Ab initio modeling of primary processes in photosynthesis : protein induced activation of bacteriochlorophylls for efficient light harvesting and charge separation

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Chapter 2

Theoretical Methods

2.1 Introduction

This chapter provides a short description of theoretical approximations and methods used in this work. First, the Born-Oppenheimer approximation will be reviewed, followed by a brief overview of Density Functional Theory. Next, the basis set approximation will be discussed together with Pople's notation, followed by a discussion on the exchange-correlation functionals. Finally, the perturbative derivative of DFT, the time-dependent DFT, will be presented.

2.2 Born-Oppenheimer Approximation

The time-dependent Schrödinger Equation

$$\widehat{\mathrm{H}}\Psi(\mathbf{r},\mathbf{R},t) = i\hbar\frac{\partial\Psi(\mathbf{r},\mathbf{R},t)}{\partial t} \tag{2.1}$$

is a non-relativistic description of the system and it is valid when particle velocities are small compared to the speed of light. Since $\widehat{\mathrm{H}}$ does not depend on time the equation 2.1 can be simplified to the time-independent Schrödinger Equation:

$$\widehat{\mathrm{H}}\Psi(\mathbf{r},\mathbf{R}) = E\Psi(\mathbf{r},\mathbf{R}) \tag{2.2}$$

Following the Born interpretation of the wavefunction, Ψ has to be normalized:

$$\langle \Psi | \Psi \rangle = 1 \tag{2.3}$$

The Hamiltonian consists of kinetic and potential energy terms:

$$\widehat{\mathrm{H}} = \widehat{\mathrm{T}}_n(\mathbf{R}) + \widehat{\mathrm{T}}_e(\mathbf{r}) + \widehat{\mathrm{V}}_{n-n}(\mathbf{R}) + \widehat{\mathrm{V}}_{e-e}(\mathbf{r}) + \widehat{\mathrm{V}}_{e-n}(\mathbf{r}, \mathbf{R}) \tag{2.4}$$

The kinetic energy operators for nuclei and electrons are written as

$$\widehat{\mathrm{T}}_n = -\frac{\hbar^2}{2} \sum_I^N \frac{1}{M_I} \left(\frac{\partial^2}{\partial x_I^2} + \frac{\partial^2}{\partial y_I^2} + \frac{\partial^2}{\partial z_I^2} \right) \tag{2.5}$$

and

$$\widehat{\mathrm{T}}_e = -\frac{\hbar^2}{2} \sum_i^n \frac{1}{m_i} \left(\frac{\partial^2}{\partial x_i^2} + \frac{\partial^2}{\partial y_i^2} + \frac{\partial^2}{\partial z_i^2} \right) \tag{2.6}$$

The potential energy contains three parts: nuclear–nuclear repulsion, electron–electron repulsion and electron–nuclear attraction, represented as

$$\begin{aligned} \widehat{\mathrm{V}}_{n-n} =& \frac{1}{4\pi\varepsilon_0} \sum_I^N \sum_{J>I}^N \frac{Z_I Z_J e^2}{R_{IJ}}, \\ \widehat{\mathrm{V}}_{e-e} =& \frac{1}{4\pi\varepsilon_0} \sum_i^n \sum_{j>i}^n \frac{e_i e_j}{r_{ij}}, \\ \widehat{\mathrm{V}}_{e-n} =& -\frac{1}{4\pi\varepsilon_0} \sum_i^n \sum_I^N \frac{Z_I e_i^2}{r_{iI}} \end{aligned} \tag{2.7}$$

Since the nuclear mass is much larger than the mass of an electron, it is reasonable to assume that the electronic distribution in a molecule depends mainly on nuclear positions and not on their velocities, and will adapt immediately to any changes in nuclear coordinates. The Born-Oppenheimer approximation introduces therefore the electronic Hamiltonian

$$\begin{aligned} \widehat{\mathrm{H}}_e =& -\frac{\hbar^2}{2} \sum_i^n \frac{1}{m_i} \left(\frac{\partial^2}{\partial x_i^2} + \frac{\partial^2}{\partial y_i^2} + \frac{\partial^2}{\partial z_i^2} \right) + \frac{1}{4\pi\varepsilon_0} \sum_I^N \sum_{J>I}^N \frac{Z_I Z_J e^2}{R_{IJ}} \\ &+ \frac{1}{4\pi\varepsilon_0} \sum_i^n \sum_{j>i}^n \frac{e_i e_j}{r_{ij}} - \frac{1}{4\pi\varepsilon_0} \sum_i^n \sum_I^N \frac{Z_I e_i^2}{r_{iI}}, \end{aligned} \tag{2.8}$$

which describes the electron motion in the field of fixed nuclei. By introducing atomic units ($e = m = \hbar = 1$) and the Laplacian operator

$$\Delta \equiv \nabla^2 \equiv \left(\frac{\partial^2}{\partial x^2} + \frac{\partial^2}{\partial y^2} + \frac{\partial^2}{\partial z^2} \right) \tag{2.9}$$

equation (2.8) can be rewritten as

$$\widehat{\mathrm{H}}_e = -\frac{1}{2} \sum_i^n \Delta_i + \sum_I^N \sum_{J>I}^N \frac{Z_I Z_J}{R_{IJ}} + \sum_i^n \sum_{j>i}^n \frac{1}{r_{ij}} - \sum_i^n \sum_I^N \frac{Z_I}{r_{iI}} \tag{2.10}$$

Solving the electronic Schrödinger equation for fixed nuclear coordinates

$$\widehat{\mathrm{H}}_e \Psi_e(\mathbf{r}; \mathbf{R}) = E_{eff}(\mathbf{R}) \Psi_e(\mathbf{r}; \mathbf{R}) \tag{2.11}$$

leads to an effective nuclear potential E_{eff} that describes the potential energy surface of the system and characterize the nuclear Hamiltonian:

$$\widehat{\mathrm{H}}_n = \widehat{\mathrm{T}}_n(\mathbf{R}) + E_{eff}(\mathbf{R}) \tag{2.12}$$

2.3 Density Functional Theory

The well-known wave function *ab initio* approach to solving the Schrödinger equation forms a well defined hierarchy offering systematic improvement towards the exact solution of the equation. However, a wavefunction for a closed-shell system, which contains all information about a given state of a system of electrons, is defined in 3N dimensional space. Hence the complexity of the problem increases with the size of the system. An alternative approach is offered by density functional theory where only the electron density is considered. This significantly reduces the complexity of the problem, as the electron density is a function of only three coordinates, independently of the number of electrons:

$$\rho(r) = \int \cdots \int |\Psi(\mathbf{r_1}, \mathbf{r_2}, \ldots, \mathbf{r_n}|^2 d\mathbf{r_2} \ldots d\mathbf{r_n} \tag{2.13}$$

The concept of DFT[†] has been mathematically proven by Hohenberg and Kohn by showing that a one-to-one mapping between the ground-state electron density ρ_0 and the external potential υ_{ext} exists. In the case of molecules,

[†]For overview see ref. [72]

the external potential is given by the nuclear Coulomb potential υ_{nuc}. This relation implies that the external potential and hence the Hamiltonian can be determined from a given ground-state electron density. By definition, also all the properties derivable from the Hamiltonian, such as the ground-state wavefunction and energy, excited-state wavefunctions and energies, can in principle be determined from the electron density.

Therefore, for a given external potential υ_{ext} a density functional exists, which provides an energy for any trial electron density in this potential

$$E \equiv E_\upsilon[\rho(\mathbf{r})] \equiv \int \upsilon_{ext}(\mathbf{r})\rho(\mathbf{r})d\mathbf{r} + F[\rho(\mathbf{r})] \tag{2.14}$$

where the integration variable $\mathbf{r}$ runs over all space. The theorem proves also a variational principle for the electron density. For any density $\rho(\mathbf{r})$, the corresponding energy functional $E_\upsilon[\rho]$ gives an energy that is larger than or equal to the ground-state energy, *i.e.*

$$E_\upsilon[\rho] \geqslant E_0 \qquad \forall\rho, \tag{2.15}$$

and the ground-state energy $E_\upsilon[\rho] = E_0$ is obtained only with the ground-state electron density ρ_0. Thus, for a given external potential the total energy is at a minimum for the ground-state electron density and if the functional $F[\rho(\mathbf{r})]$ is known, the ground-state energy and density for any electronic system can be determined, independent of the number of electrons.

The total energy functional can be decomposed into different contributions:

$$E_\upsilon[\rho] = T[\rho] + V_{ne}[\rho] + V_{ee}[\rho] \tag{2.16}$$

where $T[\rho]$ is the electronic kinetic energy, $V_{ne}[\rho]$ is the electrostatic attraction of the electrons and the nuclei and $V_{ee}[\rho]$ is the electron–electron repulsion energy, which can be decomposed into classical Coulomb and nonclassical terms:

$$V_{ee}[\rho] = J[\rho] + V_{ee}^{nc}[\rho] \tag{2.17}$$

While the $V_{ne}[\rho]$ and $J[\rho]$ can be calculated explicitly in terms of the electron

density:

$$\begin{aligned} V_{ne}[\rho] &= \int \upsilon_{nuc}(\mathbf{r})\rho(\mathbf{r})d\mathbf{r} \\ J[\rho] &= \int \frac{\rho(\mathbf{r})\rho(\mathbf{r}')}{|\mathbf{r}-\mathbf{r}'|}d\mathbf{r}d\mathbf{r}' \end{aligned} \tag{2.18}$$

the explicit form of the density functionals of the interacting kinetic energy and the nonclassical electron–electron repulsion energy are not known. To simplify calculations of the kinetic energy functional, Kohn and Sham proposed to separate the kinetic energy of non-interacting electrons of density $\rho(\mathbf{r})$, according to

$$T[\rho] = T_c[\rho] + T_s[\rho] \tag{2.19}$$

and to combine the remaining $T_c[\rho]$ contribution, together with the nonclassical electron–electron repulsion term, as the exchange and correlation functional:

$$E_{xc}[\rho] = T_c[\rho] + V_{ee}^{nc}[\rho] \tag{2.20}$$

The total energy functional can now be written as:

$$E_v[\rho] = T_s[\rho] + V_{ne}[\rho] + J[\rho] + E_{xc}[\rho] \tag{2.21}$$

By applying the variational principle (eq. 2.15) a set of one-electron self-consistent equations, called Kohn-Sham equations, can be derived:

$$\left[-\frac{\nabla^2}{2} + \upsilon_{nuc} + \int \frac{\rho(\mathbf{r}')}{|\mathbf{r}-\mathbf{r}'|}d\mathbf{r}' + \upsilon_{xc}(\mathbf{r})\right]\phi_i(\mathbf{r}) = \varepsilon_i\phi_i(\mathbf{r}) \tag{2.22}$$

where i runs over the number of electrons. The first term is the single-particle kinetic operator, the second term is the external potential, the integral corresponds to the classical electrostatic potential and the last term is the exchange-correlation potential defined as:

$$\upsilon_{xc}(\mathbf{r}) \equiv \frac{\partial E_{xc}[\rho(\mathbf{r})]}{\partial\rho(\mathbf{r})} \tag{2.23}$$

The auxiliary single particle wavefunctions $\phi_i(\mathbf{r})$ in Kohn-Sham orbitals give the electron density:

$$\rho(\mathbf{r}) = \sum_{i=1}^{n} |\phi_i(\mathbf{r})|^2 \tag{2.24}$$

2.4 Basis Set Approximation

To solve the KS equations in practice, the Kohn-Sham orbitals are expanded in a linear combination of known functions called the basis set, according to:

$$\phi_i = \sum_{\mu=1}^{k} c_{\mu i}\chi_\mu \tag{2.25}$$

where k is the number of basis functions. The choice of the χ functions depends on the application and for molecular systems typically atom-centered functions similar to atomic orbitals are used, such as Slater-type functions

$$\chi^{STF}_{\zeta,n,l,m}(r,\theta,\varphi) = NY_{l,m}(\theta,\varphi)r^{n-1}e^{-\zeta r} \tag{2.26}$$

or Gaussian-type functions

$$\chi^{GTF}_{\zeta,n,l,m}(r,\theta,\varphi) = NY_{l,m}(\theta,\varphi)r^{(2n-l-2)}e^{-\zeta r^2} \tag{2.27}$$

There are two major differences in the shape of Slater-type and Gaussian-type functions, as may be seen in Fig. 2.1. For $x = 0$ the GTF exhibits a zero

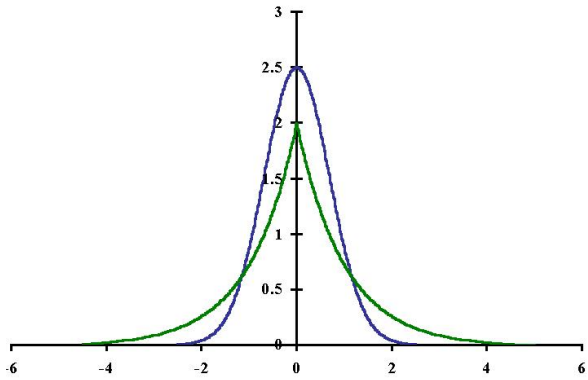

Figure 2.1: Unit exponent normalized GTF (blue line) and STF (green line). The functions are centered at the nucleus.

slope, while the STF has a discontinuous derivative. The other difference is that a GTF has problems in representing the near-nucleus region and falls

off too rapidly in comparison with STF. Therefore, a relatively large number of GTFs is necessary to describe energetically important but chemically unimportant core electrons. To reduce the computational cost, those functions (called *primitive GTFs*) are combined into a smaller set of *contracted GTFs* by forming a fixed linear combination:

$$\chi_\mu = \sum_p^l d_{\mu p} \chi_p \tag{2.28}$$

The smallest possible basis set, using one function for each occupied atomic orbital, is called a minimum basis set. This means that for elements from the second row of periodic table two s-functions (1s, 2s) and one set of p-functions ($2p_x$, $2p_y$, $2p_z$) are used. The so-called *Double Zeta* (DZ) basis set doubles the minimum basis set, assigning twice as many functions for each orbital — 1s, 1s', 2s, 2s', 2p, 2p'. As a compromise between accuracy and efficiency, *Split Valence Basis Sets* have been proposed, which double only the functions for valence orbitals. Similarly *Triple Zeta* (TZ), *Quadruple Zeta* (QZ), *Quintuple Zeta* (5Z) and higher sets have been developed, also in the valence split version.

In most cases, higher angular momentum functions, known also as *polarization functions*, are required to properly describe polarization of orbitals when a chemical bond is formed. Although not populated in the atomic ground state, they can be safely used both for hydrogens and heavy atoms. Also *diffuse functions*, *i.e.* s- and p-type functions with very small exponents, can be used for all the elements. Those functions improve standard basis sets, which are optimized mainly to reproduce energies with high accuracy, by a more detailed description of regions far away from nuclei. They should be in use whenever long-distance interactions, anions, excited states, molecules with electron lone pairs or properties such as polarizability are studied.

2.5 Exchange-Correlation Functionals

The exact form of the exchange-correlation functional $E_{xc}[\rho]$ is not known and there are no prescriptions how to approximate and systematically improve this functional. One of the earliest approximations is the local density

approximation in which the system is treated as a uniform electron gas:

$$E_{xc}^{\mathrm{LDA}}[\rho] = \int \epsilon_{xc}^{uniform}(\rho(\mathbf{r}))\rho(\mathbf{r})d\mathbf{r} \tag{2.29}$$

where $\epsilon_{xc}^{uniform}$ is the exchange-correlation energy per electron of a uniform electron gas of density ρ, derived from Quantum Monte-Carlo calculations. This functional is by definition exact for a homogeneous electron gas but works also surprisingly well for metals, failing however in applications for molecules, especially in predicting binding energies. The more accurate generalized gradient approximation

$$E_{xc}^{\mathrm{GGA}}[\rho, \nabla\rho] = \int f(\rho(\mathbf{r}), \nabla\rho(\mathbf{r}))d\mathbf{r} \tag{2.30}$$

considers also the gradient of the density. New generations of meta-GGA functionals include also the Laplacian of the density or the kinetic energy density, according to

$$E_{xc}^{\mathrm{mGGA}}[\rho, \nabla\rho, \nabla^2\rho] = \int f(\rho(\mathbf{r}), \nabla\rho(\mathbf{r}), \nabla^2\rho(\mathbf{r}))d\mathbf{r} \tag{2.31}$$

The most popular GGA functionals are the BP (Becke, Perdew) [73, 74] and BLYP [73, 75], combining the exchange functional of Becke with the correlation functional of Lee, Yang and Parr.

A separate family is the family of hybrid functionals. They mix a portion of exact exchange energy derived from Hartree-Fock method with the exchange and correlation GGA functional:

$$E_{xc}^{\mathrm{hybrid}}[\rho] = E_{xc}^{\mathrm{GGA}}[\rho, \nabla\rho] + c_x(E_x^{HF}[\rho] - E_x^{GGA}[\rho]) \tag{2.32}$$

The c_x coefficient controls the mixing between the Hartree-Fock and GGA exchanges. One of the remarkably successful hybrid functionals is the B3LYP functional. [75–77]

2.6 Time-dependent Density Functional Theory

The Time-dependent DFT[‡] originates from the Runge-Gross theorem, which is a time-dependent version of the Hohenberg-Kohn theorem, it follows that

[‡]For overview see ref. [78]

the time-dependent electron density $\rho(\mathbf{r},t)$ uniquely determines the external time-dependent potential $v_{ext}(\mathbf{r},t)$. Therefore, it is possible to formulate a set of time-dependent Kohn-Sham equations:

$$\left[-\frac{\nabla^2}{2}+v_{ext}(\mathbf{r},t)+\int\frac{\rho(\mathbf{r}',t)}{|\mathbf{r}-\mathbf{r}'|}d\mathbf{r}'+v_{xc}(\mathbf{r},t)\right]\phi_i(\mathbf{r},t)=i\frac{\partial}{\partial t}\phi_i(\mathbf{r},t) \quad (2.33)$$

where $v_{xc}(\mathbf{r},t)$ is the unknown time-dependent exchange-correlation potential. Similar to ground-state DFT, the density is obtained from the noninteracting orbitals:

$$\rho(\mathbf{r},t)=\sum_{i=1}^{n}|\phi_i(\mathbf{r},t)|^2 \quad (2.34)$$

For the determination of properties like excitation energies and polarizabilities, only the knowledge of the linear density response of the system to the perturbation of the potential (v_1) is required:

$$v_{ext}(\mathbf{r},t)=\begin{cases} v_0(\mathbf{r}) & ;\ t\leqslant t_0 \\ v_0(\mathbf{r})+v_1(\mathbf{r},t) & ;\ t>t_0 \end{cases} \quad (2.35)$$

Using the perturbation theory, it is possible to expand the density $\rho(\mathbf{r},t)$ as a functional of the external potential v_{ext} in a Taylor series:

$$\rho(\mathbf{r},t)=\rho_0(\mathbf{r})+\rho_1(\mathbf{r},t)+\rho_2(\mathbf{r},t)+\ldots \quad (2.36)$$

The first term corresponds to the unperturbed density at $t<t_0$, which can be obtained from the ground-state KS equations in the potential $v_0(\mathbf{r})$.

The first-order time-dependent density can be calculated therefore from the exact linear response function χ, evaluated at the ground-state potential v_0:

$$\chi(\mathbf{r},t;\mathbf{r}',t')=\frac{\delta\rho[v_{ext}](\mathbf{r},t)}{\delta v_{ext}(\mathbf{r}',t')}\bigg|v_0 \quad (2.37)$$

as

$$\rho_1(\mathbf{r},t)=\int d\mathbf{r}'\int\chi(\mathbf{r},t;\mathbf{r}',t')v_1(\mathbf{r}',t')dt' \quad (2.38)$$

The unknown response function can be obtained from the unperturbed KS orbitals, their occupation numbers f_j and their orbital energies ε_j through:

$$\chi_s(\mathbf{r},\mathbf{r}';\omega)=\sum_{j,k}(f_k-f_j)\frac{\phi_j(\mathbf{r})\phi_k^*(\mathbf{r})\phi_j^*(\mathbf{r}')\phi_k(\mathbf{r}')}{\omega-(\varepsilon_j-\varepsilon_k)+i\eta} \quad (2.39)$$

where η is a positive infinitesimal. In this way absorption energies ω are accessible directly from the ground-state electron density. For the real density response of a molecule in an electric field, real Kohn-Sham orbitals ϕ_j and $\eta = 0$ can be used.

2.7 Chemical Models

The accuracy of a theoretical study depends both on computational method and chemical models chosen to represent the studied system. Proteins, due to their size, are in general beyond the current capabilities of full quantum theoretical description and therefore either a combined quantum mechanics/molecular mechanics (QM/MM) treatment or a model approach must be used. In the first methodology, the most crucial parts of proteins are described quantum mechanically, while the remaining part is considered on the MM level. The second approach, used in this thesis, is based on studying a model for the functional core of a protein under consideration. Usually the model is built with a reference to the protein's X-ray structure and contains residues essential for the investigated mechanism. In order to reproduce the missing protein environment, specific geometrical constraints may be additionally introduced. In this thesis, all the models were systematically refined in an evidence-based preparation procedure, *i.e.* until a satisfactionary agreement with available NMR data was achieved.