Quantum–biased umbrella sampling for mixed quantum/classical simulation: The potential of mean force between hydrated electrons

Ross E. Larsen and Benjamin J. Schwartz
Department of Chemistry and Biochemistry,
University of California, Los Angeles, CA 90095–1569

(Dated: November 9, 2006)

Abstract

We introduce a simulation method, called quantum–biased umbrella sampling (QBUS), that extends umbrella sampling (Umb-S) to quantum mechanical degrees of freedom. The method is based on classical Umb-S, in which a bias potential is applied to cause rare configurations to be sampled preferentially and the effects of the bias are later removed analytically. Standard Umb-S cannot be used when the bias must be applied to quantum–mechanical degrees of freedom because the bias potential must commute with the system Hamiltonian. For QBUS, we construct bias potentials that commute approximately with the Hamiltonian, allowing Umb-S to be applied directly to quantum degrees of freedom. We demonstrate the usefulness of QBUS by calculating the potential of mean force between two hydrated electrons at room temperature using full configuration interaction mixed quantum/classical simulation. We find, consistent with what has been inferred from experiment, that two hydrated electrons form a stable (by ∼1.6 k_BT) complex when they are separated by ∼6.75 Å.

One of the first steps in understanding physical or chemical processes involves predicting the probability of the system to achieve some special configuration. For most systems, such special configurations are usually associated with a local maximum or saddle point on the relevant free energy surface. In practice, the search for these points is accomplished by computing the free energy of the system as a function of the reaction coordinate, a quantity known as the potential of mean force (PMF),

$$W(q) = -k_B T \ln \left[P(q)/P(q_0) \right] \ , \tag{1}$$

where $P(q)$ is the probability of finding the system at a particular value of the reaction coordinate q, k_B is Boltzmann's constant, T is the temperature, and q_0 is the coordinate whose free energy is zero. Eq. 1 defines the PMF as the function whose Boltzmann factor produces the equilibrium population distribution, $P(q)$.

For systems that obey Newton's laws, many statistical mechanics techniques have been developed to bias systems to calculate free energies efficiently,[1, 2] but there is almost no methodology in the literature for finding the PMF when the reaction coordinate depends on quantum mechanical (QM) degrees of freedom, e.g., where q measures the amount of electrical charge on the donor in a charge transfer reaction. In this Letter, we generalize the classical method of umbrella sampling [2] (Umb-S) to allow the efficient calculation of PMFs for quantum mechanical systems. We then apply our new method, called quantum–biased umbrella sampling (QBUS), to study the PMF between two hydrated electrons (e^-_{hyd}). The PMF between two hydrated electrons is of considerable interest not only because of the e^-_{hyd}'s status as the canonical quantum solute,[3, 4] but also because the e^-_{hyd}–e^-_{hyd} interaction plays an intrinsic role in their annihilation reaction,[5] which is central to understanding radiation chemistry and damage.[4] In fact, it is believed that e^-_{hyd}–e^-_{hyd} pairs form short–lived bound complexes *en route* to annihilation.[5]

The chief difficulty in calculating a PMF is that it is extremely inefficient to find $P(q)$ by direct simulation because most of the configurations generated are near free energy minima, so that interesting regions such as local maxima or saddle points are undersampled. There are several approaches to improving sampling of rarely–visited reaction coordinates,[1] but here we focus on Umb-S.[2] In Umb-S, a bias potential is added to the system's Hamiltonian to force the system to preferentially sample reaction coordinates in regions of interest and the effect of this bias on the sampling is removed at a later stage of the calculation. For a classical system described by a Hamiltonian, H, the average in the canonical ensemble of any quantity f (which depends on some or all of the degrees of freedom) may be written

$$\begin{aligned}\langle f\rangle &= \frac{Tr\left(fe^{-\beta H}\right)}{Tr\left(e^{-\beta H}\right)} = \frac{Tr\left(fe^{\beta U}e^{-\beta(H+U)}\right)}{Tr\left(e^{\beta U}e^{-\beta(H+U)}\right)} \\ &= \frac{\langle fe^{\beta U}\rangle_U}{\langle e^{\beta U}\rangle_U}\ , \qquad (2)\end{aligned}$$

where Tr denotes the trace over all degrees of freedom, $\beta = 1/k_BT$, and $\langle\ \rangle_U$ denotes an ensemble average using $H + U$ as the Hamiltonian. In the second equality, we multiply and divide by one to introduce the umbrella potential, U. The last equality in Eq. 2 shows that $\langle f\rangle$ can also be computed in the presence of the U. To use this formalism to calculate the PMF between two classical particles, one computes $g(r;U) = \langle\delta(r - r_{12})\exp{(\beta U)}\rangle_U$, where r_{12} is the interparticle distance, using a series of potentials U that restrict r_{12} to a desired range of values. With perfect statistics, each $g(r;U)/\langle\exp{(\beta U)}\rangle_U$ generated this way would be identical, but in practice, finite sampling causes each distribution to be peaked near the value allowed by U. Thus, the final step in Umb-S is to create an unbiased $g(r)$ by properly combining the simulated $g(r;U)$.[2, 6]

Umb-S is well established for classical simulations,[2] but a similar derivation cannot be applied when the bias potential acts on quantum degrees of freedom: the second equality in Eq. 2 requires that $e^{-\beta\hat{H}}e^{-\beta\hat{U}} = e^{-\beta(\hat{H}+\hat{U})}$, which is true for QM systems only when $\hat{H}$ and $\hat{U}$ commute. For some mixed quantum/classical systems, this problem may be side-stepped by applying the umbrella bias to classical degrees of freedom in a such a way that the mixed quantum/classical reaction coordinate samples the desired values. Staib and Borgis took this approach when they calculated the PMF between an excited electron and a chlorine atom in liquid water;[7] their umbrella sampling potential tethered the (classical) chlorine atom to the centroid of the QM electron's position, so the bias did not directly affect the QM electron's wave function. It is difficult to see how such an approach can be used for systems such as pairs of hydrated electrons, in which there is no obvious classical degree of freedom that can be biased instead of the quantum degrees of freedom.

How can we modify Umb-S so that a bias can be directly applied to quantum mechanical degrees of freedom? One approach would be to use the Baker–Campbell–Hausdorff (BCH) formula[8] to write $e^{-\beta\hat{H}}e^{-\beta\hat{U}} = e^{-\beta\hat{V}}$, with $-\beta\hat{V} = -\beta(\hat{H}+\hat{U}) - \beta^2[\hat{H},\hat{U}]/2 + \ldots$ (the additional terms are various nested commutators), and to choose U such that the resulting infinite series can be resummed to find the biased Hamiltonian, $\hat{V}$. We attempted to do this by choosing $\hat{U}$ to have a Gaussian form in the hopes that the resulting series of Hermite polynomials would be summable but we found no convenient closed form solution. Therefore, we took a different approach and constructed the bias potential so as to allow the classical derivation of Umb-S (Eq. 2) to work even when the bias acts directly on the quantum degrees of freedom. The key to our method, which we call quantum-biased umbrella sampling (QBUS), is to construct $\hat{U}$ so that the commutator $[\hat{H}, \hat{U}] \sim 0$. We considered only bias potentials that are functions of the QM particle's position, r, so that the only difficulties with non-commutation of $\hat{H}$ and $\hat{U}$ come from the kinetic energy operator in the Hamiltonian, $\hat{T}$. It is straighforward to show that if $\hat{U} = \hat{U}(r)$, the commutator is

$$[\hat{T}, \hat{U}] = -(\hbar^2/2m)\nabla^2\hat{U}(r) - i(\hbar/m)\nabla\hat{U}(r) \cdot \hat{p} \; , \tag{3}$$

where $\hat{p}$ is the momentum operator (with an obvious generalization for multiple QM particles).

To make the commutator in Eq. 3 small, we must construct a class of quantum bias potentials so that $[\hat{T}, \hat{U}] \sim 0$ for a choice of $\hat{U}$ that forces the QM degrees of freedom to sample preferentially a particular range of spatial locations. The first term in Eq. 3 suggests that we should choose for our quantum umbrella potential any function that satisfies Laplace's equation in regions where the quantum degrees of freedom have significant amplitude. We found that it sufficed to construct two–center umbrella sampling potentials from products of one–dimensional, piecewise–linear functions. After some experimentation with various piecewise–linear forms, we found that products of inverted, "truncated pyramid" functions form multiple potential wells that commute with $\hat{T}$ well enough that correction factors to Eq. 2 from BCH would be negligible. The inverted truncated pyramid potentials we form act on both QM particles and are chosen to constrain the particles' positions near $\pm x_i$,

$$U(\mathbf{r}; x_i) \;=\; V_0\left[u_+(x)u_0(y)u_0(z) + u_-(x)u_0(y)u_0(z)\right] \tag{4}$$

$$u_\pm(x; x_i) \;=\; \begin{cases} -1 \; , & |x \pm x_i| < x_a \\ -1 + \frac{|x \pm x_i| - x_a}{x_b - x_a}, & x_a < |x \pm x_i| < x_b \\ 0 \; , & |x \pm x_i| > x_b \; , \end{cases} \tag{5}$$

where V_0 is the well depth and $u_0(x)$ denotes $u_\pm(x; 0)$. With this piecewise–linear form for the umbrella potential, two QM objects can be made to preferentially sample separations near $2x_i$. The values of the parameters V_0, x_a, and x_b must be determined according to the shape of the quantum particles' wave functions.

Because $[\hat{T}, \hat{U}] \sim 0$ when $\hat{U}$ has the form of Eq. 5, we can use Eq. 2 to find the PMF between two hydrated electrons. To ensure that the umbrella potential would not modify the shape of each e^-_{hyd} too much, we chose the flat attractive region, $|x \pm x_i| < x_a$, to be as wide as the average electron diameter; the e^-_{hyd} within our model has a radius of gyration ∼2 Å, so we took x_a to be 2.0 Å. We found that we could stably confine one electron to each well by choosing $V_0 = 25$ eV. We made no attempt to optimize V_0 because the initial choice worked satisfactorily. To fix x_b, we experimented with several widths before arriving at $x_b = 2.67$ Å. We found that making x_b much larger allowed substantial fluctuations in the electron–electron separation, thus defeating the purpose of umbrella sampling; making x_b too small confined the electron too sharply and produced electron wave functions whose shapes were noticeably altered by the presence of the well. To demonstrate that this umbrella potential can control the distance between the electrons, we display in Figure 1 representative cuts of the two–electron density along the x axis for different values of x_i. The charge density is confined largely to the two wells and the distance between the maxima is determined by the separation between the wells.

For all of the calculations presented in this paper, we generated equilibrium configurations with constant–energy mixed quantum/classical molecular dynamics simulation. The details of the simulations, including how the two–electron wave functions were computed using full configuration interaction (CI), are described in detail elsewhere.[9, 10] We chose to use CI because when the electrons occupy cavities near each other, the single–electron eigenstates can have amplitude in both cavities so exchange and correlation effects need to be taken into account; we assumed singlet pairing in all of our calculations. For each of 27 values of the umbrella separation, $2x_i$ =5.375, 5.5, 5.625,. . . , 8.625 Å, we equilibrated the system and then collected data for 20–40 ps. We were unable to run Umb-S trajectories with $2x_i \leq 5.25$ Å because, even after we reduced x_b and deepened the potential, one e^-_{hyd} tunnelled into the other's cavity to form a dielectron (i.e., two strongly correlated electrons confined to a single cavity).[10] Initially, we ran 20 ps for each value of x_i and computed the PMF as described below; to reduce the error bars for undersampled separations, we then ran an additional 20 ps for separations near the local maxima in the PMF. To test $[\hat{T}, \hat{U}] \sim 0$, we used the fact that commuting operators have the same eigenfunctions: We formed the single–electron eigenstates, $|n\rangle$, of $\hat{H}+\hat{U}$ and found that the matrix elements of $\langle m|\hat{U}|n\rangle/\langle n|(\hat{H}+\hat{U})|n\rangle$ are of order 1 for $n=m$ and less than 10^{-3} for $n \neq m$. Thus, correction factors in Eq. 2 from BCH are negligible (of order 10^{-3}) in comparison to statistical uncertainties.

Because the two electrons in our calculation are identical, the distance between them is rigorously zero,[10] but to form the PMF as a function of the separation between the electrons we need a measure of the interelectron separation. The density cuts in Figure 1 clearly show two separated regions of charge on the left and right sides of the simulation cell, so we define the e^-_{hyd}–e^-_{hyd} separation, r_{12}, as the distance between the centers of mass on the left and right sides of the cell. The upper panel of Figure 2 displays the probability distributions, $P(r;U)=\langle\delta(r-r_{12})\rangle_U$, calculated from each of the 27 umbrella potentials described above. We find that the distributions pile up for separations $r \simeq 6.75$ Å, which suggests that this separation is particularly stable. To further show this stability, the lower panel of Figure 2 displays the average and root–mean–squared (RMS) deviation for each distribution of r. For umbrella separations $6.25 \leq 2x_i \leq 7.375$ Å, the two electrons are separated by ~6.75 Å with an RMS of about 0.2 Å; it is only when significant amounts of electron density would be forced up the walls of the umbrella potential that the electrons can be moved to separations other than 6.75 Å.

Now that we have the distributions of r for each umbrella separation, we must combine the $g(r;U)$ to form the PMF. The most common approach is the weighted histogram averaging method (WHAM),[2] which forms an unbiased $g(r)$ as a weighted average of the $g(r;U)$, with the weights determined self–consistently to be proportional to the exponential of a free energy, $\exp(\beta F_U)=\int dr g(r)\exp(\beta U(r))$. For QBUS, this approach is not possible because the analogous weight factor is not a simple integral over the inter–electron separation, r, but instead is a functional that depends on the QM particles' wave function. Therefore, we have chosen to compute the PMF using an alternative approach due to Kästner and Thiel called umbrella integration (UI).[6] In brief, with UI one converts each $g(r;U)$ into an unbiased $g_u(r;U)$ and forms the derivative of the PMF for each umbrella potential, $-\beta W'(r;U)=g'_u(r;U)/g_u(r;U)$, where the prime denotes a derivative with respect to r. The derivative of the PMF is the weighted average of these derivatives, $W'(r)=\sum_U p(r;U)\ W'(r;U)$, where the normalized weights are $p(r;U) = N_U g(r;U)/\sum_{U'} N_{U'} g(r;U')$, and N_U is the number of configurations sampled with umbrella potential U. With this weighting, $W'(r)$ gets its largest contribution from each umbrella potential where the sampling is best and the smallest weight where the sampling is worst. By forming the derivative of the PMF, UI eliminates the computationally expensive step of calculating the free energies, F_U, from a functional for each umbrella potential.

In our calculations we found no correlation between r and U: $g_u(r;U) = g(r;U) = P(r;U)$. Thus, the derivative of the umbrella potential becomes

$$W'(r) = \sum_U N_U P'(r;U) / \sum_{U'} N_U P(r;U). \tag{6}$$

To reduce the noise associated with taking the derivative of the simulated $P(r;U)$ we followed Ref. [6] and replaced each umbrella–sampled distribution by a Gaussian distribution with the same average and standard deviation. To find the PMF, we calculated $W'(r)$ from Eq. 6 for discrete values of r with a spacing of 0.01 Å, and then integrated using the trapezoid rule.

Figure 3 shows the resulting PMF; because UI does not fix the zero of the PMF and our simulations have not approached the asymptotic limit for large separations, $W(r) = e^2/\epsilon r$ (where ϵ is the static dielectric constant of water), we have chosen the zero of energy to match the flat (within our error) regions on either side of the stable well. To produce the error bars, we divided each umbrella sampling run into ten subsets, computed the PMF for ten possible combinations of P, and calculated the mean and standard deviation. The QBUS results show that there is a stable, $\sim$1.6 k_BT deep minimum in the free energy for separations $r \sim 6.75$ Å, and no other statistically significant features for $5.25 \leq r \leq 8.25$ Å. (The repulsive peak at $r \sim 8.4$ Å may or may not be physical given radius of the e^-_{hyd}, which cause these separations to encroach on half the box size, 9.085 Å.) Thus, our calculations predict that e^-_{hyd} should pair up to form stable complexes, with $r \simeq 6.75$ Å. This prediction is consistent with Schmidt and Bartels' conclusion, based on the independence of the electron–electron annihilation reaction rate on ionic strength, that there is a bound e^-_{hyd}–e^-_{hyd} complex at separations of 6–9 Å.[5]

In summary, we have presented a new method for quantum umbrella sampling, QBUS. QBUS works by constructing a bias potential that commutes approximately with the Hamiltonian, so that methods developed for classical Umb-S can be used. We used QBUS to calculate the PMF between two hydrated electrons and found a stable complex at $r \sim 6.75$ Å, in agreement with experiment. Finally, QBUS provides a general approach for constraining the positions of electrons while correctly calculating free energies. Because QBUS allows for mixed quantum/classical simulations of thermodynamically unlikely QM configurations, we anticipate that QBUS will enable a sort of “chemistry by fiat” in which electrons can be made to form bonds or charge–transfer states that would otherwise be impossible to simulate.

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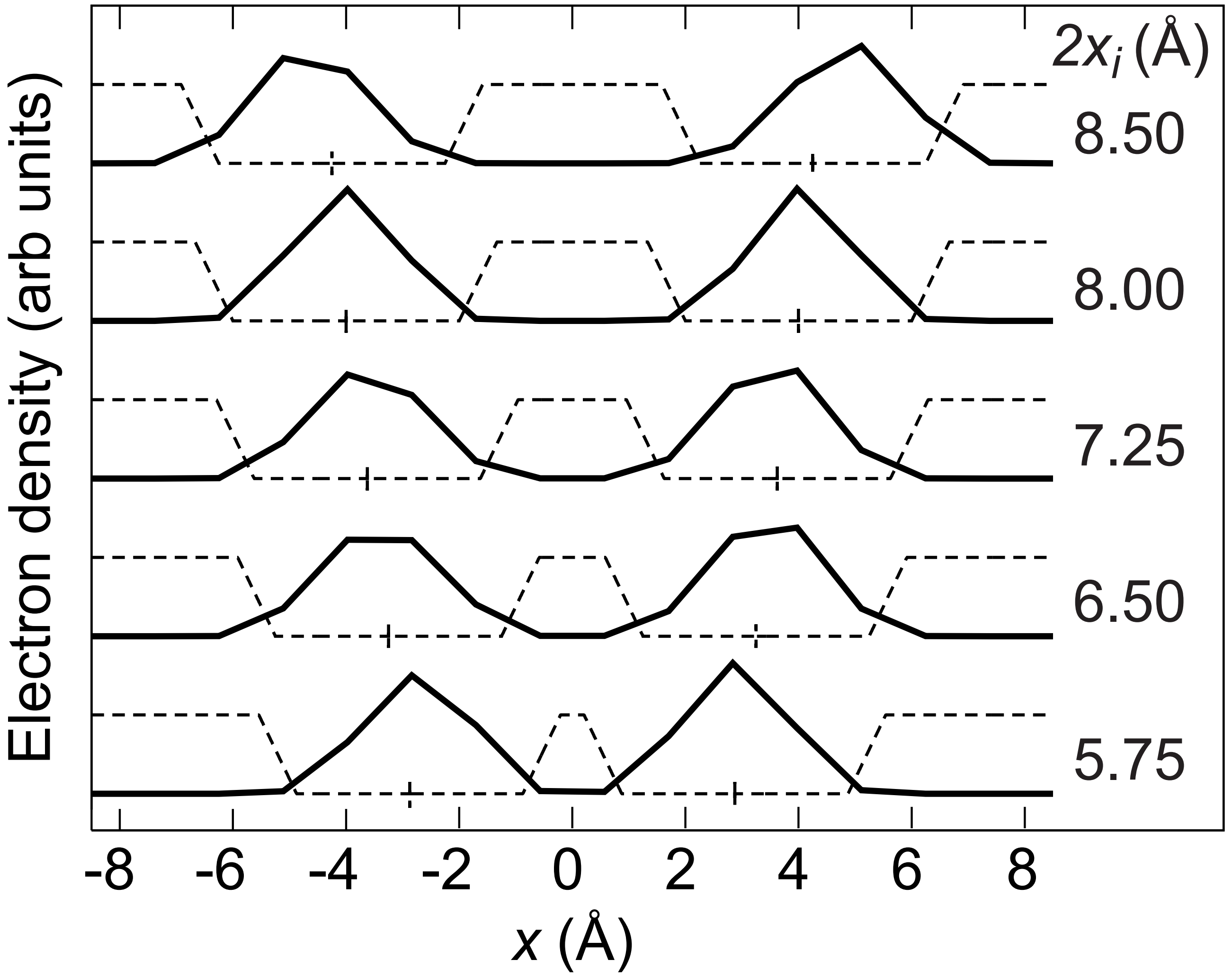
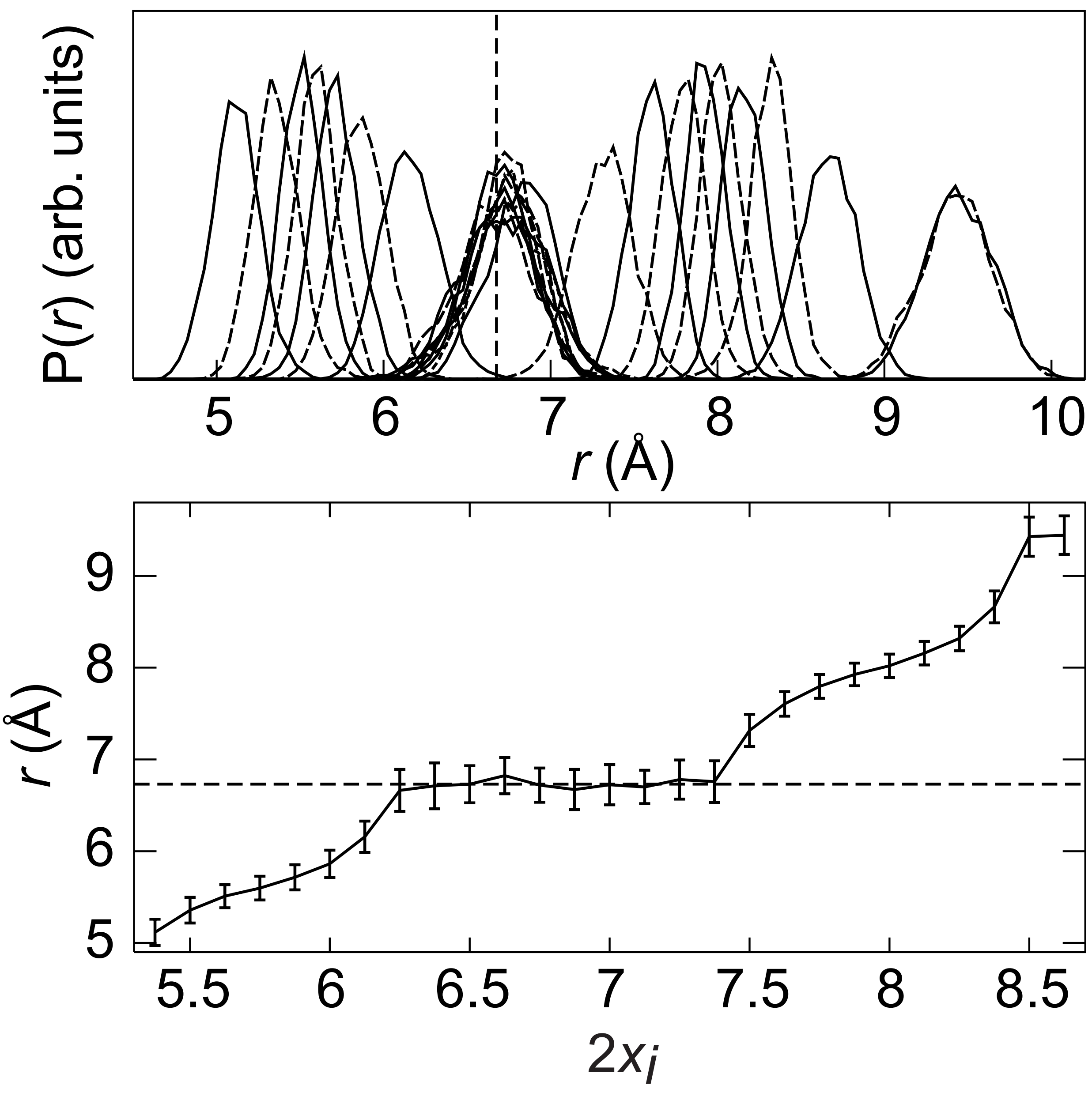
FIG. 1: Cuts of the two–electron density (thick curves) along the x axis ($y = z = 0$) from representative snapshots for the indicated umbrella potential separations, $2x_i$. The umbrella potentials, Eq. 5, used for each simulation are displayed (in arbitrary units) as the thin dashed lines and the vertical tic marks indicate the centers of the wells.

FIG. 2: Upper panel: Distributions of electron separations, $P(r) = \langle \delta(r - r_{12}) \rangle_U$, for the 27 umbrella separations described in the text. Lower panel: Average (data points) and root–mean–square deviation (bars) of r versus the separation between the centers of the wells, $2x_i$. The lines connecting the points serve only to guide the eye. The straight dashed lines in both panels indicate r=6.75 Å.

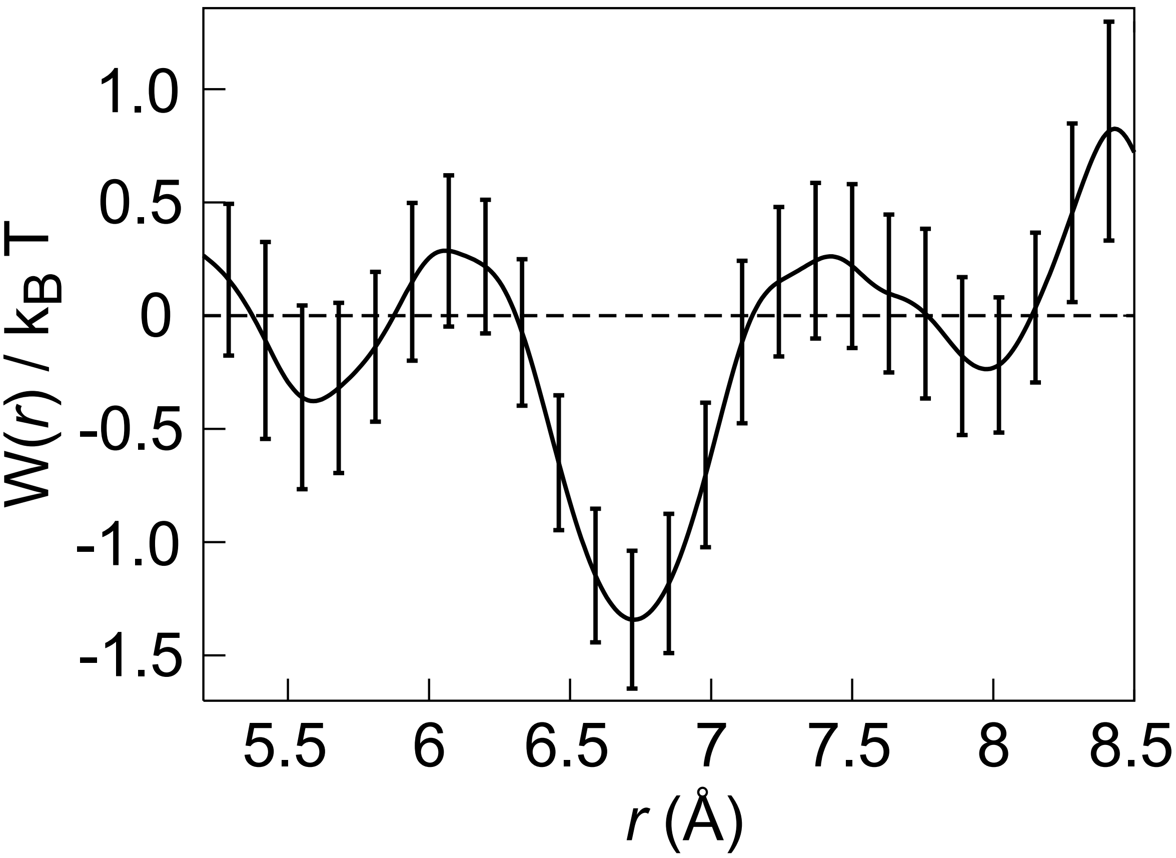
FIG. 3: Potential of mean force, W, between two hydrated electrons as a function of their separation, r. The temperature in the simulations is ~300 K, so $k_B T \simeq 0.025$ eV. The error bars are plus or minus two standard deviations and are calculated as described in the text. The zero of energy we have chosen is not necessarily the same as that defined by two infinitely separated electrons; see text.



Electron density (arb units)
$2x_i$ (Å)
8.50
8.00
7.25
6.50
5.75
-8
-6
-4
-2
0
2
4
6
8
x (Å)



Larsen & Schwartz, Figure 2



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