

THERMODYNAMIC PERTURBATION THEORY FOR ASSOCIATING MOLECULES

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CONTENTS

I. Introduction	
II. A Brief Introduction to Cluster Expansions	
III. Single Association Site: Bond Renormalization	
IV. Single Association Site: Two-Density Approach	
A. The Monovalent Case	
B. The Divalent Case	
V. Multiple Association Sites: Multi-Density Approach	
VI. The Two-Site AB Case	
A. Steric Hindrance in Chain Formation	
B. Ring Formation	
C. Bond Cooperativity	
VII. Spherically Symmetric and Directional Association Sites	
VIII. Density Functional Theory	
IX. Concluding Remarks	
Acknowledgments	
References	

I. INTRODUCTION

Since the time of van der Waals, scientists have sought to describe the macroscopic behavior of fluids in terms of the microscopic interactions of the constituent molecules. By the early 1980s, accurate theories based on statistical mechanics had primarily been developed for near-spherical molecules. Successes of the 1960s and 1970s particularly by Chandler, Weeks, and Andersen [1] and by Barker and Henderson [2] produced perturbation theories for the properties of Lennard-Jones (LJ) fluids. Site–site theories such as reference interaction site model (RISM) [3] were developed,

in part, to provide reference fluid structure to extend these perturbation theories to polyatomic molecules. However, for certain classes of fluids, the accurate description of the fluid phase in terms of the microscopic interactions has proven much more challenging. Hydrogen bonding interactions are strong, short-ranged, highly directional interactions that lie somewhere between a dipole/dipole attraction and a covalent bond. The short range and directionality of hydrogen bonds result in the phenomena of bond saturation, giving a limited valence of the hydrogen bonding attractions.

The same properties of the hydrogen bond, which complicate the theoretical description of these fluids, also give rise to a number of macroscopic physical properties that are unique to fluids that exhibit hydrogen bonding. Hydrogen bonding is responsible for the remarkable properties of water [4], folding of proteins [5] and is commonly exploited in the self-assembly [6] of advanced materials. More recently patchy colloids, a new class of materials that shares many qualities with hydrogen bonding fluids, have been developed. Patchy colloids are colloids with some number of attractive surface patches giving rise to association like anisotropic inter-colloid potentials [7]. For the purposes of this review, patchy colloids and hydrogen bonding fluids are treated on equal footing and will simply be termed “associating fluids.”

The first models used to describe hydrogen bonding fluids were developed using a chemical approach, where each associated cluster is treated as a distinct species created from the reaction of monomers and smaller associated clusters [8, 9]. The “reactions” are governed by equilibrium constants that must be obtained empirically. This type of approach has been incorporated into various equations of state including a van-der-Waals-type equation of state [10], the perturbed anisotropic chain theory equation of state (APACT) [11], and the Sanchez–Lacombe [12] equation of state.

Alternatively, lattice theories may be employed to model hydrogen bonding fluids. These approaches generally follow the method of Veytsman [13] who showed how the free energy contribution due to hydrogen bonding could be calculated in the mean field by enumerating the number of hydrogen bonding states on a lattice. Veytsman’s approach was incorporated into the Sanchez–Lacombe equation of state by Panayiotou and Sanchez [14] who factored the partition function into a hydrogen bonding contribution and a non-hydrogen bonding contribution. The lattice approach has also been applied to hydrogen bond cooperativity [15] and intramolecular [16] hydrogen bonds.

Both the chemical and lattice theory approaches to hydrogen bonding yield semi-empirical equations of state, which are useful for several hydrogen bonding systems [8]. The drawback of these approaches is a result of their simplistic development. As discussed earlier, it is desired to describe the macroscopic behavior of fluids through knowledge of the microscopic intermolecular interactions and distributions. This cannot be accomplished using a lattice or chemical theory. To accomplish this goal, we must incorporate molecular details of the associating fluid from the outset.

The starting place for any molecular theory of association is the definition of the pair potential energy $\phi(12)$ between molecules (or colloids). Molecules are treated as rigid bodies with no internal degrees of freedom. In total, six degrees of freedom describe any single molecule: three translational coordinates represented by the vector $\vec{r}_1$ and three orientation angles represented by Ω_1 . These six degrees of freedom are represented as $1 = \{\vec{r}_1, \Omega_1\}$. It is assumed that the intermolecular potential can be separated as

$$\phi(12) = \phi_{ref}(12) + \phi_{as}(12) \quad (1)$$

where $\phi_{as}(12)$ contains the association portion of the potential and $\phi_{ref}(12)$ is the reference system potential, which contains all other contributions of the pair potential including a harsh short-ranged repulsive contribution.

Considering molecules (or colloids) that have a set of association sites $\Gamma = \{A, B, C, \dots, Z\}$, where association sites are represented by capital letters, the association potential is decomposed into individual site–site contributions

$$\phi_{as}(12) = \sum_{A \in \Gamma} \sum_{B \in \Gamma} \phi_{AB}(12) \quad (2)$$

The potential $\phi_{AB}(12)$ represents the association interaction between site A on molecule 1 and site B on molecule 2. One of the challenges in developing theoretical models for associating fluids stems from the short-ranged and directional nature of the association potential ϕ_{AB} , which results in the phenomena of bond saturation. For instance, considering molecules which consist of a hard spherical core of diameter d

$$\phi_{ref}(12) = \phi_{HS}(r_{12}) = \begin{cases} \infty & r < d \\ 0 & r \geq d \end{cases} \quad (3)$$

and a single association site A (see Fig. 1), bond saturation arises as follows. When spheres 1 and 2 are positioned and oriented correctly such that an association bond is formed, the hard cores of these two spheres may, depending on the

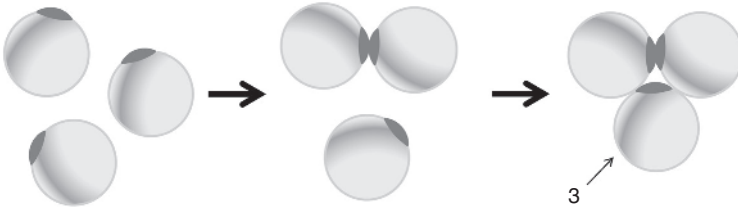


Figure 1. Illustration of bond saturation for hard spheres with a single monovalent association site. (See insert for color representation of the figure.)

size and range of the association site, prevent sphere 3 from approaching and sharing in the association interaction. That is, if $\phi_{as}(12) < 0$ and $\phi_{as}(13) < 0$, then $\phi_{HS}(r_{23}) = \infty$, meaning that each association site is singly bondable (has a valence of 1). In hydrogen bonding it is usually the case that each association bond site is singly bondable, although there are exceptions. For the case of patchy colloids, the patch size can be controlled to yield a defined valence controlling the type of self-assembled structures that form.

Conical square well (CSW) association sites are commonly used as a primitive model for the association potential ϕ_{AB} . First introduced by Bol [17] and later reintroduced by Chapman *et al.* [18, 19], CSWs consider association as a square well interaction which depends on the position and orientation of each molecule. Kern and Frenkel [20] later realized that this potential could describe the interaction between patchy colloids. For these CSWs the association potential is given by

$$\begin{aligned}\phi_{AB}(12) &= -\epsilon_{AB} O_{AB}(12) \\ O_{AB}(12) &= \begin{cases} 1, & r_{12} \leq r_c; \theta_{A1} \leq \theta_c; \theta_{B2} \leq \theta_c \\ 0 & \text{otherwise} \end{cases} \\ f_{AB}(12) &= (\exp(\epsilon_{AB}/k_{BT}) - 1) O_{AB}(12) = f_{AB} O_{AB}(12)\end{aligned}\quad (4)$$

where r_c is the maximum separation between two colloids for which association can occur, θ_{A1} is the angle between $\vec{r}_{12}$ and the orientation vector passing through the center of the patch on colloid 1, and θ_c is the critical angle beyond which association cannot occur. Equation (4) states that if the spheres are close enough $r_{12} < r_c$, and both are oriented correctly $\theta_{A1} < \theta_c$ and $\theta_{B2} < \theta_c$, then an association bond is formed and the energy of the system is decreased by ϵ_{AB} . Figure 2 gives an illustration of two single-site spheres interacting with this potential. The size of the patch is dictated by the critical angle θ_c that defines the solid angle to be $2\pi(1 - \cos\theta_c)$. The patch size determines the maximum number of other spheres to which the patch can bond. Specifically considering a hard sphere reference fluid with association occurring at hard sphere contact $r_c = d$, it is possible for a

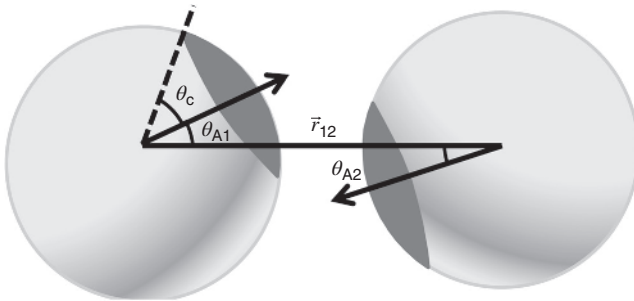


Figure 2. Association parameters for conical association sites. (See insert for color representation of the figure.)

patch to associate at most once for $0^\circ \leq \theta_c < 30^\circ$, twice for $30^\circ \leq \theta_c < 35.3^\circ$, thrice for $35.3^\circ \leq \theta_c < 45^\circ$, and four times for $45^\circ \leq \theta_c < 58.3^\circ$ [21]. The advantage of the CSW model is that it separates the radial and angular dependence of the potential and allows for analytic calculations in the model while allowing for quick calculation of association in a simulation since only two dot products are needed to determine that the molecular orientation criteria is satisfied for association.

In the following sections we review some of the existing theories to model associating fluids with potentials of the form of Eqs. (1)–(2). We focus mainly on the multi-density formalism of Wertheim [22, 23], which has been widely applied across academia and industry. In Sections III and IV.A, only association sites that are singly bondable are considered and steric hindrance between association sites is neglected. Extensions of Wertheim’s multi-density approach for the divalent case is described in Section IV.B. Section V addresses the case of multiple association sites on a molecule within Wertheim’s multi-density formalism. Section VI extends the theory to the case of a small angle between two association sites, so that the sites cannot be assumed to be independent, and for the case of cooperative hydrogen bonding. Section VII extends the theory to account for association interactions between molecules with spherically symmetric and directional association sites (e.g., ion–water solvation). A brief description of applying the density functional theory (DFT) approach for associating molecules is presented in Section VIII. Finally, Section IX gives concluding remarks. Prior to exploring the theory, a brief introduction to cluster expansions is provided in Section II.

II. A BRIEF INTRODUCTION TO CLUSTER EXPANSIONS

In this section we give a very brief overview of cluster expansions. For a more detailed introduction the reader is referred to the original work of Morita and Hiroike [24] and also to the reviews by Stell [25] and Andersen [26]. Cluster expansions were first introduced by Mayer [27] as a means to describe the structure and thermodynamics of non-ideal gases. In cluster expansions Mayer f functions are introduced:

$$f(12) = \exp\left(\frac{-\phi(12)}{k_B T}\right) - 1 \quad (5)$$

The replacement $\exp(-\phi(12)/k_B T) = f(12) + 1$ in the grand partition function and the application of the lemmas developed by Morita and Hiroike [24] allows for the pair correlation function $g(12)$ and Helmholtz free energy A to be written as an infinite series in density where each contribution is an integral represented pictorially by a graph. A graph is a collection of black circles and white circles with bonds connecting some of these circles. The bonds are represented by

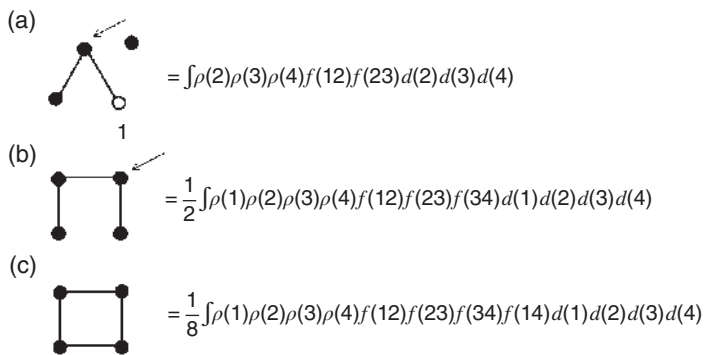


Figure 3. Examples of integral representations of graphs. Arrows point towards articulation circles.

two-molecule functions such as Mayer functions $f(12)$ and the black circles are called “field points” represented by single-molecule functions such as fugacity $z(1)$ or density $\rho(1)$ integrated over the coordinates (1). The white circles are called “root points” and are not associated with a single-molecule function, and the coordinates of a root point are not integrated. Root points are given labels 1, 2, 3, The value of the diagram is then obtained by integrating over all coordinates associated with field points and multiplying this integral by the inverse of the symmetry number S of the graph. Figure 3 gives several examples. The volume element $d(1)$ is given by $d(1) = d\vec{r}_1 d\Omega_1$, representing the differential position and orientation of the molecule.

Before giving graphical representations of the pair correlation function $g(12)$ and the Helmholtz free energy A , a few definitions must be given as follows:

1. A graph is connected if there is at least one path between any two points. Graph **a** in Fig. 3 is disconnected, and graphs **b** and **c** are both connected.
2. An articulation circle is a circle in a connected graph whose removal makes the graph disconnected, where at least one part contains no root point and at least one field point. Arrows in Fig. 3 point to articulation circles.
3. An irreducible graph has no articulation circles. Graph **c** in Fig. 3 is an example of an irreducible graph.

Using these definitions, the pair correlation function and Helmholtz free energy are given as

$$g(12) = \left\{ \begin{array}{l} \text{sum of topologically different irreducible graphs that have two root} \\ \text{points labelled 1 and 2, any number of field points } \rho, \text{ and at most} \\ \text{one } f \text{ bond between each pair of points} \end{array} \right\} \quad (6)$$

and

$$\frac{A}{k_B T} = \int \rho(1) \left(\ln(\rho(1) \Lambda^3) - 1 \right) d(1) - c^{(o)} \quad (7)$$

where Λ is the de Broglie wavelength, $\rho(1)$ is the density where $\rho(\vec{r}) = \int \rho(1) d\Omega$, and $c^{(o)}$ is the graph sum given by

$$c^{(o)} = \left\{ \begin{array}{l} \text{sum of topologically different irreducible graphs that have no root} \\ \text{points any number of field points } \rho, \text{ and at most one } f \text{ bond between} \\ \text{each pair of points} \end{array} \right\} \quad (8)$$

Equations (6)–(8) are rigorous and exact mathematical statements. Unfortunately, the exact evaluation of these infinite sums cannot be performed and numerous approximations must be made to obtain any usable result. In these approximations only some subset of the original graph sum is evaluated.

Performing these partial summations in hydrogen bonding fluids is complicated by both the strength of the association interaction and the limited valence of the interaction. Hydrogen bond strengths can be many times that of typical van der Waals forces giving Mayer functions which are very large. If the entire cluster series were evaluated for $g(12)$ and $c^{(o)}$ many of these large terms would cancel; however, when performing partial summations, care must be taken to eliminate divergences if meaningful results are to be obtained. Similarly, in most hydrogen bonding fluids, each hydrogen bonding group is singly bondable. Hence, any theory for hydrogen bonding fluids must account for the limited valence of the attractions. Again, if the full cluster series were evaluated for $g(12)$ this condition would be naturally accounted for; however, when performing partial summations care must be taken to ensure this single bonding condition holds. There have been three general methods to handle these strong association interactions using cluster expansions. The first was the pioneering work of Andersen [28, 29] who developed a cluster expansion for associating fluids in which the divergence was tamed by the introduction of renormalized bonds, the second is the approach of Chandler and Pratt [30] who used physical clusters to represent associated molecules, and the third is the method of Wertheim [22, 23, 31–33] who used multiple densities. Both Andersen and Wertheim took the approach of incorporating the effects of steric hindrance early in the theoretical development in the form of mathematical clusters. In what follows, for brevity, we restrict our attention to the approaches of Andersen and Wertheim, however, when possible we draw parallels between these approaches and that of Chandler and Pratt.

III. SINGLE ASSOCIATION SITE: BOND RENORMALIZATION

Before discussing the more general case of associating fluids with multiple association sites, we will discuss the simpler case of molecules with a single association site A. For a single association site, the Mayer function is decomposed as

$$f(12) = f_{ref}(12) + F_{AA}(12) \quad (9)$$

where

$$\begin{aligned} F_{AA}(12) &= e_{ref}(12) f_{AA}(12) \\ e_{ref}(12) &= \exp\left(\frac{-\phi_{ref}(12)}{k_B T}\right) = 1 + f_{ref}(12) \\ f_{AA}(12) &= \exp\left(\frac{-\phi_{AA}(12)}{k_B T}\right) - 1 \end{aligned} \quad (10)$$

In Eq. (10) the $f_{AA}(12)$ accounts for the anisotropic/short-ranged attraction of the association interaction and the function $e_{ref}(12)$ prevents the overlap of the cores of the molecules. It is the functions $e_{ref}(12)$ that give rise to the single bonding condition. Now inserting Eq. (9) into Eq. (6) and simplifying

$$g(12) = \left\{ \begin{array}{l} \text{sum of topologically different irreducible graphs that have two} \\ \text{root points labelled 1 and 2, any number of field points } \rho, f_{ref} \text{ and} \\ F_{AA} \text{ bonds, and at most one bond between each pair of points} \end{array} \right\} \quad (11)$$

Andersen [28, 29] defines a renormalized association Mayer function $\tilde{F}_{AA}(12)$ as the sum of the graphs in Eq. (11) which are most important in the determination of $g(12)$. Since the Mayer functions F_{AA} may take on very large numerical values in the bonding region, the most important graphs in the calculation of $g(12)$ are the ones whose root points are connected by an F_{AA} bond. Hence, it is natural to define $\tilde{F}_{AA}$ as

$$\tilde{F}_{AA}(12) = \left\{ \begin{array}{l} \text{sum of graphs in (11) whose root points are connected} \\ \text{by an } F_{AA} \text{ bond} \end{array} \right\} \quad (12)$$

Andersen assumes that the intermolecular potential was such that the association site was singly bondable. This single bonding condition was exploited in the

cluster expansion by use of the *cancelation theorem* as described by Andersen, who was able to sum the diagrams in Eq. (12) as

$$\tilde{F}_{AA}(12) = F_{AA}(12)Y_p(12) \frac{1 + 2\Delta_{AA} - \sqrt{1 + 4\Delta_{AA}}}{2\Delta_{AA}^2} \quad (13)$$

where the term Δ_{CD} is given by (where for a homogeneous fluid $\rho = \int \rho(1) d\Omega_1$)

$$\Delta_{CD} = \frac{\rho}{\Omega} \int Y_p(12) F_{CD}(12) d(2) \quad (14)$$

and $\Omega = \int d\Omega'$ is the total number of orientations. The function $Y_p(12)$ is given by

$$Y_p(12) = \left\{ \begin{array}{l} \text{sum of graphs in (11) which have no } F_{AA} \text{ bond attached} \\ \text{to either root, and no bond between the roots} \end{array} \right\} \quad (15)$$

It is easily shown that $\tilde{F}_{AA}(12)$ is bounded as follows:

$$0 \leq \frac{\rho}{\Omega} \int \tilde{F}_{AA}(12) d(2) \leq 1 \quad (16)$$

Equation (16) shows that the renormalized association bond remains finite even when the association potential ϕ_{AA} takes on infinitely large negative values. Using this renormalized bond the average number of hydrogen bonds per molecule is calculated as follows:

$$N_{HB} = \frac{\rho}{\Omega} \int \tilde{F}_{AA}(12) d(2) \quad (17)$$

Comparing Eqs. (16) and (17) it is easy to see

$$0 \leq N_{HB} \leq 1 \quad (18)$$

Equation (18) demonstrates that the single bonding condition is satisfied and that the method of Andersen was successful. Unfortunately, the function $Y_p(12)$ must be obtained through the solution of a series of integral equations using approximate closures.

To the author's knowledge, this approach has never been applied for numerical calculations of the structure or thermodynamics of one-site-associating fluids. Here we will show how a single simple approximation allows for the calculation

of N_{HB} . To approximate $Y_p(12)$ we note that this function can be decomposed into contributions from graphs that contain k association bonds F_{AA}

$$Y_p(12) = \sum_{k=0}^{\infty} Y_p^{(k)}(12) \quad (19)$$

The terms $Y_p^{(k)}$ give the contribution to Y_p from graphs that contain k association bonds. The simplest possible case is to keep only the first contribution $k=0$ and disregard all $Y_p^{(k)}$ for $k>0$. For this simple case

$$Y_p(12) = y_{ref}(12) \quad (20)$$

where y_{ref} is the cavity correlation function of the reference fluid, meaning association is treated as a perturbation to the reference fluid. This approximation is not necessarily intuitive since the structure of a fluid is expected to be strongly affected by association. Combining these results, the monomer fraction (fraction of molecules that do not have an association bond) can be written as

$$X_o = 1 - N_{NB} = \frac{-1 + \sqrt{1 + 4\Delta_{AA}}}{2\Delta_{AA}} \quad (21)$$

where Δ_{AA} is now given by $\Omega\Delta_{AA} = \rho \int y_{ref}(12) F_{AA}(12) d(2)$. Equation (21) gives a very simple relationship for the monomer fraction. This same equation was later derived by Chandler and Pratt [30] and Wertheim [22] using very different cluster expansions. Equation (21) has been shown to be highly accurate in comparison to simulation data [19, 34, 35]. Now we will introduce Wertheim's two-density formalism for one-site-associating fluids.

IV. SINGLE ASSOCIATION SITE: TWO-DENSITY APPROACH

In the previous section it was shown that Andersen's formalism can be applied to derive a highly accurate and simple relationship for the monomer fraction. In order to obtain this result the renormalized association Mayer functions $\tilde{F}_{AA}$ were employed. The applicability of Andersen's approach to more complex systems (mixtures, multiple bonds per association site, etc.) is limited by the fact that for each case the renormalized Mayer functions must be obtained by solving a rather complex combinatorial problem. A more natural formalism for describing association interactions in one-site-associating fluids is the two-density formalism of Wertheim [22, 31].

Instead of using the density expansion of the pair correlation function $g(12)$ or Helmholtz free energy A , Wertheim uses the fugacity expansion of $\ln \Xi$, where Ξ

is the grand partition function, as the starting point. Building on the ideas of Lockett [36], Wertheim then regroups the expansion such that individual graphs are composed of s -mer graphs. An s -mer represents a cluster of points that are connected by paths of F_{AA} bonds; each pair of points in an s -mer, which are not directly connected by a F_{AA} bond, receives an $e_{ref}(12)$ bond. This regrouping serves to include the geometry of association with the $e_{ref}(12)$ bonds enforcing the limited valence of the association interaction. In the s -mer representation, graphs that include unphysical core overlap are identically zero. That is, if the association site is singly bondable all graphs composed of s -mers of size $s > 2$ immediately vanish due to steric hindrance. This is not the case in Andersen's approach where these unphysical contributions are allowed in individual graphs, with the single bonding condition being exploited with the *cancelation theorem*.

This regrouping of the fugacity expansion allows for the easy incorporation of steric effects. Now, unlike Andersen who tamed the arbitrarily large F_{AA} bonds through the introduction of a renormalized $\tilde{F}_{AA}$, Wertheim uses the idea of multiple densities, splitting the total density of the fluid as

$$\rho(1) = \rho_o(1) + \rho_b(1) \quad (22)$$

where $\rho_o(1)$ is the density of monomers (molecules not bonded) and $\rho_b(1)$ is the density of molecules that are bonded. The density $\rho_o(1)$ is composed of all graphs in $\rho(1)$ which do not have an incident F_{AA} bond, and $\rho_b(1)$ contains all graphs which have one or more incident F_{AA} bonds. Performing a topological reduction from fugacity graphs to graphs which contain $\rho_o(1)$ and $\rho(1)$ field points, allowed Wertheim to arrive at the following exact free energy

$$\frac{A}{k_B T} = \int \left(\rho(1) \ln \left(\rho_o(1) \Lambda^3 \right) - \rho_o(1) \right) d(1) - c^{(o)} \quad (23)$$

where for this case the graph sum $c^{(o)}$ is given as follows:

$$c^{(o)} = \left\{ \begin{array}{l} \text{sum of all irreducible graphs consisting of monomer points carrying} \\ \text{factors of } \rho, s\text{-mer graphs with } s \geq 2 \text{ and every point carrying a factor} \\ \text{of } \rho_o, \text{ and } f_{ref}\text{-bonds between some sets of points in distinct } s\text{-mers.} \end{array} \right\} \quad (24)$$

The first few graphs in the infinite series for $c^{(o)}$ are given in Fig. 4. In Fig. 4 crossed lines $\text{---} \times \text{---} \times \text{---} \times \text{---} \times \text{---}$ represent F_{AA} bonds, dashed lines represent e_{ref} bonds, and solid lines represent f_{ref} bonds. All points with one or more incident F_{AA} bonds carry a factor $\rho_o(1)$, and each point with no incident F_{AA} bonds carries a factor $\rho(1)$. All graphs without any F_{AA} bonds (graphs **a**, **c**, **g**, **h**, and **i** in Fig. 4) represent

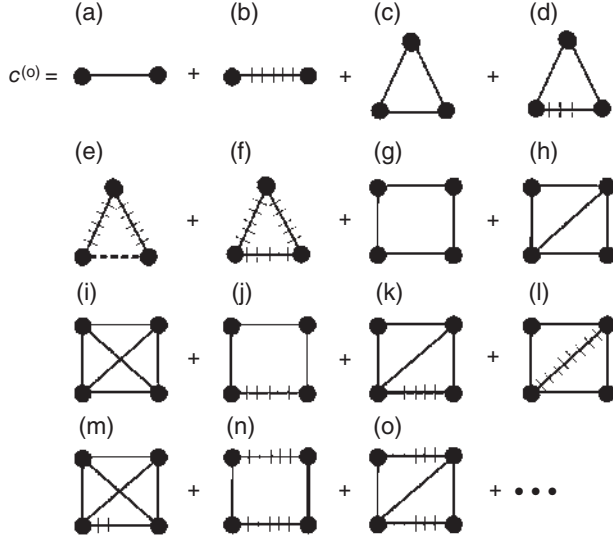


Figure 4. Graphical representation of Eq. (24) where crossed lines $\text{---} \text{+} \text{+} \text{+} \text{+} \text{---}$ represent F_{AA} bonds, dashed lines represent e_{ref} bonds, and solid lines represent f_{ref} bonds.

the reference system contribution $c_{ref}^{(o)}$. Any point that has two incident F_{AA} bonds (graphs **e** and **f** in fig. 4 are $s=3$ -mers) represents a molecule with an association site which is bonded to two other molecules.

A. The Monovalent Case

If $\phi(12)$ is chosen such that the single bonding condition holds, then all s -mer graphs with $s > 2$ vanish (e.g., graphs **e** and **f** in Fig. 4 are zero) and Eq. (24) can be summed exactly to yield the following:

$$c^{(o)} = c_{ref}^{(o)} + \frac{1}{2} \int \rho_o(1) f_{AA}(12) g_{oo}(12) \rho_o(2) d(1) d(2) \quad (25)$$

Note that Eq. (25) contains monomer densities since only monomers can associate. The use of monomer densities bounds the association term. The quantity $g_{oo}(12)$ is the monomer/monomer pair correlation function which can be ordered by graphs that contain k F_{AA} bonds:

$$g_{oo}(12) = \sum_{k=0}^{\infty} g_{oo}^{(k)}(12) \quad (26)$$

Similar to the approximation made for Y_p in the formalism of Andersen (Eq. 19), only the lowest-order contribution is retained, and all contributions with $k > 0$ are neglected. This is the single chain approximation, that yields the following:

$$g_{oo}(12) = g_{ref}(12) = y_{ref}(12)e_{ref}(12) \quad (27)$$

Equation (27) forms the basis of Wertheim's TPT, which assumes the monomer–monomer correlation function is the same as that of the reference fluid. This amounts to neglecting all graphs in Eq. (24) which contain more than a single F_{AA} bond (e.g., neglecting graphs **n** and **o** in Fig. 4). Although this is the same approximation that we introduced in Eq. (20) for Andersen's theory, the approximation is more intuitive in terms of the monomer–monomer distribution. Considering a dense fluid of hard spheres associating at contact, the packing fraction of the fluid does not change with extent of association. Therefore, we might expect that the monomer–monomer distribution function would remain relatively unchanged with association. For association near hard sphere contact (or sigma for LJ molecules), molecular simulation results show this to be a reasonably accurate approximation [18, 19, 35, 37–39].

To obtain an equation for $\rho_o(1)$, Eq. (23) is minimized:

$$\frac{\delta A / k_B T}{\delta \rho_o(1)} = \frac{\rho(1)}{\rho_o(1)} - 1 - \int f_{AA}(12) g_{ref}(12) \rho_o(2) d(2) = 0 \quad (28)$$

The operator $\delta/\delta\rho_o(1)$ represents the functional derivative. Combining Eqs. (23), (25), and (28) the free energy is simplified as

$$\frac{A - A_{ref}}{k_B T} = \int \rho(1) \left(\ln X_o(1) - \frac{X_o(1)}{2} + \frac{1}{2} \right) d(1) \quad (29)$$

where A_{ref} is the Helmholtz free energy of the reference system and $X_o(1) = \rho_o(1) / \rho(1)$ is the fraction of monomers. Now, assuming a homogeneous fluid $\rho = \rho(1) \Omega$ and solving Eq. (28), the monomer fraction Eq. (21) is obtained.

As can be seen, under the single bonding condition when treated as a perturbation theory, both Andersen's and Wertheim's approaches give the same result for homogeneous fluids. Indeed, Eq. (13) can be rewritten in terms of monomer fractions

$$\tilde{F}_{AA}(12) = F_{AA}(12) y_{ref}(12) X_0^2 = f_{AA}(12) g_{ref}(12) X_0^2 \quad (30)$$

and for a homogeneous fluid the renormalized Mayer functions can be used to represent $c^{(o)}$.

$$c^{(o)} = c_{ref}^{(o)} + \frac{1}{2} \frac{V \rho^2}{\Omega} \int \tilde{F}_{AA}(12) d(2) \quad (31)$$

Note that the monomer fraction provides the scaling that keeps the perturbation bounded even for large association energies. While Andersen's and Wertheim's approaches produce identical results for singly bondable sites in the single chain approximation (perturbation theory), the two-density approach of Wertheim is much more versatile than the approach of Andersen. For instance, for the case that the association site can bond a maximum of n times, there is a clear path forward in the development of a perturbation theory using Wertheim's approach (keep all s -mer graphs with $s \leq n$). Attempting to apply Andersen's formalism to this case would be hopelessly complex. Also, Eqs. (28) and (29) are generally valid for inhomogeneous fluids where the density and monomer fraction vary with position and orientation. In fact, DFTs based on Wertheim's TPT have proven to be very accurate in the description of inhomogeneous one-site-associating fluids [40, 41]. It seems unlikely the approach of Andersen could be utilized to derive the inhomogeneous form of the theory.

The accuracy of the theory for hard spheres and LJ spheres with a single association site is remarkable in comparison with molecular simulation results for the extent of association, fluid pressure, and internal energy to high association energy [18, 35, 37]. In the limit of infinite association energy, the theory accurately predicts the equation of state for a fluid of diatomic hard spheres or diatomic LJ molecules [18, 33, 35, 37]. Interestingly, in the limit of infinite association energy, the residual free energy in the theory predicts a correction to the ideal gas term to convert from an ideal gas of spheres to an ideal gas of diatomics. For LJ diatomics, the theory accurately predicts the change in potential energy from a fluid of independent LJ spheres to a fluid of LJ diatomics. Accurately predicting the equation of state of the species produced by association is necessary to accurately model the association equilibrium.

B. The Divalent Case

One of the main assumptions in the development of Wertheim's first-order thermodynamic perturbation theory (TPT1) is that association sites are singly bondable. Indeed, the entire multi-density formalism of Wertheim is constructed to enforce this condition. For the case of hydrogen bonding, the assumption of singly bondable sites is justified; however for patchy colloids (see Section I for a background on patchy colloids), it has been shown experimentally [42, 43] that the number of bonds per patch (association site) is dependent on the patch size. It has been 30 years since Wertheim first published his two-density cluster

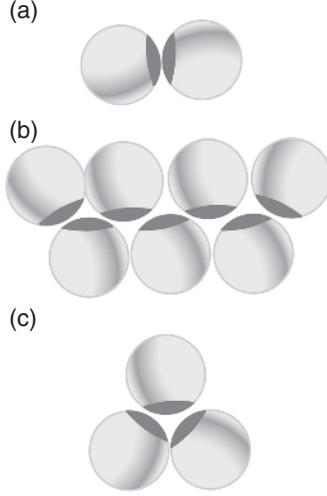


Figure 5. Associated clusters for patchy colloids with a single double bondable patch: (a) dimers, (b) chains with double bonded sites, and (c) triatomic rings of double-bonded sites. (*See insert for color representation of the figure.*)

expansion for associating fluids, and only very recently have researchers applied his approach (or a similar approach developed for associating fluids with spherically symmetric association potentials [44]) to the case that association sites are divalent [21, 45, 46].

Application of TPT to divalent association sites is complicated by the fact that three-body terms must be included to account for blocking effects caused between two molecules attempting to bond to an association site on a third molecule. For a pure component fluid of associating spheres with a single divalent association site the dominant types of associated clusters are chains and triatomic rings of doubly bonded sites as shown in Fig. 5. The application of TPT to this divalent case is an excellent teaching example of how to extend TPT beyond first-order (monovalent sites). For clarity we consider the specific case of a homogeneous fluid of patchy hard spheres (PHS) whose potential model is defined with a hard sphere reference (Eq. 3) and a single conical square well association site (Eq. 4).

To begin we first separate $\Delta c^{(o)}$ into contributions for chain and ring formation as follows:

$$\Delta c^{(o)} \approx \Delta \hat{c}_1^{(o)} = \Delta c_{chain}^{(o)} + \Delta c_{ring}^{(o)} \quad (32)$$

The contribution $\Delta c_{chain}^{(o)}$ is further decomposed into contributions from chains of n bonds and $n + 1$ colloids as follows:

$$\Delta c_{chain}^{(o)} = \sum_{n=1}^{\infty} \Delta c_n^{chain} \quad (33)$$

For instance, graph **e** in Fig. 4 belongs to the contribution Δc_2^{chain} and graph **f** belongs to $\Delta c_{ring}^{(o)}$. Each of these contributions consists of an infinite series of graphs with a single associated cluster interacting with the reference fluid. These series can be summed as follows:

$$\frac{\Delta c_n^{chain}}{V} = \frac{1}{2} \rho_o^{n+1} f_{AA}^n \int g_{HS}(1 \dots n+1) \prod_{k=1}^n O_{AA}(k, k+1) \frac{d(k+1)}{\Omega} \quad (34)$$

and

$$\frac{\Delta c_{ring}^{(o)}}{V} = \frac{1}{6} \rho_o^3 f_{AA}^3 \int g_{HS}(123) O_{AA}(12) O_{AA}(23) O_{AA}(13) \frac{d(2)}{\Omega} \frac{d(3)}{\Omega} \quad (35)$$

Here $\Omega = 4\pi$ and the functions $g_{HS}(1 \dots k)$ are the k body correlation functions of the hard sphere reference system. Since little is known about the correlation functions $g_{HS}(1 \dots k)$ for $k > 3$, we must approximate the higher order $g_{HS}(1 \dots k)$ in superposition. For the current case, a particularly convenient approximation for the *chain contributions* will be the following:

$$g_{HS}(1 \dots k) = \prod_{j=1}^{k-1} g_{HS}(r_{j,j+1}) \prod_{i=1}^{k-2} e_{HS}(r_{i,i+2}) \quad (36)$$

The superposition given by Eq. (36) prevents overlap between nearest and next nearest neighbors in the chain and should be most accurate at low densities. We note that the probability that an isolated associated chain of $n+1$ colloids has a configuration $(1 \dots n+1)$ is given by the following equation:

$$P_{chain}^{(n)}(1 \dots n+1) = \frac{\prod_{k=1}^n O_{AA}(k, k+1) e_{HS}(r_{k,k+1}) \prod_{i=1}^{n-1} e_{HS}(r_{i,i+2})}{Z_{chain}^{(n)}} \quad (37)$$

The probability in Eq. (37) accounts for steric interactions between nearest and next nearest neighbors in the chain, and the term $Z_{chain}^{(n)}$ is the chain partition function given by the following equation:

$$Z_{chain}^{(n)} = \int \prod_{i=1}^{n-1} e_{HS}(r_{i,i+2}) \prod_{k=1}^n O_{AA}(k, k+1) e_{HS}(r_{k,k+1}) d(k+1) \quad (38)$$

Combining Eqs. (34) and (36)–(38) we obtain the following:

$$\frac{\Delta c_n^{chain}}{V} = \frac{1}{2} \rho_o^{n+1} f_{AA}^n \frac{Z_{ch}^{(n)}}{\Omega^n} \left\langle \prod_{j=1}^n y_{HS}(r_{j,j+1}) \right\rangle_{P_{chain}} \quad (39)$$

The cavity correlation function $y_{HS}(r_{j,j+1}) = g_{HS}(r_{j,j+1}) / e_{HS}(r_{j,j+1})$. The brackets in Eq. (39) represent an average over the distribution function Eq. (37). To an excellent approximation this average can be evaluated as a product of individual averages over the bonding range

$$\left\langle \prod_{j=1}^n y_{HS}(r_{k,k+1}) \right\rangle_{P_{chain}} = \langle y_{HS}(r) \rangle_{br}^n \quad (40)$$

where

$$\langle y_{HS}(r) \rangle_{br} = \frac{4\pi \int_d^{r_c} y_{HS}(r) r^2 dr}{4\pi \int_d^{r_c} r^2 dr} = \frac{\xi}{v_b} \quad (41)$$

The constant v_b is the volume of a spherical shell defined by the denominator of the second term in Eq. (41) and ξ is defined by the numerator. As has been shown [21], integrals of similar form to $Z_{chain}^{(n)}$ can be very accurately factored as

$$Z_{chain}^{(n)} = \left(Z_{chain}^{(1)} \right)^n \Phi_{chain}^{n-1} \quad (42)$$

where

$$\Phi_{chain} = \frac{Z_{chain}^{(2)}}{\left(Z_{chain}^{(1)} \right)^2} = \frac{1}{(v_b \kappa)^2} \int O_{AA}(12) O_{AA}(23) e_{HS}(r_{12}) e_{HS}(r_{23}) e_{HS}(r_{13}) \frac{d(2)}{\Omega} \frac{d(3)}{\Omega} \quad (43)$$

The accuracy of the factorization in Eq. (42) stems from the fact that double bonding of a patch is dominated by two- and three-body effects. When $\Phi_{chain} = 0$, multiple bonding of an association site (patch) is impossible; while for the case $\Phi_{chain} = 1$, there is no steric hindrance between two PHS bonding to the same association site on a third. Indeed, the geometric integral Φ_{chain} encodes the effect of steric hindrance for doubly bonded sites. Combining the previous results, we obtain the following:

$$\frac{\Delta C_n^{chain}}{V} = \frac{1}{2} \rho_o^{n+1} (f_{AA} \xi \kappa)^n \Phi_{chain}^{n-1} \quad (44)$$

The constant κ represents the probability that two colloids are in mutual bonding orientations and is given by the following equation:

$$\kappa = \frac{(1 - \cos \theta_c)^2}{4} \quad (45)$$

Now using Eq. (44) to evaluate the infinite sum in Eq. (33) we obtain the following:

$$\frac{\Delta c_{chain}^{(o)}}{V} = \frac{\frac{1}{2} \rho_o^2 f_{AA} \xi \kappa}{1 - f_{AA} \xi \kappa \rho_o \Phi_{chain}} \quad (46)$$

When multiple bonding of a patch is impossible $\Phi_{chain} \rightarrow 0$, and we recover the TPT1 result Eq. (25) for the case $g_{oo} = g_{HS}$.

Now we turn our attention to the ring contribution $\Delta c_{ring}^{(o)}$ Eq. (35). For this case we approximate the triplet correlation function using Kirkwood superposition. Following a similar process to the one described above in the development of Eq. (46), we obtain the following result:

$$\frac{\Delta c_{ring}^{(o)}}{V} = \frac{1}{6v_b} (\rho_o f_{AA} \xi)^3 \kappa^2 \Phi_{ring} \quad (47)$$

In Eq. (47) Φ_{ring} is given by

$$\Phi_{ring} = \frac{1}{(v_b \kappa)^2} \int O_{AA}(12) O_{AA}(23) O_{AA}(13) e_{HS}(r_{12}) e_{HS}(r_{23}) e_{HS}(r_{13}) \frac{d(2)}{\Omega} \frac{d(3)}{\Omega} \quad (48)$$

When multiple bonding of a site becomes impossible, $\Phi_{ring} = 0$, resulting in $\Delta c_{ring}^{(o)} = 0$. Now that $\Delta c^{(o)}$ has been completely specified the free energy is minimized with respect to ρ_o giving the following relation:

$$\rho = \rho_o + \frac{\rho_o^2 f_{AA} \xi \kappa}{1 - f_{AA} \xi \kappa \rho_o \Phi_{chain}} + \frac{1}{2} \rho_o^3 \Phi_{chain} \left(\frac{f_{AA} \xi \kappa}{1 - f_{AA} \xi \kappa \rho_o \Phi_{chain}} \right)^2 + \frac{1}{2v_b} (\rho_o f_{AA} \xi)^3 \kappa^2 \Phi_{ring} \quad (49)$$

Equation (49) is simply conservation of mass. From Eq. (49) we identify the density of colloids bonded twice in rings ρ_2^{ring} , bonded once in a chain ρ_1^{chain} , and bonded twice in a chain ρ_2^{chain} as follows:

$$\rho_2^{ring} = \frac{1}{2v_b} (\rho_o f_{AA} \xi)^3 \kappa^2 \Phi_{ring} \quad (50)$$

$$\rho_1^{chain} = \frac{\rho_o^2 f_{AA} \xi \kappa}{1 - f_{AA} \xi \kappa \rho_o \Phi_{chain}} \quad (51)$$

$$\rho_2^{chain} = \frac{1}{2} \rho_o^3 \Phi_{chain} \left(\frac{f_{AA} \xi \kappa}{1 - f_{AA} \xi \kappa \rho_o \Phi_{chain}} \right)^2 \quad (52)$$

Using these density definitions the free energy can be simplified to

$$\frac{A - A_{HS}}{Vk_B T} = \rho \ln \frac{\rho_o}{\rho} + \rho - \rho_o - \frac{\rho_1^{chain}}{2} - \frac{\rho_2^{ring}}{3} \quad (53)$$

Equation (53) completes the theory for molecules/colloids with a single doubly bondable association site. To obtain the free energy, Eq. (49) is first evaluated for ρ_o which allows the free energy to be calculated through Eq. (53).

All that remains to be done is to calculate the integrals Φ_{chain} (43) and Φ_{ring} (48). To evaluate these integrals we exploit the mean value theorem and employ Monte Carlo integration [47] to obtain the following:

$$\Phi_{chain} = \left\{ \begin{array}{l} \text{The probability that if the positions of two colloids are generated} \\ \text{such that they are correctly positioned to associate with a third colloid,} \\ \text{that there is no core overlap between the two generated colloids} \end{array} \right\} \quad (54)$$

$$\Phi_{ring} = \left\{ \begin{array}{l} \text{The probability that if the positions and orientations of two colloids} \\ \text{are generated such that they are positioned and oriented correctly to} \\ \text{bond to a third colloid, that there is no core overlap between the} \\ \text{two generated colloids and that these two generated colloids are} \\ \text{oriented and positioned such that they share an association bond} \end{array} \right\} \quad (55)$$

Equations (54) and (55) are easily evaluated on a computer; the calculations are independent of temperature and density—they depend only on the potential parameters r_c and θ_c . Table I gives calculations for a critical radius of $r_c = 1.1d$.

Numerical results are given in Fig. 6, for theoretical predictions of the reduced excess internal energy $E^* = E_{AS}/Nk_B T$ as well as the fraction of PHS that are bonded twice in chains X_2^{chain} and rings X_2^{ring} . Results are plotted against reduced association energy $\varepsilon^* = \varepsilon_{AA}/k_B T$ at a packing fraction of $\eta = 0.2$. For comparison

TABLE I
Numerical Calculations of Integrals Φ_{chain} and Φ_{ring} for a
Critical Radius $r_c = 1.1d$

θ_c	Φ_{chain}	Φ_{ring}
27°	0	0
28°	2.89×10^{-5}	0
29°	5.91×10^{-4}	0
30°	2.82×10^{-3}	0
31°	7.42×10^{-3}	5.10×10^{-8}
32°	1.44×10^{-2}	2.41×10^{-6}
33°	2.35×10^{-2}	1.79×10^{-5}
34°	3.45×10^{-2}	6.20×10^{-5}
35°	4.70×10^{-2}	1.51×10^{-4}
40°	0.123	1.52×10^{-3}
45°	0.207	4.37×10^{-3}
50°	0.285	8.03×10^{-3}
55°	0.355	1.18×10^{-2}

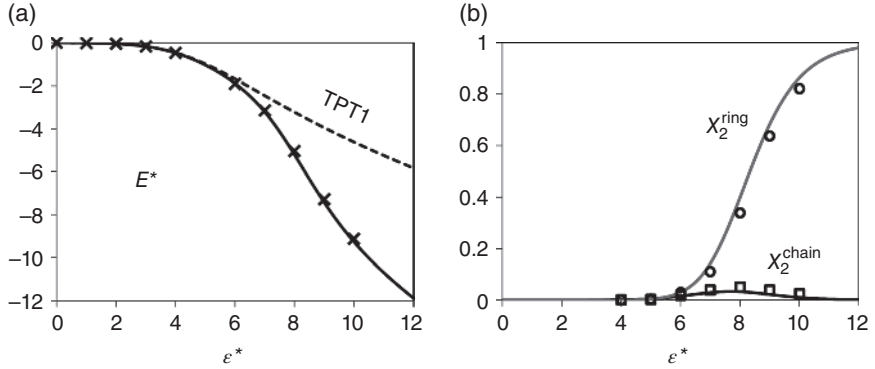


Figure 6. Left: Reduced internal energy versus reduced association energy. Dashed curve gives theory predictions assuming a monovalent association site and solid curve gives theory predictions when double bonding of a site is accounted for and symbols give Monte Carlo simulation [45] results. Right: Fraction of spheres bonded twice in chains and spheres. Squares and circles give respective Monte Carlo simulations [45], and curves are from divalent theory.

we include the simulation results of Marshall *et al.* [45] and predictions of TPT1. As can be seen, TPT1 significantly under predicts the magnitude of E^* due to the fact that the possibility of two bonds per patch is not accounted for. The theory derived here (solid curve) is in excellent agreement with the simulation data over the full range of ϵ^* . In addition to the internal energy, the theory also accurately predicts the structure of the fluid. In agreement with simulation the theory shows that triatomic rings dominate at strong association.

V. MULTIPLE ASSOCIATION SITES: MULTI-DENSITY APPROACH

Now the case of molecules with a set of association sites $\Gamma = \{A, B, C, \dots, Z\}$ will be considered. The majority of hydrogen bonding molecules contain multiple association sites: water, alcohols, proteins, hydrogen fluoride, etc. Theoretically, this case is more difficult to model than the single-site case due to the fact that these molecules can form extended hydrogen bonded structures.

The two-density approach of Wertheim allows the development of accurate and simple theories for molecules with a single association site. To extend this idea to the case of multiple association sites $n(\Gamma) > 1$, Wertheim again begins with the fugacity expansion of $\ln \Xi$ which he regroups into the s -mer representation. Where, as for the one-site case, an s -mer represents a cluster of s points (hyperpoints here) connected by association bonds f_{ij} . However, in contrast to the two-density case, all points in an s -mer are not connected by e_{ref} bonds. Only points with bond-connected association sites within an s -mer are connected by e_{ref} bonds. Wertheim defines two association sites as bond connected if there is a continuous path of association sites and bonds between these two association sites. Figure 7 demonstrates this for the case of a two-site AB molecule. The wavy lines represent f_{AB} bonds and the dashed lines represent e_{ref} bonds, remembering $f_{AB}(12)e_{ref}(12) = F_{AB}(12)$. All molecules that share f_{AB} bonds are bond connected receiving e_{ref} bonds. Molecules that do not share association bonds (e.g., molecules 1 and 3 and 3 and 5 in Fig. 7) can only be bond connected if an association site is bonded more than once. This is the only way two association sites not directly connected by a f_{AB} bond can be connected by a continuous path of sites and f_{AB} bonds. For this reason, molecules 1 and 3 receive an e_{ref} bond and molecules 3 and 5 do not. This choice to only fill with e_{ref} bonds between bond connected sites greatly facilitates the formulation of approximation methods.

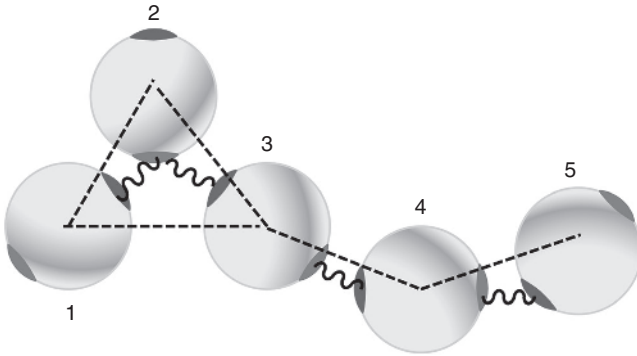


Figure 7. Representation of graph for two-site-associating fluids, where wavy lines represent association bonds and dashed lines represent reference system e bonds. (See insert for color representation of the figure.)

In the two-density formalism for one-site-associating molecules, separate densities were assigned to molecules that were bonded and those that were not bonded. For multiple association sites this choice would result in the loss of information on site–site-level interactions. For this reason, Wertheim expresses the total density as the sum over densities of individual bonding states of the molecules

$$\rho(1) = \sum_{\alpha \in \Gamma} \rho_{\alpha}(1) \quad (56)$$

where $\rho_{\alpha}(1)$ is the density of molecules bonded at the set of sites α . For example, $\rho_{AB}(1)$ is the density of molecules with sites A and B bonded. To aid in the reduction to irreducible graphs Wertheim defines the density parameters:

$$\sigma_{\gamma}(1) = \sum_{\alpha \subset \gamma} \rho_{\alpha}(1) \quad (57)$$

Two important cases of Eq. (57) are $\sigma_o = \rho_o$ and $\sigma_{\Gamma} = \rho$. Using these density parameters, Wertheim transforms the theory from a fugacity expansion to an expansion in σ_{γ} through the use of topological reduction, ultimately arriving at the following exact free energy.

$$\frac{A}{k_B T} = \int \left(\rho(1) \ln(\rho_o(1) \Lambda^3) + Q(1) \right) d(1) - c^{(o)} \quad (58)$$

The graph sum in Eq. (58) is now defined as follows:

$$c^{(o)} = \left\{ \begin{array}{l} \text{sum of all irreducible graphs consisting of } s\text{-mer graphs (including} \\ \text{monomer hyperpoints) and } f_R \text{ bonds. Points which are bonded} \\ \text{at a set of sites } \alpha \text{ carry a factor } \sigma_{\Gamma-\alpha}(1) \end{array} \right\} \quad (59)$$

The term $Q(1)$ is given by

$$Q(1) = -\rho(1) + \sum_{\substack{\alpha \subset \Gamma \\ \alpha \neq \emptyset}} \sigma_{\Gamma-\alpha}(1) c_{\alpha}(1) \quad (60)$$

with

$$c_{\alpha}(1) = \frac{\delta c^{(o)}}{\delta \sigma_{\Gamma-\alpha}(1)} \quad (61)$$

The densities are related to the $c_\alpha(1)$ by the relation

$$\rho_\alpha(1) = \rho_o(1) \sum_{P(\alpha)=\{\gamma\}} \prod_\gamma c_\gamma(1) \quad (62)$$

where $P(\alpha) = \{\gamma\}$ is the partition of α into subsets indexed by $\{\gamma\}$. For instance, the density $\rho_{AB}(1)$ is given by $\rho_{AB}(1) = \rho_o(1)(c_{AB}(1) + c_A(1)c_B(1))$.

The reference system Helmholtz free energy is given as follows:

$$\frac{A_{ref}}{k_B T} = \int \left(\rho(1) \ln(\rho(1) \Lambda^3) - \rho(1) \right) d(1) - c_{ref}^{(o)} \quad (63)$$

The reference system $c_{ref}^{(o)}$ contains all of the graphs in Eq. (59) which are devoid of association bonds. Subtracting Eq. (63) from (58) we obtain the following:

$$\frac{A - A_{ref}}{k_B T} = \int \left(\rho(1) \ln \left(\frac{\rho_o(1)}{\rho(1)} \right) + Q(1) + \rho(1) \right) d(1) - \Delta c^{(o)} \quad (64)$$

The association graph sum $\Delta c^{(o)} = c^{(o)} - c_{ref}^{(o)}$ contains all the graphs in Eq. (59) which contain association bonds. Figure 8 gives examples of graphs in the sum $\Delta c^{(o)}$ for the two-site AB case discussed in Fig. 7.

Equation (64) provides a very general starting point for the statistical mechanics of associating fluids and is exact so long as the system is pairwise additive, and the intermolecular potential can be separated into a reference and association portion as in Eq. (1). The challenge is to approximate the graph sum $\Delta c^{(o)}$ (here we assume the properties of the reference fluid are known).

A simple and widely used approximation of this sum forms the foundation of Wertheim's TPT [32, 33]. To start we decompose $\Delta c^{(o)}$ as

$$\Delta c^{(o)} = \sum_{k=1}^{\infty} \Delta \hat{c}_k^{(o)} \quad (65)$$

where $\Delta \hat{c}_k^{(o)}$ is the contribution for graphs which contain k associated clusters. For example, graph **d** in Fig. 8 belongs to the sum $\Delta \hat{c}_2^{(o)}$, while the remaining graphs all belong to $\Delta \hat{c}_1^{(o)}$. TPT can be defined as the neglect of all $\Delta \hat{c}_k^{(o)}$ for $k > 1$ giving

$$\Delta c^{(o)} \approx \Delta \hat{c}_1^{(o)} \quad (66)$$

The approximation Eq. (66) accounts for interactions within the associated cluster and between the clusters and the reference fluid, but not the interactions between associated clusters. This approximation is accurate for cases in which the pair correlation function between associating molecules is similar to that of the reference fluid.

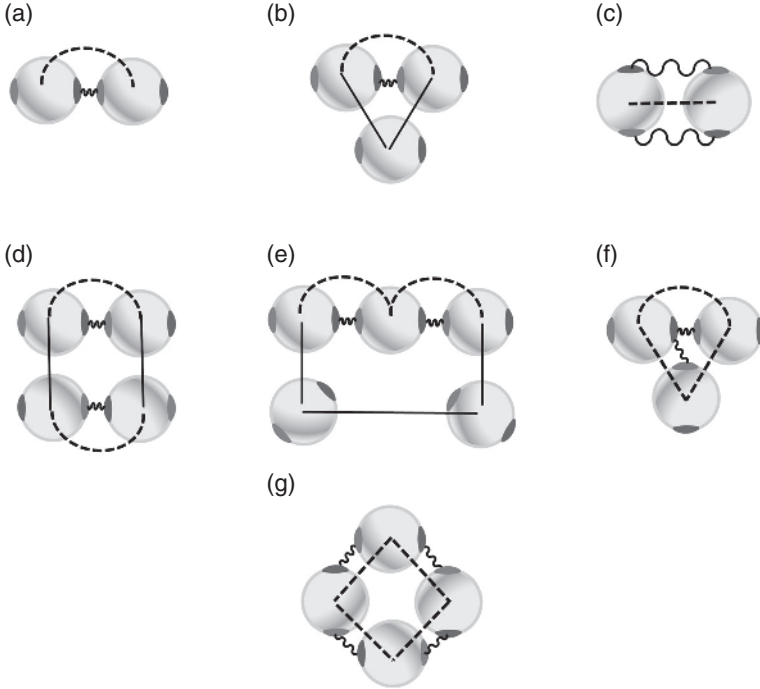


Figure 8. Examples of graphs in $\Delta c^{(o)}$ for the two site AB case. Wavy lines represent f_{AB} bonds, dashed lines represent e_{ref} bonds, and solid lines represent f_{ref} bonds.

Equation (66) accounts for multiple bonded association sites (graph **f** in Fig. 8 belongs to this class), cycles of association bonds (graph **g** in Fig. 8), multiple bonds between two molecules (graph **c** in Fig. 8), and chains (trees) of association bonds (graphs **a**, **b**, and **e** in Fig. 8). For the time being, it will be assumed that the intermolecular potential and placement of association sites is such that contributions from cycle formation, multiple bonded association sites, and multiple bonds between molecules can all be ignored, leaving only contributions for the formation of chain and tree like clusters. With these restrictions $\Delta \hat{c}_1^{(o)}$ can now be written as

$$\Delta \hat{c}_1^{(o)} = \Delta c_{TPT1}^{(o)} + \Delta c_{TPT2}^{(o)} + \Delta c_{TPT3}^{(o)} + \dots \quad (67)$$

where $\Delta c_{TPT1}^{(o)}$ is the first-order contribution that contains all contributions for association between a pair of molecules (graph **a** and **b** in Fig. 8 are examples), $\Delta c_{TPT2}^{(o)}$ is the second-order contribution that contains information about the simultaneous association of three molecules (graph **e** in Fig. 8 belongs to this class) etc. For the case of molecules with a single association site $\Delta \hat{c}_1^{(o)} = \Delta c_{TPT1}^{(o)}$.

If it can be assumed that steric hindrance between association sites is small, the sum in Eq. (67) can be truncated at first order (TPT1) giving the simple result [32]

$$\Delta c^{(o)} \approx \Delta \hat{c}_1^{(o)} \approx \Delta c_{TPT1}^{(o)} = \frac{1}{2} \sum_{A \in \Gamma} \sum_{B \in \Gamma} \int \sigma_{\Gamma-A}(1) g_{ref}(12) f_{AB}(12) \sigma_{\Gamma-B}(2) d(1) d(2) \quad (68)$$

It should be noted that while $\Delta c_{TPT1}^{(o)}$ only accounts for interactions between pairs of molecules, all possible trees of associated clusters can be reproduced. However, in first order, the only steric interactions are between nearest neighbors in the cluster giving a theory that is independent of bond angles.

The combination of Eqs. (64) and (68) summarizes Wertheim's first-order theory for multiple association sites. The density parameters in Eq. (57) are determined by minimizing the free energy with respect to variations in these parameters. Once an association model is specified, the free energy function and equations for the density parameters can be derived from Eqs. (64) and (68).

Since the association sites on a molecule are independent at first order in perturbation, Chapman derived a closed-form solution for mixtures of molecules with any number of association sites [18, 34].

$$\frac{A - A_{ref}}{k_B T} = \sum_i \sum_{A \in \Gamma^{(i)}} \int \rho^{(i)}(1) \left(\ln X_A^{(i)}(1) - \frac{X_A^{(i)}(1)}{2} + \frac{1}{2} \right) d(1) \quad (69)$$

The fractions of molecules of species i that are not bonded at site A, $X_A^{(i)}$, are solved for self-consistently by minimizing the free energy with respect to the density parameters in Eq. (57) as

$$X_A^{(i)}(1) = \frac{\sigma_{\Gamma^{(i)}-A}(1)}{\rho^{(i)}(1)} = \frac{1}{1 + \sum_j \int \rho^{(j)}(1) g_{ref}(12) \sum_{B \in \Gamma^{(j)}} f_{AB}(12) X_B^{(j)}(2) d(2)} \quad (70)$$

For homogeneous fluids, the densities and $X_A^{(i)}$ parameters are no longer functions of position. The primary approximation in Wertheim's perturbation theory is that the unbonded site–unbonded site distribution function can be approximated by the pair correlation function of the spherical reference fluid. Since the structure of an associating fluid is known to be much different from that of a simple fluid, this approximation might seem surprising. In the section on single association sites, we stated that, for association near sphere contact, the packing fraction of the fluid does not change with extent of association, and therefore the monomer–monomer pair correlation function is assumed independent of the extent of association. In this case, approximating the unbonded site–unbonded site correlation function

with the reference fluid pair correlation function is in reasonably good agreement with molecular simulation results [18, 19, 35, 37, 38, 48]. Since association is short ranged and commonly modeled as a square well, it is common to approximate the integral in Eq. (70) using the pair correlation function at contact [18, 19, 34, 39]. Numerical solution of Eq. (70) is simplified since the $X_A^{(i)}$ parameters are the solution to an unconstrained minimization of the free energy [49]. Given that the association sites are independent of one another at first order in perturbation, the monomer fraction of component i can be calculated from the product of the $X_A^{(i)}$'s.

This simple TPT1 result has proven to be a very powerful tool in the theoretical description of associating fluids. Equations (69) and (70) have been shown to be accurate for bulk fluids composed of hard spheres with one [19], two [19, 50], and four association sites [38, 51]. The theory has also been shown to be accurate for associating LJ spheres with one, two [37], and four [38] association sites and associating molecules with a square well reference fluid [52]. Also, TPT1 has been shown to accurately describe novel phase behavior in patchy colloid fluids [50, 53–57]. In addition to spherical molecules, TPT1 has been shown to be accurate for associating chains [18] of tangentially bonded hard [48], LJ [37, 38, 48, 58, 59] and square well [52] spheres. When applying TPT1 to associating chains, a chain reference fluid must be used, which is obtained using TPT1 in the complete association limit [18].

Given the accuracy of the theory in describing the properties of networking forming fluids, one might imagine using the associating spheres as molecular building blocks to build specific structures. By defining a mixture of molecules with one, two, or more association sites that can only bond to specific sites on other molecules, it is possible to define the structure that will form in the limit of strong association. For example, if molecule 1 can only bond to the A site on molecule 2, and the B site on molecule 2 can only bond to the A site on molecules 3, etc. until the A site on molecule $(m - 1)$ can only bond to the B site on molecule m , a linear chain of length m segments can form given a stoichiometric ratio of components and large enough association energy. In this way, by taking the limit of infinite association energy, the perturbation theory produces an equation of state for polyatomic molecules [18, 34] that is in reasonable agreement with molecular simulation results for polyatomic molecules made of chains of hard spheres, LJ chains, and square well chains [18, 33, 34, 37, 58–61].

The theory was further extended to mixtures of associating polyatomic molecules [18, 34, 37, 48, 62–64]. This requires the pair correlation function between unbonded sites on the molecules. The simplest approximation is that the pair correlation function between unbonded sites is the same as that in the reference fluid. This is valid as long as the angle between association sites is large enough that the sites do not affect each other. One might question using the pair correlation function for spheres as an estimate of the pair correlation function between association sites on chain-like molecules. Some may suggest that this contradicts the correlation hole effect seen in site–site distribution functions; however, the correlation hole effect is largely a result of averaging over spherically symmetric

potentials. Over the small range of angles for which molecules can associate, the approximation of the unbonded–unbonded distribution function with that for spheres (particularly for hard sphere chains) has been shown to be a good approximation [37, 38, 48, 58, 59].

When LJ spheres (or square well spheres) associate with each other, we expect that the LJ (or square well) contribution to the internal energy (and free energy) should be a function of the extent of association due to shielding of molecules in the associated cluster. In other words, the dispersion contribution to the internal energy should be different from that of a fluid of independent LJ spheres. The TPT1 predicts the change in internal energy due to association or chain formation in good agreement with molecular simulation results particularly for dense fluids [37, 38, 48, 58, 59].

In addition to model systems, TPT1 has been widely applied in both academia and industry as an engineering equation of state for hydrogen bonding fluids. The equation of state resulting from the extension of Wertheim's TPT1 to mixtures of associating polyatomic molecules is called the statistical associating fluid theory (SAFT) [18, 34, 37, 59, 62, 63]. Many of the SAFT forms [63, 65–67] have found wide application among scientists and engineers in academia and industry to describe the properties and phase behavior of solvents to associating polymers as well as patchy colloids.

Though widely applied, TPT1 is far from perfect with a number of limitations resulting from the simplifying approximations employed. These approximations are summarized as follows:

1. Single chain approximation—Neglects all graphs with more than one associated cluster. This is TPT, which assumes that the structure of unbonded sites in the fluid is similar to that of the reference fluid. The single chain approximation will fail, for instance, for fluids with a nematic phase [68].
2. Singly bondable association sites—Assumes each association site saturates after sharing in a single association bond. This approximation is not valid for patchy colloids with large patch sizes [43].
3. No multiple bonding of molecules—Assumes that any two molecules can share at most one association bond. Carboxylic acids [69] and water [70] are known to violate this condition.
4. No cycles of association bonds—Only chains and trees of association bonds are accounted for. Cycles are irreducible and cannot be reproduced in TPT1. It is well known that hydrogen fluoride exhibits significant ring formation [71].
5. No steric hindrance between association sites—All contributions to the irreducible graph sum with more than a single association bond were neglected. For this reason, association at one site is independent of association at all other sites. Most polyfunctional associating molecules will exhibit some degree of steric hindrance between association sites.

6. Association is independent of bond angles—There is no information in TPT1 on location of association sites. This is intimately related to approximations 3–5 above.
7. In Wertheim’s multi-density formalism, pairwise additivity of the pair potential was assumed. Most polyfunctional hydrogen bonding molecules exhibit some degree of bond cooperativity (non-pairwise additivity) [72]. Hydrogen bond cooperativity is particularly important for hydrogen fluoride [71].

In recent developments, a number of these approximations have been relaxed. The remainder of this chapter will review some of these extensions of the theory and development of a molecular DFT for inhomogeneous fluids.

VI. THE TWO-SITE AB CASE

In Section V it was shown how Wertheim’s multi-density approach could be used to develop an equation for associating fluids with an arbitrary number of association sites provided a number of assumptions were satisfied. The simplicity of the TPT1 solution results from the fact that the solution is that of an effective two-body problem. Only one bond at a time is considered. This allows the theory to be written in terms of pair correlation functions only, as well as obtain analytical solutions for the bond volume. Moving beyond TPT1 is defined as considering irreducible graphs that contain more than one association bond.

The simplest case to illustrate this extension is for molecules with a single type A and type B association site, where the center of these two sites is separated by the angle α_{AB} . We loosely call α_{AB} the bond angle. Figure 9 gives examples of association into linear chains for both cases of large (case **a**), and small (case **b**) α_{AB} . In case **a**, since the sites are widely separated, association at each site will be

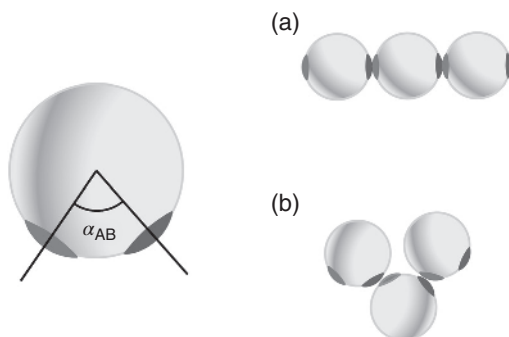


Figure 9. Examples of linear triatomic clusters for two angles α_{AB} . (See insert for color representation of the figure.)

independent. For case **b** this is not the case. Due to the small bond angle, association at one site may block a third molecule coming to associate with the other site. There is steric hindrance. Further, for simplicity, we will assume that there is only attraction between unlike sites. That is there are AB attractions, but no AA or AB attractions. This could serve as a primitive model for a bifunctional hydrogen bonding molecule such as hydrogen fluoride, monomer in a supramolecular polymer, globular protein, or patchy colloid.

To extend the TPT1 results, such that systems with small α_{AB} can be considered, we need to introduce the effect of steric hindrance. However, inclusion of steric hindrance alone is not sufficient due to the fact that as α_{AB} is decreased, the probability of forming small rings increases. Indeed, as has been shown [39, 73], for small bond angles rings become the dominant type of associated cluster. In what follows we outline the methodology to include these types of higher-order interactions into an accurate equation of state which explicitly depends on α_{AB} .

A. Steric Hindrance in Chain Formation

To incorporate steric effects in chain formation we must employ Wertheim's TPTM. In TPTM, $\Delta c^{(o)}$ is approximated by considering all chain diagrams that contain a single chain of M or less association bonds and is given as [33]

$$\Delta c^{(o)} \approx \Delta \hat{c}_1^{(o)} = \sum_{n=1}^M \Delta c_{TPTn}^{(o)} \quad (71)$$

where $\Delta c_{TPTn}^{(o)}$ is the n th-order contribution (involves chains of n association bonds) and is given by (assuming a homogeneous fluid)

$$\frac{\Delta c_{TPTn}^{(o)}}{V} = \sigma_A \sigma_B \rho_o^{n-1} I_n \quad (72)$$

The integrals I_n are given by

$$I_n = \frac{1}{\Omega^n} \int f_{AB}(12) \dots f_{AB}(n, n+1) G_{ref}(1 \dots n+1) d(2) \dots d(n+1) \quad (73)$$

where $\Omega = 8\pi^2$ and the $f_{AB}(ij)$ are the association Mayer functions. Wertheim defines the functions $G_{ref}(1 \dots n+1)$ as “the subset of graphs in $g_{ref}(1 \dots n+1)$ such that combining them with the chain produces an irreducible graph; $g_{ref}(1 \dots s)$ denotes the s particle correlation function of the *reference* system” [33]. This means, for instance, that in a TPT2 the contribution Δc_{TPT2} will include the triplet correlation function $g_{ref}(123)$, but one must subtract off the contribution from the first-order term $\Delta c_{TPT1}^{(o)}$ to keep from double counting. We then obtain the $G_{ref}(1 \dots s)$ by summing $g_{ref}(1 \dots s)$ and all products of g_{ref} 's obtained by partitioning $1 \dots s$ into

subsequences which share the switching point and associating a negative 1 with each switching point [33]. A few examples include the following:

$$\begin{aligned}
 G_{ref}(12) &= g_{ref}(12) \\
 G_{ref}(123) &= g_{ref}(123) - g_{ref}(12)g_{ref}(23) \\
 G_{ref}(1234) &= g_{ref}(1234) - g_{ref}(123)g_{ref}(34) - g_{ref}(12)g_{ref}(234) \\
 &\quad + g_{ref}(12)g_{ref}(23)g_{ref}(34)
 \end{aligned} \tag{74}$$

The general idea of TPTM is then to build up chains by adding in higher-order contributions and subtracting off lower-order contributions.

Returning our attention to case **a** in Fig. 9, all $\Delta C_{TPTn}^{(o)}$ with $n > 1$ can be neglected due to the fact that there will be little steric hindrance between sites. For case **b** the situation is more complex as there are steric effects between association sites. To include these steric effects we must go to a minimum of TPT2. For clarity we will now assume a hard sphere reference system with CSW association sites as given in Eq. (4). In TPT2 we keep all contributions in Eq. (71) up to and including $M=2$. The integrals I_1 and I_2 are evaluated as

$$\begin{aligned}
 I_1 &= \frac{1}{\Omega} \int f_{AB}(12) g_{HS}(12) d(2) = \Delta_{AB} = \kappa f_{AB} \xi \\
 I_2 &= \frac{1}{\Omega^2} \int f_{AB}(12) f_{AB}(23) G_{HS}(123) d(2) d(3) - \Delta_{AB}^2 = \Delta_{AB}^2 (\langle y_o(123) \rangle - 1)
 \end{aligned} \tag{75}$$

In Eq. (75) the triplet function $y_o(123)$ is defined as

$$y_o(123) = \frac{y_{HS}(123)}{y_{HS}(12)y_{HS}(23)} \tag{76}$$

and $\langle \rangle$ represents the average over all states where both sites on the molecule are bonded

$$\langle y_o(123) \rangle = \frac{\int O_{AB}(12) O_{AB}(23) e_{HS}(12) e_{HS}(23) e_{HS}(13) y_o(123) d(2) d(3)}{(\kappa v_b \Omega)^2} \tag{77}$$

The steric effects in TPT2 are now wholly included in this average. Employing the mean value theorem Eq. (77) can be further simplified as

$$\langle y_o(123) \rangle = \Psi_{ch} \langle y_o(123) \rangle_{AS} \tag{78}$$

where Ψ_{ch} is given by

$$\Psi_{ch} = \left\{ \begin{array}{l} \text{The probability that if the positions of two molecules are generated} \\ \text{such that site A on molecule 1 is bonded to site B on molecule 2 and} \\ \text{that site B on molecule 3 is bonded to site A on molecule 2, that there} \\ \text{is no overlap between molecules 1 and 3} \end{array} \right\} \quad (79)$$

and $\langle \rangle_{AS}$ represents the average over all associated states of the cluster in which there is no hard sphere overlap. In short, the average in Eq. (77) includes states with hard sphere overlap in the normalization $(\kappa \nu_b \Omega)^2$, while the average $\langle \rangle_{AS}$ does not with the normalization $\Psi_{ch} (\kappa \nu_b \Omega)^2$.

Equation (78) splits the TPT2 contribution into a geometric contribution Ψ_{ch} , which accounts for the decrease in bond volume due to steric hindrance, and a density dependent contribution $\langle y_o(123) \rangle_{AS}$ which accounts for the effect of bond angle on the fluid packing. At this point $\langle y_o(123) \rangle_{AS}$ has not been evaluated; however, this average should be relatively easy to evaluate using the fitting function of Müller and Gubbins [74] in combination with Monte Carlo integration.

A desirable limit of this approach is that the density of molecules bonded at both sites ρ_{AB} vanishes as the angle $\alpha_{AB} \rightarrow 0$. In this limit it becomes impossible for a molecule to be bonded at both sites. To check this limit we set $\Psi_{ch} \rightarrow 0$ and evaluate ρ_{AB} through Eq. (62) as (enforcing $\sigma_A = \sigma_B$).

$$\left(\frac{\rho_{AB}}{\rho_o} \right)_{\alpha_{AB} \rightarrow 0} = c_{AB} + c_A c_B = \left(\sigma_A \rho_o \Delta_{AB}^2 \right)^2 - 2 \sigma_A^2 \rho_o \Delta_{AB}^3 \neq 0 \quad (80)$$

As can be seen, TPT2 does not satisfy this limit showing that TPT2 does not include full steric information between the two association sites. This deficiency results from the way in which reducible graphs are created from irreducible graphs through elimination of the density parameters σ_A and σ_B .

To include full steric information it is necessary to consider perturbation to infinite order. Unfortunately, we know very little of correlation functions beyond the triplet case. To proceed further we note that the TPT2 contribution given in Eq. (78) is split into a purely geometric contribution and a density dependent contribution which depends on knowledge of the triplet correlation function. A simplification of Eq. (78) would be to assume that the average $\langle y_o(123) \rangle_{AS}$ was approximately unity giving

$$\langle y_o(123) \rangle \approx \Psi_{ch} \quad (81)$$

Equation (81) will account for blocking effects between the two association sites by correcting the decrease in the total number of associated states of the cluster.

Equation (81) will be exact in the low-density limit, and should be a fair approximation at higher densities, becoming more accurate as α_{AB} increases.

To apply the theory as an infinite-order perturbation theory we must approximate $g_{HS}(1 \dots n+1)$ in such a way that the infinite sum over all chain graphs can be performed. For this we take the same approach as in Section IV.B and approximate the multi-body correlation functions with Eq. (36). Like Eq. (81), the superposition Eq. (36) treats higher-order effects in a density-independent way by incorporating purely geometric constraints in the association model. With Eq. (36), the infinite sum in Eq. (71) for $M \rightarrow \infty$ can be approximated as follows:

$$\frac{\Delta c_{ch}^{(o)}}{V} = \frac{\sigma_A \sigma_B \kappa f_{AB} \xi}{1 + (1 - \Psi) \kappa f_{AB} \rho_o \xi} \quad (82)$$

Now we use Eq. (82) to evaluate the density of molecules bonded at both sites as follows:

$$\frac{\rho_{AB}}{\rho_o} = \Psi_{ch} \left(\frac{\sigma_A \xi \kappa f_{AB}}{1 + (1 - \Psi_{ch}) f_{AB} \xi \kappa \rho_o} \right)^2 \quad (83)$$

It is easy to see from Eq. (83) that as $\Psi_{ch} \rightarrow 0$ the density of molecules bonded twice vanishes. This shows that, in contrast to TPT2, the theory properly accounts for blocking effects between the two association sites.

B. Ring Formation

In addition to steric effects, when bond angles are small as in case **b**, ring formation can become significant. Where now we are assuming association sites are singly bondable and rings are composed of cycles of AB bonds as depicted in Fig. 10. It was Sear and Jackson (SJ) [75] who were the first to introduce contributions for association into rings. In this approach the associated rings were treated

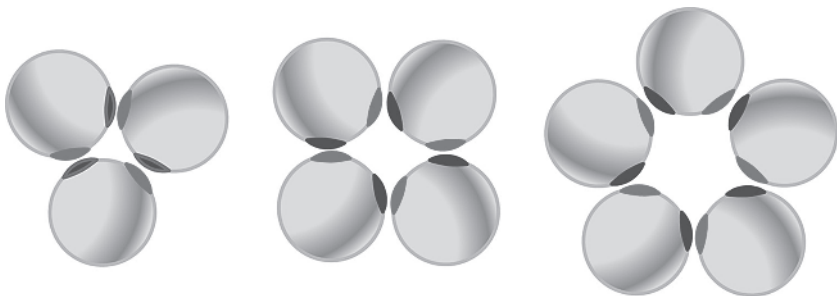


Figure 10. Examples of associated rings. (See insert for color representation of the figure.)

ideally such that non-adjacent neighbors along the ring can overlap. The probability that a chain of colloids was in a valid ring state was approximated by the expression of Treolar [76] for the distribution of the end-to-end vector in a polymer chain. In this approach any dependence on α_{AB} is neglected when in reality α_{AB} plays a dominant role in determining if association into rings will occur. A recent study using lattice simulations has shown that ring formation is strongly dependent on α_{AB} [73]. For instance, it is impossible to form 4-mer rings (and satisfy the one-bond-per-site condition) when $\alpha_{AB} = 180^\circ$; however, decreasing α_{AB} to 90° this type of ring would be possible. Tavares *et al.* [77] explored the possibility of ring formation in two patch colloid fluids with $\alpha_{AB} = 180^\circ$ by extending the approach of SJ [75] and found that to achieve appreciable ring formation the parameters of the association potential had to be chosen such that the one-bond-per-patch condition would be violated. To correct for this in the simulations they used a model that restricts bonding to at most one bond per patch [78].

Recently, Marshall and Chapman [39] extended TPT to account for the effect of α_{AB} on ring formation. To allow for rings of all sizes the ring contribution to the graph sum is split into contributions from rings of size m

$$\Delta c_{ring}^{(o)} = \sum_{m=3}^{\infty} \Delta c_m^{ring} \quad (84)$$

where Δc_m^{ring} is the contribution for rings of size m . The contributions Δc_m^{ring} are obtained by summing over all graphs that contain a single ring of m association bonds.

$$\frac{\Delta c_m^{ring}}{V} = \frac{(\rho_o f_{AB})^m}{m(8\pi^2)^{m-1}} \int O_{AB}(12) \dots O_{AB}(m-1, m) O_{AB}(1, m) g_{HS}(\vec{r}_1 \dots \vec{r}_m) d\vec{r}_2 d\Omega_2 \dots d\vec{r}_m d\Omega_m \quad (85)$$

Pictorially, graph **g** in Fig. 8 represents the low-density limit of Δc_4^{ring} . Evaluation of Eq. (85) is much more difficult than for the chain contribution due to the presence of the additional association bond that closes the ring, rendering the graph irreducible irrespective of the superposition used to approximate $g_{HS}(\vec{r}_1 \dots \vec{r}_m)$. To proceed, we consider the following simple superposition of $g_{HS}(\vec{r}_1 \dots \vec{r}_m)$:

$$g_{HS}(\vec{r}_1 \dots \vec{r}_m) = \prod_{\substack{\text{bonded pairs} \\ \{i,j\}}} y_{HS}(r_{ij}) \prod_{\substack{\text{all pairs} \\ \{l,k\}}} e_{HS}(r_{lk}) \quad (86)$$

In Eq. (86) each pair of spheres in the ring receives an $e_{HS}(r_{lk})$, meaning the ring is fully self-avoiding. This is in contrast to a similar approximation for chain formation in Eq. (36), for which the steric effects are limited to first and second

neighbors along the chain, which ultimately allows for the factorization of the chain into dimer and triplet contributions. Here, since the ring graph cannot be factorized regardless of the superposition used, the additional connectivity of Eq. (86) imposes no penalty. Using Eqs. (85) and (86) Marshall and Chapman [39] arrived at the following form for Δc_m^{ring}

$$\frac{\Delta c_m^{ring}}{V} = \frac{(f_{AB} \rho_o \hat{g}_{HS} K)^m}{m d^3} \Gamma^{(m)} \quad (87)$$

where

$$\hat{g}_{HS} = \frac{2^p g_{HS}(d)}{(r_c/d + 1)^p} \quad (88)$$

and $\Gamma^{(m)}$ is proportional to the partition function of an isolated ring of size m .

Both $\Gamma^{(m)}$ for $m=3-10$ and ψ have been evaluated numerically for CSW association sites with potential parameters $\theta_c = 27^\circ$, $r_c = 1.1d$ over the full bond angle range [39]. Figure 11 gives results for Ψ and $\Gamma^{(m)}$ for rings of size $m=3$ and 4. As expected, Ψ vanishes for small α_{AB} due to steric hindrance, and becomes unity for large α_{AB} when association at one site no longer interferes with the ability of the other site to bond. The ring integrals $\Gamma^{(m)}$ are peaked around an optimum bond angle for ring formation, and the maximums of $\Gamma^{(m)}$ decrease and shift to larger bond angles as m increases. It is the relative magnitudes of these geometric integrals which control the types of associated structures that exist.

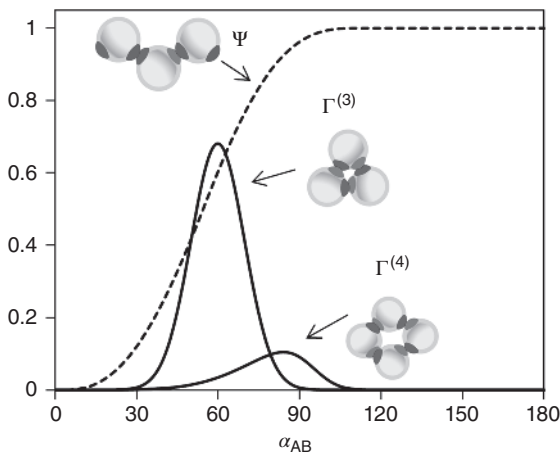


Figure 11. Numerical evaluation of geometric integrals for the two-site case [79]. Ψ represent the probability that there is no core overlap in a triatomic chain and ring integrals $\Gamma^{(m)}$ are proportional to the partition function of an isolated ring of size m .

The Helmholtz free energy for the two-site case with steric hindrance and ring formation can be developed from the results of Sections V and VI as follows:

$$\frac{A - A^{HS}}{Nk_B T} = \left(\frac{A - A^{HS}}{Nk_B T} \right)_{TPT1} + \Delta a_{HO} \quad (89)$$

Where the first term on the right-hand side represents the TPT1 solution obtained from Eq. (69) and Δa_{HO} represents the higher-order correction given by

$$\Delta a_{HO} = \ln \frac{X_o}{X_A X_B} - \sum_{m=3}^{\infty} \frac{X_m^{ring}}{m} \quad (90)$$

Here, X_m^{ring} is the fraction of molecules in rings of size m given by [39]

$$X_m^{ring} = \frac{(f_{AB} \rho_o \hat{g}_{HS} K)^m}{\rho d^3} \Gamma^{(m)} \quad (91)$$

From Eq. (90), we see the first-order limit will be obtained when α_{AB} is large enough that ring formation becomes improbable $X_m^{ring} = 0$, and steric hindrance between sites is small enough that association at one site is essentially independent of the other. When association sites are independent due to the lack of ring formation and steric hindrance, the relation $X_o = X_A X_B$ holds. Under these conditions, Δa_{HO} will vanish and a treatment in TPT1 will be justified.

Figure 12 compares theory predictions and Monte Carlo simulations for the fraction of spheres bonded in rings of size $m=3-4$, and the fraction of spheres that

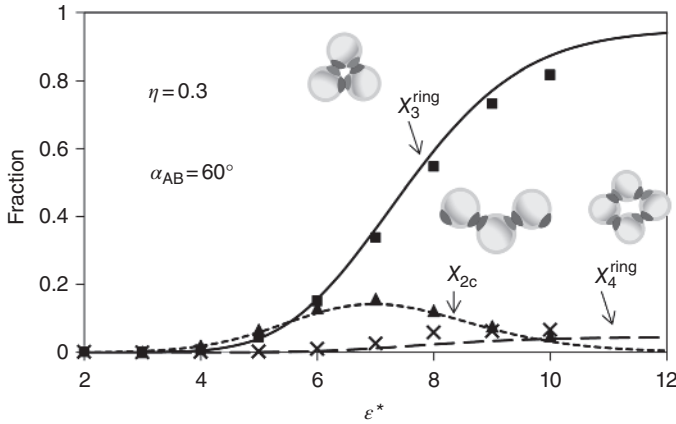


Figure 12. Comparison of TPT (curves) and simulation results (symbols) for the fraction of two-site molecules in trimer rings, 4-mer rings, and chain centers X_{2c} (chains of all sizes) versus reduced association energy. Potential parameters are $\theta_c = 27^\circ$ and $r_c = 1.1 d$. The figure is modified from Ref. 39.

are bonded at both sites in chains of any size X_{2c} (spheres in the middle of a chain) [39]. The comparison is made for an angle $\alpha_{AB} = 60^\circ$ and a liquid-like packing fraction of $\eta = 0.3$. For low $\varepsilon^* = \varepsilon_{AB}/k_B T$, the majority of fully bonded colloids are in the center of triatomic chains resulting in X_{2c} being the dominant contribution. Increasing ε^* , X_3^{ring} rapidly becomes the dominant type of associated cluster in the fluid forcing a maximum in X_{2c} which becomes very small in strongly associating systems. The fraction X_4^{ring} shows a nearly linear increase with ε^* , overtaking X_{2c} near $\varepsilon^* \sim 9.5$.

As can be seen, theory and simulation are in excellent agreement. This may come at a surprise to many. After all, the superpositions Eqs. (36) and (86) neglect any density-dependent packing effects beyond nearest neighbors in the cluster. What this shows is that the accuracy of the theory is largely (not completely) determined by getting the geometry right. That is, if the number of associated states of an isolated cluster can be calculated, TPT can give good predictions over a wide range of densities. Of course, at some density, packing effects must become important. Marshall and Chapman [39] showed that the theory loses accuracy somewhat for $\eta = 0.4$; however, even at this high density, the theory still performed well.

C. Bond Cooperativity

In the previous sections we have shown how TPT can be extended to describe a wide variety of associating fluids. In each case, the distribution of associated clusters and the resulting equation of state were strongly dependent on a delicate balance between the energetic benefits of association and the resulting entropic penalty. In each case it was assumed that the total system energy is pairwise additive, there is no bond cooperativity. In nature, hydrogen bond cooperativity arises from the fact that when a multi-functional hydrogen bonding molecule forms hydrogen bonds, the polarization of the molecule is necessarily increased [72]. As has become increasingly apparent in recent years, hydrogen bond cooperativity plays a significant role in many physical processes. Both hydrogen fluoride (HF) [71] and alcohols [80] have been shown to exhibit strong hydrogen bond cooperativity. In addition, hydrogen bond cooperativity has been shown to stabilize peptide hydrogen bonds [81]. Indeed, it is believed that all polyfunctional hydrogen bonding molecules exhibit some degree of bond cooperativity [72].

The assumption of a pairwise additive association potential, Eq. (2), forms the foundation from which Wertheim's multi-density formalism is built. Strictly speaking, TPT cannot be applied to non-pairwise additive association potentials in a rigorous way. However, it was recently [79, 82] demonstrated how the same ideas used to develop Eq. (82) can be applied to develop an equation of state for hydrogen bonding fluids that exhibit bond cooperativity. The approach employs the potential model of SJ [83] for a fluid composed of N_p hard spheres of

diameter d with two association sites A and B (only AB attractions and singly bondable sites) with a total energy composed of pairwise and triplet contributions [83]

$$U(1 \dots N_p) = \frac{1}{2} \sum_{i,j} (\phi_{HS}(r_{ij}) + \phi_{as}^{(2)}(ij)) + \frac{1}{6} \sum_{i,j,k} \phi_{as}^{(3)}(ijk) \quad (92)$$

The term $\phi_{as}^{(2)}(ij)$ is the pairwise contribution given by Eqs. (2), (4) and $\phi_{as}^{(3)}(ijk)$ is the triplet association contribution:

$$\begin{aligned} \phi_{as}^{(2)}(ij) &= -\varepsilon^{(1)} (O_{AB}(ij) + O_{BA}(ij)) \\ \phi_{as}^{(3)}(ijk) &= -(\varepsilon^{(2)} - \varepsilon^{(1)}) (O_{AB}(ij)O_{BA}(ik) + O_{BA}(ij)O_{AB}(ik) \\ &\quad + O_{AB}(ji)O_{BA}(jk) + O_{BA}(ji)O_{AB}(jk) \\ &\quad + O_{AB}(ki)O_{BA}(kj) + O_{BA}(ki)O_{AB}(kj)) \end{aligned} \quad (93)$$

The triplet contribution $\phi_{as}^{(3)}$ serves to add a correction $-(\varepsilon^{(2)} - \varepsilon^{(1)})$ for each sphere bonded twice. With this potential an associated chain of n spheres will have a cluster energy:

$$\varepsilon_{ch}^{(n)} = -\varepsilon^{(1)} - (n-2)\varepsilon^{(2)}. \quad (94)$$

Strictly speaking, Wertheim's formalism cannot be rigorously applied to this potential; however, employing the same ideas used to develop Eq. (82), a very accurate approximation of $\Delta c_{ch}^{(o)}$ can be derived for this potential model. The derivation begins with the observation that the energy given by Eq. (94) can be partitioned such that the first association bond in a chain receives an energy $\varepsilon^{(1)}$, while each remaining bond in the chain receives an energy $\varepsilon^{(2)}$. This partitioning is illustrated in Fig. 13. Partitioning the bond energies in this manner allows one to replace the product of association Mayer functions in Eq. (73) with the following:

$$f_{AB}(12) \dots f_{AB}(n, n+1) \rightarrow f_{AB}^{(1)}(12) f_{AB}^{(2)}(23) \dots f_{AB}^{(2)}(n, n+1) \quad (95)$$

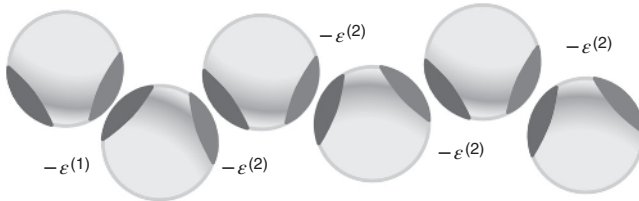


Figure 13. Diagram of bond energy distribution in associated chain with bond cooperativity as given by Eq. (93).

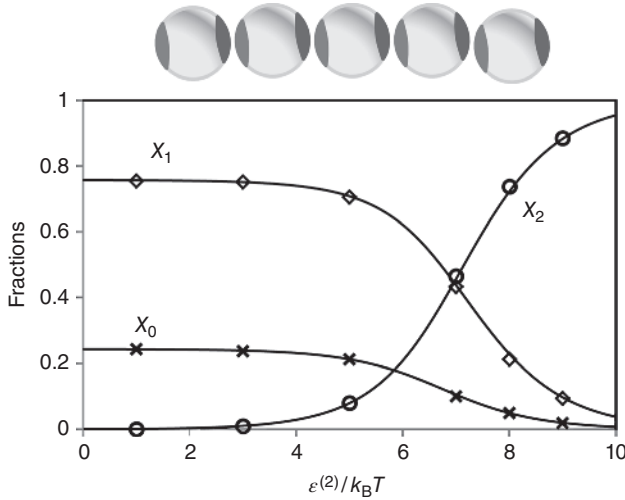


Figure 14. Comparison of theory and simulations for the bonding fractions (fraction of spheres bonded k times) of two-site-associating spheres with bond cooperativity. The pairwise association energy and density are held constant at $\varepsilon^{(1)} = 7k_B T$ and $\rho = 0.6d^3$. Curves give theory predictions and symbols give Monte Carlo simulation results. The figure is modified from Ref. 79.

where the Mayer functions $f_{AB}^{(k)}(12) = (\exp(\varepsilon^{(k)}/k_B T) - 1) O_{AB}(12)$. Combining Eqs. (73) and (95) effectively map the non-pairwise additive association potential onto Wertheim's multi-density formalism. Following this approach it was shown that when the transformation Eq. (95) is combined with the superposition approximation (36), Eq. (71) can then be summed in the limit of an infinite-order perturbation theory as [79, 82] follows:

$$\frac{\Delta c_{ch}^{(o)}}{V} = \frac{\sigma_A \sigma_B f_{AB}^{(1)} \xi \kappa}{1 + \left(f_{AB}^{(1)} - f_{AB}^{(2)} \Psi \right) \xi \kappa \rho_o} \quad (96)$$

Equation (96) is a very simple result which accounts for both steric hindrance and hydrogen bond cooperativity in two-site-associating fluids. When hydrogen bonding is non-cooperative $f_{AB}^{(1)} = f_{AB}^{(2)}$, and Eq. (96) simplifies to Eq. (82). To demonstrate the accuracy of this approach, Fig. 14 compares theory predictions to Monte Carlo simulations for the fraction of molecules which are monomers X_0 , bonded once X_1 and bonded twice X_2 . For simplicity we consider the case of a bond angle $\alpha_{AB} = 180^\circ$, pairwise association energy $\varepsilon^{(1)} = 7k_B T$ and density $\rho = 0.6d^3$. For $\varepsilon^{(2)} = 0$, there is no energetic benefit for a sphere to bond twice which results in $X_2 \rightarrow 0$. Increasing $\varepsilon^{(2)}$ results in a steady increase in X_2 and the fractions X_1 and X_0 remain nearly constant until $\varepsilon^{(2)} \sim 5k_B T$ at which point they decline sharply.

The lack of fully bonded molecules for small $\epsilon^{(2)}$ is due to the fact that there is little energetic benefit to a molecule to becoming fully bonded, while the entropic penalty must still be paid in full. For large $\epsilon^{(2)}$ the energetic push for molecules to become fully bonded overpowers the entropic penalty resulting in $X_2 \rightarrow 1$ for large $\epsilon^{(2)}$. Theory and simulation are in near-perfect agreement.

In addition to chains, rings can also be included in the bond cooperative perturbation theory through the simple transformation $f_{AB} \rightarrow f_{AB}^{(2)}$ in Eq. (85). Including the effect of bond angle, bond cooperativity, and ring formation, Marshall *et al.* [82] were able to show that both bond angle and bond cooperativity play a huge role in the types of associated clusters which are formed. In agreement with detailed quantum calculations [71], it was shown that bond cooperativity favors ring formation.

VII. SPHERICALLY SYMMETRIC AND DIRECTIONAL ASSOCIATION SITES

Throughout this chapter association has been defined as being between two molecules that must be positioned and *oriented* correctly for association to occur. That is, both molecules participating in the association bond have directional association sites. Another common case would be an association interaction between two molecules where one has a directional association site, while the other has a spherically symmetric association site. This type of interaction could describe ion–water solvation or mixtures [42] of patchy and spherically symmetric colloids.

The single-component version of this type of interaction is the Smith and Nezbeda [84] model of associating fluids. This model considers a spherical core with a single directional bonding site. The directional association sites are singly bondable and the spherical cores are treated as spherically symmetric association sites, with the maximum number of bonds the spherical core can receive being determined by steric constraints. Wertheim [85] developed an integral equation theory for this model of associating fluids, which was later solved analytically by Kalyuzhnyi and Nezbeda [86]. Also, we may draw parallels with the study of highly asymmetric electrolyte solutions. These solutions contain large polyions and small single-charge counterions. Previous multi-density integral equation theory studies of these solutions [87–89] have treated the counterions as singly bondable and the maximum number of times the polyion ion can bond is unrestricted and determined by steric constraints.

Very recently Marshall and Chapman [90, 91] developed a new TPT to model mixtures of these types. Specifically, they considered a mixture of molecules with directional association sites (d molecules) and molecules with a single spherically symmetric associations site (s molecules). The d molecules have CSW association sites as given in Eq. (4) with an association energy between d molecules $\epsilon_{AB}^{(d,d)}$,

the s molecules do not attract other s molecules, and the association between s molecules and d molecules is governed by the following association potential

$$\phi_A^{(s,d)}(12) = \begin{cases} -\varepsilon_A^{(s,d)}, & r_{12} \leq r_c \text{ and } \theta_A \leq \theta_c \\ 0 & \text{otherwise} \end{cases} \quad (97)$$

which states that if s molecule 1 and d molecule 2 are within a distance r_c of each other, and the d molecule is oriented such that the angle between the site A orientation vector and the vector connecting the two segments θ_A is less than the critical angle θ_c , the two molecules are considered bonded and the energy of the system is decreased by a factor $\varepsilon_A^{(s,d)}$.

In what follows, attention will be restricted to the case that both s and d molecules have a hard spherical core Eq. (3), equal diameters, and the d molecules will be restricted to having a single association site. For this case, this mixture can be treated as a binary mixture of associating molecules in Wertheim's two-density formalism outlined in Section IV. As done throughout this chapter, we will consider a perturbation treatment with a hard sphere reference fluid. Like previous cases, the challenge is determining the graph sum $\Delta c^{(o)}$.

For the current case, the s molecule is a single spherical association site which can clearly not be modeled in the single bonding condition. The maximum number of bonds is simply the maximum number of d molecules n^{max} that can pack in the s molecule's bonding shell $d \leq r \leq r_c$. To account for all association possibilities, we will have to include contributions for each association possibility explicitly (one s molecule with one d molecule, two d molecules, three d molecules, etc.). To accomplish this, we decompose $\Delta c^{(o)}$ as follows:

$$\Delta c^{(o)} = \sum_{n=1}^{n^{max}} \Delta c_n^{(o)} \quad (98)$$

where $\Delta c_n^{(o)}$ is the contribution for n directional molecules bonded to a s molecule. Figure 15 gives a pictorial representation of Eq. (98).

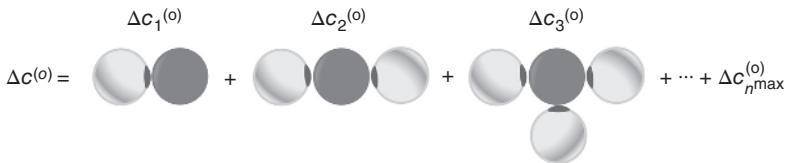


Figure 15. Illustration of graph sum contributions Eqs. (98) and (99) for a binary mixture of s molecules and d molecules.

The development of $\Delta c_n^{(o)}$ follows a similar path to the chain contribution for doubly bonded association sites Eq. (39). The final result is (in a slightly different form) [91]

$$\frac{\Delta c_n^{(o)}}{V} = \frac{1}{n!} \rho_o^{(s)} \tilde{\Delta}_n \delta^{(n)} Z_n^{(s,d)} \quad (99)$$

where

$$\tilde{\Delta} = \frac{1}{\Omega} \left(\exp \left(\frac{\varepsilon^{(s,d)}}{k_B T} \right) - 1 \right) \rho_o^{(d)} y_{HS}(d) \quad (100)$$

with $\rho_o^{(s)}$ being the monomer density of s molecules, $\rho_o^{(d)}$ the monomer density of directional molecules and $\delta^{(n)}$ being a second-order correction to the superposition approximation Eq. (86). Here $Z_n^{(s,d)}$ is the cluster partition function for an isolated cluster of n directional molecules bonded to a single s molecule.

As with the other perturbation theories discussed in this chapter, the key quantity in the theory is the cluster partition function which enumerates the number of associated states for which an isolated associated cluster can exist. For this case the cluster partition function is simplified as follows:

$$Z_n^{(s,d)} = \left(v_b \Omega \sqrt{\kappa} \right)^n P^{(n)} \quad (101)$$

The term $P^{(n)}$ is the probability that if n directional molecules are randomly generated in the bonding shell of the s molecule that there is no hard sphere overlap. An interesting feature of this result is that the square root $\sqrt{\kappa} = (1 - \cos \theta_c) / 2$ appears in the equations, as opposed to κ as in Eq. (46). The reason for this is that when one d molecule forms an association bond to an s molecule, there is a total orientation entropic penalty of $k_B \ln \sqrt{\kappa}$. On the other hand, when two d molecules form association bond, there is a total orientation entropic penalty of $k_B \ln \kappa$. The difference in the two cases lies in the fact that the s molecules do not pay a penalty in decreased orientational entropy when an association bond is formed. The number n^{max} is defined as the largest integer n for which the probability $P^{(n)}$ is nonzero. For bonding at hard sphere contact $n^{max} = 12$.

Figure 16 compares theoretical predictions and Monte Carlo simulation results for a mixture d and s molecules with an association energy $\varepsilon^{(s,d)} = 7k_B T$ at both low and high densities. The average “solvation number” of s molecules $\bar{n}$, or average number of bonds per s molecule, is plotted against the number fraction of s molecules $x^{(s)}$. For each case, $\bar{n}$ increases with decreasing $x^{(s)}$ reaching a maximum when $x^{(s)} \rightarrow 0$. This is due to the fact that when $x^{(s)}$ is small, there is an abundance of d molecules available to bond to the s molecules. As $x^{(s)}$ is increased, $\bar{n}$ decreases

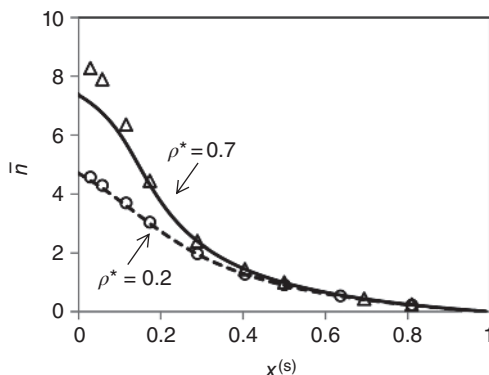


Figure 16. Comparison of theory (curves) and Monte Carlo simulation (symbols) results for the average solvation number of s molecules versus number fraction of s molecules at an association energy $\varepsilon^{(s,d)} = 7k_B T$ and densities $\rho^* = \rho d = 0.2$ (circles, dashed curve) and 0 (triangles, solid curves). The figure is modified from Ref. 91.

because there are less d molecules available for association due to a decreased fraction of d molecules and competition with other s molecules. Overall, theory and simulation are in good agreement. In addition to average solvation numbers, it was shown that the theory accurately predicts the distribution of s molecules bonded n times [91].

Going beyond the single site case, the theory was recently extended such that the d molecules can have an arbitrary number of association sites [90]. In this approach the interaction between s molecules was also that of the hard sphere reference fluid. To add spherically symmetric attractions (square well, LJ, etc.) between s molecules, one simply needs to employ the appropriate reference system (square well, LJ, etc.). Work is currently under way to employ this association theory as a model for ion–water solvation.

VIII. DENSITY FUNCTIONAL THEORY

Thus far, the focus of this review has been homogeneous fluids. For many interesting phenomena observed in biological and soft material systems, the micro- or mesoscale structure determines the properties of the system. DFT provides a valuable tool to predict mesoscale structure and interfacial properties assuming a suitable free energy functional can be developed. Excellent reviews of DFT for associating molecules have been written [92–94], so only a brief introduction will be provided here.

Calculating the inhomogeneous fluid structure of associating molecules based on Wertheim’s perturbation theory was first proposed by Chapman [18]. At that time, accurate molecular DFTs for non-polar spherical molecules (e.g., Tarazona’s

weighted density approximation [95] for hard spheres) had been developed. Two methods were suggested to include a perturbation for association in a DFT for nonpolar spheres. One approach was to include association using the local density approximation [52, 96] or using weighted densities of the bulk free energy due to association in a similar way to that used to create a hard sphere free energy functional by Tarazona or later Rosenfeld [97]. The second approach was to take advantage of the fact that Wertheim's TPT for associating molecules was already written in the form of a free energy functional (see Eqs. 69 and 70). A challenge with the associating free energy functional is to approximate the inhomogeneous cavity correlation function required by the theory.

Kierlik and Rosinberg [68, 98, 99] were the first to apply Wertheim's theory in the form of a free energy functional to produce a DFT for non-associating polyatomic molecules. As input to the theory, they estimated the cavity correlation function from a first-order functional Taylor series around the homogeneous result [99]. Results were in good agreement with molecular simulation results for hard sphere chains.

Segura *et al.* [51, 100] used two perturbation approaches to produce DFTs for associating molecules with one, two, and four association sites. In the first approach, they calculated the bulk free energy due to association at the same weighted densities as from Tarazona's DFT [95] for hard spheres. The theory results were in good agreement with molecular simulation for associating hard spheres near a hydrophobic surface. Further studies have showed accurate results in comparisons with molecular simulation for mixtures and confined associating molecules with hydrophobic and hydrophilic surfaces as described in the reviews [92, 93]. The same approach has been applied using various weighted densities or fundamental measure theory with similar accurate agreement with molecular simulation. Still other studies have used gradient theory or a local density approximation for vapor-liquid interfaces and shown good agreement with interfacial tension data [92, 93, 101, 102]. Extensions of the weighted bulk association free energy approach of Segura *et al.* have resulted in an accurate DFT for polyatomic molecules [103–106] by taking the limit of complete association in the bulk as described earlier.

The second approach of Segura *et al.* [51] was to use the free energy functional of Eqs. (69) and (70) as a perturbation to a hard sphere DFT. To minimize the system free energy requires the functional derivative of Eq. (69) with respect to the singlet density. The result is

$$\begin{aligned} \frac{\delta \beta A^{ex,assoc}}{\delta \rho_j(\mathbf{r})} = & \sum_{A \in \Gamma^{(j)}} (\ln \chi_A^j(\mathbf{r})) \\ & - \frac{1}{2} \iint d\mathbf{r}_1 d\mathbf{r}_2 \sum_{i=1}^N \sum_{k=1}^N \rho_i(\mathbf{r}_1) \rho_k(\mathbf{r}_2) \sum_{A \in \Gamma^{(i)}} \sum_{B \in \Gamma^{(k)}} \chi_A^i(\mathbf{r}_1) \chi_B^k(\mathbf{r}_2) \left(\frac{\delta \Delta_{AB}^{ik}(\mathbf{r}_1, \mathbf{r}_2)}{\delta \rho_j(\mathbf{r})} \right) \end{aligned} \quad (102)$$

Based on Eq. (102), Jain *et al.* [107] proposed a DFT for heteronuclear polyatomic molecules by taking the limit of the free energy functional for complete association of a fluid of spheres. Interestingly, in this limit, the theory automatically corrects the ideal gas free energy functional from an ideal gas of spheres to predict the exact free energy and density distribution for an ideal gas chain. Bymaster and Chapman [108] have shown that, in addition to associating spheres, Eq. (102) is applicable to associating polyatomic molecules. Results based on this DFT for associating molecules and non-associating polyatomics are in good agreement with molecular simulation results for associating molecules near a hydrophobic surface [109], associating grafted polymers [110], surfactants [111], and mixtures of associating polyatomics with intermolecular and intramolecular association [112]. For further information, we recommend reviews available in the literature as well as more recent literature [92, 94, 110, 113–116].

IX. CONCLUDING REMARKS

In this chapter, the basics of Wertheim's and Andersen's cluster expansions for associating fluids have been reviewed, specifically focusing on thermodynamic perturbation theory (TPT). Despite the severe approximations made in TPT, the approach yields equations of state that accurately reproduce simulation data, and are widely used for modeling the properties and phase behavior of solvents to polymers in the engineering community. As was shown throughout the chapter, TPT can be applied to develop theories for complex associated structures with steric effects, so long as the number of associated states of an isolated cluster can be calculated. Of course, this TPT approach will fail once the correlation functions of the real fluid begin to deviate from that of the reference fluid; for instance, association of monomers into rigid chains resulting in a nematic transition.

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REFERENCES

1. Weeks, J. D.; Chandler, D.; Andersen, H. C. *The Journal of Chemical Physics* 1971, **54**, (12), 5237–5247.
2. Barker, J. A.; Henderson, D. *The Journal of Chemical Physics* 1967, **47**, (11), 4714–4721.
3. Chandler, D.; Andersen, H. C. *The Journal of Chemical Physics* 1972, **57**, (5), 1930–1937.

4. Jeffrey, G. A. *An Introduction to Hydrogen Bonding*. Oxford University Press New York: 1997; Vol. **12**.
5. Dill, K. A. *Biochemistry* 1990, **29**, (31), 7133–7155.
6. Whitesides, G. M.; Grzybowski, B. *Science* 2002, **295**, (5564), 2418.
7. Bianchi, E.; Blaak, R.; Likos, C. N. *Physical Chemistry Chemical Physics* 2011, **13**, (14), 6397–6410.
8. Economou, I. G.; Donohue, M. D. *AIChE Journal* 1991, **37**, (12), 1875–1894.
9. Dolzalek, F. Zur Theorie der Biniiren Gemische und Konzentrierten Loungen. *Z. Phys. Chem.* 1908, (64), 727–747.
10. Heidemann, R. A.; Prausnitz, J. *Proceedings of the National Academy of Sciences* 1976, **73**, (6), 1773–1776.
11. Ikonomou, G.; Donohue, M. *AIChE Journal* 1986, **32**, (10), 1716–1725.
12. Panayiotou, C. G. *The Journal of Physical Chemistry* 1988, **92**, (10), 2960–2969.
13. Veytsman, B. *Journal of Physical Chemistry* 1990, **94**, (23), 8499–8500.
14. Panayiotou, C.; Sanchez, I. *The Journal of Physical Chemistry* 1991, **95**, (24), 10090–10097.
15. Gupta, R. B.; Brinkley, R. L. *AIChE Journal* 1998, **44**, (1), 207–213.
16. Brinkley, R. L.; Gupta, R. B. *Industrial & Engineering Chemistry Research* 1998, **37**, (12), 4823–4827.
17. Bol, W. *Molecular Physics* 1982, **45**, 605.
18. Chapman, W. G., PhD Thesis. 1988, Cornell University: Ithaca, NY.
19. Jackson, G.; Chapman, W. G.; Gubbins, K. E. *Molecular Physics* 1988, **65**, (1), 1–31.
20. Kern, N.; Frenkel, D. *The Journal of Chemical Physics* 2003, **118**, 9882.
21. Kalyuzhnyi, Y.; Docherty, H.; Cummings, P. *The Journal of Chemical Physics* 2010, **133**, 044502.
22. Wertheim, M. *Journal of Statistical Physics* 1984, **35**, (1), 19–34.
23. Wertheim, M. *Journal of Statistical Physics* 1986, **42**, (3), 459–476.
24. Morita, T.; Hiroike, K. *Progress of Theoretical Physics* 1961, **25**, (4), 537–578.
25. Frisch, H. L.; Lebowitz, J. L., *The Equilibrium Theory of Classical Fluids: A Lecture Note*. W. A. Benjamin New York: 1964.
26. Andersen, H. C. Cluster methods in equilibrium statistical mechanics of fluids. In *Statistical Mechanics*, Springer New York: 1977; pp 1–45.
27. Mayer, J. E.; Mayer, M. G., *Statistical Mechanics*. John Wiley & Sons, Inc. New York: 1940.
28. Andersen, H. C. *The Journal of Chemical Physics* 1973, **59**, 4714.
29. Andersen, H. C. *The Journal of Chemical Physics* 1974, **61**, 4985.
30. Chandler, D.; Pratt, L. R. *The Journal of Chemical Physics* 1976, **65**, (8), 2925–2940.
31. Wertheim, M. *Journal of Statistical Physics* 1984, **35**, (1), 35–47.
32. Wertheim, M. *Journal of Statistical Physics* 1986, **42**, (3), 477–492.
33. Wertheim, M. *The Journal of Chemical Physics* 1987, **87**, 7323.
34. Chapman, W. G.; Jackson, G.; Gubbins, K. E. *Molecular Physics* 1988, **65**, (5), 1057–1079.
35. Joslin, C. G.; Gray, C. G.; Chapman, W. G.; Gubbins, K. E. *Molecular Physics* 1987, **62**, (4), 843–860.
36. Lockett III, A. *The Journal of Chemical Physics* 1980, **72**, 4822.
37. Chapman, W. G. *The Journal of Chemical Physics* 1990, **93**, (6), 4299–4304.
38. Ghonasgi, D.; Chapman, W. G. *Molecular Physics* 1993, **79**, (2), 291–311.
39. Marshall, B. D.; Chapman, W. G. *Physical Review E* 2013, **87**, (5), 052307.
40. Segura, C. J.; Vakarin, E. V.; Chapman, W. G.; Holovko, M. *The Journal of Chemical Physics* 1998, **108**, 4837.
41. Tripathi, S.; Chapman, W. G. *Journal of Chemical Physics* 2003, **118**, (17), 7993–8003.
42. Feng, L.; Dreyfus, R.; Sha, R.; Seeman, N. C.; Chaikin, P. M. *Advanced Materials* 2013, **25**, (20), 2779–2783.
43. Wang, Y.; Wang, Y.; Breed, D. R.; Manoharan, V. N.; Feng, L.; Hollingsworth, A. D.; Weck, M.; Pine, D. J. *Nature* 2012, **491**, (7422), 51–55.

44. Kalyuzhnyi, Y. V.; Stell, G. *Molecular Physics* 1993, **78**, (5), 1247–1258.
45. Marshall, B. D.; Ballal, D.; Chapman, W. G. *The Journal of Chemical Physics* 2012, **137**, (10), 104909.
46. Marshall, B. D.; Chapman, W. *Soft Matter* 2014, **10**, 5168–5176.
47. Frenkel, D.; Smit, B., *Understanding Molecular Simulation: From Algorithms to Applications*. Academic Press New York: 2001; Vol. **1**.
48. Ghonasgi, D.; Chapman, W. G. *Molecular Physics* 1993, **80**, (1), 161–176.
49. Michelsen, M. L.; Hendriks, E. M. *Fluid Phase Equilibria* 2001, **180**, (1), 165–174.
50. Sciortino, F.; Bianchi, E.; Douglas, J. F.; Tartaglia, P. *The Journal of Chemical Physics* 2007, **126**, (19), 194903.
51. Segura, C. J.; Chapman, W. G.; Shukla, K. P. *Molecular Physics* 1997, **90**, (5), 759–771.
52. Gloor, G. J.; Jackson, G.; Blas, F. J.; Del Río, E. M.; de Miguel, E. *The Journal of Chemical Physics* 2004, **121**, 12740.
53. de las Heras, D.; Tavares, J. M.; da Gama, M. M. T. *Soft Matter* 2011, **7**, (12), 5615–5626.
54. de las Heras, D.; Tavares, J. M.; da Gama, M. M. T. *The Journal of Chemical Physics* 2011, **134**, 104904.
55. de Las Heras, D.; Tavares, J. M.; da Gama, M. M. T. *Soft Matter* 2012, **8**, (6), 1785–1794.
56. Rovigatti, L.; Tavares, J. M.; Sciortino, F. *Physical Review Letters* 2013, **111**, (16), 168302.
57. Russo, J.; Tavares, J.; Teixeira, P.; da Gama, M. M. T.; Sciortino, F. *The Journal of Chemical Physics* 2011, **135**, 034501.
58. Ghonasgi, D.; Llanorestrepo, M.; Chapman, W. G. *Journal of Chemical Physics* 1993, **98**, (7), 5662–5667.
59. Ghonasgi, D.; Chapman, W. G. *AIChE Journal* 1994, **40**, (5), 878–887.
60. Ghonasgi, D.; Chapman, W. G. *Journal of Chemical Physics* 1994, **100**, (9), 6633–6639.
61. Banaszak, M.; Chiew, Y.; Radosz, M. *Physical Review E* 1993, **48**, (5), 3760.
62. Chapman, W. G.; Gubbins, K. E.; Jackson, G.; Radosz, M. *Fluid Phase Equilibria* 1989, **52**, 31–38.
63. Chapman, W. G.; Gubbins, K. E.; Jackson, G.; Radosz, M. *Industrial & Engineering Chemistry Research* 1990, **29**, (8), 1709–1721.
64. Ghonasgi, D.; Chapman, W. G. *Molecular Physics* 1994, **83**, (1), 145–158.
65. Gilvillegas, A.; Galindo, A.; Whitehead, P. J.; Mills, S. J.; Jackson, G.; Burgess, A. N. *Journal of Chemical Physics* 1997, **106**, (10), 4168–4186.
66. Gross, J.; Sadowski, G. *Industrial & Engineering Chemistry Research* 2002, **41**, (22), 5510–5515.
67. Huang, S. H.; Radosz, M. *Industrial & Engineering Chemistry Research* 1990, **29**, (11), 2284–2294.
68. Kierlik, E.; Rosinberg, M. *The Journal of Chemical Physics* 1992, **97**, 9222.
69. Jakobsen, R.; Mikawa, Y.; Brasch, J. *Spectrochimica Acta, Part A: Molecular Spectroscopy* 1967, **23**, (7), 2199–2209.
70. Dyke, T. R.; Mack, K. M.; Muentner, J. S. *The Journal of Chemical Physics* 1977, **66**, 498.
71. Rincón, L.; Almeida, R.; García-Aldea, D.; y Riega, H. D. *The Journal of Chemical Physics* 2001, **114**, 5552.
72. Reed, A. E.; Curtiss, L. A.; Weinhold, F. *Chemical Reviews* 1988, **88**, (6), 899–926.
73. Almaraz, N. G. *Physical Review E* 2012, **86**, (3), 030101.
74. Müller, E.; Gubbins, K. *Molecular Physics* 1993, **80**, (4), 957–976.
75. Sear, R. P.; Jackson, G. *Physical Review E* 1994, **50**, (1), 386–394.
76. Flory, P. J., *Statistical Mechanics of Chain Molecules*. Interscience Publishers New York: 1969.
77. Tavares, J. M.; Rovigatti, L.; Sciortino, F. *The Journal of Chemical Physics* 2012, **137**, (4), 044901.
78. Zaccarelli, E.; Buldyrev, S.; La Nave, E.; Moreno, A.; Saika-Voivod, I.; Sciortino, F.; Tartaglia, P. *Physical Review Letters* 2005, **94**, (21), 218301.
79. Marshall, B. D.; Chapman, W. G. *The Journal of Chemical Physics* 2013, **139**, (21), 214106.
80. Barlow, S. J.; Bondarenko, G. V.; Gorbaty, Y. E.; Yamaguchi, T.; Poliakov, M. *The Journal of Physical Chemistry. A* 2002, **106**, (43), 10452–10460.

81. Guo, H.; Karplus, M. *The Journal of Physical Chemistry* 1994, **98**, (29), 7104–7105.
82. Marshall, B. D.; Haghmoradi, A.; Chapman, W. G. *The Journal of Chemical Physics* 2014, **140**, 161401.
83. Sear, R. P.; Jackson, G. *The Journal of Chemical Physics* 1996, **105**, (3), 1113.
84. Smith, W. R.; Nezbeda, I. *The Journal of Chemical Physics* 1984, **81**, 3694.
85. Wertheim, M. *The Journal of Chemical Physics* 1988, **88**, (2), 1145.
86. Kalyuzhnyi, Y. V.; Nezbeda, I. *Molecular Physics* 1991, **73**, (3), 703–713.
87. Kalyuzhnyi, Y. V.; Holovko, M.; Vlachy, V. *Journal of Statistical Physics* 2000, **100**, (1–2), 243–265.
88. Kalyuzhnyi, Y. V.; Vlachy, V. *Chemical Physics Letters* 1993, **215**, (5), 518–522.
89. Kalyuzhnyi, Y. V.; Vlachy, V.; Holovko, M.; Stell, G. *The Journal of Chemical Physics* 1995, **102**, 5770.
90. Marshall, B. D.; Chapman, W. G. *Soft Matter* 2013, **9**, (47), 11346–11356.
91. Marshall, B. D.; Chapman, W. G. *The Journal of Chemical Physics* 2013, **139**, (10), 104904.
92. Emborsky, C. P.; Feng, Z.; Cox, K. R.; Chapman, W. G. *Fluid Phase Equilibria* 2011, **306**, (1), 15–30.
93. Feng, Z. Z.; Bymaster, A.; Emborsky, C.; Ballal, D.; Marshall, B.; Gong, K.; Garcia, A.; Cox, K. R.; Chapman, W. G. *Journal of Statistical Physics* 2011, **145**, (2), 467–480.
94. Wu, J.; Li, Z. *Physical Chemistry* 2007, **58**, (1), 85.
95. Tarazona, P. *Physical Review A* 1985, **31**, (4), 2672.
96. Gloor, G. J.; Jackson, G.; Blas, F.; Del Rio, E. M.; De Miguel, E. *The Journal of Physical Chemistry C* 2007, **111**, (43), 15513–15522.
97. Rosenfeld, Y. *Physical Review Letters* 1989, **63**, (9), 980–983.
98. Kierlik, E.; Rosinberg, M. *The Journal of Chemical Physics* 1993, **99**, 3950.
99. Kierlik, E.; Rosinberg, M. *The Journal of Chemical Physics* 1994, **100**, 1716.
100. Segura, C. J.; Vakarin, E. V.; Chapman, W. G.; Holovko, M. F. *Journal of Chemical Physics* 1998, **108**, (12), 4837–4848.
101. Kalyuzhnyi, Y.; Iacovella, C.; Docherty, H.; Holovko, M.; Cummings, P. *Journal of Statistical Physics* 2011, **145**, (2), 481–506.
102. Kalyuzhnyi, Y. V.; Cummings, P. T. *The Journal of Chemical Physics* 2003, **118**, (14), 6437–6445.
103. Cao, D.; Jiang, T.; Wu, J. *The Journal of Chemical Physics* 2006, **124**, 164904.
104. Cao, D.; Wu, J. *The Journal of Chemical Physics* 2004, **121**, 4210.
105. Yu, Y.; Wu, J. *The Journal of Chemical Physics* 2002, **117**, 2368.
106. Yu, Y. X.; Wu, J. *The Journal of Chemical Physics* 2002, **116**, 7094.
107. Jain, S.; Dominik, A.; Chapman, W. G. *The Journal of Chemical Physics* 2007, **127**, 244904.
108. Bymaster, A.; Chapman, W. *The Journal of Physical Chemistry B* 2010, **114**, (38), 12298–12307.
109. Ballal, D.; Chapman, W. G. *The Journal of Chemical Physics* 2013, **139**, (11), 114706.
110. Gong, K.; Marshall, B. D.; Chapman, W. G. *The Journal of Chemical Physics* 2013, **139**, (9), 094904.
111. Emborsky, C. P.; Cox, K. R.; Chapman, W. G. *The Journal of Chemical Physics* 2011, **135**, (8), 084708.
112. Marshall, B. D.; García-Cuellar, A. J.; Chapman, W. G. *The Journal of Chemical Physics* 2012, **136**, 154103.
113. Marshall, B. D.; Chapman, W. G. *The Journal of Chemical Physics* 2013, **138**, 044901.
114. Marshall, B. D.; Cox, K. R.; Chapman, W. G. *The Journal of Physical Chemistry C* 2012.
115. Marshall, B. D.; Cox, K. R.; Chapman, W. G. *Soft Matter* 2012, **8**, 7415–7425.
116. Gnan, N.; de las Heras, D.; Tavares, J. M.; da Gama, M. M. T.; Sciortino, F. *The Journal of Chemical Physics* 2012, **137**, (8), 084704.

