# A general-purpose biasing scheme for Monte Carlo simulation of associating fluids

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We present a method for accelerating convergence of Monte Carlo simulations of associating fluids. Such fluids exhibit strong, short-ranged, orientation-specific intermolecular attractions which are difficult to sample via conventional molecular simulation. We propose a bias scheme that preferentially attempts Monte Carlo trials that lead to ''unbonding'' or ''bonding'' (UB) transitions of the associating molecules. The proposed method is most like the recently introduced aggregation volume bias Monte Carlo (AVBMC) algorithm of Chen and Siepmann. Both algorithms are much simpler, more efficient, and more generally applicable than previously proposed association-bias schemes. We study the UB algorithm via application to the simple ideal-association model of van Roij. Although unrealistic, the model contains the basic features of association that cause problems for simulation, and its simple nature facilitates analysis of the performance of the simulation algorithm. We find, at least in application to this model, that the UB algorithm exhibits better convergence properties when compared to AVBMC, and through analysis of the acceptance probability distributions we can develop an explanation for this difference. We also demonstrate the UB algorithm in the context of the Gibbs ensemble, reproducing the phase coexistence behavior of a dimerization model originally proposed by Tsangaris and de Pablo. © *2001 American Institute of Physics.* [DOI: 10.1063/1.1369131]

## I. INTRODUCTION

Associating fluids are characterized by an intermolecular potential that exhibits strong but short-ranged, orientationally dependent attractions. Such fluids can form clusters and ordered structures, even at low density. Usually the origin of these attractive interactions is hydrogen bonding, and examples of associating fluids include water, acetic acid, and hydrogen fluoride, among many others. Molecular simulation of associating fluids is problematic. Typically, the configuration space of such fluids is not sampled accurately by a standard molecular dynamics or Metropolis Monte Carlo simulation.[1] Associated configurations occupy a small portion of configuration space, and consequently they are difficult to find and enter via random, unbiased sampling methods. However, such configurations contribute substantially to ensemble averages because their Boltzmann weighting is made high by their favorable energetics. Thus when such configurations are found, dissociation is rare. So, the delicate balance between associated and disassociated configurations is poorly characterized by simulations of reasonable length.

Recently progress in the area of simulation of associating fluids has been made through the application of biasing algorithms in Monte Carlo simulation. Several algorithms have been put forth. All methods treat the problem similarly, and entail Monte Carlo trial moves that preferentially place a molecule into the bonding volume surrounding another molecule. This bias is removed by also performing trials that preferentially remove a bound molecule from the binding region of its associated partner. The earliest approaches are due to Seaton and Glandt,[2–5] and Kranendonk and Frenkel,[6] who developed algorithms to handle the extreme case of the ''sticky sphere'' model, in which the association volume is zero but the association energy is infinite. Following this, the first more generally applicable approach was the association-bias Monte Carlo (ABMC) put forth by Busch *et al.*[7,8] in the context of associating biological macromolecules. Subsequently Tsangaris and de Pablo[9] proposed the bond-bias Monte Carlo (BBMC) method, Visco and Kofke[1,10] presented the monomer addition/subtraction algorithm (MASA), and most recently Chen and Siepmann[11] described the aggregation volume-bias Monte Carlo (AVBMC) technique. With the exception of the AVBMC method, each of these algorithms has limitations or drawbacks that make it inappropriate for general use. In the present work we describe a method that is similar to the AVBMC approach, but which displays performance advantages without sacrificing simplicity and general applicability.

One of the key difficulties in formulating an association-bias scheme is quantitative evaluation of the bias introduced with the special MC trials. In most approaches, this step requires a calculation of the bias volume. A bias trial is constructed to move a molecule into a particular subregion of the whole simulation cell, and it is necessary to know the volume of this region to remove the bias introduced by the preferential sampling. This subregion is defined as the union over all molecules of some simple region that surrounds each, and for each molecule the volume of its bonding region is simple to evaluate. Problems arise when the bonding region of one molecule overlaps with the bonding region of one or more other molecules. Then the volume evaluation

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becomes a difficult geometric problem that can quickly become intractable. The ABMC method of Busch *et al.*[7,8] adds further complications, but in the end provides a general-purpose method for simulating associating fluids. However, the algorithm is not simple to implement, and it involves the numerical evaluation of the volume integrals, which adds significant computational expense to the method. The BBMC method of Tsangaris and de Pablo[9] is much simpler, but is limited to a model in which only associating dimers can form (thus greatly simplifying the problem of evaluating the association volume). The MASA method of Visco and Kofke[1,10] is similarly limited in applicability, permitting simulation of only linear and cyclic associating chains.

We have found, as Chen and Siepmann[11] have recently described, that great simplification can be achieved by formulating bias moves that do not involve the union of all bonding regions. Instead the trial is given simply in terms of the region about individual molecules. This makes for an algorithm that is simpler to implement than any previously proposed method, yet is generally applicable, and not restricted to particular types of aggregates (unlike BBMC and MASA). Chen and Siepmann applied their AVBMC algorithm to models of water, hydrogen fluoride, and acetic acid and demonstrated the favorable convergence of the simulation averages. The algorithm we propose here is very similar to AVBMC, but differs in important ways which we describe in this work.

The remainder of this paper is organized as follows. In Sec. II we review the basis of association bias MC methods. In Sec. III we describe our new method, which we call the unbound–bound (UB) algorithm. Then in Sec. IV we demonstrate the UB algorithm through application to two simple model systems, and in one case compare it to the AVBMC method. In Sec. V we discuss in detail the origin of the differing behaviors of the UB and AVBMC algorithms, and we conclude in Sec. VI.

## II. BACKGROUND: ASSOCIATION-BIAS ALGORITHMS

We consider association bias moves that are performed in a canonical ensemble; extension of the basic approach to other ensembles is straightforward. The probability distribution in this ensemble is simply[12]

$$\Pi_i = \exp(-\beta U_i)/Q, \tag{1}$$

where $Q$ is the canonical partition function, $\beta = 1/kT$ with $T$ the absolute temperature and $k$ Boltzmann's constant, and $U_i$ is the energy of state $i$.

In Metropolis Monte Carlo,[13–15] a move from (micro)state $i$ to a state $j$ is completed via a two-step process. In the first step, the trial is performed with probability $T_{ij}$; in the second step a decision is made as to whether to accept the trial, with probability $A_{ij}$. Thus the overall probability to complete the move $i \to j$ in a given step is $T_{ij}A_{ij}$. Trial and acceptance probabilities for the reverse move $j \to i$ are defined also, and together the forward and reverse trial and acceptance probabilities are constructed to satisfy detailed balance

$$\Pi_i T_{ij} A_{ij} = \Pi_j T_{ji} A_{ji}. \tag{2}$$

If the process is ergodic, then transition probabilities that satisfy this condition will converge to the desired limiting distribution, Eq. (1), for a sufficiently long sample. The Metropolis prescription for the acceptance probabilities is asymmetric, and can be expressed compactly in terms of an acceptance parameter $\chi$,

$$\Pi_i T_{ij} \min(1,\chi) = \Pi_j T_{ji} \min(1,1/\chi), \tag{3}$$

from which $\chi$ is found

$$\chi = \frac{\Pi_j T_{ji}}{\Pi_i T_{ij}}. \tag{4}$$

Thus, different Metropolis Monte Carlo algorithms are constructed through the formulation of the trial probabilities $T_{ij}$. Although all (ergodic) algorithms should yield the same limiting distribution, the performance of each, as characterized by the rate with which they converge to the limit, can vary widely.

One should note that at the beginning of each MC step, a decision is made regarding what type of move will be attempted next. Depending on the ensemble and the design of the MC algorithm, one might choose, for example, to make a volume-change trial, or a simple molecule-displacement trial, or perhaps an association-bias trial. This selection should be made at random, with some fixed probability assigned to each type of trial. Most important, if the forward and reverse trials of a particular move are not selected with the same probability, this bias must be reflected in the acceptance probabilities. In all of the following, we assume that this decision is made with no bias toward the forward or reverse moves of the trial under consideration.

Now let us focus specifically on trials that result in the displacement of a particular molecule from its position $\mathbf{r}_i$ to another position $\mathbf{r}_j$. In a standard MC simulation, such a move is made by selecting a molecule at random, and displacing it to a position selected with uniform probability from within a cubic region centered on its present location. Movement to positions outside this region have zero probability to occur (in one MC trial). We let $\Delta$ be the volume of the cubic displacement region; usually this value is adjusted to result in a 50% (or so) rate of acceptance of the trial moves. The trial probabilities for the forward and reverse moves are the same, and are equal to $1/(N\Delta)$. Thus from Eq. (4), the acceptance parameter is simply

$$\chi = \exp[-(U_j - U_i)/kT]. \tag{5}$$

An association bias MC algorithm introduces trials that move a molecule in to or out of the bonding region of another molecule. The ''region'' may include an orientational component, so that placement of a molecule into the bonding region of another could involve bias of both the position and orientation of the molecule being moved. The definition of a ''bonding region'' is completely arbitrary, but it is usually selected to coincide with the region about a molecule where another molecule would have strong favorable energetic interactions. But the bonding region need not be defined in such a restrictive manner. It could have a less physical basis, and be something as simple as a small cubic region centered on another molecule. Placement into such a region could

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sometimes actually lead to overlap (very unfavorable energetics), but such trials (although sometimes rejected) could nevertheless work well in enhancing the sampling of clustering (strongly favorable interactions) molecules. If one wishes to analyze cluster statistics of molecules, then a more physically based definition of bonding would be appropriate, but this matter can be disconnected from the way bonding is defined to formulate a MC association-bias algorithm.

Thus we will adopt a nomenclature in this work that considers two molecules ''bound'' or ''bonded'' if they lie within each other's association-bias (bonding) region, regardless of their actual energy of interaction. Likewise, two molecules not within each other's bonding region will be considered ''unbound.'' If the bonding region is selected to coincide well with the region of favorable energetics, then this definition falls in accord with the usually understood meaning of ''bound,'' but we wish in this work to apply the notion in a less restrictive sense. The implementation of association-bias algorithms requires a clear definition of the bonding region, but the effectiveness of these algorithms requires only that the energetically favorable region lies within the bonding region. It may be easier at times to work with a perhaps simpler, arbitrarily defined bonding region, instead of the smaller and probably more complicated energetically favorable subset of it.

One way to perform association-bias trials is to consider movement of a molecule into the region formed by the union of all the bonding regions about every molecule in the system. If the volume of this region for state $i$ is $\Phi_i V$, where $V$ is the volume of the entire system, then the transition probability for moving a molecule, selected at random from all other molecules, into a position $\mathbf{r}_j$ selected uniformly within this volume is proportional to $1/(\Phi_i V)$. The overall trial probability is then $T_{ij}=1/(N\Phi_i V)$. The reverse move, which must be considered with probability equal to the forward move, begins by selecting at random one of the $N_{Aj}$ associated molecules. This molecule is then placed at a position selected at random within the entire simulation system. The trial probability is then $T_{ji}=1/(N_{Aj}V)$. The acceptance parameter is

$$\chi=\frac{N\Phi_i}{N_{Aj}}\exp[-(U_j-U_i)/kT]. \tag{6}$$

For the associating systems to which this algorithm is applied, the exponential will be large (the energy of state $j$ will be very favorable compared to the energy of state $i$), while the bonding volume fraction $\Phi$ will be small (assuming it is selected to roughly coincide with the energetically favorable region). If the balance is right the acceptance parameter $\chi$ will be near unity for both forward and reverse moves, leading to a large likelihood of acceptance in either case. As indicated in Sec. I, calculating the volume of the association region (and thereby $\Phi$) can be difficult if the regions for each molecule have substantial overlap. A related problem is the difficulty of choosing a point with uniform probability in this region, as required by the algorithm. The ABMC method tackles this problem and pays the computational price, while the BBMC and MASA algorithms circumvent it by prohibiting configurations in which the association volumes might overlap.

The approach taken by the AVBMC method is different.[11] In the algorithm it is possible to accomplish the move of a molecule from $\mathbf{r}_i$ to $\mathbf{r}_j$ via many independent routes. One way to ensure that the algorithm satisfies detailed balance involves enumeration of all possible routes with their transition probabilities, each constructed so that the overall transition probabilities—considering all routes together—for the moves $i\rightarrow j$ and $j\rightarrow i$ satisfy the criterion. This is difficult and, fortunately, unnecessary. Instead it is sufficient that the algorithm satisfy ''super-detailed balance.'' [15] This means that each of the independent ways to accomplish $i\rightarrow j$ has a unique counterpart that results in $j\rightarrow i$, and that each of these pairs by themselves satisfy detailed balance. In fact, this idea is tacitly assumed in the conventional association-bias methods just described. Since a MC simulation usually would use both biased and unbiased molecule-displacement trials, there are certain moves that can be accomplished by both. Yet the transition probability for each trial does not take into account how the same move could be performed using the other trial. They do not have to, because super-detailed balance ensures overall detailed balance.

Thus, the AVBMC method proceeds as follows. A molecule $i$ is selected, and another molecule $j$ is selected to define the bias region. A decision is made with some preset probability whether to move the molecule $i$ into the bonding region of $j$ (''in'' trial), or whether to move it to a point anywhere outside of this region (''out'' trial). Molecule $i$ is then moved to a position selected uniformly within the chosen region. Four cases can arise, differing in whether the old/new position of $i$ was/was not already in the bonding region of $j$. Acceptance probabilities are formulated appropriately. The question of whether molecule $i$ was or will be in the association region of any other molecule (other than $j$) does not factor into the algorithm. Note that positions that lie within the bonding region of two or more molecules will have an enhanced probability of being selected—there is more than one way such a point could result as a trial in the algorithm. This complication does not matter, however, because the super-detailed balance condition is met for each route. Clearly, this approach is much simpler and more generally applicable than the other methods, and it is no less effective.

## III. UNBONDING–BONDING (UB) ALGORITHM

We describe now the biasing algorithm that forms the focus of this work. We developed this method independently, but it shares some of the basic features of the AVBMC approach. This main difference in the proposed algorithm is less reliance on super-detailed balance, and more explicit promotion of trials that form and break bonded molecules. We formulate the acceptance probabilities considering all the ways that a bias move could result in the same outcome as the current trial.

The UB algorithm defines two complementary trial moves, and each bias trial begins by selecting one of these

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moves randomly with equal probability. Here is the recipe. The quantity in parentheses at the end of each step indicates the multiplicative factor that the step introduces into the overall trial probability.

Select whether to perform an unbonding trial or a bonding trial. $(\frac{1}{2})$

*1. Unbonding trial*

(a) Select a molecule (label it A) uniformly from among the $N_{ai}$ molecules that are currently in the bonding region of at least one other molecule. If $N_{ai}=0$, the trial is rejected and the current configuration is taken as the next one in the Markov chain. Otherwise, molecule A is at position $\mathbf{r}_i$ where it is in the bonding region of $n_i \geqslant 1$ other molecules. $(1/N_{ai})$

(b) Place molecule A at a point $\mathbf{r}_j$ selected uniformly from the entire simulation volume, where it will be in the bonding region of $n_j \geqslant 0$ other molecules. $(1/V)$

*2. Bonding trial*

(a) Select a molecule (A) uniformly from the $N$ molecules being simulated. Molecule A is at position $\mathbf{r}_i$ where it is in the bonding region of $n_i \geqslant 0$ other molecules. $(1/N)$

(b) Select another molecule, labeled B. $(1/(N-1))$

(c) Place molecule A with uniform probability at a point $\mathbf{r}_j$ in the bonding region (of volume $\phi V/N$) of B. At this new location, molecule A will be in the bonding region of $n_j \geqslant 1$ other molecules, including B. Thus there are $n_j$ equivalent ways that the molecule could arrive at this position via this trial move, so the trial probability is multiplied accordingly. $(n_j N/\phi V)$

So now we need to figure the trial probabilities for movement of a molecule from position $\mathbf{r}_i$ to $\mathbf{r}_j$ using a bias trial. In general, the move may arise in either the unbonding or the bonding trial. The bonding-trial probability is

$$T_{ij}^{(B)}=\frac{1}{2}\times\frac{1}{N}\times\frac{1}{N-1}\times\frac{n_j}{\phi V/N}. \tag{7}$$

The unbonding-trial probability is

$$T_{ij}^{(U)}=\frac{1}{2}\times\frac{1}{N_{ai}}\times\frac{1}{V}\times\delta_i, \tag{8}$$

where $\delta_i$ is zero if the molecule is not bound in state $i$, and is one if the molecule is bound. So the overall trial probability is the sum

$$T_{ij}=\frac{1}{2V}\left[\frac{\delta_i}{N_{ai}}+\frac{n_j}{\phi(N-1)}\right]. \tag{9}$$

The reverse trial, from $\mathbf{r}_j$ to $\mathbf{r}_i$ occurs via the same process, so the trial probability will have the same form

$$T_{ji}=\frac{1}{2V}\left[\frac{\delta_j}{N_{aj}}+\frac{n_i}{\phi(N-1)}\right]. \tag{10}$$

From Eq. (6), the acceptance parameter is

$$\chi=\frac{(N-1)\phi\delta_j+n_iN_{aj}}{(N-1)\phi\delta_i+n_jN_{ai}}\times\frac{N_{ai}}{N_{aj}}\times\exp[-\beta(U_j-U_i)]. \tag{11}$$

If $N_{aj}$ is zero (no associated molecules in state $j$), this formula needs clarification

$$\chi=\frac{n_iN_{ai}}{(N-1)\phi}\times\exp[-\beta(U_j-U_i)]. \tag{12}$$

Likewise if $N_{ai}$ is zero (both cannot be zero, so we need not consider such a case)

$$\chi=\frac{(N-1)\phi}{n_jN_{aj}}\times\exp[-\beta(U_j-U_i)]. \tag{13}$$

In contrast to the AVBMC method, the proposed biasing algorithm uses more information in deciding acceptance of a trial. In particular, it requires knowledge of the number of bonding regions a molecule has moved into, the total number of bound molecules, and a list of the molecules that are in the bonding volume of at least one other molecule. Evaluation or tracking of this information requires some computational resources, but they are negligible. The number of bound molecules can be updated with each accepted MC trial, while the determination of whether a molecule is in another's bonding region can be performed while evaluating their pair energy (which must be done anyway). It is not necessary to identify clusters of associated molecules, or to do any difficult geometric calculations for the union of bonding volumes. The biasing scheme requires only a sum of associates. In light of this, a biasing/bonding array can be used and updated each trial.

We performed tests of the proposed unbonding–bonding (UB) algorithm using two models: the ideal association model (IAM) of van Roij;[16,17] and the dimerization model of Tsangaris and de Pablo.[9] The IAM is very simple and unrealistic, but it captures the essential features that make simulation of associating systems difficult. Its advantage is that its properties are solvable (almost) exactly, so we can examine the convergence and correctness of the simulation algorithms under consideration. The simplicity of the model also exposes more starkly the features and limitations of the biasing algorithms. We examine it in Sec. IV. The model of Tsangaris and de Pablo is idealized too, but is significantly more realistic than the IAM. It was studied for its phase coexistence behavior by Tsangaris and de Pablo,[9] and in Sec. V we examine the ability of the UB algorithm to provide results comparable to those given by them.

## IV. SIMULATION TESTS: IDEAL-ASSOCIATION MODEL

### A. Model definition

The ideal association model[16] (IAM) is defined by a two-site attractive square-well molecule (Fig. 1). The sites, arbitrarily labeled A and B, are placed a fixed distance apart. The A-type sites interact via a square well of pure attraction with the B-type sites on other molecules,

$$u_{ij}=\begin{cases}-\epsilon, & r_{\mathrm{Ai,Bj}}<R_{\mathrm{eff}}\\ 0, & r_{\mathrm{Ai,Bj}}\geqslant R_{\mathrm{eff}}\end{cases}. \tag{14}$$

There are no other interactions defined in the model. In particular, there is no steric repulsion, nor any type of isotropic attraction. van Roij presented a solution to this model with

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the provision that no branched or ring structures form. His model is defined in a way that has, for example, the energy associated with two B sites in the attractive region of one A site as equal to only $-\epsilon$, not $-2\epsilon$. In our simulations, we have applied a different approach to preclude branching: We prohibit each binding site from having more than one complementary site in its attractive region, effectively imposing a hard repulsion to sites attempting to occupy a nonvacant site. We prohibit the formation of rings in a like manner, rejecting any move that leads to formation of a ring structure. The difference between our approach and van Roij's choice is minor at the low densities of interest to our study. It shows up as a small deviation of our simulation energy from the van Roij solution, while having a lesser effect on the heat capacity. The main contribution to the deviation from his solution is the limitation on the range of rotation of each molecule when in the binding site of another, a limitation needed to prevent the two molecules from double bonding with each other (i.e., forming a two-member ring). The discrepancy becomes smaller as the A–B separation is increased, and it can be approximately accounted for in the exact solution, but it is not worth the effort.

In van Roij's solution, the energy per molecule is

$$u=-\frac{\epsilon}{N}\sum_i \frac{N}{A}(i-1)Y^i \tag{15}$$

and

$$Y=1-\frac{H-1}{2A} \tag{16}$$

with $H\equiv(4A+1)^{1/2}$ and $A\equiv\rho V_{\mathrm{eff}}\exp(\beta\epsilon)$, where $V_{\mathrm{eff}}=4\pi R_{\mathrm{eff}}^3/3$ is the volume of one of the binding sites. In addition, the constant-volume heat capacity is given by

$$\frac{C_v}{Nk_{\mathrm{B}}}=\frac{\beta^2\epsilon^2}{A}\sum_i (i-1)\left(iY^{i-1}\left(\frac{H-1}{2A}-\frac{1}{H}\right)-Y^i\right). \tag{17}$$

The sums in these formulas are over clusters of different sizes, and in principle they extend from 1 to infinity. But for comparison to our simulation results they should extend to only $N$, since this is the largest possible cluster that can be observed in a simulation. The difference is apparent only at the lowest temperatures.

The intramolecular A–B separation $R_{\mathrm{AB}}$ does not enter into the van Roij solution, but it must be set at some value to conduct the simulations. For reasons just discussed, this choice has a small effect on the properties as measured in the simulation. For most simulations we set $R_{\mathrm{AB}}$ equal to $4R_{\mathrm{eff}}$.

### B. Simulation details

Monte Carlo (MC) simulations were performed for 256 IAM molecules using the UB biasing algorithm, or the AVBMC method, or no bias at all. Consistent with our model definition, only linear molecules were allowed to form: any trial that resulted in the formation of a ring aggregate or branched structure was rejected. Cubic periodic boundaries were applied, and the maximum displacement and maximum rotation were adjusted independently to yield 50% acceptance rates for these (unbiased) standard MC moves. We considering two types of initial configuration. In the first the molecules were placed on a fcc lattice, for which no molecule is bound to another. In the second, all molecules were placed such that they formed a single $N$-member bonded chain, with each molecule's binding well (except the first and last) in the binding well of another (i.e., all molecules in the most energetically favorable condition). These initial conditions represent the extreme cases of no clustering and full clustering, and permit us to examine how well each algorithm converges to the equilibrium energy from each direction.

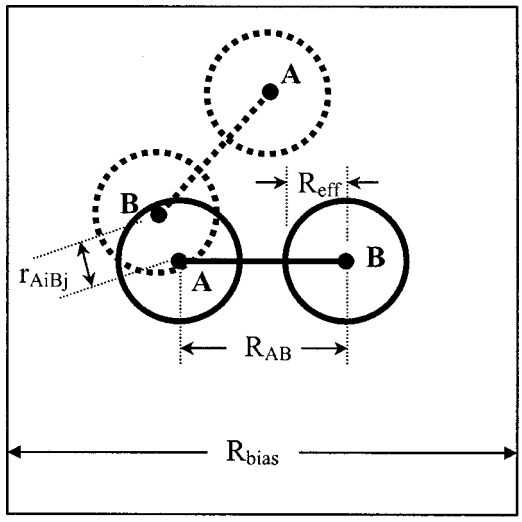


FIG. 1. Illustration of the ideal association model (IAM), with the various geometric features defined. A second IAM molecule is depicted in broken lines, showing it in a configuration where it is separated by a distance just within the attractive association well of one of their bonding sites of the central (solid-line drawn) molecule. Also shown is the cubic Monte Carlo biasing region associated with the central IAM molecule.

The systems were allowed to equilibrate for $N_e$ cycles, followed by a production period of $N_p$ cycles; specific values are indicated in the following. A cycle consisted of $N$ Monte Carlo trials. In each trial, one of the following types of move was selected with equal probability: (a) a simple unbiased displacement of a molecule within a small cubic region centered on its present position (i.e., a standard MC molecule displacement); (b) a rotation within a cone centered on its present orientation; (c) a ''bonding'' trial if an UB-bias simulation, or an ''in'' trial if an AVBMC simulation; or (d) an ''unbonding'' trial if a UB-bias simulation, or an ''out'' trial if an AVBMC simulation. Averages were taken every 1000 cycles, and errors were calculated on all measurements by Kolafa's method.[18] Heat capacities were measured using standard fluctuation formulas.[12]

A bias-trial bonding region (which, to reiterate, has no necessary connection to the interaction energy) was defined for each molecule as a cube centered on the midpoint between the A–B sites (and thus extends outside the attractive well), as shown in Fig. 1. The width $R_{\mathrm{bias}}$ of the bonding cube was selected to be from 2 to 10 times the well-site radius, although for any given simulation it is fixed at one value. In a bias trial move the center (midpoint between the A and B sites) of a molecule was placed at a random point in the cubical bonding region of another molecule, as described

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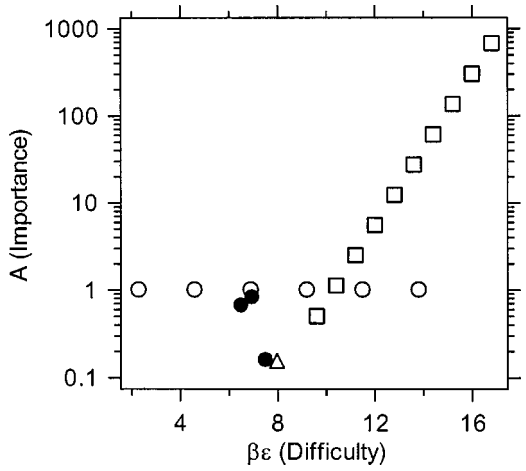


FIG. 2. State conditions for study of the biasing algorithms as applied to the IAM model. The ordinate is the parameter $A=\rho V_{\mathrm{eff}}\exp(\beta\epsilon)$, which describes the importance of clusters to the thermodynamic properties, while the abscissa is the reciprocal temperature $\beta\epsilon$, which characterizes the difficulty of simulating the systems. The open symbols are simulation state points examined in this study (squares describe a line of constant $\rho V_{\mathrm{eff}}=3.43\times10^{-5}$, circles a line of constant $A=1.0$, and the triangle is the point focused on in Sec. VI). The closed circles characterize the experimentally observed state of hydrogen fluoride at three pressures where the superheated vapor shows a large heat-capacity maximum.

previously. The orientation vector of the displaced molecule was chosen at random on the unit sphere.

The thermodynamic state of the system can be specified with two dimensionless groups. Visco and Kofke[1] emphasized the parameters $A$ and $\beta\epsilon$ as particularly appropriate to associating systems. The parameter $A$ [see Eq. (15)]characterizes the importance of associated clusters to the thermodynamic properties (in fact, in the van Roij solution these properties depend only on $A$). A large value is obtained if the association volume is large relative to the system volume, and/or if the association energy is large relative to the temperature. Large $A$ indicates that clusters are relevant. The parameter $\beta\epsilon$ characterizes the rate at which an unbiased simulation converges to an equilibrated distribution of clusters. A large value indicates more difficulty in converging. Our studies were performed for a range of values of these parameters, and the conditions studies are summarized in Fig. 2. Each simulation indicated in Fig. 2 performed $N_e$ equilibration cycles and $N_p$ production cycles as follows $((N_e,N_p)$, in thousands of cycles): open circles (100, 100); open squares (200, 500); triangle (50, 50). To provide some context, we also show in Fig. 2 rough values of these parameters for superheated hydrogen fluoride (HF) vapor, at conditions where its heat capacity exhibits a highly anomalous maximum. The displayed values are based on experimental measurements[19,20] of the temperature and density of the heat-capacity maxima (at pressures of 96.1, 56.0, and 15.5 kPa, respectively), and use the characteristic values of $\epsilon$ (4 kcal/mol) and $V_{\mathrm{eff}}$ (29.7Å$^3$) suggested by Visco and Kofke[10] via characterization of the HF molecular model of Cournoyer and Jorgensen.[21]

### C. Results

The energy and constant-volume heat capacities measured in the simulations are compared to van Roij's analytic

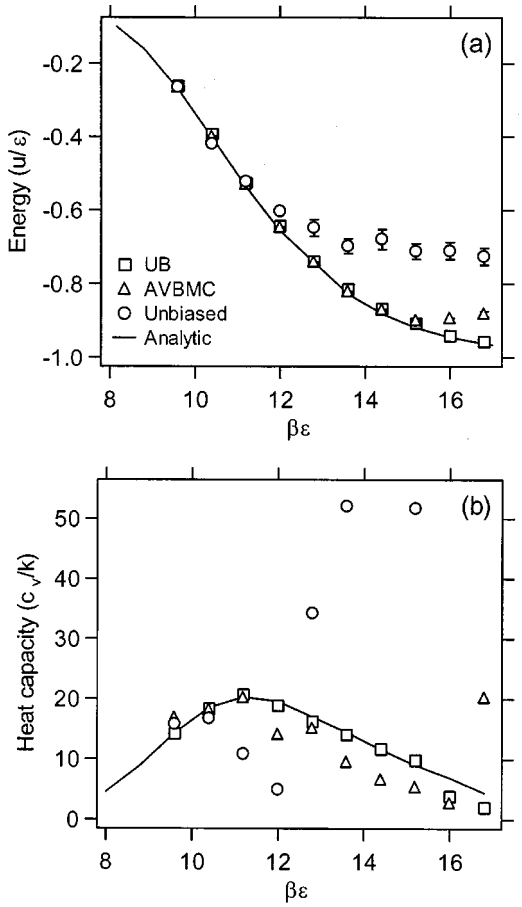


FIG. 3. Measured values of (a) the energy and (b) the heat capacity as a function of reduced reciprocal temperature, given by Monte Carlo simulations of the IAM employing biasing algorithms as indicated by the symbols. All data are for the same value of $\rho V_{\mathrm{eff}}=3.43\times10^{-5}$. Large-$\beta$ data for the heat capacity using the unbiased algorithm are off the scale. Confidence limits are not shown on any of the data. Solid line represents the analytic solution of van Roij.

solution in Fig. 3. The plots show the results as a function of $\beta\epsilon$ and describe a line of constant $\rho V_{\mathrm{eff}}=3.43\times10^{-5}$. For low enough $\beta\epsilon$ (high temperature), association is unimportant and all simulation methods produce satisfactory results for the energy. At intermediate values of $\beta\epsilon$, the unbiased method begins to yield results that differ from the analytic value. Particularly bad is the heat capacity, which begins to show highly erratic behavior. Of course, this happens because the heat capacity relies on proper characterization of fluctuations for its measurement, and these fluctuations are especially poorly sampled in unbiased simulations. Both the proposed UB algorithm and the AVBMC method greatly improve the averages in comparison to the unbiased simulations.

A similar comparison is presented in Fig. 4. Here we hold $A$ fixed while again varying $\beta\epsilon$. Since the properties depend only upon $A$, the data fall on a horizontal line. The results are much as in Fig. 3, with the biasing methods yielding data of much higher quality than the unbiased simulation results, particularly at low temperatures. The conditions here are not as extreme as in Fig. 3, and the AVBMC and UB algorithms provide results of comparable quality.

At the most severe conditions the UB algorithm suc-

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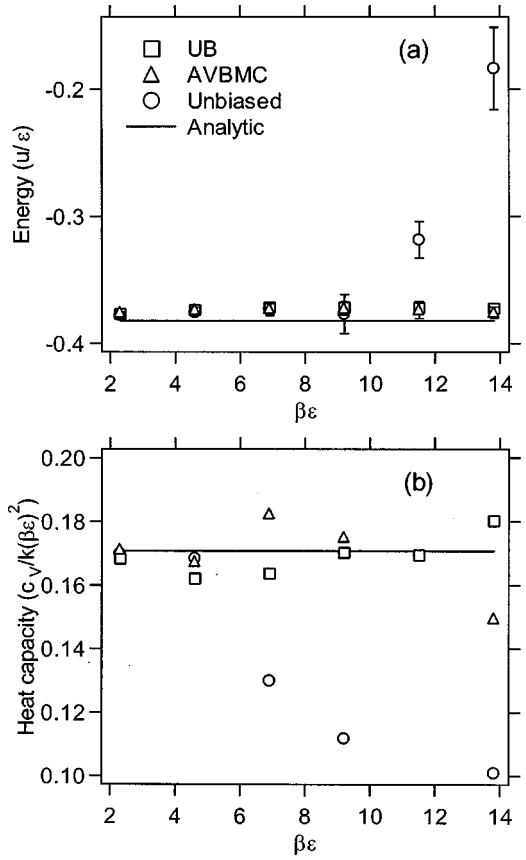


FIG. 4. Same as Fig. 3, except data are for constant $A=1.0$.

ceeds in describing both the energy and heat capacity, whereas in the AVBMC method begins to fail. The difference in convergence of the methods is highlighted in Fig. 5, which shows the block averages (each over 1000 cycles) of the energy over the course of the simulation, for each algorithm. In an attempt to provide a more fair comparison, the convergence data are presented in terms of the CPU time, since there is slightly more overhead in the UB algorithm,

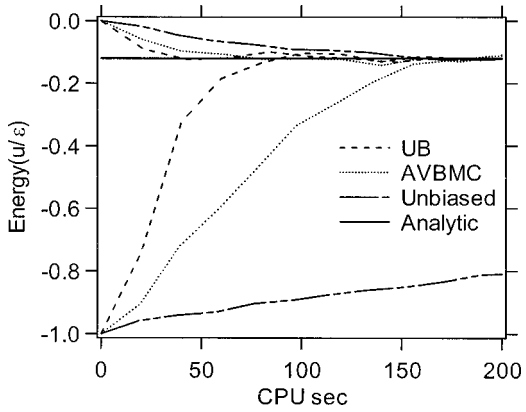


FIG. 5. Convergence of the energy of the IAM model using various Monte Carlo algorithms. Block averages of the configurational energy are presented as a function of CPU expended in each simulation. Lines beginning from energy 0.0 are simulations beginning from an underbonded configuration, while those beginning from $-1.0$ are from an overbonded condition. The state conditions are $\beta\epsilon=8.0$; $A=0.153$; $V_{\text{bias}}=1000\ \text{A}^3$ (indicated in Fig. 2 by the open triangle).

but the qualitative outcome is not much different when presented instead in terms of number of bias trials; each curve describes about ten block averages. State conditions are $\beta\epsilon=8.0$, $A=0.154$ (indicated by the triangle symbol in Fig. 2). Two sets of simulations are presented, one beginning from a system of IAM molecules on fcc lattice, with none interacting (i.e., no attractive-well overlaps), and the other beginning from a chain of IAM molecules, with every molecule (except the first and last in the chain) interacting with two others. Of some interest is the difficulty of converging to an equilibrium condition when starting from an overbonded state. Here the UB algorithm clearly outperforms the others. This outcome is true too, although to a lesser extent, when beginning from the underbonded initial configuration. We note that this state condition is one of moderate difficultly on the scale presented in Fig. 2, and corresponds roughly to one of the conditions where the heat-capacity maximum is observed experimentally in HF.

## V. SIMULATION TESTS: DIMERIZATION MODEL

We applied the UB algorithm to the dimerization model of Tsangaris and de Pablo, to demonstrate that the method can be applied to Gibbs-ensemble phase equilibria calculations. We did not attempt a comparison with other algorithms in this application.

### A. Model definition

The Tsangaris–de Pablo dimerization model[9] uses a vector to define the orientation of each molecule, and the pair potential depends on the angle $\theta$ between the orientation vector and the center-to-center distance vector $\mathbf{r}_{ij}$ between the pair of particles. The potential consists of an orientationally dependent square-well site

$$U_{SS}=\begin{cases}-\epsilon_{\text{SW}} & \text{if } 0<\mathbf{r}_{ij}<r_c,\ \theta_i<\theta_c,\ \theta_j<\theta_c\\ 0 & \text{otherwise}\end{cases} \tag{18}$$

attached to an isotropic Lennard-Jones potential

$$U_{cc}(r_{ij})=4\epsilon\left[\left(\frac{\sigma}{r_{ij}}\right)^{12}-\left(\frac{\sigma}{r_{ij}}\right)^{6}\right], \tag{19}$$

where $r_{ij}=|\mathbf{r}_{ij}|$. This results in an off-center conically shaped attractive site[9] which favors configurations in which the orientation vectors of two particles point toward each other. The geometry of the molecule is such that each particle is incapable of forming associations with more than one other particle, so only dimer aggregates can form.

For our study we adopted the potential parameters used by Tsangaris and de Pablo. In particular $\theta_c=27°$ and $r_c=\sigma$. We examined two values of the well depth studied by them: $\epsilon_{\text{SW}}=8\epsilon$ and $\epsilon_{\text{SW}}=20\epsilon$.

### B. Simulation details

Gibbs ensemble simulation was performed of the dimerization model, with UB bias moves conducted within each phase. No biasing moves were conducted in association with the interphase molecule-transfer steps performed as part of the Gibbs ensemble simulation. The simulation results were collected after 10 k cycles of volume and translation move-

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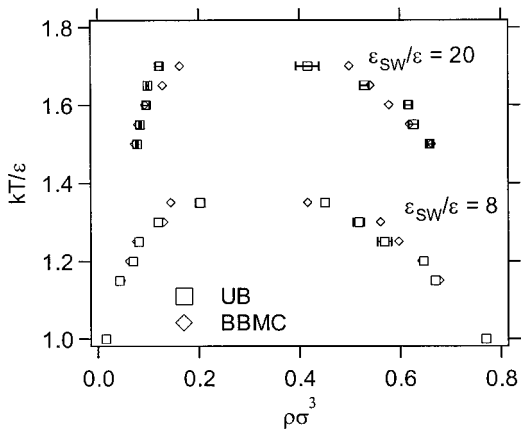


FIG. 6. Vapor–liquid coexistence data obtained from Gibbs-ensemble Monte Carlo simulations of the dimerization association model. Data taken using UB-bias trials are compared to the results reported by Tsangaris and de Pablo.

ments, 15 k relaxation cycles consisting of translation, volume, and particle transfer moves, and 100 k production cycles. Other simulation details are as described by Tsangaris and de Pablo.

### C. Results

Simulation data for the coexistence curves are displayed in Fig. 6. Results are shown for both systems studied, varying the bonding well depth relative to the Lennard-Jones energy parameter. The results are in good agreement with the data reported by Tsangaris and de Pablo, with some deviation beginning to be noticeable in both instances as the critical point becomes near. We also examined the monomer fractions in the saturated liquid and vapor phases, and find results largely in agreement with the observations of Tsangaris and de Pablo.

## VI. DISCUSSION

The UB algorithm is effective in enhancing the exploration of configurations in which association is important but difficult to sample well. The AVBMC algorithm is also very effective, but in our study of the IAM model, it seems to reach its limits of effectiveness before the UB algorithm fails. It is worthwhile to consider further how these very similar algorithms differ when applied in this situation.

In Fig. 7, for each type of trial (unbonding and bonding) we present histograms of the values of the acceptance probability ($\chi$) encountered in an UB-bias Monte Carlo simulation of the IAM model at $\beta\epsilon=8.0$, $A=0.153$ (the point depicted by the triangle in Fig. 2). Histrograms were taken for 10 k cycles, beginning from an equilibrated system; this yields about 1.2 million bias trials. Trials with small values of $\chi$ are less likely to be accepted, while transitions with $\chi>1$ are always accepted. The plots exhibit several prominent peaks, each of which can be associated with a different type of energetic transition that accompanies the placement or removal of one molecule in/out of another's square-well sphere of attraction. We label these peaks with ''F'' and ''W'' to indicate the state of being free or in a well before/

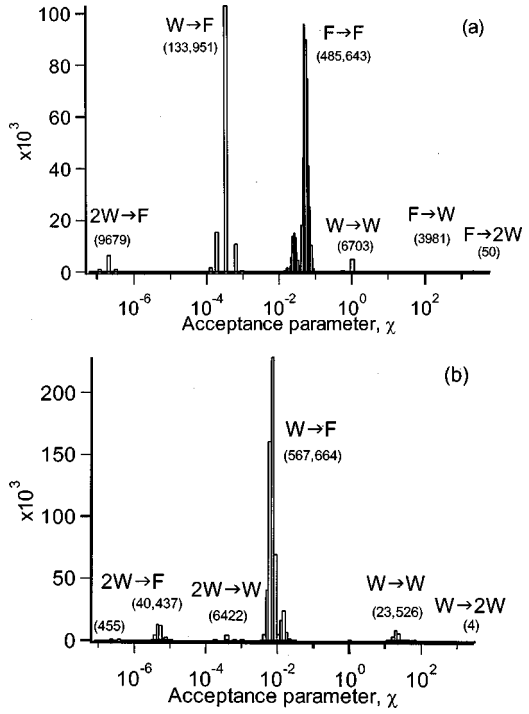


FIG. 7. Histogram of the Monte Carlo acceptance parameter $\chi$ as observed in simulations of the IAM using the UB bias algorithm. (a) Values observed in bonding trials; (b) values observed in unbonding trials. Annotation indicates the energetic state of the displaced molecule before and after the trial: ''F'' (free) indicates the molecule is not interacting with any others; ''W'' indicates it is in the attractive well of one other molecule; ''2W'' indicates it is in the well of two other molecules. The parameters are set as in Fig. 5. The sampling was started from an equilibrated system. The number in parentheses is the sum of nearby histograms.

after the trial move (this should not be confused with being ''unbonded'' or ''bonded,'' which reflects only whether the molecule is in an association-bias bonding region). The sharpness of these peaks is a consequence of the simplicity of the IAM model, and the small broadening that they do show results from the role of the configuration-dependent parameters $n_i, N_{ai}$, etc. [cf. Eq. (11)] in the acceptance probabilities.

The bonding-trial histogram has a peak at $\chi$ near 0.0003 and another at about 0.04. The first of these corresponds to bonding trials that select (equally from among the $N$ molecules) a molecule that is in the well of another, and places it in the bonding region of the target molecule without actually putting it in the attractive well. This is unfavorable and almost all of these trials are rejected. In this case $\delta_i=\delta_j=1$, and (approximately) $n_i=n_j=1$, $N_{ai}=N_{aj}$. Thus the acceptance probability is approximately equal to $\exp(-\beta\epsilon)=\exp(-8)$. These are essentially wasted trials, and their occurrence could be reduced considerably (or even eliminated) by taking the bonding volume to be much closer in size to the energetically favorable well region (in this study it is almost 1000 times larger). In a few instances this trial does result in placement into the attractive well of the target molecule, and this occurrence is represented by the small peak at about $\chi=1.0$.

The peak near 0.04 corresponds to trials in which a molecule moves from an unbound state (in which it is therefore

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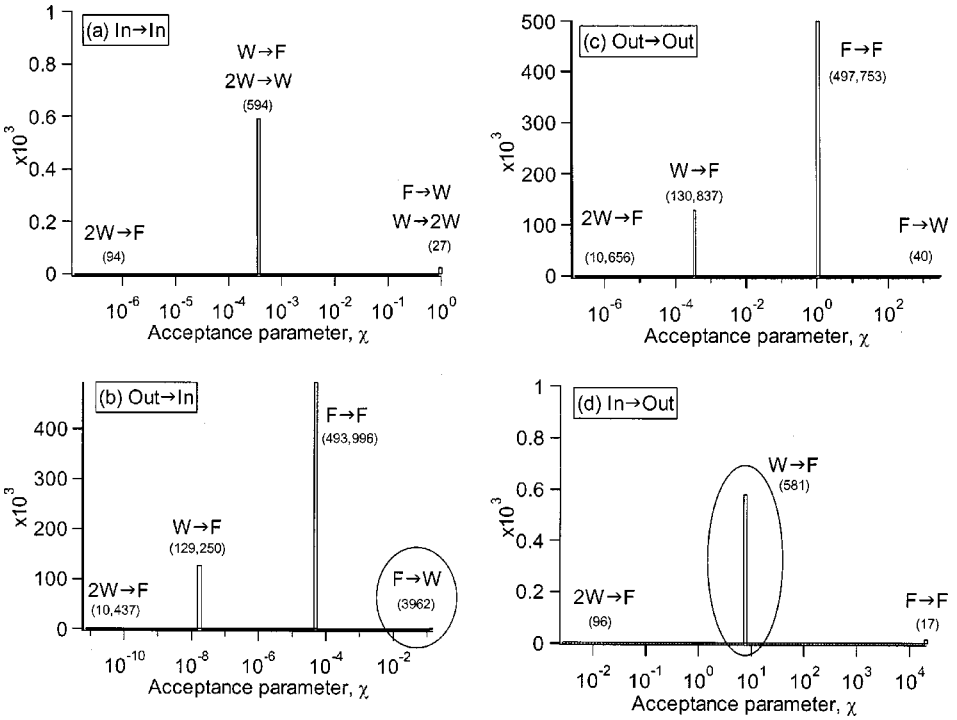


FIG. 8. Histograms of the Monte Carlo acceptance parameter $\chi$ as observed in simulations of the IAM using the AVBMC bias algorithm. Parts (a) through (d) differ in the type of move being performed, varying in whether the molecule being moved started and finished ''In'' or ''out'' of the association-bias region of another molecule. ''F'' and ''W'' annotations are used as in Fig. 7. Trials that contribute most to the creation or breakup of energetically bound molecules are indicated by the enclosing ovals. Note the greatly expanded scale of the ordinate in (a) and (d). The parameters are set as in Fig. 5. The sampling was started from an equilibrated system. The number in parentheses is the sum of nearby histograms.

also not any energetic well) to one where it is placed in the bonding region of the target but again without finding the energetically favorable well. The acceptance fraction of these moves is much greater, since they do not have the penalty associated with pulling a molecule from a well state to a free state. Here $\delta_i=n_i=0$, $\delta_j=1$, and $n_j=1$, $N_{ai}=N_{aj}$; thus (approximately) $\chi=\rho V_{\text{bias}}/(N_{ai}/N)=0.04$. There is an another, much smaller peak at about $\chi=\rho V_{\text{bias}}/(N_{ai}/N)\exp(+8)=140$, corresponding to similar trials that instead end with the displaced molecule in with the attractive well of the target. Decreasing $V_{\text{bias}}$ so that it coincides better with the well region would decrease $\chi$ for both of these types of moves, but it would still benefit the simulation convergence. It would result in more F→W moves at the expense of the (less useful) F→F moves. Moreover, the F→W moves with a reduced $\chi$ would still be always accepted because $\chi$ in the present approach is already much greater than 1.0.

The unbonding-trial histogram exhibits one prominent peak at about 0.01. This corresponds to W→F trials in which a molecule in the well of another is placed outside any other molecule's well. This is a useful move for the sampling of the associating system. Here $\delta_i=1$, $\delta_j=0$, and (approximately) $n_i=1$, $n_j=0$, $N_{ai}=N_{aj}$, so $\chi=/(N_{ai}/N)/\rho V_{\text{bias}}\exp(-8)=0.007$. Decreasing $V_{\text{bias}}$ would enhance acceptance of these moves too.

This detailed analysis of the observed acceptance-probability values indicates that even though the UB algorithm greatly improves the sampling of association, this example has applied it in a way that is far from optimal. Decreasing the bonding-bias region to a point where it coincides with the attractive well would yield many more useful trials (those in which movement into and out of the energetically favorable regions is attempted) without reducing the rate of acceptance of the moves. We have deliberately avoided implementing the algorithm in the optimal way because in some applications it may not be so easy to form an optimal bonding region. It is good then to see that even in this worst-case formulation, in which the bonding region is 1000 times larger than the well region and the bias is very inefficient, that substantial improvement to sampling is obtained.

In the AVBMC algorithm, there are four types of events that can occur with a bias move:

(1) in–in: A trial places into a molecule's bonding region another molecule that was already in that region.
(2) out–in: A trial places into a molecule's bonding region another molecule that was previously outside it.
(3) out–out: A trial places outside a molecule's bonding region another molecule that was already outside it.
(4) in–out: A trial places outside a molecule's bonding region another molecule that was previously in it.

In Fig. 8 we present $\chi$ histograms for these categories of events. The most prevalent of these are the *out–in* and *out–out* events. Most of the *out–out* events are F→F, and even though always accepted they do nothing to enhance the sampling of bound states. Some of these events are W→F, but the acceptance probability of these is small (0.0003), so they are not consequential. Of all the *out–in* moves, only a small fraction (0.008) effect a F→W change in binding state, and because of the need to remove the bias, their acceptance rate is only 0.14. Still, these form the bulk of the contribution of the AVBMC trials that make a F→W transition. The remainder of the trials do not contribute to the sampling (the tiny number that are not rejected do not change the binding state). The other event types, *in–in* and *in–out*, occur in much smaller proportion (about 1000 times less often). The *in–in* moves contribute a yet smaller fraction to the change in

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binding state (F→W). The *in–out* moves contribute most. The most common occurrence here is a W→F transition, which is always accepted.

In summary, of all the AVBMC moves, there are two basic types that contribute to the sampling of the association states, and both moves are accepted in equal but very small fractions (about 0.001) of all moves: (1) the F→W transition in the *out–in* trial and (2) the W→F transition of the *in–out* trial. The details of this result can be altered by adjusting the bias volume, but this will not improve the outcome. If the bias volume were decreased, even to the point of making it coincident with the bonding volume, many more of the *out–in* moves would be of the type F→W, but their acceptance probability would be diminished by an exactly compensating amount (this must be so because the *in–out* W→F reverse move balancing it would still be always accepted and occur no more frequently). One of the main problems with the algorithm is that many of the moves are F→F, and do not actually enhance the sampling of bound states. The main way to improve sampling within this framework is to decrease the probability $P_{\text{bias}}$ of selecting an *in* move. This will increase the occurrence of *in–out* trials and W→F events. This can occur without any acceptance penalty down to a $P_{\text{bias}}$ that gives about 12% *in* trials. But even then the overall fraction of moves that accomplish useful association sampling at most doubles to about 0.2%.

The real hindrance to the algorithm is that there is no trial that states ''these two molecules, which are bonded to each other, will be preferentially taken apart.'' Separation of bound molecules occurs only indirectly, in either of two ways.

(1) Molecule 1 is selected, and molecule 2, which happens to be bound to some molecule other than 1, is selected. Molecule 2 is then placed outside the association region of 1. Such a move is not uncommon, but its acceptance is simply $\exp(-\Delta U/kT)$, and thus does not benefit from the biasing algorithm. Consequently these moves are accepted no more often than in an unbiased algorithm.

(2) Molecule 1 is selected, and molecule 2, which happens to be bound to 1, is selected. Acceptance of such a move benefits from the biasing algorithm, but these moves occur with relatively low frequency, since the selection probability for the molecule bound to molecule 1 is $1/N$.

The fraction of all AVBMC bias trials that resulted in an accepted move F→W or W→F was about 0.1%; for the UB algorithm this fraction is about 0.8%. So although the AVBMC algorithm does indeed improve convergence relative to an unbiased algorithm, it does so less efficiently. And, unlike the UB algorithm, AVBMC in this application cannot be markedly improved by adjusting the parameters of the algorithm.

Finally, we note that super-detailed-balance condition enforced in the AVBMC algorithm allows for the straightforward combination of AVBMC and common tricks used in particle swap moves (e.g., configurational-bias Monte Carlo CBMC and multiple insertions of the first bead). All AVBMC simulations for molecular systems described in Ref. 11 made use of such additional biasing schemes, and it was reported that they lead to large gains in efficiency (one order of magnitude). We have not considered such extensions in the context of the UB algorithm, but with proper attention to the formulation of acceptance probabilities we see no reason they could not be applied here as well.

## VII. CONCLUSION

We have presented an algorithm that aids in the simulation of systems of associating molecules. The method shares features with the recently proposed AVBMC algorithm of Chen and Siepmann. Both methods require the arbitrary definition of a bonding volume about each molecule, and both consider Monte Carlo trials in which one molecule is preferentially placed into or removed from the bonding volume of another. Both methods are much simpler and more generally applicable than previously proposed methods, and both are effective in accelerating the convergence of associating systems. The methods differ in the details of their implementation. The AVBMC algorithm is slightly simpler to implement, but it does not use quite as much configuration information as the proposed UB algorithm when performing the bias trials. We find that the AVBMC algorithm does not converge as quickly as the UB algorithm when applied in the simple IAM test system, and we have presented an analysis that indicates the origin of these differing behaviors. In this study we purposely avoided applying the UB algorithm in a most efficient manner, and our analysis indicates that the performance of the UB algorithm could be greatly improved with a better selection of the bonding-bias volume; further analysis indicates that AVBMC could not be comparably improved.

One should be careful in drawing conclusions from this limited study. We have examined a highly idealized model for association, and there may be effects unconsidered here that become important to the behavior of the biasing algorithms when more realism is introduced to the models. However, the study does highlight some of the considerations that are likely to be important to the behavior of these association-bias algorithms, and gives us some guidance about what to consider when applying and improving upon them. As both the AVBMC and the UB algorithms are used in future work we will learn more about which is most appropriate in different situations.

## ACKNOWLEDGMENTS

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