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Communication

Gridding and fast Fourier transformation on non-uniformly sparse sampled multidimensional NMR data

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ABSTRACT

For multidimensional NMR method, indirect dimensional non-uniform sparse sampling can dramatically shorten acquisition time of the experiments. However, the non-uniformly sampled NMR data cannot be processed directly using fast Fourier transform (FFT). We show that the non-uniformly sampled NMR data can be reconstructed to Cartesian grid with the gridding method that has been wide applied in MRI, and sequentially be processed using FFT. The proposed gridding-FFT (GFFT) method increases the processing speed sharply compared with the previously proposed non-uniform Fourier Transform, and may speed up application of the non-uniform sparse sampling approaches.

1. Introduction

Multidimensional (mD) NMR spectroscopy can dramatically reduce peak overlapping, and provide molecular structural information such as chemical bond linkages, and spatial distances between nuclei, therefore it has been widely used in the structure, interaction and dynamic studies of biological macromolecules. However, the experimental time of the mD NMR spectroscopy increases dramatically when expanding sampling dimensions, which results in that massive instrument time is required in 3D/4D NMR experiment [1], hence improving the efficiency of data acquisition and processing has attracted more and more attention [2,3].

There are numerous approaches have been developed, such as reduced dimensionality (RD) [4,5], GFT [6–8], projection reconstruction (PR) [9–12], covariance NMR [13,14], filter diagonalization method (FDM) [15–17], maximum entropy (MaxEnt) [18–20], multidimensional decomposition (MDD) [21,22], hyperdimensional NMR [23–25], Hadamard encoding [26–28], Single-Scan [29–31], relaxation delay optimization [32–34], and non-uniform Fourier transformation (NU-FT) [35–37]. Most of the methods utilize non-uniform sparse or nonlinear sampling patterns in indirect dimensions with particular data processing methods. Although, data processing takes less time than acquisition for mD NMR, the procedure is generally repeated several times in order to optimize the parameters and to obtain high quality spectra. Therefore, fast and widely applicable processing method is highly demanded.

Without the restraints of sampling pattern, line shape, parameters tuning, or previous spectral information, NU-FT becomes the most robust processing approach. However, in case of non-uniform sampling (NUS), the time domain data points may not locate on the knots of Cartesian grids, fast Fourier transformation (FFT) cannot be used in a straight forward manner, which slows down the speed of NU-FT very much. To take the advantage of the high efficiency of FFT, Zhou et al. proposed to replace the off-grid sampling points with their nearest grid points [38]; Marion used Lagrange interpolation to recast the non-uniformly sampled data into the uniformly sampled data [39]. Recently, Matsuki proposed a iterative method SIFT using the Gerchberg–Papoulis (G-P) algorithm on the on-grid non-uniformly sampled NMR data [40]. However, on-grid non-uniform sampling pattern results in problem known as primary and secondary aliasing [37,41], and SIFT must incorporate the previous spectral information, such as empty regions in the NMR spectra. Herein, we described an alternative processing strategy, gridding-FFT (GFFT), to perform FFT on arbitrary non-uniformly sampled NMR data without any requirement of previous spectral information. The method is generally applicable to multidimensional FT of off-grid sampled data.

2. Theoretical basis

The key point of the GFFT technique is using gridding algorithm [42–45], which is much less error prone than interpolation [44] and has been widely applied in radio astronomy and magnetic resonance imaging (MRI) [45], to reconstruct the non-uniformly

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sampled data to Cartesian grids required for FFT. The procedure of the algorithm is shown in Fig. 1. Assume $f(t)$ is the non-uniformly sampled data, then the aim of GFFT is to quickly obtain its Fourier transform $\hat{f}(v)$, i.e. NMR spectrum, through FFT. The first step of gridding method is to numerically compute convolution product [44] on the Cartesian grid, as shown in the following equation:

$$g(t) = (c * f)(t) = \int c(t - t')f(t')dt', \tag{1}$$

where c is convolution function. Here we use a Kaiser–Bessel function [43,44],

$$KB(t) = I_0(\beta\sqrt{1 - (2t/W)})/W, \tag{2}$$

where W is the convolution width, β is a free design parameter, and I_0 denotes zero-order modified Bessel function of the first kind. According to Nyquist theorem, the unit size of grid is determined by spectral width. When calculating a 2D grid, $c(t_1, t_2)$ can be written as $c(t_1)c(t_2)$, and similarly, $c(t_1, t_2, t_3)$ as $c(t_1)c(t_2)c(t_3)$ in 3D case. Since the domain of $c(t)$ is a zero-centered interval and the acquisition times of NMR experiments are always positive, the sampled data must be shifted into a centered interval before convolution, which results in an phase change in spectrum according to Fourier transform shift theorem. Because the convolution function can be set very narrow to reduce calculation amount, this convolution calculation must be fast. In this step, the raw data may be processed ahead with sampling density function to reduce the artifact induced by the point spread function of non-uniform sampling pattern [43,46].

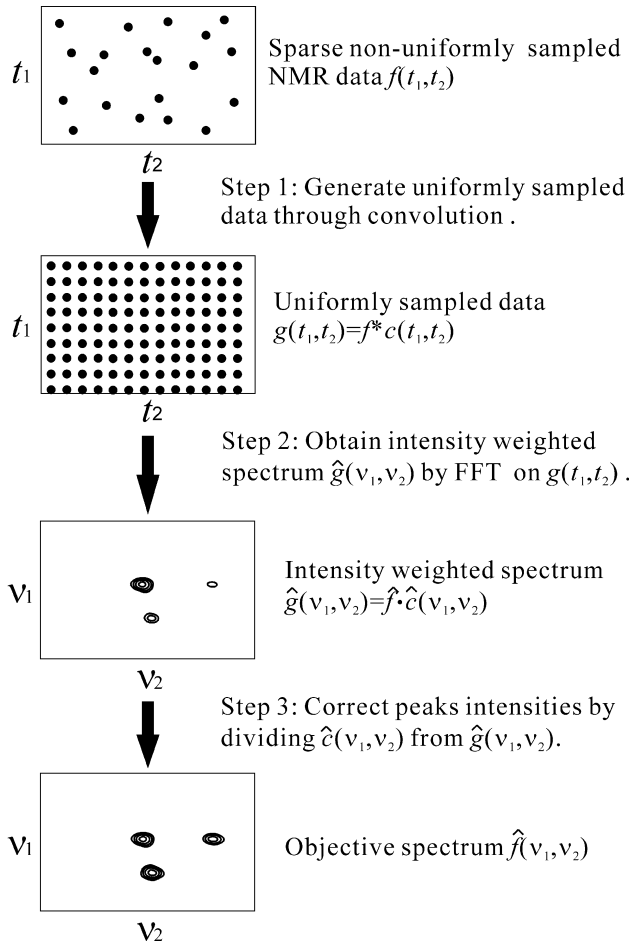

Fig. 1. Procedure of the proposed GFFT strategy, where $f(t_1, t_2)$ is non-uniformly sampled NMR data in the indirect dimensions in case of 3D NUS experiment .

The second step is to perform FFT on the gridded data $g(t)$ as in conventional NMR spectrum processing, to get its Fourier transform $\hat{g}(v)$. Since $g(t) = c * f(t)$, from convolution theorem we know $\hat{g}(v) = \hat{c} \cdot \hat{f}(v)$. When Kaiser–Bessel function is used as convolution function, the weight correction function [44] is shown in the following equation.

$$\hat{c}(v) = KB(v) = \frac{\sinh\sqrt{\beta^2 - \pi^2 W^2 v^2}}{\sqrt{\beta^2 - \pi^2 W^2 v^2}} \tag{3}$$

This function will enhance the intensities of peaks in the center of spectrum, while weaken those in the fringe of spectrum. To obtain the spectrum $\hat{f}(v)$, the weight correction function $\hat{c}(v)$ must be divided from $\hat{g}(v)$, which is just the final step of the gridding reconstruction process.

3. Experimental validation and discussion

To verify the feasibility and speed advantage of the GFFT, conventional 3D HNCO experiment and its indirect dimensional spiral sampling version [35,47] were performed. The sample was a 1 mM aqueous solution (10% D_2O) of uniformly ^{13}C and ^{15}N labeled ubiquitin. The NMR experiments were carried out on a Bruker Avance III 800 spectrometer equipped with cryoprobe. In the conventional 3D HNCO experiment, the indirect dimensional evolution steps were 48 and 32 for t_1 and t_2, respectively. In the spiral sampling experiment, the total number of the indirect dimensional sampling points was 403, as shown in Fig. 2.

Both GFFT and NU-FT [35] were applied to spiral sampled HNCO data for comparison. After the conventional processing along the direct dimension, every t_1–t_2 plane was extracted to perform GFFT or NU-FT to obtain the whole NMR spectrum. The processing programs were written in C++ language and available upon request from the authors. As shown in Fig. 3, all spectral information was recovered by GFFT (Fig. 3B) or NU-FT (Fig. 3C), however, the former cost 0.875 s while the latter cost 52.922 s for a 256 × 256 F_1–F_2 plane on our computer equipped with Intel Core2 Duo CPU E8300. When the spectral resolution was extended to 512 × 512, the processing time was 1.25 s with GFFT, while it took 212.522 s with NU-FT. It is known that higher digital resolution or higher dimensionality requires more data points and longer processing time, in such cases, the speed advantage of GFFT is more obvious.

The speed advantage of GFFT over NU-FT is due to its much lower computational complexity. For a size $SI_1 \times SI_2$ spectrum

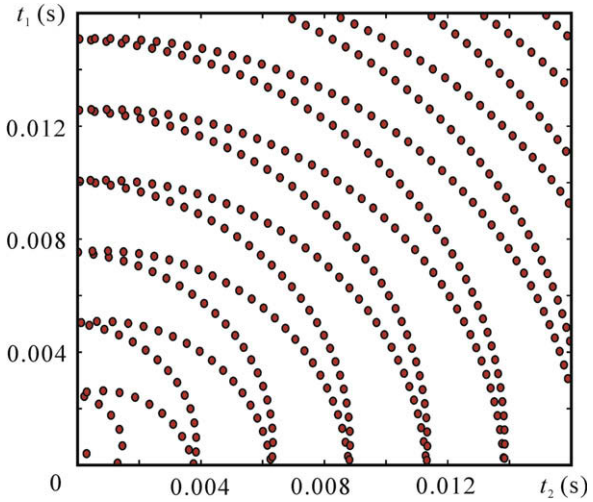

Fig. 2. The sampling points in the t_1–t_2 plane of the spiral HNCO experiment.

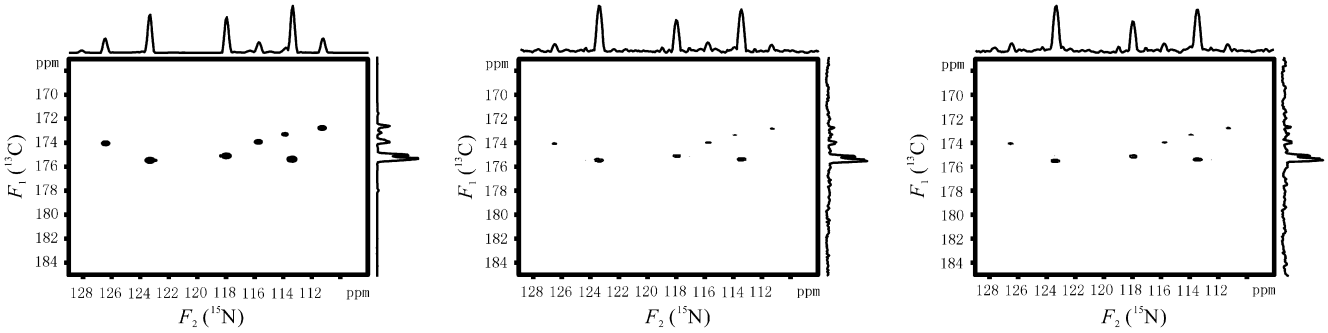

Fig. 3. Comparison of F_1/F_2 planes of HNCO spectra of ubiquitin for $\omega_3(^1H, \delta\ 8.46)$. (A) Conventional HNCO; spiral sampled HNCO, processed using (B) GFFT (processing time 0.875 s) and (C) NU-FT (processing time 52.922 s). Kaiser–Bessel function $KB(t) = I_0(\beta\sqrt{1-(2t/W)})/W$ was chosen as convolution function of this gridding calculation, where I_0 denotes zero-order modified Bessel function of the first kind. According to Ref. [44], $W = K/(d \cdot TD)$, where d is the spectral resolution (reciprocal of acquisition time), TD is the number of reconstructed points along the certain dimension, and $K \ll TD$, which confines the convolution function width as shown in Fig. 4; and $\beta = \alpha\pi Wr$, where r is the spectral width along the certain dimension, and α is another parameter to adjust the shape of Kaiser–Bessel function ($\alpha \geqslant 1$). In this gridding calculation, W was 0.001656 in t_1 dimension, or 0.002936 in t_2 dimension, β was 28.274334 in t_1 dimension, or 23.561945 in t_2 dimension.

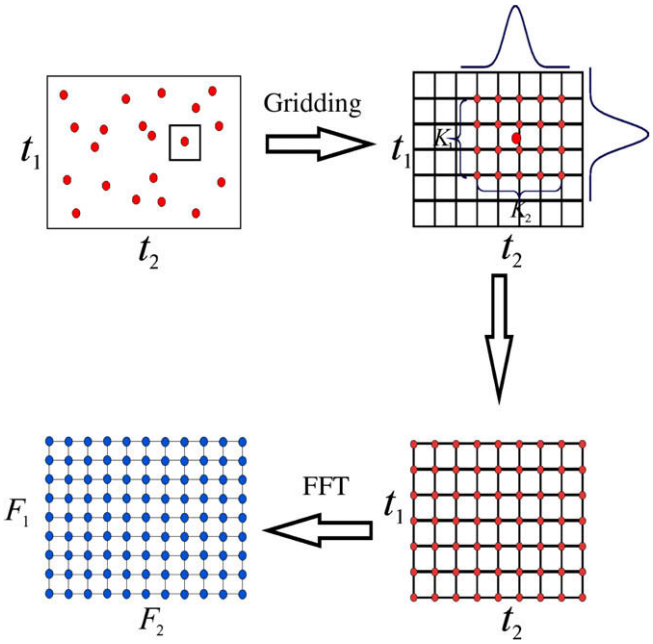

Fig. 4. The computational procedures of (A) NU-FT (MFT) and (B) GFFT. For GFFT, each non-uniformly sampled data point is reconstructed to a $K_1 \times K_2$ submatrix through convolution calculation, and the final gridded matrix for FFT is just the superposition of all these submatrices, so the Computational complexity of gridding is $O(nK_1K_2)$, where n is the number of sampling points.

transformed from n sampling points, the computational complexity of NU-FT is $O(nN)$, where $N = SI_1 \times SI_2$. As shown in Fig. 4, in gridding procedure each sampled data point is reconstructed to a $K_1 \times K_2$ submatrix through convolution calculation, and the final gridded matrix for FFT is just the superposition of all these submatrices due to the linearity of convolution. From this procedure, it can be seen that the computational complexity of gridding is $O(nK_1K_2)$. Remind the well known computational complexity of FFT is $O(N \log N)$, where $n \ll N$, and $K_1K_2 \ll N$, it can be concluded that GFFT has much higher efficiency than NU-FT.

The non-uniform sampling pattern is always accompanied with the artifact induced by the point spread function of its sampling function [48]. In NMR experiments, the acquired data is actually not the true continuous signal $f(t)$, but the product with the sampling function, $s(t)f(t)$. From the convolution theorem of FT, the frequency domain spectrum calculated from the sampled data is $\hat{s}(v) * \hat{f}(v)$, which is different from the true spectrum $\hat{f}(v)$. $\hat{s}(v)$ is called the point spread function of the sampling procedure. In case of uniform sampling pattern, $\hat{s}(v)$ does not cause artifact in spectrum, because $s(t)$ is constant and there is only one frequency component in $\hat{s}(v)$. However, when non-uniform sampling pattern is used, $\hat{s}(v)$ will induce artifacts in the spectrum. Dividing each sampling point with sampling density $\rho(t_1, t_2) = s(t_1, t_2) * c(t_1, t_2)$ before the convolution calculation in step 1 of GFFT, can compensate the sampling density and reduce the artifact induced by the point spread function [43], as shown in Fig. 5.

Compared with other processing approaches on non-uniformly sampled NMR data, GFFT owns many advantages. As a FT based

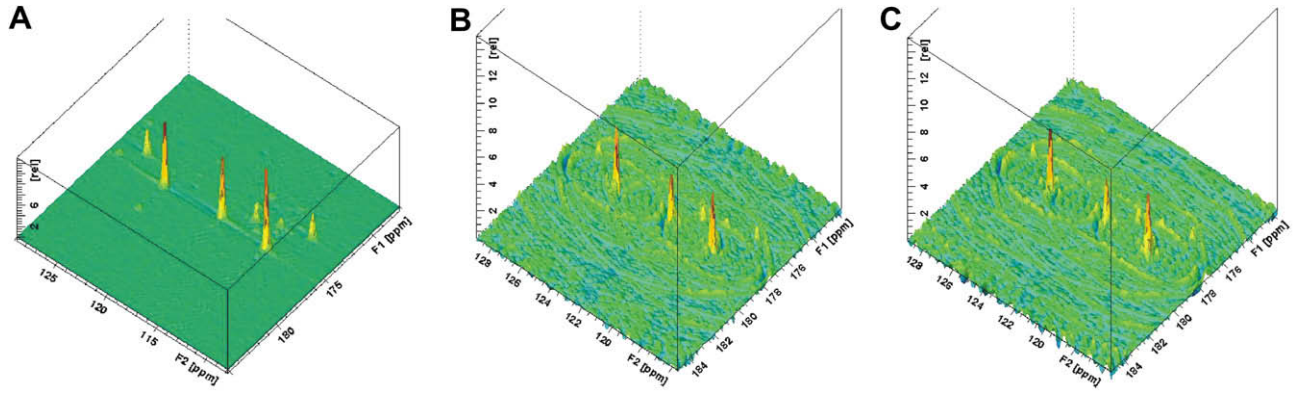

Fig. 5. Oblique view of comparison of F_1/F_2 planes of HNCO spectra of ubiquitin for $\omega_3(^1H, \delta\ 8.46)$. (A) Conventional HNCO; spiral sampled HNCO, processed using (B) GFFT and (C) NU-FT. The ring shape artifacts caused by the point spread function of spiral sampling in (B) is weaken than (C) to some extent.

method, GFFT is highly robust, so that it is not influenced by spectral quality, line shape, and signal overlapping, and does not need parameter tuning or trial-and-error approach either. In the aspect of processing speed, GFFT is much faster than NU-FT. GFFT is able to handle any kinds of non-uniform sampling patterns, no matter on-grid or off-grid, spiral distribution or radial distribution, which means off-grid sampling pattern can be used to avoid aliasing.

4. Conclusions

As a general processing method for NMR data with non-uniform sparse sampling, GFFT is amenable for arbitrary sampling pattern, and any dimensionality. Compared with NU-FT, the speed advantage of GFFT is distinct, and may be more remarkable when wider spectral width, higher resolution or higher dimensionality is required, because the size of spectra should be larger in these kinds of situations. Sampling density compensating in gridding can reduce the artifacts induced by point spread function of non-uniform sampling pattern.

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