Available online at www.sciencedirect.com
ScienceDirect
Journal of Magnetic Resonance 187 (2007) 363–370
JMR Journal of Magnetic Resonance
www.elsevier.com/locate/jmr

Communication

Phasing arbitrarily sampled multidimensional NMR data

John M. Gledhill, A. Joshua Wand *

Johnson Research Foundation and Department of Biochemistry & Biophysics, University of Pennsylvania, 905 Stellar-Chance Laboratories, 422 Curie Blvd., Philadelphia, PA 19104-6059, USA

Received 9 April 2007; revised 5 May 2007
Available online 6 June 2007

Abstract

The recent re-introduction of the two-dimensional Fourier transformation (2D-FT) has allows for the transformation of arbitrarily sampled time domain signals. In this respect, radial sampling, where two incremented time dimensions (t_1 and t_2) are sampled such that $t_1 = \tau\cos\alpha$ and $t_2 = \tau\sin\alpha$, is especially appealing because of the relatively small leakage artifacts that occur upon Fourier transformation. Unfortunately radially sampled time domain data results in a fundamental artifact in the frequency domain manifested as a ridge of intensity extending through the peak positions perpendicular to +/− the radial sampling angle. Successful removal of the ridge artifacts using existing algorithms requires absorptive line shapes. Here we present two procedures for retrospective phase correction of arbitrarily sampled data.

Keywords: NMR spectroscopy; Two-dimensional Fourier transformation; Phase correction; Time domain sampling

1. Introduction

The high probability of degenerate frequencies in NMR spectra of complex biopolymers such as proteins presented a great barrier to detailed analysis. The combination of multidimensional NMR spectroscopy and high magnetic field strengths has overcome the resulting resonance assignment problem for proteins less than 50 kDa. Furthermore, recent advances in NMR instrumentation have largely removed sensitivity as a limiting parameter for protein samples in the millimolar concentration range. As a consequence, the orthogonal linear sampling requirements of conventional multidimensional NMR spectroscopy have required longer acquisition times than potentially needed with respect to signal-to-noise. A number of approaches have been introduced to escape the linear sequential sampling requirements of the standard fast Fourier transform usually employed to deal with processing of the time domain NMR signal [1]. Many of the new approaches find their roots in the so-called accordion spectroscopy introduced by Bodenhausen and Ernst over two decades ago where two or more incremented time domains are linked [2].

Recently the two-dimensional Fourier transformation (2D-FT) has been re-introduced to transform arbitrarily sampled time domain signals [3–5]. In principle the 2D-FT allows the use of non-linear time domain sampling. In this respect, the so-called radial sampling protocol, where two incremented time dimensions (t_1 and t_2) are sampled such that $t_1 = \tau\cos\alpha$ and $t_2 = \tau\sin\alpha$, is especially appealing because of the absence of the aliasing artifacts of random sampling that occur upon Fourier transformation. However, transformation of radially sampled time domain data results in a fundamental artifact manifested as a ridge of intensity extending through the peak positions perpendicular to +/− the radial sampling angle. A number of algorithms have been introduced to remove these ridges [6–8] but, as we will emphasize below, successful removal of the ridge artifacts requires absorptive line shapes. Unfortunately, no general procedure for phasing radially sampled NMR data has been presented. Indeed, the emphasis thus

* Corresponding author. Fax: +1 215 573 7290.
E-mail address: wand@mail.med.upenn.edu (A.J. Wand).

1090-7807/$ - see front matter © 2007 Elsevier Inc. All rights reserved.
doi:10.1016/j.jmr.2007.05.017

far has been on the collection of time domain data that is free of phase distortion or error. Obviously a procedure for retrospective phase correction of radially sampled data is a distinct advantage. Here we present two methods capable of phase correcting arbitrarily sampled NMR data as a solution to this problem.

2. Theory

The discrete 2D-FT can be described as [3–5,9]:

$$S(\omega_1,\omega_2)=\sum_{t_1=0}^{t_1^{\max}}\sum_{t_2=0}^{t_2^{\max}}\exp(-i\omega_1 t_1)\times\exp(-j\omega_2 t_2)f(t_1,t_2)g(t_1,t_2)w(t_1,t_2) \quad (1)$$

where i and j are quarternion numbers; t_1 and t_2 are the incremented times, ω_1 and ω_2 comprise the frequency pair being determined, $f(t_1,t_2)=\exp(-i\Omega_1 t_1)\exp(-j\Omega_2 t_2)$ is the data being transformed, Ω_1 and Ω_2 are the chemical shifts for time domain t_1 and t_2, respectively, $w(t_1,t_2)$ is a weighting factor to account for the unequally spaced sampling of the time domain and is typically applied as a two-dimensional apodization function, and $g(t_1,t_2)$ describes the lifetime of the signal, which we will subsequently ignore. In the case of radial sampling $t_1=\tau\cos\alpha$ and $t_2=\tau\sin\alpha$ where τ is the incremented time and α is the sampling angle.

In accordance with standard Fourier transform quadrature theory, if the carrier frequency is set in the middle of the spectral ranges, eight pieces of data must be collected in order to determine the sign of the frequency components for a three-dimensional spectrum. Typically the proton dimension is processed separately; therefore we will only deal with the indirect evolution terms here. This simplification leaves four terms that are modulated by a mixture of cosine and sine as presented below.

$$f_{CC}(t_1,t_2)=\cos(t_1\Omega_1)\cos(t_2\Omega_2) \quad (2a)$$

$$f_{CS}(t_1,t_2)=\cos(t_1\Omega_1)\sin(t_2\Omega_2) \quad (2b)$$

$$f_{SC}(t_1,t_2)=\sin(t_1\Omega_1)\cos(t_2\Omega_2) \quad (2c)$$

$$f_{SS}(t_1,t_2)=\sin(t_1\Omega_1)\sin(t_2\Omega_2) \quad (2d)$$

Four real Fourier transformations can be used to process the four data sets, which we term the cos–cos Fourier transform (CC-FT), the cos–sin Fourier transform (CS-FT), the sin–cos Fourier transform (SC-FT) and the sin–sin Fourier transform (SS-FT). The CC-FT is used to transform the cos–cos modulated data set [Eq. (2a)], the CS-FT to transform the cos–sin modulated data set [Eq. (2b)], and so on. For example, the CC-FT becomes:

$$S_{CC}(\omega_1,\omega_2)=\sum_{t_1=0}^{t_1^{\max}}\sum_{t_2=0}^{t_2^{\max}}\cos(t_1\omega_1)\times\cos(t_2\omega_2)f(t_1,t_2)w(t_1,t_2) \quad (3)$$

The three remaining transformations are similarly defined [3,9]. In order to select the appropriate quadrature image the four resulting spectra, $S_{CC}(\omega_1,\omega_2)$, $S_{CS}(\omega_1,\omega_2)$, $S_{SC}(\omega_1,\omega_2)$ and $S_{SS}(\omega_1,\omega_2)$ are summed, canceling the quadrature images and artifact peaks.

$$S_{RR}(\omega_1,\omega_2)=S_{CC}(\omega_1,\omega_2)+S_{CS}(\omega_1,\omega_2)+S_{SC}(\omega_1,\omega_2)+S_{SS}(\omega_1,\omega_2) \quad (4)$$

To demonstrate the four Fourier transforms and summing procedure, we use four computer generated radially sampled time domain data sets modulated by a mixture of cos and sin as dictated by Eqs. (2a)–(2d) with one peak. The peak position for the data sets was set at (−300 Hz, 75 Hz) and the sampling angle set to 45°. The linewidth was adjusted to 10 Hz by multiplying the data sets by an exponential decay. The data sets were Fourier transformed with their respective transform as outlined by Eq. (3). Sixteen peaks are visible in the $S_{CC}(\omega_1,\omega_2)$ spectrum. Four peaks are the quadrature images at ±300, ±75 Hz and the twelve arise from intersection of the ridge artifact appearing at ±400, 0; ±200, 0; 0, ±300; 0, ±150, ±100, ±225. The other three spectra $S_{CS}(\omega_1,\omega_2)$, $S_{SC}(\omega_1,\omega_2)$ and $S_{SS}(\omega_1,\omega_2)$ have the same four quadrature image peaks with varying signs. The variation in signs causes the artifact patterns to change. In the case where two negative ridges intersect a negative artifact peak is present, when two ridges of varying sign intersect no peak is present. When all four spectra are summed the variations in sign of the quadrature and artifact peaks cause them to cancel resulting in a spectrum with just the authentic peaks remaining (Fig. 1).

In addition to the authentic peaks, ridges also extend from the peak at the sampling angle in the $S_{RR}(\omega_1,\omega_2)$ spectrum. Most often one wishes to remove the ridges and in the case where signal to noise is not limiting the lower value (LV) algorithm is preferred [6]. Here multiple data sets are collected at various sampling angles and the data is Fourier transformed independently. Subsequent to the transforms the intensities of multiple $S_{RR}(\omega_1,\omega_2)$ spectra are compared point-wise and the smallest magnitude value at each point is kept in a separate spectrum. If a sufficient number of angle data sets are collected a final spectrum free of ridges is generated.

Providing the data is free of phase error, the above Fourier transform method combined with the lower value algorithm works quickly and accurately to generate a ridge-free frequency spectrum. However, this approach is severely limited by its inability to deal with phase distorted data. If a phase error is present the lowest value algorithm will delete authentic peaks. This occurs because the lineshape of dispersive peaks causes the intensity to be zero inside the linewidth of the peak. The zero values are different for each sampling angle, therefore when multiple angles are compared by the LV algorithm the peak will be eliminated.

In order to circumvent this shortcoming, the current strategy is to optimize data collection to reduce phase distortions. Nevertheless, non-ideal spectrometer performance and inherent limitations of pulse sequences often preclude