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Aue W P, Bartholdi E & Ernst R R. Two-dimensional spectroscopy. Application to nuclear magnetic resonance. *J. Chem. Phys.* 64:2229-46, 1976.
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The paper discusses the possibilities for the extension of spectroscopy to two dimensions and develops the basic theory of two-dimensional spectroscopy. Numerous possible variants are treated including the elucidation of energy-level diagrams and the observation of multiple quantum transitions. [The *SCI*® indicates that this paper has been cited in over 815 publications.]

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The history of this paper started in late summer 1971. One of my students, Thomas Baumann, attended the Ampère Summer School in Basko Polje, Yugoslavia, where Jean Jeener suggested in a lecture a mysterious new two-pulse nuclear magnetic resonance (NMR) technique that was supposed to deliver two-dimensional (2D) spectra. However, nothing was published about his suggestion. Without lecture notes at hand, we tried to figure out the purpose and inner workings of the technique. We soon realized its potential and were intrigued by the possibility of replacing cumbersome double-resonance measurements, used for assigning NMR spectra, with a more powerful and elegant scheme.

In 1972 another student, Enrico Bartholdi, began extensive calculations on various 2D experiments for specific spin systems. The prospects looked very promising, although we did not yet believe in the practical applicability because of enormous computer storage and time requirements for handling the 2D data matrices. In 1973 we had some interesting discussions on the subject with Jeener at a conference in Poland.

Finally, we decided to perform experiments, because we urgently needed to present results at the Sixth International Conference on Magnetic Resonance in Biological Systems, Kandersteg, Switzerland (September 1974). And surprisingly, the experiments worked! We obtained the first 2D spectra ever recorded, although they were of very simple molecules and with limited resolution. We were excited and started a full-blown research project on 2D spectroscopy that included Anil Kumar, Luciano Müller, and particularly Walter P. Aue. We soon found many additional intriguing 2D techniques and discovered 2D resolution, 2D multiple quantum spectroscopy, and heteronuclear 2D experiments. At the same time, the basic theoretical framework for 2D spectroscopy was developed. This led finally to the first comprehensive paper on 2D spectroscopy, submitted to the *Journal of Chemical Physics* in November 1975 and published in 1976.

At that time, two other groups started work on the further development of 2D techniques: John S. Waugh with a 2D solid-state technique and Ray Freeman and Geoffrey Bodenhausen contributing to heteronuclear 2D spectroscopy.

Since the appearance of the paper, the field has experienced (after a slow start) an explosive development. Indeed, a new dimension of spectroscopy has become accessible, and an almost uncountable number of useful techniques has emerged.[1-3] Perhaps the most useful application of 2D spectroscopy is for determining the structure of biological macromolecules in solutions.[4] The initial steps and much of the development were done in a fruitful collaboration with Kurt Wüthrich that started in 1976 and that continues today.

Certainly, the development of powerful laboratory computer systems capable of handling large data matrices has been essential for the practical success. But the decisive factor has been the ease of visual perception of the enormous information content in 2D spectra that made the technique highly attractive to chemists. It also led to numerous references to the paper, despite its comprehensive scope that renders it somewhat difficult to read.

1. **Bax A.** *Two-dimensional nuclear magnetic resonance in liquids.* Boston: Reidel, 1982. 200 p. (Cited 350 times.)
2. **Ernst R R, Bodenhausen G & Wokaun A.** *Principles of nuclear magnetic resonance in one and two dimensions.* Oxford: Clarendon Press, 1987. 650 p.
3. **Chandrakumar N & Subramanian S.** *Modern techniques in high-resolution FT-NMR.* New York: Springer-Verlag, 1987. 388 p.
4. **Wüthrich K.** *NMR of proteins and nucleic acids.* New York: Wiley, 1986. 292 p.