MAGNETIC RESONANCE ZEUGMATOGRAPHY

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ABSTRACT

Spatial resolution of magnetic resonance signals may be achieved by the use of various combinations of magnetic field gradients. The experiments are examples of a new general technique, 'zeugmatography', by which images may be formed by the use of induced local interactions. Methods for the generation of magnetic resonance images of objects, including living organisms, are described, and a number of applications are illustrated and discussed.

INTRODUCTION

Magnetic resonance techniques were originally developed and used to determine the properties of atomic nuclei and to study the static and dynamic interactions among nuclei and electrons in atoms, molecules and crystals. Such information on the properties and behaviour of matter on the molecular scale is most readily obtained if the static magnetic fields responsible for the Zeeman splittings of nuclear and electronic spin energy levels are homogeneous, so that the field variations within the samples give rise to resonance widths small compared with the interactions being investigated. When the magnetic field gradients imposed upon objects are large compared with the peak widths produced by intrinsic effects, the inhomogeneously broadened signals contain information on the spatial distributions of the nuclei or electrons at resonance. Under these circumstances, magnetic resonance becomes a technique for studying structure above the molecular level[1, 2]. When such experiments are combined with those in which molecular properties are studied, the data allow the spatial distributions of spectroscopic properties to be determined[3].

GENERAL PRINCIPLES

The experimental techniques that can give rise to spatial resolution of resonances are not, strictly speaking, spectroscopic in nature. They depend upon the interaction of matter with a radiation field *in the presence of a second field* whose influence is a function of laboratory spatial coordinates. The image that is generated represents the distribution, in the spatial coordinates determined by the defining field, of the entities that couple that field to the radiation field. The fundamental principle involved suggested the general name 'zeugmatography' for these techniques. It is derived from the Greek ζευγμα, 'that which joins together'.

Whenever the spectral response of an object can be made dependent upon an inhomogeneous field, a zeugmatographic experiment is possible in principle. Whether it is also possible in practice depends upon the accuracy with which the effect of an applied field gradient on peak shapes can be distinguished from the intrinsic shapes and from other distorting influences. Because magnetic resonance spectra often contain lines whose widths are much smaller than their frequencies, and reproducible magnetic field gradients are readily produced, magnetic resonance zeugmatography is the most experimentally convenient form of the technique, which permits the resolution of detail much smaller than that theoretically distinguishable with radio waves and microwaves if conventional imaging methods were used in a homogeneous field.

PRACTICAL CONSIDERATIONS

Practical realization of these possibilities depends upon the development of appropriate combinations of experimental apparatus and techniques, as well as data processing methods capable of generating true images from the results of actual experiments. There are a number of ways in which the effects of field inhomogeneities on magnetic resonance signals can be used to produce useful pictures. All of them depend upon knowledge of the distribution of surfaces of constant magnetic field within the object being studied. If the frequency of the spectrometer is swept, and if all parts of the object are equally coupled to the radio-frequency transmitter and receiver coils, the integrated signal intensity at each frequency will be the sum of the intensities from all of the spins located in the corresponding constant field surface. An especially simple analysis is possible if these surfaces may be approximated by a family of parallel flat planes perpendicular to the gradient axis. The intensities then correspond to one-dimensional projections perpendicular to the gradient. Relative rotation of the gradient and the object about an axis perpendicular to the gradient generates a set of such projections, which can be combined by image reconstruction techniques[4] to give a two-dimensional projected image of the object as viewed from the direction of the rotation axis. Relative rotations about other axes will permit the generation of other views, which can be combined to give a complete three-dimensional image of the object in terms of its local magnetic resonance signal intensities. If the surfaces of constant magnetic field are not uniformly spaced planes, corresponding to the same linear field gradient throughout the object, the plots of signal strength as a function of frequency no longer correspond to simple linear projections, and optical analogies and image reconstruction methods are not quite so straightforward. In arbitrary inhomogeneous magnetic fields, generalized projections, defined as surface integrals, may be used to construct images if the shape of the field can be determined.

The necessary one-dimensional projections can be obtained from frequency-sweep experiments, from field-sweep experiments or from transient experiments with appropriate Fourier transform or other data processing to give a plot of signal intensity as a function of frequency. Each will have advantages under certain circumstances. The data can be made to respond to relaxation time differences by performing progressive differential saturation experiments or by perturbing the magnetization with suitable pulses before observing a free induction decay or echo in a gradient. Images produced from perturbed spin systems will contain information on quantities, such as the various relaxation times and the local diffusion coefficients, that can affect the observed magnetization under appropriate conditions.

The simplifying assumption that the resonance signal is a single narrow peak, identical in all parts of the object, will often be inapplicable to real objects. The simplest way to suppress the effects of peak shapes is to use a gradient large enough for the entire peak to fall within one resolution element in the final picture. For example, if the chemical shifts in a spectrum were to cover a range of 500 Hz, a spatial resolution of one part in a hundred would require that the magnetic field gradient over the object correspond to 50000 Hz. The chemical shift information would then be filtered out of the data and only the distribution of the resonant nuclei would be obtained from the image. For those contributions to line shape and width that are field-dependent, such as chemical shifts and internal demagnetizing fields, operation at a low magnetic field will allow the use of smaller gradients. When field-independent effects such as spin–spin couplings are limiting, operation at high magnetic fields may often be desirable to give the highest possible signal-to-noise ratio.

Zeugmatographic imaging techniques are potentially applicable to a wide variety of magnetic resonance signals. Proton n.m.r. spectra of mobile tissue constituents other than water may be used, and the signals of other nuclei will give pictures of their distributions, although signal-to-noise ratios will, of course, usually be much lower than for water protons in organisms and their parts. The resonances of solids can be employed if the lines are narrow, if large gradients are used or if line-narrowing techniques can be applied[5]. ESR zeugmatography is also possible, and should permit studies of the locations of free radicals and paramagnetic ions within materials and complex structures, including biological objects.

APPLICATIONS

The condition that the field inhomogeneity be much larger than the intrinsic spectral width is most easily met in the nuclear magnetic resonance spectra of liquids. The most common objects for which a simple sharp resonance is accompanied by interesting structural features are plants and animals. Although the water concentrations and relaxation times are different in various tissues and organs, most of the water contributes to an apparently single strong proton resonance. Relatively simple experiments in slightly modified n.m.r. spectrometers can generate data from which pictures of living organisms can be constructed in terms of the concentration and properties of water in their tissues. A resolution of several tenths of a millimetre has been achieved in experiments on water in glass capillaries and on a small clam, and other objects up to about 30 millimetres in diameter have been studied. The upper size limit is now set only by the available magnet gap, and much larger objects could be examined in an instrument with a greater volume of homogeneous magnetic field. NMR zeugmatography may thus become a generally useful technique for the study of microscopic and macroscopic biological structures, complementing the use of light, x-rays and ultrasonic imaging.

EXAMPLES

All of the examples given here are from experiments in which an object was scanned in a conventional n.m.r. spectrometer in the presence of a field gradient lying in the plane of the receiver coil. Twelve different gradient orientations were obtained by turning the object about an axis perpendicular to the direction of the main magnetic field and to the direction of the fixed field gradient. The 12 projections, taken 15° apart, were digitized and were used by an iterative image reconstruction program similar to 'multiplicative ART'[6] to form a 32 × 32 array of intensities. Interpolated intensity values were displayed on a line printer, using a 16-level grey scale produced by various combinations of conventional symbols. Some of the pictures have been made more pleasing by photographic processing to improve contrast and to suppress distracting symbols by focusing adjustments.

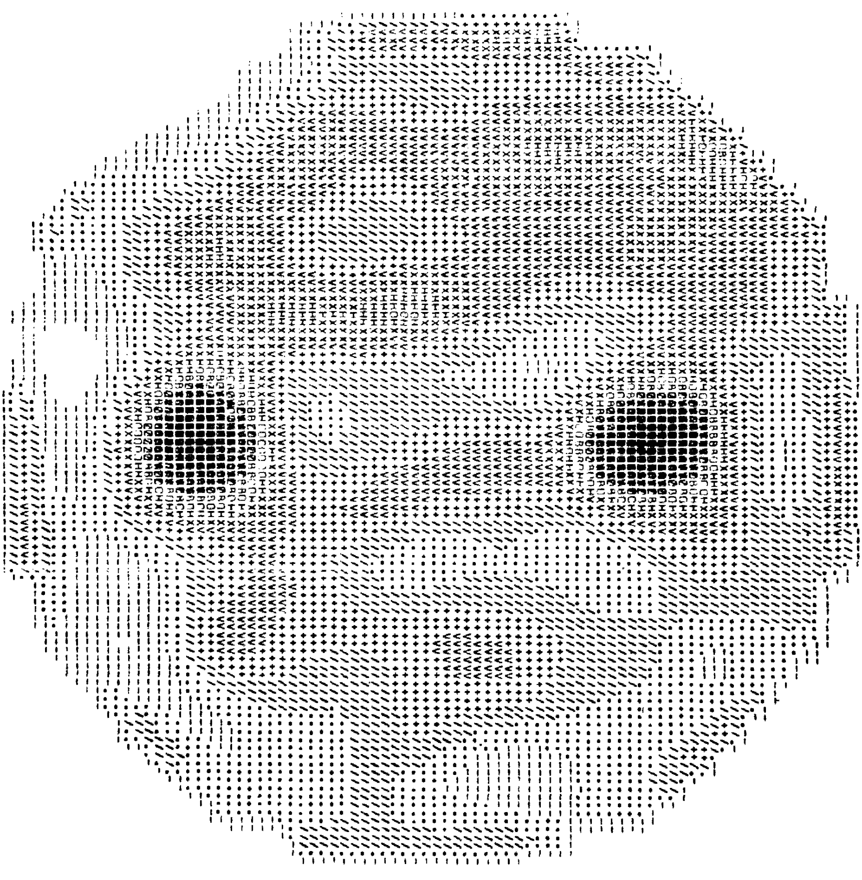

Figure 1. Proton n.m.r. zeugmatogram of two 1 mm capillaries of water in a 4.2 mm inside diameter tube containing a mixture of H_2O and D_2O.

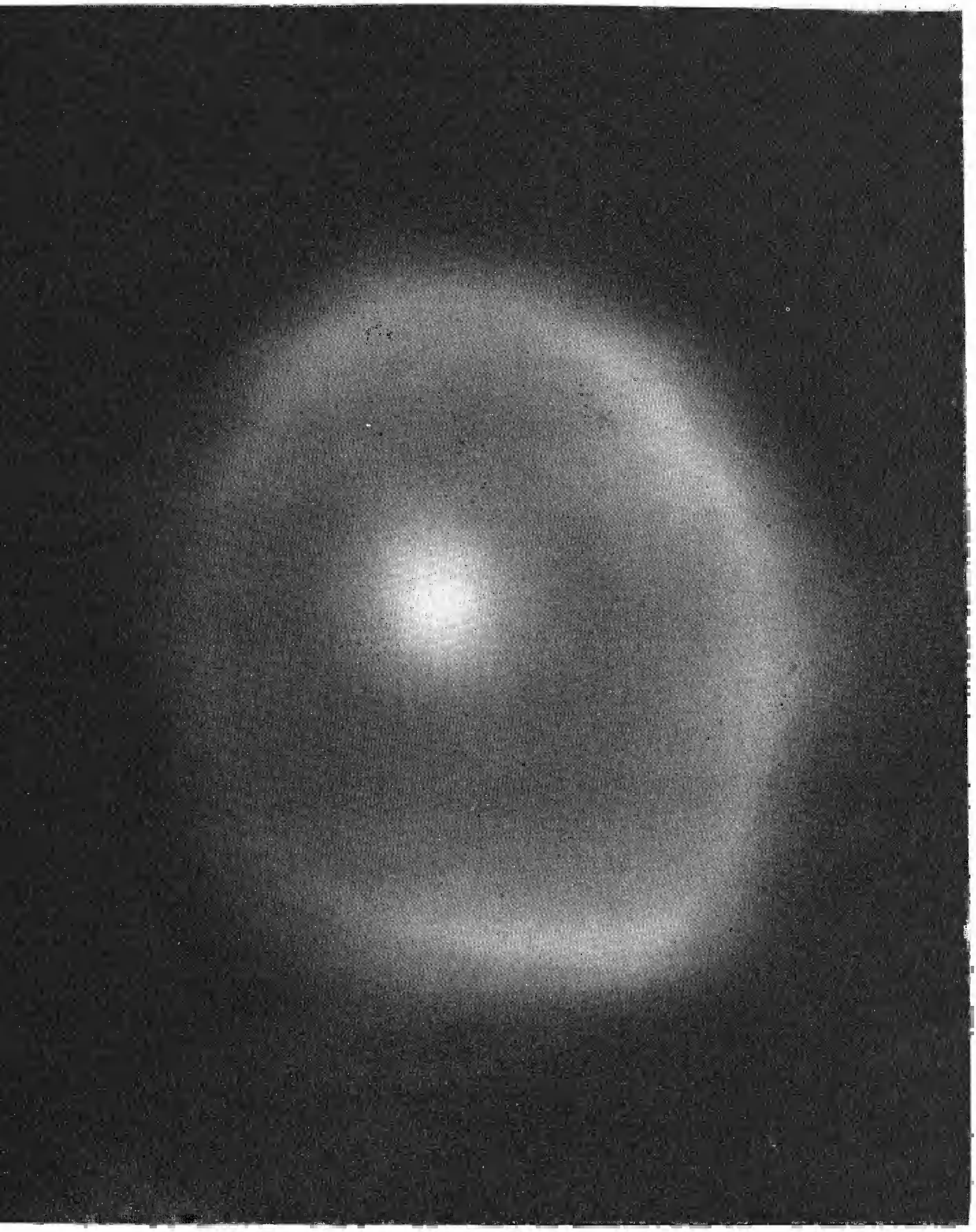

Figure 2. Proton n.m.r. zeugmatogram of the water distribution in a pine branch. The computer output has been photographically filtered and enhanced.

Figure 1 shows a proton n.m.r. zeugmatogram of a simple test object, two 1 mm diameter glass capillaries of H_2O in a standard 4.2 mm inside diameter sample tube containing a mixture of H_2O and D_2O. The resolution, about 0.2 mm, was limited by gradient distortions and by the use of only 12 gradients. A Varian A-60 spectrometer, with extra field gradient controls, was used for these experiments, which employed gradients of less than 10 μT across the sample. *Figure 2* shows the water distribution inside a conifer branch about 20 mm in diameter. The sample was surrounded by air, and was held, inside a tube with an inside diameter of 28 mm, in a special cross-coil probe operating

Figure 3. Proton n.m.r. zeugmatogram of the oil distribution within an intact pecan nut (*Carya illinoensis*).

at 8.13 MHz which was also used for the other experiments described below. Gradients of about 0.1 mT cm^{-1} were employed. The instrument was a Varian DA-60 spectrometer, modified by the addition of a pulsed time-sharing system. *Figure 3* shows the oil distribution inside a pecan nut, which contains only a few per cent of water, but gives a signal about 2 p.p.m. wide

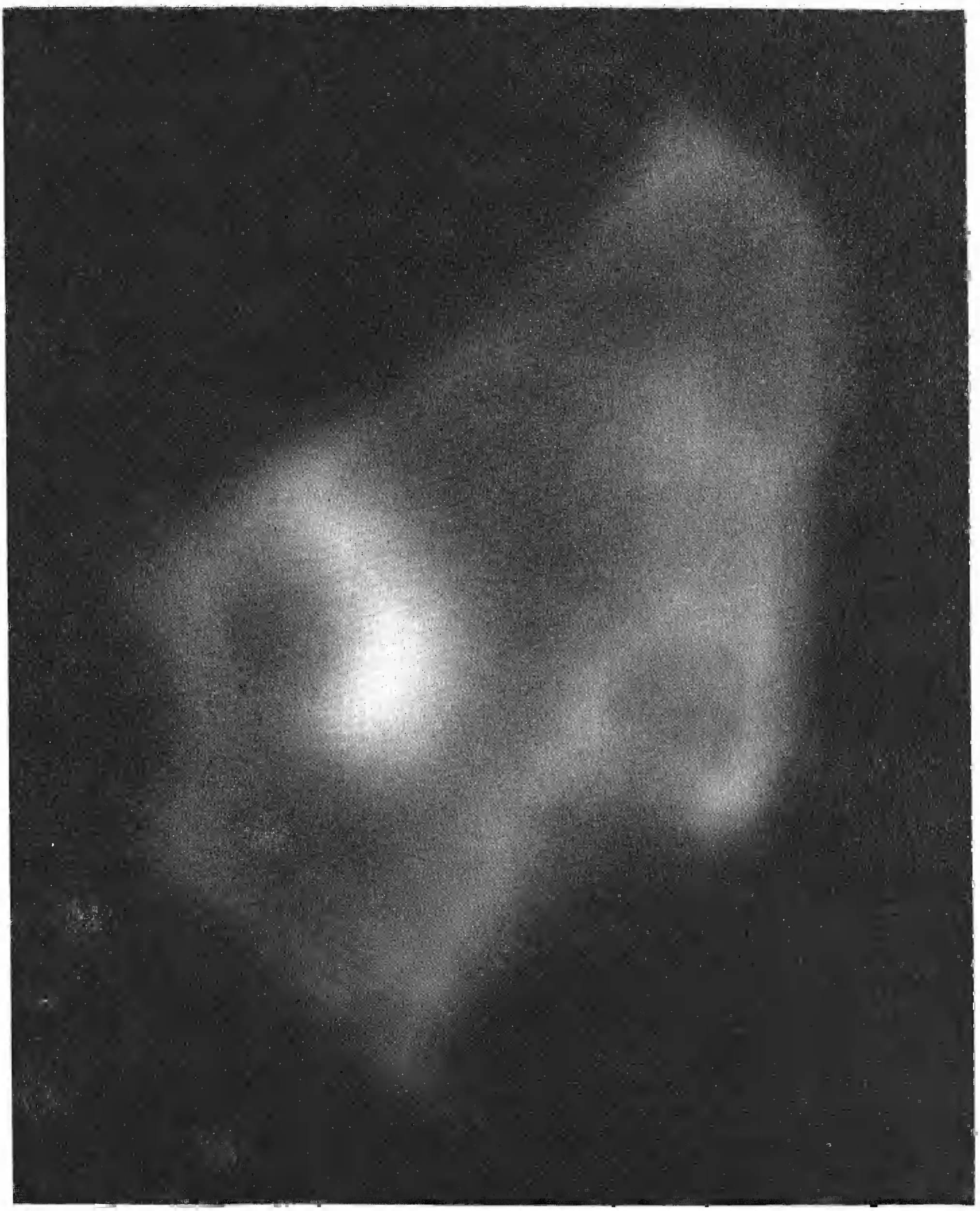

Figure 4. Proton n.m.r. zeugmatogram of a cherrystone clam (small *Venus mercenaria*) viewed edge-on. The animal was alive and enclosed within its shell. The bright regions in the photographically processed image represent regions of high projected water content. The computer output has been photographically filtered and enhanced.

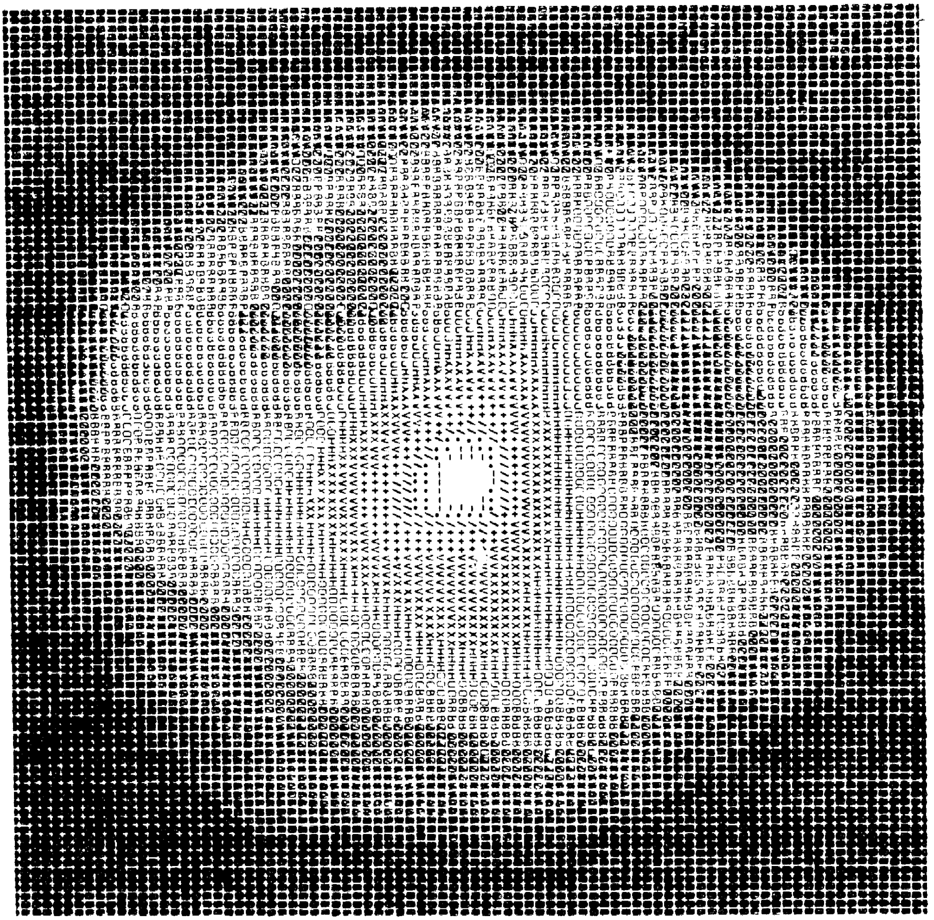

Figure 5. Proton n.m.r. zeugmatogram of the thoracic cavity of a live mouse. The plane of the receiver coil passed through the lungs at right angles to the long axis of the body, and the image is similar to that which would be obtained from a thick transverse section.

from the oils in the nut meat. The shell does not affect the image in any way. Similarly, the distribution of soft tissues and fluids within a clam about 30 mm across is shown in *Figure 4.* The animal was in its closed shell, surrounded by air. The plane between the shells lies parallel to the viewing direction. In *Figure 5* a partial proton n.m.r. zeugmatogram of a live mouse is shown. The receiver coil was centred on the thoracic region and was sensitive only to that part of the body. The lungs may be clearly seen, but no other detail is visible (the bright spot in the centre is an artefact). Twelve 15 s scans, recorded over a 20 min period, were used for the reconstruction, as for those in *Figures 2–4.*

CONCLUSIONS

Images of objects have hitherto been obtained by taking advantage of their intrinsic ability to interact with radiation, and the resolution in such images has been limited by the wavelength of the radiation used. Induced interactions between matter and radiation, such as magnetic resonance phenomena dependent upon the presence of an applied magnetic field, may be employed to generate a new kind of image. The portion of the object within which the interaction with a given frequency of radiation takes place may be controlled by using an inhomogeneous magnetic field, and resolution in images constructed from such data is independent of the wavelength of the radiation. The quality of the images depends, instead, upon a number of other factors, such as the linearity of the field gradients, the uniformity of the radiation field and the details of image reconstruction algorithms or other techniques for generating images from the data. Relatively crude low-resolution pictures have been generated by the use of one possible combination of experimental and computational techniques, and some examples have been shown in this paper. Higher resolution, and applications to both larger and smaller objects, seem likely to be readily attainable as instruments and techniques are refined.

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