Local changes of solubility induced by electrolytes: salting-out and ionic hydration

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Abstract - A comparative examination of electrostatic distribution treatments of salting-out and other approaches such as "scaled particle theory" is given. Treatments that take into account some ion-specific parameter such as the radius of the primary solvation co-sphere or some related equivalent quantity such as the ion's partial molal volume, give best agreement with experiment. Structural effects of a non-electrostatic kind are important in associated solvents but are most difficult to deal with in a satisfactory a priori way.

Analogies are drawn between salting-out of non-electrolytes at ions and the surface-charge dependence of adsorption of neutral molecules in the double-layer at polarized electrode interfaces.

INTRODUCTION

Phenomenology and approaches

The solubility of non-electrolyte solutes (1) in solvents (2) is usually specific to the molecular structure, polarity and donicity of the 1,2 binary system, corresponding to the standard free energy change, $\Delta\mu°$, of the solution process. If component 1 is a dilute gas, solute-specific effects arising from intermolecular interactions in the solid or liquid lattices of 1 are avoided, making the interpretation of specific $\Delta\mu°$ values for 1,2 mixtures one stage less complex.

Since salting-out (or salting-in) effects are measured by changes of solubility, we are fortunately not concerned directly with the specificities that arise in solute solubility itself on account of solute size, polarity and polarizability, H-bonding etc., although these specificities have some indirect role in determining the changes of solubility induced by ions through non-electrolyte and ion-solvation co-sphere interactions in near neighbor encounters.

In the presence of a dissolved dissociated electrolyte, a fraction of the solvent molecules, dependent on the concentration and stoichiometry of the dissolved salt, suffer solvational interaction with the ions and thus becomes diminished in activity, leading to "salting-out" of the dissolved non-electrolyte solute (2). The solvation of the ions of the electrolyte also leads to a self-salting-out effect which is a significant factor determining the activity behavior (Refs. 2,3) of electrolytes at concentrations > ca. 1M. The formal thermodynamics of these situations is easily represented by the equations below but an a priori quantitative account of salting-out effects is quite difficult to achieve if salt ion specificities are to be at all well accounted for.

Adequate theories of salting out must take into account:

a) the structure of the solvent (Refs. 4,5) in the absence of solutes, and its own radial distribution function;

b) changes of structure and entropy of the solvent (Ref. 6) in the neighborhood of cations and anions of the electrolyte and in the neighborhood of the non-electrolyte solute;

c) the distribution functions for solvent around the ions and the non-electrolyte solute;

d) the electric polarization and associated dipole orientation about the cations and anions of the electrolyte (usually ion- and charge-specific)

and

e) the average integrated effects associated with factors (a) to (d) about the ions out to several molecular diameters of solvent molecules from the ions.

Calculations of salting-out effects thus involve most of the complexities of calculations of ion solvation (Ref. 7) with the added complication of the distribution of a polar, or non-polar, non-electrolyte near the ions in the region where the ions' strongest influences on the solvent structure and polarization normally arise.

Several types of calculation of salting-out effects have been performed or may be envisaged:

   a) electrostatic distribution calculations for solvent and non-electrolyte solutes (Debye and MacAulay (Ref. 8); Butler (Ref. 9); Belton (Ref. 10); Conway, Desnoyers and Smith (Ref. 11));
   b) quasi-thermodynamic calculations (McDevit and Long (Ref. 12)), taking account of volumes of the species involved;
   c) scaled-particle theory (Ref. 13),based on empirical density information Refs. 14,15));
   d) molecular dynamics calculations (e.g. of Heinzinger (Ref.16)) of the type applied to ion-solvent interaction, and distribution (not yet applied to salting-out, to our knowledge);
   e) dispersion and electrostatic energy calculations in distribution-type evaluations of salting-out effects (Bockris, Bowler-Reed and Kitchener (Ref. 17)).

Most work on salting-out has been done in highly associated solvent media - water and alcohol/water mixtures (Ref. 17). In some ways, however, such solvents present the greatest difficulties in developing quantitative, ion-specific accounts of salting-out owing to the role of structural changes (and associated entropy effects) induced locally in the H-bonded solvents by the ions of the added electrolyte. Easier interpretations might be achieved in work on unassociated but polar aprotic solvents such as CH_3CN and DMSO. However, in such solvents, a complication of a different kind arises: in all but the most dilute solutions, electrolytes that are employed to study the salting effect remain substantially ion-paired.

Some advantage arises in treating the salting-out of spherical or quasi-spherical non-electrolyte solutes, e.g. noble gases, CH_4, $C(CH_3)_4$ since the geometric distribution of solvent molecules around the solute is spherical and no localized dipole, asymmetrically situated in the molecule, is present.

TREATMENTS OF SALT EFFECT ON NON-ELECTROLYTE SOLUBILITIES

1. __Formal thermodynamics.__ Saturation solubility equilibrium of a substance between e.g. the gas-phase, g, and a solution phase, s, is determined by the condition $\mu_g = \mu_s$, i.e.

$$\mu^°_g + RT \ln f_g = \mu^°_s + RT \ln S^° + RT \ln \gamma^° \qquad (1)$$

where f_g is the fugacity of the gas, $S^°$ the saturation solubility in pure solvent and γ the activity coefficient, usually taken as 1 in the pure solvent. In the presence of a salt, $S^°$ is changed to S and $\gamma^°$ to γ, due mainly to the interaction of the salt ions with the solvent. Then

$$\ln S^°/S = \ln \gamma. \qquad (2)$$

Salting-out arises when $\gamma > 1$ and salting-in when $\gamma < 1$. Usually the change of $\ln \gamma$ is linear with salt concentration, c_+, in dilute solutions so that $\ln S^°/S = kc_+$ (Setschenow's relation). From eqn. (2), it is clear that calculations of the solubility ratio or of Setschenow's constant k require evaluation of the non-ideal free energy of non-electrolyte solute caused by the presence of ions. By noting that $S^°-S = \Delta S$, the change of solubility, an alternative relation

$$\Delta S/S^° = kc_\pm \qquad (3)$$

arises from Setschenow's equation for sparingly soluble solutes.

2. __Electrostatic theories.__ Early electrostatic theories were based on the following approaches:

   a) calculation of RT ln γ is made (Debye and MacAulay (Ref. 8)) in terms of the difference of charging energy of the ions of the electrolyte in the pure solvent and in the non-electrolyte-containing solution brought about by the fact that the non-electrolyte, i, usually changes the dielectric constant of the solvent. RT ln γ is then obtained in terms of the dielectric decrement δ of i in the solvent. For most non-electrolyte solutions in water, this treatment predicts salting-out. In a number of cases, these predictions for various salts are neither

quantitatively nor qualitatively in agreement with experiment. This treatment
has all the well-known (Ref. 11) deficiencies associated with use of the Born
equation in a very polar medium such as water.

b) $\Delta S/S^\circ$ (eqn. 3) is calculated by means of a treatment in which the distribution
of solute i in comparison with that of solvent molecules is evaluated around the
ions of the electrolyte. A Boltzmann relation is generated in terms of the
difference ΔU_e of electrostatic polarization energy suffered by the "gas"
molecule in the field of an ion in comparison with that of an equal volume of
solvent at the same distance r from the ion. Integration of this effect from
the radius of the ion a to infinity [or to a co-sphere radius R, dependent on
ionic concentration c_+^- (R = $3000/4\pi N_A c_\pm)^{1/3}$], gives the relative solubility
change $\Delta S/S^\circ$. This was the basis of Butler's method (Ref. 9), as also employed
by Bockris and Egan (Ref. 17), and Bockris, Bowler-Reed and Kitchener
(Ref. 17).

These treatments suffer from three serious weaknesses: (i) the Boltzmann factor in the
polarization energy difference $\Delta U_e/kT$ was linearized which, near the ion, where the field
is high, is inadmissable; (ii) dielectric saturation effects, important near the ion,
were not considered (this factor makes it more inadmissible to linearize the Boltzmann
exponent); (iii) the term used (Refs. 9,17) for electrostatic polarization of the sol-
vent was inappropriate for an associated liquid such as water where dipole reaction-field
and correlation effects in the polarization have to be considered (Belton (Ref. 10)
recognized some, but not all, of the latter difficulties). However, Bockris, Bowler-Reed
and Kitchener (Ref. 17) introduced a quantitative treatment of dispersion interactions
into salting-out theory which is important in salting effects between relatively large
polarizable solutes and large ions, e.g. of the R_4N^+ type, where salting-in may arise.

Conway, Desnoyers and Smith (Ref. 11) improved the distribution-type theories by taking
account of the dielectric saturation effects and avoiding linearization of the Boltzmann
factor by performing the required integration (Refs. 9,10,11) over two integrands: one,
near the ion (Fig. 1) where $U_e/kT \gg 1$ and dielectric saturation is important, and the
other further from the ion, beyond the primary hydration shell of radius r_h, (Fig. 1),
where linearization is permissible. Fortunately, near the ion, the dielectric saturation
effects do not have to be numerically evaluated since they appear in U_e for conditions
where $U_e/kT \gg 1$, so that $\exp[-U_e/kT] \to 0$.
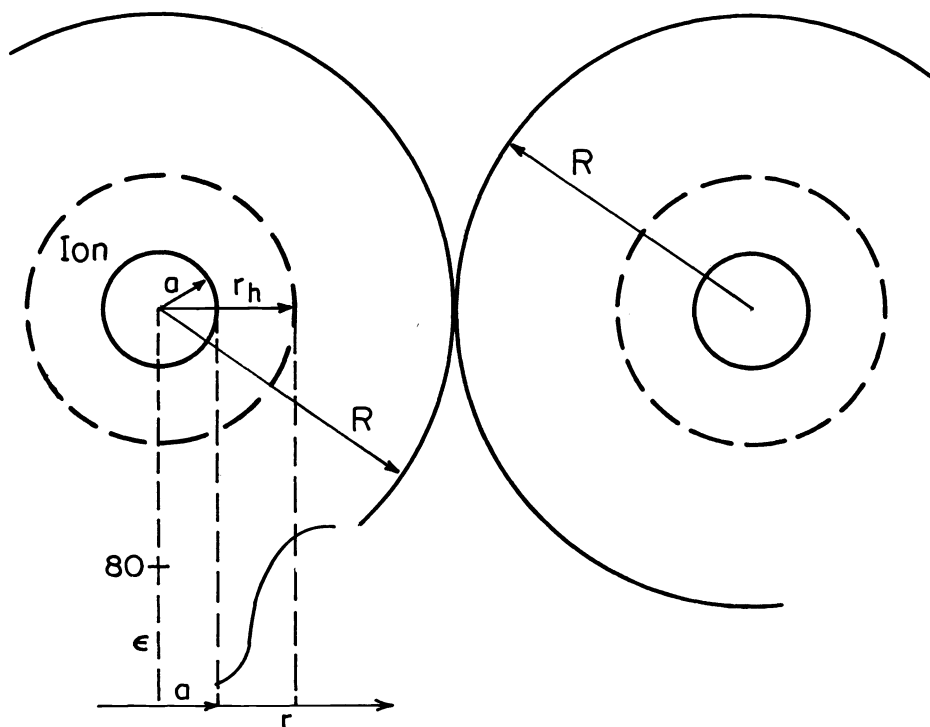

Fig. 1   Schematic diagram of region of polarization influence about two
ions showing the cosphere radii r_h and R.

Their equation for $\Delta S/S°$ was (Ref. 11)

$$k = \Delta S/S° \ c_\pm = \frac{4\pi N_A}{1000} \int_a^R (1-\exp[-\Delta U_e/kT])r^2 dr \tag{4}$$

$$= \frac{4\pi N_A}{1000} \int_a^{r_h} (1-\exp[-\Delta U_e/kT])r^2 dr + \frac{4\pi N_A}{1000} \int_{r_h}^R \frac{\Delta U_e}{kT} r^2 dr \tag{5}$$

The electrostatic energy ΔU_e was taken as

$$\Delta U_e = (E^2/8\pi N_A)(\bar{V}\varepsilon_o - 9P/2) \tag{6}$$

where P is the polarization of non-electrolyte given by $\frac{4}{3}\pi N_A(\alpha + \mu\bar{\mu}/3kT)$, $\bar{V}$ is the partial molar volume of non-electrolyte, ε_o the dielectric constant of the solvent and α the polarizability of i. $\mu\bar{\mu} = 1/9(n^2 + 2)^2_o\mu^2$ where n is the refractive index and μ the dipole moment of the non-electrolyte. $(\varepsilon E^2/8\pi N_A)$ $\bar{V}$ corresponds to the polarization energy which solvent molecules experience in the field E of the ion. The first integral in eqn. (5) can easily be evaluated when $\Delta U_e/kT \gg 1$, as it normally is near the ion $(a < r < r_h)$. It is simply the volume of the primary hydration shell of the ion from which the non-electrolyte solute i is virtually completely excluded.

Introduction of this parameter r_h allows specificity of ion-solvent interaction to be taken into account since r_h measures an effective radius of the primary solvation shell (Ref. 19) within which the ion-solvent interaction energy is usually $\gg kT$ and dielectric saturation obtains. Within this region, no errors of linearization of the exp function arise.

A further improvement (Ref. 20) to this type of theory is the introduction of the radial distribution function $g_{\pm,s}(r)$ of the solvent, s, about the ions, $\pm$, since the integration should not be performed, especially near the ion, as though the solvent were a continuum. $g_{\pm,s}(r)$ allows some account to be taken of the discontinuous nature of the solvent near the ions. In practice, however, few data are yet available for $g_{\pm,s}$ functions except for a few salts studied by Narten (Ref. 5). Introduction of $g_{\pm,s}$ transforms eqn. (5) into

$$\Delta S/S° \ c_\pm = \frac{4\pi N_A}{1000}\left[\int_a^{r_h} r^2 g_{\pm,s}(r)dr + \int_{r_h}^R (E^2/8\pi kTN_A)\bar{V}\varepsilon g_{\pm,s}(r)r^2 dr - \int_{r_h}^R (E^2/8\pi kTN_A)\frac{9}{2} P \ r^2 \ dr\right] \tag{7}$$

$g_{\pm,s}(r)$ does not enter into the last integral since that term involves interaction between non-electrolyte (n.e.) and the ions and nothing is known about $g_{ne,s}(r)$ for non-electrolytes, although it is important for refinement of calculations involving ion non-electrolyte co-sphere encounters. As in eqn. (5), the first integral in eqn. (7) deals with the almost complete exclusion of i from the primary solvation shell of the ion. In practice, eqns. (5) or (7) must be written (for a simple 1:1 electrolyte) as the sum of two sets of terms, one for the cation and one for the anion, each with its respective ionic parameters (a, r_h).

While electrostatic calculations of salting-out of gases give a fair account of the trend of $\Delta S/S°$ with ionic charge and radius for a given gas salted-out by a series of salts, they do not give any basis for specific solute and solvent structure effects in salting-out. Such effects are very difficult to calculate from first principles and would require detailed knowledge of the radial distribution functions $g_{+,ne}(r)$, $g_{-,ne}(r)$ and $g_{ne,s}(r)$, and of any dependence of $g_{ne,s}(r)$ on the presence of the ion for situations where n.e. is near an ion (co-sphere interaction effects).

3. Non-electrostatic factors. Usually, dissolution of a solute is accompanied by an enthalpy change and for a series of solutes in a given solvent or for a given solute in a series of solvents, the $\Delta H°$ and $\Delta S°$ changes compensate each other to give a standard free energy change for the dissolution process that is relatively less sensitive to the nature of the solute or solvent. This "compensation effect" is especially significant for water where heat changes associated with H-bond breaking or making are accompanied by respective positive or negative entropy changes. Specificities in salt effects on gas solubility can arise because of changes in either or both the $\Delta H°$ or the $T\Delta S°$ components of the free energy of solution of the gas, due to local changes of H bonding in the water, brought about by the ion-water interaction.

Dissolution of a gas atom or molecule requires first the formation of a cavity (Ref. 21) of suitable size in the solvent. The cavity formation process itself involves an entropy and enthalpy change. After the gas particle has entered the cavity, new interactions between the solvent particles and the solute arise with a corresponding entropy change. Restriction of the particle to a "free volume box" in the solvent usually involves a substantial loss of translational entropy while the reaction of the solvent particles surrounding the solute may involve an increase or decrease of entropy, especially in water, depending on whether hydrophilic or hydrophobic interactions predominate.

In the case of a polyatomic gas, dissolution will also result in loss of some rotational entropy as the particle suffers restrictions to its rotational freedom (libration). The partition function for libration is

$$q_L = \frac{8\pi^2(8\pi^3 I_1 I_2 I_3 k^3 T^3)^{1/2}}{h^3} \cdot \frac{\sinh U_L/kT}{U_L/kT}$$

i.e., the rotational partition quotient, which is the term before the sinh, is multiplied by the function $\sinh U_L/kT$ / U_L/kT where U_L is the potential well in which restricted rotational oscillations arise. It is obvious that as $U_L/kT \rightarrow 0$, $q_L \rightarrow q_{rot}$ and the entropy increases; conversely, when $U_L/kT \gg 1$, the entropy is decreased.

In the case of polyatomic gases, the entropy associated with restricted rotation will itself be sensitive to solvent-structure around the cavity in which the librations are executed, since U_L will depend on how the H-bonding amongst water molecules in the cavity is affected by the gas particles occupying the cavity.

General factors in salting-out are listed in Table 1.

TABLE 1.   Factors in salting-out

A) **Energy factors**

(i)   Difference of electrostatic polarization energy of non-electrolyte solute and an equal volume of solvent, by the ionic field.

(ii) Van der Waals dispersion forces [significant for large non-electrolytes and large ions (giving salting-in tendency; cf. Ref. 17)].

B) **Structural energy and entropy factors**

(i)   Modification of radial distribution function for solvent by (a) ions and (b) gas solute.

(ii)   Modification of cavity formation energy for cavities formed near ions.

(iii) Modification of cavity reaction behavior when gas enters cavity near an ion in comparison with cavity in free bulk solvent.

(iv)   Hydrophobic bonding with certain ions by sharing of structure-enhanced regions around ion and gas solute (co-sphere and cavity sharing).

(v)   Dependence of librational entropy of polyatomic gases on cavity properties near an ion.

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4. Treatments based on scaled-particle theory. In recent years, applications of scaled-particle theory (Ref. 13) to calculation of salting-out effects (Refs. 14,15) and related matters have been made. The approach is based on Pierotti's (Ref. 13) use of the scaled-particle theory of Reiss et al. (Ref. 13) to calculate gas solubilities. Shoor and Gubbins (Ref. 15) applied this method to calculation of solubilities of He, H_2, Ar, O_2, CH_4, SF_6 and $C(CH_3)_4$ in concentrated aq. KOH (10-50 wt % - an unfortunate choice of conditions for testing of any theory related to electrolyte solution behavior). Masterton and Lee (Ref. 14) extended Shoor and Gubbins' treatment to calculation of the salting effects for any salt/non-electrolyte pair.

The solubility S in the salt solution is evaluated by regarding the electrolyte solution as a different type of "solvent" for the non-electrolyte from that in the absence of salt.

The following relation for S is obtained (Refs. 14,15)

$$-kT \ln S = g_c + g_{c,ne} + \ln kT \sum \rho_j \qquad (9)$$

where g_c is the free-energy of cavity formation, $g_{c,ne}$ the free-energy of introduction of non-electrolyte into the cavity (this includes the energy of interaction with molecules in the walls of the cavity, plus any energy associated with "reaction" of the cavity [changes of H bonding and orientation] to the presence of the non-electrolyte). ρ_j are number densities (particles per cc) of the various species j in solution taken as empirical parameters in the scaled-particle theory. The use of these empirical ρ_j, it is to be noted, introduces an unfortunate empirical aspect into the treatment since specificities of ion-solvent polarization and interaction are hidden in these terms.

Evaluation of the Setschenow coefficient k (eqn. 3) requires evaluation of the derivatives of g_c, $g_{c,ne}$ and $\ln \sum \rho_j$ with respect to ionic concentration. The last factor is relatively easily evaluated and gives a contribution to the overall salting-out coefficient of

$$k_{(\rho)} = 0.016 - 4.34 \times 10^{-4} \ \bar{V}^\circ \ (= k_3 \ [\text{see below}]) \qquad (10)$$

where $\bar{V}^\circ$ is the partial molar volume of salt at infinite dilution and thus contains most of the factors of interest with regard to ion-solvent polarization interactions and electrostriction (cf. the treatment of McDevit and Long (Ref. 12).

The contributions to k from $dg_c/dc_{\pm}$ and $dg_{c,ne}/dc_{\pm}$ are more difficult to calculate but the results, after some extensive mathematics, are (Ref. 14)

$$g_{c,ne}/2.3 \ RT = - \frac{32\pi C_{\pm}}{9000T} \left[\varepsilon_{1,3}\sigma_{1,3}^3 + \varepsilon_{1,4}\sigma_{1,4}^3 \right] - \frac{4\pi d_2}{3M_2 T} \left[1 - \frac{C_{\pm}\bar{V}}{1000} \right] \times \left[\frac{8}{3} \varepsilon_{1,2}\sigma_{1,2}^3 + \frac{\mu^2 \alpha}{\sigma_{1,2}^3} \right] \qquad (11)$$

where μ is the dipole moment and α the polarizability of water, σ_{ij} are intermolecular distances between 1 = non-electrolyte, 2 = water, 3 = cation and 4 = anion. ε_{ij} terms are corresponding pair interaction potentials in the mixture, taken as $\varepsilon_{ij} = (\varepsilon_i \varepsilon_j)^{1/2}$, while $\sigma_{ij} = (\sigma_i + \sigma_j)/2$. Eqn. (11), it is seen, involves again $\bar{V}$, which characterizes the ion-solvent interaction in this theory.
And

$$g_c/kT = -\ln(1-\tau_3) + A \qquad (12)$$

where

$$A = \frac{3\tau_2\sigma_1}{1-\tau_3} \left[1 + \frac{\tau_1\sigma_1}{\tau_2} + \frac{3\tau_2\sigma_1}{2(1-\tau_3)} \right] \qquad (13)$$

The terms τ_1, τ_2 and τ_3 involve $\bar{V}$, the radii of the species in solution, the ionic concentrations, and the density and molecular weight of the solvent. An expression can be derived for $dg_c/dc_{\pm}$ which involves only a series of numerical factors, the diameters σ and the $\bar{V}^\circ$ for the ionic components. The quantities required for the calculation of the overall k are, in summary, V° for the salt, the diameters and polarizabilities of the cation and anion, the diameter of non-electrolyte solute, the energy parameter ε_1/k and the polarizability α_1 of the non-electrolyte.

The relative values of the three salting-out coefficient contributions $dg_c/dc_{\pm}$ (= k_1), $dg_{c,ne}/dc_{\pm}$ (= k_2) and $d \log \Sigma \rho_j$ (= k_3) are quoted (Ref. 14) for several systems:

System	k_1	k_2	k_3	Overall k (eqn. 3)
H_2/NaCl	0.126	-0.023	0.008	0.111
H_2/KI	0.115	-0.031	-0.004	0.080
CH_4/NaCl	0.203	-0.080	0.008	0.131
CH_4/KI	0.182	-0.102	-0.004	0.076
SF_6/NaCl	0.387	-0.194	0.009	0.202
SF_6/KI	0.343	-0.226	-0.004	0.113

For all systems k_1 is positive which implies that it is more difficult to form a cavity in the ionic solution than in water itself. This is understandable, since the attractive interaction between an ion and solvent dipoles will make it more difficult to form cavities near the ions, i.e., where the salting-out effects originate.

The negative values of k_2 are interpreted (Ref. 14) in terms of the non-electrolyte expe-
riencing a net attractive force in the cavity when water molecules in the surrounding
walls of a cavity are replaced (in part) by an ion. This is expected, since the non-
electrolyte experiences polarization interactions due to the field E of the ion
($-1/2\ \alpha_{total}\ E^2$). This effect is thus analogous to part of the dielectric polarization
energy difference term ΔU_e employed in the distribution type theories. The k_3 terms are
relatively small. The other part is involved in the energy required to form a cavity
near an ion, a process in which water molecules must be removed from their favorable
position of interaction with the ion. It is evident that this part corresponds to the
ion-solvent dielectric polarization component of the U_e term of eqn. (4). The advantage
of the distribution type theories is that these energies are calculated directly and
their difference determines the salting-out coefficient after integration over the volume
of solvent influenced by the ions. Specificities in ion-solvent interaction which are
reflected in the experimental dependence of k on the identity and charge-type of the salt
are included in the scaled-particle treatment in the V and σ terms.

It has been stated (Ref. 15) that an advantage of the scaled-particle theory is that all
structural aspects of the interaction of the solute with the solvent (cf. Ref. 6) are
eliminated. The method therefore obscures the electrostatic ion/solvent and ion/solute
interactions that are of essential interest in salting-out and are predominant and often
specific for small ions. Structural and electrostatic properties of the solvent or
solution are contained in the number densities for components of the solution (which are
required as empirical data) and in g_c which is mainly entropic (Ref. 20) in the aqueous
medium case.

In the application of this theory to salting-out phenomena, it is claimed (seemingly as
an advantage) that the treatment "makes no appeal to assumptions concerning solvent
structure, ionic hydration, etc.", and that, in addition, "the ionic charge has little
direct influence on salting-out". It must be stressed, however, that there is clearly
demonstrable experimental dependence of salting-out constants (Refs. 11,12), k, on ionic
charge and radii in salt solutions, but that the effects are obscured by use of empirical
densities in the scaled-particle theory; the essential electrostatic effects (primary
hydration, solute and solvent polarization, etc.) are contained in the densities or V
data introduced empirically, as they are in McDevit and Long's theory (Ref. 12).

In fact, the salting-out is really evaluated as the difference of solubility in two kinds
of solvents, the ion-free and the ion-containing one without any direct reference to the
essential electrostatic interactions and structural modifications which ions are known to
make in polar solvents, especially water.

Statistical-mechanical treatments of salting-out effects have been given by Haugen and
Friedman (Ref. 22) and by Krishnan and Friedman (Ref. 23). In the former paper, simpli-
fications were introduced which made the treatment equivalent to earlier electrostatic
calculations. In the latter paper, Setschenow coefficients were calculated on the basis
of a model, similar to that used in previous ion-ion and ion-solvent interaction calcula-
tions, for which the interaction potential U_{ij} as a function of distance r is given by

$$U_{ij} = COR_{ij}(r) + e_i e_j/\varepsilon r + CAV_{ij}(r) + GUR_{ij}(r) \tag{14}$$

The COR term is a core repulsion term, the CAV accounts for dielectric effects and the
GUR term is a solvation-shell co-sphere overlap effect characterized by a parameter A_{ij}
having the significance of a free energy change per mole of solvent displaced from the
co-sphere of i and j due to their overlap. Unfortunately, one of the main ion-specific
factors in salting-out, viz., the GUR term, was adjusted to fit the experimental data by
matching experimental k values by empirical introduction of the A_{ij} values in $GUR_{ij}(r)$
for cation and anion. It seems that much of the elegance of the method of Friedman et
al. is negated by the empirical assignment of the $GUR_{ij}(r)$ term which expresses the main
interaction causing salting-out (i = non-electrolyte, j = cation or anion). In discuss-
ing the case of benzene-ion interactions, Krishnan and Friedman (Ref. 23) conclude that
the main defect in their model is the omission of dispersion and charge polarization
interactions. To us, these seem to be the main electrostatic interactions of interest in
salting-out.

5. Hydrophobic co-sphere interactions leading to salting-in contributions

(i) Structure-promotion and co-sphere sharing

Salting-in arises with a number of systems for which simple electrostatic theory
(Refs. 8,9,11) would predict salting-out. Bockris et al. (Ref. 17) showed how
introduction of dispersion interactions could account for such effects. However,
calculation of their dielectric polarization contribution was based on over-sim-
plified dielectric theory for water. Desnoyers et al. (Ref. 24) showed how
sharing of co-spheres of an hydrophobic non-electrolyte (benzene) and an

hydrophobic ion (R_4N^+ type) could lead to salting-in effects without recourse to calculation of dispersion interactions (although these will always be significant [cf. 17,20] for large ions). A statistical mechanical approach to calculation of such effects with neutral molecules was given by Ben-Naim (Ref. 25) on the basis of free energies of solution of "monomer" and equivalent "dimer" species, associated on account of "hydrophobic bonding". The case of CH_4 and C_2H_6 ("dimer of methane") was considered; the free energy of hydrophobic association was expressed as the difference of the standard free energies of solution, $\Delta\mu^\circ_{C_2H_6} - 2\Delta\mu^\circ_{CH_4}$, of ethane and methane. The anomalous nature of water as a medium leading to hydrophobic bonding is closely connected with its anomalous behavior for dissolution of such solutes at infinite dilution where unusual entropies and heat capacities of solution commonly arise.

Despite the elegant statistical mechanical presentation of the hydrophobic interaction effect by Ben-Naim, its evaluation is referred to relatively simple empirical quantities such as $\Delta\mu^\circ_{C_2H_6}$ and $\Delta\mu^\circ_{CH_4}$.

   (ii) An equally interesting approach can be made in terms of surface tension and cavity area, where co-sphere sharing leads to a diminution of local solute/water interface area and a net attractive interaction.

6. <u>Comparative summary of theories of salting-out.</u> Theories of salting-out and salting-in are summarized comparatively in Table 2 below:

TABLE 2.   Comparison of theories of salting-out and salting-in

Theory	Comments	Authors/Ref.
a) Born polarization energy treatment	Has weaknesses of Born polarization type of calculation (problems of continuum dielectric, dielectric saturation, ionic radii, etc.)	Debye and MacAulay[8]
b) Distribution treatments		
(i) Butler	Oversimplified dielectric polarization calculation. Unjustified linearization of exponentials.	Butler[9]; Bockris and Egan[17]
(ii) Belton	Improved treatment of non-electrolyte distribution; more realistic polarization terms suggested.	Belton[10]
(iii) Bockris, Bowler-Reed and Kitchener	As in b(i), but inclusion of dispersion interactions gives prediction of salting-in.	Bockris, Bowler-Reed and Kitchener[17]
(iv) Conway, Desnoyers and Smith; Conway, Novak and Laliberté; Desnoyers and Arel	Linearization problem and dielectric saturation taken into account. Special role of primary hydration shell included and solvent-structure entropy effects recognized.	Conway, Desnoyers and Smith[11]; Conway, Novak and Laliberté[20]; Desnoyers and Arel[24]
c) Scaled-particle theory treatments	Gives good account of salting-out behavior and specificity for various salts. Ion/solvent/non-electrolyte electric polarization effects obscured by use of empirical density factors. Includes cavity effects.	Shoor and Gubbins[15]; Masterton and Lee[14]
d) Thermodynamic compression (electrostriction) treatment	Gives good account of salting-out/in but is based on empirical electrostriction term which includes specificities in ion-solvent interaction.	McDevit and Long[12]

TABLE 2. Comparison of theories of salting-out and salting-in (cont'd)

Theory	Comments	Authors/Ref.
e) Statistical-mechanical treatments	Very sound in principle, but weakened by necessity for extensive simplifications and introduction of empirical factors if numerical evaluations are to be made, e.g., use of empirical Gurney term.	Haugen and Friedman[22]; Krishnan and Friedman[23]; Hall[26]

7. **Salting-out in relation to field effects on adsorption at charged interfaces:** The problem of calculation of salting-out of non-electrolytes near ions is closely related to that of evaluation of potential or surface-charge dependence of adsorption of neutral molecules in the double-layer at electrified interfaces. The field due to ions is replaced by a double-layer field determined by the surface charge density σ on the electrode (or colloid) surface. Primary hydration has its analogue in solvent orientation in the double-layer in response to the field established by the charged surface.

The adsorption of a non-electrolyte is normally a maximum at or near the potential of zero charge. Increasing σ causes polarization of both solvent and non-electrolyte. The non-electrolyte is relatively excluded ("salting-out" field effect) from the compact region of the double-layer in relation to the solvent when the latter is more polarizable, per unit volume, than the adsorbate. Even for highly polar adsorbates, such as glycine (dipole moment, ca. 15D), adsorption from water at the Hg electrode is decreased by increasing electrode charge density.

The adsorption problem can be treated in terms of classical dielectric theory with an appropriate polarization energy term for associated polar dielectrics. Alternatively, in recent treatments, the change of energy of adsorption with increasing σ can be evaluated by calculating the energy required for displacing oriented solvent molecules in the double-layer by the non-electrolyte adsorbate. The energy of the solvent molecules increases with surface charge as also does their relative orientation. A two-state model with ↑ or ↓ orientation was used. An adsorption maximum at $\sigma = 0$ is predicted with an almost correct diminishing extent of adsorption, analogous to salting-out, with increasing ± σ.

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