

CHAPTER II

MOLECULAR DYNAMICS SIMULATIONS

2.1 Introduction to molecular dynamics (MD) simulations

In general, the simulation techniques can be classified into 2 types, namely, Monte Carlo (MC) and molecular dynamics (MD). For the treatment of condensed-phase systems, MD technique is more preferential than MC since it can provide not only the structural data, but also the dynamics details, *e.g.*, providing the information related to time dependent behaviors of the system under investigation.

The performance of MD simulation is based on Newton's second law, $F = ma$, where F represents force on particle, m is its mass, and a is its acceleration. According to the schematic details of the MD simulation shown in Figure 2.1, the simulation starts with reading in the starting configurations, velocities, accelerations and forces. In practice, since there are no explicitly time-dependent or velocity dependent forces that shall act on the system, the time integration algorithms will be employed to obtain the details of positions, velocities and accelerations of two successive time steps. The energy of the system can be obtained from either molecular mechanics (MM) or quantum mechanics (QM) calculations. The force on each atom in the system can be derived from the derivative of the energy with respect to the change in the atom's position. All particles in the system will be moved by their new forces to the new configurations. This process will be repeated until the system reaches its equilibrium. After that, the coordinates, velocities, accelerations, forces and so on of all particles in the system will be collected for further structural and dynamical property calculations.

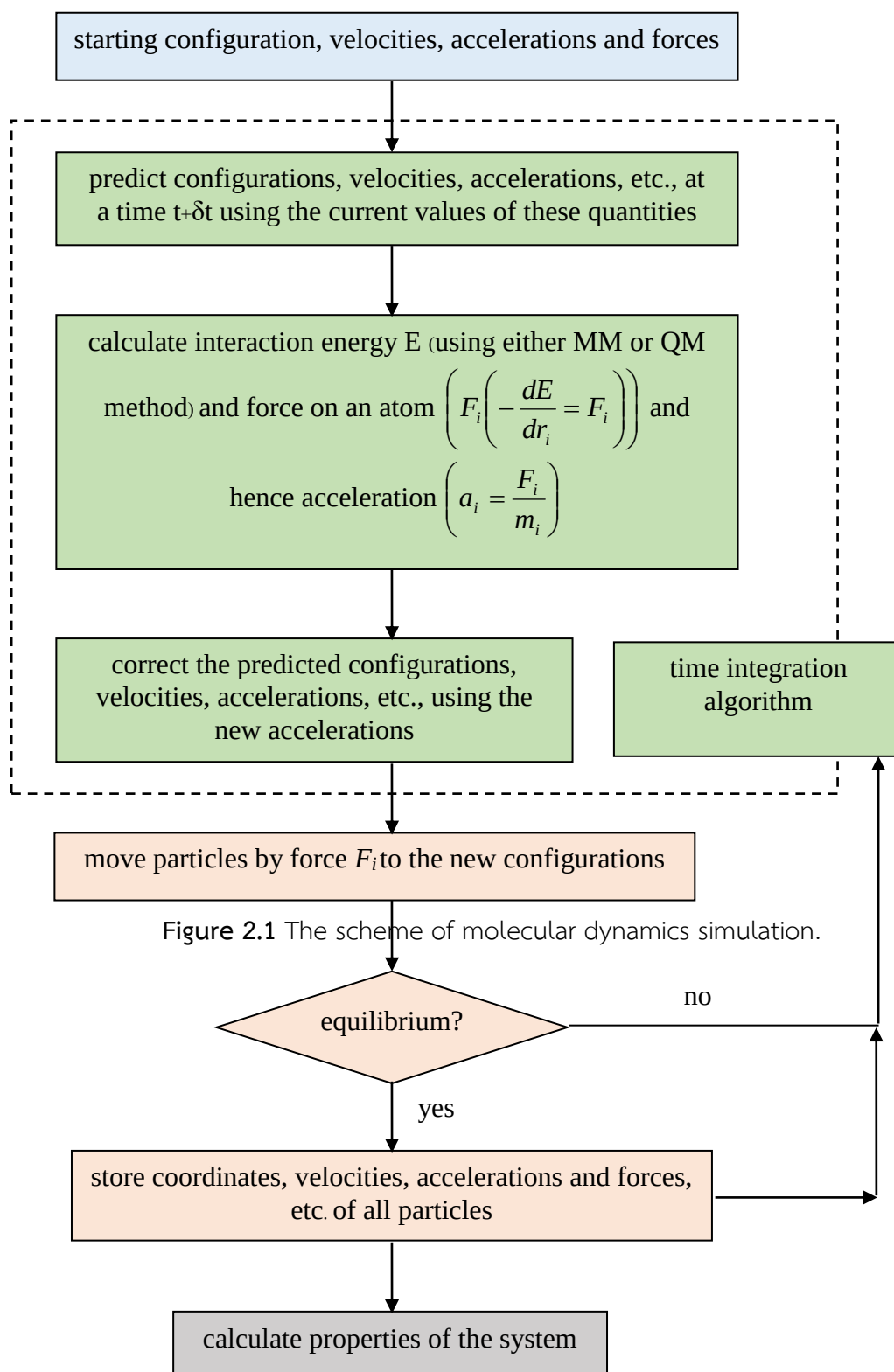


Figure 2.1 The scheme of molecular dynamics simulation.

Figure 2.1 The scheme of molecular dynamics simulation.

2.2 Periodic boundary conditions

One of the common problems found in computer simulations is the boundary effects or surface effects due to system size, *i.e.*, the interactions between particles and the wall usually reflect in wrong properties of bulk. This problem can be solved by using periodic boundary (PB) condition. By this scheme, the particles in the box are replicated in all directions to give a periodic array, which can be represented in Figure 2.2.

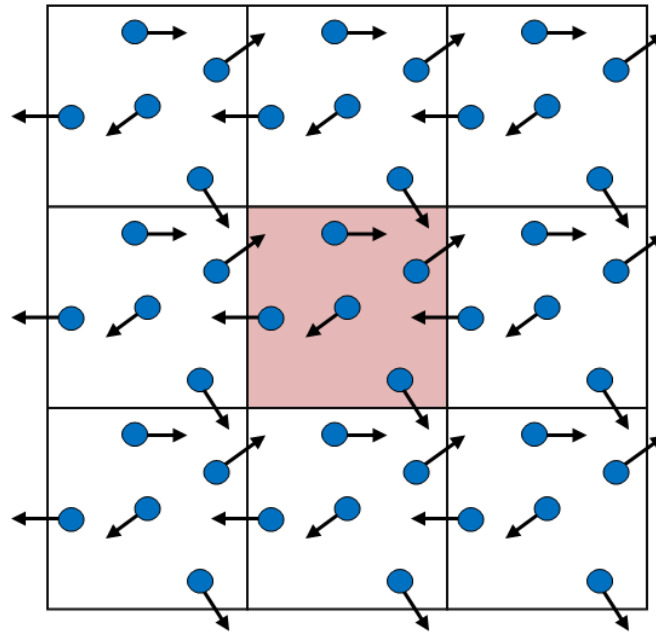


Figure 2.2 The periodic boundary conditions in two dimensions.

The concept of the periodic boundary conditions is that the coordinates of the particles in the image boxes can be computed by adding or subtracting integral multiples of the box sides. If a particle leaves the box during the simulation, it is replaced by an image particle that enters from the opposite side at the same time,

as illustrated in Figure 2.2. Consequently, the number of particles within the central box remains constant.

2.3 Cut-off and minimum image convention

In earlier MC and MD studies, most of which are relied on MM-based models, in which one of the very time-consuming of the simulations is the calculation of non-bond energies and forces. The simple way of reducing the time expense is to use a cut-off and to apply the minimum image convention. The minimum image convention is a common form of the PB condition, in which each atom interacts with only its neighboring atoms in the system. The energies and forces are computed with respect to the closest atom or image, as shown in Figure 2.3.

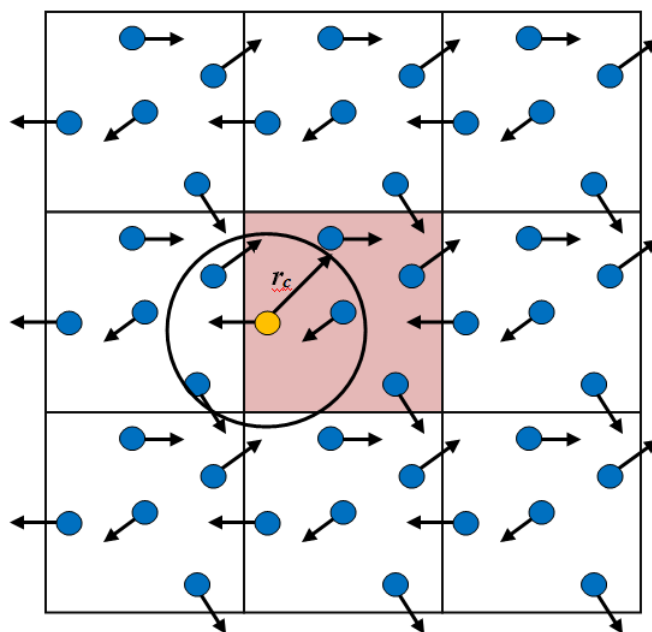


Figure 2.3 The spherical cut-off and the minimum image convention.

By using the cut-off, the interactions between all pairs of atoms that are further apart from the cut-off value are set to zero. In this regard, the cut-off distance should not be greater than half of the length of their image. However, the use of cut-off leads to a serious problem in the simulation, as can be seen in Figure 2.4

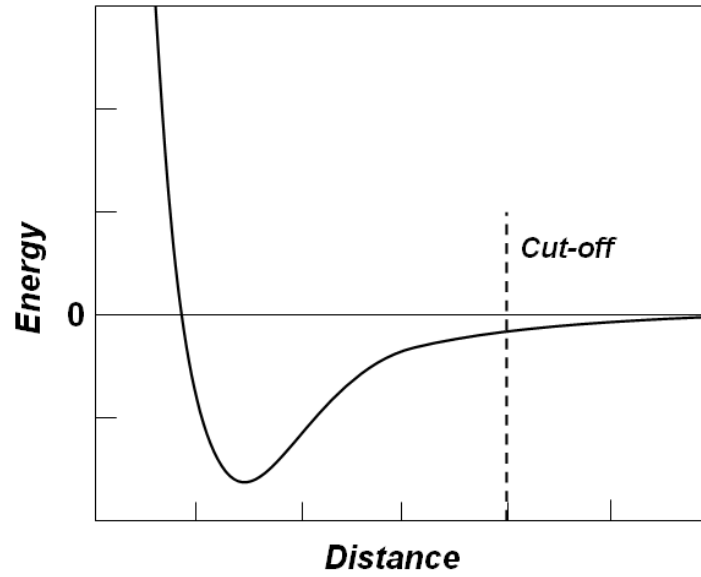


Figure 2.4 A discontinuity of cut-off.

In accordance with the use of cut-off limit, this reflects in the discontinuity in both the potential energy and the force after the cut-off value, as depicted in Figure 2.4. One way for solving this problem is to use a *shifted potential function* by an amount V_c , in which a constant term is subtracted from the potential at all values as

$$V'(r) = \begin{cases} V(r) - V_c & \text{if } r \leq r_c \\ 0 & \text{if } r > r_c \end{cases}, \quad (2.1)$$

where r_c is the cut-off distance and V_c corresponds to the value of the potential at the cut-off distance. In this respect, the energy conservation can be improved by the shifted potential. By this scheme, however, the discontinuity in the force with the shifted potential still exists. At the cut-off distance, since the force will have a finite value, the suitable shifted potential would be of the form

$$V'(r) = \begin{cases} V(r) - V_c - \left(\frac{dV(r)}{dr} \right)_{r=r_c} (r - r_c) & \text{if } r \leq r_c \\ 0 & \text{if } r > r_c \end{cases} . \quad (2.2)$$

In practice, the application of shifted potential is not easy for inhomogeneous systems containing many different types of atom. An alternative way is to eliminate discontinuities in the energy and force by using a *switching function*. The switched potential ($V^S(r)$) is related to the true potential ($V(r)$) as

$$V'(r) = V(r)S(r). \quad (2.3)$$

Some switching functions are applied to the entire range of the potential up to the cut-off point. In general, the switching function has a value of 1 at $r = 0$ and a value of 0 at $r = r_c$, while the switching function values between two cut-offs are varied. The example of a switching function applied to the Lennard-Jones potential is given in Figure 2.5.

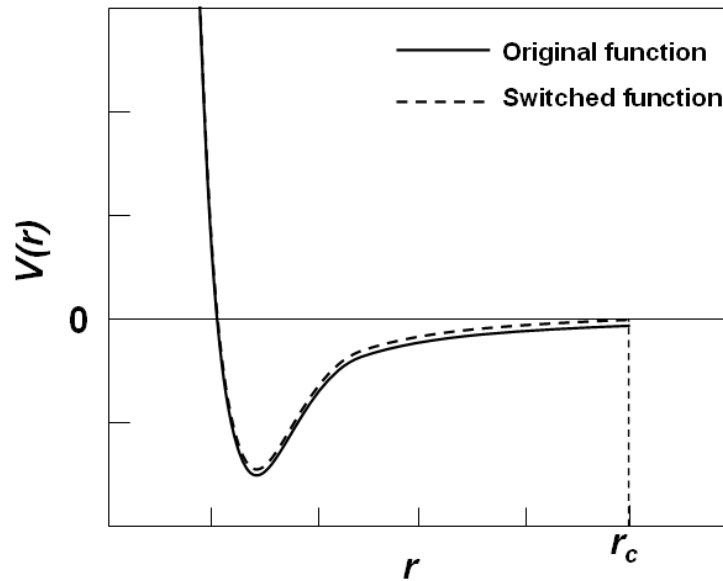
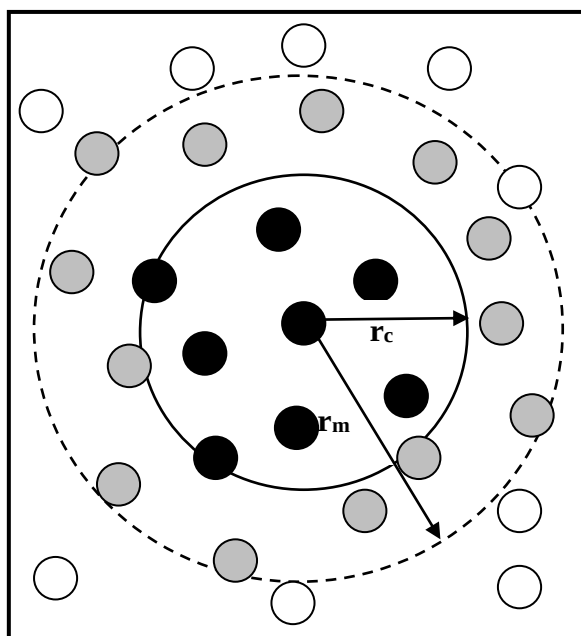


Figure 2.5 The effect of a switching function applied on the Lennard-Jones potential.

2.4 Non-bonded neighbor lists

In practice, the use of cut-off and minimum image convention can not actually reduce the time in the simulation, since all the non-bonded distances must firstly be calculated and checked whether it is inside or outside the cut-off distance. A useful technique for solving this problem is to use the *non-bonded neighbor list*. The first non-bonded neighbor list has been proposed by Verlet (Verlet, 1967). As depicted in Figure 2.6, the Verlet neighbor list stores all atoms within the cut-off distance (the solid circle (r_c)) and atoms are slightly further away than the cut-off distance (the dashed circle (r_m)). The neighbor list will frequently be updated throughout the simulation. In practice, the distance used to calculate each atom's neighbors should be slightly larger than the actual cut-off distance in order to ensure that the atoms outside the cut-off will not move closer than the cut-off distance before the neighbor list is updated again.



2.5 Long-range interactions

Since the charge-charge interactions in range greater than half of the box length are still significance, the neglect of long-range interactions beyond cut-off may

introduce serious errors in the simulation. There are two common methods used for the treatment of long-range forces. The first one is Ewald summation (Ewald, 1921), This method studies the energetics of ionic crystals, which allow a particle to interact with all the other of particles in the simulation box and with all of their images in an infinite array of periodic cell. The charge-charge contribution to the potential energy of the Ewald summation can be expressed as

$$V = \frac{1}{2} \sum'_{|\mathbf{n}|=0} \sum_{i=1}^N \sum_{j=1}^N \frac{q_i q_j}{4\pi\epsilon_0 |\mathbf{r}_{ij} + \mathbf{n}|}, \quad (2.4)$$

where the prime on the first summation indicates that the series does not include the interaction $i = j$ for $\mathbf{n} = \mathbf{0}$, q_i and q_j are charges and $\mathbf{n}$ is a cubic lattice point. The Ewald summation method is the most correct way to accurately include all the effects of long-range forces in the computer simulation. However, this method is rather expensive to implement since the equation (2.4) converges extremely slowly.

Another method for the treatment of long-range interactions is to apply the *reaction field method* (Foulkes and Haydock, 1989). This method constructs the sphere around the molecule with a radius equal to the cut-off distance. All interactions within the sphere are calculated explicitly, while those outside of the sphere are modeled as a homogeneous medium of dielectric constant (ϵ_s). The electrostatic field due to the surrounding dielectric is given by

$$E_i = \frac{2(\epsilon_s - 1)}{\epsilon_s + 1} \left(\frac{1}{r_c^3} \right) \sum_{j; r_{ij} \leq r_c} \mu_j, \quad (2.5)$$

where μ_j are the dipoles of the neighboring molecules that are located within the cut-off distance (r_c) of the molecules i . The interaction between molecule i and the reaction field equals to $E_i \cdot \mu_i$.

2.6 The QM/MM MD based on ONIOM-XS method

Schematic diagram of the ONIOM-XS method (Kerdcharoen and Morokuma, 2002) is given in Figure 2.7. Regarding the ONIOM-XS MD technique, the system is divided into a high-level (QM) sphere, *i.e.*, a sphere which contains the ion and its surrounding water molecules, and the “low-level” MM region, *i.e.*, the bulk water. A thin switching shell located between QM and MM subsystems is introduced in order to smooth the transition due to the solvent exchange.

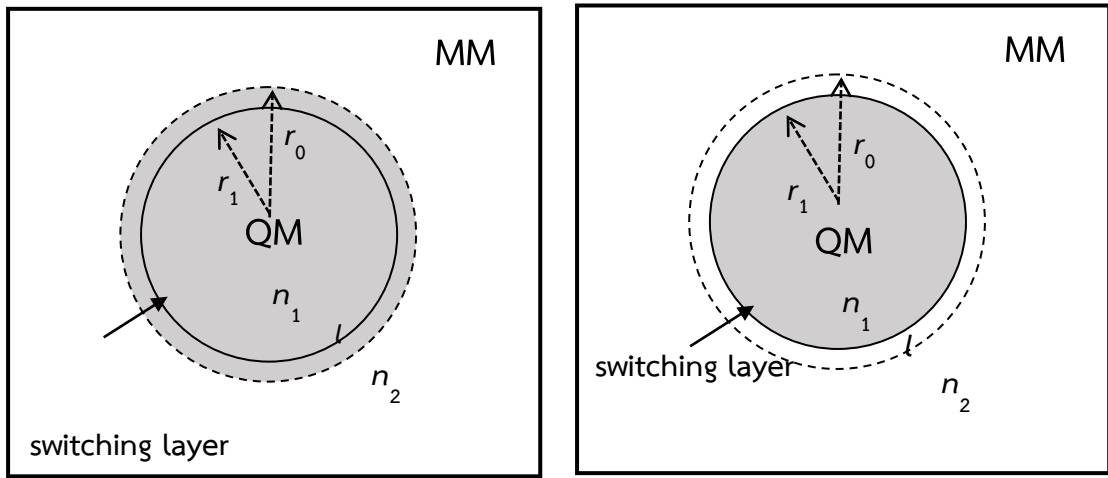


Figure 2.7 Schematic diagram of the ONIOM-XS method.

Given n_1 , l and n_2 as number of particles in the QM region, the switching shell and the MM region, respectively, and $N=n_1+l+n_2$ is the total number of particles, the potential energy term can be written according to the ONIOM extrapolation scheme (Svensson *et al.*, 1996). If the switching layer is included into the high-level QM sphere, the energy expression is defined as

$$E^{\text{ONIOM}}(n_1 + l; N) = E^{\text{QM}}(n_1 + l) - E^{\text{MM}}(n_1 + l) + E^{\text{MM}}(N). \quad (2.6)$$

If the switching layer is considered as part of the “low-level” MM region, the energy expression can be written as

$$E^{ONIOM}(n_1; N) = E^{QM}(n_1) - E^{MM}(n_1) + E^{MM}(N). \quad (2.7)$$

Then, the potential energy of the entire system is taken as a hybrid between both energy terms (1) and (2),

$$E^{ONIOM-XS}(\{r_l\}) = (1 - \bar{s}(\{r_l\})) \cdot E^{ONIOM}(n_1 + l; N) + \bar{s}(\{r_l\}) \cdot E^{ONIOM}(n_1; N), \quad (2.8)$$

where $\bar{s}(\{r_l\})$ is an average over a set of switching functions for individual exchanging particle in the switching shell $s_i(x_i)$ (Tasaki, McDonald, and Brady, 1993),

$$\bar{s}(\{r_l\}) = \frac{1}{l} \sum_{i=1}^l s_i(x_i), \quad (2.9)$$

The switching function $s_i(x_i)$ in equation (4) is written in a polynomial form as

$$s_i(x_i) = 6\left(x_i - \frac{1}{2}\right)^5 - 5\left(x_i - \frac{1}{2}\right)^3 + \frac{15}{8}\left(x_i - \frac{1}{2}\right) + \frac{1}{2}, \quad (2.10)$$

where $x_i = ((r_l - r_0)/(r_1 - r_0))$, and r_0 and r_1 are the radius of inner and outer surfaces of the switching shell, respectively, and r_l is the distance between the center of mass of the exchanging particle and the center of the QM sphere. Then, the gradient of the energy can be written as

$$\begin{aligned} \nabla_R E^{ONIOM-XS}(\{r_l\}) = & (1 - \bar{s}(\{r_l\})) \cdot \nabla_R E^{ONIOM}(n_1 + l; N) + \bar{s}(\{r_l\}) \\ & \cdot \nabla_R E^{ONIOM}(n_1; N) + \frac{1}{(r_1 - r_0)} \nabla \bar{s}(\{r_l\}) \\ & \cdot (E^{ONIOM}(n_1; N) - E^{ONIOM}(n_1 + l; N)), \end{aligned} \quad (2.11)$$

2.7 Construction of pair potential functions

In this study, the pair potential functions for describing $\text{PH}_4^+ \text{-H}_2\text{O}$ interactions were newly constructed. A set of $\text{PH}_4^+ \text{-H}_2\text{O}$ configurations can be generated by moving a water molecule with respect to the PH_4^+ ion according to the variations of θ (*i.e.* between 0° and 180°) and Φ (*i.e.* between 0° and 360°) angles, as depicted in Figure 2.8. Along with the variations of θ and Φ angles, 20 different types of water's orientations were employed (see Figure 2.9).

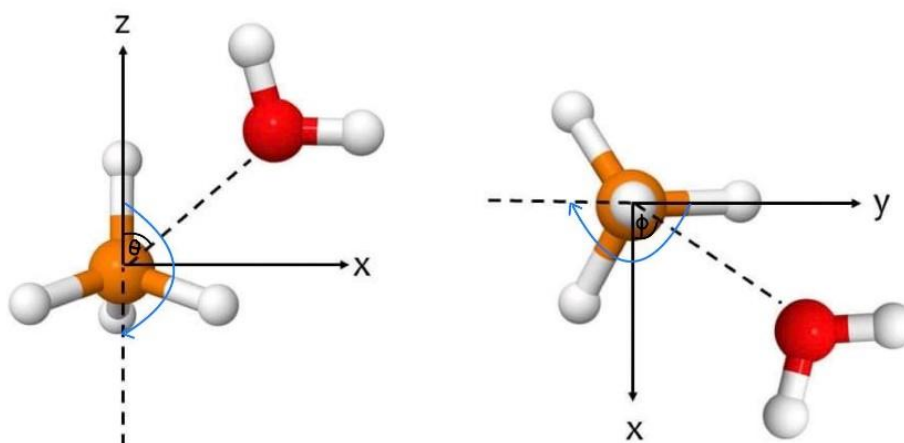


Figure 2.8 Movements of H_2O around PH_4^+

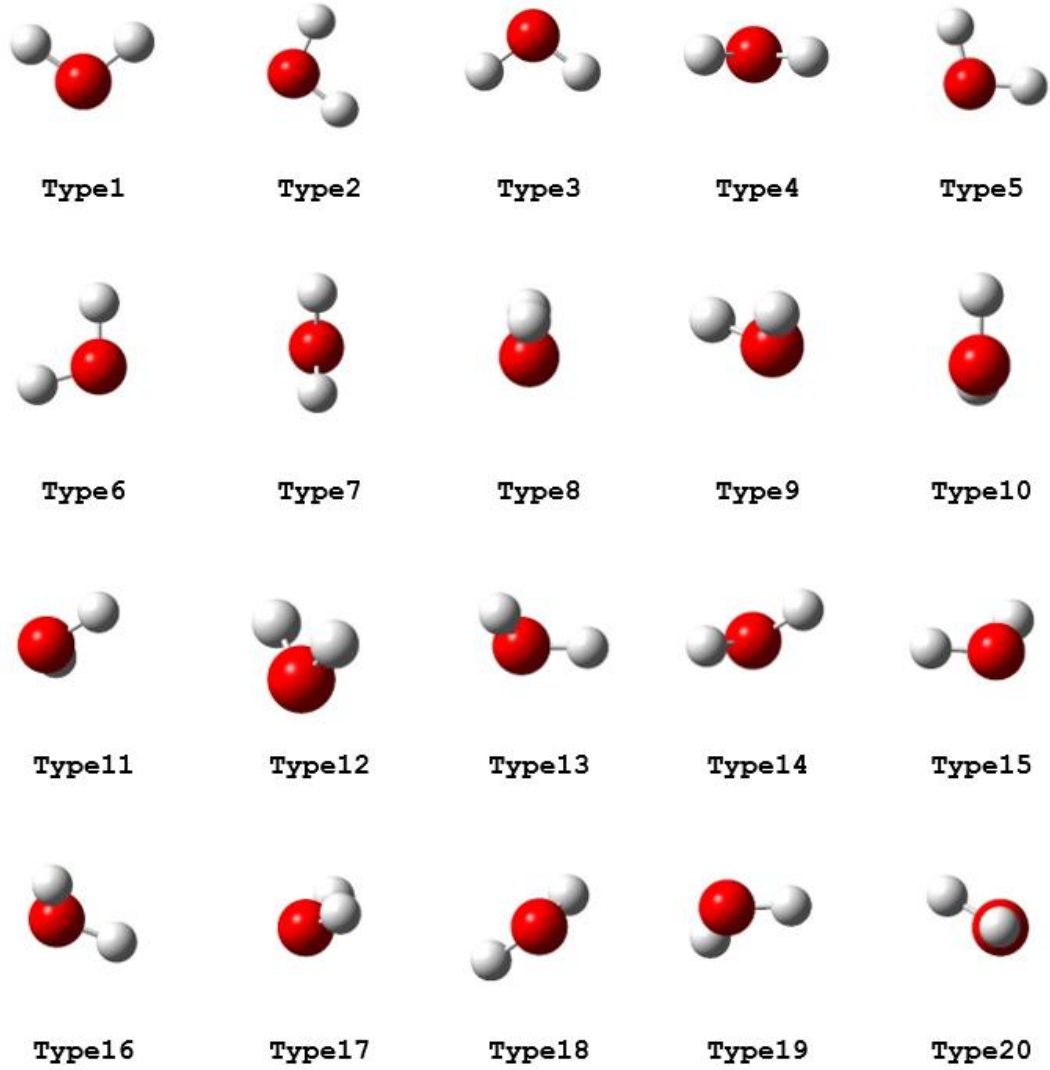


Figure 2.9 Variation of water's orientations.

The 20,347 HF and 28,163 B3LYP interaction energy points for various PH₄⁺-H₂O configurations, obtained from TURBOMOLE 7.3 software package (Ahlrichs *et al.*, 2018), using def2-SVP basis set were fitted to the analytical forms of

$$\Delta E_{\text{PH}_4^+-\text{H}_2\text{O}} = \sum_{i=1}^3 \left(\frac{A_{ic}}{r_{ic}^4} + \frac{B_{ic}}{r_{ic}^6} + C_{ic} \exp(-D_{ic} r_{ic}) + \frac{q_i q_c}{r_{ic}} \right), \quad (2.12)$$

where A , B , C and D are the fitting parameters (see Table 2.1 and 2.2), r_{ic} denotes the distances between the ions and the i -th atom of water, and q are the atomic net charges. The charge on P and H of PH_4^+ were obtained from Mulliken charge analysis of the corresponding HF and B3LYP calculations. They were set to 0.31653 and 0.17087 (HF), and to 0.2087 and 0.1978 (B3LYP), respectively. The charge on O and H of water molecule were adopted from the BJH-CF2 water model (Stillinger and Rahman, 1976) as -0.6598 and 0.3299, respectively.

Table 2.1 Optimized parameters of the analytical pair potentials for the interaction of water with PH_4^+ , which correspond to the HF calculations of PH_4^+ -water complex (interaction energies in kcal mol^{-1} and distances in Å).

	A	B	C	D
P-O _w	1610130.302	-18942832.18	125152285.8	3.176355545
P-H _w	-601982.9273	1556801.26	182262.353	1.017906464
H _P -O _w	-223025.9858	88117.42239	2258598.871	2.618844254
H _P -H _w	88756.39527	61824.60328	416209.7638	2.256920555

Table 2.2 Optimized parameters of the analytical pair potentials for the interaction of water with PH_4^+ , which correspond to the B3LYP calculations of PH_4^+ -water complex (interaction energies in kcal mol^{-1} and distances in Å).

	A	B	C	D
P-O _w	1788433.348	-19241797.2	134748173.4	3.214770578
P-H _w	-307180.052	833709.7276	118892.9838	1.052463438
H _P -O _w	-207552.833	83623.14564	2515289.674	2.806444338
H _P -H _w	-67229.1863	41678.31531	463993.2206	2.514972482

2.8 Selection of QM size, QM method and basis set

Based on the ONIOM-XS MD technique, the selection of QM method, as well as QM size and basis set, is very crucial in order to obtain reliable results. In practice, these important parameters must be optimized, compromising between the quality of the simulation results and the requirement of CPU time. With regard to previous ONIOM-XS MD studies of liquid water (Thaomola, Tongraar and Kerdcharoen, 2012), which provided data for the requirements of CPU time for the different levels of QM calculations of water clusters using DZP basis set (see Figure 2.10) it is apparent that the correlated QM calculations using even moderate basis set, like DZP, are still very time-consuming. In this work, the requirements of CPU times for the HF force calculations of $\text{PH}_4^+(\text{H}_2\text{O})_n$ complexes, where $n=1-15$, using def2-SVP, and def2-TZVP basis sets, were also investigated, as shown in Figure 2.11. It is obvious that the HF calculations using the TZVP basis set is still rather expensive. In this respect, the performance of the ONIOM-XS MD simulations using the HF or B3LYP calculations and the moderate basis set, like def2-SVP, is expected to be a promising condition to obtain reliable simulation results according to the available computational facilities.

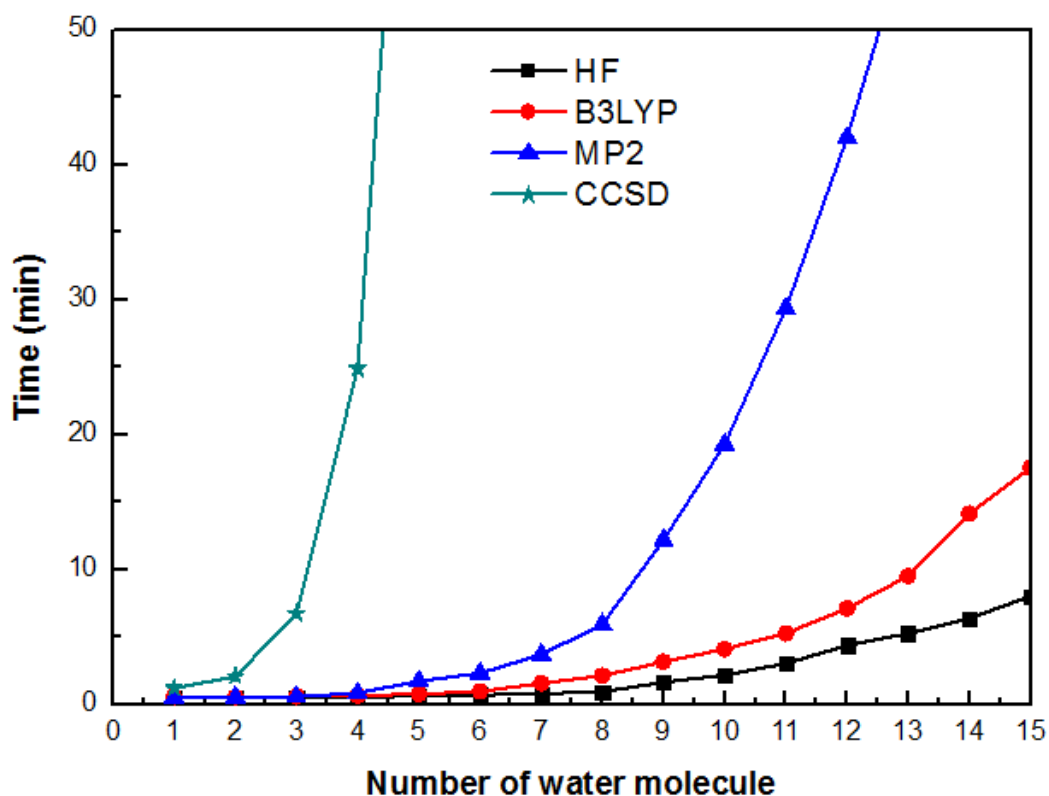


Figure 2.10 Requirements of CPU times for HF, B3LYP, MP2 and CCSD force calculations of $(\text{H}_2\text{O})_n$, $n = 1, 15$ complexes using DZP basis set. All calculations were performed on CCRL cluster with Intel Core^{TM2} Quad of CPU and 4GB of Ram. (Thaomola, Tongraar and Kerdcharoen, 2012)

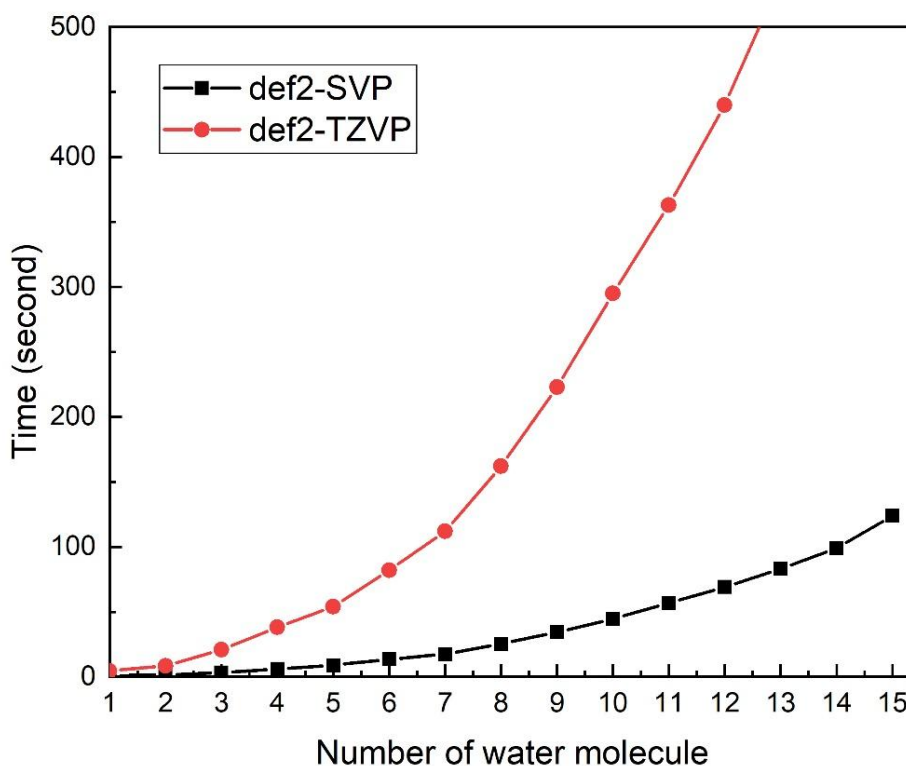


Figure 2.11 Requirements of CPU times for HF force calculations of $\text{PH}_4^+(\text{H}_2\text{O})_n$ complexes, where $n = 1-15$, using def2-SVP, and def2-TZVP basis sets. All QM calculations were performed on computational facilities at NECTEC.

In the present ONIOM-XS MD studies, the phosphorus atom of PH_4^+ was set as the center of the QM region, and QM radius of 4.6 Å and a switching width of 0.2 Å were chosen, which correspond to the ONIOM-XS parameters r_0 and r_1 of 4.4 and 4.6 Å, respectively. This QM size is considered to be large enough to include most of the many-body interactions and the polarization effects, *i.e.*, at least within the whole solvation shell of PH_4^+ , and the remaining interactions beyond the QM region are assumed to be well accounted for by the MM potentials. Since the correlated QM calculations, even at the simple MP2 and CCSD are rather too time-consuming for our current computational feasibility, all interactions within the QM region were

evaluated by performing *ab initio* calculations at the Hartree-Fock (HF) and B3LYP levels of accuracy using the def2-SVP basis set. It should be noted that the electron correlation and the charge transfer effects are not typically well-described by the HF theory, and that the use of DFT method, like the B3LYP, may lead to overestimation of the ion-water interactions (Xenides, Randolph and Rode 2005). In addition, it should be realized that the use of the def2-SVP basis set could result in a high basis set superposition error and an exaggeration of the ligand-to-metal charge transfer.

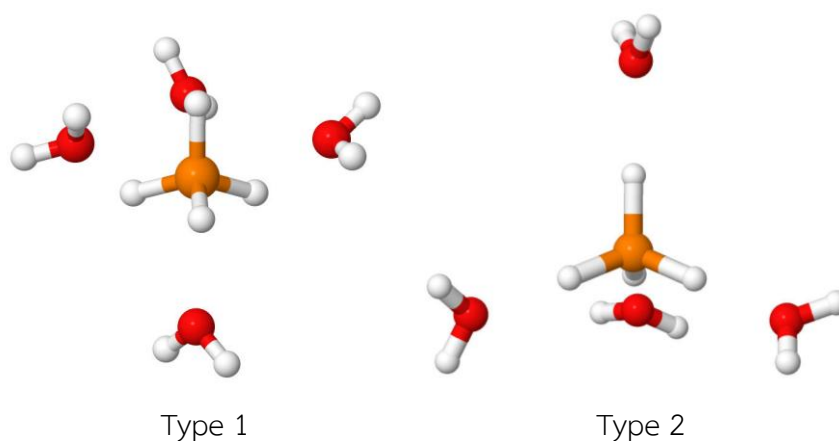


Figure 2.12 Geometry optimizations of $\text{PH}_4^+(\text{H}_2\text{O})_4$ complexes in gas phase.

To simply check the validity of the QM methods (HF and B3LYP) and the def2-SVP basis set employed in the ONIOM-XS MD studies of PH_4^+ in aqueous solution, the geometry optimizations of the $\text{PH}_4^+(\text{H}_2\text{O})_4$ complex have been carried at the HF, B3LYP, MP2 and CCSD levels of accuracy using the def2-SVP basis set. In this respect, the geometry optimizations of $\text{PH}_4^+(\text{H}_2\text{O})_4$ complex have been performed for 2 types of ion-water complexes, namely type 1 where each of water molecule is trifurcated HB to three hydrogens of PH_4^+ and type 2 in which each of water molecule directly HBs to each of PH_4^+ hydrogen, as summarized in Table 2.3 and 2.4, respectively. According to the data in Tables 2.3 and 2.4, the stabilization energies of the $\text{PH}_4^+(\text{H}_2\text{O})_4$ complex have been calculated from

$$\Delta E = E_{\text{complex}} - (E_{\text{ion}} + E_{\text{W1}} + E_{\text{W2}} + E_{\text{W3}} + E_{\text{W4}}), \quad (2.13)$$

where E_{complex} refers to the total energy of the $\text{PH}_4^+(\text{H}_2\text{O})_4$ complex, E_{ion} represents the energy of PH_4^+ and E_{Wi} , where $i = 1, 4$, correspond to the energy of each water molecule. For Type1 complex, the B3LYP method clearly provides the geometry optimization results in good agreement with the MP2 and CCSD calculations, while the HF method reveals underestimation of the ion-water interactions. For Type2 complex, as compared to the MP2 and CCSD calculations, the HF method consistently yields underestimation of the ion-water interactions, whereas the B3LYP method oppositely predicts the overestimation of the ion-water interactions. In particular, it has been reported that the use of simple DFT functionals may result in too strong ion- H_2O interactions, leading to more rigidity of the structure of ion- H_2O complexes (Schwenk, Loeffler, and Rode, 2001; Vande Vondel, Mohamed, Krack, Hutter, Sprik, and Parrinello, 2005). According to the data in Tables 2.3 and 2.4, it should be remarked that the ONIOM-XS MD results obtained by the HF and B3LYP calculations using the def2-SVP basis set must be discussed with caution, *i.e.*, it should be interpreted according to the reliability of the QM methods and the quality of the basis set employed.

Table 2.3 Optimized geometries of $\text{PH}_4^+(\text{H}_2\text{O})_4$ complex (type 1), calculated at the HF, B3LYP, MP2 and CCSD levels of accuracy using the def2-SVP basis sets.

Method	HF	B3LYP	MP2	CCSD
ΔE (kcal/mole)	-58.3151	-63.2463	-64.0894	-64.5081
P-O _w (Å)	2.86	2.78	2.79	2.78
H _p -O _w (Å)	2.73	2.67	2.66	2.66
$\angle \text{O}_w\text{PO}_w$ (deg)	109.4	109.4	109.3	109.3
O-H (Å)	0.9474	0.9681	0.9648	0.9657
$\angle \text{HOH}$ (deg)	105.2	103.9	103.0	102.9

Table 2.4 Optimized geometries of $\text{PH}_4^+(\text{H}_2\text{O})_4$ complex (type 2), calculated at the HF, B3LYP, MP2 and CCSD levels of accuracy using the def2-SVP basis sets.

Method	HF	B3LYP	MP2	CCSD
ΔE (kcal/mole)	-48.9579	-62.31678	-56.8793	-57.7251
P-O _w (Å)	3.50	3.34	3.39	3.39
H _P -O _w (Å)	2.10	1.91	1.98	1.98
$\angle \text{O}_w\text{PO}_w$ (deg)	109.5	109.5	109.5	109.5
O-H (Å)	0.9471	0.9687	0.9646	0.9656
$\angle \text{HOH}$ (deg)	105.3	104.6	103.3	103.2

2.9 Simulation details

In this work, the ONIOM-XS MD simulations based on the HF and the B3LYP methods were separately carried out in a canonical ensemble (NVT) at 298 K with periodic boundary conditions. The system's temperature was kept constant using the Berendsen algorithm (Berendren, Postma, van Gunsteren, and Hermans, 1981). The periodic box, with a box length of 18.19 Å, contains one PH_4^+ ion and 199 water molecules, which corresponds to the experimentally observed density of pure water. The QM size, with radius of 4.6 Å, is employed. The reaction-field method (Adams, Adams and Hills, 1979) was employed for the treatment of long-range interactions. The Newtonian equations of motions were treated by a general predictor-corrector algorithm. The time step size was set to 0.2 fs, allowing for the explicit movement of the hydrogen atoms of water molecules. Note that the time step size employed in the MD simulation refers to the small increment of time over which the simulation updates the positions and velocities of particles (atoms or molecules). In practice, a common choice for the simulation of water is around 1 fs to 2 fs. In this study, the time step of 0.2 fs was employed to ensure stability and accuracy when simulating the dynamics of water. For each of the ONIOM-XS MD simulations, the system was

initially equilibrated by performing the ONIOM-XS MD simulations for 20,000 steps step, followed by 300,000 time steps to collect configurations every 10th step.

2.10 References

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