# Theoretical prediction of thermodynamic equilibrium constants of chemical reactions in water

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## Abstract

In this work we characterize the thermodynamics of two simple chemical reactions in water. Applying the quasi-gaussian entropy theory to the molecular dynamics calculations, we model the equilibrium constant and its temperature dependence along the typical water isochore. Such a theoretical–computational approach could be useful to predict the optimal condition for chemical reactions in condensed phase at a very low computational cost.
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## 1. Introduction

Understanding and predicting the thermodynamics of chemical reactions in condensed phase at different conditions has always represented a 'holy grail' for chemists. The possibility of virtually handling the matter is in fact extremely appealing not only intrinsically but also for many applications ranging from organic synthesis to industrial processes. However a reliable modelling of liquid solutions has been for many years extremely challenging and only in the last decades has become computationally accessible [1]. In this respect many efforts have been done for the calculation of excess partial molar properties and in particular the excess chemical potential [2,3], which is the key parameter for addressing the whole chemical thermodynamics in liquid solution. In a number of recent publications [4,5], we have proposed a rigorous and relatively low-cost approach for evaluating the whole statistical mechanics and thermodynamics of highly diluted liquid solutions in the framework of The Quasi Gaussian Entropy Theory (QGE) [6]. The most appealing feature of this approach, whose computational procedure is essentially based on classical molecular dynamics (MD) simulations of a box of one solute molecule embedded in a meaningful number of solvent molecules, is the possibility of evaluating the excess chemical potential variation accompanying whatever chemical reaction at whatever temperature.

In this paper we have applied this method for studying the thermodynamics of two simple chemical reactions in water solution which are of a certain fundamental and practical interest. The first one is the so-called water–gas shift reaction.

$$CO_{(aq)} + H_2O_{(aq)} \rightarrow CO_{2(aq)} + H_{2(aq)} \tag{1}$$
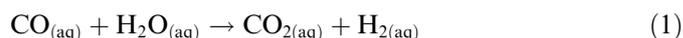
which, because of its importance, has been extensively studied by several investigators in particular at non-

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standard conditions (e.g. supercritical and near-supercritical conditions) [7,8].

The second one is the $S_N2$ hydrolysis of chloromethane which is a benchmark reaction both for synthetic organic chemistry and for mechanistic studies

$$CH_3Cl_{(aq)} + OH^-_{(aq)} \rightarrow CH_3OH_{(aq)} + Cl^-_{(aq)} \qquad (2)$$

This paper is organized as follows. In the first part, we briefly describe the essential features of the theoretical approach. In the methodological section the technical details are provided and, finally, the results and the conclusions are illustrated.

## 2. Theoretical section

The large body of QGE theory for the evaluation of statistical mechanics and thermodynamics of highly diluted solutions is described elsewhere [4–6,9–17]. In this paper we only report the essential theoretical features utilized in the present investigation. Let us consider a solution containing $N$ highly diluted solute molecules and $N_s$ solvent molecules. As shown in previous papers [5,6], for highly diluted solutes their partial molar thermodynamics can be fully obtained by a solution containing a single solute molecule embedded in $n_s = N_s/N$ solvent molecules. The excess Helmholtz free energy of such a system, i.e. the free energy variation between the actual system and its reference condition where the total potential energy (the excess energy $\mathcal{U}'$) has been removed, [6] is

$$A'(T) = n_s a'_s + a' \qquad (3)$$

where $a'_s$ and $a'$ are the partial molecular excess free energies of the solvent and solute, respectively. The partial molecular excess free energy is obviously related to the excess chemical potential $\mu'$ according to the relations: [5]

$$a'_s = \mu'_s - p'v_s \qquad (4)$$
$$a' = \mu' - p'v \qquad (5)$$

where $p'$, $v$ and $v_s$ stand for the excess pressure and the partial molecular volume of the solute and of the solvent, respectively. The excess (Helmholtz) free energy of the system can be written as [5]

$$A'(T) = kT \ln\langle e^{\beta\mathcal{U}'}\rangle - kT \ln \epsilon \qquad (6)$$

where $k \ln \epsilon$ is the confinement term taking into account the presence of effectively or virtually unaccessible phase space regions [5,6], which can be evaluated as indicated at the end of this section. The first term in Eq. (6), according to QGE theory, can be calculated assuming a 'quasi-Gaussian' distribution of the excess energy $\mathcal{U}'$. In particular, it has been shown [5,6,9,10,12–16] that one of the simplest 'quasi-Gaussian' distribution, i.e. the Gamma distribution, provides a simple and accurate model for treating fluid-state thermodynamics.

Hence, for Gamma state thermodynamics [5] we have

$$n_s a'_s + a' = U'_0 - T_0 C'_{V0}\Lambda(T) - kT \ln \epsilon \qquad (7)$$

$$\Lambda(T) = \frac{1}{\delta_0} + \frac{T}{T_0\delta_0^2} \ln\{1 - \delta(T)\} \qquad (8)$$

$$\delta(T) = \frac{T_0\delta_0}{T(1 - \delta_0) + T_0\delta_0} \qquad (9)$$

where $U'_0 = U'(T_0)$ and $C'_{V0} = C'_V(T_0)$ represent the excess internal energy and heat capacity of the system of $n_s$ solvent molecules and one solute molecule at the reference temperature $T_0$ and $\delta_0$ is a dimensionless intensive property [6] independent of the temperature, that in the case of high dilution, can be directly determined by the solvent.

Subtracting the solvent partial excess free energy from Eq. (7) it immediately follows the solute excess chemical potential [5]

$$\mu' = u'_0 - c'_{V0}T_0\Lambda(T) - kT \ln \bar{\epsilon} + p'v \qquad (10)$$

where $u'_0$ and $c'_{V0}$ are the solute partial molecular excess internal energy and heat capacity evaluated at the reference temperature $T_0$, and $-kT \ln \bar{\epsilon}$ represents the partial solute molecular excess free energy due to the confinement.

It is therefore clear that according to this model it is possible to derive the whole statistical mechanics and thermodynamics of a highly dilute solution by using MD simulations of a single solute embedded in $n_s$ solvent molecules.

The parametrization of the model, Eq. (10), may be obtained considering the confined excess chemical potential $\mu^*$ and Helmholtz free energy $A^*$ via

$$\mu^* = \mu' + kT\left(\frac{\partial \ln \epsilon}{\partial n}\right)_{V,n_s} = \left(\frac{\partial A^*}{\partial n}\right)_{V,T,n_s} = \Delta A^* \qquad (11)$$

$$A^* = A' + kT \ln \epsilon \qquad (12)$$

where $\Delta A^*$ is the difference between the confined excess Helmholtz free energies of the solute–solvent system and of the pure solvent one, at fixed volume, and $n$ is the solute molecular number which can be used as a continuous variable given the macroscopic nature of the thermodynamic system considered.

From Eqs. (7), (10) and (11) we then have

$$\mu^* = u'_0 - c'_{V0}T_0\Lambda(T) + p^*v \qquad (13)$$

$$p^* = p' - \xi T \qquad (14)$$

$$\xi = k\left(\frac{\partial \ln \epsilon}{\partial V}\right)_{n,n_s} \qquad (15)$$

where $\Lambda(T)$, $p^*$, $p'$, $\xi$, being intensive properties, are given by the Gamma state obtained by the pure solvent simulations [5].

Therefore by fitting $\Delta A^*$ as provided by MD simulation with Eq. (13), we can evaluate $u'_0$, $c'_{V0}$ and the partial molecular volume $v$.

The confinement term, $kT \ln \epsilon$ may be associated with hard body excluded volume. In our previous studies [4,5] we have shown that its calculation can be relatively straightforward in the case of simple spherical solutes by

the use of hard body equations of state. In this paper, following our previous studies, we utilize a recently developed hard sphere mixture equation of state (BMCSL) [18–20].

In the case of non-spherical molecules for which hard sphere equation of state would be inaccurate, we may obtain the confinement properties to be used in our model, simply performing at one temperature a thermodynamic integration calculation to evaluate $\mu'$ as described in detail in a previous paper [5].

Finally, in order to obtain the complete chemical potential ($\mu = \mu' + \mu_{ref}$) of each solute, we need to evaluate $\mu_{ref}$, i.e. the chemical potential at the reference condition which, for rigid molecules as in the present case, is fully equivalent to the actual gas-phase condition. Therefore we obtained, $\mu_{ref}$, via quantum chemical calculations on the isolated molecule.

## 3. Methodological section

We performed molecular dynamics (MD) simulations over a wide temperature range (280–1200 K), using a cubic box of 256 simple point charge (SPC) [21] water molecules, at 55.32 mol/l, plus a solute molecule: water (SPC), methanol [5], hydrogen, carbon monoxide, carbon dioxide, chloride [5], methyl chloride and hydroxide anions [22].

Note that in these models non polar hydrogens are not explicitly present (united atoms approximation). All the simulations were performed using Gromacs software package [23–25] modified to use the isokinetic temperature coupling [26]. This was done in order to obtain results fully consistent with statistical mechanics [9,28]. For all the simulations the number of steps was 3 000 000 with three different time steps: 2 fs for simulations in the range 280–450 K, 1 fs in the range 450–800 K and 0.5 fs in the range 800–1200 K. Hence the corresponding simulation time lengths were about 6, 3 and 1.5 ns and in each simulation the initial 250 000 steps were considered as equilibration and so removed from the analysis. Short range interactions were evaluated within 0.9 nm cut off radius and the long range electrostatics was calculated using the Particle Mesh Ewald (PME) method, [29] with 34 wave vectors in each dimension and a 4th order cubic interpolation. All the solute molecules were constrained for the internal and roto-translational motions via the roto-translational [9] and bond length [30] constraints, or using the freezing option in GROMACS. Hence, in the simulations we treated the solutes as rigid molecules with no roto-translational motions. This procedure, which speeds up the solvent relaxation around the solute, provides the correct statistical mechanics and thermodynamics of the system (SPC plus a rigid solute). Thermodynamic integration (TI) calculations were also carried out with the routine implemented in GROMACS (soft core potential with $\alpha = 1.51$, $\sigma = 0.3$ nm) on methanol, cholorometnane, hydroxide anion at 800 K to obtain the confinement term in our models (see theory section).

The calculations of the reference chemical potential ($\mu_{ref}$) were carried out using standard quantum chemical calculations within the harmonic approximation at the G2 computational level [31] for improving the accuracy of the electronic energies. These calculations were carried out using the program Gaussian 98 [32].

## 4. Results

In Table 1 we compare the excess chemical potential values ($\mu'$), calculated at 300 K, and the related available experimental data at the same temperature.

Results indicate a very good agreement between the QGE-derived excess chemical potential and the corresponding experimental values. It is also interesting to remark that our theoretical data, systematically overestimating the experimental finding, practically match water-SPC excess chemical potential. This may be ascribed to the fact that SPC has been parametrized for reproducing pure-water properties. Nevertheless our data further confirm that SPC does actually provide a sufficiently good model even for solutions.

The excess chemical potential $\mu'$ values were then calculated as a function of the temperature along the isochore at 55.32 mol/l, according to the theoretical approach outlined in the Theory section, providing the values of the reaction

Table 1
Calculated and experimental [35] excess chemical potential (kJ/mol) at 300 K

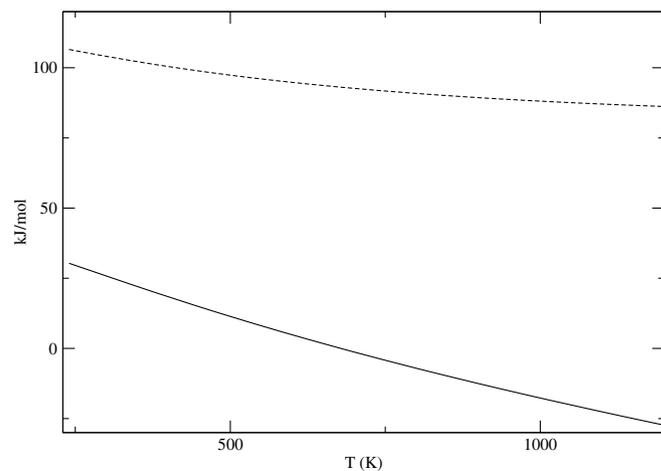| $\mu'$ | QGE | Exp. | Diff. |
|---|---|---|---|
| CH$_3$Cl | 5.0 | −2.3 | 7.3 |
| OH– | −489.0 | −496.9 [34] | 7.9 |
| CH$_3$OH | −14.4 | −21.3 | 6.9 |
| Cl– | −365.6 | −369.6 [34] | 4.0 |
| H$_2$O | −26.0 | −26.5 | 0.5 |
| CO | 12.7 | 9.3 | 3.4 |
| H$_2$ | 11.2 | 9.8 | 1.4 |
| CO$_2$ | 4.5 | 0.5 | 4.0 |



Fig. 1. Calculated excess reaction free energy $\Delta\mu'$ for reaction (1) (dotted line) and (2).

excess free energy $\Delta\mu'$, for reactions (1) and (2) as reported in Fig. 1.

It is interesting to observe that both reactions show a monotonic decreasing $\Delta\mu'$ as temperature is increased.

In Table 2 we report the calculated standard reaction free energy in the reference (gas-phase) condition $\Delta\mu_{\text{ref}}^{\ominus}$ for the same reactions at 300 K, termed as $\Delta\mu_{\text{ref1}}^{\ominus}$ and $\Delta\mu_{\text{ref2}}^{\ominus}$, respectively, and also in this case we observe a rather good agreement between calculated and experimental data with absolute errors not exceeding 8 kJ/mol. Via calculation in temperature of $\Delta\mu_{\text{ref}}^{\ominus}$ for both reactions, the standard reaction free energy, $\Delta\mu^{\ominus} = \Delta\mu' + \Delta\mu_{\text{ref}}^{\ominus}$, was then obtained as a function of temperature along the isochore as shown in Figs. 2 and 3. Interestingly, while for reaction 1 the temperature increase provides a monotonic $\Delta\mu^{\ominus}$ decrease, like for $\Delta\mu'$, reaction 2 shows a well defined $\Delta\mu^{\ominus}$ minimum, at about 550 K, corresponding to the products highest relative thermodynamic stability. As expected from the good quantitative reproduction of both $\Delta\mu_{\text{ref}}^{\ominus}$ and $\Delta\mu'$ at 300 K, the model provides rather accurate corresponding $\Delta\mu^{\ominus}$ values: $-93$ kJ/mol versus the experimental $-96.7$ kJ/mol for reaction (1) and 0 kJ/mol versus the experimental $-7.5$ kJ/mol for reaction (2).

Unfortunately, we may compare our theoretical predictions with experimental data only at about 300 K where our isochore density matches the usual isobaric water conditions, i.e. about 55 mol/l. However, prediction of chemical reaction thermodynamics along an isobar, may well be achieved with this theoretical/computational procedure by investigating the thermodynamics along a set of isochores within the density range spanned by the isobar considered.

Table 2
Calculated and experimental standard reaction free energies (kJ/mol) at 300 K in the reference (gas-phase) condition

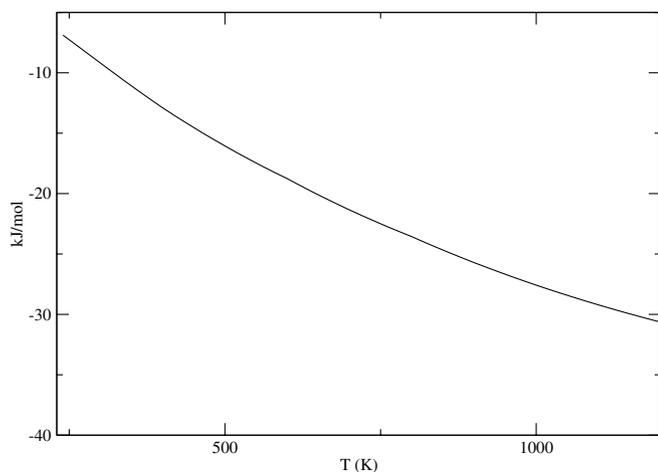| $\Delta\mu_{\text{ref1}}^{\ominus}$ | Exp. [33] | $\Delta\mu_{\text{ref2}}^{\ominus}$ | Exp. [33] |
|---|---|---|---|
| $-29$ | $-35$ | $-197$ | $-205$ |



Fig. 2. Calculated standard reaction free energy $\Delta\mu^{\ominus}$ for reaction (1).
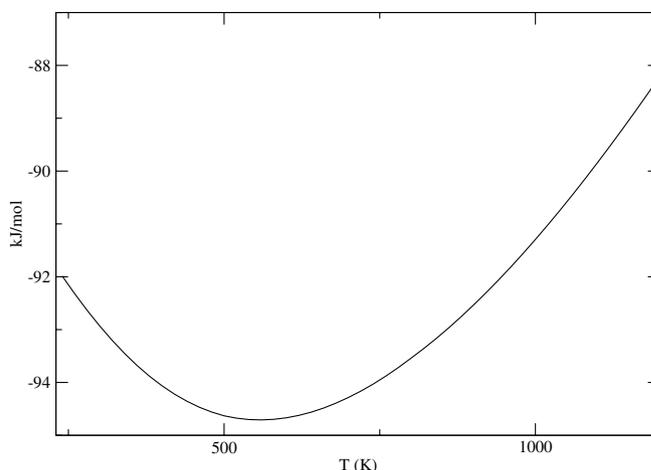


Fig. 3. Calculated standard reaction free energy $\Delta\mu^{\ominus}$ for reaction (2).

## 5. Conclusions

In this paper we present a straightforward application of the QGE theory for modelling chemical reaction thermodynamics able to provide valuable predictions of the reaction efficiency over a large temperature range along an isochore. Such an approach, which proved to be rather accurate for the two chemical reactions studied in this paper, may be easily extended to treat also the effects of density variations hence furnishing a complete equation of state for chemical equilibria.

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