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THEORETICAL DETERMINATION OF THE GIBBS ENERGY OF SOLUTION AND TRANSFER BETWEEN IMMISCIBLE SOLVENTS, WITH COMMENTS ON THE DYNAMICS OF PHASE TRANSFER *

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ABSTRACT

A method for the ab initio evaluation of solvation and solvent transfer Gibbs energies is presented and illustrated with some results.

The method provides for the complete determination of ΔG. The results, however, show that for many purposes a less detailed description is sufficient and the work of computation can be drastically reduced.

The model is extended to the construction of free energy surfaces describing the change in the energy (or chemical potential) for a solute near the boundary between two liquid phases. The results agree with chemical intuition.

INTRODUCTION

The activity of our group in the elaboration of theoretical and computational models for the study of chemical processes in solutions represents a natural extension of earlier theoretical studies on the nature and properties of molecular interactions involving a limited number of partners. Our approach to the study of solutions is influenced by our previous history and places more emphasis on the accurate description of the microscopic, submolecular aspects of the problem than on the elaboration of macroscopic, large-scale, empirical models and rules.

Because many aspects of the properties of chemical systems in a fluid phase that we have investigated, starting from our initial quantum-mechanical model for solvent effects [1], lie outside the field of interest of the present journal (for a recent synopsis of our work see ref. 2), we shall here deal solely with our elaboration for the evaluation of the free energy change of a system due to a change in the environment. More specifically, we shall only

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consider solvation free energies, $\Delta_{\text{sol}}G^{\ominus}$, and solvent transfer free energies, $\Delta_{\text{trf}}G^{\ominus}$ for infinitely diluted solutions.

THE METHOD

Our quantum mechanical approach relies on the solution of a Schroedinger equation, in which the molecular Hamiltonian of the solute M (i.e., $H_{\text{M}}^{\ominus}$) is accompanied by an effective interaction operator, V_{int}, accounting for the interactions with the surrounding medium. Further terms necessary for the evaluation of G according to statistical thermodynamics are obtained either via the same Hamiltonian, or with models (at the molecular level) of general use in the statistical treatment of liquids.

Solution of the Schroedinger equation

$$\left(H_{\text{M}}^{\ominus} + V_{\text{int}}\right)\Psi' = E'\Psi' \tag{1}$$

presents different possibilities that depend on the application sought. The solvation free energy for one mole of M may be written in the following form

$$\Delta_{\text{sol}}G^{\ominus} = W(\text{M/S}) - RT\left(\ln \frac{q_{(\text{g})}^{\text{rot}}}{q_{(\text{lq})}^{\text{rot}}} + \ln \frac{q_{(\text{g})}^{\text{vib}}}{q_{(\text{lq})}^{\text{vib}}} + \ln \frac{q_{(\text{g})}^{\text{tr}}}{q_{(\text{lq})}^{\text{tr}}}\right) + \Delta(PV) \tag{2}$$

the first term of which represents the interaction energy between solute M and solvent S, and the remaining terms express the contributions of motion through the appropriate molecular partition functions.

We shall adopt the Ben-Naim approach [3] because it is well suited for the application considered at the end of the paper.

We are firstly interested in a more precise definition of $W(\text{M/S})$. This term may be divided into electrostatic, dispersion and repulsion contributions. All the terms may be evaluated according to quantum mechanics, but it is convenient to adopt different approaches.

The electrostatic contribution includes the difference in the reversible electrical work necessary to assemble the electrical subunits of M (electrons and nuclei) in vacuo and in solution. When the corresponding part of V_{int}, eqn. (1), uses a continuous description of the thermally averaged distribution of solvent molecules around M, the electrostatic contribution also contains the work necessary to bring the continuous distribution into the opportune polarisation state. If limited to this term, V_{int} may be assimilated to a generalisation of the solvent reaction potential used in semi-classical theories of solvation (V_σ) [4]. The electrostatic contribution is obtained as the difference in the analogous quantities computed in solution and in vacuo

$$\Delta G_{\text{el}} = E' - \tfrac{1}{2}\langle\Psi'(V_\sigma)\Psi'\rangle - E^{\ominus} \tag{3}$$

E' (total energy, including nuclear contributions), Ψ' and V_σ come from eqn. (1) and $E^{\ominus}$ (including nuclear contributions) is the solution of the equation with $V_{\mathrm{int}} = 0$. More details on the derivation of eqn. (3) are given in earlier papers [1,2,5]. We stress here the fact that both E' and $E^{\ominus}$ have the status of a free energy contribution.

For practical applications it is convenient, even if not necessary, to maintain the level of calculation within the Hartree–Fock level. In the following examples, therefore, $H_{\mathrm{M}}^{\ominus}$ in eqn. (1) is replaced by the Fock operator $F_{\mathrm{M}}^{\ominus}$, with the usual recipes for the calculation of E' and $E^{\ominus}$.

The Hartree–Fock approximation is not sufficient for the evaluation of dispersion contributions. Instead of using a full Hamiltonian, with accurate description of the solute M as well as of the solvent molecules, we have recently elaborated an efficient algorithm which makes use of atomic (or group) contributions to the dispersion energy [6]. The energy obtained as an output of the calculations has again the status of a free energy contribution, G_{disp}.

Repulsion effects are the cause of the formation of the appropriate empty space where M is situated in the bulk of the solvent; they also represent a contribution to the solute–solvent interaction energy. The calculation via quantum mechanics of the first repulsion contribution is a formidable task which can be approximated by semi-classical molecular dynamics simulations (still very expensive). A simpler method is offered by the scaled particle theory [7], and we shall adopt the expression given by Pierotti [8] to evaluate the free energy for the formation of a cavity of appropriate size, G_{cav}. The second repulsion contribution may be evaluated with the approach used for the dispersion contributions, again using group contributions [9].

Summing up, the solute–solvent interaction term may be decomposed in the following way

$$W(\mathrm{M/S}) = \Delta G_{\mathrm{el}} + G_{\mathrm{disp}} + G_{\mathrm{rep}} + G_{\mathrm{cav}} \tag{4}$$

with appropriate computational algorithms for each term. An important and characterising feature of the computational procedure outlined is the reduction of all the single terms of eqn. (4) to contributions defined on the surface of M, a surface computed with an original algorithm [10,11] which is more effective than those available in the literature. Reduction of solvent interaction to molecular surface contributions constitutes an interesting bridge between calculation of a single physical property (as here for $\Delta_{\mathrm{sol}}G^{\ominus}$) and the extremely detailed information offered by quantum calculation. The examination of contributions on the surface enables the researcher to set up new correlations between physical properties of different material systems via pattern recognition and image processing.

The remaining terms of $\Delta_{\mathrm{sol}}G^{\ominus}$, eqn. (2), are treated with the normal methods of statistical mechanics.

The partition function, q^{vib}, in the gas phase as well as in solution can be evaluated via quantum mechanical calculation (for the evaluation of vibrational frequencies in solution with our approach see ref. 12). The calculations are relatively costly, especially for solutes of large dimensions.

Evaluation of the partition function for rotational motions in solution makes use of empirical values for the potential forbidding free rotation: we primarily direct our attention to the strength of local interaction between solute and solvent molecules (especially hydrogen bonds), following a treatment similar to that outlined by Némethy and Scheraga [13].

The term related to the momentum partition function gives rise to the liberation free energy, in the Ben–Naim terminology. Given the temperature and solute density in the liquid, this quantity is independent of the properties of the surrounding medium.

The method described, with some details for evaluation of the free energy changes, can also be adapted, with minor modifications and a few additional calculations, for the corresponding enthalpy changes. By exploiting the Gibbs–Helmholtz equation, the derivative of G with respect to T is divided into separate contributions, each evaluated with appropriate partial derivatives. Where convenient, use is also made of experimental values. Some details are given in refs. 1 and 14. The method seems to work, but we have so far paid less attention to the separate evaluation of enthalpy and entropy.

ESTIMATES OF SOLVATION FREE ENERGIES

Each component of $\Delta_{\mathrm{sol}}G^{\ominus}$ is subject to uncertainties and errors of its own. The physical model, the mathematical algorithm and the parameters used in the calculation are approximate and are all possible sources of errors. Unfortunately, information on the single components into which we have divided $\Delta_{\mathrm{sol}}G^{\ominus}$ cannot be extracted from the direct experimental data. The checks we have performed, and are still performing, are based on the congruence of the final results over a wide set of properties (solvation energies, spectral data, chemical processes, equilibrium geometry in solution). Discussion of this checking must be confined here to the presentation of a few results, which may be of general interest.

SOLUTES AT FIXED GEOMETRY

The quality of the basis set employed in the evaluation of ΔG_{el} has a remarkable influence on the quality of the results. Figure 1 shows the results for the evaluation of $\Delta_{\mathrm{hyd}}G^{\ominus}$ (water at 298.15 K) using eqn. (2) for a small set of organic solutes containing oxygen (alcohols, aldehydes, ketones, ethers and esters) with different basis sets of common use in quantum mechanical calculations. The correlation between computed and experimental values is acceptable for all basis sets; but there are clear hints that more accurate calculations give better agreement with experiment.

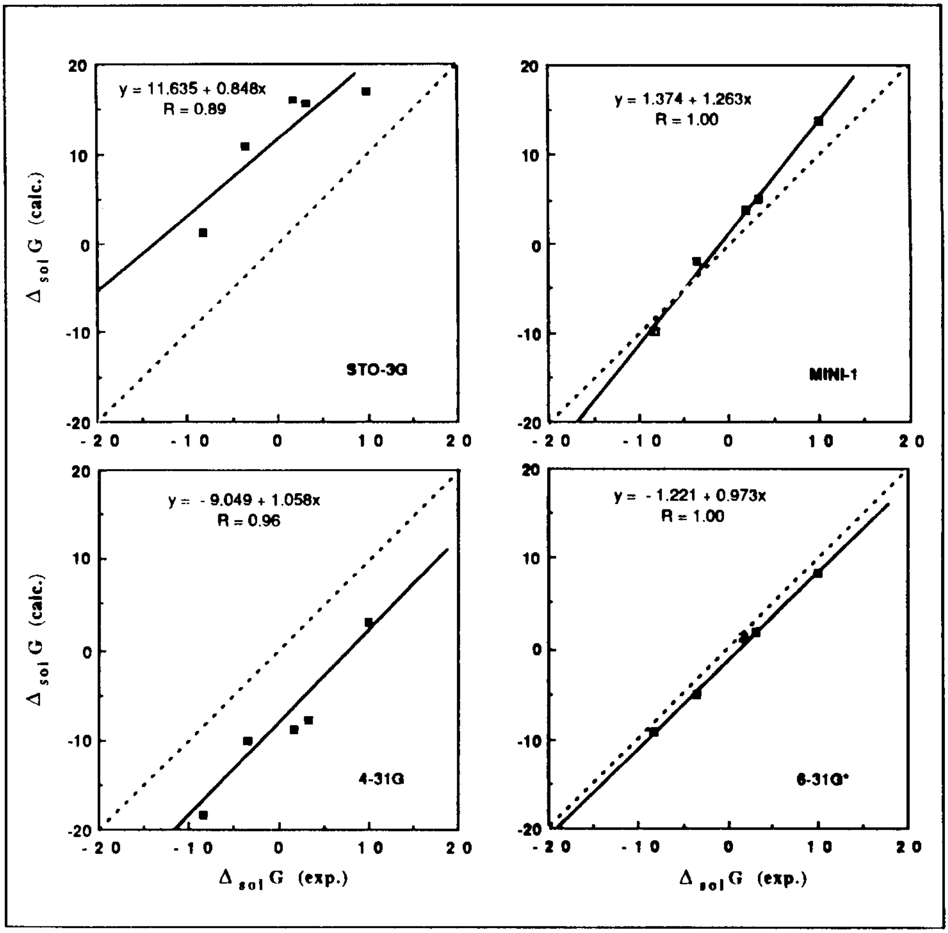


Fig. 1. Comparison of the computed and experimental values of $\Delta_{\text{sol}}G^{\ominus}$ (solvent water, $T = 298.15$ K) for a restricted specimen of small molecules. Each graph refers to a different basis set. Linear correlation expressions and regression coefficients are reported in the graphs (values in kJ mol^{-1}). The dependence of the results on the basis set is noticeable, but basis sets of good quality give satisfactory results. The data are taken from ref. 2.

A tentative conclusion, which has so far passed several tests, is rather encouraging: as already stated, the components of $\Delta_{\text{sol}}G^{\ominus}$ most subjected to arbitrary assumptions in the calculations are those related to the evaluation of $-RT \ln q_{\text{sol}}(\text{M})$. In several sets of related compounds there is a good correlation between ΔG_{el}, eqn. (3), and $\Delta_{\text{sol}}G^{\ominus}$, eqn. (2). The solution of some simple amides in water (298.15 K) is illustrated in Fig. 2. The quality of the computed values of $\Delta_{\text{sol}}G^{\ominus}$ with respect to the experimental ones is comparable to those shown in Fig. 1 (basis set 6.31 G*).

The method seems applicable to water as well as to non-polar solvents. Application to the evaluation of free energy of transfer (and then of the partition coefficients) is under way, with encouraging results. Figure 3

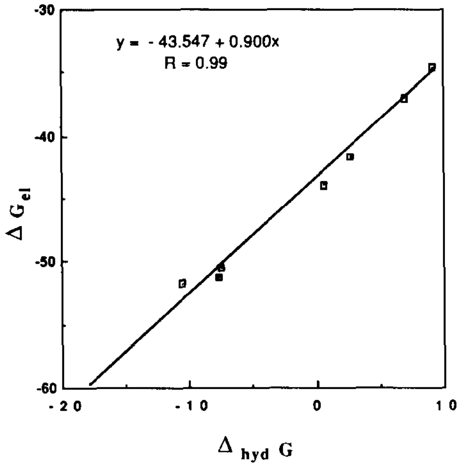


Fig. 2. Comparison of computed ΔG_{el} and $\Delta_{\mathrm{sol}} G^{\ominus}$ values for some amides. Calculations done with the 6-31G* basis set.

compares the experimental and computed values for $\Delta_{\mathrm{trf}} G$ (water → *p*-toluene) for a set of linear amines $C_nH_{2n+1}NH_2$. The computed values refer to the ΔG_{el} component only (STO-4G calculations) [15].

These few examples suffice to show that *ab initio* low-cost methods (the computational times are smaller by a factor of 10^3 or 10^4 than those necessary for computer simulations) allow reasonable appreciation of solvation free energies for neutral solutes in various solvents.

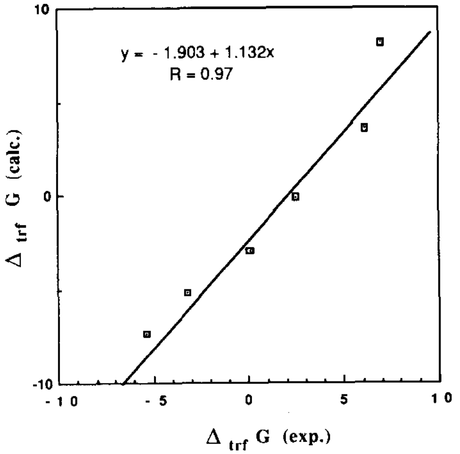
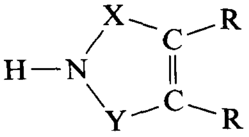


Fig. 3. Comparison of the calculated and experimental values for the water $\Delta_{\mathrm{trf}} G^{\ominus}$ (water → *p*-toluene, $T = 298.15$ K) for some linear amines. Data from ref. 15.

CHANGES IN THE GEOMETRY OF THE SOLUTE

A comparison of ΔG_{el} and $\Delta_{\mathrm{hyd}}G^{\ominus}$ values for a set of different tautomers related to the molecular skeleton given in Scheme 1 is made in Fig. 4.



$$\mathrm{X, Y}\left\{\begin{array}{l}\mathrm{C{=}O}\\ \mathrm{C{=}NH}\end{array}\right.$$

Scheme 1.

The agreement between the two sets of computed values is good, as in the preceding examples. To the best of our knowledge, there are no reliable estimates of the experimental $\Delta_{\mathrm{hyd}}G^{\ominus}$ for these compounds. But the experimental estimates of the relative percentage of the tautomers in solution, when available [16], agree with the computed ratios within 2–3%. More detailed experimental estimates are available for the neutral–zwitterion tautomeric equilibrium in solution of glycine; in this case we also present estimates of ΔH and $T\Delta S$ (see Table 1).

For these evaluations, the value of $\Delta_{\mathrm{hyd}}G$ must be accompanied by the changes in the in vacuo energy, or, to be more precise, by the changes of free energy in vacuo due to changes in the internal geometry.

These considerations justify extension of the concept of free energy commonly used in thermodynamics to the concept of a free energy hypersurface in the space defined by the nuclear coordinates of M. Justifications and a precise definition of this concept may be found, for example, in a review paper by Laidler and Polanyi [20]. Free energy hypersurfaces may be defined in the following way

$$G^{\mathrm{sol}}(\mathrm{M};R) = G^{\mathrm{vac}}(\mathrm{M};R) + \Delta_{\mathrm{sol}}G(\mathrm{M};R) \tag{5}$$

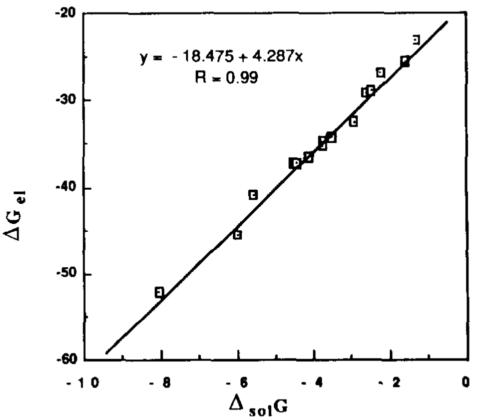


Fig. 4. Comparison of computed ΔG_{el} and $\Delta_{\mathrm{sol}}G^{\ominus}$ values for a set of tautomers related to the general formula given in scheme 1. The ΔG_{el} values will be also employed in ref. 26.

TABLE 1

Prospect of some thermodynamic quantities for processes involving tautomeric changes between the neutral (NT) and the zwitterionic (ZW) form of glycine (kJ mol^{-1})

Quantity	(NT) (g) → (ZW) (aq)		(NT) (aq) → (ZW) (aq)	
	Computed [a]	Experimental [b]	Computed [a]	Experimental [c]
ΔG	−69.0	–	−27.2	−32.2
ΔH	−81.6	−80.3	−37.2	−41.4
$-T\Delta S$	12.6	–	10.0	9.2

[a] The calculations refer only to electrostatic contributions. Values taken in part from Bonaccorsi et al. [17] and in part from unpublished calculations.

[b] Estimate provided by Gaffney et al. [18].

[c] Estimated provided by Haberfield [19].

which indicates the nuclear coordinates (R) on which the single terms depend. Some additional remarks on the thermodynamical status of eqn. (5) may be found in ref. 21. The use of eqn. (5) for the determination of relative stabilities of conformers, especially of large molecules, is examined in detail in refs. 22 and 23.

SOLVATION ENERGY AT A LIQUID PHASE SEPARATION

While the concept of free energy surface in the space of the nuclear coordinates of the molecule is now regularly used in molecular sciences, other phenomena require further extension of the concept. When one passes from isotropic solutions to more complex systems where there are fields (it is not necessary to specify here the origin and nature of the field) that have an effect on W(M/S) depending on the position of M in the Euclidean space, $\Delta_{sol}G^{\ominus}$ also depends on this position. The definition of Laidler and Polanyi already quoted can also be applied to this case. Ben-Naim's definition of starred thermodynamics quantities, related to the insertion of the solute at a fixed, preselected, point of the solution, may be of some use. The "liberation free energy" assumes a different meaning in the cases considered here and depends on the problem and the model under examination.

Let us consider the case of two immiscible liquids, separated by a flat infinite boundary. Computer simulations indicate that the effect of the boundary is limited to a layer with a depth of approximately two molecular diameters (for the water–benzene system see Linse [24]). We found similar effects on $\Delta_{sol}G^{\ominus}$ (M; z,ω) for solutes, M, near the water–benzene surface; z and ω are the distance and orientation of M with respect to the surface. Figure 5 reports the $\Delta G_{el}(z, \theta)$ values for $C_2H_5NH_2$ (only rotation, θ, which maintains the main inertia axis in a fixed plane normal to the separation boundary). The values of ΔG_{el} at large positive and negative z values

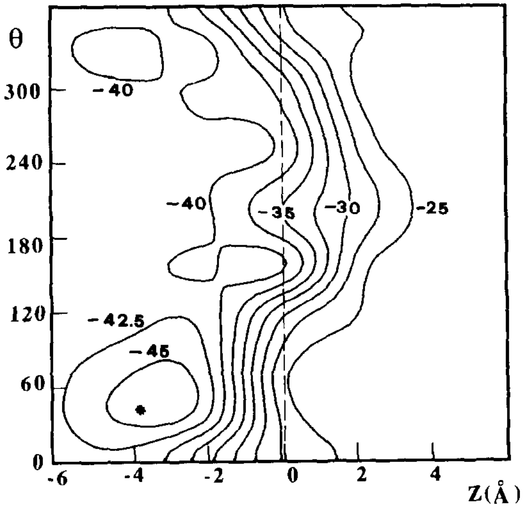


Fig. 5. Map for ΔG_{el} ($M; z, \theta$) for ethylamine in the water–benzene system ($T = 298.15$ K). The separation surface is put at $z = 0$. The benzene is in the region with positive z values. The positions on the map refer to the centre of mass of the solute. The rotation axis θ is perpendicular to the separation surface. The curves are spaced by 2.5 kJ mol^{-1}. Calculations were performed with the 4-31G basis set.

correspond to the $\Delta G_{el}(M)$ values in the bulk benzene and water, respectively. There is a propensity for the solute molecule (we are considering infinitely dilute solutions) to stay in the proximity of the boundary on the water side.

A final computer experiment is presented in Fig. 6. It concerns $C_nH_{2n+1}NH_2$ molecules with their hydrocarbon tails in the extended conformation, allowing motion only along the z coordinate. The minima of these sections of the $\Delta_{sol}G^{\ominus}$ ($M; z, \omega$) surface correspond to a buoyancy condition,

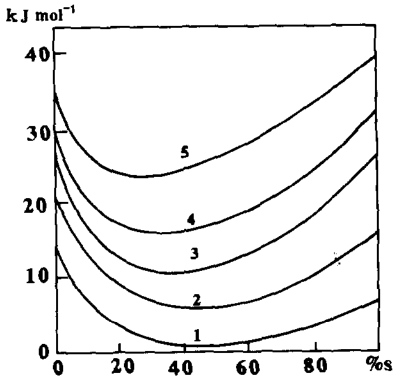


Fig. 6. Plots of ΔG_{el} (z, $\theta = 0$) for the passage of some linear amines $C_nH_{2n+1}NH_2$ ($n = 1$, 2, 3, 4 or 5) from benzene to water ($T = 298.15$ K) with respect to the % of the molecular surface, S, in contact with water. STO-4G calculations from ref. 15.

with the polar head in water and the hydrocarbon tail in benzene. This effect is familiar, at the macroscopic level, to those working on liquid interfaces. Different buoyancy conditions have been found for other classes of compounds, while for hydrocarbon solutes, there is an engulfing process (for the definition of engulfing, see, for example, Israelachvili [25], and ref. 15 for our computed data).

As stated in the introduction, with these last examples we are shifting from the field of classic thermodynamics of liquid solution to a less well-defined field, where topics of equilibrium thermodynamics are mixed with static and dynamic considerations at the molecular level: the underlying unity of the phenomena occurring in the material world makes it sometimes necessary to explore unitary approaches in which different methods are combined.

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