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Direct Free Energy Calculation in the Continuous Fractional Component Gibbs Ensemble

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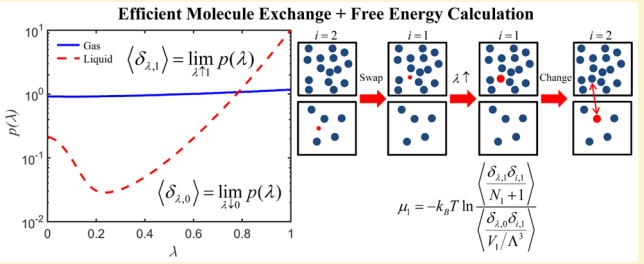
ABSTRACT: A new formulation of the Gibbs ensemble (GE) combined with the continuous fractional component Monte Carlo method is presented. In the proposed formulation, only a single fractional molecule per component is used instead of two in the original formulation by Shi and Maginn (*J. Comput. Chem.* **2008**, *29*, 2520−2530). This has the following advantages: (1) one directly obtains chemical potentials, without using test particles. We show analytically that the expressions for the chemical potential are identical to those in the conventional Gibbs ensemble; (2) biasing is applied to each simulation box independently; (3) maximum allowed changes in the scaling parameter of intermolecular interactions can be chosen differently in each simulation box. Obtaining chemical potentials directly facilitates thermodynamic modeling using equations of state, and it can be used as an independent check to ensure that chemical equilibrium is achieved. As a proof of principle, our method is tested for Lennard-Jones (LJ) particles and the TIP3P-Ew water model. Results are compared with the conventional GE. Excellent agreement was found both for average densities and chemical potentials. In our new approach, the acceptance probability for molecule exchanges between the boxes is much higher (typically larger than 40% for LJ particles) than for the conventional GE (typically lower than 2% for LJ particles). It is also shown that the contribution of the fractional molecule should be disregarded when computing ensemble averages such as the average energy per molecule and the average densities. The algorithm can be easily extended to mixtures and molecules with intramolecular interactions.



1. INTRODUCTION

Knowledge regarding vapor−liquid equilbria (VLE) is of great importance in many processes in chemical industry.[1−3] Equilibrium densities and other thermodynamic properties of the two coexisting phases can be computed directly by means of molecular simulation.[4−6] Monte Carlo simulation in the Gibbs ensemble (GE), introduced in the 1980s of the last century by Panagiotopoulos,[7−9] is widely applied for simulating phase coexistence of pure components and mixtures.[10−14] In this ensemble, two separate simulation boxes are considered that can exchange molecules and volume in such a way that the total volume and total number of molecules are constant. Equilibrium is achieved when the pressures and chemical potentials are equal in both simulation boxes.[15] Alternative simulation methods to study VLE such as histogram reweighting in the grand-canonical ensemble[16−18] can be more efficient, provided that the number of components is limited and the acceptance probability for insertions/deletions of molecules is sufficiently high. Still, the GE provides a straightforward route to determine accurate coexistence densities and critical parameters using relatively small system sizes.[14] Simulations in the grand-canonical ensemble and GE rely on a sufficient number of molecule exchanges with either the reservoir or the other simulation box. Unfortunately, the acceptance probabilities for these exchanges can be close to zero. This is typically the case when molecules are large or when densities are high (e.g., a liquid phase at low temperature). When faced with low acceptance probabilities for molecule exchanges in the GE, it is not trivial to verify whether or not the system is at chemical equilibrium. In principle, the chemical potentials of both boxes follow from average energy changes of attempted molecule transfers,[15] but in practice the statistics of this calculation are poor at conditions where the probability of accepted molecule exchanges is low. Hence, to ensure identical chemical potentials in both boxes, one should perform separate free energy calculations.

Beside simulating direct coexistence (two phases are directly in contact),[19,20] there are two classes of solutions to overcome the problem of low acceptance probabilities for molecule exchanges in the GE: methods based on the insertion of whole molecules such as configurational-bias Monte Carlo (CBMC) or related methods,[21−24] and methods inspired by expanded ensembles[18,25,26] such as the continuous fractional component Monte Carlo (CFCMC) method developed by Shi and Maginn.[27,28] The advantage of the latter approach is that molecules are not inserted in a single trial move such as in

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CBMC but in a gradual way. Therefore, the method does not depend on the occurrence of spontaneous cavities in the system that have the same size as the exchanged molecule. CFCMC is frequently used for computing solubilities of various gases in ionic liquids,[29−36] and this method is often significantly more efficient than CBMC, even for small molecules such as CO_2 and CH_4.[37] The CFCMC approach can also be combined with reaction ensemble Monte Carlo.[38,39] For more details on the challenges of Monte Carlo simulations in open ensembles, the reader is referred to refs 40 and 41.

In the Gibbs ensemble version of CFCMC, the conventional GE is expanded with two fractional molecules per component, one in each simulation box.[28] Interactions of the fractional molecule with the surrounding are scaled by a coupling parameter λ, such that $\lambda = 0$ means no interactions with the surroundings (the fractional molecule is an ideal gas molecule) and $\lambda = 1$ means full interactions with the surroundings (the fractional molecule has the same interactions as other molecules of the same component). The coupling parameters of fractional molecules in two boxes are constrained by $\lambda_{\text{box 1}} + \lambda_{\text{box 2}} = 1$.[28] In addition to conventional trial moves in the GE, attempts are made to change the coupling parameters, using $\lambda_{\text{n,box 1}} = \lambda_{\text{o,box 1}} + \Delta\lambda$. Here, n and o denote the new and old configurations, respectively. Due to the constraint $\lambda_{\text{box 1}} + \lambda_{\text{box 2}} = 1$, the coupling parameter of the fractional molecule in the other simulation box also changes according to $\lambda_{\text{n,box 2}} = \lambda_{\text{o,box 2}} - \Delta\lambda$. When $\lambda_{\text{n,box 1}} > 1$ or $\lambda_{\text{n,box 1}} < 0$, molecule transfer between the simulation boxes occurs. For more details, we refer the reader to the original publications by Shi and Maginn.[28] Although the CFCMC GE algorithm significantly facilitates the exchange of molecules between the simulation boxes, one cannot directly obtain chemical potentials, and hence no direct check for chemical equilibrium is possible. Moreover, due to the constraint $\lambda_{\text{box 1}} + \lambda_{\text{box 2}} = 1$ the two fractional molecules have to adapt to their surrounding molecules simultaneously. This may reduce the efficiency of the method when the density of at least one of the phases is high.

In this work, an alternative formulation for CFCMC GE with only a single fractional molecule per component is introduced. As a proof of principle, our method is tested and validated for Lennard-Jones (LJ) particles and the TIP3P-Ew water model.[42] The reason to choose these simple systems is that conventional GE yields accurate results for coexistence densities and chemical potentials, so a detailed numerical comparison can be made. In the new method, the chemical potential of each box is directly obtained without using test particles and therefore chemical equilibrium between the two phases can be checked directly. We show analytically that the chemical potentials obtained are identical to those in the conventional GE, but no test particles are required and hence the approach will be efficient for dense fluids. Knowledge of the chemical potentials facilitates thermodynamic modeling using the simulation results (e.g., fugacity coefficients and activity coefficient follow directly from the simulations). In addition, the issue regarding how to count the fractional molecule is investigated. When computing average energies and densities, it is best not to count the contribution of the fractional molecule. Our method is now implemented in the RASPA software package.[43]

2. METHODOLOGY

In our new formulation of the CFCMC GE method, we consider a single component system consisting of N_T whole molecules. These molecules are indistinguishable and are referred to as whole molecules as they interact via the full unscaled interaction potential. The total volume V_T of the simulation boxes is fixed while the boxes can exchange volume. Molecules can be distributed between the two simulation boxes. In addition to the N_T whole molecules, there is a single fractional molecule present in the system that is distinguishable from the whole molecules. This fractional molecule can be located in either of the two simulation boxes. The interactions of the fractional molecule with the whole molecules are scaled with a coupling parameter $\lambda \in [0,1]$ (hence the name "fractional molecule"). For the LJ potentials it is convenient to scale interactions as[28]

$$u_{\text{LJ}}(r) = \lambda 4\varepsilon\left(\frac{1}{\left[\frac{1}{2}(1-\lambda)^2 + \left(\frac{r}{\sigma}\right)^6\right]^2} - \frac{1}{\left[\frac{1}{2}(1-\lambda)^2 + \left(\frac{r}{\sigma}\right)^6\right]}\right) \tag{1}$$

Electrostatic interactions are scaled according to[27,28,37]

$$u_{\text{Coul}}(r) = \lambda^5 \frac{1}{4\pi\varepsilon_0}\frac{q_i q_j}{r} \tag{2}$$

where ε_0 is the dielectric constant in vacuum and q_i is the partial charge of atom i. To avoid singularities at low λ, interaction sites that only carry partial charges are protected by adding a blocking radius of 1 Å. Note that other choices for scaling the interactions of fractional molecule are also possible.[44−46]

Following the guidelines presented in the work of Frenkel and Smit[15,47] and Shi and Maginn,[27,28] the partition function of such a system is

$$\begin{aligned} Q_{\text{CFCMC}} = {} & \frac{1}{\Lambda^{3(N_T+1)}(N_T)!}\sum_{i=1}^{2}\sum_{N_1=0}^{N_T}\int_0^1 \mathrm{d}\lambda \\ & \times \int_0^{V_T} \mathrm{d}V_1\, V_1^{N_1+\delta_{i,1}}(V_T - V_1)^{N_T-N_1+\delta_{i,2}}\frac{(N_T)!}{(N_1)!(N_T-N_1)!} \\ & \times \int \mathrm{d}s^{N_1}\exp[-\beta U_{\text{int},1}(s^{N_1})]\int \mathrm{d}s^{N_T-N_1}\exp[-\beta U_{\text{int},2}(s^{N_T-N_1})] \\ & \times (\delta_{i,1}\int \mathrm{d}s^1_{\text{frac}}\exp[-\beta U_{\text{frac},1}(s^1_{\text{frac}}, s^{N_1}, \lambda)] \\ & + \delta_{i,2}\int \mathrm{d}s^2_{\text{frac}}\exp[-\beta U_{\text{frac},2}(s^2_{\text{frac}}, s^{N_T-N_1}, \lambda)]) \end{aligned} \tag{3}$$

in which $\beta = 1/(k_B T)$ and Λ is the thermal wavelength. The parameter i indicates the box in which the fractional molecule is located. $U_{\text{int},j}$ indicates the energy of the indistinguishable whole molecules in box j, and $U_{\text{frac},j}$ indicates the interaction energy of the fractional molecule in box j with the indistinguishable (whole) molecules in box j. The scaled coordinates of molecules are indicated by the symbol s. The function $\delta_{i,j}$ equals 1 when $i = j$ and zero otherwise. Because the fractional molecule can be located in either of the simulation boxes, we need to consider both possibilities in eq 3. In principle, one could reformulate the partition function with more than one fractional molecule per component. This increases the number of combinations in the last term of eq 3, and therefore this is not considered here.

In MC simulation in the GE ensemble, we have three different categories of trial moves: displacement of a randomly selected molecule (including the fractional molecule), volume changes (in such a way that V_T is conserved), and molecule exchanges between the simulation boxes. It is trivial to show that the acceptance rule for molecule displacements is the same as in the conventional GE.[15,48] For volume changes, one should

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take care that the fractional molecule is taken into account. From eq 3, it immediately follows that the acceptance criterion for random volume changes equals[15]

$$\mathrm{acc}(o\rightarrow n) = \min\left(1, \frac{(V_1^n)^{N_1+\delta_{i,1}}(V_T - V_1^n)^{N_T-N_1+\delta_{i,2}}}{(V_1^o)^{N_1+\delta_{i,1}}(V_T - V_1^o)^{N_T-N_1+\delta_{i,2}}} \exp[-\beta\Delta U]\right) \tag{4}$$

in which ΔU is the total energy change resulting from the trial move, and the symbols n and o are used to denote the new and old configurations, respectively. For ergodic sampling of the ensemble of eq 3, three different types of trial moves are devised for exchanging molecules (that are schematically illustrated in Figures 1−3).

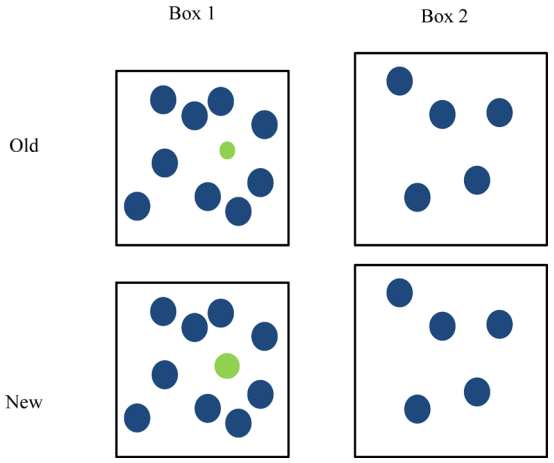

Figure 1. Schematic representation of the trial move attempting to change the coupling parameter, λ, while the fractional molecule stays in the same simulation box. The green sphere is the fractional molecule, and the blue spheres are the whole molecules. In this example, the interactions of the fractional molecule in box 1 are increased. These trial moves are accepted or rejected according to eq 7 (or eq 17 when a weight function is used).

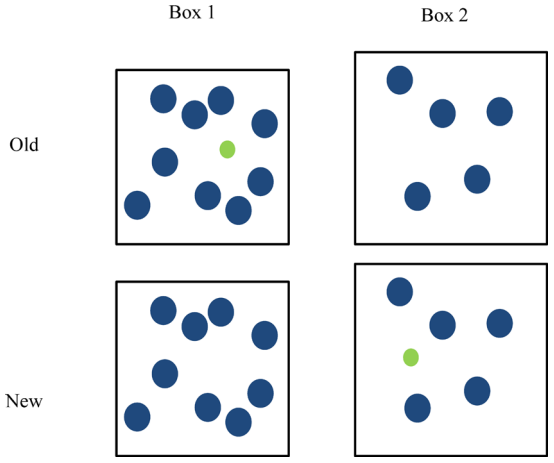

Figure 2. Schematic representation of the trial move attempting to swap the fractional molecule between the simulation boxes. The green sphere is the fractional molecule, and the blue spheres are the whole molecules. In this example, the fractional molecule is moved from box 1 to a randomly selected position in box 2, while keeping the value of λ fixed. These trial moves are accepted or rejected according to eq 11 (or eq 18 when a weight function is used).

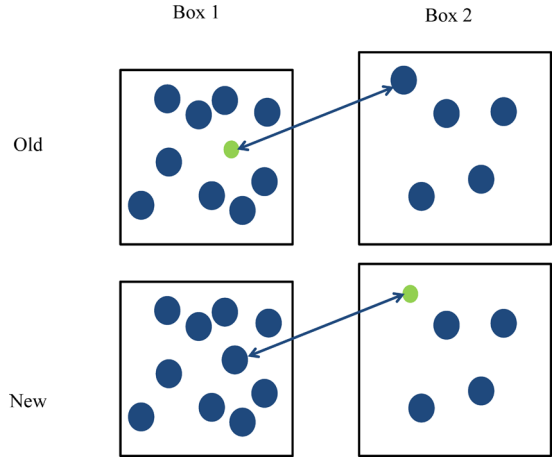

Figure 3. Schematic representation of the trial move attempting to change the fractional molecule into a whole molecule while keeping its position fixed, and, simultaneously, changing a (randomly selected) whole molecule in the other simulation box into a fractional molecule while not changing the value of λ. In this example, the fractional molecule (green sphere) in box 1 is exchanged with a whole molecule in box 2. These trial moves are accepted or rejected according to eq 15 (or eq 19 when a weight function is used).

(1) Changing the parameter λ by adding a uniformly distributed random value from the interval $[-\Delta\lambda,\Delta\lambda]$, while the fractional molecule stays in the same simulation box at the same position (see Figure 1). Assume here that the fractional molecule is in box 1 (the resulting acceptance rule when the fractional molecule is in the other box is similar). Since the parameter λ is constrained to the interval between 0 and 1, trial moves that take λ outside this range are automatically rejected. The probabilities for the system to be in the old (o) and new (n) configurations are respectively

$$\begin{aligned} p_o &= \frac{1}{Q_{\mathrm{CFCMC}}}\frac{1}{\Lambda^{3(N_T+1)}(N_T)!}V_1^{N_1+1}(V_T - V_1)^{N_T-N_1}\frac{(N_T)!}{(N_1)!(N_T-N_1)!} \\ &\quad \times \exp[-\beta U_{\mathrm{int},1}(s^{N_1})]\exp[-\beta U_{\mathrm{int},2}(s^{N_T-N_1})] \\ &\quad \exp[-\beta U_{\mathrm{frac},1}(s_{\mathrm{frac}}, s^{N_1}, \lambda_o)] \\ p_n &= \frac{1}{Q_{\mathrm{CFCMC}}}\frac{1}{\Lambda^{3(N_T+1)}(N_T)!}V_1^{N_1+1}(V_T - V_1)^{N_T-N_1}\frac{(N_T)!}{(N_1)!(N_T-N_1)!} \\ &\quad \times \exp[-\beta U_{\mathrm{int},1}(s^{N_1})]\exp[-\beta U_{\mathrm{int},2}(s^{N_T-N_1})] \\ &\quad \exp[-\beta U_{\mathrm{frac},1}(s_{\mathrm{frac}}, s^{N_1}, \lambda_n)] \end{aligned} \tag{5}$$

in which λ_n is the new value of the coupling parameter and λ_o is the old one. From this it follows that the ratio of these probabilities equals

$$\frac{p_n}{p_o} = \exp[-\beta(U_{\mathrm{frac},1}(s_{\mathrm{frac}}, s^{N_1}, \lambda_n) - U_{\mathrm{frac},1}(s_{\mathrm{frac}}, s^{N_1}, \lambda_o))] \tag{6}$$

and therefore the acceptance rule reduces to the conventional Metropolis acceptance rule[15,48]

$$\begin{aligned} &\mathrm{acc}(o\rightarrow n) \\ &\quad = \min(1, \exp[-\beta(U_{\mathrm{frac},1}(s_{\mathrm{frac}}, s^{N_1}, \lambda_n) - U_{\mathrm{frac},1}(s_{\mathrm{frac}}, s^{N_1}, \lambda_o))]) \\ &\quad = \min(1, \exp[-\beta\Delta U]) \end{aligned} \tag{7}$$

in which ΔU is the energy change resulting from the trial move. It is important to note that the maximum change in λ (denoted by $\Delta\lambda$) can be chosen differently for each simulation box. The value of $\Delta\lambda$ can be much larger in the gas phase than in the liquid phase.

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(2) Swapping the fractional molecule between the simulation boxes, while keeping the value of λ fixed (see Figure 2). The rest of the system is unchanged in this trial move. Assume that the fractional molecule is removed from its current position s_{frac} in box 1 and inserted at a random position s^n_{frac} in box 2. The probabilities to be in the old and new configurations are respectively:

$$p_o = \frac{1}{Q_{\mathrm{CFCMC}}}\frac{1}{\Lambda^{3(N_T+1)}(N_T)!}V_1^{N_1+1}(V_T-V_1)^{N_T-N_1}\frac{(N_T)!}{(N_1)!(N_T-N_1)!} \times \exp[-\beta U_{\mathrm{int},1}(s^{N_1})]\exp[-\beta U_{\mathrm{int},2}(s^{N_T-N_1})]\exp[-\beta U_{\mathrm{frac},1}(s_{\mathrm{frac}}, s^{N_1}, \lambda)] \quad (8)$$

$$p_n = \frac{1}{Q_{\mathrm{CFCMC}}}\frac{1}{\Lambda^{3(N_T+1)}(N_T)!}V_1^{N_1}(V_T-V_1)^{N_T-N_1+1}\frac{(N_T)!}{(N_1)!(N_T-N_1)!} \times \exp[-\beta U_{\mathrm{int},1}(s^{N_1})]\exp[-\beta U_{\mathrm{int},2}(s^{N_T-N_1})] \times \exp[-\beta U_{\mathrm{frac},2}(s^n_{\mathrm{frac}}, s^{N_T-N_1}, \lambda)] \quad (9)$$

The ratio of these probabilities equals

$$\frac{p_n}{p_o} = \frac{V_T-V_1}{V_1}\exp[-\beta(U_{\mathrm{frac},2}(s^n_{\mathrm{frac}}, s^{N_T-N_1}, \lambda) - U_{\mathrm{frac},1}(s_{\mathrm{frac}}, s^{N_1}, \lambda))] \quad (10)$$

and therefore the acceptance probability equals

$$\mathrm{acc}(o\to n) = \min\left(1, \frac{V_T-V_1}{V_1}\exp[-\beta (U_{\mathrm{frac},2}(s^n_{\mathrm{frac}}, s^{N_T-N_1}, \lambda) - U_{\mathrm{frac},1}(s_{\mathrm{frac}}, s^{N_1}, \lambda))]\right) = \min\left(1, \frac{V_T-V_1}{V_1}\exp[-\beta\Delta U]\right) \quad (11)$$

It is important to note that when λ is very small, this equation reduces to

$$\mathrm{acc}(o\to n) = \min\left(1, \frac{V_T-V_1}{V_1}\right) \quad (12)$$

This result is expected, as the distribution of an ideal gas molecule over two volumes equals the ratio of the two volumes.

(3) Changing the fractional molecule into a whole molecule while keeping its position fixed and, simultaneously, changing a (randomly selected) whole molecule in the other simulation box into a fractional molecule, while not changing the value of λ (see Figure 3). Consider here the situation in which the fractional molecule is initially located in box 1. This molecule is transformed into a whole molecule and a randomly selected molecule in box 2 is transformed into a fractional molecule. We can write for the probabilities for being in the old and new configurations respectively

$$p_o = \frac{1}{Q_{\mathrm{CFCMC}}}\frac{1}{\Lambda^{3(N_T+1)}(N_T)!}V_1^{N_1+1}(V_T-V_1)^{N_T-N_1}\frac{(N_T)!}{(N_1)!(N_T-N_1)!} \times \exp[-\beta U_{\mathrm{int},1}(s^{N_1})]\exp[-\beta U_{\mathrm{int},2}(s^{N_T-N_1})] \times \exp[-\beta U_{\mathrm{frac},1}(s^1_{\mathrm{frac}}, s^{N_1}, \lambda)]$$

$$p_n = \frac{1}{Q_{\mathrm{CFCMC}}}\frac{1}{\Lambda^{3(N_T+1)}(N_T)!}V_1^{N_1+1}(V_T-V_1)^{N_T-N_1} \frac{(N_T)!}{(N_1+1)!(N_T-N_1-1)!} \times \exp[-\beta U_{\mathrm{int},1}(s^{N_1+1})]\exp[-\beta U_{\mathrm{int},2}(s^{N_T-N_1-1})] \times \exp[-\beta U_{\mathrm{frac},2}(s^2_{\mathrm{frac}}, s^{N_T-N_1-1}, \lambda)] \quad (13)$$

The ratio of these probabilities equals

$$\frac{p_n}{p_o} = \frac{N_T-N_1}{N_1+1}\exp[-\beta\Delta U] \quad (14)$$

in which ΔU is the energy change of the two simulation boxes due to the trial move. The acceptance probability then becomes

$$\mathrm{acc}(o\to n) = \min\left(1, \frac{N_T-N_1}{N_1+1}\exp[-\beta\Delta U]\right) \quad (15)$$

For λ close to 1, the energy change ΔU is small and hence the acceptance criterion reduces to

$$\mathrm{acc}(o\to n) = \min\left(1, \frac{N_T-N_1}{N_1+1}\right) \quad (16)$$

It is convenient to bias the probability distribution of λ in such a way that the sampled probability distributions $p_i(\lambda)$ are flat and that the fractional molecule is equally likely to be in box 1 and box 2 (in principle by changing the applied bias one could tune this ratio to any desired value). In practice, this is realized by multiplying the statistical weight of each system state by a factor $\exp[W(\lambda,i)]$ (i being the box in which the fractional molecule is located). It is important to note that because the fractional molecule can be located in two boxes, the weight function $W(\lambda,i)$ is a two-dimensional function that depends both on λ and the box the fractional molecule is located in (i). The acceptance criterion for changing the parameter λ (Figure 1) then becomes

$$\mathrm{acc}(o\to n) = \min(1, \exp[-\beta\Delta U + W(\lambda_n, i) - W(\lambda_o, i)]) \quad (17)$$

The acceptance criterion for swapping the fractional molecule (Figure 2) becomes

$$\mathrm{acc}(o\to n) = \min\left(1, \frac{V_T-V_1}{V_1}\exp[-\beta\Delta U + W(\lambda, 2) - W(\lambda, 1)]\right) \quad (18)$$

The acceptance criterion for the trial move of Figure 3 changes to

$$\mathrm{acc}(o\to n) = \min\left(1, \frac{N_T-N_1}{N_1+1}\exp[-\beta\Delta U + W(\lambda, 2) - W(\lambda, 1)]\right) \quad (19)$$

To obtain the correct Boltzmann averages, the ensemble average of an observable X should be computed using

$$\langle X\rangle_{\mathrm{Boltzmann}} = \frac{\langle X\exp[-W(\lambda, i)]\rangle_{\mathrm{modified}}}{\langle\exp[-W(\lambda, i)]\rangle_{\mathrm{modified}}} \quad (20)$$

$W(\lambda,i)$ can be determined iteratively[15] or by the Wang−Landau algorithm.[49,50] The algorithm can be easily extended to mixtures[51] and the NPT version of the Gibbs ensemble.[9] For molecules with intramolecular degrees of freedom, the trial move of Figure 2 can be performed by inserting the fractional molecule at a random position with a random orientation in the new simulation box, while keeping the internal configuration of the molecule the same as in the old configuration. For ergodic sampling, trial moves that attempt to change the internal configuration of flexible molecules should be added to the MC scheme.[15,52,53]

In ref 47, it is shown that the chemical potential of molecules in box i of the conventional GE equals

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$$\mu_i = -k_B T \ln\left\langle \frac{V_i/\Lambda^3}{N_i+1} \exp[-\beta\Delta U_i^+] \right\rangle_{GE} \quad (21)$$

in which ΔU_i^+ is the energy change when a molecule is inserted at a random position in box i. We will show that the term $\left\langle \frac{V_i/\Lambda^3}{N_i+1} \exp[-\beta\Delta U_i^+] \right\rangle_{GE}$ corresponding to the conventional GE can be computed using simulation in the ensemble of eq 3, but without using test particles. This can be done as follows for box 1 (using the brackets $\langle ... \rangle$ to indicate averages in the ensemble of eq 3 and $\langle ... \rangle_{GE}$ to indicate averages in the conventional GE):

$$\begin{aligned}\left\langle \frac{\delta_{\lambda,1}\delta_{i,1}}{V_1/\Lambda^3} \right\rangle &= \frac{1}{Q_{CFCMC}} \frac{1}{\Lambda^{3(N_T+1)}(N_T)!} \\ &\times \sum_{N_1=0}^{N_T} \int_0^{V_T} dV_1\, V_1^{N_1+1} (V_T - V_1)^{N_T-N_1} \frac{(N_T)!}{(N_1)!(N_T-N_1)!} \\ &\times \frac{1}{V_1/\Lambda^3} \int ds^{N_1} \exp[-\beta U_{int,1}(s^{N_1})] \\ &\times \int ds^{N_T-N_1} \exp[-\beta U_{int,2}(s^{N_T-N_1})] \\ &= \frac{1}{Q_{CFCMC}} \frac{1}{\Lambda^{3N_T}(N_T)!} \\ &\times \sum_{N_1=0}^{N_T} \int_0^{V_T} dV_1\, V_1^{N_1} (V_T - V_1)^{N_T-N_1} \frac{(N_T)!}{(N_1)!(N_T-N_1)!} \\ &\times \int ds^{N_1} \exp[-\beta U_{int,1}(s^{N_1})] \\ &\times \int ds^{N_T-N_1} \exp[-\beta U_{int,2}(s^{N_T-N_1})] \end{aligned} \quad (22)$$

$$\begin{aligned}\left\langle \frac{\delta_{\lambda,1}\delta_{i,1}}{N_1+1} \right\rangle &= \frac{1}{Q_{CFCMC}} \frac{1}{\Lambda^{3(N_T+1)}(N_T)!} \\ &\times \sum_{N_1=0}^{N_T} \int_0^{V_T} dV_1\, V_1^{N_1+1} (V_T - V_1)^{N_T-N_1} \frac{(N_T)!}{(N_1)!(N_T-N_1)!} \\ &\times \frac{1}{N_1+1} \int ds^{N_1} \exp[-\beta U_{int,1}(s^{N_1})] \\ &\times \int ds^{N_T-N_1} \exp[-\beta U_{int,2}(s^{N_T-N_1})] \\ &\times \int ds_{frac}^{1} \exp[-\beta U_{frac,1}(s_{frac}^{1}, s^{N_1}, 1)] \\ &= \frac{1}{Q_{CFCMC}} \frac{1}{\Lambda^{3N_T}(N_T)!} \\ &\times \sum_{N_1=0}^{N_T} \int_0^{V_T} dV_1\, V_1^{N_1} (V_T - V_1)^{N_T-N_1} \frac{(N_T)!}{(N_1)!(N_T-N_1)!} \\ &\times \int ds^{N_1} \exp[-\beta U_{int,1}(s^{N_1})] \\ &\times \int ds^{N_T-N_1} \exp[-\beta U_{int,2}(s^{N_T-N_1})] \\ &\times \frac{V_1/\Lambda^3}{N_1+1} \int ds_{frac}^{1} \exp[-\beta U_{frac,1}(s_{frac}^{1}, s^{N_1}, 1)] \end{aligned} \quad (23)$$

In these equations, the notations $\langle \delta_{\lambda,1} \rangle$ and $\langle \delta_{\lambda,0} \rangle$ are used for $\lim_{\lambda \uparrow 1} p_1(\lambda)$ and $\lim_{\lambda \downarrow 0} p_1(\lambda)$, respectively. It is important to note that in the limit where the value of λ approaches one, the fractional molecule is still distinguishable from the whole molecules. Because the partition function of the conventional GE equals[47]

$$\begin{aligned} Q_{GE} &= \frac{1}{\Lambda^{3N_T}(N_T)!} \sum_{N_1=0}^{N_T} \int_0^{V_T} dV_1\, V_1^{N_1} (V_T - V_1)^{N_T-N_1} \frac{(N_T)!}{(N_1)!(N_T-N_1)!} \\ &\times \int ds^{N_1} \exp[-\beta U_{int,1}(s^{N_1})] \int ds^{N_T-N_1} \exp[-\beta U_{int,2}(s^{N_T-N_1})] \end{aligned} \quad (24)$$

we have

$$\frac{\left\langle \frac{\delta_{\lambda,1}\delta_{i,1}}{N_1+1} \right\rangle}{\left\langle \frac{\delta_{\lambda,0}\delta_{i,1}}{V_1/\Lambda^3} \right\rangle} = \left\langle \frac{V_1/\Lambda^3}{N_1+1} \exp[-\beta\Delta U_i^+] \right\rangle_{GE} \quad (25)$$

and therefore

$$\mu_{CFCMC,1} = -k_B T \ln\left(\frac{\left\langle \frac{\delta_{\lambda,1}\delta_{i,1}}{N_1+1} \right\rangle}{\left\langle \frac{\delta_{\lambda,0}\delta_{i,1}}{V_1/\Lambda^3} \right\rangle} \right) \quad (26)$$

This means that the chemical potential in box 1 for CFCMC GE simulations directly follows from the probabilities that λ approaches zero or one and that the obtained result is identical to that in the conventional GE. For sufficiently large systems, the volume and number of whole molecules in box 1 is uncorrelated to the value of λ and hence eq 26 reduces to

$$\mu_{CFCMC,1} \approx -k_B T \ln\left(\frac{\left\langle \frac{\delta_{i,1}}{N_1+1} \right\rangle}{\left\langle \frac{\delta_{i,1}}{V_1/\Lambda^3} \right\rangle} \right) - k_B T \ln\left(\frac{p_1(\lambda \uparrow 1)}{p_1(\lambda \downarrow 0)} \right) \quad (27)$$

$$\approx -k_B T \ln\left\langle \frac{V_1/\Lambda^3}{N_1+1} \right\rangle - k_B T \ln\left(\frac{p_1(\lambda \uparrow 1)}{p_1(\lambda \downarrow 0)} \right) \quad (28)$$

Equation 28 is identical to the chemical potential obtained by thermodynamic integration in the canonical ensemble.[40,54,55] Since $p_i(\lambda)$ can be steep for the liquid phase in the region $\lambda \approx 1$, extrapolation to $\lambda \rightarrow 1$ may be required. We found that in practice a linear extrapolation is sufficiently accurate.

For computing ensemble average energies and densities of the simulation boxes, it is not obvious how to deal with the fractional molecule. For example, consider a system with N_1 molecules and the fractional molecule in box 1. One could define the instantaneous density as N_1/V_1, but also as $(N_1+\lambda)/V_1$, or, in general as $(N_1+f(\lambda))/V_1$ in which $f(\lambda)$ is an arbitrary function of λ. Similarly, for the average energy of the total system we can compute the ensemble average of the quantity $[U_{int}+g(\lambda)]$ in which $g(\lambda)$ is a similar arbitrary function. At the first sight, logical choices may be to set $g(\lambda) = U_{frac}$ or $g(\lambda) = 0$. With these general definitions of the ensemble average loading and total energy, it is instructive to consider the change in the average number of molecules in one of the boxes when the temperature is increased. In the CFCMC GE we can write[48]

$$\begin{aligned}\frac{\partial\langle N_1 + f(\lambda)\rangle}{\partial\beta} &= \langle N_1 + f(\lambda)\rangle\langle U_{int} + U_{frac}\rangle \\ &- \langle (N_1 + f(\lambda))(U_{int} + U_{frac})\rangle \end{aligned} \quad (29)$$

and in the same way

$$\begin{aligned}\frac{\partial\langle U_{int} + g(\lambda)\rangle}{\partial\beta} &= \langle U_{int} + g(\lambda)\rangle\langle U_{int} + U_{frac}\rangle \\ &- \langle (U_{int} + g(\lambda))(U_{int} + U_{frac})\rangle \end{aligned} \quad (30)$$

Combining these equations we obtain

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Table 1. Coexistence Densities and Chemical Potentials for Vapor−Liquid Equilibria of LJ Particles for Different System Sizes and Reduced Temperatures Computed with the Conventional GE and the Proposed CFCMC GE Methods[a]

	GE				CFCMC GE			
T	ρ_l	ρ_g	μ_l	μ_g	ρ_l	ρ_g	μ_l	μ_g
				$N_T = 256$				
0.7	0.788(2)	0.0074(1)	−3.52(1)	−3.51(1)	0.786(2)	0.0074(2)	−3.52(2)	−3.52(2)
0.8	0.731(1)	0.0198(2)	−3.34(1)	−3.34(1)	0.729(1)	0.0198(3)	−3.35(1)	−3.35(1)
0.9	0.664(1)	0.0450(3)	−3.20(1)	−3.20(1)	0.662(1)	0.0451(5)	−3.21(1)	−3.22(1)
0.95	0.623(1)	0.0659(8)	−3.14(1)	−3.14(1)	0.621(1)	0.0660(8)	−3.15(1)	−3.16(1)
				$N_T = 512$				
0.7	0.788(2)	0.0074(1)	−3.52(1)	−3.52(1)	0.786(1)	0.0075(1)	−3.52(1)	−3.52(1)
0.8	0.731(1)	0.0199(1)	−3.34(1)	−3.33(1)	0.730(1)	0.0199(3)	−3.34(1)	−3.34(1)
0.9	0.664(1)	0.0451(2)	−3.20(1)	−3.20(1)	0.663(1)	0.0449(2)	−3.21(1)	−3.21(1)
0.95	0.624(1)	0.0661(6)	−3.14(1)	−3.14(1)	0.623(1)	0.0665(4)	−3.14(1)	−3.15(1)

[a]Numbers in brackets are uncertainties in the last digit, i.e., −3.52(1) means −3.52 ± 0.01. A weight function was used in the CFCMC GE simulations to flatten the probability distribution of the coupling parameter λ and to ensure that the fractional molecule is equally likely to be in both simulation boxes. The total volume $V_T = 2 \times 8^3$ for $N_T = 256$ and 2×10^3 for $N_T = 512$.

$$\frac{\partial\langle U_{int} + g(\lambda)\rangle}{\partial\langle N_1 + f(\lambda)\rangle} = \frac{\langle U_{int} + g(\lambda)\rangle\langle U_{int} + U_{frac}\rangle - \langle (U_{int} + g(\lambda))(U_{int} + U_{frac})\rangle}{\langle N_1 + f(\lambda)\rangle\langle U_{int} + U_{frac}\rangle - \langle (N_1 + f(\lambda))(U_{int} + U_{frac})\rangle} \quad (31)$$

This partial derivative is related to the total energy change when an additional molecule is present in box 1. Consider the case in which there is an external field present in box 1, and that the interactions of molecules (including the fractional one) with the field are much stronger than the intermolecular interactions. A typical example of this would be the presence of a porous host structure such as a zeolite in box 1, and a low number of molecules in box 1, so that intermolecular interactions are much weaker than interactions with the field. In this situation, U_{int} is independent from U_{frac}, $f(\lambda)$, and $g(\lambda)$ and N_1 is independent from $f(\lambda)$. Subsequently, eq 31 reduces to

$$\frac{\partial\langle U_{int} + g(\lambda)\rangle}{\partial\langle N_1 + f(\lambda)\rangle} = \frac{\langle U_{int}\rangle^2 - \langle U_{int}{}^2\rangle + \langle g(\lambda)\rangle\langle U_{frac}\rangle - \langle g(\lambda)U_{frac}\rangle}{\langle N_1\rangle\langle U_{int}\rangle - \langle N_1U_{int}\rangle + \langle f(\lambda)\rangle\langle U_{frac}\rangle - \langle f(\lambda)U_{frac}\rangle} \quad (32)$$

It is important to note that the terms $[\langle g(\lambda)\rangle\langle U_{frac}\rangle - \langle g(\lambda) U_{frac}\rangle]$ and $[\langle f(\lambda)\rangle\langle U_{frac}\rangle - \langle f(\lambda) U_{frac}\rangle]$ are not equal to zero (except for the trivial case $f(\lambda) = 0$, $g(\lambda) = 0$). Similarly, from the partition function of the conventional GE, (eq 24) we can derive the change in energy when a molecule is added to box 1[48]

$$\frac{\partial\langle U_{int}\rangle_{GE}}{\partial\langle N_1\rangle_{GE}} = \frac{\langle U_{int}\rangle_{GE}{}^2 - \langle U_{int}{}^2\rangle_{GE}}{\langle N_1\rangle_{GE}\langle U_{int}\rangle - \langle N_1U_{int}\rangle_{GE}} \quad (33)$$

For sufficiently large systems, ensemble averages computed in the conventional GE and the CFCMC GE will be identical. This means that the most logical choice is to set $f(\lambda) = 0$ and $g(\lambda) = 0$, because the computed values of $\partial U/\partial N_1$ will be identical in both ensembles and eq 31 reduces to eq 33. Hence, when computing average energies and the number of molecules, the fractional molecule should be excluded.

3. SIMULATION DETAILS

As a proof of principle, simulations are performed in the conventional GE and the proposed CFCMC GE to study the vapor−liquid equilibria of Lennard-Jones particles. All properties are defined in reduced units (i.e., the Lennard-Jones parameters σ and ϵ are set as units of length and energy, respectively), and for convenience the thermal wavelength Λ is set to 1.[15] The interactions are truncated and shifted at 2.5σ. Interactions of the fractional molecule are scaled according to eq 1. Two system sizes (256 and 512 molecules) and four reduced temperatures (T = 0.7, 0.8, 0.9, and 0.95) are considered. The weight function is determined iteratively such that the probability distributions $p_i(\lambda)$ in the proposed CFCMC GE ensemble are flat and the fractional molecule is equally likely to be in the two simulation boxes. Ensemble averages are computed using eq 20, and the fractional molecule is not counted when computing average densities. Simulations are started with 0.2 million Monte Carlo cycles to equilibrate the system, followed by 2 million production cycles. The number of Monte Carlo steps per cycle equals the total number of molecules in the system, with a minimum of 20. In each Monte Carlo step, a trial move is selected at random with the following probabilities: 1% volume changes, 49.5% molecule displacements, and 49.5% molecule exchanges. In the conventional GE, there is only one type of trial move for molecule exchange. In contrast, the proposed CFCMC GE requires three types of trial moves for facilitating molecule transfers: 50% changes in the λ space (Figure 1), 25% swapping the fractional molecule to the other simulation box (Figure 2), and 25% changing the fractional molecule with a whole molecule in the other simulation box (Figure 3). Maximum displacements in volume, positions, and λ were set such that on average 50% of the trial moves are accepted. To store the probability distribution of λ, 100 bins are used. In the CFCMC GE method, the chemical potentials of the two simulation boxes are computed from eq 27. In the conventional GE, the chemical potentials are computed from the average energy change during particle insertions (eq 21).[47]

To validate the proposed method for systems with partial charges, the VLE of the TIP3P-Ew water model at three different temperatures (400, 450, and 473 K) is investigated. The TIP3P-Ew is a rigid water model with three point charges optimized for the Ewald summation.[42] A cutoff radius of 13 Å is used for both Lennard-Jones and electrostatic interactions. LJ interactions are truncated and smoothed, and no tail corrections are used. The Ewald summation with a relative precision of 10^{-6} is used for the electrostatic interactions. Typically, around 800 water molecules are distributed over the

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Table 2. Acceptance Probabilities for the Molecule Exchange Trial Moves in the Conventional GE and the CFCMC GE Methods for Different Reduced Temperatures and System Sizes, For the Simulations Reported in Table 1 (LJ Particles)[a]

	N_T = 256		N_T = 512	
T	$P_{acc}(\text{swap})_{GE}$	$P_{acc}(\text{change})_{CFCMC\ GE}$	$P_{acc}(\text{swap})_{GE}$	$P_{acc}(\text{change})_{CFCMC\ GE}$
0.7	8.93×10^{-4}	4.20×10^{-1}	9.12×10^{-4}	4.38×10^{-1}
0.8	3.59×10^{-3}	4.66×10^{-1}	3.60×10^{-3}	4.76×10^{-1}
0.9	1.18×10^{-2}	4.96×10^{-1}	1.17×10^{-2}	5.04×10^{-1}
0.95	2.07×10^{-2}	5.00×10^{-1}	2.04×10^{-2}	5.12×10^{-1}

[a]The acceptance probabilities of swap trial moves in the conventional GE are compared to the acceptance probabilities of exchanging the fractional molecule with a whole molecule in the other simulation box (Figure 3), using the proposed CFCMC GE method (eq 19). A weight function was used in the CFCMC GE simulations to flatten the probability distribution of the coupling parameter λ and to ensure that the fractional molecule is equally likely to be in both simulation boxes.

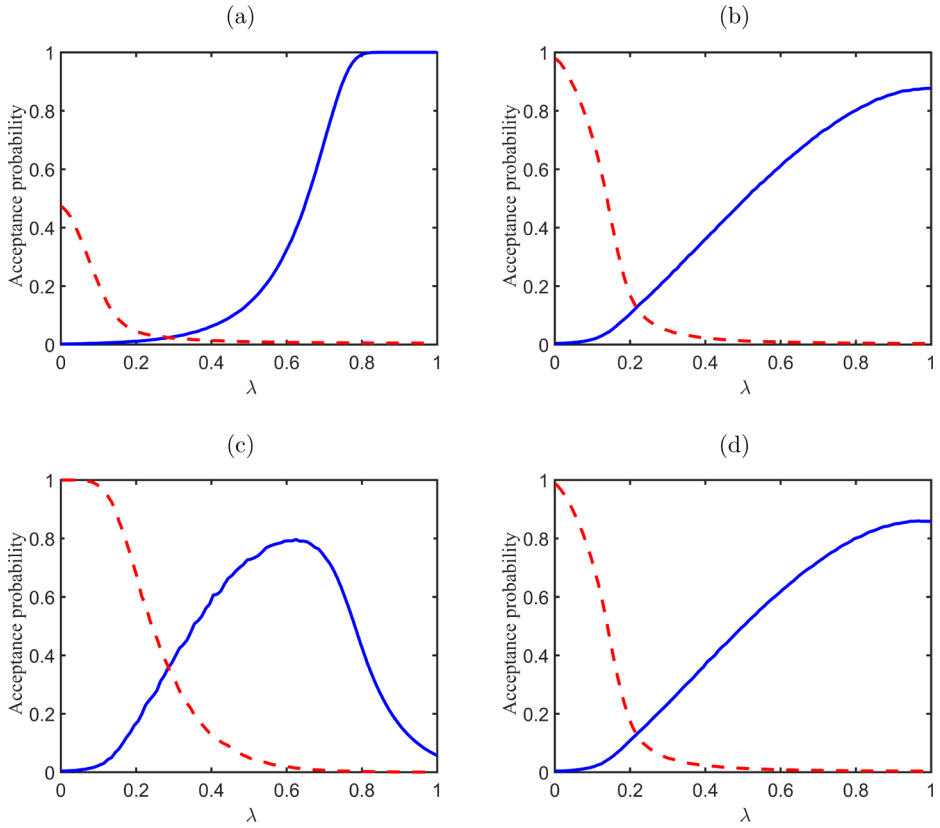

Figure 4. Acceptance probabilities for swapping the fractional LJ molecule between the two simulation boxes, while keeping λ constant (dashed line, Figure 2), and changing the fractional molecule with a randomly chosen whole molecule in the other simulation box (solid line, Figure 3) as a function of λ, for CFCMC GE at T = 0.8: (a) without weight function ($W(\lambda,i)$ = 0), fractional molecule in the gas phase (old configuration); (b) with weight function such that the observed distribution of λ is flat, fractional molecule in the gas phase (old configuration); (c) without weight function ($W(\lambda,i)$ = 0), fractional molecule in the liquid phase (old configuration); (d) with weight function such that the observed distribution of λ is flat, fractional molecule in the liquid phase (old configuration).

two simulation boxes. Additional trial moves to rotate water molecules are used. Simulations are started with 0.1 million equilibration cycles followed by 2 million production cycles. To store the probability distributions of λ, 41 bins are used. Uncertainties reported for the chemical potential of water include the uncertainties due to extrapolation to $\lambda \rightarrow 1$ as well. The value of the thermal wavelength Λ is set to 1 Å for all temperatures.

4. RESULTS

4.1. Lennard-Jones Particles. In Table 1, the average densities and chemical potentials of the two coexisting phases computed using the conventional GE and the proposed CFCMC GE are compared. The values obtained from the two methods are in excellent agreement. This comparison shows that the algorithm is correctly implemented. The chemical potential computed from eqs 26 to 28 yield nearly identical values (not shown). We have confirmed numerically that CFCMC GE simulation results do not depend on the weight function. The easiest way to compare the efficiency of the two approaches is to compare the acceptance probabilities for exchanging molecules between the two simulation boxes. In Table 2, the acceptance probability for the exchange trial move in the conventional GE (moving one molecule from one simulation box to the other) is compared to the probability of changing the fractional molecule into a whole molecule while keeping its position fixed, and, at the same time, changing a (randomly selected) whole molecule in the other simulation

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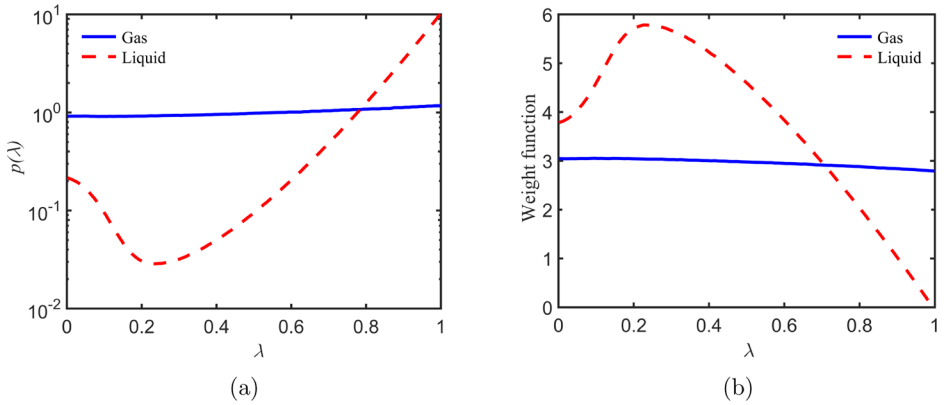

Figure 5. (a) Probability distribution of λ for the gas and the liquid phases as used in CFCMC GE of LJ particles at $T = 0.8$; (b) weight functions to flatten the corresponding probability distributions of λ (as in panel a) and to ensure that the fractional molecule is equally likely to be in both simulation boxes.

Table 3. Coexistence Densities and Chemical Potentials for Vapor−Liquid Equilibria of TIP3P-Ew Water for Different Temperatures, Computed with the Conventional GE and the Proposed CFCMC GE Method[a]

GE					
T/K	ρ_l/(kg m^{-3})	ρ_g/(kg m^{-3})	μ_l/(kJ mol^{-1})	μ_g/(kJ mol^{-1})	$P_{acc}(\text{swap})_{GE}$
400	882(2)	1.7(1)	−32.0(2)	−33.1(1)	2.86×10^{-3}
450	798(2)	6.8(1)	−32.2(8)	−32.9(2)	6.83×10^{-3}
473	754(5)	12.2(5)	−32.4(7)	−33.0(3)	9.52×10^{-3}
CFCMC GE					
T/K	ρ_l/(kg m^{-3})	ρ_g/(kg m^{-3})	μ_l/(kJ mol^{-1})	μ_g/(kJ mol^{-1})	$P_{acc}(\text{change})_{CFCMC\ GE}$
400	882(2)	1.7(1)	−33.2(6)	−33.0(1)	7.75×10^{-2}
450	798(2)	6.7(1)	−33.3(5)	−32.8(1)	8.71×10^{-2}
473	753(2)	12.2(2)	−33.4(5)	−32.9(1)	1.01×10^{-1}

[a]The acceptance probabilities of swap trial moves in the conventional GE are compared to the acceptance probabilities of exchanging the fractional molecule with a whole molecule in the other simulation box (see Figure 3). Numbers in brackets are uncertainties in the last digit, i.e., 882(2) means 882 ± 2. A weight function was used in the CFCMC GE simulations to flatten the probability distribution of the coupling parameter λ and to ensure that the fractional molecule is equally likely to be in both simulation boxes. The total number of water molecules in the simulations is typically around 800. The value of the thermal wavelength Λ is set to 1 Å for all temperatures.

box into a fractional molecule, while not changing the value of λ (Figure 3). These trial moves both result in the exchange of whole molecules between the simulation boxes. The data presented in Table 2 show that the acceptance probability for exchanging molecules between the two simulation boxes is considerably higher when the proposed CFCMC GE is used (more than 2 orders of magnitude at $T = 0.7$). In other words, molecule exchange between the two simulation boxes is significantly facilitated in the proposed CFCMC GE approach. When insertions/deletions are considered as the bottleneck of the simulations, using CFCMC GE instead of conventional GE increases the efficiency of the simulation significantly. The average acceptance probability for the change trial move in CFCMC GE (Figure 3) is slightly reduced from ca. 0.4 to ca. 0.2 when $W(\lambda,i) = 0$, showing that an appropriate biasing improves the efficiency of the method.

In Figure 4, the acceptance probabilities of swapping the fractional molecule between the two simulation boxes (Figure 2) and exchanging the fractional with a randomly chosen whole molecule in the other simulation box (Figure 3) are plotted as a function of the coupling parameter λ. No biasing was used in Figure 4a,c. In comparison, the probability distribution of λ was flattened by adding a weight function; see Figure 4b,d. Without biasing and λ being close to 0, almost 50% of the attempts to swap the fractional molecule from the gas phase to the liquid phase are accepted. We verified that this ratio is exactly equal to the ratio of the volumes of the two boxes; see eq 12. By increasing the coupling parameter λ, interactions of the fractional molecule with the surrounding molecules increase and therefore this trial move becomes more similar to the swap trial move in conventional GE. It is not surprising that the acceptance probability for swapping the fractional molecule reduces when the value of the coupling parameter is increased. When no biasing is used and λ is close to 1, all attempts to change the fractional molecule in the gas phase into a whole molecule and simultaneously changing a whole molecule in the liquid phase into a fractional molecule are accepted. This is due to the fact that the energy change associated with this trial move is almost zero when λ is close to 1. Therefore, the acceptance rule reduces to eq 16, and since more molecules are present in the liquid phase, this trial move is always accepted. When λ is close to 0, the energy change associated with this trial move is almost identical to the energy change associated with a swap trial move in conventional GE. Hence, such a trial move is rarely accepted at λ close to 0. In Figure 4, the acceptance probabilities of the same trial moves are plotted as a function of λ, in the case where the fractional molecule is initially located in the liquid phase. The acceptance probability for the change trial move (Figure 3) first increases and subsequently decreases with increasing coupling parameter. When λ is close to 0, surrounding molecules in the liquid phase are very closely positioned to the fractional molecule. As a

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result, changing the fractional molecule into a whole molecule leads to repulsive interactions between the new whole molecule and surrounding molecules. As a consequence, this trial move is rarely accepted for λ close to 0. By increasing λ, the effective volume occupied by the fractional molecule increases, and changing it to a whole molecule results in less repulsive and more attractive interactions. For large values of λ, the energy change associated with this trial move is limited and the prefactor in eq 15 becomes increasingly important. As a result, for high values of λ, the acceptance probability of the change trial move (with fractional molecule initially in the liquid phase) reduces.

In Figure 5, the probability distributions of λ ($p_i(\lambda)$) and the optimized weight functions for the gas and the liquid phase are shown. The shape of $p_i(\lambda)$ is similar to the original CFCMC GE formulation.[28] The weight function for the gas phase is almost independent of the value of λ. This is due to the fact that the average distance between molecules in the gas phase is much larger than in the liquid phase. We verified that changing V_T in the simulations only results in a shift of the weight functions, while their shape remains the same. From Figure 5 it becomes clear that maximum changes in λ can be much larger in the gas phase than in the liquid phase, and this is an advantage compared to the original CFCMC GE formulation with two fractional molecules. In the acceptance rule for the changing and swapping the fractional molecule (eqs 18 and 19), the term "$\exp[W(\lambda,2) - W(\lambda,1)]$" accounts for the biasing. Graphically, this corresponds to the difference between the weight functions in Figure 5b at a constant value of λ. From Figure 4, it is clear that this biasing significantly enhances molecule transfers.

4.2. Water. In Table 3, the average densities and chemical potentials computed using the conventional GE and the proposed CFCMC GE method for the two coexisting phases of TIP3P-Ew water at different temperatures are compared. Values obtained with the two approaches are in excellent agreement, showing the applicability of the proposed method for systems with partial charges. For liquid water, the computed excess chemical potential at 400 K equals 21.5 kJ mol^{-1}, which agrees very well with the value of 21.8 kJ mol^{-1} reported in ref 56. In Table 3, the acceptance probabilities for the swap move in the conventional GE are compared with the acceptance probabilities of the change move (Figure 3) in the proposed CFCMC GE. It is clear that the particle exchange between the two simulation boxes is significantly improved by using the proposed CFCMC GE instead of the conventional GE.

5. CONCLUSION

We introduced an alternative formulation for the Gibbs ensemble (GE) combined with the continuous fractional component Monte Carlo (CFCMC) method. The main advantages of this method over the original formulation of CFCMC GE by Shi and Maginn[28] are (1) the direct calculation of chemical potentials in both simulation boxes, without the use of test particles; (2) the biasing is applied to each simulation box independently; and (3) the maximum change of the λ parameter ($\Delta\lambda$) can be different for each simulation box. We verified our method for a system of LJ particles and molecules with partial charges (water using the TIP3P-Ew force field). Densities and chemical potentials obtained with the proposed method are in excellent agreement with those computed in the conventional GE. We showed that the CFCMC GE significantly increases the acceptance probability for exchanging molecules between the two simulation boxes and that the use of appropriate weight functions can facilitate molecule exchanges further. It was shown that it is best not to count the fractional molecule while computing averages such as the average energy per molecule and the density. Our approach can easily be extended to mixtures and molecules with intramolecular interactions. For the latter systems, one could consider using molecular dynamics to sample the degrees of freedom of each simulation box, while using the three proposed trial moves for molecule transfers. The simulation method is now implemented in the RASPA software package.[43]

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Notes

The authors declare no competing financial interest.

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