Computing absolute free energies of disordered structures by molecular simulation

T. Schilling and F. Schmid

Citation: J. Chem. Phys. **131**, 231102 (2009); doi: 10.1063/1.3274951
View online: http://dx.doi.org/10.1063/1.3274951
View Table of Contents: http://jcp.aip.org/resource/1/JCPSA6/v131/i23
Published by the AIP Publishing LLC.

Computing absolute free energies of disordered structures by molecular simulation

T. Schilling[a] and F. Schmid[b]
Institut für Physik, Johannes Gutenberg-Universität, Staudinger Weg 7, D-55099 Mainz, Germany

(Received 15 October 2009; accepted 25 November 2009; published online 17 December 2009)

We present a Monte Carlo simulation technique by which the free energy of disordered systems can be computed directly. It is based on thermodynamic integration. The central idea is to construct an analytically solvable reference system from a configuration which is representative for the state of interest. The method can be applied to lattice models (e.g., the Ising model) as well as off-lattice molecular models. We focus mainly on the more challenging off-lattice case. We propose a Monte Carlo algorithm, by which the thermodynamic integration path can be sampled efficiently. At the examples of the hard sphere liquid and a hard disk solid with a defect, we discuss several properties of the approach. © *2009 American Institute of Physics*. [doi:10.1063/1.3274951]

The fundamental equation $S=f[U,V,(N_\alpha)]$, which connects the entropy S with the internal energy U, the volume V, and the numbers N_α of particles of type α, contains all information about a system that is accessible within classical thermodynamics. Thermodynamic potentials such as the free energy are related to the fundamental equation by the Legendre transform, hence they equally contain this information.[1] Therefore, there is a large interest in computing free energies in many areas of science, i.e., statistical physics, materials science, theoretical chemistry, and biology.[2] Computing the free energy of disordered systems such as lipid membranes, solids with defects, or nematic liquid crystals, is one of the long-standing unsolved problems in computer simulations.

There are only very few, special cases in which the free energy of a system can be computed directly: Either the accessible phase space volume can be enumerated completely (as for a lattice gas on a small lattice) or the problem can be solved analytically in the first place (as for the ideal gas). In all other cases, one must resort to approximations or to computer simulations. Unfortunately, the latter only give access to free energy derivatives and free energy differences. Several advanced techniques have been developed that allow to relate free energies of different state points to each other, and a large body of literature has been written on this topic.[2–8] Nevertheless, comparing the free energies of arbitrary systems remains a challenge, and alternative approaches that allow to determine the absolute free energy for each individual system are clearly of interest.

In principle, absolute free energies can be obtained by connecting the system of interest with a reference system of known free energy. For a large class of systems, however, this insight is idle because no suitable reference system has been identified yet. In this letter, we propose a general strategy for the construction of analytically solvable reference systems that can be connected with disordered target structures via thermodynamic integration.

Thermodynamic integration[9,10] is a widely applied method to determine free energy differences. Here, we briefly repeat the main ideas: Consider a system with a Hamiltonian $H(\boldsymbol{r}^N,\boldsymbol{p}^N,\varepsilon)$, which explicitly depends on some parameter ε. In order to obtain an expression for its free energy, one uses the relation $\partial F/\partial\varepsilon=\langle\partial H(\varepsilon)/\partial\varepsilon\rangle$, where $\langle\ldots\rangle$ denotes the thermodynamic average. Here and in the following, we set $k_BT=1$. In general, $\langle\partial H(\varepsilon)/\partial\varepsilon\rangle$ is directly accessible in a simulation. Thus, the expression above can be used to evaluate the free energy difference between two systems at different ε: One samples $\langle\partial H(\varepsilon)/\partial\varepsilon\rangle$ for a range of ε and integrates

$$\Delta F = F(\varepsilon_1) - F(\varepsilon_0) = \int_{\varepsilon_0}^{\varepsilon_1} d\varepsilon' \left\langle \frac{\partial H(\varepsilon')}{\partial \varepsilon'} \right\rangle_{\varepsilon'}. \tag{1}$$

If the free energy is known for one ε_0 (reference system), one can calculate absolute free energies for a whole range of ε. However, it is crucial that the evolution of $\langle\partial H(\varepsilon)/\partial\varepsilon\rangle$ on the integration path is reversible, i.e., no phase transition of first order may be crossed. This limits the choice of suitable integration paths and reference systems considerably, and hence a large class of problems could not be tackled by thermodynamic integration up to now. For gases, the ideal gas is a useful reference system, for frozen solids the "Einstein crystal" (where the particles are bound to fixed sites by harmonic potentials[11–15]). To the best of our knowledge, no general strategy to construct reference systems has been introduced so far that can be used for arbitrary disordered systems. Additionally, even if a dense system can be connected to an ideal gas, the integration path is long and therefore errors accumulate leading to low accuracy of the results.

To remedy this situation, we propose to take a configuration that is representative for the structure of interest (obtained within a typical simulation of an equilibrated system) and to construct a reference system by first "pinning" this configuration with suitable external fields, and then switching off the internal interactions. In the remainder of this letter, we will show how this idea can be exploited to evaluate

[a]Electronic mail: schillit@uni-mainz.de.
[b]Electronic mail: friederike.schmid@uni-mainz.de.

absolute free energies in practice. For the purpose of illustration, we begin by considering the Ising model $H_0=-J\Sigma_{\langle ij\rangle}s_is_j$, where $\langle ij\rangle$ denotes neighboring i and j and $s_i=\pm 1$. To evaluate the free energy F_0 at a given temperature, we simulate the system until it is equilibrated, and then pick a typical configuration $\{s_i^R\}$ as "representative" reference configuration. The reference system is then defined by the Hamiltonian

$$H_{\mathrm{ref}}(\varepsilon) = -\varepsilon\sum_i s_i s_i^R \tag{2}$$

and its free energy can be computed easily, $F_{\mathrm{ref}}(\varepsilon)=-N\ln(2\cosh(\varepsilon))$. To establish the connection with the original system, we proceed in two steps: First, we define an intermediate model $H'(\varepsilon)=H_0+H_{\mathrm{ref}}(\varepsilon)$, which reduces to H_0 at $\varepsilon=0$. The free energy difference $\Delta F_1(\varepsilon)=F_0-F'(\varepsilon)$ between the original system and the intermediate system can be calculated for arbitrary ε by thermodynamic integration, using $\langle\partial H'/\partial\varepsilon\rangle=-\langle\Sigma_i s_i s_i^R\rangle$. The second step is to connect the intermediate system to the reference system. The free energy difference between the two systems at the same value of ε, $\Delta F_2(\varepsilon)=F'(\varepsilon)-F_{\mathrm{ref}}(\varepsilon)$, is evaluated by carrying out a simulation with additional Monte Carlo (MC) moves that switch on and off the interaction J according to a Metropolis criterion. [ε is chosen large enough that the spins in the system $H'(\varepsilon)$ hardly fluctuate about the reference value.] We obtain $\Delta F_2(\varepsilon)=-\ln(P_{\mathrm{on}}/P_{\mathrm{off}})$, where $P_{\mathrm{on,off}}$ is the fraction of configurations with interactions switched on (off). Combining everything, we obtain the absolute free energy of the target system H_0, $F_0=F_{\mathrm{ref}}(\varepsilon)+\Delta F_1(\varepsilon)+\Delta F_2(\varepsilon)$.

Now, we transfer this idea to off-lattice particle models. For clarity, we only discuss monatomic liquids and solids in the *NVT* ensemble in the following. Our method can be easily generalized to molecular systems, and, as we shall demonstrate below, to constant pressure simulations. Furthermore, we disregard the kinetic contribution to the free energy, which can be evaluated trivially.[16]

Let configurations be characterized by a set of coordinates $\{\boldsymbol{r}_i\}$ and the configurational energy be given by a Hamiltonian $H_0=U(\{\boldsymbol{r}_i\})$. To calculate the free energy of a given, arbitrary equilibrium structure, we choose a representative configuration $\{\boldsymbol{r}_i^R\}$, obtained from a simulation of an equilibrated system, and construct a reference system by imposing local potentials

$$H_{\mathrm{ref}}(\varepsilon) = \varepsilon\sum_i \Phi\left(\frac{|\boldsymbol{r}_i-\boldsymbol{r}_i^R|}{r_{\mathrm{cutoff}}}\right) \tag{3}$$

that pin the particles' positions $\boldsymbol{r}_i$ to the reference positions $\boldsymbol{r}_i^R$. Here, Φ defines attractive potential wells centered at each position $\boldsymbol{r}_i^R$, with $\Phi(x)<0$ for $x<1$ and $\Phi\equiv 0$ elsewhere. Note that particle i can only be trapped by well i and not by the other wells. To make the particles indistinguishable as they should be, we allow them to swap identities (i.e., labels i,j) at regular intervals during the simulations. We will show below that such identity swaps are also necessary to equilibrate the system efficiently.

The (configurational) reference free energy is given by

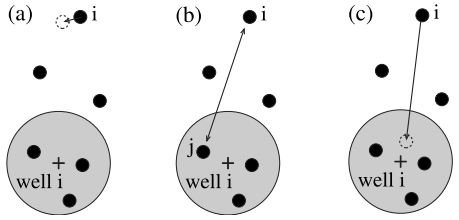

FIG. 1. Sketch of moves in our MC algorithm. (a) Simple particle displacements. (Could be replaced, e.g., by short molecular dynamics runs.) (b) Smart particle swaps. (c) Smart particle relocations. See text for explanation.

$$\frac{F_{\mathrm{ref}}(\varepsilon)}{N} = \ln\left(\frac{N}{V}\right) - \ln\left(1+\frac{V_0}{V}g_\Phi(\varepsilon)\right), \tag{4}$$

where V_0 is the volume of the sphere of radius r_{cutoff} and $g_\Phi(\varepsilon):=d\int_0^1 dx\, x^{d-1}(e^{-\varepsilon\Phi(x)}-1)$ for a d-dimensional problem. Here, we mostly used a linear well potential $\Phi(x)=x-1$, giving $g_\Phi(\varepsilon)=d/\varepsilon^d(e^\varepsilon-\Sigma_{k=0}^d\varepsilon^k/k!)$. As before, we define an intermediate model $H'(\varepsilon)=H_0+H_{\mathrm{ref}}(\varepsilon)$, and evaluate $\Delta F_2(\varepsilon)$ at high ε with a MC simulation where the interaction H_0 is switched on and off (if necessary, in several steps). $\Delta F_1(\varepsilon)$ is computed by sampling $\partial F'/\partial\varepsilon=\langle\Sigma_i\Phi(|\boldsymbol{r}_i-\boldsymbol{r}_i^R|/r_{\mathrm{cutoff}})\rangle$ and performing a thermodynamic integration. The remaining challenge is to devise an algorithm for sampling the intermediate model efficiently for arbitrary ε.

We first note that the range r_{cutoff} of the reference potential must be chosen finite when looking at liquid systems. Otherwise, $\partial F'/\partial\varepsilon$ diverges at $\varepsilon\to 0$ and cannot be sampled efficiently in large systems. (In practice, the particular choice of r_{cutoff} turns out to be not crucial.) This, however, introduces a problem: The particles need to find their respective wells of attraction. We therefore introduce two MC moves that help particles i explore their well i (Fig. 1). One move [Fig. 1(b)] swaps particles in a smart way. It works as follows:

- Pick a random particle i and find the set of particles $\{n_i\}$ that are within the attraction range of well i.
- If particle $i\notin\{n_i\}$, pick a particle j from $\{n_i\}$ and swap i and j with the probability $\min\{1,(n_i/N)e^{-\Delta H'}\}$.
- Otherwise, pick a particle j from all particles;
- if $j\notin\{n_i\}$, swap with probability $\min\{1,(N/n_i)e^{-\Delta H'}\}$.
- if $j\in\{n_i\}$, swap with probability $\min\{1,e^{-\Delta H'}\}$.

Here, $\Delta H'$ is the difference in the energies (according to the intermediate model) of the old and new configuration. This algorithm promotes particle swaps that bring particles close to their respective well and nevertheless satisfies detailed balance.

The other move [Fig. 1(c)] relocates particles i with a bias toward the neighborhood of their well i.

- Pick a random particle i (with position $\boldsymbol{r}_i$).
- Choose a new position $\boldsymbol{r}_i'$ from a given (biased) distribution $P_i(\boldsymbol{r}_i')=\exp(-W(|\boldsymbol{r}_i'-\boldsymbol{r}_i^R|))$.

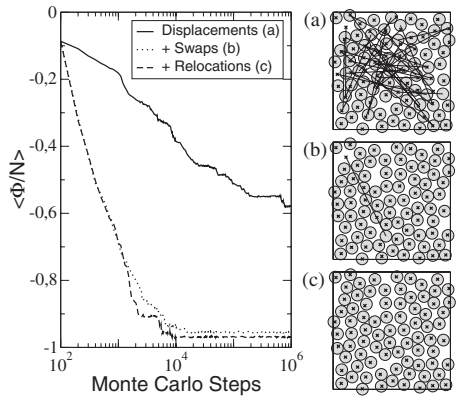

FIG. 2. Illustration of the effect of the moves of Fig. 1 on the equilibration of a system of 80 hard disks (diameter D) at a density $\rho=0.8/D^2$, after switching on linear well potentials with strength $\varepsilon=50$ ($r_{\text{cutoff}}=2D$). Swap moves and relocation moves (one per bead) were attempted one per 100 MC sweeps. Left: Evolution of $\langle\Phi\rangle$ in simulations that include different moves as indicated. Right: Corresponding final configurations. Circles indicate particle positions, crosses give well positions. Particles and their respective wells are connected by straight lines.

- Relocate the particle from $\boldsymbol{r}$ to $\boldsymbol{r}_i'$ with probability $\min\{1, P(\boldsymbol{r}_i)/P(\boldsymbol{r}_i')e^{-\Delta H'}\}$.

Obvious choices for $W(r)$ which we have tested are $W(r)=\varepsilon\Phi(r/r_{\text{cutoff}})$ or $W(r)=\text{const.}$ for $r<r_{\text{cutoff}}$. At high ε, the relocation move helps to overcome trapped situations where most particles are bound to a well, and a few cannot escape from a local cage. To illustrate the effect of the different moves, Fig. 2 shows the evolution of the observable $\langle\Phi_i\rangle$, averaged over all particles i, in a two-dimensional system of hard disks, after ε had been raised from zero to a high value. In a MC simulation that includes only random particle displacements, the system is far from equilibration after one million MC sweeps (a). The smart swap moves speed up equilibration considerably, but the system gets trapped in a configuration where one particle cannot enter its well (b). This problem is solved by including smart relocation moves (c).

We will now demonstrate the power of our approach at a few examples. We have studied hard spheres in two (2d) and three dimensions (3d). The simulations were carried out on ordinary workstations with test programs within a few days. Optimized programs would yield even higher accuracy. For the remainder of this letter, we use the particle diameter D as unit of length.

TABLE I. Results for the free energy of hard spheres. F/N_{CS} is the value according to the Carnahan–Starling equation of state (Ref. 17).

N/V	F/N	$(F/N)_{\text{CS}}$
0.25	0.620 ± 0.002	0.625
0.5[a]	1.541 ± 0.002	1.544
0.5[b]	1.540 ± 0.002	1.544
0.5[c]	1.549 ± 0.002	1.544
0.75	3.009 ± 0.005	3.005

[a]Linear potential Φ, liquid reference state.
[b]Linear Φ, hcp reference state.
[c]Harmonic Φ, liquid reference state.

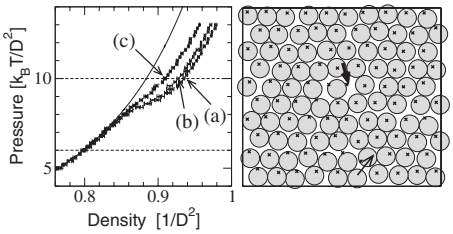

FIG. 3. Characterization of the dense two-dimensional systems discussed in the text. Left: Pressure vs density as obtained from constant pressure simulations at $\varepsilon=0$. (a) $N=100$ particles, expanded from an ordered solid phase, (b) $N=99$ particles, expanded from an ordered solid phase with one vacancy, (c) $N=100$ particles (diameter D), compressed from the fluid phase. The solid line shows the theoretical estimate (Ref. 18) $P=\hat{\rho}/(1-[\pi/4]\hat{\rho})^2$ with $\hat{\rho}=(N+1)/\langle V\rangle$. Right: A configuration with one vacancy at the beginning (crosses) and the end (circles) of a MC run. The thin and thick arrows mark the respective positions of the defect.

Table I shows results for the free energy of a liquid in 3d. The simulations were performed on a system of $N=256$ particles, using 50 values of ε and 6×10^5 MC sweeps for each value at $N/V=0.25$ and $N/V=0.5$, and 200 values of ε times 1 Mio. MC sweeps at $N/V=0.75$. The results agree with the values obtained by integration of the Carnahan–Starling equation of state[17] within the error bars. For $N/V=0.5$, we compared the cases (a) linear potential Φ and liquid reference state, (b) linear Φ and crystalline reference state, and (c) harmonic Φ and liquid reference state. Within the error bars, these variations produce the same result. However, for more accurate calculations the linear potential seems to be most useful because the particles get trapped most efficiently. In case (b), we did not see a hysteresis on increasing/decreasing ε. This will presumably be different closer to liquid/solid coexistence. Nevertheless, we can conclude that our method is robust and may work even if the reference configuration is not "ideal," i.e., not representative of the target structure.

Next, we show an example for the application of the method to dense disordered systems, where the dynamics is driven by cooperative processes. We studied hard disks in 2d up to densities where the equilibrium phase is a solid, and enforced a vacancy defect by taking one particle out of an otherwise ordered configuration. These simulations were carried out at constant pressure P in a rectangular simulation box of varying area, but fixed side ratio $1:\sqrt{3/4}$, to accommodate a triangular lattice. The defect is then stable, but highly mobile (see Fig. 3, right).

We compare three different structures (Fig. 3, left): An ordered solid (a), an ordered solid with a vacancy (b), and a metastable disordered jammed phase (c), which was obtained by compressing the system from the fluid phase. Free energy calculations were carried out at $P=10$ for these three cases, and additionally at $P=6$, in the fluid regime. To calculate the free energy in the enthalpic ensemble, we use a reference system that is defined in terms of scalable coordinates (i.e., the positions of the well centers are rescaled along with the particle coordinates if the volume of the system changes), and pin the volume of the system by an additional term $\varepsilon(V-V_{\text{ref}})^2$ in the reference Hamiltonian. The resulting free enthalpies G can be related to the chemical potential μ by

virtue of the thermodynamic relation $G=\mu N$.

At $P=6$, the free energy calculation yields the free enthalpy per particle $\mu=8.997\pm0.002$, which is in reasonable agreement with the theoretical estimate $\mu=9.047$.[18] At $P=10$, we found $\mu_{\mathrm{solid}}=13.617\pm0.002$ in the solid state and $\mu_{\mathrm{jam}}=13.675\pm0.002$ in the jammed state, which establishes that the solid is indeed the stable phase. For the system with one defect, we obtained the total enthalpy $G_{\mathrm{defect}}=1361.7\pm0.2$. This result can be used to estimate the core free energy of the vacancy $\mu_c=G_{\mathrm{defect}}-\mu_{\mathrm{solid}}N+\ln(N)=7.1\pm0.3$, which corresponds to a relative vacancy frequency of roughly 10^{-3}. (For comparison, the frequency of vacancies at liquid/solid coexistence[19] in 3d is roughly 10^{-4}.) Probably, μ_c is largely overestimated due to finite size effects, hence the value given above is at best an upper bound. More detailed studies shall be carried out in the future. Here, the example mainly serves to illustrate the use of our approach in situations where free energies are difficult to access with other methods.

In summary, we have introduced a general method to compute absolute free energies for a wide range of structures. We have illustrated the method for monatomic simple systems, but it can be applied equally well to molecular fluids and mixtures. We anticipate that our method will be useful to calculate free energies of systems that are not directly connected with the ideal gas, such as liquid crystal phases or membranes. In combination with additional smart moves such as configurational bias,[9] it should also be applicable to macromolecular systems. Another promising field of application is defects in solids. From a fundamental point of view, it should be interesting to study how well the method can be applied to glassy systems, which have not just one, but a whole set of representative configurations, one for each local minimum in a rugged free energy landscape.

We thank M. Oettel for stimulating discussions. We are grateful to the DFG (Emmy Noether Program SCHI 853/1-3 and SFB 625) for financial support.

[1] R. Jelitto, *Thermodynamik und Statistik* (Aula Verlag, Wiesbaden, 1989).
[2] *Free Energy Calculations. Theory and Applications in Chemistry and Biology*, edited by C. Chipot and A. Pohorille (Springer Verlag, Berlin, 2007).
[3] D. Earl and M. Deem, Phys. Chem. Chem. Phys. **7**, 3910 (2005).
[4] Y. Okamoto, J. Mol. Graphics Modell. **22**, SI425 (2004).
[5] A. Panagiotopoulos, J. Phys. Condens. Matter **12**, R25 (2000).
[6] J. de Pablo, Q. Yan, and F. Escobedo, Annu. Rev. Phys. Chem. **50**, 377 (1999).
[7] A. D. Bruce, A. N. Jackson, G. J. Ackland, and N. B. Wilding, Phys. Rev. E **61**, 906 (2000).
[8] N. B. Wilding and A. D. Bruce, Phys. Rev. Lett. **85**, 5138 (2000).
[9] D. Frenkel and B. Smit, *Understanding Molecular Simulation* (Academic, London, 2002).
[10] D. P. Landau and K. Binder, *A Guide to Monte Carlo Simulations in Statistical Physics* (Cambridge University Press, Cambridge, 2005).
[11] A. Einstein, Ann. Phys. **22**, 180 (1907).
[12] D. Frenkel and A. Ladd, J. Chem. Phys. **81**, 3188 (1984).
[13] R. B. Speedy, Mol. Phys. **80**, 1105 (1993).
[14] C. Vega and E. Noya, J. Chem. Phys. **127**, 154113 (2007).
[15] B. M. Mladek, P. Charbonneau, C. N. Likos, D. Frenkel, and G. Kahl, J. Phys. Condens. Matter **20**, 494245 (2008).
[16] J. P. Hansen and I. R. McDonald, *Theory of Simple Liquids* (Academic, London, 2000).
[17] N. Carnahan and K. Starling, J. Chem. Phys. **51**, 635 (1969).
[18] E. Helfand, H. L. Frisch, and J. L. Lebowitz, J. Chem. Phys. **34**, 1037 (1960).
[19] S. Pronk and D. Frenkel, J. Phys. Chem. B **105**, 6722 (2001).