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MULTIDIMENSIONAL NMR SPECTROSCOPY

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1- ABSTRACT

A scheme allowing the entire sampling of multidimensional NMR domain names inside a unmarried non-stop acquisition is added and exemplified. Provided that an analyte's sign is adequately strong, the purchase time of multidimensional NMR experiments can as a consequence be shortened through orders of magnitude. This may want to permit the characterization of temporary activities inclusive of proteins folding, 2D NMR experiments on samples being chromatographed, carry the length of better dimensional experiments (e.g., 4D NMR) into the life of maximum proteins below physiological conditions, and facilitate the incorporation of spectroscopic 2D sequences into in vivo imaging investigations. The protocol is well matched with present multidimensional pulse sequences and may be carried out through the usage of traditional hardware; its overall performance is exemplified right here with numerous homonuclear 2D NMR acquisitions.

Key-words: NMR, Multidimensional, spectroscopy, Structural elucidation

INTRODUCTION

Nuclear Magnetic Resonance

NMR-spectroscopy observes the resonance interaction of atomic nuclei with electromagnetic waves. The effect is only detectable in a strong magnetic field. Every atomic nucleus is observed separately [1-3] and in addition interactions between nuclei can be visualized. NMR therefore corresponds well to the chemists view of a molecule as atoms connected by bonds. NMR is very powerful in the determination of the constitution of natural products NMR can help to determine the 3D structure of proteins at atomic resolution, in solution as well as in the solid state NMR can be used to detect the interaction between proteins and ligands.[4]

Basic principles of NMR-spectroscopy

Basis of the effect of nuclear magnetic resonance is the nuclear spin, that can be imagined as a mixture of gyroscope and magnetic needle A gyroscope has an angular momentum whose axis is stable in three-dimensional space An alignment of the “magnetic needle“ with an external magnetic field is prevented by the properties of a gyroscope, a precession begins The resonance frequency of the spins is determined by the magnetic field, as is the sensitivity and the resolution of the spectra.[5-8]

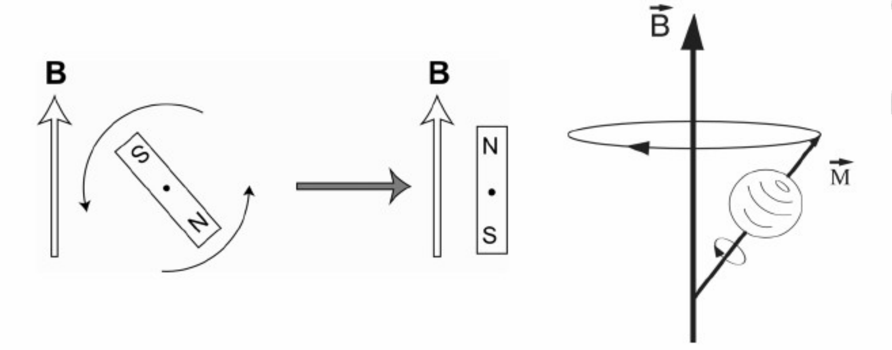

Fig. no. 01: Principle of NMR spectroscopy

Parameters in NMR-spectroscopy

1. Chemical shift

Electrons around the nucleus shield it from the external magnetic field, the more electrons the weaker the field. Each atom in the molecule gives rise to a resonance line The chemical shift depends on the chemical environment An important factor influencing the chemical shift are anisotropy effects, that are created by small additional fields.[9-10]

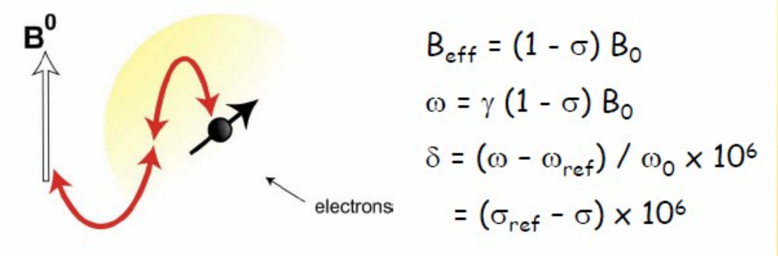

Fig. no.02: Chemical Shift

2. Scalar or J-coupling

Electrons in the bonds between the nuclei mediate an interaction; the scalar coupling Scalar coupling splits the signals according to the number of neighboring nuclei Scalar coupling contains structural information [11]

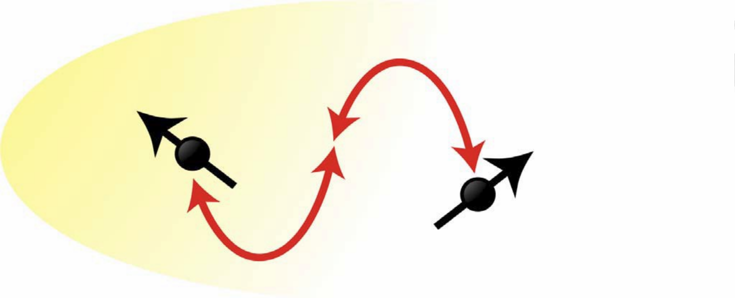

Fig. no.03: J-coupling

3. Dipolar coupling

The nuclei interact directly through space via a dipol-dipol interaction In solution NMR this interaction is averaged to zero due to the fast isotropic movement of the molecules but it is still a source of relaxation One aspect of relaxation is the NOE-Effect, that depends on the distance between two nuclei Since the intensity drops quickly with increasing distance the effect can only be observed up to 500 pm [12]

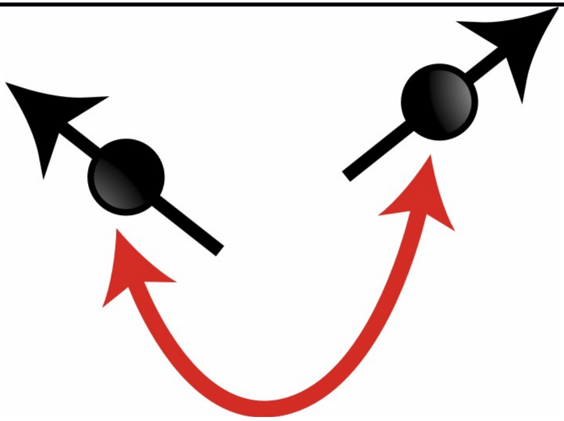

Fig. no.04 : NOE effect

2.0 MULTIDIMENSIONAL NMR-SPECTROSCOPY

The two major advantages of multidimensional NMR are: Improved resolution: Signals are spread over a surface (2D) or in a three-dimensional space (3D, 4D) Magnetization transfer: Signals result from the interaction between nuclei. That can be interactions through bond (via J-coupling) or through space (via NOE). Taken together this eases the interpretation and the assignment of the spectra considerably.[13-17]

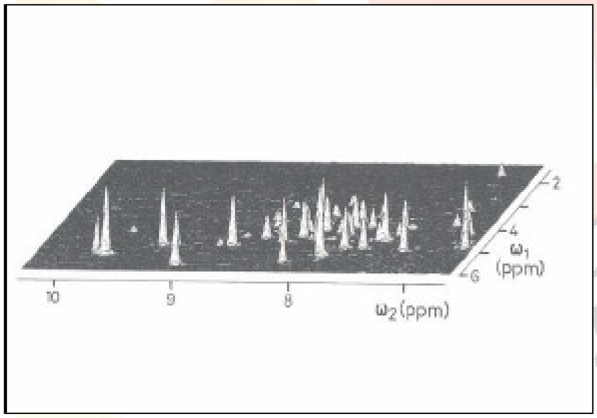

Fig. no. 05: 2D-NMR

Homonuclear spectra

Transfer of magnetization takes place between like nuclei. Both axis exhibit the chemical shift of the same type of nucleus. If a transfer has taken place, the signal has different frequencies in the two dimensions: cross peak If no transfer has taken place, the shifts are the same in both dimensions: diagonal signal [18-20]

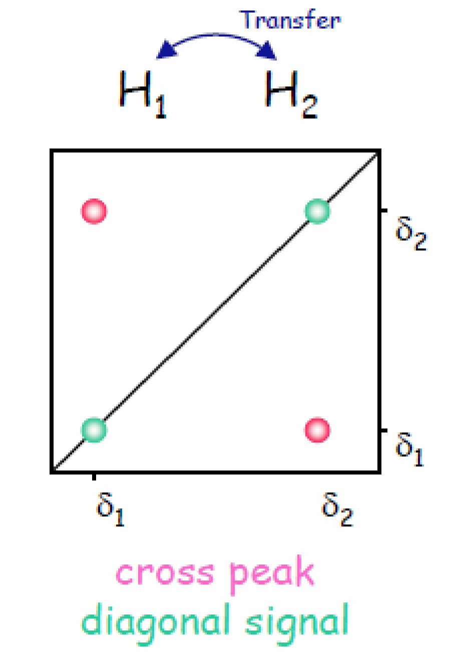

Fig. no.06: Homonuclear spectra

Heteronuclear spectra

Transfer of magnetization takes place between nuclei of different types. The two axis show the chemical shift of the respective type of nucleus. If a transfer has taken place, a signal appears at the intersection of the two frequencies, without a transfer there is no signal.[21]

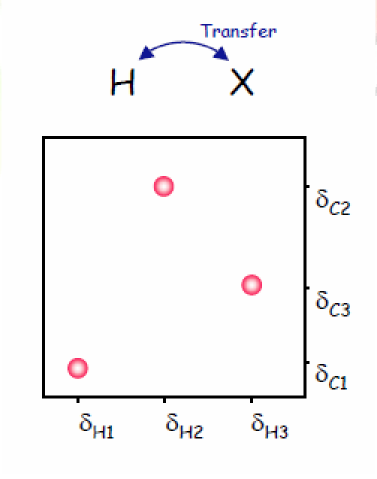

Fig. no. 07: Heteronuclear spectra

NMR-spectroscopy of proteins

The major problem of protein NMR results from the fact that proteins are polymers, i.e. the repetition of almost identical subunits Differences in chemical shifts can be produced by structure and the accompanying anisotropy effect [22-23]

Sequence specific assignment

The solution of the assignment problem is the sequence-specific assignment Two strategies exist: In case of small proteins or peptides where usually only unlabeled material is available the strategy is based on homonuclear spectra (COSY,TOCSY, NOESY) In case of larger proteins labeling with 13C and 15N is necessary and heteronuclear triple resonance experiments (CBCA(CO)NNH,CBCANNH) are recorded [24]

a. Which amino acid type is present (which color)

b. Which amino acid is next to which (neighborhood)

c. Comparison of subsequences with that of the protein

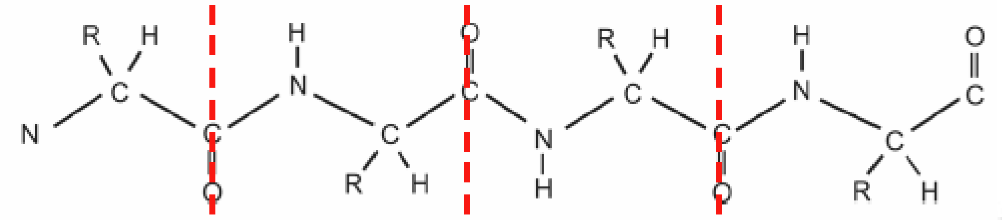

Fig. no. 08: Sequence specific assignment

Assignment using homonuclear spectra:

Each amino acid represents a separate set of signals, a spin system, since amino acids are separated by the carbonyl carbon that does not have a proton attached. Homonuclear spectra that utilize scalar couplings (COSY, TOCSY) are used to establish the amino acid type The neighborhood of the amino acids are then detected by through space interactions, i.e. in NOESY spectra. Inter- and intra-residue signals are separated by comparison between the scalar-coupling spectra that can only show intra-residual peaks and the NOESY The distance from the H N to the Hα of the same amino acids, d N α(i,i), is always short enough to yield an NOE. The same is true for the distance from the H N to the Hα of the amino acid (i-1), d α N A neighborhood of amino acids is thus established. [25]

Triple resonance experiments use the couplings between 1H, 13C und 15 N Main chain assignment using triple resonance experiments

A protein structure determination

With increasing size of the protein the interpretation of homonuclear spectra alone becomes increasingly difficult. With the introduction of nitrogen and carbon labels this problem can be ameliorated because of the better resolution in the heteronuclear spectra and the option to record well resolved 3D spectra.[26]

Ligand-screening using NMR spectroscopy

An increasingly important application of NMR spectroscopy is the screening of compound libraries to identify new interaction partners for a given protein and subsequently lead structures There are two major types of approach, the „ligand detecting techniques“ and the „protein detecting techniques“ A technique of major importance from the class of protein-detecting techniques is called „SAR-by-NMR“ Starting point is a completely assigned two dimensional HSQC spectra of the protein of interest HSQC-spectra with and without the addition of a potential ligand are compared. A shift in the spectrum with ligand relative to the one without indicates an interaction The method can be used in a „high-throughput “manner There are numerous techniques in the class of the „ligand detecting techniques“Two techniques of particular importance are WATERlogsy and STD-NMR The major principle is the alteration of certain properties of the ligand by the protein when bound [27-30]

3.0 **CONCLUSION**

As is clear from the dialogue above, Multidimensional NMR spectroscopic approach will extensively lessen the time taken to decide the shape of complicated herbal products. Systems which could address actual global issues are already available, and are probably to boom in variety and enhance in capacity withinside the close to future. Apart from elucidating systems those structures can also be capable of assist the spectroscopist in assigning chemical shift facts to a proposed shape. One manner wherein multidimensional spectroscopic approach might be precious is in figuring out whether or not or now no longer there may be a unmarried precise approach to a given hassle the usage of the given spectroscopic facts. In the instances wherein multiple answer is again to the operator, those regularly come as a surprise, due to the fact they do now no longer adhere to biosynthetic regulations or the user’s prejudices. If multiple manageable shape is produced with the aid of using the system, then the spectroscopist have to decide the best one thru the really apt use of reference chemical shifts and version compound facts.

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