

4.5 An Effective Hamiltonian Method from Simulations: ASEP/MD

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4.5.1 The ASEP/MD Method

The ASEP/MD method, acronym for Averaged Solvent Electrostatic Potential from Molecular Dynamics, is a theoretical method addressed at the study of solvent effects that is half-way between continuum and quantum mechanics/molecular mechanics (QM/MM) methods. As in continuum or Langevin dipole methods, the solvent perturbation is introduced into the molecular Hamiltonian through a continuous distribution function, i.e. the method uses the mean field approximation (MFA). However, this distribution function is obtained from simulations, i.e., as in QM/MM methods, ASEP/MD combines quantum mechanics (QM) in the description of the solute with molecular dynamics (MD) calculations in the description of the solvent.

The MFA [1] introduces the perturbation due to the solvent effect in an averaged way. Specifically, the quantity that is introduced into the solute molecular Hamiltonian is the averaged value of the potential generated by the solvent in the volume occupied by the solute. In the past, this approximation has mainly been used with very simplified descriptions of the solvent, such as those provided by the dielectric continuum [2] or Langevin dipole models [3]. A more detailed description of the solvent has been used by Ten-no *et al.* [4], who describe the solvent through atom–atom radial distribution functions obtained via an extended version of the interaction site method. Less attention has been paid, however, to the use of the MFA in conjunction with simulation calculations of liquids, although its theoretical bases are well known [5]. In this respect, we would refer to the papers of Sesé and co-workers [6], where the solvent radial distribution functions obtained from MD [7] calculations and its perturbation are introduced *a posteriori* into the molecular Hamiltonian.

The main advantage of the MFA is that it permits one to dramatically reduce the computational requisites associated with the study of solvent effects. This allows one to focus attention on the solute description, and it consequently becomes possible to use calculation levels similar to those usually employed in the study of systems and processes in the gas phase. Furthermore, in the case of ASEP/MD this high level description of the solute is combined with a detailed description of the solvent structure obtained from molecular dynamics simulations. Thanks to these features ASEP/MD [8] enables the study of systems and processes where it is necessary to have simultaneously a good description of the electron correlation of the solute and the explicit consideration of specific solute–solvent interactions, such as for VIS–UV spectra [9] or chemical reactivity [10].

Details of the Method

As usual in QM/MM methods, the ASEP/MD Hamiltonian is partitioned into three terms [11]

$$\hat{H} = \hat{H}_{\text{QM}} + \hat{H}_{\text{MM}} + \hat{H}_{\text{QM/MM}} \quad (4.140)$$

corresponding to the quantum part, \hat{H}_{QM} , the classical part, \hat{H}_{MM} and the interaction between them, $\hat{H}_{\text{QM/MM}}$. The quantum part comprises only the solute molecule. The classical part comprises all the solvent molecules.

The energy and wavefunction of the solvated solute molecule are obtained by solving the effective Schrödinger equation:

$$\left(\hat{H}_{\text{QM}} + \hat{H}_{\text{QM/MM}} \right) |\Psi\rangle = E |\Psi\rangle \quad (4.141)$$

The interaction term, $\hat{H}_{\text{QM/MM}}$ takes the following form [8]:

$$\hat{H}_{\text{QM/MM}} = \hat{H}_{\text{QM/MM}}^{\text{elect}} + \hat{H}_{\text{QM/MM}}^{\text{vdw}} \quad (4.142)$$

$$\hat{H}_{\text{QM/MM}}^{\text{elect}} = \int dr \cdot \hat{\rho} \cdot \langle V_s(r; \rho) \rangle \quad (4.143)$$

where $\hat{\rho}$ is the solute charge density operator and the brackets denote a statistical average. The term $\langle V_s(r; \rho) \rangle$, named ASEP, is the average electrostatic potential generated by the solvent at the position r , and is obtained from MD calculations where the solute molecule is represented by the charge distribution ρ and a geometry fixed during the simulation. The term $\hat{H}_{\text{QM/MM}}^{\text{vdw}}$ is the Halmiltonian for the van der Waals interaction, in general represented by a Lennard-Jones potential. A few clarifications are relevant at this point. Firstly, not all the configurations generated by the simulation are included in the ASEP calculation. We include only configurations separated by 0.05 ps. In this way, we decrease the statistical correlation between the selected configurations. Secondly, only the electrostatic term enters into the electron Hamiltonian. Other contributions to the solute–solvent interaction energy (repulsion and dispersion terms included in $\hat{H}_{\text{QM/MM}}^{\text{vdw}}$) are treated with empirical classical potentials, and since they depend only on the nuclear coordinates, they do not affect the solute electron wavefunction.

For computational convenience, the potential $\langle \hat{V}_s(r; \rho) \rangle$ is discretized and represented by a set of point charges $\{q_i\}$ that simulate the electrostatic potential generated by the continuous solvent distribution

$$\langle \hat{V}_s(r; \rho) \rangle = \sum_i \frac{q_i}{r - r_i} \quad (4.144)$$

The set of charges $\{q_i\}$ is obtained in three steps:

- (1) Each selected configuration is translated and rotated in such a way that all of the solvent coordinates can be referred to a reference system centred on the centre of mass of the solute with the coordinate axes parallel to the principal axes of inertia of the solute.
- (2) Next, one explicitly includes in the ASEP the charges belonging to solvent molecules that, in any of the MD configurations selected, lie inside a sphere of radius a and that include at least the first solvation shell (Figure 4.26). The value of any charge is then divided by the number of solvent configurations included in the determination of the ASEP. Next, in order to reduce the number of charges, one adds together all the charges closer to each other than a certain distance. This distance is generally taken as 0.5 Å.
- (3) Finally, one includes a second set of charges representing the effect of the solvent molecules lying outside the first solvation shell (Figure 4.27). These charges are obtained by a least

squares fit to the values of the ASEP originated by the outer solvent molecules in a three-dimensional grid defined inside the volume occupied by the solute molecule. The solute volume is defined through a set of interlocking spheres of radius fR_{vdw} , where f is a numerical factor close to unity, and R_{vdw} are the Bondi radii.

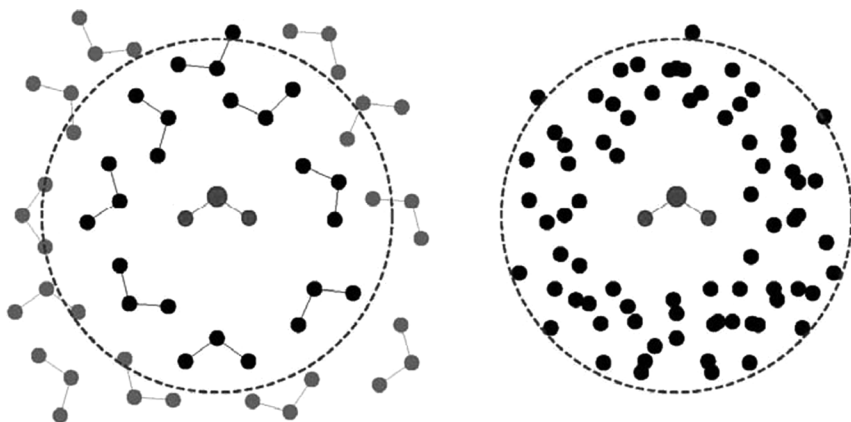


Figure 4.26 Charges representing the ASEP generated by the first solvation shell.

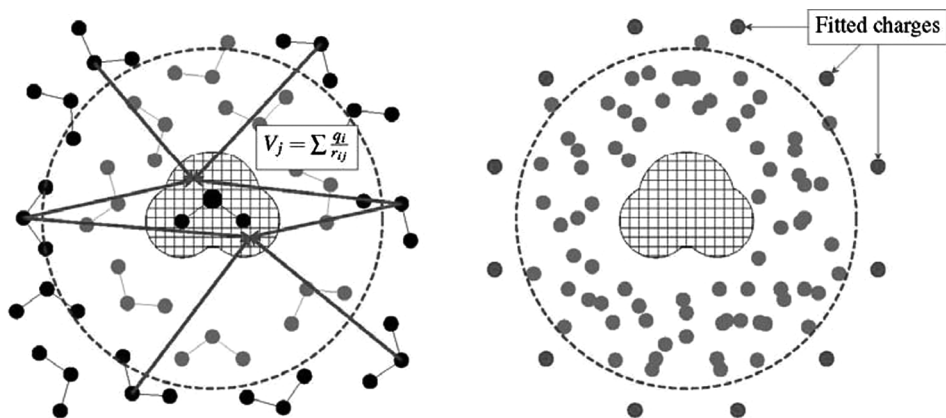


Figure 4.27 Charges representing the ASEP generated by the outer solvation shell.

The total number of charges introduced into the perturbation Hamiltonian is generally between 25 000 and 35 000.

The basic scheme of ASEP/MD is very simple:

- (1) The procedure is begun by performing one quantum calculation for the solute molecule in the gas phase and obtaining, by any of the procedures currently available, a set of point charges representing the solute charge distribution. By default, in ASEP/MD the solute charges are obtained by fitting to the molecular electrostatic potential of the solute molecule.

- (2) The solute charge distribution obtained from the quantum calculation is then used as input in the molecular dynamics calculation. The solute–solvent Lennard-Jones parameters and the complete solvent–solvent force field are obtained from the literature.
- (3) Once the structure of the solvent around the solute molecule has been obtained from the MD data, the charges representing the ASEP are determined by the procedure described above, and introduced into the molecular Hamiltonian of the solute.
- (4) The electronic wavefunction of the solute, now in solution, can be obtained by solving the associated effective Schrödinger equation.
- (5) A new solute charge distribution can be calculated from the solute wavefunction and used again as input in a new molecular dynamics calculation.

This process is repeated until convergence in the solute charges is achieved. In general, only a few cycles, 4–5, of quantum calculation/molecular dynamics simulations are needed for convergence. However, it is convenient to continue the procedure for another 10–15 cycles. In this way, the final results can be obtained with the associated statistical error by averaging over the last 5–10 last cycles. The scheme of the method is shown in Figure 4.28.

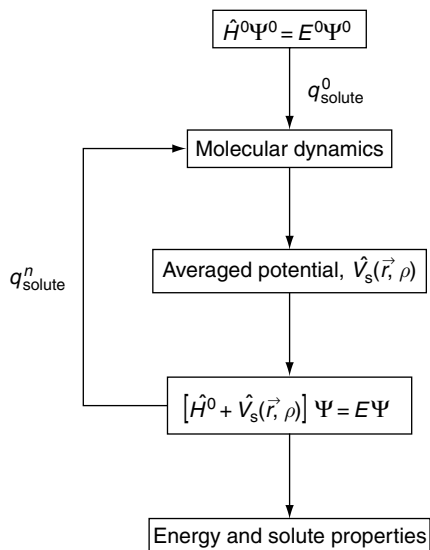


Figure 4.28 ASEP/MD scheme.

Figures 4.29 and 4.30 display the co-evolution of the formamide dipole moment and of the oxygen(formamide)–oxygen(water) radial distribution function during the polarization process [12]. As the dipole moment of the formamide increases, the position of the first peak of the RDF is shifted inward and its height increases. Once the dipole moment has reached its equilibrium value, it begins to fluctuate. Fluctuations are related to the statistical error associated with the finite length of the simulations. From Figures 4.29 and 4.30 it is clear that: (1) ASEP/MD permits one to simultaneously equilibrate the

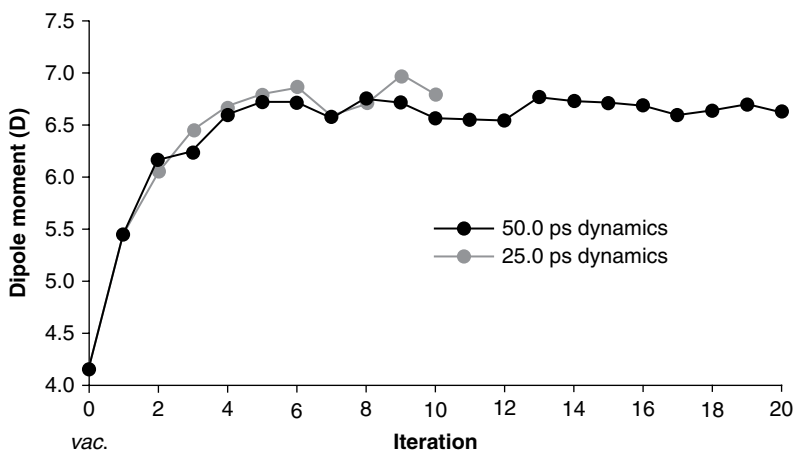


Figure 4.29 Evolution of the formamide dipole moment during the ASEP/MD iteration.

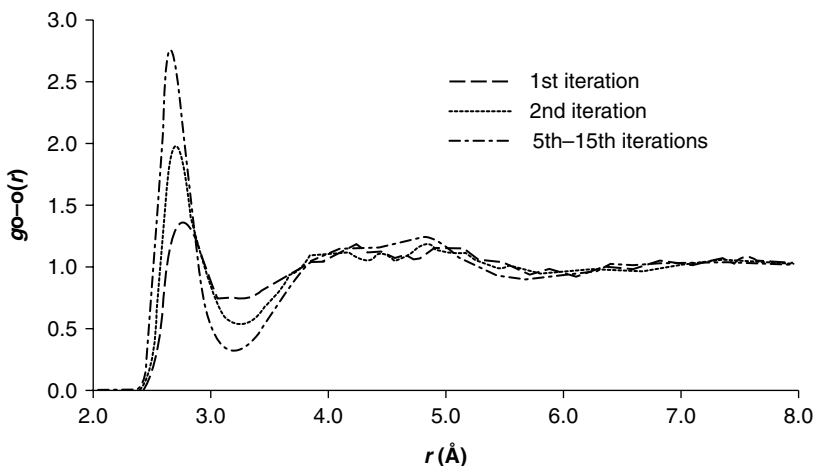


Figure 4.30 Evolution of the oxygen(water)–oxygen(formamide) RDF during the ASEP/MD procedure.

solite charge distribution and the solvent structure around it; (2) the use of *in vacuo* charges (step 1) in MD simulations can yield completely erroneous results.

Comparison of ASEP/MD with Other Methods

With respect to other QM/MM methods, ASEP/MD introduces two approximations:

- (1) It makes use of the mean field approximation. The mean value of any property (which in QM/MM methods is obtained by averaging over all the system configurations) is replaced in ASEP/MD by the value obtained from an averaged configuration. This means that MFA neglects the correlation between the motion of the solvent nuclei and the response of the solute

electron polarizability. The energy associated with this correlation is usually known as the Stark component [1, 13, 14].

- (2) In its current formulation the ASEP/MD method introduces a dual representation of the solute molecule. At each cycle of the ASEP/MD calculation, the solute charge distribution is updated using quantum mechanics but during the molecular dynamics simulations the solute charge distribution is represented by a set of fixed point charges. The use of an inadequate set of charges in the solute description can introduce errors into the estimation of the solvent structure, and hence of the solute's properties

The errors associated with the use of the mean field approximation, the Stark energy, can be easily estimated. As an example, we give in Table 4.7 the magnitude of the errors for the case of liquid alcohols. The calculations were performed at Hartree–Fock and MP2 levels, and the basis set used was the aug-cc-pDZV from Dunning and co-workers [15]. For methanol, the results obtained by averaging over 100 or 1000 configurations are compared with the result obtained using the MFA. For ethanol and propanol, only 100 configurations were used. The Stark energy ranges between 0.3 and 0.8 kcal mol⁻¹, representing errors lower than 5 % in all cases. The differences in dipole moments are even lower: 0.01–0.02 D, representing 0.4–1 %. Furthermore, the small errors in the energy introduced by this approximation can easily be corrected through the use of approximate formulae (see ref. [1]) which permit a very easy and rapid estimation of the Stark component.

Table 4.7 Interaction energy, Stark component (in kcal mol⁻¹), and dipole moment (in debyes) of alcohols in the liquid state calculated as a mean value ($\langle E \rangle$ and $\langle \mu \rangle$) or with the mean field approximation (E_{MFA} and μ_{MFA})

| | $\langle E \rangle$ | E_{MFA} | W_{Stark} | $\langle \mu \rangle$ | μ_{MFA} | $\langle \mu \rangle - \mu_{\text{MFA}}$ |
|---------------|---------------------|------------------|--------------------|-----------------------|--------------------|--|
| <i>HF</i> | | | | | | |
| Methanol 1000 | -19.0 | -18.6 | 0.4 (2.1 %) | 2.46 | 2.45 | 0.01 (0.4 %) |
| Methanol 100 | -19.1 | -18.7 | 0.4 (2.1 %) | 2.46 | 2.45 | 0.01 (0.4 %) |
| Ethanol 100 | -16.5 | -16.0 | 0.5 (3.0 %) | 2.27 | 2.25 | 0.02 (0.9 %) |
| Propanol 100 | -14.3 | -14.0 | 0.3 (2.1 %) | 2.15 | 2.13 | 0.02 (0.9 %) |
| <i>MP2</i> | | | | | | |
| Methanol 1000 | -18.3 | -17.9 | 0.4 (2.2 %) | | | |
| Methanol 100 | -18.3 | -17.9 | 0.4 (2.2 %) | | | |
| Ethanol 100 | -15.8 | -15.4 | 0.4 (2.5 %) | | | |
| Propanol 100 | -13.7 | -13.5 | 0.2 (1.5 %) | | | |

The magnitude of the second source of error, the use of a classical representation for the solute during the simulation, can be estimated by comparing the results provided by ASEP/MD with those obtained with a QM/MM method using the same level of calculation. As an example we present the results obtained for liquid water, Table 4.8, and formamide in aqueous solution, Table 4.9. In both cases, the basis set quality was N,C,O(7111/411/1) H(41/1) [16]. During the DFT calculations the VWN [17] functional with the density-gradient-corrected exchange-correlation functional proposed by Becke and Perdew [18] was used. The DFT/MM calculations were performed with the set of programs [19] developed in Nancy by the group of Professor Ruiz López. DFT/MM and

Table 4.8 Comparison between the DFT/MM and ASEP/MD results for liquid water

| | DFT/MM | ASEP/MD |
|--|--------|---------|
| μ (D) | 2.63 | 2.68 |
| μ^0 (D) | 2.08 | 2.08 |
| $\Delta\mu$ (D) | 0.55 | 0.60 |
| E_{int} (kcal mol ⁻¹) | -19.5 | -20.3 |

Table 4.9 Comparison between the DFT/MM and ASEP/MD results for the formamide–water system

| | DFT/MM | ASEP/MD |
|--|--------|---------|
| μ (D) | 6.89 | 6.91 |
| μ^0 (D) | 4.09 | 4.09 |
| $\Delta\mu$ (D) | 2.80 | 2.82 |
| E_{int} (kcal mol ⁻¹) | -44.8 | -44.9 |

ASEP/MD yield quite close results. For instance, for water [12], the difference in the induced dipole moment is only 0.05 D and the difference in interaction energy is about 0.8 kcal mol⁻¹. In percentage terms, this represents 3 % of the value of the in-solution dipole moment and 4 % of the energy. Similar results are obtained in the formamide–water system [12]: the difference in the values obtained for the induced dipole moment with ASEP/MD and DFT/MM is only 0.02 D, which represents about 1 %. The interaction energy has a similar behaviour: the values obtained with the two methods differ only by 0.1 kcal mol⁻¹ (0.2 %).

A somewhat more problematic situation was found in triazene [20] in aqueous solution. In this case, ASEP/MD completely failed to reproduce the solvent structure around N2 and N3 (see Figure 4.31) as obtained with QM/MM methods, and hence it underestimated the solute–solvent interaction energy. A detailed analysis of the situation showed that the problem was the incorrect description of the solute charge distribution of triazene during the MD calculation. By default, and following the trend used for most force fields, the ASEP/MD method places a charge on each nucleus of the molecule. In the case of triazene this prescription yielded incorrect results. The inclusion of additional charges representing the lone electron pairs notably improved the results both for the RDFs and for the solute–solvent interaction energies. The study validated the use of the ASEP/MD method provided a physically correct and accurate description of the solute charge distribution is used during the MD step.

4.5.2 Location of Critical Points on the Free Energy Surface

In this section we address the important question of the determination of the critical points on the free energy surface (FES). The FES is defined as the energy associated with the time average of the forces acting on each atom of the solute molecule. In optimizing

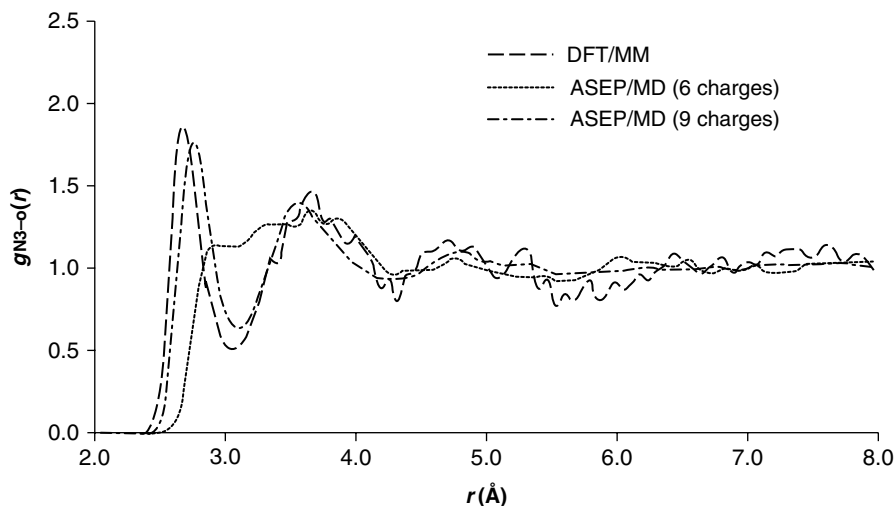


Figure 4.31 Oxygen(water)–nitrogen(triazene) RDF. Comparison between the DFT/MM and ASEP/MD results using six and nine point charges to represent the triazene molecule.

geometries, ASEP/MD uses a free-energy gradient method [21–23]. In this method the forces experienced by the solute atoms are obtained from simulations where the solute molecule has a fixed geometry. From the mean gradient, a new geometry closer to the minimum can be generated. The process is repeated until the gradient converges to a desired precision. The method permits one to obtain both stable structures and transition states.

Because of its use of average quantities, the free-energy gradient method is especially suited for use together with the MFA. Their joint application permits a considerable saving of computation time. The force experienced by the solute nuclei when the geometry is defined by the point r of the FES is: [21–23]

$$F(r) = -\frac{\partial G(r)}{\partial r} = -\left\langle \frac{\partial V(r)}{\partial r} \right\rangle \quad (4.145)$$

where $G(r)$ is the free energy, V is the sum of intra- and intermolecular contributions to the potential energy associated with the interaction with the other atoms of the solute molecule, V_{QM} , and with the solute–solvent interaction energy, $V_{QM/MM}$, respectively. The brackets denote a statistical average. The Hessian is:

$$H = \left\langle \frac{\partial^2 V}{\partial r \partial r} \right\rangle - \beta \left\langle \frac{\partial V}{\partial r} \frac{\partial V^T}{\partial r} \right\rangle + \beta \left\langle \frac{\partial V}{\partial r} \right\rangle \left\langle \frac{\partial V}{\partial r} \right\rangle^T \quad (4.146)$$

$$H = \left\langle \frac{\partial^2 V}{\partial r \partial r} \right\rangle - \beta \left[\langle F^2 \rangle - \langle F \rangle^2 \right] \quad (4.147)$$

where the superscript T denotes the transposition and $\beta = 1/RT$. The last terms in Equations (4.146) and (4.147) are related to the thermal fluctuation of the force.

In our method, the MFA is also used to simplify the calculation of the force and the Hessian. Because we assume a fixed geometry and a fixed charge distribution of the solute during the simulation, the average value of the force can be replaced by the force of the mean configuration [24]:

$$F(r) \approx -\frac{\partial \langle V \rangle}{\partial r} \quad (4.148)$$

$$H \approx \frac{\partial^2 \langle V \rangle}{\partial r \partial r} - \beta \left\langle \frac{\partial V}{\partial r} \frac{\partial V^T}{\partial r} \right\rangle - \beta \frac{\partial \langle V \rangle}{\partial r} \frac{\partial \langle V \rangle^T}{\partial r} \approx \frac{\partial^2 \langle V \rangle}{\partial r \partial r} \quad (4.149)$$

In Equation (4.149) we have introduced an additional approximation: we have neglected the contribution of the force fluctuations to the Hessian. Given that the Hessian is used only to accelerate the optimization procedure, this approximation has no effect on the optimized geometries (but does affect the calculation of the frequencies). In any case, preliminary estimations show that the errors introduced in the trace of the Hessian in the formamide–water systems when one neglects the fluctuation term are less than 5 % [24].

Once the gradient and Hessian are available, the positions of the minimum and saddle point on the FES are determined by the RFO [25] algorithm. It is important to stress that we assume that at any instant the solvent is in equilibrium with the charge distribution of the solute. As a consequence, nonequilibrium contributions are completely neglected, and if necessary must be included *a posteriori*.

4.5.3 Free Energy Differences

In most practical applications, one needs to know the free energy difference between two states, reactants and products or reactants and transition state, for instance. This magnitude provides the evolution direction for P and T constant. In ASEP/MD the standard free energy difference between the initial and final state in solution is approximated as

$$\Delta G_s = \Delta E_{\text{solute}} + \Delta G_{\text{int}} + \Delta \text{ZPE}_{\text{solute}} \quad (4.150)$$

where ΔE_{solute} is the *ab initio* energy difference between the two QM models, ΔG_{int} is the difference in the solute–solvent interaction free energy and $\Delta \text{ZPE}_{\text{solute}}$ include the zero-point energy and the entropy and thermal contributions to ΔE_{solute} .

Calculation of ΔE_{solute}

The *ab initio* energy difference between the two QM structures is defined as

$$\Delta E_{\text{solute}} = E_B - E_A = \langle \Psi_B | \hat{H}_B^0 | \Psi_B \rangle - \langle \Psi_A | \hat{H}_A^0 | \Psi_A \rangle \quad (4.151)$$

Here, \hat{H}_X^0 is the *in vacuo* Hamiltonian of the structure X, and Ψ_X is the electron wavefunction of the structure X calculated in the presence of the perturbation due to the solvent. Ψ_X is obtained by solving the effective Schrödinger equation, Equation (4.141). E_B and E_A are calculated using the geometries optimized in solution.

Calculation of $\Delta ZPE_{\text{solute}}$

This term is calculated in a completely equivalent way to that used for *in vacuo* calculations. The only additional consideration is that the vibrational frequencies and molecular geometries necessary for the calculation of the vibrational, rotational and translational partition functions of the solute are calculated in solution.

Calculation of ΔG_{int}

The free energy perturbation method [26,27] is used to determine the free energy change. The solute geometry is assumed to be rigid and a function of the perturbation parameter (λ) while the solvent is allowed to move freely. When $\lambda = 0$, the solute geometry and charges and the solute–solvent Lennard-Jones parameters correspond to the initial state. When $\lambda = 1$, the charges, Lennard-Jones parameters, and geometry are those of the final state. For intermediate values, a linear interpolation is applied.

We must remark that this term is calculated classically. This point needs clarification. In the determination of the energies, geometries, and charge distribution of the initial and final states in solution, the solute is represented quantum mechanically. However, once one has determined these magnitudes, the calculation of ΔG_{int} is performed through molecular dynamics simulations where the solute is represented by a set of point charges. This approximation permits one to reduce markedly the computational cost. Furthermore, if a sufficiently good solute charge distribution is used, no improvement is expected from replacing the classical by the quantum representation. A more detailed discussion of this point can be found in ref. [20].

As an application example [10], Table 4.10 presents the different contributions to the activation free energy for the Menshutkin reaction between NH_3 and CH_3Cl . The solvent decreases the activation free energy as expected given that reactants are neutral while the transition state is characterized by a strong charge separation. This fact is reflected in the value of $\Delta G_{\text{int}}^\ddagger$. More striking is the fact that the charge separation in the transition state is lower in solution than in the gas phase. The explanation is that in solution, as a consequence of the decrease of the activation energy, the TE is reached earlier (a measure of the reaction advance degree is the C – Cl distance) and the charge separation is hence lower. As a consequence, the solute internal energy in solution decreases with respect to the gas-phase value. This energy makes a substantial contribution to the decrease in the activation free energy.

Table 4.10 Activation free energy and its components for the Menshutkin reaction. Energies are in kcal mol^{-1} , distances in ångströms and dipoles in debyes

| DFT/aug-cc-pVDZ | <i>in vacuo</i> | <i>in solution</i> | Exp(CH3I) |
|---------------------------------------|-----------------|--------------------|-----------|
| $\Delta E_{\text{solute}}^\ddagger$ | 32.70 | 27.48 | |
| $\Delta ZPE_{\text{solute}}^\ddagger$ | 12.23 | 11.86 | |
| $\Delta C_{\text{int}}^\ddagger$ | — | –13.70 | |
| ΔC^\ddagger | 44.93 | 25.64 | 23.5 |
| $d(\text{C} - \text{Cl})^\ddagger$ | 2.44 | 2.18 | |
| $\mu^\ddagger(\text{D})$ | 12.48 | 11.09 | |

4.5.4 Electron Transitions

If the electron solvent polarization is neglected, the study of electron transitions and the determination of the solvent shift do not require appreciable modifications in the basic scheme of ASEP/MD. During a Franck–Condon transition the solute and solvent nuclei remain fixed and hence the ASEP obtained for the initial state can be used for the rest of the states of interest. However, it is known that the electron degrees of freedom of the solvent can respond to the sudden change of the solute electron charge distribution. In fact, the polarization component can contribute appreciably to the final value of the solvent shift. The determination of this component requires additional calculations where the solute and solvent charge distributions are equilibrated. Each electronic state requires a separate calculation of the solvent polarization component. It is hence necessary to perform as many polarization calculations as electronic states being considered.

The inclusion of the solvent polarization in ASEP/MD involves two types of calculations: (1) the solvent structure and the solute geometry for the initial state (the ground state in an absorption process or the excited state in an emission process) are determined using the ASEP/MD procedure with no polarizable solvent; (2) the electron solvent polarization is determined for the state of interest by coupling the quantum mechanical solute in the state under study with the electron polarization of the solvent using the solvent structure and solute geometry obtained in the first step. To do this, one assigns a molecular polarizability to every solvent molecule. Simultaneously, one replaces the effective water charge distribution used in the MD calculation (TIP3P or SPC, for instance, that implicitly include the solvent polarization) by the gas-phase values of the solvent molecule, q_{solvent}^0 . The details of the procedure can be found elsewhere [9].

The solvent shift, δ , and its different contributions are obtained as the difference between the internal energies, U , of the excited and ground states:

$$\delta = U_{\text{ex}} - U_{\text{g}} = \frac{1}{2}\delta_{\rho q} + \delta_{\rho q} + \frac{1}{2}\delta_{\rho\rho} + \delta_{\text{dist}}^{\text{solute}} \quad (4.152)$$

Here, q refers to the permanent charges of solvent molecules, p to the solvent induced dipoles, and ρ is the solute charge density. The last term in Equation (4.152) is the distortion energy of the solute, i.e., the energy spent in polarizing it.

The above procedure has been successfully applied to the study of solvent effects in the electron spectra of several chromopheres in solution: carbonyl compounds [9a], acrolein [9c] retinal [9d] etc. As an example, Table 4.11 presents the different contributions to the solvent shift in the $n \rightarrow \pi^*$ transition in acrolein. The largest contribution to the solvent shift comes from the interaction between the solute and the permanent charges of the solvent. However, the contribution of the solvent polarization (components associated with the induced dipoles) is also important, representing about 26–35 % of the total solvent shift. Values in parentheses include the dynamic correlation energy of the solute calculated using the CASPT2 method as implemented in the MOLCAS program package [28]. When this component is included, the solvent shift values become $4.5 \pm 0.2 \text{ kcal mol}^{-1}$. The experimental solvent shift for acrolein in water was estimated to be $4.50 \text{ kcal mol}^{-1}$.

Table 4.11 Solvent shift and its components (in kcal mol⁻¹) for the vertical absorption and emission transitions of the acrolein in water solution

| | $\frac{1}{2}\delta_{pq}$ | $\delta_{\rho q}$ | $\frac{1}{2}\delta_{pp}$ | $\delta_{\text{dist}}^{\text{solute}}$ | δ |
|------------|--------------------------|-------------------|--------------------------|--|-----------|
| Absorption | 0.02 | 5.45 | 1.02 | -2.10 | 4.3 (4.5) |
| Emission | 0.01 | 1.22 | 0.67 | 0.69 | 1.3 (1.7) |

4.5.5 Summary

The mean field approximation permits one to reduce markedly the computational cost associated with the inclusion of solvent effects, and does not introduce significant errors in the evaluated quantities. Thanks to these characteristics it has had great success in computational chemistry as is demonstrated by the great number of methods that use this approximation: continuum models, Langevin dipoles, RISM/SCF, and the program developed by our group named ASEP/MD. The feature that characterizes and distinguishes ASEP/MD from the rest of models is that it represents the solvent through a classical force field, i.e. the perturbation due to the solvent is obtained from molecular dynamics simulations. This special combination of MFA and simulations enables the study of systems and processes where a good description of the solute wavefunction must be combined with the consideration of specific solute-solvent interactions. These features are required in fields such as electron transitions, intermolecular interactions, and chemical reactivity, for instance.

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