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Linear phase correction of folded multidimensional NMR data by zero inter-filling

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Abstract

We describe a procedure to enable linear phase correction of extensively folded multidimensional NMR data. This involves adding zeros in between data points in the indirect dimension to increase the effective bandwidth in the associated spectral window. A standard linear phase correction can then be applied to the data and a properly phased spectrum obtained after additional shuffling of the data in many instances.

Keywords: Linear phase error; NMR data reduction; Phase correction; Zero inter-filling

1. Introduction

In multidimensional NMR methods it can sometimes be useful to undersample the data in an indirect dimension to reduce the total experiment time or data file size. This approach was applied early in the development of 2D methods [1], and is now especially relevant for some 3D methods. An example might be a situation where the third dimension provides evolution under a chemical shift plus a residual dipolar coupling constant, while another dimension already provides that particular chemical shift alone. To measure the coupling constant then this third dimension only need cover the range of couplings likely to be encountered, thereby reducing the required indirect Nyquist frequency one or two orders of magnitude in comparison to what would be required for the chemical shifts.

When undersampling is employed in this type of situation the frequency spectrum will be extensively folded. This poses a problem when the data needs to have a linear phase correction applied, i.e., one in which the phase correction is a linear function of the spectral frequency. This may be required because of either a necessary or an unintentional non-zero delay in acquiring the first point in the interferogram. Linear phase errors can also be a consequence of an insufficient B_1 field to cover the bandwidth that the observed resonances span. Although the best experimental practice is to arrange for an experiment to result in no needed linear phase correction, it is not uncommon to have acquired a data set over several days to find that its only shortcoming is a linear phase error in one of the indirect dimensions. A method to phase correct such data would be a useful alternative to acquiring a new data set with different timing or without spectral foldover.

2. Phase correction by zero inter-filling

The reason such a data set cannot be phase corrected is simply that the linear phase error of a folded line can be very much greater than its apparent frequency coordinate will indicate. If the data is extensively folded, a standard linear phase correction then cannot be applied. This is illustrated in Fig. 1 where we depict a numerically simulated 2D shift-correlation spectrum in which the indirect dimension t_1 had a significant effective acquisition delay. One line in the center of the spectrum has no phase error, as it is at zero frequency. Lines displaced further from resonance have an increasingly larger phase error. The same spectrum is shown in the next panel,

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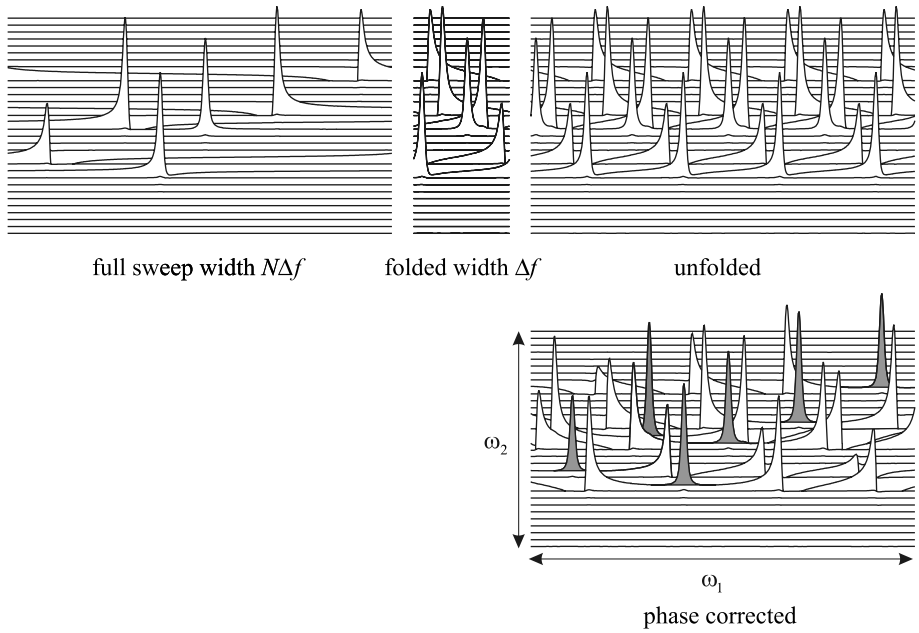

Fig. 1. These data sets were generated using a computer program written in Perl that generates a simulated free-induction decay based on multiplying $\cos(\omega t)$ by a decaying exponential. The simulated data set was then converted into the proper format and processed using Varian VNMR 6.1 as the data reduction software. The upper left panel depicts a 2D correlation spectrum consisting of 6 lines and having a linear phase error due to an acquisition delay in t_1. Sampling this same time domain data at 1/4 the rate gives the next panel after the Fourier transform. The spectral width in ω_1, denoted here as Δf, is 1/4 that in the first spectrum. Zero inter-filling this data, by adding 3 zero points in between all successive t_1 points, brings the Nyquist frequency back to $4\Delta f$. The resulting 2D spectrum in the third panel now has the folded lines repeated every Δf. In each ω_1 slice one of the lines will appear at the actual resonance position. When the linear phase correction is applied, as shown in the bottom right panel, only the lines at the true positions now appear properly phased. These have been shaded in for easy identification.

where the data was undersampled so that the spectrum was folded 4 times over. The line in the center of the spectrum is still purely absorptive, but the phase errors the other lines display bear no direct relation to their frequency coordinate in the folded spectrum.

As long as there is no significant spectral overlap caused by the folding, it is possible to partially unfold the indirect dimension spectrum by adding zeros in between the data points. *Zero inter-filling* by inserting $N-1$ null points between every pair of original data points produces an indirect dimension free induction decay (FID) whose Fourier transform will have N times the bandwidth Δf of the original. The resulting FID is the same that would be obtained if the data were actually taken at this higher sampling rate, but then multiplied by a periodic windowing function $w(t)$ consisting of delta functions every N data points. In essence zero inter-filling produces a FID much like that which is obtained by first oversampling and then decimating the resultant data [2]. The Fourier transform of the zero inter-filled data is the convolution of the Fourier transform of the FID obtained at the higher sampling rate, with the Fourier transform of $w(t)$. Fourier transform of the full FID gives the entire unfolded spectrum, while Fourier transform of $w(t)$ is a picket fence of equally spaced and equally intense lines at a frequency $1/N$ of the full spectral width. Their convolution then simply duplicates the entire spectrum shifted repeatedly by Δf across the full spectral width of $N\Delta f$ [2,3].

This is demonstrated pictorially in the third panel of Fig. 1. To produce this spectrum we started with the undersampled data set that produced the heavily folded 2D spectrum in the second panel. Zero inter-filling the indirect time dimension t_1 twice inserts 3 zeros in between the actual data points. Upon Fourier transformation the spectra in ω_1 now appear as a set of equal intensity sidebands spaced Δf apart, Δf being the spectral width of the folded data in the indirect dimension.

The utility of the zero inter-filling procedure becomes clear when we compare this 2D zero inter-filled spectrum to the original where the data was sampled at the N-fold lower rate, which was sufficiently high to uniquely determine the frequency of every line. In each slice, one of the peaks in the ω_1 spectrum appears at its actual frequency. That particular line will then become absorptive when the correct linear phase correction corresponding to the acquisition delay in t_1 is applied. The replicate lines will of course not phase properly, but as long as the original Δf was large enough to avoid significant overlap in ω_1 this will be easy to recognize. When the proper phase correction for one off-resonance line in a single ω_1 slice is applied, there will be one properly phased line in all the other ω_1 slices. This is

shown in the fourth panel in Fig. 1, where a linear phase correction has now been applied to the zero inter-filled 2D spectrum. The peaks appearing at the actual peak positions are now absorptive as desired. When the data is sparse enough a phase corrected 2D map of the folded data can be reconstructed by picking out the phased sections Δf in width in each ω_1 slice. In the situation described earlier where the two frequencies being correlated differ only by a small coupling constant, the properly phased lines will be easy to recognize as they will be those close to the diagonal in the unfolded spectrum.

There are of course limitations to this approach to repairing undersampled data having a linear phase error. The spectra in ω_1 must either be sparse, or at least highly resolved. In solution NMR applications it is unlikely that all of the lines in an ω_1 slice will actually originate from the same Δf window, and therefore will appear properly phased in different sections of the zero inter-filled spectrum. As long as the lines are well resolved this is only a limitation if the purpose is to obtain an artistically pleasant picture of the 2D spectrum. Recognizing which Δf window a particular line is properly phased in is straightforward. If a line requires a phase correction $\Delta\varphi$ to appear absorptive, in the nth replication it will be rotated by $n\Delta\varphi$. As demonstrated in Fig. 1 the properly phased line will have the maximum intensity, while those on either side will be progressively more out of phase, and thus lower in amplitude.

Phasing errors can be a significant source of uncertainty in determining peak positions [4]. Application of the zero inter-filling method to facilitate a linear phase correction on folded multidimensional data used to measure residual dipolar couplings then should result in more accurate results and improved structures. This method may also have some utility for high-dimensional spectra that are aliased to reduce the overall time required for the experiment [5]. In spectra where all of the peaks lie near to the diagonal, this method could be used as an alternative to other methods of deconvoluting undersampled spectra, such as in FOCSY [1]. In solid state NMR the method should find some application in multiple quantum magic angle spinning (MQMAS) NMR spectroscopy. In this type of spectroscopy there are typically a small number of lines, and the various MQMAS transitions are usually well resolved. In such spectra the slices could typically be separated when applying the linear phase correction as described.

As with any Fourier transform based data processing technique, there are several other possible approaches to this problem. A frequency domain equivalent for instance would be to concatenate copies of the original folded frequency domain spectrum end to end, and then to apply the phase correction in the manner described. Many of the alternatives to the Fourier transform in principle could similarly be adapted to provide the means to obtain proper linear phasing corrections for each line. Our intent here has not been to provide an exhaustive study of the solutions to the problem of linear phasing of folded data sets, and we would not claim the method presented here will work in every situation that might be encountered, nor that it is even the most computationally efficient. Zero inter-filling does however provide an extremely convenient and easy to implement solution. One only need add the appropriate number of zeros in between the experimental time domain data points, and then process the data using the Fourier transform based NMR data processing package of one's preference.

3. Summary

A number of situations arise in which it is desirable to intentionally fold multidimensional NMR data. If a linear phase error is present, either inadvertent or intentional, the zero inter-filling method proposed here provides a convenient means of artificially increasing the indirect dimension Nyquist frequency. In many instances this is sufficient to make linear phase correction of lines in the subsequent 2D spectrum possible when using standard Fourier transform based processing software.

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