biopolymers.

## 4. Results

### 4.1. Polystyrene–polyisoprene–toluene

A quite extensive study of the phase behaviour of this system (at 45°C) was published in 1987 by Tseng and Lloyd and provided a stimulus for the present development of the direct method of tie line analysis. The principle of this

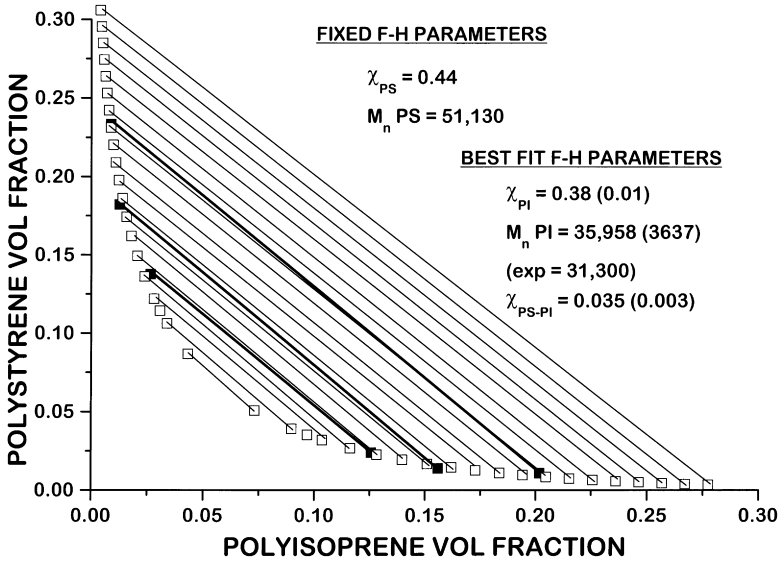


Fig. 2. Flory–Huggins direct analysis of polystyrene–polyisoprene tie line data (Tseng & Lloyd, 1987) for polystyrene, $M_n = 51,130$.

method was described by these authors, even though they appear not to have applied it correctly, in that they assumed that arbitrary molecular weights could be assigned when solving linear equations (see above). In the present re-analysis of their data, tie line concentrations were taken (wt%) from their Table 2 for systems involving a fixed molecular weight fraction of polyisoprene ($M_n = 31,300$), and variable molecular weight polystyrene samples ($M_n = 17,500$; 51,130; 87,770 and 220,500). Three tie lines were available in each case, but one had to be dropped from the 220,500 data set, as it contained a very small (and not very accurately determined) volume fraction, which led to an anomaly in the calculation.

In the calculations performed, the $\chi 12$ value, i.e. the polystyrene–toluene energy parameter was fixed at 0.44 in agreement with the original estimate by Tseng and Lloyd based on literature data, and the polystyrene molecular weights were fixed at the values specified above. The resulting calculated (average) values (DIRCH2) of $\chi 13$, $\chi 23$ and $P3$ (the polyisoprene molecular weight) appear in Figs. 1–4, which also show the experimental phase diagram data, and theoretical tie lines based on these final averages. In these figures, tie lines are expressed in volume fraction terms, but could equally well have been presented as corresponding weight fractions. There is clearly a significant systematic increase in $\chi 13$ as $P2$ increases, and the average value of 0.38 is higher than suggested for polyisoprene by the range of literature estimates (0.27–0.35) quoted by Tseng and Lloyd. Variation is also found for the polymer–polymer interaction parameter $\chi 23$, there being

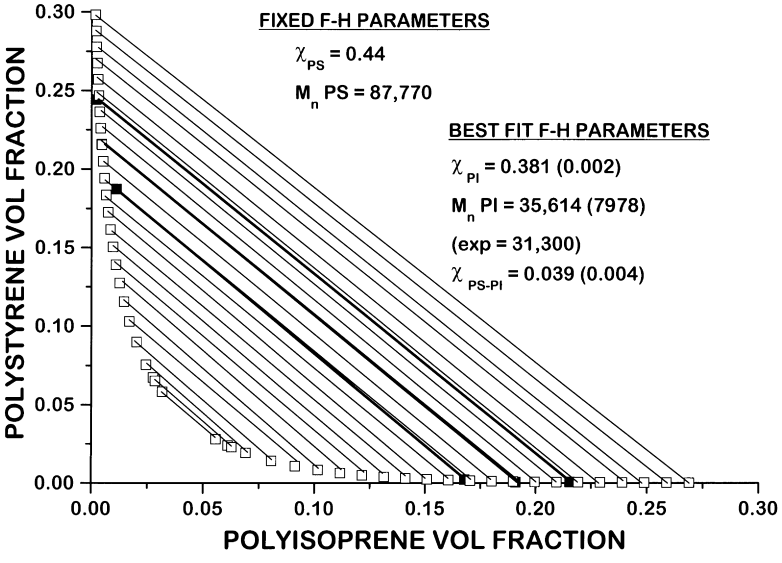


Fig. 3. Flory–Huggins direct analysis of polystyrene–polyisoprene tie line data (Tseng & Lloyd, 1987) for polystyrene, $M_n = 87,770$.

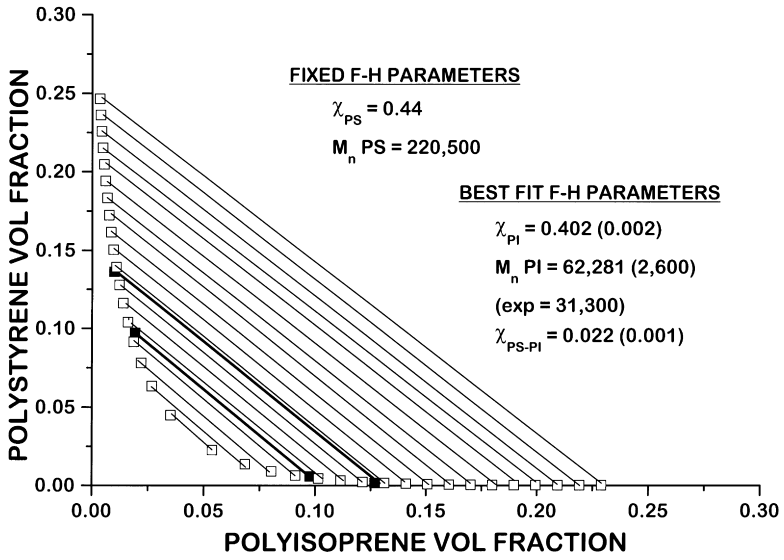


Fig. 4. Flory–Huggins direct analysis of polystyrene–polyisoprene tie line data (Tseng & Lloyd, 1987) for polystyrene, $M_n = 220,500$.

a systematic fall in this parameter with rising $P2$, and its spread lying outside the appropriate range of uncertainty. These values of $\chi 23$, which lie in the range 0.022–0.063 (average value 0.04), cannot be tested directly against experiment (no data available from, for example, light scattering) but may (according to Tseng & Lloyd, 1987) be compared with values such as 0.01–0.013 for polystyrene–polybutadiene, 0.007–0.040 for polystyrene–polyisobutylene, and 0.08 for polystyrene–polypropylene.

$P3$ also shows variations, increasing as $P2$ is increased, and agreeing well with experiment only in the cases shown in Figs. 2 and 3 where parameter consistency is at a maximum (i.e. for the intermediate polystyrene molecular weights 51,130 and 87,770). Thus, despite the apparent appropriateness of the system for application of Flory–Huggins theory (linear uncharged organic polymers in an organic solvent), discrepancies are evident, taking the form of systematic variation of $\chi$ parameters as a component molecular weight is changed, and disagreements between $\chi 13$ and $P3$ and independently measured experimental results.

A further unsatisfactory feature is an observed trend in calculated parameter values from tie line to tie line within each molecular weight analysis. For example, $P3$, in particular, was found to vary systematically from one tie line to another, within a set. This, and the other inconsistencies mentioned, warn against real effectiveness of the Flory–Huggins model as a reliable quantitative predictor of phase behaviour for such mixtures over a wide range of molecular weight.

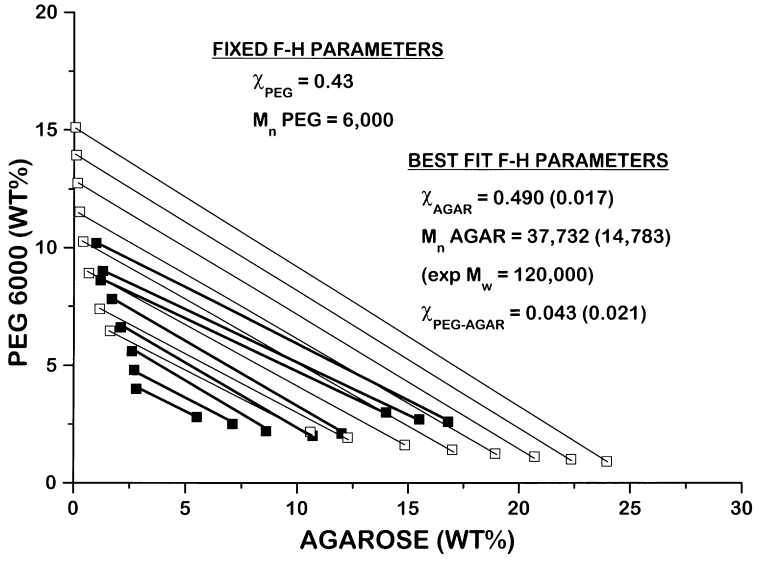


Fig. 5. Flory–Huggins direct analysis of PEG–agarose tie line data (Medin & Janson, 1993) for PEG, $M_n = 6000$.

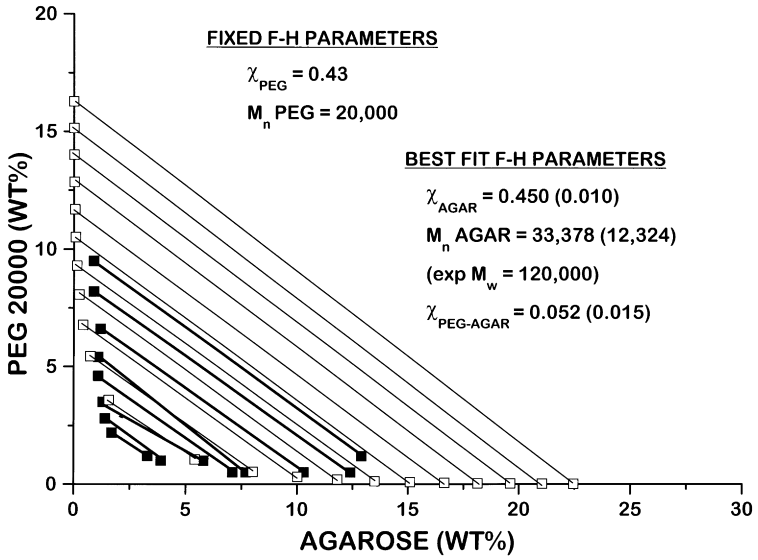


Fig. 6. Flory–Huggins direct analysis of PEG–agarose tie line data (Medin & Janson, 1993) for PEG, $M_n = 20,000$.

### 4.2. PEG–agarose–water

Tie line data for aqueous PEG–agarose systems (at 80°C) have been published by Medin and Janson (1993) for an agarose sample of weight average molecular weight 120,000, and for PEG samples of number average molecular weights: 6000, 20,000 and 35,000. In the present work, when analysing this data by direct methods, the PEG $\chi 12$ and $P2$ parameters were fixed at 0.43, and at the appropriate molecular weight averages just quoted. The $\chi 12$ value was taken as an average from a number of publications, including an article by Edmond and Ogston (1968), and finds support from virial coefficient data. The results of applying direct tie line analysis to experimental phase diagram data are presented in Figs. 5–7 which this time display phase diagrams in weight percent terms. For the PEG 6000 and 20,000 samples, eight tie lines were available, whilst for the PEG 35,000 the number was six. One obvious conclusion from the figures is that the calculated agarose molecular weight is much lower than the experimental weight average, and that it falls significantly as PEG molecular weight is increased. A second observation is that the agarose–water $\chi 13$ interaction parameter also falls as the PEG molecular weight increases while the value of $\chi 23$ increases (interestingly the average value of $\chi 23 = 0.053$ is similar to that for the synthetic polymer system described above). $\chi 13$ is generally smaller than the value expected for agarose (an uncharged, potentially gelling polymer), though the average value of 0.45 obtained is within three standard deviations of the more reasonable value of 0.48–0.49 sometimes

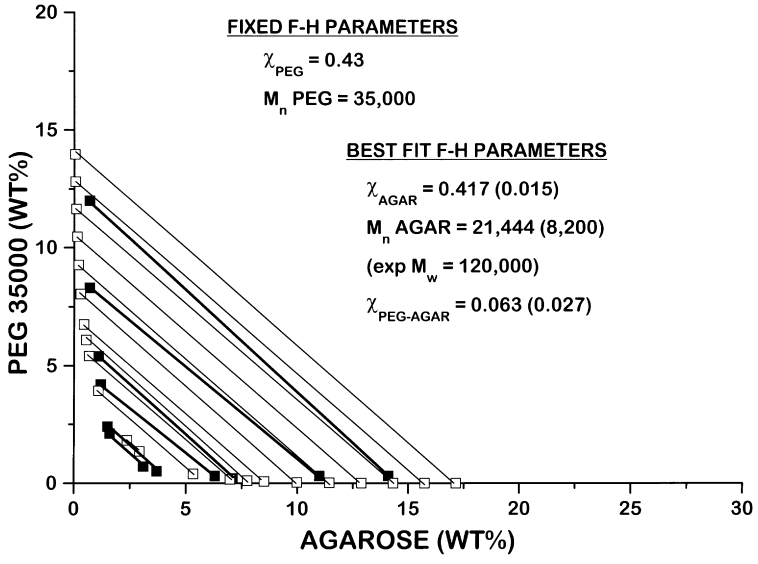


Fig. 7. Flory–Huggins direct analysis of PEG–agarose tie line data (Medin & Janson, 1993) for PEG, $M_n = 35,000$.

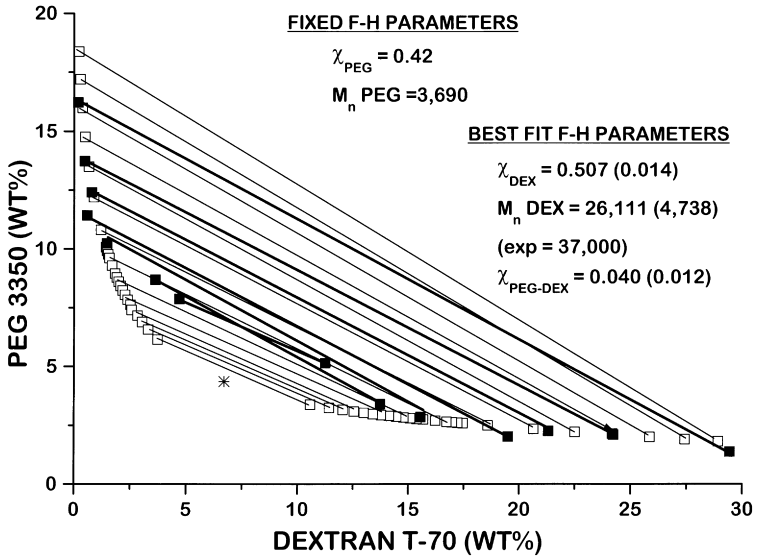


Fig. 8. Flory–Huggins direct analysis of PEG–dextran tie line data (King et al., 1988) for PEG, $M_n = 3690$. Theoretical critical point is indicated by asterisk.

assumed. This discrepancy is particularly noticeable for the higher molecular weight PEG systems, and may simply reflect a lack of true phase equilibration (and/or incomplete physical phase separation) for what must be very viscous systems. This would produce a change in tie line slope (as shown in Figs. 6 and 7) and a corresponding change in $\chi$13.

The most serious problem emerging from the analyses of PEG/agarose data, in terms of a satisfactory description of the system, is the discrepancy in values obtained for the agarose molecular weight when compared with experiment. One explanation for this could be polydispersity in the agarose sample making the number average much smaller than the weight average. The authors of the original paper do not give a value for $M_n$, but certainly $M_n$ would be expected to be the more appropriate average with which to make comparisons (although one must admit that, for a polydisperse sample, it may be that no single average is entirely satisfactory). Another explanation, however, could relate to the different segment sizes of the two polymers in this system, making volume ratios in relation to water an inappropriate way of handling their relative molecular weights. Finally, it is also possible that incomplete phase equilibration (and/or separation) is contributing to the molecular weight discrepancy just as was suggested above for the agarose $\chi$ value.

### 4.3. PEG–dextran–water

Data for this system was taken from two sources

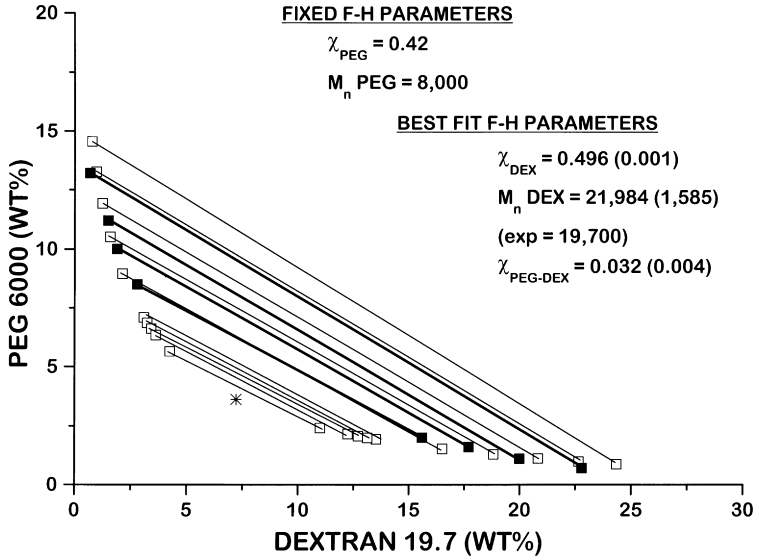


Fig. 9. Flory–Huggins direct analysis of PEG–dextran tie line data (Edmond & Ogston, 1968) for PEG, $M_n = 8000$. Theoretical critical point is indicated by asterisk.

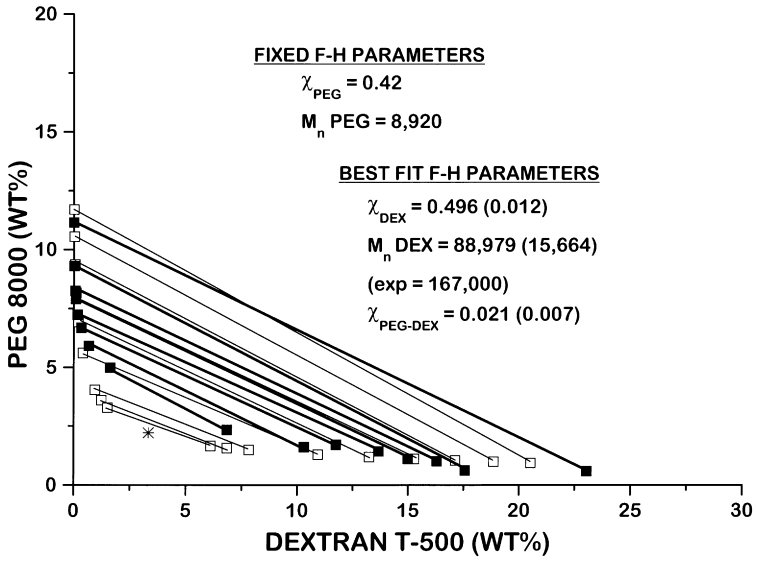


Fig. 10. Flory–Huggins direct analysis of PEG–dextran tie line data (King et al., 1988) for PEG, $M_n = 8920$. Theoretical critical point is indicated by asterisk.

(Edmond & Ogston, 1968; King, Blanch & Prausnitz, 1988), the PEG samples of interest having molecular weights ($M_n$) equal to 3690, 8000 and 8920 (relatively low molecular weight samples labelled PEG 3350, 6000 and 8000, respectively), while for dextran, molecular weights were $M_n = 37,000$, 19,700 and 167,000, respectively. In the direct tie line analyses performed, PEG molecular weights were fixed at the above number average values, whilst $\chi 12$ for PEG was fixed at 0.42, a slightly lower value than adopted in the section above for PEG–agarose, but a value consistent with results from Edmond and Ogston (1968) where low molecular weight PEGs were particularly discussed. The difference is not highly significant, however, and would lead only to a small increase in $\chi 13$, if $\chi 12$ were increased to the 0.43 used for PEG–agarose.

Results of direct tie line analyses for PEG–dextran systems (25–28°C) are shown in Figs. 8–10, seven tie lines being used for PEG 3690, four for PEG 8000 and eight for PEG 8920. Consistent $\chi$ values are obtained for the dextran, though these are perhaps surprisingly high (close to theta solvent values, while virial coefficient data might suggest a more hydrophilic polymer, $\chi = 0.48$). In the figures the molecular weight results for $P3$ are compared with the experimental number averages 37,000, 19,700 and 167,000. Only the fit corresponding to the last of these molecular weights (i.e. for the PEG 8920 system) is seriously in disagreement with experiment, but the standard

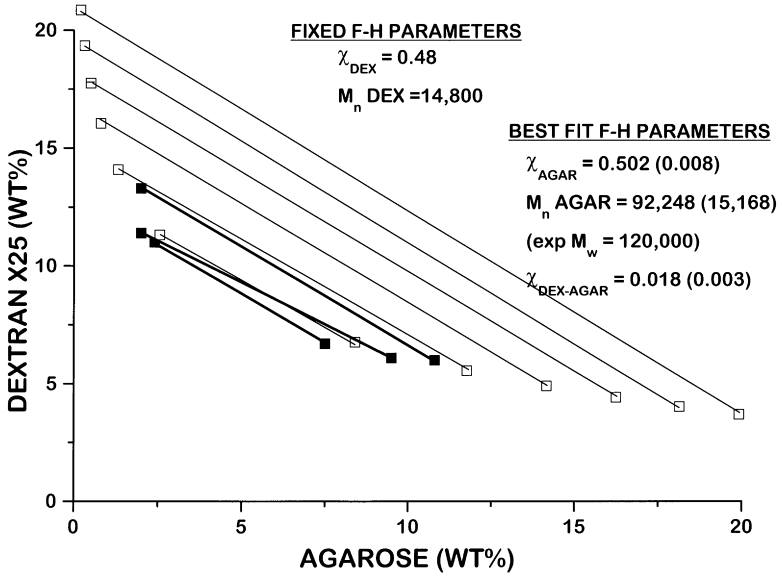


Fig. 11. Flory–Huggins direct analysis of dextran–agarose tie line data (Medin & Janson, 1993) for dextran, $M_n = 14,800$.

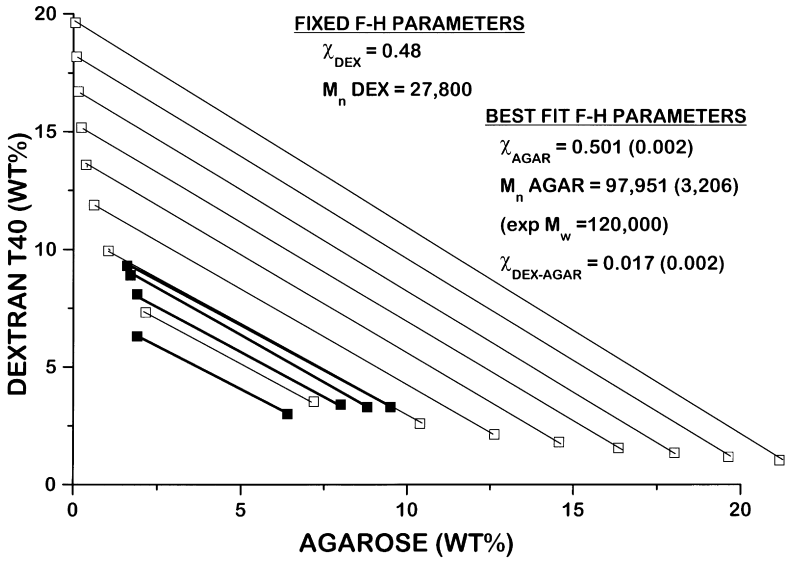


Fig. 12. Flory–Huggins direct analysis of dextran–agarose tie line data (Medin & Janson, 1993) for dextran, $M_n = 27,800$.

deviation here is high. One explanation for this might be that the high molecular weight dextran is significantly branched and is not expected to be well described by Flory–Huggins theory, and there is also the ill-defined problem of molecular weight polydispersity which may also be relevant.

The parameter $\chi 23$ is similar in value to that for the other polymer mixtures described so far, and again varies from system to system (average = 0.031), though in this case not too seriously. Overall, the results are encouraging, considering that the dextran is a branched polysaccharide, and PEG is not a polysaccharide at all, and has a significantly different segment size. Interestingly, no strong trends were found over the range of tie lines involved in any particular analysis, indicating random errors in tie line data in relation to the model, rather than systematic discrepancies.

### *4.4. Dextran–agarose–water*

Data from Medin and Janson (1993) were again used in this analysis of tie lines measured for three dextran–agarose systems (80°C). Number average values for dextran molecular weights were assumed, i.e. 14,800, 27,800 and 48,500 for the dextran samples used (dextran X-25, T-40 and T-70). In this work, the dextran $\chi 12$ value was held constant at 0.48, a slightly lower value than emerged during the calculations of the previous section. This was a value obtained from second virial coefficient data. Increasing this

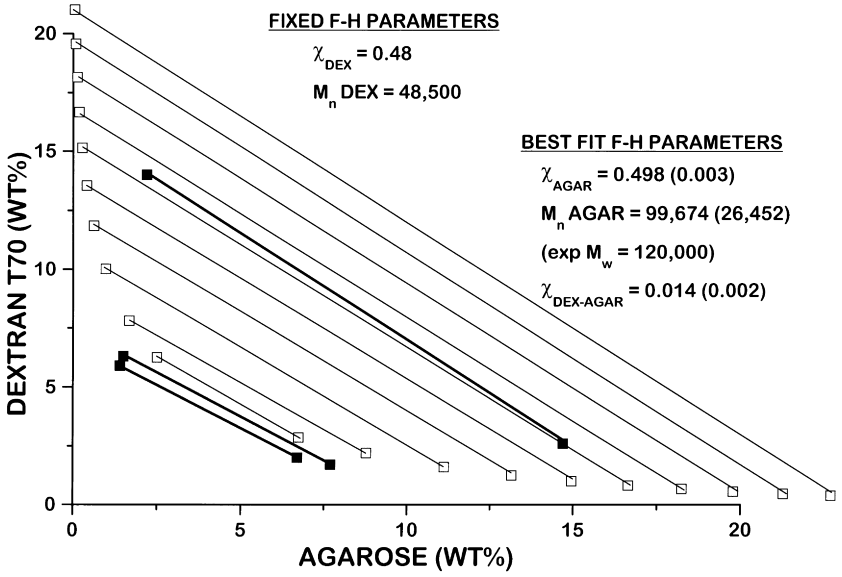


Fig. 13. Flory–Huggins direct analysis of dextran–agarose tie line data (Medin & Janson, 1993) for dextran, $M_n = 48,500$.

constrained parameter to 0.49 or 0.50 would simply increase the agarose $\chi 13$ determined by direct analysis by about the same amount, and would affect nothing else.

Results of the direct analyses are shown in Figs. 11–13, three tie lines being used in the dextran 14,800 case, four for dextran 27,800, and three for dextran 48,500. As before, the agarose molecular weight was $M_w = 120,000$, no number average value being available. Although standard deviations are quite high, the $\chi 13$ and molecular weight ($P3$) values are very consistent as $P2$ varies, with $\chi 13$ quite close to the value expected for agarose (0.48–0.49) and $P3$ within error of the experimental $M_w$. $\chi 23$ also varies little, and is in reasonable agreement with values for the previous systems, though results are somewhat lower (average = 0.016). All this good agreement should be viewed in the context of the branched nature of dextran, however, and the fact that the agarose molecular weight is a weight average. The good agreement may thus be partly fortuitous, and of course it is based on only very limited tie line data. Systematic trends in parameter values obtained in individual analyses were almost absent, however.

Interestingly, it appears that for the dextran–agarose combination, unlike for the PEG–agarose systems, fewer problems have been experienced in achieving phase equilibration and complete macroscopic phase separation.

## 5. Conclusions

1. The mathematical approach to direct tie line analysis described here works extremely well as a quick computational procedure though, as has been discussed above, it is unable to provide all five Flory–Huggins model parameters from a single, or even a larger collection of measured tie lines. The polymer–solvent interaction parameter for one of the polymers, and one polymer molecular weight, have to be introduced as fixed constraints in any successful analysis. The same problem would be encountered, however, even if the iterative least-squares approach could be made to work, this problem having its origin in a fundamental correlation property of the model, i.e. between $\chi 12$ and $\chi 13$ and between $P2$ and $P3$.
2. Application of direct analysis to at least one synthetic organic polymer–organic solvent system provides the warning that $\chi$ values are not truly independent of the polymer molecular weights (or indeed polymer concentration), nor are calculated molecular weight values always in good agreement with experimental estimates. This, despite the apparent appropriateness of the synthetic polymer system for Flory–Huggins description. This indicates that the theory in its original form (five parameters) is unlikely to be applicable in a quantitatively predictive way, i.e. the effect on the phase behaviour of a system, of changing the molecular weight of the polymer components, is unlikely to be accurately predicted by a calculation based on $\chi$ values obtained by fitting the phase behaviour established in one particular case. There is also the implication that complete a priori prediction of the phase behaviour of a system through knowledge of number average molecular weights for the components, and $\chi$ values from osmotic pressure measurements (or light scattering), would be even less reliable. In this last connection it has to be said that such prediction was not a real ambition, as the work involved to establish all three $\chi$ values for a system (particularly the polymer–polymer interaction parameter) using techniques such as osmotic pressure measurements and light scattering would no doubt rival that involved in establishing the phase diagrams themselves. It was also an objective of the present work to examine only the simplest form of the theory. More highly parameterised versions are possible in which some of the problems found here are considered but the feeling was that such additional parameterisation would reduce the practical value of the model. The idea was to establish the utility, if any, of the lowest parameter version as a means of rationalising mixed biopolymer phase behaviour. The conclusion reached here that such success is likely to be of a qualitative (or at best, semi-quantitative) kind only, seems to be consistent with the results of Monte Carlo simulation studies of two polymer–one solvent systems by Sariban and Binder (1988) who explored the approximations/assumptions involved in Flory–Huggins theory in some depth.
3. Application to biopolymer–water systems, in the case of uncharged polymers, led to a reasonably encouraging description of three sets of phase diagrams, with parameter consistency (and agreement with experiment) being no worse than for the synthetic polymer case, and sometimes much better. This was achieved despite the branched nature of one of the biopolymers—dextran, and the different repeat segment sizes between PEG and the polysaccharides (and, of course, the stiffened nature of polysaccharides). Such inconsistencies as were found, however, warned again that the model was unlikely to have an accurate (quantitative) predictive role to play in the biopolymer case, which was not surprising given the results for the synthetic polymer system. The agreement and consistency actually achieved, however, were good enough to suggest that valuable (if mainly qualitative) conclusions could be reached about such systems on the basis of tie line analyses, i.e. that such analyses were worth doing, and added value to phase diagram data, revealing the most significant implications of the polymer structures and their interactions with solvent in relation to phase behaviour.It is to be noted that in no case (including the synthetic polymer examples) was it possible to check $\chi 23$ against an experimental estimate. Interestingly, however, this parameter did not vary enormously from system to system (0.013–0.063), and while the number of systems examined here is small, the big chemical difference between synthetic polymers and biopolymers suggests that this lack of large variation may

be a useful property. It is interesting also that the lowest values found for $\chi 23$ were for the case of the two polysaccharides, and that for these too, the best consistency of results, and agreement with experiment, was obtained. Lastly, it should be noted that where biopolymers such as stiffened high molecular weight polysaccharides are concerned, the caution must be added that some discrepancies between theory and experiment might well relate to incomplete equilibration and separation of phases, caused by the high viscosities involved, i.e. have an experimental rather than a theoretical origin.

4. As discussed in Appendix A no large differences in fit quality were found on applying the (truncated and more empirical) Edmond and Ogston second virial coefficient approach to the data, suggesting: (a) that higher virial coefficients are important for these systems (since the Edmond–Ogston description is clearly not perfect), and warning (b) that the Flory–Huggins formulation of the required higher virial coefficients is inadequate (still significant discrepancies between theory and experiment) even though some marginal improvement is probably gained by adding these terms (improved polymer–solvent $\chi$ values in some cases). Indeed, the need for higher virial coefficients to describe PEG–dextran phase behaviour has been emphasised previously (Gustafsson, Wennerstrom & Tjerneld, 1986; Haynes, Beynon, King, Blanch & Prausnitz, 1989) and the inadequacy of the Flory–Huggins description to achieve this has been suggested by Haynes et al., who quote strongly concentration dependent values for the PEG–water $\chi$ parameter as obtained from activity data. All of these conclusions are subject to neglect of polymer molecular weight polydispersity, however, for in the forms implemented here, neither the Edmond–Ogston nor Flory–Huggins theories deal with this explicitly, molecular weights being fixed at number or weight averages. Polydispersity has in fact been shown to significantly influence binodal shape (see, for example, Kang & Sandler, 1988).
5. The present work has only considered uncharged systems, and has not explored temperature influences on tie line data. Programs DIRCH2 and DIRCH3, however, do allow ion effects to be included in chemical potential calculations, and temperature can be handled also by treating $\chi$ values in free energy terms. Charged systems can thus be treated (in the presence of added electrolyte, if necessary) and this application will be explored in a future report dealing with biopolymers such as gelatin, alginate and pectin.

## Appendix A. Comparison of Flory–Huggins and Edmond–Ogston approaches to tie line description

The Flory–Huggins model is based on some very particular assumptions about the nature of the polymers involved in a ternary mixture (Flory, 1953). These molecules are assumed to be random coils built up from segments of similar size, and of a size similar to that of an individual solvent molecule. Entropy of mixing is formulated using a lattice model and combinatorial arguments, and energy via a mean field description, and segment–solvent and segment–segment interaction parameters. Evidently, such an approach is likely to fail where polymers vary greatly from these ideals, e.g. when they are stiff, or become highly branched, or fold into some specific conformation (e.g. a globular protein), or indeed involve segments of many different kinds (proteins).

In 1968, Edmond and Ogston discussed a theoretical description of polymer phase behaviour which was, in principle, applicable to any polymer type, as it was thermodynamic in nature, rather than a statistical mechanical model. Chemical potentials for the components were written as series expansions in terms of second and higher virial coefficients. An actual model only became involved when some attempt was made to calculate the virial coefficients in relation to polymer structure and interaction (essentially what the Flory–Huggins theory does for a particular model polymer type). In principle, if the virial coefficients can be measured experimentally, together with the polymer molecular weights, phase behaviour for the system is automatically predicted through the usual chemical potential balances. Of course measurement of the relevant virial coefficients is likely to be just as time consuming as measuring phase behaviour, particularly if higher virial coefficients are important. Indeed, it may only be practically possible to measure the lowest order members, i.e. the so-called second virial coefficients.

In the 1968 paper, Edmond and Ogston proposed that for many dilute polymer mixtures phase behaviour would be dominated by the second virial coefficients alone, and wrote down expressions for the chemical potentials of the solvent, and of the polymers, in terms of these. In molality concentration units these expressions were:

$$\Delta\mu 1/\mathrm{R}T = -M1\{m2 + m3 + 0.5cm2^2 + 0.5dm3^2 + am2m3\}/1000 \quad \text{(A.1)}$$

$$\Delta\mu 2/\mathrm{R}T = \ln(m2) + \mathrm{cm}2 + am3 \quad \text{(A.2)}$$

$$\Delta\mu 3/\mathrm{R}T = \ln(m3) + dm3 + am2 \quad \text{(A.3)}$$

where $m$ symbolises molality, $c$, $d$ and $e$ are second virial coefficients expressed in molal terms, $M1$ is the solvent molecular weight, and the other symbols have their usual meanings. The more usually defined (and more nearly molecular weight independent) second virial coefficients for the polymer solutions, i.e. $A12$ and $A13$, and that for the polymer–polymer interaction $A23$, can be written in terms of the molal values as,

$$A12 = 1000v_1c/2M2^2 \quad \text{(A.4)}$$

$$A13 = 1000v_1d/2M3^2 \quad \text{(A.5)}$$

$$A23 = 1000v_1a/2M2M3 \quad \text{(A.6)}$$

where $v_1$ is the solvent partial specific volume, and $M2$ and $M3$ are the polymer molecular weights.

Also molal concentrations can be written in terms of the weight fractions of the components, i.e. $X1$, $X2$ and $X3$, these units being independent of molecular weight, and those most commonly used to specify phase diagrams. The relationships are:

$$m1 = 1000/M1 \quad \text{(A.7)}$$

$$m2 = 1000X2/(M2X1) \quad \text{(A.8)}$$

$$m3 = 1000X3/(M3X1) \quad \text{(A.9)}$$

Substitution of Eqs. (A.4)–(A.9) in Eqs. (A.1)–(A.3) leads to expressions for the chemical potentials in terms of the polymer molecular weights and the molecular weight independent virial coefficients, molecular weights now appearing explicitly in the relationships. Balancing chemical potentials of all three components between two phases ultimately leads to three linear equations in the second virial coefficients A12, A13 and A23, analogous to Eqs. (4)–(6) described earlier for Flory–Huggins $\chi$ values. The coefficients of these equations contain the molecular weights, as well as of course the component weight fractions describing the ends of the tie line.

As before, solution of the equations for a particular set of tie line concentrations is not straightforward, as the equations are ill-conditioned. This forces adoption of an experimental value for $A12$ as a constraint, to reduce the equation set to three, now defining $A13$ and $A23$. As before, it is also necessary to fix the molecular weight for at least one of the polymer components (at an experimental value) to solve these, but the other polymer molecular weight is then uniquely determined by the condition of there being a common solution to all three equations.

The close analogy with the Flory–Huggins situation is not fortuitous. It can easily be shown that the Flory–Huggins Eqs. (1)–(3) are equivalent to those of the Edmond–Ogston analysis if (1) the Flory–Huggins equations are truncated to depend only on linear terms in the polymer volume fractions and (2) if the second virial coefficients are written in terms of Flory–Huggins $\chi$ parameters as,

$$A12 = (1/2 - \chi 12)v_2^2/(v_1M1) \quad \text{(A.10)}$$

$$A13 = (1/2 - \chi 13)v_3^2/(v_1M1) \quad \text{(A.11)}$$

$$A23 = (1 + \chi 23 - \chi 12 - \chi 13)v_2v_3/(2v_1M1) \quad \text{(A.12)}$$

Here $v2$ and $v3$ are the polymer partial specific volumes. The more complete Flory–Huggins theory (higher polymer volume fractions) is seen to differ from the Edmond–Ogston approach in that it contains higher order virial coefficients formulated in a very model specific way in terms of $\chi$ values, molecular weights, etc.

In the present work, a program OGSDIR was written to apply direct tie line analysis in terms of molecular weights and second virial coefficients only (Edmond and Ogston method). It seemed interesting to compare results for the same phase diagrams using this and the previous DIRCH2 or DIRCH3 treatment based on the full Flory–Huggins model. Such a comparison would establish (a) whether higher virial coefficients were playing a significant part in the tie line analyses and were necessary to describe the data, and (b) if this was so, whether the forms of the higher virial coefficients offered by the Flory–Huggins approach, achieved a real improvement in data description. Such an improvement could be judged in terms of parameter consistency over a tie line range, the actual graphical quality of fit achieved using final average parameters, and the agreement between calculated molecular weight and second virial coefficients with corresponding experimental results, where available. A summary of findings was as follows:

1. For the polystyrene–polyisoprene–toluene systems only the polyisoprene $\chi$ value (and hence the second virial coefficient) was significantly different between the two fits, the values output by the Flory–Huggins approach being lower and more nearly in agreement with literature estimates. The discrepancy was greatest for the most concentrated system ($M_n$ polystyrene = 17,500 data).
2. For the PEG–agarose–water systems, even less difference was found between the two sets of analyses. The agarose $\chi$ value was determined slightly more realistically by the Flory–Huggins model, but the differences in relation to expectation were still very large for both models, particularly for the PEG 20,000 and 35,000 examples.
3. For the PEG–dextran–water system, the situation was more equivocal. In terms of experimental second virial coefficients, the Flory–Huggins method seemed to overestimate the dextran $\chi$ value, while the Edmond–Ogston underestimated it. In general, however, the Edmond–Ogston method got a better result for the dextran molecular weight if this was compared with an experimental number average. Figs. 14 and 8 show a comparison of results obtained by the two analysis procedures when applied to the PEG 3690–dextran T-70 system. Discrepancies between the two approaches are probably at their greatest here and seem to relate mainly to description of behaviour around the critical point. Actual measurement of the latter, and nearby tie lines, could thus produce a better discrimination of models than is currently possible.
4. For the dextran–agarose–water system, $\chi$ parameters obtained by the two methods are very similar. The Edmond–Ogston method gives molecular weights for agarose which are higher, and which are in better agreement with the experimental $M_w$, but this is not

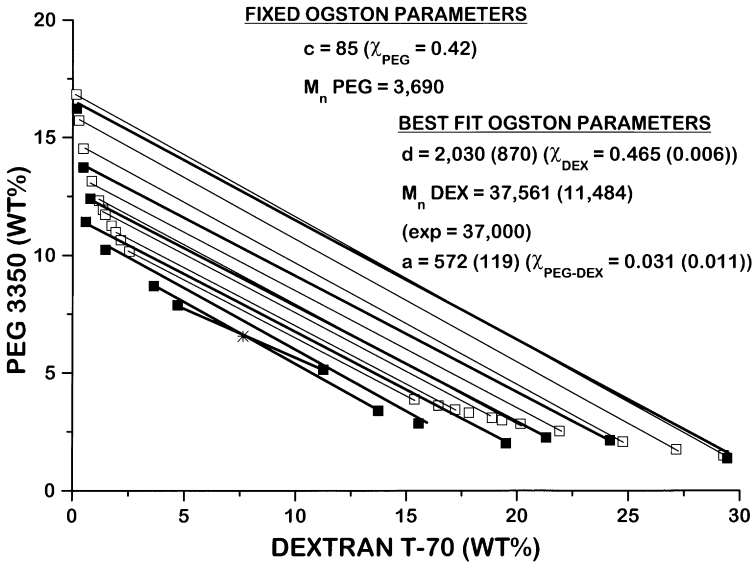


Fig. 14. Results of Edmond–Ogston analysis for PEG 3350–dextran T70 (cf. Fig. 8).

necessarily the best average to consider, the unknown $M_n$ being probably more appropriate.

Overall, the fact that significant discrepancies between calculated and experimental parameters are still found when using the Edmond and Ogston (truncated Flory–Huggins theory), suggests that virial coefficients higher than second are important in describing phase behaviour for the systems discussed, a conclusion which seems reasonable in the light of the quite high polymer concentrations generally involved. The marginally improved description achieved by the full Flory–Huggins model in some cases seems to confirm this, as this model does include such higher terms, albeit formulated in a very model-dependent way. However, the fact that the improvement offered is so small suggests that the Flory–Huggins treatment of the higher virial coefficients is itself inadequate to describe the phase behaviour of systems of the type discussed here in a really accurate and quantitative way, even though some useful qualitative trends can be identified.

Of course, all of this assumes that the discrepancies demonstrated by the present work are the result of higher virial coefficient effects, and that they are not due to experimental problems in obtaining separated and equilibrated phases, or to molecular weight polydispersity. While these last may be problems for some of the biopolymer-containing systems cited (very likely for the PEG–agarose solutions), they are unlikely to have strongly influenced the synthetic polymer results, as highly monodisperse polymer samples were chosen in the original experimental studies and these more flexible polymers (and hence less viscous solutions) should have equilibrated and separated fairly easily. Overall, one is tempted to conclude from this appendix that the apparent lack of strong benefit in proceeding from the Edmond–Ogston approach to the full Flory–Huggins theory, justifies the former as a first choice, particularly as it is simple and more general, being applicable to systems containing highly branched polymers (or even globular proteins) for which the Flory–Huggins theory would seem inappropriate. A previous study of the PEG–dextran system (Gustafsson et al., 1986) reached a different conclusion, however. These authors criticise the Edmond–Ogston analysis on the grounds that the second virial coefficients extracted are only apparent (necessary higher virials ignored in the treatment) and are not readily interpreted in molecular terms (usual excluded volume model inadequate). While the present work confirms the need for higher virial coefficients in any treatment of the data discussed, it is less certain that the Flory–Huggins theory offers a better and more 'molecular' description. The variation of $\chi$ parameters with molecular weight and concentration that is found here, and the well-known interpretation of these as free energies rather than energies, seem to negate this. Overall the Flory–Huggins theory should only be strongly preferred if it provides a more globally consistent and better description of binodals and tie lines for semi-dilute mixtures of biopolymers. Such advantages have not been conclusively demonstrated by the present calculations.

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