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A critique of a thermodynamic description of hydrophobic aggregation in aqueous solution

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Abstract

The conclusions recently summarised by A. Marmur [J. Am. Chem. Soc. 122 (2000) 2120] concerning hydrophobic aggregation of solutes in aqueous solution are examined. The thermodynamic analysis is critically reviewed and the impact of implicit extrathermodynamic assumptions discussed. These assumptions are questioned and shown to lead to a model for hydrophobic aggregation which is flawed.

Keywords: Aqueous solutions; Hydrophobic aggregation; Clustering; Chemical potentials

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1. Introduction

The importance of hydrophobic solute–solute interactions in aqueous solution at ambient temperature and pressure has been recognised for almost 50 years prompted by a key publication by Kauzmann [1]. Nevertheless, controversy and debate concerning such interactions and hydrophobic hydration have been intense [2,3]. Recently, Marmur suggested that aggregation of neutral solutes in aqueous solution can be quite extensive [4]. For ethanol(aq) and *n*-butanol(aq), Marmur calculated aggregation numbers of 2.5 and 119, respectively [4]. This surprising conclusion is based on a novel model for aqueous systems together with a detailed thermodynamic analysis [4].

Nevertheless, solubility data for a wide range of systems [5] do not conform to the model developed by Marmur [4]. Therefore, the question remains as to the validity of the thermodynamic analysis set out by Marmur [4]. Here we show that the derived equations are based on three extrathermodynamic assumptions which are doubtful.

2. Thermodynamic analysis

2.1. Liquid mixture I

A given liquid mixture I contains two components; $n_1(\mathrm{I})$ moles of water and $n_X(\mathrm{I})$ moles of chemical substance X. Then the Gibbs energy of the mixture $G_\mathrm{I}(\mathrm{mix})$ is defined by Eq. (1) [6].

$$G_\mathrm{I}(\mathrm{mix}) = G_\mathrm{I}[T, p, n_1(\mathrm{I}), n_X(\mathrm{I})] \quad (1)$$

Then,

$$G_\mathrm{I}(\mathrm{mix}) = n_1(\mathrm{I})\mu_1(\mathrm{mix\,I}) + n_X(\mathrm{I})\mu_X(\mathrm{mix\,I}) \quad (2)$$

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Here and below, we confine attention to closed systems at thermodynamic equilibrium. Further, we assume that the systems are at ambient pressure and at 298.2 K although Marmur [4] specifies neither. Here μ_1(mix I) and μ_X(mix I) are the chemical potentials of the two liquid components in the binary liquid mixture. We use Raoult's law descriptions of the properties of components 1 and X in the system where the thermodynamic reference states are the pure liquid chemical substances at the same T and p [7,8].

Thus,

$$G_I(\text{mix}) = n_1(\text{I})[\mu_1^*(\ell) + RT\ln(x_1 f_1)_I] + n_X(\text{I})[\mu_X^*(\ell) + RT\ln(x_X f_X)_I] \quad (3)$$

Here $\mu_1^*(\ell)$ and $\mu_X^*(\ell)$ are the chemical potentials of pure water and liquid X at the same T and p. Further, by definition [7,8], at all T and p,

$$\text{limit}[x_1(\text{I}) \to 1](f_1)_I = 1 \quad (4)$$

$$\text{limit}[x_X(\text{I}) \to 1](f_X)_I = 1 \quad (5)$$

Further, mole fraction

$$x_1(\text{I}) = \frac{n_1(\text{I})}{[n_1(\text{I}) + n_X(\text{I})]} \quad (6)$$

and mole fraction

$$x_X(\text{I}) = \frac{n_X(\text{I})}{[n_1(\text{I}) + n_X(\text{I})]} \quad (7)$$

Here the n-quantities refer to the amounts of chemical substances in the system. Marmur [4] develops the argument in terms of the Gibbs energy of mixing. Thus, for a system comprising the same amounts of two pure liquids, 1 and X, but in the unmixed state, the Gibbs energy is given by Eq. (8).

$$G_I(\text{no-mix}) = n_1(\text{I})\mu_1^*(\ell) + n_X(\text{I})\mu_X^*(l) \quad (8)$$

Thus, we envisage a closed system with a very thin membrane separating the two pure liquids. The two liquids are now allowed to mix.

By definition,

$$\Delta_{\text{mix}} G_I = G_I(\text{mix}) - G_I(\text{no-mix}) \quad (9)$$

Then,

$$\frac{\Delta_{\text{mix}} G_I}{RT} = n_1(\text{I})\ln(x_1 f_1)_I + n_X(\text{I})\ln(x_X f_X)_I \quad (10)$$

Then, the molar Gibbs energy of mixing is given by Eq. (11) (cf. Eq. (4) in [4]).

$$\frac{\Delta_{\text{mix}} G_{\text{mI}}}{RT} = x_1(\text{I})\ln(x_1 f_1)_I + x_X(\text{I})\ln(x_X f_X)_I \quad (11)$$

The latter equation is similar to Eq. (6) in [4].

2.2. Liquid mixture II

We turn our attention to a liquid mixture prepared using three liquid components, water, liquid X and liquid Y at the same T and p. For such a mixture, the Gibbs energy G_{II}(mix) is defined by Eq. (12) [6].

$$G_{II}(\text{mix}) = G_{II}[T, p, n_1(\text{II}), n_X(\text{II}), n_Y(\text{II})] \quad (12)$$

Then using a Raoult's law description, G_{II}(mix) is related to the composition of the system using Eq. (13),

$$G_{II}(\text{mix}) = n_1(\text{II})[\mu_1^*(\ell) + RT\ln(x_1 f_1)_{II}] + n_X(\text{II})[\mu_X^*(\ell) + RT\ln(x_X f_X)_{II}] + n_Y(\text{II})[\mu_Y^*(\ell) + RT\ln(x_Y f_Y)_{II}] \quad (13)$$

Thus, at all T and p,

$$\text{limit}[x_X(\text{II}) \to 1](f_X)_{II} = 1.0 \quad (14)$$

Similar equations define $(f_1)_{II}$ and $(f_Y)_{II}$.

Further,

$$x_X(\text{II}) = \frac{n_X(\text{II})}{[n_1(\text{II}) + n_X(\text{II}) + n_Y(\text{II})]} \quad (15)$$

Similar equations define x_1(II) and x_Y(II).

At this point, Marmur [4] defines the composition of a particular liquid mixture II such that $n_1(\text{I}) = n_1(\text{II})$, $n_X(\text{II}) = (1-\alpha)n_X(\text{I})$ and $n_Y(\text{II}) = (\alpha/k)n_X(\text{I})$. In these terms, chemical substance Y is an aggregate of chemical substance X. Thus, α, a composition variable, is the fraction of chemical substance X present as substance Y, aggregation number k. The important point to note is that it is assumed that the liquid mixture is prepared using three chemical substances, water, monomer X and aggregate X_k. It is not envisaged that a chemical equilibrium exists between monomers and aggregates. Nevertheless, the composition of the system is determined by the variables, n_1(I), n_X(I), α and k. Then, with respect to mole fractions of chemical substances in system (II),

$$x_1(\text{II}) = \frac{n_1(\text{I})}{\beta} \quad (16)$$

where

$$\beta = n_1(\mathrm{I}) + (1-\alpha)n_{\mathrm{X}}(\mathrm{I}) + \left(\frac{\alpha}{k}\right) n_{\mathrm{X}}(\mathrm{I}) \qquad (17)$$

Similarly,

$$x_{\mathrm{X}}(\mathrm{II}) = \frac{(1-\alpha)n_{\mathrm{X}}(\mathrm{I})}{\beta} \qquad (18)$$

And,

$$x_{\mathrm{Y}}(\mathrm{II}) = \frac{\alpha n_{\mathrm{X}}(\mathrm{I})}{\beta} \qquad (19)$$

Then, with reference to the liquid mixture II, the Gibbs energy $G_{\mathrm{II}}(\mathrm{mix})$ is given by Eq. (20).

$$\begin{aligned} G_{\mathrm{II}}(\mathrm{mix}) = {} & n_1(\mathrm{I})[\mu_1^*(\ell) + RT\ln(x_1 f_1)_{\mathrm{II}}] \\ & + (1-\alpha)n_{\mathrm{X}}(\mathrm{I})[\mu_{\mathrm{X}}^*(\ell) + RT\ln(x_{\mathrm{X}} f_{\mathrm{X}})_{\mathrm{II}}] \\ & + \left(\frac{\alpha}{k}\right) n_{\mathrm{X}}(\mathrm{I})[\mu_{\mathrm{Y}}^*(\ell) + RT\ln(x_{\mathrm{Y}} f_{\mathrm{Y}})_{\mathrm{II}}] \end{aligned} \qquad (20)$$

In the event that the system comprised the ‘no-mix’ liquids in the manner described above, then G_{II} (no-mix) is given by Eq. (21).

$$\begin{aligned} G_{\mathrm{II}}(\text{no-mix}) = {} & n_1(\mathrm{I})\mu_1^*(\ell) + (1-\alpha)n_{\mathrm{X}}(\mathrm{I})\mu_{\mathrm{X}}^*(\ell) \\ & + \left(\frac{\alpha}{k}\right) n_{\mathrm{X}}(\mathrm{I})\mu_{\mathrm{Y}}^*(\ell) \end{aligned} \qquad (21)$$

Then,

$$\begin{aligned} \frac{\Delta_{\mathrm{mix}} G_{\mathrm{II}}}{RT} = {} & n_1(\mathrm{I}) \ln(x_1 f_1)_{\mathrm{II}} + (1-\alpha)n_{\mathrm{X}}(\mathrm{I}) \ln(x_{\mathrm{X}} f_{\mathrm{X}})_{\mathrm{II}} \\ & + \left(\frac{\alpha}{k}\right) n_{\mathrm{X}}(\mathrm{I}) \ln(x_{\mathrm{Y}} f_{\mathrm{Y}})_{\mathrm{II}} \end{aligned} \qquad (22)$$

The molar Gibbs energy of mixing $\Delta_{\mathrm{mix}} G_{\mathrm{IIm}}$ is given by Eq. (23) where β is given by Eq. (17).

$$\begin{aligned} \frac{\Delta_{\mathrm{mix}} G_{\mathrm{II}m}}{RT} = {} & \left[\frac{n_1(\mathrm{I})}{\beta}\right] \ln(x_1 f_1)_{\mathrm{II}} + \left[\frac{(1-\alpha)n_{\mathrm{X}}(\mathrm{I})}{\beta}\right] \\ & \times \ln(x_{\mathrm{X}} f_{\mathrm{X}})_{\mathrm{II}} + \left[\frac{(\alpha/k)n_{\mathrm{X}}(\mathrm{I})}{\beta}\right] \\ & \times \ln(x_{\mathrm{Y}} f_{\mathrm{Y}})_{\mathrm{II}} \end{aligned} \qquad (23)$$

Up to this point, the thermodynamic analysis is straightforward although complicated by the extensive use of symbols defining the various systems. The symbols are, however, important as we now show.

At this point, we suggest that in order to obtain Eq. (8) in [4] (or, its equivalent, Eq. (27) below), Marmur [4] makes three extrathermodynamic assumptions.

Assumption I. $\Delta_{\mathrm{mix}} G_{\mathrm{Im}} = \Delta_{\mathrm{mix}} G_{\mathrm{II}m}$.

Assumption II. $x_1(\mathrm{I})\ln(x_1 f_1)_{\mathrm{I}} = [n_1(\mathrm{I})/\beta]\ \ln(x_1 f_1)_{\mathrm{II}}$.

Assumption III. $\alpha \ll 1$ such that $\beta \cong n_1(\mathrm{I}) + n_{\mathrm{X}}(\mathrm{I})$.

These assumptions allow Eqs. (11) and (23) to be combined. Then,

$$\begin{aligned} x_{\mathrm{X}}(\mathrm{I}) \ln(x_{\mathrm{X}} f_{\mathrm{X}})_{\mathrm{I}} = {} & \left[\frac{(1-\alpha)n_{\mathrm{X}}(\mathrm{I})}{\beta}\right] \ln(x_{\mathrm{X}} f_{\mathrm{X}})_{\mathrm{II}} \\ & + \left[\frac{(\alpha/k)n_{\mathrm{X}}(\mathrm{I})}{\beta}\right] \ln(x_{\mathrm{Y}} f_{\mathrm{Y}})_{\mathrm{II}} \end{aligned} \qquad (24)$$

Hence,

$$\begin{aligned} & x_{\mathrm{X}}(\mathrm{I}) \ln(x_{\mathrm{X}} f_{\mathrm{X}})_{\mathrm{I}} \\ & = [(1-\alpha)x_{\mathrm{X}}(\mathrm{I})] \ln[(1-\alpha)x_{\mathrm{X}}(\mathrm{I}) f_{\mathrm{X}}(\mathrm{II})] \\ & \quad + \left[\left(\frac{\alpha}{k}\right) x_{\mathrm{X}}(I)\right] \ln\left[\left(\frac{\alpha}{k}\right) x_{\mathrm{X}}(\mathrm{I}) f_{\mathrm{Y}}(\mathrm{II})\right] \end{aligned} \qquad (25)$$

Then,

$$\begin{aligned} \ln[f_{\mathrm{X}}(\mathrm{I})] = {} & \left[(1-\alpha) \ln[f_{\mathrm{X}}(\mathrm{II})] + \left(\frac{\alpha}{k}\right)\right] \\ & \times \ln\left[\left(\frac{\alpha}{k}\right) f_{\mathrm{Y}}(\mathrm{II})\right] + (1-\alpha) \ln[x_{\mathrm{X}}(\mathrm{I})] \\ & + \left(\frac{\alpha}{k}\right) \ln[x_{\mathrm{X}}(\mathrm{I})] - \ln[x_{\mathrm{X}}(\mathrm{I})] \end{aligned} \qquad (26)$$

Or,

$$\begin{aligned} & \ln[f_{\mathrm{X}}(\mathrm{I})] \\ & = \left[(1-\alpha) \ln[f_{\mathrm{X}}(\mathrm{II})] + \left(\frac{\alpha}{k}\right)\right] \ln\left[\left(\frac{\alpha}{k}\right) f_{\mathrm{Y}}(\mathrm{II})\right] \\ & \quad - \left[\frac{\alpha(k-1)}{k}\right] \ln[x_{\mathrm{X}}(\mathrm{I})] \end{aligned} \qquad (27)$$

The latter is essentially Eq. (8) in the analysis given by Marmur [4].

3. Discussion

The analysis presented here was prompted by the analysis given by Marmur [4]. In particular, we were concerned with the magnitude of aggregate numbers reported by Marmur [4] for aqueous solutions.

Here our aim was to explore the extrathermodynamic assumptions invoked in Marmur's analysis [4]. We suggest that the derived aggregation numbers taken together with the disagreements with solubility data [5] point to the unsatisfactory nature of the extrathermodynamic assumptions. We see no basis for Assumption I because the two solutions are quite different. Assumption II is invalid because the amounts of solutes in the two solutions differ. Then, for example, van't Hoff properties, such as depression of freezing point, would confirm the point. Assumption III requires in any case that there is little of chemical substance Y in the system. We should add that a similar set of extrathermodynamic assumptions are required if the analysis uses a Henry's law description of the thermodynamic properties of solutes X, Y and aggregates. In such an analysis, the reference state for a solute is an ideal solution, having unit molality at the same T and p. The activity coefficients are defined, for example, in the case of chemical substance X such that $\text{limit}(m_X \rightarrow 0)\gamma_X = 1.0$ at all T and p. The final equation making the same assumptions described by Marmur [4] leads to the same conclusion. In any event, we suggest that the analysis does not advance our understanding of hydrophobic interactions in aqueous solution.

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