

Chapter 2

Simplistic Theory of the Functions of the Ensemble of the Electrons, Atoms, Molecules, Nuclei, in the Brain

2.1 Simple Macroscopic Brain Model

One should realize that the quantum science is not as much a common knowledge as the Newtonian Science is. It thus becomes a formidable task, to propagate further about the new developments in the brain science. The neuroscience audience who this work should attract the most would normally have little and basically no exposure to the basics of the quantum physic so deeply rooted in the dynamics of the atoms, molecules, tissues, etc., in the brain. However an effort at grass roots level is made in this work in that direction. To keep it simple explanation is made by reference to diagrams drawn. It is a rough spin model picture of the brain MRI that is exposed here. It is as if it were a collection of ordered spins in an ensemble of molecules in the direction of the static magnetic field naturally present around the nucleus. Spins in molecules are surrounded by smeared out orbital electron cloud of the molecules, fluids, tissue, etc. There are as many electrons in the orbital state as there are the protons in the nuclei in a small region consisting of several molecules.

An approximate spin model picture is illustrated here globally (Fig. 2.1) over the brain. The brain on the whole is electrically neutral as if it were a single atom. From this rudimentary equivalent over simplified picture to progress further towards reality one has to add regional perturbations in space and time. These are due to the local fine structure of individual atoms, molecules, tissues, fluids, etc., and the functions they perform. Then it will take the knowledge about brain science a step closer to the otherwise a very complex picture. In the regional areas there are various forces e.g. coulomb, nuclear, quantum, etc., which control the regional behavior in carrying out moment to moment brain functions. In a broad sense there is an overall system within the brain that looks after the intricate and wider functions of the brain. Figure 2.1 is a broad pictorial representation of the spin model of the brain. This is as if the orbiting electrons in molecules are circulating in copper coils and influence neighbors through self and mutual electrical induction.

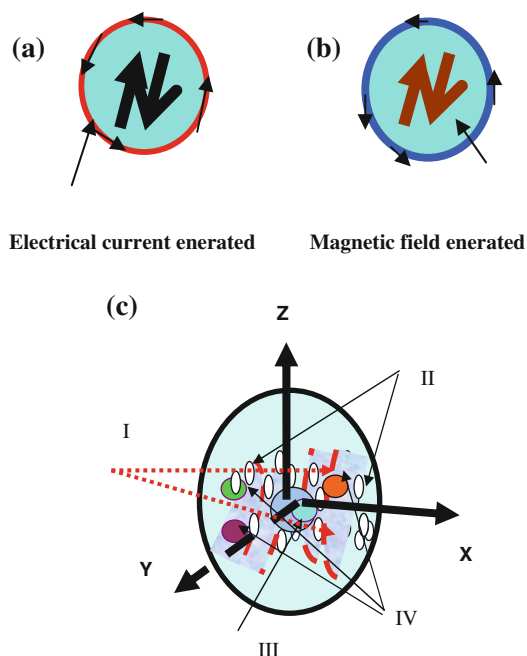


Fig. 2.1 **a** Electric current generated around the copper coil due to alternating magnetic field at the centre. **b** Alternating magnetic field generated at the centre of the coil due to alternating current flowing around the copper coil. **a–c** In this Figure is shown a pictorial depiction of an over simplified model of the brain. One can visualize a group of molecules (or macromolecules) in the brain under RF radiation behaving like copper coils carrying oscillating electrical current. This will lead to a generation of oscillating magnetic field through and around the molecules. The electromagnetic field created due to the RF radiation excitation encourages interaction between molecular dipole magnets. **a, b** Simple analogy to an experiment which can be conducted in a laboratory. It is a rough picture of a representation of the famous more than a century old copper coil experiment, by Hertz, the physicist, after whose name the unit of frequency of radiation Hz was adopted. **c** An approximate picture of a regional local order assumed present in pockets, in the brain, created by the internal magnetic field of around 1 Tesla, due to a group of nuclei, at a point. Small elliptical spots shown are examples of the several local micro-order regions in space. There is also an order on the global scale but is a weak one

The order can be regional as well as long range one. In the long (but on macro-molecular scale) range orbiting electrons are shown as a smeared out cloud as if they were a part of single giant molecule with single giant nucleus. But on this order is superimposed a regional (and long range) quantum-order due to quantum correlations between atoms and molecules. This order can be measured through multi-quantum coherence imaging from small voxels of 1 micron^3 to 1 mm^3 size. One can also mathematically model and get computational results and compare it with experiment. Both approaches where they will meet ultimately, to an agreement, will lead to the understanding of, the real, the unknown brain science. Thus there are four parts of the model of the brain as follows. I The effective internal

surrounding magnetic field lines of force are imagined as if the whole brain were made of several macromolecular dipole magnet grouped with N-S poles. They interact quantum mechanically to produce long range orders. II The electrons as if belonging to a group of molecules as a unit surrounding the central positive nuclear charge of protons. III The filled ellipses represent sort of scattered short range ordered macromolecules submerged in the surrounding electron cloud depicted by unfilled circles. IV The giant nucleus of a local order is as if belonging to a group of macro-molecules as a unit in a local volume say a voxel.

The spatial density, $\rho(x, y, z)$ variation of the spins can be worked out from the measured k space (k_x, k_y, k_z) intensity distribution in the MRI. The wave number in k -space, is given as, $k = 1/\lambda$, λ being the wavelength of the RF radiation. The measured k -space intensity variation (converted into the x - y - z space picture produced) has one to one correspondence to the spatial variation of spins density in the real (x, y, z) space in the brain. The density of spins (their number per unit volume) is related to the magnetic moment per unit volume created by the spins at a point. Due to the multinuclear structure of the brain the spin density sharply varies from point to point. The procedure of the transformation of the data from the k -space to the real space is a standard procedure well established in the conventional MRI. It is called as Fourier Transform Technique (FTT). It is a simple physics principle in electricity that an alternating current through a copper coil (Fig. 2.1a) induces an alternating magnetic field at the centre of the coil. This alternating magnetic field at the centre also influences a current in the same coil. This is called as the self induction. Similarly in a reverse manner an alternating magnetic field at the centre of a coil generates an alternating current through the coil and the generated current influences the magnetic field at the centre. Also a current in one coil induces a current in the neighboring coil which also generates a magnetic field at the centre of the second coil. This is called as the mutual induction. Atoms and molecules in our brain are a sort of copper coils with circulating electrons around the nucleus. The atomic orbits act like copper coils. The single electron in the outermost orbit of an atom is called as the valence electron. It has an intrinsic magnetic moment called as spin $S_z = \pm 1/2\hbar$. This is added to the atomic magnetic moment produced by the circulating electron in the orbit of an atom. One should remember that it is the valence electron in an atom that is the reactive one and creates interaction with its neighbors through its charge and spin. The Na-K pump which is the source of life in our brain is typical example of interest in this book. On the long range the influence on the neighbors in the short range is smeared out. This is what we get in conventional MRI. In the short range the quantum nature of the atom and the molecules can be seen. This is what QMRI is about.

In the real situation like the human brain in a small region of it referred to as a voxel the atoms and molecules overlap and the electron cloud charge spreads over a smeared out region. The shared electrons in a voxel represent signatures of the local interactions between the molecules, atoms, nuclei, as if there were a single large molecule and many electrons were bound to it due to the coupling between the electron spins. The overlapping electrons become a sort of shadow of the

chemical structure in the local region. In the small region which may be spherically symmetric in regard to the distribution of spins the spin effects over-all cancel out. Thus there is no structural abnormality shown in the image of the region. The brain is thus a normal healthy one. If there is an asymmetry at a point due to say a tumor the symmetry is broken down and the spins appear as an outstanding spot in the MRI scan of the brain. This would be the most rudimentary form of image and is called as the chemical shift imaging (CSI). In this conventional MRI an RF pulse is applied along the X and Y directions perpendicular to the applied static magnetic field which is in the Z direction. A macroscopic average three dimensional spin asymmetry of the region can be projected as a planar asymmetry on the X–Y plane. In this plane the atomic spins evolve in time by interactions among themselves and the environment. The dynamics of the spins can be mapped in macro space and time to produce images of the local molecular events. One can venture now with the multi-quantum coherence technology newly emerging to explore spin dynamics in a multi-quantum regime. It is possible to look for quantum correlations among spins as a source of imaging rather than just be satisfied with the conventional topological echo planar imaging (EPI).

2.2 The Relationship Between the Angular Momentum L of the Orbiting Electron Around the Nucleus and the Associated Magnetic Moment μ_L

2.2.1 The Induced Electrical Signals Created by the Incident RF Radiation

An electron spins around its axis and thus has an intrinsic angular momentum referred to by symbol S . But the electron also orbits around the nucleus and thus there is an orbital momentum for the electron associated with the atom. It is referred to by the symbol L . Normally in an ensemble like human brain the intrinsic electron and atomic angular momentum are randomly oriented in space. They cancel themselves on a macroscopic scale. But on a microscopic scale the internal magnetic field of a group of nuclei makes the two types of angular momentum add up to produces a resultant $J = L + S$. It is called as the spin-orbit interaction. This is the result referring to a single electron and an atom in isolation with no atom to atom interactions (correlations). But in an ensemble like the brain there are around 10^{23} (Avogadro number) nuclei including different species in a mole of the soft matter. Most of the spins in the absence of an applied (or internal) magnetic field cancel out in a small region say a voxel used for examination. In the presence of a magnetic field the spins have all their L' (multi-particle) and S' (multi-particle)s added up to produce a resultant $J' = L' + S'$.

Since an electron is a charged particle its rotation produces an electric current over the nano size area traced by it. This orbital motion of an electron in an orbit in

the atom makes an atom a nano-magnet. There is an intrinsic relationship between angular momentum and the tiny magnet generated due to it. The product of the electric current i generated by the electron and the area of the orbit traced A is called as the magnetic dipole moment $\mu_i (=iA)$. In a very small volume of the order of tens and hundreds of nano meter³ the local nuclear magnetic field induces a resultant orientational force on magnetic moment μ_j as if trying to align the tiny magnet, along its own direction. The situation however enhances in the presence of an external applied magnetic field H_{z_0} .

In an externally applied field all the spins order themselves with their resultant magnetic moment tending to be pointing in the H_{z_0} direction. The disturbance due to the local environment in which the spins are present however tend to disorient spins from the externally applied field direction and try to return them to their natural random behavior. The result is a compromise i.e. μ_j (the resultant magnetic moment corresponding to the total angular momentum \mathbf{J}) rotates around the static magnetic field. The spin vector corresponding to it moves in a cone around the field. A single rotating vector around the static magnetic field H_{z_0} is a representative of many spins grouped together as a bunch. Individual spins corresponding to different species of nuclei will rotate at different flip angles. But it is very hard to observe them on individual basis experimentally. It is the group effect that is observed.

One chooses to use a band of frequency of RF radiation to observe a small group of spins at a time. The tip of the spin (of a group corresponding to say a macromolecule) may be located anywhere at any moment in space and time. The angular momentum controls the position of the magnetic moment at any time. The angular momentum however can not be measured in a laboratory. The magnetic moment as a group representation can however be measured. On the scale of micrometer to mm to cm a large electrical signal is generated by the RF radiation. This signal created by the application of RF (radio frequency) radiation due to the magnetic spins vibration produces an electrical signal. An average magnetic moment per unit volume over a region is called as the magnetization of the soft matter. It is not constant over different points in space and its susceptibility to external RF radiation also varies in space and time. In fact this is what provides the secrets of the human brain science.

2.2.2 The Magnitude and the Quantum Nature of the Atomic Magnetic Moment

The angular momentum and the associated magnetic moment of the electrons and atoms are quantized. This means they can only occupy fixed quantum energy levels. In the process of transition above and down in the energy levels the energy is absorbed and re-radiated in quantum jumps, $\Delta J = 0, \pm 1, \pm 2, \dots$. The angular momentum J and the magnetic moment μ_j are oppositely directed for an electron

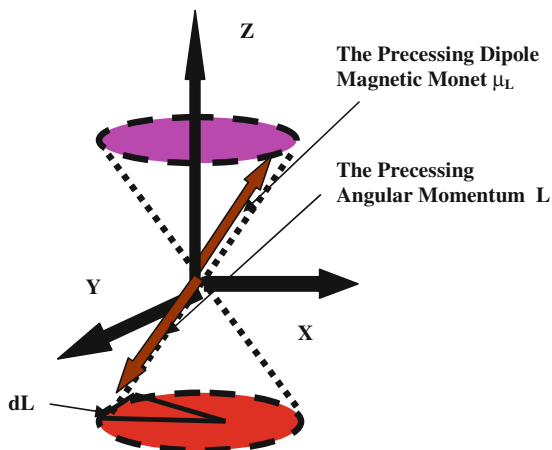


Fig. 2.2 The static magnetic field H_0 is applied along the Z-direction through the skull of the brain under scan. An electron being a charged particle produces an electric current in the orbit around the atom. This electric current say i when multiplied by the area A generated by the orbit is equal to the term called as the orbital dipole magnetic, $\mu_L = iA$, of the atom. Normally μ_L is randomly oriented at any point in space and time in the absence of the field H_0 . So the resultant effect overall is zero. H_0 is perpendicular to the X–Y plane of the orbit and remains situated at the centre of the orbit

in an atom. Application at an angle θ of the RF pulse to the static field produces a rotation of spins by an angle θ from the static field. Normally $\theta = 90^\circ$ is used to rotate spin from Z-direction to say X or Y direction. These pulses are called as 90° pulses. The static field exerts a torque τ on the spins. The torque is on the plane of an atomic orbit and it tries to orient the plane perpendicular to the static field and consequently keeps the spins in its own direction. RF pulse oscillations make the spins vibrate. Their vibration produces an electrical signal which is measured. By choosing suitable magnitude direction and frequency of the RF radiation applied the study of the quantum nature of the spins helps bring out the quantum secrets of the brain from the real time quantum images produced. Figure 2.2 is an approximate pictorial depiction of the macroscopic relationship between L and μ_L , in the presence of an externally applied magnetic field applied in the Z-direction.

The angular momentum vector L of the orbiting electron that produces the magnetic moment is not static in space along the Z-direction. It is under precession at an angle θ to the static magnetic field. This happens because though the spins are under force to remain oriented in the Z-direction the local activities, e.g. metabolism, neurotransmission, etc., try to keep the spins oriented, away from the Z-axis. This results in an equilibrium i.e. the precession of the spins at an angle θ to the Z-axis. The length of the vector of the angular momentum L i.e. its magnitude remains fixed for a particular frequency of resonance and amplitude of the RF radiation. However as a result of the precession in space its direction is changing at the rate of a fixed angular frequency. Due to the quantum nature of the

angular momentum a fixed quantum of energy is supplied by H_0 , i.e. $E = \mu_L H_0 \cos\theta$. Here θ is the angle between μ_L and H_0 . L remains quantized in space. But it rotates around H_0 in random fashion i.e. it can be anywhere in X–Y plane at any time. It can change its values up and down in quantum jumps. The magnitude of the jump is $L_z = \hbar m_z$, where m_z is the magnetic quantum number with values, $\pm(0, 1, 2, \dots)$ and \hbar is the angular Planck constant. The tip of L moves in a circle generating a cone around H_0 . This angular momentum cone generated is shown in the lower part of the diagram (Fig. 2.2). Since the magnetic moment is oppositely directed to the angular momentum due to the negative charge of the electron the corresponding cone generated by the magnetic moment is shown in the upper part of the diagram (Fig. 2.2).

The rotation of the angular momentum L in a circle is due to the precession of the magnetic moment μ_l . The precession frequency is referred to by the symbol Ω . The orbital magnetic moment of the electron is given as $\mu_l = g_l (\mu_b L/\hbar)$. It is coupled to the angular momentum and rotates at the same frequency. The precessional frequency Ω of the spin magnetic moment μ_s is given as $\Omega = g_s (\mu_b H_0/\hbar)$. g_l = orbital spectroscopy splitting factor. $\mu_b = (e\hbar/2m_e) = 0.927 \times 10^{-23}$ amp-m² (or Joules/Tesla) is the fundamental unit of the dipole magnetic moment μ_l , m_e being the mass of the electron and e its charge. In a multi-particle system one deals with total spectroscopy splitting factor g_J . An electron in an atomic orbit is also rotating around its own axis. It is called as the intrinsic angular momentum (spin) of the electron S . In the presence of the field H_0 there is the resultant angular momentum $J = L + S$ of the atom which one need to consider. The brain ensemble is a hetero-nuclear one. In a small volume one need to take some kind of an average of the magnetic moments and also in regard to the resultant angular momentum J . The ratio of the magnetic moment to the angular momentum is called as the gyro-magnetic ration GMR. The $GMR = (\mu_J/J) = g_J (\mu_b/\hbar)$. Here μ_b is the fundamental unit of the magnetic moment and \hbar provides the fundamental unit of energy (has units of joules second) and is called as the Planck's constant of the RF radiation, g_l is the resultant spectroscopic splitting factor. This ratio has very important place in the MRI literature. There are many species (hetero-nuclear situation) of nuclei in a small selected volume in the brain. For examination one needs to take into account the resultant effect of all the local interactions among the nuclei. It is a common practice now to take spectroscopy of a small region of say mm³ – cm³ dimension as part of MRI. This small volume is referred to as a voxel in the medical MRI literature.

Spectroscopy is very helpful in determination of the distribution in space of the relative and absolute metabolic concentration in the brain. The spectroscopy also helps in the diagnostics of the brain tumors. The precessional frequency of the magnetic spins around H_0 is $\Omega = g_J (\mu_b H_0/\hbar)$. Here g_J is the spectroscopy splitting factor that determines the splitting of the energy levels in a voxel and is a measure of the distribution of the metabolite concentrations. In Fig. 2.2 there is only a rough depiction of the precession of the diamagnetic dipole moment. The μ_l shown is representative of a single electron or a proton. In fact it can very well be the resultant of several neighboring electrons and protons. Furthermore in a small selected region i.e. a voxel in the brain for imaging the outer orbital electrons in

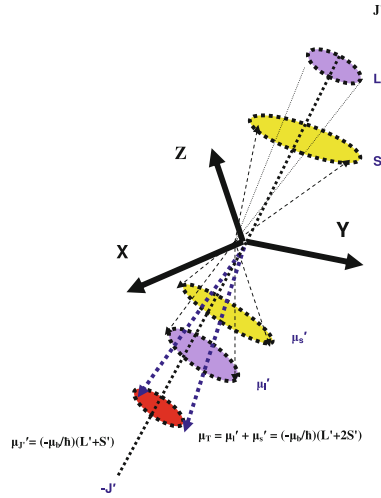


Fig. 2.3 Above is a picture representation of how the multi-electron intrinsic spin angular momentum $S' = \pm 1/2\hbar$ and the multi-atomic angular momentum L' are oriented and add together in space in a multi-particle system. The resultant produced is modulated due to the interactions e. g. metabolism, neuronal synapses etc. events in-between the molecules. This is induced due to the presence of the internal the nature's magnetic field in the brain. In each little volume (voxel) in the brain there is a resultant angular momentum J' due to all the local spins present. Because of the local nuclear magnetic field spins try to align themselves along the local Z-direction the internal local direction of the local order. One should remember that the local order direction being called as z-direction is purely arbitrary. This is just to keep analogy with the real laboratory MRI situation where the Z-direction is taken as the direction along which the static magnetic field is applied

the neighboring molecules and the protons in the nuclei will all couple together to produces a resultant angular momentum $J = L + S$. Here L precisely could be the resultant of angular momentum of atomic angular momentum and that of the nuclear one. The over all S would be the intrinsic angular momentum of outermost orbital electrons in the neighboring molecules. In larger size voxels diffusion dynamics of the molecules modulates the received signal.

It is part of the space and time functional dependence of the fluids e.g. blood circulation on the angular momentum J . A typical example where the spin dynamics can be seen in action is the BOLD (blood oxygen level dependent)-MRI. One should always remember that it is not the angular momentum J that is a measurable quantity. Instead it is the changes associated with the precession frequency of the magnetic moment and the phase (time of arrival of signals) due to varying angles between spins created by the RF radiation that is measured. Finally the received modulated radiation is the consequence of the variations of the magnetic dipole moment which oscillates because of the precession of the angular momentum J . According to the simple physics principles of dynamic electricity an oscillating magnet in space produces electrical signals around it. Its space and time variation detected by the sensor forms the image.

2.3 The Multi-Particle Angular Momentum Has a Resultant Due to the Internal Nuclear Magnetic Field of ~ 1 Tesla

In a multi-particle system the internal magnetic field due to various nuclei (generated due to relative motion of electron and nucleus) in macromolecule situation adds up to a resultant, locally, and tends to orient the neighboring spins around it along its own-order-Z-direction. The angular momentum of a spin (the atomic magnet) is given as $L = I\omega$. Here I is the moment of inertia of rotation of an electron around its axis of rotation and ω is the frequency of rotation due to the electron rotation around the nucleus. In a voxel L 's and S 's are the resultant due to various atoms, molecules, etc., given as $L' = L_1 + L_1 + \dots$; $S' = S_1 + S_1 + \dots$. The resultants (Fig. 2.3) consist of the components of the angular momentum of the neighboring interacting particles. Then due to the internal magnetic field, L 's and S 's, add up to produce a resultant $J' = L' + S'$, and thus a local order is produced. Spin-Orbit (L-S) interaction breaks the degeneracy of the doublet quantum state of S ($\pm 1/2 \hbar$). It makes instead, $J' = L' + 2S'$. The resultant magnetic moment μ_j' is thus not exactly oppositely directed to J' . This offset is suppressed in MRI by the externally applied static magnetic field. Figure 2.3 depicts Z as the internal magnetic field direction and shows how the internal order along J' is created locally.

In MRI the brain's internal order is suppressed by the external static magnetic field which is applied in the laboratory in the Z -direction. A suitable sequence of RF pulses is applied along X and Y directions, to excite the spins for imaging. The $J' = L' + S'$ interaction is commonly used in chemical shift imaging in the conventional MRI. The quantum energy correlation between nuclei in molecules on the other hand is excited by the magnetic field gradient-pulsed radiation and the correlations can be imaged. The quantum order can be detected on a micron to mm region scale. This is what makes the QMRI (quantum magnetic resonance imaging). In QMRI also the spins are projected to new positions in the X, Y plane as in conventional MRI. One tries to produce gradient echoes using the incident gradient RF pulses and is analyzed through the received signals. Specifically in QMRI we are particularly looking for multi-quantum correlations between molecules. This is different from just an average overall resultant of local environmental effects due to the molecules in a voxel. The spins vibrate due to the incident RF radiation gradient magnetic field pulses and produce the electrical signals.

In QMRI the gradient magnetic field pulses are applied in different directions to reinforce quantum correlation among multinuclear molecules. Further the signals in particular due to the quantum interactions are measured. In between the pulses the spins undergo a relaxation back to their original equilibrium position with quantum correlation relaxation times. As in the conventional MRI there are two main types of relaxations. One is called as the longitudinal relaxation. This characteristic time is also referred to as spin-lattice relaxation time T_1 . T_1 basically originates from spins rotated or deflected away from $+Z$ direction by the incident RF radiation; eventually they try to comeback to the $+Z$ -direction. The second type of relaxation is called as the transverse relaxation. The characteristic

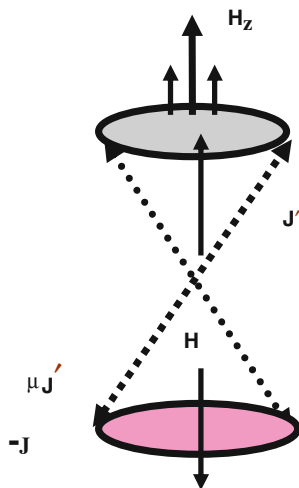


Fig. 2.4 In the presence of an externally applied field H_z , the internal magnetic moment $\mu_{J'}$ is suppressed and only the externally (in the laboratory) created μ_{H_z} survives and is measured. For the particular case of a single electron (e.g. electron in Hydrogen atom) the intrinsic electron spin S will produce for the energy level of the atom a doublet split ($g_s = 2$) as shown. In a multi-atom molecule, multiple splitting will be observed that will include the effect of the angular momentum quantum numbers $l = 0, 1, 2, \dots$ in each main orbit $n = 1, 2, \dots$

time of this relaxation is called as T_2 . In this relaxation the spins are kept in the X-Y plane while evolving. They are initially focused in +Y direction. Then they are reversed in the plane along the -Y direction. The repeated reversal generates gradient echoes and thus the electrical signals are measured. This relaxation is also called as the spin-spin relaxation.

There can be interactions in-between the voxels too. The process is a resultant effect overall over large (mm^3 to cm^3) volumes. The overlapping resultant orbital angular momentum is $L'' = L'_1 + L'_2 + \dots$, over all particles and the overlapping spin angular momentum is $S'' = S'_1 + S'_2 + \dots$, over all particles. The overall resultant is $J'' = L'' + S''$...over all particles. Because the electron-spin angular momentum S has duplicity ($S_z = \pm 1/2 \hbar$), actually speaking,, we have, $J'' = L'' + 2S''$. The spin-orbit ($L''-S''$) interaction, does not allow $\mu_{J''}$ to be exactly aligned in opposition to the J'' . The overlapping space in between the voxels becomes the source of continuity in the overall global image of the brain. Internally the magnetic moment does not follow the same precessional rule as does the angular momentum. What exactly happens in the brain is not exactly the same thing what we can measure in laboratory. The magnetic moment is supposed to be an exact replica of the angular momentum but it is not.

One should note in passing here that the conventional MRI does not take much notice of the intermolecular quantum level interactions. They are treated as if they were scalar J-couplings producing the average effect in imaging. In QMRI the quantum interactions are encouraged by applying suitable magnetic field gradients of the order of mT/m (milli Tesla per meter) in x, y, z-directions. These gradients

tend to concentrate molecular spins in one direction more than the other, thus producing localization of the molecules in a desired quantum state. The concept of the two relaxation times and the echo still remains the same as in the conventional MRI. But the reason for relaxation is different for the QMRI. Here one selects zero quantum coherence (ZQC), double quantum coherence (DQC), etc., as the source of analysis in a particular voxel.

2.4 Application of an External Static Magnetic Field H_z Along the Z-direction Suppresses the Random Internal Magnetic Order

There is no technology yet which can work out the arrangement of internal magnetic field around a nucleus and its influence on nature's intricacies of the brain functions. MRI tries to impose an order of its own on the brain and find out whatever it can. Figure 2.4 shows a rough depiction of an average measurable magnetic moment μ_H , created by the external static field applied in the z-direction.

The multi-nuclear ensemble like the brain produces a complex spectrum. It can be a rich source of information gathering about a tumor in the brain. Over a small region when there is no externally applied magnetic field the internal magnetic field creates an order of its own. Due to the degeneracy of $g_s = 2$, of the electron's intrinsic angular momentum, $S_z = \pm 1/2\hbar$, the multi-particle resultant is $J' = L' + 2S'$ and not $J' = L' + S'$. One should note the coupling between S' and μ_S' is twice as much stronger than the coupling between L' and μ_L' . Thus the magnetic moment μ_J' does not follow $J' = L' + S'$ but instead follows $J' = L' + 2S'$. Accordingly the total magnetic moment, $\mu_T' = \mu_L' + \mu_S'$ is not exactly oppositely directed to J' i.e. it is not along $-J'$. By applying an external field H_z the above offset between the total multi-particle angular momentum J' and the total magnetic moment μ_J' is removed. They then follow each other and make the analysis simpler. The Z component of the total magnetic moment μ_H on the application of the RF radiation can now be easily manipulated with little modulations from the internal nuclear magnetic field.

The quantum correlations between the spins within a voxel become a source of detailed spectroscopy. The quantum numbers according to the main orbital n are, $n = 0, 1, 2, \dots$. For each main total quantum number n there are the familiar spectroscopic sub shells, s, p, d, ... corresponding to the orbital quantum numbers $l = 0, 1, 2, 3, \dots$. The angular momentum sub-shells accommodate the number of electrons as, $n_l = 2, 6, 10, \dots$ according to $2(2l + 1) \dots$ in each sub-shell. For the total spectroscopic effect of the electrons, protons, nuclei, etc. the total spectroscopic splitting factor due to all the interactions, $g_{J\mu_L'} = g_l\mu_L' + g_s\mu_L'$, will be used. In the simplest case like that of a Hydrogen atom as an illustration there will be a doublet split of the single energy level of an electron in the orbit. This is the ideal lowest level splitting. This doublet split will be present in the each orbit n for different levels corresponding to different sub-shells in any other tom.

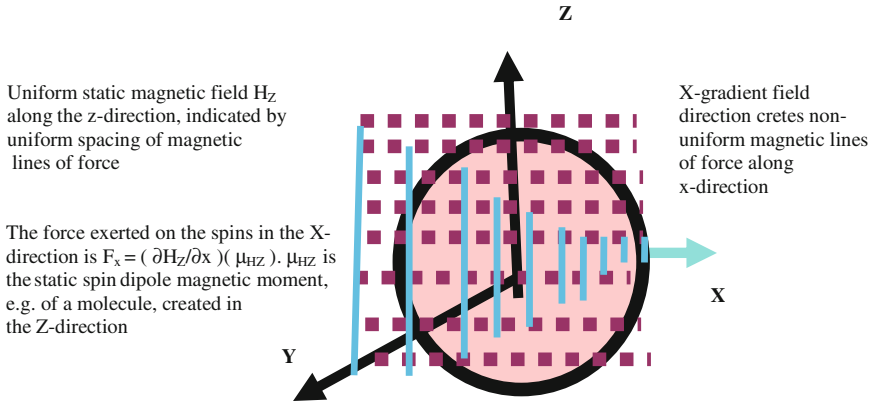


Fig. 2.5 In this figure a uniform static magnetic field is shown applied in the Z-direction. A static magnetic field gradient is also shown applied in the X-direction. Uniform spacing of the magnetic lines of force (*dotted lines*) in space along the Z-direction (X–Z plane) is representative of the uniform magnetic field along the Z-direction. On the other hand a non-uniform spacing of the magnetic lines of force (concentrating in the +X direction and dilating in the –X direction) represents the presence of the gradient field in the +X direction. In a gradient magnetic field spins are focused in the direction of the gradient. This is the result of a force $F_x = (\partial H_Z / \partial x) (\mu_{HZ})$ on the spins, superimposed on the strong static magnetic field (representing uniform spacing of spins in the X–Z plane) applied in the Z-direction. It is as if trying to divert a fraction of the total number of Z-directed spins, into the X direction. The result is a translational motion of the spins in the direction of the x-gradient

The total quantum number can be written as $n = 1 + l + s$ where the spin quantum number, s , of the electron produces doublet of its own. This is referred to as the multiplet-structure in spectroscopy due the l sub-shells and the s -degeneracy. The internal atomic-nuclear magnetic field produces dynamic interactions among the atoms and molecules due to the various brain activities happening all the time. The overall resultant multi-particle-effect will thus further split the sub-shells. This is called as the hyperfine-splitting. Thus a detailed spectroscopy will show the signatures of, what exactly is happening in a small volume called as the voxel. This information is commonly collected by using the technique called as the proton magnetic resonance spectroscopy (PMRS). For a voxel PMRS is done at the same time when the image scan is performed. In the single particle spin only case the spectroscopic splitting factor, is referred to by the symbol, g_s . This will be the case e.g. for the electron in the simplest atom. This is the case of the Hydrogen atom. Here the gyromagnetic ratio (GMR) is given by, $g = g_s = 2$. This is an ideal situation when there are no interactions among the atoms and molecules as if they are isolated atoms with no interactions.

2.5 Effect of the Application of a Magnetic Field Gradient: Illustration of the Effect on a Single Spin (Orbiting Electron in an Atom)

A uniform static magnetic field applied in space at any moment of time directed say in the Z direction orients atomic spins in that direction. Now suppose we superimpose a gradient field of relatively small magnitude on the uniform field in another selected say X direction. This gradient exerts a directed force on the resultant magnetic moment $\mu_j = \mu_l + \mu_s$ over a small volume in the X direction. This is as if trying to make a linear displacement of a group of spins in the X direction. By changing the sign of the gradient i.e. applying it in the opposite direction the force will be exerted in the opposite direction. If one makes the applied gradient field vibratory (or pulsed gradient) in time with positive and negative amplitudes included the spins in the localized volume will vibrate and produce electrical signals. This is due to the vibrating magnetic field produced by the oscillating gradient pulse. Electrical signals can be generated in a plane perpendicular to the direction of the vibration of the spins (in a selected slice ΔZ , in the z-direction) i.e. in the Y–Z plane. A sensor can then detect the signals for mapping of the brain. These signals will have all the information about the molecules and the nuclei as to what activities they are performing. This will be in reference to a particular instant, in space and time. This information is collected and stored during a scan of the brain (Fig. 2.5).

Quick reversal of the gradient in space and time forward (+x) and backward (–x) by means of an RF gradient pulse will produce echoes with electrical signals representative of the signatures of the dynamic events happening in the brain. One can use the directed gradient pulse simultaneously or one at a time in all the three x, y, and z directions. We can thus build a three dimensional dynamics of the brain in space and time. One can think as if a three dimensional virtual RF wave diffraction grating has been created in the brain. An optical grating is fairly well known. It is a structure with fine line grooves on a glass plate made in one direction. The width and spacing of the lines is very close to the wavelength of optical light.

When light is incident on the optical grating it produces a diffracted spectrum of the light into various components (colors) i.e. in wavelengths, orders, etc., on a screen. The above analogy may not be a perfect one but similar things are happening in both situations. In MRI we are creating in the time–space a dynamic RF grating. In an optical grating one uses a coherent source of light to produce the spectrum from static grating. In the brain application of the frequency selected RF gradient pulses in different directions becomes a source of detailed imaging of the artifacts and of the modulated spectroscopy observed. This is as if a three dimensional virtual diffraction grating has been created in the brain in the time–space.

The artificially created grating by MRI provides an ordered structure in time. It is required for an ordered collection of signals. But one should remember that our brain physically is a microscopic order (remember on a macroscopic scale we

are able to make imaged portions according to the functions of the various regions) and is not an ordered structure like a crystal. That is what distinguishes the brain from easily discernable three dimensional diffraction gratin we are so accustomed to, e.g. in X-ray and electron diffraction in solids (crystals). The spatial non-uniformity in our brain is transformed into a uniform and periodic time space by using carefully designed structure of RF pulses. The reader is reminded that the above effort trying to describe the microscopic MRI analysis of the brain in words is not an exact description that could have been created by including some mathematical equations. Then unfortunately the book will go more in the direction of the PCM experts version. Some compromise has been struck here to make things simpler. A reader interested in a detailed mathematical treatment should refer to a normal text book in MRI.

2.6 The Quantum Model of the Brain

One can think as a first level of physical impression of the quantum brain as made of several macromolecules arranged in a random manner locally. Suppose each macromolecule has a central processing unit (CPU) like the desk top electronic computer we are so familiar with an equivalent giant nucleus. There are peripherals in the macromolecule. These are the quantum spin-correlations. They comprise electron–electron correlations e.g. the chemical shift, multi-quantum correlations, etc., etc. Wide spread are the correlations for the resultant multi-particle angular momentum L' and the spin S' producing $J' = L' + S'$, i.e. the J-coupling and similarly others. Aside the couplings on a macroscopic scale created by spin–orbit interactions there can be pure quantum coherence couplings at the nm to micron scale level. These are generated by the demagnetizing field created by the distant dipole spins. This field can activate coherence between spins pointing in the same direction or in the opposite direction. These coherences lead to multi-quantum effects. There can be zero and double quantum coherences in addition to the single quantum coherences which are easily observed.

The coordinated macro-molecules in the brain in a small volume can be thought as if jointly having a giant nucleus at the center with several protons and neutrons in it. There is a group of, correlated electrons orbiting around a group of nuclei in a macromolecule. A nucleus intrinsically has a magnetic field of its own which varies in direction and magnitude over small distances. This creates a magnetic order over distances of nano-meters to micrometers and to millimeters. This order influences the activities of the electrons, atoms and molecules. Under the influence of the nuclear magnetic field atoms and molecules are busy in carrying out communication and regional activities e.g. metabolism, electrical communication, etc. The energy transfer between the metabolic and other connected activities is quantized. The energy is passed on as bundles called as quantum of energy rather than transferred in a continuous manner.

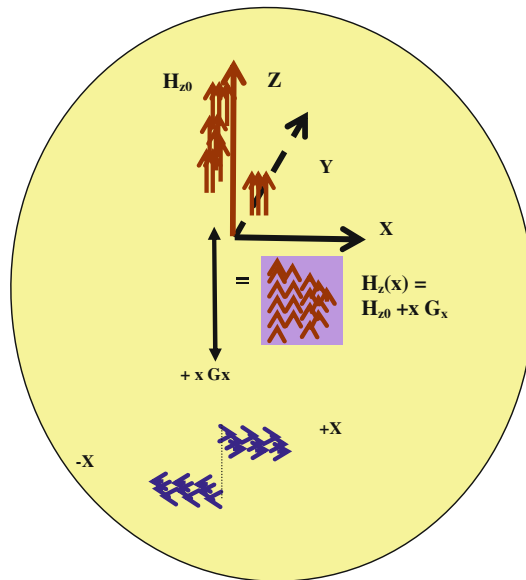


Fig. 2.7 This figure makes a pictorial depiction of the effect of the X-field gradient in the X–Z plane on the spins directed along the +z-direction. Magnetic Field Gradients in X, Y, Z directions can be used to induce quantum correlations in the brain in space and time thus creating the scenario for QMRI. In the above situation the gradiated spins along the +x direction are shown added at point x to the uniformly spaced z-oriented spins. The final result of addition is shown on the right hand side of the figure. One can notice in the Figure a uniformly distributed spins along the z-direction. A bunch of spins are created in the voxel pointing along the z-direction but are non uniformly spaced along the X-direction. A gradient of magnetic field along the +x direction is applied to a small selected volume. It produces focused spins along +x direction. Same will hold when gradient is applied along the -X direction

coherences and triple, etc. coherences. In order to sustain multi-quantum coherences (MQCs) in time a phase cycling process is repeated in time. This means repeated cycle of 90° pulses along X, $-X$, Y, $-Y$ is applied to reinforce MQCs.

2.7 Quantum Magnetic Resonance Imaging in Brain

The phenomena of interference of waves in one, two or three dimensions in a medium are well known. An application of magnetic field gradients pulses in the X, Y, Z directions can effectively simulate this phenomena in the brain. It can provide frequency selection and interaction of the spins with modulations of the brain activities in space and time. This can consequently be imaged. The following diagrams (Figs. 2.7 and 2.8) illustrate how the QMRI can be realize.

By applying the magnetic field gradient pulses in three directions one can collect information in space and time from the re-radiated back RF radiation. The signatures

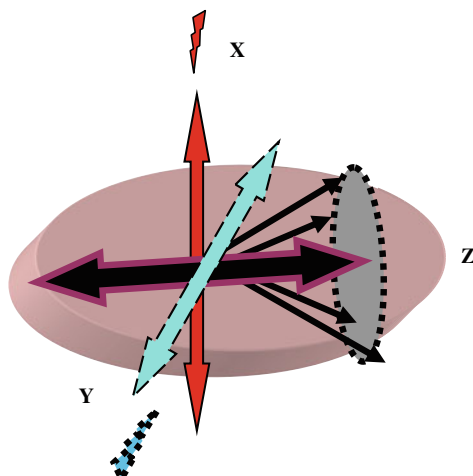


Fig. 2.8 This figure depicts an illustration of application of magnetic field gradients which can be applied in the X, Y, directions. The static magnetic field is applied along the z-direction. This arrangement allows a desired space and time modulation of spins in the brain to be measured. The selected (resonance frequency) RF radiation application allows to choose the spins of hetero-nuclear components. The procedure has to be quantum mechanically manipulated to allow imaging in the X–Y–Z planes. It amounts to a pulsating spin model corresponding to macromolecule in the Brain. One should remember the global brain picture would be an ideally replica of the macromolecule model with added modulations of spins in space and time. One follows voxel by voxel scan to obtain a coordinated and continuous picture through computer programs. Gradient pulses here are shown applied along x and y, directions here

of the events happening at the level of quantum coherence can be detected by a receiver. One should realize that the picture depicts as if the RF gradient pulses are being applied globally over the brain. In fact one would choose a small volume around 1 mm^3 size called as the voxel for analysis at a time. The chance of observing quantum correlations is much greater on distance scale of $1 \mu\text{m}$ (10^{-6}m) to 1 mm than on scale of mms–cms. An overall global picture of the brain is shown in the Fig. 2.8. It is to emphasize as if brain were a three dimensions RF diffraction grating. In fact what happens in MRI is not exactly a normal wave diffraction phenomenon. The re-radiated RF radiation is channeled out in different quantum channels referred to in the literature as CTPs. In a small volume ($<1 \text{ mm}^3$) the atoms and molecules behave as if they were a single large molecule. The macromolecule acts with a common structure of spin-orbit and other quantum interactions. A simplified pictorial representation of the as if, RF radiation diffraction model, of the brain is represented in book (Fig. 2.8).

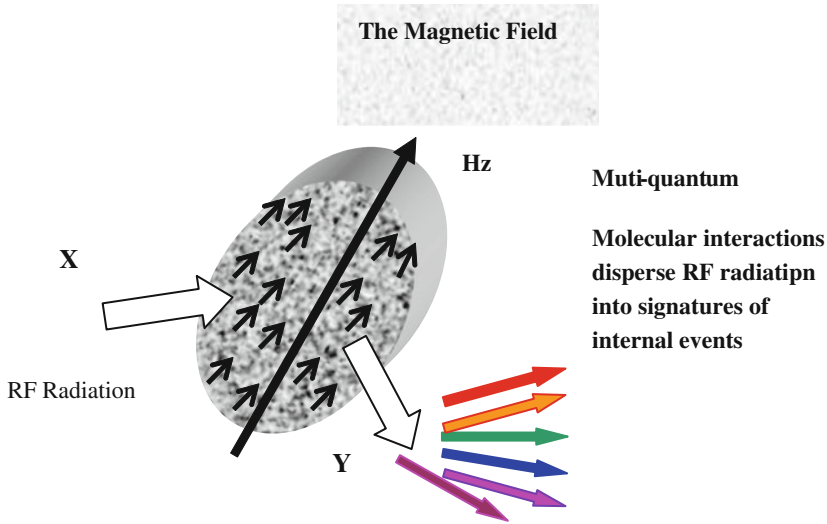


Fig. 2.9 The model presented here for illustration sake is as if the brain were a wave dispersive medium (e.g. an optical prism). The Figure is a rough illustrative dispersive model of the brain. Low energy radiation (radio-waves) is incident on the brain. The in-going and the out-coming radiation here is an invisible (RF) radiation. However the brain is a much more complex medium rather than just being a dispersive medium. It has intricate contagious spread of the various artifacts. There are real time events happening inside. The situation is much more complex and is in real time. Incident RF radiation excites the macromolecules present in the heterogeneous (species) medium of the brain. The magnetic field H_z applied along the z-direction aligns spins in macromolecules in the brain in the z-direction. A macromolecules group of spins disperses the RF radiation as if it were diffracted in different orders (frequencies and wavelengths) of spectrum representative of the various events happening

2.8 How QMRI Can Be Produced

2.8.1 A Rough Radiation Dispersive Medium Model of the Brain

One can start with a very simple interpretation of the model of the brain. Figure 2.9 presents a rudimentary pictorial representation of it. There is an ordered group of spins created by the Z-directed external static magnetic field along the Z-direction. These spins act as if they are behaving like lines as in an optical diffraction grating. In fact more exactly they are like atomic discs. They can be a source of diffraction for the RF radiation. One can derive a simplified model picture by analogy to the rainbow scene observed in nature about the dispersion of light. We may say the spins are like tiny rain drops of water hanging in the air in the sky after the rain. When the sun shines on them we see the beautiful rainbow. The sun light goes through the rain drops and is dispersed into beautiful rainbow with seven visible natural colors of different wavelengths. Each color corresponding to a specific

wavelength and is dispersed in space according to the dispersion produced in the water droplet. In fact if the sky were a diffraction media rather than the dispersive one would see very sharp line spectrum instead of the usual fussy rainbow. The spectrum would be discrete and sharp in contrast as well. Also one would see many more wavelengths not visible in rainbow. Situation with RF radiation is quite a different one particularly in reference to interaction with our brain. Firstly its an invisible radiation. Secondly our brain is complex structure. It has tissues, water, membranes, arteries, veins, etc. White light can not pass through the brain as it is opaque to it. The RF radiation also can not pass through the brain. But RF radiation can excite the local spins of atoms, molecules etc., to their higher energy states.

The ordered spins in the brain are taken as representative model of the soft matter of the brain in the presence of the applied static magnetic field. For simplicity sake we can imagine as if the spins were sitting, in a kind of variable dispersive medium. The RF radiation when incident on the brain gets dispersed by the spins with information from the dispersive medium that is present in the brain. Mere dispersion of radiation and its detection in different directions however does not serve much purpose as a model. The model has to be a bit more comprehensive commensurate with the more complex problems of the brain. We are interested in moment to moment and point to point modulations of the spins by the local events. We have to be able to record the local events through the received back electrical signals generated by the spins. The spin-spin quantum interactions are missing in the dispersion model (closer to the conventional MRI) of the brain. The RF radiation signals generated are invisible (dark light) to a naked eye. The reradiated RF radiation output from the spins is measured in MRI. They have a region to region information from the protons (e.g. water molecules), blood oxygen level dependent (BOLD) movements, metabolic activities between molecules and tissues, neuro-transmission, etc. The measurement of the dispersed RF radiation by virtue of the presence of spins in a dispersive medium is the approach taken in the conventional MRI. One may say that conventional MRI in a simple expression (in common persons' language) detects dispersed RF radiation from spins associated with different artifacts of the brain which when collated in space and time is reconstructed into a real picture. But the individual components of information collected do not include quantum-coherent interactions among the spins. The mutual interaction of spins in conventional MR is as result of the medium in which they reside and move. Below is a rough pictorial presentation in terms of the oversimplified dispersive model of the brain.

Our brain is a strongly interacting quantum-molecular medium. If the incident radiation were only visible white (optical) light the output from the imagined optical brain prism one may imagine would be something akin to seven rainbow colors. The brain has a dispersive (fluids, artifacts, etc.) medium. In MRI we use the invisible RF radiation. The spins in the brain are in fact part of the dispersive medium in which they are present. The method of dispersion in MRI is the absorption of the RF radiation by the molecules, tissues, fluids, etc. and re-radiated back with modulation in amplitude frequency and phase from the local medium. One may think of RF radiation used in MRI for simplicity sake illustrated above as if it were going through some kind of dispersive biological prism. But the brain is

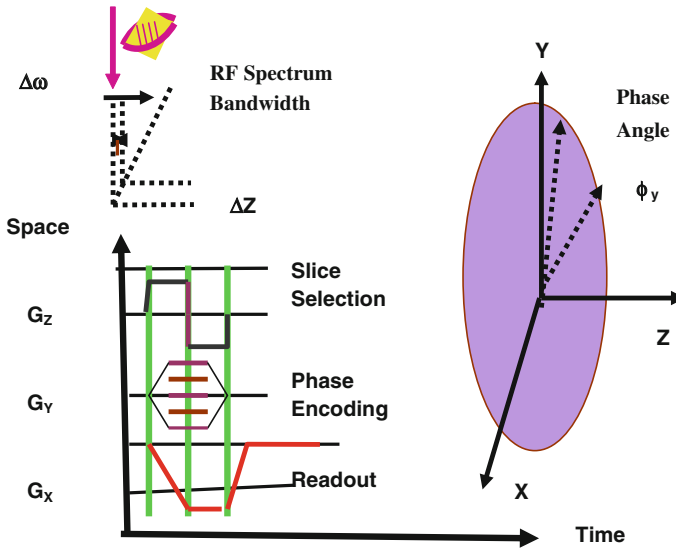


Fig. 2.10 It is a pictorial representation of the basic pulse sequence technique of imaging of the brain. A series of magnetic field gradient pulses with positive and negative components are used along X, Y, Z directions. One can follow the pulses in a sequential structure with a typical arrangement as shown. But in a commercial situation different machines would have their own specific routines to follow. H_z is the static magnetic field applied in the Z-direction. Y-gradient is the phase encoding gradient. The phase angle is $\phi_y = \gamma y G_y t_y$. Here γ is called as the gyro-magnetic ratio = the ratio of the magnetic moment μ to the angular momentum L , G_y is the field gradient in the Y-direction, y is a coordinate point in the Y-direction and t_y is any instant of time. The X-Gradient, G_x is then applied in the X direction to select the output. The resonance frequency selection along X at a position x is $\omega(x) = \omega_0 + \gamma \times Gx$

not as simple as the optical type dispersive medium. It is a complex biological structure. The brain consists of atoms, molecules, tissues, fluids, etc. It makes it internally an irregular medium. One can say it is somewhat a spheroid shaped complex biological medium. In the presence of a static magnetic field applied in z direction to the brain and the RF electromagnetic field applied in the x direction one observes in the y direction like a diffracted RF beam of radiation. This modulated beam of RF radiation brings out what is happening in the brain over space and time. This is converted into a map of the brain. In a nut shell one can say if one wants to know about the detailed intricate-dynamic-quantum mechanical structure of the brain just the single quantum conventional MRI technology we have at present is not adequate.

2.8.1.1 A Basic Quantum Imaging Technique

The use of magnetic field gradients along the three x , y , z directions can be exploited to stimulate RF electronic excitations of the macromolecules in the brain

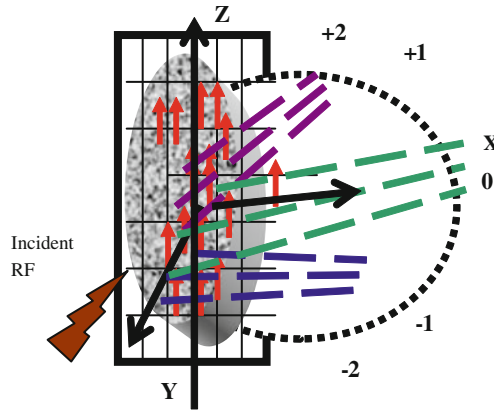


Fig. 2.11 The above pictorial representation depicts a more refined (from the macroscopic medium -dispersive) model of the brain. It is as if the brain were a three dimensional diffraction gratin. This model in fact is seen very close to reality. On the left hand side (LHS) is shown round about a three dimensional ellipse (representing the brain) with arrangement of spins pointing in the Z-direction created by the static magnetic field applied in the Z-direction. Suppose now a small gradient magnetic field is superimposed on this order in the X-direction. The result will be a fraction of the spins will be moved in the X-direction. If the gradient is in the form of pulsed gradient, echoes will be generated, by the vibrating spins. These spins will tend to dissipate in the X–Y plane. A phase (angle with respect to Y-axis) reversal by 180 pulse is applied around the X-axis. The spins now flip to –Y axis first bunch together towards –Y and then start dissipating towards + Y axis. This bunching and de-bunching (phase recycling) is repeated in-between a time (called as the relaxation time T_2) several times. It provides the amplified signal required for the Quantum MRI (QMRI)

and build a multi-quantum imaging. Figure 2.10 provides a round about illustration giving a brief description of the simple three basic steps involved in quantum imaging. First a slice selection (the X–Y plane) is done in the brain space along the Z-direction. Then the spins are then projected on the X–Y plane using a 90° pulse. The maximum amplitude signal arrived due to the spins in the X–Y plane is recorded at an angle ϕ ($=0$ initially) along the Y-axis (X–Y plane) like a reference point. In subsequent phase encoding steps (Y-direction) the strength of the Y-magnetic field gradient (phase) gradient is gradually increased. This enables more and more participation of the regional (X–Y plane) molecules. A readout gradient in X-direction then makes selection of the signal in a particular bandwidth and is recorded. The three steps are repeated in succession over a period of time called as the repetition time (TR). Each time a new slice selection (X–Y plane) is made the procedure is repeated. This procedure enables systematic data information being collected about the events happening in all the X–Y planes progressing gradually in the Z-direction and finally recorded. It is later converted into a global image of the brain. Figure 2.10 is only an over-simplified pictorial representation of the steps one carries out in succession and thus builds up the data. The data is used to make a picture using a standard mathematical package

e.g. Mathematica, Matlab, etc. The reader is referred to further sections for some more details about imaging. One should refer to a standard text book on MRI for exact techniques followed in the imaging. This book is more on conceptual physical principles of multi-quantum imaging rather than on imaging technology itself.

2.8.1.2 The Quantum Approach to Imaging

Today we are in the process of refining MRI further i.e. designing the QMRI machine. In the presence of a magnetic field gradient applied in a narrow region along a chosen direction the output RF radiation will have in its components different orders of coherence-of-interaction between spins, in the dispersed state. These components are the natural result of different quantum orders of coherences between spins. The multiple orders of coherence originate from the fact that a bunch of spins is excited into different levels of energy within a macromolecular structure or due to interaction in-between the macro-molecules. The spins can correlate to each other in many different ways. The spins may be pointing in opposite ($\pm Z$) directions i.e. correlation corresponding to spins being anti-parallel. This is the lowest level bound state of energy. These correlations give rise to ZOC. But there can be spins in correlation a distance apart pointing in the same direction. These correlations give rise to DQC. There can be multiple coherences as well.

Multiple coherences of higher orders are difficult to observe. One normally observes coherences in lower orders, i.e. +2, +1, 0, -1, -2, etc. The digits 2, 1 and 0 correspond to double, single and zero quantum level coherences. These coherence arise due to the distant dipole field (DDF) created among spins in the otherwise uniform applied magnetic field in the z-direction. The selection of the quantum orders in the brain takes place in the presence of RF radiation by natural selection of the principle of the conservation of the angular momentum. Both positive and negative coherence transfer paths (CTPs) are possible but in the end it is the -1 (single quantum coherence) which is detected. Others are not directly observable. One can illustrate as a typical example shown below that our brain has the capacity to perform multiple quantum coherences. The digit 2 chosen is purely incidental. Each of these coherences may be a part of some collective activity e.g. the metabolism, etc. Having correlated the event the brain then dissipates along five different channels the messages collating different actions.

The use of the phenomena of dispersion of light in a prism or say in a rainbow as analogy discussed before was purely an over-simplification in a layman's language. That was a rough illustration for the sake of analogy and simplicity without involving a detailed PCM (physics, chemistry and mathematics) of the phenomena involved. But in the real brain there are several complex correlations of activities happening. MRI is yet a humble tool to see the distinct out puts of the several electronic happening simultaneously. It does not bring out an exact scientific truth underneath which is much more complex. It is not possible to design an MRI machine which in one go can be perfect to the finest details. One should not forget it has taken more than half a century to create the MRI machine

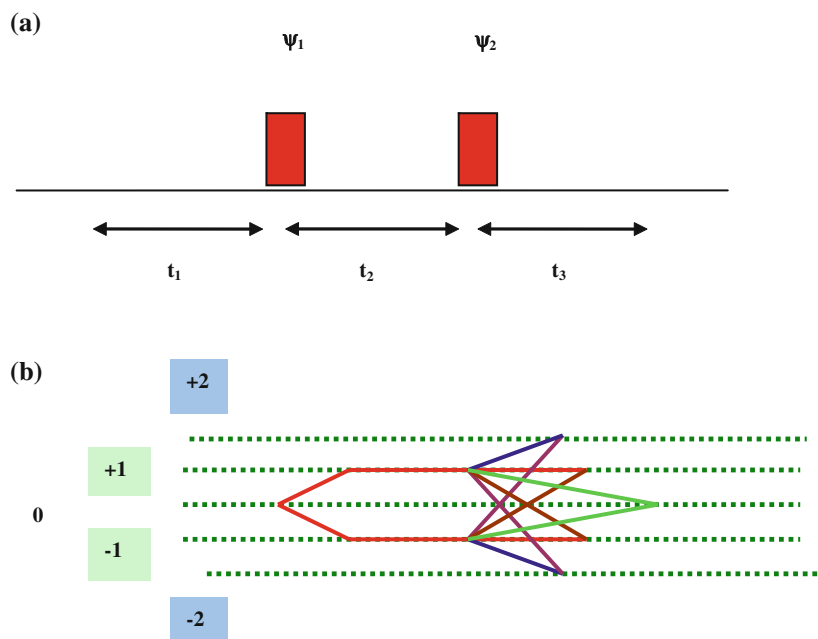


Fig. 2.12 **a** The ψ_1 , ψ_2 , phase angle (in the X–Y plane) pulses, are applied along the X-direction in succession. Normally the 90 angle (rotation along X or Y) pulses are used, and the time intervals t_1 , t_2 , t_3 in between the pulses, are allowed, and then repeated. The intervals can be variable or kept constant. The duration of the pulses, is normally kept fixed, $=\tau$ seconds. **b** The number of pulses applied depends upon the number of CTPs desired. Normally the number of pulses used is one higher than the quantum coherence order required

which we have today. It is a common knowledge that an optical prism disperses white light into seven rainbow colors. But in MRI we use RF (radio frequency) radiation which is invisible to eye and the brain is not an optical prism either. In MRI RF radiation impinges on the brain. The brain is first polarized with spins pointing in the z-direction by the applied static magnetic field.

The RF radiation excites hetero-nuclear species of atoms and molecules to higher energy states. These molecules when they come back to their ground state emit back the RF radiation. This re-emitted radiation is a random mixture of various frequencies and phases (emitted at different times). In order to get useful information out of this radiation one needs to reinforce certain signals and eliminate others. The gradient echo technique selects the required constructive interference of the important events and destroys others. One can apply oscillatory magnetic field gradients along the x, y, z directions. In general the x, y, z magnetic pulsed field gradients make the molecular spins to vibrate about their mean position and different species isolate themselves from each other in response in space and time. The receiver of the signal classifies the incoming signal into different categories according to their magnetic moments and thus a quantum

image of the brain is formed in space and time. Figure 2.11 is a rough pictorial diffraction model representation of the brain as if it were a three dimensional diffraction grating but not in the real x, y, z space but in the time–space for the spins.

In between the pulses there will be time for the spins to interact and create quantum correlations between them. Correlation between spins aligned in opposite directions leads to ‘zero quantum coherence (ZQC)’. Correlation between spins pointing in the same direction separated due to magnetic repulsion over a distance leads to ‘double quantum coherence (DQC)’. ZQCs and DQCs provide imaging signals which are smaller in intensity than the SQC (single quantum coherence) signals used in the conventional MRI but provide better resolution in the image. A single quantum coherence assumes that all the spins have the same identity over large volumes in the brain. But this is very far from reality and that is where QMRI steps into unravel the true mystery of the brain.

2.8.2 A Pulse Sequence Used to Explore Quantum Model of the Brain

The following is a typical pictorial illustration of the use of pulses to explore the secret of our brain. It is used as a routine technique and allows creation of many coherence paths possible for the quantum correlations under the applied RF radiation in the brain. But the quantum science of correlations among the atoms and molecules allows only a few selected correlation paths in preference to others. The selection comes from the overall conservation of the angular momentum in a selected region in space and time. The paths carry information due to the metabolic and other events happening in the brain. Figure 2.12 is a pictorial representation of the arrangement of two pulses used in a typical experiment and the resulting quantum coherences possible. One can select the coherence one is interested in and eliminate the others.

The reader is advised that the support information presented in the Appendices A and B at the end of the book will be very helpful in enhancing knowledge about the various concepts involved in the modern day MRI. The appendices provide greater insights in brief about the technical aspects which otherwise for details one need to look into a routine text book on MRI.

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

Kaila, M.M.; Kaila, R.

2013, LX, 388 p., Hardcover

ISBN: 978-3-642-30301-2