SOLUBILITY OF SELECTED SYSTEMS AND INFLUENCE OF SOLUTES

5.1 EXPERIMENTAL METHODS OF EVALUATION AND CALCULATION OF SOLUBILITY PARAMETERS OF POLYMERS AND SOLVENTS. SOLUBILITY PARAMETERS DATA.

VALERY YU. SENICHEV, VASILIY V. TERESHATOV
Institute of Technical Chemistry
Ural Branch of Russian Academy of Sciences, Perm, Russia

5.1.1 EXPERIMENTAL EVALUATION OF SOLUBILITY PARAMETERS OF LIQUIDS

The value of solubility parameter can be calculated from the evaporation enthalpy of liquid at given temperature:[1]

$$\delta = \left(\frac{\Delta H_p - RT}{V} \right)^{1/2} \qquad [5.1.1]$$

where:

ΔH_p latent heat of vaporization
V molar volume

5.1.1.1 Direct methods of evaluation of the evaporation enthalpy

For measurement of the evaporation enthalpy of volatile substances, adiabatic apparatuses were developed. They require significant quantities of highly purified substances. The accuracy is determined to a large degree by equipment design and precision of measurement.

Most calorimeters that measure a latent heat of vaporization work under isobaric conditions. The measurement of a latent heat of vaporization requires monitoring heat input into calorimeter and the amount of liquid evaporated during measurement time.[2-4]

In calorimeters of a flowing type,[5-6] a liquid evaporates from a separate vessel of a calorimeter. The vapors are directed into the second calorimeter where the thermal capacity of gas is measured. The design of such calorimeters ensures a precise measurement of the stream rate. Heaters and electrical controls permit control of heat flow with high precision and highly sensitive thermocouples measure temperature of gas. There are no excessive thermal losses, thus single-error corrections for the heat exchange can be used to increase precision of measurement.

The calorimeters used for the measurement of the heat of reaction can also be used for a measurement of the latent heat of vaporization. These are calorimeters for liquids, micro-calorimeters, mass calorimeters, and double calorimeters.[7]

The calorimeters with carrier gas are also used.[8-9] Evaporation of substance is accelerated by a stream of gas (for example, nitrogen) at reduced pressure. The heat loss by a calorimeter, due to evaporation, is compensated by an electrical current to keep temperature of calorimeter constant and equal to the temperature of the thermostating bath.

5.1.1.2 Indirect methods of evaluation of evaporation enthalpy

Because the calorimetric methods of measurement of enthalpy of vapor formation are very difficult, the indirect methods are used, especially for less volatile substances. The application of generalized expression of the first and second laws of thermodynamics to the heterogeneous equilibrium between a condensed phase in isobaric- thermal conditions is given in the Clausius-Clapeyron equation that relates enthalpy of a vapor formation at the vapor pressure, P, and temperature, T. For one component system, the Clausius-Clapeyron equation has the form:[7]

$$dP / dT = \Delta H_p / T\Delta V \qquad [5.1.2]$$

where:

ΔV difference between molar volumes of vapor and liquid

The ratio that neglects volume of a condensed phase with assumption that vapor at low pressure is ideal can be derived from the above equation:

$$d\ln P / d(1/T) = -\Delta H_p / R \qquad [5.1.3]$$

After integration:

$$\ln P = -\Delta H_p / RT + const \qquad [5.1.4]$$

Introducing compressibility factors of gas and liquids, ΔZ, the Clausius-Clapeyron equation can be written as:

$$d\ln P / d(1/T) = -\Delta H_p / R\Delta Z \qquad [5.1.5]$$

where:

ΔZ difference between compressibility factors of gas and liquids

The value ΔZ includes corrections for volume of liquid and non-ideality of a vapor phase. The simplifying assumptions give the equation:

$$\ln P = A + B / T \qquad [5.1.6]$$

Approximate dependence of a vapor pressure on inverse temperature is frequently linear but the dependence may also be non-linear because of changing ratio of $\Delta H_p/\Delta Z$ on heating. The mathematical expressions of the dependence lnP on 1/T of real substances in a wide range of temperatures should be taken into account. If $\Delta H_p/\Delta Z = a + bT$, it results in an equation with three constants:

$$\ln P = A + B/T + C\ln T \qquad [5.1.7]$$

In more complicated dependancies, the number of constants may further increase.

Another convenient method is based on empirical relation of ΔH_p at 25°C with the normal boiling point, T_b, of non-polar liquids:[1]

$$\Delta H_p = T_b^2 + 23.7T_b - 2950 \qquad [5.1.8]$$

Methods of evaluation of vapor pressure may be divided into static, quasi-static, and kinetic methods.

5.1.1.3 Static and quasi-static methods of evaluation of pair pressure

Manometric method[10] consists of thermostating with a high precision (0.01K) and vapor pressure measurement by a level of mercury with the help of a cathetometer or membrane zero-manometer. The accuracy of measurement is 0.1-0.2 mm Hg.

Ebulliometric method[11] is used for a simultaneous measurement of the boiling and condensation temperature that is required for evaluation of purity of a substance and its molecular mass.

5.1.1.4 Kinetic methods

These methods were developed based on the molecular kinetic theory of gases. The Langmuir method is based on the evaporation of substance from a free surface into a vacuum. The Knudsen method is based on the evaluation of the outflow rate of a vapor jet from a mesh.

The basic expression used in Langmuir method[12] is:

$$P = \left(\frac{m}{St\alpha}\right)\left(\frac{2\pi RT}{M}\right)^{1/2} \qquad [5.1.9]$$

where:

m	mass of evaporated substance
S	surface of evaporation
t	time of evaporation.

The Knudsen method[13] is based on a measurement of the mass rate of the vapor outflow through a hole. Knudsen proposed the following expression:

$$P_k = \left(\frac{\Delta m}{S_h t\beta}\right)\left(\frac{2\pi RT}{M}\right)^{1/2} \qquad [5.1.10]$$

where:

Δm	mass output of substance
S_h	surface area of the hole
t	time of vaporization
β	Clausing parameter
M	molecular mass

The method uses special effusion cameras with holes of a definite form, maintaining high vacuum in the system. The method is widely applied to the measurements of a vapor pressure of low volatile substances.

The detailed comparative evaluation of experimental techniques and designs of equipment used for determination of enthalpy of evaporation can be found in the appropriate monographs.[7,14] Values of solubility parameters of solvents are presented in Subchapter 4.1.

5.1.2 METHODS OF EXPERIMENTAL EVALUATION AND CALCULATION OF SOLUBILITY PARAMETERS OF POLYMERS

It is not possible to determine solubility parameters of polymers by direct measurement of evaporation enthalpy. For this reason, all methods are indirect. The underlining principles of these methods are based on the theory of regular solutions that assumes that the best mutual dissolution of substances is observed at the equal values of solubility parameters (see Chapter 4).

Various properties of polymer solutions involving interaction of polymer with solvent are studied in a series of solvents having different solubility parameters. A value of a solubility parameter is related to the maximum value of an investigated property and is equated to a solubility parameter of polymer.

This subchapter is devoted to the evaluation of one-dimensional solubility parameters. The methods of the evaluation of components of solubility parameters in multi-dimensional approaches are given in the Subchapter 4.1.

According to Gee,[15] a dependence of an equilibrium swelling of polymers in solvents on their solubility parameters is expressed by a curve with a maximum where the abscissa is equal to the solubility parameter of the polymer. For exact evaluation of δ, a swelling degree is represented by an equation resembling the Gaussian function:

$$Q = Q_{max} \exp\left[-V_1(\delta_1 - \delta_2)^2\right] \qquad [5.1.11]$$

where:

Q_{max} the degree of swelling at the maximum on the curve
V_1 molar volume of solvent
δ_1, δ_2 solvent and polymer solubility parameters.

Then

$$\delta_2 = \delta_1 \pm \left(\frac{1}{V_1}\ln\frac{Q_{max}}{Q}\right)^{1/2} \qquad [5.1.12]$$

The dependence $[(1/V_1)\ln(Q_{max}/Q)]^{1/2}=f(\delta_1)$ is expressed by a direct line intersecting the abscissa at $\delta_1 = \delta_2$. This method is used for calculation of the parameters of many crosslinked elastomers.[16-19]

The Bristow-Watson method is based on the Huggins equation deduced from a refinement of the lattice approach:[20]

$$\chi = \beta + (V_1 / RT)(\delta_1 - \delta_2)^2 \qquad [5.1.13]$$

where:

β $=(1/z)(1-1/m)$
z a coordination number
m the chain length.

β may be rewritten as χ_S entropy contribution to χ (see Chapter 4).

Accepting that Eq. [5.1.12] represents a valid means of assignment of a constant δ_2 to polymer, the rearrangement of this equation gives:

$$\frac{\delta_1^2}{RT} - \frac{\chi}{V_1} = \left(\frac{2\delta_2}{RT}\right)\delta_1 - \frac{\delta_2^2}{RT} - \frac{\chi_S}{V_1} \qquad [5.1.14]$$

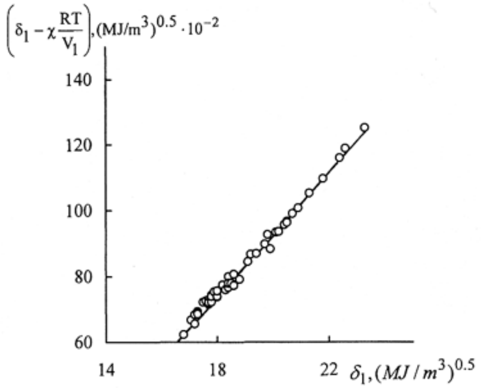

Figure 5.1.1. Dependence for equilibrium swelling of crosslinked elastomer on the base of polyether urethane. [Adapted, by permission, from V.Yu. Senichev in Synthesis and properties of cross-linked polymers and compositions on their basis. *Russian Academy of Sciences Publishing*, Sverdlovsk,1990, p.16]

Now it is assumed that χ_S is of the order of magnitude suggested above and that, in accordance with the Huggins equation, it is not a function of δ_2. Therefore χ_S/V_1 is only about 3% or less of δ_2^2/RT for reasonable values of δ_2 of 10-20 $(MJ/m^3)^{1/2}$. Hence Eq. [5.1.14] gives δ_2 from the slope and intercept on plot against δ_1 (see Figure 5.1.1).

This method was improved[21] by using calculations that exclude strong deviations of χ. When ($\chi_S RT/V_1 \approx$ const), Eq. [5.1.14] is close to linear (y = A + Bx), where $y = \delta_1^2 - \chi_S(RT/V_1)$, $A = -\chi_S(RT/V_1) - \delta_2^2$, $B = 2\delta_2$, $x = \delta_1$.

But δ_2 enters into expression for a tangent of a slope angle and intercept which is cut off on the ordinates axes. This can be eliminated by introduction of a sequential approximation of $\chi_S(RT/V_1)$ and grouping of experimental points in areas characterized by a definite interval of values $\chi_S(RT/V_1)$. Inside each area $\chi_S(RT/V_1) \rightarrow$ const and Eq. [5.1.14] becomes more precise.

The intervals of values $\chi_S(RT/V_1)$ are reduced in the course of computations. For n experimental points, the files X ($x_1, x_2, \ldots x_n$) and Y ($y_1, y_2, \ldots y_n$) are gathered. Tangent of the slope angle is defined by the method of least squares and the current value (at the given stage) of a solubility parameter of a polymer is:

$$\delta_{2j} = \frac{\sum_{i=1}^{n} x \sum_{i=1}^{n} y - n\sum_{i=1}^{n} xy}{\left(\sum_{i=1}^{n} x\right)^2 - n\sum_{i=1}^{n} x^2} \qquad [5.1.15]$$

where:

j a stage of computation

$\chi_S(RT/V_1)$ is then calculated using the equation derived from Eqs. [5.1.13] and [5.1.14]:

$$\left(\chi_S \frac{RT}{V_1}\right)_j = -y_i - \delta_{2j}^2 + 2x_i\delta_{2j} \qquad [5.1.16]$$

Table 5.1.1. Modification of $\bar{\delta}_{2j}$ values during stages of computation

Polymer	j = 1	j = 2	j = 3	j = 4
	$\bar{\delta}_{2j}$, $(MJ/m^3)^{1/2}$			
polydiene urethane epoxide	17.64	17.88	17.78	17.8
polydiene urethane	17.72	18.17	17.93	17.82
poly(butylene glycol) urethane	19.32	18.89	18.95	18.95
poly(diethylene glycol adipate) urethane	19.42	19.44	19.44	-

where:

δ_{2j} value of δ_2 at the given stage of computation

By sorting of all experimental points into a defined amount of intervals (for 30-50 points it is more convenient to take 5-6 intervals), it is possible to calculate δ_2 for each interval separately. The current average weighted value (contribution of δ_2 is defined), obtained for each interval, is proportional to the amount of points in the interval according to the following formula:

$$\bar{\delta}_{2j} = \frac{1}{M}\sum_{k=1}^{k}\delta_{2k}m_k \qquad [5.1.17]$$

where:

k = 1,2,.... k, number of intervals
m_k number of points in k-interval
M the total number of points
j stage of computation.

The shaping of subarrays of points is made in the following order, ensuring that casual points are excluded: 1) account is made in a common array of points of δ_2 and $\chi_S(RT/V_1)_i$; 2) partition of a common array into a population of subarrays of $\chi_S(RT/V_1)$ in limits defined for elimination of points not included in intervals and points which do not influence consequent stages of computation, 3) reductions of intervals in each of the subarrays (this stage may be repeated in some cases).

At the each stage the sequential approximation to constant value of $\chi_S(RT/V_1)$ is produced in a separate form, permitting one to take into account the maximum number of points. The procedure gives a sequence of values δ_{2j} as shown in Table 5.1.1.

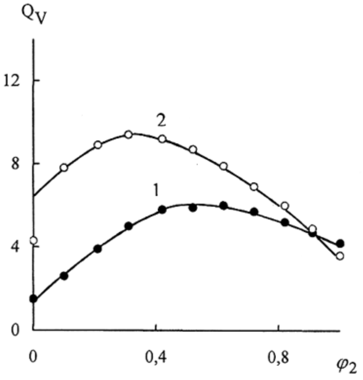

Figure 5.1.2. Dependence of equilibrium swelling of crosslinked elastomer of polyester urethane (1) and polybutadiene nitrile rubber (2) on the volume fraction of acetone in the toluene-acetone mixture. [Adapted, by permission, from V.V. Tereshatov, V.Yu. Senichev, A.I. Gemuev, *Vysokomol. soed.*, **B32**, 412 (1990)]

In still other methods of evaluation,[22] the solvents are selected so that the solubility parameter of polymer occupies an intermediate position between solubility parameters of solvents. Assumption is made that the maximum polymer swelling occurs when the solubility parameters of the solvent mixture and polymer are equal. This is the case when the solubility parameter of polymer is lower than the solubility parameter of the primary solvent and the solubility parameter of the secondary solvent is higher. The dependence of the swelling ratio on the composition of solvent mixture has a maximum (see Figure 5.1.2). Such mixed solvents are called symmetric liquids. The reliability of the method is examined by a narrow interval of change of the solubility parameter of a binary solvent. The data obtained by this method in various mixtures differ by no more than 1.5% with the data obtained by other methods. Examples of results are given in Tables 5.1.2, 5.1.3.

Table 5.1.2. Values of solubility parameters for crosslinked elastomers from swelling in symmetric liquids. [Adapted, by permission, from V.V. Tereshatov, V.Yu. Senichev, A.I. Gemuev, *Vysokomol. soed.*, B32, 412 (1990).]

Elastomer	Symmetric liquids	φ_2^H at Q_{max}	δ_p, $(MJ/m^3)^{1/2}$
Polyether urethane	Toluene(1) - acetone (2) Cyclohexane (1) -acetone (2)	0.11 0.49	18.4 18.2
Ethylene-propylene rubber	Hexane (1) - benzene (2) Toluene (1) - acetone (2)	0.38 0.32	16.2 18.9
Butadiene-nitrile rubber	Ethyl acetate (1) - acetone (2) Benzene (1) - acetone (1)	0.22 0.27	19.1 19.1
Polyester-urethane	Toluene (1) - acetone (2) o-Xylene (1) - Butanol -1(2)	0.62 0.21	19.6 19.5
Butyl rubber	Octane (1) - benzene (2)	0.26	16.1

Table 5.1.3. Values of solubility parameters of crosslinked elastomers from swelling in individual solvents and symmetric liquids. [Adapted, by permission, from V.V. Tereshatov, V.Yu. Senichev, A.I. Gemuev, *Vysokomol. soed.*, B32, 412 (1990).]

Elastomer	Symmetric liquids	Individual solvents	
		Gee method	Bristow-Watson method
	$(MJ/m^3)^{1/2}$		
Polyether-urethane	18.3±0.1	17.8, 18.4, 19.4	19.2
Ethylene-propylene rubber	16.2	16.1-16.4	-
Butadiene-nitrile rubber	19.0±0.1	18.9-19.4	18.7
Polyester-urethane	19.5-19.6	19.3, 19.9	19.5
Butyl rubber	16.1	15.9-16.6	14.9

The calculations were made using equation:

$$\delta_p = \delta_{mix} = \left[\delta_1^2 \left(1 - \varphi_1''\right) + \delta_2^2 \varphi_1'' - \Delta H_{mix} / V_{12} \right]^{1/2} \qquad [5.1.18]$$

where:

φ_1''	volume fraction of a solvent in a binary mixture of solvents causing a maximum of equilibrium swelling
ΔH_{mix}	experimental value of the mixing enthalpy of components of binary solvent. It can be taken from literature.[23-24]
V_{12}	the molar volume of binary solvent

If there are no volume changes, V_{12} can be calculated using the additivity method:

$$V_{12} = V_1\varphi_1 + V_2\varphi_2 \qquad [5.1.19]$$

Attempts[25] were made to relate intrinsic viscosity [η] to solubility parameters of mixed solvents. δ_2 of polymer was calculated from the equation: $[\eta] = f(\delta_1)$. The authors assumed that the maximum value of [η] is when $\delta_1 = \delta_2$ of polymer. However, studying [η] for polymethylmethacrylate in fourteen liquids, the authors found a large scatter of experimental points through which they have drawn a curve with a diffusion maximum. Thus the precision of δ_2 values was affected by 10% scatter in experimental data.

This method was widely used by Mangaray et al.[26-28] The authors have presented [η] as the Gaussian function of $(\delta_1 - \delta_2)^2$. Therefore, dependence $\{(1/V_1)\ln[\eta]_{max}/[\eta]\}^{1/2} = f(\delta_1)$ can be expressed by a straight line intersecting the abscissa at a point for which $\delta_1 = \delta_2$. For natural rubber and polyisobutylene, the paraffin solvents and ethers containing alkyl chains of a large molecular mass were studied.[26] For polystyrene, aromatic hydrocarbons were used. For polyacrylates and polymethacrylates esters (acetates, propionates, butyrates) were used.[27,28] The method was used for determination of δ_2 of many polymers.[29-31] In all cases, the authors observed extrema in the dependence of $[\eta] = f(\delta_1)$, and the obtained values of δ_2 coincided well with the values determined by other methods. But for some polymers it was not possible to obtain extremum in dependence of $[\eta] = f(\delta_1)$.[32]

A method of the evaluation [η] in one solvent at different temperatures was used for polyisobutylene[33] and polyurethanes.[34]

For polymers soluble in a limited range of solvents, more complex methods utilizing [η] relationship are described.[35-37]

In addition to the above methods, δ_2 of polymer can be determined from a threshold of sedimentation[38] and by critical opalescence.[39] In recent years the method of inverse gas-liquid chromatography has been used to evaluate δ_2 of polymers.[40,41] One may also use some empirical ratios relating solubility parameters of polymers with some of their physical properties, such as, surface tension[42-44] and glass transition temperature.[45]

The solubility parameters for various polymers are given in Table 5.1.3.

Table 5.1.4. Solubility parameters of some polymers[36,46]

Polymer	δ		Polymer	δ	
	$(cal/cm^3)^{1/2}$	$(MJ/m^3)^{1/2}$		$(cal/cm^3)^{1/2}$	$(MJ/m^3)^{1/2}$
Butyl rubber	7.84	16.0	Polydimethylsiloxane	9.53	19.5
Cellulose diacetate	10.9	22.2	Polydimethylphenyleneoxide	8.6	17.6
Cellulose dinitrate	10.6	21.6	Polyisobutylene	7.95	16.2
Polyamide-66	13.6	27.8	Polymethylmethacrylate	9.3	19.0

Polymer	δ		Polymer	δ	
	$(cal/cm^3)^{1/2}$	$(MJ/m^3)^{1/2}$		$(cal/cm^3)^{1/2}$	$(MJ/m^3)^{1/2}$
Natural rubber	8.1	16.5	Polymethylacrylate	9.7	19.8
Neoprene	8.85	18.1	Polyoctylmethacrylate	8.4	17.2
Cellulose nitrate	11.5	23.5	Polypropylene	8.1	16.5
Polyacrylonitrile	14.5	29.6	Polypropylene oxide	7.52	15.4
Polybutadiene	8.44	17.2	Polypropylene sulphide	9.6	19.6
Poly-n-butylacrylate	8.7	17.8	Polypropylmethacrylate	8.8	18.0
Polybutylmethacrylate	8.7	17.8	Polystyrene	8.83	18.0
Polybutyl-tert-methacrylate	8.3	16.9	Polyethylene	7.94	16.2
Polyvinylacetate	9.4	19.2	Polyethyleneterephthalate	10.7	21.8
Polyvinylbromide	9.55	19.5	Polyethylmethacrylate	9.1	18.6
Polyvinylidenechloride	12.4	25.3	Polybutadienenitrile (82:18 w)	8.7	17.8
Polyvinylchloride	9.57	19.5	Polybutadienenitrile (75:25)	9.38	19.2
Polyhexyl methacrylate	8.6	17.6	Polybutadienenitrile (70:30)	9.64	19.7
Polyglycol terephthalate	10.7	21.8	Polybutadienenitrile (61:39)	10.30	21.0
Polydiamylitaconate	8.65	17.7	Polybutadienevinylpyridine (75:25 mas.)	9.35	19.1
Polydibutylitaconate	8.9	18.2	Polybutadienestyrene (96:4)	8.1	16.5
Polysulfone	10.5	21.4	Polybutadienestyrene (87.5:12.5)	8.31	17.0
Polytetrafluorethylene	6.2	12.7	Polybutadienestyrene (85:15)	8.5	17.4
Polychloroacrylate	10.1	20.6	Polybutadienestyrene (71.5:28.5)	8.33	17.0
Polycyanoacrylate	14.0	28.6	Polybutadienestyrene (60:40)	8.67	17.7
Polyethylacrylate	9.3	19.0	Chlorinated rubber	9.4	19.2
Polyethylenepropylene	7.95	16.2	Ethylcellulose	10.3	21.0

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5.2 PREDICTION OF SOLUBILITY PARAMETER

NOBUYUKI TANAKA
Department of Biological and Chemical Engineering
Gunma University, Kiryu, Japan

5.2.1 SOLUBILITY PARAMETER OF POLYMERS

For the purpose of searching for the solvents for a polymer, the solubility parameter of polymers, δ_p, is defined as:[1-11]

$$\delta_p = (h_0 / v)^{1/2} \qquad [5.2.1]$$

where:

h_0	the cohesive enthalpy per molar structural unit for a polymer (cal/mol)
v	the volume per molar structural unit for a polymer (cm^3/mol)

because δ_p is equivalent to the solubility parameter of solvents, δ_s, that shows the minimum of the dissolution temperature[7] or the maximum of the degree of swelling[1,2] for the polymer. For δ_s, h_0 is the molar energy of vaporization that is impossible to measure for polymers decomposed before the vaporization at elevated temperatures, and v is the molar volume of a solvent. The measurements of the dissolution temperature and the degree of swelling are only means to find the most suitable solvents for a polymer by trial and error.

In order to obtain easily the exact value of δ_p at a temperature, T, the possibility of δ_p prediction from the thermal transition behaviors such as the glass transition and the melting has been discussed.[9-11] Consequently, it was found that the sum of their transition enthalpies gave h_0 in equation [5.2.1] approximately:

for crystalline polymers,

$$h_0 \approx h_g + h_x + h_u \qquad T \le T_g \qquad [5.2.2]$$

$$h_0 \approx h_x + h_u \qquad T_g < T < T_m \qquad [5.2.3]$$

for amorphous polymers,

$$h_0 \approx h_g + h_x \qquad T \le T_g \qquad [5.2.4]$$

where:

h_g	the glass transition enthalpy per molar structural unit for a polymer
h_u	the heat of fusion per molar structural unit for a polymer
h_x	the transition enthalpy per molar structural unit due to ordered parts in the amorphous regions
T_g	the glass transition temperature; here the onset temperature of heat capacity jump at the glass transition
T_m	the melting temperature

In the following sections, the physical meanings of h_g and h_x are shown in the theoretical treatments of the glass transition, and for several polymers, δ_p is predicted using these thermodynamic quantities.

5.2.2 GLASS TRANSITION IN POLYMERS

The glass transition in polymers is the same kind of physical phenomenon as observed generally for amorphous materials.[12] At T_g in the cooling process, polymers are frozen glasses and the molecular motions are restricted strictly. However, the actual states of glasses are dependent on the cooling rate; if the cooling rate is rapid, the glasses formed should be imperfect, such as liquid glasses or glassy liquids.[13,14] The annealing for imperfect glasses results in the enthalpy relaxation from imperfect glasses to perfect glasses. At T_g in the heating process, the strong restriction of molecular motions by intermolecular interactions is removed and then the broad jump of heat capacity, C_p, is observed.[15] Annealing the glasses, the C_p jump curve becomes to show a peak.[15,16]

5.2.2.1 Glass transition enthalpy

For polymer liquids, the partition function, Ω, normalized per unit volume is given by:[10,14,17,18]

$$\Omega = \left(Z^N / N!\right)\left(2\pi mkT / \mathbf{h}^2\right)^{3Nx/2}\left(q / v_f\right)^{Nx} \exp\left\{-Nxh^{\mathrm{int}} / (RT)\right\} \qquad [5.2.5]$$

with $v_f = qv\exp\{-h^{\mathrm{int}}/(RT)\}$

where:

h^{int}	the intermolecular cohesive enthalpy per molar structural unit for a polymer
$\mathbf{h}$	Planck's constant
k	Boltzmann's constant
m	the mass of a structural unit for a polymer
N	the number of chains
q	the packing factor of structural units for a polymer
R	the gas constant
v_f	the free volume per molar structural unit for a polymer
x	the degree of polymerization
Z	the conformational partition function per a chain

From equation [5.2.5], the enthalpy and the entropy per molar chain for polymer liquids, H_l and S_l, are derived:[10]

$$H_1 = RT^2 d\ln Z / dT + (3/2)RxT - RxT^2 d\ln v_f / dT + xh^{\mathrm{int}} \qquad [5.2.6]$$

$$S_1 = \left(R\ln Z + RTd\ln Z/dT\right) + \left(3/2\right)Rx - x\left(R\ln v_f + RTd\ln v_f/dT\right) + xS_d \qquad [5.2.7]$$

with $S_d = (3R/2)\ln(2\pi mkT/\mathbf{h}^2) - (1/x)(R/N)\ln N! + R\ln q$

The first terms on the right hand side of equations [5.2.6] and [5.2.7] are the conformational enthalpy and entropy per molar chain, xh^{conf} and xs^{conf}, respectively.[19] Assuming that chains at T_g are in quasi-equilibrium state, the criterions on T_g are obtained:

$$f_{flow}\ (= h_{flow} - T_g s_{flow}) \approx 0 \qquad [5.2.8]$$

$$\text{and } s_{flow} \approx 0 \ \text{(hence } h_{\mathrm{flow}} \approx 0) \qquad [5.2.9]$$

with $h_{\mathrm{flow}} = H_l/x - 3RT_g/2$ and $s_{\mathrm{flow}} = S_l/x - 3R/2$

From equations [5.2.8] and [5.2.9], which show the conditions of thermodynamic quasi-equilibrium and freezing for polymer liquids, the conformational enthalpy and entropy per molar structural unit at T_g, h_g^{conf} and s_g^{conf}, are derived, respectively:

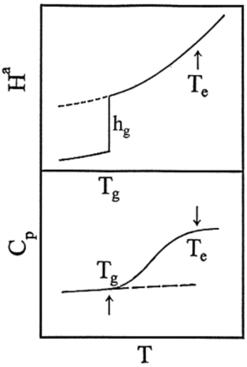

Figure 5.2.1. Schematic curves of H^a and C_p in the vicinity of T_g for an amorphous polymer. Two lines of short and long dashes show H^a for a supercooled liquid and C_p for a superheated glass (hypothesized), respectively. T_e is the end temperature of C_p jump. [after reference 10]

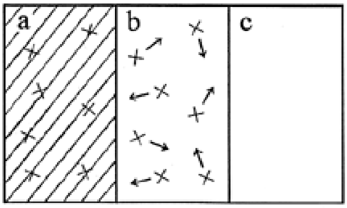

Figure 5.2.2. State models for an amorphous polymer in each temperature range of (a) $T \le T_g$, (b) $T_g < T \le T_e$, and (c) $T_e < T$, where hatching: glass parts, crosses: ordered parts, and blank: flow parts. The arrows show the mobility of ordered parts. [after reference 10]

$$h_g^{conf}\left\{=RT_g^2\left(d\ln Z/dT\right)/x)\right\}=RT_g^2 d\ln v_f/dT-h_g^{int} \qquad [5.2.10]$$

$$s_g^{conf}\left\{=\left(R\ln Z+RT_g d\ln Z/dT\right)/x\right\}=R\ln v_f+RT_g d\ln V_f/dT-S_d \qquad [5.2.11]$$

Rewriting equation [5.2.10], the glass transition enthalpy per molar structural unit, h_g $(=h_g^{int}+h_g^{conf})$, is obtained:

$$h_g=RT_g^2 d\ln v_f/dT\approx RT_g^2/c_2 \qquad [5.2.12]$$

with $c \approx \phi_g/\beta$

where:

h_g^{int}	h^{int} at T_g
c_2	the constant in the WLF equation[20]
β	the difference between volume expansion coefficients below and above T_g
ϕ_g	the fractional free volume at T_g

The WLF equation on the time - temperature superposition of viscoelastic relaxation phenomena is given by:[20]

$$\log a_T=-c_1\left(T-T_g\right)/\left(c_2+T-T_g\right) \qquad [5.2.13]$$

where:

a_T	the shift factor
c_1	the constant

Figure 5.2.1 shows the schematic curves of H^a and C_p for an amorphous polymer, where H^a is the molar enthalpy for an amorphous polymer. Substituting H_l/x for H^a, H^a at T_g corresponds to $3RT_g/2$, because of $h_{flow} = 0$. At T_g, the energy of h_g is given off in the cooling process and absorbed in the heating process.

Table 5.2.1 shows the numerical values of h_g $(= h_g^{int} + h_g^{conf})$ and c_2 from equation [5.2.12], together with T_g,[12,16] h_g^{int}, h_g^{conf}, and s_g^{conf}, for several polymers. As the values of h_g^{int}, the molar cohesive energy of main residue in each polymer, e.g. -CONH- for N6 and

N66, -CH(CH_3)- for iPP, -CH(C_6H_5)- for iPS, and -C_6H_4- for PET, was used.[21] The predicted values of c_2 for PS and PET are close to the experimental values, 56.6K and 55.3K, respectively.[20,22] The standard values of c_1 and c_2 in equation [5.2.13] are 17.44 and 51.6K, respectively.[20,23]

Table 5.2.1

Polymer	T_g K	h_g^{int} cal/mol	h_g^{conf} cal/mol	s_g^{conf} cal/(K mol)	h_g (=h_g^{int}+h_g^{conf}) cal/mol	c_2 K
N6	313	8500	475	11.2	8980	21.7
N66	323	17000	976	22.6	17980	11.5
iPP	270	1360	180	0.98	1540	94.1
iPS	359[16]	4300	520	2.03	4820 (4520)	53.1 (56.6)
PET	342	3900	282	7.10	4180 (4200)	55.6 (55.3)

The numerical values in parentheses are the experimental values[20,22] of c_2 and h_g (from c_2). N6: polycaproamide (nylon-6), N66: poly(hexamethylene adipamide) (nylon-6,6), iPP: isotactic polypropylene, iPS: isotactic polystyrene, PET: poly(ethylene terephthalate).

5.2.2.2 C_p jump at the glass transition

The mechanism of C_p jump at the glass transition could be illustrated by the melting of ordered parts released from the glassy states.[10] Figure 5.2.2 shows the state models for an amorphous polymer below and above T_g.

The ordered parts are generated near T_g in the cooling process; in the glasses, the ordered parts are contained. In the heating process, right after the glassy state was removed at T_g, the melting of ordered parts starts and continues up to T_e, keeping an equilibrium state between ordered parts and flow parts. In this temperature range, the free energy per molar structural unit for polymer liquids contained ordered parts, f_m, is given by:[10]

$$f_m = f_x X_x + f_{flow}\left(1 - X_x\right) \qquad [5.2.14]$$

where:

f_x	the free energy per molar structural unit for ordered parts
f_{flow}	the free energy per molar structural unit for flow parts
X_x	the mole fraction of ordered parts

From $(df_m/dX_x)_p = 0$, an equilibrium relation is derived:

$$f_m = f_x = f_{flow} \qquad [5.2.15]$$

Whereas, C_p is defined as:

$$C_p = \left(dh_q / dT\right)_p \qquad [5.2.16]$$

with $h_q = f_q - T(df_q/dT)_p$, q = m, x or flow

From equations [5.2.15] and [5.2.16], it is shown that C_p of ordered parts is equal to that of flow parts. Therefore, h_x is given by:[10]

$$h_x \approx h_g + \Delta h \qquad [5.2.17]$$

with $\Delta h = \int_{T_g}^{T_e} \Delta C_p dT$ and $\{RT_g \ln(Z_g/Z_0)\}/x \le \Delta h \le T_g\{s_g^{conf} - (R\ln Z_0)/x\}$,

where:

ΔC_p	the difference in the observed C_p and the hypothesized super heated glass C_p at the glass transition
Z_g	the conformational partition function per a chain at T_g
Z_0	the component conformational partition function per chain regardless of the temperature in Z
s_g^{conf}	the conformational entropy per molar structural unit at T_g

h_x is also given by rewriting the modified Flory's equation, which expresses the melting point depression as a function of the mole fraction of major component, X, for binary random copolymers:[24-27]

$$h_x \approx 2h_u(1 - 1/a) \qquad [5.2.18]$$

with $a = -h_u(1/T_m(X) - 1/T_m^0)/(R\ln X)$

where:

$T_m(X)$	the melting temperature for a copolymer with X
T_m^0	the melting temperature for a homopolymer of major component

Table 5.2.2

Polymer	h_u cal/mol	h_x(eq.[5.2.17]) cal/mol	h_x(eq.[5.2.17]) - h_u cal/mol	h_x (eq.[5.2.18]) cal/mol	h_x from δ_p cal/mol
N6	5100	9590 (10070)	4490 (4970)	4830	-
N66	10300	19300 (20280)	9000 (9980)	9580	10070
iPP	1900	1600 (1780)	-	1470	1420
iPS	2390[12]	5030 (5550)	2640 (3160)	-	2410 - 5790
PET	5500	5380 (5670)	-	6600	6790

The numerical values in parentheses were calculated using equation [5.2.17] with the second term of $T_g\{s_g^{conf} - (R\ln Z_0)/x\}$.

Table 5.2.2 shows the numerical values of h_x from equations [5.2.17] and [5.2.18], and from the reference values[7,8] of δ_p using equations [5.2.1] ~ [5.2.4], together with the values[12,28,29] of h_u, for several polymers. The second term in the right hand side of equation [5.2.17] was calculated from $\{RT_g \ln(Z_g/Z_0)\}/x$. The numerical values in parentheses, which were calculated using equation [5.2.17] with the second term of $T_g\{s_g^{conf} - (R\ln Z_0)/x\}$, are a little more than in the case of $\{RT_g \ln(Z_g/Z_0)\}/x$. The relationship of h_x(eq.[5.2.17]) » h_u found for N6 and N66 suggests two layer structure of ordered parts in the glasses, because, as shown in the fourth column, h_x(eq.[5.2.17]) - h_u is almost equal to h_x ($\approx h_u$) from equation [5.2.18] or δ_p (=13.6 (cal/cm^3)$^{1/2}$). For iPP, h_x(eq.[5.2.17]) is a little more than h_x from equation [5.2.18] or δ_p (=8.2 (cal/cm^3)$^{1/2}$), suggesting that the ordered parts in glasses seem to be related closely to the helical structure. For iPS, h_x(eq.[5.2.17]) and h_x(eq.[5.2.17]) - h_u are in the upper and lower ranges of h_x from δ_p (=8.5~10.3 (cal/cm^3)$^{1/2}$), respectively. For PET, h_x(eq.[5.2.17]) is almost equal to h_u, but h_x from equation [5.2.18] or δ_p (=10.7 (cal/cm^3)$^{1/2}$) is a little more than h_u, resulting from glycol bonds in bulk crystals distorted more than in ordered parts.[10,25,30]

5.2.3 δ_p PREDICTION FROM THERMAL TRANSITION ENTHALPIES

Table 5.2.3 shows the numerical values of δ_p predicted from equations [5.2.1] ~ [5.2.4] using the results of Tables 5.2.1 and 5.2.2, together with h_x, h_u, h_g, h_0, and $\delta_p{}^r$ (reference values)[7,8] for several polymers. The predicted values of δ_p for each polymer are close to $\delta_p{}^r$.

Table 5.2.3

Polymer	h_x cal/mol	h_u cal/mol	h_g cal/mol	h_0 cal/mol	δ_p (cal/cm^3)$^{1/2}$	$\delta_p{}^r$ (cal/cm^3)$^{1/2}$
N6	9590*	-	8980	18570	13.4	-
	(10070)	-	8980	(19050)	(13.6)	-
	4830**	5100	8980	18910	13.5	-
N66	19300*	-	17980	37280	13.4	13.6
	(20280)	-	17980	(38260)	(13.6)	13.6
	9580**	10300	17980	37860	13.5	13.6
iPP	1600*	1900	-	3500	8.4	8.2[7]
	(1780)	1900	-	(3680)	(8.6)	8.2[7]
	1470**	1900	-	3370	8.3	8.2[7]
iPS	5030*	-	4820	9850	9.9	8.5 - 10.3
	(5550)	-	4820	(10370)	(10.2)	8.5 - 10.3
PET	5380*	5500	4180	15060	10.2	10.7
	(5670)	5500	4180	(15350)	(10.3)	10.7
	6600**	5500	4180	16280	10.6	10.7

The numerical values attached * and ** are h_x from equations [5.2.17] and [5.2.18], respectively. The numerical values in parentheses were calculated using equation [5.2.17] with the second term of $T_g\{s_g{}^{conf} - (R\ln Z_0)/x\}$.

For atactic polypropylene (aPP) that could be treated as a binary random copolymer composed of meso and racemi dyads,[26,27,31] δ_p is predicted as follows.

For binary random copolymers, h_g is given by:

$$h_g = h_g^{\text{int}} + h_g^{conf}(X_A) \qquad [5.2.19]$$

with $h_g{}^{\text{int}} = h_g{}^{\text{int}}(1) - (h_g{}^{\text{int}}(1) - h_g{}^{\text{int}}(0))(1 - X_A)$

where:

$h_g{}^{conf}(X_A)$	the conformational enthalpy per molar structural unit for a copolymer with X_A at T_g
$h_g{}^{\text{int}}(1)$	the intermolecular cohesive enthalpy per molar structural unit for a homopolymer of component A (X_A=1) at T_g

$h_g^{int}(0)$ the intermolecular cohesive enthalpy per molar structural unit for a homopolymer of component B (X_A=0) at T_g
X_A the mole fraction of component A

Further, h_x is obtained from equation [5.2.17], but Z_g is the conformational partition function for a copolymer with X_A at T_g and Z_0 is the component conformational partition function for a copolymer with X_A regardless of the temperature in Z. Whereas for binary random copolymers, T_g is given by:[32,33]

$$T_g = T_g(1)(h_g^{\text{int}} + h_g^{conf}(X_A)) / \{h_g^{\text{int}}(1) + h_g^{conf}(1) - T_g(1)(s_g^{conf}(1) - s_g^{conf}(X_A))\} \qquad [5.2.20]$$

where:

$h_g^{conf}(1)$ the conformational enthalpy per molar structural unit for a homopolymer (X_A=1) at T_g
$s_g^{conf}(1)$ the conformational entropy per molar structural unit for a homopolymer (X_A=1) at T_g
$s_g^{conf}(X_A)$ the conformational entropy per molar structural unit for a copolymer with X_A at T_g
$T_g(1)$ the glass transition temperature for a homopolymer (X_A=1)

Thus, using equations [5.2.19] and [5.2.20], δ_p for binary random copolymers, including aPP, could be predicted.

Table 5.2.4

1 - X_A	**T_g K**	**h_g cal/mol**	**h_x cal/mol**	**h_0 cal/mol**		**δ_p(cal/cm^3)$^{1/2}$**	
				$T>T_g$	$T<T_g$	$T>T_g$	$T<T_g$
0	270	1540	1600 (1780)	3500 (3680)	5040 (5220)	8.42 (8.62)	10.10 (10.23)
0.05	265	1480	1510	3410	4900	8.31	9.95
0.1	261	1450	1470	3370	4830	8.26	9.88
0.15	259	1440	1460	3360	4790	8.24	9.85
0.2	257	1430	1440	3340	4770	8.23	9.83
0.3	255	1420	1440 (1500)	3340 (3400)	4760 (4820)	8.22 (8.29)	9.82 (9.87)
0.4	254	1420	1450	3350	4770	8.23	9.83
0.5	255	1440	1470	3370	4810	8.26	9.86
0.6	256	1450	1490	3390	4840	8.28	9.90
0.7	258	1470	1520	3420	4890	8.32	9.95
0.8	262	1500	1560	3460	4960	8.37	10.02
0.85	264	1510	1580	3480	4990	8.39	10.05
0.9	266	1520	1600	3500	5030	8.42	10.09
0.95	268	1540	1620	3520	5060	8.45	10.12
1	270	1550	1650 (1840)	3550 (3740)	5100 (5300)	8.48 (8.69)	10.16 (10.34)

The numerical values in parentheses were calculated using equation [5.2.17] with the second term of $T_g\{s_g^{conf}(R\ln Z_g)/x\}$.

Table 5.2.4 shows the numerical values of δ_p for aPP, together with T_g, h_g, h_x, and h_0, which give the concave type curves against 1 - X_A, respectively. Where X_A is the mole fraction of meso dyads. As h_u of crystals or quasi-crystals in aPP, 1900 cal/mol was used, because h_u(=1900 cal/mol) of iPP[28] should be almost equal to that of syndiotactic PP (sPP); $h^{conf} + h^{int} \approx 1900$ cal/mol at each T_m for both PP, where $h^{conf} = 579.7$ cal/mol at $T_m = 457K$[28] for iPP, $h^{conf} = 536.8$ cal/mol at $T_m = 449K$[34] for sPP, and $h^{int} = 1360$ cal/mol for both PP. Here quasi-crystals are ordered parts in aPP with 1 - $X_A \approx 0.30 \sim 0.75$, which do not satisfy the requirements of any crystal cell. As T_g of iPP and sPP, 270K was used for both PP.[12,35] The experimental values of T_g for aPP are less than 270K.[36-41] In this calculation, for aPP with 1 - X_A = 0.4, the minimum of T_g, 254K, was obtained. δ_p in $T>T_g$ showed the minimum, 8.22 $(cal/cm^3)^{1/2}$, at 1 - X_A = 0.3, which is 0.20 less than 8.42 $(cal/cm^3)^{1/2}$ of iPP, and δ_p in $T<T_g$ showed the minimum, 9.82 $(cal/cm^3)^{1/2}$, at 1 - X_A = 0.3 and 10.10 $(cal/cm^3)^{1/2}$ for iPP. Substituting $T_g\{s_g^{conf} - (R\ln Z_0)/x\}$ for the second term in equation [5.2.17],[42,43] the numerical values of h_x, h_0, and δ_p become a little more than in the case of $\{RT_g\ln(Z_g/Z_0)\}/x$, as shown in Table 5.2.4. However, the increase of h_x for iPP led T_e (=375K) near the experimental values,[35] e.g. 362K and 376K, where T_e was approximated by:

$$T_e \approx 2\left(h_x - h_g\right) / \Delta C_p^0 + T_g \qquad [5.2.21]$$

where:

ΔC_p^0 the difference in liquid C_p and glass C_p before and after the glass transition; 4.59 cal/(K mol) for iPP[12]

Thus, we can browse the solvents of aPP which satisfy $\delta_p = \delta_s$.

Equations [5.2.2], [5.2.3] and [5.2.4] would be available as tools to predict δ_p from thermal transition behaviors.

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5.3 METHODS OF CALCULATION OF SOLUBILITY PARAMETERS OF SOLVENTS AND POLYMERS

Valery Yu. Senichev, Vasiliy V. Tereshatov
Institute of Technical Chemistry
Ural Branch of Russian Academy of Sciences, Perm, Russia

The methods of calculation of solubility parameters are based on the assumption that energy of intermolecular interactions is additive. Thus, the value of an intermolecular attraction can be calculated by addition of the contributions of cohesion energy of atoms or groups of atoms incorporated in the structure of a given molecule. Various authors use different physical parameters for contributions of individual atoms.

Dunkel proposed to use a molar latent heat of vaporization[1] as an additive value, describing intermolecular interactions. He represented it as a sum of the contributions of latent heat of vaporization of individual atoms or groups of atoms at room temperature.

Small's method[2] received the greatest interest. Small has used the data of Scatchard[3] showing that the square root of a product of cohesion energy of substance and its volume is a linear function of a number of carbon atoms in a molecule of substance. He also proposed additive constants for various groups of organic molecules that permit calculation of $(EV)^{1/2}$ value. He named these constants as molar attraction constants, F_i:

$$(EV)^{1/2} = \sum_i F_i \qquad [5.3.1]$$

Cohesion energy and solubility parameters could then be estimated for any molecule:

$$E = \frac{\left(\sum_i F_i\right)^2}{V}, \quad \delta = \frac{\sum_i F_i}{V} \qquad [5.3.2]$$

where:

V molar volume of solvent or a repeating unit of polymer

The molar attraction constants were calculated by Small based on literature data for a vapor pressure and latent heat of vaporization of liquids. The comprehensive values of these constants are given in Table 5.3.1.

Table 5. 3.1. Molar attraction constants

Group	Small[2]	Van Krevelen[5]	Hoy[7]
	F, $(\text{cal cm}^3)^{1/2}$ mol^{-1}		
>C<	-93	0	32.0
>CH-	28	68.5	86.0
$-CH_2-$	133	137	131.5
$-CH_3$	214	205.5	148.3
$-CH(CH_3)-$	242	274	(234.3)
$-C(CH_3)_2-$	335	411	(328.6)
>C=CH-	130	148.5	206.0
-CH=CH-	222	217	243.1
$-C(CH_3)=CH-$	(344)	354	(354.3)
Cyclopentyl	-	676.5	633.0
Cyclohexyl	-	813.5	720.1
Phenyl	735	741.5	683.5
1,4-Phenylene	658	673	704.9
-O-	70	125	115.0
-OH	-	368.5	225.8
-CO-	275	335	263.0
-COO-	310	250	326.6
-COOH	-	318.5	(488.8)
-O-CO-O-	-	375	(441.6)
-CO-O-CO-	-	375	567.3
-CO-NH-	-	600	(443.0)
-O-CO-NH-	-	725	(506.6)
-S-	225	225	209.4

Group	Small[2]	Van Krevelen[5]	Hoy[7]
	F, (cal cm^3)$^{1/2}$ mol^{-1}		
-CN	410	480	354.6
-CHCN-	(438)	548.5	(440.6)
-F	(122)	80	41.3
-Cl	270	230	205.1
-Br	340	300	257.9
-I	425	-	-

The Scatchard equation is correct only for nonpolar substances because they have only dispersive interactions between their molecules. Small eliminated from his consideration the substances containing hydroxyl, carboxyl and other groups able to form hydrogen bonds.

This method has received its further development due to Fedors' work,[4] who extended the method to polar substances and proposed to represent as an additive sum not only the attraction energy but also the molar volumes. The lists of such constants were published in several works.[5-8] The most comprehensive set of contributions to cohesion energy can be found elsewhere.[9]

Askadskii has shown[10] that Fedors' supposition concerning the additivity of contributions of volume of atoms or groups of atoms is not quite correct because the same atom in an environment of different atoms occupies different volume. In addition, atoms can interact with other atoms in different ways depending on their disposition and this should be taken into account for computation of cohesion energy. Therefore, a new scheme of the solubility parameters calculation was proposed that takes into account the nature of an environment of each atom in a molecule and the type of intermolecular interactions. This approach is similar to that described in the work of Rheineck and Lin.[6]

$$\delta = \left(\frac{\sum_i \Delta E_i}{N_A \sum_i \Delta V_i} \right)^{1/2} \qquad [5.3.3]$$

where:

N_A	Avogadro number
ΔE_i	increment (contribution) to cohesion energy of atom or group of atoms
ΔV_i	increment to the van der Waals volume of atom

The volume increment ΔV_i of an atom under consideration is calculated as volume of sphere of the atom minus volumes of spherical segments, which are cut off on this sphere by the adjacent covalently-bound atoms:

$$\Delta V_1 = \frac{4}{3}\pi R^3 - \sum_i \frac{1}{3}\pi h_i^3 (3R - h_i) \qquad [5.3.4]$$

where:

R van der Waals (intermolecular) radius of a considered atom
h_i a height of segment calculated from the formula:

$$h_i = R - \frac{R^2 + d_i^2 - R_i^2}{2d_i} \qquad [5.3.5]$$

where:

d_i bond length between two atoms
R_i van der Waals radius of the atom adjacent to the covalently-bonded atoms under consideration

The increments to the van der Waals volume for more than 200 atoms in various neighborhoods is available elsewhere.[11]

Using data from Tables 5.3.2 and 5.3.3, van der Waals volumes of various molecules can be calculated. The increments to the cohesion energy are given in Table 5.3.4. An advantage of this method is that the polymer density that is important for estimation of properties of polymers that have not yet been synthesized does not need to be known.

The calculation methods of the solubility parameters for polymers have an advantage over experimental methods that they do not have any prior assumptions regarding interactions of polymer with solvents. The numerous examples of good correlation between calculated and experimental parameters of solubility for various solvents support the assumed additivity of intermolecular interaction energy.

The method has further useful development in calculation of components of solubility parameters based on principles of Hansen's approach.[12] It may be expected that useful results will also come from analysis of donor and acceptor parameters used in TDM-approach (see Chapter 4).

In Table 5.3.5, the increments required to account for contributions to solubility parameters related to the dipole-dipole interactions and hydrogen bonds are presented.[13] Table 5.3.6 contains Hansen's parameters for some common functional groups.

Table 5.3.2. Intermolecular radii of some atoms

Atom	R, Å	Atom	R, Å	Atom	R, Å	Atom	R, Å
C	1.80	F	1.5	Si	2.10	P	1.90
H	1.17	Cl	1.78	Sn	2.10	Pb	2.20
O	1.36	Br	1.95	As	2.00	B	1.65
N	1.57	I	2.21	S	1.8		

Table 5.3.3. Lengths of bonds between atoms

Bond	d_i, Å	Bond	d_i, Å	Bond	d_i, Å	Bond	d_i, Å
C–C	1.54	C–F	1.34	C–S	1.76	N–P	1.65
C–C	1.48	C–F	1.31	C=S	1.56	N–P	1.63
C–C^{arom}	1,40	C–Cl	1.77	H–O	1.08	S–S	2.10
C=C	1.34	C–Cl	1.64	H–S	1.33	S–Sn	2.10

Bond	d_i, Å	Bond	d_i, Å	Bond	d_i, Å	Bond	d_i, Å
C≡C	1.19	C–Br	1.94	H–N	1.08	S–As	2.21
C–H	1.08	C–Br	1.85	H–B	1.08	S=As	2.08
C–O	1.50	C–I	2.21	O–S	1.76	Si–Si	2.32
C–O	1.37	C–I	2.05	O–Si	1.64	P–F	1.55
C=O	1.28	C–P	1.81	O–P	1.61	P–Cl	2.01
C–N	1.40	C–B	1.73	N–O	1.36	P–S	1.81
C–N	1.37	C–Sn	2.15	N–N	1.46	B–B	1.77
C=N	1.31	C–As	1.96	O=N	1.20	Sn–Cl	2.35
C=N	1.27	C–Pb	2.20	O=S	1.44	As–Cl	2.16
$C–N^{arom}$	1.34	C–Si	1.88	O=P	1.45	As–As	2.42
C≡N	1.16	C–Si	1.68	$N–P^{arom}$	1.58		

Table 5.3.4. Values of ΔE^*_i for various atoms and types of intermolecular interaction required to calculate solubility parameters according to equation [5.3.3] (Adapted from refs. 10,11)

Atom and type of intermolecular interaction	Label	ΔE^*_i, cal/mol
C	ΔE^*_C	550.7
H	ΔE^*_H	47.7
O	ΔE^*_O	142.6
N	ΔE^*_N	1205.0
F	ΔE^*_F	24.2
S	ΔE^*_S	1750.0
Cl	ΔE^*_{Cl}	-222.7
Br	ΔE^*_{Br}	583
I	ΔE^*_I	1700
Double bond	$\Delta E^*_{\neq}$	-323
Dipole-dipole interaction	ΔE^*_d	1623
Dipole-dipole interaction in nonpolar aprotic solvents of amide type	$\Delta E^*_{a,N}$	1623
Dipole-dipole interaction in nonpolar aprotic solvents as in dimethylsulfoxide	$\Delta E^*_{a,S}$	2600
Aromatic ring	ΔE^*_{ar}	713
Hydrogen bond	ΔE^*_h	3929
Specific interactions in the presence of $=CCl_2$ group	$\Delta E^*_{=CCl_2}$	2600
Specific interactions in 3-5 member rings in the presence of O atom	$\Delta E^*_{O,r}$	2430
Isomeric radicals	ΔE^*_i	-412

Table 5.3.5 Increments of atoms or groups of atoms required in equation [5.3.3]

Atoms or their groups	**ΔV_i, Å^3**	**Atoms or their groups**	**ΔV_i, Å^3**
$-CH_3$	23.2 (22.9)	$>CH_2$	17.1 (16.8, 16.4)
$>CH$	11.0 (10.7,10.4)	C	5.0 (4.7,4.5)
$=CH_2$	21.1	$-CH=$	15.1 (14.7)
$-O-$	3.4 (2.7, 2.1)	$-OH$	10.3 (9.9)
$>CO-$	18.65 (18.35,18.15)	$-NH-$	8.8 (8.5)
$-NH_2$	16.1	$-CN$	25.9
$-F$	9.0 (8.9)	$-Cl$	19.9 (19.5)

The values in brackets correspond to one and two neighboring aromatic carbon atoms. In other cases values are given for the aliphatic neighboring carbon atoms.

Table 5.3.6. Hansen's parameters[12]

Atom (group)	**ΔV, cm^3/mol**	**$V\delta_p$, (cal cm/mol)$^{1/2}$**	**$V\delta_h^2$, cal/mol**	
			aliphatic	aromatic
$-F$	18.0	12.55±1.4	~0	~0
$-Cl$	24.0	12.5±4.2	100±200	100±20
$>Cl_2$	26.0	6.7±1.0	165±10	180±10
$-Br$	30.0	10.0±0.8	500±10	500±100
$-I$	31.5	10.3±0.8	1000±200	-
$-O$	3.8	53±13	1150±300	1250±300
$>CO$	10.8	36±1	800±250	400±125
$>COO$	18.0	14±1	1250±150	800±150
$-CN$	24.0	22±2	500±200	550±200
$-NO_2$	33.5	15±1.5	400±50	400±50
$-NH_2$	19.2	16±5	1350±200	2250±200
$>NH$	4.5	22±3	750±200	-
$-OH$	10.0	25±3	4650±400	4650±500
$(-OH)_n$	n 10.0	n (17±2.5)	n (4650±400)	n (4650±400)
$-COOH$	28.5	8±0.4	2750±250	2250±250

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5.4 MIXED SOLVENTS, A WAY TO CHANGE THE POLYMER SOLUBILITY

LIGIA GARGALLO AND DEODATO RADIC
Facultad de Quimica
Pontificia Universidad Católica de Chile, Santiago, Chile

5.4.1 INTRODUCTION

In general, a mixture is often found to be unexpectedly potent for a particular purpose. Examples are known in several branches of Science and Technology. In the field of solubility, the synergistic effect is, sometimes, spectacular. Innumerable cases of synergism in solvent extraction are known.[1-9]

Eucaliptus oil has been found to act as a cosolvent, special type of synergistic solvent in case of water-ethanol-gasoline.[10]

It has been frequently observed that certain polymers can be readily dissolved in mixtures of two or more solvents, whereas they are not soluble in the individual constituents of this mixture. This phenomenon, known as cosolvency is of great practical importance.

The scientific and technological importance of polymers has led to extensive study of their solution properties. Most techniques rely on dilute solution methods such as viscometry, light scattering, osmometry, gel swelling or dipole moments. However, these need solvents which completely dissolve the polymer, and many important polymers either are not very soluble, or completely insoluble. In general, polymer solubility normally increases with rising temperature, but negative temperature coefficients are also observed. Increase in polymer molecular weight reduces solubility. Certain combinations of two solvents may become nonsolvents. However, mixtures of non-solvents may sometimes become solvents. In this article, we will review major information for the evaluation of solubility behavior of polymers in binary solvents. Experimental results are compiled and discussed. The emphasis here is on solubility-cosolvency phenomenon, the thermodynamical description of ternary systems and the influence of the polymer structure on preferential adsorption. Finally, interrelationships between polymer structure and thermodynamic properties of the mixture will be discussed relative to the properties and conformation of the dissolved polymer.

Some new cosolvent effects will be also described particularly of polymer-supercritical CO_2 mixtures.

5.4.2 SOLUBILITY-COSOLVENCY PHENOMENON

The addition of a second liquid to a binary liquid-polymer system to produce a ternary system is used widely for a variety of purposes. If the second liquid is a poor solvent, or a precipitant for the polymer, the dissolving potential of the liquid medium can be reduced and eventually phase separation may even occur. This does not necessarily take place in every case and sometimes mixtures of two relatively poor solvents can even produce an enhancement of the solvent power.[11-16] The mixed solvent is then said to exhibit a synergistic effect.[17]

Cosolvency usually refers to a certain range of temperatures of practical use. Within that range, the polymer dissolves in the mixed solvent but not in the pure liquids. The term, "true cosolvency" has been coined to designate those more strict cases, in which the polymer does not dissolve in the pure liquids at any temperature, not just in a given range.[18]

An analysis of the phase behavior in terms of the free volume theory of polymer solutions has revealed that cosolvency has enthalpic origin.[19] In a classic cosolvent system, the single liquids are both very poor solvents for the polymer and the number of polymer-liquid contacts formed in each binary system are not enough to stimulate dissolution of the polymer, except at very short chain lengths. Mixing to produce a ternary system results in a combination of liquid(1)/polymer(3) and liquid(2)/polymer(3) contacts, which according to Cowie et al.[20] is sufficient to cause the polymer to dissolve if these contacts are of a different nature, i.e., if the two liquids tend to solvate the polymer at different sites along the chain and so lead to a reinforcement of solvation. If this occurs then, it is also likely that the expanded coil will allow further liquid-polymer contacts to develop even though these may be energetically weak.

This idea of a favorable solvation sheath is in agreement with observations made during preferential adsorption studies in ternary systems exhibiting cosolvency.[21] Maximum coil expansion is usually found to occur at a mixed solvent composition where there is not preferential adsorption. In other words, the driving force is an attempt to maintain the most favorable composition, thereby minimizing polymer-polymer contacts. However, the balance of interactions giving rise to cosolvency and to inversion in preferential sorption are different, so that both phenomena have to be studied separately. This has been exemplified by a series of systems in which the molecular sizes of the liquid solvents and the nature of their interactions are varied and each plays its role in determining maximum sorption and inversion in preferential sorption.[22-25]

The interesting phenomenon where a mixture of two poor solvents or nonsolvents for a polymer provides a medium that acts as a good solvent for the polymers[26,27] has been the objective of many studies, by light scattering,[21,29,30-34] viscometry,[35,36] sorption equilibrium,[37] and fluorescence.[38] From these techniques, it has been possible to appreciate how the second virial coefficient A_2[39,17,40-42] and the intrinsic viscosity $[\eta]$[13,43-45] preferential adsorption coefficient λ and excimer and monomer emission ratio I_E/I_M are involved by changing solvent composition. They present ($[\eta]$, A_2) a maximum or a variation at a certain solvent composition where the polymer behaves as through it were dissolved in a good solvent.

The quality of solvent or the cosolvent action has been established by determining the magnitude of the miscibility range between the two critical temperatures, UCST and LCST.[19,45-58] The application of pressure can widen the miscibility range.[59,60]

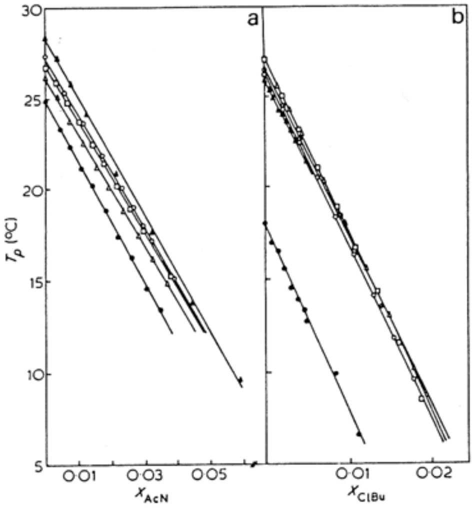

Figure 5.4.1. Phase separation temperature (T_p), as a function of solvent mixture composition, determined on the system PMMA-acetonitrile + chlorobutane, at several polymer concentrations, x(x 10^2/g cm^{-3}): (a): c = Δ, 12.2; O, 9.17; ☐ 7.14; Δ, 4.36: ●, 2.13. (b): c = O, 9.47; **O**, 8.22; Δ, 5.89; ☐, 3.69; Δ, 2.17; ●, 0.442. From Fernandez-Pierola and Horta.[65] (Copyright by Hüthig & Wepf Verlag (Basel), used with permission).

The cosolvency phenomenon was discovered in 1920's experimentally for cellulose nitrate solution systems.[61] Thereafter cosolvency has been observed for numerous polymer/mixed solvent systems. Polystyrene (PS) and polymethylmethacrylate (PMMA) are undoubtedly the most studied polymeric solutes in mixed solvents.[62,63]

Horta et al.[64] have developed a theoretical expression to calculate a coefficient expressing quantitatively the cosolvent power of a mixture $(dT_c/dx)_0$, where T_c is the critical temperature of the system and x is the mole fraction of liquid 2 in the solvent mixture, and subscript zero means $x \to 0$. This derivative expresses the initial slope of the critical line as a function of solvent composition (Figure 5.4.1).[65] Large negative values of (dT_c/dx) are the characteristic feature of the powerful cosolvent systems reported.[65] The theoretical expression developed for $(dT_c/dx)_0$ has been written in terms of the interaction parameters χ_i for the binary systems:

$$(dT_c \; / \; dx)_0 = \frac{\left(\chi_{23} - \chi_{13} - \frac{V_2}{V_1}\chi_{12}\right)}{(-d\chi_{13} \; / \; dT)} \qquad [5.4.1]$$

where:

V_i the volume fraction of polymer and solvent, respectively

All the magnitudes on the right hand side of this equation are to be evaluated at the critical temperature corresponding to x = 0.

The expression provides a criterion to predict whether or not the mixed solvent is expected to be a cosolvent of the polymer. When T_{c1}, is a UCST (as is the case in these phase separation studies), $-d\chi_{13}/dT > 0$ and $(dT_c/dx)_0$ has the same sign as the numerator of the equation. Choosing solvent 1 such that $T_{c2} < T_{c1}$, then $(dT_c/dx)_0 < 0$ guarantees that the system will be a cosolvent one. Since $\chi_{23} - \chi_{13} > 0$, at T_{c1}, the numerator in the equation [5.4.1] is negative (cosolvent system) if the unfavorable interaction between the two liquids is large enough to compensate for their different affinity towards the polymer. The equation proposed gives a more detailed criterion for cosolvency than the simple criterion of $G^E > 0$. The information needed to predict $(dT_c/dx)_0$ from equation [5.4.1] includes the binary interaction parameters of the polymer in each one of the two solvents as a function of temperature, and $\chi_{12}(G^E)$ for the mixed solvent too. Table 5.4.1 summarizes results reported by Horta et al.[64] for some cosolvents of polymethylmethacrylate (PMMA).[65]

Table 5.4.1. Comparison between theory and experiment in cosolvents of PMMA. From Fernandez-Pierola.[65] (Copyright by Hüthig & Wepf Verlag (Basel), used with permission)

Solvent 1	Solvent 2	Experiment $(dT_p/dx)_0$ x 10^{-2} K	Theory $(dTc/dx)_0$ x 10^{-2} K
Acetonitrile	Amylacetate	-11.1	-18.0
Acetonitrile	Chlorobutane	-9.4	-9.4
Acetonitrile	CCl_4	-12.3	-7.2
Acetonitrile	BuOH	-7. 6	-12.5
4-Chloro-n-butane	Acetonitrile	-3.2	-4.6
1-Chloro-n-butane	BuOH	-17.0	-14.0

Table 5.4.2 Liquid mixtures which are cosolvents of PMMA. From Horta and Fernandez Pierola.[64] (Copyright by Butterworth-Heineman Ltd., used with permission)

Acetonitrile (AcN) + 4-Heptanone (Hna)[a)]	Formamide (FA) + Ethanol (EtOH)[a)]
Acetonitrile (AcN) + Isopentyl acetate (iPac)[a)]	1-Chlorobutane (BuCl) + Isopentyl alcohol (iPOH)[a)]
Acetonitrile (AcN) + Pentylacetate (Pac)[a)]	1-Chlorobutane (BuCl) + Pentyl alcohol (POH)[a)]
Acetonitrile (AcN) + 1-Chlorobutane (BuCl)[a)]	1-Chlorobutane (BuCl) + 2-Butanol (sBuOH)[b)]
Acetonitrile (AcN) + Carbon tetrachloride (CCl_4)[a)]	1-Chlorobutane (BuCl) + Isopropyl alcohol (iPrOH)[a)]
Acetonitrile (AcN) + Isopentyl alcohol (iPOH)[a)]	Carbon tetrachloride (CCl_4) + 1-Butanol (BuOH)[c)]
Acetonitrile (AcN) + Pentyl alcohol (POH)[a)]	Carbon tetrachloride (CCl_4) + Ethanol (EtOH)[c)]
Acetonitrile (AcN) + 1-Butanol (BuOH)[a)]	Carbon tetrachloride (CCl_4) + Methanol (MeOH)[c)]
Acetonitrile (AcN) + Isopropyl alcohol (iPrOH)[a)]	

a) Ref. 65, b) Ref. 47, c) Ref. 6 6

In the case of PMMA, several powerful cosolvent mixtures have been reported.[65,46,47] In such systems, a small proportion of liquid 2, added to the polymer-liquid 1 solution, is enough to produce a large decrease in T_p, these cosolvents are accessible to phase separation determinations.

In Table 5.4.2, a number of liquid mixtures are listed to act as cosolvents of polymethylmethacrylate (PMMA).[65,47,64,67] Intrinsic viscosity [η] has been reported in cosolvent mixtures containing CCl_4: $CC1_4$/methanol,[42,66] ethanol,[66] 1-propanol,[66] 1-butanol,[66] 1-chlorobutane,[67] and acetonitrile,[68] and acetonitrile/methanol.[68] It was also reported the [η] of PMMA in the cosolvent mixture acetonitrile/1-chlorobutane.[42] The last system is a powerful cosolvent. Acetonitrile forms powerful cosolvents for PMMA too with other liquids having a wide variety of chemical groups.[65] [η] has been reported for PMMA in acetonitrile/pentylacetate as a powerful cosolvent.[44] On the contrary, the mixture of 1-chlorobutane/pentyl acetate is a co-nonsolvent of the polymer.[44] Mixing acetonitrile, with pentylacetate or mixing acetonitrile with 1-butanol greatly increases solubility and produces a large increase in [η]. This large increase of [η] in the cosolvents contrasts with the approximate constancy of [η] in the l-chlorobutane/pentylacetate mixture.

The increase of [η] in a mixed solvent over its weighed mean value in the pure liquids is usually expressed as:

$$\Delta[\eta] = [\eta] - [\eta]_1 \phi_1 - [\eta]_2 \phi_2 \qquad [5.4.2]$$

where $[\eta]_1$ and $[\eta]_2$ refer to values in the pure liquids 1 and 2, and [η] refers to the value in the mixture. This increase in [η] has been attributed to the existence of unfavorable interactions between the two liquids .[39] For a given molecular weight, Δ[η] is usually taken to be proportional to the excess in Gibbs function of the mixture: $\Delta[\eta](\phi) \sim G^E(\phi)/RT$.[39]

The values of G^E and S^E for these cosolvent mixtures[69,70] at equimolecular composition, and 25°C, are given in Table 5.4.3.

Table 5.4.3. Thermodynamic properties of the liquid mixtures used as cosolvents of PMMA. Excess Gibbs function G^E, and excess entropy S^E, of the binary mixtures at equimolecular composition (at 25°C). From Prolongo et al.[44] (Copyright by Butterworth-Heineman Ltd., used with permission)

Cosolvent mixture	G^E, J mol^{-1}	S^E, J mol^{-1} K^{-1}
MeCN + BuOH	1044	3.70
MeCN + PAc	646	-0.58
MeCN + ClBu	1032	-

The values of G^Es have allowed for a qualitative interpretation of the relative values of [η] in these three cosolvent systems studied.[44]

Mixing cosolvents is much more effective in expanding the polymer coil than increasing temperature.[44] In fact, the same increase in [η] experienced by one sample in pure acetonitrile in going from 25°C to 45°C is reached at 25°C by adding just 9% pentyl acetate or 8% 1-butanol or 6% in the case of 1-chlorobutane,[71] for polymethylmethacrylate.

The sign of Δ[η] was in contradiction with the cononsolvent character attributed to this mixture by cloud point studies.[72] This apparent inconsistency could be due to the different range of concentrations in which [η] and cloud point temperature were determined.[44]

Systematic study of the cosolvency phenomenon has been practically limited to polymethylmethacrylate[42,46,64-68,72-81] and polystyrene.[45,82,83] The cosolvency is usually explained in terms of the molecular characteristics of the system, specially in terms of molecular interactions. In the powerful cosolvents of PMMA described in the literature[72,65,42,44,46,64] one of the liquid components is always either acetonitrile or an alcohol. These are non-random liquids with a certain degree of order in their structure. Two important characteristics seem to be present in these polymer cosolvent systems: the liquid order structure and the tendency of the polymer towards association.[65,14,66] The roles of these two factors were considered to interpret solvation of PMMA chains in cosolvent systems.[43,14] The mechanisms of cosolvent action have been discussed in terms of the competitive interactions between liquid components and one liquid component and the polymer.[44] The best example is the case of acetonitrile and a second liquid having a high proportion of methylene units in its molecule, the unfavorable nitrile-methylene interactions between acetonitrile and PMMA favor the nitrile ester group interaction and an extensive polymer solvation becomes possible. According to Prolongo et a1.,[44] the number of methylene units or length of the n-alkyl chain is very important for reaching cosolvency when the second liquid is an ester (acetate). Another factor G^E of the acetonitrile + acetate mixtures is larger for long alkyl chains such as in pentyl acetate, favors cosolvency.

In the majority of cases, the cosolvent mixtures for PMMA contain either CCl_4[73,77,80,81] or acetonitrile[13,42-44,67] as one of the liquid components. A study of the mixture formed by these two liquids and a comparison with the results obtained in the other cosolvents studied before has been also reported.[84] The total sorption of the coil (PMMA) was calculated from second virial coefficient and intrinsic viscosity data. According to these authors, acetonitrile can interact favorably with the ester group of PMMA and is unfavorable with its methylene backbone. The role of these opposing interactions and of liquid order in acetonitrile are taken into account to explain the dilute solution properties of PMMA in this cosolvent system.[84]

On the other hand, in the case of PMMA, in powerful cosolvents, a small proportion of liquid 2, added to the polymer/liquid 1 solution, is enough to produce a large decrease in the phase separation temperature (T_p).[64]

Katime et al.[85] have studied the influence of cosolvency on stereo-complex formation of isotactic and syndiotactic PMMA. The formation of PMMA stereo-complex has been attributed to the interactions between the ester group of the isotactic form and the α-methyl group of the syndiotactic form.[86]

The stereo-complex was obtained at different compositions of the cosolvent mixtures acetonitrile/carbon tetrachloride, acetonitrile/butyl chloride and butyl chloride/carbon tetrachloride. The results show a high yield of complex formation in pure solvents and when approaches its solvency maximum a decrease of the yield of stereo-complex was observed, indicating that the interactions are impeded.[85]

The dilute solution viscosity of PMMA in the cosolvent mixture formed by acetonitrile (MeCN) and 1-chloro-n-butane (ClBu) at 25°C has been studied.[42,87] The cosolvent effect in this system is extremely large. It has been observed a large increase in the hydrodynamic volume of the macromolecule in solution,[42,17] and a step depression in the critical temperature of phase separation (UCST).[64,88] The quantitative determination of the magnitude of these effects has been reported.[42,64,88] Horta et al.,[71] have compared a relative capacities of temperature and of cosolvent mixing on expanding the macromolecular coils and the tendency of the polymer to associate in poor solvents. They have also shown that there is a connection which relates the dependencies of $[\eta]$ on temperature and solvent composition with the depression in critical temperature (UCST) caused by cosolvency.[71] The action of the cosolvent was much more effective in expanding the macromolecule than temperature was.[71] These authors have concluded that the comparison between the temperature and solvent composition variations of $[\eta]$ allows for a correct prediction of the cosolvent depression of the UCST. The comparison between cloud points and $[\eta]$ - T gives, in general, inconsistent results, but the combination of $[\eta]$ - T and $[\eta]$ - ϕ compensates such inconsistency and establishes a valid link between T_c and $[\eta]$.

It was found that when the cosolvent power of the binary mixture increases, the complexing capacity decreases. These results were explained by taking into account the excess Gibbs free energy, G^E, and the order of the liquid.

5.4.3 NEW COSOLVENTS EFFECTS. SOLUBILITY BEHAVIOR

Cosolvent effect of alkyl acrylates on the phase behaviour of poly(alkyl acrylate)supercritical CO_2 mixtures has been reported.[89] Cloud-point data to 220 and 2000 bar are presented for ternary mixtures of poly(butyl acrylate)-CO_2-butyl acrylate (BA) and poly(ethylhexyl acrylate)-CO_2-ethylhexyl acrylate) (EHA). The addition of either BA or EHA to the respective polymer-solvent mixtures decreases the cloud-point pressures by as much as 1000 bar and changes the pressure-temperature slope of the cloud-point curves from negative to positive, which significantly increases the single-phase region.

The literature presents many studies on coil dimensions of synthetic polymers in mixed solvents. Most investigations involve liquid mixtures composed of a good and a poor solvents for the polymer. The action of mixed solvents has been reported to change coil dimensions, not only because of excluded volume effect or due to the interactions existing between the two liquids[90,91] but also due to the preferential adsorption of one of the solvent by the polymer.

Recently, the behavior of polysiloxanes with amino end-groups in toluene/nitromethane mixtures has been reported.[92] This mixture is solvent/non-solvent for the polymer.

The transition concentrations separating the concentration domain[93] chain flexibility aspects, excluded volume effects[94] and total and preferential adsorption coefficients[95] of the same system have been discussed.

The solubility curves, the cloud point curves and vitrification boundaries for several poly(lactide)-solvent-nonsolvent systems have been reported.[96] The liquid-liquid miscibility gap for the systems with the semicrystalline poly(L-lactide) (PLLA) were located in a similar composition range as the corresponding systems with the amorphous poly(DL-lactide) (PDLLA). The solvent-nonsolvent mixtures used for the experiments were: dioxane/water, N-methyl pyrrolidone (NMP)/water, chloroform/methanol and dioxane/methanol. For all PLLA solvent-nonsolvent systems studied solid-liquid demixing was preferred thermodynamically over liquid-liquid demixing. Attempts were made to correlate the experimental finding with predictions on the basis of the Flory-Huggins theory for ternary polymer solutions using interaction parameters derived from independent experiments. Qualitative agreement was found for the relative locations of the liquid-liquid miscibility gaps. The Flory-Huggins description of the solubility curves was less satisfactory.

The phase separation processes occurring in poly(L-lactide) (PLLA)-chloroform-methanol mixtures and poly(DL-lactide) (PDLLA)-chloroform-methanol mixtures have been also studied using differential scanning calorimetry, cloud point measurements and optical microscopy.[97] It was demonstrated that liquid-liquid demixing occurs in ternary solutions of PDLLA at sufficient high methanol concentrations. For PLLA-containing-solutions, both liquid-liquid demixing processes and soli-liquid demixing processes occur. Only a low cooling rates and high polymer concentration does solid-liquid demixing take place without the interference of liquid-liquid demixing.[97]

Another interesting effects are the changes of a polyelectrolyte in binary solvents. The complex inter and intramolecular interactions that take place due to the presence of hydrophilic and hydrophobic structural units in the macroion can modify the balance of the interactions and for this reason can change the solubility.[98]

5.4.4 THERMODYNAMICAL DESCRIPTION OF TERNARY SYSTEMS. ASSOCIATION EQUILIBRIA THEORY OF PREFERENTIAL ADSORPTION

Polymers dissolved in mixed solvents show the phenomenon of Preferential Adsorption. Experimentally, the preferential adsorption coefficient, λ, is determined. λ is the volume of one of the liquids sorbed in excess by the polymer (per unit mass of polymer). In general, the Flory-Huggins model of polymer solutions is used to describe the Preferential Adsorption. More recently, equation of state theories have been applied.[13,43,99-101]

Description of experimental results of λ (and another properties as intrinsic viscosities, second virial coefficients, etc.) necessitates the use of correcting terms in the form of ternary interaction parameters. Using equation of state theory it has been shown that such correcting terms can in part be explained by free volume and molecular surface effect.[100] Non-random interactions are important in many systems (hydrogen bonding, complex formation, etc.) (see Table 5.4.1). Strongly interacting species can be described taking into account the formation of associates in equilibrium with unassociated molecules (Association Equilibria Theory).

Experimental results[102] for polymethylmethacrylates in 1,4-dioxane/methanol have been reported , which indicate that the size of the substituent in the polymer ester group exerts an influence on the specific interaction between the methanol molecule and the carbonyl of the ester. In fact, the preferential adsorption of methanol is completely hindered when the lateral group is bulky enough. Similar results have been reported for substituted poly(phenyl methacrylate)s in the mixture tetrahydrofuran/water.

The description of these systems was not in agreement with predictions of classical thermodynamic theories.[39,103-105]

This behavior was analyzed in terms of specific interactions among the components of the ternary system. If the oxygen atoms of 1,4-dioxane can interact specifically with methanol by accepting a proton, then, methanol hydrogen bonds not only to poly(methacrylate)s but also to 1,4-dioxane. The new theoretical formation takes into account the case of solvent which is self-associated and interacts specifically with sites in the polymer chain and with sites in the other solvent molecule. Therefore, it must consider association constants of the solvent molecule and association constants of the self-associated-solvent (2) with (3) the polymer. It was assumed that the polymer molecule has one site for specific interactions with 2, that the constant for such specific interaction between one 2 molecule and one sites is η_1 and that the self-association of 2 over the 2 molecule attached to a site in 3 is characterized by constant σ_2, η_2 or σ_2 values, or both, should vary from polymer to polymer depending on the size of the substituent pending from the ester group. In addition, also association constants of 2 with the other solvent molecule (1) have been postulated. These are: η_1 and σ_1. The number of sites on molecule 1 was called t. The constant for the specific interaction of one 2 molecule with one site in 1 is η_1, and the self-association of 2 over the already attached 2 molecule is σ_1. With all these constants a quantitative description of the experimental results for the three poly(alkyl methacrylates) (alkyl + Me, Et, iBu) in 1,4-dioxane/methanol was reported.[106] In conclusion, the theory applied by Pouchly and Zivny to the simpler case in which one of the liquids is inert, was extended to more complex mixture.[106]

Table 5.4.4 summarizes the glossary of association constants and interaction parameters used in the theory in the case of poly(alkyl methacrylates). The results that are obtained for the minimum standard deviation in each case are shown on Table 5.4.4.

Table 5.4.4. Parameter values giving the minimum deviation (δ) between theory and experiment, for the preferential adsorption coefficient, λ, calculated according to the Association Equilibria Theory. Reprinted with permission from Horta et al.[106] (Copyright (1989) American Chemical Society)

	Polymer	σ	gBA'	η_a	σ_c	gAC'-r rAgBC'	η_c	δ
1	**PMMA**	400	0.85	244	400	0.0	5.7	0.034
2	**PEMA**	400	0.85	244	400	-1.2	59.3	0.028
3	**PiBMA**	400	0.85	244	400	-2.3	129.5	0.018
4	**PMMA**	400	0.30	100	400	-3.4	243.2	0.013
5	**PEMA**	400	0.30	100	400	-2.75	169.2	0.014
6	**PiBMA**	400	0.30	100	400	-1.6	188.2	0.009
7	**PMMA**	400	0.85	244	375	-0.1	11.2	0.034
8	**PEMA**	400	0.85	244	375	-2.2	145.4	0.028
9	**PiBMA**	400	0.85	244	375	-1.6	100.7	0.035
10	**PMMA**	400	0.30	100	375	-2.45	195.5	0.013
11	**PEMA**	400	0.30	100	375	-1.75	125.0	0.016
12	**PiBMA**	400	0.30	100	375	-0.5	45.6	0.016

The results obtained are a good description of the experimental data on these ternary systems. Effectively, the shape of the variation of λ with solvent composition was well reproduced by the association equilibria theory, as it is shown in Figure 5.4.2.

It has extended the same theoretical treatment to other closely related systems, a family of poly(dialkyl itaconates).[107] Preferential adsorption coefficient λ was determined and calculated according to the association equilibria theory, and using classical thermodynamic theories.[108,103,104,105]

The dependence of the preferential adsorption coefficient for poly(dimethyl itaconate) (PDMI), poly(diethyl itaconate) (PDEI), poly(dipropyl itaconate) (PDPI) and poly(dibutyl itaconate) (PDBI), in 1,4-dioxane/methanol mixtures, as a function of the methanol composition (u_{BO}) is shown in Figure 5.4.3. The results are very similar to those of poly(alkyl methacrylates) in the same solvent.[106]

Comparison between theory and experimental for λ, by using classical thermodynamic theories[103-105,108] are shown in Figure 5.4.4.

The results obtained are a good description of the experimental data on these ternary systems. Effectively, the shape of the variation of λ with solvent composition was well reproduced by the association equilibria theory. It can be concluded that the association equilibria theory of preferential adsorption in systems with solvent-solvent and solvent-polymer interactions describe in a quantitative way the experimental results of λ. Although, the systems in which the theory has been applied are closely related. More recently, there was no other systems studied to apply this theory.

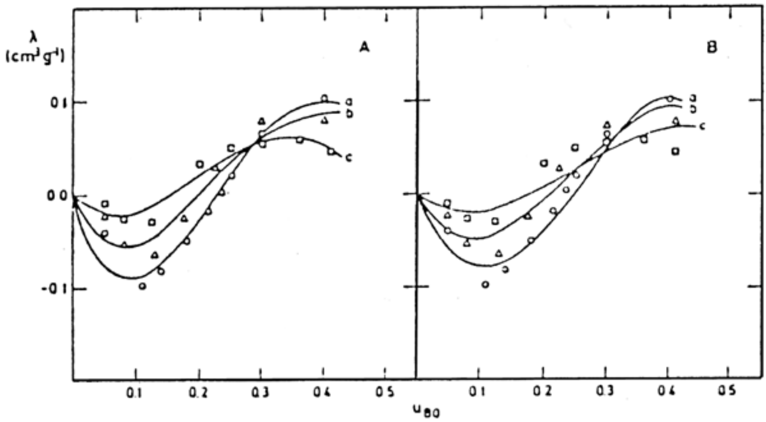

Figure 5.4.2. Comparison of theory and experiment for preferential adsorption coefficient, λ, of poly(alkyl methacrylate)s in 1,4-dioxane-methanol. (u_{BO}=methanol volume fraction). Points: Experimental results from ref.[6]. (O) PMMA (alkyl = Me); (Δ) PEMA (Et); (☐) PiBMA (iBu). Association equilibria theory. (8A) Calculated with the parameter values shown in Table 5.4.4 and numbered as 4-6. Curves: (a) PMMA; (b) PEMA; c) PiBMA. (7B) Calculated with the parameter values shown in Table 5.4.4 and numbered as 10-12. Curves: (a) PMMA; (b) PEMA; c) PiBMa. Reprinted with permission from Horta et al.[106] (Copyright (1989) American Chemical Society).

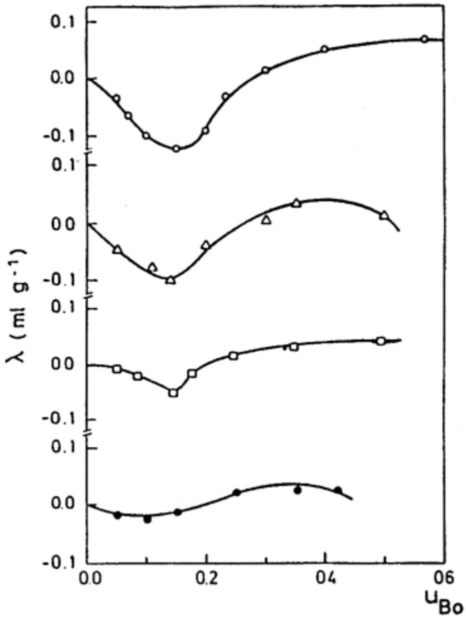

Figure 5.4.3. Variation of preferential adsorption coefficient, λ, as function of methanol volume fraction u_{BO}, for PDMI (O), PDEI (Δ), PDPI (☐), and PDBI (●), at 298 K. Reprinted with permission from Horta et al.[107] (Copyright (1990) American Chemical Society).

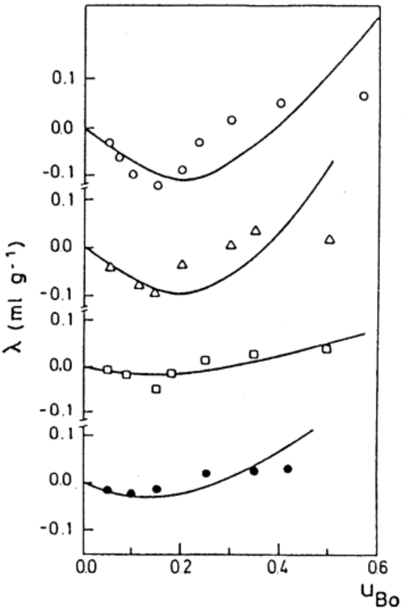

Figure 5.4.4. Comparison between theory and experiment for the preferential adsorption coefficient, λ, by using classical thermodynamic theories.[103] Points: experimental result of λ. Curves: classical thermodynamic theories.[108] Reprinted with permission from Horta et al.[107] (Copyright (1990) American Chemical Society).

5.4.5 POLYMER STRUCTURE OF THE POLYMER DEPENDENCE OF PREFERENTIAL ADSORPTION. POLYMER MOLECULAR WEIGHT AND TACTICITY DEPENDENCE OF PREFERENTIAL ADSORPTION

There are some important structural aspects of the polymer which are necessary to take into account in the analysis of the polymer behavior in mixture solvents, such as its polarity, chemical structure, microtacticity, molecular weight. The analysis of these properties shows that they are determinant factors in preferential adsorption phenomena involved. It has been pointed out[73] that the effect of tacticity, and particularly the molecular weight, is a complex problem. In the case of poly(2-vinylpyridine), when the polar solvent is preferentially adsorbed, preferential solvation is independent of molecular weight; but when the non-polar solvent is adsorbed, there is a dependence on the molecular weight.[62]

The reported experimental evidence[109-111,67,73,77] seems to show that the coefficient of preferential adsorption λ, for a given polymer in a mixed solvent of fixed composition depends on molecular weight of the polymer sample. It is important to remember, however, that this dependence of λ on M has not been always detected. Particularly for molecular weights lower than a certain value.[100,111,91]

According to Dondos and Benoit,[109] Read,[104] and Hertz and Strazielle,[112] the dependence of preferential adsorption coefficient λ, with molecular weight or with segment density can be expressed empirically as:

$$\lambda = \lambda_\infty + AM^{-1/2} \tag{5.4.4}$$

or

$$\lambda = \lambda_\infty + K[\eta]^{-1} \tag{5.4.5}$$

where:

λ_∞	the value of λ extrapolated to $M \to \infty$
$[\eta]$	the intrinsic viscosity
A and K	constants

It is interesting to note that the variation of λ with M is more pronounced. A in equation [5.4.4] is larger in mixtures which are poor solvents close to θ-conditions than in mixtures with excluded volume.[109,111,112]

Apparently, there will not be exhaustive results either with the chemical structure of the polymer on the preferential adsorption,[113] or the influence of the tacticity on the preferential adsorption. In the last years, investigations regarding the effect of ortho-substituents in polymers with aromatic bulky side groups on the preferential adsorption and viscometric behavior have been reported for poly(phenyl methacrylate) and its dimethyl and diisopropyl ortho derivatives in tetrahydrofuran/water.[114] Figure 5.4.5 from ref.[114] shows the λ values for three polymers in THF/water.

The λ values diminish when the volume of the side groups increases and there is a strong water adsorption. The behavior reported[114] indicates that the cosolvent effect decreases or disappears when the preferential adsorption is very small or is not observed.[114]

In another publication,[102] the systems studied were a series of poly(alkyl methacrylates) including the methyl (PMMA), ethyl (PEMA), isobutyl (PiBMA) and cyclohexyl (PCHMA) substituents in the mixture solvent 1,4-dioxane/methanol. The experimental results[113] indicate that the size of the substituents on the polymer ester group exerts an influence on the specific interaction between the methanol molecule and the carbonyl of the ester. It has been shown that the preferential adsorption of methanol is completely hindered when the lateral groups are bulky enough.

Several attempts have been made to take into account the geometrical character of the polymer segment and the solvent molecule. None of them seems to give a unique explanation for the experimental results about the cosolvent effect.

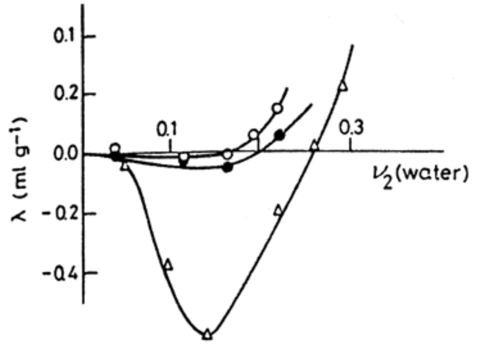

Figure 5.4.5. Variation of the preferential adsorption as a function of solvent composition (Δ) PPh (Gargallo et al., 1984): (●) PDMPh: (O) PDPPh. From Gargallo et al.[114] (Copyright by Springer Verlag, used with permission).

The most important task in the field of research on ternary systems polymer in binary solvents is to examine the state of the macromolecular chain in solution and the analysis of the changes in solubility and then in composition involved in the total system itself.

The goal of this review was to present aspects of the preferential adsorption phenomena of solvents and polymers with a focus on their thermodynamic aspects. The idea behind this was to attract the attention of polymeric physico-chemists to this area, which is sufficiently related to a lot of different effects. In fact, preferential adsorption occupies a special place in the solubility of polymers in mixed solvents.

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5.5 THE PHENOMENOLOGICAL THEORY OF SOLVENT EFFECTS IN MIXED SOLVENT SYSTEMS

KENNETH A. CONNORS
School of Pharmacy, University of Wisconsin, Madison, USA

5.5.1 INTRODUCTION

We do not lack theories dealing with solvent effects on chemical and physical processes, as is made clear by other sections and authors in the present book. Some of these theories are fundamental in the sense that they invoke detailed physical descriptions of molecular phenomena (electrostatic interactions or the dispersion interaction, for example) whereas others are extensively empirical (such as the UNIQUAC and UNIFAC schemes for estimating activity coefficients, or extrathermodynamic correlations with model processes, exemplified by the Dimroth-Reichardt E_T value). Given the abundance of theoretical and empirical approaches, it might seem that new attacks on the general problem of solvent effects would be superfluous. Yet when a solvent effect problem (in particular a solubility problem) arises, the extant theories often are in some measure inadequate. The empirical approaches tend to constitute special rather than general methods of attack, and the physical theories are either too complexly detailed or must be overly simplified to be usable. (It should be noted that our present concern is dominated by an interest in pharmaceutical systems, and therefore by aqueous and mixed aqueous solvents). The consequence is that a chemist or pharmacist confronted with a solubility problem (and such problems usually arise in situations allowing little commitment of time to the problem) often finds it more fruitful to solve the problem experimentally rather than theoretically. This is perfectly valid, but seldom does the solution lead to deeper understanding, and moreover the time required for the experimental effort may be excessive. Another factor is the frequent availability of only milligram quantities of material. It is these considerations that led to the development of this phenomenological theory of solvent effects in mixed aqueous-organic solvent systems. The theory is termed "phenomenological" because it includes elements of description such as equilibrium constants whose evaluation is carried out experimentally, yet it is based on physicochemical ideas.

5.5.2 THEORY

In the following development, the symbol x represents mole fraction, c is the molar concentration, component 1 is water, component 2 is a water-miscible organic cosolvent, and component 3 is the solute.

5.5.2.1 Principle

Before we can carry out any solution chemistry we must have a solution, and so we begin with the process of dissolution of a solid solute in a liquid solvent (which may itself be a mixture), the system being at equilibrium at constant temperature T.[1] The experimentally measured equilibrium solubility of the solute is x_3. Eq. [5.5.1] gives the free energy of solution per molecule, where k is the Boltzmann constant.

$$\Delta G^{*}_{soln} = kT \ln x_3 \qquad [5.5.1]$$

Conventionally the standard free energy of solution is given by eq. [5.5.2],

$$\Delta G^{0}_{soln} = kT \ln a_3 \qquad [5.5.2]$$

where a_3 is the mole fraction solute activity. Since we can write $a_3 = f_3x_3$, eq. [5.5.3] relates ΔG^{*}_{soln} and ΔG^{0}_{soln}.

$$\Delta G^{*}_{soln} = \Delta G^{0}_{soln} + kT \ln f_3 \qquad [5.5.3]$$

The traditional approach would be to develop a theory for the activity coefficient f_3, which measures the extent of nonideal behavior. This seems to be a very indirect manner in which to proceed, so we will henceforth make no use of activity coefficients, but instead will develop an explicit model for ΔG^{*}_{soln}.

The general principle is to treat ΔG^{*}_{soln} as the sum of contributions from the three types of pairwise interactions: solvent-solvent interactions, which give rise to the *general medium effect*; solvent-solute interactions, or the *solvation effect*; and solute-solute interactions (the *intersolute effect* in the present context). Thus we write.

$$\Delta G^{*}_{soln} = \Delta G_{gen\,med} + \Delta G_{solv} + \Delta G_{intersol} \qquad [5.5.4]$$

Our problem is to develop explicit expressions for the solvent-dependent quantities on the right-hand side of eq. [5.5.4].

5.5.2.2 The intersolute effect: solute-solute interactions

There are two contributions to the intersolute effect. One of these comes from solute-solute interactions in the pure solute, which for solid solutes constitutes the crystal lattice energy. We will make the assumption that this contribution is independent of the nature (identity and composition) of the solvent. Usually this is a valid assumption, but exceptions are known in which the composition of the solid depends upon the composition of the solvent. Theophylline, for example, forms a hydrate in water-rich solvents, but exists as the anhydrous form in water-poor solvents; thus its crystal energy varies with the solvent composition.[2-4] Although the final theory is capable of empirically describing the solubility of such systems, it lacks a valid physical interpretation in these cases. Fortunately such solid solute behavior is not common, and our assumption that the pure solute interaction energy is solvent-independent is usually a good one.

The second contribution to the intersolute effect comes from solute-solute interactions in the solution phase. In pharmaceutics our motivation for incorporating organic solvents into an aqueous system commonly arises from an unacceptably low equilibrium solubility of a drug in pure water. This means that in water and in water-rich mixed solvents the extent of solution phase solute-solute interactions will be negligible because the solute concentration is in the extremely dilute range. At higher concentrations of the organic cosolvent it is true that the solute concentration may rise well above the dilute range, but in some degree this is offset by the diminished tendency for solute-solute interaction in such systems. Thus the hydrophobic interaction is sharply decreased by incorporating organic cosolvents. We will recognize these solution phase solute-solute interactions as a possible source of perturbation in our theory because of our assumption either that they are negligible, or that they do not vary with solvent composition.

5.5.2.3 The solvation effect: solute-solvent interaction

Our approach is to treat solvation as a stoichiometric equilibrium process. Let W symbolize water, M an organic cosolvent, and R the solute. Then we postulate the 2-step (3-state) system shown below.

$$RW_2 + M \xrightleftharpoons{K_1} RWM + W \qquad [5.5.5]$$

$$RWM + M \xrightleftharpoons{K_2} RM_2 + W \qquad [5.5.6]$$

In this scheme K_1 and K_2 are dimensionless solvation equilibrium constants, the concentrations of water and cosolvent being expressed in mole fractions. The symbols RW_2, RWM, RM_2 are not meant to imply that exactly two solvent molecules are associated with each solute molecule; rather RW_2 represents the fully hydrated species, RM_2 the fully cosolvated species, and RWM represents species including both water and cosolvent in the solvation shell. This description obviously could be extended, but experience has shown that a 3-state model is usually adequate, probably because the mixed solvate RWM cannot be algebraically (that is, functionally) differentiated into sub-states with data of ordinary precision.

Now we further postulate that the solvation free energy is a weighted average of contributions by the various states, or

$$\Delta G_{solv} = \Delta G_{WW} F_{WW} + \Delta G_{WM} F_{WM} + \Delta G_{MM} F_{MM} \qquad [5.5.7]$$

where F_{WW}, F_{WM}, and F_{MM} are fractions of solute in the RW_2, RWM, and RM_2 forms, respectively. Eq. [5.5.7] can be written

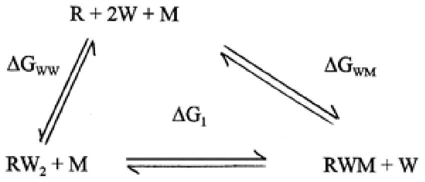
$$\Delta G_{solv} = (\Delta G_{WM} - \Delta G_{WW}) F_{WM} + (\Delta G_{MM} - \Delta G_{WW}) F_{MM} + \Delta G_{WW} \qquad [5.5.8]$$

By combining definitions of K_1, K_2, F_{WM}, and F_{MM} we get

$$F_{WM} = \frac{K_1 x_1 x_2}{x_1^2 + K_1 x_1 x_2 + K_1 K_2 x_2^2} \qquad F_{MM} = \frac{K_1 K_2 x_2^2}{x_1^2 + K_1 x_1 x_2 + K_1 K_2 x_2^2} \qquad [5.5.9]$$

for use in eq. [5.5.8]

Now observe this thermodynamic cycle [5.5.10]:



From this cycle we get

$$\Delta G_1 = \Delta G_{WM} - \Delta G_{WW} = -kT \ln K_1 \qquad [5.5.11]$$

A similar cycle yields eq. [5.5.12].

$$\Delta G_2 = \Delta G_{MM} - \Delta G_{WW} = -kT \ln K_1 K_2 \tag{5.5.12}$$

Combination of eqs. [5.5.8] - [5.5.12] then gives

$$\Delta G_{solv} = \frac{(-kT \ln K_1) K_1 x_1 x_2 + (-kT \ln K_1 K_2) K_1 K_2 x_2^2}{x_1^2 + K_1 x_1 x_2 + K_1 K_2 x_2^2} + \Delta G_{ww} \tag{5.5.13}$$

Obviously when $x_2 = 0$, $\Delta G_{solv} = \Delta G_{WW}$.[5] Eq. [5.5.13] is the desired expression relating the solvation energy to the solvent composition.

5.5.2.4 The general medium effect: solvent-solvent interactions

Here we make use of Uhlig's model,[6] writing eq. [5.5.14] as the energy required to create a molecular-sized cavity in the solvent.

$$\Delta G_{gen\,med} = gA\gamma \tag{5.5.14}$$

In eq. [5.5.14] g is a curvature correction factor, an empirical quantity that corrects the conventional surface tension γ for the curvature of the cavity needed to contain a solute molecule. A is the surface area of this cavity in Å^2 molecule^{-1}; in Sections 5.5.3 and 5.5.4 we treat the meaning of A in more detail, but here we only make the assumption that it is essentially constant, that is, independent of x_2.

There is a subtlety in assigning the value of γ, for implicit in our model (but treated more fully in reference 1) is the condition that the γ of eq. [5.5.14] is the surface tension of the cavity surface at its equilibrium composition. But this is the composition of the solvation shell immediately adjacent to the molecule, and this is in general different from the composition (x_1, x_2) of the bulk solvent mixture. Let f_1 and f_2 be the equilibrium mean fractional concentrations of water and cosolvent, respectively, in the solvation shell, so $f_1 + f_2 = 1$. These fractions are defined

$$f_1 = \frac{1}{2}(2F_{WW} + F_{WM}) \tag{5.5.15}$$

$$f_2 = \frac{1}{2}(F_{WM} + 2F_{MM}) \tag{5.5.16}$$

Now we define, for use in eq. [5.5.14],

$$\gamma = \gamma_1 f_1 + \gamma_2 f_2 \tag{5.5.17}$$

$$\gamma = \gamma_1 + (\gamma_2 - \gamma_1) f_2 \tag{5.5.18}$$

where γ_1 and γ_2 are the surface tensions of pure component 1 (water) and 2, respectively. Combining eqs. [5.5.14, 5.5.16, and 5.5.18] gives for the general medium effect

$$\Delta G_{gen\,med} = gA\gamma_1 + \frac{gA\gamma' K_1 x_1 x_2 + 2gA\gamma' K_1 K_2 x_2^2}{x_1^2 + K_1 x_1 x_2 + K_1 K_2 x_2^2} \tag{5.5.19}$$

where $\gamma' = (\gamma_2 - \gamma_1)/2$. Notice that the general medium and solvation effects are coupled through the solvation constants K_1 and K_2.

When $x_2 = 0$, eq. [5.5.19] yields $\Delta G_{gen\,med} = gA\gamma_1$. We interpret this as a quantitative expression for the *hydrophobic effect*. In general, eq. [5.5.19] describes the solvophobic effect. This is a phenomenological description, not a detailed structural description.

5.5.2.5 The total solvent effect

The solution free energy is now obtained by inserting eqs. [5.5.13] and [5.5.19] into eq. [5.5.4]. We obtain

$$\Delta G^*_{soln}(x_2) = gA\gamma_1 + \Delta G_{intersol} + \Delta G_{WW}$$
$$+ \frac{(gA\gamma' - kT\ln K_1)K_1x_1x_2 + (2gA\gamma' - kT\ln K_1K_2)K_1K_2x_2^2}{x_1^2 + K_1x_1x_2 + K_1K_2x_2^2} \qquad [5.5.20]$$

When $x_2 = 0$, eq. [5.5.20] gives

$$\Delta G^*_{soln}(x_2 = 0) = gA\gamma_1 + \Delta G_{intersol} + \Delta G_{WW} \qquad [5.5.21]$$

With the Leffler-Grunwald delta operator symbolism[7] we define

$$\delta_M \Delta G^* = \Delta G^*_{soln}(x_2) - \Delta G^*_{soln}(x_2 = 0) \qquad [5.5.22]$$

which, applied to eqs. [5.5.20] and [5.5.21], gives our final result:

$$\delta_M \Delta G^*_{soln} = \frac{(gA\gamma' - kT\ln K_1)K_1x_1x_2 + (2gA\gamma' - kT\ln K_1K_2)K_1K_2x_2^2}{x_1^2 + K_1x_1x_2 + K_1K_2x_2^2} \qquad [5.5.23]$$

The quantity $\delta_M\Delta G^*_{soln}$ can be read “the solvent effect on the solution free energy.” Because of eq. [5.5.1], $\delta_M\Delta G^*$ is proportional to the “relative solubility,” $\log[(x_3)_{x_2} / (x_3)_{x_2=0}]$, that is, the logarithm of the solubility in the mixed solvent of composition x_2 relative to the solubility in pure water. The subtraction that yields eq. [5.5.23], a workable equation with just three unknown parameters (gA, K_1, and K_2), has also prevented us from dealing with absolute solubilities.

5.5.3 APPLICATIONS

5.5.3.1 Solubility

It will be no surprise that the first use of eq. [5.5.23] was to describe the equilibrium solubility of solid nonelectrolytes in mixed aqueous-organic solvents.[1] Equilibrium solubility in mol L^{-1}, c_3, is converted to mole fraction, x_3, with eq. [5.5.24], where ρ is the saturated solution density, w is the wt/wt percentage of organic cosolvent, and M_1, M_2, M_3 are the molecular weights of water, cosolvent, and solute.[8]

$$x_3 = \frac{c_3}{c_3(1000\rho - c_3M_3)\left(\frac{w}{M_2} + \frac{(1-w)}{M_1}\right)} \qquad [5.5.24]$$

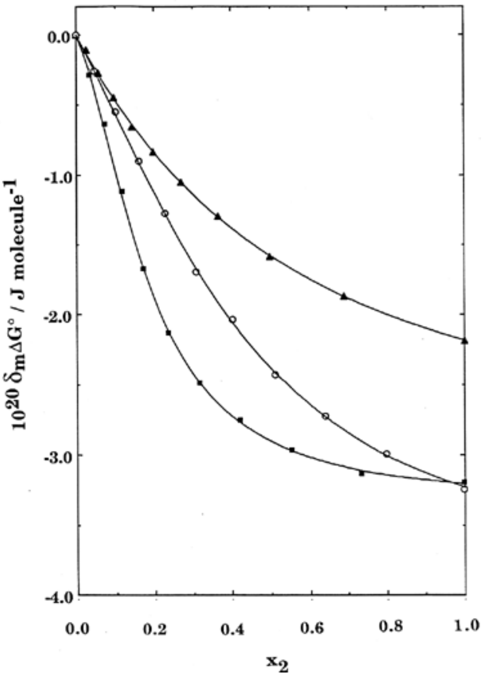


Figure 5.5.1. Solvent effect on the solubility of diphenylhydantoin. Cosolvents, top to bottom: glycerol, methanol, ethanol. The smooth lines were drawn with eq. 5.5.23. (Reproduced with permission from the *Journal of Pharmaceutical Sciences* reference 1.)

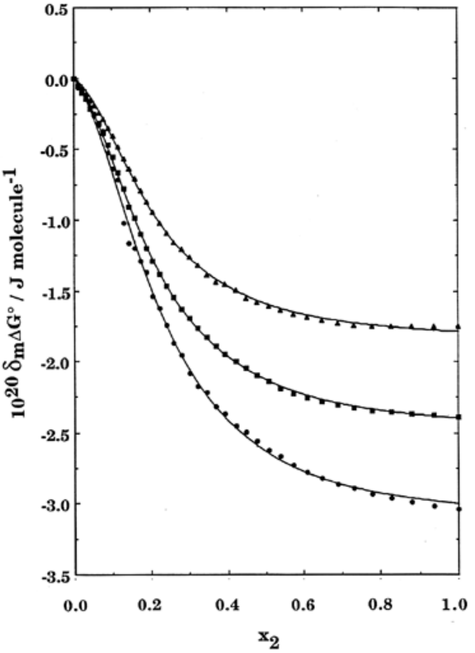


Figure 5.5.2. Solvent effect on the solubilities of barbituric acid derivatives in ethanol-water mixtures. Top to bottom: metharbital, butabarbital, amobarbital. The smooth lines were drawn with eq. 5.5.23. (Reproduced with permission from the J*ournal of Pharmaceutical Sciences*, reference 1.)

The free energy of solution per molecule is then calculated with eq. [5.5.1], $\delta_M\Delta G^*$ is found with eq. [5.5.22], and $\delta_M\Delta G^*$ as a function of x_2 is fitted to eq. [5.5.23] by nonlinear regression, with gA, K_1, and K_2 being treated as adjustable parameters.[9] Figures 5.5.1 and 5.5.2 show some results.[1]

Clearly eq. [5.5.24] possesses the functional flexibility to describe the data. (In some systems a 1-step (2-state) equation is adequate. To transform eq. [5.5.24] to a 1-step version, set $K_2 = 0$ and let $\gamma' = \gamma_2 - \gamma_1$.) The next step is to examine the parameter values for their possible physical significance. It seems plausible that K_1 and K_2 should be larger than unity, but not "very large," on the basis that the solutes are organic and so are the cosolvents, but the cosolvents are water-miscible so they are in some degree "water-like." In fact, we find that nearly all K_1 and K_2 values fall between 1 and 15. Likewise the gA values seem, in the main, to be physically reasonable. Earlier estimates of g (reviewed in ref.[1]) put it in the range of 0.35-0.5. A itself can be estimated as the solvent-accessible surface area of the solute, and many of the gA values found were consistent with such estimates, though some were considerably smaller than expected. Since gA arises in the theory as a hydrophobicity parameter, it seemed possible that A in the equation represents only the nonpolar surface area of the molecule. An experiment whose results are summarized in Table 5.5.1 was designed to examine this possibility.[10]

Table 5.5.1. Surface area estimates of biphenyls[10]

Compound	A_{total}	$A_{nonpolar}$	gA
Biphenyl	179 (3)	179 (3)	74 (0.6)
4-Hydroxybiphenyl	185 (4)	155 (7)	69 (0.3)
4,4'-Dihydroxybiphenyl	203 (5)	126 (7)	53 (0.5)
4-Bromobiphenyl	217 (7)	217 (7)	87 (1.4)

Areas in Å^2 molecule; standard deviations in parentheses. The cosolvent was methanol.

Evidently the experimental gA estimate is correlated with $A_{nonpolar}$ rather than with A_{total}, and the linear relationship yields the estimate g = 0.37. On the other hand, there was evidence[1] that g depends upon cosolvent identity (for a given solute), and LePree and Mulski[8,11] examined this possibility. Their findings led to an empirical but quite general correlation between gA and properties of the cosolvent and solute:

$$gA = -42 \log P_M + 11 \log P_R \tag{5.5.25}$$

In eq. [5.5.25] P_M is the 1-octanol/water partition coefficient of the pure organic cosolvent and P_R is the partition coefficient of the solute. Table 5.5.2 gives examples of the application of eq. [5.5.25].

Table 5.5.2 Experimental and calculated gA values[8,11]

Solute	Solvent	gA, Å^2 molecule^{-1}	
		Calculated	Observed
Naphthalene	Methanol	66	63
Naphthalene	Ethanol	48	54
Naphthalene	2-Propanol	35	43
Naphthalene	1,2-Propanediol	92	71
Naphthalene	1,2-Ethanediol	116	102
Naphthalene	Acetone	45	69
Naphthalene	DMSO	120	127
4-Nitroaniline	Methanol	46	35
4-Nitroaniline	Ethanol	29	21
4-Nitroaniline	2-Propanol	15	11
4-Nitroaniline	1,2-Ethanediol	96	84
4-Nitroaniline	Acetone	25	37

Solute	Solvent	gA, Å^2 molecule^{-1}	
		Calculated	Observed
4-Nitroaniline	DMSO	101	86
4-Nitroaniline	Acetonitrile	30	29

We now encounter a curious observation. The parameter gA is constrained, in the nonlinear regression fitting program, to be constant as x_2 varies over its entire range from 0 to 1. We have identified A as the nonpolar surface area of the solute (though it may actually be the corresponding area of the solvent cavity, and so may show some cosolvent dependency, which we have ignored). The quantity g can then be estimated. For example, from Table 5.5.2 for naphthalene (A = 147 Å^2 molecule^{-1}), g varies from 0.29 (for 2-propanol) to 0.86 (for DMSO). Yet how can g possess these different values in different cosolvents, maintain its constancy as x_2 varies, and then collapse to the unique value it must possess in water, the reference solvent for all systems? An independent calculation gives g = 0.41±0.03 in water.[8] Some tentative explanations for this puzzle have been offered,[8] and we return to this issue in Section 5.5.4.

Turning to the K_1 and K_2 parameters, we have observed that these are relatively insensitive to the identity of the solute, but that they depend upon the cosolvent, whose polarity is a controlling factor. Table 5.5.3 gives some empirical correlations that provide routes to the prediction of K_1 and K_1K_2. In Table 5.5.3, P_M is the 1-octanol/water partition coefficient of the pure cosolvent,[12] and E_T is the Dimroth-Reichardt solvatochromic polarity parameter.[13] We thus have the capability of predicting gA, K_1, and K_1K_2, which extends the utility of eq. [5.5.23] from the merely descriptive to the predictive.

Table 5.5.3. Empirical relationships for estimating solvation constants

Equation	n	r	Restrictions
$\log K_1 = -0.0316\ E_T + 2.24$	10	0.91	-
$\log (K_1/K_2) = 0.0171\ E_T - 9.23$	4	0.98	$E_T > 51$
$\log (K_1/K_2) = -0.0959\ E_T + 4.60$	6	0.85	$E_T < 52$
$\log K_1K_2 = 1.31 \log P_M + 1.81$	6	0.91	$\log P_M > -1.0$

5.5.3.2 Surface tension

In the development of the basic phenomenological model, eq. [5.5.23], we derived a relationship for the surface tension of the solvation shell. Combining eqs. [5.5.16] and [5.5.18] yields

$$\gamma = \gamma_1 + \gamma' \left[\frac{K_1 x_1 x_2 + 2K_1 K_2 x_2^2}{x_1^2 + K_1 x_1 x_2 + K_1 K_2 x_2^2} \right] \qquad [5.5.26]$$

where $\gamma' = (\gamma_2 - \gamma_1)/2$. Now if we identify the solute-solvation shell system with the air-solvent interface, we are led to test eq. [5.5.26] as a description of the composition dependence

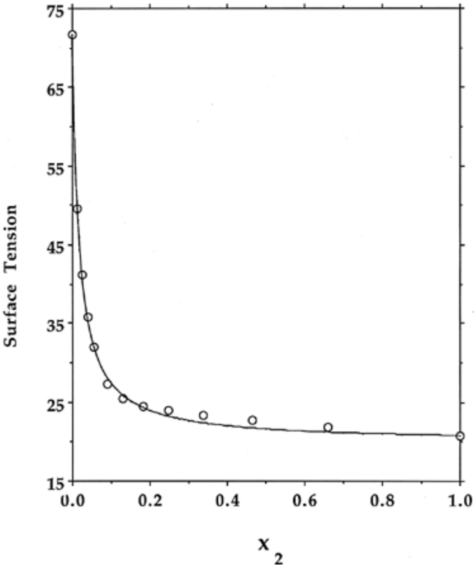


Figure 5.5.3. Surface tension of 2-propanol-water mixtures. The smooth line is drawn with eq. 5.5.26. (Reproduced with permission from the *Journal of Solution Chemistry*. reference 14.)

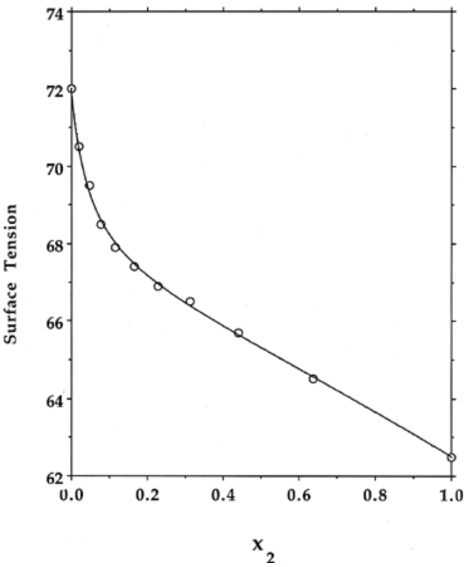


Figure 5.5.4. Surface tension of glycerol-water mixtures. The smooth line is drawn with eq. 5.5.26. (Reproduced with permission from the *Journal of Solution Chemistry*. reference 14.)

of surface tension in mixed solvent systems, air playing the role of the solute. Figures 5.5.3 and 5.5.4 show examples of these curve-fits.[14]

When $K_2 = 0$, eq [5.5.26] gives the 1-step model, eq. [5.5.27], where $\gamma' = \gamma_2 - \gamma_1$.

$$\gamma = \gamma_1 + \gamma' \left[\frac{K_1 x_2}{x_1 + K_1 x_2} \right] \qquad [5.5.27]$$

We had earlier[15] published an equation describing the dependence of surface tension on composition, and a comparison of the two approaches has been given;[14] here we will restrict attention to eqs. [5.5.26] and [5.5.27].

Suppose we set $K_1 = 2$ and $K_2 = 1/2$ in eq. [5.5.26]. This special condition converts eq. [5.5.26] to

$$\gamma = \gamma_1 x_1 + \gamma_2 x_2 \qquad [5.5.28]$$

which corresponds to ideal behavior; the surface tension is a linear function of x_2. The restriction $K_1 = 2$, $K_2 = 1/2$ is, however, a unique member of a less limited special case in which $K_1 = 4K_2$. This important condition (except when it happens to occur fortuitously) implies the existence of two identical and independent binding sites.[16] Inserting $K_2 = K_1/4$ into eq. [5.5.26] yields, upon simplification, eq. [5.5.29], where $\gamma' = \gamma_2 - \gamma_1$.

$$\gamma = \gamma_1 + \gamma' \left[\frac{(K_1 / 2) x_2}{x_1 + (K_1 / 2) x_2} \right] \qquad [5.5.29]$$

Eq. [5.5.29] will be recognized as equivalent to eq. [5.5.27] for the 1-step model. The interpretation is as follows: the 2-step model, eq. [5.5.26], can always be applied, but if the result is that $K_1 \approx 4K_2$ the 1-step model will suffice to describe the data. Moreover, if $K_1 \approx 4K_2$ from the 2-step treatment, no physical significance is to be assigned to the second parameter.

These considerations are pertinent to real systems. Table 5.5.4 lists K_1 and K_2 values obtained by applying eq. [5.5.26] to literature data.[15] Several systems conform reasonably to the $K_1 \approx 4K_2$ condition. Recall that ideal behavior requires the special case $K_1 = 2$, $K_2 = 1/2$. The less restrictive condition $K_1 \approx 4K_2$ we call "well-behaved." Figure 5.5.3 shows a well-behaved system; Figure 5.5.4 shows one that is not well-behaved. The distinction is between a hyperbolic dependence on x_2 (well-behaved) and a non-hyperbolic dependence.

Table 5.5.4. Solvation parameter estimates for surface tension data according to eq. [5.5.26]

Cosolvent	K_1	K_2	K_1/K_2
Methanol	19.8	2.9	6.8
2-Propanol	130	29.4	4.4
1-Propanol	232	50	4.6
t-Butanol	233	65	3.6
Acetic acid	115	2.7	42.6
Acetone	138	7.1	19.4
Acetonitrile	33.4	14.5	2.3
Dioxane	62.1	7.4	8.4
THF	136	25.9	5.3
Glycerol	22.7	0.80	28.4
DMSO	12.3	1.43	8.6
Formamide	5.52	2.57	2.1
Ethylene glycol	9.4	2.62	3.6

A further observation from these results is that some of the K_1 values are much larger than those encountered in solubility studies. Correlations with log P_M have been shown.[14]

5.5.3.3 Electronic absorption spectra

The energy of an electronic transition is calculated from the familiar equation

$$E_T = h\nu = \frac{hc}{\lambda} \qquad [5.5.30]$$

where h is Planck's constant, c is the velocity of light, v is frequency, and λ is wavelength. If λ is expressed in nm, eq. [5.5.31] yields E_T in kcal mol^{-1}.

$$E_T = 2.859 \times 10^4 / \lambda \qquad [5.5.31]$$

The phenomenological theory has been applied by Skwierczynski to the E_T values of the Dimroth-Reichardt betaine,[13] a quantity sensitive to the polarity of the medium.[17] The approach is analogous to the earlier development. We need only consider the solvation effect. The solute is already in solution at extremely low concentration, so solute-solute interactions need not be accounted for. The solvent cavity does not alter its size or shape during an electronic transition (the Franck-Condon principle), so the general medium effect does not come into play. We write E_T of the mixed solvent as a weighted average of contributions from the three states:

$$E_T(x_2) = F_{WW}E_T(WW) + F_{WM}E_T(WM) + F_{MM}E_T(MM) \qquad [5.5.32]$$

where the symbolism is obvious. Although $E_T(WW)$ can be measured in pure water and $E_T(MM)$ in pure cosolvent, we do not know $E_T(WM)$, so provisionally we postulate that $E_T(WM) = [E_T(WW) + E_T(MM)]/2$. Defining a quantity Γ by

$$\Gamma = \frac{E_T(x_2) - E_T(WW)}{E_T(MM) - E_T(WW)} \qquad [5.5.33]$$

we find, by combining eqs. [5.5.9], [5.5.10], and [5.5.32],

$$\Gamma = \frac{K_1 x_1 x_1 / 2 + K_1 K_2 x_2^2}{x_1^2 + K_1 x_1 x_2 + K_1 K_2 x_2^2} \qquad [5.5.34]$$

The procedure is to fit Γ to x_2. As before, a 1-parameter version can be obtained by setting $K_2 = 0$:

$$\Gamma = \frac{K_1 x_2}{x_1 + K_1 x_2} \qquad [5.5.35]$$

Figure 5.5.5 shows a system that can be satisfactorily described by eq. [5.5.35], whereas the system in Figure 5.5.6 requires eq. [5.5.34]. The K_1 values are similar in magnitude to those observed from solubility systems, with a few larger values; K_2, for those systems requiring eq. [5.5.34], is always smaller than unity. Some correlations were obtained of K_1 and K_2 values with solvent properties. Figure 5.5.7 shows log K_1 as a function of log P_M, where P_M is the partition coefficient of the pure organic solvent.

5.5.3.4 Complex formation.

We now inquire into the nature of solvent effects on chemical equilibria, taking noncovalent molecular complex formation as an example. Suppose species S (substrate) and L (ligand) interact in solution to form complex C, K_{11} being the complex binding constant.

$$S + L \xrightleftharpoons{K_{11}} C \qquad [5.5.36]$$

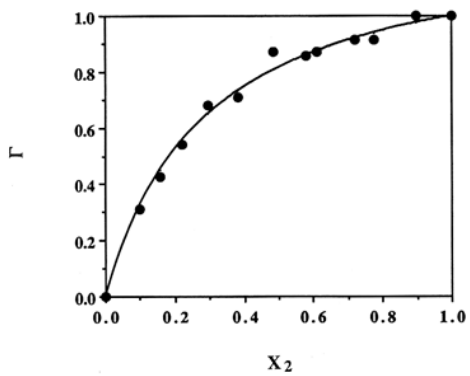


Figure 5.5.5. Dependence of E_T on composition for the methanol-water system. The smooth line was drawn with eq. 5.5.35. (Reproduced with permission from the *Journal of the Chemical Society. Perkin Transactions 2*, reference 17.)

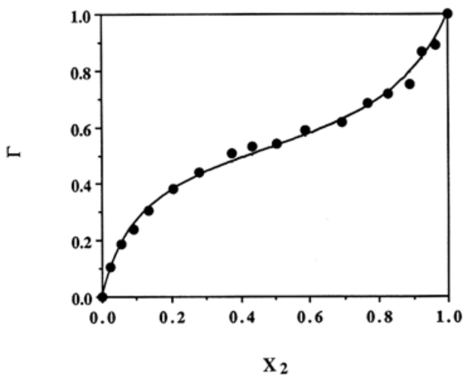


Figure 5.5.6. Dependence of E_T on composition for the acetone-water system. The smooth line was drawn with eq. 5.5.34. (Reproduced with permission from the *Journal of the Chemical Society. Perkin Transactions 2*,. reference 17.)

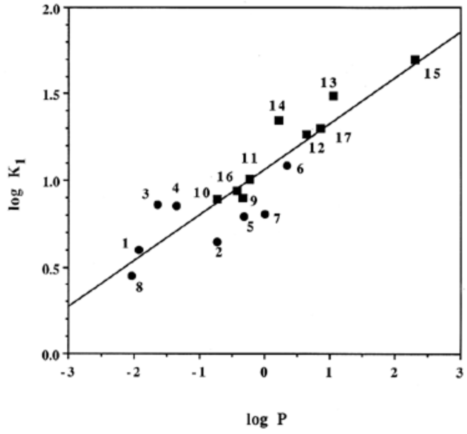


Figure 5.5.7. A plot of log K_1 from the E_T data against log P_M; the circles represent 1-step solvents (eq. 5.5.35) and the squares, 2-step solvents (eq. 5.5.34). (Reproduced with permission from the *Journal of the Chemical Society, Perkin Transactions 2*, reference 17.)

It is at once evident that this constitutes a more complicated problem than those we have already considered inasmuch as here we have three solutes. We begin with the thermodynamic cycles shown as Figure 5.5.8; these cycles describe complex formation in the solid, solution, and gas phases horizontally, and the energy changes associated with the indicated processes. ΔG_{latt} corresponds to the crystal lattice energy (solute-solute interactions), ΔG_{cav} represents the energy of cavity formation (identical with the general medium effect of Section 5.5.2). ΔG_{comp} is the free energy of complex formation, which in the solution phase is given by eq. [5.5.37].

$$\Delta G_{comp}(l) = -kT\ln K_{11} \quad [5.5.37]$$

Eq. [5.5.37] gives the free energy with respect to a 1M standard state, because the unit of K_{11} is M^{-1}. To calculate the unitary (mole fraction) free energy change we write, instead of eq. [5.5.37], eq. [5.5.38]:

$$\Delta G_{comp}(l) = -kT\ln\left(K_{11}M^{*}\rho\right) \qquad [5.5.38]$$

where M* is the number of moles of solvent per kg of solvent and ρ is the solution density. The unitary free energy does not include the entropy of mixing.

From cycle gl in Figure 5.5.8 we obtain eq. [5.5.39].

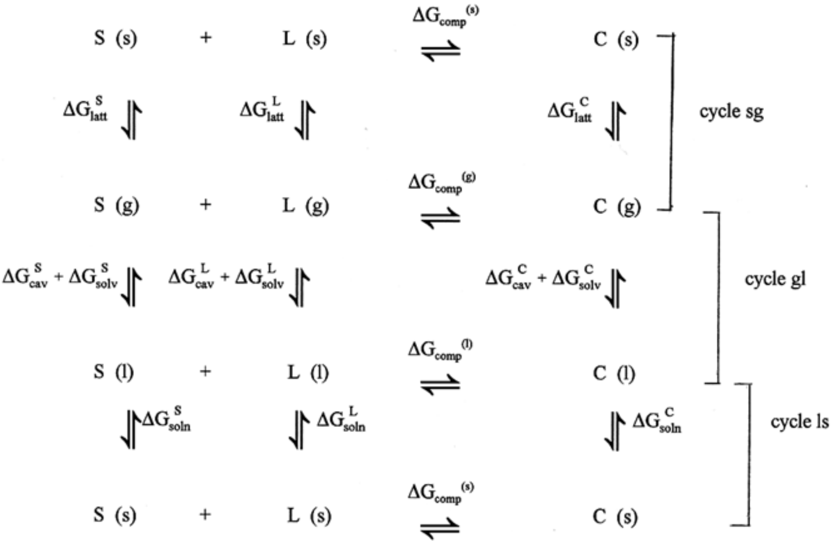


Figure 5.5.8. Thermodynamic cycles for bimolecular association. The symbols s, l, g represent solid, liquid, and gas phases; the superscripts refer to substrate S, ligand L, and complex C. (Reproduced with permission from the *Journal of Solution Chemistry*, reference 18.)

$$\Delta G_{comp}(g) + \left(\Delta G_{cav}^{C} + \Delta G_{solv}^{C}\right) - \Delta G_{comp}(l) - \left(\Delta G_{cav}^{L} + \Delta G_{solv}^{L}\right) - \left(\Delta G_{cav}^{S} + \Delta G_{solv}^{S}\right) = 0 \qquad [5.5.39]$$

We apply the δ_M operator to eq. [5.5.39]

$$\delta_M \Delta G_{cav}^{C} - \delta_M \Delta G_{cav}^{S} - \delta_M \Delta G_{cav}^{L} + \delta_M \Delta G_{solv}^{C} - \delta_M \Delta G_{solv}^{S} - \delta_M \Delta G_{solv}^{L} = \delta_M \Delta G_{comp}(l) \qquad [5.5.40]$$

where we have assumed $\delta_M \Delta G_{comp}(g) = 0$, which is equivalent to supposing that the structure of the complex (the spatial relationship of S and L) does not depend upon solvent composition, or that the intersolute effect is composition independent.

Also applying the δ_M treatment to eq. [5.5.4] gives

$$\delta_M \Delta G_{soln} = \delta_M \Delta G_{cav} + \delta_M \Delta G_{solv} \qquad [5.5.41]$$

for each species; recall that $\Delta G_{gen\ med}$ and ΔG_{cav} are identical. Use eq. [5.5.41] in [5.5.40]:

$$\delta_M \Delta G_{comp}(l) = \delta_M \Delta G_{soln}^{C} - \delta_M \Delta G_{soln}^{L} - \delta_M \Delta G_{soln}^{S} \qquad [5.5.42]$$

Eq. [5.5.42] says that the solvent effect on complex formation is a function solely of the solvent effects on the solubilities of reactants (negative signs) and product (positive sign). This is a powerful result, because we already have a detailed expression, eq. [5.5.23], for each of the three quantities on the right-hand side of eq. [5.5.42]. Thus the problem is solved in principle.[18]

In practice, of course, there are difficulties. Each of the $\delta_M \Delta G_{soln}$ terms contains three adjustable parameters, for nine in all, far too many for eq. [5.5.42] to be practicable in that form. We therefore introduce simplifications in terms of some special cases. The first thing to do is to adopt a 1-step model by setting $K_2 = 0$. This leaves a six-parameter equation, which, though an approximation, will often be acceptable, especially when the experimental study does not cover a wide range in solvent composition (as is usually the case). This simplification gives eq. [5.5.43].

$$\delta_M \Delta G^*_{comp} = \frac{(gA^C\gamma' - kT\ln K_1^C)K_1^C x_2}{x_1 + K_1^C x_2} - \frac{(gA^S\gamma' - kT\ln K_1^S)K_1^S x_2}{x_1 + K_1^S x_2} - \frac{(gA^L\gamma' - kT\ln K_1^L)K_1^L x_2}{x_1 + K_1^L x_2} \qquad [5.5.43]$$

Next, in what is labeled the *full cancellation approximation*, we assume $K_1^C = K_1^S = K_1^L = K_1$ and we write $\Delta gA = gA^C - gA^S - gA^L$. The result is

$$\delta_M \Delta G^*_{comp} = \frac{(kT\ln K_1 + \Delta gA\gamma')K_1 x_2}{x_1 + K_1 x_2} \qquad [5.5.44]$$

and we now have a 2-parameter model. The assumption of identical solvation constants is actually quite reasonable; recall from the solubility studies that K_1 is not markedly sensitive to the solute identity.

The particular example of cyclodextrin complexes led to the identification of another special case as the *partial cancellation approximation*; in this case we assume $K_1^C = K_1^S < K_1^L$, and the result is, approximately.[19]

$$\delta_M \Delta G^*_{comp} = \frac{(kT\ln K_1 - gA\gamma')K_1 x_2}{x_1 + K_1 x_2} \qquad [5.5.45]$$

Functionally eqs. [5.5.44] and [5.5.45] are identical; the distinction is made on the basis of the magnitudes of the parameters found. Note that gA in eq. [5.5.45] is a positive quantity whereas ΔgA in eq. [5.5.44] is a negative quantity. In eq. [5.5.45] it is understood that gA and K_1 refer to L. Eqs. [5.5.44] and [5.5.45] both have the form

$$\delta_M \Delta G^*_{comp} = \frac{(kT\ln K_1 + G\gamma')K_1 x_2}{x_1 + K_1 x_2} \qquad [5.5.46]$$

where G = ΔgA in eq. [5.5.44] and G = -gA in eq. [5.5.45]. Table 5.5.5 shows G and K_1 values obtained in studies of α-cyclodextrin complexes.[19,20] The assignments are made on the basis of the magnitude of K_1; those values substantially higher than typical solubility K_1 values suggest that the full cancellation condition is not satisfied. After the assignments are made, G can be interpreted as either ΔgA (full cancellation) or -gA (partial cancellation).

Notice in Table 5.5.5 that all full cancellation systems give substantial negative ΔgA values. If g is constant, $\Delta gA = g\Delta A$, and the negative ΔA value leads to a solvophobic driving force of $g\Delta A\gamma$ for complex formation. (The dioxane system in Table 5.5.5 is unassigned because its K_1 value suggests partial cancellation whereas its G value suggests full cancellation).

Table 5.5.5. Parameter values of the 4-nitroaniline/α-cyclodextrin and methyl orange/α-cyclodextrin systems[19,20]

Cosolvent	$\mathbf{K_1}$	$\mathbf{G^a}$	**Cancellation assignment**
		4-Nitroaniline	
Acetonitrile	55	+3	Partial
2-Propanol	46	-3	Partial
Ethanol	29	-9	Partial
Acetone	10	-57	Full
Methanol	3.1	-68	Full
		Methyl orange	
Acetone	46	-3	Partial
2-Propanol	43	-11	Partial
Acetonitrile	40	-13	Partial
Dioxane	31	-38	(Unassigned)
Ethylene glycol	7.7	-58	Full
DMSO	6.4	-66	Full
Methanol	4.9	-43	Full

[a] Units are Å^2 molecule^{-1}

5.5.3.5 Chemical kinetics

Treatment of the solvent effect on chemical reaction rates by means of the phenomenological theory is greatly facilitated by the transition state theory, which postulates that the initial and transition states are in (virtual) equilibrium. Thus the approach developed for complex formation is applicable also to chemical kinetics. Again we begin with a thermodynamic cycle, Figure 5.5.9, where R represents the reactant (initial state) in a unimolecular reaction, $R^\ddagger$ is the transition state, and P is the product. From Figure 5.5.9 we write eq. [5.5.47], where $\Delta G^\ddagger_{rxn(1)}$ subsequently writ-

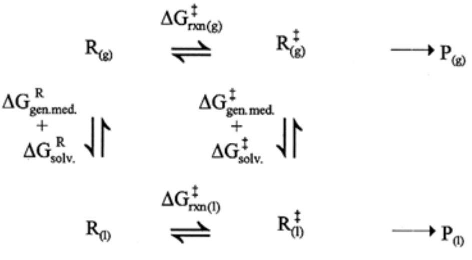


Figure 5.5.9. Thermodynamic cycle for a unimolecular reaction. (Reproduced with permission from the *Journal of Pharmaceutical Sciences*, reference 21.)

ten $\Delta G^{\ddagger}_{rxn}$, is the free energy of activation in the solution phase.

$$\Delta G^{\ddagger}_{rxn(1)} = \Delta G^{\ddagger}_{rxn(g)} + (\Delta G^{\ddagger}_{gen\ med} + \Delta G^{\ddagger}_{solv}) - (\Delta G^{R}_{gen\ med} + \Delta G^{R}_{solv}) \qquad [5.5.47]$$

Applying the δ_M operation gives eq. [5.5.48]:

$$\delta_M \Delta G^{\ddagger}_{rxn} = \Delta G^{\ddagger}_{rxn(x_2)} - \Delta G^{\ddagger}_{rxn(x_2=0)} \qquad [5.5.48]$$

The quantity $\Delta G^{\ddagger}_{rxn(g)}$, disappears in this subtraction, as do other composition-independent quantities. We make use of eq. [5.5.13] and eq. [5.5.19] to obtain a function having six parameters, namely K_1^R, K_2^R, $K^{\ddagger}_1$, gA^R, and $gA^{\ddagger}$. This function is made manageable by adopting the full cancellation approximation, setting $K_1^R = K^{\ddagger}_1 = K_1$ and $K_2^R = K^{\ddagger}_2 = K_2$. We then obtain

$$\delta_M \Delta G^{\ddagger}_{rxn} = (\Delta gA^{\ddagger}\gamma' K_1 x_1 x_2 + 2\Delta gA^{\ddagger}\gamma' K_1 K_2 x_2^2)/(x_1^2 + K_1 x_1 x_2 + K_1 K_2 x_2^2) \qquad [5.5.49]$$

where $\Delta gA^{\ddagger} = gA^{\ddagger} - gA^R$; this is the difference between the curvature-corrected molecular surface areas of the cavities containing the transition state and the reactant. This quantity may be positive or negative.

LePree[21] tested eq. [5.5.49] with the decarboxylative dechlorination of N-chloroamino acids in mixed solvents

$$\mathrm{RCH(NHCl)COOH + H_2O \rightarrow RCHO + NH_3 + HCl + CO_2} \qquad [5.5.50]$$

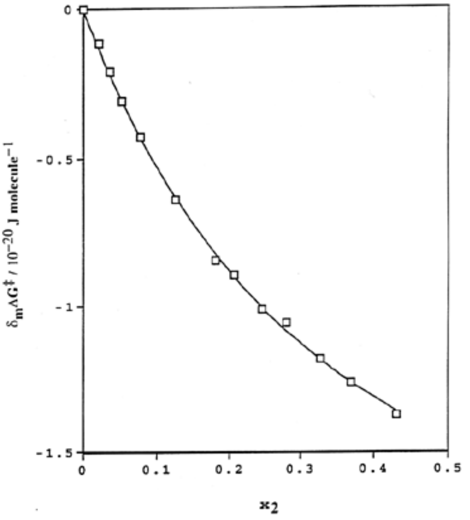


Figure 5.5.10. Solvent effect on the decomposition of N-chloroaniline in acetonitrile-water mixtures. The smooth curve is drawn with eq. 5.5.49. (Reproduced with permission from the *Journal of Pharmaceutical Sciences*, reference 21.)

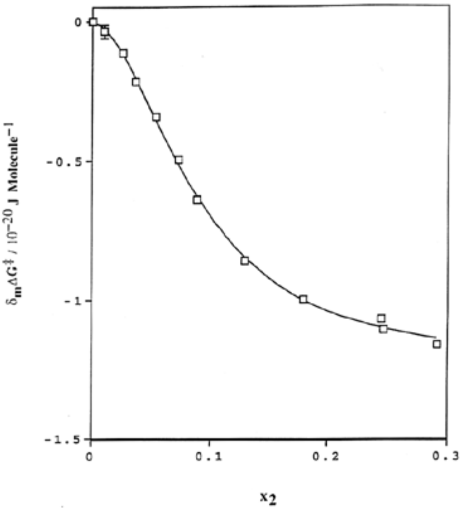


Figure 5.5.11. Solvent effect on the decomposition of N-chloroleucine in 2-propanol-water mixtures. The smooth curve is drawn with eq. 5.5.49. (Reproduced with permission from the *Journal of Pharmaceutical Sciences*, reference 21.)

For this test, the reaction possesses these very desirable features: (1) the kinetics are first order, and the rate-determining step is unimolecular; (2) the reaction rate is independent of pH over the approximate range 4-13; (3) the rate-determining step of the process is not a solvolysis, so the concentration of water does not appear in the rate equation; and (4) the reaction is known to display a sensitivity to solvent composition. Figures [5.5.10] and [5.5.11] show curve-fits, and Tables 5.5.6 and 5.5.7 give the parameter values obtained in the curve-fitting regression analysis. Observe that $\Delta gA^{\ddagger}$ is positive. This means that the transition state occupies a larger volume than does the reactant. This conclusion has been independently confirmed by studying the pressure dependence of the kinetics.[21,22]

Table 5.5.6. Model parameters for solvent effects on the decomposition of N-chloroalanine[21]

Cosolvent	K_1	K_2	$\Delta gA^{\ddagger}$, Å^2 molecule^{-1}
Methanol	2.8	3.1	16.8
Ethanol	5.7	2.8	23.8
1-Propanol	13.0	3.2	22.0
2-Propanol	5.9	11	20.6
Ethylene glycol	4.4	1.7	34.8
Propylene glycol	5.2	6.0	27.0
Acetonitrile	7.0	2.0	42
Dioxane	8.9	4.3	55

Table 5.5.7. Model parameters for solvent effects on the decomposition of N-chloroleucine[21]

Cosolvent	K_1	K_2	$\Delta gA^{\ddagger}$, Å^2 molecule^{-1}
Methanol	2.5	4.0	19.3
2-Propanol	2.7	40	24.2
Ethylene glycol	4.4	3.2	38
Acetonitrile	7.5	3.9	43

The success shown by this kinetic study of a unimolecular reaction unaccompanied by complications arising from solvent effects on pH or water concentration (as a reactant) means that one can be confident in applying the theory to more complicated systems. Of course, an analysis must be carried out for such systems, deriving the appropriate functions and making chemically reasonable approximations. One of the goals is to achieve a practical level of predictive ability, as for example we have reached in dealing with solvent effects on solubility.

5.5.3.6 Liquid chromatography

In reverse phase high-pressure liquid chromatography (RP HPLC), the mobile phase is usually an aqueous-organic mixture, permitting the phenomenological theory to be applied. LePree and Cancino[23] carried out this analysis. The composition-dependent variable is the capacity factor k′, defined by eq. [5.5.51],

$$k' = \frac{V_R - V_M}{V_M} = \frac{t_R - t_M}{t_M} \qquad [5.5.51]$$

where V_R is the retention volume of a solute, t_R is the retention time, V_M is the column dead volume (void volume), and t_M is the dead time. It is seldom possible in these systems to use pure water as the mobile phase, so LePree reversed the usual calculational procedure, in which water is the reference solvent, by making the pure organic cosolvent the reference. This has the effect of converting the solvation constants K_1 and K_2 to their reciprocals, but the form of the equations is unchanged. For some solvent systems a 1-step model was adequate, but others required the 2-step model. Solvation constant values (remember that these are the reciprocals of the earlier parameters with these labels) were mostly in the range 0.1 to 0.9, and the gA values were found to be directly proportional to the nonpolar surface areas of the solutes. This approach appears to offer advantages over earlier theories in this application because of its physical significance and its potential for predicting retention behavior.

5.5.4 INTERPRETATIONS

The very general success of the phenomenological theory in quantitatively describing the composition dependence of many chemical and physical processes arises from the treatment of solvation effects by a stoichiometric equilibrium model. It is this model that provides the functional form of the theory, which also includes a general medium effect (interpreted as the solvophobic effect) that is functionally coupled to the solvation effect. The parameters of the theory appear to have physical significance, and on the basis of much experimental work they can be successfully generated or predicted by means of empirical correlations. The theory does not include molecular parameters (such as dipole moments or polarizabilities), and this circumstance deprives it of any fundamental status, yet at the same time enhances its applicability to the solution of practical laboratory problems. Notwithstanding the widespread quantitative success of the theory, however, some of the observed parameter values have elicited concern about their physical meaning, and it is to address these issues, one of which is mentioned in 5.5.3.1, that the present section is included.

5.5.4.1 Ambiguities and anomalies

Consider a study in which the solubility of a given solute (naphthalene is the example to be given later) is measured in numerous binary aqueous-organic mixed solvent systems, and eq. [5.5.23] is applied to each of the mixed solvent systems, the solvent effect $\delta_M \Delta G^*_{soln}$ being calculated relative to water (component 1) in each case. According to hypothesis, the parameter gA is independent of solvent composition. This presumably means that it has the same value in pure solvent component 1 and in pure solvent component 2, since it is supposed not to change as x_2 goes from 0 to 1. And in fact the nonlinear regression analyses support the conclusion that gA is a parameter of the system, independent of composition.

But in the preceding paragraph no restriction has been placed on the identity of solvent component 2, so the conclusion must apply to any cosolvent 2 combined with the common solvent 1, which is water. This means that all mixed solvent systems in this study as described should yield the same value of gA. But this is not observed. Indeed, the variation in gA can be extreme, in a chemical sense; see Table 5.5.2. This constitutes a logical difficulty.

There is another anomaly to be considered. In nearly all of the nonelectrolyte solubility data that have been subjected to analysis according to eq. [5.5.23] the solute solubility increases as x_2, the organic cosolvent concentration, increases, and gA is positive, the physically reasonable result. But in the sucrose-water-ethanol system, the sucrose solubility decreases as x_2 increases, and gA is negative. There appears to be no physically reasonable picture of a negative gA value.

A further discrepancy was noted in 5.5.3.2, where we saw that some of the solvation constants evaluated from surface tension data did not agree closely with the corresponding numbers found in solubility studies.

5.5.4.2 A modified derivation

Recognizing that the original condition that g and A are independent of composition was unnecessarily restrictive, we replace eq. [5.5.18] with eq. [5.5.52], where the subscripts 1 and 2 indicate values in the pure solvents 1 and 2.

$$\hat{g}\hat{A}\gamma = g_1A_1\gamma_1 + (g_2A_2\gamma_2 - g_1A_1\gamma_1)f_2 \qquad [5.5.52]$$

It is important for the moment to maintain a distinction between gA in the original formulation, a composition-independent quantity, and $\hat{g}\hat{A}$ in eq. [5.5.52], a composition-dependent quantity. Eq. [5.5.52] combines the composition dependence of three entities into a single grouping, $\hat{g}\hat{A}\gamma$, which is probably an oversimplification, but it at least generates the correct values at the limits of $x_2 = 0$ and $x_2 = 1$; and it avoids the unmanageable algebraic complexity that would result from a detailed specification of the composition dependence of the three entities separately. Eq. [5.5.14] now is written $\Delta G_{gen\ med} = \hat{g}\hat{A}\gamma$ and development as before yields eq. [5.5.53] as the counterpart to eq. [5.5.23], where $\delta_M gA\gamma = g_2A_2\gamma_2 - g_1A_1\gamma_1$.

$$\delta_M\Delta G^*_{soln} = \frac{(\delta_M gA\gamma/2 - kT\ln K_1)K_1x_1x_2 + (\delta_M gA\gamma - kT\ln K_1K_2)K_1K_2x_2^2}{x_1^2 + K_1x_1x_2 + K_1K_2x_2^2} \qquad [5.5.53]$$

Comparison of eqs. [5.5.23] and [5.5.53] gives eq. [5.5.54], which constitutes a specification of the meaning of gA in the original formulation in terms of the modified theory.

$$gA(\gamma_2 - \gamma_1) = g_2\gamma_2A_2 - g_1\gamma_1A_1 \qquad [5.5.54]$$

Now, the right-hand side of eq. [5.5.54] is a constant for given solute and solvent system, so the left-hand side is a constant. This shows why gA in the original theory (eq. [5.5.23]), is a composition-independent parameter of the system. Of course, in the derivation of eq. [5.5.23] gA had been assumed constant, and in effect this assumption led to any composition dependence of gA being absorbed into γ. In the modified formulation we acknowledge that the composition dependence of the product $\hat{g}\hat{A}\gamma$ is being accounted for without claiming that we can independently assign composition dependencies to the separate factors in the product.

5.5.4.3 Interpretation of parameter estimates

Eq. [5.5.54] constitutes the basis for the resolution of the logical problem, described earlier, in which different cosolvents, with a given solute, yield different gA values, although gA had been assumed to be independent of composition. As eq. [5.5.54] shows, gA is determined by a difference of two fixed quantities, thus guaranteeing its composition independence, and at the same time permitting gA to vary with cosolvent identity.

Eq. [5.5.53] is therefore conceptually sounder and physically more detailed than is eq. [5.5.23]. Eq. [5.5.53] shows, however, that in the absence of independent additional information (that is, information beyond that available from the solubility study alone) it is not possible to dissect the quantity ($g_2\gamma_2A_2$ - $g_1\gamma_1A_1$) into its separate terms. In some cases such additional information may be available, and here we discuss the example of naphthalene solubility in mixed aqueous-organic binary mixtures. Table 5.5.8 lists the values of $gA(\gamma_2$-$\gamma_1)$ obtained by applying eq. [5.5.23] to solubility data in numerous mixed solvent systems.[8] In an independent calculation, the solubility of naphthalene in water was written as eq. [5.5.55],

$$\Delta G^*_{soln}(x_2 = 0) = \Delta G_{cryst} + g_1A_1\gamma_1 \qquad [5.5.55]$$

which is equivalent to eq. [5.5.4]. ΔG_{cryst} was estimated by conventional thermodynamic arguments and ΔG_{solv} was omitted as negligible,[24] yielding the estimate $g_1A_1\gamma_1 = 4.64 \times 10^{-20}$ J molecule^{-1}. With eq. [5.5.54] estimates of $g_2A_2\gamma_2$ could then be calculated, and these are listed in Table 5.5.8.

Table 5.5.8. Parameter estimates and derived quantities for naphthalene solubility in water-cosolvent mixtures at 25°C[a]

Cosolvent	γ_2, erg cm^{-2}	10^{20} $gA(\gamma_2$-$\gamma_1)$, J molecule^{-1}	10^{20} $g_2A_2\gamma_2$, J molecule^{-1}
Methanol	22.4	-3.11	+1.53
Ethanol	21.8	-2.70	1.94
Isopropanol	20.8	-2.19	2.45
Propylene glycol	37.1	-2.46	2.18
Ethylene glycol	48.1	-2.24	2.22
Acetone	22.9	-3.37	1.27
Dimethylsulfoxide	42.9	-3.67	0.97

[a] Data from ref. (8); $\gamma_1 = 71.8$ erg cm^{-2}, $g_1A_1\gamma_1 = 4.64 \times 10^{-20}$ J molecule^{-1}.

Observe that $g_1A_1\gamma_1$ and $g_2A_2\gamma_2$ are positive quantities, as expected; $gA(\gamma_2$-$\gamma_1)$ is negative because of the surface tension difference. It is tempting to divide each of these quantities by its surface tension factor in order to obtain estimates of gA, g_1A_1, and g_2A_2, but this procedure may be unsound, as proposed subsequently.

5.5.4.4 Confounding effects

Solute-solute interactions

It is very commonly observed, in these mixed solvent systems, that the equilibrium solubility rises well above the dilute solution condition over some portion of the x_2 range. Thus solution phase solute-solute interactions must make a contribution to ΔG^*_{soln}. To some extent these may be eliminated in the subtraction according to eq. [5.5.22], but this operation cannot be relied upon to overcome this problem. Parameter estimates may therefore be contaminated by this effect. On the other hand, Khossravi[25] has analyzed solubility data for biphenyl in methanol-water mixtures by applying eq. [5.5.23] over varying ranges of x_2; he found that $gA(\gamma_2-\gamma_1)$ was not markedly sensitive to the maximum value of x_2 chosen to define the data set. In this system the solubility varies widely, from $x_3 = 7.1 \times 10^{-7}$ (3.9×10^{-5} M) at $x_2 = 0$ to $x_3 = 0.018$ (0.43 M) at $x_2 = 1$.

Coupling of general medium and solvation effects

In this theory the general medium and solvation effects are coupled through the solvation exchange constants K_1 and K_2, which determine the composition of the solvation shell surrounding the solute, and thereby influence the surface tension in the solvation shell. But the situation is actually more complicated than this, for if surface tension-composition data are fitted to eq. [5.5.26] the resulting equilibrium constants are not numerically the same as the solvation constants K_1 and K_2 evaluated from a solubility study in the same mixed solvent. Labeling the surface tension-derived constants K_1' and K_2', it is usually found that $K_1'>K_1$ and $K_2'>K_2$. The result is that a number attached to γ at some x_2 value as a consequence of a nonlinear regression analysis according to eq. [5.5.23] will be determined by K_1 and K_2, and this number will be different from the actual value of surface tension, which is described by K_1' and K_2'. But of course the actual value of γ is driving the general medium effect, so the discrepancy will be absorbed into gA. The actual surface tension (controlled by K_1' and K_2') is smaller (except when $x_2 = 0$ and $x_2 = 1$) than that calculated with K_1 and K_2. Thus $g_{apparent} = g_{true} \times \gamma(K_1',K_2')/\gamma(K_1,K_2)$. This effect will be superimposed on the curvature correction factor that g represents, as well as the direct coupling effect of solvation mentioned above.

The cavity surface area

In solubility studies of some substituted biphenyls, it was found (see 5.5.3.1) that gA evaluated via eq. [5.5.23] was linearly correlated with the nonpolar surface area of the solutes rather than with their total surface area; the correlation equation was $gA = 0.37\,A_{nonpolar}$. It was concluded that the A in the parameter gA is the nonpolar surface area of the solute. This conclusion, however, was based on the assumption that g is fixed. But the correlation equation can also be written $gA = 0.37\,F_{nonpolar}A_{total}$, where $F_{nonpolar} = A_{nonpolar}/A_{total}$ is the fraction of solute surface area that is nonpolar. Suppose it is admitted that g may depend upon the solute (more particularly, it may depend upon the solute's polarity); then the correlation is consistent with the identities $A = A_{total}$ and $g = 0.37\,F_{nonpolar}$.

Thus differences in gA may arise from differences in solute polarity, acting through g. But A may itself change, rather obviously as a result of solute size, but also as a consequence of change of solvent, for the solvent size and geometry will affect the shape and size of the cavity that houses the solute.

The role of interfacial tension

In all the preceding discussion of terms having the $gA\gamma$ form, γ has been interpreted as a surface tension, the factor g serving to correct for the molecular-scale curvature effect. But a surface tension is measured at the macroscopic air-liquid interface, and in the solution case we are actually interested in the tension at a molecular scale solute-solvent interface. This may be more closely related to an interfacial tension than to a surface tension. As a consequence, if we attempt to find (say) g_2A_2 by dividing $g_2A_2\gamma_2$ by γ_2, we may be dividing by the wrong number.

To estimate numbers approximating to interfacial tensions between a dissolved solute molecule and a solvent is conjectural, but some general observations may be helpful. Let γ_X and γ_Y be surface tensions (vs. air) of pure solvents X and Y, and γ_{XY} the interfacial tension at the X-Y interface. Then in general,

$$\gamma_{XY} = \gamma_X + \gamma_Y - W_{XY} - W_{YX} \qquad [5.5.56]$$

where W_{XY} is the energy of interaction (per unit area) of X acting on Y and W_{YX} is the energy of Y acting on X. When dispersion forces alone are contributing to the interactions, this equation becomes[26]

$$\gamma_{XY} = \gamma_X + \gamma_Y - 2\left(\gamma_X^d \gamma_Y^d\right)^{1/2} \qquad [5.5.57]$$

where $\gamma_X{}^d$ and $\gamma_Y{}^d$ are the dispersion force components of γ_X and γ_Y. In consequence, γ_{XY} is always smaller than the larger of the two surface tensions, and it may be smaller than either of them.

Referring now to Table 5.5.8, if we innocently convert $g_2A_2\gamma_2$ values to estimates of g_2A_2 by dividing by γ_2, we find a range in g_2A_2 from 23 Å^2 molecule^{-1} (for dimethylsulfoxide) to 118 Å^2 molecule^{-1} (for isopropanol). But if the preceding argument is correct, in dividing by γ_2 we were dividing by the wrong value. Taking benzene ($\gamma = 28$ erg cm^{-2}) as a model of supercooled liquid naphthalene, we might anticipate that those cosolvents in Table 5.5.8 whose γ_2 values are greater than this number will have interfacial tensions smaller than γ_2, hence should yield g_2A_2 estimates larger than those calculated with γ_2, and vice versa. Thus, the considerable variability observed in g_2A_2 will be reduced.

On the basis of the preceding arguments it is recommended that $gA\gamma$ terms (exemplified by $g_1A_1\gamma_1$, $g_2A_2\gamma_2$, and $gA(\gamma_2-\gamma_1)$) should not be factored into gA quantities through division by γ, the surface tension, (except perhaps to confirm that magnitudes are roughly as expected). This conclusion arises directly from the interfacial tension considerations.

Finally let us consider the possibility of negative gA values in eq. [5.5.23]. Eq. [5.5.54] shows that a negative gA is indeed a formal possibility, but how can it arise in practice? We take the water-ethanol-sucrose system as an example; gA was reported to be negative for this system. Water is solvent 1 and ethanol is solvent 2. This system is unusual because of the very high polarity of the solute. At the molecular level, the solute in contact with these solvents is reasonably regarded as supercooled liquid sucrose, whose surface tension is unknown, but might be modeled by that of glycerol ($\gamma = 63.4$ erg cm^{-2}). In these very polar systems capable of hydrogen-bonding eq. [5.5.57] is not applicable, but we can anticipate that the sucrose-water interaction energies (the W_{XY} and W_{XY} terms in eq. [5.5.56] are greater than sucrose-ethanol energies. We may expect that the sucrose-water interfacial tension is very low.

Now, gA turned out to be negative because $gA(\gamma_2-\gamma_1)$, a positive quantity as generated by eq. [5.5.23], was divided by $(\gamma_2-\gamma_1)$, a difference of surface tensions that is negative. Inevitably gA was found to be negative. The interfacial tension argument, however, leads to the conclusion that division should have been by the difference in interfacial tensions. We have seen that the interfacial tension between sucrose and water may be unusually low. Thus the factor $(\gamma_2-\gamma_1)$, when replaced by a difference of interfacial tensions, namely [γ(sucrose/ethanol) - γ(sucrose/water)], is of uncertain magnitude and sign. We therefore do not know the sign of gA; we only know that the quantity we label $gA(\gamma_2-\gamma_1)$ is positive. This real example demonstrates the soundness of the advice that products of the form $gA\gamma$ not be separated into their factors.[27,28]

5.5.5 NOTES AND REFERENCES

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