Solvation thermodynamics in a van der Waals liquid

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Abstract

The expression of the chemical potential of a solute in a solvent is derived exploiting the van der Waals model of liquids using a statistical thermodynamical approach. Then the solvation thermodynamics is determined, and discussed in detail for the case of an infinitely dilute solution. The analysis shows that the definitions introduced by Ben-Naim are exact and need no corrections. Moreover, the results obtained are in line with the theoretical approach devised by Lee to rationalize the experimental thermodynamic data of solvation.
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1. Introduction

There is a general and strong interest in trying to reach a better understanding of solute–solvent interactions [1–8]. However, a great deal of confusion does exist among scientists working in the field also for the definition of solvation [9,10]. Ben-Naim [11–14], in a series of important works, has shown that the physically correct definition of solvation refers to the transfer of a solute molecule from a fixed position in the ideal gas phase to a fixed position in the liquid, at constant temperature and pressure. The corresponding Ben-Naim standard Gibbs energy change reflects only the coupling work of the solute with the surrounding solvent molecules and does not contain contributions from the difference in the molar volume available in the two phases, in the assumption that the

internal partition function of the solute molecule—rotational, vibrational, electronic and nuclear degrees of freedom—is not affected by the transfer process. In addition, this quantity is directly related to the ratio of the molar concentrations of the solute in the gas and liquid phases at equilibrium [14]. However, some authors [15–22] have claimed that a correction should be added to the Ben-Naim standard Gibbs energy change.

Honig and co-workers [15–17] advocated that the mixing entropy, accounting also for the different molar volumes of the chemical species involved, has to be subtracted from the Ben-Naim standard Gibbs energy change. But, as pointed out by Lee [23], such a correction represents the mixing entropy of a system consisting of ideal gases, not that of the real system. The latter, as for the usual liquid solutions, is a crowded assembly of finite size particles, and its entropy is greatly reduced with respect to an ideal gas system by both excluded volume effects and attractive interactions among particles. On the other hand, Chan and Dill [19,20] claimed that the Flory–Huggins interaction parameter, the so-called

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contact free energy, is the physical quantity that has to be extracted from solubility measurement data in order to estimate the solute–solvent interactions. Actually, the Flory–Huggins theory [24], being entirely based on a rigid lattice model of the liquid state, is not able to properly account for the excluded volume effects [25]. The latter, however, play a major role in both pure liquids and solutions and cannot be underestimated.

Recently, Vitha and Carr [26], starting from the van der Waals equation of state, claimed that both the transfer Gibbs energies based on the molar concentration scale and those based on the mole fraction scale do not "purely reflect attractive solute–solvent interactions free from volume entropy effects". In order to avoid these problems, they suggested that the solute concentration has to be based on the so-called free volume, not the total volume of the system [26].

In the present article, we would like to disprove the claim by Vitha and Carr and to confirm the general validity of the analysis by Ben-Naim, using the same van der Waals model of liquids. The van der Waals equation of state provides a simple but non-trivial and insightful model of liquids because it considers that each particle occupies a finite volume and interacts with all the others. In fact, the successful Weeks–Chandler–Andersen theory confirms the qualitative correctness of the van der Waals picture for liquids [27]. We start with the derivation of the chemical potential of a solute in a van der Waals liquid. Then the thermodynamics of transfer from ideal gas to the van der Waals liquid is determined and discussed in detail for the case of an infinitely dilute solution. As a result, the analysis performed by Ben-Naim proves to be correct, and a simplified version of the theoretical approach devised by Lee [28–30] to rationalize the solvation thermodynamics emerges.

2. Chemical potential of van der Waals fluids

The canonical partition function for a monoatomic van der Waals fluid is reported in several textbooks of statistical mechanics [31–33]. The canonical partition function for a binary mixture of monoatomic van der Waals fluids is an extension of the former and can be written in the following manner:

$$
\begin{aligned}
Q(N_1, &N_2, V, T) \\
&= \left[\frac{V^{N_1+N_2}}{N_1! \Lambda_1^{3N_1} N_2! \Lambda_2^{3N_2}} \right] \\
&\quad \times \left[\frac{V - (b_1 N_1 + b_2 N_2)}{V} \right]^{N_1+N_2} \\
&\quad \times \exp \left[\frac{(a_1 N_1 + a_2 N_2)^2}{kTV} \right]
\end{aligned}
\tag{1}
$$

where V is the volume of the system; N_i the number of molecules i; $\Lambda_i \equiv h/(2\pi m_i kT)^{1/2}$ the momentum partition function or the thermal de Broglie wavelength of molecules i; parameter b_i the measure of the size and so of the short-range repulsive interactions; parameter a_i the measure of the long-range attractive interactions of molecules i (note that a_i and b_i are positive and temperature independent); k the Boltzmann constant and T is the absolute temperature. It is well known that in the van der Waals model each molecule moves in the free volume $[V - (b_1 N_1 + b_2 N_2)]$, where the average attractive potential energy corresponds to $-(a_1 N_1 + a_2 N_2)^2/V$, and is practically independent of the others.

It has to be noted that, according to van der Waals [34], its equation of state can be applied to binary mixtures by considering that the parameters a and b vary in the following manner with composition:

$$
a = a_{11} x_1^2 + 2 a_{12} x_1 x_2 + a_{22} x_2^2
\tag{2}
$$

$$
b = b_{11} x_1^2 + 2 b_{12} x_1 x_2 + b_{22} x_2^2
\tag{3}
$$

where the x_i are the mole fractions of the components; a_{ii} and b_{ii} are just the parameters for the pure components; the a_{12} and b_{12} parameters characterize the interactions between unlike molecules. The canonical partition function of Eq. (1) corresponds to the prescription by van der Waals if $a_{ii} = a_i^2$, $b_{ii} = b_i$, $a_{12} = a_1 a_2$ and $b_{12} = (b_1 + b_2)/2$. The latter conditions practically correspond to the commonly used Lorentz–Berthelot combining rules for passing from the parameters characterizing the interactions between like molecules to those characterizing the interactions between unlike molecules [31–33]. Therefore, Eq. (1) has to be considered of general validity.

The Helmholtz free energy of the system is readily obtained from the general statistical mechanical

relation $A = -kT \ln Q$. Then, it is possible to calculate the chemical potential of component 2 in the mixture:

$$\mu_2 \equiv \left(\frac{\partial A}{\partial N_2} \right)_{T,V,N_1} \tag{4}$$

Performing the derivative, one obtains

$$
\mu_2 = kT \ln \rho_2 \Lambda_2^3 - kT \ln \\
\times \left[\frac{V - (b_1 N_1 + b_2 N_2)}{V} \right] \\
+ kT \left\{ \frac{(N_1 + N_2) b_2}{[V - (b_1 N_1 + b_2 N_2)]} \right\} \\
+ \left\{ \frac{-2a_2(a_1 N_1 + a_2 N_2)}{V} \right\} \tag{5}
$$

where $\rho_2 = N_2/V$ is the number density of component 2. Eq. (5) is the complete expression of the chemical potential of component 2 in a binary mixture of monoatomic van der Waals fluids. According to the analysis by Ben-Naim [14], Eq. (5) can be rewritten as

$$\mu_2 = \mu_2^\bullet + kT \ln \rho_2 \Lambda_2^3 \tag{6}$$

where $\mu_2^\bullet$ is the so-called Ben-Naim standard chemical potential (Ben-Naim standard quantities are denoted by a superscript ($\bullet$)). As emphasized by Eq. (5), this quantity accounts for all the interactions of the component 2 in the liquid phase, except for the classical translational degrees of freedom. Actually, the quantity $\mu_2^\bullet$, also referred to as the coupling work of the solute molecule to the system [14], is the average free energy of interaction of the solute molecule, fixed at any position in the solution, with its entire surroundings, with no restriction on the solute concentration in the system (i.e. since the liquid phase is considered to be homogeneous and isotropic, the solute molecule can be placed at any point in the system). It has to be noted that: (a) this interpretation comes directly from the statistical mechanical derivation; (b) there is no need to define any standard state, in contrast to what happens in the framework of thermodynamics; (c) the quantity $\mu_2^\bullet$ depends upon the composition of the solution, because the coupling work depends upon such variable (this is a fundamental property to correctly address the role of solvation in fundamental biochemical processes, such as protein folding, protein–protein and protein–DNA associations).

On the other hand, it is well known that the chemical potential of the monoatomic component 2 in the ideal gas phase is [31–33]:

$$\mu_2 = kT \ln \rho_2 \Lambda_2^3 \tag{7}$$

In fact, since there are no interactions among particles in the ideal gas phase, only the classical translational degrees of freedom contribute to μ_2 and so $\mu_2^\bullet = 0$. Eqs. (6) and (7) show that according to statistical thermodynamics, the natural concentration unit to be used in expressing the chemical potential is the number density.

3. Thermodynamics of solvation

3.1. Gibbs energy change

Knowing the chemical potential of component 2 in the ideal gas phase and in a van der Waals fluid, we can study the transfer of component 2 from the ideal gas phase to the van der Waals fluid at constant temperature and pressure (i.e. the solvation process, if the van der Waals fluid is considered a model of the liquid state). The thermodynamic equilibrium condition is [14]

$$\mu_2(\text{ig}) = \mu_2(\text{vdW}) \tag{8}$$

where ig stands for ideal gas and vdW for van der Waals. By inserting Eqs. (6) and (7) into Eq. (8), one obtains

$$kT \ln \rho_2(\text{ig}) \Lambda_2^3 = \mu_2^\bullet(\text{vdW}) + kT \ln \rho_2(\text{vdW}) \Lambda_2^3 \tag{9}$$

Clearly, since the contribution from the momentum partition function is identical in the two phases and cancels out, Eq. (9) is readily transformed in

$$\Delta G^\bullet = \mu_2^\bullet(\text{vdW}) = kT \ln \left[\frac{\rho_2(\text{ig})}{\rho_2(\text{vdW})} \right] \tag{10}$$

where $\Delta G^\bullet$ is the Ben-Naim standard Gibbs energy change associated with the solvation process; and according to the first equality on the right-hand side of Eq. (10), $\Delta G^\bullet$ corresponds to the solute–solvent coupling work. Moreover, according to the second equality on the right-hand side of Eq. (10), as advocated by Ben-Naim [11–14], the direct application of statistical thermodynamics indicates that the ratio of

the molar concentrations of component 2 in the two phases allows the evaluation of the standard Gibbs energy change associated with the transfer from a fixed position in the ideal gas to a fixed position in the liquid, at constant temperature and pressure (i.e. $\Delta G^\bullet$ values are readily obtained from experimental data).

Given that the quantity $\Delta G^\bullet$ is not based on any standard state and there is no restriction regarding the concentration of the solute in the two phases [14], Eq. (10) is valid over the whole range of concentrations. There is no need to add a correction, as incorrectly claimed by Honig and co-workers. This fact has already pointed out and discussed by various authors using different arguments and routes [9,23,25,35–40].

Now, we specialize the analysis by considering an infinitely dilute solution of the component 2 in the van der Waals fluid 1, in order to reach a better physical understanding. In this case, the expression of $\Delta G^\bullet$ is readily obtained by taking the limit of the corresponding terms in Eq. (5) for $N_2 \to 0$, and by considering that, for $N_2 \to 0$, $N \cong N_1$ and $V \cong N_1 v_1$, where v_1 is the molecular volume of component 1. Accordingly, $\Delta G^\bullet$ is given by

$$\Delta G^\bullet = \mu_2^\bullet(\text{vdW})$$
$$= -kT \ln\left[\frac{v_1 - b_1}{v_1}\right] + kT\left[\frac{b_2}{v_1 - b_1}\right] - \frac{2a_1 a_2}{v_1} \tag{11}$$

Finally, it is convenient to pass from microscopic to macroscopic quantities multiplying all the terms by the Avogadro's number:

$$\Delta G^\bullet = -RT \ln\left[\frac{v_1 - b_1}{v_1}\right] + RT\left[\frac{b_2}{v_1 - b_1}\right] - \frac{2a_1 a_2}{v_1} \tag{12}$$

where v_1 is now the molar volume of component 1, and the parameters a_i and b_i refer to molar units. In order to gain physical insight, it is necessary to attach a reliable meaning to the three terms on the right-hand side of Eq. (12). The first two should represent the work to create a cavity suitable to host the molecule of component 2 in the van der Waals fluid 1:

$$\Delta G_c = -RT \ln\left[\frac{v_1 - b_1}{v_1}\right] + RT\left[\frac{b_2}{v_1 - b_1}\right] \tag{13}$$

In principle, they correspond to the first and fourth terms in the expression of ΔG_c provided

by the scaled particle theory, SPT [41,42]. In fact, $-RT \ln[(v_1 - b_1)/v_1]$ should correspond to the SPT term $-RT \ln(1 - \xi_1)$, where ξ_1 is the volume packing density of fluid 1; and $RT[b_2/(v_1 - b_1)] \cong P(\text{vdW})b_2$ should be the pressure–volume work done to introduce a molecule of component 2 in the van der Waals fluid 1. Actually, Eq. (13) is less accurate than the expression provided by the scaled particle theory, because the latter takes explicitly into account the mutual correlations existing between the positions occupied by individual molecules, in order to fulfill the non-overlap requirement operating in real liquids [41,43].

The existence of these mutual correlations cannot be accounted for by the van der Waals model because it handles the excluded volume effect in a rough manner, by considering only the so-called free volume $(v_1 - b_1)$ of the liquid. The latter is a large quantity in real liquids (50–60% of the total volume), whereas the volume available to insert a molecular-sized cavity is significantly smaller (orders of magnitude), because the non-overlap requirement has to be fulfilled. A very small fraction of the entire free volume of the liquid is relevant for the insertion of a real solute (i.e. only the cavities large enough to accommodate the solute molecule). If the free volume is not divided to provide cavities whose size is at least equal to the diameter of the solute to be inserted, all the free volume proves to be not available to the solute, as it were occupied by solvent molecules. This reasoning emphasizes that the partitioning of the free volume is a fundamental property of the liquid that cannot be accounted for by the van der Waals model. Computer simulations have provided invaluable information on the cavity size distribution in pure liquids [44–48].

In this respect, it is worth noting that the predictions of the van der Waals equation of state do not fit the experimental results, mainly because the expression accounting for the short-range repulsive interactions is not correct [49]. Other authors have pointed out and discussed the limitations of the van der Waals model for the molecular description of the chemical potential in the liquid phase [50,51].

On the other hand, according to the physical meaning of the parameters a_1 and a_2, the third term on the right-hand side of Eq. (12) should represent the average interaction energy of component 2 at infinite

dilution in the van der Waals fluid 1:

$$\Delta G_a = -\frac{2a_1 a_2}{v_1} \tag{14}$$

The analysis of Eq. (12) confirms that the solvation process can be correctly decomposed in two sub-processes having a well defined physical meaning [28–30]: (a) creation of a cavity in the solvent suitable to host the solute molecule; (b) turning-on the solute–solvent attractive potential. Therefore, both the excluded volume effect due to the finite size of real molecules, and the attractive interactions due to the charge distribution in real molecules play a role in solvation and are accounted for by the quantity $\Delta G^\bullet$, as advocated by Ben-Naim [11–14]. Contrary to the claim by Vitha and Carr [26], the concept of free volume inherent in the van der Waals model, even though qualitatively right and useful, is not quantitatively correct to account for the excluded volume effect associated with the insertion of the solute molecule; therefore, it has not to be used to avoid dangerous ambiguities.

3.2. Enthalpy and entropy changes

It is useful to calculate the enthalpy and entropy contributions associated with the two sub-processes under the constant pressure condition. For the cavity creation step, one readily obtains

$$\Delta H_c = -T^2 \left[\frac{\partial(\Delta G_c/T)}{\partial T} \right]$$
$$= RT^2 \left[\frac{\alpha_1}{v_1 - b_1} \right] \left\{ b_1 + \left[\frac{v_1 b_2}{v_1 - b_1} \right] \right\} \tag{15}$$

$$\Delta S_c = -\frac{\partial \Delta G_c}{\partial T}$$
$$= R \ln \left[\frac{v_1 - b_1}{v_1} \right] - R \left[\frac{b_2}{v_1 - b_1} \right] + \frac{\Delta H_c}{T}$$
$$= \Delta S_x + \frac{\Delta H_c}{T} \tag{16}$$

where $\Delta S_x = -\Delta G_c/T$ and represents the excluded volume entropy contribution due to cavity creation; and α_1 is the thermal expansion coefficient of the van der Waals fluid 1. The solvent undergoes a structural reorganization as a consequence of cavity creation, but such contribution, directly proportional to α_1, affects

the enthalpy and entropy in an exactly compensating manner [52]. In other words, the creation of a cavity under the constant pressure condition causes a change in the volume of the system, which, in turn, determines an enthalpy change (remember that the internal energy of a van der Waals fluid is inversely proportional to the volume). This enthalpy change has to be ascribed to solvent reorganization since there is no other source, and is exactly balanced by a corresponding entropy contribution. Note that, if the cavity is made under the constant volume condition, the enthalpy change is zero, and all the entropy change is due to the excluded volume effect, $\Delta S_c = \Delta S_x$.

For the attractive potential turning-on step, one obtains

$$\Delta H_a = -T^2 \left(\frac{\partial(\Delta G_a/T)}{\partial T} \right) = -\frac{2a_1 a_2}{v_1}(1 + \alpha_1 T) \tag{17}$$

$$\Delta S_a = -\frac{\partial \Delta G_a}{\partial T} = -\frac{2a_1 a_2 \alpha_1}{v_1} \tag{18}$$

where again the solvent structural reorganization upon turning-on the solute–solvent attractive potential proves to be directly proportional to α_1, and to affect the enthalpy and entropy in an exactly compensating manner. The finding that the solvent structural reorganization is proportional to the thermal expansion coefficient of the solvent is correct from the physical point of view because α is a measure of the ensemble correlations between enthalpy fluctuations and volume fluctuations [28,42,53] (i.e. $\alpha \equiv < \delta H \, \delta V > /kT^2 < V >$, where $\delta H = H- < H >$ and $\delta V = V- < V >$ represent the enthalpy and volume fluctuations with respect to their ensemble average values).

Such results are in line with the general theory devised by Lee [28–30], and with the analysis by Qian and Hopfield [54] aimed at explaining the occurrence of enthalpy–entropy compensation in many processes [55]. These authors showed that the action of a small perturbation on a thermodynamic system can be dissected into two parts: a direct interaction between the perturbation and the unperturbed system; and a response of the system by means of a redistribution of its subsystems, which are in thermal equilibrium, according to the Le Chatelier principle [54]. Such redistribution is a function of the environmental constraints applied to the system: the relaxation depends on the

type of microscopic fluctuations that the thermodynamic system can do. The latter process proves to be characterized by a perfect enthalpy–entropy compensation and so the Gibbs energy change is entirely due to the direct interaction between the perturbation and the unperturbed system. Clearly, in the case of solvation, the perturbation is represented by the insertion of the solute molecule at a fixed position into the solvent. The direct part of the perturbation consists of both cavity creation and turning on solute–solvent attractive potential; solvent structural reorganization is the response of the system to the direct perturbation.

4. Conclusion

The van der Waals model of liquids is qualitatively correct but not quantitatively exact. With respect to solvation, its fundamental merit is the possibility to obtain analytical expressions for the thermodynamic functions associated with the process. We have exploited such possibility and confirmed the general validity of the analysis by Ben-Naim. The solute–solvent coupling work, $\Delta G^{\bullet}$, is the only quantity that really accounts for the energetic and entropic contributions arising from both the repulsive and attractive solute–solvent interactions.

Acknowledgements

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