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Optimal Filtering in Fourier Transform NMR

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It has been suggested that convolution functions other than Ernst's optimal matched filter may be efficacious for resolution enhancement of NMR spectra. For the purposes of comparison, the possible line distortions and signal-to-noise and resolution enhancement ratios in the Ernst filter are explicitly derived. The general limitation inherent in the digital transformation on the minimum linewidth obtainable by any convolution filter is also derived.

Several recent publications (*1–6*) have suggested that convolution functions other than the optimal matched filter proposed by Ernst (*7*) may be effective in enhancing the resolution of NMR spectra. In spite of continued progress in increasing the field strength of spectrometers, such enhancement techniques are likely to remain useful or necessary for much high-resolution NMR, and the establishment of the conditions for enhancements is therefore of considerable practical importance. A common misconception concerning the Ernst filter is that an exact knowledge of the original lineshapes is required. We show mathematically that such an exact estimate is unnecessary and that any resulting line distortion is negligible. We also calculate the limitations on enhancement inherent in the digital transformation, and the linewidth, signal to noise, and distortion resulting from application of the Ernst filter. We point out that the original Ernst filter is easily programmable, and its calculation can be as rapid as any other.

We are concerned with filtering a given function into another weakly defined function. Although the discussion in this article is concerned with Fourier transform NMR (FTNMR), most of the results are clearly independent of this topic. We assume that we begin with an input signal, a free-induction decay, $F(t)$ a function of time t, and its associated Fourier cosine transform, the spectrum, $f(s)$ a function of frequency s. It is assumed that peaks exist in $f(s)$ which are not resolved and that we wish to filter $f(s)$ into $\mathbf{f}(s)$ so that the unresolved peaks in $f(s)$ are resolved in $\mathbf{f}(s)$. We also require that this filtering process maintain a maximal signal-to-noise (S/N) ratio.

By "resolved" we mean that the separation of peaks is greater than some measure of their linewidth. The choice of the measure of peakwidths is somewhat arbitrary, but the customary measure (W) of full width at half height is inadequate for our present purposes since it depends on only two points of the lineshape function. Instead we have chosen the continuous measure of energy bandwidth, β, as the

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measure of linewidth

$$\beta = \frac{2\pi \int F^2\,dt}{\left[\int F\,dt\right]^2}. \qquad [1]$$

This parameter, β, has the desirable properties that it is an integral property of the lineshape and is mathematically tractable. It is the width of a rectangle whose height is equal to the height of the input signal and whose energy bandwidth is equal to the energy bandwidth of the input line; i.e.,

$$\beta[f(0)]^2 = \int [f(s)]^2\,ds. \qquad [2]$$

For Lorentzian lines this definition reduces to

$$\beta = W\pi/4. \qquad [3]$$

Using the above definitions and assumptions, Ernst (*7*) has shown that there exists an optimal filter which satisfies the following criteria: (1) The linewidth is measured by the energy bandwidth; (2) S/N is maximal for a given filtered linewidth; (3) the filter is linear; (4) $F(t)$ is a continuously differentiable function of t and $F(t)$ is integrable over the half-open interval $[0, \infty)$; (5) the noise is assumed to be white, i.e., the noise density function is uniformly distributed over the frequency space. This filter is given by

$$g(t) = \frac{c(q)F(t)}{1 + F^2(t)}, \qquad [4]$$

where q is an enhancement parameter with values in $[0, \infty)$ and $c(q)$ is a normalization function depending on the enhancement factor q alone.

It should be noted that nonlinear filters are excluded from discussion because their use inevitably leads to the generation of spurious peaks.

The input signals for FTNMR may be assumed to be Lorentzian lines of width 2a. The optimal filter for resolution enhancement with maximal signal to noise is then

$$g(t) = \frac{c(q)\,e^{-at}}{1 + q\,e^{-2at}}. \qquad [5]$$

The filtered output signal, $\mathbf{f}(s)$, may be calculated exactly in some cases. In general, however, the initial linewidth, 2a, is unknown, and α, an estimate of a, must be used:

$$g(t) = \frac{c(q)\,e^{-\alpha t}}{1 + q\,e^{-2\alpha t}}. \qquad [6]$$

For $q > 0$ and $\alpha > a$ we may obtain the lineshape $\mathbf{f}$ as

$$\mathbf{f}(s) = \int F(t)g(t)\,e^{ist}\,dt. \qquad [7]$$

To obtain a more useful representation of $\mathbf{f}(s)$, [7] may be integrated using the theory of residues (*8*) in the complex plane around a contour, Γ, describing the rectangle between $(R, 0i)$, $(R, i\pi/\alpha)$, $(-R, i\pi/\alpha)$, and $(-R, 0i)$, where R is a positive real number greater than $\log(q)$; i.e.,

$$\Gamma=\left[|z|<R, \operatorname{Im}(z)=0 \text{ or } \frac{i\pi}{\alpha}\right] \cup \left[z=R+iy, 0<y<\frac{i\pi}{\alpha}\right]. \qquad [8]$$

From this calculation we obtain

$$\mathbf{f}(s)=\frac{c\pi q^{[is-a-\alpha]/2a}}{2\alpha \cos(\pi[is-a]/2\alpha)}. \qquad [9]$$

The filtered spectrum Φ, which in general is a function of frequency s, the experimental linewidth a, the postulated linewidth α, and the enhancement factor q, is given by the real part of $\mathbf{f}(s)$,

$$\operatorname{Re}(\mathbf{f})=\frac{c\pi q^{-(a+\alpha)/2\alpha}(\cos(rs)\cosh(ps)\cos(pa)+\sin(rs)\sinh(ps)\sin(pa))}{\alpha(\cosh(2ps)+\cos(2pa))} \qquad [10]$$

where $p=\pi/2\alpha$ and $r=\log(q)/2\alpha$. In addition to this general form for Φ, we require the form when $a=\alpha$; i.e., we wish to evaluate $\lim \Phi(s, a, \alpha, q)=\lim \operatorname{Re}(\mathbf{f})$ as $\alpha \to a$. Note that the integrand in [7] is square integrable over the positive part of the real line and is less in absolute value than $k \exp(-wt)$ for some positive values of k and w; therefore the dominated convergence theorem (*8*) applies so that

$$\lim_{a\to\alpha} \Phi(s, a, \alpha, q)=\Phi(s, a, a, q). \qquad [11]$$

Thus the case of the matched resolution enhancement filter may be calculated as the limit as α approaches a to give

$$\Phi(s, a, a, q)=\frac{\pi \sin(\log(q)s/2a)}{a \log(q) \sinh(\pi s/2a)}, \qquad [12]$$

where we have used the requirement that the filter be height preserving to calculate the normalization function $c(q)$ as $2/\log(q)$. The function Φ has a removable singularity at $s=0$, where for continuity we define $\Phi(0, a, a, q)=1/a$. Qualitatively the shape of the signal is that of an exponentially damped cosine wave with asymptotic decay constant of $\pi/2a$ and oscillatory at frequency $\log(q/2a)$, i.e., a peak with wiggles on the baseline.

To obtain physically interesting properties of the filtered lineshape relevant to the NMR experiment it is necessary to approximate the transcendental equation [10] over various parameter ranges. For the lineshape given in [6] we calculate the asymptotic effects of using a mismatched filter: the asymptotic linewidth, the asymptotic signal to noise, and the distortion for $a<\alpha$.

Mismatched Filters

The effect of mismatching the filter by using $\alpha=a+\varepsilon$, where $0<\varepsilon \ll a$, is easily calculated by a regular perturbation scheme. We wish to find a simple expression for $\Phi(s, a, a+\varepsilon, q)$ when ε is a small positive parameter. To accomplish this, we expand between $(R, 0i)$, $(R, i\pi/\alpha)$, $(-R, i\pi/\alpha)$, and $(-R, 0i)$, where R is a positive real number greater than $\log(q)$; i.e.,

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where $p = \pi/2\alpha$ and $r = \log(q)/2\alpha$. In addition to this general form for Φ, we require the form when $a = \alpha$; i.e., we wish to evaluate $\lim \Phi(s, a, \alpha, q) = \lim \mathrm{Re}(\mathbf{f})$ as $\alpha \to a$. Note that the integrand in [7] is square integrable over the positive part of the real line and is less in absolute value than $k \exp(-wt)$ for some positive values of k and w; therefore the dominated convergence theorem (*8*) applies so that

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$$\Phi(s, a, a+\varepsilon, q) = [1+(\varepsilon/a)]\Phi(s, a, a, q) + g(s)(\varepsilon/a)^2. \qquad [13]$$

The function $g(s)$ is the error in the approximation of the function Φ by a two-term Taylor series and is easily seen to be bounded uniformly in s by

$$|g(s)| \leqq \frac{\|\Phi(s, a, a, q)\| (\log[q])^2}{8}; \qquad [14]$$

i.e., a slight mismatch in the filter results only in a small perturbation of the amplitudes, leaving the lineshape function intact. In practice, mismatches of a and α of the order of $\leq 10\%$ result in spectra that are insignificantly different for cases such as those discussed later.

Linewidth

Calculation of the asymptotic linewidth is another perturbation and the result is that the first zero of $\Phi(s, a, a, q) = 1/2a$ is at

$$s = \frac{1.56a}{(1+2[\log(q)/\pi]^2)^{1/2}} \qquad [15]$$

and so for an input linewidth of $2a$ Hz the output linewidth will be given by

$$\Delta = \frac{3.5a}{\log(q)} \qquad [16]$$

for the full width at half height.

Signal-to-Noise Ratio

Yet another application of perturbation theory gives the asymptotics for the change in the signal-to-noise ratio of the optimally matched resolution enhancement filtered spectra to the unfiltered spectra.

$$\Psi = \frac{2(1+q)^{1/2} \log(q)}{q} \qquad [17]$$

or in terms of a and Δ

$$\Psi = \frac{7.0a\, e^{-1.75a/\Delta}}{\Delta}. \qquad [18]$$

Distortion

The distortion generated by a filtering process may be defined in several ways (*7*). For our purposes in this paper, we define the distortion, η, as the maximum deviation of the filtered signal below the baseline normalized by the constant amplitude at the center of the peak.

$$\eta(q)=\frac{\max(-\Phi(s, a, a, q))}{\Phi(0, a, a, q)}. \qquad [19]$$

Thus if the peak remains positive after filtering the distortion will be zero, and if there are wiggles on the filtered signal, the distortion will be the ratio of the amplitude of the largest wiggle to the amplitude of the center of the peak. It is clear that for the optimally matched resolution enhancement filter the maximum of the wiggles will occur between the first two zeros of the equation $\Phi(s, a, a, q)=0$. For $q \gg \exp(\pi)$ we may calculate this distortion asymptotically to obtain

$$\eta(q)=\frac{\pi \operatorname{csch}[3\pi^2/2\log(q)]}{\log(q)}, \qquad [20]$$

which has as an asymptote $\eta=2/(3\pi)\approx 21\%$. Thus for the optimal matched resolution enhancement filter, the distortion, i.e., the maximum deviation of the filtered lineshape below the baseline, is always less than one-fifth the height of the original signal.

We need to estimate the effects of a digital representation of the input data. It is obvious that one cannot increase the resolution beyond the limit allowed by the datablock size, i.e., we have a limit Λ_1, in achievable resolution

$$\Lambda_l=2\Xi/N, \qquad [21]$$

where Ξ is the sweep width and N is the number of data points in the FID. For data which are exactly represented in the ordinate axis and for a fixed sweep rate, increasing the number of data samples, N, will reduce inversely this bound on the achievable resolution.

It may be noted that while this limit on resolution in terms of peak separation is quite strict it is usually possible to discriminate more precisely than Λ_1 by using line-fitting procedures which assume a lineshape.

A more restrictive limit of enhancement, Λ_2, is brought about by the digitization in the vertical axis. Assume that we have a w-bit computer and that the FFT algorithm is based on an integer data representation. Also assume that the data have been collected in such a way that the limits of the digitizer resolution are negligible (as is usually the case in FTNMR (*9*)); then we can calculate Λ_2 in the following manner. Consider an input signal $F(t)=\exp(-at)$. Let us accumulate data, with each single scan lasting a time t^*, so that $\exp(-at^*)<2^{1-w}$, i.e., after t^* seconds the computer represents $F(t)$ as strictly zero. Then the spectrum after filtering with any linear filter $g(t)$ will be given by

$$f(s)=\int_0^{t^*} g(t)\, e^{t(-a+is)}\, dt. \qquad [22]$$

Assume that we have performed the optimal resolution enhancement so that

$g(t)\exp(-at) = 1$ for $t < t^*$. Then $f(s)$ is given by

$$f(s) = (\sin(ks))/s, \tag{23}$$

where $k = (\log 2)(w-1)/a$ and $f(0) = k$. The abscissa s^* such that $f(s^*) = \frac{1}{2}f(0)$ is given by

$$ks^* = 0.32 + \pi/2 = 1.89 \tag{24}$$

and this implies a full width at half height of

$$\Lambda_2 = 3.78/k \tag{25}$$

and a maximal achievable resolution enhancement factor, E, for any filtering technique given by

$$E = \frac{\text{input linewidth}}{\Lambda_2} = 0.36(w-1). \tag{26}$$

Table 1 gives some values of the enhancement factor E for various values of the word length w.

For example, if one accumulates a free-induction decay of a 10-Hz Lorentzian line with a dwell time of 0.0005 sec on a computer with a 20-bit word, then after approximately 2.634 sec or 5268 data points, the signal will be represented as strictly zero. This implies that the optimal resolution enhancement for any filtering process would be less than 6.9; i.e., the 10-Hz line could not be filtered to less than 1.5 Hz regardless of the type of filtering used. This limitation has been experimentally verified by calculating lineshapes using a floating-point algorithm from a calculated input masked to the various word sizes.

Given a fixed word length, two methods of circumventing this limitation are to use a floating-point averaging technique and to use multiple-precision averaging. Clearly the floating-point representation is the better technique as it generally maintains a higher dynamic range of the data. Note that the precision and dynamic range of these representations must be maintained for all subsequent calculations after the acquisition. As the cost of solid-state memory and other computer components continues to decline and as more complex problems are tackled in NMR techniques, the desirability of a spectrometer–computer with a hardwired floating-point processor and a 32-bit or larger word would seem to be very great.

TABLE 1

Word length w (bits)	Maximal enhancement factor E
8	2.5
16	5.4
20	6.9
32	11.2
64	22.7
Floating point 10-bit exponent, 30-bit mantissa	130.0

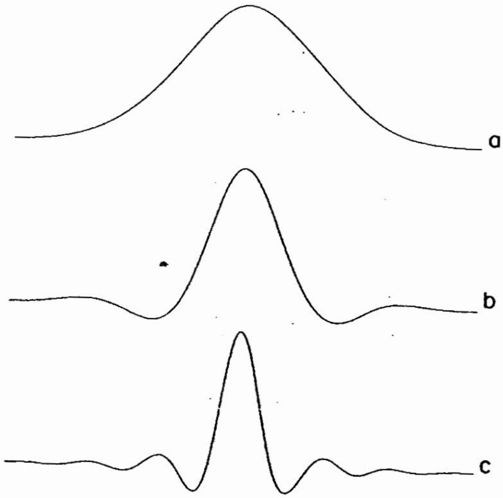

FIG. 1. The calculated lineshapes shown are for a 5-Hz Lorentzian input line filtered with the optimal resolution enhancement filter function. The width of display is 10 Hz (a) $q = 10.0$, (b) $q = 100.0$, (c) $q = 10{,}000$.

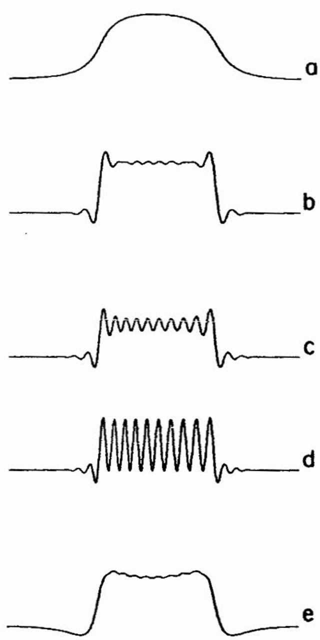

FIG. 2. Ten Lorentzian lines with linewidths of 5 Hz separated from each other by 2 Hz were subjected to various filtering procedures. The spectral width is 50 Hz. Spectra (b), (c), and (d) are filtered with the optimal matched resolution enhancement filter with a linewidth of 2 Hz. (a) Normal (unfiltered) spectrum. (b) $q = 1.0E5$. (c) $q = 1.0E6$. (d) $q = 1.0E7$. (e) sinebell filtering.

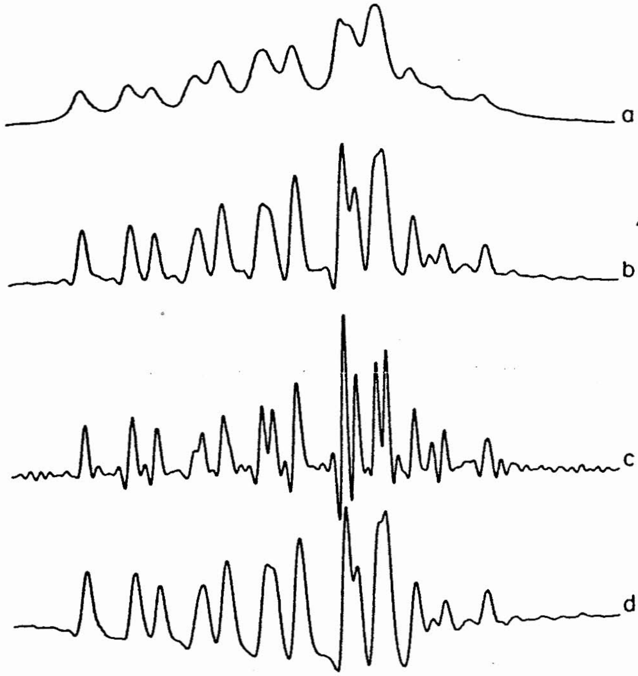

FIG. 3. Effects of filtering are demonstrated on a spectrum of the peptide arginine vasopressin. This sample was run at 20°C in deuterium oxide at a pD of 3.8 on a Bruker WH-360 spectrometer. The region shown contains the β protons of Cys^6, Phe^3, Tyr^2, and Asn^5. (a) Normal spectrum, signal-to-noise (S/N) = 375. (b) Resolution-enhanced spectrum using the Ernst filter with parameters $1 = 2.8$ Hz and $q = 400$, S/N = 275. (c) Same filtering as in (b) but with a q of 100,000, S/N = 40. (d) Sinebell filtering, S/N = 161.

We present several examples of the filtering process for an overview of current filtering methods. Figure 1 displays the lineshapes to be expected from the optimally matched resolution enhancement filter as a function of the enhancement factor q. Figure 2 shows an extreme case in which the input signal is the sum of 10 Lorentzian lines of full width at half height of 5 Hz, all equal in amplitude and of constant separation of 2 Hz. The excellence of the calculated result (d) should be tempered by the fact that for a final signal-to-noise ratio of over 10 to 1, an initial signal-to-noise ratio of over 2000 to 1 is required. This example was unresolvable by other enhancement techniques (*2*). Figure 3 shows the effects of filtering on a 360-MHz proton sample of [8-arginine]vasopressin. A sine-bell-filtered spectrum is included for comparison.

Implementation of the optimally matched resolution enhancement filter on a digital computer is trivial if one uses a floating-point algorithm, but on most minicomputers in common use with NMR spectrometers the execution times using this method are very long. As an alternative, a fixed-point algorithm may be used but care must be taken to scale the filtered data so that the complete word length of the computer is utilized. The method used in this laboratory is first to compute

$$K = 2^{1-w} \max(g(j)F(j)), \qquad [27]$$

where j varies over all the data. Then the use of the renormalized filtering function

$$g^*(t) = g(t)/K \qquad [28]$$

will utilize the full word length of the computer, for now

$$\max(fg^*) = \max(fg/K) = 2^{w-1}. \qquad [29]$$

A scheme for maintaining scaling factors for derivation of absolute intensities is obviously feasible. The filtering function used in the fixed-point algorithm is first calculated exactly for a 128-word table and the intermediate values are interpolated linearly. For all cases we have investigated, the degree of accuracy permitted by the algorithm has proved sufficient, as have similarly sized tables in other applications (*10*).

In conclusion, we have shown analytically and experimentally that the matched resolution enhancement filter is optimal. The only drawback to its application is the requirement of *a priori* knowledge of the linewidth, but this objection is relatively mild so long as a reasonable estimate of the linewidth is available.

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