

Preface for First Part of the Book

Humans on earth out of curiosity have developed powerful telescopes to look into the structure of the universe around us. We are striving to look for signs of life whether in the galaxy in which we live or in other galaxies. Are we so special? Is there need to be looking for our image billions and billions of kilometers away? As a matter of curiosity and knowledge there is such a need. The dynamics of the motions of the stars, planets, etc., is explained by Newton's gravitational laws and is a well-established science in theory and experiment. There is another aspect of science. We have several elements in the earth's crust, e.g., iron, copper, calcium, sodium, potassium, silicon, etc. Some of these elements, e.g., sodium, potassium, chlorine, in the form of some compounds, etc., form an essential part of the survival of life, plant, or animal. We should look deep inside the atomic structure of the elements and of the molecules they form, e.g., the water molecule H_2O , the essential ingredient for our survival. The dynamics of the electrons, protons, nuclei in our body is as intriguing as puzzling. For example, the electrons stay in stable orbits around the nuclei. It is no different from, say, the planet earth going around our Sun. One needs to go to nanometer distances (10^{-9}) deep from the surface of a macromolecule to work out the amazing science inside the atoms and molecules. This branch of science which deals with the deep down discrete structure of matter, i.e., atoms and molecules, is called quantum science.

Quantum science also has its laws in nature worked out though not in as clear a way as the gravitational ones. In a practical use, e.g., in our brain one can see quantum laws of dynamics as clearly brought out through MRI. They are related to simple concepts in physics. The quantum magnetic resonance used in Magnetic resonance imaging (MRI) is a typical example. As a machine, MRI is seen very prevalent in hospitals, medical centers, universities, etc., as a part of our health system. We can hardly miss to look at it through a diagnostic picture to find what has gone wrong in our body when we fall sick. Multi-quantum spectroscopy which reveals the multi-quantum structure of atoms and molecules is century old. It is now being applied to in vivo brain imaging over the past of couple of decades. It acts as a complement to find out the concentration and specific functional role of various chemicals present in our brain. Multi-quantum coherence imaging (MQCI)

does both (spectroscopy and imaging) together in an integrated form. This book which has purely educational aim behind it tries to put together quantum science and the imaging of the brain together. For some readers, e.g., for clinicians to learn quantum science in-depth can be a difficult task. This book has avoided the phenomenological development of the physics, chemistry, and mathematics (PCM) that form a detailed exposure of brain imaging. The approach taken here instead, is to let the reader learn through practical visualization of the concepts in action.

Preface for the Second Part of the Book

Nature has evolved though essential elements like oxygen, hydrogen, nitrogen, iron, zinc, etc., via their inorganic and organic compounds, e.g., NaCl, H₂O, KCl, FeO, etc. There are various organic matter macromolecules encompassing the basic isotopes, e.g., ¹H, ¹³C, ²³Na, ³⁵Cl, ³¹P, ³⁹K, ⁵⁷Fe, etc., which have regulated the animal and plant life evolved over millions of years on the earth. Deep down in life which evolves all the time are tiny building blocks, atoms, and molecules, which conglomerate to form bigger molecules, the macromolecules, the tissue, and ultimately the body. Atoms, when looked into deeply, have a nucleus with a positive charge at the center surrounded by negatively charged electrons. The magnitude of the positive charge at the center of the nucleus (basically due to the protons) is equal to the negative charge of the surrounding electrons. This keeps the atoms and the molecules electrically neutral as it should. One should remember that there are always some ionized free radicals present in our body. The electrons in atomic and molecular situations are not stationary but orbit around the nucleus and stay in a number of stationary orbits so as not to collapse into the nucleus. The orbital motion of an electron around the nucleus generates an electric current. This electric current when multiplied by the area of the orbit of the electron is called the magnetic dipole (in analogy with the earth's giant, the north-south pole dipole-magnet) moment. The tiny atomic dipole magnets in our body coordinate with other atoms to form bigger molecular magnets. The molecules expand their electron correlations with their surrounding molecules to form cohesive charge and spin configured macromolecules. The macromolecules which form the essential part of the dynamics of life in the human body (and even in the plants and animals) retain the feature of the magnetic (over a large molecular space) dipole character. These macromolecules are tens and hundreds of nano (10^{-9}) m in size and control the dynamics of the life of all living creatures.

One needs to remember that orbital motion of electrons (and of protons and neutrons inside the nucleus) generates a basic physical quantity in motion dynamics, the angular momentum locally in macromolecules in our body. This local basic physical quantity, the macromolecular angular momentum, becomes the source of all the activities coordinated in the brain. The dipole magnetic

moment is a naturally associated part of the angular momentum. Unfortunately, angular momentum in the molecular situation cannot be measured in the laboratory. But fortunately, nature is kind to let us find the secrets of life through the molecular dipole magnetic moment associated with the annular momentum. Nature's secret is that the magnetic dipole moment creates electrical signals which we measure and help to create the MRI we know. How lucky are we? We are at the center of a vast universe which is formed of atoms and molecules. The atoms and molecules have evolved over millions of years in such a way as to create the most intelligent form of life on earth. Intelligence does not progress without a healthy scientific environment and the interaction of the body and mind with the universe which surrounds us. The magnetic resonance (MR) phenomena observed through MRI in our body is like many other resonance phenomenae observed in nature. These can be seen all around us and are used in many technologies, e.g., Radio and TV broadcast, Lasers, etc. The development of MR into a practical MRI machine we are so familiar with now has been the result of more than half a century of research and development efforts. It is now not only a routine health care technology in hospitals and medical centers but is also a valuable noninvasive tool of research and education about the science of the human body. Sodium is an important element and there are several others found in almost every organ of the human body involved in the functioning of organs on a moment and day-to-day basis.

Sodium nuclear magnetic resonance imaging (SNMRI) is now being used in the area of diagnostics of diseases of several organs of the body, e.g., the brain, liver, heart, kidney, etc. In the present day MRI we have the single-quantum (conventional) MRI technology approach. It is a routine versatile technological tool in the diagnostics of the human brain disorders. It is important to point out here that the single quantum basically means that we assign a single resultant spin covering all the spins of the group of molecules in a voxel (a small volume) under measurement. The dispersion in the output signal observed in time and space is the result of the various dynamic activities in the brain. These are measured by various techniques, e.g., the blood oxygen level dependence MRI, called the fMRI (functional MRI), SNMRI, etc.

The multi-quantum means the subvoxel molecular level structure dynamics. It does not form part of the present (conventional) MRI technology. MRI enables scientific research follow-up through monitoring the effects of a treatment therapy. During the practice of following this research scientists discover new and better treatments for a disorder. A useful secretive knowledge gathered through the MRI about our brain creates literacy about our brain and how it works. In essence, in the conventional MRI, which we have at present one is looking for the spin (tiny atomic and molecular magnets) interactions over the wider average volume (mm^3 – cm^3) as the medium in which they reside and move. This medium provides the environment of generation of the spin electrical signals. Through the brain medium of tissues, fluids, etc., spins perform dynamic activities, e.g., metabolism, communication, etc. In the conventional MRI model we assume spins behave like an averaged entity over a selected volume. Over the voxel-to-voxel situation they are

magnetic entities with little multi-quantum interactions with other molecular spins. Their imaging identity is through their interaction with the environment in which they respond to the applied static magnetic field and the radio frequency (RF) radiation that is applied.

The physical and chemical multi-quantum interactions on a molecular level between spins are of little consideration in the conventional MRI. The result is more like mapping rather than a picture of the precise dynamical events happening in the brain. This is the limit (called as single quantum) on which the conventional MRI has been founded. In-depth MRI would allow one to understand the basic science of the human brain. Sodium and potassium are very basic elements involved in life controlling the familiar sodium–potassium pump in our body. They perform essential energy transport and metabolic functions for the natural life-running mechanisms in the body. Typically in the brain, e.g., in the ischemic situation, it is known that the healthy natural sodium concentration inside the cell membrane is disturbed. There is extra uptake of sodium ions in the cell inside a tissue than the healthy normal balance requires. The life giving sodium–potassium equilibrium pump then does not perform in a normal healthy manner, anymore. The brain becomes disordered and the person ends up with a stroke. Normally, sodium is in a bound state inside the cell; it is not a free, nucleus. It is a part of the macromolecule structure inside the cell. On the other hand, outside the cell there is sodium in a free state as part of the fluids, e.g., blood and other fluids around the cell. In an MRI situation sodium nuclei are exposed to a relatively strong static magnetic field (around say 3 T).

The direction along which this static magnetic field is applied is referred to as the z-direction in the MRI literature. This is along the axis of the direct current (DC) carrying coil that produces the static magnetic field inside which the human body is placed for imaging. A much weaker (milli-Tesla) radio frequency (RF) electro-magnetic field is subsequently applied in different X–Y directions in the Z-planes to cover 3D space of the organ under investigation. The purpose of the RF field is to project the spins in different directions with respect to the main static magnetic field and excite them to their higher energy states. The sodium nuclei in a selected small volume (the voxel) on de-excitation reradiates back the RF radiation carrying the signatures of the local events in the voxel. In the diseased state of a tissue, modified activities are happening inside and outside the tissue as compared to a healthy body. The changed interactions between the sodium nuclear magnetic dipole and the electrical quadrupole (charge) moment inside and around the cell act as a barometer of the diseased dynamic state of the tissue. Inside the cell, normally one observes two types of relaxation mechanisms, the fast and the slow. This is during the de-excitation of the spins. We now have the two characteristic relaxation times, the fast and the slow, for examination. In MRI, the fast and the slow T_1 and T_2 relaxation times become the source of imaging in a stroke situation. These two relaxation times routinely form the weighting parameters in the imaging produced in the conventional MRI. In the particular case of sodium imaging we look for the interactions between the electric (charge) quadrupole character of the sodium ion (Na^+) and the fluctuating electric field created by the

variable nuclear ion concentration around it. Each relaxation time has a fast and a slow component.

The observed behavior of spins is now a nature of the perturbed abnormal charge distribution inside and outside the cell. It can be compared to the case of a healthy normal brain and use it as a diagnostic tool, for the disease. In essence the changed T_1 and T_2 relaxation times in a voxel are used as the source of conventional sodium MRI. MQ-MRI will take it to the molecular level. It is important to remind the reader here that in the sodium MRI (S-MRI) we are after the result of interaction between the electric quadrupole sodium nucleus and the surrounding electric field gradient. But the external static magnetic field applied in the Z-direction is still the key in the investigation process. The magnetic dipole of the sodium nucleus points in that direction and is the source of a standard reference for the analysis.

One should note that inside the cell the sodium nucleus is in the bound state within a macromolecule of the tissue. The quantum correlations among the spins of various nuclei are very strong. The quantum science principles guide, that inside the cell the spin relaxation mechanism, should be bi-exponential, that is there will be two distinct decay rates for the relaxation times. It arises due to the sodium nuclei being in a bound state in macromolecule inside the cell. The bound nuclei interact with the free sodium nuclei surrounding the cell. There is a charge concentration gradient due to sodium ions inside the cell and the surrounding area in which the cell is present. This gradient is non-uniform in its character. Sodium nuclei have electric quadrupole (four poles, two positive, and two negative) moment character. This is in addition to the nuclear magnetic dipole character which is inherently present in the sodium nucleus. The electric field gradient (due to the varying sodium concentration) from inside to outside of the cell is asymmetric and thermally dynamic in character. The electric field gradient fluctuations trigger electric quadrupole–magnetic dipole interaction among the nuclei. This produces a split of the magnetic state $I = 3/2$ of the sodium nucleus into the four degenerate levels, $-3/2$, $-1/2$, $+1/2$, and $+3/2$. The result is a mixture of two prominent fast and slow decay rates in response to the electro-magnetic RF radiation.

Outside the cell the free nature of the sodium nuclei still allows a unique single exponential decay. Thus the sodium nuclei inside and outside the cell with a separating membrane in-between behave in different manners when exposed to RF field. The longitudinal (T_1) and transverse (T_2) relaxation times of the sodium nuclei inside and outside the cell become a source of differential chemistry in space and time for imaging. The conventional single-quantum MRI in use has been developed over half a century now. It is implicitly expressed as being single quantum in the MRI literature. Why it is called as single quantum is that it is assumed that all nuclei have the same identity as a single magnetic dipole and do not interact coherently between each other quantum-mechanically during the process of imaging. One needs to see the underlying microscopic events in detail. Microscopically the interactions are very far from the single-quantum type. The multi-quantum MRI now is felt as a basic necessity. It has found way to success

very recently. This approach allows the molecular level physics and chemistry among the nuclei as the source of imaging. Any organ of the body say e.g. human brain is a heterogeneous ensemble of very many species of nuclei among the macromolecules. These, macromolecules are surrounded by other macromolecules; several types of fluids with complex chemistry of their own in a dynamic state.

We know that the atomic chemical elements when in a free state in nature have their characteristic signature called as the electronic-quantum energy structure. In a confined state like the soft condensed matter in our body the discrete atomic and molecular, quantum energy structure is modulated by the region where they are present and the functions they perform as a group. The individual discrete single atom electronic quantum structure inside a macromolecule environment is part of a wider discrete macromolecular quantum structure. This is spread over all in space and time. A macromolecule has its characteristic charge and retains it through equilibrium with neighbors in a unique discrete energy structure of its own. At the cell level there is a much broader quantum character in space and time as an ensemble. The smearing electron clouds in-between among the macromolecules provide the conventional region of chemical shift mapping. The molecular magnetic dipole-dipole interaction provide the source of a reference axis in MRI.

In the imaging the sodium quadrupole characteristics are depicted with respect to the fixed Z-axis of the magnetic dipole spins produced by the application of the applied static magnetic field in the Z-direction. As one goes deeper to the nuclear level of the macromolecules the quantum correlations among the nuclei reveal the real quantum chemistry events happening in micro-space-and-time imaging domain. Multi-quantum sodium imaging is a step in the forward direction. It will develop quantum coherence imaging (QCI) through the understanding of the nanomolecular science phenomena. Unfortunately the magnitude of the electrical signals created at the electric-quadrupole, nano-quantum coherence level, are much weaker in magnitude as compared to the case of $\text{mm}^3\text{--cm}^3$, volume, generating, the single quantum signal. The magnetic field inhomogeneities due both to static and the RF fields add to the complications of the multi-quantum MRI (MQMRI). We are trying to observe in the MQMRI much weaker multi-quantum coherence imaging signals. This book presents a first hand picture of the research and development efforts in progress to date in the newly emerging field of the multi-quantum, sodium, electric-quadrupole, magnetic-dipole imaging.

Molecular Imaging of the Brain
Using Multi-Quantum Coherence and Diagnostics of
Brain Disorders

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