# Appendixes

Appendix A.— NMR: Technical Background

NMR Spectroscopy—Technical Background

Ordinarily the magnetic moments of hydrogen atoms (the vector representations of the net magnetic properties of hydrogen atoms) will point in random directions. [1] When exposed to an externally applied magnetic field, however, these magnetic moments tend to align themselves either parallel to or antiparallel to the magnetic field.[2] Because the energy state of a hydrogen nucleus is lower when its magnetic moment is pointing in the direction of the applied magnetic field than when it is pointing in the opposite direction, more of the magnetic moments will point in the direction of the applied field than in the opposite direction. In quantum mechanical terms, hydrogen nuclei exposed to an externally applied magnetic field, B, will reside in one of two possible magnetic energy levels (see fig. A-l). For hydrogen nuclei to go from the lower energy level, E_1, to the higher energy level, E_2, an $E_2 - E_1$ amount of energy needs to be added to the system. When hydrogen nuclei go from the higher energy level to the lower energy level, in contrast, $E_2 - E_1$ energy is emitted from the system.

---

[1] For simplicity, the remainder of this discussion will pertain to hydrogen, which has a spin of one-half (a quantum nuclear spin number of one-half to describe the rotation of the hydrogen nucleus)

[2] Other forces, such as thermal agitation, will influence the orientation of these magnetic moments. but consideration of such forces is beyond the scope of this case study

Figure A-1 .—Energy Levels of Hydrogen Atoms in Applied Magnetic Fields
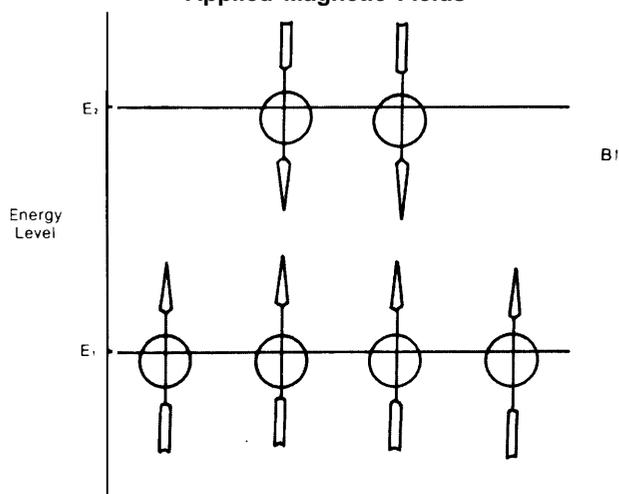
SOURCE E P Steinberg, Johns Hopkins Medical Institutions, Baltimore. MD, 1983

According to quantum theory, hydrogen nuclei will move from E_1 to E_2 *only* when *exactly* the right amount of energy (namely $E_2 - E_1$) is applied to the system. In NMR experiments, excitational energy is provided in the form of radiofrequency (RF) waves. In order for hydrogen nuclei residing in energy level E_1 to be excited into level E_2 by such radiofrequency energy, the RF waves must be applied at exactly the same rotational frequency as that at which the magnetic nuclei in E_1 are processing.[3] This frequency is known as the Larmor frequency.

When an NMR system is appropriately constructed (see fig. A-2), the energy emitted by excited hydrogen nuclei during the process of relaxation can be detected as an NMR signal. The intensity of the signal will be proportional to the number of hydrogen nuclei in the sample being studied.

Variations in the local magnetic field give rise to variations in the frequency at which nuclei spin. These spin differences depend on the exact molecular environment in which each nucleus exists. This observed "shift" in nuclear precessional frequency, and therefore the radiofrequency at which NMR signals are detected, has been termed "chemical shift. " These slight variations in NMR signals induced by variations in molecular environment provide the basis for NMR spectroscopy and its use in acquisition of information about molecular structure and conformation.

Application of NMR Principles to Imaging—Technical Background

A decade ago, scientists realized that exciting possibilities emerged if, instead of applying a *uniform* magnetic field across an experimental sample, they established a magnetic field *gradient* across it (see fig. A-3). In so doing, the strength of the magnetic field, B, varies from one line (L_1) to another (L_2). Because of the one-to-one relationship between the magnetic field strength in which magnetic nuclei exist and the frequency of radiofrequency energy that will excite them, a pulse of radiofrequency energy applied to the system depicted in figure A-3 will be absorbed (and subsequently re-emitted) only by nuclei that are located in the vertical line L_x of magnetic field strength B_x that corresponds to the Larmor frequency of the energy being applied. By sequentially varying the frequency of the energy being supplied, one can thus selectively excite nuclei, line by line. The establishment of a magnetic field gradient across a sample thus "spa-

---

[3] Precession is a term describing the motion of a proton in an external magnetic field or of a top in the Earth's gravitational field

Figure A-2.—Schematic Diagram of NMR System
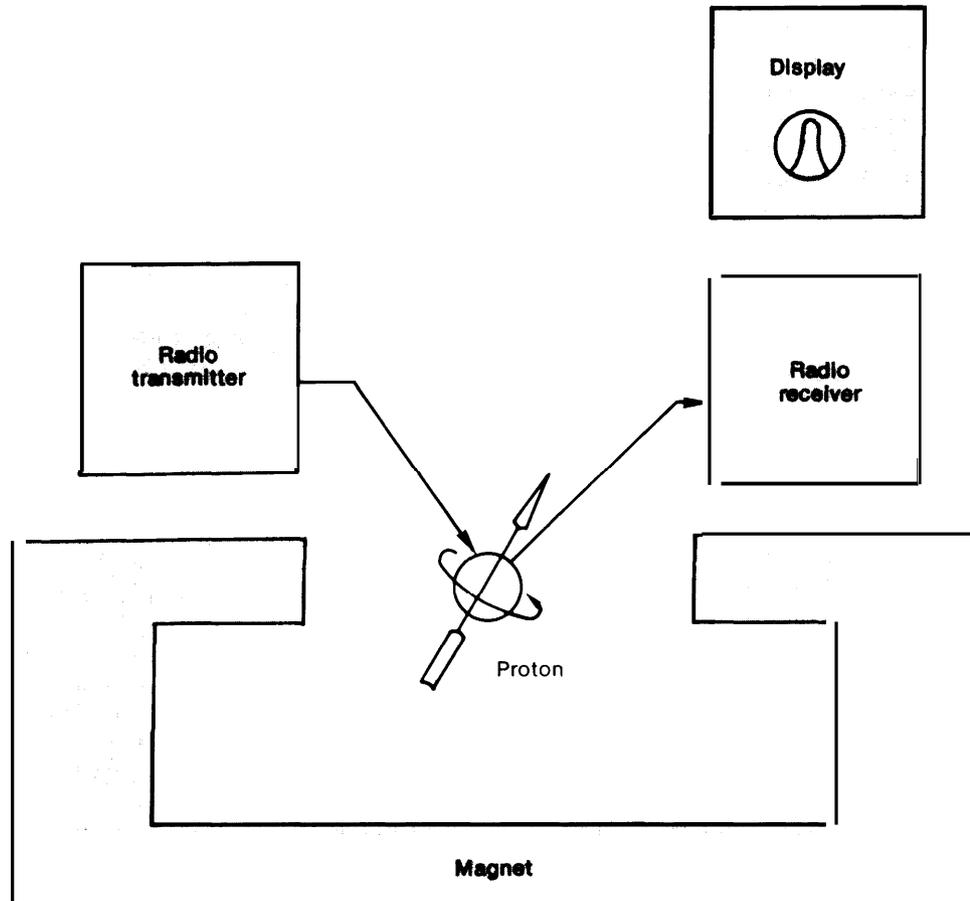
The radiotransmitter provides radiowaves at the appropriate rotational frequency to excite the proton. When the radiowaves are turned off, the excited protons precess in phase, thereby producing radiowaves that are detected with a radio receiver and then displayed.

SOURCE E. P Steinberg, Johns Hopkins Medical Institutions, Baltimore. MD, 1983

tially encodes" the NMR information inherent in a system. This type of spatial encoding of the origin of a NMR signal forms the basis of NMR imaging.

Radiofrequency Pulse Sequences

As explained earlier, NMR signals are obtained through the excitation of magnetic nuclei with RF waves. In a typical NMR experiment, the nuclei to be excited (and imaged) are repeatedly exposed to RF waves in a pulsed fashion. Specific "pulse sequences" are characterized by the duration and intensity of each pulse used, as well as by the interval between repeated pulses.

Several different types of pulse sequences can be utilized to produce NMR images. Probably the three most common types of sequences currently employed in NMR imaging are Saturation Recovery, Inversion Recovery, and Spin-Echo sequences (27,55,77). Although the exact technical details of how these sequences are produced are beyond the scope of this report, it should be mentioned that Saturation Recovery and Inversion Recovery sequences result in NMR signals (and therefore images) that tend to reflect

Figure A-3.— Experimental Sample in Magnetic Field Gradient

Magnetic field strength (B)
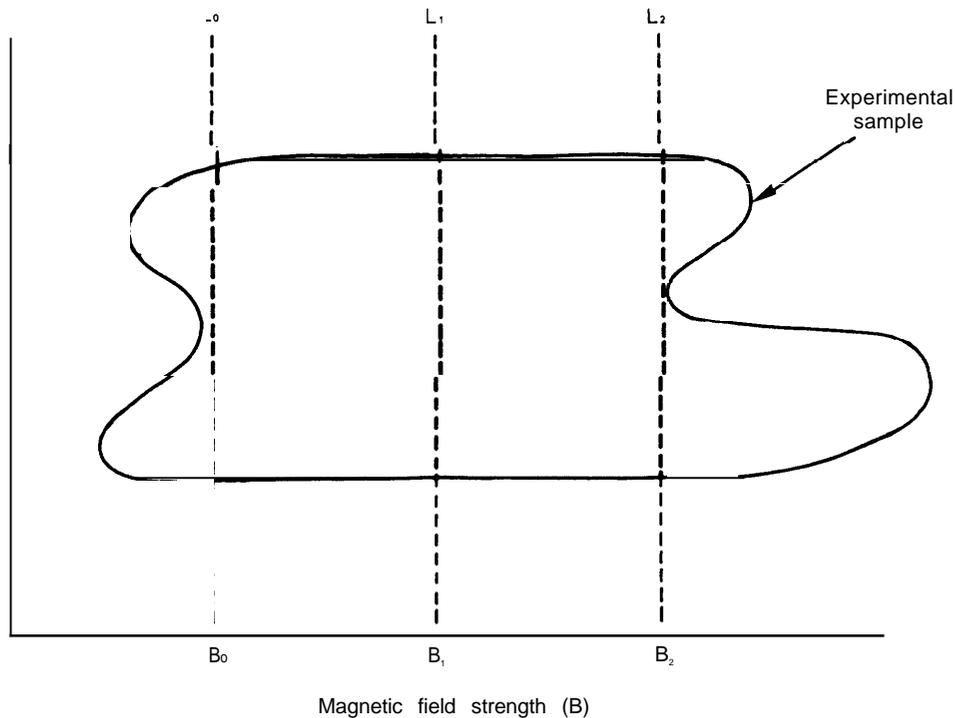
(Magnetic field strength in line Lo is Bo; in line L, is B,; and
in line L₂ is B₂.)
SOURCE E P Steinberg, Johns Hopkins Medical Institutions, Baltimore, MD, 1983

predominantly the T_1 character of tissues (i. e., they are T_1 weighted), whereas Spin-Echo sequences tend to reflect more T_2 information (i.e., they are T_2 weighted). NMR images will thus vary depending upon the particular pulse sequences used to produce them. Considerable effort is being expended on trying to define pulse sequences that optimally demonstrate different types of morphologic and pathologic abnormalities. This task is formidable, given the infinite number of pulse sequences that can be used.

Techniques for Spatial Encoding and Image Acquisition

Several different techniques have been developed through which NMR information can be spatially encoded, acquired, and transformed into an image. The first such technique, adapted from use in X-ray computed tomography (CT) reconstructions, was the projection-reconstruction method of NMR imaging used by Lauterbur (115). In this technique, magnetic gradients are electronically rotated to produce multiple projections of the sample being imaged. These projections are then "pieced together" with the help of a computer to construct an NMR image. Imaging methods developed subsequently employ a variety of techniques to "selectively excite" nuclei. These techniques have acquired names based on whether they excite nuclei on a point-by-point (sequential point methods), line-by-line (sequential line methods), plane-by-plane (planar imaging) or whole-volume (three-dimensional imaging) basis **(8).** The latter techniques require less time to form images (8). The recently developed echo-planar method of imaging permits scans to be obtained in milliseconds, raising the possibility of dynamic, or real-time, NMR imaging (133).