CHAPTER NO. 1

INTRODUCTION

In 1794, Johann Gadolin, a French chemist, while investigating a rare Swedish mineral, discovered a new element in impure form, which he believed to be a new element and to which he gave the name Ytterbia, from Ytterby, the village where the ore was found. The name, however, was soon shortened to Yttria. Owing to the close chemical similarities between the members of the lanthanide series, they resisted easy purification and separation from one another. Numerous misidentifications, false claims and counter claims are scattered through the pages of lanthanide chemical history. The following Table 1.01 gives a picture about the history of lanthanides.

Table 1.01 : Discovery of the lanthanides

<table>
<thead>
<tr>
<th>Lanthanide</th>
<th>Year of identification</th>
<th>Discoverer</th>
<th>Origin of name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lanthanum</td>
<td>1839</td>
<td>Mosander</td>
<td>Lanthanum: Greek for &quot;to lie hidden&quot;</td>
</tr>
<tr>
<td>Cerium</td>
<td>1803</td>
<td>1. Berzelius and Hisinger 2. Klaproth</td>
<td>Ceres, an asteroid discovered in 1801</td>
</tr>
<tr>
<td>Praseodymium</td>
<td>1885</td>
<td>Von Welsbach</td>
<td>From Greek : prasios = green; dymium = twin</td>
</tr>
<tr>
<td>Neodymium</td>
<td>1885</td>
<td>Von Welsbach</td>
<td>From Greek : Neo = new; Dymium = twin</td>
</tr>
<tr>
<td>Promethium</td>
<td>1947</td>
<td>1. Marinsky 2. Glenenin 3. Coryell</td>
<td>Promethus, the Greek God who stole fire from heaven for men's use</td>
</tr>
<tr>
<td>Samarium</td>
<td>1879</td>
<td>De Boisbaudran</td>
<td>From its ore, Samarskite, named after the Russian engineer Samarski</td>
</tr>
</tbody>
</table>
### Table 1.02: Some properties of lanthanide atoms and ions

<table>
<thead>
<tr>
<th>Atomic number</th>
<th>Name</th>
<th>Symbol</th>
<th>Electronic configuration</th>
<th>$E^0(V)$</th>
<th>Radius $M^{3+}(\text{Å})$</th>
</tr>
</thead>
<tbody>
<tr>
<td>57</td>
<td>Lanthanum</td>
<td>La</td>
<td>5d$^1$6s$^2$</td>
<td>[Xe]</td>
<td>-2.37</td>
</tr>
<tr>
<td>58</td>
<td>Cerium</td>
<td>Ce</td>
<td>4f$^1$5d$^1$6s$^2$</td>
<td>4f$^1$</td>
<td>-2.34</td>
</tr>
<tr>
<td>59</td>
<td>Praseodymium</td>
<td>Pr</td>
<td>4f$^2$6s$^2$</td>
<td>4f$^2$</td>
<td>-2.35</td>
</tr>
<tr>
<td>60</td>
<td>Neodymium</td>
<td>Nd</td>
<td>4f$^3$6s$^2$</td>
<td>4f$^3$</td>
<td>-2.32</td>
</tr>
</tbody>
</table>


#### 1.1: General Feature of Lanthanides

The term lanthanides refer to the very similar fourteen elements following lanthanum (La, At. No. 57) to Lutetium (Lu, At. No. 71), which resemble each other in their physical and chemical properties and are characterized by gradual filling up of electrons in the inner lying 4f-shell. The general electron configuration of lanthanides is (n-2)f$^1$-4f$^1$(n-1)d$^1$ns$^2$. Since 4f-electrons are relatively less involved in binding, these highly electropositive elements have their prime oxidation number +3.

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**Introduction**

<table>
<thead>
<tr>
<th>Name</th>
<th>Year of Discovery</th>
<th>Discoverer</th>
<th>Termination</th>
</tr>
</thead>
<tbody>
<tr>
<td>Europium</td>
<td>1889</td>
<td>Crookes, Marignac</td>
<td>Europe</td>
</tr>
<tr>
<td>Gadolinium</td>
<td>1880</td>
<td>Marignac, After the Finnish chemist Gadolin</td>
<td>After the town of Ytterby in Sweden</td>
</tr>
<tr>
<td>Terbium</td>
<td>1843</td>
<td>Mosander</td>
<td>After the town of Ytterby in Sweden</td>
</tr>
<tr>
<td>Dysprosium</td>
<td>1886</td>
<td>De Boisbaudran</td>
<td>Dysprositos=hard to get at Holmia, Latinized version of Stockholm After the town of Ytterby in Sweden</td>
</tr>
<tr>
<td>Holmium</td>
<td>1879</td>
<td>1. Cleve, 2. Soret</td>
<td>After the town of Ytterby in Sweden</td>
</tr>
<tr>
<td>Erbium</td>
<td>1843</td>
<td>Mosander</td>
<td>After the town of Ytterby in Sweden</td>
</tr>
<tr>
<td>Ytterbium</td>
<td>1878</td>
<td>Marignac</td>
<td>After the town of Ytterby in Sweden</td>
</tr>
<tr>
<td>Lutetium</td>
<td>1908</td>
<td>1. Von Welsbach, 2. Urbain</td>
<td>Lutetia, Latin for Paris</td>
</tr>
<tr>
<td>Ytterium</td>
<td>1794</td>
<td>Gadolin</td>
<td>After the town of Ytterby in Sweden</td>
</tr>
</tbody>
</table>

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An important feature of lanthanide elements is the occurrence of “Lanthanide Contraction”, a steady decrease in ionic and atomic size with increasing atomic number. The major cause of lanthanide contraction is the screening effect of the increasing nuclear charge by inner sphere 4f-electrons.

<table>
<thead>
<tr>
<th>Atomic Number</th>
<th>Lanthanide</th>
<th>Electron Configuration</th>
<th>Atomic Radius</th>
<th>Ionic Radius</th>
</tr>
</thead>
<tbody>
<tr>
<td>61</td>
<td>Promethium</td>
<td>Pm (4f⁶6s²)</td>
<td>4f⁴</td>
<td>-2.29</td>
</tr>
<tr>
<td>62</td>
<td>Samarium</td>
<td>Sm (4f⁶6s²)</td>
<td>4f⁵</td>
<td>-2.30</td>
</tr>
<tr>
<td>63</td>
<td>Europium</td>
<td>Eu (4f⁶6s²)</td>
<td>4f⁶</td>
<td>-1.99</td>
</tr>
<tr>
<td>64</td>
<td>Gadolinium</td>
<td>Gd (4f⁷5d⁶6s²)</td>
<td>4f⁷</td>
<td>-2.29</td>
</tr>
<tr>
<td>65</td>
<td>Terbium</td>
<td>Tb (4f⁹6s²)</td>
<td>4f⁸</td>
<td>-2.30</td>
</tr>
<tr>
<td>66</td>
<td>Dysprosium</td>
<td>Dy (4f¹⁰6s²)</td>
<td>4f⁹</td>
<td>-2.29</td>
</tr>
<tr>
<td>67</td>
<td>Holmium</td>
<td>Ho (4f¹¹6s²)</td>
<td>4f¹⁰</td>
<td>-2.33</td>
</tr>
<tr>
<td>68</td>
<td>Erbium</td>
<td>Er (4f¹²6s²)</td>
<td>4f¹¹</td>
<td>-2.31</td>
</tr>
<tr>
<td>69</td>
<td>Thulium</td>
<td>Tm (4f¹³6s²)</td>
<td>4f¹²</td>
<td>-2.31</td>
</tr>
<tr>
<td>70</td>
<td>Ytterbium</td>
<td>Yb (4f¹⁴6s²)</td>
<td>4f¹³</td>
<td>-2.22</td>
</tr>
<tr>
<td>71</td>
<td>Lutetium</td>
<td>Lu (4f¹⁴5d⁴6s²)</td>
<td>4f¹⁴</td>
<td>-2.30</td>
</tr>
</tbody>
</table>

Figure 1.01 Shapes of 4f-orbitals
The reduction in size from one lanthanide to the next makes their separation possible but the smallness and regularity of the reduction in size makes the separation difficult. By the time Ho$^{3+}$ is reached, the radius has been sufficiently reduced to be almost identical with that of Y$^{3+}$, that is why with much lighter element is associated with heavier lanthanide. The total lanthanide contraction is of the similar magnitude to the expansion found in passing from the first to the second transitions series, which might therefore have been expected to occur from passing from second to third. This interaction of lanthanides in fact almost cancel this anticipated increase with the result, i.e. in each group of transition elements the second and third member have almost similar sizes and properties.$^{1-3}$.

According to Hard and Soft Acid Bases concept, lanthanides behave as typical hard acids and so its bonding preference is to fluorine (F) and oxygen (O) donor ligands. In the presence of water, complexes with nitrogen, sulphur and halogen (except fluorine) are not stable, but if these donor sites are a part of multidonor ligands these donor sites are involved in strong complexation with lanthanides$^{4,5}$. The absence of extensive interaction with 4f-orbitals, minimizes ligand field stabilization energy (LFSE). Low LFSE reduces overall stability, but on the other hand provides a greater flexibility in geometry and coordination number because LFSE is not lost e.g. when an octahedral complex is transformed into trigonal prismatic or square anti prismatic geometry. Furthermore, the complexes tends to be labile in solution. Table 1.03 presents a summary of these differences between lanthanides and transition metal ions.
In spite of the fact that f-block elements, the members of lanthanide and actinide transition series, have no known essential role in life processes, they no doubt pose some of the most fascinating, challenging and important chemical and biochemical problems of all inorganic elements of the periodic table. The reasons for this, primarily stem from the properties conferred by their outer electron configuration and associated

### Table 1.03: Comparison of transition metal ions and lanthanide ions

<table>
<thead>
<tr>
<th>Property</th>
<th>Lanthanide ions</th>
<th>First series transition metal ions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metal orbitals</td>
<td>4f</td>
<td>3d</td>
</tr>
<tr>
<td>Ionic radii</td>
<td>106-85 pm</td>
<td>75-60 pm</td>
</tr>
<tr>
<td>Common coordination no.</td>
<td>6,7,8,9</td>
<td>4,6</td>
</tr>
<tr>
<td>Typical coord. Polyhedra</td>
<td>Trigonal prism, square antiprism, dodecahedron</td>
<td>Square planar, tetrahedron, octahedron</td>
</tr>
<tr>
<td>Bonding</td>
<td>Little metal-ligand orbital interaction</td>
<td>Strong metal-ligand orbital interaction</td>
</tr>
<tr>
<td>Bond direction</td>
<td>Little preference in bond direction</td>
<td>Strong preference in bond direction</td>
</tr>
<tr>
<td>Bond strengths</td>
<td>Bond strengths correlate with electronegativity, decreasing in the order: F⁻, OH⁻, H₂O, NO₃⁻, Cl⁻</td>
<td>Bond strengths determined by orbital interaction normally decreasing in the following order: CN⁻, NH₃, H₂O, OH⁻, F⁻</td>
</tr>
<tr>
<td>Solution complexes</td>
<td>Ionic; rapid ligand exchange</td>
<td>Often covalent; covalent complexes may exchange slowly</td>
</tr>
</tbody>
</table>

### 1.2: The Biochemistry of Lanthanides and Actinides

In spite of the fact that f-block elements, the members of lanthanide and actinide transition series, have no known essential role in life processes, they no doubt pose some of the most fascinating, challenging and important chemical and biochemical problems of all inorganic elements of the periodic table. The reasons for this, primarily stem from the properties conferred by their outer electron configuration and associated
energy levels coupled with their chemical toxicity which are low for lanthanides and with their radio toxicities which are a major problem for actinides.

The paramagnetic nature of lanthanides is responsible for higher magnetic moment due to number of unpaired electrons in 4f orbitals. This makes them of great practical value for their application in Nuclear Magnetic Resonance Spectroscopy (NMR) as well Nuclear Magnetic Resonance Imaging (MRI).

Gadolinium(III) complexes especially with polyamino-polycarboxylic acids, make good contrast enhancing agent because of their high magnetic moment coupled with good relaxation efficiencies. Dysprosium and Thulium chelates have been proved excellent SHIFT REAGENTS in following compartmentalization of sodium during onslaught of Ischaemia. Other important biological and biochemical applications are as follows:

(i) Lanthanides can be used as heavy atom ‘STAINS’ in electron microscopy or x-ray diffractions studies.

(ii) Thermodynamic properties of metal ion binding site, e.g. for Calcium(II) can be elucidated through competition or exchange reactions with lanthanide ions. This is most important because calcium, one of the most important and ubiquitous of essential elements, has very few properties, which can be used to PROBE its Biochemistry in situ. The lanthanide(III) ions, make almost BIOMIMETIC agent for Ca(II) [Table 1.04]
(iii) Kinetic properties of biochemical react involving metal ions, can likewise be investigated and mechanistic information gained.

(iv) Fine structural features of biological systems may be researched and defined using NMR, ESR and 4f-4f transition spectra and energy transfer leading to fluorescence.
(v) Further applications include in vivo targeting and localization in tumors using appropriate lanthanide ion complexes.\(^7\)

### 1.2.1: Biochemistry in Body Compartments

After entry into the body by whatever route, transport of lanthanide or actinides, secondary disposition sites is mainly via the plasma in blood stream. Within body compartment it is convenient to consider the f-element as being placed between the three (or perhaps four) fractions which are in equilibrium with one another and which are responsible for transport and intracellular uptake. We take iron as important essential elements to illustrate this concept. Iron is partitioned between fractions, which exist in a labile and thermodynamic equilibrium with one another. There a fourth fraction in which the metal is bound inertly and which is also exchangeable with the other three fractions. This latter fraction can be thought as storage compartment.

<table>
<thead>
<tr>
<th>Inert and or Thermodynamically</th>
<th>Labile</th>
<th>and</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-reversible</td>
<td>Thermodynamically Reversible</td>
<td></td>
</tr>
</tbody>
</table>

**Hemoglobin**

**Myoglobin**

**Transferrin**

**Ferritin**

Low molecular mass 

Fe\(^{3+}\) Complexes with

free aquo ion and 

\([\text{Fe(H}_2\text{O)}_6]^{3+}\) and citrate

Inert and labile forms of metal ions in vivo
With respect to metal transport, it is the three labile compartments, which are of interest. Transferrin, the protein which is responsible for transporting iron in and out of cells via receptor mediated endocytosis, appears to play a major role in f-element transport within the bloodstream.\(^7\) Transferrin is a glycoprotein (molecular mass 80k Da) containing 800 amino acid residues. The protein is bilobular with one metal binding site in each lobe. These metal bindings are designated as N- and C- terminal sites. In addition to binding and transporting Fe\(^{3+}\) ions, transferrin is also responsible for binding lanthanides and actinides in vivo.

The protein also binds to both lanthanide and actinides. Comparative Studies in vitro and in vivo have shown the binding of lanthanides.\(^9\)-\(^11\) UV difference spectroscopy and other studies in vitro with Pu(IV), Th(IV) and a number of trivalent lanthanides have very clearly demonstrated that, like iron, two lanthanide or actinide metal atoms are bound per transferrin molecule.\(^12\)

Data on the formation constants for actinide and lanthanide complexes with transferrin is very sparse. Harris\(^13\) however reported conditional values of equilibrium formation constants of Nd(III) and Sm(III) transferrin complexes, using absorption difference and comparative absorption spectra. However the data published on conditional stability constants of human serum transferrin with lanthanides and actinides have important implications with regard to actinide/lanthanide distribution within the human body. It has been shown that in binding to human serum transferrin, the f elements are participating in certain aspects of iron transport pathways in vivo. However, no plutonium e.g. is found within RBC following incorporation and there is no unequivocal evidence that plutonium and the other actinides or lanthanides are
The interactions of various lanthanides with a very wide range of proteins have been reviewed in depth by Evans (1990). The range of proteins which have been investigated is large and includes enzymes such as Trypsins, Elastase, Collagenase, Amylase, Nuclease, ATPase, Phospholipase—A$_2$ and Acetylcholinesterase, the contractile proteins Actins, Myosin and molecular oxygen carriers such as Haemocyanin. These studies have shown that the major ligand for Ln(III) ion is the carboxyl group with additional coordination through carboxyl or hydroxylic oxygen. Often lanthanides occupy Ca$^{2+}$ binding sites. However, Ln$^{3+}$ ions may also bind to sites
of proteins, which are not known to bind Ca\(^{2+}\) or any other metal. Because of their higher charge to volume ratio, Ln\(^{3+}\) ions usually have higher affinity for proteins than Ca\(^{2+}\). The affinities of different lanthanides vary widely but in general they increase with decreasing hydration of sequestered lanthanide ion and with increasing cationic charge of binding site. In addition to protein study the Ln\(^{3+}\) binding to other types of biomolecules in vitro can also provide valuable structural and other information. The biomolecules include Nucleic acid, Phospholipids, Phospholipid membrane, Porphyrins, Vitamin B\(_{12}\) and high-density Lipoproteins.

The most important aspect of lanthanide binding to biomolecule is the fact that these MIMIC interaction of these biomolecules with radioactive actinides. Increasing use of nuclear reactor, radioactive isotopes, nuclear medicines, the medicinally compatible Ln(III) interaction has been extremely useful in exploring biochemistry and biological chemistry of actinides.\(^{16-18}\)

**1.2.2 : Similarities and Differences in Trivalent Lanthanide and Actinide-Ions:**

While comparing the absorption spectra of lanthanides and actinide ions having same number of f-electron the most evident difference lies in the absolute values for molar absorptivities. Actinide ion molar absorptivities, generally decrease across actinide series to Am\(^{3+}\). For Cm\(^{3+}\) and heavier actinides the molar absorptivity becomes more or less constant but continue to be significantly larger than the lanthanide having similar number of f-electrons,

The entire energy range of calculated “free ion” f-states is shown in Figure 1.02 for trivalent lanthanide ions and in Figure 1.03 for trivalent actinide ions. Several features are evident in comparing Figure 1.02 and 1.03 Actinide ions tend to have a somewhat
more open energy-level structure near their ground state, but a less open energy-level structure for higher-lying states. This arises from larger spin-orbit coupling parameters, but reduced Slater parameter values in the actinide series when parameter values for actinide and lanthanide ions having the same number of f-electrons are compared. For mid-series and actinide ions, it is evident that many or even most f-sates occur at energies corresponding to vacuum-ultraviolet or shorter wave length light (i.e. at energies where little observed data on f-state energies exist). The fingerprinting character of f-state successfully used for analytical purposes as characteristics. Birnbaum et al. by using absorption difference and comparative absorption spectra could demonstrate the binding sites of Transferrin, Albumin and Trypsin, which were given sound support by other studies. The changes in the f-state energies are large enough for the observed spectra to permit the determination of complexation, but not so large enough as to make assignments of complexed metal ion bands. What we think the emphasis should be given more on intensity data, which definitely yields better and more useful findings. With sophistication and better understanding of solution absorption spectroscopy will definitely prove boon for lanthanide/actinide coordination and biochemistry.

Figure 1.02 Calculated free ion energy-level structure of 4f states of trivalent lanthanide ions

Figure 1.03 Calculated free ion energy-level structure of 5f states of trivalent actinide ions
Table 1.05: Listing of absorption bands with calculated $U^{(2)} > 0.01$ for aquated trivalent lanthanide ions to 50000 cm$^{-1}$ and trivalent actinides to 31000 cm$^{-1}$.

<table>
<thead>
<tr>
<th>Lanthanide ion</th>
<th>Excited state</th>
<th>Transition energy (cm$^{-1}$)</th>
<th>Calculated $U^{(2)}$</th>
<th>Actinide ion</th>
<th>Excited state</th>
<th>Transition energy (cm$^{-1}$)</th>
<th>Calculated $U^{(2)}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pr$^{3+}$</td>
<td>$^3H_4$</td>
<td>2322</td>
<td>0.1095</td>
<td>Pa$^{3+}$</td>
<td>$^4I_{9/2}$</td>
<td>2007</td>
<td>0.0194</td>
</tr>
<tr>
<td>($^3H_4$)</td>
<td>$^3H_4$</td>
<td>5149</td>
<td>0.5089</td>
<td></td>
<td>$^4I_{11/2}$</td>
<td>4007</td>
<td>0.0214</td>
</tr>
<tr>
<td></td>
<td>$^3H_4$</td>
<td>6540</td>
<td>0.0654</td>
<td></td>
<td>$^2H_{9/2}$</td>
<td>9631</td>
<td>0.0544</td>
</tr>
<tr>
<td></td>
<td>$^3H_4$</td>
<td>6973</td>
<td>0.0187</td>
<td></td>
<td>$^4F_{3/2}$</td>
<td>9921</td>
<td>0.2016</td>
</tr>
<tr>
<td></td>
<td>$^3H_4$</td>
<td>16840</td>
<td>0.0026</td>
<td></td>
<td>$^4G_{5/2}$</td>
<td>11220</td>
<td>0.7029</td>
</tr>
<tr>
<td></td>
<td>$^3H_4$</td>
<td>22535</td>
<td>~0</td>
<td></td>
<td>$^4F_{7/2}$</td>
<td>11518</td>
<td>0.0392</td>
</tr>
<tr>
<td>Nd$^{3+}$</td>
<td>$^4I_{11/2}$</td>
<td>2007</td>
<td>0.0194</td>
<td>U$^{3+}$</td>
<td>$^4I_{9/2}$</td>
<td>4563</td>
<td>0.0214</td>
</tr>
<tr>
<td>($^4I_{9/2}$)</td>
<td>$^4G_{5/2}$</td>
<td>17167</td>
<td>0.8979</td>
<td></td>
<td>$^2H_{9/2}$</td>
<td>9631</td>
<td>0.0544</td>
</tr>
<tr>
<td></td>
<td>$^2G_{7/2}$</td>
<td>17333</td>
<td>0.0757</td>
<td></td>
<td>$^4F_{3/2}$</td>
<td>9921</td>
<td>0.2016</td>
</tr>
<tr>
<td></td>
<td>$^4G_{7/2}$</td>
<td>19103</td>
<td>0.0550</td>
<td></td>
<td>$^4G_{5/2}$</td>
<td>11220</td>
<td>0.7029</td>
</tr>
<tr>
<td>Pm$^{3+}$</td>
<td>$^5I_5$</td>
<td>1577</td>
<td>0.0246</td>
<td>Np$^{3+}$</td>
<td>$^5I_4$</td>
<td>3954</td>
<td>0.0192</td>
</tr>
<tr>
<td>($^5I_4$)</td>
<td>$^5G_2$</td>
<td>17857</td>
<td>0.7215</td>
<td></td>
<td>$^5I_6$</td>
<td>7231</td>
<td>0.0134</td>
</tr>
<tr>
<td></td>
<td>$^5G_3$</td>
<td>18256</td>
<td>0.1444</td>
<td></td>
<td>$^5F_2$</td>
<td>8197</td>
<td>0.2275</td>
</tr>
<tr>
<td></td>
<td>$^3G_3$</td>
<td>21102</td>
<td>0.0228</td>
<td></td>
<td>$^3H_4$</td>
<td>10752</td>
<td>0.0215</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>$^5F_3$</td>
<td>11588</td>
<td>0.0114</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>$^5G_2$</td>
<td>11853</td>
<td>0.4629</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>$^5G_3$</td>
<td>12732</td>
<td>0.1493</td>
</tr>
<tr>
<td>Ion</td>
<td>Configuration</td>
<td>Energy (eV)</td>
<td>Oscillator Strength</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-----</td>
<td>---------------</td>
<td>-------------</td>
<td>---------------------</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sm³⁺</td>
<td>(⁶H₉/₂)</td>
<td></td>
<td></td>
<td></td>
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<td>⁷F₄</td>
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<td>Dy³⁺</td>
<td>(⁶H₁₃/₂)</td>
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<tr>
<td>⁶H₁₃/₂</td>
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<td>(⁶H₁₃/₂)</td>
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<td>⁶H₁₃/₂</td>
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<td>0.2098</td>
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</table>
1.2.3: Clinical Applications of Lanthanides

Radioactivity and radioactive species of various lanthanides formed significant use in localizing tumors and exposing the high potential of lanthanide compounds as
The trivalent lanthanide ions have unique spectroscopic properties. Since the $4f$ shell is effectively shielded by closed $5s$ and $5p$ shells, the ligand environment has only a weak influence on the electronic cloud of lanthanide ion. Although weak, this perturbation is responsible for the spectral fine structure. The line width of the bands is small and its peak position reveals the electronic structure (of a part) of the $4f^n$ configuration. The crystal field splitting gives information about the symmetry of the rare earth site and about the shape of the coordination polyhedron.\(^{21}\)

The main idea behind this present work is to explore the potential of these fascinating lanthanides as spectral and structural probe in biochemical reaction of immense importance in human metabolism.

**1.3 : Spectroscopic Features of Lanthanides**

The trivalent lanthanide ions have unique spectroscopic properties. Since $4f$ shell is effectively shielded by closed $5s$ and $5p$ shells, the ligand environment has only a weak influence on the electronic cloud of lanthanide ion. Although weak, this perturbation is responsible for the spectral fine structure. The line width of the bands is small and its peak position reveals the electronic structure (of a part) of the $4f^n$ configuration. The crystal field splitting gives information about the symmetry of the rare earth site and about the shape of the coordination polyhedron.\(^{21}\)
Absorption and luminescence spectroscopy are important techniques in the study of lanthanide system as they allow determining the natural frequencies of lanthanide.

The absorption spectra of lanthanide doped single crystals of lanthanide compounds show group of narrow lines in solution or in glasses, however the lines within group broaden to one absorption band, these bands have to be ascribed to

Figure 1.04 Absorption spectra of Pr$^{3+}$, Nd$^{3+}$, electronic to electronic transition Pm$^{3+}$, Sm$^{3+}$, Eu$^{3+}$, Dy$^{3+}$, Ho$^{3+}$, Er$^{3+}$, Tm$^{3+}$ and inside the 4f shell. Each group or Yb$^{3+}$ in dilute acid solution band corresponds to the transition between $^{2S+1}L_J$ free ion levels (or J-manifolds). They are not accompanied by a change in configuration and hence named as Intra-configurationally Transition. Three mechanisms must be considered for the interpretation of the observed transitions$^{22}$.

(i) Magnetic-Dipole Transitions

(ii) Induced Electric Dipole Transitions

(iii) Electric Quadrupole Transition.
1.3.1: Magnetic Dipole Transition

The magnetic dipole transition is caused by the interaction of spectroscopic active ion with magnetic field component of the light through a magnetic dipole. Magnetic dipole radiations can also be considered as rotational displacement of charge. Because the sense of rotation is not reversed under inversion through a point (or inversion centre) a magnetic dipole transition has even parity. Therefore a magnetic dipole operator possesses even transformation properties between states of equal parity (or intra-configurational transition).

1.3.2: Induced Electric Dipole Transition

The majority of observed optical transition of lanthanides are Induced Electric Dipole Transition, which have consequence of interaction of spectroscopically active ion/ the lanthanide ion with the Electric Filed vector through an electric dipole. The creations of electric dipole suppose a linear movement of charge, and such transition has odd parity. The electric dipole operator has therefore odd transformation properties under inversion with respect to an inversion centre. Intra configurational electric dipole transitions are forbidden by the Laporte Selection rules. The induced electric dipole transitions are described in details in Judd\textsuperscript{23} - Ofelt\textsuperscript{24} theory.

1.3.3: Electric Quadrupole Transition

The electric quadrupole transition arises from the displacement that has a quadrupole nature. An electric quadrupole consists of four point charges with overall zero charge and zero dipole moment. It may visualized as two dipoles arranges in a way to annul each other’s dipole moment. An electric quadrupole has even parity. Electric quadrupole transitions are much weaker than magnetic dipole, which in turn are
weaker than induced electric dipole transitions. However *hypersensitive transitions* are considered as pseudoquadrupole transitions as these transitions obey the selection rules of quadrupole transitions.

### Selection Rules

Selection rules are only valid in strict conditions and can be relaxed under circumstances. The selection rules for $\Delta L$ and $\Delta S$ are only applicable for Russell Saunders Coupling Scheme. These selection rules are relaxed in intermediate coupling scheme, because in this scheme $L$ and $S$ are not good numbers. Since $J$ remains a good quantum number in the intermediate coupling scheme, the selection rules on $\Delta J$ are harder to break down; it can be relaxed only by $J$-mixing, which is a weak effect.

The selection rules on $\Delta M$ depend on point group symmetry of the rare earth site. The selection rules for magnetic dipole and induced electric dipole transitions are given in Table 1.06.

**Table 1.06: Selection rules for magnetic dipole and induced electric dipole transitions:**

<table>
<thead>
<tr>
<th>Magnetic Dipole Transition (MD)</th>
<th>Induced Electric Dipole Transition (ED)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\Delta \tau=\Delta S=\Delta L=0$</td>
<td>$\Delta L=\pm 1$, $\Delta \tau=0$, $\Delta S=0$, $</td>
</tr>
<tr>
<td>$\Delta J=0$, $\pm 1$ but $0\leftrightarrow 0$ is forbidden</td>
<td>$</td>
</tr>
<tr>
<td>$M'-M=-P$, where $P=\pm 1$</td>
<td>$M'-M=-(q+p)$</td>
</tr>
</tbody>
</table>

A well known example of the breakdown of selection rules of the Judd-Ofelt theory is the occurrence of $^7F_0 \rightarrow ^5D_0$ and $^5D_0 \rightarrow ^7F_0$ transitions in some Eu(III) complexes. The $^7F_0 \leftrightarrow ^5D_0$ transitions are forbidden by the selection rules, as $\Delta J$ ($0 \leftrightarrow 0$) is
forbidden. The breakdown of closure approximation in Judd-Ofelt can be explained to this exceptional behaviour was ascribed by Tanaka et al. Wybourne has shown that the second order matrix element $U^{(0)}$ is zero, so that no intensity can come from this mechanism. Wybourne proposed a mechanism in which spin selection rule is relaxed by scalar third order contribution involving spin-orbit interaction acting within higher lying perturbing states. This model was later developed further by Burdick.  

1.3.5: Intensity Parameterization of Transition between Crystal Field Levels

1.3.5.1: Static Coupling (SC) Model for Line Transition

The induced electric dipole matrix elements between two states $B$ and $B'$ of the $f'$ configuration can be written as:

$$
\langle B | \hat{m}_p^{(l)} | B' \rangle = \langle B | -e \hat{D}_p^{(l)} | B' \rangle = -e \sum_M a_M a'_{M'} \sum_{T,S,L,T',S',L'} \hbar(TSL)h'T'S'L' \times \sum_{k,q \lambda=even} \sum A_{kq} \Xi(k,\lambda)(-1)^{q+p+(J-M)+(S+L'+J+\lambda)} \times \left( \begin{array}{ccc} 1 & \lambda & k \\ p-q & -p & q \end{array} \right) \left( \begin{array}{ccc} \lambda & J & \lambda' \\ -M & q+p & M' \end{array} \right) \left( \begin{array}{c} J' \\ S \\ J \end{array} \right) \times (2\lambda + 1)(2J + 1)(2J' + 1) \left( f^N \right) \left( \hat{U}^{(2)} \right) \left( f^N T'S'L' \right) \right)
$$

(1)

The matrix element in above equation (1) is valid for transitions between two crystal field levels. Because of the radial integrals, the calculation of matrix elements is very tedious and can in fact be done by using some approximations. Axe treated the quantities $A_{kq} = (k, \lambda)$ in equation in equation (1) as adjustable parameter with $\lambda$ is equal to 2, 4 and 6 and $k$ is restricted to the values of $\lambda \pm 1$. The values of $q$ are determined by crystal field symmetry constraints and lie between 0 and $\pm k$. Porchner and Caro introduced notation $B_{kq}$ for the intensity parameters.
\[ B_{\lambda,kq} = A_{kq} = (k,\lambda) \] (2)

At the first local minimum. Starting values chosen for those parameters, because the minimisation procedure stops at the first local minimum. 

The optimised phenomenological intensity parameters depend to a large extent on starting values chosen for those parameters, because the minimisation procedure stops at the first local minimum. 

The equations to be solved are of the form:

\[ \frac{1}{\chi_{ED}} \left[ D_{exp} - \chi_{MD} D_{MD} \right] = \left[ \sum_{kq} \alpha_{kq}^{\text{opt}} B_{kq} \right] \] (3)

or

\[ D_{exp}^0 = \left[ \sum_{kq} \alpha_{kq}^{\text{opt}} B_{kq} \right]^2 \] (4)

Where \( D_{exp}^0 \) is the experimental dipole strength for the magnetic dipole contribution and \( p \) is the polarization number. The symbol \( \alpha \) and \( \beta \) stands for ground and excited state respectively. In general one has to write down such an equation for each of the \( M \) transitions for which a value of the experimental dipole strength is available and \( M \geq N \) (\( N \) is the number of intensity parameters). The parameters are determined by finding the minimum of a function, which consists of sum of \( M \) nonlinear quadratic functions in \( N \) variables. The equations to be solved are of the form:

\[ \sum_{A'} \sum_{kq} \left[ \sum_{kq} \alpha_{kq}^{\text{opt}} B_{kq} \right]^2 - D_{exp}^0 = 0 \] (5)

\begin{align*}
D_{exp} \sim x p \\
\text{is the experimental dipole strength for the magnetic dipole contribution and p is the polarization number. The symbol } \alpha \text{ and } \beta \text{ stands for ground and excited state respectively. In general one has to write down such an equation for each of the M transitions for which a value of the experimental dipole strength is available and } M \geq N \text{ (N is the number of intensity parameters). The parameters are determined by finding the minimum of a function, which consists of sum of M nonlinear quadratic functions in N variables. The equations to be solved are of the form:}
\end{align*}
Intensity parameterisation of spectral transitions between crystal field levels for lanthanide doped single crystal have been reported for LaAlO₃ : Pr³⁺ (Diricks), LaF₃ : Pr³⁺, Pr₂Mg₃(NO₃)₁₂.2₄H₂O (Gorller-Walrand et al)⁴¹, LiYF₄ : Nd³⁺ (Gorller – Walrand et al)⁴², LiYF₄ : Eu³⁺ (Fluyet et al)⁴³, Na₅Eu(MoO₄)₃ and Na₅Eu(WO₄)₃ (Holsa et al)⁴⁴.

The parameterisation scheme given by Judd-Ofelt for J-multiplate transition intensities in terms of \( T_x \) parameters is general and is limited by the assumption of one electron one photon interaction. The parameterisation scheme is independent of the nature of metal ligand interaction. The parameterisation scheme of Axe of describing the intensities of crystal field transition is not general in terms of its applicability. In addition to one electron and one photon assumption, the parameterisation scheme required that the superposition approximation is valid which requires all metal-ligand pair wise interactions to be cylindrically symmetric and independent.⁴⁵ The superposition approximation poses problems for lanthanide systems with polyatomic ligands with highly anisotropic charge distribution.

### 1.3.5.2: Reid-Richardson Intensity Model

Reid – Richardson⁴⁶-⁵⁰ developed a parameterisation scheme, which is very similar to that given by Newman and Subramanian⁴⁵. They pointed out that the intensity parameters can be interpreted and calculated in terms of two intensity mechanism namely STATIC COUPLING (SC) and DYNAMIC COUPLING (DC). In both SC and DC models the interactions are considered purely electrostatic and thus an overlap between the change distributions between the ligand and central metal ion in neglected. In SC coupling model the electronic configuration of the lanthanide ion is perturbed by the ligands and the ligands produced a static potential of odd parity
around lanthanide ion, so the 4f states of mixed parity are formed. Transitions between these states can be polarised isotropically by the \( \text{Ln}^{3+} \) ion. The basic assumption in the Static Coupling Model is however; that the ligands are not perturbed by the radiation field of the incident light. The intermediate perturbing wave functions are fully localized on the lanthanide ion. Judd-Ofelt theory is an example of Static Coupling Model.

1.3.5.3 : **Dynamic Coupling (DC) Model**

In DC model the change in the distribution of the ligand charges under the influence of radiation field of light is taken into account. The electric dipole component of the light induces transient dipoles on the ligands, which in turn induce 4f-4f transitions in lanthanide ions. These are two possibilities (1) isotropic polarisability and (2) anisotropic polarisability. In the former the ligands are isotropic and ligand-ligand polarisation is cylindrically symmetric and independent. In case of the anisotropic polarisation the ligand are anisotropic (\( \text{BO}_3^3 \), \( \text{NO}_3^- \), ODA, GSH) and thus lanthanide-ligands interactions cannot be considered cylindrically symmetric. The perturbing wave functions in DC mechanism are localised on ligands. Reid-Richardson used a combination of DC and SC mechanism and made ‘ab initio’ calculation of intensity parameters in such a way that an easy differentiation between SC and DC mechanism can be made. Their intensity parameters \( A_{\lambda}^{\lambda_p} \), the \( t=\lambda \) parameter reflect the lanthanide ligand pair wise interactions, which are not cylindrically ellipsoids. These extra parameters are symmetry allowed in all point groups except \( C_{xyz} \).

The static coupling scheme gives rise to \( A_{\lambda}^{\lambda_p} \) parameters with \( \lambda =2,4,6 \) are with
\[ v = \lambda \pm 1 \] and employing Reid-Richardson (SC) and (DC) models, parametric calculations were made successfully by Burdick et al.\textsuperscript{31,52} and Chertanov et al.\textsuperscript{53}

The agreement between the experimental and calculated oscillator strength (P) of transitions between the ground state and \( ^{2S+1}L_J \) manifolds is good, but the relative intensities of crystal field transitions are still not well produced.

Placing the samples in a magnetic field induces optical activity. The differential absorption of left and right circularly polarised light in a longitudinal magnetic field can be measured. In the longitudinal magnetic field, the magnetic lines are parallel to the light beam. This technique is known as MCD (Magnetic Circular Dichroism), which is based upon Zeeman Effect. The simulation of MCD spectrum and calculation of MCD signals do not require more parameters than crystal field and intensity parameters extracted from absorption spectrum.\textsuperscript{54,55}

1.3.6: Carnall’s \( \Xi \) Intensity Parameters and \( \Omega \) Intensity Parameters

These are very commonly used in solution spectral analysis studies. Carnall et al used new parameter \( T_\lambda \) and thus described Oscillator Strength as:

\[
P_{\exp} = \sum_{\lambda=2,4,6} \Xi_\lambda \frac{\bar{v}_\lambda}{2J+1} \left| \left( f^N \Psi J || f^N \Psi' J \right) \right|^2
\]

The parameter \( \Xi_\lambda \) (Carnall et al.) is related to Judd-Ofelt (\( T_\lambda \)) parameter through

\[
\Xi_\lambda = (2J+1)cT_\lambda
\]

This is essentially only an extraction of \( (2J+1)^{-1} \) weighing factor out of the \( T_\lambda \) parameter. The factor \( c \) (the speed of light) is used to convert frequency \( v_\lambda \) into the wavenumber \( \bar{v}_\lambda \left( v_\lambda = c \bar{v}_\lambda \right) \). Workers studying absorption spectra of lanthanide
The parameter $\Omega_\lambda$ is introduced by $\Lambda_\varepsilon$ which is related to $\mathcal{F}_\lambda$ by

$$\Omega_\lambda = \left( \frac{8\pi^2mc}{3\hbar} \chi_{\text{ED}} \right)^{-1} \mathcal{F}_\lambda \quad (8)$$

or

$$\Omega_\lambda = \left( 1.085 \times 10^{11} \chi_{\text{ED}} \right)^{-1} \mathcal{F}_\lambda \quad (9)$$

The $\chi_{\text{ED}}$ is the correction factor included in the $\mathcal{F}_\lambda$ parameters but not in $\Omega_\lambda$ parameters. Similarly $\Omega_\lambda$ parameters are also related to $A_{1p}^1$ parameters as follows:

$$\Omega_\lambda = \frac{1}{2\lambda + 1} \sum_i |A_{1p}^1|^2 \quad (10)$$

**1.3.6.1: Standard Least Square Fit Procedure**

The standard least square method minimizes the absolute differences between experimental and calculated values. This method is much simpler than Chi-square fit method, but has the disadvantage that a small discrepancy in a large experimental value has the same influence as a large error in small experimental value. Hence the magnitude of $T_\lambda$ or $\Omega_\lambda$ parameters depend largely on the relative magnitude of the Oscillator Strength of transitions used in the fit. However, the parameter set is able to predict both small and large Oscillator Strength.

$$\Delta_{\text{exp}} = \frac{(2J + 1)D_{\text{exp}}}{e^2\chi_{\text{ED}}} \quad (11)$$

then,

$$\Delta_{\text{exp}} = \Omega_2 U^{(2)} + \Omega_4 U^{(4)} + \Omega_6 U^{(6)} \quad (12)$$
The same thing can be used for writing down such an equation for each spectral transition resulting in a system of equation for \( n \) transitions.

\[
\Delta_1^{\text{exp}} = \Omega_2 U_1^{(2)} + \Omega_4 U_1^{(4)} + \Omega_6 U_1^{(6)}
\]

\[
\Delta_2^{\text{exp}} = \Omega_2 U_2^{(2)} + \Omega_4 U_2^{(4)} + \Omega_6 U_2^{(6)}
\]

\[
\Delta_3^{\text{exp}} = \Omega_2 U_3^{(2)} + \Omega_4 U_3^{(4)} + \Omega_6 U_3^{(6)}
\]

..............................

\[
\Delta_n^{\text{exp}} = \Omega_2 U_n^{(2)} + \Omega_4 U_n^{(4)} + \Omega_6 U_n^{(6)}
\]

We want to find a good estimate for the parameter set \((\Omega_2', \Omega_4', \Omega_6')\) or \((T_2', T_4', T_6')\)

The set of equation (13) is of form:

\[
Y_i = a_1 X_{i1} + a_2 X_{i2} + a_3 X_{i3} + \ldots + a_k X_{ik}
\]

\[
Y_2 = a_1 X_{21} + a_2 X_{22} + a_3 X_{23} + \ldots + a_k X_{2k}
\]

\[
Y_3 = a_1 X_{31} + a_2 X_{32} + a_3 X_{33} + \ldots + a_k X_{3k}
\]

..............................

\[
Y_n = a_1 X_{n1} + a_2 X_{n2} + a_3 X_{n3} + \ldots + a_k X_{nk}
\]

The \( Y_i \) is the values of the observations and \( X_{ik} \) is coefficients and \( a_i \) is the unknown parameters. The observational model is a general linear model, because the dependent variable \( Y_i \), is described as a function of several independent variables \( X_{ik} \). The function is a linear function (there are no terms of degree higher than 1). The matrix method is used to solve the problem. The equation (14) can be written in terms of the response random vector containing the response values of \( n \) observations:
The matrix representation for any set of observations \( Y_1, Y_2, Y_3, \ldots, Y_n \) becomes

\[
Y = \begin{bmatrix}
y_1 \\
y_2 \\
y_3 \\
\vdots \\
y_n
\end{bmatrix}
\]

(15)

the model parameter vector

\[
a = \begin{bmatrix}
a_1 \\
a_2 \\
a_3 \\
\vdots \\
a_n
\end{bmatrix}
\]

(16)

the vector of errors associated with \( n \) observations:

\[
E = \begin{bmatrix}
e_1 \\
e_2 \\
e_3 \\
\vdots \\
e_n
\end{bmatrix}
\]

(17)

and the \( n \times k \) design matrix

\[
X = \begin{bmatrix}
x_{11} & x_{12} & x_{13} & \cdots & x_{1k} \\
x_{21} & x_{22} & x_{23} & \cdots & x_{2k} \\
x_{31} & x_{32} & x_{33} & \cdots & x_{3k} \\
\vdots & \vdots & \vdots & \ddots & \vdots \\
x_{n1} & x_{n2} & x_{n3} & \cdots & x_{nk}
\end{bmatrix}
\]

(18)

The matrix representation for any set of observation \( Y_1, Y_2, Y_3, \ldots, Y_n \) becomes
\[ Y = Xa + E \]  \hspace{1cm} (19)

Let the matrix

\[
\hat{a} = \begin{bmatrix}
\hat{a}_1 \\
\hat{a}_2 \\
\hat{a}_3 \\
\vdots \\
\hat{a}_n
\end{bmatrix}
\]

Equation 20 represents the matrix of the least square estimates for the parameters of the general linear model. The matrix can be calculated as follows:

\[
\hat{a} = (\chi^TX)^{-1}X^TY \hspace{1cm} (21)
\]

Where \( \chi^T \) is the transpose of \( X \). The matrix \( \chi \) is an \( n \times k \) matrix. \( X^T \) is a \( k \times n \) matrix and \( \chi^TX \) is a \( K \times K \) matrix with \( n \geq k \). The matrix solution gives the set of parameter estimates \( d_1, d_2, \ldots, d_k \) in general linear model that minimizes \( \sum (y_i - \bar{y}_i)^2 \) for the data collected.

After the parameter estimates (\( T_2, T_4, T_6 \) or \( \Omega_2, \Omega_4, \Omega_6 \)) have been obtained \( D'_{ED} \) or \( P'_{ED} \) can be calculated

\[
P'_{ED} = e^2 (\Omega_2 U_i^{(2)} + \Omega_4 U_i^{(4)} + \Omega_6 U_i^{(6)}) \hspace{1cm} (22)
\]

\[
\text{RMS} = \left[ \frac{\text{Sum of square of deviation}}{\text{Number of observation} - \text{Number of parameters}} \right]^{1/2} \hspace{1cm} (23)
\]
1.3.6.2: Chi-Square Method

If one wants to weigh each value of dipole strength or Oscillator Strength by its own uncertainty, the Chi-Square method has to be chosen as the minimizing quantity. Caird et al.\textsuperscript{61}, Seeber et al.\textsuperscript{62} and Goldner and Auzel.\textsuperscript{63}

This method minimizes the relative difference between the experimental and calculated values rather than their absolute differences. The uncertainty in the measured intensity of each transition is often difficult to estimate. Goldner and Auzel\textsuperscript{63} take a constant fraction of the experimental Oscillator Strength for the uncertainty. The RMS of this method is independent of the number or magnitude of the included transition. The Chi-square method is analogous to the matrix calculation presented for the standard least square method except that the design matrix $X$ is now given as:

$$\begin{bmatrix}
\frac{x_{11}}{\sigma_1} & \frac{x_{12}}{\sigma_1} & \cdots & \frac{x_{1k}}{\sigma_1} \\
\frac{x_{21}}{\sigma_2} & \frac{x_{22}}{\sigma_2} & \cdots & \frac{x_{2k}}{\sigma_2} \\
\cdots & \cdots & \cdots & \cdots \\
\frac{x_{n1}}{\sigma_n} & \frac{x_{n2}}{\sigma_n} & \cdots & \frac{x_{nk}}{\sigma_n}
\end{bmatrix}$$

(24)

And the vector $Y$ with the observation is now given by:
The fit is applied to the quantities $P/\sigma_i$ where $\sigma$ is the uncertainty in the experimental Oscillator Strength $P_{\text{exp}}$. The error of a parameter is given by square root of the respective diagonal matrix elements of the matrix $(X^TX)^{-1}$.

Judd-Osfeft theory though is quite commanding yet for Pr$^{3+}$, this theory does not seem work well. Difficulties are experienced if one tries to fit both the $^3H_4 \rightarrow ^3F_3, ^3F_4$ and $^3H_4 \rightarrow ^3P_{2,1,0}$ transition groups with the same set of $T_A$ intensity parameter. Instead of determining parameter set with the inclusion of all the transitions the $^3H_4 \rightarrow ^3F_3, ^3F_4$ transitions can be excluded. A number of authors preferred to exclude $^3H_4 \rightarrow ^3P_2$ transition.

Eyal et al have included $\Omega_3$ and $\Omega_5$ parameters in the intensities of 4f-4f transitions of Pr$^{3+}$. White Flore et al also included odd intensity parameters and also include $^3H_4 \rightarrow ^1I_6$ transition in the fitting procedure.

It should be mentioned that the hypersensitive transition for Pr$^{3+}$, $^3H_4 \rightarrow ^3F_2$ has to be included in the fit of Pr$^{3+}$, because otherwise a negative value of $T_2$ will be found which has no relevance. Extraction of reliable $\Omega_2$ parameter is often a problem for Pr$^{3+}$, because $^3H_4 \rightarrow ^3F_2$ transition is situated in infrared spectral region and thus cannot be observed in aqueous and in aquated organic solvent in absorption spectrum in UV-Visible region. In order to obtain more reliable intensity parameters Quimby
and Miniscalo\textsuperscript{69} introduced a modified Judd-Ofelt theory in which luminescence branching ratios are included in the fit. We have found that by including $T_5$ and $T_3$ parameters and by including $^3H_4 \to ^1I_6$ transition. Oscillator Strengths for computing purposes improves the closeness between the observed and calculated Oscillator Strength of 4f – 4f transition.

1.3.7 : Hypersensitivities

The environment does not affect the intensities of the induced dipole transitions in lanthanides significantly. The dipole strength of particular transition of the lanthanide(III) ion in different matrices does not vary more than a factor two or three. However, a few transitions are very sensitive to the environment and these are much more intense in lanthanides complex, than that for lanthanide (III) aquo ion complex.\textsuperscript{70-72}

The high sensitivity of spectral intensities for ligand environment as a general phenomenon was first noticed by Moeller et al\textsuperscript{73-75} for β-diketonate and EDTA complexes of Nd\textsuperscript{3+}, Ho\textsuperscript{3+} and Er\textsuperscript{3+} much before the advent of Judd-Ofelt Theory. Jorgensen and Judd have called such transitions HYPERSENSITIVE and these transitions obeyed selection rules $|\Delta S|=0$; $|\Delta L|\leq2$; $|\Delta J|\leq2$ and these rules are the same as the selection rules for pure quadrupole transitions. But calculations have revealed that the intensities to have a quadrupole character, therefore, hypersensitive transitions have been called pseudoquadrupole in character.\textsuperscript{76-77}

Karraker\textsuperscript{78} has investigated the hypersensitive transitions of Nd\textsuperscript{3+}, Ho\textsuperscript{3+} and Er\textsuperscript{3+} and considered the absorption spectra of six, seven and eight coordinated β-diketonates in nonaqueous media to determine effect of coordination number on the intensity and
fine structure of the spectra. The β-diketonate ligands were chosen because all of them bind to lanthanides (III) in bidentate manner involving two oxygen donor atoms yielding six membered chelate ring. Thus the two main variables were coordination number and geometry of the bonded ligands. Solvents chosen were with low polarity to reduced the solvent effect to the crystal field splitting of the lanthanide ion. His excellent study showed that the hypersensitive transitions showed differences that were characteristic, for the coordination and symmetry of the lanthanide ion. The conclusion was based on following findings:

i) There is a difference between the appearance of the absorption bands for hypersensitive transitions between six, seven and eight coordinated lanthanide ion;

ii) Addition of unidentate ligand to solution of six or seven coordinated complexes results in changing the spectra to spectra resembling those of seven or eight coordinated complexes.

iii) The removal of water from the solution of hydrated complexes results in changing the spectra to spectra resembling the spectra of lower coordination lanthanide;

iv) There is a correlation between the intensities of hypersensitive transition and coordination number of lanthanide.

In his latter paper Karraker investigated the effect of strong aqueous chloride on perchlorate solution on hypersensitive transitions. The change in the shape of the band was considered diagnostic marker for the change in the coordination number of lanthanides.
Chopin et al have made excellent contribution into the absorption spectral intensities of lanthanide complexes in solutions. While systematically analyzing Ln(III) complexes with Poly (amino carboxylic) acids they have suggested different sequence for oscillator strength of hypersensitive transitions for Nd$^{3+}$ and Ho$^{3+}$. The chelates order of oscillator strength was

- EDTA>HEDETA>DTPA>DCTA>NTA for Nd(III)
- HEDTA>DTPA>NTA>EDTA>DCTA for Ho(III)

However these workers could not give any explanation for different behaviour of Nd$^{3+}$ and Ho$^{3+}$. Fellow and Choppin and Choppin, however found a good correlation between the oscillator strength and sum of the ligand pKa for dibasic acid. These workers made three generalizations concerning intensity of hypersensitive transitions:

i) An increasing basic character of coordination ligand results in increasing ligand absorption intensity;

ii) Decreasing metal ligand bond distance results in intensity enhancement;

and

iii) The greater is the number of more basic ligand greater is the degree of enhanced intensity.

During our solution spectral studies on Pr(III), Nd(III) and Er(III) complexes with variety of ligands we also have made a number of generalizations. The alkoxides and bimetallic alkoxides of lanthanides in nonpolar solvents like benzene gave quite intense 4f-4f bands and the intensities of both hypersensitive as well as some of the non-hypersensitive (not obeying $|\Delta J|$ selection rules) transitions are affected very significantly by the bulkiness of the alkoxy ligands.
1.4.1: Function of Glutathione

The branched alky group also were responsible for the lowering of the molecular complexity of metal alkoxides irrespective of lanthanide (III) ion. The solvent effect of these alkoxides was also quite prominent. The polar solvents like DMF, DMSO enhanced the intensities of the both hypersensitive and pseudohypersensitive transitions again irrespective of the nature of metal. Detailed account of hypersensitivity and our new observation on Ligand Mediated Pseudohypersensitivity will be discussed in details in Chapter IV.

1.4: Glutathione

The primary < secondary < tertiary alkoxides group,

n-butanol < isobutanol < secondary butanol < tertiary butanol,
n-pentanol < secondary pentanol < tertiary pentanol < neo pentanol

Figure 1.05: Overview of the metabolism and function of glutathione
Most, but not all, cells contain glutathione. This molecule, which has been conserved through evolution, is adopted to perform many diverse functions. Glutathione is synthesised within the cells and exerts many of its functions intracellularly. Transport of glutathione out of the cell seems to be associated with cell membrane functions such as transport and protection. In higher animals and human, cellular transport of glutathione is related to the transport of amino acid sulphur to other cell: Figure 1.05 summarise information available about the metabolism of glutathione and indicates the biochemical pathways that seem to be connected with the several functions of glutathione. These include cellular protection (against reactive organic oxygen compounds, other toxic compounds of exogenous and endogenous origin. Free radicals) catalysis, metabolism and transport.

The multifunctional properties of glutathione are perhaps most dramatically reflected by continually increasing interest in this molecule by investigation of such diverse subjects as organic chemical mechanism enzymology, molecular biology, intermediary, agriculture toxicology, aging and still many other fields.

Intracellular total glutathione consists of greater than 99.5% glutathione, the small amounts of glutathione disulphide present may be an artefact. Glutathione is the major transport form. The Table 1.06 shows the different glutathione levels in different body fluids.
Table 1.07 : Glutathione Levels in different Body Fluids :

<table>
<thead>
<tr>
<th>Body Organ</th>
<th>Total</th>
<th>% Glutathione</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rat :</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatic vein plasma</td>
<td>26.0±4.2 µM</td>
<td>~80</td>
</tr>
<tr>
<td>Aortic plasma</td>
<td>14.5±2.7 µM</td>
<td>~80</td>
</tr>
<tr>
<td>Renal vein plasma</td>
<td>2.6±0.6 µM</td>
<td>~80</td>
</tr>
<tr>
<td>Inferior vena cava plasma</td>
<td>8.1±2.0 µM</td>
<td>~70</td>
</tr>
<tr>
<td>Arterial plasma (no anaesthesia)</td>
<td>25-35 µM</td>
<td>~85</td>
</tr>
<tr>
<td>Bile</td>
<td>2.4 mM</td>
<td>~80-90</td>
</tr>
<tr>
<td>Pancreatic juice</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>Mouse :</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arterial blood plasma</td>
<td>25-35 µM</td>
<td>~85</td>
</tr>
<tr>
<td>Urine (after AT-125)</td>
<td>25-30 mM</td>
<td>30-70</td>
</tr>
<tr>
<td>Human lymphoid cells</td>
<td>0.12-3.4 nM</td>
<td>&gt; 90</td>
</tr>
</tbody>
</table>

The cellular export of glutathione serves to protect cell membranes against oxidative and other types of damage by maintaining essential thiol groups or other components of the membrane. Export of glutathione also provides a mechanism for reducing compounds in the immediate environment of the cell membrane. Such export facilitates the transport of certain compounds especially disulphides.

Depletion of cellular glutathione has been of great importance as an experimental tool in investigations on mechanism and functions of tripeptide.

(i) Depletion of glutathione via inhibition of γ-glutamylcysteine synthetase.

(ii) Depletion of glutathione by the use of oxidising agent.

(iii) Depletion of glutathione by the use of the compounds such as diamide.
(iv) Depletion of glutathione by the use of compounds that react with glutathione (diethyl maleate, 1-chloro-2,4-dinitrobenzene).

(v) The decreasing cellular level of glutathione by inhibiting glutathione synthetase level.

(vi) Depletion of glutathione by administration of buthionine sulfoximine has considerable member of effect on metabolic activity.

Figure 1.06: Scheme for synthesis and transport of glutathione in mitochondria and cytoplasm

After administration of buthionine sulfoximine, the level of glutathione in liver and kidney is significantly affected. Figure 1.06 clearly demonstrates the synthesis of glutathione and its transport in mitochondria and cytoplasm. Reversible conversion of glutathione disulphide occurs in both mitochondria and cytoplasm, but the synthesis of glutathione occurs only in cytoplasm. Glutathione, rather the glutathione disulphide, is probably the major transport form, since glutathione is the predominant intra-cellular form. Transport of glutathione-disulphide, which may be formed in mitochondria that are under severe oxidative stress, serves as a mechanism for
protection. The observed rapid labelling of mitochondrial glutathione after administration of isotopically labelled cysteine is in the accord with the view that there is an exchange carrier in the mitochondrial membrane, that is, accessible to both mitochondrial and cytoplasmic glutathione. Glutathione is essential for mitochondrial function. The net efflux of glutathione from mitochondria is very slow. This suggests that, this transport mechanism functions in a manner that conserves mitochondrial glutathione during periods of cytoplasmic glutathione depletion, which may be produced by nutritional factors and also by phenomenon associated with oxidation and the presence of toxic compounds.\(^8^2\)

**1.4.2 : Metal Complex of Glutathione**

Glutathione is a polydentate ligand, offering as potential binding sites of two carboxylate oxygen, an amino nitrogen, a sulphydryl group and two amide groups.\(^8^3\) The structure of glutathione is such that all its potential binding sites cannot be simultaneously coordinated to the same metal ion, and therefore the coordination chemistry of glutathione is characterized by the formation of protonated and polynuclear complexes. The coordination chemistry of glutathione is very important and is of great interest as a model system. For the binding of metal ion by larger peptides and proteins and because metal-glutathione complexes are involved in the toxicology of several metals. Glutathione present in the cellular system at a relatively high concentration and generally it is the most abundant nonprotein thiol. Because of high affinity of a sulphur for many heavy metals glutathione is involved in their uptake and excretion.\(^8^4,8^5\) And naturally their complexation can explain very well their inter-cellular competition.
The complex of several heavy metals by glutathione in intact erythrocytes has been detected directly and noninvasively by $^1$H NMR spectroscopy.\textsuperscript{86-87}

### 1.4.3: Acid-Base Chemistry of Glutathione

The acid-base chemistry of glutathione at the molecular level is described by eight microscopic constant as shown in the scheme (Figure 1.07)

![Diagram of acid dissociation scheme for glutathione](image)

**Figure 1.07**: Macroscopic acid dissociation scheme for glutathione

\[
K_i = \frac{[H^+][H_{4-L}]}{[H_{5-L}]} \]

Proton NMR data indicate that two carboxylic acid groups ionize simultaneously over the pH 0.5-6.0 while sulphydryl and ammonium groups ionize simultaneously over the pH range 7-12.\textsuperscript{88} The value of microscopic constants for sulphydryl ammonium
group is highly affected by the nature of solvent. Increase in the acetonitrile content in the aquated organic solvent dielectric constant decreases, this has dramatic effect on the relative activity of sulphydryl and ammonium group (decrease in the $K_a$ value from 1.6 to 0.4)\(^8\).

**Table 1.08**: Microscopic Acid Dissociation Constant of GSH

<table>
<thead>
<tr>
<th>$pK_1$</th>
<th>2.19(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$pK_2$</td>
<td>3.22</td>
</tr>
<tr>
<td>$pK_{12}$</td>
<td>3.45</td>
</tr>
<tr>
<td>$pK_{21}$</td>
<td>2.42</td>
</tr>
<tr>
<td>$pK_{123}$</td>
<td>8.92(^a)</td>
</tr>
<tr>
<td>$pK_{124}$</td>
<td>9.20</td>
</tr>
<tr>
<td>$pK_{1234}$</td>
<td>9.44</td>
</tr>
<tr>
<td>$pK_{1243}$</td>
<td>9.16</td>
</tr>
<tr>
<td>$K_5$</td>
<td>1.9</td>
</tr>
</tbody>
</table>

\(^a\) Determined by pH titration; $I=0.16$, 25\(^\circ\)C

\(^b\) Determined by $^1$H NMR; $I=0.2-0.5$, 25\(^\circ\)C

\(^c\) Determined by pH titration; $I=0.15$, 25\(^\circ\)C

\(^d\) Determined by spectrophotometric titration; $I=0.10$, 25\(^\circ\)C

The $K_{124}$, $K_{1234}$ pathways, which involves the more highly charged zwitter-ionic intermediate as acetonitrile content increases. This change in the acid base chemistry with decreasing dielectric constant is of great interest in view of the hydrophobic regions of low dielectric constant in protein. Therefore our study of complexation of glutathione with one, two or three different metal ion simultaneously investigated in different mixed solvents (DMF-H\(_2\)O, Dioxane-H\(_2\)O and Acetonitrile-H\(_2\)O) of different
Introduction

stoichiometry, will be important and relevant in understanding hetero metal complexation of large proteins involving endogenous metal ions.

The thesis presents the quantitative absorption spectral intensity data analysis with absorption difference, comparative absorption spectroscopy involving 4f-4f transition as PROBE in understanding the coordination and binding characteristics of Glutathione reduced (GSH) and Glutathione oxidise (GSSG) in presence of hard metal ions Pr(III) and Nd(III) and a soft metal ion Zn(II) in process of simultaneous coordination. Since such hetero-bimetallic complexation of GSH/GSSG involving Pr(III)/Nd(III)/Er(III) and Ca(II)/Zn(II) MIMICS the in vitro hetero bimetallic simultaneous complexation of these sulphur containing peptides with Ca(II) and Zn(II) occurring both intra and extra cellularly. The effectivity of such effort made in present thesis opens up new vistas of structure and spectra correlation which pave way to make 4f-4f transition spectroscopy on very effective tool in following the progress of several biochemical reaction involving most essential metal ions like Ca$^{2+}$ and Zn$^{2+}$ ions.

The thesis has been divided into following chapters:

(1) Introduction
(2) Review
(2) Experimental
(3) Tables and Figures
(4) Results and Discussion
(5) Summary and Conclusion
References:


