Zero-Field Splitting in Gd(III) complexes – Towards a molecular understanding of paramagnetic relaxation

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Abstract

The prime objectives of contrast agents in Magnetic Resonance Imaging (MRI) is to accelerate the relaxation rate of the solvent water protons in the surrounding tissue. Paramagnetic relaxation originates from dipole-dipole interactions between the nuclear spins and the fluctuating magnetic field induced by unpaired electrons. Currently Gadolinium(III) chelates are the most widely used contrast agents in MRI, and therefore it is incumbent to extend the fundamental theoretical understanding of parameters that drive the relaxation mechanism in these complexes.

Traditionally the Solomon-Bloembergen-Morgan equations have been utilized to describe relaxation times in terms, primarily of the Zeeman interaction, which is the splitting of degenerate energy levels due to an applied magnetic field. However, in compounds such as Gadolinium(III) complexes with total electron spins higher than 1 (in this case S=7/2) other interactions such as the Zero-Field Splitting (ZFS) play a significant role. ZFS is the splitting of degenerate energy levels in the absence of an external magnetic field. For this purpose, the current research delves into an understanding of the relaxation process, focusing on ZFS in various complexes of interest, using quantum chemical methods as well as molecular dynamic simulations.
List of Papers

The following papers, referred to in the text by their Roman numerals, are included in this thesis.

PAPER I:  **Systematic theoretical investigation of the zero-field splitting in Gd(III) complexes: Wave function and density functional approaches**  
S. Khan, A. Kubica-Misztal, D. Kruk, J. Kowalewski, M. Odelius  
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PAPER II: **Theoretical investigation of the zero-field splitting in aqueous Gd(III) and Eu(II)**  
S. Khan, J. Kowalewski, M. Odelius  
*In Manuscript*
Author’s contribution

PAPER I: I was responsible for writing and organizing the manuscript and carried out all computations.

PAPER II: I was responsible for writing and organizing the manuscript and carried out all computations.
## Contents

Abstract iv  
List of Papers v  
Author’s contribution vii  
List of Figures xi  
List of Tables xiii  
Acknowledgements xv  

1 Quantum Chemistry 17  
  1.1 Introduction ........................... 17  
  1.2 Wavefunction and Density Functional methods ........................... 18  
    1.2.1 Hartree-Fock and CASSCF ........................... 18  
    1.2.2 Density Functional Theory ........................... 20  
  1.3 Relativistic Quantum Chemistry ........................................... 22  
    1.3.1 The Dirac Equation ........................................... 22  
    1.3.2 ZORA approximation ........................................... 23  
    1.3.3 DKH approximation ........................................... 24  

2 NMR Relaxation 25  
  2.1 Introduction ........................................... 25  
  2.2 Relaxation ........................................... 26  
    2.2.1 Dipole-Dipole Interactions ........................................... 27  
    2.2.2 Other interactions ........................................... 27  
  2.3 Paramagnetic Parameters ........................................... 28  
    2.3.1 Paramagnetic Relaxation Enhancement ........................................... 28  
    2.3.2 Pseudocontact Shift ........................................... 29  
    2.3.3 Residual Dipolar Couplings ........................................... 29  
  2.4 Solution Dynamics from MD ........................................... 29
List of Figures

3.1 The ZFS of the Kramer doublets in symmetrical Gd(III) compounds expressed in the cylindrical $D$ parameters. When the rhombic $E$ parameter is included, the graphical representation does not apply. ................................. 32

3.2 Comparison of the artificial ZFS of the Kramer Doublets in the Symmetrical Complexes ................................. 34

3.3 ZFS of Kramers Doublets under Axial Distortion of Gd(III)F$_6$$^{3-}$ in panel (a), of Gd(III)H$_2$O$_6$$^{3+}$ in panel (b) and of Mn(II)H$_2$O$_6$$^{2+}$ in panel (c). For the Gd(III)F$_6$$^{3-}$ complex, we have included CASSCF results for negative distortions, which shows that the curves are smooth and the ZFS $D$ parameter changes sign while passing through the structure of $O_h$ symmetry. ..................................................... 34

3.4 Ground Octet State Splitting of the Kramer Doublets: a comparison of the three systems of interest. The CASSCF/MRCI0 values are shown as solid lines whereas the $D$-derived values are shown as dashed lines. ..................................................... 36

4.1 Radial Distribution function(left) and cumulative radial distribution function(right) using classical molecular dynamics for aqueous Gd(III) complexes. The various distribution functions result from the inclusion of 1, 2 or 3 Gd(III) in the simulation cell. ..................................................... 40

4.2 A comparison of the $D$-parameter between the inner shell Gd(III) and the inclusion of the outer shell in the aqua complex. ..................................................... 42
4.3 A comparison of optimized M(H$_2$O)$_n$ complex where M is Eu(II) or Gd(III) and n = 7, 8 or 9. The left-hand figure shows the splitting of the ground state octet. The right-hand figure shows the lowest excited state sextets where the left axis corresponds to Eu(II) and the right axis corresponds to the energy values for Gd(III).

4.4 A comparison of the splitting of the ground state octet when using different geometries. A@B corresponds to using A as the metal ion center whilst using the optimized geometry of B.
List of Tables

3.1 Gd(III)DTPA$^{2-}$ ZFS parameters as computed using the DFT formalism. The experimental $D$ value is 0.048 cm$^{-1}$ and E/D = 0.2[1] ........................................... 35

3.2 Comparing the *ab-initio* ZFS [cm$^{-1}$] from CASSCF/MRCI0 calculations to previously reported experimental values . . . . 36

3.3 ZFS parameters from CASSCF/MRCI0 calculations using various geometries for the Gd(III)DOTA$^-$ and Gd(III)DOTA(H$_2$O)$^-$ ........................................... 37

3.4 ZFS parameters from CASSCF/MRCI0 calculations as the Gd-O bond distance(between the connected water molecule) is increased for Gd(III)DOTA(H$_2$O)$^-$ using the TPSSh optimized geometry ........................................... 38

4.1 Optimized Geometry Parameters for M(H$_2$O)$_n$$^{3+}$, M = Eu(II)/Gd(III) and n = 7, 8, 9 ........................................... 41

4.2 D[cm$^{-1}$] and E/D values for M(H$_2$O)$_n$$^{3+}$, M = Eu(II)/Gd(III) and n = 7, 8, 9 ........................................... 45
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1. Quantum Chemistry

1.1 Introduction

One of the founding principles on which a large part of modern science is based, is a consequence of the famous equation first written down in 1926, in a slightly different form, but which is now recognized as the (time-independent) Schrödinger Equation:

\[ E\Psi(r, R) = -\frac{\hbar^2}{2m} \nabla^2 \Psi(r, R) + \hat{V}\Psi(r, R) \]  

(1.1)

This equation was born out of the mind of the Austrian scientist Erwin Schrödinger and for the first time laid down an accurate description of the internal distribution of electrons around a nucleus. It is an energy eigenvalue problem, the first and second terms on the right hand side of the equation include kinetic and potential operators respectively, corresponding to the classical total kinetic and potential energies. The solutions give us a set of eigenfunctions which are associated with energy eigenvalues describing different electronic quantum states of the system. With this equation, we are capable of explaining a huge amount of atomic and molecular phenomena accurately and quantitatively, except those involving magnetism and relativity. However, even though it is a starting point for any electronic phenomenon, the complexity of the problem increases exponentially with each additional particle, and this places a severe limitation not only on computation, but in fact, the mathematics involved inherently in the problem becomes too complicated to solve analytically as soon as we go on to systems of atoms even with as little as two electrons.

Since the Schrödinger Equation was first written down in the 1920’s, a whole range of techniques and approximations has been developed to provide reasonable computations for phenomena that occur in atomic and molecular systems. To circumvent the high dimensionality of the Schrödinger Equation, the Born-Oppenheimer approximation was proposed by Max Born and Robert J. Oppenheimer in 1927 [2], which is now often treated almost ubiquitously in wave function calculations. Since the nuclear mass is much greater than the electronic mass, the motion associated with the kinetic energy of nuclei is much
slower than the electrons. When solving for the electronic wavefunction, the nuclei are essentially static and the inter-nuclear repulsion thus becomes a constant contribution to the Hamiltonian. The nuclear and electronic motions are thus separated and we can search for the solutions of the Schrödinger Equation separately:

$$\Psi_{\text{total}}(r; R) = \Psi_{\text{nuclear}}(R) \times \Psi_{\text{electronic}}(r; R) \quad (1.2)$$

where \( r \) represents electronic coordinates and \( R \) represents all nuclear coordinates. The electronic wavefunction of the Schrödinger Equation under the Born-Oppenheimer approximation is given by:

$$H_{\text{el}} \Psi_{\text{el}}(r; R) = E_{\text{el}} \Psi_{\text{el}}(r; R) \quad (1.3)$$

The Born-Oppenheimer is a relatively mild assumption and easily justifiable in many cases. In fact, it does not go too far in helping to solve more complicated problems, and even with this approximation there is only one molecular species that can be solved exactly: that of the Hydrogen-ion \( \text{H}^+ \) which contains only one electron along with the two nuclei of the hydrogen atoms. However from a conceptual point of view the approximation has some profound implications, such as the concept of the Potential Energy Surface (PES) which is defined by the electronic energy over all possible nuclear coordinates. Other concepts such as equilibrium and transition state geometries are also born out of this approximation, since they are manifested through the PES.

### 1.2 Wavefunction and Density Functional methods

#### 1.2.1 Hartree-Fock and CASSCF

In this section, I will briefly explain the concepts behind the wave function methods and density functional theory. Adopting the Born-Oppenheimer approximation, the central problem left to solve in quantum chemistry is to find the ground state energy of the electronic Hamiltonian for fixed nuclei. In 1928 a powerful approximation attempting to solve this ground state problem was proposed by Hartree [3] in what came to be known as the Hartree equations. The many particle wavefunction is represented as a product of \( N \) one-electron wavefunctions.

$$\Psi(r_1, \ldots, r_N) = \prod \psi_i(r_i) \quad (1.4)$$

Here, the electronic spin and the Pauli exclusion principle, which states that two identical fermions cannot occupy the same quantum state simultaneously, were not taken into account. To overcome the problem of the indistinguishability of electrons, Fock [4] and Slater [5] independently proposed a variational scheme for the total wavefunction that makes use of a determinant, the
so-called Slater determinant. This determinant ensures that the wavefunction has the correct symmetry properties. Under an exchange of particle indexes fermions require an anti-symmetric wavefunction, thus obeying the Pauli exclusion principle. A linear combination of different N-electron Slater determinants is also antisymmetric. The Slater determinant is written as:

$$\Psi_{HF} = \frac{1}{\sqrt{N!}} \begin{vmatrix} \psi_1(x_1) & \psi_1(x_2) & \cdots & \psi_1(x_N) \\ \psi_2(x_1) & \psi_2(x_2) & \cdots & \psi_2(x_N) \\ \vdots & \vdots & \ddots & \vdots \\ \psi_N(x_1) & \psi_N(x_2) & \cdots & \psi_N(x_N) \end{vmatrix}$$

The Hartree-Fock one-electron orbitals are conveniently orthonormalized so that:

$$\langle \psi_i | \psi_j \rangle = \delta_{ij} \quad i, j = 1, \ldots, N$$

The one-electron wavefunctions can be expanded as products of spatial functions $\phi(r)$ and spin functions $\sigma(s)$, and are thus known as spin-orbitals. An initial guess of spatial functions is used to form a Slater determinant and then the goal is to seek the Slater determinant that minimizes the energy expectation value. For each spin-orbital we will be solving an equation of the form:

$$F \psi_i = \varepsilon_i \psi_i \quad i = 1, \ldots, N \quad (1.5)$$

which are the canonical Hartree-Fock equations. $F$ is the Fock operator and comprises of the following terms:

$$F = \sum_{i=1}^{N} H_i + \frac{1}{2} \sum_{i=1}^{N} \sum_{j=1}^{N} (J_{ij} - K_{ij}) \quad (1.6)$$

The first sum of terms on the right hand side of Equation 1.6 contains the one electron operators consisting of the electron kinetic operator and the potential operator between electrons and the nucleus. The $J$ and $K$ terms are operators that contain information of the 2-electron integrals, the Coulomb potential between electrons and the so-called 'Exchange' integral, respectively. The Exchange energy arises due to the Pauli principle and is a purely quantum mechanical contribution.

A physical interpretation of the Hartree-Fock method is that each electron moves in a potential which is due to the nuclei and the average of the potential of all other electrons. This means that all other electronic spin-orbitals must be known when computing the one-electron wavefunction. Therefore, an approximate starting set of spin-orbitals are usually used and then the Hartree-Fock equations are applied to calculate the matrix elements of the
Fock operator, diagonalizing it and obtaining a set of new orbitals. The total energy is then calculated and the new orbitals are used to calculate a new Fock operator and the process repeated iteratively until the energy converges to a precision that lies within a given threshold. Therefore, the underlying problem is to search a global minimum of the energy functional $\langle \Psi | \hat{H} | \Psi \rangle$ with the constraint that the wavefunction be represented as a Slater determinant of one-electron spin-orbitals.

One of the major short-comings of the Hartree-Fock method is what is known as correlation energy. It does not consider instantaneous coulombic interactions between electrons. It neglects quantum mechanical effects on electron distributions because it treats the effects of the $N - 1$ electrons on the electron of interest in an average way. We deal with these shortcomings by making use of post-Hartree-Fock methods. In the Configuration Interaction (CI) method, possible $N$-electron Slater determinants are used as basis themselves, so that the exact ground-state or excited-state wavefunctions can be expressed as linear combinations of all possible $N$-electron Slater determinants:

$$\Psi = C_o \Phi_{HF} + \sum C^p_a \Phi^a_p + \sum C^{pq}_{ab} \Phi^{pq}_{ab} + \sum C^{pqr}_{abc} \Phi^{pqr}_{abc} + \cdots$$  \hspace{1cm} (1.7)$$

Any equation of this form is known as CI [6]. The first term is the Hartree-Fock term and the difference between the HF limit and the energy of the CI is called the correlation energy. Whereas in CI, only the coefficients in Equation 1.7 are optimized, in the multiconfiguration self-consistent field method (MCSCF) the orbital coefficients, along with the expansion coefficients $C^i_j$ from Equation 1.7 are optimized simultaneously. One scheme of the MCSCF method is the complete active-space self-consistent field method (CASSCF) [7] where spin-orbitals are divided into inactive orbitals that are usually the lowest energy spin-orbitals and doubly occupied, virtual orbitals that are normally high energy unoccupied spin-orbitals and the active orbitals in which the orbital occupation varies in different determinants. After an initial SCF(HF) calculation is performed to determine orbitals, a full-CI wavefunction is calculated within the active space by taking all possible permutations of the electrons across the various orbitals (obeying the basic quantum mechanical laws of course).

1.2.2 Density Functional Theory

Most of the wave-function based methods are an extension of the Hartree-Fock equations. As we reach larger systems with large basis sets, the computational effort of calculations is exponentially increased. An alternative method was developed for solving a many-body interacting system utilizing its electronic probability density, which also takes into account electron correlation. This
sort of method is in principle exact and very effective. Present approximations have shown to consistently produce accurate results comparable to multi configuration wave-functional based methods when analyzing experimental data. Since it is based on the electronic probability density it came to be known as Density Functional Theory (DFT). The foundational pillars of DFT were first put forth by Kohn and Hohenberg during the 1960’s [8]. The theorems described in the paper show that, given the exact density functionals, one can find the exact ground-state density and energy of an N-electron system in an external scalar potential using the total density as variational objects. Because of its computational efficiency and relatively agreeable accuracy for larger systems, DFT has come to dominate many aspects of quantum chemistry, computational physics and condensed matter systems.

Very simply put DFT provides an exact energy correspondence for the many-electron wave function from knowledge of just the electron density. The ground state energy associated with the density is available through the functional.

\[ E[\rho] = \int \rho(r) V_{ext} dr + F[\rho] \]  (1.8)

In orbital free DFT the kinetic energy can be approximated in terms of the density, for example by making use of the Thomas-Fermi model [9] [10]. In 1965 Kohn and Sham derived a set of one-electron equations from which the electron density could be obtained [11]. In Kohn-Sham DFT, indirectly interacting electrons in single particle states are described by the one-electron orbitals that map the problem onto the DFT formalism. By using electron orbitals we get a better approximation of the kinetic energy for the density functional.

\[ E_{kin} = -\frac{1}{2} \sum_i \langle \phi_i | \nabla^2_i | \phi_i \rangle \]  (1.9)

Here the one-electron spatial orbitals \( \phi_i \) are the Kohn-Sham orbitals, and using these, Kohn and Sham showed that the exact ground state energy can be written as:

\[ E[\rho] = -\frac{1}{2} \sum_i \langle \phi_i | \nabla^2_i | \phi_i \rangle + \int \rho(r) \mu(r) d^3r + E_{coulomb}[\rho] + E_{xc}[\rho] \]  (1.10)

which consists of electron kinetic energy, electron-nuclear attraction and coulomb contributions respectively. Since the coulomb potential energy does not include contributions due to exchange-correlation effects, an additional exchange correlation term must be added to the total energy contribution \( E_{xc} \).

The use of multi-determinental wave function based methods results in an exponential increase in calculations with each additional particle, but using the
occupied orbitals or fictitious one-electron wavefunctions the number of equations to compute is drastically decreased. For example to represent one electron in a mesh of 10 points each along the x, y and z axis would require $10^3$ numbers, but a 17 electron system would require $10^{51}$ numbers for a correlated wavefunction. An orbital description would require only $17 \times 10^3$ numbers to compute, which is a much simpler problem to solve. The main problem with DFT methods is that the exact functional is unknown and a lot of approximate XC-functionals have been developed. There is no a priori way to determine which functionals may benefit which calculations and usually with time one is able to say that a particular functional works for calculating a particular property of a complex, but it is only with empirical experience that DFT methods seem to be the most successful.

1.3 Relativistic Quantum Chemistry

Although the Schrödinger equation is capable of describing many phenomena, it does not take relativistic effects into account. Relativistic effects can effect orbital sizes and shapes, and hence interaction energies and molecular properties, and become increasingly important for heavier atoms, where the electrons begin to obtain relativistic speeds. In this thesis we are interested in the Zero-Field-Splitting, which is influenced by spin-orbit coupling, a relativistic effect. Zero-Field Splitting is the splitting of degenerate energy levels of an open-shell ground state in the absence of an external magnetic field. There are several ways that relativistic calculations can be performed and here I present two of the most common methodologies that are used today and were used in our studies: the Zeroth-Order Regular Approximation(ZORA) and the Douglas-Kroll-Hess(DKH) approximation.

1.3.1 The Dirac Equation

Under Einstein’s theory of special relativity all physical laws must be invariant under Lorentz transformation. This condition is not fulfilled by the Schrödinger Equation since temporal and spatial derivatives appear in non-symmetric form. Paul Dirac was the first to combine the wave mechanics of Schrödinger and the theory of special relativity and was able to deduce a formula that fulfilled both conditions [12]. This symmetric treatment of time and space is fulfilled by the Dirac Hamiltonian:

$$H_D = c \alpha \cdot p + (\beta - 1)mc^2 + V$$ (1.11)
Here $\alpha$ is a 3-vector whose elements $\alpha_k$ consist of $4 \times 4$ matrices,

$$
\alpha_k = \begin{pmatrix}
0 & \sigma_k \\
\sigma_k & 0
\end{pmatrix}, \quad k = x, y, z
$$

(1.12)

where $\sigma_k$ are the Pauli spin matrices, and $\beta$ is a diagonal matrix with entries $(1, 1, -1, -1)$. Equation 1.11 is the starting point of all molecular relativistic calculations and may be written as two coupled differential equations for the two spinor components.

$$
\begin{pmatrix}
V(r) - E & c(\sigma \cdot p) \\
c(\sigma \cdot p) & V(r) - E - 2mc^2
\end{pmatrix}
\begin{pmatrix}
\Psi^L(r) \\
\Psi^S(r)
\end{pmatrix} = 0
$$

(1.13)

Since the Dirac equation is only valid for a one-electron system, the one-electron Dirac Hamiltonian has to be extended to a many-electron Hamiltonian to treat the chemically interesting many-electron systems.

### 1.3.2 ZORA approximation

An elegant approach by making use of elimination procedures to the four-component Dirac equation was proposed by Chang et al. [13] as well as Heully et al. [14] and later developed into a computational algorithm by the Amsterdam group [15] [16]. This came to be known as the Zeroth-Order Regular Approximation (ZORA). By writing out Equation 1.13 in terms of two 2-component equations:

$$
V\Psi^L + c\sigma \cdot p\Psi^S = E\Psi^L
$$

(1.14)

$$
c\sigma \cdot p\Psi^L + (V - 2mc^2)\Psi^S = E\Psi^S
$$

(1.15)

we can use Equation 1.15 to describe $\Psi^S$ in terms of $\Psi^L$:

$$
\Psi^S = \left(\frac{c\sigma \cdot p}{E - V + 2mc^2}\right)\Psi^L
$$

(1.16)

and substituting back into Equation 1.14 reveals,

$$
V\Psi^L + \frac{1}{2}\sigma \cdot pK\sigma \cdot p\Psi^L = E\Psi^L
$$

(1.17)

where

$$
K = \left(1 + \frac{E - V}{2mc^2}\right)^{-1}
$$

(1.18)

The regular approximation takes this value of $K$ and expands it into a power series, which is the starting point for calculations.

$$
K = \left(1 + \frac{E - V}{2mc^2}\right)^{-1} = 2c^2(2mc^2 - V)^{-1} - 2c^3E(mc^2 - V)^{-2} + \cdots
$$

(1.19)
By just including the first term of this expansion we get the Zeroth Order Regular Approximation.

\[ H_{ZORA} = V + \sigma \cdot p \frac{c^2}{2mc^2 - V} \sigma \cdot p \]  

(1.20)

The inclusion of the second term is called the First Order Regular Approximation (FORA), but the one-electron ZORA Hamiltonian is already a reliable relativistic correction. The mass-velocity correction as well as part of the Darwin term are missing from ZORA, and since the missing term is positive for bound states, ZORA results in energies that are too low. However, since it is bounded from below it makes the method variationally stable.

1.3.3 DKH approximation

The Dirac Hamiltonian from Equation 1.13 can be block-diagonalized with a suitable unitary operator \( U \):

\[ U H_D U^\dagger = \begin{pmatrix} H_+ & 0 \\ 0 & H_- \end{pmatrix} \]  

(1.21)

\( H_+ \) and \( H_- \) are the positive and negative energy values of the full Dirac spectrum respectively, and the two-component equation can be written in terms of the positive energy solutions:

\[ H_+ \Phi = E \Phi \]  

(1.22)

Douglas and Kroll noted in the appendix of their paper on the fine structure of helium [17] a possible scheme to carry out sequential unitary decoupling transformations. The method they suggested used the external potential \( V \) to classify contributions to \( H_+ \). This appendix note was not utilized by quantum chemists until it was discovered by Hess [18] who sought its practical implementation by making use of the upper component of the Dirac eigenvector.

The unitary transformation can be represented as a sequence of simpler unitary transformations:

\[ U = \cdots U_3 U_2 U_1 U_0 \]  

(1.23)

The unitary matrices \( U_m \) are chosen so that off-diagonal terms from the Dirac Hamiltonian vanish step by step and this procedure leads to even terms \( H \) and odd terms \( O \), and if a complete decoupling is achieved than the odd terms vanish and we will be left with a completely block-diagonal Hamiltonian. Furthermore, the \( H_+ \) and \( H_- \) operators may be categorized into spin-free(\( H^f \)) and spin-dependent(\( H^d \)) parts. By truncating Equation 1.23 to a pre-defined order in the external potential \( V \), the order of the scheme is defined.
2. NMR Relaxation

2.1 Introduction

Nuclear Magnetic Resonance (NMR) spectroscopy is an important tool to determine the structure and properties of atoms and molecules by observing the interaction of constituent nuclear spins of a sample with an external magnetic field. Each nucleus has an intrinsic spin quantum number $I$ determined by the number of unpaired neutrons and protons, and is associated with $2I+1$ energy levels, corresponding to each different magnetic quantum number $m_I$ (where $m_I = -I, -I+1, ..., I-1, I$). These energy levels are degenerate in the absence of an external magnetic field, but when a magnetic field is applied they lose their degeneracy, an effect known as the Zeeman effect. In an applied magnetic field $B_0$ the energy for a given spin state $m_I$ is given by:

$$E_{m_I} = -\hbar m_I \gamma B_0$$

(2.1)

where $\gamma$, the gyromagnetic ratio of an isotope, is the ratio of its magnetic dipole moment to its angular momentum and is unique for each nucleus. The difference in energy between two consecutive energy levels is given by:

$$\Delta E = \hbar \gamma B_0 = h \mu_0$$

(2.2)

The resonance frequency $\mu_0$ is known as the Larmor frequency and is therefore:

$$\mu_0 = \frac{\gamma B_0}{2\pi}$$

(2.3)

The populations of energy levels $n_i$ for an $N$ spin system can be written as Boltzmann distributions and the ratio of populations can be expressed as:

$$\frac{n_a}{n_b} = \exp\left(-\frac{\Delta E}{k_B T}\right)$$

(2.4)

The population difference is directly proportional to the intensity of NMR signals and therefore, high magnetic fields and low temperatures result in more intense resonances. The chemical shift ($\delta$) represents the difference in resonance positions of an observed sample and a reference sample. The interaction is caused by electrons in the vicinity of a nucleus, and shifts the Zeeman energy levels influencing the frequency of transition between levels.
2.2 Relaxation

The concept of relaxation invokes the image that the system under considerations is being perturbed, and relaxes back into an equilibrium state. In NMR spectroscopy this perturbation may be attributed to a radio pulse. When molecules absorb an electromagnetic pulse they are transferred from lower energy states to higher energy states. Light in the radio-frequency range cause spins to 'flip' or jump to higher energy states. Then, relaxation is the process by which spins return to an equilibrium configuration. This equilibrium configuration can be described as the state where the populations of energy levels follow a Boltzmann distribution and where no coherences are present in the system. Relaxation can be described in terms of two relaxation times: $T_1$, the spin-lattice, and $T_2$, the spin-spin relaxation. Spin-lattice relaxation refers to the component of the magnetization vector along the applied magnetic field(the 'spin') reaching equilibrium with its surroundings(the 'lattice'). Spin-lattice relaxation is a first order kinetic process:

$$\frac{dM_z}{dt} = -\frac{M_z - M_0}{T_1}$$

(2.5)

where $M_0$ is the equilibrium magnetization and $M_z$ is the magnetization at time $t$.

$$M_z = M_0 e^{-t/T_1}$$

(2.6)

For the energy transfer to occur the motion of the lattice must cause a fluctuating magnetic field at the site of the spin involved, and only the $x$ and the $y$ components of the local field can cause $T_1$ relaxation.

On the other hand, spin-spin relaxation is the exponential decay of the transverse component of the magnetization vector $M_{xy}$. It takes the form:

$$M_{xy} = M_{xy,0} e^{-t/T_2}$$

(2.7)

where $M_{xy,0}$ is the initial value of the transverse magnetization and $M_{xy}$ is the transverse component of magnetization at time $t$. Under perturbation the decay of the signal in the $xy$-plane is faster than the decay of the magnetization along the $z$-axis. This decay is due to the loss of phase coherence of the microscopic components, which is partially caused by the differences in the Larmor frequencies induced by the applied magnetic field at different locations in the sample. It is also caused by chemical exchange, which can lead to line broadening, an important tool for the measurement of relaxation rates. In the next sections I will briefly look at some of the mechanisms that drive relaxation. Thereafter, I give a brief section on how molecular dynamics and quan-
tum chemical calculations can assist in understanding the relaxation process in NMR.

2.2.1 Dipole-Dipole Interactions

Each spin has a magnetic moment which gives rise to a local magnetic field which can interact with other spins. This mechanism is therefore, due to two spins, one that generates the magnetic moment, and the other that experiences it. The size of the interaction between two spins is proportional to the inverse cube of the distance between them (the interaction falls quickly as \( \frac{1}{r^3} \)) and the product of the gyromagnetic ratios of the two nuclei involved; it is dependent on the magnetic dipoles of the two spins \( \mu_I \) and \( \mu_S \). Furthermore the orientation of the vector joining the two spins relative to magnetic field also influences the dipolar mechanism.

\[
E_{dd} = \frac{\mu_I \cdot \mu_S}{r_{IS}^3} - \frac{(\mu_I \cdot r_{IS})(\mu_S \cdot r_{IS})}{r_{IS}^5} \tag{2.8}
\]

Here \( \mu_I = \hbar \gamma_I I \) and \( \mu_s = \hbar \gamma_S S \). Dipole interaction provides a path by which energy can be transferred from the spin to the lattice. Dipole-dipole interaction turns molecular motion into an oscillating magnetic field which causes spin transitions. The relaxation is caused if the fluctuations occur at the Larmor precession frequency. The correlation time for dipole-dipole relaxation is governed by molecular motion.

2.2.2 Other interactions

Two other interactions are discussed here that affect the relaxation mechanism: chemical shift anisotropy (CSA) and quadrupolar relaxation. Chemical shifts reflect the electronic environments that modify the local magnetic fields experienced by different nuclei. Electrons in a molecule may induce local fields at the nucleus. The Larmor frequency is therefore shifted, since it experiences the sum of the applied and induced field. These chemical shifts may provide structural information. The precession frequency is written as:

\[
\omega = -\gamma(1 - \phi)B_0 \tag{2.9}
\]

\( \phi \) is a dimensionless quantity depicting the isotropic nuclear shielding. The chemical shift is defined in terms of the NMR frequency of a given resonance and a reference sample:

\[
\delta_{\text{sample}} = \frac{\omega_{\text{sample}} - \omega_{\text{ref}}}{\omega_{\text{ref}}} = \frac{\phi_{\text{ref}} - \phi_{\text{sample}}}{1 - \phi_{\text{ref}}} \tag{2.10}
\]
Chemical shielding is described by a chemical shift tensor, which transforms the static field into an effective field. Due to these shielding effects the effective field $B_{\text{eff}}$ may deviate from the direction of the static field $B_0$. Because of the rapid rotation of the molecule in solution the observed chemical shift is an average over the shifts corresponding to the different orientations. The magnetic field experienced by the nucleus depends on the orientation of the molecule relative to the applied magnetic field. This phenomenon is termed CSA. CSA is described as the difference in chemical shift between the isotropic and anisotropic states.

Nuclei with spin angular momentum $I > 1/2$ are characterized by an additional mechanism for relaxation, the quadrupolar interaction which arises due to the non-spherical distribution of charge in the nucleus. These nuclei have an electric quadrupole moment $Q$ which interacts with the electric field gradient present at the nucleus, and the interaction is anisotropic (it depends upon orientation). The high efficiency of quadrupolar relaxation is associated with the large strength of the quadrupolar coupling constant which in certain cases may be magnitudes larger than the dipolar coupling constant.

2.3 Paramagnetic Parameters

2.3.1 Paramagnetic Relaxation Enhancement

Paramagnetic species contribute strongly to the nuclear spin relaxation which is why they have garnered significant interest. In systems that contain a paramagnetic central ion, this enhancement is due to the large magnetic moment associated with unpaired electron spins around the metal center. The dipole-dipole interaction between the nuclear spin $I$ and electron spin $S$, generally dominate the effects. $^{17}O$ is an exception to this rule where the scalar interactions of the hyperfine interaction are the primary contributors. When dealing with paramagnetic relaxation enhancement we must deal with two cases, the inner-sphere relaxation, where the nuclear spin resides in the first coordination sphere of the paramagnetic ion, and the outer sphere relaxation. Luz and Meiboom [19] showed that the PRE in the inner-sphere longitudinal relaxation is related to the solution composition, exchange lifetime and the in-complex relaxation rate.

The Paramagnetic Enhancement effect is large, owing to the large magnetic moment of the unpaired electron and fast electron spin relaxation, which makes it suitable for larger systems at distances of up to 35 Å. Paramagnetic Relaxation Enhancement can be manifested through direct dipole-dipole interactions
or through Curie-Spin Interactions. The Curie-Spin Relaxation arises from dipole-dipole interaction between a nucleus and the time-averaged magnetization of the electrons.

2.3.2 Pseudocontact Shift

The electron magnetic moment is usually treated by its isotropic spin contribution and its anisotropic orbital contribution. When the orbital contribution is large the induced magnetic moment shifts in intensity, inducing an anisotropic change in the magnetic susceptibility tensor. The net contribution by the dipole interaction in this case does not equal zero, and there will be a shift in the external magnetic field which is termed the pseudocontact shift $\delta_{PCS}$. The theoretical framework to describe the relationship between pseudocontact shift and dynamics is still an active area of research and has not been fully established yet.

2.3.3 Residual Dipolar Couplings

The partial orientation of molecules result in incomplete rotational averaging of the dipolar and quadrupolar couplings which causes splittings in the NMR spectra. These incomplete average couplings are termed Residual Dipolar Couplings (RDC) and provide a source for structural information by defining long-range ordering in a molecule [20] [21]. RDC generated by paramagnetic alignment with the external magnetic field allow unique opportunities to probe conformational variation.

2.4 Solution Dynamics from MD

Having discussed the general methodologies used in quantum chemistry in Chapter 1, it is now time to relate some of the ideas discussed to the parameters that are produced from NMR relaxation experiments. When speaking about the dynamics in solution we are particularly interested in those mechanisms that will effect the relaxation times $T_1$ and $T_2$, the spin-lattice and spin-spin relaxation times explained in the relaxation section. Being a dynamic process, to have direct correspondence with experiment, one must resort to dynamical simulations such as Molecular Dynamics (MD). There are several ways in which these kinds of simulations can help when comparing to experimental data. Correlation times for translational, angular rotational and re-orientational motions are some of the components that can be extracted from MD simulations and related to relaxation theories.
Furthermore, from the MD simulations one is able not only to extract correlation times, but indeed correlation functions which can provide deeper insight into molecular motions and interactions. In general, the rotational diffusion or tumbling is an extremely important dynamic mechanism in NMR spectroscopy and is what makes NMR structure determination possible. The proton relaxation can for example arise from the rotational motion of a rigid molecule. Molecular dynamics simulations can directly explore the molecular rotational diffusion at picosecond and nanosecond time scales and are an extremely useful tool for this purpose. Vibrations are normally considered to contribute to the average coupling. Through molecular dynamics we can get insight into the internal vibrations, librations, rotations/re-orientations and translations.

The mechanisms thought to have been the most effective in reducing $T_1$ were molecular tumbling and inner-sphere water exchange. However, the importance of electronic spin relaxation on the shortening of $T_1$ that is caused by Gd(III) contrast agents has in recent years begun to catch the attention of scientists. Longer electronic relaxation $T_{1e}$ allows strong hyperfine interactions between nuclear and electronic spins leading to faster $^1$H relaxation times. The electronic spin relaxation is caused due to the effect of fluctuations of the zero-field splitting (ZFS) spin Hamiltonian in the laboratory frame. The ZFS is the result of electron repulsion, spin-orbit coupling and the effect of the ligand field on the ground state. The overall ZFS will be dependent on the orientation of the complex and its instantaneous conformation in the laboratory frame. Furthermore, one is to assume that amidst a mean equilibrium conformation of the compound the various components undergo vibration and libration around the molecular frame to which it is rigidly bound. In this frame, the ZFS spin Hamiltonian has a time average value which is time independent and therefore called the static ZFS. The difference $\Delta F(t) = F_{S,T}(t) - F_{S,T}$ is called the transient ZFS. Fast molecular re-orientation introduces stochastic time dependence on the electron nuclear dipole-dipole coupling interaction which effects the paramagnetic relaxation enhancement.
3. Results PAPER I: ZFS of Gd(III) complexes

The zero-field splitting (ZFS) of the electronic ground state in paramagnetic ions is a sensitive probe of the variations in the electronic and molecular structure. In particular the ZFS in Gd(III) complexes has a profound effect on the paramagnetic relaxation enhancement, which influences the spin relaxation parameters. The paramagnetic Gd(III) ion is an interesting study from a fundamental physical chemistry perspective because of its highly symmetrical $^8S$ ground state comprising of 7 $f$-electrons. It is also an interesting case study from a practical point of view since it has applications as a contrast agent in medical resonance imaging. In our study we compare various complexes using multiconfigurational complete-active-space self-consistent field wave functions and density functional theory (DFT) calculations. First, we performed a series of systematic tests on idealized models with high symmetry, such as the free Gd(III) ion and Gd(III)F$_6$ to test our computational methodology and to compare DFT to the wavefunction methods. Next we performed tests on realistic systems Gd(III)DOTA(H$_2$O)$^-$, Gd(III)DTPA(H$_2$O)$_2^-$, and Gd(III)(H$_2$O)$_8^{3+}$ in order to analyze how the theoretical results compare to experimental values. In contrast to approximations based on density functional theory, the multiconfigurational methods produce results for the ZFS of Gd(III) complexes on the correct order of magnitude.

3.1 Theoretical Details

To investigate ZFS one can invoke the spin Hamiltonian formalism upto second-order, which is parametrized with the cylindrical $D$ and rhombic $E$ parameters:

$$\hat{H}_{ZFS} = D[S^2_z - \frac{1}{2}S(S+1)] + E[S^2_x - S^2_y].$$

The ZFS term may be represented as a matrix in Hilbert space spanned by the $|S,M_s\rangle$ kets and in the case of Gd(III), since $S=7/2$ the dimensionality of the matrix will be 8. The matrix will be represented in terms of the two parameters
$D$ and $E$, which are related to the principal components of $D$ in the principal axes frame:

\[
D = D_{zz} - \frac{1}{2}(D_{xx} + D_{yy}),
\]
\[
E = \frac{1}{2}(D_{xx} - D_{yy}).
\]  

For axial symmetry (no rhombic distortions), the rhombic parameter, $E$, is zero and as a consequence $D_{xx} = D_{yy}$. Therefore, neglecting rhombic contributions, one can express the energies of the Kramer doublets in Gd(III) compounds solely in terms of the ZFS parameter, $D$. The energy levels of the ground octet state will then be split in accordance to Figure 3.1. However, in practical quantum chemical calculations the energies of the Kramer doublet might deviate from the relationships formulated in Figure 3.1. This shows the limitation of the second order formulation of the spin-Hamiltonian.

![Figure 3.1: The ZFS of the Kramer doublets in symmetrical Gd(III) compounds expressed in the cylindrical $D$ parameters. When the rhombic $E$ parameter is included, the graphical representation does not apply.](image)

In this study we consider an active space of 7 electrons included in the 7 $f$-orbitals (14 spinorbitals). In the given active space there are 1 octet, 48 sextets, 392 quartets and 784 doublet states, generating altogether $\binom{14}{7}$ electronic states. However, for most of our calculations we only consider including the
3.2 Symmetrical Systems

We began by investigating the free Gd(III) ion. The purpose was to assess the scale of error we may expect in the ZFS calculations on Gadolinium(III) complexes. The free ion produced an artificial splitting of the ground state octet utilizing the CASSCF method, but this splitting is quenched and we were able to obtain a degenerate ground state when a further MRCI calculation on top of the CASSCF (known forthwith as CASSCF/MRCI0) was performed. We also tested for various convergence criteria and basis set dependence.

Next we look at two idealised Gadolinium(III) complexes Gd(III)F$_6^{3−}$ and Gd(III)(H$_2$O)$_6^{3+}$ characterized by $O_h$ and $T_h$ symmetry respectively. A third complex Mn(II)(H$_2$O)$_6^{2+}$ was also used to compare to $S = 5/2$ systems. The geometries were obtained using constrained optimization in order to preserve symmetry. Because of these symmetry constraints we would expect there to be no splitting of the ground state in these complexes.

A comparison of the splitting of energy levels is shown in Figure 3.2 and we see that the octahedral complex Gd(III)F$_6^{3−}$ has a slightly lower splitting than the hexa-aqua Gd(III) complex, of $T_h$ symmetry. These ground state splitting of both complexes is less than 0.01 cm$^{-1}$ which is quite small, although they should ideally be 0. The hexa-aqua Mn(II) system shows a degenerate energy level up to the precision recorded, and we only witnessed the artifact for heavy $f$-electron systems.

We chose to distort the complexes Gd(III)F$_6^{3−}$, Gd(III)H$_2$O$_6^{3+}$ and Mn(II)H$_2$O$_6^{2+}$ along a single axis and see the effect of this axial distortion on the splitting of the Kramer doublets as depicted in Figure 3.3. The distortion has a larger effect on the splitting of Gd(III)F$_6^{3−}$ as compared to the other two complexes. The response to distortion of the ZFS is of similar magnitude in the aqueous Gd(III) and Mn(II) complexes. It was found that the off-diagonal SOC elements in the SI matrix for Gd(III) complexes are an order of magnitude larger than for the Mn(II) complex and this may explain the similar magnitude, since the energy separation between the ground state and low-lying excited state is much lower in energy for the hexaaqua Mn(II).
Figure 3.2: Comparison of the artificial ZFS of the Kramer Doublets in the Symmetrical Complexes

Figure 3.3: ZFS of Kramers Doublets under Axial Distortion of Gd(III)F$_6^{3-}$ in panel (a), of Gd(III)H$_2$O$_6^{3+}$ in panel (b) and of Mn(II)H$_2$O$_6^{2+}$ in panel (c). For the Gd(III)F$_6^{3-}$ complex, we have included CASSCF results for negative distortions, which shows that the curves are smooth and the ZFS $D$ parameter changes sign while passing through the structure of $O_h$ symmetry.
3.3 ZFS parameters from Density Functional Theory

We did various tests to determine the accuracy of the DFT formalism to compute the ZFS on Gd(III)F$_6^{3-}$ and Gd(III)H$_2$O$_6^{3+}$. It was found that the DFT results are highly functional dependant and in particular the hybrid functionals are rather inaccurate when compared to CASSCF results, the error of which increases as a larger amount of Hartree-Fock exchange is added to the functional. To compare directly to experimental values we ran DFT computations on the compound Gd(III)DTPA$_{2-}$ which has an experimental $D$ parameter of 0.048 cm$^{-1}$ and $E/D=0.2$[1]. The DFT results for the Coupled-Perturbed (CP) and Pederson-Khanna (PK) method using various hybrid and non-hybrid functionals is shown in Table 3.1. The computed $D$ values seem unrealistic compared to the experimental values and highly functional dependent regardless of whether the PK or CP method is used. The DFT formalism to compute the ZFS parameters was therefore deemed unreliable especially as compared to the post-HF methods discussed in the next sections. However, it should be pointed out that DFT does have a significant edge when considering computational speed and therefore it is important to improve DFT methods to use for dynamical sampling where a tremendous amount of calculations may be needed [22]

Table 3.1: Gd(III)DTPA$^{2-}$ ZFS parameters as computed using the DFT formalism. The experimental $D$ value is 0.048 cm$^{-1}$ and $E/D = 0.2$[1]

<table>
<thead>
<tr>
<th></th>
<th>CP</th>
<th></th>
<th>PK</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$D$ [cm$^{-1}$]</td>
<td>$E/D$</td>
<td>$D$ [cm$^{-1}$]</td>
<td>$E/D$</td>
</tr>
<tr>
<td>B3LYP</td>
<td>1.720</td>
<td>0.127</td>
<td>1.200</td>
<td>0.007</td>
</tr>
<tr>
<td>BLYP</td>
<td>-0.193</td>
<td>0.123</td>
<td>1.299</td>
<td>0.007</td>
</tr>
<tr>
<td>BP86</td>
<td>-0.185</td>
<td>0.140</td>
<td>-0.166</td>
<td>0.054</td>
</tr>
<tr>
<td>PBE0</td>
<td>2.418</td>
<td>0.285</td>
<td>1.717</td>
<td>0.221</td>
</tr>
</tbody>
</table>

3.4 Larger Systems of Clinical Relevance

We have taken three complexes that are of relevance to paramagnetic-NMR experiments: the Gd(III)DOTA(H$_2$O)$^-$ and Gd(III)DTPA(H$_2$O)$_2^{2-}$ complexes, which form the first generation of clinical contrast agents for use in medical MRI and Gd(III)(H$_2$O)$_8^{3+}$, since the Gd(III) ion usually form 8 or 9 co-ordination complexes when in aqueous solution.

Experimental ZFS parameters may vary since the acquisition is performed under dynamical conditions and molecular vibrations and solvent collisions may effect the result. It is for this reason that we have used several geometries
Figure 3.4: Ground Octet State Splitting of the Kramer Doublets: a comparison of the three systems of interest. The CASSCF/MRCI0 values are shown as solid lines whereas the $D$-derived values are shown as dashed lines.

to acquire the ZFS. We have taken a previously reported optimized geometry [23] for Gd(H$_2$O)$_8^{3+}$, in an idealized D$_{4h}$ symmetry with a Gd-O distance of 2.471 Å, whereas experimental geometries have been reported to lie between the range of 2.4-2.6 Å [24]. We also used previously reported optimized geometries under the TPSSh functional for the Gd(III)DOTA(H$_2$O)$^-$ and Gd(III)DTPA(H$_2$O)$_2^{2-}$ [25] along with optimizing these structures with the B3LYP functional.

Table 3.2: Comparing the *ab-initio* ZFS [cm$^{-1}$] from CASSCF/MRCI0 calculations to previously reported experimental values

<table>
<thead>
<tr>
<th></th>
<th>Exp. Value</th>
<th>TPSSh geom</th>
<th>B3LYP geom</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gd(III)DOTA(H$_2$O)$^-$</td>
<td>0.230 [1]</td>
<td>0.179</td>
<td>0.100</td>
</tr>
<tr>
<td>Gd(III)DTPA(H$_2$O)$_2^{2-}$</td>
<td>0.576 [1]</td>
<td>0.592</td>
<td>0.375</td>
</tr>
<tr>
<td>Gd(III)(H$_2$O)$_8^{3+}$</td>
<td>0.2-0.5 [26]</td>
<td>0.970</td>
<td></td>
</tr>
</tbody>
</table>

Figure 3.4 shows a comparison of the splitting between the Kramer doublets of the three complexes as well as the ZFS splitting obtained from the $D$ values. The experimental splittings, corresponding to $12D$, for Gd(III)DOTA(H$_2$O)$^-$ and Gd(III)DTPA(H$_2$O)$_2^{2-}$ of 0.23 and 0.576 cm$^{-1}$ respectively are in reasonable agreement with those obtained using the TPSSh optimized structure as can be seen from Table 3.2. On the other hand, the Gd(III)(H$_2$O)$_8^{3+}$ under the symmetrical model shows a total splitting of 0.9695 cm$^{-1}$, more than double experimental values which lie in the range of 0.2-0.46 cm$^{-1}$. We take a closer look at why this may be so in our next study where the $D$ parameter is closer to that of experimental value once the symmetry constraints were removed. It
is clear that certain discrepancies arise due to the sensitivity to geometry and a more extensive sampling may provide deeper insight. However, the overall scheme produces reasonable estimates. In Figure 3.4, we notice that there are also limitations of the second order formulation of the spin-Hamiltonian, since the $D$ and $E$ values fitted to the ZFS splitting tensor are not exactly aligned with the splittings of the exact Kramer doublets.

3.5 Dynamic Fluctuations in Gd(III)DOTA(H$_2$O)$^-$

Next we look at the dynamic effects of Gd(III)DOTA(H$_2$O)$^-$ by distorting the distance of the water molecule from the Gd(III) center and viewing the resulting fluctuations in the ZFS. Three geometry structures were used: one experimental [27], a previously reported optimized structure using the TPSSh functional [25] and one optimized using the B3LYP functional.

<table>
<thead>
<tr>
<th></th>
<th>Exp.Geom</th>
<th>Supp (TPSSh)</th>
<th>Optimized (B3LYP)</th>
<th>Exp. Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gd(III)DOTA$^-$</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$D$ value [cm$^{-1}$]</td>
<td>0.050</td>
<td>0.033</td>
<td>0.028</td>
<td></td>
</tr>
<tr>
<td>$E/D$</td>
<td>0.219</td>
<td>0.013</td>
<td>0.004</td>
<td></td>
</tr>
<tr>
<td>Splitting [cm$^{-1}$]</td>
<td>0.662</td>
<td>0.398</td>
<td>0.330</td>
<td></td>
</tr>
<tr>
<td>Gd(III)DOTA(H$_2$O)$^-$</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$D$ value [cm$^{-1}$]</td>
<td>0.028</td>
<td>0.015</td>
<td>0.078</td>
<td>-0.019</td>
</tr>
<tr>
<td>$E/D$</td>
<td>0.226</td>
<td>0.081</td>
<td>0.165</td>
<td></td>
</tr>
<tr>
<td>Splitting [cm$^{-1}$]</td>
<td>0.370</td>
<td>0.179</td>
<td>0.100</td>
<td>0.230</td>
</tr>
</tbody>
</table>

Experimental values for the ZFS $D$ parameter of Gd(III)DOTA(H$_2$O)$^-$ have been reported as -0.019 cm$^{-1}$ which results in a maximal multiplet splitting of 0.23 cm$^{-1}$ assuming that the complex maintains axial symmetry[1]. Unfortunately, we were unable to reproduce the negative sign of $D$ and in upcoming projects we hope to look more deeply into the reason behind this discrepancy. However, the negative value is of little significance to actual electronic spin relaxation calculations since the square of terms is required for the equations, but it is of principal importance also for the calibration of the calculations. Currently it is difficult to know whether there is any structural relation to the sign of the ZFS parameter. This is subject to one of our current
research projects that we are investigating.

The CASSCF/MRCI0 calculations follow the relationship of the spin Hamiltonian formalism and maintain a splitting of $2D$, $4D$ and $6D$, yet our value of $D > 0$, is in contrast to experimental work. From Table 3.3 we see that depending on the geometry of the complex we should expect a variation of the total induced splitting. From the reference experimental value of $0.23 \text{ cm}^{-1}$ the most representative geometries seem to be generated from the TPSSh functional as presented in reference [25] and our treatment produces a total splitting of $0.1787 \text{ cm}^{-1}$, which lies close to the experimental range. Utilizing the TPSSh geometry we varied the distance of the water molecule to the central complex to see the variation in the ZFS, and this is shown in Table 3.4. The variation in the $D$ parameter is rather small and it can be concluded that the distance of the water molecule does not significantly effect the ZFS.

**Table 3.4:** ZFS parameters from CASSCF/MRCI0 calculations as the Gd-O bond distance (between the connected water molecule) is increased for Gd(III)DOTA(H$_2$O)$^-$ using the TPSSh optimized geometry

<table>
<thead>
<tr>
<th>Distance [Å]</th>
<th>2.646</th>
<th>2.70</th>
<th>2.75</th>
<th>2.80</th>
</tr>
</thead>
<tbody>
<tr>
<td>$D$ [cm$^{-1}$]</td>
<td>0.015</td>
<td>0.015</td>
<td>0.016</td>
<td>0.016</td>
</tr>
<tr>
<td>$E/D$</td>
<td>0.081</td>
<td>0.050</td>
<td>0.033</td>
<td>0.023</td>
</tr>
<tr>
<td>Splitting [cm$^{-1}$]</td>
<td>0.179</td>
<td>0.181</td>
<td>0.188</td>
<td>0.200</td>
</tr>
</tbody>
</table>
4. Results PAPER II: Gd(III) and Eu(II) in aqueous solution

Aqueous Eu(II) and Gd(III) form an inner shell that bind to 7, 8 or 9 water molecules. These complexes form an interesting study since they are isoelectronic, each containing 7 unpaired $f$ electrons in the outer shell. Investigating the effects of zero-field splitting (ZFS) in these complexes is the subject of our current report. In order to evaluate the effect of long-range interactions we tackled this problem from several angles. *Ab-initio* and classical MD simulations were performed on aqueous Gd(III) in order to acquire data on radial distribution functions (RDF’s). In addition to supplying us with coordination numbers, these simulations allowed us to extract cluster configurations of the inner and outer shell, which we were able to use to compute differences in the ZFS before and after the inclusion of the second shell. It was established that inclusion of the second shell does not contribute significantly to the ZFS and for all practical purposes it should be sufficient to include only the first solvation shell for investigating fluctuations in the ZFS. Geometry optimizations were performed for Gd(III)$\cdot$(H$_2$O)$_n^{3+}$ and Eu(II)$\cdot$(H$_2$O)$_n^{2+}$ (for $n = 7, 8, 9$) after which we compute the ZFS of these complexes and analyse the similarities and differences that arise from various considerations.

4.1 Computational Details

Classical MD simulations were performed in Gromacs [28] [29] and *ab-initio* MD simulations were performed using the CPMD [30] [31] code on the aqueous Gd(III) ion with a density of 0.997 [g/cm$^3$] to sample structural data and determine RDF’s. The electronic structure was described by density functional theory with a gradient corrected functional (BLYP). Geometry optimizations on the Gd(III) and Eu(II) aqua complexes were performed in Gaussian09 [32] using the PBE0 functional with a TZVPP basis set on the water molecules (oxygen and hydrogen atoms) along with the Stuttgart-pseudo relativistic effective core potential [33] on the Gd(III) and Eu(II) metal centers. For computation of the spin-orbit coupling effects the ORCA suite of packages was utilized [34] and in calculating the ZFS the CASSCF method was used with
Figure 4.1: Radial Distribution function (left) and cumulative radial distribution function (right) using classical molecular dynamics for aqueous Gd(III) complexes. The various distribution functions result from the inclusion of 1, 2 or 3 Gd(III) in the simulation cell.

a set-up similar to the one employed in Paper I [35] using 7 f-electrons spread over 7 orbitals as the active space.

4.2 MD simulation

After initial equilibration the MD simulation was conducted over 10 ns. We used Cl− ions to counter the effects of the positive charge of the system. We computed RDF’s and evaluate the co-ordination number of the Gd(III) ion to water molecules in aqueous solution. In Figure 4.1 the Gd-O RDF’s are presented for the varying conditions. The first peak occurs at 2.45 Å and the single Gd(III) system has a peak height of around 23, whereas the peak height is around 16 for the 2 and 3 Gd(III) systems. In all cases the concentration was kept constant and the box size varied. Figure 4.1 b shows the n(r) analysis of coordination numbers which varies between 8 or 9 water molecules. Since the value fluctuates between these numbers, this led us to look more carefully at such systems and evaluate systems with 7, 8 or 9 water molecules binding to the central lanthanide in our quantum chemistry evaluation. The change in coordination number is possibly due to the smaller box-size of 14.1927 Å for the single Gd(III) which restricts the cut-off to a smaller value. These calculations were not meant to provide highly accurate solvation configurations but rather to be used as a generator for fluctuating geometries of the Gd3+(aq) complex for analyzing the effect of the second shell on the ZFS.
4.3 Optimization of complexes

Table 4.1 shows the optimized bond lengths of the complexes. Through calculation of the hessian matrix we confirmed that minima for the 7 and 9 coordinated complexes were determined. In our previous work [35] we had used a reference geometry for Gd(III)(H$_2$O)$_8^{3+}$ optimized using the TPSSH functional [23]. This optimization made use of symmetry constraints and thus the geometry was constrained to a $D_{4d}$ symmetry with a Gd-O distance of 2.471 Å. The resulting splitting of the $^8$S state was 0.9695 cm$^{-1}$, nearly double that of experimental values. Here we re-optimized the geometry using the PBE0 functional which resulted in $C_{4v}$ symmetry and extracted a bond length of 2.438 Å for four of the Gd-O bonds and 2.435 Å for the other four. It should be noted that the experimental geometry for the complex has been reported to lie in the range of 2.4-2.6 Å [24]. This geometry resulted in a total splitting of the ground state of 0.3861 cm$^{-1}$ which is in good agreement with the experimental data for aqueous solution (0.38-0.46 cm$^{-1}$) [26]. A more in-depth analysis of the structure dependence on symmetry is presented in the article. Similarly the Eu(II) complexes were optimized and the results are shown in Table 4.1. In general the bond length of the Eu(II) complexes are longer than those of the corresponding Gd(III) complexes. We also notice that with an increase in hydration number the average bond length of the central lanthanide and the oxygen molecules increases.

**Table 4.1:** Optimized Geometry Parameters for M(H$_2$O)$_n^{3+}$, M = Eu(II)/Gd(III) and n = 7, 8, 9

<table>
<thead>
<tr>
<th></th>
<th>Gd(III)(H$_2$O)$_n^{3+}$</th>
<th>Eu(II)(H$_2$O)$_n^{3+}$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 7</td>
<td>n = 8</td>
</tr>
<tr>
<td>M-O1</td>
<td>2.407</td>
<td>2.438</td>
</tr>
<tr>
<td>M-O2</td>
<td>2.413</td>
<td>2.438</td>
</tr>
<tr>
<td>M-O3</td>
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4.4 Zero-Field splitting for aqueous Gd(III) and Eu(II)

From the trajectory of our CPMD simulation we extracted several data points using the first shell with a cut-off radius of 3 Å which generally included 8 water molecules and the second shell with a cut-off of 5 Å which included a total of 22-24 water molecules. The values for the inner and outer shell are determined from the RDF in Figure 4.1. These cluster configurations from a limited sampling of the MD simulation were used to compare the effect of including the second shell on the ZFS. The comparison of the $D$ parameter of the two configuration samples is depicted in Figure 4.2. We see that though the points deviate slightly from perfect correlation, the effect of the second-shell is quite small and considering the balance between accuracy and statistical sampling, it is much more computationally efficient to only include the first shell in the calculations.

In Figure 4.3 the splitting of the ground state octet into kramer doublets is depicted for the various complexes $M(H_2O)_n$ where $M$ is Eu(II) or Gd(III), and the corresponding lowest lying excited sextet states are shown on the right hand side. For the case of Gd(III) the 9 co-ordinated complex has the lowest amount of splitting ($0.0838 \text{ cm}^{-1}$) and from the splitting it can be seen that the $D$ parameter is negative, whereas the $D$ parameter is positive for the 7 or 8 co-ordinated complex. The excited state sextet of the 9 co-ordinated complex lies the highest in energy relative to the ground state at $40285 \text{ cm}^{-1}$ compared to the 8 co-ordinated complex($40253 \text{ cm}^{-1}$) and the 7 co-ordinated complex($40254 \text{ cm}^{-1}$). The order of the lowest lying excited state corresponds directly to the splitting of the ground state: the larger the energy difference between the ground states octet and the lowest sextet excited state, the smaller the ZFS.
**Figure 4.3:** A comparison of optimized $\text{M(H}_2\text{O)}_n$ complex where M is Eu(II) or Gd(III) and $n = 7, 8$ or $9$. The left-hand figure shows the splitting of the ground state octet. The right-hand figure shows the lowest excited state sextets where the left axis corresponds to Eu(II) and the right axis corresponds to the energy values for Gd(III).

In the case of Eu(II) the least amount of splitting of the ground state occurs in the 8 co-ordinated complex, followed by the 9 co-ordinated complex and the 7 co-ordinated complex. Similar to the Gd(III) complexes the splitting of the ground state has a direct relation to the energy levels of the excited states. In general, the $D$ parameters of the Eu(II) complex are much less than at least half the $D$ parameters of the corresponding Gd(III) complexes. Whereas the Gd(III) complexes have the lowest lying excited states close to approximately $40200 \text{ cm}^{-1}$, the lowest lying excited states of the Eu(II) complexes are much lower in energy around the $35700 \text{ cm}^{-1}$ mark. Surprisingly, despite the Eu(II) and Gd(III) ions being iso-electronic there is no systematic trend in the ZFS for each system size.

To investigate the differences in Eu(II) and Gd(III), we decided to use the Eu(II) optimized geometry and replace the metal center with Gd(III) and vice versa and see the effect this would have on the splitting of the ground state. This would give us deeper insight into the nature of the ZFS since Eu(II) and Gd(III) are iso-electronic and allow us to see the sensitivity of the splitting to the geometry under consideration. The results are depicted in Figure 4.4 where A@B corresponds to using A as the center while using the optimized geometry of the complex B. In panel a) we see that in the case of Eu(II), changing the geometry to the Gd(III) optimized geometry has a dramatic effect on the 7 and 8 co-ordinated complexes, increasing the splitting from $0.1264 \text{ cm}^{-1}$ to $0.4979 \text{ cm}^{-1}$ and from $0.0557$ to $0.8334 \text{ cm}^{-1}$ respectively, while the 9 co-ordinated complex remains almost the same, and decreasing
Figure 4.4: A comparison of the splitting of the ground state octet when using different geometries. A@B corresponds to using A as the metal ion center whilst using the optimized geometry of B.

only slightly from 0.2425 cm$^{-1}$ to 0.22370 cm$^{-1}$. The least splitting for the Eu(II) metal center is witnessed with the 8 co-ordinated complex whereas, in the case of Gd(III) the lowest amount of splitting occurs in the 9 co-ordinated complex. In panel d) for the case of Gd(III), changing the geometry to Gd@Eu lowers the total amount of splitting of the ground state octet in the case of the 7 and 8 co-ordinated complex from 0.3646 cm$^{-1}$ to 0.2536 cm$^{-1}$ and from 0.3861 cm$^{-1}$ to 0.2768 cm$^{-1}$ respectively, whereas for the 9 co-ordinated complex the splitting is increased very slightly from 0.0838 cm$^{-1}$ to 0.0912 cm$^{-1}$. The $D$ values for the various complexes are shown in Table 4.2.

Overall, we see that changing the geometry has a more dramatic effect on Eu(II) as compared to Gd(III). Replacing Gd(III) at the Eu(II) cluster geometries shows the same trend as Figure 4.3. Since there are no apparent general trends in the data relating the geometry to the ZFS, perhaps a better way to approach the problem may be by analyzing the individual spin-orbit coupling elements and re-orienting the molecules to the principal axis frame of the ZFS.
Table 4.2: D [cm$^{-1}$] and E/D values for M(H$_2$O)$_n^{3+}$, M = Eu(II)/Gd(III) and n = 7, 8, 9

<table>
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<tr>
<th></th>
<th>Gd(III)(H$_2$O)$_n^{3+}$</th>
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<th>Eu@Gd</th>
</tr>
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5. Outlook

Up to now we have looked at the direct contributions of the ZFS to various complexes and observed the effects of various geometries and distortions. For a more complete picture and to reach one step further in our goal to investigate the molecular foundation of paramagnetic nuclear spin relaxation, we will try and relate these effects to electron spin dynamics. This can be done by studying the simultaneous correlated electronic fluctuations and molecular dynamics of a system. For this purpose we have a number of projects that we anticipate.

Firstly, we wish to study the normal mode vibrations of complexes. By distorting the complex along the normal mode vibrations we can determine which dynamic degrees of freedom contribute the most to the ZFS. We have decided to look at the complexes Ni(II)(H$_2$O)$_6$ and Mn(II)(H$_2$O)$_6$ in one of our studies since they have valence $d$-orbitals and are computationally not as demanding as Gd(III) system and yet may provide us valuable insight into the nature of how vibrational modes can be related to fluctuations in the molecular dynamics. For example, in the case of the Ni(II)(H$_2$O)$_6$ complex, it is presumed that among the 51 normal modes only 3 to 5 normal modes may be important to contributing to the ZFS, whereas the effects of the other distortions along the vibrational modes is negligible. We can then compare these normal mode vibrations to molecular dynamics simulations and determine which distortions can be projected on top of which normal modes, enabling us to study the effects of dynamical systems.

Secondly, we wish to relate our ZFS study to high level \textit{ab-initio} MD simulations. This is done by taking conformations of geometries for a particular complex in solution and extracting the inner shell of the complex. We then compute the ZFS for the various geometries using wave-function methods and once this is done one is able to write out the time auto-correlation function of the contribution of the ZFS from the elements of the $D$-tensor. This is one of the parameters that can assist in computing the electron spin relaxation.

We also anticipate calculating other parameters that are important in analyzing NMR parameters for the relaxation process. We will be particularly interested
in shifts that arise in lanthanide systems. We will derive parameters for the spin Hamiltonian (g-tensor, D-tensor and the A-tensor) from quantum chemical calculations, which can then be related to compute shifts.

Therefore the overall scope of the project extends what we have accomplished so far, i.e. calculating ZFS tensors for complexes, and bridging the high-level \textit{ab-initio} calculations to dynamical values so that we can find a direct relationship to the equations that govern electron spin relaxation.


