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Mini Review

Current Bioinformatic Resources in NMR Spectrum Analysis

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Abstract

To date, a large number of biological studies have been reported using Nuclear Magnetic Resonance (NMR). This technique provides identification and quantification of diverse compounds in a complex biological sample. Moreover, its non-destructive and high reproducibility nature made it popular for biologists.

NMR-based studies generates large amount of complex and multi-dimensional data. Processing, analyzing and statistical analysis of such datasets require specialized bioinformatics tools and online databases. This review focuses on the current bioinformatic resources in NMR spectrum analysis. The article describes features of available software packages as well as online websites.

Keywords: *Bioinformatic Resources; NMR Spectrum Analysis*

Introduction

Mass Spectrometer (MS) and Nuclear Magnetic Resonance (NMR) are the most popular platforms to investigate biological samples because of their ability in analyzing of few hundred components in one experiment simultaneously [1-5].

NMR has numerous advantages compare to MS approach. The NMR open a window to view and precise quantification of biological, cell extracts, and tissues without needs to laborious work for sample preparation and/or fractionation. Likewise, NMR could detect compounds that are difficult to ionize or require derivatization in MS. Moreover, in NMR, identification of compounds with identical masses like those with different isotopomer distributions is achievable. NMR also could determine the structures of un-known compounds. Through using stable isotope labels, NMR could be used to clarify the dynamics and mechanisms of metabolite conversions and to discover the compartmentalization of metabolic pathways. Finally, NMR could be utilized for metabolic studies in living organisms by site-specific NMR imaging and spectroscopy approaches [3].

Analyzing NMR spectrum

Analyzing of NMR spectrum can be grouped into two main steps namely spectral processing and spectral identification and quantification [6].

Processing of spectra

All NMR analysis in metabolomics is initiated by the transformation of the time-domain free induction decay (FID) into the frequency domain spectrum. These steps are simple and usually include the apodization, zero-filling, Fourier transformation, and phase correction [6].

Identification of metabolites

Identification of metabolites is one of the most important steps in metabolomics studies, since final results of such studies are based upon identification procedure. Advanced NMR techniques and subsequent analytical strategies are recommended for accurate metabolite identification in biological samples [7]. This step is carried out after processing steps. There are several methods for identification of metabolites including:

a. Chemical shift of ^{1}H, coupling patterns (singlet, doublet, triplet, and etc.), and coupling constants (the distance between the doublet, the triplet, and etc.) [2].

b. Cross-checking with reference databases and previously published data.

c. Spiking (adding the small amounts of a pure metabolite to a sample before spectrum acquisition [8].

d. Matching of standard spectrum to NMR spectrum [3].

e. Two dimensional NMR (^{1}H-^{13}C HSQC, ^{1}H-^{1}H TOCSY, ^{1}H-^{1}H COSY) [3].

Some software packages and web sites which are used for processing of NMR spectrum and identification of metabolites are represented in table 1. The standard spectrum of some biological metabolites could also be accessed in table 2.

Software name	Installable/web based	Free/commercial	1D/2D	Processing ability	Database	Automatic identification	Automatic quantification
Chenomx	Installable	Commercial	1D	✓	✓	✓	✓
mNOVA	Installable	Commercial	1D/2D	✓	No	No	✓
Top Spin	Installable	Commercial	1D/2D	✓	✓	✓	✓
rNMR	Installable	Free	1D/2D	No	No	No	✓
ASICS	Installable	Free	1D	No	✓	✓	✓
MetaboMiner	Installable	Free	1D/2D	✓	✓	✓	No
MetaboHunter	Web based	Free	1D	No	No	✓	No
MMCD	Web based	Free	1D/2D	No	✓	✓	✓
HMDB	Web based	Free	1D/2D	No	✓	✓	No

Table 1: *Some of Software programs and web based algorithms developed for processing of NMR spectrum and identification of metabolites.*

Data base name	URL	Number of metabolites	Type of Spectra	Free to Download
BMRB	http://www.bmrb.wisc.edu/	906	1H, 13C, DEPT 90, DEPT 135, J-resolve, COSY, HSQC, TOCSY, HMBC	✓
HMDB	http://www.hmdb.ca/	916	1H, HSQC	✓
MMCD	http://mmcd.nmrfam.wisc.edu/	794	1H, DEPT 90, DEPT 135, J-resolve, COSY, HSQC, TOCSY, HMBC	✓
SpinCople	http://emar.riken.jp/spincpl/	598	J-resolved	No
BML-NMR	http://www.bml-nmr.org/	208	1H, J-resolved	✓

Table 2: *Database containing standard spectra [2].*

Conclusion

NMR-based approach is one of the comprehensive methods used in metabolomics area, but because of complexity of spectra, special skills and expertise is required for its analysis. As shown on table 1, the commercial software packages like Chenomx and Top Spin as well as MMCD web site are most user friendly than other software packages or web sites because of automatic identification and quantification of spectra. This short article could provide worthwhile information about software packages and web sites that are used for a NMR-based spectrum analysis.

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