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Historical Perspective

The 'DANTE' experiment

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ABSTRACT

The selective excitation scheme known as 'DANTE' emerged from a confluence of several ideas for new NMR experiments, some more fanciful than others. DANTE offers a simple and effective way to restrict excitation to a very narrow frequency band, usually that of a single resonance line. Initially applied to the study of individual proton-coupled carbon-13 spin multiplets, the method has been extended to water presaturation, relaxation measurements, and chemical exchange studies. Through the imposition of a magnetic field gradient it offers a simple method to enhance resolution by restricting the effective volume of the sample. Multiple DANTE excitation (with Hadamard encoding) can speed up multidimensional spectroscopy by orders of magnitude. Applied to magnetic resonance imaging, the DANTE sequence has been used to superimpose a rectangular grid onto a cardiac image, permitting motional distortions to be monitored in real time.

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.2011.08.020.

One might fondly imagine that any *really* new NMR technique should emerge from that fabled 'eureka' moment – a sudden inspiration at bath-time; indeed this is often how these experiments are written up for publication. In practice there may be a long and complex history behind the evolution of the idea, and this was in fact the case with the DANTE selective excitation experiment. The story can be traced back as far as 1968. At that time there was already interest in *selective* excitation experiments using 'soft' pulses where the radiofrequency intensity $\gamma B_1/2\pi$ was reduced to the same order as the line width, and the pulse duration increased accordingly. Attention is focused on the behavior of a single chemical site, and its spin-lattice or spin–spin relaxation times are recorded. One practical implementation of this idea involves the creation of an excitation field in the form of a weak modulation sideband of the intense transmitter radiofrequency field. In this manner quite simple audiofrequency equipment makes it easy to implement a soft pulse, calibrate its duration, change the phase, and indeed observe the NMR response during the pulse [1,2]. Later, the general introduction of pulsed Fourier transform techniques made it possible to measure several relaxation times in a single experiment, and consequently the sideband method fell into disuse.

The revolutionary paper of Ernst and Anderson [3] comprehensively covers all the key aspects of pulsed Fourier transform NMR, even including a detailed analysis of the steady-state effects on longitudinal magnetization. An optimum flip angle (the 'Ernst angle') is defined to cover the situation where the interpulse interval is shorter than the spin-lattice relaxation time T_1. Steady-state effects on *transverse* magnetization are also considered, but in their understandable desire to demonstrate this new technique, Ernst and Anderson decided not to follow up the troubling practical consequences. Because considerations of sensitivity dictate that the pulses be reapplied as soon as the signal has decayed through instrumental effects (T_2^*) there are significant steady-state effects when the spin–spin relaxation time T_2 is longer than T_2^*.

A later detailed analysis [4] of these steady-state effects focuses on the fact that each chemical site undergoes a different degree of free precession between pulses. When the inter-pulse interval is short compared with T_2, the resulting spectrum is marred by intensity (and phase) anomalies. Here we focus specifically on pulses of small flip angle. In this case the steady-state signal is strong for free-precession angles near $2n\pi$ (where n is zero or an integer) and very weak elsewhere. Indeed for spins that precess through $(2n+1)\pi$ there is no net excitation. A sequence of weak radiofre-

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quency pulses has a cumulative effect only when close to the transmitter frequency F_0, or close to sidebands at $F_0 \pm nF_R$, where F_R is the pulse repetition rate. At all other irradiation frequencies free precession disperses the transverse components of magnetization and the pulses have little cumulative effect. Here lies the germ of the idea for the 'DANTE' sequence. Excitation is highly frequency-selective in the steady-state regime when small flip angle pulses are employed. If this sequence is truncated after (say) tens or hundreds of milliseconds, it becomes a *transient* excitation scheme with a frequency-domain selectivity defined by the inverse of the pulse sequence duration, making it suitable for picking out a single resonance line in a high-resolution spectrum.

Gareth Morris was studying the Tomlinson–Hill paper [5] where a 'tailored' frequency-domain excitation pattern is created by time-domain radiofrequency modulation computed as the Fourier transform. This was one trigger for the first DANTE experiment, the realization that a simple monochromatic excitation could be very useful [6]. But there were related ideas 'in the air'. There was a different project – the suggestion that a sequence of transient nutations (during which the signals decay by a combination of T_1 and T_2 mechanisms) could be used to identify resonances with abnormally short T_2 values. Excitation was preceded by a train of 360° pulses, separated by short delays, aimed at preferential attenuation of lines with a short T_2. In orthodichlorobenzene we expected the ^{13}C-Cl resonances to be most affected but to our dismay, separate experimental trials at Oxford and Palo Alto gave completely conflicting results. It turned out that poor calibration of the 360° condition had converted the small excess nutations into a long train of small flip angle pulses, saturating any line that happened to fall on resonance. Fortunately, the machine code program for the ill-fated transient nutation experiment required only a trivial change to adapt it for DANTE.

Gareth set out to cover the theoretical background of selective excitation in a comprehensive manner, and to suggest several possible applications [7]. As usual, significant effort was expended on finding an appropriate acronym for the new scheme. Gareth noticed that the trajectory of a magnetization vector at the first sideband condition closely resembled the path prescribed by Dante Alighieri for souls in *'Purgatorio'* (barring a trivial time reversal). The unfortunate protagonists are required to negotiate seven circular ledges running around a mountain, circumnavigating each ledge before moving up to the next. Each ledge represents one of the cardinal sins, and the main idea appears to be to graduate towards the more attractive misdemeanors (gluttony, lust) at the top of the mountain. This analogy suggested the acronym '*D*elays *A*lternating with *N*utations for *T*ailored *E*xcitation' and the appellation has stuck. Although some frequency-selective experiments could already be performed at that time using a second radiofrequency transmitter, DANTE has two key advantages: it is easy to fine-tune the sideband condition, and the excitation is phase-coherent with the hard pulses, making the method applicable to selective excitation as well as for inversion or saturation.

The vector model, representing the transient solutions of the Bloch equations, gives a clear pictorial representation of the DANTE experiment. Magnetization vectors 'on resonance' with the transmitter frequency or with one of the sidebands ($\theta = 0$), undergo small successive nutations about the X axis of the rotating frame, reaching a cumulative flip angle (usually set to 90°) and generating a final response M_Y corresponding to pure absorption-mode. Vectors at different offsets precess through a small excess angle θ in each interval between pulses, thus following a zig-zag trajectory that carries them out of the YZ plane, approximating the motion caused by a single off-resonance soft pulse. The overall result is a frequency-domain excitation pattern made up of a regular array of sinc functions, one centered at each sideband condition. To the extent that the excitation is linear, the frequency-domain pattern is the convolution of an infinite train of delta functions with a sinc function representing the Fourier transform of the time-domain pulse envelope. This suggests that the DANTE sequence could be 'cured' of sinc function wiggles simply by shaping the envelope, and this has been demonstrated experimentally for a Gaussian shaping function [8]. A purely rectangular pulse envelope is non-ideal for another reason. A closer approximation to the ideal soft pulse is achieved by halving the amplitudes of the first and last pulses of the DANTE sequence [9].

There were several immediate applications of the DANTE sequence:

(1) Excitation of individual proton-coupled ^{13}C multiplets [6,7].
(2) Presaturation of an unwanted resonance, usually water [7].
(3) Spin–spin and spin–lattice relaxation measurements, one line at a time [7].
(4) Chemical exchange studied by magnetization transfer [10].
(5) 'Burning a hole' in an inhomogeneously broadened line [7].
(6) Enhancing resolution by reducing the *effective* sample length by excitation in an applied field gradient [11].

Selective excitation at two *arbitrary* frequencies is achieved by interleaving two DANTE sequences of different pulse repetition rates, terminating at the same instant, with allowance for near-coincidences between pulses [7,12]. Later improvements in spectrometer hardware have made it possible to extend this idea to multiply-selective irradiation to implement band-selective excitation schemes [13], and even to excite an entire high-resolution spectrum with 2048 *individual* radiofrequencies spaced 1 Hz apart across a 2 kHz band [14]. An extension of this idea speeds up two-dimensional NMR spectroscopy by a large factor by direct selective excitation of chemical sites (using Hadamard encoding), thereby avoiding the usual comprehensive stepwise exploration of all evolution space [15].

The interval between successive individual pulses in a DANTE sequence can be exploited to monitor the instantaneous NMR signal, offering a window on the motion of the nuclear spins. For example, the complex evolution of magnetization vectors during band-selective excitation by the 'E-BURP' sequence [13] has been mapped out in detail by recording the real and imaginary NMR responses between pulses [16]. A related principle can be used to suppress the severe broadening of the water line by radiation damping in aqueous solutions. The radiation damping field (along the X axis) exerts a torque proportional to the strong time-dependent signal M_Y, and causes a very fast decay of the water response. This effect can be countered by compensating rotations generated by an opposed DANTE sequence with flip angles that decrease at a rate that just matches the decay of M_Y [17]. Thus a 13.5 Hz broadening of the water line was reduced to 0.8 Hz.

Just as new experiments can have roots that are far from obvious, so too they may have unanticipated applications, and DANTE has proved surprisingly versatile in other fields. Magnetic resonance imaging has extensively exploited selective excitation in applied field gradients. One popular scheme uses DANTE excitations during field gradient pulses applied along two orthogonal directions to impose a two-dimensional grid on a cardiac image in order to monitor the motions and distortions caused by breathing [18]. DANTE has even been used to assess the success of heart transplants [19]. Perhaps we have not yet heard the last of DANTE?

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