

Molecular Dynamics Simulation and Molecular Orbital Method

53

Ya-Pu Zhao, Feng-Chao Wang, and Mei Chi

Contents

53.1	Introduction 1				
53.2	Molecular Dynamics Simulation				
	53.2.1	Basic Theory	1562		
	53.2.2	Force Fields	1562		
	53.2.3	Boundary Conditions	1564		
	53.2.4	Energy Minimization	1566		
	53.2.5	Integrators	1567		
	53.2.6	Analysis of the MD Results	1568		
	53.2.7	Water Models Used in MD Simulations	1570		
	53.2.8	Examples of MD Implements	1571		
53.3	Molecular Orbital Method				
	53.3.1	Introduction	1576		
	53.3.2	Density Functional Theory	1578		
	53.3.3	Examples of DFT Calculations	1582		
53.4	Hybrid	Quantum Mechanics/Molecular Mechanics (QM/MM) Methods	1585		
	53.4.1	Basic Theory	1586		
	53.4.2	QM/MM Boundary Treatments	1588		
	53.4.3	Examples of QM/MM Simulations	1588		
53.5	Ab Initio Molecular Dynamics (AIMD)				
53.6	Conclusion 1				
References 1					

Abstract

Computer simulations have provided a powerful technique in understanding the fundamental physics and mechanics of adhesion. In this chapter, various

e-mail: yzhao@imech.ac.cn; wangfc@lnm.imech.ac.cn; wangfc@ustc.edu.cn; chim@lnm.imech.ac.cn

Y.-P. Zhao (🖂) · F.-C. Wang · M. Chi

State Key Laboratory of Nonlinear Mechanics (LNM), Institute of Mechanics, Chinese Academy of Sciences, Beijing, China

[©] Springer International Publishing AG, part of Springer Nature 2018

L. F. M. da Silva et al. (eds.), *Handbook of Adhesion Technology*, https://doi.org/10.1007/978-3-319-55411-2_52

simulation methods pertaining to adhesion technology are introduced, such as the molecular dynamics simulations, the quantum mechanics calculations, the molecular orbital method, the density functional theory, and the molecular mechanics simulations. Besides, some combined methods such as the hybrid quantum mechanics/molecular mechanics simulations, ab initio molecular dynamics, and the density-functional-based tight-binding method are reviewed. General features and routines of these methods as well as the basic theory are described. The advantages and disadvantages of these methods are compared and discussed. Each method has the distinctive advantage and is suitable for specific condition. Some examples are proposed to give the direct perception when investigating adhesion issues using various simulation methods. All these instances are expected to be helpful to readers when performing the corresponding simulations and analyzing of the results.

53.1 Introduction

As hierarchical, multiscale, and complex properties in nature, as shown in Fig. 1, adhesion is an interdisciplinary subject, which undergoes vast experimental, numerical, and theoretical investigations from microscopic to macroscopic levels. As an example, adhesion in micro- and nano-electromechanical systems (MEMS/NEMS) is one of the outstanding issues in this field including the micromechanical process



Fig. 1 Hierarchical and multiscale nature of adhesion

of making and breaking of adhesion contact; the coupling of physical interactions; the trans-scale (nano-micro-macro) mechanisms of adhesion contact, adhesion hysteresis; and the new effective ways of adhesion control (Zhao et al. 2003).

Computer simulations including quantum mechanics (OM) calculations and molecular dynamics (MD) simulations have provided a powerful technique in understanding the fundamental physics of micro- and nanoscale adhesion (Shi et al. 2005; Yin et al. 2005; Chi and Zhao 2009; Yuan et al. 2009). QM method has been proven accurate and provided fundamental understanding for a wide variety of phenomena, including the energy levels of atoms, the band structure of lattice, and the chemical reaction of the materials. The key rule of the QM is to establish the Hamiltonians of the system and to solve the many-body Schrödinger equation (Leach 2001). QM method has the advantage over MD simulations that it includes the effects of charge transfer, polarization, and bond breaking and forming from the beginning. However, the QM computation is always expensive. So QM simulation is employed for the investigation of the chemical reaction in which a few number of atoms are needed, while MD simulation is well suited for the investigation of the dynamics process and time-dependent properties for relatively large systems (Allen and Tildesley 1989). Besides, the molecular mechanics (MM) simulation method is used to study the conformational transformation of the system. Due to some drawbacks of classical MD, ab initio MD (AIMD) is proposed to describe the molecular system dynamic behavior directly from the electronic structure. The development of the hybrid quantum mechanics/molecular mechanics (QM/MM) algorithm (Field et al. 1990) is guided by the general idea that an electronically important region of the system is treated with OM and the remainder admits a classical description, which combines both merits of QM and MM. The QM/MM method is a powerful and effective tool to investigate the adhesion issues such as the polymer interaction with metals. The density-functional-based tightbinding (DFTB) method is also one of the combined simulation methods which integrates the density functional theory (DFT) and the tight binding (TB) method. It should be noted that any one of the aforementioned methods has both advantages and disadvantages. One should pay extra attention when choosing a method before performing simulations.

53.2 Molecular Dynamics Simulation

Molecular dynamics (MD) is a computer simulation technique with which one can obtain the time evolution of a system of interacting particles (atoms, molecules, coarse-grained particles, granular materials, etc.). It was first introduced to study the interactions of hard spheres by Alder and Wainwright in the late 1950s (Alder and Wainwright 1959). With the rapid developments of the computer technology, MD simulations have become a powerful technique and are widely used in the study of proteins and biomolecules, as well as in materials science. This method is now routinely used to investigate the structure, dynamics, and thermodynamics of

biological molecules and their complexes addressing a variety of issues including tribology and adhesion (Bharat 2004).

53.2.1 Basic Theory

The basic idea of the MD simulations is to generate the atomic trajectories of a system of N particles by numerical integration, of a set of Newton's equations of motion for all particles in the system

$$m_i \frac{\partial^2 \vec{r_i}}{\partial t^2} = \vec{F_i} \tag{1}$$

where F_i is the force exerted on particle *i*, m_i is the mass of particle *i*, and r_i is its current position. The force can be derived from the gradient of the potential energy

$$\vec{F}_i = -\frac{\partial U(\vec{r}_1, \vec{r}_2, \dots, \vec{r}_N)}{\partial \vec{r}_i}$$
(2)

in which $U(\vec{r}_1, \vec{r}_2, ..., \vec{r}_N)$ is the empirical interaction potential, depending on the position of the N particles. Given certain boundary conditions, as well as an initial set of positions and velocities, which are referenced as the initial condition, the equations of motions for a specific interatomic potential can be solved and then the information including atomic positions and velocities generated. One may have an interest in the conversion of this microscopic information to macroscopic observables such as pressure, energy, temperature, etc., which requires statistical mechanics. In contrast with the Monte Carlo method, MD is a deterministic technique: The subsequent time evolution is in principle completely determined. Two basic assumptions of the MD simulations are: (i) The motions of all the particles obey the classical Newton's laws of motion, and (ii) the interactions between any pair of the particles satisfy the superposition theorem.

To summarize, the highly simplified description of the MD simulation algorithm is illustrated in Fig. 2.

53.2.2 Force Fields

In a MD simulation, a force field which includes the functional form and parameter sets needs to be specified in order to describe the interaction between atoms and molecules, which is also called the potential energy of a system of particles. Force field functions and parameter sets are derived from both experimental work and high-level quantum mechanical calculations. Most force fields are empirical and consist of a summation of bonded forces associated with chemical bonds, bond angles, bond dihedrals, out-of-plane bending, and nonbonded forces associated with



Fig. 2 Simplified flowchart of a standard MD simulation

van der Waals forces and the Coulomb forces. The most commonly used functional forms are

$$U = U_{\text{nobond}} + U_{\text{bond}} + U_{\text{angle}} + U_{\text{dihedral}} + U_{\text{improper}} + U_{\text{elec}}$$
(3)

Van der Waals interaction can be expressed as the best well-known Lennard–Jones (LJ) 12–6 function (Jones 1924),

$$U_{\text{nobond}} = 4\varepsilon \left[\left(\frac{\sigma}{r} \right)^{12} - \left(\frac{\sigma}{r} \right)^{6} \right]$$
(4)

where ε is the depth of the potential well, σ is the distance at which the interatom potential is zero, and *r* is the distance between atoms. In a MD simulation, the truncation schemes are always adopted. Here, we introduce the simplest one in which the potential is discontinuous at $r = r_c$

$$U_{\text{nobond}}(r) = \begin{cases} U_{\text{nobond}}(r) - U_{\text{nobond}}(r_c), & r < r\\ 0 & r \ge r \end{cases}$$
(5)

The interaction between pairs of bonded atoms has the form of

$$U_{\text{bond}} = k_b (r - r_0)^2 \tag{6}$$

where k_b is the stiffness of the bond with the usual 1/2 factor included and r_0 is the equilibrium bond distance. The interaction of valence angles in the molecule can be written as

$$U_{\text{angle}} = k_a (\theta - \theta_0)^2 \tag{7}$$

where k_a is the stiffness of the bond angle with the usual 1/2 factor included and θ and θ_0 are the bond angle and its reference value, respectively.

The dihedral interaction, also referred to as torsional terms, can be written as

$$U_{\text{dihedral}} = k_d [1 + \cos\left(n\phi - \gamma\right)] \tag{8}$$

in which φ is the dihedral angle, γ acts as an equilibrium angle, k_d is the force constant, and n is the multiplicity which gives the number of minimum points in the function as the bond is rotated through 360°. The improper torsion is used to describe the out-of-plane bending term. It can be modeled using the form of

$$U_{\rm improper} = k_i (\psi - \psi_0)^2 \tag{9}$$

in which k_i is the improper torsion force constant and ψ and ψ_0 are the improper torsion angle and its reference value, respectively.

The columbic pairwise interaction is given by

$$U_{\text{elec}} = \frac{Cq_i q_j}{r} \tag{10}$$

where *C* is an energy conversion constant and q_i and q_j are the charges on the two atoms.

The abovementioned potentials can be classified into the empirical ones, which may not be sufficiently accurate to reproduce the dynamics of molecular systems in some cases. There are also a wide variety of semiempirical potentials, known as TB potentials, which use QM matrix representation whose elements are obtained through empirical formulae. For more accurate cases, ab initio QM methods are used to calculate the potential energy of the system on the fly, which is the combination of first principles electronic structure methods with MD based on Newton's equations of motion.

53.2.3 Boundary Conditions

There are two major types of boundary conditions: isolated boundary condition and periodic boundary condition (PBC). PBC enables a simulation to be performed using

a relatively small number of particles in such a way that the particles behave as if it was infinite in size and there were no edge effects. All the particles are expected to experience forces as though they were in a bulk solution. When using PBC, particles are enclosed in a box, and one can imagine that this box is replicated to infinity by rigid translation in all the Cartesian directions, completely filling the space. In a two-dimensional (2D) example, each simulation box is surrounded by 8 mirror images, while in 3D the mirror image number would be 26. The concept of 2D PBC is illustrated in Fig. 3 . The shaded box (marked as "E") represents the system being simulated, while the surrounding boxes are the copies in every detail. Even the velocities (indicated by the arrows) and the forces are exactly the same. When a particle leaves the simulation cell, it is replaced by another with exactly the same velocity, entering from the opposite cell face. So the number of particles in the cell is conserved. Furthermore, no particle feels any surface force, as these are now completely removed.

Forces on the primary particles are calculated from particles within the same box as well as in the image box. In Fig. 3, R_{cut} is the cutoff radius that is normally applied when calculating the force between two particles. As one can see, a particle may



Fig. 3 Illustration of 2D periodic boundary conditions. The shaded box E represents the system being simulated and the other ones are the images of E

interact with one in the neighboring cell (which is an image of one of the particles in the simulation cell) because it is within the cutoff radius. It ignores the equivalent particle in the simulation cell because it is too far away. In other cases the interaction comes from a particle in the simulation cell itself. Thus the interaction that is calculated is always with the closest image. This is known as the minimum image convention. These operating conditions greatly simplify the set up of a MD program and are commonly used. Of course, the size of the simulation box must also be large enough. If the simulation box is too small, a particle may interact with its own image in a neighboring box, which produces highly unphysical dynamics. The cutoff should be chosen such that a particle in the primary box does not see its image in the surrounding boxes. A practical suggestion is that one must always make sure that the box size is at least two times R_{cut} along all the directions where PBCs are effective.

There are boundaries existing inherently in some cases, where PBC cannot be used in computer simulations. Simulations which require no periodic boundaries are best suited to in vacuo simulations, such as the conformational study of an isolated polymer molecule. When simulating surfaces, it is particularly useful to apply the slab boundary conditions in which boundaries are periodic only in X and Y. The periodic cell in the XY plane can be any parallelogram. The origin of the X and Y atomic coordinates lies on an axis perpendicular to the center of the parallelogram. The origin of the Z coordinate is where the user specifies it, but it is recommended at or near the surface. The correct treatment of boundary conditions and boundary effects is crucial in MD simulations, which use relatively small numbers of particles (Leach 2001).

53.2.4 Energy Minimization

In MM simulations, energy minimization (also called energy optimization or geometry optimization) methods are used to compute the equilibrium configuration of biomolecules, liquids, and solids. Moreover, MD simulations focusing on adhesion always deal with complex molecules or systems, in which the added hydrogens and broken hydrogen bond network in water would lead to quite large forces and structure distortion if the MD simulations were started immediately. To remove these forces, it is often preferable to carry out a short energy minimization on the conformation before MD simulations. Energy minimization is usually performed by gradient optimization; atoms are moved so as to reduce the net forces on them. The minimized structure has small forces on each atom and therefore serves as an excellent starting point for MD simulations. At that point, the configuration will hopefully be in local potential energy minimum. This can be done with two representative methods which involve the steepest descent algorithm and the conjugate gradient algorithm. In a steepest descent algorithm, at each iteration, the search direction is set to the downhill direction corresponding to the force vector (negative gradient of energy), while in a conjugate gradient algorithm, the force gradient is

combined at each iteration with the previous iteration information to compute a new search direction perpendicular (conjugate) to the previous search direction. Typically, steepest descent method will not converge as quickly as the conjugate gradient method, but may be more robust in some situations.

53.2.5 Integrators

MD simulation implement involves solving a system of three N second-order differential equations. Due to the complicated nature of this function, there is no analytical solution to the equations of motion, and they must be solved numerically. A standard method for solution of ordinary differential equations such as Eq. 1 is the finite difference approach. Given the initial conditions and the boundary conditions, one can solve the equations step by step. The time interval δt is always chosen to be one or several femtoseconds, which should be significantly smaller than the typical time taken for a molecule to travel its own length. Many different algorithms fall into the general finite difference pattern, such as Verlet, leapfrog, velocity Verlet, Beeman, and predictor–corrector algorithms. When choosing an algorithm to use, the following criteria should be computationally efficient and it should permit a long time step for integration. To illustrate the principles of the method, the velocity Verlet algorithm is selected, and its technical details which affect the choice in practice are discussed.

The velocity Verlet algorithm starts with the position r(t) and the velocity v(t) at time *t* and is carried out by repeating these instructions:

1. Calculate a(t),

$$a(t) = \frac{\partial^2 r(t)}{\partial t^2} \tag{11}$$

2. Calculate the position of the particle for the following time step,

$$r(t + \delta t) = r(t) + \delta t \cdot v(t) + \frac{1}{2}\delta t^2 \cdot a(t)$$
(12)

3. Calculate velocities at mid-step using

$$v\left(t+\frac{1}{2}\delta t\right) = v(t) + \frac{1}{2}\delta t \cdot a(t)$$
(13)

4. Calculate $a(t+\delta t)$

$$a(t+\delta t) = \frac{\partial^2 r(t+\delta t)}{\partial t^2}$$
(14)

5. Complete the velocity move using

$$v(t+\delta t) = v\left(t+\frac{1}{2}\delta t\right) + \frac{1}{2}\delta t \cdot a(t+\delta t)$$
(15)

The velocity Verlet algorithm provides both the atomic positions and velocities at the same instant of time and for this reason may be regarded as the most complete form of Verlet algorithm. The advantage of this algorithm is that it requires less computer memory, because only one set of positions, forces, and velocities need to be carried at any one time. This convenience is not apparent in the original equations. Besides, this algorithm conserves energy well even with relatively long time steps and is numerically stable as well as simple to program.

53.2.6 Analysis of the MD Results

MD simulations provide the means to solve the equations of motion of the particles and output the desired physical quantities in the term of some microscopic information. In a MD simulation, one often wishes to explore the macroscopic properties of a system through the microscopic information. These conversions are performed on the basis of the statistical mechanics, which provide the rigorous mathematical expressions that relate macroscopic properties to the distribution and motion of the atoms and molecules of the N-body system. With MD simulations, one can study both thermodynamic properties and the time-dependent properties. Some quantities that are routinely calculated from a MD simulation include temperature, pressure, energy, the radial distribution function, the mean square displacement, the time correlation function, and so on (Allen and Tildesley 1989; Rapaport 2004).

The temperature of the system in MD simulations is calculated by

$$T = E_k / \left(\frac{d}{2}Nk_B\right) \tag{16}$$

where E_k is the total kinetic energy of all the N particles, k_B is the Boltzmann constant, and d = 2 or 3 is the dimensionality of the simulation. The kinetic energy of the system is obtained simply by the summation over all the particles,

$$E_k = \sum_{i=1}^{N} \frac{1}{2} m_i v_i^2, \tag{17}$$

where m_i and v_i are the mass and velocity of the ith particle, respectively. The radial distribution function describes how the atomic density varies as a function of the distance from one particular atom. It provides a particularly effective way of describing the average structure of disordered molecular systems such as liquids. The mathematical formula of the radial distribution function, g(r), is

$$g(r) = \frac{n(r)}{4\pi\rho r^2\Delta r},\tag{18}$$

in which n(r) is the mean number of atoms in a shell of width Δr at distance r and ρ is the mean atom density. The method needs not be restricted to one atom. All the atoms in the system can be treated in this way, leading to an improved determination of the radial distribution function as an average over many atoms.

The mean square displacement is a measure of the average distance a molecule travels. It is defined as

$$msd(t) = \left\langle \left[r_i(t) - r_i(0) \right]^2 \right\rangle, \tag{19}$$

where $\langle ... \rangle$ denotes here averaging over all the atoms and $r_i(t) - r_i(0)$ is the distance traveled by atom *i* over some time interval of length *t*. The slope of the mean squared displacement versus time is proportional to the diffusion coefficient *D* of the diffusing atoms, which is given by the following Einstein relation,

$$D = \lim_{t \to \infty} \frac{1}{2dt} \left\langle \left[r_i(t) - r_i(0) \right]^2 \right\rangle,\tag{20}$$

where d has the same meaning as in Eq. 16.From a MD simulation, time-dependent properties such as correlation functions can also be calculated. A time correlation function is defined as

$$C(t) = \langle A(0)A(t) \rangle, \tag{21}$$

where $\langle ... \rangle$ represents an ensemble average and A is the dynamic variable of interest. Many other properties can be calculated based on the integral of this correlation function, such as diffusion coefficient D, the shear viscosity η , and the thermal conductivity λ . The corresponding computing formulas are listed as follows (Rapaport 2004):

$$D = \frac{1}{dN} \int_0^\infty \left\langle \sum_{i=1}^N v_i(0) v_i(t) \right\rangle dt,$$
(22)

in which d has the same meaning as in Eq. 16.

$$\eta = \frac{V}{3k_BT} \int_0^\infty \left\langle \sum_{x < y} p_{xy}(0) p_{xy}(t) \right\rangle dt,$$
(23)

where p_{xy} is the component of the pressure tensor (the negative of which is known as the stress tensor), V is the volume of the simulation box, and T is the temperature of the system.

$$\lambda = \frac{V}{3T^2} \int_0^\infty \langle S(0)S(t)\rangle dt,$$
(24)

where

$$S = \frac{1}{V} \left[\sum_{i} e_{i} v_{i} + \frac{1}{2} \sum_{i \neq j} r_{ij} \left(f_{ij} \cdot v_{i} \right) \right], \tag{25}$$

and the instantaneous excess energy of the ith atom is

$$e_i = \frac{1}{2}m_i v_i^2 + \frac{1}{2}\sum_{i\neq j}u(r_{ij}) - \langle e \rangle.$$

$$(26)$$

In order to get the surface energy, for example, the surface energy of nanofilm, one should calculate the energy of nanofilm with PBC and the slab boundary conditions, respectively.

Then the surface energy can be expressed as

$$\gamma = \frac{E_{\rm pbc} - E_{\rm slab}}{2A},\tag{27}$$

in which E_{pbc} is the total energy of the nanofilm with PBC, while E_{slab} is that with slab boundary conditions.

When carrying out a MD simulation, coordinates of the system can be obtained, which is called the trajectory of the system. It can be displayed graphically and also used for the analysis. To visualize (and analyze) the snapshots from MD simulations, one can use a variety of visualization programs including VMD (Humphrey et al. 1996) and AtomEye (Li 2003). At present there are several high-quality MD codes, which have been widely used by researchers. Some of them are open-source codes, such as LAMMPS (Plimpton 1995), GROMACS (Berendsen et al. 1995; Lindahl et al. 2001), and NAMD (Nelson et al. 1996; Kale et al. 1999). The last two show extra attention on the simulations of biomolecules. Besides, CHARMM (Brooks et al. 1983) and AMBER (Pearlman et al. 1995) are not free but are standard and extremely powerful codes in biology.

For more details of the MD simulations, there are numerous excellent books available on this subject (Allen and Tildesley 1989; Leach 2001; Rapaport 2004).

53.2.7 Water Models Used in MD Simulations

When dealing with adhesion issues of biomolecules surrounded by water, the solvent environment always has a significant influence on the properties of the biomolecules. Different types of the water models are illustrated in Fig. 4.



Fig. 4 Illustration of three types of water model. The red, blue, and green balls represent O and H atoms and the massless charge, respectively

Model	Type	σ (Å)	εkImol ^{−1}	1. (Å)	12 (Å)	a. (e)	a ₂ (e)	h∘	φ°
	TJPC	0 ()	0 110 11101	-1 ()	-2 ()	41 (0)	q ₂ (c)	0	Ψ
SPC	A	3.166	0.650	1.0000	-	+0.410	-0.8200	109.47	-
SPC/E	A	3.166	0.650	1.0000	-	+0.4238	-0.8476	109.47	-
TIP3P	Α	3.15061	0.6364	0.9572	-	+0.4170	-0.8340	104.52	-
TIP4P	В	3.15365	0.6480	0.9572	0.15	+0.5200	-1.0400	104.52	52.26
TIP5P	C	3.12000	0.6694	0.9572	0.70	+0.2410	-0.2410	104.52	109.47

 Table 1
 Parameters for water molecular models

The parameters of five representative and commonly used water models in MD simulations are listed in Table 1. SPC is the short term for "simple point charge," and SPC/E denotes the extended simple point charge model with charges on the oxygen and hydrogen modified to improve the classical SPC water model; the SPC/E model results in a better density and diffusion constant than the SPC model. "TIP" in "TIPnP" stands for transferable intermolecular potential, while "nP" means there are n points used in the corresponding water model.

53.2.8 Examples of MD Implements

Barnacle cement is an underwater adhesive that is used for permanent settlement. Its main components are insoluble protein complexes. In the following simulations, 36-KD protein which has 38 amino acids and Mrcp-100K protein with 28 amino acids were chosen to study the adhesion properties of the barnacle cement (Yin et al. 2005). Energy minimization was performed first at the temperature of absolute zero in order to avoid improper structure of proteins. Then, the temperature of the system was increased to 300 K by giving every atom a prime velocity according to Boltzmann distribution, and the system was then thermally equilibrated for a short period of time. All the MD simulations were performed using GROMACS version

3.1. For the proteins, the standard GROMACS amino acid residue topology and parameters based on the GROMOS-96 force field (Lindahl et al. 2001) were used. The SHAKE algorithm (Ryckaert et al. 1977) was used to fix hydrogen bonds during the simulation. Leapfrog algorithm was employed to integrate the Newton's equations of motion for all the atoms, with a time step of 1 fs. The temperatures of the system were always controlled at 300 K, where the week coupling Berendsen scheme was used to control the temperature.

In this simulation, the proteins were stretched in a water solvent modeled by TIP3P water molecules (Jorgensen et al. 1983). The dimension of the simulation box was $40 \times 40 \times 200$ Å with the PBC applied in all the three directions. The proteins were stretched at a velocity of 0.01 Å/ps.

It was found that there are mainly two regimes of protein deformation: fluctuation regime and extension regime. In the fluctuation regime, resistance to stretching is mostly due to the hydrogen bonds, while in the extension regime, the main resistance force is due to bonded interaction. Moreover, the hydrogen bonds in proteins play an important role in the adhesive ability of the protein. In Fig. 5, the stretching force becomes bigger when more hydrogen bonds are breaking and almost every peak of the force curve corresponds to a trough of the hydrogen bond number curve (indicated by the arrows). For proteins, the average energy needed to break or form a hydrogen bond is about 15-30 kJ/mol. It can also be found that the total energy of the Mrcp-100K protein decreases with the increasing hydrogen bond number. All of this information shows that in fluctuation regime, hydrogen bonds are more significant than many other interactions, such as entropic force, van der Waals force, and so on. With this background knowledge, the efforts directed toward more detailed understanding of the properties of this adhesive and molecular biology studies would significantly contribute to progress in the basic field and potential applications such as biofouling prevention (Khandeparker and Anil 2007).

Since the barnacle is a saltwater organism, 36-KD protein stretching in seawater was also simulated. Na⁺ and Cl⁻ ions were also added to the water box with a concentration of about 17% to simulate the neutral seawater system. Figure 6 shows that the stretching force of 36-KD protein in seawater is larger than that in water. The more structural stability of 36-KD protein in seawater is due to two reasons. First, the electrostatic interaction between proteins and ions in seawater makes the structure more stable. Second, 36-KD protein forms more hydrogen bonds in seawater in fluctuation regime (there are 27 hydrogen bonds in seawater while only 19 hydrogen bonds in water).

Another example of MD simulations was performed to study adhesion and peeling of a short fragment of single-stranded DNA (ssDNA) molecule from a graphene surface (Shi et al. 2005). A short homogeneous ssDNA oligonucleotide containing 8 adenine bases in the B-helix form was placed on top of 3 graphene layers each containing 928 carbon atoms, with an average separation of about 7 Å. After energy minimization, the system was equilibrated at 300 K for 400 ps. In order to simulate the process of peeling ssDNA from graphene, a dummy atom was linked to one end of the ssDNA with a constraint force constant of 8 kcal/mol/Å². Then the dummy atom was pulled at different peeling angles under a constant pulling velocity,



Fig. 5 The variation of hydrogen bonds, strain (stretching), and total energy (stretching) (Reprinted from Materials Science and Engineering A, 409, Yin J and Zhao YP, Molecular Dynamics Simulation of Barnacle Cement, 160–166, Copyright (2005), with permission from Elsevier)

with the graphene fixed. All these simulations were performed using the code CHARMM (Brooks et al. 1983). Figure 7 depicts several snapshots of ssDNA peeled away from graphene under a constant velocity of 0.1 Å/ps and at a peeling angle of 90° .



Fig. 7 Steered MD simulation snapshots of peeling ssDNA from graphene at a peeling angle of 90° (With kind permission from Springer Science+Business Media: Shi et al. (2005), Fig. 3)

During the simulation, the pulling force was calculated and was represented in Fig. 8, which indicated that the pulling force reaches a local maximum value when a tightly attached DNA base is pulled off the surface and is relaxed before the next tightly attached base is to be pulled off. The peel-off force can be calculated from the global maximum of the force profile. Simulations of the peeling process under various pulling rates (from 0.01 to 0.4 Å/ps) and peeling angles (75°, 90°, 120°, and 135°) were also performed, with the calculated peel-off forces summarized in Fig. 9.

The black line in Fig. 9 shows the prediction of the critical peel-off forces using the homogeneous peeling model (Kendall 1975),

$$F(1 - \cos \theta) + F\varepsilon - \int_0^\varepsilon g(\varepsilon) d\varepsilon = \Delta \gamma$$
(28)



Fig. 9 The critical peel-off forces of ssDNA oligonucleotide on graphene as a function of the peeling angle. The blue closed triangles are the results of direct MD simulations at peeling angles of 75° , 90° , 120° , and 135° , respectively (With kind permission from Springer Science+Business Media: Shi et al. (2005), Fig. 8)

where *F* is the peeling force at a peeling angle θ from a substrate, $g(\varepsilon)$ is used to describe the elasticity of the polymer, ε is the elastic strain along the length of the chain, and $\Delta \gamma$ denotes the work of adhesion between the chain and the substrate. Considering the work of adhesion between ssDNA and substrate is not constant, the homogeneous peeling model can be modified as

$$F(1 - \cos \theta) + F\varepsilon - \int_0^\varepsilon g(\varepsilon)d\varepsilon = \Delta \gamma' \left(1 - \left|\sin\frac{\pi}{l}x\right|\right)$$
(29)

where the constant work of adhesion is replaced by a sinusoidal function with l being the period of modulation of adhesion energy and x denoting the position along the chain. Equation 29 is the generalized elastic band model, and the corresponding results are illustrated as the red line in Fig. 9, which are in good agreement with the MD results. The simulations and models demonstrated that, for the same adhesion energy, the critical peel-off forces also depend on the peeling angle.

53.3 Molecular Orbital Method

53.3.1 Introduction

Molecular orbital (MO) theory is a method for determining molecular structure in which electrons are not assigned to individual bonds between atoms, but are treated as moving under the influence of the nuclei in the whole molecule (Daintith 2004). In this theory, each molecule has a set of MOs, in which it is assumed that each MO wave function ψ_i can be written as a summation of the following form (Pople and Beveridge 1970):

$$\psi_i = \sum_{\mu=1}^K c_{\mu i} \varphi_\mu, \tag{30}$$

where ψ_i is a (spatial) MO, ϕ_{μ} is one of *K* atomic orbitals, and $c_{\mu i}$ is the coefficient. This method is called the linear combination of atomic orbitals (LCAO) approximation and is widely used in computational chemistry.

MOs are often divided into bonding, antibonding, and nonbonding orbitals. In a bonding orbital, the electrons have a higher probability of being between nuclei than elsewhere. Electrons in the antibonding orbital tend to spend more time elsewhere than between the nuclei, while electrons in nonbonding orbital prefer to be in deep orbitals (nearly atomic orbitals) associated almost entirely with one nucleus.

In the MO theory, three necessary conditions must be satisfied when atomic orbitals combine together to form MOs:

- 1. The combining atomic orbitals must have the same symmetry about the molecular axis.
- 2. The combining atomic orbitals must be able to overlap to the maximum extent to form MOs, since the greater is the extent of overlap between the combining atomic orbitals, the greater will be the electron density in the region between the nuclei of the combining atoms and hence the stronger the bond between them.
- 3. The combining atomic orbitals must have the same or almost the same energy.

The first one is the most important, which decides whether these atomic orbitals can form MOs or not. The other two just affect the combination efficiency.

For diamagnetic species, MO method starts by assigning electrons in pairs to spatial functions $\psi_1, \psi_2, \ldots, \psi_n$, which are then used in the construction of a manyelectron wave function as a single determinant (Roothaan 1951; Pople and Beveridge 1970; Hehre 1976)

$$\Psi(1,2,\ldots,2n) = \frac{1}{2n} \times \begin{vmatrix} \psi_1(1)\alpha(1) & \psi_1(1)\beta(1)\cdots & \psi_n(1)\beta(1) \\ \psi_1(2)\alpha(2) & \cdots & \\ \ddots & \\ \psi_1(2n)\alpha(2n) & \psi_1(2n)\beta(2n)\cdots & \psi_n(2n)\beta(2n) \end{vmatrix}, \quad (31)$$

where α and β are spin functions. The MOs ψ_i are chosen so as to minimize the total energy of the system, that is, the expectation value of the many-electron Hamiltonian *H*,

$$E = \int \dots \int \Psi(1, 2, \dots 2n) H \Psi(1, 2, \dots 2n) d\tau_1 d\tau_2 \dots d\tau_{2n},$$
(32)

is in practice written in terms of a linear combination of nuclear centered atomic functions, as shown in Eq. 30. The coefficients, $c_{\mu i}$, in Eq. 30 are obtained at by solution of the Roothaan equations

$$\sum_{\nu} \left(F_{\mu\nu} - \varepsilon_i S_{\mu\nu} \right) c_{\mu i} = 0, \tag{33}$$

where $S_{\mu\nu}$ is an overlap integral

$$S_{\mu\nu} = \int \varphi_{\mu}(1)\varphi_{\nu}(1)\mathrm{d}\tau_{1}, \qquad (34)$$

 ε_i is the one-electron energy associated with ψ_i , and $F_{\mu\nu}$ is an element of the Fock matrix

$$F_{\mu\nu} = H_{\mu\nu} + \sum_{\lambda} \sum_{\sigma} P_{\lambda\sigma} [(\mu\nu|\lambda\sigma)(\mu\lambda|\nu\sigma)].$$
(35)

Here $H_{\mu\nu}$ is the element

$$H_{\mu\nu} = \int \varphi_{\mu}(1) \left[-\frac{1}{2} \nabla^{2} \right] \varphi_{\nu}(1) d\tau_{1} + \sum_{A}^{\text{nuclei}} \int \varphi_{\mu}(1) \left[\frac{1}{r_{1}A} \right] \varphi_{\nu}(1) d\tau_{1}.$$
(36)

which describes the motion of a single electron in a field of bare nuclei, and $(\mu v | \lambda \sigma)$ is a two-electron integral

$$(\mu\nu|\lambda\sigma) = \iint \varphi_{\mu}(1)\varphi_{\nu}(1) \left[\frac{1}{r_{12}}\right] \varphi_{\lambda}(2)\varphi_{\sigma}(2)d\tau_{1}d\tau_{2}.$$
(37)

The one-electron density matrix, P, is given by

$$P_{\lambda\sigma} = 2\sum_{i} c_{\lambda i} c_{\sigma i},\tag{38}$$

where the summation is over the manifold of occupied MOs. Note that the Roothaan equations are not readily amenable to solution in closed form. This is simply because the quantity sought (the $c_{\mu i}$) appears, disguised as $P_{\lambda\sigma}$, in their formulation.

53.3.2 Density Functional Theory

The two basic methods in QM calculations are MO theory and density functional theory (DFT). These two methods, often contrasting, but mostly cooperating, are different approaches to tackling the electronic problems. MO method is always adopted by the chemists who think that the MO is expressed as LCAO. The DFT method is always used to treat infinite periodic systems by the physicists.

DFT is founded on the Hohenberg–Kohn (H–K) theorems (Hohenberg and Kohn 1964), which comes in two parts. The first one states that the ground state properties of a many-electron system are uniquely functional of the ground state electron density which depends on only three spatial coordinates. This implies that all properties of the system are completely determined given only the ground state density.

The Hohenberg–Kohn Theorem

The second part of the H–K theorem states that the total energy of the ground state of a many-electron system in an external potential $V_{\text{ext}}(\vec{r})$ is a unique functional of the electron density

$$E[n] = F[n] + \int n\left(\vec{r}\right) V_{\text{ext}}\left(\vec{r}\right) d\vec{r}.$$
(39)

This functional has its minimum (i.e., the ground state energy E_0) for the ground state electron density $n_0(\vec{r})$

$$E_0 = E\left[n_0\left(\vec{r}\right)\right] = \min_{n\left(\vec{r}\right)} E[n].$$
(40)

The functional F[n] is a universal function, independent of the external potential $V_{\text{ext}}(\vec{r})$ and the same for all systems.

Levy gave a particularly simple proof of the Hohenberg–Kohn theorem (Levy 1979): A functional O is defined as

$$O\left[n\left(\vec{r}\right)\right] = \min_{\left|\Psi\rangle \to n\left(\vec{r}\right)\right.} \langle \Psi | \hat{O} | \Psi \rangle, \tag{41}$$

where the expectation value is found by searching over all wavefunctions, ψ , giving the density $n(\vec{r})$ and selecting the wave function which minimizes the expectation value of \hat{O} .

 $F\left[n\left(\vec{r}\right)\right]$ is defined by

$$F\left[n\left(\vec{r}\right)\right] = \min_{|\Psi\rangle \to n\left(\vec{r}\right)} \langle \Psi | \hat{F} | \Psi \rangle, \tag{42}$$

so

$$\hat{F} = \sum_{i} -\frac{1}{2}\nabla_{i}^{2} + \frac{1}{2}\sum_{i \neq j} \frac{1}{\left|\vec{r}_{i} - \vec{r}_{j}\right|}.$$
(43)

Considering an N-electron ground state wavefunction Ψ_0 which yields a density $n(\vec{r})$ and minimizes $\langle \Psi | \hat{F} | \Psi \rangle$, then from the definition of the functional *E*

$$E\left[n\left(\vec{r}\right)\right] = F\left[n\left(\vec{r}\right)\right] + \int n\left(\vec{r}\right) V_{\text{ext}}\left(\vec{r}\right) d\vec{r} = \langle \Psi | \hat{F} + V_{\text{ext}} | \Psi \rangle.$$
(44)

The Hamiltonian is given by $\hat{F} + V_{\text{ext}}$, and so $E\left[n\left(\vec{r}\right)\right]$ must obey the variational principle,

$$E\left[n\left(\vec{r}\right)\right] \ge E_o. \tag{45}$$

This completes the first part of the proof, which places a lower bound on $E\left[n\left(\vec{r}\right)\right]$. From the definition of $F\left[n\left(\vec{r}\right)\right]$ in Eq. 42, the following is obtained

$$F\left[n_0\left(\vec{r}\right)\right] \le \langle \Psi_0 | \hat{F} | \Psi_0 \rangle, \tag{46}$$

since Ψ_0 is a trial wave function yielding $n_0(\vec{r})$. Combining $\int n(\vec{r}) V_{\text{ext}}(\vec{r}) d\vec{r}$ with the above equation gives

$$E\left[n_0\left(\vec{r}\right)\right] \le E_o,\tag{47}$$

which in combination with Eq. 46 yields the key result

$$E\left[n_0\left(\vec{r}\right)\right] = E_o. \tag{48}$$

The Kohn–Sham (KS) Equations

Kohn and Sham derived a coupled set of differential equations enabling the ground state density $n_0(\vec{r})$ to be found. The variational problems of minimizing the energy functional $E[n(\vec{r})]$ can be solved by applying the Lagrangian method of undetermined multipliers (Hohenberg and Kohn 1964). First, one considers an energy functional that does not explicitly have an electron–electron interaction energy term,

$$E_{s}\left[n\left(\vec{r}\right)\right] = \left\langle \Psi_{s}\left[n\left(\vec{r}\right)\right] \middle| \hat{T}_{s} + \hat{V}_{s} \middle| \Psi_{s}\left[n\left(\vec{r}\right)\right] \right\rangle, \tag{49}$$

where \hat{T}_s is defined as the kinetic energy of a non-interacting electron gas and \hat{V}_s is an external effective potential in which the non-interacting electrons are moving. Obviously, $n_s(\vec{r}) \stackrel{\text{def}}{=} n(\vec{r})$ if \hat{V}_s is chosen to be

$$\hat{V}_{s} = \hat{V} + \hat{U} + (\hat{T} - \hat{T}_{s}).$$
(50)

Thus, to find the ground state energy, E_0 , and the ground state density, n_0 , the one-electron Schrödinger equation,

$$\left[-\frac{\hbar^2}{2m}\nabla^2 + V_s\left(\vec{r}\right)\right]\phi_i\left(\vec{r}\right) = \varepsilon_i\phi_i\left(\vec{r}\right),\tag{51}$$

should be solved self-consistently with

$$n(r) \stackrel{\text{def}}{=} n_s \left(\vec{r} \right) = \sum_{i}^{N} \left| \phi_i \left(\vec{r} \right) \right|^2.$$
(52)

The effective single-particle potential can be written in more detail as

$$V_{s}\left(\vec{r}\right) = V\left(\vec{r}\right) + \int \frac{e^{2}n_{s}\left(\vec{r}'\right)}{\left|\vec{r}-\vec{r}'\right|} d^{3}r' + V_{xc}\left[n_{s}\left(\vec{r}\right)\right],$$
(53)

where the second term is the so-called Hartree term describing the electron–electron Coulomb repulsion, while the final term $V_{\rm xc}$ is an implicit definition of the exchange–correlation potential. Here, $V_{\rm xc}$ includes all the many-particle interactions, which is given formally by the functional derivative $V_{\rm XC}\left(\vec{r}\right) = \frac{\delta E_{\rm xc}[n(\vec{r})]}{\delta n(\vec{r})}$.

Since the Hartree term and $V_{\rm xc}$ depend upon the density $n(\vec{r})$, which depends on the $\phi_{\rm i}$, which in turn depends on V_s , the problem of solving the KS equation has to be done in a self-consistent (i.e., iterative) way. Usually, one starts with an initial guess for $n(\vec{r})$, then calculates the corresponding V_s , and solves the KS equations for $\phi_{\rm i}$. Then, one calculates a new density and starts again. This procedure is then repeated until the input and output densities satisfy the accuracy.

Exchange–Correlation Functionals

To solve Kohn–Sham equations, the exchange–correlation energy $E_{xc}[n]$ must be known. However, because of the many-body effects, $E_{xc}[n]$ cannot be derived exactly. Therefore, certain approximations are required for $E_{xc}[n]$. In physics, the most widely used approximation has been the local-density approximation (LDA), where the functional depends only on the density at the coordinate where the functional is evaluated,

$$E_{\rm xc}[n] = \int \varepsilon_{\rm xc}(n) n\left(\vec{r}\right) d^3r, \qquad (54)$$

where $\varepsilon_{xc}(n)$ is the exchange–correlation energy per particle of a uniform electron gas of density n. LDA has yielded valuable quantitative or at least semiquantitative results, especially for equilibrium structures of molecules and solids. The local spindensity approximation (LSDA) is a straightforward generalization of the LDA to include electron spin

$$E_{\rm xc}[n_{\uparrow},n_{\downarrow}] = \int \varepsilon_{\rm xc}(n_{\uparrow},n_{\downarrow})n(\vec{r})d^{3}r.$$
(55)

Highly accurate formulae for the exchange–correlation energy density $\varepsilon_{xc}(n_{\uparrow}, n_{\downarrow})$ have been constructed from quantum Monte Carlo simulations of a free electron model (Perdew et al. 2005).Generalized gradient approximations (GGA) have yielded substantial improvements over the LDA for binding energies of molecules and solids as well as for barrier heights of chemical reactions. GGA are still local but also take into account the gradient of the density at the same coordinate

$$E_{\rm xc}[n_{\uparrow},n_{\downarrow}] = \int \varepsilon_{\rm xc} \Big(n_{\uparrow},n_{\downarrow},\overrightarrow{\nabla} \quad n_{\uparrow},\overrightarrow{\nabla} \quad n_{\downarrow}\Big) n\Big(\overrightarrow{r}\Big) d^{3}r.$$
(56)

Potentially more accurate than the GGA functionals are the so-called hybrid functionals, which have the generic form

$$E_{\rm xc}[n_{\uparrow},n_{\downarrow}] = \gamma E_{\rm x}^{\rm exact} \left[n\left(\vec{r}\right) \right] + \int \varepsilon_{\rm xc}' \left(n_{\uparrow},n_{\downarrow},\vec{\nabla} \quad n_{\uparrow},\vec{\nabla} \quad n_{\downarrow} \right) n\left(\vec{r}\right) {\rm d}^{3}r, \quad (57)$$

where E_x^{exact} is the exact exchange energy evaluated with KS orbitals and γ is a constant between 0 and 1.

53.3.3 Examples of DFT Calculations

Gas sensors based on metal oxide–semiconductor materials as well as metal-doped graphene have attracted considerable attention during the past decade. Zinc oxide (ZnO), tin dioxide (SnO ₂), and Al-doped graphene have been chosen as sensing materials because of their excellent characteristics such as low cost, high sensitivity, rapid response, and fast recovery. Here two examples are given to show the general routine of DFT calculations and the analysis of the results.

DFT calculations were employed to explore the gas-sensing mechanisms of zinc oxide (ZnO) with surface reconstruction taken into consideration (Yuan et al. 2009). Mix-terminated $(10\bar{1}0)$ ZnO surfaces were examined. Simulations of the adsorption process of various gases, that is, H₂, NH₃, CO, and ethanol (C₂H₅OH) gases, on the ZnO ($10\bar{1}0$) surface, were carried out. All the ab initio calculations were performed using DFT implemented in the DMol³ program (Delley 2000, 2002). The widely used GGA with the exchange–correlation functional parameterized by Perdew and Wang (PW91) was adopted, calculating with restricted spin. Compared with LDA, GGA will not lead to a strong bonding of molecules. So if the calculated molecules are adsorbed on the ZnO surface, they will definitely bind in a real system. However, GGA overestimates binding distance and underestimates binding energy consequently.

A plane-wave basis set with an orbital cutoff distance of 3.9 Å was used. All-electron calculations and a double numerical basis set with polarization functions (DNP) were employed. Wave function integration in reciprocal space was performed via fine grid sampling of k points with a separation of 0.02 Å ⁻¹. For the calculation of the density of states (DOS), a $5 \times 8 \times 3$ Monkhorst–Pack grid was used. Charge transfer was calculated based on the Mulliken population analysis (MPA) (Mulliken 1955).

The ethanol (C_2H_5OH) molecule adsorption on the ZnO surface is shown in Fig. 10. When an ethanol molecule approaches the ZnO surface, electronic

Fig. 10 Optimized configuration of the ethanol molecule on the ZnO surface. Blue line represents hydrogen bond between H and O atoms (Reprinted with permission from Yuan et al. (2009). Copyright 2009 American Chemical Society)



interactions among nuclei and electrons disturb the initial configuration, inducing adsorption of the gas molecule on the ZnO surface. After the surface reconstruction induced by adsorption, energy-level splitting is found (Fig. 11a). Band structure is deflexed because of charge transfer (Fig. 11b).



Fig. 11 Band structure and PDOS of the (**a**) reconstructed and (**b**) ethanol–molecule-adsorbed ZnO surface (Reprinted with permission from Yuan et al. (2009). Copyright 2009 American Chemical Society)

Based on these calculations, two gas-sensing mechanisms were proposed and revealed that both surface reconstruction and charge transfer result in a change of electronic conductance of ZnO. When the gas molecule is adsorbed upon the surface, the electronic conductance of the gas sensor changes because of the joint effect of these two mechanisms. These results show good accordance with existing experiments and could help in understanding the sensing mechanism of ZnO-based gas sensors.

To search for a high sensitivity sensor for formaldehyde (H₂CO), the adsorptions of H₂CO on the intrinsic and Al-doped graphene were investigated using DFT calculations (Chi and Zhao 2009). Structure optimizations as well as the corresponding total energy calculations were performed based on the GGA function with the Perdew–Burke–Ernzerhof (PBE) correction (Perdew et al. 1996). The DFT semicore pseudopotential (DSPP) core treatment (Delley 2002) was implemented for relativistic effects, which replaces core electrons by a single effective potential. To ensure that the results of the calculations are comparable, identical conditions were employed for the isolated H₂CO molecule, the graphene substrate, and also the adsorbed graphene system. The k-point was set to $6 \times 6 \times 1$ for all slabs, which brought out the convergence criterion of $10-^5$ a.u. on energy and electron density and that of maximum force of 0.002 Ha/Å. Self-consistent field procedure was carried out with a convergence criterion of $10-^6$ a.u. on energy and electron density. All DFT calculations were performed using DMol³ code (Delley 1990, 2000).

In these calculations, the PBCs were applied to the supercells. A vacuum width of 16 Å above was constructed, which ensured that the Z-axis of the periodic supercell (perpendicular to the graphene layer) was large enough so that there was no interaction between graphene sheets of adjacent supercells. Optimized configurations of intrinsic graphene and Al-doped graphene are illustrated in Fig. 12. The binding energy of the adsorbed systems is defined as

$$E_b = E_{\text{total}} - (E_{\text{sheet}} + E_{\text{H}_2\text{CO}}), \tag{58}$$

where the E_{total} , E_{sheet} , and E_{H2CO} denote the total energy of intrinsic or Al-doped graphene adsorbed system, isolated graphene or Al-doped graphene, and a H₂CO molecule, respectively. A negative E_b corresponds to a stable adsorption structure.

To investigate the changes of electronic structures in graphene caused by the adsorption of H₂CO molecule, electron density difference $\Delta \rho$ is calculated, which illustrates how the charge density changes during this adsorption process. $\Delta \rho$ is defined as

$$\Delta \rho = \rho_{\text{total}} - \left(\rho_{\text{sheet}} + \rho_{\text{H}_2\text{CO}}\right),\tag{59}$$

in which ρ_{total} , ρ_{sheet} , and ρ_{H2CO} denote electron density of the intrinsic or Al-doped graphene adsorbed system, graphene or Al-doped graphene, and a H₂CO molecule for the adsorbed system, respectively. The electronic density differences of energy



Fig. 12 Optimized most stable configurations of (**a**) intrinsic graphene and (**b**) Al-doped graphene (Reprinted from Chi and Zhao (2009), Copyright (2009), with permission from Elsevier)

favorable intrinsic and Al-doped graphene with H_2CO adsorptions are shown in Fig. 13. The net electron transfer from the Al-doped graphene to H_2CO is four times more than that in the intrinsic grapheme, which indicates that the Al-doped graphene can be used as a novel sensor for the detection of H_2CO molecules.

53.4 Hybrid Quantum Mechanics/Molecular Mechanics (QM/MM) Methods

As stated above, MD simulations and QM calculations show enormous capacity in handling problems in adhesion. However, in many cases, current force fields used in MD as well as MM simulations are not sufficiently accurate to reproduce the dynamics of molecular systems. At the same time, QM methods cannot deal with large systems because the simulations will be time-consuming or even become impossible. The simulation techniques have been expanded to combine the strength



Fig. 13 The electronic density difference isosurfaces for (a) H_2CO -graphene system and (b) H_2CO -Al-doped adsorbed systems with energy preferred configuration (graphene systems). The blue region shows the electron accumulation, while the yellow region shows the electron loss (Reprinted from Chi and Zhao (2009), Copyright (2009), with permission from Elsevier)

of both MM simulations and QM calculations, which is called the hybrid quantum mechanics/molecular mechanics (QM/MM) approach.

53.4.1 Basic Theory

The basic strategy for the QM/MM method lies in the hybrid potential in which a classical MM potential is combined with a QM one (Field et al. 1990). The energy of the system, E, is calculated by solving the Schrödinger equation with an effective Hamiltonian, $H_{\rm effb}$ for the mixed quantum mechanical and classical mechanical system

$$H_{\rm eff}\psi(r, R_{\rm QM}, R_{\rm MM}) = E(R_{\rm QM}, R_{\rm MM})\psi(r, R_{\rm QM}, R_{\rm MM}), \tag{60}$$

where ψ is the electronic wave function of the quantum system, *r* is for the coordinates of the electrons, $R_{\rm QM}$ is the position of the quantum mechanical nuclei, and $R_{\rm MM}$ is for the molecular mechanical nuclei. The wave function, ψ , depends directly on *r*, $R_{\rm QM}$, and $R_{\rm MM}$. The effective Hamiltonian for the mixed quantum and classical system is divided into three terms (Lyne et al. 1999)

$$H_{\rm eff} = H_{\rm QM} + H_{\rm MM} + H_{\rm QM/MM},\tag{61}$$

where H_{QM} is the contribution from complete QM section (see QM in Fig. 14), H_{MM} is from the pure MM section (see MM in Fig. 14), and $H_{\text{QM/MM}}$ is the interaction between the QM and MM portions of the system. Similarly, the total energy of the system calculated by solving the Schrödinger equation can likewise be divided into three component parts



$$E_{\rm eff} = E_{\rm QM} + E_{\rm MM} + E_{\rm QM/MM}.$$
 (62)

However, the pure MM term can be removed from the integral because it is independent of the electronic positions. So another way to express the total energy of the system is as the expectation value of $H_{\rm eff}$

$$E_{\rm eff} = \langle \psi | H_{\rm OM} + H_{\rm OM/MM} | \psi \rangle + E_{\rm MM}, \tag{63}$$

where $H_{\rm QM}$ is the Hamiltonian that can be obtained by either semiempirical, Hartree–Fock, or DFT. $E_{\rm MM}$ is an energy calculated based on a classical force field. $H_{\rm QM/MM}$ is the key term which involves combinations of the interaction of the MM atom "cores" with the electron cloud of the QM atoms, the repulsion between the MM and QM atomic cores, as well as the LJ term. The form of $H_{\rm QM/MM}$ is

$$H_{\rm QM/MM} = -\sum_{\rm iM} \frac{q_M}{|r_{\rm iM}|} + \sum_A \frac{q_M Z_A}{|R_{\rm AM}|} + \sum_{\rm AM} 4\varepsilon_{\rm AM} \left(\frac{R_{\rm min,\,AM}^{12}}{R_{\rm AM}^{12}} - 2\frac{R_{\rm min,\,AM}^6}{R_{\rm AM}^6}\right) \quad (64)$$

where q_M is the atomic point charge on the MM atom, r_{iM} is the QM electron to MM atom distance, Z_A is the core charge of QM atom A, R_{AM} is the QM atom A to MM atom M distance, and ε_{AM} and $R_{\min,AM}$ are the LJ parameters for QM atoms A interacting with MM atom M. The critical term that allows the QM region to "see" the MM environment is the first term in the right side of Eq. 64 where the summation is over all interactions between MM atoms and QM electrons. The second term in Eq. 64 represents the core electron interaction between MM and QM atoms and is incorporated into the QM Hamiltonian explicitly. The van der Waals interaction between QM part and MM part is described by the third term in Eq. 64. As the integrated molecular orbital/molecular mechanics (IMOMM) method (Maseras and Morokuma 1995) is taken, the introduction of new parameters is avoided and the number of geometry variables is reduced as much as possible.

53.4.2 QM/MM Boundary Treatments

An important aspect of the formation of a hybrid potential is how to handle the covalent bonds between atoms that are described with different potentials, that is, the bonds existing at the interface of the QM and MM regions. Several methods have been proposed to deal with this problem, including the simple link-atom method (Field et al. 1990), the sophisticated hybrid-orbital technique (Ferre et al. 2002), and the pseudo-bond approach (Zhang et al. 1999).

In many situations, it is necessary to split a molecule between QM and MM regions, which means that there are covalent bonds between QM and MM atoms. These cleavage bonds must be treated in some way because the presence of broken bonds and unpaired electrons at the boundary of the QM region dramatically changes the electronic structure of the QM subsystem. As long as the QM and MM atoms are in different molecules, no such problem arises.

Here, the classical link-atom method was introduced as a typical example. The link atoms as shown in Fig. 14 are treated exactly like QM hydrogen atoms in the QM/MM scheme, and they are invisible to the MM atoms because no interactions between the link atoms and the MM atoms are calculated. Each bond that crosses the boundary between the two regions must be defined. The link atom should be placed along the bond between the QM and MM atoms. The exact distance does not matter since the position of the link atoms is optimized in subsequent calculations. For the IMOMM scheme, the introduction of link atom is modified to study organometallic reactions by subtracting the classical MM interactions with the real QM system.

53.4.3 Examples of QM/MM Simulations

The hybrid QM/MM method is employed to simulate the His-tagged peptide adsorption to ionized region of nickel surface. "His-tags" are used in nanomechanical systems and biosensors due to their functional side chains. Noji et al. exploited the high affinity of polyhistidine-tagged β -subunits for Ni-nitrilotriacetate (NTA) to immobilize an F1–ATPase $\alpha 3\beta 3\gamma$ subcomplex on a solid surface as shown in Fig. 15 (Noji et al. 1997). His-tags were used by Montemagno et al. (Montemagno and Bachand 1999) to attach a biomolecular motor, F1–ATPase, to metal substrates, and they have tested the binding strength of a $6 \times$ His-tagged synthetic peptide attached to Au-, Cu-, and Ni-coated coverslips.

The $6 \times$ His-tagged synthetic peptide attachment to the ionized region in Ni substrate was studied with the peptide chelating with Ni ion considered (Yang and Zhao 2006). GAMESS (Schmidt et al. 1993) and TINKER (Ponder and Richards 1987) were employed for the QM/MM calculation of the His-tagged peptide chelating with Ni ion. GAMESS/TINKER can perform the IMOMM scheme (Maseras and Morokuma 1995), which spearheads the entry of hybrid QM/MM approaches in computational transition metal chemistry. In the QM/MM calculation, the imidazoles on the side chain of the peptide and the metal ion with several neighboring water molecules are treated as a QM part calculated by "GAMESS," and the remaining



	ΔΕ	D (N-Ni)	D (C1-L)	D (C1-C2)	D (Ni-O)	∠(N–Ni–N)
Two His-tags chelate with Ni ²⁺						
HF(6-31+G**)/MM	-231.626	2.056	1.081	1.347	1.962	86.43
B3LYP(6-31+G**)/MM	-247.913	2.065	1.083	1.350	1.969	89.62
Four His-tags chelate with Ni ²⁺						
HF(6-31+G**)/MM	-314.077	2.083	1.072	1.341	1.973	93.38
B3LYP(6-31+G**)/MM	-326.062	2.090	1.075	1.342	1.976	93.40
Six His-tags chelate with Ni ²⁺						
HF(6-31+G**)/MM	-382.331	2.092	1.071	1.345	-	91.60
B3LYP(6-31+G**)/MM	-399.462	2.095	1.076	1.348	-	92.02
Experiment	-	2.112	-	1.355	2.065	93.50

 Table 2
 Binding energy and structural data for the optimized chelate structures

atoms are treated as a MM part calculated by "TINKER." The IMOMM method is used to deal with the QM part with the transitional metal.

All the geometry parameters and the binding energy are listed in Table 2. The QM/MM simulation results show that the $6 \times$ His-tagged peptide can form the most stable structure with high binding energy which is also confirmed experimentally. And the optimized structure data are obtained satisfactorily. The results obtained for the peptide–Ni chelate complexes also show that the present QM/MM approach is reasonable and effective. Such delicate properties as conformational changes and binding energy are modeled in the QM/MM calculations. It is shown that the QM/MM method can be used to probe aspects of metal chelate complexes from both fundamental and practical aspects.



D is the distance, \angle is the angle (donor atom-Ni²⁺-donor atom), and L represents the link atom. All distances are in Angstrom, and energy in kJ/mol. Experimental data comes from references (Arici et al. 2002; Petrenko et al. 2004). "Reprinted from Materials Science and Engineering A, 423, Yang ZY and Zhao YP, QM/MM and classical molecular dynamics simulation of His-tagged peptide immobilization on nickel surface, 84–91, Copyright (2006), with permission from Elsevier"

In another example, the hybrid QM/MM method is applied to study the hydration phenomena of dipalmitoylphosphatidylcholine (DPPC) headgroup (Yin and Zhao 2009). In geometry optimization, the headgroup and its bound water molecules are treated at QM level of theory and the hydrocarbon chain with MM method (Fig. 16). All the geometry optimizations were carried out using the hybrid QM/MM method without any constraints, and hydrogen atoms were used as link atoms. First the hybrid QM/MM method was demonstrated to be both accurate and efficient enough to describe the conformations of DPPC headgroup. Then, both monohydration and polyhydration phenomena were investigated. In monohydration, different water association sites were studied. Both the hydration energy and the quantum properties of DPPC and water molecules were calculated at the DFT level of theory after geometry optimization. The binding force of monohydration was estimated by using the scan method. In polyhydration, more extended conformations were found and hydration energies in different polydration styles were estimated.

53.5 Ab Initio Molecular Dynamics (AIMD)

Classical MD is based on the established force fields or predefined interatomic potential. It is a powerful tool to serve problems of adhesion. The heart of any molecular dynamics scheme is the question of how to describe the interatomic interactions which always adopt some suitable functional forms to approximate the two-body, short-range or long-range interactions. The parameters used in the functions are always fitted by the experimental data or the ab initio simulation in some given condition. Payne et al. listed some drawbacks of traditional MD in a review paper (Payne et al. 1992). Due to these reasons, AIMD has been established to describe the molecular system behavior directly from the electronic structure. In this way, the electronic system always keeps in the ground state and the dynamical behaviors of the system are all in the Born–Oppenheimer (BO) surface which is always called BOMD. Car and Parrinello introduced a new scheme (Car and Parrinello 1985) for AIMD that can perform finite temperature simulations and also did not involve electronic self-consistency at every MD step. Car–Parrinello molecular dynamics (CPMD) was the first to show that AIMD was possible. Some work has been performed using CPMD (Zang et al. 2009). The codes have been also utilized a lot in adsorption research. Mischler et al. used the CPMD to simulate the water adsorption on amorphous silica surfaces and the reaction of the water and the silicon (Mischler et al. 2005). The simulation procedures reveal that CPMD can perform a reaction dynamically.

CPMD has combined first principles electronic structure methods with MD based on Newton's equations of motion. Ground state electronic structures were described according to DFT in plane-wave pseudopotential framework.

In CPMD, considering the parameters $\{\psi_i\}, \{R_i\}, \{\alpha_v\}$ in energy function,

$$E[\{\psi_i\}, \{R_I\}, \{\alpha_\nu\}] = \sum_i \int_{\Omega} d^3 r \psi^*(r) \left[-(\hbar^2/2m) \nabla^2 \right] \psi_i(r) + U[n(r), \{R_I\}, \{\alpha_\nu\}],$$
(65)

are supposed to be time dependent, the dynamical Lagrangian,

$$L = \sum_{i} \frac{1}{2} \mu \int_{\Omega} d^{3}r |\dot{\psi}_{i}|^{2} + \sum_{I} \frac{1}{2} M_{I} \dot{R}_{I}^{2} + \sum_{\nu} \frac{1}{2} \mu_{\nu} \dot{\alpha}_{\nu}^{2} - E[\{\psi_{i}\}, \{R_{I}\}, \{\alpha_{\nu}\}], \quad (66)$$

was introduced, where the $\{\psi_i\}$ are subject to the holonomic constraints:

$$\sum_{i} \int_{\Omega} d^3 r \psi_i^*(r, t) \psi_j(r, t) = \delta_{ij.}$$
(67)

In Eqs. 65 and 66, $\{\psi_i\}$ are orbitals for electrons, $\{R_I\}$ indicate the nuclear coordinates, $\{\alpha_\nu\}$ are all the possible external constraints imposed on the system, $\psi^*(r)$ is the complex conjugate of wave function $\psi(r)$, \hbar is the reduced Planck constant, *m* is the mass of electron, and $n(r) = \sum_i |\psi_i(r)|^2$ is the electron density; the dot indicates time derivative M_i are the physical ionic masses and $\mu_i \mu_i$ are arbitrary parameters.

time derivative, M_I are the physical ionic masses, and μ , μ_{ν} are arbitrary parameters of appropriate units. Then, the equations of motion can be written as:

$$\mu \ddot{\psi}_i(r,t) = -\frac{\delta E}{\delta \psi_i^*(r,t)} + \sum_k \Lambda_{ik} \psi_k(r,t), \tag{68}$$

$$M_I \ddot{R}_I = -\nabla_{R_I} E, \tag{69}$$

$$\mu_{\nu}\ddot{\alpha}_{\nu} = -\left(\frac{\partial E}{\partial \alpha_{\nu}}\right),\tag{70}$$

where Λ_{ik} are Lagrangian multipliers introduced in order to satisfy the constraints in Eq. 67. Then the equation of kinetic energy

$$K = \sum_{i} \frac{1}{2} \mu \int_{\Omega} d^{3}r |\dot{\psi}_{i}|^{2} + \sum_{I} \frac{1}{2} M_{I} \dot{R}_{I}^{2} + \sum_{\nu} \frac{1}{2} \mu_{\nu} \dot{\alpha}_{\nu}^{2}, \tag{71}$$

is obtained (Car and Parrinello 1985). In fact, μ , μ_{ν} have the dimensions of the mass which are called "fictitious mass." In this scheme, the wave functions are treated as "particles" in which "mass" are μ . When a suitable μ is selected, the thickness of the BO surface can be controlled and the simulations are still close to the exact BO surface. So, the ground state wave function obtained by the initial configuration of the nuclei will stay close to its ground state during time evolution. Based on the technique mentioned, CPMD extends MD beyond the usual pair-potential approximation. In addition, it also extends the application of DFT to much larger systems.

Apart from the aforementioned combined simulation methods, the densityfunctional-based tight-binding (DFTB) method has been developed. DFTB is an accurate semiempirical method explicitly derived from Kohn–Sham DFT by making an expansion of the total energy functional around a reference charge density, which has been shown to be capable of producing reliable molecular structures and energy at a significantly reduced computational cost.

53.6 Conclusion

In this chapter, various simulation methods involving the adhesion technology have been reviewed, such as the MD simulations, the QM calculations, the MO method, the DFT calculations, the hybrid QM/MM simulations, the AIMD simulations, and the DFTB method. For each method, the basic theory and the general routine were described. Several representative examples of applications in the investigations of adhesion properties are given. Any one of the aforementioned methods has both advantages and disadvantages. Brief comparisons are listed in Table 3. To make a choice of the simulation method depends on the desired properties that one intends to obtain, while the computational capabilities should also be taken into account (as shown in Fig. 17).

Computer simulation forms a bridge between the molecules and the continuum mechanics of adhesion due to its multiscale, hierarchical, and complex nature (Kendall 2001). It is possible to speculate that the combined simulation methods with more efficiency and flexibility are still required and will lead the future directions of the simulation methodology in this fascinating field.

	Merits	Drawbacks
DFT	High accuracy; more details (electronic states, charge distribution, molecule orbits)	Limited to static states of small systems; slow and expensive
MD/MM	Available for large systems; fast and cheap	Disable in chemical reaction (bond breaking/forming); empirical potentials are used which lead to low accuracy
Hybrid QM/MM	Combined DFT with MM, extended the simulation system	Interactions between the QM region and MM region are difficult to describe
AIMD/ CPMD	Combined MD with DFT; a balance between the time and precision	Limited to dynamic process of small systems
DFTB	Combined DFT with TB; works well for homonuclear system	Low accuracy for some heterogeneous system

 Table 3
 Brief comparisons of some simulation methods



Fig. 17 Choices for the simulation methods

Acknowledgments Part of the work presented in this chapter was jointly supported by the National High-tech R&D Program of China (863 Program, Grant No. 2007AA021803), National Basic Research Program of China (973 Program, Grant No. 2007CB310500), and National Natural Science Foundation of China (NSFC, Grant Nos. 10772180, 60936001, and 11072244).

References

Alder BJ, Wainwright TE (1959) Studies in molecular dynamics. I. General method. J Chem Phys 31(2):459

Allen MP, Tildesley DJ (1989) Computer simulation of liquids. Oxford University Press, Oxford

- Arici C, Ercan F, Atakol O, Basgut O (2002) Crystal structure of [N,N'-bis(3,5-dinitrosalicylidene-1,3-propanediaminato)bis(3,4-dimethylpyridine)]nickel(II)dioxane solvate. Anal Sci 18(3):375
- Berendsen HJC, Vanderspoel D, Vandrunen R (1995) GROMACS: a message-passing parallel molecular dynamics implementation. Comput Phys Commun 91(1–3):43
- Bharat B (2004) Springer handbook of nanotechnology. Springer, Berlin
- Brooks BR, Bruccoleri RE, Olafson BD, States DJ, Swaminathan S, Karplus M (1983) CHARMM: a program for macromolecular energy, minimization, and dynamics calculations. J Comput Chem 4(2):187
- Car R, Parrinello M (1985) Unified approach for molecular dynamics and density-functional theory. Phys Rev Lett 55(22):2471
- Chi M, Zhao YP (2009) Adsorption of formaldehyde molecule on the intrinsic and Al-doped graphene: a first principle study. Comput Mater Sci 46(4):1085
- Daintith J (2004) Oxford dictionary of chemistry. Oxford University Press, Oxford
- Delley B (1990) An all-electron numerical method for solving the local density functional for polyatomic molecules. J Chem Phys 92(1):508
- Delley B (2000) From molecules to solids with the DMol³ approach. J Chem Phys 113(18):7756
- Delley B (2002) Hardness conserving semilocal pseudopotentials. Phys Rev B 66(15):155125
- Ferre N, Assfeld X, Rivail JL (2002) Specific force field parameters determination for the hybrid ab initio QM/MM LSCF method. J Comput Chem 23(6):610
- Field MJ, Bash PA, Karplus M (1990) A combined quantum mechanical and molecular mechanical potential for molecular dynamics simulations. J Comput Chem 11(6):700
- Hehre WJ (1976) Ab initio molecular orbital theory. Acc Chem Res 9(11):399
- Hohenberg P, Kohn W (1964) Inhomogeneous electron gas. Phys Rev B 136(3):864
- Humphrey W, Dalke A, Schulten K (1996) VMD: visual molecular dynamics. J Mol Graph 14(1):33
- Jones JE (1924) On the determination of molecular fields. II. From the equation of state of a gas. Proc R Soc A 106(738):463
- Jorgensen WL, Chandrasekhar J, Madura JD, Impey RW, Klein ML (1983) Comparison of simple potential functions for simulating liquid water. J Chem Phys 79(2):926
- Kale L, Skeel R, Bhandarkar M, Brunner R, Gursoy A, Krawetz N, Phillips J, Shinozaki A, Varadarajan K, Schulten K (1999) NAMD2: greater scalability for parallel molecular dynamics. J Comput Phys 151(1):283
- Kendall K (1975) Thin-film peeling-the elastic term. J Phys D Appl Phys 8(13):1449
- Kendall K (2001) Molecular adhesion and its applications. Kluwer/Plenum, New York
- Khandeparker L, Anil AC (2007) Underwater adhesion: the barnacle way. Int J Adhes Adhes 27(2):165
- Leach AR (2001) Molecular modelling: principles and applications. Pearson Education, New York
- Levy M (1979) Universal variational functionals of electron densities, first-order density matrices, and natural spin-orbitals and solution of the v-representability problem. Proc Natl Acad Sci U S A 76(12):6062
- Li J (2003) AtomEye: an efficient atomistic configuration viewer. Model Simul Mater Sci Eng 11(2):173
- Lindahl E, Hess B, van der Spoel D (2001) GROMACS 3.0: a package for molecular simulation and trajectory analysis. J Mol Model 7(8):306
- Lyne PD, Hodoscek M, Karplus M (1999) A hybrid QM-MM potential employing Hartree-Fock or density functional methods in the quantum region. J Phys Chem A 103(18):3462
- Maseras F, Morokuma K (1995) IMOMM: a new integrated ab initio + molecular mechanics geometry optimization scheme of equilibrium structures and transition states. J Comput Chem 16(9):1170
- Mischler C, Horbach J, Kob W, Binder K (2005) Water adsorption on amorphous silica surfaces: a Car-Parrinello simulation study. J Phys Condens Matter 17(26):4005
- Montemagno C, Bachand G (1999) Constructing nanomechanical devices powered by biomolecular motors. Nanotechnology 10(3):225

- Mulliken RS (1955) Electronic population analysis on LCAO-MO molecular wave functions. I J Chem Phys 23(10):1833
- Nelson MT, Humphrey W, Gursoy A, Dalke A, Kale LV, Skeel RD, Schulten K (1996) NAMD: a parallel, object oriented molecular dynamics program. Int J Supercomputer Appl High Perform Comput 10(4):251
- Noji H, Yasuda R, Yoshida M, Kinosita K (1997) Direct observation of the rotation of F-1-ATPase. Nature 386(6622):299
- Payne MC, Teter MP, Allan DC, Arias TA, Joannopoulos JD (1992) Iterative minimization techniques for ab initio total-energy calculations: molecular dynamics and conjugate gradients. Rev Mod Phys 64(4):1045
- Pearlman DA, Case DA, Caldwell JW, Ross WS, Cheatham TE, Debolt S, Ferguson D, Seibel G, Kollman P (1995) AMBER, a package of computer programs for applying molecular mechanics, normal mode analysis, molecular dynamics and free energy calculations to simulate the structural and energetic properties of molecules. Comput Phys Commun 91(1–3):1
- Perdew JP, Burke K, Ernzerhof M (1996) Generalized gradient approximation made simple. Phys Rev Lett 77(18):3865
- Perdew JP, Ruzsinszky A, Tao JM, Staroverov VN, Scuseria GE, Csonka GI (2005) Prescription for the design and selection of density functional approximations: more constraint satisfaction with fewer fits. J Chem Phys 123(6):062201
- Petrenko PA, Gdaniec M, Simonov YA, Stavila VG, Gulea AP (2004) Crystal structure of monoprotonated Ni(II) nitrilotriacetate tetrahydrate. Russ J Coord Chem 30(7):813
- Plimpton S (1995) Fast parallel algorithms for short-range molecular dynamics. J Comput Phys 117(1):1
- Ponder JW, Richards FM (1987) An efficient newton-like method for molecular mechanics energy minimization of large molecules. J Comput Chem 8(7):1016
- Pople JA, Beveridge DL (1970) Approximate molecular orbital theory. McGraw Hill, New York
- Rapaport DC (2004) The art of molecular dynamics simulation. Cambridge University Press, Cambridge
- Roothaan CCJ (1951) New developments in molecular orbital theory. Rev Mod Phys 23(2):69
- Ryckaert JP, Ciccotti G, Berendsen HJC (1977) Numerical integration of the cartesian equations of motion of a system with constraints: molecular dynamics of n-alkanes. J Comput Phys 23(3):327
- Schmidt MW, Baldridge KK, Boatz JA, Elbert ST, Gordon MS, Jensen JH, Koseki S, Matsunaga N, Nguyen KA, Su SJ, Windus TL, Dupuis M, Montgomery JA (1993) General atomic and molecular electronic structure system. J Comput Chem 14(11):1347
- Shi XH, Kong Y, Zhao YP, Gao HJ (2005) Molecular dynamics simulation of peeling a DNA molecule on substrate. Acta Mech Sin 21(3):249
- Yang ZY, Zhao YP (2006) QM/MM and classical molecular dynamics simulation of His-tagged peptide immobilization on nickel surface. Mater Sci Eng A 423(1–2):84
- Yin J, Zhao YP (2009) Hybrid QM/MM simulation of the hydration phenomena of dipalmitoylphosphatidylcholine headgroup. J Colloid Interface Sci 329(2):410
- Yin J, Zhao YP, Zhu RZ (2005) Molecular dynamics simulation of barnacle cement. Mater Sci Eng A 409(1–2):160
- Yuan QZ, Zhao YP, Li LM, Wang TH (2009) Ab initio study of ZnO based gas sensing mechanisms: surface reconstruction and charge transfer. J Phys Chem C 113(15):6107
- Zang JL, Yuan QZ, Wang FC, Zhao YP (2009) A comparative study of Young's modulus of singlewalled carbon nanotube by CPMD, MD, and first principle simulations. Comput Mater Sci 46(3):621
- Zhang YK, Lee TS, Yang WT (1999) A pseudobond approach to combining quantum mechanical and molecular mechanical methods. J Chem Phys 110(1):46
- Zhao YP, Wang LS, Yu TX (2003) Mechanics of adhesion in MEMS-a review. J Adhes Sci Technol 17(4):519