MOLECULAR SIMULATION OF PHASE EQUILIBRIA

ATHANASSIOS Z. PANAGIOTOPOULOS
School of Chemical Engineering
Cornell University
Ithaca, NY 14853-5201 U.S.A.

ABSTRACT. This chapter presents an introduction to the rapidly expanding field of molecular simulation methodologies for calculations of fluid-phase coexistence, with particular emphasis on high pressure and supercritical systems. The first part of the chapter deals with methodological issues. The focus is on Monte-Carlo techniques for the determination of free energies and phase equilibria. Particle insertion techniques are first briefly discussed. The Gibbs ensemble Monte Carlo method is then covered in detail. While the original method is applicable primarily to simple model potentials, recently developed configurational-bias sampling techniques allow the study of a broad range of systems. The second part of the chapter reviews applications of molecular simulation techniques to systems of interest for supercritical processes. Phase diagrams of pure components, including water, hydrocarbons, ionic and polymeric fluids are first discussed. Studies of simple mixtures reveal that conformal solution theories have a significantly greater range of applicability than previously thought. The chapter concludes with a discussion of the future promise and limitations of molecular simulation techniques for the study of fluid phase equilibria.

1. Introduction

The focus of this chapter is on molecular simulation of phase equilibria. The phase behavior of a system is typically the most crucial piece of information needed for modeling processes involving supercritical fluids. More generally, the need for accurate description of phase equilibria for the multicomponent fluid mixtures that are encountered in chemical processes has been the main driving force for the development of chemical engineering thermodynamics over the past fifty years. As a result, high-quality experimental data and good modeling techniques are now available for many classes of mixtures. Particularly useful for supercritical fluids are equation-of-state methods described in detail in the chapter by S. Sandler in this book. Nevertheless, mixtures such as aqueous or highly polar systems at elevated pressures, systems containing polymeric molecules, ionic solutions, associating fluids and solutions with amphiphilic molecules present significant difficulties. Even for systems for which current modeling techniques are adequate, the models are mostly phenomenological, relying on regression of experimental data for determination of their parameters. The models cannot be extrapolated with confidence to conditions outside the range of experimental measurements.

——————————————

The lack of accurate predictive techniques severely limits the ability of engineers to propose innovative solutions to old or new problems. For example, a promising process for the destruction of aqueous wastes is supercritical water oxidation that relies on the reaction of organic contaminants with oxygen at pressures and temperatures above the critical point of water, discussed in the chapter by G. Brunner in this book. Process design and successful scale-up without excessive pilot plant trials requires modeling techniques that can deal with aqueous/organic mixtures at high temperatures and pressures. Equations of state presently available rely on experimental data to obtain the binary mixture parameters. Experimental data for these systems, however, are scarce and expensive to measure.

An attractive alternative to conventional engineering modeling techniques is large-scale molecular simulations starting from an assumed intermolecular potential model between the components of interest. Referring to the schematic diagram of Figure 1, molecular simulation methods provide an intermediate layer between direct experimental measurements and engineering models. The latter rely on assumptions about the intermolecular forces as well as theoretical approximations (such as mixing rules for equations of state) to render the statistical mechanics tractable. Because fewer approximations are made, molecular simulation methods can provide results applicable over wider ranges of process conditions and transferable from one set of conditions to another (e.g. predicting high pressure fluid-fluid equilibria from parameters determined from low-pressure vapor-liquid measurements).
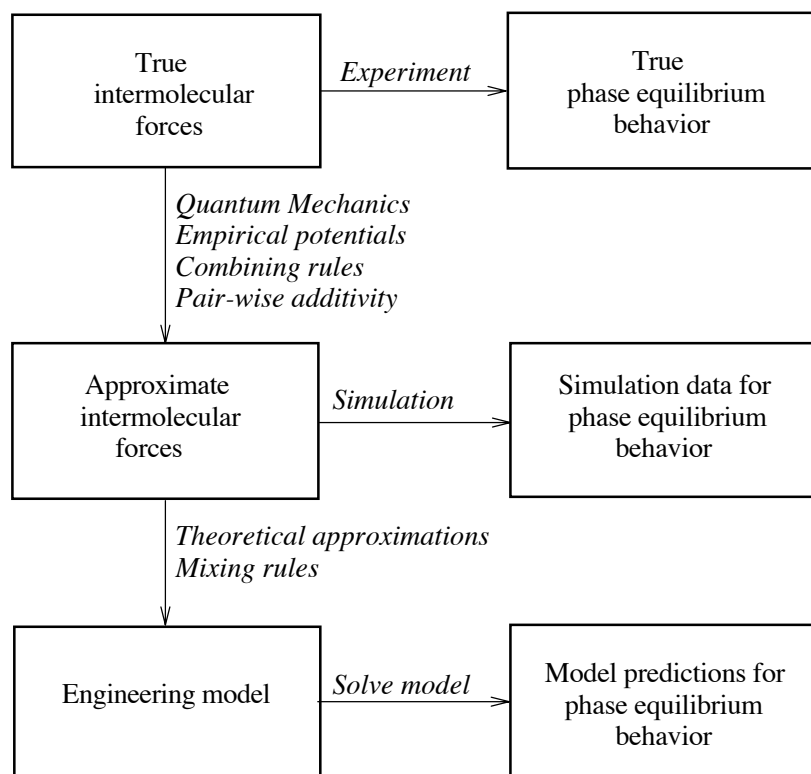

Figure 1. Relationships between engineering and molecular simulation-based predictions of phase equilibria.

In addition to their utility as a means of modeling experimental data, molecular simulations are also useful for providing accurate data for comparisons with approximate theoretical techniques. For example, integral-equation methods discussed in the chapters by Lee, Cummings, Meroni and Lomba have found widespread applications in supercritical fluid modeling. The validity of closure relationships and the accuracy of the calculated thermodynamic and structural properties can be established by comparisons of results of simulations and integral equation theories for the same model potentials.

The possibility for calculating phase equilibria by simulation has existed from the early days of computer simulation, but has been until recently impractical for multicomponent systems due to the large number of simulations required and the significant uncertainties associated with the calculations. A number of recent developments have greatly expanded the range of systems that can be practically studied by simulation. The Gibbs ensemble Monte Carlo simulation technique [1] is perhaps the most frequently used current technique for the calculation of phase equilibria in multicomponent fluid mixtures.

It is of interest to compare the relative costs of experimental, simulation-based and theoretical determination of phase equilibria. For a single coexistence point for a binary fluid mixture, the recent review of Gubbins [2] gives a cost of $2,600 and 2 days of a trained scientist's time for experimental measurement, $30 and 35 CPU hours for a Gibbs ensemble simulation of a 2-site Lennard-Jones model, and very little cost or time for applying an engineering correlation. While these figures are approximate, the *relative* cost of simulation versus experiment seems reasonable. Simulation can of course never replace experiment as a truly reliable source of data, but the rapidly expanding computing capabilities justify optimism for an increased role of phase equilibrium simulations in engineering practice.

There are two main classes of molecular simulation techniques, namely molecular dynamics and Monte Carlo methods. Molecular dynamics methods are based on solving the time-evolution equations for a system and can be used for the determination of transport properties and time correlation functions. Molecular dynamics simulations of near-critical and supercritical fluids are discussed in the chapter by Cummings in this book. The focus of the present chapter is on Monte Carlo techniques. Molecular simulation methods are covered in significantly more detail than is possible in the present book by the standard textbook in the field, Allen and Tildesley [3]. Recent progress in the field is summarized in the proceedings of a NATO School devoted to computer simulation [4]. A recent review of applications of molecular simulation to supercritical extraction is also available [5] with a somewhat different emphasis from the present chapter.

The structure of the chapter is as follows. The first half of the chapter is primarily methodological. An introduction to importance sampling Monte Carlo is given, followed by brief descriptions of the main methods available for the determination of free energies and phase equilibria. Interfacial simulations, particle insertion and thermodynamic integration methods are covered. The Gibbs ensemble methodology for direct determination of fluid phase equilibria is then described in detail. The recently proposed Gibbs-Duhem integration method for obtaining phase diagrams without particle insertions is also discussed. The section on methodology closes with a discussion of specialized techniques designed to deal with multisegment, polymeric and associating systems. The remainder of the chapter is devoted to a review of applications to date of molecular simulation techniques to systems of interest for supercritical processes. Phase diagrams of pure components, including water and hydrocarbon systems are first discussed. Recently determined phase diagrams at high pressures for pure ionic and polymeric fluids are also covered. Studies of binary and multicomponent simple mixtures reveal that simple

conformal solution theories have a significantly greater range of applicability than previously thought. The chapter concludes with a discussion of the future promise and limitations of molecular simulation techniques for the study of fluid phase equilibria.

2. Molecular Simulation Methodologies for Calculating Phase Equilibria

2.1. INTERMOLECULAR POTENTIAL MODELS AND PERIODIC BOUNDARY CONDITIONS

A recent review of intermolecular potential models useful for condensed phase simulations is available [6]. In the present section, we can offer only a brief summary of a few basic concepts. For most simulations of systems of interest to chemical engineers classical intermolecular potentials are used and quantum effects are ignored. In real fluids, three-body forces contribute significantly to the configurational energy of condensed phases [7]. However, simulations using fully explicit three-body potentials are still prohibitively expensive in terms of computational resources required, as the number of interactions that need to be calculated is proportional to the third power of the number of interactions centers. For this reason, it is common practice to utilize simplified potentials that are "effective pair-wise additive." What the last terms means is that three-body forces are effectively incorporated in the potential parameters, which do not represent the actual forces acting between a pair of isolated molecules in vacuum.

Many common intermolecular potential models contain terms of the Lennard-Jones type,

$$U_{ij}(r) = 4\varepsilon_{ij}\left[\left(\frac{\sigma_{ij}}{r}\right)^{12} - \left(\frac{\sigma_{ij}}{r}\right)^{6}\right], \tag{1}$$

where U_{ij} is the configurational energy of interaction between centers i and j located at a distance r, and ε_{ij} and σ_{ij} characteristic energy and size parameters for the ij interactions. This potential, although not a good representation of the actual intermolecular potential for any particular substance or pair of substances [7] enjoys continued popularity for reasons of computational simplicity and because of the availability of a large body of results for its properties.

More realistic potentials are often constructed by using multiple interaction centers, often of the Lennard-Jones type, to describe molecules that deviate significantly from spherical shape. For polar molecules, dipole, quadrupole and charge interaction terms can also be added. As an illustration of the type of intermolecular potential models used for water, we show in Figure 2 the Simple Point Charge (SPC) model for water [8] for which we later present phase equilibrium results obtained from molecular simulations. The model contains a single Lennard-Jones interaction center located on the oxygen atom and partial fixed charges on the oxygen and hydrogen atoms. Realistic potentials for multisegment molecules such as hydrocarbons often contain terms to describe internal molecular flexibility. Such terms could include bond bending or, less commonly, bond stretching energies, and torsional potentials that are periodic functions of the dihedral angle defined by four consecutive carbon atoms.

$$q(O) = -0.82 \text{ esu}$$
$$q(H) = 0.41 \text{ esu}$$
$$\varphi(HOH) = 109.47°$$
$$r(OH) = 1.0 \text{ Å}$$
$$\varepsilon(OO) = 0.155 \text{ kcal / mol}$$
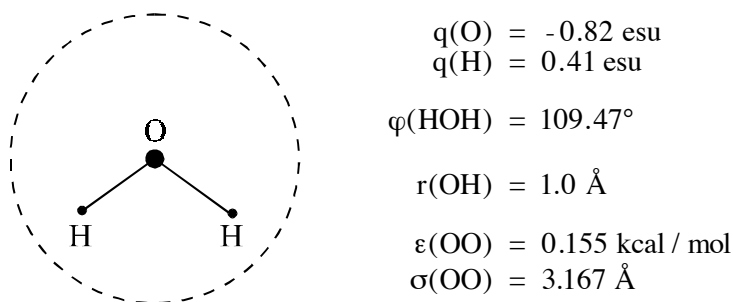$$\sigma(OO) = 3.167 \text{ Å}$$

Figure 2. SPC model of water [8].

No matter which intermolecular potential model is used, simulations must be performed on a *finite* system, although in most cases the properties we are interested in are those of a *macroscopic* collection of interacting molecules. The difference is quite significant for typical system sizes that can be comfortably handled with present-day computers. To illustrate this point, consider a spherical droplet of a liquid composed of simple spherical atoms. A droplet containing 1000 atoms has a radius of 7 atomic diameters at a typical liquid density. Correlations of atomic positions in a liquid away from a critical point extend to a distance of a few atomic diameters, and therefore the majority of atoms in such a droplet would be sufficiently close to the interface to be affected by it. The standard trick used to overcome this potential difficulty is periodic boundary conditions. The simulated system is placed in a space-filling central cell, for example a cube in three dimensions. The simulated system consists of an infinite number of replicas of the central cell. An illustration of periodic boundary conditions is given in Figure 1 of the chapter by Cummings. Despite the artificial periodicity imposed by this scheme, properties calculated for systems away from critical points are then not greatly affected by system size, and can be considered representative of the properties of a bulk fluid.

For most potential models, it is relatively straight-forward to correct the results for the effects of intermolecular potential cutoff on the calculated thermodynamic properties. The corrections are normally performed assuming that there is a uniform distribution of particles for distances greater that the ones contained within the central simulation cell. A special difficulty arises in this respect for potentials that contain polar and ionic terms, which decay with the third and first power of distance, respectively. For these systems, the most commonly used method for long-range corrections is the Ewald summation method, in which all the potential contributions from the complete infinite periodic array of cells are summed with the aid of Fourrier transformations. A tutorial introduction to Ewald sums and program segments for applying it to molecular simulations of polar and ionic systems is given in [3].

2.2. IMPORTANCE SAMPLING MONTE CARLO

The main molecular simulation method used for the calculation of free energies and phase equilibria is the Monte Carlo method, even though some of the techniques described in this section have counterparts using molecular dynamics. In general, Monte Carlo methods in statistical mechanics are used to sample configuration space of a system with a specified Hamiltonian. In the canonical ensemble (constant temperature, volume and number of particles), states occur with probability density, ρ_m^{NVT},

$$\rho_m^{NVT} = \frac{\exp(-\beta \mathcal{V}_m)}{\displaystyle\sum_{\text{all states}} \exp(-\beta \mathcal{V}_m)}, \tag{2}$$

where $\mathcal{V}_m$ is the configurational energy of a state and $\beta = 1/k_B T$, where k_B is Boltzmann's constant and T is the absolute temperature.

In order to sample configuration space with the correct probability density, the following scheme is used. An initial state is constructed, in principle arbitrarily, but preferably close to the set of states of interest. The state is then perturbed, commonly by moving a particle to a new position or orientation, thus generating a new trial state. The *a priori* probability, α_{mn}, of generating trial state n from state m must satisfy the important condition of microscopic reversibility,

$$\alpha_{mn} = \alpha_{nm}, \tag{3}$$

in order to sample the correct limiting distribution (equation 2). In addition, the set of moves selected must be *ergodic*, covering the whole of configuration space for the systems of interest. Acceptance of the new state is then performed probabilistically (hence the name Monte Carlo), most commonly according to the Metropolis criterion [9],

$$\begin{aligned}
\wp_{mn} &= \alpha_{mn} & \rho_n \geq \rho_m & \quad m \neq n \\
\wp_{mn} &= \alpha_{mn}(\rho_n / \rho_m) & \rho_n < \rho_m & \quad m \neq n \\
\wp_{mm} &= 1 - \sum_{m \neq n} \wp_{mn}
\end{aligned} \tag{4}$$

where $\wp_{mn}$ is the acceptance probability of trial state n. A significantly more extensive introduction to the topic of importance sampling Monte Carlo can be found in [3].

A Monte Carlo simulation consists of a large number of "steps" performed according to the acceptance criterion of equation 4. How large a number is required depends on the complexity of the intermolecular potential studied and the desired accuracy of the results. For determining thermodynamic properties of a fluid interacting with a Lennard-Jones potential, simulations of approximately 10^4-10^5 Monte Carlo steps per particle are normally sufficient.

2.3. SIMULATIONS WITH AN EXPLICIT INTERFACE

Conceptually, the easiest method for calculating phase equilibria by simulation is to set up a system at conditions at which more than one phases would be present in a macroscopic thermodynamic system. Applications of direct interfacial simulations have been reviewed by Rowlinson and Widom [10] and more recently by Gubbins [11]. Despite the apparent simplicity of the technique, there are several problems associated with setting up and equilibrating a system with two coexisting phases. In particular, simulations involving many particles and very long equilibration times are often required [12]. Even with large systems, a significant fraction of particles are close to the interface (see discussion in section 2.1). When the density difference between the two coexisting phases is small, it is often not possible to set up a stable two-phase

system. Finally, for fluids with low vapor pressures, for any reasonable system size, practically no particles can be found in the gas phase [13]. For these reasons, direct interfacial simulations have found relatively few application in predicting phase equilibria.

2.4. WIDOM TEST PARTICLE INSERTIONS AND GRAND CANONICAL MONTE CARLO

In classical thermodynamics, the chemical potential of a component is a quantity for which no simple mechanical interpretation can be given. The chemical potential is a "statistical" property and as such is harder to obtain from simulations than "mechanical" quantities such as the configurational energy or pressure. An elegant theorem proposed by Widom [14] provides a simple way of calculating chemical potentials by simulation.

$$\beta\mu = -\ln\langle\exp(-\beta U_{test})\rangle + \ln\rho, \tag{5}$$

where μ is the chemical potential of a component in a system (to within a temperature-dependent constant that does not affect phase equilibrium calculations), U_{test} is the energy experienced by a "test" particle of that component placed in a random position in the simulation cell and ρ is now the molar density. Figure 3 illustrates the technique. The darker-shaded circles represent "real" particles of a fluid that participate in the simulation, while the lighter-shaded "test" particles are placed at random positions in the system and their energy of interaction with the real particles determined for use with equation 5.
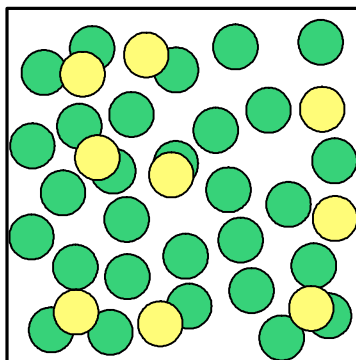

Figure 3. Schematic representation of the Widom test particle method for the determination of chemical potentials.

As illustrated in Figure 3, most attempted insertions of test particles result in overlap with existing particles in the fluid, with U_{test} large and positive. These insertions do not contribute significantly to the ensemble average in equation 5. For simple single-site intermolecular potentials, such as the Lennard-Jones potential, sampling using the Widom test particle method can be performed throughout the fluid state. Sampling fails for the ordered solid phases.

The chemical potential of a system can also be obtain from Grand Canonical Monte Carlo (GCMC) simulations, which have a comparable range of applicability as the Widom test particle technique. In GCMC, the simulated system is considered at conditions of constant temperature T ($\beta=1/k_BT$), volume V, and chemical potential μ. In addition to particle displacements, attempted

creations and destructions of particles are performed and accepted with the following probabilities.

$$\wp(N \rightarrow N+1) = \min\left[1, \frac{V}{N+1}\exp(-\beta\Delta U + \beta\mu)\right]$$
$$\wp(N \rightarrow N-1) = \min\left[1, \frac{N}{V}\exp(-\beta\Delta U - \beta\mu)\right], \tag{6}$$

where N is the instantaneous number of particles in the system. In GCMC simulations, therefore, the density of the system that corresponds to a given value of the chemical potential is obtained at the end of the simulation.

The determination of phase coexistence from Widom test particle insertions or GCMC then proceeds in the following way. Consider the schematic diagram shown in Figure 4, which refers to a one-component system. From a series of canonical simulations with Widom test particle insertions, or a series of GCMC simulations, one can obtain the dependence of the chemical potential on pressure for the gas and liquid. The coexistence condition is found at the point of intersection of the two branches. Away from the critical point, a small change in chemical potential for the liquid results in a large change in pressure, because the liquid is incompressible, and the corresponding line is almost horizontal. For this case, the number of simulations required is quite small. These ideas have been applied by Möller and Fischer [15] and Lotfi *et al*.[16] to obtain the coexistence properties of the pure Lennard-Jones fluid to a very high accuracy. Uncertainties of a fraction of a percent for the liquid density and approximately 1% for the gas density and vapor pressure were achieved.

For binary and multicomponent systems, or for one-component systems close to a critical point, the method described suffers from the serious disadvantage that the number of simulations required to locate the point of phase coexistence rapidly increases. For these systems, the method of choice is the Gibbs ensemble Monte Carlo technique described in section 2.5.
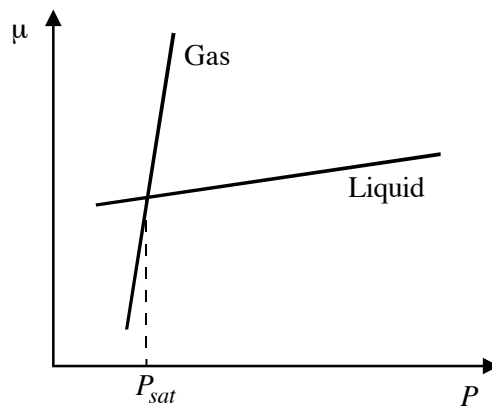

Figure 4. Schematic representation of the search technique for locating the
point for phase coexistence for a one-component system using chemical
potential determination methods. P_{sat} is the vapor pressure.

2.5. THE GIBBS ENSEMBLE TECHNIQUE

2.5.1 Basic Methodology The Gibbs ensemble Monte Carlo simulation methodology [1] was developed specifically in order to enable direct simulations of phase coexistence in fluids. A schematic of the technique is shown in Figure 5. Let us consider a macroscopic system with two phases coexisting at equilibrium. Gibbs ensemble simulations are performed in two microscopic regions within the bulk phases, away from the interface. In simulations, this implies that each region is embedded within periodic boundary conditions with replicas of itself.   The thermodynamic requirements for phase coexistence are that each region should be in internal equilibrium, and that temperature, pressure and the chemical potentials of all components should be the same in the two regions. System temperature in Monte Carlo simulations is specified in advance. The remaining three conditions are respectively satisfied by performing three types of Monte Carlo "moves", displacements of particles within each region (to satisfy internal equilibrium), fluctuations in the volume of the two regions (to satisfy equality of pressures) and transfers of particles between regions (to satisfy equality of chemical potentials of all components).

The original methodology was developed for simulations at constant total volume, appropriate for the study of equilibria in one-component systems. Panagiotopoulos *et al*. [17] extended the methodology to calculations at constant total system pressure, an approach which is commonly applied to binary and multicomponent mixture simulations. Smit et al. [18] and Smit and Frenkel [19] developed significantly the statistical mechanics of the ensemble and provide equations for the computation of chemical potentials in Gibbs ensemble simulations.

2.5.2 *Improving sampling efficiency* The main bottleneck in achieving convergence in Gibbs ensemble simulations is typically chemical potential equilibration through particle transfers between phases. For dense fluid phases, especially for complex, orientation-dependent intermolecular potentials, configurations with "holes" in which an extra particle can be accommodated are highly improbable, and the converse step of removing a particle also involves a large cost in energy. Because of these factors, the probability of successful particle transfers becomes prohibitively low. The same difficulties are present in chemical potential determination methods based on particle insertions, such as the Widom technique and grand canonical Monte Carlo. There have been several proposed modifications to the Gibbs methodology in order to improve its efficiency for dense fluids and complex potentials. The particle-identity exchange algorithm [20] is appropriate for the study of mixtures of components that differ greatly in molecular size and has been inspired by the semi-grand canonical ensemble technique [21]. Stapleton and Panagiotopoulos [22] have proposed a combination of the excluded volume map sampling technique [23] and the Gibbs ensemble, applicable to systems with very dense fluid phases. Cracknell *et al*. [24] have described a rotational insertion bias method applicable to dense phases of structured particles (e.g. water).   The method biases the orientation, rather than the position, of the particle to be transferred.

The configurational-bias sampling techniques described in section 2.7.1 are the most likely to significantly improve sampling efficiency for Gibbs ensemble simulations. Configurational-bias techniques has been combined with the Gibbs ensemble [25,26] to obtain the phase behavior of multisegment molecules.
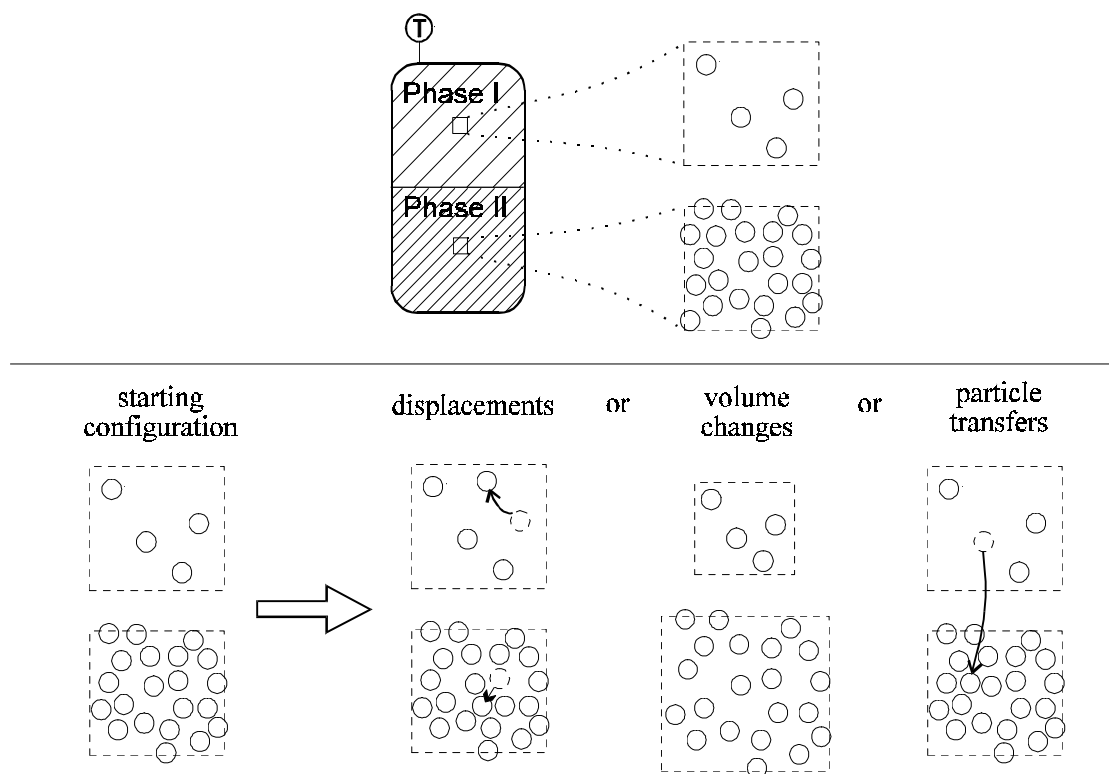
Figure 5. Schematic diagram of the Gibbs ensemble simulation technique for direct determination of phase equilibria.

2.5.3 Approaching critical points Approaching critical points by molecular simulation methods is complicated by the use of a finite system and periodic boundary conditions. At a critical point, a characteristic correlation length for the macroscopic thermodynamic system approaches infinity, in the manner described in the chapter by Levelt-Sengers in the present volume. This divergence cannot be captured by a simulation which constrains fluctuations to the box length used. The techniques of *finite size scaling*, to which an introduction is given in [27] can be used to extrapolate the results from the finite systems to the limit of infinite system size. In the following paragraph, we restrict our attention to the topic of determining critical points from Gibbs ensemble simulations, a topic of considerable interest in the study of supercritical fluids by simulation.

The recent study of Wilding and Bruce [28] for the two-dimensional Lennard-Jones fluid using Grand Canonical Monte Carlo represents the best that can be done at present using finite-size scaling ideas for continuous potentials. In that study, the location of the critical point was determined to a high accuracy by performing a series of long simulations (10^6-10^7 Monte Carlo steps *per particle*) for two different system sizes, $<N> \approx 100$ and $<N> \approx 400$, along the coexistence line in the chemical potential/inverse temperature plane. This plane is defined by the condition that the probability density of observing a given number of particles in the simulation box shows two peaks of equal height. Exactly at the critical point, the shape of the probability density function is a universal scaling function independent of system size. As Allen [27] points

out, the serious "critical point seeker" must have such a scaling function available for the chosen ensemble, boundary conditions and universality class, and have available a large amount of computing time.

For more approximate estimates of the location of the critical point, a series of Gibbs ensemble simulations for different system sizes can be used to extrapolate to infinite system size. The calculation consists of two parts, one in which the critical point for a given system size is obtained by extrapolating the coexistence curve below the critical point, and one in which the infinite system size critical point is from the critical point data for different system sizes. In many studies of continuous-space models, the rectilinear diameter rule and the scaling relationship for the width of the coexistence curve are used to estimate the location of the critical point.

$$\frac{\rho_{liq} + \rho_{gas}}{2} = \rho_c + A(T_c - T) \, ,$$
$$\rho_{liq} - \rho_{gas} \propto (T_c - T)^\beta \tag{7}$$

where β is an exponent that takes the value 1/2 according to classical (mean-field) theories, and is close to 1/3 in three dimensions for real fluids and in modern theories of critical phenomena.

The shape of the coexistence curve obtained from Gibbs ensemble simulations at the vicinity of the critical point has been examined by Mon and Binder [29] for the two-dimensional lattice Ising model, and by Recht and Panagiotopoulos [30] for a continuous-space square-well fluid in two and three dimensions. In two dimensions, a cross-over in the shape of the coexistence curve from an apparent non-classical exponent away from the critical point to a classical value at the vicinity of the critical point was observed in both lattice and off-lattice simulations. This behavior was not apparent for the three-dimensional off-lattice simulations.

2.6. GIBBS-DUHEM INTEGRATION

While the Gibbs ensemble technique can be used to obtain the densities and compositions of two coexisting phases at one temperature from a single simulation, it relies on insertions of particles to equalize the chemical potentials, and therefore experiences difficulties for dense phases and long molecules. If a single point on the coexistence curve is known (e.g. from long Gibbs ensemble simulations), the remarkably simple and novel method of Kofke [31,32] has the potential of enabling the calculation of the complete phase diagram from a series of constant-pressure simulations that do not involve any transfers of particles. For one-component systems, the method is based on integrating the Clasius-Clapeyron equation over temperature.

$$\left(\frac{dP}{d\beta}\right)_{sat} = -\frac{\Delta H}{\beta \Delta V} \, , \tag{8}$$

where "*sat*" implies that the equation holds on the saturation line, and ΔH is the difference in enthalpy between the two coexisting phases. The right-hand side of equation 8 involves only "mechanical" quantities that can be simply determined during a simulation. The method to date has been applied only to one-component systems. However, it is unique among the methods described in this chapter in that it is also applicable to equilibria involving solids.

2.7. HOW TO DEAL WITH "HARD" SYSTEMS

In the context of the present chapter, "hard" systems are ones for which the simple insertion-based techniques for the calculation of free energies and phase equilibria described in sections 2.4 and 2.5 are not practical. Such system include multisegment and polymeric molecules as well as strongly interacting or associating systems. Some of the advanced techniques applicable to these systems are covered in more detail than is possible here in [33].

2.7.1 Rosenbluth and Rosenbluth biased sampling methods The main obstacle for applying the Widom test particle or the Gibbs ensemble method to calculate chemical potentials and phase equilibria for multisegment, polymeric, or strongly interacting systems is that random insertions of a new particle in an existing system of even moderate density are likely to result to overlap with existing particles, as illustrated in Figure 6, representing a schematic snapshot from a Gibbs ensemble simulation of a pentameric fluid. On the other hand, in the exceedingly rare instances that such an insertion is successful, the resulting energy change is highly favorable, and the resulting configurations are heavily weighted in calculating the thermodynamic properties.
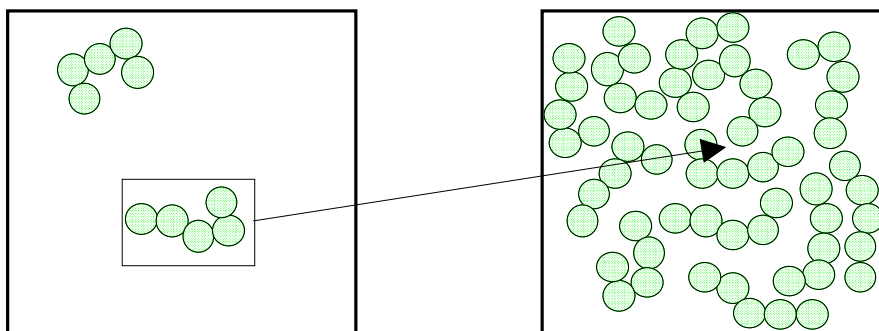

Figure 6. Illustration of the difficulty in insertion of an additional
multisegment particle in a dense phase.

Rosenbluth and Rosenbluth [34] presented a powerful idea that is currently finding numerous applications. The idea is best explained in the original context of simulation of a polymeric system constrained on a lattice, although most of applications of interest to the topic of this book would be for continuous-space models. Consider the system shown in Figure 7. It consists of a simple two-dimensional 5x5 square lattice on which 10 monomers are present. Now suppose that we would like to compute the chemical potential of a hexamer. The approximate probability of finding six unoccupied positions is, to a very crude approximation valid at the limit of infinite temperature, $\left(\frac{25-10}{25}\right)^6 \approx 5\%$, which represents the probability of success of Widom-type (unbiased) insertions. Now consider the following procedure for inserting the hexamer into the fluid. First, select an unoccupied position in the fluid to insert the first bead, and assign a "Rosenbluth weight" to the insertion equal to the fraction of sites that were unoccupied, in this case 15/25. Next, let us consider the sites at the vicinity of the first bead. Out of four possible growth directions, one is occupied (taking, of course, periodic

boundary conditions into account). We select one of these growth directions at random and assign a weight of 3/4, again equal to the fraction of unoccupied sites. For the next bead, we do not allow for the possibility of the chain "backtracking", and thus the number of available growth directions is three, out of which one is unoccupied (weight of 1/3). Growth proceeds in this fashion until all six beads have been inserted. The total Rosenbluth weight of the configuration

just generated is $\frac{15}{25} \times \frac{3}{4} \times \frac{1}{3} \times \frac{2}{3} \times \frac{1}{3} \times \frac{3}{3} = \frac{1}{30}$. The procedure just described will be almost always successful, resulting in growth of the full hexamer with Rosenbluth weight typically in the vicinity of a few percent. Any property related to the single inserted chain (e.g. the chemical potential according to equation 5) can be calculated by summing the contributions of each configuration generated multiplied by the Rosenbluth weight of each. The properties calculated in this fashion are fully equivalent, if configuration space is adequately sampled, to the properties we would have calculated with unbiased insertions. The advantage we gain is in efficiency. Instead of sampling rare events with large contributions to the properties, we sample frequent events with small contributions.
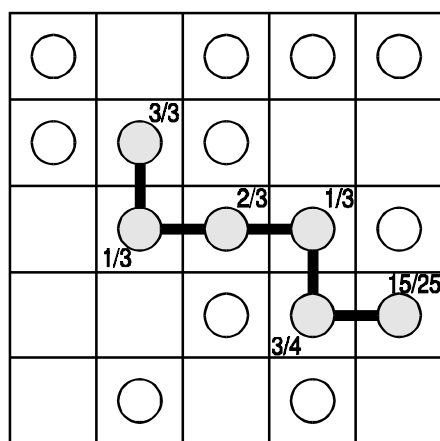

Figure 7. Schematic illustration of the Rosenbluth and Rosenbluth algorithm.

The original Rosenbluth and Rosenbluth scheme was quite limited in scope, dealing with configurational properties of single-chain systems without taking into account energy considerations. Significant contributions to the development of efficient growth-based techniques for calculating configurational properties and chemical potentials in dense chain systems have been made recently [35,36,37]. These schemes share with the original Rosenbluth and Rosenbluth algorithm the undesirable feature that system configurations are generated with a probabilities different from their Boltzmann weights. The configurational-bias Monte Carlo method [38,39] overcomes this limitation, and allows for efficient sampling of polymer conformations directly with the correct limiting distribution, thus allowing incorporation of Rosenbluth and Rosenbluth sampling within conventional Metropolis Monte Carlo simulations. The combination of configurational-bias Monte Carlo with the Gibbs ensemble to compute phase diagrams of macromolecular systems has already been mentioned [25,26].

2.7.2 Incremental Chemical Potentials of Polymeric Systems   Even with Rosenbluth and Rosenbluth sampling, the computation of free energies and phase equilibria for chain molecules of length more than 20 or 30 segments encounters serious sampling difficulties. The "Chain Increment" method [40] can be used to obtain the chemical potential difference,

$$\mu_{chain}(n+1) - \mu_{chain}(n) = -kT\ln\left\langle\exp\left(-\beta U^+\right)\right\rangle, \tag{9}$$

where $\mu_{chain}(n)$ is the chemical potential of a chain of length n and U^+ is the energy experienced by a segment added at the end of a polymeric molecule. In principle, n simulations are required to determine the chemical potential of an n-mer using this method, so it is quite expensive computationally. The number of simulations required can be reduced by one of the following two ways. The chain increment method can be combined with configurational-bias schemes described in section 2.7.1 to grow more than a single segment at a given time. In addition, it has been found [41] that the chain length dependence of the incremental chemical potential is often weak and the following approximate relationship holds.

$$\mu_{chain}(n) \approx \mu_{chain}(n_0) + (n-n_0) \times \mu_{segment}(n_0), \tag{10}$$

where n_0 is the minimum chain length above which the total chemical potential is approximately linear in chain length.

2.7.3 Cluster Algorithms   Many systems of strongly interacting particles, for example ionic systems in a medium of low dielectric constant or surfactant systems, exhibit strong clustering that makes moves of independent particles (e.g. single-ion moves) extremely sluggish. For successful simulation of such systems, it is necessary to use algorithms that facilitate the movement of large parts of the system. The Swedsen and Wang [42] algorithm was originally developed to facilitate Monte Carlo sampling of near-critical systems. The original algorithm generates configurations with a probability that is proportional to their respective Boltzmann weights, thus allowing for 100% acceptance of the trial moves [33]. Wu *et al*. [43] propose an extension of the original algorithm for self-assembling systems. The key step in the Swedsen and Wang algorithm is the creation of "virtual bonds" between neighboring particles. A schematic diagram for application of such a scheme to a continuous-space simulation is shown in Figure 8. The probability of bond formation between two particles is a function only of their distance in the Wu *et al*. modification. Once the clusters have formed, they are moved as a whole (that is, without changing the intracluster distances), as shown for one of the clusters in the right-most panel of Figure 8. The acceptance probability of the cluster moves is not simply the Metropolis criterion (equation 4), but takes into account the probabilities of bond formation of particles at the old and new cluster positions [43].
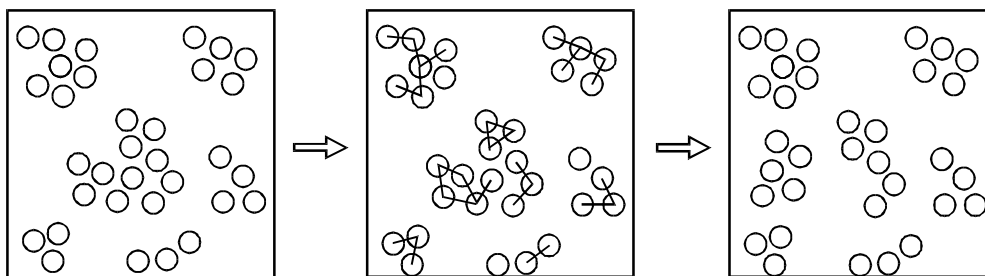
Figure 8. Cluster moves in the spirit of Swedsen and Wang [42].

3. Some Applications to High Pressure and Supercritical Systems

Section 2 of this chapter presented a brief introduction to methodologies for the calculation of free energies and phase equilibria by Monte Carlo simulation. In the present section, some representative applications to systems of potential interest to the supercritical fluid community are described. I use a broad definition of the area of supercritical fluids to include systems such as water, hydrocarbons and ionic fluids at high pressures and temperatures. Some of the more traditional areas of application of supercritical fluids, namely supercritical equilibria involving solid phases are not represented because little work has been performed in these areas using molecular simulation. The reason for this is that most of the methods described in section 2 for the determination of phase behavior are not applicable to solid phases.

3.1 WATER

Because of its technological importance, water has been the subject of a large number of simulation studies. Modeling of high pressure aqueous systems is important for development of supercritical water oxidation processes. A review of molecular simulation studies of liquid water is given in the contribution by Cummings in this book. The present section focuses on the phase behavior of realistic intermolecular models for water. The first Gibbs ensemble simulation study of such a model was by de Pablo and Prausnitz [44] who used the TIP4P model of Jorgensen *et al*. [45] and covered the range from approx. 100°C to the critical point. The same model, as well as the older TIPS2 model [46], has been studied at lower temperatures by Cracknell *et al*. [25], using the rotational insertion bias method. The SPC model [8] has been studied by Mezei [47] using a cavity-biased Gibbs ensemble technique. In these three studies, spherical truncation of the potential at distances beyond half the box length was performed. Some dependence of the results on system size is expected for polar and ionic systems when spherical truncation is used, because of the fluctuation in density and number of molecules in each of the two phases. The Ewald summation technique which is less sensitive to system size was used by de Pablo *et al*. [48] to study the SPC model for water .

Results for the coexistence curves of the TIP4P and SPC models for water are compared to experimental data in Figure 9. The SPC model reproduces the dielectric constant of water much better than the TIP4P model [49], but its phase behavior deviates significantly from experiment, especially at higher temperatures. One possible reason for this is the following [50]. One feature of the SPC model that makes it accurate at ambient conditions is that it has a dipole moment of

2.24 D, higher than the bare dipole moment of water of 1.8 D, in order to incorporate polarizability effects that are important for the high density liquid. Strauch and Cummings [50] examined the phase behavior of an SPC-like model for which the dipole moment was reduced to 1.8 D in the gas phase. The results were only slightly better than the unmodified SPC model. We conclude that an intermolecular potential model for water that reproduces accurately dielectric properties of the liquid at ambient conditions and the phase behavior at high temperatures is not yet available.
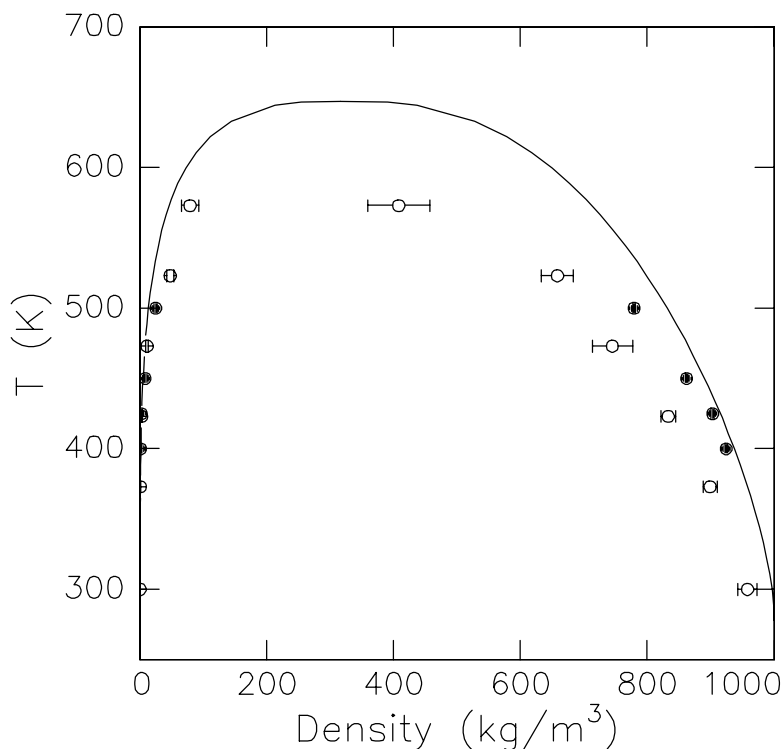

Figure 9. Phase diagrams for SPC (○) and TIP4P (●) models for water
[48,44] compared to experimental results (———).

3.2 IONIC FLUIDS

The phase behavior of fluids containing ionic species is of particular interest for applications related to supercritical water oxidation. Small concentrations of ions have a strong influence on the phase behavior of water at the vicinity of its critical point. Simulations of the vapor-liquid behavior of a mixed solvent electrolytes for which only the liquid phase contains salt were performed by Strauch and Cummings [51].

The phase behavior of a different type of ionic system consisting of a pure molten salt modeled as charged hard spheres of uniform diameter, was studied by Panagiotopoulos [52]. Study of such systems is relevant for determining the phase envelope at the very high temperatures near the critical point (approx. 3500 K for molten NaCl) at which experimental measurements are not possible. These calculations were performed in the Gibbs ensemble with

single-particle transfers. The total electroneutrality condition was satisfied by assuming that each particle is accompanied by a uniform neutralizing continuum of equal and opposite charge. The estimated critical point, at a reduced temperature $T_c^* = 0.056$ and density $\rho_c^* = 0.04$, is significantly different from previous theoretical estimates [53]. The recent calculations of Valleau [54] using the density-scaling Monte Carlo technique for the same system give $T_c^* = 0.07$, $\rho_c^* = 0.07$. The difference may be due to the use of different type of boundary conditions (Ewald sum in [52] versus minimum image in [54]). A promising approach for handling strongly interacting ionic systems is the use of configurational-bias sampling techniques and cluster algorithms described in section 2.7 [55]. Recent unpublished results from the author's laboratory for the restricted primitive model with pair transfers seem to confirm the earlier estimates of reference [52] for the location of the coexistence curve.

3.3 POLYMERIC SYSTEMS AND LONG-CHAIN HYDROCARBONS

Polymeric systems are the main topic of the chapters by Kiran, Kleintjens, Radosz and McHugh in this volume, so it will not be necessary to expand on the practical importance and challenges in modeling of the phase behavior of systems containing polymers in the present chapter. As described in section 2.7, predictions of the phase behavior of macromolecular systems from molecular simulation became possible only recently, with the development of configurational-bias methods and the Chain Increment method.

An example of the phase behavior of a macromolecular system determined using the Chain Increment method [40] is given in Figure 10, adapted from [56]. The polymeric model consists of a string of beads interacting with the Lennard-Jones potential. Stiff harmonic springs connect neighboring beads. The vapor-liquid phase envelope for chains of length n=20, 50 and 100 was determined. The vapor-liquid phase behavior is physically relevant for long-chain hydrocarbons at high temperatures, but the primary interest in the phase diagram is that it provides a means of testing polymer solution theories applicable also to polymer/solvent equilibria. The critical temperature increases with chain length and the critical density decreases, in accordance to experimental observations for polymer/solvent systems [57]. The extrapolated critical temperature at the limit of infinite chain length was found to coincide, within simulation uncertainty, to the temperature at which the second virial coefficient for polymer-polymer interactions becomes zero, and the temperature at which long chains assume quasi-ideal dimensions.

A calculation of the phase envelope for a realistic model of hydrocarbons was performed by Siepmann *et al.* [58] They applied a combination of configurational-bias Monte Carlo and the Gibbs ensemble method to obtain the vapor-liquid phase envelopes for normal alkanes of length 8, 16, 24 and 48 carbon atoms. The intermolecular potential functions used contained Lennard-Jones terms to describe methylene and methyl groups, a harmonic bending term for the bond angle, and a tortional potential term. Excellent quantitative agreement was obtained for the phase behavior of the lower alkanes for which reliable experimental data exist. For the higher alkanes, the qualitative features of the phase diagrams obtained are comparable to Figure 10: the critical temperature increases and the critical density decreases with increasing carbon number. Measurements of critical properties of long-chain alkanes is difficult because of thermal decomposition, but knowledge of these properties is important for developing reliable engineering models for hydrocarbons [59].
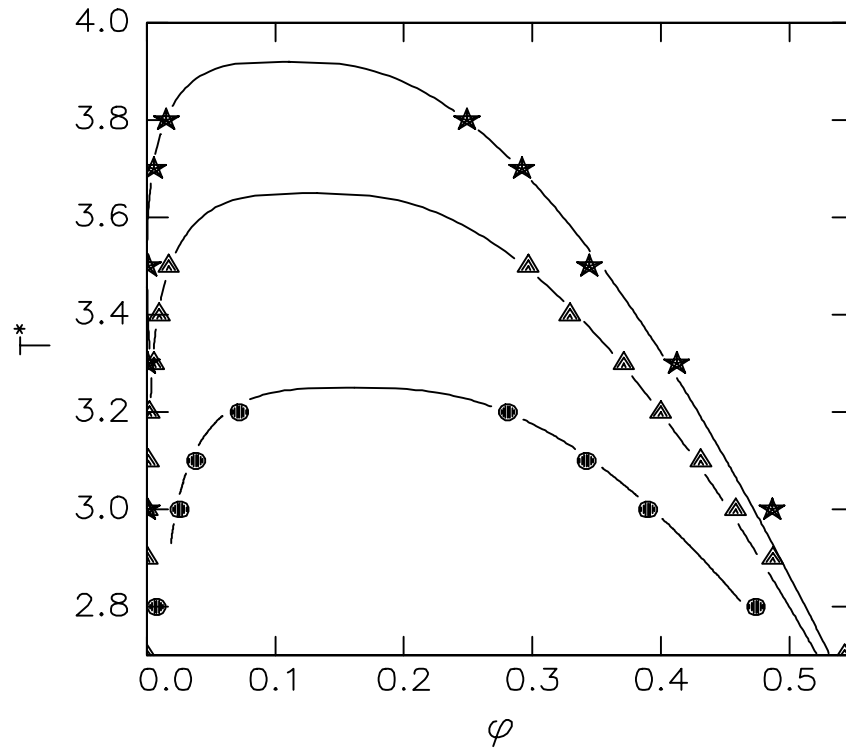
Figure 10. Phase behavior of a bead-spring polymeric model (adapted from [56]).
Monte Carlo results: (★) n=100; (▲) n=50; (●) n=20. Fitting of Monte Carlo
results to scaling relationships (equation 7) with β=0.332: (—).

3.4 PHASE EQUILIBRIA FOR SIMPLE MIXTURES AT HIGH PRESSURES

Several studies of the phase behavior of mixtures with components described by simple intermolecular potentials have been performed. Examples of studies done to test theoretical approximations are presented in section 3.5. In this section we focus on two representative examples of studies which aim at direct comparisons with experiment.

The studies of de Kuijper *et al.* [60,61] are for the system He/H_2 at very high pressures, using a potential of the α-exp-6 form,

$$U_{ij}(r) = \frac{\varepsilon_{ij}}{\alpha_{ij} - 6}\left\{6\exp\left[\alpha_{ij}\left(1 - \frac{r}{\sigma_{ij}}\right)\right] - \alpha_{ij}\left(\frac{\sigma_{ij}}{r}\right)^6\right\}, \tag{11}$$

where α_{ij} is an exponent characterizing the ij interaction, and the other symbols have the same meaning as in equation 1. Literature values for the potential were used, so that the agreement between experimental and simulation results shown in Figure 11 is quite satisfactory. An interesting comparison was made in [60] between the calculation with the full potential and a purely repulsive potential of the same form that is truncated and shifted at σ_{ij}. The results are

also shown in Figure 11 and demonstrate that repulsive forces are the primary cause of fluid-fluid phase separation in this mixture.

An application of the Gibbs ensemble methodology for the binary system He/N_2 was presented by Stapleton and Panagiotopoulos [22], using Lennard-Jones and quadrupole-quadrupole interactions with parameters taken from the literature. The results, partly reproduced here in Figure 12, show excellent agreement between experiment and simulation. The simulations reproduce well the behavior at the vicinity of the minimum temperature of the mixture critical curve. Results from perturbation theory using the same intermolecular potential parameters shown in the same Figure show significant deviations from both experiment and simulation.

Studies of phase equilibria for mixtures of noble gases modeled as Lennard-Jones particles are discussed in [9]. Agreement between experiment and simulation was obtained for the system Ar/Kr without any fitted parameters. For the more asymmetric system Ne/Xe, it was necessary to adjust one mixture parameter to obtain agreement with experimental data.
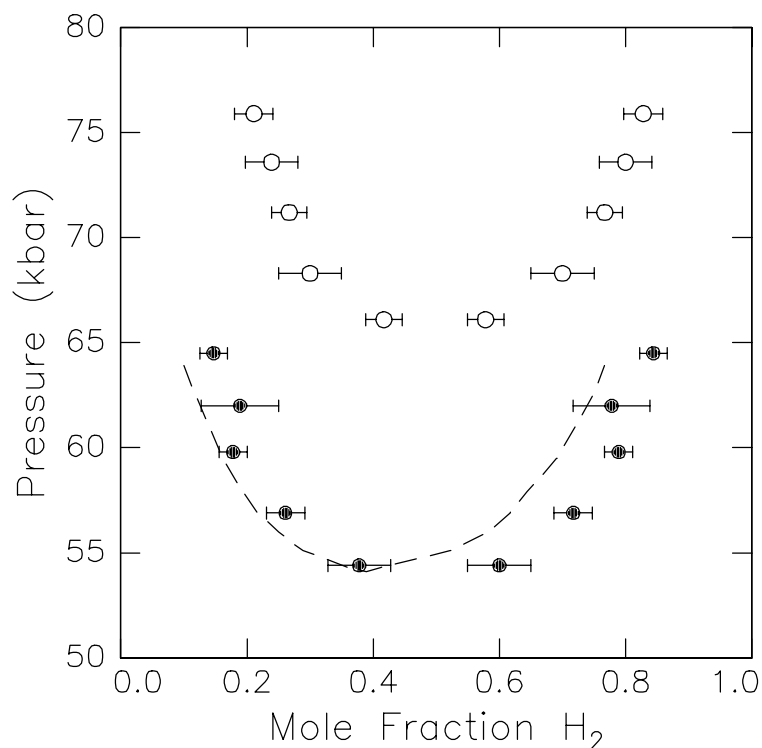

Figure 11 (adapted from [60]). Phase behavior of the system He-H_2 at T=300 K. (●) Gibbs ensemble simulation results for the full α-exp-6 potential, equation (11); (○) repulsive α-exp-6 potential; (– – –) experimental data.
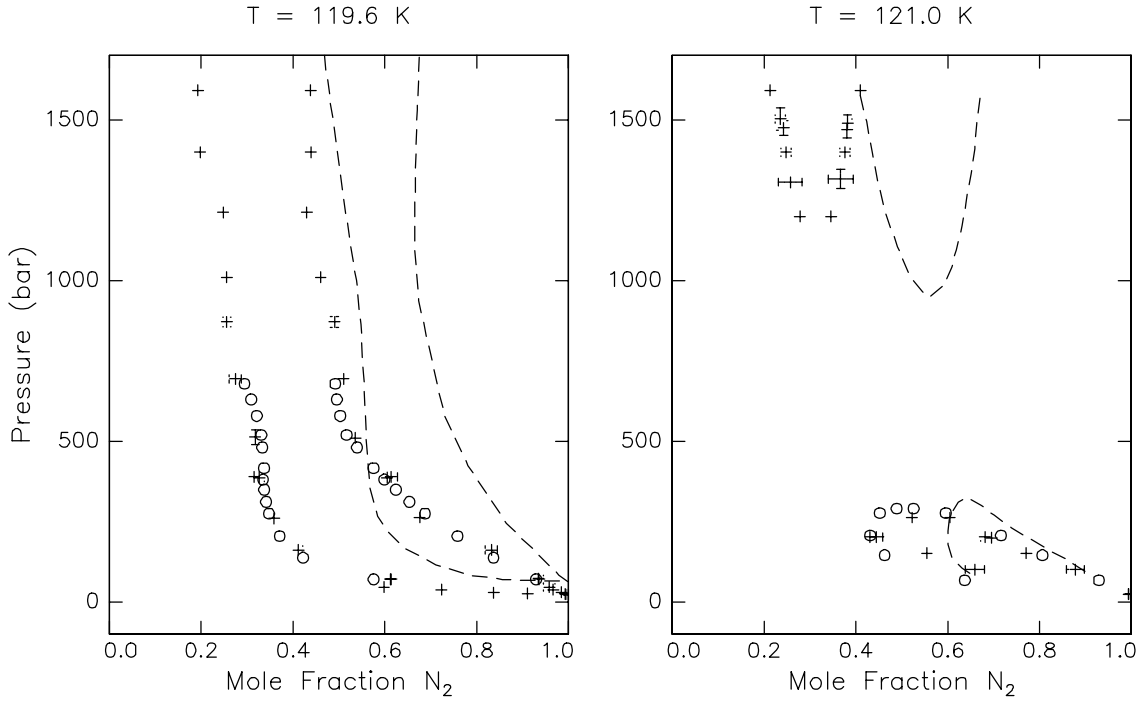
Figure 12 (adapted from [22]). Phase behavior of the system He/N$_2$. (+) Gibbs ensemble Monte Carlo; (O) experimental data; (– – –) perturbation theory.

3.5 RANGE OF VALIDITY OF VAN DER WAALS ONE-FLUID THEORY

In the previous section, comparisons were performed between molecular simulation results and experimental for phase equilibria of simple mixtures. In this section, we examine the validity of a simple theory of the fluid state, the van der Waals one-fluid approximation. The comparisons are performed using molecular-simulation generated data for phase equilibria of binary mixtures in which all interactions are of the Lennard-Jones type (equation 1). The van der Waals one-fluid theory is a particular case of the general class of "conformal solutions" theories. Such theories assume that the intermolecular potentials in a mixture are of the same functional form, an assumption that is not strictly satisfied in any real fluid, but is exact for the case under study here. According to van der Waals one-fluid theory, the configurational Helmholtz free energy, A^{conf}, of a mixture of N particles at a certain temperature T and volume V is

$$\frac{A^{conf}(T,N,V)}{Nk_BT} = \mathcal{F}\left(\frac{kT}{\varepsilon_m}, \frac{V}{N\sigma_m^3}\right), \tag{12}$$

where $\mathcal{F}$ is function that depends only on the form of the intermolecular potential and thus can be obtained from a pure fluid obeying that potential (hence the name *one-fluid* theory). The mixture parameters ε_m and σ_m are given by the equations ("mixing rules"),

$$\varepsilon_m \sigma_m^3 = \sum_i \sum_i x_i x_j \varepsilon_{ij} \sigma_{ij}^3, \tag{13}$$

$$\sigma_m^3 = \sum_i \sum_i x_i x_j \sigma_{ij}^3. \tag{14}$$

For the binary Lennard-Jones mixtures simulations, one is free to chose to study a mixture of components with specified pure component and unlike pair interactions. The Lorentz-Berthelot combining rules are frequently used to relate pure component and unlike-pair interactions. A generalized version of these rules is

$$\sigma_{ij} = \xi_{ij} \frac{\sigma_{ii} + \sigma_{jj}}{2}, \tag{15}$$

$$\varepsilon_{ij} = \zeta_{ij} \sqrt{\varepsilon_{ii} \varepsilon_{jj}}. \tag{16}$$

where ξ_{ij} and ζ_{ij} are dimensionless parameters that describe deviations from the Lorentz-Berthelot rules.

There is general agreement that the theory gives a good representation of thermodynamic properties of mixtures with components that have similar size and energy interaction parameters, but the situation is much less clear for highly asymmetric mixtures [62]. Harismiadis *et al*. [62] have performed an extensive study of phase equilibria for binary Lennard-Jones mixtures with size parameter ratios between 1 and 2, and energy parameter ratios also between 1 and 2. Unlike-pair parameters were given by the Lorentz-Berthelot rules (equations 15 and 16 with $\xi_{ij} = \zeta_{ij} = 1$). For all cases studied, Harismiadis *et al*. found excellent agreement between simulation and theoretical predictions. A representative set of pressure-composition diagrams for systems with size ratio of $\sigma_{22}/\sigma_{11}=1.5$ is shown in Figure 13.

Georgoulaki *et al*. [63] have extended the range of asymmetries to 4:1 for both energy and size parameter ratios, and have also examined the behavior of mixtures deviating from the Lorentz-Berthelot rules (ξ_{ij} or ζ_{ij} different from unity). For highly asymmetric systems and mixtures deviating from the Berthelot rule van der Waals one-fluid theory was able to describe the simulation results quite well. In contrast, for systems deviating from the Lorentz rule, performance of the theory was less satisfactory. We conclude from these studies that the range of applicability of van der Waals one-fluid theory in describing the phase behavior of Lennard-Jones mixtures is very broad. Common engineering equations of state effectively reduce to the van der Waals one-fluid theory when conventional quadratic mixing rules are used. Their inability to describe systems encountered in supercritical extraction processes is commonly attributed to the large asymmetry of the mixtures. In the light of the comparisons with simulation results mentioned here it seems that this explanation is not appropriate, and the reasons for the failure of equations of state may be related to the presence of specific interactions, such as polar or hydrogen-bonding forces.
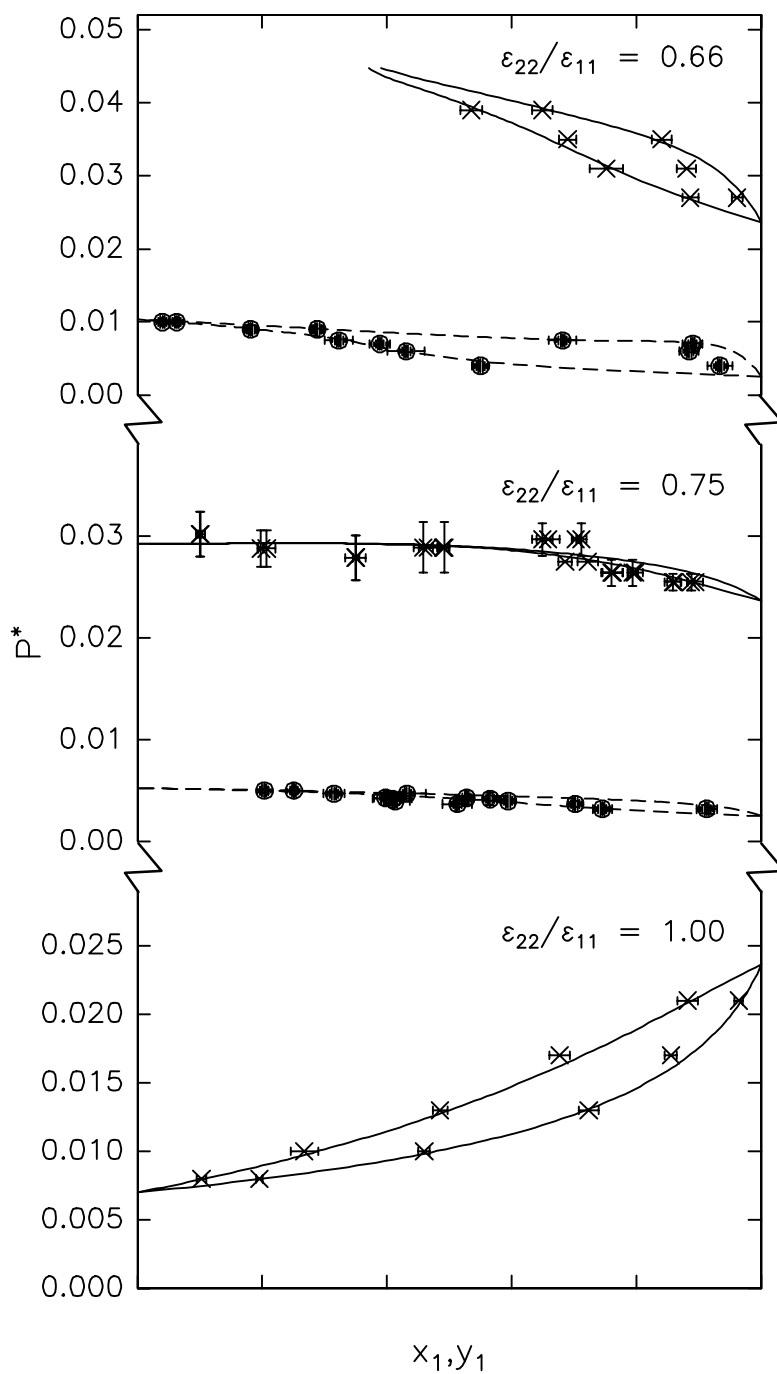
Figure 13. Phase diagrams for Lennard-Jones mixtures obeying the Lorentz-Berthelot rules, with $\sigma_{22}/\sigma_{11}=1.5$ and $\varepsilon_{22}/\varepsilon_{11} = 0.66, 0.75$ and 1.00, adapted from reference [62]. Gibbs ensemble Monte Carlo results: ($\times$) $T^*=1.00$; ($\bullet$) $T^*=0.75$. Van der Waals one-fluid theory predictions: (———) $T^*=1.00$; (– –) $T^*=0.75$.

3.6 SUPERCRITICAL EXTRACTION

There are relatively few studies of the phase behavior for systems of direct interest to supercritical extraction processes to date. Solubilities of solid naphthalene in supercritical CO_2 have been studied by Shing and Chung [64]. Agreement between simulation and experimental data was only qualitative when literature potentials for the components were used.

Studies of binary and ternary systems with water, acetone and supercritical CO_2 have been presented by Panagiotopoulos [65]. No attempt was made in [65] to use realistic intermolecular potential models for the components studied. Simple effective Lennard-Jones potentials with pure component parameters obtained from critical properties were used instead. For the cross interaction parameters, the Lorentz rule (equation 15 with ξ_{ij} =1) was used for all size parameters, and the Berthelot rule (equation 16 with ζ_{ij} =1) was used for the acetone-carbon dioxide energy interaction parameter. For the carbon dioxide-water binary system, fitting of high pressure phase equilibrium data resulted in excellent agreement with experiment for the composition of both carbon dioxide-rich and water-rich phases with an interaction parameter ζ_{ij}=0.81 [65]. Two cases were studied, (a) in which the acetone-water interaction parameter assumed the Berthelot value (ζ_{ij}=1), and (b) in which ζ_{ij} for the acetone-water interaction was set to 0.90. Table 1 summarizes the effective parameters used.

Table 1. Effective Lennard-Jones potential parameters from [65]

Interaction	ε / k_B (K)	σ (nm)
Carbon Dioxide	232.2	0.384
Acetone	443	0.467
Water	540	0.358
Carbon Dioxide/Acetone	320.7	0.426
Carbon Dioxide/Water	286.8	0.371
Acetone/Water	489.1(a) 440.2(b)	0.413

Results obtained from the simulations of the ternary systems are shown in Figure 14. Also presented on the same figure are new calculations using the conformal solutions theory described in the previous section, and experimental results from [66]. The predicted phase diagram is highly sensitive to the interaction between acetone and water. Surprisingly, conformal solutions theory does poorly in predicting the phase behavior of the ternary systems.

4. Summary and Future Outlook

In this chapter, I presented a review of molecular simulation methods for calculation of phase equilibria from assumed intermolecular interactions. There has been rapid progress in the field over the past decade. Before the mid-1980's, even the calculation of a phase diagram for a potential as simple as the Lennard-Jones potential was considered to be a major research project.
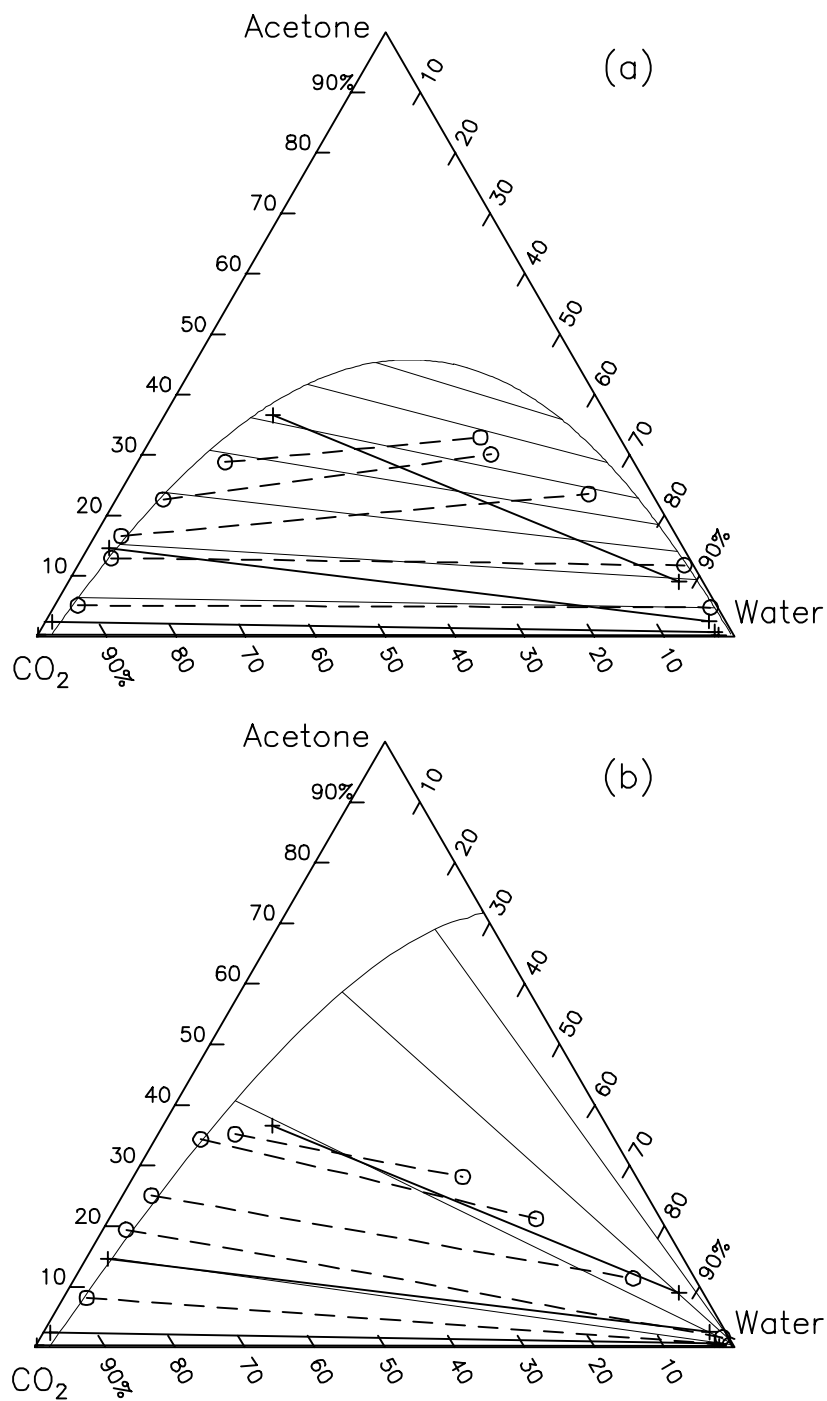
Figure 14. Phase behavior of a ternary mixture of Lennard-Jones particles with parameters shown in Table 1 at T=333 K, P=150 bar. (○– – –○) Gibbs ensemble Monte Carlo [65]; (—) conformal solutions theory; (+—+) experimental data for the acetone-water-carbon dioxide system [66].

The Gibbs ensemble technique for simple fluids greatly facilitated the calculation of phase diagrams for pure components and mixtures. Applications of finite-size scaling methods are starting to appear for continuous-space systems that promise to allow accurate determinations of critical points. The Gibbs-Duhem integration method allows rapid calculations of complete phase diagrams even for systems that include solid phases. Configurational-bias methods have greatly contributed towards a solution of the sampling problems encountered for complicated potentials and chain molecules. Cluster algorithms are available for strongly associating systems or at the vicinity of critical points.

Applications of these methods to systems of interest for high pressure and supercritical systems are, to date, restricted primarily to equilibria involving fluid phases using relatively simple potentials. The availability of methods to handle complicated potentials will certainly ensure that molecular simulation will play a continuously expanding role in modeling phase equilibria. It is worth considering what changes this is likely to bring. Direct simulations can be used to refine theoretical approximations or fit molecular-based parameters to experimental data. While the latter approach is necessarily empirical in nature, it is preferable to fitting of macroscopic model parameters, because the resulting molecular-based models are likely to be applicable outside the range of experimental conditions from which they were derived. Simulation will never replace experiment in providing primary data for process development and design. However, it can certainly play an important role in extending the range and "filling in the gaps" of experimental measurements. The recent calculations of Siepmann *et al.* for the critical properties of long-chain alkanes are a case in point. With potentials fitted to experimental data for the lower alkanes molecular simulation can be used to predict the critical properties of higher alkanes that are experimentally inaccessible due to thermal decomposition. Another example is the calculation of the critical point for molten salts mentioned in the section on ionic fluids.

The main limitation of molecular simulation is, at present, the lack of intermolecular potentials that can adequately describe complex components. *A priori* quantum mechanical techniques are not yet in position to give potentials accurate for calculations in dense phases. The most promising approach for the next few years will be using empirical potentials with parameters fitted to experimental phase equilibrium and thermodynamic data. A coordinated research effort to obtain a database of potential parameters will greatly enhance the practical usefulness of molecular simulation methods.

Acknowledgments

REFERENCES

[1]   Panagiotopoulos, A.Z. "Direct determination of phase coexistence properties of fluids by Monte Carlo simulation in a new ensemble," *Mol. Phys.* **1987**, 61, 813-826.

[2]   Gubbins, K.E. "Application of molecular theory to phase equilibrium predictions," Chapter 6 in *Thermodynamic Modeling*, Sandler, S.I. Ed.; Marcel Dekker: NY, 1992.

[3]   Allen, M.P.; Tildesley, D.J. *Computer Simulation of Liquids*, Clarendon Press: Oxford, 1987.

[4]   Allen, M.P.; Tildesley, D.J. Eds. *Computer Simulation in Chemical Physics*,; NATO ASI Ser. C: vol. 397, Kluwer Academic Publishers: Dordrecht, The Netherlands, 1993.

[5]   Shing, K.S. "Application of molecular simulation to the study of supercritical extraction," in *Supercritical fluid technology: reviews in modern theory and applications,* Bruno, T.J.; Ely, J.F. Eds, CRC Press: Boca Raton, FL, . 1991; pp. 227-244.

[6]   Sprik, M.; "Effective pair potentials and beyond," Chap. 7 in reference 4.

[7]   Maitland, G.C.; Rigby, M.; Smith, E.B.; Wakeham, W.A. *Intermolecular Forces*, Clarendon Press: Oxford, 1981.

[8]   Berendsen, H.J.C.; Postma, J.M.P.; von Gustersen W.F.; Hermans, J. "Interaction models for water in relation to protein hydration", in *Intermolecular Forces*, Pullman, B. Ed. Jerusalem Symp. Quantum Chem. Biochem. **14**, 331-342 (1981).

[9]   Metropolis, N.; Rosenbluth, A.W.; Rosenbluth, M.N.; Teller, A.H.; Teller, E., "Equation of state calculations by fast computing machines," *J. Phys. Chem.* **1953**, 21, 1087-92.

[10]   Rowlinson J.S.; Widom, B. *Molecular Theory of Capillarity*, Ch. 6, Clarendon Press: Oxford, 1982.

[11]   Gubbins, K.E. "The role of computer simulation in studying phase equilibria," *Molec. Simulation* **1989**, 2, 223-252.

[12]   Holcomb, C.D.; Clancy, P.; Thompson S.M.; Zollweg, J.A. "A critical study of the subtleties of simulations of the Lennard-Jones Liquid-Vapor interface for pure fluids and binary mixtures," presented at the 11th Symposium on Thermophysical Properties, Boulder, CO, June 23-27, 1991.

[13]   Madden, W.G. "Monte Carlo studies of the melt-vacuum interface of a lattice polymer," *J. Chem. Phys .***1987**, 87, 1405-1422.

[14]   Widom, B., "Some topics in the theory of fluids," *J. Chem. Phys.* **1963**, 39, 2808-12.

[15]   Möller, D.; Fischer, J. "Vapour liquid equilibium of a pure fluid from test particle method with NpT molecular dynamics simulations," *Molec. Phys.* **1990**, 69, 463-73.

[16]   Lotfi, A.; Vrabec, J.; Fischer, J. "Vapour liquid equilibria of the Lennard-Jones fluid from the NpT plus test particle method," *Molec. Phys.* **1992**, 76, 1319-33.

[17]   Panagiotopoulos, A.Z.; Quirke, N.; Stapleton, M.; Tildesley, D.J. "Phase equilibria by simulation in the Gibbs ensemble: alternative derivation, generalization and application to mixture and membrane equilibria," *Molec. Phys* **1988**, 63, 527-545.

[18]   Smit, B.; de Smedt Ph.;Frenkel, D. "Computer simulations in the Gibbs ensemble", *Mol. Phys.* **1989**, 68, 931-950.

[19]   Smit B.; Frenkel, D. "Calculation of the chemical potential in the Gibbs ensemble", *Mol. Phys.***1989**, 68, 951-958.

[20]   Panagiotopoulos, A.Z. "Exact calculations of fluid-phase equilibria by Monte Carlo simulation in a new statistical ensemble", *Int. J. Thermophys.* **1989,** 10, 447-457.

[21] Kofke D.A.;Glandt, E.D.; "Monte Carlo simulation of multicomponent equilibria in a semigrand canonical ensemble," *Molec. Phys* **1988**, 64, 1106-1131.

[22] Stapleton M.R.; Panagiotopoulos, A.Z. "Application of excluded volume map sampling to phase equilibrium calculations in the Gibbs ensemble", *J. Chem. Phys.* **1990**, 92, 1285-93.

[23] Deitrick, G. L.; Scriven, L. E.; Davis, H. T. "Efficient molecular simulation of chemical potentials," *J. Chem. Phys.***1989,** 90, 2370-2385.

[24] Cracknell, R.F.; Nicholson, D.; Parsonage N.G.; Evans, H. "Rotational insertion bias: a novel method for simulating dense phases of structured particles, with particular application to water", *Mol. Phys.* **1990**, 71, 931-943.

[25] Mooij, G.C.A.M.; Frenkel D.; Smit, B. *J. Phys.: Condensed Matter* **1992**, 4, L255.

[26] Laso, M.; de Pablo J.J.; Suter, U.W. "Simulation of phase equilibria for chain molecules", *J. Chem. Phys.***1992,** 97 2817-2819.

[27] Allen, M.P., "Back to basics," Chapter 3 in [4].

[28] Wilding, N.B.; Bruce, K. *J. Phys.: Condens. Matter* **1992,** 4, 3087.

[29] Mon, K.K.; Binder, K. "Finite size effects for the simulation of phase coexistence in the Gibbs ensemble near the critical point," *J. Chem. Phys.* **1992**, 96, 6989-95.

[30] Recht, J.R.; Panagiotopoulos, A.Z. "Finite-size effects and approach to criticality in Gibbs ensemble simulations," *Molec. Phys.* **1993**, in press.

[31] Kofke, D.A. "Gibbs-Duhem integration: a new method for direct evaluation of phase coexistence by molecular simulation," *Molec. Phys.* **1993**, 78, 1331-1336.

[32] Kofke, D.A. "Direct evaluation of phase coexistence by molecular simulation via integration along the saturation line," *J. Chem. Phys.* **1993**, 98, 4149-4162.

[33] Frenkel, D. "Advanced Monte Carlo techniques," Chapter 4 in [4].

[34] Rosenbluth, M.N.; Rosenbluth, A.W., "Monte Carlo calculations of the average extension of molecular chains," *J. Chem. Phys.* **1955**, 23, 356-9.

[35] Meirovitch, H. "Computer simulation technique for calculating the entropy of polymer chains, based on the scanning method with a mean-field parameter," *Macromolecules* **1985**, 18, 569-573.

[36] Harris, J.; Rice, S.A. "A lattice model of a supported monolayer of amphiphile molecules: Monte Carlo simulation," *J. Chem. Phys.* **1988**, 88, 1298-1306.

[37] Siepmann, J.I. "A method for the direct calculation of chemical potentials for dense chain systems," *Molec. Phys.* **1990**, 70, 1145-58.

[38] Siepmann, J.I.; Frenkel, D. "Configurational bias Monte Carlo: a new sampling method for flexible chains," *Molec. Phys.* **1992**, 75, 59-70.

[39] de Pablo, J.J.; Laso, M.; Suter, U.W., "Simulation of polyethylene above and below the melting point," *J. Chem. Phys.* **1992**, 96, 2395-2403.

[40] Kumar, S.K.; Szleifer, I.; Panagiotopoulos, A.Z. "Determination of the chemical potentials of polymeric systems from Monte Carlo Somulations," *Phys. Rev. Lett.* **1991**, 66, 2935-8.

[41] Szleifer, I.; Panagiotopoulos, A.Z. "Chain length and density dependence of the chemical potential of lattice polymers," *J. Chem. Phys.* **1992**, 97, 6666-73.

[42] Swendsen, R.H.; Wang, J.-S. "Nonuniversal Critical Dynamics in Monte Carlo Simulation," *Phys. Rev. Letts.* **1987**, 58, 86-88.

[43] Wu, D.; Chandler, D.; Smit, B. "Electrostatic analogy for surfactant assemblies," *J. Chem. Phys.* **1992**, 96, 4077-4083.

[44] de Pablo, J.J.; Prausnitz, J.M. "Phase equilibria for fluid mixtures from Monte Carlo simulation," *Fluid Phase Equil.* **1989**, 53, 177-89.

[45] Jorgensen, W.L.; Chandrachekhar, J.; Madura, J.D.; Impey R.W.; Klein, M.L. "Comparison of simple potential functions for simulating liquid water," *J. Chem. Phys.* **1983**, 79, 926-935.

[46] Jorgensen, W.L. "Revised TIPS for simulations of liquid water and aqueous solutions," *J. Chem. Phys.* **1982**, 77, 4156-4163.

[47] Mezei, M. "Theoretical Calculation of the Liquid-Vapor Coexistence Curve of Water, Chloroform and Methanol with the Cavity-Biased Monte Carlo Method in the Gibbs Ensemble," *Molec. Simulation* **1992**, 9, 257-267.

[48] de Pablo, J.J.; Prausnitz, J.M.; Strauch H.J.; Cummings, P.T. "Molecular simulation of water along the liquid-vapor coexistence curve from 25 °C to the critical point," *J. Chem. Phys.* **1990**, 93, 7355-7359.

[49] Strauch H.J.; Cummings, P.T. "Computer Simulation of the Dielectric Properties of Water", *Mol. Simulation* **1989**, 2, 89-104.

[50] Strauch, H.J.; Cummings, P.T. "Comment on: Molecular simulation of water along the liquid-vapor coexistence curve from 25 °C to the critical point," *J. Chem. Phys.* **1992**, 96, 864-5.

[51] Strauch, J.H.; Cummings, P.T. "Computer simulation of vapor liquid equilibria in mixed solvent electrolyte solutions," *Fluid Phase Equil.*, **1993**, 83, 213-22.

[52] Panagiotopoulos, A.Z. "Molecular simulation of phase equilibria: simple, ionic and polymeric fluids," *Fluid Phase Equil.* **1992**, 76, 97-112.

[53] Stell, G. ;Wu, K.C.;Larsen, B. "Critical point in a fluid of charged hard spheres", *Phys. Rev. Lett.* **1976**, 37, 1369-1372.

[54] Valleau, J.P. "Density-scaling: A new Monte Carlo technique in statistical mechanics," *J. Computational Phys.* **1991**, 96, 193-216.

[55] Orkoulas, G.; Panagiotopoulos, A.Z. "Phase equilibria in ionic systems from Monte Carlo simulations with distance-biased test particle insertions," *Fluid Phase Equil.* **1993**, 83, 223-231.

[56] Sheng, Y.-J.; Panagiotopoulos, A.Z.; Kumar, S.K.; Szleifer, I., "Monte Carlo calculation of phase equilibria for a bead-spring polymeric model," submitted for publication (1993).

[57] Dobashi, T.; Nakata, M.; Kaneko, M. "Coexistence curve of polystyrene in methylcyclohexane. II. Comparison of coexistence curves observed and calculated from classical theory," *J. Chem. Phys.* **1980**, 72, 6692-7.

[58] Siepmann, J.I.; Karaborni, S.; Smit, B. "Simulations of complex fluids: critical properties of *n*-alkanes," submitted for publication, 1993.

[59] Tsonopoulos, C.; Tan, Z. "The critical constants of normal alkanes from methane to poly-ethylene II. Application of the Flory Theory," *Fluid Phase Equilib.* **1993**, 83, 127-138.

[60] de Kuijper, A.; Smit, B.; Schouten, J.A.; Michels, J.P.J. "Fluid-fluid phase separation in a repulsive α-exp-6 mixture: a comparison with the full α-exp-6 mixture by means of computer simulations," *Europhys. Lett.* **1990**, 13, 679-83.

[61] Schouten, J.A.; de Kuijper, A.; Michels, J.P.J. "Critical line of He-H2 up to 2500 K and the influence of attraction on fluid-fluid separation," *Phys. Rev. B* **1991**, 44, 6630-4.

[62] Harismiadis,V.I.; Koutras, K.K.; Tassios, D.P.; Panagiotopoulos, A.Z. "How good is conformal solutions theory for phase equilibrium predictions?" *Fluid Phase Equil*. **1991**, 65, 1-18.

[63] Georgoulaki, K.; Ntouros, N.; Tassios, D.P.; Panagiotopoulos, A.Z. unpublished data.

[64] Shing, K.S.; Chung, S.T. "Computes simulation methods for the calculation of solubility in supercritical extraction systems," *J. Phys. Chem*. **1987**, 91, 1674-81.

[65] Panagiotopoulos; A.Z. "Gibbs-ensemble Monte Carlo simulations of phase equilibria in supercritical fluid systems," in *Supercritical Fluid Science and Technology*, Johnston, K.P.; Penninger, J. Eds., ACS Symposium Ser 406; American Chemical Society: Washington, DC., 1989; pp. 39-51.

[66] Panagiotopoulos, A.Z.; Reid, R.C. "High pressure phase equilibria in ternary mixtures with a supercritical component," in *Supercritical Fluids*, Squires, T.G.; Paulaitis, M.E., Eds, ACS Symposium Ser. 329; American Chemical Society: Washington, DC, 1989; pp. 115-129.