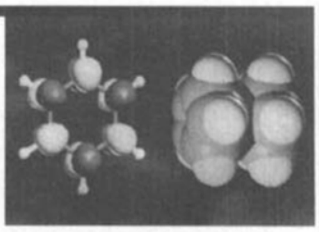
COMPUTATIONAL CHEMISTRY COLUMN



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All You Always Wanted to Know About Density Functional Theory...

Although, properly speaking, density functional theory (DFT) can not be qualified as a recent quantum chemical method (the basic theorems trace back to 1964), one observes nowadays such an increase of DFT applications in computational chemistry that we found it timely to devote one *Column* to introduce the basic concepts and gross features of this model. However, as usual in our short reports, it is out of question to carry out an in-depth presentation of the formalism, inasmuch as its physical and mathematical foundations are rather complex. Instead, we shall review the most important characteristics of DFT, as compared with more traditional quantum chemical methods, and outline some of its most promising applications in the areas of the calculation of both structural and electronic properties of a broad range of systems, and of first-principles molecular dynamics simulations as well. This is why this *Column* is immodestly entitled: 'all you always wanted to know about DFT...', and one could easily imagine to proceed with 'without daring putting too much of your fingers into it'. To make it short, our purpose is to place this model into proper perspective and to give a first impression as to the present state of this rapidly expanding field.

Before focusing on DFT, it is perhaps worthwhile to recall the basic features of the *ab initio* methods traditionally used in quantum chemistry. This denomination generally applies to models which, given an initial choice of the form of the wave function of a chemical system with *n* electrons, attempt to solve the stationary *Schrödinger* equation in the *Born-Oppenheimer* approximation:

$$H\Psi = E\Psi \tag{1}$$

where H is the hamiltonian made of the kinetic and potential energy operators, E is the molecular electronic energy and Ψ is the n-particle solution

$$\Psi(\mathrm{r}_1, \mathrm{r}_2, \ldots, \mathrm{r}_n) \tag{2}$$

Ab initio means that no empirical parameters are introduced to solve *Eqn. 1*. The simplest form of Ψ (*Eqn. 2*) is an antisymmetrized product of n one-electron functions ϕ_i, known as molecular orbitals (MOs), which are solutions of the *Hartree-Fock* (*HF*) equations:

$$h^{\mathrm{eff}}_{HF}\,\phi_i(\mathrm{r}) = \varepsilon_i\phi_i(\mathrm{r}) \qquad i = 1, \ldots, n \tag{3}$$

where h^{eff}_{HF} is the effective one-particle *HF* hamiltonian and ε_i is the energy of MO ϕ_i.

The problem with the *ab initio HF* method is that it neglects the instantaneous repulsion between electrons that is at the origin of the so-called correlation energy, which means that the behavior of each electron is dictated by the *average* position of all the others. To improve the accuracy of *HF* solutions, time-consuming, 'configuration interaction' or 'perturbation' techniques, which correct for electron correlation effects, must be used.

The basic idea of DFT is to replace the complicated n-electron wave function (*Eqn. 2*) and the associated *Schrödinger* equation (*Eqn. 1*) by the much simpler electron density $\rho(\mathrm{r})$ and its associated calculational scheme. This choice can be done without loss of rigor, as it has been shown by *Hohenberg* and *Kohn* in their famous theorem reported in 1964 [1] that the ground-state energy of a many electron system is completely and uniquely determined by its electron density, although the explicit functional dependence of the energy on density is not entirely known.

Let us open a parenthesis to refresh your mind about the notion of functional. Recall that a function $f(x)$ is a rule that associates a number with each value of the variable x. For example, the function $f(x) = x^2 + 1$ associates the number 10 with the value 3 of x. A functional $F[f]$ is a rule that associates a number with each function f. For example, the functional

$$F[f] = \int_{-\infty}^{\infty} f^2(x)\,\mathrm{d}x$$

associates a number, found by integration of $f^2(x)$ over all space, with each quadratically integrable function $f(x)$.

Coming back to DFT, *Hohenberg* and *Kohn* proved that the ground-state molecular energy (E_0), wave function, and all other electronic properties are uniquely determined by the knowledge of the electron density ρ at every point r of the molecular volume, *i.e.* a function of three variables only. One says that E_0 is a functional of ρ and writes $E_0[\rho]$, with $\rho=\rho(\mathrm{r})$. However, the *Hohenberg-Kohn* theorem does not tell us how to calculate E_0 from ρ or how to find ρ without first finding Ψ! That is, there is at present no rigorous procedure to exactly derive E_0 from ρ and one is left with approximations. Well, you are going to say, what are then the advantages to work with ρ, since we have anyway to use approximate expressions for $E_0[\rho]$? There are indeed two advantages:

- for a comparable level of accuracy, the DFT equations leading to ρ (see below) are easier to solve than the corresponding *ab initio* ones;
- the *Hohenberg-Kohn* theorem provides both impetus and theoretical foundations to strive to advance the calculational procedures to higher and higher accuracy.

Practical applications of DFT became feasible with the work of *Kohn* and *Sham* (KS) who derived in 1965 [2] a set of one-electron equations from which one could in principle obtain the exact electron density and hence the total energy. These equations write as follows:

$$h^{\text{eff}}_{\text{KS}}\ \psi_i(\text{r}) = \varepsilon_i\ \psi_i(\text{r}) \qquad i = 1, \ldots, n \qquad (4)$$

where $h^{\text{eff}}_{\text{KS}}$ is the effective *Kohn-Sham* one-electron hamiltonian, generally expressed as a functional of ρ, $\psi_i(\text{r})$ are the *Kohn-Sham* orbitals (which should not be confused with the *HF* MOs ϕ_i of *Eqn. 3*) and ε_i their associated energies. *Kohn* and *Sham* also showed that the electron density can be calculated from the ψ_i's according to

$$\rho(\text{r}) = \sum_{i=1}^{n} |\ \psi_i(\text{r})\ |^2 \qquad (5)$$

Actually, the *Kohn-Sham* orbitals ψ_i have no physical significance other than in allowing the exact $\rho(\text{r})$ to be calculated from *Eqn. 5*. Indeed, there is no DFT molecular wave function which can be built from the $\psi_i(\text{r})$. Nevertheless, it is interesting to notice that both *Hartree-Fock* and *Kohn-Sham* theories provide one-electron equations for describing many electron systems.

There is only one problem in using *Kohn-Sham* equations to find $\rho(\text{r})$: no one knows what the correct functional $h^{\text{eff}}_{\text{KS}}[\rho]$, and particularly its so-called exchange-correlation part, is for molecules. This means that approximate functionals have to be used in molecular calculations. To investigate the accuracy of a particular approximate functional, one has to use it in DFT calculations and to compare the computed molecular properties with their experimental values. The lack of a systematic procedure for improving the functional, and hence improving calculated molecular properties, is a real drawback of DFT. However, the advantages are that efficient techniques are now available to solve the *Kohn-Sham* equations more rapidly than the *Hartree-Fock* ones; in addition, some functionals recently developed for $h^{\text{eff}}_{\text{KS}}[\rho]$ incorporate correlation effects to the same extent as second-order *Rayleigh Schrodinger* perturbation theory [3–5], *i.e.* the MP2 formalism well known to the *ab initioists*.

To summarize, the *Kohn-Sham* equations are fundamental in DFT as they serve as a starting point for approximate methods. These schemes can now be considered as approximations to a rigorous theory rather than just models and the recent spectacular progresses in DFT are due both to the development of more accurate procedures to solve these equations and to their efficient implementation on mainframe computers and workstations.

Whatever the form of the exchange-correlation potential term of $h^{\text{eff}}_{\text{KS}}$, various schemes have thus been proposed to solve the *Kohn-Sham* one-electron equations. The oldest method is undoubtedly the so-called multiple scattering (MS) or scattered-wave one, where the molecular volume is partitioned into (spherical) atomic, interatomic and (spherical) extramolecular regions. The KS potential is generally taken from the Xα formalism, *i.e.* without explicit inclusion of correlation, and approximated as a spherical or volume average in each region. In spite of these simplifications, the MS-Xα model has led to good predictions of the electronic structure and related properties of transition-metal complexes. However, although it is still in use today for such calculations, this model does generally lead to an inconsistent variation of total energy as a function of structural parameters, which makes it impractical for predicting the minima of potential energy surfaces. As the optimization of geometrical parameters is often considered as priority number one in molecular modeling applications, the MS-Xα method can at best be used as a second step technique, once the geometry of the compound under study has been extracted from a structural data bank or optimized by another tool. It is, therefore, not surprising that the MS-Xα model has been supplanted by more elaborate DFT methods, which rest generally on the use of the popular LCAO approximation, to solve the *Kohn-Sham* equations.

Two different LCAO DFT schemes have been proposed almost simultaneously in the early seventies; the so-called discrete variational method (DVM) [6], which uses a *Slater*-type orbital basis set, and the linear combination of *Gaussian*-type orbital (LCGTO)-local spin density (LSD) technique suggested by *Sambe* and *Felton* [7] Both techniques, which have been considerably refined and improved in the last few years, rely on the fit of the electron density to one-center auxiliary functions so as to achieve a faster calculation of the *Coulomb* (and exchange in the case of LCGTO-LSD) operator of $h^{\text{eff}}_{\text{KS}}$. This leads roughly to a N^3 scaling of the computational effort involved by a LCAO-DFT calculation, where N is the size of the one-electron basis set, as compared with the N^4 dependence of the *Hartree-Fock* scheme. This explains the growing popularity of these LCAO-DFT schemes, as they allow to perform calculations on large clusters (comprising typically 10–20 transition metal atoms) and organometallics (made of up to 50 atoms). In addition, the range of application of these techniques has been recently extended by the development of pseudopotentials, relativistic corrections, and the calculation of energy gradients for geometry optimization purposes.

Many DFT applications have indeed been reported for a broad range of compounds, mostly inorganic or organometallic, and of properties: ground-state geometries, activation energies, dissociation energies, vibrational frequencies, dipole moments, polarizabilities, ionization energies, excitation energies, proton affinities, electrostatic potentials, chemisorption energies, *etc.* In general, the results are very satisfactory, being at least of the quality of *ab initio* calculations performed using a large (polarized) basis set at the MP2 (second-order *Moller-Plesset* perturbation theory) level, *i.e.* including a fair amount of electron correlation [3–5][8].

Several good DFT program packages are available today for such applications: DMol (developed by *B. Delley* in Zürich) [9], deMon (*D. Salahub*, Montréal) [10], DGauss (*E. Wimmer*, Minneapolis) [3], AMol (*E. Baerends*, Amsterdam) [6] and Numol (*A. Becke*, Kingston) [11]. However, it is unfortunate that they are in general available to the community of computational chemists only through commercial software companies which sell them at rather expensive conditions. In this context, we heard recently that a future release of the *Gaussian* series of programs initiated by the group of John Pople could well include a DFT code.

Finally, we should mention that DFT plays also an important role in molecular dynamics (MD) simulations through the so-called first-principles MD scheme developed recently by *Car* and *Parrinello*. In this method, the interatomic forces acting on the atoms of the system investigated are computed, as the simulation proceeds, using electronic structure calculations based on DFT. The interatomic potential is thus parameter-free and derived from first principles, with no experimental input. The *Car-Parrinello* method has been recently applied to a variety of problems which had previously been inaccessible, such as the determination of the physical properties of disordered systems in their liquid and amorphous states, the investigation of processes relevant to semi-conductor technology, *e.g.* the diffusion of hydrogen in silicium, as well as the study of surface reconstruction and molecular clusters. In addition, this method shows undeniable promises for the simulation of the behavior of molecular and biochemical systems, both in gas phase and in solution, as a function of temperature. It is not possible to present here the *Car-Parrinello* method with many more details, but we intend to come back to this promising technique in a future Column.

So, after having been through this initiation to the mysteries of density functional theory, when do you like us to proceed with a more detailed presentation and, why not, guide your first steps as a new DFT user? In the meantime, you might take advantage of excellent reviews [12][13] and textbooks [14–16] which appeared recently on this rather hot topic.

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[2] W. Kohn, L.J. Sham, *Phys. Rev.* **1965**, *140*, A1133.
[3] J. Andzelm, E. Wimmer, *J. Chem. Phys.* **1992**, *96*, 1280.
[4] C.W. Murray, G.J. Laming, N.C. Handy, R.D. Amos, *Chem. Phys. Lett.* **1992**, *199*, 551.
[5] A.D. Becke, *J. Chem. Phys.* **1992**, *97*, 9173.
[6] E.J. Baerends, D.E. Ellis, P. Ros, *Chem. Phys.* **1973**, *2*, 41.
[7] H. Sambe, R.H. Felton, *J. Chem. Phys.* **1975**, *62*, 1122.
[8] P.M.W. Gill, B.G. Johnson, J.A. Pople, M.J. Frisch, *Int. J. Quantum Chem. Symp.* **1992**, *26*, 319.
[9] B. Delley, *J. Chem. Phys.* **1990**, *92*, 508.
[10] D.R. Salahub, R. Fournier, P. Mlynarski, I. Papai, A. St-Amant, J. Ushio, in 'Density Functional Methods in Chemistry' Eds. J.K. Labanowski, and J.W. Andzelm, Springer, New York, 1991, p. 77.
[11] A.D. Becke, *Int. J. Quantum Chem. Symp.* **1989**, *23*, 599.
[12] S. Borman, *Chem. Eng. News* **1990**, *68*(15), 22.
[13] T. Ziegler, *Chem. Rev.* **1991**, *91*, 651.
[14] R.G. Parr, W. Yang, 'Density-Functional Theory of Atoms and Molecules', Oxford University Press, New York, 1989.
[15] E.S. Kryachko, E.V. Ludena, 'Density-Functional Theory of Many Electron Systems'' Kluwer, Dordrecht, 1991.
[16] N.H. March, 'Electron Density Theory of Atoms and Molecules', Academic, New York, 1992.

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Third Swiss-Japanese Joint Meeting on Bioprocess Development: Montreux, 25–27 October 1992

Hans Georg W. Leuenberger* and **H. Michael Widmer****

The Third Swiss-Japanese Joint Meeting on Bioprocess Development took place in Montreux from 25 to 27 October 1992. It was organized by Prof. Dr. *Armin Fiechter* and his team from the Institute of Biotechnology at the Swiss Federal Institute of Technology in Zürich (ETHZ) and was held under the auspices of the Swiss Coordination Committee of Biotechnolo-

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