those of AOs. Electrons fill MOs in the diagram according to the *Aufbau principle* (electrons occupy MOs in order of increasing energy), *Pauli exclusion principle* (each MO can only occupy two antiparallel electrons), and *Hund's rule* (when electrons occupy degenerate MOs, they will first fill each orbital singly with parallel spins before pairing up). Using the diagram, one can evaluate bond orders, determine paramagnetic and diamagnetic properties, and quantitatively describe conjugation, hyperconjugation, and aromaticity.

Even though localization and hybridization are concepts from VBT, it can be integrated with MOT to explain molecular geometry and bonding through, for example, the *natural bond orbital* analysis [39, 40]. Localized molecular orbitals (LMOs) are obtained through the unitary transformation of the conventional, delocalized MOs. LMOs are spatially concentrated in specific regions of a molecule and thus provide an intuitive picture of bonding that resembles the traditional Lewis structure, where bonds are localized between pairs of atoms and lone pairs are confined to specific atoms.

Molecules have symmetry, so do AOs and MOs. AOs that have the same symmetry with respect to a molecule's symmetry elements can mix and form MOs, whereas those with different symmetries do not interact, due to orthogonality. LCAO preserves the symmetry property of the molecule, leading to the *orbital symmetry conservation principle* in MOT [38]. As a result, MOs inheriting the symmetry of a molecule can be classified as σ, π, δ, or with symmetry labels such as a_1 and b_2. Based on this principle for chemical reactions, Woodward and Hoffmann proposed a set of rules, called the *Woodward–Hoffmann rules* [37, 38], to predict the outcome of pericyclic reactions.

The frontier molecular orbital (FMO) theory proposed by Kenichi Fukui is a conceptual framework in MOT to explain and predict chemical reactivity and selectivity [36, 41, 42]. It focuses on the interaction between the highest-occupied MO and the lowest-unoccupied molecular orbital of the reactants. These orbitals, referred to as the "frontier orbitals," are most important in governing the reactivity of molecules. Because of this work, Fukui shared the 1981 Nobel Prize in Chemistry with Roald Hoffmann for his contribution to establishing the Woodward–Hoffmann rules.

1.4 Density Functional Theory

DFT [9] has been the workhorse in the past few decades as the most widely used computational method to simulate the electronic structure of molecules and condensed matter alike [43]. It has become a cornerstone of materials science, chemistry, and condensed matter physics due to its balance of remarkable accuracy and computational efficiency. At its core, unlike VBT and MOT, DFT avoids directly solving the Schrödinger equation, Eq. (1.1), with an approximate many-electron wavefunction Ψ. Instead, it rewrites Eq. (1.2) as

$$E = E[\rho], \tag{1.16}$$

where $\rho \equiv \rho(\mathbf{r})$ stands for the electron density of a many-electron system in the ground state, which is a function of only three spatial coordinates and is normalized to N,

$$\int \rho(\mathbf{r}) d\mathbf{r} = N, \tag{1.17}$$

where N is the total number of electrons in the system. This electron density $\rho(\mathbf{r})$ can be obtained experimentally from X-ray crystallography. It can also be obtained from wavefunction theory from the N-body wavefunction, $\Psi(\mathbf{r}_1, \mathbf{r}_2, \ldots, \mathbf{r}_N)$,

$$\rho(\mathbf{r}) = N \iint \cdots \int |\Psi(\mathbf{r}, \mathbf{r_2}, \ldots, \mathbf{r_N})|^2 \, \mathrm{d}\mathbf{r_2} \, \mathrm{d}\mathbf{r}_3 \cdots \mathrm{d}\mathbf{r}_N, \tag{1.18}$$

or MOs $\{\psi_i(\mathbf{r})\}$,

$$\rho(\mathbf{r}) = \sum_{i=1}^{\mathrm{occ}} |\psi_i(\mathbf{r})|^2, \tag{1.19}$$

where the sum runs over all occupied MOs in the single-particle approximation, such as in Hartree–Fock theory.

The idea of describing an electronic system by its density goes back to the Thomas–Fermi model developed separately by Thomas [44] and Fermi [45]. In these early works, the electron density was used as a central variable. However, the notation was not entirely standardized then. Many authors used symbols like $n(\mathbf{r})$ or $\rho(\mathbf{r})$ interchangeably to denote the electron density. To the best of the author's knowledge, it was Dirac's 1930 paper "Note on Exchange Phenomena in the Thomas Atom" [46] that derived an expression for the exchange energy of an electron gas and formulated it in terms of the local electron density, denoted by $\rho(\mathbf{r})$. This paper can be credited as the first influential instance where the symbol $\rho(\mathbf{r})$ was used explicitly to represent the electron density.

Equation (1.16) suggests that the total energy of the system is a functional of the electron density, as opposed to Eq. (1.2), where the total energy is a functional of the many-electron wavefunction,

$$E \equiv E\left[\Psi(\mathbf{r_1}, \mathbf{r_2}, \ldots, \mathbf{r_N})\right]. \tag{1.20}$$

This reformulation of Eq. (1.16) is based on the two Hohenberg–Kohn theorems [8]. The first one states that there is a one-to-one mapping between the electron density $\rho(\mathbf{r})$ and the external potential $v_{\mathrm{ext}}(\mathbf{r})$ in the ground state. This suggests that all ground state properties of the system are functionals of the electron density, including the total energy,

$$E[\rho] = F[\rho] + \int \rho(\mathbf{r}) v_{\mathrm{ext}}(\mathbf{r}) \mathrm{d}\mathbf{r}, \tag{1.21}$$

where $F[\rho]$ is the universal density functional. The second theorem asserts that the correct ground-state electron density should minimize the total energy functional, thus providing a variational principle for Eq. (1.21) and yielding the following Euler equation,

$$\mu = \frac{\delta E[\rho]}{\delta \rho(\mathbf{r})} = \frac{\delta F[\rho]}{\delta \rho(\mathbf{r})} + \upsilon_{\text{ext}}(\mathbf{r}), \tag{1.22}$$

where μ is the chemical potential and $\delta/\delta\rho(\mathbf{r})$ is the functional derivative with respect to the electron density [9].

According to these theorems, in principle, any energetic component of the total electronic energy can be rigorously expressed by a density functional, but in practice it is impossible to do so. In DFT, a conventional partition of the total electronic energy is the following,

$$E[\rho] = T_S[\rho] + V_{ne}[\rho] + J[\rho] + E_{xc}[\rho], \tag{1.23}$$

where T_S is the noninteracting total kinetic energy, V_{ne} the electron–nucleus attraction, J the electron–electron Coulombic repulsion, and E_{xc} the exchange–correlation energy, which captures the quantum mechanical effects of electron exchange and correlation. Note that when calculating the total energy, one should add the electrostatic repulsion among nuclei, V_{nn}. Among the four components in Eq. (1.23), only two terms are known to have an explicit expression in terms of the electron density. The first is $V_{ne}[\rho]$, which is the second term at the right-hand side of Eq. (1.21), and the other is the classical electron–electron Coulombic repulsion $\mathrm{J}[\rho]$,

$$J[\rho] = \frac{1}{2}\iint \frac{\rho(\mathbf{r})\rho(\mathbf{r}')}{|\mathbf{r} - \mathbf{r}'|} \boldsymbol{d}\mathbf{r}\boldsymbol{d}\mathbf{r}'. \tag{1.24}$$

For $T_S[\rho]$ and $E_{xc}[\rho]$, their exact expression in terms of the electron density is unknown.

To overcome this difficulty, Kohn and Sham [47] introduced a fictitious system of noninteracting electrons moving in the so-called Kohn–Sham orbitals $\{\psi_i(\mathbf{r})\}$ with an effective potential $\upsilon_{eff}(\mathbf{r})$, so the same ground-state electron density $\rho(\mathbf{r})$ as the interacting system is reproduced

$$\rho(\mathbf{r}) = \sum_{i=1}^{N} |\psi_i(\mathbf{r})|^2, \tag{1.25}$$

the noninteracting total kinetic energy is expressed as

$$T_S[\rho] = -\frac{1}{2}\sum_{i=1}^{N} \int \psi_i(\mathbf{r}) \nabla^2 \psi_i(\mathbf{r}) \mathrm{d}\mathbf{r}, \tag{1.26}$$

and then the Kohn–Sham equation is obtained as,

$$\left(-\frac{1}{2}\nabla^2 + \upsilon_{eff}(\mathbf{r})\right)\psi_i(\mathbf{r}) = \epsilon_i \psi_i(\mathbf{r}), \tag{1.27}$$

where the effective Kohn–Sham potential is composed of several terms,

$$\upsilon_{eff}(\mathbf{r}) = \upsilon_{ext}(\mathbf{r}) + \upsilon_J(\mathbf{r}) + \upsilon_{xc}(\mathbf{r}), \tag{1.28}$$

with the classical Coulombic potential

$$v_J(\mathbf{r}) = \int \frac{\rho(\mathbf{r}')}{|\boldsymbol{r} - \mathbf{r}'|} d\mathbf{r}', \tag{1.29}$$

and the exchange–correlation potential

$$v_{xc}(\mathbf{r}) = \frac{\delta E_{xc}[\rho]}{\delta \rho(\mathbf{r})}. \tag{1.30}$$

In the Kohn–Sham scheme, the total kinetic energy is obtained by Eq. (1.26), so there is only one unknown left in Eq. (1.23) to approximate, which is the exchange–correlation energy density functional $E_{xc}[\rho]$.

The development and history of DFT are closely tied to the search for better exchange–correlation functionals because $E_{xc}[\rho]$ is the key approximation in the Kohn–Sham equation that determines its accuracy and applicability. The local density approximation (LDA) was the first form proposed, and it is the simplest exchange–correlation functional. It assumes that the exchange–correlation energy at any point in space depends only on the local electron density at that point,

$$E_{xc}^{\mathrm{LDA}} = \int \rho(\mathbf{r}) e_{xc}(\rho(\mathbf{r})) d\mathbf{r}, \tag{1.31}$$

where $e_{xc}(\rho)$ is the exchange–correlation energy per particle. LDA works surprisingly well for systems with slowly varying electron densities (e.g., simple metals) but fails for systems with strong inhomogeneities (e.g., atoms, molecules, surfaces). To address the limitations of LDA, the generalized gradient approximation (GGA) [48] was developed, including not only the local electron density but also its gradient,

$$E_{xc}^{\mathrm{GGA}} = \int \rho(\mathbf{r}) e_{xc}(\rho(\mathbf{r}), \nabla\rho(\mathbf{r})) d\mathbf{r}. \tag{1.32}$$

GGA functionals, such as B88 (Becke 88) [49], Lee–Yang–Parr (LYP) [50], and Perdew–Burke–Ernzerhof [51], significantly improved the accuracy of DFT for molecular systems, bond energies, and structural properties. Another popular category is the hybrid functional, such as B3LYP (Becke 3-parameter Lee-Yang-Parr), mix a portion of exact exchange from Hartree–Fock theory with GGA exchange and correlation,

$$E_{xc}^{\mathrm{Hybrid}} = aE_x^{\mathrm{HF}} + (1-a)E_x^{\mathrm{GGA}} + E_c^{\mathrm{GGA}}, \tag{1.33}$$

where E_x^{HF} is the exact exchange energy from Hartree–Fock theory.

Other kinds of approximate exchange–correlation functionals in DFT are (i) meta-GGA functionals, such as Tao–Perdew–Staroverov–Scuseria [52] and Strongly Constrained and Appropriately Normed [53], which go beyond GGA by including higher-order derivatives of the electron density (e.g., the kinetic energy density), and (ii) range-separated hybrid and double hybrid functionals [54], which further refine the treatment of exchange and correlation energies by incorporating long-range corrections and perturbative correlation, respectively.

Unlike ab initio wavefunction theory methods in Figure 1.3, where a clear pathway is available to systematically improve the accuracy, DFT does not have such a route.

Figure 1.5 The Jacob's ladder in DFT (Generated with AI using DALL·E—OpenAI).

Still, the Jacob's ladder metaphor in DFT, shown in Figure 1.5, represents the hierarchy of increasingly accurate density functionals. This "ladder" metaphor, introduced by John P. Perdew, compares functional development to climbing a ladder toward the "heaven" of chemical accuracy. Each rung of the ladder corresponds to a level of approximation, with higher rungs providing greater accuracy but also increasing computational cost. It serves as a framework to understand the tradeoff between accuracy and computational cost in DFT, guiding researchers in choosing the appropriate functional for their systems.

DFT has become immensely popular over the last few decades due to its unique combination of accuracy, versatility, and computational efficiency. While DFT is powerful and widely used, its limitations arise primarily from approximations in the exchange–correlation functional and its inability to handle specific phenomena like strong correlation, excited states, or van der Waals interactions. Manifested by, for example, the self-interaction error [55], it overestimates electron delocalization, leading to incorrect prediction of properties like band gaps, dissociation energies, and ionization potentials. On the other hand, it underestimates electron localization, causing a poor description of charge transfer, oxidation states, spin states, or

electronic configurations of localized systems such as transition metal complexes. These errors arise because DFT functionals do not fully capture the complex exchange and correlation effects. Recent developments, such as double hybrid functionals (e.g., B2PLYP), combine a portion of exact exchange with a perturbative treatment of correlation, providing a more balanced description of delocalized and localized states. Additionally, ML techniques are being used to develop new functionals that better capture the complexities of electron delocalization and localization [56–58].

1.5 Scope of This Book

We want insight, not just numbers [20]. Any electronic structure theory should provide a new understanding of traditional chemical concepts. As highlighted in Section 1.3, VBT did that with the insight into chemical bonding, and MOT provided the FMO theory, orbital symmetry conservation principle, and Woodward–Hoffmann rules. They are both orbital-based. In DFT, electron density is the basic variable. To the best of the author's knowledge, there is no systematic work to present all conceptual frameworks to harness chemical understanding using density-based ideas [59–61]. Conceptual DFT (CDFT) [9, 62–65] is the first effort in DFT to analyze chemical reactivity in terms of global and local descriptors such as electronegativity, hardness, and electrophilicity. Other efforts such as quantum theory of atoms in molecules (QTAIM) [66], electron localization function (ELF) [67], and noncovalent interaction (NCI) [68, 69] analyses are also available in the literature. However, their scope is limited, and controversies are abundant. The purpose of this book is to fill the knowledge gap by providing a systematic overview of how to employ density-based ideas to harvest chemical insights, including covalent bonding, weak interactions, conformational stability, acidity/basicity, electrophilicity, nucleophilicity, aromaticity, stereoselectivity, and catalysis, with density-based descriptors.

In what follows, in Part I of this book, we will present the four density-based frameworks, including CDFT (Chapter 2), density-associated quantities (Chapter 3), information-theoretic approach (Chapter 4), and orbital-free DFT (Chapter 5), and the interrelationships among these frameworks as well as a few recent developments (Chapter 6).

In Part II, applications of these four frameworks to real chemical problems are discussed, including covalent and noncovalent interactions (Chapter 7), cooperativity and frustration (Chapter 8), principle of chirality hierarchy and homochirality (Chapter 9), electrophilicity and nucleophilicity (Chapter 10), steric effect and stereoselectivity (Chapter 11), acidity and basicity (Chapter 12), aromaticity and antiaromaticity (Chapter 13), excited states (Chapter 14), catalysis (Chapter 15), and miscellaneous applications (Chapter 16).

In Part III, based on the ideas from this book, in the final two chapters (Chapters 17 and 18), we provide perspectives on how chemical understanding is, in general, obtained with chemical concepts (Chapter 17) and how to expand the territory of chemical reactivity theory by harvesting chemical understanding with ML and quantum computing (Chapter 18).

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