Electronics And Instrumentation

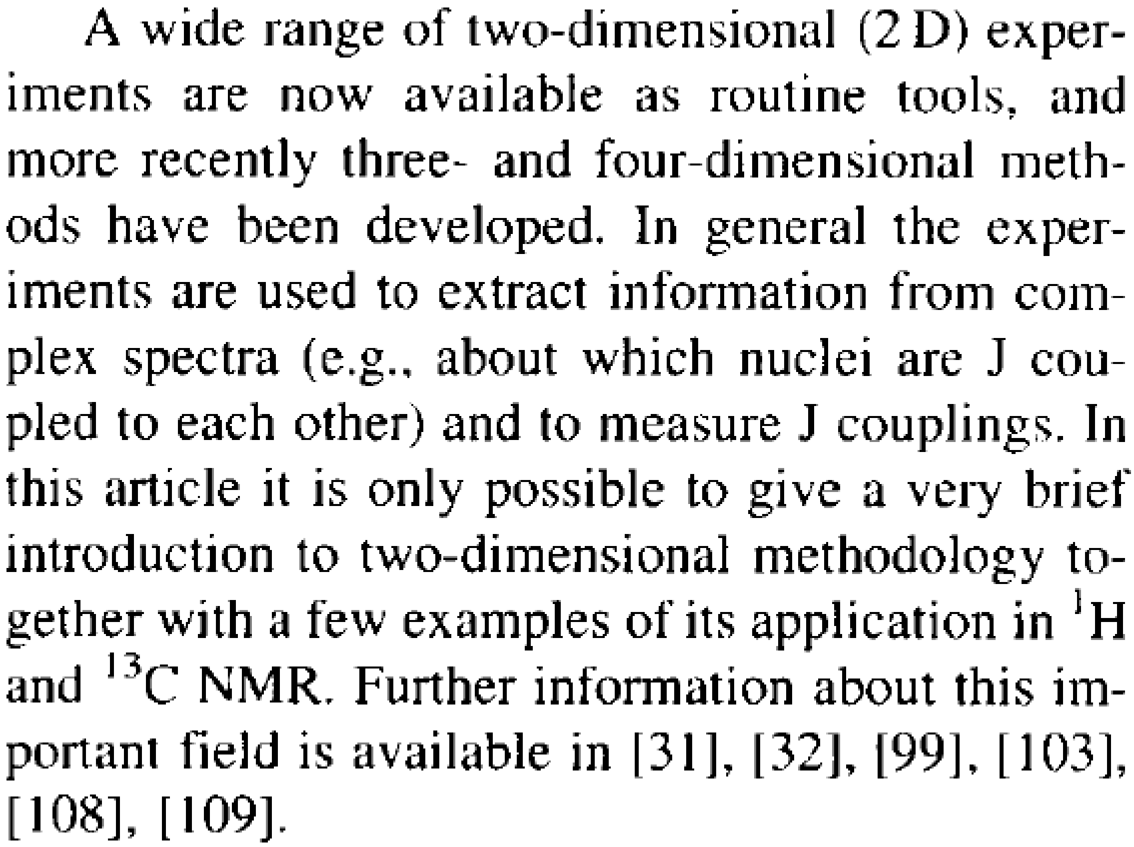
8th Semester

Subject: Analytical Instrumentation
Subject code: BT 808

Unit-5

Nuclear Magnetic Resonance Spectroscopy

3.6. Multi-Dimensional NMR



A wide range of two-dimensional (2 D) experiments are now available as routine tools, and more recently three- and four-dimensional methods have been developed. In general the experiments are used to extract information from complex spectra (e.g., about which nuclei are J coupled to each other) and to measure J couplings. In this article it is only possible to give a very brief introduction to two-dimensional methodology together with a few examples of its application in ^1H and ^{13}C NMR. Further information about this important field is available in [31], [32], [99], [103], [108], [109].

3.6.1. Basic Principles

The common feature of the 1 D multipulse experiments described above was the time sequence preparation – evolution – detection, whereby the detected signal is only a function of the detection time t_2. The important difference in 2 D NMR is that the evolution time t_1 is now a variable. In a 2 D experiment n separate experiments are performed with incremented values of t_1. For each experiment a free induction decay $S(t_2)$ is measured. In this way a matrix $S(t_1, t_2)$ is built up.

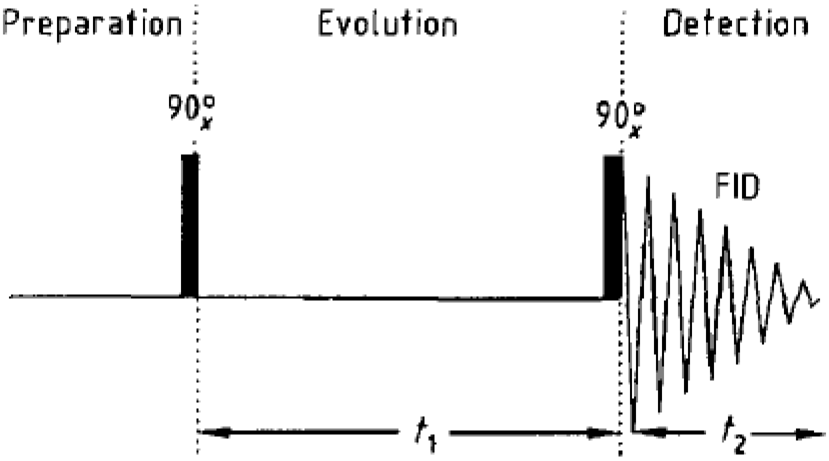


Figure 25. Basic COSY pulse sequence

Fourier transformation of this matrix with respect to t_2 gives a series of spectra $S(t_1, f_2)$. Further transformation with respect to t_1 gives a matrix $S(f_1, f_2)$ which is a spectrum in two independent frequency dimensions. The dispersion of the signals as a function of f_1 depends on the effect of the pulse sequence used on the spin system as t_1 is varied. In general there are two distinct types of 2D experiments, referred to as J-resolved and correlated spectroscopy. In a *J-resolved spectrum* one frequency axis (f_1) contains spin–spin coupling information and the other (f_2) chemical shift information. In *correlated spectroscopy* both axes contain chemical shift information, the connection between the two being via spin–spin coupling, NOE, or exchange effects.

3.6.2. J-Resolved Spectra

J-Resolved spectra provide the possibility to observe the resonance frequencies δ and the coupling constants J on two distinct frequency axes separately. This is achieved by a pulse sequence $[T_d - 90^\circ - t_1/2 - 180^\circ - t_1/2 - \mathrm{FID}(t_2)]_n$. After excitation by a 90° pulse the evolution time t_1 is divided by a 180° pulse. The signal (FID) is then detected in t_2. This experiment, known as 2D J-resolved or J,δ-spectroscopy is mainly used in analysis of crowded spectra. The overlapping absorptions in a 1D proton spectrum can sometimes be resolved by this experiment, in which chemical shifts are presented on one axis and coupling constants on the other. The projection of the 2 D spectrum onto the δ-axis is effectively a "^{1}H broad band decoupled" proton spectrum. However, the relatively long measuring time, which are usually larger than that of other 2 D methods and a number of artifacts, shown in strongly coupled spin systems, caused a decrease of the application frequency.

In heteronuclear *J*-resolved spectra chemical shifts of an arbitrary nucleus X which couples with protons (this is mostly ^{13}C) are presented on one axis and proton-X *J* couplings on the other. The information content is equivalent to that in a proton-coupled ^{13}C spectrum (Fig. 12) but without the severe overlap of multiplets which is usually encountered in the latter. In common with off-resonance proton decoupling, *J*-modulated spin echo, and DEPT experiments, it facilitates multiplicity determination. In addition, it enables proton-X coupling constants to be measured.

3.7. NMR Spectral Collections, Databases, and Expert Systems

NMR is a powerful tool for the determination of structures from first principles and the chemical shift is the most important NMR parameter in structural analysis. For estimating the relationship between chemical structures and chemical shifts three possibilities exist: the calculation of the chemical shift values by empirical methods [137], the computation by quantum chemical procedures, e.g., with the IGLO-method (Individual Gauge for Localized Orbitals [129]), or the use of large compilations of NMR spectra and the associated chemical structures. The access to relevant reference data for identical or similar compounds can facilitate the assignment process enormously. Reference data may assist by reducing the amount of experimental and/or interpretive effort required or increase confidence in the suggested structure.

Many data compilations exist, containing significant amounts of reference data, especially those dedicated to a single nucleus. In addition there are many spectral libraries, some available in hard-copy format only. One of the first ^1H NMR libraries was published by Varian Associates always in the early 1960s [33]. Such older hard-copy libraries contain only low-field data and are normally searchable by parameters such as name, molecular formula, chemical shift value, or compound type [34]–[38], [137]. However, state of

the art are search softwares in computer-readable form. Computer-searchable libraries, especially those which allow substructure searching of compound data in conjunction with spectral data searching, are much more powerful than hardcopy libraries. In 1973 BREMSER published a procedure for the description of the chemical environment of nuclei by their hierarchically ordered spheres of environment (HOSE code) [130]. Today several databases exist containing hundreds of thousands of chemical shift values in particular for ^{13}C nuclei and the corresponding information about the chemical environment of the individual carbons. Only some examples of electronically stored databases should be mentioned here: SpecInfo [39], CSEARCH [132], and CNMR [133]. Their current contents are 149 000 (500), 265 000 (0) and >67 000 (>82 000) spectra for ^{13}C NMR (^{1}H NMR) spectroscopy, respectively. All three systems listed above contain assigned NMR data which can be searched by molecular formula, name, peak positions/-spectrum similarity, and structure/substructure. Users are also able to add their own spectral data to the libraries. All databases can be used to identify known substances contained within the database, and they are an efficient tool for elucidating the structure of unknown substances.

The SpecInfo system which was originally developed in-house by BREMSER et al. at BASF and was also marketed in a searchable microfiche version [40], is the premier spectroscopic archive and interpretation system for ^{13}C, ^{1}H, hetero-NMR, IR, UV/VIS, Raman, and mass spectra. In a more automated way the structure assignment can be achieved by using a structure generator, which assembles all possible isomers for a given molecular formula and performs an automatic ranking of the candidate structures (SPECTACLE [131]). In 2000 a PC program was developed on basis of the SpecInfo database for the calculation of ^{13}C NMR spectra of any proposed organic molecular structure [134]. The spherically encoded chemical environments of more than 500 000 carbons were used here to train artificial neural networks which allow the fast determination of ^{13}C chemical shift values.