
A PRELIMINARY REPORT ON A QUANTUM-MECHANICAL MODEL FOR THE ENERGETICS OF A SOLUTE AT THE SURFACE SEPARATING TWO IMMISCIBLE LIQUID PHASES

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Dedicated to Dr R. Zahradník on the occasion of his 60th birthday.

The model considered here is directed to the problem of evaluation of free energy changes in the course of the passage of a solute M from solvent A to the second solvent B . It is applied to detailed description of the energetics of the solute passage (M in contact with the A/B separating surface) for n -alkanes, n -alcohols and n -primary amines. The difference in the behaviour due to the different composition of M is evident (engulfing versus buoyancy processes). The further text regards the transfer free energy change ($A =$ water, $B = p$ -xylene) for amines. A discussion of possible improvements of the model is presented also.

We present in this paper a first attempt to model solvent interactions at the boundary of two immiscible liquids. The phenomena we consider, is the transfer of solute molecules between the two liquid phases, and, especially, the phenomena occurring during the close contact of the solute with the separation surface.

For the reasons which shall become more evident from the following, the model considered here is rather simple. When a new model is being introduced, the most important point is a selection of an approach which enables future inclusions of new features and which gives, also at the initial and intermediate stages of elaboration, results of some interest. We hope that this general criterion is satisfied by the present contribution.

The model considered here is based on our previous experiences on quantum-mechanical description of molecular interactions — at the *ab initio* level — and represents a contribution of our group to filling the gap between studies on small molecular isolated systems and studies concerned with large bodies by far encompassing the molecular scale. Recently, Dr Zahradník has strongly stressed the necessity of filling-up this gap, starting from the molecular side of the problem¹. The choice

of this subject for a special issue in his honour, indicates, to our opinion, that analyses done by Dr Zahradník on the complex domain of investigations in molecular sciences are timely and appropriate nowadays, as well as they were in the past.

THEORETICAL

The model is composed of two immiscible liquids, characterized at this stage of elaboration by their static dielectric constants ϵ_1 and ϵ_2 (and by a set of other static properties, like molecular diameter, density, thermal expansivity) and separated by a well defined and static flat boundary surface. Within the liquid, there is a single molecule of solute M .

Physical interactions accounted for by the model are the electrostatic interactions inside M , described in a time-independent formulation by the usual electrostatic hamiltonian in the Born–Oppenheimer approximation, supplemented by interactions with the solvents, formally represented by an interaction operator \mathbf{V}_{int} , acting on the particles of M .

The physical model is then described by the following equation:

$$(\mathbf{H}_M^0 + \mathbf{V}_{\text{int}}) \Psi'_M = E' \Psi'_M. \quad (1)$$

The operator \mathbf{V}_{int} is approximated by a classical electrostatic operator, which accounts only for classical interaction terms between M and an averaged description of the solvents. It will be designated further as \mathbf{V}_σ . The solution of Eq. (1), or better, of the corresponding equation where \mathbf{V}_{int} is replaced by \mathbf{V}_σ :

$$(\mathbf{H}_M^0 + \mathbf{V}_\sigma(M)) \Psi'_M = E' \Psi'_M \quad (2)$$

gives information on the electrostatic interaction between M and solvent(s), with the inclusion of polarization effects on M due to the polarized solvent. V_σ is a generalization of the solvent reaction potential (in the common sense of this term) because $\mathbf{V}_\sigma(M)$ ultimately depends on the solvent polarized charge contribution of M (while the interaction potential usually refers to the unpolarized solvent).

The mathematical model is based on the formulation of the reaction potential operator in terms of apparent charge distributions defined at the boundaries between the portions of space filled with dielectrics at different ϵ . The principal source for σ is the surface of the cavity Σ encircling M . This cavity is defined in terms of spheres centered on atoms of M (here we have used a unique sphere for each CH_3 or CH_2 group) with radii close to the van der Waals values: the interior of the cavity has a dielectric constant $\epsilon_0 = 1$. A secondary source for σ is the flat and infinite surface separating solvents 1 and 2.

At each point of the surface separating medium i from medium j , there will occur an apparent charge distribution σ_{ij} , related to the differences in the polarization vector \mathbf{p} in the two media, or in other words, to the normal component of the derivative of the electrostatic potential which has as sources the charge distribution $\Gamma(M, r)$ of the solute (electrons and nuclei) and all the σ_{ij} charge distributions

$$\sigma_{ij}(s_k) = \frac{\epsilon_j - \epsilon_i}{4\pi\epsilon} \nabla V(r_i) \cdot n_{ij}, \quad (3)$$

where $\nabla V(r_i)$ is the gradient of the total electrostatic potential computed at r_i , and n_{ij} is the normal vector to the ij surface at r_i . The algorithm we use to compute the apparent charge distribution, starting from the definition of the spatial position of the boundaries, and on the ϵ_i values (being the only external parameters used here) has been described in preceding papers, for the simpler case of homogeneous solutions^{2,3}, as well as for the general case of different solvents^{4,5}.

It will be sufficient to recall that the solution of this nonlinear problem (the σ_{ij} 's depend on the final solution Ψ'_M of Eq. (2)) is achieved by means of an iterative procedure which converges quickly, and relies on the definition of point charges $q_{ij,k}(s_k)$ placed at the center of tesserads of area ΔS_k on the boundary surfaces:

$$q_{ij,k} = \sigma_{ij}(s_k) \Delta S_k. \quad (4)$$

From this set of charges one can immediately derive an expression for V_σ in the term of one-electron operator for current use in quantum-mechanical computational packages.

For the energy we use the following expression:

$$G_M^{si} = E_M^{\text{tot}} - \frac{1}{2} \int \Gamma'(M, r) V_\sigma(M, r) dr, \quad (5)$$

where G_M is a free energy, and corresponds to the work necessary to build up the polarized charge distribution of the solute, $\Gamma'(M, r)$, starting from an unpolarized system of dielectrics in which the void cavities Σ were present. The expression (5) emphasizes the fact that in the present utilization, the energy E_M^{tot} of the separate subsystem M is not the basic quantity. It may be designated as the electrostatic contribution to the free energy of the system.

Other contributions to the free energy could be also computed (vide infra), but they are neglected here. The only contribution taken into account is the contribution originated from the formation of the cavity, G_{cav} , evaluated in the framework of the scaled particle theory (SPT) according to the prescriptions given by Pierotti⁶ with modifications due to the non spherical shape of the cavity.

As stated above, the calculation of G_M^{e1} requires a definition of the cavity radii. These radii are empirical parameters which, according to our derivation of the model, should take into account the difference between semiclassical electrostatic calculations in discrete (and finite) M + solvent molecular clusters and electrostatic calculations with M within a continuous (in generally infinite) dielectrics. Our previous work on this subject has been mainly directed to aqueous solutions. In this case, the parallel examination of the decomposition of the interaction energy in hydration clusters of variable composition and geometry, the analysis of Monte Carlo results (both with M and with a void equivalent cavity as solute) and continuous dielectric calculations with variable cavity radii, resulted in a conclusion that the use of van der Waals radii multiplied by a constant factor, $f = 1.2$, represents a reasonable compromise for all the neutral chemical group. Such a simple rule, not based on the actual charge distribution in the solute, has been considered as sufficient for comparison of hydration energies of different molecules.

Currently, new attempts occurred to define more precisely cavity radii for the electrostatic energy based on intrinsic properties of atoms in the molecule^{7,8}.

As our problem is being related to the evaluation of differences in free energies in two solvents, we have found it convenient to explore a different strategy. Starting from the first three members of the alkane family (CH_4 , C_2H_6 , C_3H_8), we have systematically varied the cavity radii in two versions (separate radii for C and H atoms, radii for CH_3 and CH_2 groups) in two separate solvents (water and benzene), following the differences in the free energies

$$\Delta G_M^{e1}(1 \rightarrow 2) + \Delta G_{\text{cav}}(1 \rightarrow 2).$$

We have found very regular behaviour and selected the following couple of correction factors for the van der Waals radii: $f(\text{water}) = 1.2$, $f'(\text{benzene}) = 1.1$, possessing transfer free energies for all the set of n-alkanes with moderate errors.

Passing then to alcohols and primary amines, we have repeated these calculations for the cavity radii of the O, N, and H atoms in CH_3OH and CH_3NH_2 using fixed the f and f' factors for CH_3 . The resulting correction factors are $f(\text{water}) = 1.0$, $f'(\text{benzene}) = 1.2$ for alcohols and $f(\text{water}) = 0.95$, $f'(\text{benzene}) = 1.05$ for amines, with errors of the evaluation of the transfer free energy of the same order as above. The set of cavity radii defined in this way has been employed for all the solutes examined so far.

The cavitation energy has been computed using volumes and areas related to the same correction factors. When M is partially immersed in the two solvents, as in Fig. 1, G_{cav} has been computed as a sum of two components, each related to the volume of liquid displaced in the pertinent phase.

CALCULATIONS AND RESULTS

The model described in the preceding section has been applied to a set of n-alkanes, n-alcohols and n-primary amines, ranging in complexity from CH_3X to $\text{C}_6\text{H}_{13}\text{X}$ ($\text{X} = \text{H}, \text{OH}, \text{NH}_2$). In all cases the solute M has been kept in its fully extended conformation, with standard internal geometric parameters⁹. The solute has been put in contact with the surface separating the two liquids with the main axis perpendicular to this surface. Only vertical motions of M have been examined with the polar head of the solute, when present, pointing towards the aqueous phase. See Fig. 1 for a pictorial view.

The results reported here have been obtained on a GOULD 32/8205 using a suitably implemented version of GAUSSIAN 70 and refer to the STO-4G basis set. The free energy is plotted versus Σ_w , a parameter for the percentage of the M surface in water. We prefer the use of this parameter over a distance showing the position

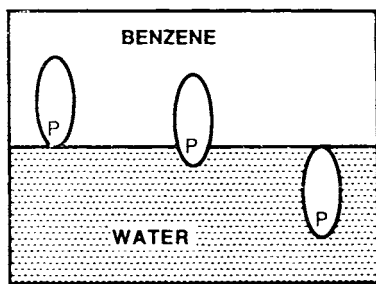


FIG. 1

A schematic representation of our material model. The solute represented by an ovoid, at three different positions. P is the polar head (when present)

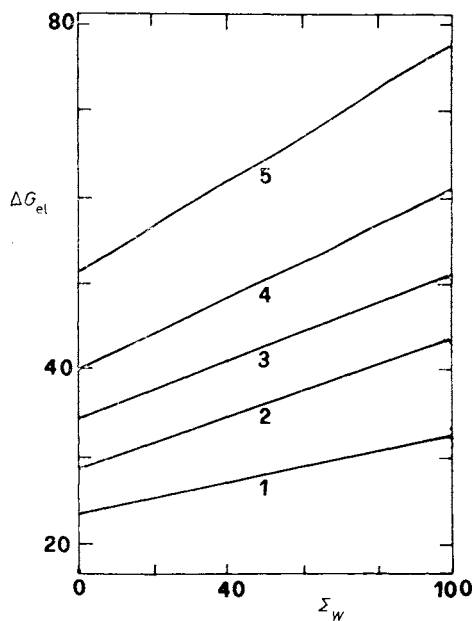


FIG. 2

Plot of the changes in ΔG_{et} with respect to Σ_w , i.e. the % of the molecular surface in the water phase for n-alkanes. Energies in kJ/mol. 1 CH_4 ; 2 C_2H_6 ; 3 C_3H_8 ; 4 C_4H_{10} ; 5 C_6H_{14}

of M with respect to the phase separation surface. The surface has been evaluated using van der Waals radii with $f = 1.0$. The simple algorithm used to compute the surface and volume of a cavity of general shape has been shown in a preceding paper¹⁰.

The results for alkanes show that for any solute occurs a clear tendency to pass into the benzene phase (engulfing process): this propensity increases with the length of the hydrocarbon chain (see Fig. 2).

On the other hand, for alcohols and amines, there exists an equilibrium position in which the buoyancy is determined by compensation of two opposite factors, the tendency of the aliphatic chain to stay in the benzene phase, and the tendency of the polar head to prefer the aqueous phase, a larger propensity for the hydration of NH_2 in comparison with OH being evident (e.g. from the comparison of the slope of the corresponding $\text{C}_n\text{H}_{2n+1}\text{X}$ curves near the 0% surface in water — see Figs 3 and 4).

Analysis of even such a limited set of results leads to interesting results which can be guessed by the reader himself. We prefer to delay this analysis until more numerical results will be available. In the following section, we shall discuss some problems related to the model, enlightening its limitations and the possible ameliorations.

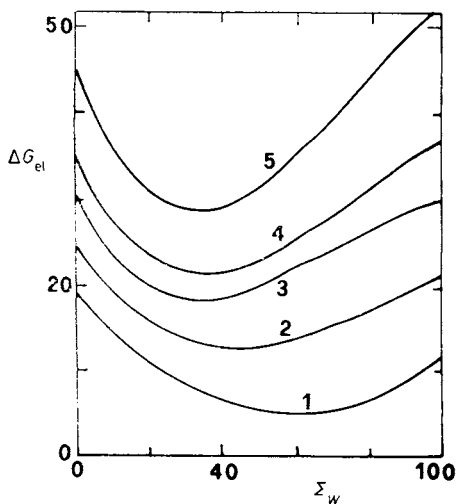


FIG. 3

As Fig. 2 for n-alcohols. 1 CH_3OH ; 2 $\text{C}_2\text{H}_5\text{OH}$; 3 $\text{C}_3\text{H}_7\text{OH}$; 4 $\text{C}_4\text{H}_9\text{OH}$; 5 $\text{C}_6\text{H}_{13}\text{OH}$

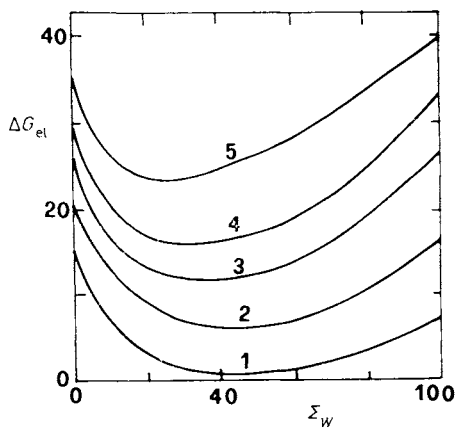


FIG. 4

As Fig. 2 for n-primary amines. 1 CH_3NH_2 ; 2 $\text{C}_2\text{H}_5\text{NH}_2$; 3 $\text{C}_3\text{H}_7\text{NH}_2$; 4 $\text{C}_4\text{H}_9\text{NH}_2$; 5 $\text{C}_6\text{H}_{13}\text{NH}_2$

DISCUSSION

As said formerly, the model has been kept purposely simple and many conceivable features have not been introduced. We shall discuss some of them, without effort of giving an order of importance.

Eq. (2) used in the calculations retains only electrostatic contributions. An important term missing here is related to dispersion contributions. Calculation of these contributions to the solvation energy is most precise, when perturbation theory techniques are used. The approach currently employed, adopting an approximate solvation cluster model and computing dispersion contributions as additive two-body terms, is unsatisfactory in several ways. Recently, we have developed a method in generalized form, for the solvent atoms¹¹ based on semiempirical dispersion atom-atom coefficients and continuous distributions. The mathematical model uses, as for the electrostatic term, an integration on the cavity surface. The calculation does not require much computer time and dispersion terms could be easily introduced in this way into the present model. Formulations expressing the solvent dispersion contributions in terms of solvent reaction field are, in addition, also possible. An attempt in this direction has been done several years ago by B. Linder¹². This approach is at present under examination in the Bajadoz group. We have not yet introduced dispersion contributions to the present model because it is convenient to explore primarily the performance of the simpler version of the model.

We should like to remark, that the strategy explained before for the determination of cavity radii has not been extended to other compounds in order to get an accurate numerical fitting. A pertinent question arises, if the rounded-off numerical factors f and f' are able to describe other transfer free energies. We report in Table I and Fig. 5 some values concerning the water \rightarrow *p*-xylene ΔG_{tr} for primary amines (regrettably, the experimental data are rather scarce and in some cases not well assessed yet).

Taking into account the change of solvents, the performances of the model are

TABLE I

Comparison of calculated and experimental¹³ free energies of transfer from water to *p*-xylene for some primary amines (in kJ/mol)

Amine	Calculated	Experiment
CH ₃ NH ₂	8.20	6.95
C ₂ H ₅ NH ₂	3.68	6.07
C ₃ H ₇ NH ₂	-0.04	2.55
C ₄ H ₉ NH ₂	-2.88	0.04
C ₅ H ₁₁ NH ₂	-5.15	-3.22
C ₆ H ₁₃ NH ₂	-7.36	-5.44

not too bad. It is worth mentioning that there exists a larger discrepancy for $(\text{CH}_3)_3\text{N}$ (calculated 11.38, experimental 20.5 kJ/mol) and a still noticeable discrepancy for $(\text{CH}_2)_2\text{NH}$ (calculated 9.16, experimental 4.7 kJ/mol; the experimental values and those in Table I are taken from Jones and Arnett¹³). It seems that the present set of parameters, if of some use for linear amines, loses efficacy passing to secondary and to tertiary amines.

For the estimation of solution free energy, as well as of transfer free energies, vibrational and translational contributions should be included also. The effect of these quantities on the solvation free energy ΔG_s° are numerically important. According to a simple model for the evaluation of the partition function of systems, the contributions neglected here are at least of the same order of magnitude as those considered here¹⁴. In addition, electrostatic contributions are heavily basis set dependent. However, the situation is not so bad as it appears, as non electrostatic contributions are less basis set dependent and it is possible to obtain reasonable estimates for ΔG_n° also without large basis set. Using some results from our preceding unpublished calculations, we present in Fig. 6 some data for simple solutes in water, computed with different basis sets, taking into account all the contributions to the solvation free energy. The experimental trend, at least, is fairly well reproduced. There are no evident reasons to suppose that in different solvents different trend will occur, even though the scarcity of the results suggests the enlargements of calculations to other cases.

The ideal experiment considered in this paper introduces an interesting problem.

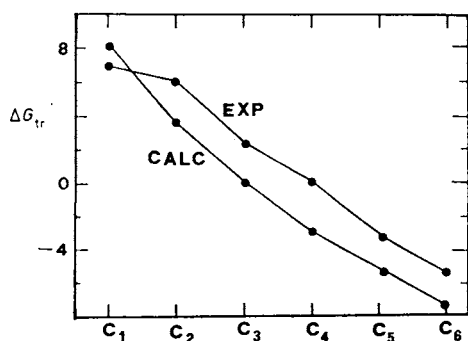


FIG. 5

Comparison of computed and experimental free energies of transfer for water to *p*-xylene (see Table I), for *n*-primary amines: C₁ CH₃NH₂; C₂ C₂H₅NH₂; C₃ C₃H₇NH₂; C₄ C₄H₉NH₂; C₅ C₅H₁₁NH₂; C₆ C₆H₁₃NH₂. Energies in kJ/mol

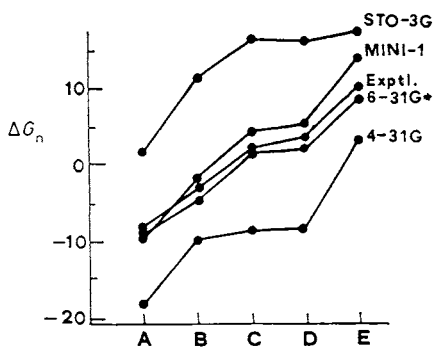


FIG. 6

Comparison of solvation free energy in water at 298 K with inclusion of vibrational, librational and translational contributions, using different basis sets. A water; B methanol; C acetone; D acetaldehyde; E dimethylether. Energies in kJ/mol

In dilute solutions, the solute molecule M is free of wandering over the entire volume. We now impose the condition that the solute must be in contact with the surface, reducing thus its wandering freedom. Generally, when M is near the surface, forces derived from the presence of the second phase will reduce this kind of freedom. The effect will be more evident when the separation surface bears an electrical charge or corresponds to a difference in the electrostatic potential. However, it occurs generally, with consequences which fade regularly when the solute increases its distance from the interface.

In many statistical models for dilute solutions — as that we employed for the data in Fig. 5 — the translational freedom of M is reduced to the evaluation of the free volume V_f available for local motions: This question has been thoroughly discussed in the literature¹⁵⁻¹⁷. A different approach, introduced by Ben Naim¹⁸ could be reconsidered for our problem: he introduced a “pseudo chemical potential” as the free energy required for the introduction of a single M molecule at some fixed point into the solution, and then a “liberation” free energy corresponding to the free energy change due to the release of this constriction. In normal solution, the liberation free energy is related to the entire volume V , while in the cases considered here, a different expression should be adopted.

Rotational contributions at the interface give origin to similar, but not identical questions. More detailed models, related to a deeper knowledge of the benzene/water interphase¹⁹ could give some information on these topics.

A different problem arises for the solutes considered here, from the vibrational contribution. In this case also the part regarding conformational changes can be included. We have considered our molecules as rigid rods without a possibility of reaching bent conformations. The irreality of this assumption is evident from the computed trend of hydration energies for alcohols and amines which shows an increment for each CH_2 group larger than that deduced from experimental data²⁰. A simple correction based on the combinatorial calculations of accessible local minima in the conformation space brings this increment to reasonable values. The remaining problem is that of a better evaluation of the relative populations of different conformers for large solutes, or to devise at least a method for obtaining information on the differential conformational behaviour in waters and in oils.

As stated at the beginning of this section, we shall not mention here all the problems left unanswered by the present model. The case considered here should be sufficient to show how the extension of methods and descriptions currently employed for isolated molecules or small clusters to large condensed systems brings up new problems which require a substantial extension and modification of the methods employed in the past.

This work of revision, and of innovation, will be done in the next future, via a co-operative effort, since the ideas and suggestions of Rudolf Zahradník will receive the attention they deserve.

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