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Bax A & Freeman R. Investigation of complex networks of spin-spin coupling by two-dimensional NMR. *J. Magn. Resonance* 44:542-61, 1981.
[Physical Chemistry Laboratory, Oxford University, England]

This article describes a series of refinements of a two-dimensional NMR experiment first proposed by J. Jeener and now known as "COSY" (correlation spectroscopy). It was used to map out the complex network of spin-spin couplings linking the 11 protons of a tricyclodecanone derivative. [The *SCI*® indicates that this paper has been cited in over 1,000 publications.]

COSY Success with 2-D NMR

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It all started with an embarrassing situation. The Delft University of Technology in The Netherlands had asked me to read a PhD thesis. I was so impressed by the work that I wrote to the author to ask whether he might be interested in working in my research group in Oxford. What I had not realized was that he already had a senior research position, having written a doctoral thesis much later than usual. He took my *faux pas* rather well and suggested that one of his young research students, Ad Bax, should visit my laboratory instead.

So Ad came to Oxford quite regularly, taking the ferryboat from the Hook of Holland to Harwich and turning my laboratory upside down with his boundless energy and enthusiasm, with a little time off for cycle racing competitions and rowing. He had "green fingers" for making new experiments work and, as a physicist, understood the theory behind the new tricks that we played on the nuclear spins. In those days everyone was inventing complicated new variations on the idea of two-dimensional NMR spectroscopy, first suggested by J. Jeener 10 years earlier.[1] Ad realized that the original, very simple experiment performed by Jeener had been virtually overlooked in the scramble for more "sophisticated" techniques such as multiple-quantum spectroscopy. He felt that this deceptively simple method (now always known as "COSY") might prove to be the most useful of all, but it had not yet been adopted by NMR spectroscopists. This may have been because the mechanism of coherence transfer is not readily described in terms of simple vector models but requires a density matrix treatment.[2]

COSY identifies two groups of coupled proton spins (A and X) that have a nonzero spin-spin coupling J_{AX}. The two-dimensional spectrum[3] takes the form of a square, with some signals lying on the principal diagonal and the rest, the cross-peaks, having coordinates (δ_A,δ_X) or (δ_X,δ_A) where δ is the chemical shift. Observation of such cross-peaks confirms that A is coupled to X, which is used as evidence of proximity within the molecule.

Ad showed how the basic experiment could be refined so that the final COSY spectrum was clear and simple to interpret. He showed how to optimize the timing parameters for the detection of very small long-range couplings and how relative signs of couplings could be obtained by inspection. He invented a "constant time" method for removing J-splittings in one frequency dimension.

We felt we had to "sell" the technique by making the explanations as clear and simple as possible and by demonstrating its practical utility. In this we were fortunate in having a good example, a derivative of tricyclodecanone, which permitted a searching test of the method. We now know that many NMR spectroscopists have tried their hand at COSY with some success.

Ad continued a meteoric career at Colorado State University and the National Institutes of Health in Bethesda. He was recently given the Outstanding Young Scientist Award by the Maryland Academy of Sciences.

1. **Jeener J.** Ampère International Summer School, Basko Polje, Yugoslavia, 1971. (Cited 175 times.)
2. **Aue W P, Bartholdi E & Ernst R R.** Two-dimensional spectroscopy. Application to nuclear magnetic resonance. *J. Chem. Phys.* 64:2229-46, 1976. (Cited 1,120 times.) [See also: **Ernst R R.** Citation Classic. *Current Contents/Engineering, Technology & Applied Sciences* 18(25):14, 22 June 1987 and *CC/Physical, Chemical & Earth Sciences* 27(25):14, 22 June 1987.]
3. **Bax A.** *Two-dimensional nuclear magnetic resonance in liquids.* Dordrecht, The Netherlands: Reidel, 1982. 200 p. (Cited 495 times.)