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Optimal temperature ladders in replica exchange simulations

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ABSTRACT

In replica exchange simulations, a temperature ladder with N rungs spans a given temperature interval. Considering systems with heat capacities independent of the temperature, here we address the question of how large N should be chosen for an optimally fast diffusion of the replicas through the temperature space. Using a simple example we show that choosing average acceptance probabilities of about 45% and computing N accordingly maximizes the round trip rates r across the given temperature range. This result differs from previous analyses which suggested smaller average acceptance probabilities of about 23%. We show that the latter choice maximizes the ratio r/N instead of r.

1. Introduction

At given computer resources, the benefit of replica exchange [1–3] (RE) simulations crucially depends on the choice of certain parameters. Having chosen a temperature range $[T_{\min}, T_{\max}]$, which should be covered by the RE simulation, the optimal form of the temperature ladder $(T_1 = T_{\min}, T_2, \ldots, T_N = T_{\max})$ is an important issue [4–10]. Aiming at a minimal average round trip time of the replicas in the temperature space and assuming a constant heat capacity C, which should approximately apply to explicit solvent simulations [11], Nadler and Hansmann [9] have derived a formula

$$N \approx 1 + 0.594\sqrt{C}\ln(T_{\max}/T_{\min}) \tag{1}$$

for the number N of rungs in the temperature ladder. In Eq. (1) the (extensive) heat capacity C is given in units of the Boltzmann constant k_B and refers to the potential energy part of the total energy. As suggested by Okamoto et al. [12], from N one can determine the temperature rungs $T_i, i = 1, \ldots, N$, in the ladder by

$$T_i = T_{\min}(T_{\max}/T_{\min})^{(i-1)/(N-1)}. \tag{2}$$

This choice is generally expected [3] to provide equal exchange probabilities $p_{\mathrm{acc}}(T_i, T_{i+1}) = p_{\mathrm{acc}}(N)$ along the N-rung ladder.

Defining the function

$$\alpha(N) \equiv (T_{\max}/T_{\min})^{1/(N-1)}, \tag{3}$$

one immediately finds that the temperature rungs are given by the recursion

$$T_{i+1} = T_i\alpha(N). \tag{4}$$

Thus, for a given N, the ratio T_{i+1}/T_i is the constant $\alpha(N)$. For such a ladder and normally distributed potential energies, which is, along with a constant heat capacity, typical for explicit solvent simulation systems, the average acceptance probabilities are very well approximated [6] by

$$p_{\mathrm{acc}}(N) = \mathrm{erfc}\left[\sqrt{C}\,\frac{\alpha(N)-1}{\alpha(N)+1}\right], \tag{5}$$

where $\mathrm{erfc}(x') = 2/\sqrt{\pi}\int_{x'}^{\infty}\exp(-x^2)\mathrm{d}x$ is the complementary error function.

In summary, for a ladder spanning the temperature range $[T_{\min}, T_{\max}]$ by the exponential spacing law Eq. (2), the temperature rungs T_i are uniquely given by N. Assuming a constant heat capacity and normally distributed potential energies, such a ladder then actually provides equal average acceptance probabilities [Eq. (5)]. Therefore, temperature ladders obeying Eqs. (2) and (5) are uniquely specified by choosing either a certain number N of rungs or a certain average acceptance probability p_{acc}.

2. Methods and simulation set-up

To check whether the formula given in Eq. (1) and suggested by Nadler and Hansmann [9] actually yields RE temperature ladders with minimal round trip times, we have designed simple test systems suited for computationally inexpensive RE Monte Carlo (REMC) simulations. The systems consist of d independent one-dimensional and harmonic oscillators in the canonical ensemble (we have chosen the same potential $E = x^2$ for all oscillators). At each REMC step the coordinates of all d oscillators in a replica are randomly drawn from the associated normal distributions, the total energy E_i of the system at temperature T_i is calculated, and an exchange of systems at neighboring [3] temperatures is attempted with the Metropolis probability [13] $p(i, i+1) = \min\{1, \exp[(1/k_BT_{i+1} - 1/k_BT_i)(E_{i+1} - E_i)]\}$. We employed the standard exchange scheme [1], which alternately attempts exchanges between 'even' (T_{2i}, T_{2i+1}) and 'odd' (T_{2i-1}, T_{2i}) replica pairs. Below

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we call this RE scheme, which combines the standard exchange with the standard Metropolis criterion, the standard RE set-up.

Note the important fact that the heat capacity of our test system is independent of the temperature and is given by $C = d/2$. Therefore, it matches the conditions assumed in the derivation of Eq. (1). Note furthermore that the force constants of the harmonic oscillator potentials are of no concern because the Metropolis probability solely depends on the overlaps of the energy distributions.

First we consider the case $d = 100$. As extremal temperatures we choose $T_{\min} = 300$ K and $T_{\max} = 800$ K. With these parameters, Eqs. (1), (2), and (5) yield $N = 5$, the temperature ladder (300, 383.4, 389.9, 626.0, 800), and the average acceptance probability $p_{\text{acc}} \approx 22\%$, respectively. Previously also Kone and Kofke [6] and Rathore et al. [5] have suggested an acceptance probability of about 23% to be optimal. Thus, choosing the number of rungs through Eq. (1) seems to yield a reasonable acceptance probability.

The question as to whether the above choice actually entails minimal round trip times in REMC simulations can be addressed by comparing the set-up outlined above with alternatives defined by different choices of N. We tested ladders with $N \in \{3, 4, \ldots, 9, 10, 12, \ldots, 18, 20\}$ each spanning the same temperature range [300 K, 800 K]. Every associated REMC simulation covered $S = 500\,000$ MC steps. From each of these REMC simulations we determined the number of round trips $M(N)$. Here, a round trip was counted whenever a selected replica that started at $T_{\min}$ subsequently reached $T_{\max}$ and eventually returned to $T_{\min}$. Considering instead of the round trip time $\tau(N)$ of a replica its inverse, the round trip rate $r(N) \equiv M(N)/S$, we asked which acceptance probability $p_{\text{acc}}(N)$ [cf. Eq. (5)] belongs to the maximal rate $r(N)$ measured in any of our simulations.

3. Results

Fig. 1 shows the measured round trip rate r as a function $r(p_{\text{acc}})$ of the average acceptance probability p_{acc}. Two data points are additionally marked by the numbers of rungs in the associated ladders ($N = 5, N = 7$). According to the graph the round trip rate r is maximal at $p_{\text{acc}} \approx 0.42$ belonging to the $N = 7$ rung ladder. This result differs from the expectation voiced above that r should be maximal at $p_{\text{acc}} \approx 0.22$ or $N = 5$, respectively.

This surprising result raises the question why Eq. (1) yields a prediction for the optimal N (or p_{acc}) differing from the measured one. Nadler and Hansmann [9] started the derivation of Eq. (1) by assuming for the round trip rate the plausible relation $r(p_{\text{acc}}, N) = k p_{\text{acc}}/N(N-1)$ with a certain constant $k > 0$. Using this assumption, one predicts that the rate $r(0.22, 5) = k\,0.22/5(5-1) \approx 0.011\,k$ should be larger than the rate $r(0.42, 7) = k\,0.42/7(7-1) \approx 0.010\,k$, which is clearly at variance with the results of our simulation. Thus, the quoted relation does not yield the correct round trip rate $r(p_{\text{acc}})$ and, correspondingly, the choice of the ladder size N through Eq. (1) does not maximize r, if the standard RE set-up is used.

To understand how r depends on p_{acc} we introduce the average (and relative) temperature move

$$\kappa(T_i, T_{i+1}) \equiv p_{\text{acc}}(T_i, T_{i+1}) \frac{T_{i+1} - T_i}{T_i} \tag{6}$$

of a replica per exchange trial (here one MC step). κ measures the average velocity of the replicas in a properly scaled temperature space. This definition is motivated by our assumption that the average replica velocity κ should be proportional to the round trip rate, i.e. that $\kappa = fr$ with a constant $f > 0$. Thus, we expect the largest round trip rates r for the largest velocities κ.

Using Eq. (4) and inverting Eq. (5) one finds for the average replica velocity

$$\kappa(p_{\text{acc}}) = p_{\text{acc}} \frac{2\text{erfc}^{-1}(p_{\text{acc}})}{\sqrt{C} - \text{erfc}^{-1}(p_{\text{acc}})}, \tag{7}$$

where erfc^{-1} denotes the inverse of the complementary error function. Thus, in contrast to the impression evoked by the definition in Eq. (6), κ is a constant within a given temperature ladder (because p_{acc} is a constant across each ladder).

The lines in Fig. 2 are the graphs of the function $\kappa(p_{\text{acc}})$ given by Eq. (7) for systems with small and large heat capacities $C = d/2$. For $d = 100$ (solid) the velocity κ becomes maximal at $p_{\text{acc}} \approx 0.42$ (i.e. at $N = 7$) and for $d = 1000$ (dashed) at $p_{\text{acc}} \approx 0.44$ (i.e. at $N = 22$). Fig. 2 additionally displays scaled round trip rates fr measured for the small ($f = 9.71$) and the large system ($f = 24.6$), respectively. The good match of the scaled rates $fr(p_{\text{acc}})$ (circles/squares) with the respective graphs $\kappa(p_{\text{acc}})$ verifies our assumption that the average velocity $\kappa(p_{\text{acc}})$ of the replicas in scaled temperature space is proportional to the round trip rate $r(p_{\text{acc}})$. Note that the value of the optimal average acceptance rate, at which the round trip rate r becomes maximal, depends only weakly on the system size d.

The noted weak dependence of the optimal average acceptance probability p_{acc} on the system size $d = 2C$ can be understood by considering the limit of large systems ($C \to \infty$). Using *Mathematica* [14] we have determined the derivative $\kappa'(p_{\text{acc}}) \equiv \mathrm{d}\kappa/\mathrm{d}p_{\text{acc}}$ and its first order Taylor expansion $\kappa'(p_{\text{acc}}) = a_0 + a_1 p_{\text{acc}} + \mathcal{O}(p_{\text{acc}}^2)$ at $p_{\text{acc}} = 0.5$. In linear approximation κ' vanishes at $p_{\text{acc}}^0 = -a_0/a_1$ which is given by

$$p_{\text{acc}}^0 \approx 0.45 + g/\sqrt{C} \tag{8}$$

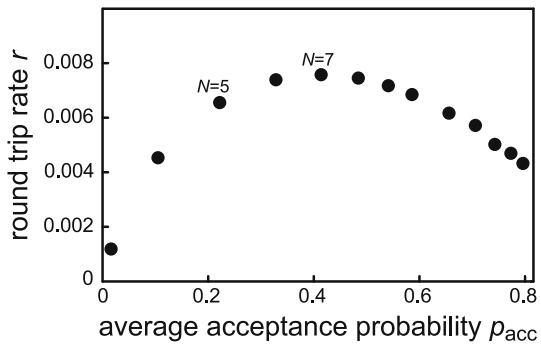

Fig. 1. Measured round trip rates r as a function of the average acceptance probability p_{acc}.

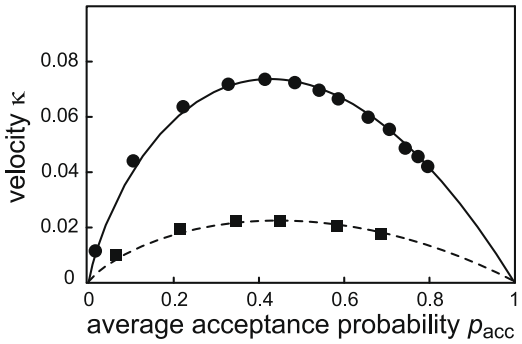

Fig. 2. Average replica velocity κ in scaled temperature space as a function of the average acceptance probability p_{acc}. The lines are graphs of $\kappa(p_{\text{acc}})$ calculated from Eq. (7) for $d = 100$ (solid) and $d = 1000$ (dashed). The dots are the round trip rates r of Fig. 1 scaled by the factor $f = 9.71$. The squares are round trip rates scaled by $f = 24.6$ and resulting from REMC simulations of $d = 1000$ oscillators. Here, the rung numbers $N \in \{10, 14, 18, 22, 30, 40\}$ increase from left to right.

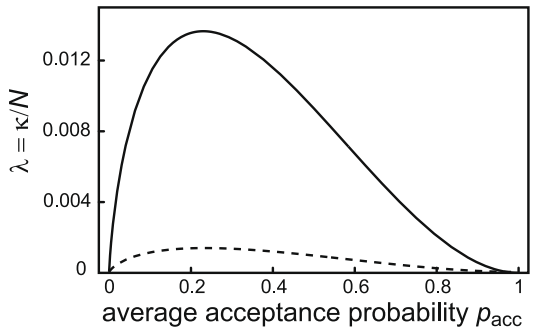

Fig. 3. $\lambda = \kappa/N$ as a function of the average acceptance probability p_{acc}. The lines are the graphs of Eq. (10) for $d = 100$ (solid) and $d = 1000$ (dashed).

with the constant g being of the order of -0.1. Thus for large systems the location p^0_{acc} of the maximum of κ approaches 0.45 from below. Note that we have also checked the limiting value 0.45 by numerically analyzing Eq. (7) for very large C.

The thus established limiting value of the optimal average acceptance probability leads to a new estimate

$$N \approx 1 + (\sqrt{C}/(2 \times 0.534) - 1/2)\ln(T_{max}/T_{min}) \tag{9}$$

for the optimal number of rungs in the associated temperature ladder. For computing Eq. (9) we have used Eq. (5), $\mathrm{erfc}^{-1}(0.45) \approx 0.534$, and $\ln[1 + 2 \times 0.534/(\sqrt{C} - 0.534)] \approx 2 \times 0.534/(\sqrt{C} - 0.534)$ for large C.

In summary, to maximize the round trip rate or minimize the round trip time, respectively, Eq. (9) has to be used instead of Eq. (1). From a practical point of view, however, instead of aiming at the maximal round trip rate, one may be content with a suboptimal rate if this choice is associated with a reduced computational effort. Instead of maximizing κ one may therefore consider the quantity

$$\lambda(p_{acc}) \equiv \kappa(p_{acc})/N(p_{acc}), \tag{10}$$

which exhibits a penalty linear in the number N of rungs. Fig. 3 shows the graphs of $\lambda(p_{acc})$ for $d = 100$ (solid line) and $d = 1000$ (dashed line). In both cases λ is maximal at $p_{acc} \approx 0.23$. Applying once again the reasoning used in the derivation of Eq. (8) one finds that the optimal p_{acc} approaches 0.234 for $C \to \infty$. This result leads to the estimate

$$N \approx 1 + (0.594\sqrt{C} - 1/2)\ln(T_{max}/T_{min}) \tag{11}$$

for the number of rungs optimizing the specific compromise $\lambda = \kappa/N$ between the round trip rate r and the number N of replicas.

Note here that Eqs. (11) and (1) become identical for large C. Thus, the number of rungs resulting from Eq. (1) effectively maximizes λ instead of κ (or, equivalently, a ladder size penalized round trip rate r/N instead of the round trip rate r). That Nadler and Hansmann [9] have effectively maximized λ instead of r can be alternatively understood by inserting the definition Eq. (6) into (10). Using subsequently Eq. (4) and the approximation $(T_{max}/T_{min})^{1/(N-1)} \approx 1 + \ln(T_{max}/T_{min})/(N-1)$, which holds for large N, one finds $\lambda \approx p_{acc}\ln(T_{max}/T_{min})/[N(N-1)]$ such that $\lambda \propto p_{acc}/[N(N-1)]$. Recall now that Nadler and Hansmann erroneously assumed a relation of this kind for the round trip rate r (i.e. for κ).

We would like to remark that our results are transferable to simulated tempering [15,16] (ST) simulations. For ST, the average acceptance probability is given by

$$p^{ST}_{acc}(N) = \mathrm{erfc}\left(\sqrt{C/2}\,\frac{\alpha(N)-1}{\alpha(N)+1}\right). \tag{12}$$

which is obtained from the RE expression Eq. (5) through replacing C by $C/2$ [5,17]. In the limit of large systems also $C/2$ becomes large and the optimal value of p^{ST}_{acc} is likewise at 45% or 23% depending on the optimized quantity. Similarly, the optimal N is given by Eqs. (9) or (11), respectively, through replacing C by $C/2$.

4. Summary

For simulations employing the standard RE set-up, we have derived with Eqs. (9) and (11) two formulas for the optimal sizes N of temperature ladders obeying Eqs. (2) and (5). Here, optimal means that either the round trip rate r or the compromise r/N with computational effort is maximized. We have furthermore shown that the suggestion Eq. (1) of Nadler and Hansmann [9] maximizes the compromise r/N and not r, as claimed by the authors. An optimal r is obtained with average acceptance probabilities of about 45%, whereas an optimal r/N requires values of 23% matching earlier suggestions [6,5]. As a practical consequence of our study one sees that average acceptance probabilities chosen in the range from 20% to 45% are definitely 'good' choices featuring, however, slightly different merits.

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