Numerical Design and Evaluation of Broadband Pulse Sequences for I=1 spin systems

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INTRODUCTION

Quadrupolar coupling constants of 170 kHz result from reduced motional averaging in biological polymers. The decay rates of Zeeman and quadrupolar order are direct measures of the spectral densities of motion. Information on the orientation-dependence of relaxation rates of Zeeman and quadrupolar order, T_{1z} and T_{1q}, respectively, assists in understanding the dynamics of molecules.[1] Sensitivity and dynamic range considerations mandate optimum efficiency and uniformity over large spectral widths. The design of composite pulses to create broadband excitation and inversion is well established for deuterium NMR.[2-11] The numerical optimization of existing composite inversion pulse sequences was performed in order to increase the uniformity of excitation over spectral widths of 250 kHz. [2-7]

Pulse sequences to create quadrupolar order over moderately broad spectral widths have recently been proposed.[12-14] The pulse sequence design of Wimperis is a good starting place from which to numerically optimize for the creation of quadrupolar order.[13] Broadband quadrupolar order is transferred to detectable magnetization with a 45 degree pulse and an additional refocusing pulse eliminates large phase corrections.[15] Numerical optimization of the conversion from quadrupolar order to well-behaved transverse magnetization is worthy of investigation.

A program developed in our laboratory for the numerical optimization of pulse sequences has been modified for I=1 spin systems.[15-18] This research is part of an ongoing investigation into the local and global dynamics of oligonucleotides utilizing solid state deuterium NMR. At the present time, the dynamics of the sugar rings of DNA are under study. The lower levels of hydration of DNA exhibit rigid-lattice lineshapes. Information on orientation dependence and the substantiation of motional models requires increased sensitivity and large spectral windows.

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METHODS

Solid state deuterium NMR spectra were obtained at 76.72 MHz on a home-built spectrometer controlled by a DEC microVAX II. Both the inversion sequences and the broadband Jeener-Broekaert experiments were phase cycled to eliminate double quantum coherence.[19,20] Phase shifting was accomplished with a homebuilt digital phase shifter. The sample, a labeled nucleoside, 2"-deutero-2'-deoxyguanosine, was prepared by Jerome Shiels at the University of Washington. Either 2K or 4K scans were taken with a recycle delay of 5.0 seconds. The field strength was 100 kHz and the dwell time was 200 nanoseconds. Each spectrum was acquired with 4096 points.

Calculations were accomplished on a DEC UNIX 3100 workstation. The strategy thus far has been to parameterize the pulse sequence and generate random trial pulse sequences. The basis set proposed by Vega and Luz was used. The coherences of interest were single basis elements rather than linear combinations of basis elements.[19] The expectation value of $-I_z$, Q_z, quadrupolar order, or I_y was compared with the target function over a specific spectral width. These quality factors quantify the performance of the pulse sequence as a function of the quadrupolar frequency. Excitation profiles of the expectation value as a function of reduced frequency illustrate overall smoothness and breadth. Evolution profiles of the elements of the density operator as a function of time demonstrate the effects of rf pulses and evolution under a strong quadrupolar Hamiltonian. Additional three-dimensional graphics developed in our laboratory assist in visualizing the transfer of coherences.[22]

RESULTS

Measurement of spin-lattice relaxation times and investigation of the orientation-dependence of T_1 in solids are important tools for understanding dynamics.[1] Inversion pulse lengths of more than 4 microseconds compromise the inversion breadth and uniformity across wide line deuterium powder patterns.[7] A variety of composite pulse schemes have been proposed for spectra with widths approaching the Rabi frequency of the radiofrequency pulse. The composite excitation triplet designed by Levitt, Suter and Ernst and supercycled in the method proposed by Levitt in order to create broadband inversion of deuterium lineshapes was numerically optimized.[3,6] The sequence consists of the composite excitation pulse, $45_0 90_{180} 135_0$, supercycled in the triplet form, $\Phi_0\ \Phi_{90}\ \Phi_0$. Only the flip angles of the excitation triplet were parametrized. The sequence has already been shown to invert rigid-lattice deuterium spectra with an rf field of 139 kHz while a weaker field led to a small loss in performance.[9]

Higher order pulses would lead to longer total pulse lengths. The total duration of the composite pulse should be short to avoid irreversible loss of magnetization during the excitation.[9] Experimental spectra acquired with the optimized composite excitation pulse of $43_0 100_{180} 142_0$, supercycled as above (B) and the Levitt triplet (A) are displayed in figure 1.

Recent application of Tycko's use of the Magnus expansion for the design of composite pulses has led to the development of new excitation schemes.[8,11]

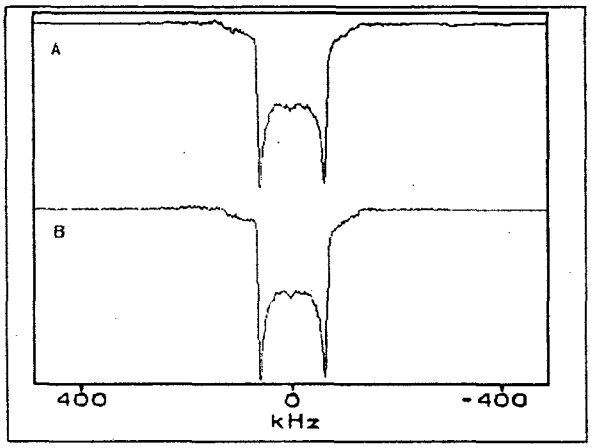
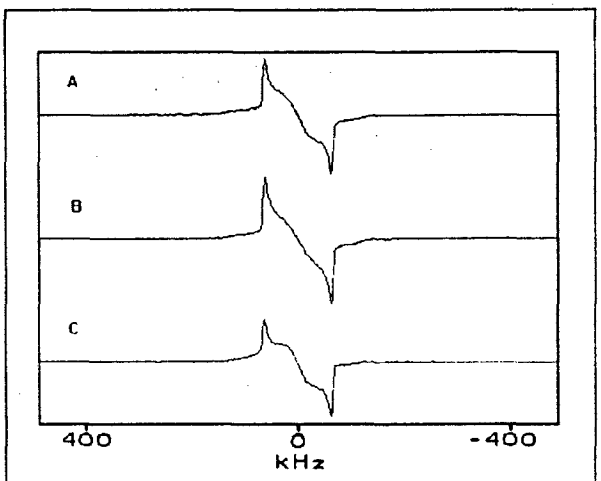


fig. 1

The modified Jeener-Broekaert pulse sequence was founded on the model of a composite excitation pulse broadband with respect to rf field strength.[13,14]

The multipulse sequence eliminated the frequency selection of the original Jeener-Broekaert experiment. The broadband sequence has been utilized to measure the spectral densities of liquid crystals.[21] Increased signal sensitivity becomes highly desired as one goes to broader linewidths, lower Larmor frequencies and smaller biological samples with dilute nuclei.

Computer search routines to create broadband quadrupolar order were performed with 10, 8 and 7 parameters. The 10 parameter search consisted of 4 pulses, 3 phases, and 3 seperate delays. The 8 parameter search had a single delay parameter. An assortment of the resulting sequences were tested experimentally. The "91" sequence was a 10 parameter search optimized over a spectral width of 300 kHz. It proved to perform well in breadth and sensitivity. Experimental spectra obtained with the Wimperis sequences A and B and the "91" pulse sequence, C, found in this study, are shown in figure 2.



A: 90_0 -4.0μ -67.5_{270} -4.0μ -45_{90} -2.0μ -45_{90}

B: 90_0 -4.0μ -75_{270}- 4.0μ -52.5_{90} -2.0μ -45_{90}

C: 113_0 -5.5μ -72_{284} -3.2μ -52_{142} -3.9μ -59_{112}

fig. 2

CONCLUSION

The use of solid state deuterium NMR as a probe of dynamics in DNA offers the luxury of selective labeling. The same luxury introduces some of the limitations of site-selective wide line spectroscopy. The technique enables one to focus on the dynamics of single positions within large molecules. The small, precious samples are dilute in the observe nuclei yet one can monitor the onset of motion in both a local and global fashion as water is added to the spaces in DNA. The technique requires high power, short pulses for broad lineshapes, resistant samples, and extensive phase cycling and signal averaging. The dry DNA has longitudinal relaxation times of several seconds making signal intensity even more elusive. For these reasons, this investigation aims to numerically optimize existing pulse sequences for the creation of selected coherences over static deuterium powder linewidths of 250 kHz. Analysis of the

evolution of the system provides clues for producing the very best tailored excitation.

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