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Nonuniform sampling of hypercomplex multidimensional NMR experiments: Dimensionality, quadrature phase and randomization

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ABSTRACT

Nonuniform sampling (NUS) in multidimensional NMR permits the exploration of higher dimensional experiments and longer evolution times than the Nyquist Theorem practically allows for uniformly sampled experiments. However, the spectra of NUS data include sampling-induced artifacts and may be subject to distortions imposed by sparse data reconstruction techniques, issues not encountered with the discrete Fourier transform (DFT) applied to uniformly sampled data. The characterization of these NUS-induced artifacts allows for more informed sample schedule design and improved spectral quality. The DFT–Convolution Theorem, via the point-spread function (PSF) for a given sampling scheme, provides a useful framework for exploring the nature of NUS sampling artifacts. In this work, we analyze the PSFs for a set of specially constructed NUS schemes to quantify the interplay between randomization and dimensionality for reducing artifacts relative to uniformly undersampled controls. In particular, we find a synergistic relationship between the indirect time dimensions and the "quadrature phase dimension" (i.e. the hypercomplex components collected for quadrature detection). The quadrature phase dimension provides additional degrees of freedom that enable partial-component NUS (collecting a subset of quadrature components) to further reduce sampling-induced aliases relative to traditional full-component NUS (collecting all quadrature components). The efficacy of artifact reduction is exponentially related to the dimensionality of the sample space. Our results quantify the utility of partial-component NUS as an additional means for introducing decoherence into sampling schemes and reducing sampling artifacts in high dimensional experiments.

1. Introduction

Nonuniform sampling (NUS) methods, and associated spectral reconstruction techniques, are increasingly used to reduce sampling requirements in multidimensional NMR. In seminal work by Barna and colleagues, data from two-dimensional NMR experiments collected using an exponentially biased selection of t_1 values from a Cartesian grid spaced at the Nyquist interval [1], were processed with maximum entropy reconstruction [2,3] to compute the spectrum. Off-grid NUS methods employing sampling along radial vectors in the indirect time dimensions were introduced in the 2000s by Ding and Gronenborn [4–6]. Spectral estimation methods such as back-projection reconstruction [7,8] and the G-matrix Fourier transform [6,9], were introduced to handle off-grid radial sampling. Because they utilize different spectral reconstruction techniques, the connection between the on-grid approach of Barna et al. and the off-grid radial sampling approaches was not immediately recognized. However, Mobli et al. [10] demonstrated the close connection by using maximum entropy reconstruction for radial sampling schemes that fall on a Cartesian grid.

The principle applications of NUS to date have been to obtain high resolution spectra while minimizing experiment time (see [11,12] for review). The omission of points from a uniform sampling grid results in gaps which, according to the Nyquist theorem, introduce aliased peaks that appear as artifacts in the final spectrum. From the earliest work by Barna et al., it has been clear that the distribution of sample times influences the distribution and magnitude of sampling artifacts. Understanding these artifacts is an important first step for improving the quality of spectra obtained from NUS experiments. Critical comparison of different sampling strategies is complicated by the non-linearity of most non-Fourier methods of spectral reconstruction. Nevertheless, a growing body of empirical evidence, coupled with theoretical insights, has yielded two fundamental principles for the design of efficient sampling schemes. The first is that randomness is

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important for minimizing sampling artifacts [13–16]. The second is that tailoring the sampling distribution to capture more samples at times when the signal envelope is larger and less samples when it is smaller helps improve sensitivity [1,17]. Beyond these general principles, more specific prescriptions have remained elusive because the quality of spectra obtained using NUS depends not only on the chosen NUS schedule, but also on the nature of the signals (e.g. noise level, dynamic range and signal decay rates), the dimensionality of the experiment and the method used to reconstruct the spectrum.

The point-spread function (PSF) is the discrete Fourier transform (DFT) of the sampling function, which is a multidimensional array with an element equal to one for each free induction decay (FID) that is sampled and equal to zero for each FID that is not sampled. Schmieder et al. [18] used the PSF as a quantitative tool for comparing sampling schemes, and despite the observation by Lustig et al. [19] that the PSF is a "natural tool to measure incoherence" of sampling schemes, the PSF has only served a minor supporting role in the investigations of NUS [20–22]. In the present work we utilize the peak-to-sidelobe ratio (PSR, an adapted form of the sidelobe-to-peak ratio of Lustig et al. [19]) which is the ratio between the magnitude of the zero-frequency component and the largest satellite (non-zero-frequency component) in the PSF. The PSR serves as a quantitative measure of the coherence among the sampled times in the sampling function. As such, PSR is an *a priori* measure akin to "signal-to-noise", in that it gives the upper bound on the ratio between the zero-frequency component and the largest NUS induced artifact expected for a given sampling function. The artifacts follow the upper bound when the NUS data is zero-augmented (i.e. FIDs not collected by the NUS schedule are zero filled) and processed by DFT, whereas the artifacts are reduced when spectral reconstruction methods make no assumptions about the missing FIDs (e.g. maximum entropy [23,24].

We present a PSR analysis of several carefully constructed sampling schemes designed to elucidate the role of dimensionality and randomization in NUS. These schemes introduce randomization along time and/or quadrature phase dimensions. The sampling schemes developed here are not intended for use in NMR experiments, but they do provide a useful perspective on the importance of decoherence and its relation to dimensionality. Our results reveal the utility of quadrature phase as an additional degree of freedom, through which randomization can further reduce coherence in NUS schemes and thereby reduce sampling artifacts relative to schedules which do not sample the quadrature phase.

2. Theory

Spectra for NUS data collected on a Cartesian grid spaced at the Nyquist interval are typically estimated using non-Fourier methods that suppress sampling artifacts relative to Fourier methods applied to zero-augmented data. The ability of these methods to suppress artifacts is subject to limitations, principally because of experiment noise. However, the DFT of NUS data (where zeros are used to augment the samples missing from the uniform grid) is a convenient tool for characterizing the relative performance of different sampling schemes because of its particularly simple relationship to the spectrum obtained by DFT of uniformly sampled data. The DFT–Convolution Theorem states that the DFT of zero-augmented NUS data is given by the convolution of the PSF with the DFT spectrum of the corresponding uniformly sampled data set.

Quadrature detection typically used to determine the sign of spectral frequencies requires separate, sequential experiments when used along indirect time dimensions (as opposed to the direct acquisition dimension, where in-phase and out-of-phase detection can be performed simultaneously) [25]. The majority of NUS schemes used to date collect all 2^d quadrature components for each sampled time point for quadrature detection conducted along d indirect dimensions. We recently described random phase detection (RPD, [26]), in which only a single quadrature component is randomly selected for detection from among the 2^d quadrature components, enabling a factor of 2^d reduction in the number of FIDs collected per time index, relative to conventional quadrature detection. RPD is one example of *partial-component NUS*, which as a class, includes any scheme that detects less than 2^d quadrature components for a sampled time point. *Full-component NUS* collects all 2^d components for each sampled time.

Partial-component NUS makes the relationship between the DFT of the zero-augmented NUS data and the PSF more complicated. The DFT–Convolution Theorem no longer applies, and there is no longer a single-valued sampling function from which the PSF can be computed. Instead there are separate sampling functions for each quadrature component of the hypercomplex data. As shown in our previous work [27], the DFT spectrum of zero-augmented partial-component NUS data is given by a linear combination of convolutions, one for each of the sampling functions; a corresponding partial-component PSF may be computed as the aggregate power of the PSFs for the individual sampling functions. In our notation for partial-component NUS, the entries in a d-dimensional partial-component sampling function (for a $(d+1)$-dimensional experiment) are defined by

$$S[k_1,\ldots,k_d]\{\phi\} \tag{1}$$

where $k_i \in \{1,\ldots,m_i\}$ is the index along indirect dimension i up to a maximum increment of m_i and ϕ is the hypercomplex component taken from $\mathcal{P}_d$, which is the set of all 2^d hypercomplex components on d-dimensions. With the real and imaginary components along each dimension referred to as "R" and "I", respectively, we have, for example, $\mathcal{P}_2 = \{$"RR", "RI", "IR", "II"$\}$. The k_i values index along the indirect time dimensions and the ϕ value indexes along the "quadrature phase dimension". Entries in S with a value of 1 indicate FIDs that are collected and values of 0 indicate FIDs that are not. Sample coverage (c) is the percentage of FIDs from a uniform sampling grid that are collected by a sample function and is computed as

$$c = \frac{\sum_{k_1,\ldots,k_d,\phi} S[k_1,\ldots,k_d]\{\phi\}}{2^d \cdot (m_1 \cdots m_d)} \tag{2}$$

If a desired sample coverage equates to a non-integer number of FIDs, the number of FIDs collected is rounded up.

3. Methods

Three types of NUS schemes are considered here: random sampling (R), constant-offset undersampling ($\overline{\mathrm{U}}$) and random-offset undersampling ($\widetilde{\mathrm{U}}$). Each of these types is deployed as either full-component ("F" subscript) or partial-component ("P" subscript). The random sample schedules ($\mathrm{R_F}$ and $\mathrm{R_P}$) are generated by the random selection of sample points across the uniform sample grid. The constant-offset ($\overline{\mathrm{U}}_\mathrm{F}$ and $\overline{\mathrm{U}}_\mathrm{P}$) and random-offset ($\widetilde{\mathrm{U}}_\mathrm{F}$ and $\widetilde{\mathrm{U}}_\mathrm{P}$) undersampling schedules are constructed as hypercomplex $(d-1)$-dimensional arrays containing copies of a uniformly undersampled 1D vector, each placed with an index offset along the first indirect dimension; these schedules are collectively referred to as 1D-generated (1DG). With respect to the notation established in Eq. (1), the index along each 1D vector is given by the time index $[k_1]$ and the location of each 1D vector within the hypercomplex $(d-1)$-dimensional array is given by the remaining time indices $[k_2,\ldots,k_d]$ along with the "quadrature phase index" $\{\phi\}$.