On the local and nonlocal components of solvation thermodynamics and their relation to solvation shell models

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A procedure for identifying the local and nonlocal components of excess partial molar quantities is presented. This procedure is based on an analysis of the excess thermodynamic quantities expressed as integrals of local estimators over the system volume. The local components can be described in terms of the solvation shell model and are independent of the condition of solute insertion. The nonlocal components are related to the asymptotic behavior of distribution functions at large distances from the solute and they give rise to the ensemble dependence of the thermodynamic quantities of solvation. It is shown that in the constant pressure process, by using natural choices for the local estimators, the nonlocal components of the excess partial molar energy, enthalpy, entropy, and volume are absent. The relationship between our analysis and a phenomenological model which expresses excess thermodynamic quantities in terms of the solute volume, surface area, and diameter is also considered and the validity of the local interpretation is discussed. © *1998 American Institute of Physics.* [S0021-9606(98)52136-8]

I. INTRODUCTION

The solvation shell model is a simple but powerful framework that has been used to analyze solvation thermodynamics.[1–7] In this model, a solute molecule is considered to perturb the structure of the solution only in a region near the solute. Excess partial molar quantities are then represented by the difference between the values of properly defined local estimators in the solvation shell and their corresponding values in the bulk. Since the solvation shell model involves only quantities averaged over a finite region proximate to the solute, it does not reflect the dependence of the excess partial molar quantities on the condition of solute insertion, i.e., on whether the solute is inserted in the solvent in a constant pressure process or in a constant volume process. It is well known, however, that the excess partial molar energy and entropy are dependent on the condition of solute insertion. In previous papers, we resolved this apparent inconsistency by analyzing the asymptotic behavior of the molecular distribution functions at distances much larger than the solute-solvent correlation length.[1,2] The major conclusion was that the dependence on insertion condition is contained in the *nonlocal* components of the excess partial molar quantities, and that the excess partial molar energy and entropy for the constant pressure process involve only *local* components.[1,2] This conclusion based on statistical mechanics justifies the solvation shell analysis of experimental data obtained at constant pressure.

A markedly different view was presented recently, on the other hand, by Cann and Patey.[8] In their study of the solute size dependence of solvation thermodynamics, Cann and Patey specified the nonlocal components within the framework of a phenomenological model and claimed that the excess partial molar energy and entropy involve nonlocal components in *both* the constant pressure and constant volume processes.[8] Using an integral equation analysis of the thermodynamics of model solutions, the nonlocal components of the excess partial molar energy and entropy specified by Cann and Patey were evaluated and found to be significant, and it was stated that the excess partial molar energy and entropy ''often cannot provide useful information about solvent structure near the solutes.''[8] They have also stated that, because the volume change in an isobaric process contributes directly to the solvent reorganization, ''the structural changes for solute insertion under isobaric conditions may not correspond, even qualitatively, to those induced by a solute under isochoric conditions.''[8] These statements appear to invalidate many of the insights obtained from the solvation shell analysis of experimental data, whereby the solvent reorganization is assumed to be localized within a finite region around the solute.

Thus, there is a disagreement concerning the decomposition of excess partial molar thermodynamic quantities into local and nonlocal components.[9] In order to resolve this disagreement and clarify the relationship between insertion conditions and structural changes of the solvent around the solute, the meaning of local and nonlocal components of the excess partial molar quantities needs to be more carefully considered. In this paper, we present consistent definitions of the local and nonlocal components of excess partial molar quantities based on statistical mechanics, and we determine the local components of the excess chemical potential and its first pressure and temperature derivatives.

We identify the local and nonlocal components of an excess partial molar quantity by studying the molecular-level cause of the dependence of the excess partial molar quantity on the insertion condition. As previously done for the solva-

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tion shell analysis of the excess partial molar energy, volume, and compressibility,[1,2] the excess partial molar quantity is first expressed as an integral over the total volume of the system of the deviation of a properly defined local estimator from its corresponding bulk value. In the thermodynamics limit, since the modification of the solvent structure due to the insertion of the solute becomes independent of the insertion condition, the value of the local estimator at a large distance from the solute approaches the corresponding pure solvent bulk value. Therefore, the solvation shell estimate of an excess partial molar quantity, obtained by restricting the domain of integration to a finite volume proximate to the solute, does not depend on the insertion condition in the thermodynamic limit. A closer analysis shows that, depending on the insertion condition, the asymptotic value of the local estimator at a large distance from the solute may deviate from the pure solvent bulk value by a factor of the order of $1/N$, where N denotes system size. This property of the local estimator gives rise to the dependence on the insertion condition of the corresponding excess partial molar quantity obtained by integrating the local estimator over the total system size N.

The local component of an excess partial molar quantity is defined by discarding the contribution arising from the deviation of the asymptotic value of the local estimator from the corresponding bulk value. We show that the local component is evaluated from the solvation shell model in the limit of a large but finite solvation shell. The formulation of the solvation shell model depends on the choice of the local estimator. We analyze the use of local estimators and the conditions of solute insertion which are most useful for extracting information about the solvation shell from experimental data.

II. LOCAL AND NONLOCAL COMPONENTS OF EXCESS THERMODYNAMIC QUANTITIES

A. Molecular distribution functions

In order to analyze the thermodynamics of solvation, it is necessary to specify the solution process precisely. We follow Ben-Naim's convention:[6] a solute molecule is inserted at a fixed origin with a fixed orientation. In this convention, the change ΔQ of a thermodynamic variable Q during the solution process represents the excess partial molar quantity at infinite dilution (hereafter, we often omit the phrase ''partial molar'' for brevity). In this work, ΔQ is typically a pressure or temperature derivative of the excess chemical potential $\Delta \mu$ (or the pseudo chemical potential in the notation of Ben-Naim[6,10]). We adopt periodic boundary conditions as implemented in computer simulations. The pure solvent system is then homogeneous and translationally invariant. In the solution, on the other hand, the solute placed at the origin produces an inhomogeneity and the solute-solvent interaction can be viewed as an external potential field acting on the solvent molecules.

The notation for the molecular distribution functions follows that given in Appendix 1 of Ref. 1. The n-body distribution functions in the pure solvent and in the solution are denoted by $\rho^{(n)}(\mathbf{x}_1,...,\mathbf{x}_n)$ and $\overline{\rho^{(n)}}(\mathbf{x}_1,...,\mathbf{x}_n)$, respectively,

where $\mathbf{x}$ denotes the position and orientation of a solvent molecule. As the solute is fixed at the origin, $\overline{\rho^{(n)}}$ is actually an $n+1$-body distribution function for one solute and n solvent molecules. It is still regarded as an n-body distribution function because the solute-solvent interaction can be viewed as an external field for the solvent molecules. In this work, the temperature of the system and the number of solvent molecules are unchanged upon solute insertion. We restrict our attention to the comparison between excess thermodynamic quantities calculated in the canonical and isothermal-isobaric ensembles.

In considering the solution process at constant volume, we denote the distribution functions by $\overline{\rho_V^{(n)}}$ and $\rho_V^{(n)}$ in order to emphasize their dependence on the total volume of the system V in the canonical ensemble. The asymptotic behavior of $\overline{\rho_V^{(n)}}$ at distances far from the solute has been analyzed in a previous paper[1] under the natural assumption that the correlation lengths among molecules in the system are finite.[11] The main result of the asymptotic analysis is presented in Eq. (A1.14) of Ref. 1 and it is equivalent to the following asymptotic expression valid when $(\mathbf{x}_1,...,\mathbf{x}_n)$ is far from the solute:

$$\overline{\rho_V^{(n)}}(\mathbf{x}_1,...,\mathbf{x}_n) \rightarrow \rho_V^{(n)}(\mathbf{x}_1,...,\mathbf{x}_n)$$
$$- \Delta V \frac{\partial \rho_V^{(n)}(\mathbf{x}_1,...,\mathbf{x}_n)}{\partial V} + o\left(\frac{1}{N}\right), \quad (1)$$

where ΔV is the excess volume for the constant pressure process, N is the number of solvent molecules, and $o(1/N)$ denotes a variable which vanishes faster than $1/N$ in the thermodynamic limit $(N \rightarrow \infty)$. The second term on the right-hand side of Eq. (1) is first order in $1/N$.[1,11] The physical meaning of this term becomes clear when Eq. (1) is rewritten as

$$\overline{\rho_V^{(n)}}(\mathbf{x}_1,...,\mathbf{x}_n) \rightarrow \rho_{V-\Delta V}^{(n)}(\mathbf{x}_1,...,\mathbf{x}_n) + o\left(\frac{1}{N}\right). \quad (2)$$

Equation (2) expresses the fact that, in the canonical ensemble, at large distances from the solute, the n-body distribution function of the solution approaches the pure solvent distribution function at the volume $V - \Delta V$, which may be interpreted as the volume effectively accessible to the solvent after the insertion of the solute.[1]

In the constant pressure process, on the other hand, we now show that the first-order term with respect to $1/N$ is absent in the asymptotic form of $\overline{\rho^{(n)}} - \rho^{(n)}$. To this end, we employ the finite-size correction formula given by Lebowitz et al., which relates an isothermal-isobaric ensemble average to the corresponding canonical ensemble average.[12] For the pure solvent, the distribution function $\rho_P^{(n)}$ in the isothermal-isobaric ensemble at pressure P can be expressed as

$$\rho_P^{(n)}(\mathbf{x}_1,...,\mathbf{x}_n) = \rho_{\tilde{V}}^{(n)}(\mathbf{x}_1,...,\mathbf{x}_n) - \frac{1}{2\beta} \frac{\partial \tilde{V}}{\partial P}$$
$$\times \left(\frac{\partial^2}{\partial V^2} \rho_V^{(n)}(\mathbf{x}_1,...,\mathbf{x}_n) \right)_{V=\tilde{V}} + o\left(\frac{1}{N}\right), \quad (3)$$

where β is the reciprocal temperature and $\tilde{V}$ is the average volume of the pure solvent at the pressure P. For the solution, on the other hand, the distribution function $\overline{\rho_P^{(n)}}$ in the isothermal-isobaric ensemble can be expressed as

$$\overline{\rho_P^{(n)}}(\mathbf{x}_1,\ldots,\mathbf{x}_n)$$

$$=\overline{\rho_{\tilde{V}+\Delta V}^{(n)}}(\mathbf{x}_1,\ldots,\mathbf{x}_n)-\frac{1}{2\beta}\frac{\partial(\tilde{V}+\Delta V)}{\partial P}$$

$$\times\left(\frac{\partial^2}{\partial V^2}\overline{\rho_V^{(n)}}(\mathbf{x}_1,\ldots,\mathbf{x}_n)\right)_{V=\tilde{V}+\Delta V}+o\left(\frac{1}{N}\right)$$

$$=\overline{\rho_{\tilde{V}}^{(n)}}(\mathbf{x}_1,\ldots,\mathbf{x}_n)+\Delta V\left(\frac{\partial\overline{\rho_V^{(n)}}(\mathbf{x}_1,\ldots,\mathbf{x}_n)}{\partial V}\right)_{V=\tilde{V}}$$

$$-\frac{1}{2\beta}\frac{\partial\tilde{V}}{\partial P}\left(\frac{\partial^2}{\partial V^2}\overline{\rho_V^{(n)}}(\mathbf{x}_1,\ldots,\mathbf{x}_n)\right)_{V=\tilde{V}}+o\left(\frac{1}{N}\right), \quad (4)$$

since $\tilde{V}+\Delta V$ is, by definition, the average volume of the solution. Because on the right-hand sides of Eqs. (3) and (4) the terms beyond the first vanish for $N\to\infty$, in the thermodynamic limit the isobaric distribution functions for the pure liquid and the solution are identical to the corresponding isochoric distribution functions regardless of the solute partial molar volume and solute-solvent interaction.

To derive the asymptotic behavior of $\overline{\rho_P^{(n)}}$ when $(\mathbf{x}_1,\ldots,\mathbf{x}_n)$ is far from the solute, we insert Eq. (2) in Eq. (4) to obtain

$$\overline{\rho_P^{(n)}}(\mathbf{x}_1,\ldots,\mathbf{x}_n)$$

$$\to\rho_{\tilde{V}}^{(n)}-\frac{1}{2\beta}\frac{\partial\tilde{V}}{\partial P}\left(\frac{\partial^2}{\partial V^2}\rho_V^{(n)}(\mathbf{x}_1,\ldots,\mathbf{x}_n)\right)_{V=\tilde{V}}+o\left(\frac{1}{N}\right). \quad (5)$$

By using Eq. (3), Eq. (5) can then be rewritten as

$$\overline{\rho_P^{(n)}}(\mathbf{x}_1,\ldots,\mathbf{x}_n)\to\rho_P^{(n)}(\mathbf{x}_1,\ldots,\mathbf{x}_n)+o\left(\frac{1}{N}\right). \quad (6)$$

Equation (6) shows that the asymptotic form of $\overline{\rho^{(n)}}-\rho^{(n)}$ does not involve first-order terms with respect to $1/N$ in the isothermal-isobaric ensemble. In summary, to first order in $1/N$, the n-body solvent density far from the solute in the isobaric process at pressure P is identical to that of the pure solvent at the same pressure, while in the isochoric process at volume V, the n-body solvent density far from the solute is identical to that of the pure solvent at volume $V-\Delta V$.

B. Excess energy

In this section, we discuss the local and nonlocal components of an excess thermodynamic quantity, focusing on the excess energy ΔE as the first example. As shown in Ref. 1, the solvation shell decomposition of ΔE can be performed in terms of the binding energies in the solution and in the pure solvent. The binding energy in the solution $\bar{B}(\mathbf{x})$ is defined as

$$\bar{B}(\mathbf{x})=u_{\mathrm{uv}}(\mathbf{x})+\frac{1}{2}\int d\mathbf{y}\frac{\overline{\rho^{(2)}}(\mathbf{x},\mathbf{y})}{\overline{\rho^{(1)}}(\mathbf{x})}u_{\mathrm{vv}}(\mathbf{x},\mathbf{y}), \quad (7)$$

where u_{uv} and u_{vv} are, respectively, the solute-solvent and solvent-solvent interaction potential functions, and the binding energy in the pure solvent $B(\mathbf{x})$ is defined similarly to Eq. (7).[13] Since the pure solvent is homogeneous, $B(\mathbf{x})$ is independent of $\mathbf{x}$ and is written as B.[14] As seen in Ref. 1, the excess energy $\Delta E_{\mathrm{const\text{-}V}}$ at a fixed volume V can be expressed exactly as

$$\Delta E_{\mathrm{const\text{-}V}}=\int d\mathbf{x}\overline{\rho_V}(\mathbf{x})(\overline{B_V}(\mathbf{x})-B_V), \quad (8)$$

where $\bar{\rho}\equiv\overline{\rho^{(1)}}$ and the domain of integration is the whole unit cell. The subscript V indicates a canonical ensemble average with volume V. The solvation shell model is introduced by restricting the domain of integration to a finite volume, the "solvation shell" V_{shell}. The exact $\Delta E_{\mathrm{const\text{-}V}}$ at a fixed V is recovered when V_{shell} is set equal to the total volume of the unit cell V. In this sense, the exact $\Delta E_{\mathrm{const\text{-}V}}$ is the limit of the solvation shell formula for $V_{\mathrm{shell}}\to V$, which we call the "large shell limit." Thus, the evaluation of the excess energy from Eq. (8) involves two limiting processes, the thermodynamic limit ($N\to\infty$, $V\to\infty$, $N/V=$ constant) and the large shell limit ($V_{\mathrm{shell}}\to V$). Since Eq. (8) is exact at any V, it provides the exact excess energy at constant volume when the large shell limit is taken before the thermodynamic limit. As will be shown, different behavior is observed for $\Delta E_{\mathrm{const\text{-}V}}$ in Eq. (8) when the order of the two limits is interchanged, i.e., when the thermodynamic limit is taken first keeping V_{shell} finite and the large shell limit is then performed by letting $V_{\mathrm{shell}}\to\infty$.

We now show that the asymptotic behavior of $\bar{B}(\mathbf{x})$ determines the effect of the order of the thermodynamic and large shell limits. Note, from Eqs. (2) and (7), that $\bar{B}_V(\mathbf{x})$ approaches $B_{V-\Delta V}+o(1/N)$ at a large distance from the solute. This result is then used to rewrite Eq. (8) as

$$\Delta E_{\mathrm{const\text{-}V}}=\int_V d\mathbf{x}\overline{\rho_V}(\mathbf{x})(\overline{B_V}(\mathbf{x})-B_{V-\Delta V})$$

$$+\int_V d\mathbf{x}\overline{\rho_V}(\mathbf{x})(B_{V-\Delta V}-B_V) \quad (9)$$

$$=\int_V d\mathbf{x}\overline{\rho_V}(\mathbf{x})(\overline{B_V}(\mathbf{x})-B_{V-\Delta V})-\Delta V\frac{\partial E}{\partial V}+o(1), \quad (10)$$

where E is the average energy in the pure solvent and $o(1)$ denotes a variable which vanishes in the thermodynamic limit.[1]

Since $\overline{B_V}(\mathbf{x})-B_{V-\Delta V}$ is of the order $o(1/N)$ at large distances from the solute, the first term on the right-hand side of Eqs. (9) and (10) is unaffected by the order of the thermodynamic and large shell limits. In other words, $\Delta E_{\mathrm{const\text{-}V}}$ as written in Eq. (8) involves a component for which the two limiting processes are interchangeable. The noninterchangeability of the thermodynamic and large shell limits in Eq. (8) is due to the presence of the second term in Eq. (9). In fact,

this term is equal to $-\Delta V \partial E/\partial V$ if the large shell limit, as in going from Eq. (9) to Eq. (10), precedes the thermodynamic limit (the integral is taken over all the solvent molecules), while it is zero if the thermodynamic limit precedes the large shell limit $(B_{V-\Delta V} - B_V \to 0$ in the thermodynamic limit). This shows that the second term of Eq. (9) is affected by the order of the thermodynamic and large shell limits.

The first term in Eqs. (9) and (10) can be identified from the thermodynamic relation

$$\Delta E_{\text{const-V}} = \Delta E_{\text{const-P}} - \Delta V \frac{\partial E}{\partial V}, \qquad (11)$$

where $\Delta E_{\text{const-P}}$ is the excess energy at constant pressure. Comparing Eqs. (9)–(11), it is easy to see that the first term in Eqs. (9) and (10) in the thermodynamic limit, as also shown in Ref. 1, is equal to the excess energy at constant pressure.

In conclusion, Eq. (8) provides the excess energy at constant volume when the large shell limit is taken before the thermodynamic limit, while it provides the excess energy at constant pressure when the thermodynamic limit is taken before the large shell limit.

In the solvation shell model, the large shell limit is not taken and a finite cutoff is instead introduced into the integral in Eq. (8). When a finite cutoff is introduced, in the thermodynamic limit the integral in Eq. (8) is independent of the ensemble. In this limit, in fact, the solution structure in any finite region containing the solute is, as Eq. (4) shows, independent of the ensemble. Thus, in the limit of a large but finite solvation shell (larger than the solute-solvent correlation length), the excess energy obtained from the solvation shell model approaches the excess energy at constant pressure, which is the excess energy evaluated from Eq. (8) by taking the thermodynamic limit first.

The second term of Eq. (9) is equal to $-\Delta V \partial E/\partial V$ when the integration is taken over the entire volume of the system. In this integral, since the integrand is first order with respect to $1/N$, the contribution from any finite region of the system is zero in the thermodynamic limit. The contribution of a solvent molecule to the integral in the second term of Eq. (9) is identical at any point irrespective of the distance from the solute. The second term is, therefore, identified as the ''nonlocal'' component of the excess energy at constant volume. For the first term of Eq. (9), on the other hand, the integrand vanishes at distances far from the solute and the integral can be approximated by restricting the domain of integration to some finite region surrounding the solute. The first term is therefore identified as the ''local'' component of the excess energy at constant volume. For the local component the thermodynamic and large shell limits are interchangeable. As discussed in Ref. 1, the solvation shell model is an approximation to the local component.

In addition, it is possible to independently show that the excess energy at constant pressure $\Delta E_{\text{const-P}}$ can be written as an integral that does not involve the nonlocal component when the local estimator is the binding energy. To do so, it is convenient to begin with an expression similar to Eq. (8). It is possible to show from the finite-size correction formula of Lebowitz et al.[12] that

$$\Delta E_{\text{const-P}} = \overline{E_{\tilde{V} + \Delta V}} - E_{\tilde{V}} + o(1), \qquad (12)$$

where $\tilde{V}$ is the average volume of the pure solvent in the isothermal-isobaric ensemble at the pressure P, and $E_{\tilde{V}}$ and $E_{\tilde{V} + \Delta V}$ are, respectively, the average total energies in the canonical ensemble of the pure solvent at volume $\tilde{V}$ and of the solution at volume $\tilde{V} + \Delta V$. Since the number of solvent molecules does not change upon solute insertion and the pure solvent is homogeneous, it is possible, by virtue of Eqs. (3) and (4), to rewrite Eq. (12) as

$$\Delta E_{\text{const-P}} = \int_{\tilde{V} + \Delta V} d\mathbf{x} \overline{\rho_{\tilde{V} + \Delta V}}(\mathbf{x})(\overline{B_{\tilde{V} + \Delta V}}(\mathbf{x}) - B_{\tilde{V}}) + o(1)$$

$$= \int_{\tilde{V} + \Delta V} d\mathbf{x} \overline{\rho_P}(\mathbf{x})(\overline{B_P}(\mathbf{x}) - B_P) + o(1), \qquad (13)$$

where the subscript P indicates that $\bar{B}$ and B are isothermal-isobaric ensemble averages. It then follows from Eq. (6) that the integrand in Eq. (13) is of the order $o(1/N)$ at distances far from the solute. Consequently, the thermodynamic and large shell limits are interchangeable in the integral of Eq. (13). The excess energy at constant pressure, therefore, does not involve a nonlocal component when the local estimator is the binding energy. This further confirms that the local component of the excess energy is independent of the condition of solute insertion and is equal to the excess energy at constant pressure.

C. General treatment

The procedure described above for determining the local and nonlocal components of the excess energy may be used to define the local and nonlocal components of other excess thermodynamic quantities. First, we find the local estimator $\bar{q}(\mathbf{x})$ in the solution and the corresponding quantity q in the pure solvent in terms of which ΔQ can be expressed as

$$\Delta Q = \int d\mathbf{x} \bar{\rho}(\mathbf{x})(\bar{q}(\mathbf{x}) - q). \qquad (14)$$

When Eq. (14) is formulated in a particular ensemble, the exact excess quantity ΔQ in that ensemble is to be evaluated by taking the large shell limit first and then the thermodynamic limit, as done above for the excess energy. The local component of ΔQ is then defined by interchanging the order of these two limits. In other words, we obtain the local component of ΔQ by first replacing $\bar{\rho}$, $\bar{q}$, and q with their corresponding values in the thermodynamic limit and then taking the large shell limit in Eq. (14). The local component of ΔQ is independent of the condition of solute insertion when $\bar{\rho}$, $\bar{q}$, and q are independent of the ensemble in the thermodynamic limit. In general, ΔQ may be different from the local component because the thermodynamic limit and the large shell limit are not necessarily interchangeable. The difference between ΔQ and its local component is defined as the nonlocal component. When the thermodynamic limit and the large shell limit can be interchanged, ΔQ itself is local in terms of $\bar{q}$ and q and the nonlocal component is absent. Conversely, when the nonlocal component is absent, the thermodynamic and large shell limits are interchangeable. It

should be noted that the definition of the local component depends on the choice of $\bar{q}$ and q. Thus, $\bar{q}$ and q need to be clearly specified when ΔQ is decomposed into local and nonlocal components. As shown in Sec. II B, for example, a local expression is obtained for $\Delta E_{\text{const-P}}$ when $\bar{q}$ is the binding energy.

The interchangeability of the thermodynamic and large shell limits is related to the large-N behavior of the asymptotic value, $\bar{q}(\infty)$, of $\bar{q}$, from which $\bar{q}(\mathbf{x})$ differs by order $o(1/N)$ at large distances from the solute. As we have seen in Sec. II B for the excess energy, the difference between $\bar{q}(\infty)$ and q, even though vanishingly small in the thermodynamic limit, is not necessarily of the order $o(1/N)$. The effect of the deviation of $\bar{q}(\infty)$ from q is clearly seen by rewriting Eq. (14) as

$$\Delta Q = \int d\mathbf{x}\,\bar{\rho}(\mathbf{x})(\bar{q}(\mathbf{x}) - \bar{q}(\infty)) + \int d\mathbf{x}\,\bar{\rho}(\mathbf{x})(\bar{q}(\infty) - q). \tag{15}$$

In the first term of Eq. (15), since the integrand is of the order $o(1/N)$ at distances far from the solute, the thermodynamic limit and the large shell limit are interchangeable and the term is local in terms of $\bar{q}$ and q. In addition, when the thermodynamic limit is taken first, Eq. (14) reduces to the first term in Eq. (15). Thus, the second term in Eq. (15) is the origin of the nonlocal component of ΔQ. When $\bar{q}(\infty)$ differs from q by order $o(1/N)$, the second term is of the order $o(1)$ upon integration and can be dropped. In this case,

$$\bar{q}(\mathbf{x}) \to q + o\left(\frac{1}{N}\right) \tag{16}$$

holds at distances far from the solute, and ΔQ itself is local in terms of $\bar{q}$ and q. When the difference between $\bar{q}(\infty)$ and q is first order in $1/N$, on the other hand, the value of the second term in Eq. (15) depends on the order of the thermodynamic and large shell limits. When the large shell limit is taken first, the second term in Eq. (15) makes a nonvanishing contribution because $(\bar{q}(\infty) - q)$ is a constant of the order of $1/N$ and the integral of $\bar{\rho}(\mathbf{x})$ gives a factor proportional to N. When the thermodynamic limit is taken first, instead, $\bar{q}(\infty)$ is set equal to q and the second term vanishes. The local and nonlocal components of ΔQ are, therefore, given by the first and second terms in Eq. (15), respectively. The interpretation of the second term on the right-hand side of Eq. (15) as being nonlocal is indeed appropriate as all the solvent molecules throughout the system contribute equally to it. The main contribution to the local component, on the other hand, comes from the solvent molecules closer to the solute. As shown in Sec. III, the solvation shell model estimate of ΔQ is an approximation to the local component of ΔQ. As usually applied, the model assumes that the entire contribution to the local component comes from the first solvation shell. In previous papers we examined the accuracy of this assumption for the excess energy, volume, and compressibility of a hydrophobic solute.[1,2]

D. Excess volume and excess enthalpy

In this section, we consider the excess volume ΔV. In the constant pressure process, by definition, ΔV is expressed as

$$\Delta V = \left(\int_{\tilde{V} + \Delta V} d\mathbf{x} \right) - \tilde{V} + o(1)$$

$$= \int_{\tilde{V} + \Delta V} d\mathbf{x}\, \overline{\rho_{\tilde{V} + \Delta V}}(\mathbf{x}) \left(\frac{1}{\overline{\rho_{\tilde{V} + \Delta V}}(\mathbf{x})} - \frac{1}{\rho_{\tilde{V}}} \right) + o(1), \tag{17}$$

because the density $\rho_{\tilde{V}}$ in the pure solvent is position independent due to the homogeneity and the number of solvent molecules does not change upon solute insertion. It is then possible to show by virtue of Eqs. (3) and (4) that[2]

$$\Delta V = \int_{\tilde{V} + \Delta V} d\mathbf{x}\, \overline{\rho_P}(\mathbf{x}) \left(\frac{1}{\overline{\rho_P}(\mathbf{x})} - \frac{1}{\rho_P} \right) + o(1). \tag{18}$$

Equation (6) shows that the integrand in Eq. (18) is of the order $o(1/N)$ at distances far from the solute. The excess volume at constant pressure is, therefore, local in terms of the inverse densities. In the constant volume process, the excess volume is zero, of course, and its local component is the excess volume at constant pressure. In this case, the nonlocal component cancels out the local component exactly. Furthermore, Eq. (18) reduces to the Kirkwood–Buff expression for the excess volume[15] in the thermodynamic limit. The excess volume is also local in the grand canonical ensemble. This is because the asymptotic behavior of the distribution functions in the grand canonical ensemble is given by an expression similar to Eq. (6) derived in the isothermal-isobaric ensemble.[11]

When Eqs. (13) and (18) are combined, the local component of the excess enthalpy at constant pressure ΔH can be derived using the thermodynamic relation

$$\Delta H = \Delta E + P\Delta V. \tag{19}$$

Equation (19) shows that the excess enthalpy at constant pressure is local when $\bar{q}$ in Eq. (14) is taken to be $(\bar{B} + P/\bar{\rho})$. The local estimator for the excess enthalpy is simply the sum of the local estimators for the excess energy and the pressure-volume term.

Interestingly, it is possible to find a variable in terms of which the excess energy at constant volume $\Delta E_{\text{const-V}}$ is local. This can be done simply by employing Eqs. (11), (13), and (18). These equations show that $\Delta E_{\text{const-V}}$ is local when $\bar{q}$ in Eq. (14) is taken to be $(\bar{B} - (\partial E/\partial V)(1/\bar{\rho}))$. The physical meaning of such a local estimator is, however, less transparent than the binding energy, the local estimator of the excess energy at constant pressure. It is also possible to choose $\bar{q}$ and q in terms of which neither of the excess energies are local. Thus, it is more accurate to refer to the integral formulas as being local or nonlocal rather than the thermodynamic quantities themselves.

E. Excess entropy and excess chemical potential

In this section, we focus on the excess entropy ΔS and the excess chemical potential $\Delta \mu$. Because the excess chemical potential does not depend on the condition of solute insertion, the excess entropy at constant pressure $\Delta S_{\text{const-P}}$ can be expressed, by virtue of Eq. (12), as

$$\Delta S_{\text{const-P}} = \overline{S_{\tilde{V}+\Delta V}} - S_{\tilde{V}} + o(1), \tag{20}$$

where $\tilde{V}+\Delta V$ and $\tilde{V}$ are, respectively, the average volumes of the solution and of the pure solvent at a fixed pressure P, and $\overline{S_{\tilde{V}+\Delta V}}$ and $S_{\tilde{V}}$ are, respectively, the total entropies of the solution and of the pure solvent in the canonical ensemble with volumes $\tilde{V}+\Delta V$ and $\tilde{V}$. In order to express the excess entropy in the form Eq. (14), we employ the Green–Wallace expansion for the entropy.[1,16–20] In this expansion, the entropy is expressed in terms of the correlation functions $\overline{\delta g^{(n)}}(\mathbf{x}_1,\ldots,\mathbf{x}_n)$ $(n=1,2,\ldots)$, which are defined from the distribution functions $\overline{\rho^{(n)}}$'s as

$$\overline{\delta g^{(1)}}(\mathbf{x}) = \overline{\rho^{(1)}}(\mathbf{x})$$

$$\overline{\delta g^{(2)}}(\mathbf{x}_1,\mathbf{x}_2) = \frac{\overline{\rho^{(2)}}(\mathbf{x}_1,\mathbf{x}_2)}{\overline{\rho^{(1)}}(\mathbf{x}_1)\overline{\rho^{(1)}}(\mathbf{x}_2)} \tag{21}$$

$$\overline{\delta g^{(3)}}(\mathbf{x}_1,\mathbf{x}_2,\mathbf{x}_3) = \frac{\overline{\rho^{(3)}}(\mathbf{x}_1,\mathbf{x}_2,\mathbf{x}_3)}{\overline{\rho^{(1)}}(\mathbf{x}_1)\overline{\rho^{(1)}}(\mathbf{x}_2)\overline{\rho^{(1)}}(\mathbf{x}_3)} \Big/$$
$$\overline{\delta g^{(2)}}(\mathbf{x}_1,\mathbf{x}_2)\,\overline{\delta g^{(2)}}(\mathbf{x}_2,\mathbf{x}_3)\,\overline{\delta g^{(2)}}(\mathbf{x}_3,\mathbf{x}_1),$$

and $\overline{\delta g^{(n)}}$'s $(n=4,\ldots)$ are similarly defined. The total entropy of the solution $\overline{S}$ is then expressed as

$$\overline{S} = \int d\mathbf{x}\,\overline{\rho}(\mathbf{x})\overline{s}(\mathbf{x}), \tag{22}$$

where $\overline{s}$ is defined as

$$\overline{s}(\mathbf{x}) = k_B \sum_{i=1} \frac{1}{i!} \int d\mathbf{y}_1 \cdots d\mathbf{y}_{i-1}$$
$$\times \frac{\overline{\rho^{(i)}}(\mathbf{x},\mathbf{y}_1,\ldots,\mathbf{y}_{i-1})}{\overline{\rho^{(1)}}(\mathbf{x})} \ln \overline{\delta g^{(i)}}(\mathbf{x},\mathbf{y}_1,\ldots,\mathbf{y}_{i-1}) \tag{23}$$

and k_B is the Boltzmann constant. In the pure solvent, a similar expression for the entropy is obtained, and the variable corresponding to $\overline{s}$ is denoted by s. It should be noted that s is independent of $\mathbf{x}$ due to the homogeneity of the pure solvent.

We now show that the excess entropy at constant pressure is local in terms of $\overline{s}$ and s. To do so, we rewrite Eq. (20), by virtue of Eqs. (3) and (4), as

$$\Delta S_{\text{const-P}} = \int_{\tilde{V}+\Delta V} d\mathbf{x}\,\overline{\rho_{\tilde{V}+\Delta V}}(\mathbf{x})(\overline{s_{\tilde{V}+\Delta V}}(\mathbf{x}) - s_{\tilde{V}}) + o(1)$$

$$= \int_{\tilde{V}+\Delta V} d\mathbf{x}\,\overline{\rho_P}(\mathbf{x})(\overline{s_P}(\mathbf{x}) - s_P) + o(1), \tag{24}$$

where the subscripts $\tilde{V}+\Delta V$ and $\tilde{V}$ indicate variables in the canonical ensemble and the subscript P indicates variables in the isothermal-isobaric ensemble. In order to analyze the asymptotic behavior of $\overline{s}(\mathbf{x})$ when $\mathbf{x}$ is far from the solute, we turn to the asymptotic behavior of $\overline{\delta g_P^{(i)}}(\mathbf{x},\mathbf{y}_1,\ldots,\mathbf{y}_{i-1})$ in Eq. (23), $\mathbf{x}$ being far from the solute. When the components of $(\mathbf{x},\mathbf{y}_1,\ldots,\mathbf{y}_{i-1})$ are separated from one another beyond a correlation length, which is assumed to be finite,[11] an argument similar to that leading to Eq. (6) gives $\overline{\delta g_P^{(i)}}(\mathbf{x},\mathbf{y}_1,\ldots,\mathbf{y}_{i-1}) \to 1+o(1/N)$ in the isothermal-isobaric ensemble. Thus, when $\mathbf{x}$ is far from the solute, the contribution of $\ln \overline{\delta g_P^{(i)}}(\mathbf{x},\mathbf{y}_1,\ldots,\mathbf{y}_{i-1})$ to Eq. (23) vanishes unless the solvent molecules with coordinates $(\mathbf{y}_1,\ldots,\mathbf{y}_{i-1})$ are also close to $\mathbf{x}$ that is in turn far from the solute. We can, therefore, obtain, from Eq. (6),

$$\overline{s_P}(\mathbf{x}) \to s_P + o\left(\frac{1}{N}\right) \tag{25}$$

at a large distance from the solute. Equation (25) shows that the excess entropy at constant pressure is local in terms of $\overline{s}$ and s.

The excess entropy at constant volume is, however, not local when the integral formula for the excess entropy is written in terms of $\overline{s}$ and s because the excess entropy depends on the condition of solute insertion. To identify the nonlocal component of the excess entropy at constant volume, we employ the ensemble independence of the excess chemical potential $\Delta \mu$ expressed as

$$\Delta \mu = \Delta E_{\text{const-P}} + P\Delta V - T\Delta S_{\text{const-P}}$$
$$= \Delta E_{\text{const-V}} - T\Delta S_{\text{const-V}}, \tag{26}$$

where $\Delta E_{\text{const-P}}$ and $\Delta E_{\text{const-V}}$ are the excess energies at constant pressure and at constant volume, respectively, and $\Delta S_{\text{const-P}}$ and $\Delta S_{\text{const-V}}$ are the excess entropies at constant pressure and at constant volume, respectively. According to Eqs. (11) and (26), the nonlocal component of $T\Delta S_{\text{const-V}}$ in terms of $\overline{s}$ and s is given by $-\Delta V(P+(\partial E/\partial V))$.

Equation (26) also shows by virtue of Eqs. (13), (18), and (24) that the excess chemical potential is local in terms of $(\overline{B}+P/\overline{\rho}-T\overline{s})$. The condition of solute insertion does not need to be specified in this case since the excess chemical potential is independent of the condition of solute insertion.

III. DISCUSSION

In order to systematically derive the solvation shell model for an excess thermodynamic quantity ΔQ, a microscopic expression of the form Eq. (14) is first formulated by making a suitable choice of $\overline{q}(\mathbf{x})$ and q. The concept of the solvation shell is then introduced into Eq. (14) by restricting the domain of integration to a finite region called the "solvation shell" V_{shell}. In the solvation shell model, ΔQ given by Eq. (14) is approximated as

$$\Delta Q_{\text{shell}} = N_{\text{shell}}(\overline{q}_{\text{shell}} - q), \tag{27}$$

where

$$N_{\text{shell}} = \int_{V_{\text{shell}}} d\mathbf{x}\,\overline{\rho}(\mathbf{x}) \tag{28}$$

and

$$\bar{q}_{\text{shell}} = \frac{\int_{V_{\text{shell}}} d\mathbf{x} \bar{\rho}(\mathbf{x}) \bar{q}(\mathbf{x})}{\int_{V_{\text{shell}}} d\mathbf{x} \bar{\rho}(\mathbf{x})}. \tag{29}$$

N_{shell} is the number of solvent molecules in the solvation shell and $\bar{q}_{\text{shell}}$ is the average of $\bar{q}(\mathbf{x})$ within the solvation shell. Since V_{shell} is finite and of molecular dimensions, in the thermodynamic limit ΔQ_{shell} is independent of the condition of solute insertion. Because in the implementation of Eq. (27) the thermodynamic limit is taken for any finite V_{shell}, in the limit $V_{\text{shell}} \to \infty$, ΔQ_{shell} approaches the value of the local component of ΔQ. The solvation shell estimate of ΔQ is, therefore, an approximation to the local component of ΔQ.

The solvation shell analysis of the excess energy at constant pressure gives information about the shift of the binding energy in the solvation shell from that in the bulk. In contrast, the solvation shell analysis of the excess energy at constant volume gives information about $(\bar{B} - (\partial E/\partial V) \times (1/\bar{\rho}))$ in the solvation shell. Thus, either a constant pressure or a constant volume process can be chosen to analyze the excess energy using the solvation shell model. The choice depends upon which local estimator of the excess energy is to be studied. Since the binding energy $\bar{B}$ has a clearer physical meaning than $(\bar{B} - (\partial E/\partial V)(1/\bar{\rho}))$, it is preferable to perform the solvation shell analysis on experimental data obtained at constant pressure. Similarly, because simple forms of the local estimators are obtained for the excess enthalpy, entropy, and volume at constant pressure, the solvation shell analysis of experimental data obtained at constant pressure appears to be the most useful.

In a recent paper, Cann and Patey presented a scheme to decompose excess thermodynamic quantities into local and nonlocal components.[8] The decomposition is based on a phenomenological model for the solute size dependence of an excess thermodynamic quantity ΔQ.[8] For a large hard-sphere solute of diameter d, ΔQ is expressed as an expansion in terms of solute volume, surface area, and diameter:

$$\Delta Q = \Delta Q_{\text{vol}} \frac{\pi d^3}{6} + \Delta Q_{\text{surf}} \pi d^2 + \Delta Q_{\text{diam}} d. \tag{30}$$

For a constant volume solute insertion process, Cann and Patey's scheme defines the volume component as being nonlocal and the surface area and diameter components as being local. By fitting excess thermodynamic quantities obtained by an integral equation calculation for six solutes of different sizes, they have determined the volume, surface area, and diameter coefficients of the expansion for the excess chemical potential, excess energy, and excess entropy of solvation for the constant volume and constant pressure solute insertion processes. They observe that the volume coefficients of the excess energy and excess entropy at constant pressure are zero and that the surface area and diameter coefficients in the constant pressure process differ from their counterparts in the constant volume process. They explain this phenomenon by stating that ''in the isobaric case the surface area and diameter coefficients of the excess properties include nonlocal

contributions,'' and conclude, in clear disagreement with our analysis, that the solvation shell model cannot be applied to analyze experimental measurements conducted at constant pressure because ''these methods rely on most of the change in thermodynamic properties coming from solvent particles in the vicinity of the solute and changes in bulk density, which give nonlocal terms, are neglected.''

In the previous sections, we have shown that, for the constant pressure process, the excess chemical potential, energy, enthalpy, entropy, and volume are all local quantities for natural choices of the local estimators. These estimators can be written in terms of the deviations of the binding energy and of the distribution functions from their corresponding value in the bulk. When integrated over a finite but large region surrounding the solute, the local estimators yield the exact excess thermodynamic properties at constant pressure. The solvation shell analysis of experimental measurements conducted at constant pressure is, therefore, a valid procedure. The accuracy and usefulness of the solvation shell approximation depends upon the number of shells that must be included to obtain the total response.[1,2]

We now provide a microscopic interpretation of the work of Cann and Patey[8] in an attempt to resolve the apparent disagreement between their approach and ours. Consider a hard-sphere solute and the expansion of an excess thermodynamic quantity ΔQ in terms of the solute diameter d using Eq. (14). The coefficients in the expansion of ΔQ with respect to d involve the corresponding expansion coefficients of the integrand function $(\bar{q}(\mathbf{x}) - q)$. Thus, the asymptotic N-dependence ($o(1/N)$ or not) of the expansion coefficients of $(\bar{q}(\mathbf{x}) - q)$ with respect to d at large distance from the solute determine whether the coefficients of the expansion for ΔQ are local or nonlocal. In Sec. II, it is shown that the asymptotic N-dependence of $(\bar{q}(\mathbf{x}) - q)$ depends only on the condition of solute insertion. The asymptotic N-dependence of $(\bar{q}(\mathbf{x}) - q)$ is independent of the solute-solvent interaction potential and, in particular, solute size. Thus, all of the expansion coefficients of $(\bar{q}(\mathbf{x}) - q)$ with respect to d have identical asymptotic behavior with respect to $1/N$. Consequently, if the excess thermodynamic quantity ΔQ is local in terms of $\bar{q}$ and q, all of its expansion coefficients with respect to the solute diameter d are local in terms of $\bar{q}$ and q. This point is in contrast with the analysis of Cann and Patey. In their work, in fact, it is the solute size dependence that labels a quantity as being local or nonlocal. In particular, the d^3 coefficient of the expansion is considered nonlocal and the d^2 and d coefficients are considered local.[8] As both local and nonlocal components appear at the same time in the expansion, Cann and Patey's definitions of the local and nonlocal components are not consistent with ours as presented in Sec. II. In addition, since Cann and Patey's analysis is based on a phenomenological expansion, the solute volume, surface area, and diameter play essential roles in determining the local and nonlocal components. On the other hand, since Eqs. (1) and (6) are valid for any type of solute-solvent interaction, our analysis of the local and nonlocal components can be developed without relying upon such phenomenological parameters as the solute volume, surface area, and diam-

eter. It is, nevertheless, possible to show that the properties of the expansion coefficients with respect to solute size can be understood in terms of the solvation shell model. It is also possible to give a simple interpretation of the dependence of the coefficients on the insertion condition that does not assume that the solvent structure around the solute is affected by the insertion condition.

Cann and Patey write for the excess chemical potential

$$\Delta\mu = P\frac{\pi d^3}{6} + \gamma\pi d^2 + \alpha d,\qquad(31)$$

where P is the pressure of the system and γ and α are scaling coefficients.[8] The form of the first term in Eq. (31) is determined from a purely macroscopic argument.[8] The excess volume ΔV is similarly expanded through pressure differentiation of Eq. (31) as

$$\Delta V = \frac{\pi d^3}{6} + \left(\frac{\partial\gamma}{\partial P}\right)_T \pi d^2 + \left(\frac{\partial\alpha}{\partial P}\right)_T d.\qquad(32)$$

The expression for the excess energy depends on the condition of solute insertion. The excess energy at constant volume $\Delta E_{\text{const-V}}$ is given by

$$\Delta E_{\text{const-V}} = -T^2\left(\frac{\partial}{\partial T}\left(\frac{P}{T}\right)\right)_V \frac{\pi d^3}{6} - T^2\left(\frac{\partial}{\partial T}\left(\frac{\gamma}{T}\right)\right)_V \pi d^2$$
$$- T^2\left(\frac{\partial}{\partial T}\left(\frac{\alpha}{T}\right)\right)_V d,\qquad(33)$$

and the excess energy at constant pressure $\Delta E_{\text{const-P}}$ is given by

$$\Delta E_{\text{const-P}} = P\left(\frac{\pi d^3}{6} - \Delta V\right) - T^2\left(\frac{\partial}{\partial T}\left(\frac{\gamma}{T}\right)\right)_P \pi d^2$$
$$- T^2\left(\frac{\partial}{\partial T}\left(\frac{\alpha}{T}\right)\right)_P d$$
$$= -\left[T^2\left(\frac{\partial}{\partial T}\left(\frac{\gamma}{T}\right)\right)_P + P\left(\frac{\partial\gamma}{\partial P}\right)_T\right]\pi d^2$$
$$- \left[T^2\left(\frac{\partial}{\partial T}\left(\frac{\alpha}{T}\right)\right)_P + P\left(\frac{\partial\alpha}{\partial P}\right)_T\right]d$$
$$= -\left[T^2\left(\frac{\partial}{\partial T}\left(\frac{\gamma}{T}\right)\right)_V - \left(\frac{\partial E}{\partial V}\right)_T\left(\frac{\partial\gamma}{\partial P}\right)_T\right]\pi d^2$$
$$- \left[T^2\left(\frac{\partial}{\partial T}\left(\frac{\alpha}{T}\right)\right)_V - \left(\frac{\partial E}{\partial V}\right)_T\left(\frac{\partial\alpha}{\partial P}\right)_T\right]d,\qquad(34)$$

where E is the average energy in the pure solvent.

By comparing Eqs. (33) and (34) it can be seen that the expressions for the surface area and diameter expansion coefficients of $\Delta E_{\text{const-P}}$ differ from the corresponding expansion coefficients for $\Delta E_{\text{const-V}}$ by factors proportional to $(\partial E/\partial V)_T$. These factors are what Cann and Patey called the nonlocal contributions to the expansion coefficients of $\Delta E_{\text{const-P}}$ concluding that not only $\Delta E_{\text{const-V}}$ but also $\Delta E_{\text{const-P}}$ cannot be predicted solely by examining a finite solvent region close to the solute.[8] However, Eq. (34) is

merely the result of macroscopic thermodynamic manipulations and therefore cannot be used to classify thermodynamic quantities as being local or nonlocal. Such classification can be carried out after introducing the microscopic definition of a distance from the solute and employing the formalism of statistical mechanics to study its implications. When the solvent binding energy is used as a local estimator, our treatment, based on inhomogeneous solution theory, correctly classifies the expansion coefficients of $\Delta E_{\text{const-V}}$ in Eq. (33) as having nonlocal components given by the corresponding expansion coefficients of $(\partial E/\partial V)_T\Delta V$. After subtracting these nonlocal components, as done in Eq. (34), the local component of $\Delta E_{\text{const-V}}$ is isolated and revealed to be equal to $\Delta E_{\text{const-P}}$. In conclusion, $\Delta E_{\text{const-P}}$ can be entirely accounted for by considering a finite region around the solute while $\Delta E_{\text{const-V}}$ is the sum of a local component ($\Delta E_{\text{const-P}}$) and the nonlocal component $(\partial E/\partial V)_T\Delta V$.

According to Eq. (34), $\Delta E_{\text{const-P}}$ does not involve a term proportional to d^3 and the leading term is proportional to the surface area of the solute. This result can be simply interpreted on the basis of the solvation shell formula Eq. (27) [note that Eq. (27) is exact for a large enough solvation shell]. We know, from the analysis in Sec. II, that the excess energy at constant pressure is a local quantity in terms of the binding energy. Furthermore, the binding energy, which is governed by the interactions between solvent molecules, as seen from Eq. (7), is independent of d when d is large (it will correspond to the binding energy of a solvent molecule near a flat surface). Thus, the dependence on d of $\Delta E_{\text{const-P}}$ derives from the factor N_{shell} which is in turn proportional to the surface area of the solute.

A solvation shell analysis can also explain the solute volume dependence of $\Delta E_{\text{const-V}}$, as shown in Eq. (33). The term proportional to d^3 can be related to the form of the local estimator $(\bar{B} - (\partial E/\partial V)(1/\bar{\rho}))$ in terms of which the excess energy at constant volume is found to be local. This local estimator diverges inside the excluded volume of the solute due to the presence of the factor $1/\bar{\rho}$. The singularity can be removed by performing the integration of the local estimator. For instance, by rewriting the solvation shell formula for the excess volume Eq. (18) as

$$\Delta V = -\int d\mathbf{x}(g_{\text{uv}}(\mathbf{x}) - 1) + o(1),\qquad(35)$$

where g_{uv} is the solute-solvent correlation function, the Kirkwood–Buff expression for the excess volume is obtained.[2,15] As shown in Ref. 2, the term $\pi d^3/6$ is recovered by integrating over the excluded volume of the solute within which g_{uv} is zero. In the same way, because inside the solute volume $\bar{\rho}(\mathbf{x})\bar{B}$ is zero and

$$\left(\frac{\partial E}{\partial V}\right)_T = T^2\left(\frac{\partial(P/T)}{\partial T}\right)_V,\qquad(36)$$

the integration of the local estimator $(\bar{B} - (\partial E/\partial V)(1/\bar{\rho}))$ over the excluded volume yields the first term in Eq. (33). The contribution outside the excluded volume, where $1/\bar{\rho}$ does not diverge, is instead expected to be proportional to d^2 in the large d limit.

In Cann and Patey's scheme, the terms proportional to the solute surface area and diameter are considered local components of the excess energy at constant volume. The corresponding terms for the excess energy at constant pressure are, instead, considered nonlocal because they involve contributions from ΔV.[8] Our analysis presented above shows, however, that the addition of the term proportional to ΔV to $\Delta E_{\text{const-V}}$ cancels the divergent factor $1/\bar{\rho}$ and makes the local estimator of the excess energy at constant pressure well-behaved. The above arguments can also be applied to the excess entropy, leading to similar conclusions.

In conclusion, we have devised a procedure to determine unambiguously the local and nonlocal components of excess thermodynamic quantities of solvation. This scheme is based on the analysis of the expressions of the excess solvation thermodynamic quantities as integrals over the system volume of local estimators,[1,2] using the finite-size asymptotic analysis by Lebowitz et al.[11,12] We find in particular that, while the excess energy and entropy at constant volume have nonlocal components, the corresponding quantities at constant pressure can be obtained by analyzing the solute-induced perturbation of the solvent structure and energetics only in a finite region surrounding the solute. The physical basis of this result resides in the generally accepted assumption that long-range correlations are absent in a fluid, except in the neighborhood of the critical point.

ACKNOWLEDGMENTS

[1] N. Matubayasi, L. H. Reed, and R. M. Levy, J. Phys. Chem. **98**, 10640 (1994).

[2] N. Matubayasi and R. M. Levy, J. Phys. Chem. **100**, 2681 (1996).

[3] *Water, A Comprehensive Treatise*, edited by F. Franks (Plenum, New York, 1972–1982), Vols. 1–7.

[4] G. Nemethy and H. A. Sheraga, J. Chem. Phys. **36**, 3401 (1962).

[5] A. Ben-Naim, *Hydrophobic Interactions* (Plenum, New York, 1980).

[6] A. Ben-Naim, *Solvation Thermodynamics* (Plenum, New York, 1987).

[7] L. R. Pratt, Annu. Rev. Phys. Chem. **36**, 433 (1985).

[8] N. M. Cann and G. N. Patey, J. Chem. Phys. **106**, 8165 (1997).

[9] We have discussed this manuscript with Cann and Patey, and they now agree with the microscopic analysis of the local and nonlocal components of solvation thermodynamics presented here.

[10] A partial molar quantity consists of an excess contribution (from differentiation of the excess chemical potential) and an ideal contribution (from differentiation of the ideal part of the chemical potential).

[11] J. L. Lebowitz and J. K. Percus, Phys. Rev. **122**, 1675 (1961).

[12] J. L. Lebowitz, J. K. Percus, and L. Verlet, Phys. Rev. **153**, 250 (1967).

[13] The integral involved in Eq. (7), although taken over the total volume of the system, is independent of the ensemble because the contribution coming from the region outside the intermolecular interaction range is absent.

[14] Although the binding energy in the pure solvent is independent of the position, its dependence on the orientation is actually first order in $1/N$. The following discussion is then valid when the orientational averaging is properly performed for $\bar{B}$ and $\bar{\rho}$ and **x** is redefined as the position of a solvent molecule. Similar points also appear in other parts of the paper. We do not state these points explicitly in the text since they can be circumvented by redefining the notation in trivial manners.

[15] J. G. Kirkwood and F. P. Buff, J. Chem. Phys. **19**, 774 (1951).

[16] H. S. Green, *The Molecular Theory of Fluids* (North-Holland, Amsterdam, 1952).

[17] D. C. Wallace, J. Chem. Phys. **87**, 2282 (1987).

[18] D. C. Wallace, Phys. Rev. A **39**, 4843 (1989).

[19] T. Lazaridis and M. E. Paulaitis, J. Phys. Chem. **96**, 3847 (1992).

[20] T. Lazaridis and M. E. Paulaitis, J. Phys. Chem. **98**, 635 (1994).