JOURNAL OF MAGNETIC RESONANCE **127,** 225–228 (1997)
ARTICLE NO. MN971196

Fresh Spins for NMR Signal Enhancement through Programmed Sample Translation Cycles

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Received January 30, 1997; revised May 17, 1997

The perennial problem in nuclear magnetic resonance is sensitivity. This problem can sometimes be attacked directly through polarization and coherence transfer (*1*). However, the most common procedure for extracting signals from noise is signal averaging where the final signal-to-noise (S/N) ratio depends on both the magnitude of the detected signal and the number (n) of transient signals accumulated. Since the full recovery of magnetization requires three to five times the spin–lattice relaxation time T_1, the repetition rate in signal averaging experiments is severely limited and the spectrometer is idle most of the time. A variety of schemes have been devised to circumvent this limitation. A standard method, especially in MRI, is to reduce T_1 by adding a paramagnetic relaxation agent (*2*). Unfortunately, such additives contaminate the sample and may produce unacceptable line broadening by shortening spin–spin relaxation times, T_2.

Noninvasive spin manipulation methods have also been developed to reduce the cycle delay time in NMR experiments. A well-known example is the use of an optimized initial flip, i.e., the so-called Ernst angle (*3*); however, this method is usually not compatible with complicated pulse sequences. Also, the rate of recovery of magnetization can be increased by means of a driven equilibrium Fourier transform (DEFT) experiment where the last RF pulse partly restores the magnetization along the B_0 (z axis) direction (*4*). Still another method for avoiding the T_1 delay is based on the concept of ''fresh spins.'' When a continuously flowing sample is observed, the signal/noise per unit time is enhanced over that of a static sample in a given detection cell by reducing saturation effects (*5*).

In this Note we demonstrate a practical fresh spin method incorporating programmed translation of the sample in a custom-built probe. The sample is locked into position during excitation and data acquisition and is then quickly moved to a new position by a stepping motor. Sampling is interlaced so that every other layer in the z direction is sampled during the $+z$ translation part of the cycle and the alternate layers are sampled during the reverse part as illustrated on the left-hand side of Fig. 1. The translation step size or layer thickness is defined by the length of the region excited by the RF pulse, and the time for a complete translation cycle back to the initial layer is several times greater than T_1. If the time required for data acquisition and sample translation for each layer is much less than T_1, the spectrometer dead time is reduced and the repetition rate is increased. Obviously, the greatest enhancements are possible when the excitation volume is restricted in the z direction and the ratio of relaxation time T_1 to the total time for one acquisition step is large.

We demonstrate the ''cyclic sampling'' technique with a fringe field diffusion experiment (*6, 7*). In the fringe field, the large magnetic field gradient (several thousand G/cm) causes the resonance frequency to vary across the sample so that only a very thin slice of sample can be excited by RF pulses. For example, in the fringe field of a wide-bore Bruker MSL 360-MHz spectrometer where the gradient strength is about 5300 G/cm, a 1.4-μs 90° RF pulse excites a sample layer only about 0.3 mm thick. Obviously, the sensitivity of the regular fringe field experiment is very low because such a very small fraction of the sample is detected (*8*), and this is an ideal situation for the implementation of cyclic sampling to improve S/N ratios.

A probe designed for fringe field diffusion experiments with cyclic sampling is shown on the right-hand side of Fig. 1. A linear actuator, a stepping motor that provides precisely controlled translational motion (Eastern Air Devices, Dover, NH), is mounted under the probe body to move the sample after each data acquisition. A Kel-F rod is used to couple the movement of the stepping motor to an NMR sample tube sitting in the fringe field. The linear actuator is powered by a stepping motor drive module (Superior Electric, Bristol, CT), and the drive module is controlled by a personal computer through an RS-232C serial port as shown in Fig. 2. A Microsoft Windows-based program was developed to perform initial setup, simple movement control, and programming for special translation cycles. The sequence of movements (Fig. 1) and the distance of each translation step are

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1090-7807/97 $25.00

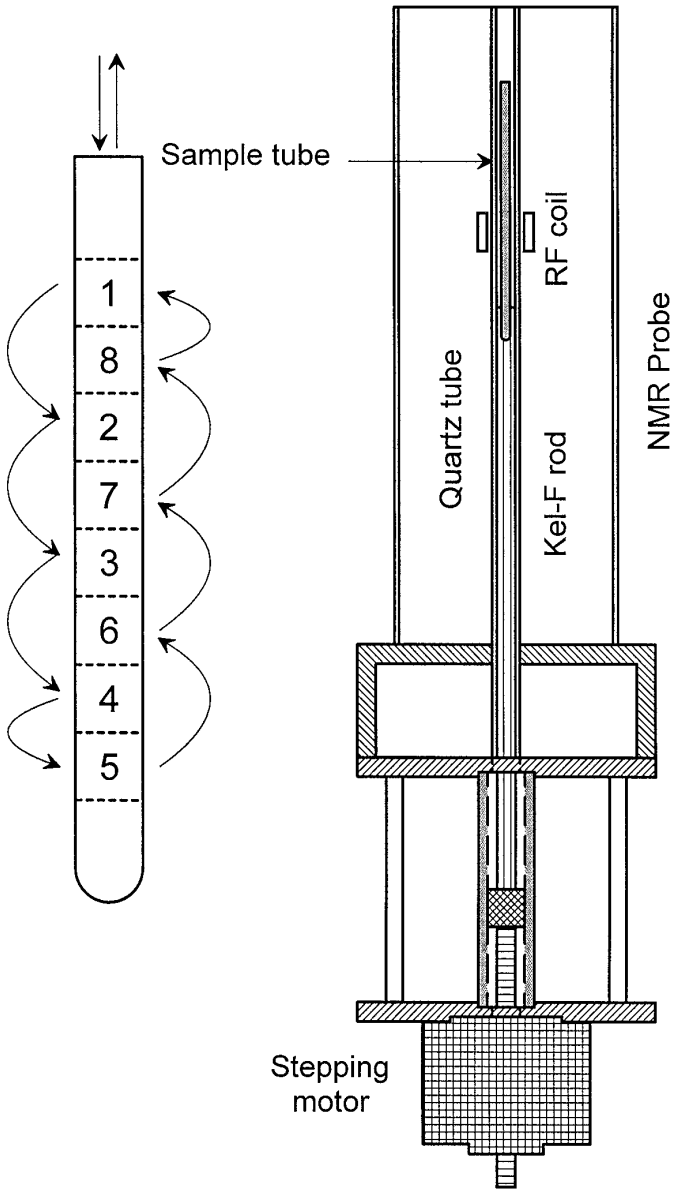

FIG. 1. The left side of the diagram shows the ''cyclic sampling'' scheme. The sample is moved for a distance of two layers in each step (except at each end of the sample) so that the entire sample is used for data acquisition during a full cycle of up and down translation. The right side of the diagram shows the fringe field NMR probe with a stepping motor mounted beneath it. A sample tube about 15 cm long sits on top of a Kel-F rod, which couples the translational motion of the stepping motor to the sample. The Kel-F rod and NMR sample tube travel inside a precision bore quartz tube, which reduces vibration in the horizontal direction and has very low friction in the direction of motion. The RF coil is mounted directly on the quartz tube, and its position is fixed.

programmed on the personal computer and then transferred to the on-board microprocessor of the drive module through the serial port. The drive module is synchronized with an NMR spectrometer through a homebuilt parallel interface board so that a TTL signal from the external control channel of the NMR spectrometer triggers one step of sample translation. Also, there are hardware ''reset'' and ''stop'' buttons on the interface board to stop the stepping motor in case of an emergency.

This arrangement permits us to move the NMR tube at a speed of about 100 mm/s (one step of 0.95 mm in 10 ms) with a position accuracy of better than 0.016 mm per step. The sample tube will become essentially steady within 50 ms after translation because of the ''lock mechanism'' of the stepping motor. However, an extra time interval, dependent on the viscosity of the solution, might be needed for the liquid inside the sample tube to become stationary. The ability to stabilize the entire sample in a short time is a very important feature for diffusion measurements in the fringe field since the experiments are extremely sensitive to movement in the sample.

A stimulated echo (STE) experiment (*9, 10*) was performed with the cyclic sampling technique on a sample of neat glycerol that has a very low diffusion coefficient at room temperature. Cyclic data sampling, 64 layers (32 in each direction) with a layer thickness of 0.47 mm, was used to acquire the NMR signal. The translation time for each step was set to 15 ms, and a settling time of 100–150 ms was added to ensure a quiescent sample for the STE experiment. The delay T between the second and third 90° RF pulses was 10 ms so that the entire process of data acquisition on a single layer was less than 200 ms; and a complete cycle of 64 layers required about 10 s, a time sufficient for the recovery of nuclear magnetization. Therefore, no additional recovery delays were necessary, and the repetition rate was 64 times higher than that in the conventional experiment for an S/N improvement of a factor of 8. In this demonstration, 16 STE experiments with gradient encoding times δ ranging

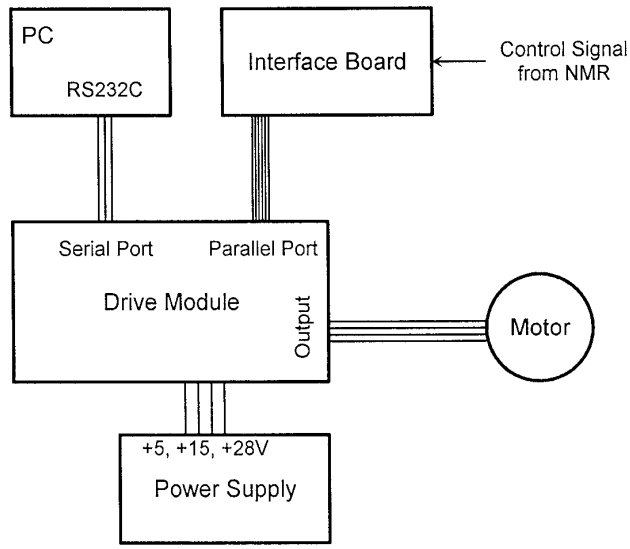

FIG. 2. Block diagram of the control system for the stepping motor (see text).

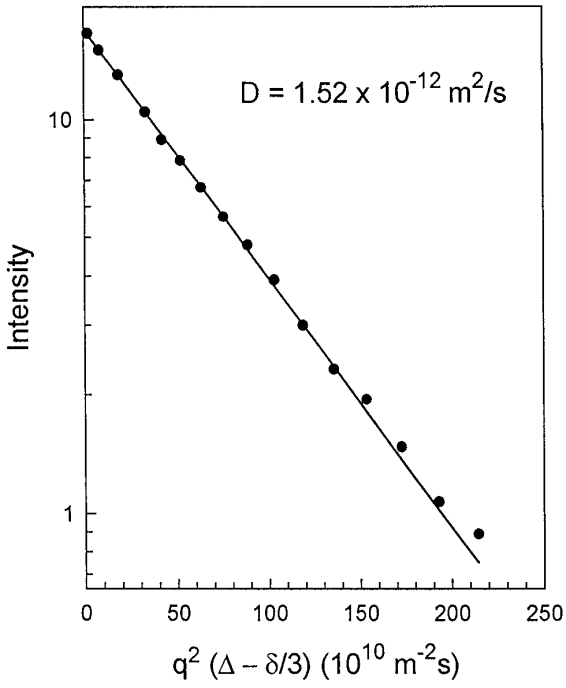

FIG. 3. STE fringe field diffusion data for glycerol recorded by cyclic sampling.

from 100 to 1000 μs were performed to obtain the signal intensities versus q^2 $(\Delta - \delta/3)$ shown in Fig. 3, where $q = \gamma g \delta$, γ is the gyromagnetic ratio, g is the gradient amplitude in the fringe field (g = 5300 G/cm), and Δ is the diffusion time ($\Delta = T + \delta$). The diffusion coefficient ($D = 1.52 \times 10^{-12}$ m^2 s^{-1}) determined by nonlinear regression is consistent with the value obtained in a conventional STE experiment with a ''steady'' sample in the fringe field. The total data acquisition time of 1 h (with cyclic data sampling and 2048 scans accumulated for each value of δ) provided a better S/N ratio than a 24-h experiment with the conventional data acquisition scheme.

This cyclic sampling scheme can also be implemented for signal enhancement in high-resolution NMR experiments as long as the length of the sample can be made several times longer than the windows of RF excitation and observation. In high-resolution experiments, the enhancement of the S/N ratio is not as dramatic as in the fringe field experiments, but cycling may still provide faster repetition rates and reduced experimental times in cases where the recycling delay for equilibration determines the total experimental time. This technique might also have an advantage for samples where low concentrations must be used, e.g., samples having low solubilities, since a sample volume much larger than the NMR coil can be observed in the acquisition cycle. Consider a sample having a volume N times as large as the volume excited by the RF field, i.e., the NMR volume. If all of the spins in the total volume could be brought into the NMR volume by increasing the concentration N-fold, the signal would be enhanced by a factor of N. If on the other hand, each of the N parts of the original sample were brought into the NMR volume separately and their signals accumulated, the S/N enhancement would only approach $N^{1/2}$. This is the maximum advantage that we can expect for samples N times larger than the RF coil.

The most important opportunities for saving time in NMR data acquisition are associated with multidimensional experiments on samples where the concentrations cannot be increased and the RF coil size is fixed. For such experiments we offer cautionary notes. The sample relocation might cause a disturbance to the NMR lock system that will introduce ''t_1 noise'' in multidimensional experiments even though no lock disturbance has been encountered in our 1D translation experiments. Sample relocation may also reduce the homogeneity of the main magnetic field in the NMR active volume because of nonuniformity of the sample in the axial direction and different susceptibilities at the ends of the sample tube. Susceptibility matching between the sample and the end plugs could be especially important in cyclic sampling experiments when the ends and not just the middle section of the sample tube are observed. These are, of course, technical problems and the potential savings may justify some engineering effort to correct them.

In summary, a ''cyclic sampling'' data acquisition strategy based on computer-controlled sample movement is demonstrated in this paper. This technique can accelerate data acquisition in NMR experiments by minimizing recycling delay times when NMR spectrometers are idle. In the extreme case of fringe field diffusion experiments reported here, the repetition rate can be increased 64 times, providing a S/N ratio enhancement of a factor of 8. This fast data acquisition scheme can also be implemented on conventional high-resolution NMR experiments, provided that the sample is several times longer than the RF coils. A modest accessory for existing spectrometers consisting of a modified probe with stepping motor assembly can potentially save valuable instrument time in routine 1D and multidimensional NMR experiments. This advance is timely since efforts are currently being made to obtain time savings of only 30% through accelerated relaxation of sensitive nuclei by means of polarization transfer (*11*).

ACKNOWLEDGMENT

This work was supported by the National Sciences Foundation under Grant CHE-9528530.

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