COMPUTER GRAPHICS FOR PULSE SEQUENCE ANALYSIS

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Introduction

The development of software for the simulation of NMR experiments has increased at an enormous pace in the last decade. Its usefulness has spread far beyond the analysis of lineshapes and spectra. Today, search-and-optimize strategies are used to develop new pulse sequences while other programs measure the performance of pulse sequences on spin systems of interest [1, 2]. Up to now, most of the output from these programs has been displayed as two-dimensional hard-copy output. With the arrival of relatively inexpensive graphics workstations, the possibility of visualizing the time development of the density operator has spurred us to develop graphics software in conjunction with our ongoing development of simulation software.

Current projects which benefit from graphical analysis include the development of "time-suspension" sequences for use with solids imaging, development of improved sequences for the creation of Zeeman or quadrupolar order in deuterium NMR, and analysis of artefacts seen in imaging experiments in the presence of flow.

Time Suspension

"Time suspension" sequences are multi-pulse sequences which remove the effects of both the dipolar coupling and the chemical shift Hamiltonians [3-5]. They are useful in pulsed-gradient imaging experiments where imaging gradients are applied only during the multi-pulse windows [6-8].

Currently implemented pulse sequences apply average Hamiltonian theory and use carefully cycled "wahuha" subcycles to achieve the suppression of internal Hamiltonians [3]. Like other multi-pulse experiments these sequences perform best at or near resonance and show decreased line-narrowing as one moves off resonance. A new "time-suspension" sequence developed with computer search-and-optimization techniques (CDIS-4) [9] achieves comparable reduction of the internal Hamiltonians but shows complementary behavior: poor line narrowing on resonance but improved performance off resonance. In an effort to understand this behavior we calculate the evolution of the density operator for a two-spin system under the influence of effective Hamiltonians defined by the multi-pulse

propagators associated with each sequence.

With perfect wahuha type sequences the trajectory of the net magnetization should be around the base of a cone whose axis is along the cube diagonal in spin space (ie. in the nodal plane of the coupling ternsor). When chemical shift offsets are small (<2Khz) this is seen to be the case (Fig. 1A). For the CDIS-4 sequence, however, rotation about an axis is modulated producing a star pattern. (Fig. 1B). As the offset is increased to

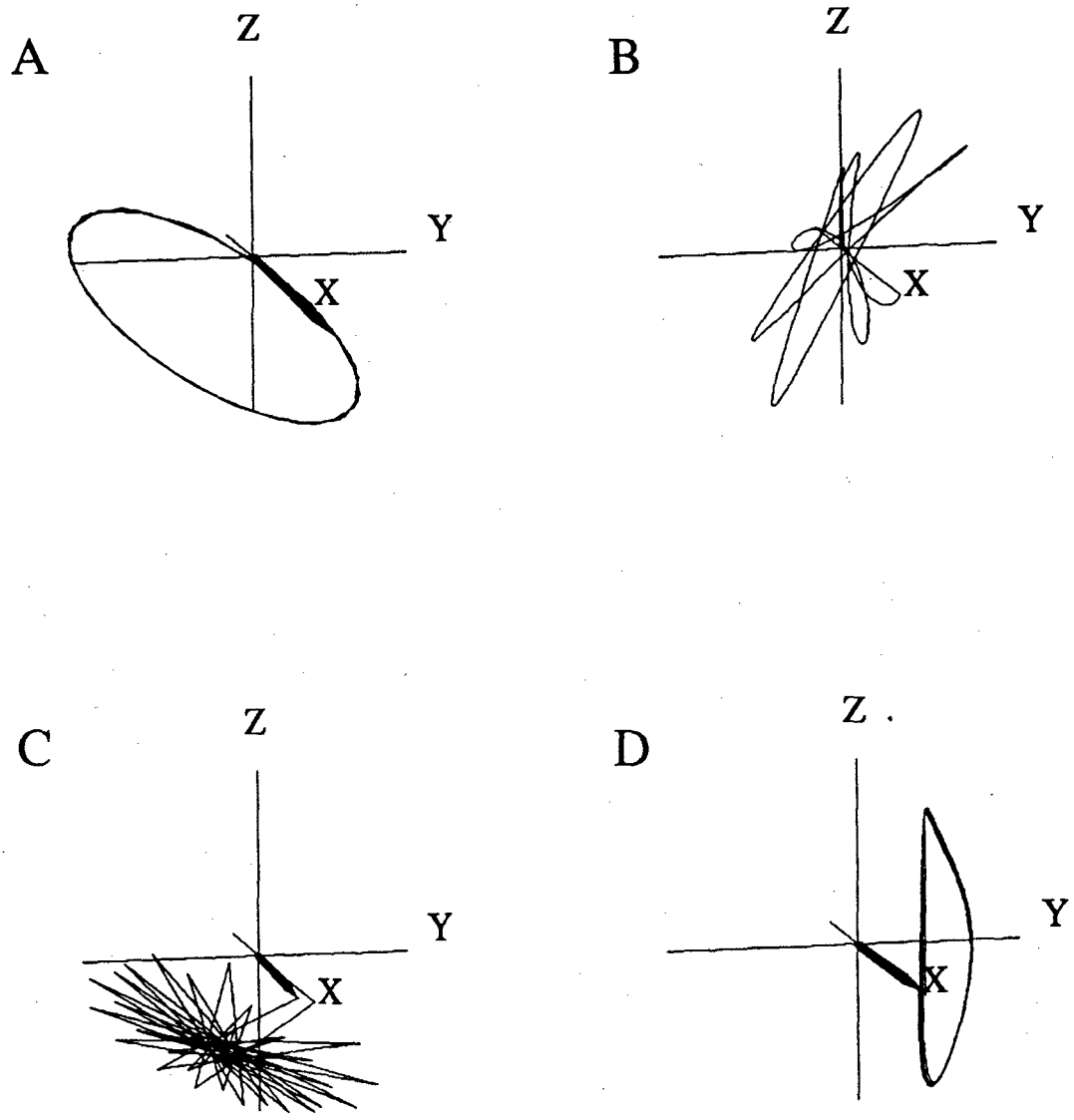

Figure 1) Net magnetization trajectories for the following experiments: A) conventional "time-suspension sequence" for a two spin system with cs1 = cs2 = 1483 Hz and dipole coupling = 2KHz; B) CDIS-4 applied to the same system; C) conventional sequence applied to cs1 = cs2 = 11483 Hz with 2KHz coupling; D) CDIS-4 applied to this large offset system.

greater than 10KHz the conventional sequence shows modulated rotation (Fig. 1C) whereas the new sequence traces out a somewhat bent circle lying in the nodal plane of the chemical shift tensor (Fig.1D). From such pictures we hope to gain a better understanding of the effect of error terms which are not easily amenable to analytical treatment.

Deuterium

The deuterium quadrupole is an excellent probe of dynamics and as such is synthetically incorporated into DNA and other biologically important molecules [10]. The same quadrupole which allows one to use deuterium as a probe also presents formidable experimental difficulties when the strength of the quadrupole approaches the strength of the rf field. This situation is realized in some of our labeled oligonucleotides. In this regime, the effective axis about which the magnetization is rotated (the sum of rf and quadrupolar terms) is substantially different from the rf axis.

Current pulse sequences which convert I_z magnetization into $-I_z$ or into quadrupolar order are found to be inefficient at higher values of the quadrupole coupling. For an inversion pulse this means incomplete inversion at the shoulders of the powder pattern. This is unacceptable in experiments where one attempts to measure the orientation dependence of spin-lattice relaxation time. Such measurements are necessary to prove or disprove particular dynamical models.

An example of non-uniform excitation is given in Fig. 2) which shows the development of spin coherences during a 180 degree pulse at five different values of the quadrupole coupling (0KHz, +/- 62.5 KHz and +/- 125KHz). The operator basis of Vega and Luz [11] is used because of the simple form of the quadrupolar operator in that basis:

I_x	I_y	I_z
$J_x=I_yI_z+I_zI_y$	$J_y=I_zI_x+I_xI_z$	$J_z=I_xI_y+I_yI_x$
$K_x=I_y^2-I_z^2$	$K_y=I_z^2-I_x^2$	$K_z=I_x^2-I_y^2$
$Q_x=I_x^2-I^2$	$Q_y=I_y^2-I^2$	$Q_z=I_z^2-I^2$

Rotation about I_x during the pulse is modified by ω_q dependent rotation about the Q_z axis. This causes a buildup of "antiphase" J_y and zero-quantum J_z. By the end of the pulse it is clear that a simple π pulse is ineffective at creating $-I_z$ over the entire range of couplings (+/-125 KHz).

We are again using search and optimize strategies to find pulse sequences which create $-I_z$ or Q_z evenly over a broad range of quadrupole couplings [12]. With its small operator basis, deuterium NMR provides us with an excellent system on which to develop interactive computer aided pulse sequence design. With user control of pulse amplitude and phase, rapid calculation of the time evolution of the spin 1 density operator and a graphical view of Hilbert space we will soon have the opportunity to design pulse sequences and shaped pulses intelligently rather than relinquishing our insight to the cpu.

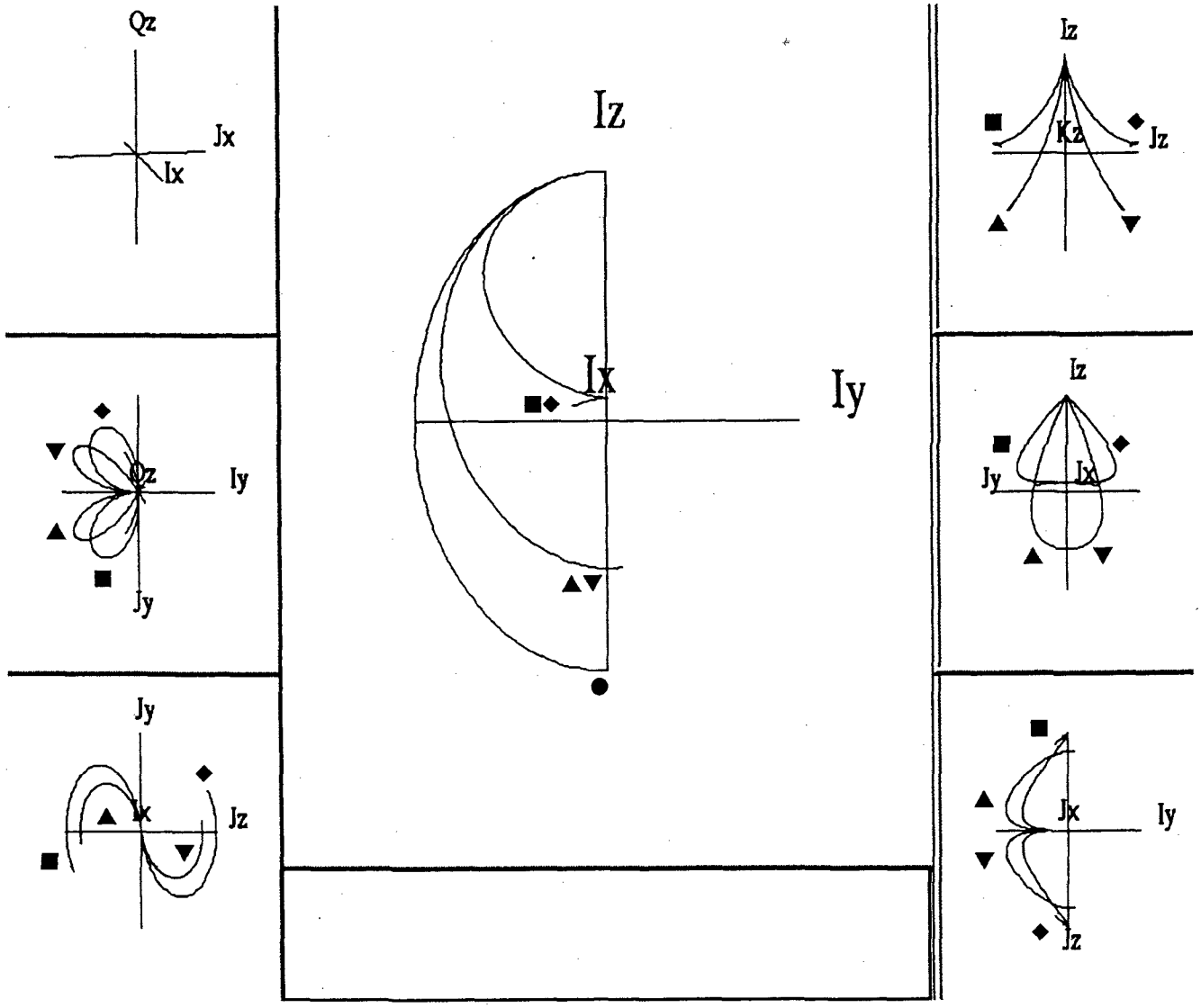

Figure 2) Evolution of spin coherences for deuterium with 0(●), +/- 62.5(▲▼) and +/- 125(■◆ KHz quadrupole coupling. The evolution is depicted in the operator basis of Vega and Luz Rotation about I_x due to the rf pulse is seen but rotation about quadrupole operator Qz is als evident. For +/- 125 KHz coupling the simple π pulse is very inefficient at creating -Iz.

Flow Imaging

Another simulation program which benefits from graphical display calculates the response of flowing spins in an NMR imaging experiment. Our interest in this area focuses on the artefacts that arise when spins move from a region with one gradient strength to a region with anothe during an imaging experiment. Ou simulation incorporates the effects c flow and of arbitrarily comple imaging sequences on an array c spins 1/2. When following an particular spin through time we kee track of its three-dimensional positio and its magnetization vector. Thus w

have for each spin seven parameters (3 space, 3 spin and time) which describe its state.

In order to understand how artefacts develop during the experiment we display the system as an array of vectors whose position corresponds to spatial position and whose orientation corresponds to magnetization state. From the z-axis we observe spatial flow of spins in the spatial x-y plane and also the magnitude and phase of transverse magnetization in the superposed spin x-y plane.

In Fig. 3) we see how the slice-select portion of an imaging experiment can be perturbed by flow in the direction of the slice-select gradient. As the rate of flow increases, the width of the slice remains fairly constant but the phase order of the spins in that slice deteriorates. Such phase disorder will lead to artefacts along the phase-encode dimension at the edges of the slice. As it now exists our simulation will allow us to evaluate imaging sequences on flow geometries

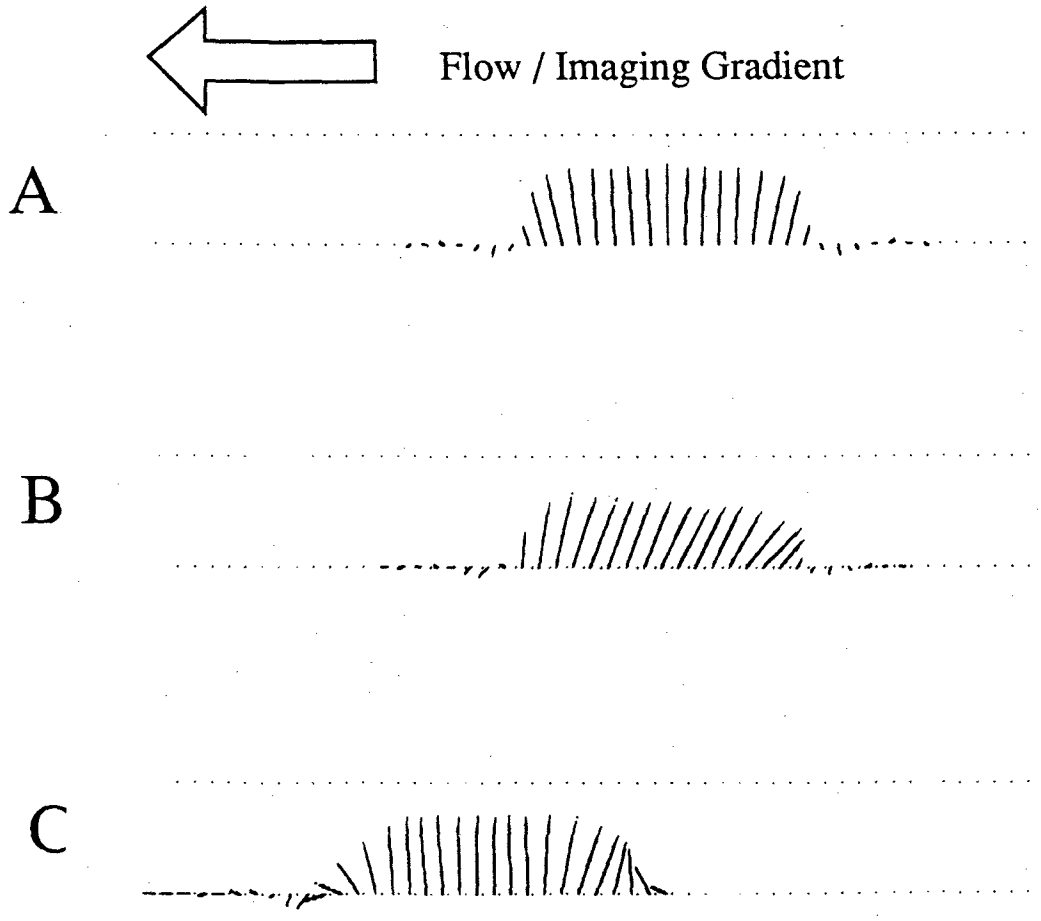

Figure 3) Excitation profiles for the slice-select portion of an imaging experiment. In this simulation the direction of flow is along the slice-select gradient causing spins to change their frequency during the sinc excitation pulse. The flow velocities are in arbitrary units but three regimes are displayed: A) static spins; B) slow flow; C) moderate flow.

of interest. A better understanding of the formation of such errors will aid us in the development of improved imaging sequences.

Conclusion

We have extended the computer techniques available to the NMR spectroscopist by presenting simulated data in multi-dimensional animations. With these animations it is much easier to see the development of spin coherences which are the result of experimental imperfection or which are intended by design. Our original goal with computer graphics was to enhance our own understanding of the experiments we perform and to aid us in experimental development In the process we have found animated simulations to be a generally useful pedagogical tool for explaining all types of NMR experiments. With computer designed pulse sequences containing unusual phases and non-analytical shapes becoming more and more common we hope to bring some of the intuition back to experimental design.

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