



## Historical Perspective

## “Development of REDOR rotational-echo double-resonance NMR” by Terry Gullion and Jacob Schaefer [J. Magn. Reson. 81 (1989) 196–200]

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## ABSTRACT

The popularity of rotational-echo double-resonance (REDOR) NMR arises from its ability to measure weak dipolar couplings and long-range heteronuclear distances accurately. This ability was not anticipated in the first REDOR experiments and resulted from the effectiveness of a simple radiofrequency phase alternation scheme to suppress amplitude and phase distortions in echo trains even after hundreds of pi pulses.

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## Interview with the author(s).

A video interview with the author(s) associated with this Historical Perspective and the original article can be found in the online version, at [doi:10.1016/j.jmr.2011.08.012](https://doi.org/10.1016/j.jmr.2011.08.012).

This perspective is all about weak heteronuclear dipolar couplings.

The rotational-echo double resonance (REDOR) story starts in 1984 when I had a solids NMR laboratory in the Physical Sciences Center of Monsanto Company in St. Louis. Ed Stejskal, Bob McKay, and I had developed  $^1\text{H} \rightarrow ^{13}\text{C} \rightarrow ^{15}\text{N}$  double-cross polarization (DCP) for the direct measurement of  $^{13}\text{C}$ – $^{15}\text{N}$  dipolar coupling in solids [1]. At that time, we were actively engaged in using this method to determine the fate of  $^{13}\text{C}$ ,  $^{15}\text{N}$ -double-labeled glyphosate in a soil bacterium which was thought to degrade the herbicide [2]. The degradation mechanism was unknown. Our idea was to move the labels around (with the help of Merck's Stable Isotope Division) and detect the metabolites directly in lyophilized whole cells, avoiding ambiguities from extractions and purifications.

DCP required the use of three radiofrequency spin-locking fields with the  $^{13}\text{C}$  and  $^{15}\text{N}$  rf amplitudes maintained to less than 1% deviations over long acquisition times [3]. Tom Dixon was a postdoctoral fellow of Robert Yaris at Washington University and was working in my laboratory at Monsanto at the time. Yaris and I were collaborators on various glassy polymer projects. Tom had just recently invented the total control of chemical-shift spinning sidebands using strategically placed pi pulses that altered the phases of sidebands according to their order, the so-called phase-altered spinning-sideband or PASS method [4]. He said that I should replace the DCP spin-lock fields with pi pulses. I didn't want to interrupt the progress of

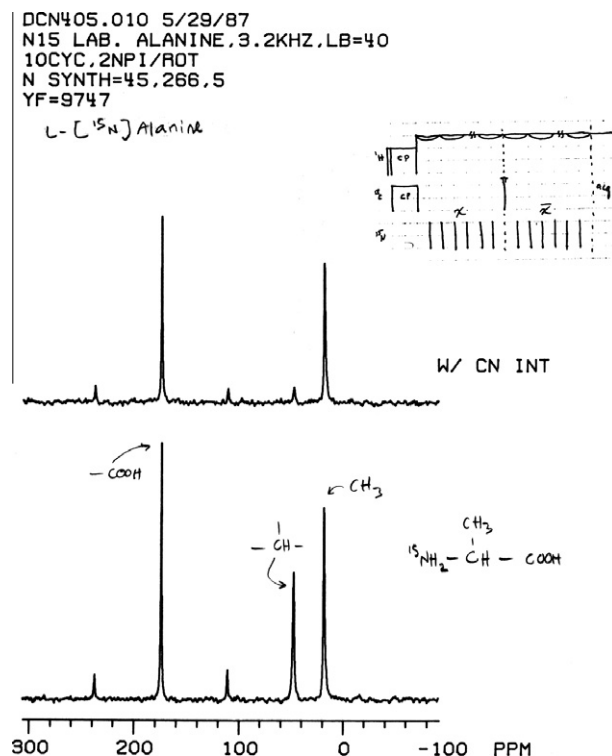
our glyphosate experiments and did not follow his suggestion. Dixon tried a few preliminary experiments (the results of which I still have) but never reduced his idea to practice before he moved to take a permanent position in the Radiology Department of the Washington University School of Medicine in 1984.

I moved from Monsanto to the Washington University Department of Chemistry late in 1986. My first two postdoctoral fellows were Vince Bork, a student of Richard Norberg in the WU Physics Department, and Terry Gullion who had just gotten his PhD with Mark Conradi at the College of William & Mary, Department of Physics. The equipment that I was moving from Monsanto to WU included a 200-MHz wide-bore magnet, a 12-in. 1.4-Tesla iron magnet, and a 2.4-Tesla horizontal-bore magnet which we were using for dynamic nuclear polarization experiments with microwaves at 40 GHz. Naturally, the renovation of the WU laboratory to house this equipment was behind schedule so I rented space at Monsanto and kept the 200-MHz system operational. Vince and Terry got Monsanto building passes and did their experiments there for more than a year. I was a commuter covering the 5-mile separation between WU and Monsanto several times a day.

Both Vince and Terry were working on improvements of DCP for measuring  $^{13}\text{C}$ – $^{15}\text{N}$  dipolar coupling. Vince eliminated the carbon spin-lock field and used a single carbon pi pulse to refocus chemical shifts during a variable dipolar evolution time [5]. This meant the difficult carbon–nitrogen Hartmann–Hahn match [6] (offset by a spinning speed) was eliminated, an important improvement. However, Terry was making even more impressive progress. He eliminated both spin-lock fields and tried various positions for car-

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**Fig. 1.** 50.3-MHz  $^{13}\text{C}\{^{15}\text{N}\}$  REDOR spectra of L- $^{15}\text{N}$ ]alanine obtained at Monsanto Company by Terry Gullion in 1987. Carbons are at natural abundance. The full echo is at the bottom of the figure and the dephased echo at the top. Dipolar evolution was for 10 rotor periods with magic-angle spinning at 3.2 kHz. The sample weight and number of accumulated scans were not recorded. ("YF" is a plotting parameter.) The  $^{15}\text{N}$  radiofrequency carrier was on resonance for alanine with a 25-MHz intermediate radiofrequency. The pulse sequence that was used is shown in the inset in Gullion's handwriting. The structure and line assignments are in my handwriting.

bon and nitrogen pi pulses to get the most dramatic reductions of full-size rotational echoes. REDOR was born.

One of the first experiments was performed on  $^{15}\text{N}$ -labeled alanine on May 29, 1987 (Fig. 1). Terry did a calculation for an isolated

$^{13}\text{C}$ – $^{15}\text{N}$  spin pair and then performed a full isotropic powder average to establish the optimum placement of the pulses. I presented the results at the ENC held in Rochester, NY in April, 1988.

There was never any question about the acronym. The connection between REDOR and Charlie Slichter's popular version [7] of Hahn's spin-echo double-resonance (SEDOR) experiment [8] was obvious. In independent work with Mark Conradi, Terry Gullion developed a new phase-alternation scheme (xy8) to enhance Carr-Purcell echo-train refocusing [9]. When we applied xy8 to the REDOR pi pulses [10], virtually all the off-resonance amplitude and phase distortions in the REDOR spectra cancelled even after hundreds of pulses [11]. In 1990, Shimon Vega visited Washington University for a sabbatical and developed a graphical analysis to explain why xy8 phase routing worked so well. Much later, Niels Nielsen told me that testing the xy8 scheme was one of his first applications of SIMPSON. With xy8, weak dipolar couplings and long-range heteronuclear distances could be measured accurately. This observation was definitely a surprise for me, and was reminiscent of the surprise that Ed Stejskal and I had in observing strong cross-polarization magic-angle spinning signals more than 10 years earlier from non-protonated carbons [12], despite spinning speeds exceeding the weak  $^1\text{H}$ – $^{13}\text{C}$  dipolar couplings for those carbons [13]. Those weak heteronuclear dipolar couplings just never seem to go away.

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