Chapter 15
Review on Simulation Models for Materials and Biomolecular Study and Design

Carlton Anthony Taft and Jose Gabriel Solano Canchaya

1 Introduction

From quantum mechanics, we know that a 3N wave function that obeys the Schrodinger equation (SE) can be used to determine the properties of an N-particle system. However, since the number of atoms of a macroscopic material is on the order of 10^{23}, for a realistic system, it is not trivial to solve SE, i.e., approximations/alternatives become necessary. Hartree eliminated the dimensionality problem of electrons yielding single-electron wave functions in a mean-field approximation for electrons. Since the nuclei are more massive than electrons and move faster, the Hamiltonian can be further simplified, i.e., motion of nuclei can be neglected in the Born-Oppenheimer (BO) approximation. Hartree's method depends on a three-dimensional space instead of a 3N-dimensional space. However, electronic correlation is not taken into account. Incorporating antisymmetry of the wave functions yields the Hartree-Fock (HF) method, whereas pairwise electron-electron repulsion is replaced by the interaction of the ith electron with the average electrostatic field, and an exchange term keeps electrons with the same spin apart. The conceptual framework for chemistry as well as the theoretical foundation of methods that model chemical compound's electronic structure is provided by quantum mechanics [1–8].

In this chapter, we review HF, post-HF (CI, MRCI, CC, MCSCF, CASSCF, MBPT, LMP2, CCSD(T)), semiempirical (Hückel, CNDO, INDO, NDDO, MNDO,

C.A. Taft (✉)
Centro Brasileiro de Pesquisas Físicas, Rua Dr. Xavier Sigaud, Urca,
22290-180, Rio de Janeiro, Brazil
e-mail: catff@terra.com.br

J.G.S. Canchaya
Universidade Católica Santa Maria, Urb. San Jose s/n, Umacol, 51-54382038,
040000, Arequipa, Peru

AM1, OMx, PM7, RM1), density functional theory ((challenges, LDA, GGA, meta-GGA, hyper-GGA, hybrids, range separation, screened, fitting, adiabatic, local, fifth rung) functionals, random phase approximation, thermochemical data sets, prediction of geometries, reaction barriers and kinetics, hydrogen bonding, response functions, performance of DFA, van der Waals forces, frontier eigenvalues and band gaps, time-dependent DFT, vdW-DF, and new trends), basis sets, plane waves and pseudopotentials, projected augmented plane wave method, generalized plane waves, wavelets, discrete variable representations, augmented and mixed basis sets, Wannier functions and real-space grids, quantum Monte Carlo, ab initio molecular dynamics, quantum mechanics/molecular mechanics, coarse-graining, and multi-scaling. An overview of selected application areas for materials and biomolecular structures, including functional materials is also presented, i.e., dielectrics, capacitors, batteries, superconductors, hydrogen storage, photovoltaics, catalysts, nanomaterials, surface adsorption, and functionalization [1–24].

2 Approaches to Solve the SE

At present, there are three approaches to solve the SE. The first is the quantum-chemical ab initio method that yields a convergent path to exact solutions of quantum-mechanical SE. Nonetheless, these methods are expensive, and for correlated/accurate approaches, they are in general restricted to small molecules. The second method is density functional theory (DFT) with a good performance/price ratio, which yields, for medium-sized molecules, sufficiently accurate calculations. Notwithstanding, the first-principle nature of DFT, the method does not yield a systematic path for improvement. The third method is quantum-chemical semiempirical, which involves parametrizations and approximations, but makes them efficient with the possibility of modeling in a realistic manner larger molecules, but with limited accuracy. The models are also divided into those that depend on wave function theory (WFT) and those that depend on DFT.

3 Valence Bond and Molecular Orbitals

Concepts of valence and bonding are central to understand reactivity and molecular structure, whereas the treatment of molecules via quantum mechanics is necessary. Valence bond (VB) and molecular orbital (MO) theories are two alternatives to explain chemical bonding. VB, chemically intuitive, helps understand chemical concepts based on bond/lone pairs. During the second half of twentieth century, with increasing computer power and programs, the attractive orthogonal MO formalism has become very tractable, in particular, for medium-sized molecules. MO theory is an extension to the molecular regime of the atomic structure. They are delocalized over nuclear framework yielding computationally tractable equations. The linear

combination of atomic orbitals (LCAO) is at the heart of the MO approach. Generating MOs from LCAOs helps understand, from an electronic structure view point, the relationship between atoms and molecules. In VB theory, electron correlation is overemphasized, whereas in simple MO theory it is neglected. In polyatomic molecules, directed valence, based on principle of maximum overlap and valence shell electron pair repulsion (VSEPR) theory, has been successful. Improvements in both VB and MO theories can lead to convergence [23].

4   HF and Post-HF

For polyatomic molecules, MO theories can be classified as electron-independent (non-self-consistent field) and electron-dependent SCF methods. The non-SCF has the possibility of modeling in a realistic manner larger molecules. Hückel's theory only includes π basis, whereas extended Hückel theory includes all valence basis. SCF methods iteratively solve many-electron SE equations in matrix form based on HF theory. They are ab initio when the Fock matrix is constructed from first principles and semiempirical when approximation and parameters are used. The HF method treats interaction of one electron with the average field of other electrons but does not consider instantaneous electrostatic interactions, whereas correlated motions of electrons are neglected, yielding higher energies. Correlation energy is the difference between exact and HF energies. Note that the quantum-mechanical exchange term, i.e., two electrons of same spin cannot occupy a single orbital, is included in HF theory [1].

For a good description of properties and structure of molecules, electron correlation is necessary and thus addressed in post-HF methods, i.e., configuration interaction (CI), multireference CI (MRCI), multiconfiguration SCF (MCSCF), coupled cluster (CC), many-body perturbation theory (MBPT), and complete active space self-consistent field method (CASSCF) [3, 13, 14].

MO theory is improved via configuration interaction (CI), whereas excitation of one or more electrons (single, double, and multiply occupied) configurations can be generated. Slater determinants can be used to describe these excited configurations. In CI methods, we note that HF determines energetically the best determinantal trial wave function which could however be improved with more configurations. Excited configurations can be generated promoting electrons from occupied to virtual orbitals. MRCI uses an expansion of Slater determinants (corresponding to excitation of ground state configurations and some excited states).

Dynamic correlation for closed shell ion addresses instant correlation between electrons occupying same spatial electrons, whereas nondynamic correlation describes electrons avoiding each other by occupying different spatial orbitals. Consequently, one Slater determinant cannot describe the ground state, and MCSCF is necessary. In the MCSF, the MOs construct the determinants whereas coefficients are optimized using the variational principle. The optimization is an iterative-like procedure.

In the CASSCF method, the selections of configurations are performed by partitioning the MOs into inactive and active spaces, whereas the active MOs have some of the lowest unoccupied as well as highly occupied MOs from an HF calculation. Other high virtual orbitals and high stable orbitals constitute the inactive orbitals (doubly occupied or completely unoccupied).

In MBPT, the Hamiltonian operator consists of the unperturbed Hamiltonian and the perturbation term, yielding corrections of various orders. As one increases from zero to finite values, the perturbation, the energy, and wave functions change continuously, which can be written as a Taylor expansion (power of perturbation parameter). Perturbation approaches (MP2, MP3, etc.) were quite powerful/popular QM methods which naturally include dispersion effects. However, they show systematic errors causing unbalance to intermolecular interactions contributions, whereas the accuracy at MP2 level is not guaranteed.

A traditional well-established WFT methods yield reliable accurate results. Correlations (electron-electron) are introduced by many-body wave function (WF) expansions, i.e., single (S), doubly (D), triply (T), etc., excited determinants (using reference wave functions). In full configuration interaction (FCI), all excited determinants are included which yields the best variational results (for given basis set). Due to high computational cost with increasing electrons and basis functions, these calculations are only performed on small systems.

The coupled cluster (CC) theory was constructed for interacting particles system using N-particle excitation operators. Once trial wave functions are expressed as determinant of HF orbitals, one obtains coupled nonlinear equations whose amplitudes are solved by some iteration technique in order to compute the CC energy. This approach emerged as very practical reference method. Consequently, CC with singles, doubles, and perturbative triples has been considered a "gold standard" for many applications (medium systems) although accuracy in large systems have not been confirmed. The CCSD(T) approach extrapolated to complete basis set (CBS) limit, i.e., CCSD(T)/CBC, is accurate for intermolecular interaction energies providing results of chemical accuracy (1 kcal/mol). For small systems with dispersive interactions, it may be necessary to use 0.1 kcal/mol subchemical accuracy.

Other approaches include complete active space with second-order perturbation theory (CASPT2) and LMP2 theory where the Hartree-Fock orbitals are localized to lone pairs and bonds from which electrons are correlated, rather than the Hartree-Fock delocalized canonical orbitals. Electronic structure quantum Monte Carlo (QMC) is a set of methods for solving the stationary Schrodinger equations using sampling of wave functions in the space of electron positions and usage of stochastic processes. This approach also indicates basis set-based limitations.

At this point, it is noteworthy that DFT reasonably includes electron correlation at a fractional cost of typical post-HF methods previously discussed.

5   Basis Sets

After selection of methods, it is necessary to represent the orbitals by basis sets, i.e., a linear combination of functions, which can represent exactly any reasonable function (limit of complete base set). Quantum chemists have used Slater-type orbitals (STOs) with a radial part that is exponentially decaying as well as Gaussian-type orbitals (GTOs), which is widely used in software. The coefficients of the linear expansions are fixed, and only the orbital expansion coefficients are optimized. Fixed linear combinations of these primitives can define angular momentum (contracted basis sets). Slater/Gaussian sets are centered at nuclei (atoms) leading to linear combination of atomic orbitals (LCAO). WF methods, unfortunately, have known imitations. The correlation energy converges slowly with size of one-particle atomic basis sets. There are often basis sets superposition and incompleteness errors. For benchmark calculations, large basis sets (augmented with diffuse basis functions) are often necessary [1, 24].

6   Plane Waves and Pseudopotentials

In order to solve the many-body problem SE (with large number of ions and electrons) more simplifications are required for practical purposes. Taking advantage of symmetry and periodicity of solid structures is one route. In addition, core electrons are typically not involved in bonding making it advantageous to write the MO in terms of plane waves with the periodicity of the crystal structure. Plane waves are rooted in solid-state theory, whereas the periodicity of the lattice yields a periodic potential, imposed on the density (Bloch's theorem). Forming a complete and orthonormal set of functions, plane waves can be used to expand orbitals where labeling can be given by vectors in reciprocal space yielding simple forms for total electronic energy and gradients. It is noteworthy that plane waves do not depend on the positions of the nuclei and are delocalized in space not favoring specific atoms or regions. To improve quality of basis set, it is necessary to increase the cutoff energy (largest reciprocal vector included in the finite expansion). Plane waves also have advantages with delocalized electrons. A plane wave basis is a lattice-symmetry-adapted three-dimensional Fourier decomposition of the orbitals. Consequently, ever larger Fourier components are necessary to solve structures in real space with decreasing small distance scales.

    Core electrons can be considered inert and thus removed explicitly. Actually, they can also be represented by smooth modeless effective potential (effective core potentials, ECPs), i.e., the pseudopotential which yields pseudo-wave functions representing valence electrons close to the nuclear core region as smoothly as possible. Nonetheless, properties that depend essentially on wave function close to core are not obtained in a straightforward manner. Valence wave functions are highly oscillatory inside core region where many terms are required for their

expansion. This leads to the usage of so-called pseudo-wave functions for valence states (replacing true all-electron wave functions). However, this method is subject to transferability errors and information on the all-electron wave function in the core region is lost [4].

7 Plane Wave Methods

In order to address pseudopotential method drawbacks, powerful techniques were introduced for plane wave calculations, i.e., "soft" norm-conserving ab initio pseudopotentials, ultrasoft pseudopotentials, and the projector augmented wave (PAW) method. The PAW method uses operators to map a smooth auxiliary wave function into the true all-electron single-particle wave function. The wave functions are decomposed into one with rapid oscillations acting only at nucleus and another that is smooth everywhere. Although each part is treated separately, information about the core region is not lost, and the all-electron wave function can at any time be retrieved [4, 25].

The above methods led to important approaches for plane wave/pseudopotential electronic structure calculation using the DFT framework. It is noteworthy, however, that for the plane waves, it may be difficult to put more required basis functions in regions of space where they are needed such as in systems with strong inhomogeneity. For some cases, an enormous cutoff parameter may be needed whereas only a few regions in real space would suffice.

8 Generalized Plane Waves

A generalization of the plane wave concept is obtained by defining them in curved space yielding orthonormal functions that form a complete basis set and used for reciprocal point sampling. As a result, the density of grid points (cutoff energy) is now highest in regions close to nuclei and lowest in vacuum regions. For a given accuracy, a lower number of generalized plane waves are required allowing even all-electron electronic structure calculations where the simple plane wave fails. Other methods consider the distortion of the metric frozen spherically around atoms via deformation functionals leading to nonuniform atom-centered meshes in real-space methods. In such approaches, locally adaptive models based on predefined coordinate transformations are used for Pulay force contributions evaluated explicitly. Freely floating Gaussians can also be used, which are distributed in space forming an originless basis set (not atom fixed/localized) [25].

9   Wavelets and Discrete Variable Representations

Similar to generalized plane waves are powerful multiscale properties of wavelets which allows exploitation of multiple length scales without introducing Pulay forces (handled efficiently by wavelet transformation). They also count on powerful routes to linear scaling. The discrete variable representation (DVR) approach consists of using continuous functions which satisfy properties of eigenfunction positions on an auxiliary grid yielding high localization about the auxiliary grid points. Plane waves are simple but lack the spatial bias of Gaussian basis sets which eliminates the problem of delocalization at the expense of increased complexity. However, DVR can be well localized about points on the grid with basis functions that satisfy orthogonality and completeness relations and constructed for simple basis functions according to boundary conditions [4, 25, 26].

10   Mixed Basis Sets

There are two extremes: plane waves on one hand and localized Gaussian basis function on the other, yielding considerable long-standing efforts to combine/exploit the mutual strengths of these approaches. The projector augmented wave method maps a smooth auxiliary wave function into true all-electron wave function using operators which yields highly oscillatory wave functions into components that contains rapid oscillations smooth and continuous everywhere as well as a contribution with rapid oscillations only in the core region for each atom. For the PAW method, for example, each part can be treated separately. Plane waves could represent delocalized wave functions. Centered radial grids (Gaussians, Bessel functions, polynomials) can be used for localized contributions. One does not lose information about core region, and all-electron wave functions can be retrieved [4, 25].

11   Wannier Functions and Real-Space Grids

For periodic solid-state theory calculations, Wannier functions can be of interest since they are formally obtained from a unitary transformation of Bloch orbitals and can be, under circumstances, localized exponentially and proven useful for electronic structure calculations. The generalized Wannier functions (maximally localized) are periodic analogs of Boys' localized orbitals for isolated systems [27].

A completely different approach consists of using real-space methods in which continuous space is substituted by discrete space whereas the derivative operator and total energy expression are discretized in some way. A number of real-space approaches have been devised including finite difference approximation with equally spaced cubic meshes in real space, nonuniform meshes, multigrid

acceleration, discretization techniques, and finite element methods. In real-space methods, we can exploit the nearsightedness of electronic matter for linear scaling, whereas the multiple length scale problem can be addressed by hierarchically adapting the grid in framework of multigrid methods [28].

12 Intermolecular Interactions

Noncovalent interactions are important in areas such as materials science, chemistry, biology, and drug design. These are weak interactions, i.e., with minimum changes in the electronic structures and geometries of the individual components. Hydrogen bonding and stacking (π-π interactions) are the most studied as they play very important roles in biochemical systems. Other noncovalent interactions identified include sigma-hole interaction, halogen bond, blue-shifting hydrogen bond, and anion-/cation-π interaction. These nonbonding interactions operate at larger (several angstroms) interatomic distances, whereas overlapping is not necessary since the attraction arises from electrical properties of participating molecules. These interactions can be described in terms of dispersion, induction (polarization), electrostatic, and exchange repulsion components. The total intermolecular interaction potential is determined by the balance of the cited interactions. The classical Coulomb interaction of the monomers electron distribution (unperturbed by the interaction) gives the electrostatic interaction. Change of the electrostatic interaction due to polarization of the monomer charge density by the interacting molecules yields the induction. Interaction of the instantaneous fluctuations of electronic density and multipoles induced by fluctuation yields the dispersion term. In other words, for induction terms, charged molecules polarize neighboring species, whereas dispersion interactions arise from the interactions between fluctuating multipoles. The dispersion is a correlation effect requiring a quantum chemical approach. The attractive short-range forces are opposed due to Pauli principle (exchange repulsion). Electrons flow from donor to acceptor in charge transfer (CT) interactions. The van der Waals (vdW) forces often describe repulsion and dispersion contributions, whereas other long-range contributions may also contribute [14, 29, 30].

13 Semi-empirical Methods

The π-electron Hückel method is one of the early semiempirical approaches. This method uses the connectivity matrix of a molecule to generate MOs. For unsaturated molecules, it provides good insight into stability, structure, and spectroscopy. All valence electrons are included in the extended Hückel theory which has been qualitatively applied to organometallic and inorganic compounds [12].

Hückel-type methods are noniterative since they only include one-electron integrals. In semiempirical self-consistent field (SCF) methods, two-electron interactions are explicitly taken into account. The Pariser-Parr-Pople method [31, 32], among the first SCF approach, was restricted to π electrons yielding, for unsaturated molecules, a reliably description. Pople introduced the generalization to valence electrons via integral approximations which satisfied rotational invariance as well as other consistency criteria. These approximations yielded the complete neglect of differential overlap (CNDO), intermediate neglect of differential overlap (INDO), neglect of diatomic differential overlap (NDDO) [31–35].

For organic molecules, Dewar introduced a new parameterization strategy by addressing the realistic description of ground-state potential surfaces via calibration against experimental reference data. This line of work yielded MINDO/3 (INDO-based method) as well as MNDO (NNDO-based method) and AM1. Parameterization of the MNDO model yielded PM3. The choice of empirical core repulsion functions determines the formal difference between MNDO and (AM1, PM3) [12, 34–36].

There are two other developments based on INDO approach before 1990, i.e., in the INDO approach, the orthogonalization corrections to the one-electron integrals by Jug et al. as well as parametrization for ground-state properties (SINDO1) [37]. This was later upgraded to MSINDO [38]. The INDO/S method by Zerner et al. focused on vertical excitation energies, using configuration interaction with single excitations (CIS) [38]. The MNDO model has progressed since the 1990 from an sp basis to an spd basis. The treatment of heavier elements has thus enabled improving results for hypervalent main-group elements. The extension to an spd basis has led to PM6 and PM7 covering the whole periodic table with applications to both solid-state and molecular properties. The usage of pairwise distance directed Gaussians (PDDG) for empirical code repulsions resulted in the PDDG/PM3 and PDDG/MNDO models. Some recent work address hydrogen bonding and dispersion by using special purpose parameterizations. Using a larger reference data set introduces the general-purpose RM1 model [39–41].

By including orthogonalization, corrections in the one-electron terms of Fock matrices yields the OM1, OM2, and OM3 models which go beyond MNDO method since they can account for the effects of Pauli exchange repulsions [42]. OM3 includes corrections to the two-center and one-electron terms of the Fock matrix to account for Pauli exchange repulsion. OM1 and OM2 include them in the one-center electron term.

We note, however, that conceptually, these semiempirical methods can be considered as simplified ab initio MO approaches. Semiempirical tight-binding (TB) versions of DFT methods have also been designed, i.e., DFTB approach, as well as the self-consistent charge (SCC) DFT method. We note that the DFTB method uses extensive integral approximations and parameterizations, especially in medium-/large-sized molecules. MNDO methods were mostly used in the 1980s and 1990s for quantum-chemical computations [43]. At present the MNDO, AM1, and PM3 approaches are still used along with more recent versions such as PM6 and PM7. Although DFT calculations have become dominant, OMx methods appear to

have merit for electronically excited states. INDO/S methods are still useful in many applications. In biochemistry and materials science, DFTB methods are popular. Recently, graphic processing units (GPUs) have been used on hybrid platforms to accelerate numerically the calculations [12].

14 Density Functional Theory

It was recognized in the early 1920s that in a uniform electron gas approximation, the kinetic energy density could lead (via constraints) to the ground-state energy functional minimization. However, only in 1964 did Hohenberg and Kohn show that properties of many-body systems are a function of the ground-state density and could thus be determined. Consider any system of electrons in an external potential. Except for a constant, the latter potential will be determined uniquely, and all the properties of the system as well as the many-body wave function are determined. Another theorem indicates that for all-electron system, a universal functional for the energy of the density could be defined. The global minimum for a given external potential would yield the exact ground-state energy. A new independent electron problem was provided to substitute the many-body problem. The independent electron problem can be solved by requiring the ground-state density and the exact density to be the same. The Kohn-Sham (KS) DFT, in use today, defines equations (self-consistent) to be solved for a set of orbitals whose density is defined to be exactly that of the real system.

DFT, with a better cost/performance than WFT, has become, in electronic structure problems, a very popular tool allowing us to solve the electron correlation problem which is included in the exchange-correlation potential. However, the exact formula is not known which yields different approximations for implementations (B3LYP and PBE are among the popular approximations [2, 9, 15–18, 44–56].

15 Some DFT Challenges

The early basic DFT challenges focused on functionals that could yield a description of dissociation energies and geometries of molecules. Subsequent challenges were to address barrier heights of reactions to determine van der Waals interactions and kinetics of chemical reactions. There is still much debate about the ability of DFT to predict the small van der Waals interactions. Current research still tries to determine whether nonlocal functionals of the density are required for these interactions. Although this is one of the weakest interactions, it is essential for a good understanding of biological processes involved in protein-drug/protein interactions [15, 18, 57].

In DFT, simple systems can indicate intricacies of larger systems such as strong correlations and encompass breakdown of the single-particle picture, based on a

determinant of single-particle Kohn-Sham orbitals. The quantum nature of matter is described by a Hamiltonian which for a Coulombic system is determined by a specified set of nuclei with charges and positions as well as a number of electrons. One needs to minimize the energy over all possible antisymmetric wave functions in order to find the appropriate wave function and thus the ground-state energy. In DFT, the external potential is a ground-state density functional. The observable 3D space density can be used to describe the interactions between electrons. Consequently, everything is determined. DFT is very useful for systems with many electrons. Kohn-Sham theory is formulated as a ground-state energy expression where the kinetic energy, the nucleus electron potential energy, and the classical electron-electron repulsion energy are known. Although an explicit form is not available, much is known about the principal remaining term, the exchange-correlational, which can be expressed via density functionals.

One of the important challenges of DFT is to maintain simplicity. The DFT functionals should not become too complicated. However, the method should not be empirical, and the cost of the simplicity should not be too high. Density functional approximations (DFA) lie in between. DFT was important for accurate description of binding energies and geometries of simple molecules. The solid-state community also widely used DFT since local-density approximation (LDA) was not performing well, overbinding molecules but yielding good geometries. The introduction of generalized gradient approximation followed by exact Hartree-Fock exchange led to B3LYP that has indicated a great performance over numerous systems becoming the most widely used functional serving as a route for improving DFT functionals [15, 18, 57].

Another challenge for DFT is to improve description of dispersion/van der Waals interaction and reaction barriers. One needs to go past equilibrium geometry and better describe transition states and weakly interacting molecules. However, LDA-/GGA-type functions underestimate by several kilocalories/mole the transition state barriers. Basic arguments include the need for a $1/R^6$ decaying attractive part of the energy, when the interaction distance increases. LDA or GGA functional do not show this behavior. Hartree-Fock nonlocal functional indicates repulsive long-range behavior. For weakly bound dimers, for example, popular functionals often yield poor results. There is still thus a challenge in DFT to correctly describe covalent bonding and van der Waals attraction [15, 18, 57].

It is important in developing DFT functional to remember the connection to the exact exchange-correlation functional and understand how the popular approximations yields known properties of the exact functional. For this purpose, the uniform/slowly varying electron gas has been very useful. The use of eigenvalues and orbitals to describe the Kohn and Sham reference system is the basis of most approximations. It is also possible to consider this as a mathematical artifact not effectively linked to density/total energy. Some authors suggest substitution of the electron density by the potential.

Most authors solve single-electron systems using the wave function, whereas DFT considers their total density. Thus, single electrons could unphysically self-interact. However, including full exact Hartree-Fock exchange cancels the Coulomb

term exactly and consequently corrects the self-interaction error. For DFT to remain strong in the future, it is important to understand theoretical/practical inconsistencies. In simple systems, we can still find errors of 100 kcal/mol.

Strongly correlated systems are still a challenge/important frontier for DFT. If we consider infinitely separated protons with different number of electrons, most functionals fail, and the integer nature of electrons is important to better understand correlation. For integer number of electrons, the energy functionals should indicate correctly the discontinuous behavior in order to yield the energy gap and describe correctly strong correlation.

16 Exchange-Correlation Functionals

16.1 LDA

The form of the uniform electron gas exchange (as a functional of density) was known from the time of Dirac in 1930. However, Monte Carlo simulations (not first principles) served to investigate high-/low-density limits. Vosko, Perdew, and others developed popular LDA correlation functionals. The uniform electron gas has played an important role in the development of functionals [58, 59].

16.2 GGA

The uniform electron gas can indicate different density from that of molecular/atomic systems. We note that the gradient of the density at the nucleus tells what the nucleus is and that the Hohenberg-Kohn proof applies to any external potential (including nucleus), yielding some insight regarding the importance of the knowledge of gradient of the density at a fundamental level.

Using the dimensionless reduced gradient for slowly varying uniform electrons gas, the gradient expansion yields major problems when applied directly to molecules and atoms due to the fact that their densities are not varying slowly. This can be attributed not to the well-defined nuclei but to the exponentially decaying atomic tails. This led to development of the generalized gradient approximation (GGA) with the introduction of functionals for exchange. With mathematical derivations as well as solid-state physics/chemistry involved, gradient functionals took some time to be developed. Although many functionals have been developed, LYP and PBE are among the main ones established [59–62].

16.3   Meta-GGA

GGA brought an order of magnitude improvement in binding energies with respect to LDA. There was thus much expectation for inclusion of higher order density derivatives. Perdew and Schmidt introduced the term meta-GGA via the Jacob's ladder of approximation to the exact exchange-correlation functional. The ladder starts with LDA and continues with GGA. Next, meta-GGA is incorporated with local ingredients including the kinetic energy density [63].

16.4   Hyper-GGA

Subsequently, at the fourth ring, nonlocal functional of the occupied orbitals involving functionals with Hartree-Fock exchange terms (hyper-GGA) is introduced. In the ladder, each rung should satisfy some constraints, whereas each step up the ladder should have previous rung functionals (B88C, B95, TPSS, and others) [64–68].

17   Hybrid Functionals

In 1993, an important advance came via inclusion in the functional of some Hartree-Fock exchange using a linear model that mixed correlation type functionals with local DFA exchange yielding BHLYP among others. Subsequently, this model was improved using experimental data (G1 data set of Pople and co-workers) yielding the B3LYP model (implemented in Gaussian package) which is a linear combination of HF, LDA, B88, LYP, and VWN [69–76].

18   Range Separation

Another idea is to separate the electron-electron interaction into short-range and long-range interactions using an error function and different functions for each interaction. The long-range LDA exchange energy can be calculated from the exchange-hole explicit form, and the Hartree-Fock potential can be considered correct in the asymptotic limit. It is thus possible to mix short-range DFA with long-range Hartree-Fock to yield a corrected functional [77–81].

19   Screened Functionals

These solid-state types of functionals use long-range DFA and short-range HF yielding an area with interesting applications in solid-state chemistry with improvements in excitation energies and other properties [82, 83].

20   Fitting

It is difficult to determine an accurate form from first principles. A more accurate exchange correlation functional can be obtained from a fitting approach, which consists of using experimental information to determine/test the functionals using some form of parameterization. Although this model has been successfully used in B3LYP and B97 functionals, it is not clear how many parameters are required. Nonetheless, this model has led to development of numerous functionals including (VS98, τ-HCTH, MO6-L, MO6, MO6-2X, MO6-HF) some of which indicate good improvement over standard B3LYP [66, 67, 76, 84].

21   Adiabatic Functionals

The idea of the adiabatic connection is that the interaction between electrons can vary with a family of Hamiltonians (H_λ) and minimizing wave functions ψ_λ such that $H_\lambda \psi_\lambda = \psi_\lambda$ and $\rho_\lambda(r) = \rho(r)$ for all λ. The exchange-correlation energy can thus be expressed by integral over λ. The path is from the noninteracting Kohn-Sham system ($\lambda = 0$) to the real physical system ($\lambda = 1$). An important advance in the functional development comes from including Hartree-Fock fraction in the hybrid functional based on adiabatic connections. Functionals can be developed from the adiabatic connection integrand, using both linear and nonlinear models, as well as the exact adiabatic connection [65, 85–89].

22   Local Hybrids

Another method consists of using a variable amount of exact exchange at each point in space. This can be done by using a local variant of exact exchange with a local mixing function. The mixing function now plays a key role [90–93].

23 Fifth Rung Functionals

Usage of fifth rung functionals involves unoccupied eigenvalues and orbitals, whereas the MP2 (second-order many-body perturbation theory) functional is the simplest form when the eigenvalues are from Hartree-Fock [94–96].

24 Random Phase Approximation

The difference between the single-particle excitations and the many-body formulation yields the random phase approximation (RPA) correlation energy. RPAX and RPAE differ in choice of eigenvalues and orbitals. Some models combine the coupled cluster formulation with RPA, whereas others connect range-separation and second-order screened exchange (SOSEX) with the RPA method [96–99].

25 Performance with Selected Properties

25.1 Thermochemical Data Sets

An important challenge in DFT is to test the results with experimental data of high quality. Pople and collaborators developed the G1, G2, and G3 sets including large molecules, ionization energies, heats of formation, proton affinities, and electron affinities. Boese and Handy and Truhlar's group as well as Grimme have also developed data sets (including AE6 and BH6) that can be used to test/benchmark DFT performance [100–103].

25.2 Prediction of Geometries

DFT has done well with geometries. Even the early LDA, without a satisfactory energetic performance, yields reasonable geometries. Sometimes, the geometries are better than GGA (with magnitudes of order better formation heats). For many geometric quantities, there is also very good performance from hybrid functionals [18, 104].

25.3   Reaction Barriers and Kinetics

Functionals indicate good performance for atomization energies but yield poor results for barrier heights of reactions even for the simplest reactions. Even hybrid functionals are known to underestimate reaction barriers by 3 kcal/mol. Reaction rates are also not well addressed. Truhlar's group work included modification of exact exchange to yield new functionals (MPW1K, HTBH42, NHTB38) that address reaction barriers and kinetics [105, 106].

26   Hydrogen Bonding, Inorganic Chemistry, and Transition Metals

Hydrogen bonding is much weaker than ionic and covalent bonds and is on the order of 1–10 kcal/mol. They are however much stronger than van der Waals interactions and weak dispersion. There exists a good difference between functionals that perform on hydrogen bonding. Since there are electrostatic interactions between fragments and overlap of electron density, functionals for hydrogen bonding has been a challenge, yielding wide differences [107].

For inorganic chemistry and main periodic group, there appears to be improvements on going from semilocal GGA to meta-GGA and forward to hybrids. When barriers are included, the trend is to include/increase Hartree-Fock exchange. For inorganic/transition metal chemistry, the opposite is suggested, i.e., there is a better performance with smaller percentages of exchange [18, 108].

27   Response Functions

In general, GGAs overestimate for small molecules the polarizability. Hybrid functionals improve the performance. Again for polymer chains, polarizability is overestimated by LDA/GGA and corrected by HF and hybrid functionals. Similarly, range-separated hybrids perform better for long-distance charge transfer excitations. On the other hand, for NMR shielding constants, hybrid functionals make the performance worse [109].

28   Performance of DFA

LDA does well in geometries but not for energetic differences. For energetics, GGA/meta-GGA is superior to LDA. However, the three models overestimate polarizabilities and underestimate reaction barriers. For weak interactions and

hydrogen bonding, there is a wide variance among the methods. For some of the most recent functionals, a much better description is obtained including Hartree-Fock exchange in hybrids and range-separated functionals. Inclusion of theoretical and physically motivated corrections sometimes can yield a worse description of chemistry although they may yield good results in other areas [18].

29   Van Der Waals Forces and Simple Corrections

For the exact theory, dispersion forces are not a problem, but local/semilocal functions cannot capture the asymptotic $1/R^6$ behavior. There may be basic/mathematical flaws in the DFT functional, and thus failure to give correct energy for two fixed densities at long distances has originated simple corrections.

Since LDA and GGA cannot describe van der Waals long-range behavior, the correct $1/R^6$ will be missing. Empirical $1/R^6$ pairwise correction has been thus proposed. These can also be functionals of both the density and the nuclear geometry and extended to higher-order corrections. The coefficients can be calculated from ab initio methods or derived from experimental information. Nonempirical functionals can also be developed from the dipole moment of the exact exchange hole. Pseudopotentials can also be used to capture the dispersion interaction. It is also possible to develop explicit functionals from the density of two separate fragments that are weakly interacting [110–113].

30   New Trends

One of the new trends consists of constructing approximate functionals and minimizing the total energy. One can also allow the interaction between electrons to vary using a family of Hamiltonians and minimizing the wave functions. Another approach would be development of models based on implicit density functionals [15, 18, 57].

Another way to carry out energy minimization with orbital functionals is the optimized effective potential (OEP) method which depends, however, on the choice of balanced potential basis sets and orbitals. The theoretical foundation of potential-centric view was established as potential functional theory (PFT). For nonlocal OEP, one can optimize the ground-state energy, whereas the optimization variables are orbitals. Using functionals such as the exact exchange (E_{xx}) yields the generalized Kohn-Sham (GKS) equations. These are also called Hartree-Fock-Kohn-Sham equations. For a functional such as B3LYP, GKS and OEP methods can yield similar results [114, 115].

Although DFT is reaching success and maturity, it is important to understand the errors which arise from the approximate functionals used in the calculations. Understanding the root of the errors can offer good insight into improving the

physics, chemistry, biology, and engineering involved, i.e., delocalization errors, self-interaction, many-electron self-interaction, and fractional charges errors [116].

Since a system of fractional number of electrons does not supposedly exist, what is the important perspective of fractional charges? Is the purpose to look at the properties of the functional rather than the chemistry? [18]

The initial/simple way to use approximate functionals to calculate fractional charge was to perform calculation on molecules with odd number of electrons. These were then stretched to infinity. However, the stretching can cause technical challenges. Another route involves modifications of code to involve fractional occupation. Generalization to fractional numbers can also be obtained by using fractional numbers for the frontier orbitals.

Another important question regards the correctness of ensemble or factional occupation. We must keep in mind that the importance of really understanding calculations on integer systems is that the density matrix appears to have been separated into fractional pieces. In other words, it is important to understand the role of functionals for calculations with fractionals essentially because of their appearance in real integer calculations [117, 118].

It is known that approximate functionals deviate from linearity condition for fractional charges with a convex behavior. They will thus give low energies for delocalized charge distribution or favor delocalized charge distributions over integer or localized ones yielding delocalization errors. For functionals with concave behavior, for fractional charges, delocalization will raise the energy yielding localization errors. The delocalization error is essentially an example of delocalized densities and can have physical consequences [119].

From a quantum perspective, static correlation and degeneracies are inherently multideterminental. The methods used for these cases are often built upon a multiconfigurational starting point yielding methods such as CASDFT where a deep understanding of the method is required [120].

Formal occupation numbers apply in the case of exact degeneracy. This idea could be extended to near degeneracy or density functional approximation (DFA) where orbital are not exactly degenerate. Degenerate ensemble of states (spatial degeneracies) can yield fractional-spin states. Both charge and fractional-spin errors can produce wrong densities. DFA has been used successfully with fractional spin to describe spin state splitting in open-shell singlet molecules [18, 121].

For the simple case of one and two electrons with a proton, the long-range asymptotic DFA behavior indicates challenges in the construction of functions which raises questions regarding usage of long-range Hartree-Fock exchange. The screening of the long-range electron-electron interactions is important in solid-state systems having different external potentials [122].

Although strongly correlated systems are difficult to describe, the problem in DFT can be focused from the functional perspective, whereas it is necessary to find one functional that works for all systems. Quantum chemistry divides the correlation energy into dynamic or nondynamic correlation, whereas the correlation energy is given by $E_c = E_{exact} - E^{HF}$. DFT dynamic correlation is describable by functionals such as E_c^{LYP} and E_c^{PBE}, i.e., not unlike correlations of uniform electron gas.

Static correlation functionals of DFT appears for cases with multiple determinants associated with degeneracy. It can be considered as the deviation from the constancy condition for fractional spins, whereas we can detect if a DFA describes it correctly [18, 123].

A fundamental understanding of band gap lies in the change in derivative when orbitals change between LUMO and HOMO. In band theory, the eigenvalue picture for the Mott insulators breaks down. The frontier KS and GKS eigenvalues are the chemical potentials when E_{xc} is an explicit and differentiable functional of the noninteracting density matrix or orbital functionals. However, the exact functional cannot be a differentiable and explicit functional of the noninteracting density matrix for all physical densities/matrices. For E_{xc} the functionals can be non-differentiable. For a Mott insulator, with zero eigenvalue difference, the gap can thus be written as $E_{gap} = I - A = _{xc,}$ which includes the explicit discontinuity of the exchange-correlation term which implies that there is a change in the functional itself (not only a change in the density or orbitals that functional acts on). $_{XC}$ represents only the explicit discontinuity of the exchange-correlation term, I is the ionization potential, and A is the electron affinity. For a pure Mott insulator, only a change in E_{xc} can yield a gap. This is a new difficult concept [124, 125].

We note that the rapid rise of DFT was supported by the similarity of computation solving KS equations using simple ab initio methods (HF). However, there is a strong philosophical difference between both methods, i.e., wave functional versus exchange functional of density. The actual challenge is concentrated on finding $E_{xc,}$

31   Frontier Eigenvalues and Band Gaps

The fundamental band gap for solids is the difference between the electron affinity and the ionization potential, whereas for molecules, it is the chemical hardness (a one-half factor neglected). For energetics, structure, defects, interfaces, and electron transport as well as electromagnetic responses, the band gap plays a key role. The frontier orbitals are either the highest occupied molecular orbital (HOMO) or the lowest unoccupied molecular orbital (LUMO).

When the exchange functional is an explicit functional of the electron density, (local or nonlocal), the frontier KS or GKS eigenvalues are the chemical potentials. The total energy is a linear interpolation between integer points. For functionals that satisfy exact linearity conditions, those are simple differentiable and depend explicitly on electron density $\varepsilon_{HOMO} = -I$ (ionization potential) and $\varepsilon_{LUMO} = -A$ (electron affinity). The functional satisfy linearity conditions will determine how well the frontier KS and GKS determine experiments. Molecules that include long-range Hartree-Fock exchange should improve the description of the frontier eigenvalues [18, 121, 126].

We also note that the fundamental band gap can also be understood from the behavior of E versus N, i.e., as the difference between the electron affinity and the ionization, whereas this can be compared with derivatives with respect to N

(difference between derivative to the right and to the left). For an exact functional, we would observe that the $E_{\text{gap}}^{\text{integer}} = E_{\text{gap}}^{\text{derivative}}$. This may explain some of difficulties of approximate functionals to determine accurate band gaps of solids [124, 127].

32 vdW-DF Method

Even nearly 100 years after van der Waals received the Nobel Prize in Physics, the complex manifestations of the vdW force is still a challenging research area. In physical chemistry, vdW includes a permanent dipole and corresponding induced dipole (Debye force), two permanent dipoles (Keesom force), and London dispersion force (two instantaneously induced dipoles). For the condensed-matter scientist, the latter nonclassical term is the vdW force. The vdW interaction is a true quantum phenomenon which emanates from dynamic electron correlation causing a net attraction between fragments of electrons in many-electron systems. Since it is a correlation effect, vdW interactions are included in exact DFT functional, but in practice, approximate forms are necessary. Analysis of polarizabilities of interacting inert atoms, molecules, and surfaces yield for inert atoms molecules and surfaces the R^{-6} asymptotic form of London force for atomic and molecular dimers, the Z^{-3} law for a neutral molecule on a surface and d^{-2} interaction law for pairs of solids [128].

The vdW has been important to investigate physical and chemical properties of functional materials. Indeed, today's emphasis in computational materials science has shifted from metals and semiconductors to biological materials and nanomaterials due to many low-density vdW regions. The applications of vdW functionals include interaction of atoms, molecules and solids, molecular solids, surfaces, adsorption, graphene, metal, oxides, polymers, nanosystems, adsorbate interactions, clusters, nanotubes, water, and others [15].

Initial vdW-DF work focused on nonlocal correlation. Asymptotic behavior such as R^{-6}, z^{-3}, and d^{-2} offered simple vdW parameters/formulas yielding promising results. Significant improvements for description of vdW-bonded regions originated vdW-DF0 and vdW-DF1 functionals. vdW-DF2 included nonlocal correlation energy and exchange energy update to address overestimation of separation and molecule-molecule interactions. Recently, the focus has been placed on exchange to improve performance, internal inconsistencies, covalent solids, and systems with different binding characteristics yielding energies that now approach chemical accuracy. The vdW-DF-cx functional attempts to use an exchange functional derived from the same plasmon-based model originating nonlocal correlation energy. An ultimate solution would be generalization to a unified treatment with an explicit solution of the electrodynamics to smaller separation. vdW-DF0 attempts to do such a generalization. The vdW-DF method also has a good potential for transferability [15].

Phenomena and processes where flexibility of DFT could be important include molecules on metal surfaces (strongly differing from bulk), charge transfer, and

screening at grain boundaries. Weaknesses of vdW-DF include lack of spin, exchange mechanisms, low accuracy for noble-gas dimers, d and f electron effects, and incorrect asymptotic power laws of low-dimensional structures. Dispersion interactions are ubiquitous and still challenging but are essential not only for typical weakly bound systems but also for materials (where they were traditionally considered negligible). New application areas should include disordered systems, liquids, several length scale systems, biological/competing interactions systems [15].

33 Time-Dependent DFT

Time-dependent density functional theory (TD-DFT) is an extension of ground-state (GS) DFT which allows electronic modeling of excited states (ESs). Runge and Gross in 1984 defined the fundamental equations [129]. Casida provided, 11 years later, linear-response expression for calculation of excitation energies (TD-DFT) [46, 130, 131]. For adiabatic approximation, considering the exchange-correlation independent of the frequency, the so-called memory effect is lost, yielding a pseudo eigenvalue matrix formulation. When the de-excitation matrix is set to zero, one obtains Tamm-Dancoff approximation (TDA), which corresponds to configuration interaction singles (CIS) when HF wave functions are used. The Casida formulation has been successful for a number of approaches since all single-reference theories using TD-DFT is straightforward/accessible. The method can treat photoactive compounds in a realistic environment, i.e., once coupled to environmental models, large compounds can be considered via scaling [54].

Nonetheless, with this formulation, it is difficult to properly investigate excited states (ESs), high-spin states, and multi-reference systems although the method has a good accuracy/computational cost accuracy. Many calculations use the vertical approximation, whereas frozen geometries (ground-state DFT/X-Ray geometries) are used, and vibronic effects (coupling between electronic and nuclear degrees of freedom) are neglected yielding Rydberg, localized, charge-transfer effects, but not a good comparison with experiment (measured optical spectra). The vertical excitation limits have stimulated new research in computing 0-0 energies/vibrationally resolved band shapes. However, this implies on one hand expensive Hessians (second geometrical derivatives of TD-DFT energy) to yield improved potential energy surfaces (PESs). On the other hand, important information can be obtained. Analytical geometrical derivative (at least first two) has been increasingly important in this line of research [46].

TD-DFT approaches that provide data comparable to experiment should become standard. Development of new exchange functionals such as range-separated hybrids should allow more accurate studies including charge-transfer effects. Constricted variational DFT [56], less sensitive than TD-DFT to selected functional, may be better suited for investigating states with double excitation character. The equation of motion coupled-cluster expansion, an alternative single-reference theory, such as CC2, includes contributions for double excitations and can be

consequently more accurate than TD-DFT. With a computational cost three times smaller than CC2 with an equivalent accuracy, we have algebraic diagrammatic construction (ADC). These models can be improved with more correlation effects and high-computational requirements yielding (CCSD, CC3). Another popular alternative from solid-state physics is BSE/GW with enhanced accuracy [132].

Continuous developments of TD-DFT permits calculation of larger/more complex systems whereas the role of nonadiabatic coupling cannot be ignored requiring models such as quantum-dynamical wave packet propagation from multiconfigurational time-dependent Hartree (MCTDH) and its multilayer expansion [133].

34   Force Fields

For large systems with temporal/length scales of ns/hundreds of Á, where QM is clearly limited, a less expensive computational model such as force fields (FF) are required. This method uses inter-site potentials to describe interactions between sites (atomic) requiring a different parameterization (data from QM or experiments) for each system. The number of bonds is fixed in a conventional FF simulation, whereas it is possible to capture dynamics and formation/destruction of covalent bonds in a reactive FF simulation. The classical potential contains bonded and nonbonded contributions. Molecular bonded potentials contain bond stretch as well as bond bending and torsion (3-body and 4-body terms). Harmonic functions can be used to describe stretching and bending, whereas periodic functions can be used for torsional energy. Nonbonding interactions are typically electrostatic (Coulomb), whereas for van der Waals, a simple description is quantum fluctuation of charges whose interaction can be given by the Lennard-Jones (L-J) M model, i.e., a repulsion 12th power term (Pauli repulsion due to overlapping electron orbitals) and an attractive sixth power (dispersion force of neutral atoms) term. It was shown that it was possible to reduce scaled L-J term to a single universal binding energy curve for numerous materials laying the basis for bond-order concept [8, 134, 135].

35   Characterization of PES (MC/MD)

Molecular simulations and computational chemistry have evolved as major techniques to study physics and chemistry of materials, whereas one of the objectives of molecular simulation is characterization of system's potential energy surface (PES) due to the interest in locating minima and saddle point connections on the PES. Approaches based on energy minimization may work well for well-ordered, high symmetry, small systems, whereas for other more complex systems, characterization of the PES requires extensive sampling. There are two traditional classes of techniques for dynamics and sampling, i.e., Monte Carlo (MC) and molecular dynamics (MD).

35.1   Monte Carlo

MC methods employ random number in order to solve a wide range of problems, including simulation of physical processes, solution of integral and linear operator equations, and evaluation of multidimensional integrals. In this method, the PES is characterized using extensive statistical sampling (accessible basins). Random changes are made in the method to an existing configuration so as to generate new configurations. A criterion such as the Metropolis criterion can be used to either accept or reject these configurations [10, 14].

35.2   Quantum Monte Carlo

MC techniques can be applied to problems in quantum mechanics whereas the intersection of MC and QM methods is referred to as quantum Monte Carlo (QMC) methods, which are accurate tools for studying molecular quantum mechanics including thorough treatment of static and dynamic correlation effects and are not constrained by considerations of many-particle expansions and basis set considerations. In QMC, a trial wave function approximates the true/exact Schrodinger wave function, and its parameters can be varied to obtain a more accurate function. The method can be considered as a family of stochastic methods for solving quantum many-body problems such as the stationary Schrodinger equation. Stochastic methodologies offer direct/correct particle correlations, favorable scaling, and a wide range of chemical/physical mechanisms. QMC is a unique approach combining known analytic insights/direct constructions with robustness of stochastic methods to capture many-body effects efficiently. Effective core potentials, periodicity, and noncovalent interactions are addressed in QMC [10, 14].

QMC approach offers new insights of the nature of quantum correlations that are stimulating for WFT methods. A complete basis set is used for stochastic sampling (determined automatically) with explicit inclusion of exact nonanalytical behavior (electron-electron cusps). The smooth, long-range, medium correlations are captured with efficiency. Limitations/challenges include the fundamental Fermion sign problem, better understanding of errors related to QMC procedures, and development of new fast algorithms.

The most common approaches to QMC include variational MC (VMC), fixed-node diffusion MC (FN-DMC), Green's function MC (GFMC), Fermion MC (FMC), self-healing diffusion MC (SH DMC), auxiliary field quantum MC (AFQMC), reputation quantum MC (RQMC), and full-CI Quantum MC (FCI-QMC). These methods rely on random walks in space of electron configurations. Time-dependent quantum Monte Carlo (TDQMC) can be seen as a set of coupled time-dependent Schrodinger equations for the guiding waves in physical space. Although QMC methods are among the most accurate tools for studying molecular quantum mechanics, the computed time for each step of a QMC calculation increases roughly as N^3 where N describes the size/number particles of the system [10, 14].

Important advantages in QMC include accurate description of noncovalent interactions, larger molecular systems than current WFT approaches (due to low-order polynomial scaling) and favorable parallelism of algorithms for supercomputer usage and straightforward treatment of periodicity [136–141].

35.3   Molecular Dynamics

In MD, the PES is sampled, whereas the initial configuration is propagated and explored with time using Newton's equation of motion yielding a trajectory (series of molecular configurations). Classical molecular dynamics, with force fields and predefined potentials are based on independent electronic structure calculations or empirical data. At the heart of this model is the description/approximation of the interatomic interactions mostly determined in advance. The full interaction comprises two-body, long-range/short-range interactions, many-body contributions, electrostatic/non-electrostatic interactions represented by appropriate functional forms. Elaborate methods, including analytic potentials, have been developed. However, despite significant success, there are serious drawbacks due to the need to devise fixed predefined potential, i.e., when the electronic structure/chemical bonding pattern changes qualitatively during simulation or when different atom/molecules yield different interatomic interactions/parameterizations and no suitable set of potentials is already available [4, 19, 142, 144].

35.4   Ab Initio Molecular Dynamics

Despite the success of MD, the necessity to construct a predefined/fixed potential is a drawback in particular for complex systems. Consequently, traditional MD was extended to (AIMD) ab initio MD or Carr-Parinello (CP), first-principles MD (FPMD) on the fly, directed extended Lagrangian MD (ELMD), density functional MD (DFMD), quantum chemical, Fock matrix, Hellmann-Feynman MD, and quantum MD (QMD). How does this theory work? As the molecular dynamics trajectory is generated, the forces acting on the nuclei are determined by "on-the fly" electronic structure calculations. The electronic variables are not represented by fixed interaction potentials and are not integrated out beforehand. Complex system can thus be handled by AIMD. The approximation is shifted from constructing an interaction potential to selecting an approximation for solving Schrodinger equation [4, 19, 142–144].

AIMD joins ab initio electronic structure theory (solving the wave equation numerically for Schrodinger and using HF or KS/LDA) with classical molecular dynamics (for a given interaction Newton's equation of motion is solved numerically). However, the relaxation times and correlation lengths are relatively smaller which is sometimes addressed by increasing computer power. Also, AIMD can yield promising results in terms of the electronic structure and chemical bonding.

36   Quantum Mechanics/Molecular Mechanics

Quantum mechanics/molecular mechanics (QM/MM) is one of the first hybrid models which includes the combination of more accurate QM strength with faster and more efficient MM methods in order to generate a stronger tool for investigating larger more complex systems. In this model, the system is divided into two regions, whereas the outer region is described by a force field and the inner region is treated quantum-mechanically. Often a small region of the system can be modeled by ab initio quantum chemistry, whereas the other can be treated more approximately. The interface between the QM and MM regions is the key issue [3, 145]. A less expensive alternative is the usage of self-consistent reaction field (SCRF) approaches, for the coupling of quantum chemical calculations with continuum models, which has been implemented over the decades in quantum chemical softwares [3, 5, 6].

37   Coarse-Grained and Multiple Scale Models

The traditional approaches using all atoms are still not adequate for appropriately simulating large temporal/spatial scales. In the coarse-grained (CG) model, one neglects some of the atomistic degrees of freedom (DOFs). The CG models can increase over temporal/spatial limitations of all-atom models. The physics of the detailed system may be sensitive to small-scale phenomena, and there is a challenge to develop accurate/transferable force fields, which can be extracted from atomistic simulations or by reproducing key experimental data [8, 20, 22, 146–152].

CG creates lower resolution/simplified model of the system by grouping atoms into CG beads (pseudoatoms) whose number determines the level of coarse-graining (degree depends on number of atoms represented). A lower-resolution model can be obtained by increasing atom-to-bead ratio, whereas total number of degrees of freedom is reduced. CG beads interact with each other via potentials yielding considerable increase in time/space accessibility. The basic idea of simulations with coarse-graining is thus to represent the system with reduced number of degrees of freedom (compared to all-atom representation).

In energy-based CG, interaction potentials of beads are derived/parameterized so that it is possible to reproduce energies of all atom system. In force-matching method, sum of atomistic forces are mapped onto corresponding CG beads. Structure-based CG methods depend on reproducing interactions obtained from atomistic simulations (radial distribution functions). The CG models can relate phenomena such as energy, force and structure molecular dynamics, or experimental results. The aim is to provide most efficient computational model with adequate details. Using coarse-graining, we can achieve a simpler description by reducing the structural details of a complicated system by grouping into fewer interaction sites. Challenges of designing CG models include choice of pseudoatom sites

(represent combined groups of multiple atoms), effective energy function (defines interaction between the pseudoatoms), and effective dynamical equations (necessary for dynamic properties).

One of the popular energy-based approaches CG models is the Martini model which uses a four-to-one mapping scheme (average four heavy atoms are represented by one interaction site or bead). Standard masses of each bead are assigned to yield a more computationally efficient model. Main types of interaction considered are polar, apolar, nonpolar, and charged with subtypes that describe the hydrogen-bonding capabilities whose combination yields different bead types (diversity leads to more accurate description of chemical nature and structure).

CG models can simulate large systems with size ($100 \times 100 \times 100$ nm^3) which contains millions of particles as well as slow micro- to millisecond range processes. High-throughput studies can be done via thousands of parallel runs indicating location/importance of detailed insights regarding fundamental driving forces for novel pathways at a much smaller computation cost than other available models.

It is of interest to link CG simulations with that of detailed models, whereas behavior can be determined at multiple scales (different scales share information regarding interactions). This can be done *bottom-up*, whereas fundamental physical principles at detailed scale parametrize a CG scale model, or *top-down* when larger scale behavior is used to inform more detailed scale interactions.

The CG Boltzmann inversion (BI) method aims to obtain an accurate reproduction of structural details via interaction potentials, based on the idea that for particles to interact with each other via forces that only depend on the scalar distance that separates them, it is necessary a one-to-one correspondence between potential and radial distribution function. The radial distribution function indicates correlations in distribution of particles due to forces exerted on each other from pair potentials. When atomistic simulations yield CG interactions, the BI method is an example of multiscale method.

Another model, the force matching method, is also an example of a multiscale method, whereas the interaction potentials are determined from atomistic simulations (structural information not used).

Another approach is the thermodynamic-based model, whose premise is that if the local thermodynamic properties are correct, dynamics on long time scales will be also correct, whereas analytical potentials are often chosen (Lennard-Jones potentials for nonbonded interactions, harmonic bond stretching/bending potentials as in atomistic simulations).

Physical and mechanical properties for systems including polymeric materials can depend on phenomena at different temporal and spatial scales making it necessary to use multiscale techniques for modeling purposes, whereas it is necessary to establish a link between macroscopic mechanical properties and molecular constituents. Difficulties arise from a wide range of spatial and temporal scales involved.

For covalent bonds, typical vibrations are on the length scale of Á with sub-picosecond time scale. Typical length of a monomer is nanometers (nm with tens of picoseconds relevant dynamics. Polymer chains are ~10–100 nm with single-chain

interactions of 10–1000 nanoseconds (ns). Polymeric networks are on the order of 1–100 μm indicating relaxation times of micro- to milliseconds. Bulk polymeric materials indicate length scales of millimeters to centimeters, whereas aging and relaxation of polymeric materials happen in seconds/hours/years range. These wide ranges of temporal/length scales show clearly that it is necessary to introduce multiscale modeling if one wants to characterize correctly the hierarchy of scales.

Future predictions? Our present limitation is for systems containing 10^7 interacting atoms and 1 μs which can be investigated using particle-based simulations. Even if we could count on doubling yearly computational performance (Moore's law), we could not model with atomistic resolution 10^{14} atoms (complete cell) although a bacterial cell may be feasible in the future. Let us go another step further and consider a typical membrane patch of length L, whereas it is assumed that the computational effort to increase membrane size scales as L^6. Assuming again Moore's law, it would take us 40 years to increase the membrane size by a factor of 10.

38 Simulation of Materials and Biomolecular Structures

The underlying physical laws (encapsulated in the Schrodinger equation) for the mathematical theory of a large part of physics and chemistry are known from the 1920s. The exact solutions of these laws are not tractable for realistic materials. Nonetheless, the application of numerous approximations previously discussed reduces considerable the number of electrons to be simulated. This advancement, coupled with computational advancements allows techniques such as DFT to solve the fundamental laws of SE and predict properties of materials and biomolecular structures.

Inputs of DFT calculations including identities and coordinates of atoms in the material's repeating lattice is often used as well as exchange correlation functional and algorithms for convergence and methods such as pseudopotential approach to treat the core electrons. The choice of the exchange correlation functional can often improve the calculation. DFT codes can tackle periodic unit cells with $\sim$1000 atoms. Difficulties can arise in modeling weak van der Walls interactions, long period dynamics, and finite temperature excited states. However, there are methods for overcoming these limitations. Linear scaling approaches can be used for larger systems. TD-DFT can address the electronic excitations. Approaches previously discussed can model the van der Walls interactions. In order to screen for materials properties using DFT, the input is given via crystal structure (atomic positions, unit cells) of hypothetical material, as well as "choice" of approximations/convergence parameters yielding total energies, charge densities, band, and crystal structures. Outputs produce descriptors for relevant applications [8, 11, 153–187].

Total energy calculations can yield important properties. The energy difference between a point defect and the perfect crystal can yield the thermodynamic

properties of the defects. The energetics of diffusion barriers can be evaluated as the energy differences along an atom's migration path. Analyzing the resultant force on remaining atoms, after displacing some atoms, it is possible to determine phonon modes (vibrational heat capacity). In the field of catalysis, we can use DFT results as descriptors to be used in scaling relations or heuristics.

Lithium-ion batteries will provide for the next-generation electric vehicles, whereas the expected voltage determines energy stored per unit charge. Using electron localization, it is possible to predict voltage increase in hypothetical doped materials. High-throughput automation virtual screening of materials can be used to predict new cathode and anodes [154–156].

Hydrogen can be generated from hydrocarbons via a steam reforming process, whereas the necessary catalysts can be predicted theoretically and the binding energies related to catalytic behavior. Since hydrogen can be embedded in a solid compound, theoretical methods can be used to identify new compound mixtures for hydrogen storage [16–160].

Traditional superconductors (electron pairing interactions arise from electron-phonon coupling) can in principle be predicted in systems with anomalously high-electron density at the Fermi level. Since many materials exhibit phase transition as a function of pressure, it may be possible to use crystal structure determination to predict high-pressure superconductivity in materials with unknown structures. Theoretical methods are expected to evolve to screen for novel higher T_c compounds [161–164].

Contribution of photovoltaics to the total electricity generation is small. Theoretical screening can be made on a wide range of materials (chalcogenides, organic photovoltaics, copolymers, transparent conducting films, alloys). PVs can be analyzed by looking at the HOMO energy level relative to air and charge-transfer energy offset of LUMO as well as band gaps [165–167].

Thermoelectric materials drive electrical currents via temperature differences. Despite their potential applications (transportation vehicles, power generation), the performance of these materials can be determined by ZT (figure of merit) which is proportional to electronic conductivity, Seebeck coefficient, and electronic conductivity). Due to inherent trade-off among these properties, there is a limit on attainable ZT. In large complex materials, it is not straightforward to obtain, from DFT, accurate band gaps and carrier lifetimes. Despite difficulties, screening of materials with improved ZT is still feasible [168, 169].

Using the polarization of an electric field within a material, the capacitor stores electrostatic energy, i.e., pseudocapacitors, carbon-based supercapacitors, ferroelectrics, dielectric capacitors. A dielectric capacitor should have high breakdown strength, good cycling stability, and high dielectric constant. The electronic component of the dielectric constant depends on the band gap. The dielectric constant can be evaluated as a function of structural and chemical properties. For most materials, it is not necessary to do, in silico, the entire material design, but focus the experimental efforts within a structural and chemical space [153, 170].

Molecular modeling is appropriate for developing quantitative and qualitative knowledge of structure-properties relationships (selective adsorption, catalysis,

separation technology) for a wide range of systems (bulk, interfaces, molecules) yielding important information regarding pore size, temperature, shape, and other variables in selectivity adsorption. Simulation methods are important for computational study/design of synthetic sorbents and catalysts (zeolites, aluminophosphates, aluminosilicates, nano, mesotubes, fullerenes, heterofullerenes, pillared clays, disordered porous solids) as well as surface heterogeneity/equilibrium and kinetics of fluid adsorption, thermal desorption, surface diffusion, and surface reactions. Solid oxide fuel cells can be improved by studying the effects of doping one the ionic conductivity [8, 11]. Future trends should include development/application of widely understood modern techniques to study adsorption experiments in order to design new types of catalysts and adsorbents. Usage of experimental databases, artificial intelligence, and advanced simulation techniques will open new strategic technologies [11, 153].

Nanotechnology with its applications for electronics, batteries, drug/gene delivery, water desalination, and diagnostics has an increasing participation in sustainable technologies that address society needs, i.e., clean water/air/energy supplies. On the other end, the usage of small size/reactive nature of nanomaterials in addition to positive contributions, raise issues regarding potential health, environmental, and safety concerns. There are challenging chemical, biological, and physical issues involving interactions between biological and nanomaterials that span spatial and broad length scales. Nanomaterials may be involved in electron transfer in cells, generation of damaging reactive oxygen species as well as undergo undesired chemical transformations. Theoretical and computational studies are expected to play important roles in elucidating the complexity of nano/bio interfaces. Coarse-grained models (structure and dynamics) may be necessary to access the large length (>100 nm) and time (>μs-ms) scales relevant to behavior and impact of nanomaterials with biological settings. Top-down approaches that depend on semiempirical methods can also provide insights into effects of nanomaterials on biological structures such as lipid membranes.

In modern surface science technology, modeling the reactions and adsorption of organic molecules at metal surfaces has important applications in molecular switches, sensors, photovoltaics, energy devices, and catalysis. The highly tunable properties of organic molecules and the electrical conductivity of metals can result in new functionalities not present in either material. An accurate description of bonding between substrate and adsorbate is essential for control and understanding functionality and design of these types of hybrid systems in which there is a delicate balance between van der Waals (vdW), covalent, hydrogen bond, Pauli repulsion, and charge transfer [144].

Due to nontoxicity, high stability, and abundance, metal oxides such as TiO_2 (nano) materials have been the subject of numerous theoretical investigations regarding chemical and physical fundamental properties. It was challenging for a long time to correctly describe relative stabilities of anatase and rutile bulk phases. Inclusion of dispersion in DFT calculations have been suggested to be important for reproducing the greater stability of rutile. Stable in nanoparticles, anatase indicates higher photocatalytic/photovoltaic activity, whereas the electronic

structure plays an important role in these applications, i.e., positions of valence and conduction band edges relative to the potentials of relevant redox couples determine occurrence of photocatalytic reactions. The optical absorption is determined by the band gap. States near conduction and valence band edges have more influence on chemical reactivity and electrical conductivity. Accurate theoretical description of band gap is important allowing quantitative energetic prediction of trap states, impurity levels, defects as well as influence of doping on optical absorption which is crucial for design of oxides with improved properties. It is also important whether charge carriers (reducing defects, doping, and photoexcitation) are in delocalized band states or coupled to lattice polarization forming localized polaronic states. Choice of electronic structure method is important, and nonstandard DFT methods are sometimes used [171]. Fullerenes, nanotubes, nanowires, and other nano systems have been designed and investigated using semiempirical, ab initio, density functional, and molecular dynamics methods [172–175].

Surface functionalization/modification is used to induce new material's properties (hybrid photovoltaics and dye-sensitized solar cells). Molecular dynamics simulations based on force fields potential allows modeling the sintering of oxide nanoparticles. Photoelectrochemical and photocatalytic processes can be elucidated using modern parallel computers and computational algorithms expanding first-principles electronic structure simulations to better understand realistic oxide nanocrystals of a few nm size. Simulation models are being applied to an ever increasing number of diversified areas including crystal structure, phase stability, mechanical properties, elasticity, theoretical strength, fracture, magnetism, conductivity, phonon frequencies, liquids, amorphous, semiconductor, insulators, metals), surfaces, interfaces, and thin films [144].

The earliest example of CG approach in structural biology was developed in the mid-1970s, i.e., a simplified simulation model of proteins. The field has branched out considerable since then, yielding many variants of protein representation, sampling models, and interaction potentials, whereas the growing number of experimentally solved structures of large biomolecules is too large to be addressed by all-atom simulations. Some of the CG models enable protein structure prediction. Interaction schemes are typically based on mean-force potentials (derived from known protein structures), and the simulation processes can be controlled by the MC method. One of the future trends of CG dynamics lies in design of approaches for efficient/reliable transition between atomic resolution and simplified levels. Using CG approaches, we will be able to send CG scale simulations to detailed all-atomic simulations (vice versa). CG simulation is playing an increasing role in protein mechanostability, folding, unfolding, and understanding mechanisms of virus binding to its host cell. CG simulation of protein-protein interaction dynamics is now in the spotlight of biomedical research since these interaction dynamics can yield essential insight into important biological processes as well as causes of diseases/drug-receptor interactions. Membrane proteins are responsible for molecular transport across lipid bilayers, signaling, maintaining cell structural stability, and control of cell-cell interactions. Nonetheless, 1% of all known 3D protein structures account for membrane proteins. The complexity of these biomolecular structures

makes CG molecular dynamics (CG-MD) simulations a very valuable approach to investigate stability, dynamics, and structure-function relationships. The MARTINI force field is of the most recognized and best performing CG-MD approaches that uses four-to-one atom mapping enabling treatment of more than 500,000 atoms with time scales above 100 μs (far beyond classical all-atom MD) [8, 22, 146–152].

Although thermodynamically stable, protein conformation was treated as responsible for biological functions; it is now known that intrinsically disordered proteins (IDP) can retain their functionality. Conformational studies of protein systems remain highly challenging. Nonetheless, CG approaches have been used to yield insights into the binding mechanisms of these complexes. CG protein simulation thus enables studies of larger protein systems and longer time scales compared with atomistic models.

Processes which are photoinitiated play very important roles in living organisms, whereas photosynthesis is performed via absorption of sunlight by bacteria, algae, and plants. Carbon dioxide and water are converted into oxygen and carbohydrates, yielding basis for Earth life. Using the rhodopsin protein, vision of animals/humans is accomplished in the eye, whereas absorption of a photon performs isomerization of the central retinal chromophore. Phototaxis of plants/bacteria begins with photoexcitation of protein pigment followed by excitation energy transfer, electron transfer isomerization among other reactions. For some of these reactions, the important ultrafast processes occur in very small spatial regions of the protein environment with only a few nuclear degrees of freedom of the pigment. The remaining protein environment has often only negligible influence on relevant excited states of pigment. Consequently, for these systems, DFT can be successfully applied within QM/MM schemes [176].

The properties of polymers depend on numerous time and length scales which are coupled. These systems indicate unique viscoelastic properties arising from atomistic level interactions. There is thus a need to probe polymers across length/time scales in order to capture their behavior making their computational modeling very challenging. With increasing molecular weight, these systems become entangled yielding long-time diffusive regimes (not accessible to atomistic simulations). Coarse-graining the polymer, i.e., increasing the time scale and reducing the degrees of freedom, is one path to overcome the theoretical/computational challenges posed by polymeric systems [8, 150].

Multiscale top-down and bottom-up approaches have been used to investigate complex biological systems, whereas an emerging approach is the middle-out approach which starts with an intermediate biological cell which is gradually expanded to include both smaller and larger spatial scales [22]. 3D multiscale numerical models were used to analyze stress/deformation of cells subject to mechanical loads. There has also been modeling of organ-level bone modeling, physical and coronary artery processes, wounded epithelial cell monolayers, simulation of heart, and immunological interactions. Future trends aim to describe complex bio systems and develop predictive models of human disease. CG representations of the DNA are being developed which should enable extensive simulations that could permit, in a reasonable amount of time, a better comprehension of essential

physical/chemical/biological processes involved [146]. Docking, molecular dynamics, pharmacophore modeling, and ADME/Tox predictions have been used in simulations to propose new drugs for cancer, aids, Alzheimer's, diabetes, and other diseases [177–187].

Although protein folding takes several minutes, their hydrogen bonds and van der Waals interactions occur within picoseconds. Corrosion of metals, in material engineering, destroy or compromise billions of dollars of advance products/process of fundamental importance to society. It takes femtoseconds for a single-electron transfer at metallic surface, minutes for multiple reaction cascades diffusion) and decades/hundreds of years for macroscopic corrosion and decomposition of metallic structures. For both materials and biomolecular systems, the underlying phenomena span a very large hierarchically organized sequence (length and time scales).

Understanding, describing, and predicting these multiscale and multi-physics/chemistry/biology/engineering phenomena with advanced theoretical-computational methods is a very important task to assure the well-being of our society.

References

1. Helgaker T, Jorgensen P, Olsen J (2000) Molecular electronic structure theory. Wiley, Chichester
2. Geerlings P, De Proft F, Langenaeker W (2003) Conceptual density functional theory. Chem Rev 103:1793
3. Friesner RA (2005) PNAS 102:6648
4. Mark D, Hutter J (2009) Ab initio molecular dynamics, basic theory and advanced methods. Cambridge University Press
5. Taft CA, da Silva CHTP (eds) (2010) New developments in medicinal chemistry, vol 1. U.A.E. Bentham Science, Saif Zone Sharjah
6. Taft CA, da Silva CHTP (eds) (2014) New developments in medicinal chemistry, vol 2. U.A.E. Bentham Science, Saif Zone Sharjah
7. Taft CA, da Silva CHTP (2013) J Biomol Struc Dyn 31:1001. doi:10.1080/07391102.2012.748540
8. Canchaya JGS, Furtado NC, Taft CA (2015) Curr Phys Chem 5:223
9. Jones RO (2015) Rev Mod Phys 87:897
10. Austin BM, Zubarev DY, Lester WA Jr (2012) Chem Rev 112:263
11. Canchaya JGS, Rebaza AVG, Lemelle DS, Taft CA (2014) Curr Phys Chem 4:45
12. Thiel W (2013) Comput Mol Sci doi:10.102/wcms.1161
13. Rezac J, Dubecky M, Jurecka P, Hobza P (2015) Phys Chem Chem Phys 17:19268
14. Dubecky M, Mitas L, Jurecka P (2016) Chem Rev 116:5188
15. Berland K, Cooper VR, Lee K, Schröder E, Thonhauser TT, Hyldgaard P, Lundqvist BI (2015) Prog Phys 78:066501
16. Domingo LR, Gutiérrez MR, Pérez P (2016) Molecules 21:748
17. Becke AD (2014) J Chem Phys 140:18A301
18. Cohen AJ, Sanchez PM, Yang W (2011) Chem Rev 112:289
19. Kuhne TD (2014) WIREs Comput Mol Sci 4:391

20. Kamerlin SCL, Dryga A, Vicatos S, Warshel A (2011) Annu Rev Phys Chem 62:41
21. Voth GA (2008) Coarse-graining of condensed phase and biomolecular systems. CRC Press, New York
22. Noid WG (2013) J Chem Phys 139:90902
23. Chattaraj PK (2009) Chemical reactivity theory, a density functional view. CRC Press (Taylor & Francis Group), Boca Raton
24. Riley KE, Pitonak M, Jurecka P, Hobza P (2010) Chem Rev 110:5023
25. Singh DJ (1994) Planewaves, pseudopotentials and the LAPW method. Kluwer, Dordrecht
26. Goedecker S, Ivanov OV (1998) Comput Phys 12:548
27. Marzari N, Vanderbilt D (1997) Phys Rev B 56
28. Chelikowsky JR, Troullier N, Saad Y (1994) Phys Rev Lett 72:1240
29. Stone A (2002) The theory of intermolecular forces. Calerdon Press, Oxford
30. Hobza P, Dethlefs KM (2010) Non-covalent interactions, RSC theoretical and computational chemistry series. RSC Publishing
31. Pariser R, Parr RG (1953) J Chem Phys 21:466
32. Pople JA (1953) Trans Farad Soc 49:1375
33. Pople JA, Santry DP, Segal GA (1965) J Chem Phys 43:S129
34. Dewar MJS, Thiel W (1977) J Am Chem Soc 99:4907
35. Dewar MJS, Zoebish E, Healy EF, Stewart JP (1985) J Am Chem Soc 107:3902
36. Stewart JJP (1989) J Comput Chem 10:221
37. Jug K, Iffert R, Schulz J (1987) Int J Quant Chem 32:265
38. Ahlswede B, Jug K (1999) J Comput Chem 20:563
39. Bacon AD, Zerner MC (1979) Theor Chim Acta 53:21
40. Tubert-Brohman I, Guimaraes CRW (2004) J Comput Chem 25:138
41. Rocha GB, Freire RO, Simas AM, Stewart JJP (2006) J Comput Chem 27:1101
42. Weber W, Thiel W (2000) Theor Chem Accounts 103:495
43. Korth M, Thiel W (2011) J Chem Theory Comput 7:2929
44. Grimme S, Antony J, Schwabe T, Lichtenfeld CM (2007) Org Biomol Chem 5
45. Yoo S, Zahariev F, Sok S, Gordon MS (2008) J Chem Phys 129:144112
46. Casida ME, Huix-Rotllant M (2011) Annu Rev Phys Chem 63:287
47. Burke K (2012) J Chem Phys 136:150901
48. Mourik T, Bühl M, Gaigeot MP (2012) Phil Trans R Soc A 372:4088
49. Peverati R, Truhlar DG (2014) Philos Trans R Soc A 10:372
50. Kohn W, Sherrill CD (2014) J Chem Phys 140:18A201
51. Maitra NT (2016) J Chem Phys 144:220901
52. Kryachko ES, Ludeña EV (2014) Phys Rep 544:123
53. Pribram-Jones A, Gross DA, Burke K (2015) Annu Rev Phys Chem 66:283
54. Santoro F, Jacquemin D (2016) WIREs Comput Mol Sci. doi:10.1002/wcms.1260
55. Kraisler E, Kronik L (2014) J Chem Phys 140:18A540
56. Ziegler T, Krykunov M, Seidu I, Park Y (2015) Density functional methods for excited states. Springer, Berlin/Heidelberg, pp 1–35
57. Cramer CJ, Truhlar DG (2009) Phys Chem Chem Phys 11:10757
58. Vosko SH, Wilk SHL, Nusair LM (1980) Can J Phys 58:1200
59. Perdew P, Burke K, Ernzerhof M (1996) Phys Rev Lett 77:3865
60. Langreth DC, Perdew JP (1979) Solid State Commun 31:567
61. Gross EKU, Dreizler RMZ (1981) Phys A: Hadrons Nucl 302:103
62. Levy M, Perdew JP (1985) Phys Rev A 32:2010
63. Perdew JP, Schmidt K (2001) Jacob's ladder of density functional approximations for the exchange_correlation energy. In: VanDoren V, VanAlsenoy C, Geerlings P (eds) Density functional theory and its application to materials, vol 577. American Institute of Physics, Melville, New York, pp 1–20
64. Van Voorhis T, Scuseria GE (1998) J Chem Phys 109:400
65. Perdew JP, Kurth S, Seidl M (2001) Int J Mod Phys B 15:1672
66. Boese AD, Handy NC (2002) J Chem Phys 116:9559

67. Zhao Y, Truhlar DG (2006) J Chem Phys 125:194101
68. Perdew JP, Ruzsinszky A, Tao J, Csonka GI, Scuseria GE (2007) Phys Rev A 76:42506
69. Becke AD (1993) J Chem Phys 98:1372
70. Stephens PJ, Devlin FJ, Chabalowski CF, Frisch MJJ (1994) J Phys Chem 98:11623
71. Becke AD (1997) J Chem Phys 107:8554
72. Adamo C, Barone VJ (1999) J Chem Phys 110:6158
73. Lynch BJ, PL Fast, M. Harris, DG Truhlar (2000) J Phys Chem A 104:4811
74. Wilson PJ, Bradley TJ, Tozer DJ (2001) J Chem Phys 115:9233
75. Keal TW, Tozer DJ (2005) J Chem Phys 123:121103
76. Zhao Y, Truhlar DG (2008) Theor Chem Accounts 120:215
77. Yanai T, Tew DP, Handy NC (2004) Chem Phys Lett 51:393
78. Toulouse J, Colonna F, Savin A (2005) J Chem Phys 122:14110
79. Vydrov OA, Heyd J, Krukau AV, Scuseria GE (2006) J Chem Phys 125:074106
80. Cohen AJ, Mori-Sanchez P, Yang WT (2007) J Chem Phys 126:191109; (81) Bylander DM, Kleinman L (1990) Phys Rev B 41:7868
81. Chai JD, Head-Gordon MJ (2008) Chem Phys 128:84106; (82) Heyd J, Scuseria GE, Ernzerhof MJ (2003) Chem Phys 118:8207
82. Heyd J, Scuseria GE, Ernzerhof M (2006) J Chem Phys 124:219906
83. Krukau AV, Vydrov OA, Izmaylov AF, Scuseria GE (2006) J Chem Phys 125:224106
84. Chan GKL, Handy NC (2000) Chem Phys 112:5639
85. Langreth DC, Perdew JP (1977) Phys Rev B 15:2884
86. Mori-Sanchez P, Cohen AJ, Yang WT (2006) J Chem Phys 124:91102
87. Teale AM, Coriani S, Helgaker T (2010) J Chem Phys 133:164112
88. Liu ZF, Burke K (2009) Phys Rev A 79:64503
89. Gori-Giorgi P, Seidl M (2010) Phys Chem Chem Phys 12:14405
90. Jaramillo J, Scuseria GE, Ernzerhof MJ (2003) J Chem Phys 118:1068
91. Becke AD (2005) J Chem Phys 122:064101
92. Becke AD, Johnson ER (2007) J Chem Phys 127:124108
93. Arbuznikov AV, Kaupp M (2007) Chem Phys Lett 440:160
94. Grimme S (2006) J Chem Phys 124:34108
95. Karton A, Tarnopolsky A, Lamere JF, Schatz GC, Martin JML (2008) J Phys Chem A 112:12868
96. Zhang Y, Xu X, Goddard WA (2009) Proc Natl Acad Sci U S A 106:4963
97. Scuseria GE, Henderson TM, Sorensen DC (2008) J Chem Phys 129:231101
98. Toulouse J, Gerber IC, Jansen G, Savin A, Angyan JG (2009) J G Phys Rev Lett 102:96404
99. Gruneis A, Marsman M, Harl J, Schimka L, Kresse G (2009) Chem Phys 131:154115
100. Curtiss LA, Raghavachari K, Redfern PC, Pople JA (2000) J Chem Phys 112:7374
101. Amin EA, Truhlar DG (2008) J Chem Theory Comput 4:75
102. Zhao Y, Truhlar DG (2008) Acc Chem Res 41:157
103. Schultz NE, Zhao Y, Truhlar DG (2005) J Phys Chem A 109:4388
104. Staroverov VN, Scuseria GE, Tao JM, Perdew JP (2003) J Chem Phys 119:12129
105. Zhao Y, Lynch BJ, Truhlar DG (2004) J Phys Chem A 108:2715
106. Zhao Y, Schultz NE, Truhlar DG (2005) J Chem Phys 123:161103
107. Zhao Y, Truhlar DG (2005) J Chem Theory Comput 1:415
108. Schultz NE, Zhao Y, Truhlar DG (2008) J Comput Chem 29:185
109. Hieringer W, Gorling A (2006) Chem Phys Lett 426:234
110. Wu Q, Yang WT (2002) J Chem Phys 116:515
111. Grimme S, Antony J, Ehrlich S, Krieg HJ (2010) J Chem Phys 132:154104
112. Di Labio GA (2008) Chem Phys Lett 455:348
113. Johnson ER, Becke AD (2006) J Chem Phys 124:174104
114. Seidl A, Gorling A, Vogl AP, Majewski JA, Levy M (1996) Phys Rev B 53:3764
115. Yang WT, Ayers PW, Wu Q (2004) Phys Rev Lett 92:146404
116. Vandevondele J, Sprik M (2005) Phys Chem Chem Phys 7:1363
117. Perdew JP (1985) Int J Quantum Chem 28:497

118. Yang WT, Zhang YK, Ayers PW (2000) Phys Rev Lett 84:5172
119. Mori-Sanchez P, Cohen AJ, Yang WT (2008) Phys Rev Lett 100:146401
120. Grafenstein J, Cremer D (2005) Mol Phys 103:279
121. Cohen AJ, Mori-Sanchez P, Yang WT (2008) J Chem Phys 129:121104
122. Janesko BG, Henderson TM, Scuseria GE (2009) Phys Chem Chem Phys 11:443
123. Handy NC, Cohen AJ (2001) Mol Phys 99:403
124. Mori-Sanchez P, Cohen AJ, Yang WT (2009) Phys Rev Lett 102:66403
125. Johnson ER, Contreras-Garcia J (2011) J Chem Phys 135:81103
126. Janak JF (1978) Phys Rev B 18:7165
127. Perdew JP, Levy M (1993) Phys Rev Lett 51:1884
128. Margenau H, Kestner NR (1969) Theory of interatomic, forces, 2nd edn. Pergamon Press, Oxford
129. Runge E, Gross EKU (1984) Phys Rev Lett 52:997
130. Casida ME (1995) In: Chong DP (ed) Time-dependent density-functional response theory for molecules, vol 1, Chap. 5. World Scientific, Singapore, pp 155–192
131. Casida ME, Jacquemin D, Chermette H (2009) J Mol Struct Theochem 914:1
132. Faber C, Boulanger P, Attaccalite C, Cannuccia E, Duchemin I, Deutsch T, Blasé X (2015) Phys Rev B 91:155109
133. Meyer HD, Gatti F, Worth GA (eds) (2009) Multidimensional quantum dynamics: MCTDH theory and applications. Wiley-VCH, Weinheim
134. Hughes ZA, Walsh TR (2015) Nanoscale Rev 7:6883
135. Jorgensen WL, Maxwell D, Tirado-Rives J (1996) J Am Chem Soc 118:11225
136. Azadi S, Foulkes WMC (2015) J Chem Phys 143:102807
137. Shulenburger L, Mattsson TR (2013) Phys Rev B Condens Matter Mater Phys 88:245117
138. Wagner LK, Abbamonte P (2014) Phys Rev B Condens Matter Phys 90:125129
139. Morales MA, McMinis J, Clark BK, Kim J, Scuseria GE (2012) J Chem Theory Comput 8:2181–2188
140. Drummond ND, Monserrat B, Lloyd-Williams JH, López Ríos P, Pickard CJ, Needs RJ (2014) Nat Commun 6:7794
141. Clay R, Morales MA (2015) J Chem Phys 142:234103
142. Tuckerman ME (2002) J Phys Condens Matter 14:1297
143. Kirchner B, di Dio PJ, Hutter J (2012) Top Curr Chem 307:109
144. Liu W, Tkatchenko A, Scheffler M (2014) Top Catal 57:40
145. Menikarachi LC, Gascon JA (2010) Curr Top Med Chem 10:46
146. Potoyan DA, Savelyev A, Papoian GA (2012) WIREs Comput Mol Sci. doi:10.1002/wcms.1114
147. Saunders MG, Voth GA (2013) Annu Rev Biophys. doi:10.1146/annurev-biophys-083012-130348
148. Carbone P, Avendaño C (2014) WIREs Comput Mol Sci 4:62–70. doi:10.1002/wcms.1149
149. Karimi-Varzaneh HA, Muller-Plathe F (2012) Top Curr Chem 307:295
150. Salerno KM, Anupriya A, Perahia D, Grest GS (2016) Phys Rev Lett 116:058302
151. Balaji V, Benson R, Wyman B, Held I (2016) Geosci Model Dev Discuss. doi:10.5194/gmd-2016-114
152. Li Y, Abberton BC, Kroger M, Liu WK (2013) Polymers 5:751
153. Jain A, Shin Y, Persson KA (2016) Nat Rev/Mater 1. doi:10.1038/natrevmats.2015
154. Aydinol M, Kohan A, Ceder G, Cho K, Joannopoulos J (1997) Phys Rev B 56:1354
155. Zhou F, Cococcioni M, Kang K, Ceder G (2004) Electrochem Commun 6:1144
156. Ceder G (2010) MRS Bull 35:693
157. Greeley J, Jaramillo TF, Bonde J, Chorkendorff IB, Nørskov JK (2006) Nat Mater 5:909
158. Alapati SV, Johnson JK, Sholl DS (2006) J Phys Chem B 110:8769
159. Siegel D, Wolverton C, Ozolins V (2007) Phys Rev B 76:134102
160. Persson KA, Waldwick B, Lazic P, Ceder G (2012) Phys Rev B 85:235438
161. Chang KJ, Cohen MML (1984) Phys Rev B 30:5376
162. Pickard CJ, Needs RJ (2006) Phys Rev Lett 97:045504

163. Mazin II (2010) Nature 464:183
164. Li Y, Hao J, Liu JH, Li Y, Ma Y (2014) J Chem Phys 140:174712
165. Yu Y, Zunger A (2012) Phys Rev Lett 108:068701
166. Körzdörfer T, Brédas JL (2014) Chem Res 47:3284
167. Shin Y, Liu J, Quigley JJ, Luo H, Lin X (2014) ACS Nano 8:6089
168. Tritt T, Subramanian M (2006) MRS Bull 31:188
169. Madsen GKH (2006) J Am Chem Soc 128:12140
170. Wang CC, Pilania G, Ramprasad R (2013) Phys Rev B 87:35103
171. De Angelis F, Di Valentin C, Fantacci S, Vittadini A, Selloni A (2014) Chem Rev 114:9708
172. Silva JCF, dos Santos JD, Taft CA, Longo E (2016) Curr Phys Chem 6:805
173. Silva GO, Santos JD, Martins JBL, Taft CA, Longo E (2016) Curr Phys Chem 6:10
174. Costa RJ, Martins JBL, Longo E, Taft CA, Santos JD (2016) Curr Phys Chem 6:60
175. Sodre JM, Longo E, Taft CA, Martins JBL, dos Santos JD Comptes Reundus Chimie. doi:10.1016/j.crci2016.05.023
176. Dreuw A (2006) Chem Phys Chem 7:2259
177. da Silva CHTP, Taft CA (2004) J Biomolec Struc Dyn 22:59
178. da Silva CHTP, Carvalho I, Taft CA (2005) J Comp Aided Molec Des 19:83
179. da Silva CHTP, Taft CA, Carvalho I (2006) J Theor Computat Chem 5:579
180. da Silva VB, Andrioli WJ, Carvalho I, Taft CA, da Silva CHTP (2007) J Theor Comput Chem 6:811
181. da Silva VB, Kawano DF, Gomes AS, Carvalho I, Taft CA, da Silva CHTP (2008) J Phys Chem A 112:8902
182. Hage-Mellin LIS, da Silva CHTP, Semighini EP, Taft CA, Sampaio SV (2009) J Biomolec Struct Dyn 27:27–36; (185) da Silva CHTP, da Silva VB, Resende J, Rodrigues PF, Bononi FC, Benevenuto CG, Taft CA (2010) J Molec Graph Model 28:513
183. da Silva VB, Leopoldino AM, da Silva CHTP, Taft CA (2011) Drug Metab Lett 5:267
184. Ferreira FP, Couto WF, Fontana F, Taft CA, da Silva CHTP (2014) Curr Phys Chem 4:94105
185. Federico LB, de Almeida JR, Taft CA, da Silva CHTP (2015) Curr Phys Chem 3:253; (188) Hage-Melim L, Sampaio S, Taft CA, da Silva CHTP (2013) Mini Rev Med Chem 13:1348
186. de Souza R, Picanço RM, Pinheiro AA, da Silva KR, Taft CA, da Silva CHTP, dos Santos CBR, da Silva LR, Hage-Melim L (2016) Curr Phys Chem 1:40
187. da Silva CHTP, Taft CA (2016) J Biomolec Struct Dyn. doi.org/10.1080/07391102.2016.1237382