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Construction of Phase Cycles of Minimum Cycle Length: MakeCycle[1]

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An algorithm for the generation of a phase cycle of minimum length for a pulse sequence is developed from the basic requirement that only specified coherence transfer pathways will be accumulated. The efficacy of the algorithm is shown by determining the phase cycles of minimum length for DQFCOSY, GHMBC, and INEPT pulse sequences. © 2000 Academic Press

Key Words: **pulse sequence; phase cycle; DQFCOSY; INEPT; GHMBC.**

INTRODUCTION

The creation of a new pulse sequence to obtain information about one particular process and/or one type of molecular fragment always involves the invention of a program for the cycling of the phases of the pulses and receiver (a phase cycle) in order to achieve the desired selectivity. In their ground-breaking paper on coherence transfer pathways and phase-cycling, Bodenhausen *et al.* (*1*) described the evolution of the spin system during the pulse sequence from the initial longitudinal magnetization of one of the nuclei present until transverse magnetization is detected as travel along a coherence transfer pathway. If coherences which follow a particular coherence transfer pathway m experience a change, Δp_{mn}, in coherence level when the nth pulse in the pulse sequence is applied, their signals acquire a phase factor $\exp(-i\Delta p_{mn}\phi_{nl})$, where ϕ_{nl} is the phase of the pulse in the lth step in the phase cycle. For a pulse sequence which has N pulses, M possible pathways, and a phase cycle of length L, the phase factor, $\mathscr{A}_{ml}$, for signals from the mth pathway in the lth step in the cycle, including the receiver phase factor $\exp(-i\phi_{Rl})$, is

$$\mathscr{A}_{ml} = \exp(-i \sum_{n=1}^{N} \Delta p_{mn}\phi_{nl} - i\phi_{Rl}). \quad [1]$$

The phases $\{\phi_{nl}, \phi_{Rl}\}_{l=1}^{L}$ must be chosen so that

$$\sum_{l=1}^{L} \mathscr{A}_{ml} = \begin{cases} LC_m & \text{if } m \text{ is a selected pathway,} \\ 0 & \text{otherwise,} \end{cases} \quad [2]$$

where C_m is a complex constant (usually 1) which reflects the phase of the signal acquired for selected pathway m. Bodenhausen *et al.* (*1*) showed that if the phase ϕ_{nl} of the nth pulse is cycled independently of other pulses through values

$$\phi_{nl} = \frac{2\pi(l-1)}{L_n} \quad [3]$$

for $l = 1, \ldots, L_n$, with corresponding receiver phases

$$\phi_{Rl} = -K\phi_{nl}, \quad [4]$$

only pathways for which the coherence level changes caused by the nth pulse are

$$\Delta p_{mn} = K \pm kL_n, \quad [5]$$

where $k = 0, 1, \ldots,$ are selected. These ideas imply that one can construct a phase cycle which selectively acquires signals which have traversed a particular coherence transfer pathway defined by the coherence level changes $\Delta p_1, \Delta p_2, \ldots, \Delta p_N$ by superimposing independent cycles of each of the pulses with suitable receiver phase. However, in many pulse sequences, the phases of some pulses are held fixed throughout and/or the phases of other pulses are cycled in concert. Clearly the creation of an effective phase cycle still remains a rather intuitive endeavor and the length of a phase cycle rather empirical.

A properly constructed phase cycle must effectively suppress signals which arise from coherences which follow undesired pathways, while accumulating signals from the selected pathway(s). Pulse imperfections open up large numbers of coherence transfer pathways which are not accessible with perfect pulses, and signals arising from all such pathways must be suppressed by the phase cycle. The first pulse in any pulse

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sequence is expected to convert longitudinal magnetization (coherence level 0) into transverse magnetization (coherence levels ± 1). If this pulse is a perfect 90° pulse, all of the zero-level coherence is converted into coherences in the ± 1 levels; but if the pulse is an imperfect 90° pulse (or intentionally has a flip angle different from 90°), some zero coherence remains after the pulse. Any 90° pulse applied later in the sequence, whether perfect or imperfect, can convert coherences in any level into coherences in levels $-n, -(n-1), -(n-2), \ldots, n-1, n$, where n is the number of spin-$\frac{1}{2}$ nuclei to which the pulse is applied, i.e., all values of Δp are possible for 90° pulses. When a perfect 180° pulse is applied to one type of nucleus in the spin system, the pulse converts coherences in level p (for that nucleus) to coherences in level $-p$, but when the 180° pulse is imperfect, all values of Δp are possible. Therefore, imperfections in the first 90° pulse and in all 180° pulses provide a large number of pathways whereby spurious signals can reach the detector. The phase cycle must block these pathways as well as the undesired ones which are accessible even with perfect pulses.

Two recent articles (*2, 3*) describe methods for determining the coherence transfer pathways which are selected when a particular pulse program is executed with a given phase cycle. The first article (*2*) uses simulation to identify the selected pathways. In the second article (*3*), the coherence level changes $\{\Delta p_{mn}\}_{n=1}^{N}$ for the selected pathways m are determined directly from the values of the phases in the phase cycle. It was shown (*3*) that the Δp_{mn} must satisfy the set of congruences

$$\sum_{n=1}^{N} \Delta p_{mn}\phi_{nl} + \phi_{Rl} \equiv \mathscr{C}_m \pmod{2\pi},\ l = 1, 2, \ldots, L, \qquad [6]$$

where $\mathscr{C}_m$ is the phase of the acquired signal from selected pathway m. The values of the Δp_{mn} can be determined by solving this set of congruences (*4*). In this article, we use the fundamental congruences [6] to derive a set of conditions which the phases $\{\phi_{nl}, \phi_{Rl}\}_{l=1}^{L}$ must satisfy for *all* possible coherence transfer pathways defined by the coefficients Δp_{mn} and use this as the basis for construction of an algorithm to determine the set of phases which constitutes a phase cycle of minimum length.

THEORY

For a pulse sequence with N pulses, M pathways, and a phase cycle of length L, the phase of the signal Φ_{ml} from the mth pathway in the lth step in the cycle will be

$$\Phi_{ml} \equiv \sum_{n=1}^{N} \Delta p_{mn}\phi_{nl} + \phi_{Rl} \pmod{2\pi}, \qquad [7]$$

where ϕ_{nl} is the phase of the nth pulse in the sequence, ϕ_{Rl} is the phase of the receiver, and Δp_{mn} is the coherence level change caused by the nth pulse to signals traversing the mth pathway. For a "selected" pathway, the phase of the signal must be the same for each of the L steps in the phase cycle so that the signals add constructively. For any "blocked" pathway, the phases of the acquired signals must vary during the phase cycle in such a way that they interfere destructively and the sum of the signals, over the complete phase cycle, is zero. In this article, we will restrict our attention to phase cycles which use modulo 4 arithmetic and define the modular phase variables F and f, which correspond to Φ and ϕ, by

$$F_{ml} = \left(\frac{2}{\pi}\right)\Phi_{ml},$$

$$f_{nl} = \left(\frac{2}{\pi}\right)\phi_{nl},$$

$$f_{Rl} = \left(\frac{2}{\pi}\right)\phi_{Rl}, \qquad [8]$$

so that the modulo 4 equivalent of Eq. [7] is

$$F_{ml} \equiv \sum_{n=1}^{N} \Delta p_{mn} f_{nl} + f_{Rl} \pmod 4. \qquad [9]$$

The accumulated signal for the mth pathway will therefore be proportional to

$$\sum_{l=1}^{L} \exp\left[-\frac{i\pi}{2} F_{ml}\right] = LC_m, \qquad [10]$$

where C_m will be zero if m is a blocked pathway, and C_m will be nonzero if m is a selected pathway. Note that C_m in Eqs. [2] and [10] is a complex constant belonging to the set $(\pm 1, \pm i, 0)$, while $\mathscr{C}_m$ in Eq. [6] is a phase angle which, in principle, can have any value in the range $(0, 2\pi)$. Most often C_m will be equal to 1 for selected pathways, but if signals from more than one path are selected, C_m may depend on the specific pathway. Any phase program $\{\{f_{nl}\}_{n=1}^{N}, f_{Rl}\}_{l=1}^{L}$ which satisfies the M conditions given in Eq. [10] is a suitable phase cycle for the pulse sequence. It is useful to require that the phase cycle also satisfy the requirement that the accumulated signals be free of the detector offset voltage. This additional requirement is met if

$$\sum_{l=1}^{L} \exp\left[-\frac{i\pi}{2} f_{Rl}\right] = 0, \qquad [11]$$

which is equivalent to including, as a blocked pathway, one in which all of the Δp's are zero.

In order to facilitate a concise mathematical description of the problem, it is necessary to express Eq. [9] in matrix form. The phases F_{1l}, F_{2l}, . . . , F_{Ml}, F_{M+1l}, where $F_{M+1l} = f_{Rl}$, are arranged into an $M + 1 \times L$ phase matrix,

$$\mathbf{F} = \begin{pmatrix} F_{11} & F_{12} & \cdots & F_{1L} \\ F_{21} & F_{22} & \cdots & F_{2L} \\ \vdots & \vdots & \ddots & \vdots \\ F_{M1} & F_{M2} & \cdots & F_{ML} \\ F_{M+1\,1} & F_{M+1\,2} & \cdots & F_{M+1\,L} \end{pmatrix}, \qquad [12]$$

so that Eq. [9] can be written as

$$\mathbf{F} \equiv \mathbf{P} \cdot \mathbf{f} \pmod 4, \qquad [13]$$

where the pathway matrix, **P**, is defined by

$$\mathbf{P} = \begin{pmatrix} \Delta p_{11} & \Delta p_{12} & \cdots & \Delta p_{1N} & 1 \\ \Delta p_{21} & \Delta p_{22} & \cdots & \Delta p_{2N} & 1 \\ \vdots & \vdots & \ddots & \vdots & \vdots \\ \Delta p_{M1} & \Delta p_{M2} & \cdots & \Delta p_{MN} & 1 \\ 0 & 0 & \cdots & 0 & 1 \end{pmatrix} \qquad [14]$$

and the pulse/receiver phase array, **f**, by

$$\mathbf{f} = \begin{pmatrix} f_{11} & f_{12} & \cdots & f_{1L} \\ f_{21} & f_{22} & \cdots & f_{2L} \\ \vdots & \vdots & \ddots & \vdots \\ f_{N1} & f_{N2} & \cdots & f_{NL} \\ f_{R1} & f_{R2} & \cdots & f_{RL} \end{pmatrix}. \qquad [15]$$

By choosing $C_{M+1} = 0$, we see that requirement [11] is equivalent to the requirement that the elements in the $(M + 1)$th row of **F** satisfy Eq. [10]. The order of the rows and columns in **P** is arbitrary, but it is expedient to arrange the rows so that the selected pathways form the first S rows of **P**, and the last $M + 1 - S$ rows correspond to pathways which are to be blocked by the phase cycle. A collection vector, **C**, defined by

$$\mathbf{C} = \begin{pmatrix} C_1 \\ C_2 \\ \vdots \\ C_S \\ 0 \\ 0 \\ \vdots \\ 0 \end{pmatrix}, \qquad [16]$$

is constructed from the elements C_m and has dimension $M + 1$.

It must be emphasized that each row in the **P** matrix corresponds to one of the pathways which begins with longitudinal magnetization in the 0 coherence level and ends with transverse magnetization of the appropriate spin in the -1 coherence level. Matrix **P** may include all possible pathways (see DQFCOSY and INEPT examples below) or only those pathways not blocked by a judicious selection of pulsed field gradients (see GHMBC example). It could also be tailored to contain only pathways which are accessed when a specified number of pulses or fewer are imperfect.

The arrangement of rows (and columns) of the arrays **F**, **f**, **P**, and **C** is arbitrary. In the following analysis, the rows and columns of these arrays are reordered in order to obtain transformed arrays which have simple canonical forms. These rearranged matrices will be denoted with primes and will be referred to as the canonical forms of the matrices.

We now seek to determine the minimum number of independent phases (referred to as *key* phases below) which must be determined in order to obtain a satisfactory phase cycle. This process involves the determination of a linear transformation which transforms the matrix **P** into a matrix, $\mathbf{V}'$, whose first K rows and columns form a $K \times K$ unit matrix, where $K \leq N + 1$, and the lower $M + 1 - K$ rows are zero:

$$\mathbf{V}' = \left(\begin{array}{cccc|cccc} 1 & 0 & \cdots & 0 & V'_{1\,K+1} & V'_{1\,K+2} & \cdots & V'_{1\,N+1} \\ 0 & 1 & \cdots & 0 & V'_{2\,K+1} & V'_{2\,K+2} & \cdots & V'_{2\,N+1} \\ \vdots & \vdots & \ddots & \vdots & \vdots & \vdots & \ddots & \vdots \\ 0 & 0 & \cdots & 1 & V'_{K\,K+1} & V'_{K\,K+2} & \cdots & V'_{K\,N+1} \\ \hline 0 & 0 & \cdots & 0 & 0 & 0 & \cdots & 0 \\ 0 & 0 & \cdots & 0 & 0 & 0 & \cdots & 0 \\ \vdots & \vdots & \ddots & \vdots & \vdots & \vdots & \ddots & \vdots \\ 0 & 0 & \cdots & 0 & 0 & 0 & \cdots & 0 \end{array}\right). \qquad [17]$$

This transformation is determined using the algorithm given in Table 1 and is essentially the Gauss–Jordan elimination process (*5*, *6*) with row and column interchange. The required linear transformation is described by two matrices: an $M + 1 \times M + 1$ matrix **Q** which contains the required linear combinations and interchanges of the rows of **P** which produces a $K \times K$ unit matrix in the upper right block of $\mathbf{V}'$ and makes all elements in rows $K + 1, K + 2, \ldots, M + 1$ of $\mathbf{V}'$ zero; and an $N + 1 \times N + 1$ matrix **T** which defines the required column interchanges in the columns of $\mathbf{Q} \cdot \mathbf{P}$ so that the matrix $\mathbf{V}'$ defined by

$$\mathbf{V}' \equiv \mathbf{Q} \cdot \mathbf{P} \cdot \mathbf{T} \pmod 4 \qquad [18]$$

is of the form given in Eq. [17]. The number K of nonzero rows in $\mathbf{V}'$ is related to the number of key phase variables whose cycles must be determined as shown below.

The application of a column ordering transformation **S** to matrix **Q** gives

TABLE 1
Algorithm for Construction of Q′, Q, V′, S, and T Matrices and Determination of *K*

set $\mathbf{V}^{(0)} = \mathbf{P}$, $\mathbf{Q} = \mathbf{1}$.
set $q = 0$.
for[a] $n = 1, N + 1 - q$
  while (column $n + q$ of $\mathbf{V}^{(n-1)}$ contains no element $V^{(n-1)}_{r\,n+q}$ with absolute value 1 for $r \geq n$)[b]
    increment q
  end while
  if ($|V^{(n-1)}_{n\,n+q}| \neq 1$)[b]
    set $\mathbf{R}^{(n)}$ to permute row n with a row n' for which $|V^{(n-1)}_{n'\,n+q}| = 1$
  else
    set $\mathbf{R}^{(n)} = \mathbf{1}$
    set $n' = n$
  end if
  set $V^{(n-1)}_{n'r} \equiv V^{(n-1)}_{n'r} \times V^{(n-1)}_{n'n+q}$ (mod4) for $r = n + q, n + q + 1, \ldots, N + 1$
  initialize $\mathbf{Q}^{(n)} = \mathbf{1}$
  set $Q^{(n)}_{rn} \equiv \begin{cases} -(\mathbf{R}^{(n)} \cdot \mathbf{V}^{(n-1)})_{n\,n+q} \times (\mathbf{R}^{(n)} \cdot \mathbf{V}^{(n-1)})_{r\,n+q} (\mathrm{mod}\ 4) & \text{for } r \neq n \\ (\mathbf{R}^{(n)} \cdot \mathbf{V}^{(n-1)})_{n\,n+q} (\mathrm{mod}\ 4) & \text{for } r = n \end{cases}$
  set $\mathbf{V}^{(n)} \equiv \mathbf{Q}^{(n)} \cdot \mathbf{R}^{(n)} \cdot \mathbf{V}^{(n-1)} (\mathrm{mod}\ 4)$
  replace $\mathbf{Q}$ by $\mathbf{Q}^{(n)} \cdot \mathbf{R}^{(n)} \cdot \mathbf{Q} (\mathrm{mod}\ 4)$
end for n
set $\mathbf{S}$ to permute columns of $\mathbf{Q}$ to block form in Eq. [20]
set $\mathbf{Q}' = \mathbf{Q} \cdot \mathbf{S}$
set $\mathbf{V} = \mathbf{V}^{(N+1-q)}$
set $\mathbf{T}$ to permute columns of $\mathbf{V}$ to block form in Eq. [17]
set $\mathbf{V}' = \mathbf{V} \cdot \mathbf{T}$
set $K = N + 1 - q$

[a] In *for* loops, the upper bound is recalculated at the end of each iteration.
[b] $|3| \equiv 1$ (mod 4). If all possible pathways are included in **P**, this reduction algorithm which restricts pivot elements to those with magnitude 1 will give the required reduction.

$$\mathbf{Q}' = \mathbf{Q} \cdot \mathbf{S}, \qquad [19]$$

where the $\mathbf{Q}'$ matrix is an $M + 1 \times M + 1$ linear transformation matrix of the form

$$\mathbf{Q}' = \left(\begin{array}{ccccc|cccc} Q'_{11} & Q'_{12} & \cdots & Q'_{1\,K-1} & Q'_{1\,K} & 0 & 0 & \cdots & 0 \\ Q'_{21} & Q'_{22} & \cdots & Q'_{2\,K-1} & Q'_{2\,K} & 0 & 0 & \cdots & 0 \\ \vdots & \vdots & \ddots & \vdots & \vdots & \vdots & \vdots & & \vdots \\ Q'_{K-1\,1} & Q'_{K-1\,2} & \cdots & Q'_{K-1\,K-1} & Q'_{K-1\,K} & 0 & 0 & \cdots & 0 \\ 0 & 0 & \cdots & 0 & 1 & 0 & 0 & \cdots & 0 \\ \hline Q'_{K+1\,1} & Q'_{K+1\,2} & \cdots & Q'_{K+1\,K-1} & 0 & 1 & 0 & \cdots & 0 \\ Q'_{K+2\,1} & Q'_{K+2\,2} & \cdots & Q'_{K+2\,K-1} & 0 & 0 & 1 & \cdots & 0 \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \ddots & \vdots \\ Q'_{M+1\,1} & Q'_{M+1\,2} & \cdots & Q'_{M+1\,K-1} & 0 & 0 & 0 & \cdots & 1 \end{array}\right). \qquad [20]$$

All elements in the upper right $K \times (M + 1 - K)$ portion of $\mathbf{Q}'$ are zero. The elements of the lower left $(M + 1 - K) \times K$ portion of $\mathbf{Q}'$ will be shown below to define important relationships from which the phase cycle can be determined, and the elements of the lower right $(M + 1 - K) \times (M + 1 - K)$ portion of $\mathbf{Q}'$ form a unit matrix. The upper left $K \times K$ portion of $\mathbf{Q}'$ is a matrix which is the inverse of the upper left $K \times K$ portion of the matrix $\mathbf{P}'$ defined by

$$\mathbf{P}' = \mathbf{S}^{\dagger} \cdot \mathbf{P} \cdot \mathbf{T}, \qquad [21]$$

where $\mathbf{S}^{\dagger}$ is the transpose of $\mathbf{S}$. $\mathbf{P}'$ is a pathway matrix in which the rows and columns are ordered in a more optimum manner than in $\mathbf{P}$. Congruence [18] can be rewritten as

$$\mathbf{V}' \equiv \mathbf{Q}' \cdot \mathbf{P}' \ (\mathrm{mod}\ 4). \qquad [22]$$

It is convenient to define reordered or canonical forms of the pathway array

$$\mathbf{F}' = \mathbf{S}^{\dagger} \cdot \mathbf{F}, \qquad [23]$$

pulse/receiver phase array

$$\mathbf{f}' = \mathbf{T}^{\dagger} \cdot \mathbf{f}, \qquad [24]$$

and collection array

$$\mathbf{C}' = \mathbf{S}^{\dagger} \cdot \mathbf{C}, \qquad [25]$$

where $\mathbf{T}^{\dagger}$ is the transpose of $\mathbf{T}$, so that Eqs. [13] and [10] can be written as

$$\mathbf{F}' \equiv \mathbf{P}' \cdot \mathbf{f}' \ (\mathrm{mod}\ 4) \qquad [26]$$

and

$$\sum_{l=1}^{L} \exp\left[-\frac{i\pi}{2} F'_{ml}\right] = LC'_m. \qquad [27]$$

It should be noted that the **S** matrix is constructed in such a way that any of the first K rows of $\mathbf{F}'$ for which the corresponding elements of $\mathbf{C}'$ are nonzero precede rows for which the corresponding elements of $\mathbf{C}'$ are zero.

From Eqs. [22] and [26],

$$\mathbf{V}' \cdot \mathbf{f}' \equiv \mathbf{\Psi} \ (\mathrm{mod}\ 4), \qquad [28]$$

where the phase array $\mathbf{\Psi}$ is defined by

$$\mathbf{\Psi} \equiv \mathbf{Q}' \cdot \mathbf{F}' \ (\mathrm{mod}\ 4). \qquad [29]$$

If the elements of $\mathbf{\Psi}$ were known, one could determine the elements of the pulse and receiver phase array $\mathbf{f}'$ by solving Eq. [28]. Examination of the form of matrix $\mathbf{V}'$ (Eq. [17]) shows that only the first K rows are nonzero and that the determinantal rank of matrix $\mathbf{V}'$ is K. This implies that there are $N + 1 - K$ degrees of freedom in the determination of the $N + 1$ rows of $\mathbf{f}'$: only K of these rows are linearly independent, and the remaining $N + 1 - K$ rows may be assigned arbitrarily (*5*). It is convenient to choose the lower $N + 1 - K$ rows of $\mathbf{f}'$ as the arbitrary rows and set them to zero so that

$$f'_{jl} = \begin{cases} \Psi_{jl} & \text{for } 1 \le j \le K, \\ 0 & \text{for } K + 1 \le j \le N + 1. \end{cases} \qquad [30]$$

Since the lower $N + 1 - K$ rows of $\mathbf{V}'$ are zero, the corresponding rows of $\boldsymbol{\Psi}$ are also zero. Equation [30] implies that the determination of the first K rows of $\boldsymbol{\Psi}$ is equivalent to the determination of the linearly independent rows of $\mathbf{f}'$.

The Kth row of $\mathbf{f}'$ (and $\boldsymbol{\Psi}$) contains the receiver phases for each step of the phase cycle. The values must be chosen to satisfy Eq. [11], and they can be chosen to be

$$f'_{Kl} = \Psi_{Kl} = (0\ 2\ 1\ 3\ 0\ 2\ 1\ 3 \ldots 0\ 2\ 1\ 3) \qquad [31]$$

independent of the values of all other phases.

In order to determine the phases $\Psi_{\alpha l}$, we recognize that $\Psi_{\alpha l}$ is identically zero for $\alpha > K$ (see Eqs. [17] and [28]) and that the αth row of $\mathbf{Q}'$, for $\alpha > K$, contains nonzero elements only in columns $\mu = 1, 2, \ldots, K - 1$ and $\mu = \alpha$ (Eq. [20]). From the definition of $\boldsymbol{\Psi}$, Eq. [29],

$$\sum_{\mu=1}^{K-1} Q'_{\alpha\mu} \cdot F'_{\mu l} + F'_{\alpha l} \equiv 0 \pmod 4 \qquad [32]$$

for $K + 1 \le \alpha \le M + 1$. Hence,

$$F'_{\alpha l} \equiv -\sum_{\mu=1}^{K-1} Q'_{\alpha\mu} \cdot F'_{\mu l} \pmod 4, \qquad [33]$$

and, from Eq. [27],

$$\sum_{l=1}^{L} \exp\left[\frac{i\pi}{2} \sum_{\mu=1}^{K-1} Q'_{\alpha\mu} \cdot F'_{\mu l}\right] = LC'_{\alpha}. \qquad [34]$$

The phases $F'_{1l}, F'_{2l}, \ldots, F'_{K-1l}$ are henceforth referred to as *key* phases since all phases $F'_{\alpha l}$, for $\alpha > K$, are just linear combinations of these key phases (see Eq. [33]).

Equation [34] defines the fundamental relationships which the $K - 1$ key phases must satisfy. It is important to recognize that the index α in Eq. [34] takes on values $K + 1, K + 2, \ldots, M + 1$, and that the additional requirements which the key phases must satisfy are given in Eq. [27]. These two sets of requirements can be included in a single equation,

$$\sum_{l=1}^{L} \exp\left[-\frac{i\pi}{2} \sum_{\mu=1}^{K-1} X_{\alpha\mu} \cdot F'_{\mu l}\right] = LC'_{\alpha}, \qquad [35]$$

where the $(M + 1) \times K$ matrix $\mathbf{X}$ has elements

$$X_{\alpha\mu} \equiv \begin{cases} \delta_{\alpha\mu} & \text{for } 0 \le \alpha \le K, \\ -Q'_{\alpha\mu} \pmod 4 & \text{for } K + 1 \le \alpha \le M + 1. \end{cases} \qquad [36]$$

The determination of the phase cycle for the pulse sequence is therefore reduced to the determination of the elements of the key phases which satisfy Eq. [35].

The determination of the elements of the key phases $F'_{\mu l}$ is not a trivial task. From the outset, the task seems impossible: the length L of the phase cycle is not known since we seek a phase cycle of minimum length; and it would appear that one must solve a myriad of transcendental Eqs. [35] in an unknown number of variables $F'_{\mu l}$. However, an iterative process to determine L and $F'_{\mu l}$ has been devised and is presented below.

In order to begin the solution process, it should be recognized that F'_{1l} is constant for all l because the first row of the pathway matrix $\mathbf{P}'$ and the collection vector $\mathbf{C}'$ corresponds to one of the collected pathways. Therefore one begins with $L = 1$ and chooses the value of F'_{11} consistent with the value of C'_1. It is easiest to describe the iterative key phase determination process by considering the determination of the jth row of the phase matrix $\mathbf{F}'$. One assumes that phases $F'_{1l}, F'_{2l}, \ldots, F'_{j-1l}$ are known for $0 \le l \le L$, where L is the length of the phase cycle which has been obtained in the determination of the elements F'_{j-1l}. (The process begins with $j = 2$, given $L = 1$ and F'_{11} consistent with C'_1.) To determine the phases F'_{jl}, one selects from Eq. [35] those relations which involve only the known key phases $1, 2, \ldots, j - 1$ and phase j, i.e., those for which $X_{\alpha j} \neq 0$ and $X_{\alpha\mu} = 0$ for $j < \mu \le K$. If there are n_1 rows of matrix $\mathbf{X}$ in which the jth element equals 1 or 3 and in which the $(j + 1)$th and higher elements are zero, Eq. [35] yields a set of n_1 simultaneous equations

$$\mathbf{A}^{(1)} \cdot \vec{\mathbf{B}}^{(1)} = \vec{\mathbf{G}}^{(1)} \qquad [37]$$

in the unknown variables $B_l^{(1)}$, where $\vec{\mathbf{B}}^{(1)}$ is a vector of dimension L with elements

$$B_l^{(1)} = \left\{\exp\left[-\frac{i\pi}{2} F'_{jl}\right]\right\}^1, \qquad [38]$$

$\mathbf{A}^{(1)}$ is a matrix of dimension $n_1 \times L$ with elements

$$A_{\alpha l}^{(1)} = \exp\left[-\frac{i\pi}{2} \sum_{k=1}^{j-1} X_{\alpha k} \cdot F'_{kl}\right], \qquad [39]$$

and $\vec{\mathbf{G}}^{(1)}$ is a vector of dimension n_1 with elements

$$G_{\alpha}^{(1)} = LC'_{\alpha}. \qquad [40]$$

The rows of $\mathbf{X}$ in which $X_{\alpha j} = 3$ are included in Eq. [37] since the relation

$$\sum_{l=1}^{L} \exp\left[-\frac{i\pi}{2}\sum_{k=1}^{j-1} X_{\alpha k}\cdot F'_{kl}\right]\left\{\exp\left[-\frac{i\pi}{2}F'_{jl}\right]\right\}^3 = LC'_{\alpha} \qquad [41]$$

implies the complex conjugate relation

$$\sum_{l=1}^{L} \exp\left[+\frac{i\pi}{2}\sum_{k=1}^{j-1} X_{\alpha k}\cdot F'_{kl}\right]\left\{\exp\left[-\frac{i\pi}{2}F'_{jl}\right]\right\}^1 = LC'^{*}_{\alpha}, \qquad [42]$$

because $\exp[-i\pi/2\ F'_{jl}]$ can have only values $\pm 1,\ \pm i$.

In cases where there are n_2 rows of matrix $\mathbf{X}$ in which the jth element is 2 and in which the $(j+1)$th and higher elements are zero, Eq. [35] yields a set of n_2 simultaneous equations

$$\mathbf{A}^{(2)}\cdot\vec{\mathbf{B}}^{(2)} = \vec{\mathbf{G}}^{(2)} \qquad [43]$$

in the unknown variables $B_l^{(2)}$, where $\vec{\mathbf{B}}^{(2)}$ is a vector of dimension L with elements

$$B_l^{(2)} = \left\{\exp\left[-\frac{i\pi}{2}F'_{jl}\right]\right\}^2, \qquad [44]$$

$\mathbf{A}^{(2)}$ is a matrix of dimension $n_2 \times L$ with elements

$$A_{\beta l}^{(2)} = \exp\left[-\frac{i\pi}{2}\sum_{k=1}^{j-1} X_{\beta k}\cdot F'_{kl}\right], \qquad [45]$$

and $\vec{\mathbf{G}}^{(2)}$ is a vector of dimension n_2 with elements

$$G_{\beta}^{(2)} = LC'_{\beta}. \qquad [46]$$

Equations [37] and [43] are usually underdetermined sets of simultaneous equations in the variables $B_l^{(1)}$ and $B_l^{(2)}$.

The development of Eqs. [37] and [43] assumes that the phase cycle has length L and that all of the elements of $\vec{\mathbf{B}}^{(1)}$ obtained by solving Eq. [37] will have values in the set $(\pm 1, \pm i)$, that all of the elements of $\vec{\mathbf{B}}^{(2)}$ obtained by solving Eq. [43] will have values ± 1, and, if a set of simultaneous Eqs. [43] was present in the determination of the jth phase variables, that

$$B_l^{(2)} = [B_l^{(1)}]^2 \qquad [47]$$

for all l. If these conditions are met, then the values of the phase variables F'_{jl} are determined from the values of $B_l^{(1)}$ using Eq. [38], and no expansion of the length of the phase cycle is required.

The most interesting and enigmatic part of the determination of the phase variables comes about when the elements of $\vec{\mathbf{B}}^{(1)}$ obtained by solving Eq. [37] and/or the elements of $\vec{\mathbf{B}}^{(2)}$ obtained by solving Eq. [43] do not have values which belong to the required sets, but instead

$$B_l^{(1)} = 0 \quad \text{for } 0 \le l \le L, \qquad [48]$$

and, possibly,

$$B_l^{(2)} = 0 \quad \text{for } 0 \le l \le L. \qquad [49]$$

Clearly a value of zero for $B_l^{(1)}$ or $B_l^{(2)}$ is inconsistent with their definitions (Eqs. [38] and [44]). These zero values can only be rationalized by expanding the length of the phase cycle to $4L$. (In some cases an expansion to $2L$ may be sufficient, so this case is included in the algorithm presented below.) In the phase cycle expansion, each element in a "known" row k of the $\mathbf{F}'$ array, with $1 \le k \le j-1$, is replaced by a block of four replicas of that element so that

$$\begin{array}{c}(F'_{k1}\ F'_{k2}\ \ldots\ F'_{kL})\\ \Downarrow \\ (F'_{k1}\ F'_{k1}\ F'_{k1}\ F'_{k1}\ F'_{k2}\ F'_{k2}\ F'_{k2}\ F'_{k2}\ \ldots\ F'_{kL}\ F'_{kL}\ F'_{kL}\ F'_{kL})\end{array}, \qquad [50]$$

and the jth phase variable is taken to be a simple repetition of the four elements h_1, h_2, h_3, and h_4:

$$F'_{jl} = (h_1\ h_2\ h_3\ h_4\ h_1\ h_2\ h_3\ h_4\ \ldots\ h_1\ h_2\ h_3\ h_4), \qquad [51]$$

whose values are to be chosen appropriately (see below). For this expanded phase cycle, sets of simultaneous Eqs. [37] and [43] are still obtained from the relations in Eq. [35] for which $X_{\alpha j} \neq 0$ and $X_{\alpha\mu} = 0$ for $j < \mu \le K$, the vectors $\vec{\mathbf{B}}^{(1)}$ and $\vec{\mathbf{B}}^{(2)}$ are still of dimension L, and $\mathbf{A}^{(1)}$ and $\mathbf{A}^{(2)}$ still have dimensions $n_1 \times L$ and $n_2 \times L$ with values defined by Eqs. [39] and [45]; but the elements of $\vec{\mathbf{G}}^{(1)}$ and $\vec{\mathbf{G}}^{(2)}$ are four times larger than in Eqs. [40] and [46], and the elements of $\vec{\mathbf{B}}^{(1)}$ and $\vec{\mathbf{B}}^{(2)}$ are given by

$$B_l^{(1)} = \sum_{\kappa=1}^{4} \exp\left[-\frac{i\pi}{2}h_{\kappa}\right] \qquad [52]$$

and

$$B_l^{(2)} = \sum_{\kappa=1}^{4} \left\{\exp\left[-\frac{i\pi}{2}h_{\kappa}\right]\right\}^2, \qquad [53]$$

rather than by Eqs. [38] and [44]. Since the elements of $\vec{\mathbf{B}}^{(1)}$ and/or $\vec{\mathbf{B}}^{(2)}$ were found to be zero, the elements h_κ must be chosen so that

$$\sum_{\kappa=1}^{4} \exp\left[-\frac{i\pi}{2} h_\kappa\right] = 0, \qquad [54]$$

if the zero result [48] was encountered, and

$$\sum_{\kappa=1}^{4} \left\{\exp\left[-\frac{i\pi}{2} h_\kappa\right]\right\}^2 = 0, \qquad [55]$$

if the zero result [49] was encountered. The phase cycle expansion therefore accounts for the zero values of the elements in $\vec{\mathbf{B}}^{(1)}$ and/or $\vec{\mathbf{B}}^{(2)}$, and, conversely, phase cycle expansion is required if the solutions to Eqs. [37] and [43] are the zero results [48] and/or [49].

The determination of the elements F'_{jl} and expansion of the length of the phase cycle from the solutions to Eqs. [37] and [43] is effected using the algorithm:

- If the values of $B_l^{(1)}$ are in the set $(\pm 1, \pm i)$, and if a set of simultaneous Eqs. [43] was involved in the determination of the jth phase variables, Eq. [47] is true for all l, no expansion of the phase cycle is required, and one simply chooses the values of F'_{jl} consistent with the values of $B_l^{(1)}$ (Eq. [38]).
- If one obtains zero values for all elements of $\vec{\mathbf{B}}^{(1)}$ and $\vec{\mathbf{B}}^{(2)}$, the length of the phase cycle must be increased from L to $4L$. The known phases are expanded using Eq. [50], and the jth row of $\mathbf{F}'$ is given by Eq. [51] with $h_\kappa = (0\ 1\ 2\ 3)$, since these elements satisfy both Eqs. [54] and [55].
- If one obtains zero values for all elements of $\vec{\mathbf{B}}^{(1)}$, but not for $\vec{\mathbf{B}}^{(2)}$, the length of the phase cycle is increased from L to $4L$, the known key phases are revised using [50], and the jth key phase variables are given by Eq. [51] with $h_\kappa = (0\ 2\ 1\ 3)$. Since the sets of elements $h_\kappa = (0\ 2)$, $h_\kappa = (1\ 3)$, and $h_\kappa = (0\ 2\ 1\ 3)$ all satisfy [54], it is uncertain whether a twofold or a fourfold increase in the phase cycle is necessary here. This is noted by setting a *halfcycle flag* for this phase cycle expansion step to indicate that the potential validity of a phase cycle obtained by taking only half of the elements in this expansion should be tested once the final phase cycle has been obtained.
- If one encounters zero values for all elements of $\vec{\mathbf{B}}^{(2)}$, but not for $\vec{\mathbf{B}}^{(1)}$, the length of the phase cycle is increased from L to $4L$, the known key phases are revised using [50], and the F'_{jl} are given by Eq. [51] with $h_\kappa = (0\ 1\ 2\ 3)$. Since the sets of elements $h_\kappa = (0\ 1)$, $h_\kappa = (2\ 3)$, and $h_\kappa = (0\ 1\ 2\ 3)$ all satisfy [55], it is again uncertain whether a twofold or a fourfold increase in the phase cycle is necessary. Therefore the halfcycle flag for this expansion is set.

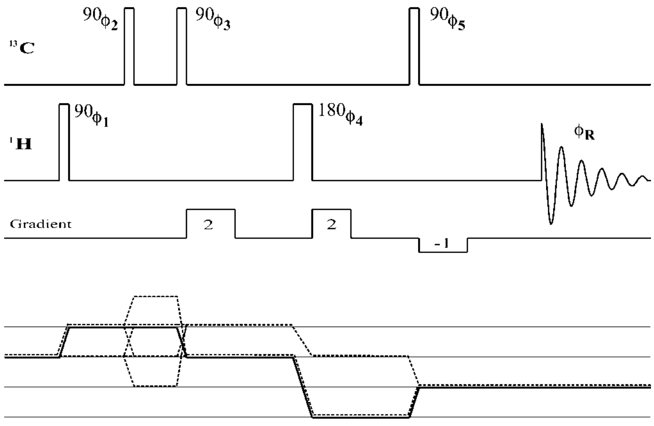

FIG. 1. Pulse sequence and coherence transfer pathways for GHMBC. The solid trajectory is the selected pathway, and the dotted ones are to be blocked by the phase cycle. Pathways which are blocked by the pulsed field gradients are not shown.

The above algorithm allows one to determine the minimum length, L, of the phase cycle and the elements $F'_{\alpha l}$ of the key phases from which the phases of the pulses and receiver are determined (see Eqs. [28] and [30]). The process is illustrated by detailed consideration of some representative pulse sequences in the next section.

APPLICATIONS

In this section, the algorithm developed above is applied to the determination of phase cycles for some representative pulse sequences. In each case, it is assumed that the pathway and phase matrices are in canonical form so that only "primed" matrices need be considered. In all examples, the pathway matrix $\mathbf{P}'$ is constructed by including all pathways which begin in the zero coherence level and end in coherence level -1 of the detected spin. Every pulse is viewed as imperfect, so that all pathways which are opened up by imperfect pulses are included. The elements of the collection vector $\mathbf{C}'$ are the phase factor(s) of the desired signal(s) and are zero for all blocked pathways (see Eqs. [16] and [25]). Arrays $\mathbf{V}'$ and $\mathbf{Q}'$ are determined from $\mathbf{P}'$ using the algorithm given in Table 1, and the elements of the $\mathbf{X}$ matrix are determined from the elements of $\mathbf{Q}'$ using Eq. [36].

GHMBC

The gradient enhanced heteronuclear correlation (GHMBC) of ^{1}H nuclei which are not directly bonded to ^{13}C (*7*) can be achieved using the modified HMQC pulse sequence (*8*) shown in Fig. 1 and conventionally uses an eight-step phase cycle. There are 27 possible coherence transfer pathways for GHMBC, but 21 of them are assumed to be blocked by careful selection of the pulsed field gradient amplitudes and durations.

The arrays involved in determining the phase cycle for GHMBC to select one pathway and block five others are

$$\mathbf{f}' = \begin{pmatrix} f_{11} & f_{12} & \cdots & f_{1L} \\ f_{21} & f_{22} & \cdots & f_{2L} \\ f_{31} & f_{32} & \cdots & f_{3L} \\ f_{R1} & f_{R2} & \cdots & f_{RL} \\ f_{41} & f_{42} & \cdots & f_{4L} \\ f_{51} & f_{52} & \cdots & f_{5L} \end{pmatrix},$$

$$\mathbf{P}' = \begin{pmatrix} 1 & 0 & 3 & 1 & 2 & 1 \\ 0 & 3 & 2 & 1 & 3 & 3 \\ 0 & 0 & 1 & 1 & 3 & 3 \\ 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 1 & 0 & 1 & 3 & 3 \\ 1 & 3 & 0 & 1 & 2 & 1 \\ 1 & 1 & 2 & 1 & 2 & 1 \end{pmatrix}, \ \mathbf{C}' = \begin{pmatrix} 1 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix},$$

$$\mathbf{V}' = \begin{pmatrix} 1 & 0 & 0 & 0 & 1 & 0 \\ 0 & 1 & 0 & 0 & 3 & 3 \\ 0 & 0 & 1 & 0 & 3 & 3 \\ 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix},$$

$$\mathbf{Q}' = \begin{pmatrix} 1 & 0 & 1 & 2 & 0 & 0 & 0 \\ 0 & 3 & 2 & 3 & 0 & 0 & 0 \\ 0 & 0 & 1 & 3 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 1 & 2 & 0 & 1 & 0 & 0 \\ 3 & 3 & 1 & 0 & 0 & 1 & 0 \\ 3 & 1 & 3 & 0 & 0 & 0 & 1 \end{pmatrix},$$

$$\mathbf{X} = \begin{pmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \\ 0 & 3 & 2 & 0 \\ 1 & 1 & 3 & 0 \\ 1 & 3 & 1 & 0 \end{pmatrix}. \qquad [56]$$

There are four linearly independent phases: the receiver phase and three key phases. One begins with $L = 1$ and $F'_{11} = 0$, since $C'_1 = 1$. Row 2 of the $\mathbf{X}$ and $\mathbf{C}'$ matrices gives the relationship

$$(1) \cdot B_1^{(1)} = 0. \qquad [57]$$

This equation has solution [48], so the length of the phase cycle is increased to $L = 4$ and the two known rows of $\mathbf{F}'$ are

$$\mathbf{F}' = \begin{pmatrix} 0 & 0 & 0 & 0 \\ 0 & 2 & 1 & 3 \end{pmatrix}. \qquad [58]$$

The halfcycle flag is set because a twofold expansion of the phase cycle is sufficient to satisfy Eq. [57].

Rows 3, 6, and 7 of $\mathbf{X}$ and $\mathbf{C}'$ give the equation

$$\begin{pmatrix} 1 & 1 & 1 & 1 \\ 1 & -1 & -i & i \\ 1 & -1 & -i & i \end{pmatrix} \vec{\mathbf{B}}^{(1)} = \begin{pmatrix} 0 \\ 0 \\ 0 \end{pmatrix} \qquad [59]$$

and row 5 gives the equation

$$(1 - 1 \quad i - i)\vec{\mathbf{B}}^{(2)} = (0). \qquad [60]$$

The mutually compatible solutions to Eqs. [59] and [60] are

$$\vec{\mathbf{B}}^{(1)} = \begin{pmatrix} -i \\ i \\ -1 \\ 1 \end{pmatrix} \quad \text{and} \quad \vec{\mathbf{B}}^{(2)} = \begin{pmatrix} -1 \\ -1 \\ 1 \\ 1 \end{pmatrix}. \qquad [61]$$

Hence the known rows of $\mathbf{F}'$ have values

$$\mathbf{F}' = \begin{pmatrix} 0 & 0 & 0 & 0 \\ 0 & 2 & 1 & 3 \\ 3 & 1 & 2 & 0 \end{pmatrix}. \qquad [62]$$

All key phases have been determined, so the phases of the pulses may now be determined using Eqs. [29] and [30]. The results, including phases of the receiver and pulses 4 and 5, are

$$\mathbf{f}' = \begin{pmatrix} 3 & 1 & 0 & 2 \\ 2 & 2 & 2 & 2 \\ 3 & 3 & 1 & 1 \\ 0 & 2 & 1 & 3 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}, \qquad [63]$$

with consecutive rows corresponding to the phases of pulses 1, 2, and 3, the receiver phase, and the phases of pulses 4 and 5. The phases $\mathbf{F}'$ computed from this $\mathbf{f}'$ using Eq. [26] satisfy the requirements in Eq. [27] and the pulse/receiver phases in Eq. [63] represent a valid phase cycle for the GHMBC sequence. The half cycle

$$\mathbf{f}' = \begin{pmatrix} 3 & 1 \\ 2 & 2 \\ 3 & 3 \\ 0 & 2 \\ 0 & 0 \\ 0 & 0 \end{pmatrix} \qquad [64]$$

does not give a set of phases $\mathbf{F}'$ which satisfies Eq. [27], and it is concluded that the four-step cycle [63] is the phase cycle of minimum length which selects the required pathway and sup-

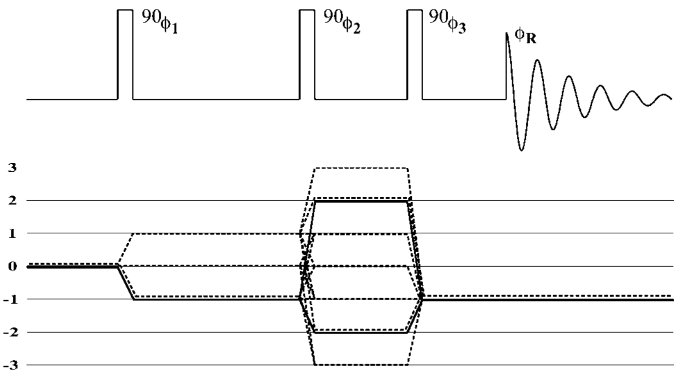

FIG. 2. Pulse sequence and coherence transfer pathways for DQFCOSY. The solid trajectories are the selected pathways, and the dotted ones are to be blocked by the phase cycle.

presses signals associated with other pathways, including those accessed when the pulses are imperfect.

DQFCOSY

The double quantum filtered COSY pulse sequence (*9*) shown in Fig. 2 contains three 90° pulses. The selected and blocked pathways are also shown in Fig. 2. The canonical forms of the phase, pathway, collect, and transformation matrices are

$$\mathbf{f}' = \begin{pmatrix} f_{11} & f_{12} & \cdots & f_{1L} \\ f_{21} & f_{22} & \cdots & f_{2L} \\ f_{31} & f_{32} & \cdots & f_{3L} \\ f_{R1} & f_{R2} & \cdots & f_{RL} \end{pmatrix}, \quad \mathbf{P}' = \begin{pmatrix} 3 & 3 & 1 & 1 \\ 3 & 2 & 2 & 1 \\ 0 & 3 & 0 & 1 \\ 0 & 0 & 0 & 1 \\ 3 & 0 & 0 & 1 \\ 3 & 1 & 3 & 1 \\ 0 & 0 & 3 & 1 \\ 0 & 1 & 2 & 1 \\ 1 & 2 & 0 & 1 \\ 1 & 3 & 3 & 1 \\ 1 & 0 & 2 & 1 \\ 1 & 1 & 1 & 1 \end{pmatrix},$$

$$\mathbf{C}' = \begin{pmatrix} 1 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix}, \quad \mathbf{V}' = \begin{pmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix},$$

$$\mathbf{Q}' = \begin{pmatrix} 2 & 1 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 3 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 3 & 1 & 3 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 2 & 1 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 1 & 2 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 3 & 1 & 3 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 \\ 2 & 2 & 3 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 \\ 2 & 3 & 2 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 \\ 1 & 0 & 2 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 1 & 2 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 \\ 3 & 2 & 2 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 \end{pmatrix},$$

$$\mathbf{X} = \begin{pmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \\ 2 & 3 & 0 & 0 \\ 3 & 2 & 0 & 0 \\ 1 & 3 & 1 & 0 \\ 2 & 2 & 1 & 0 \\ 2 & 1 & 2 & 0 \\ 3 & 0 & 2 & 0 \\ 0 & 3 & 2 & 0 \\ 1 & 2 & 2 & 0 \end{pmatrix}. \qquad [65]$$

Although signals from two pathways are selectively accumulated as shown in Fig. 2, the collection array $\mathbf{C}'$ contains only one nonzero element because the two selected pathways are equivalent in modulo 4. There are four nonzero rows in $\mathbf{V}'$, so there are four linearly independent phases: the receiver phase, which is given by Eq. [31], and three key phases whose elements are to be determined. There are no phases whose elements can be arbitrarily set to zero.

We begin the solution process with $L = 1$ and $F'_{11} = 0$, since $C'_1 = 1$. To determine the second row of $\mathbf{F}'$, we recognize that rows 2, 5, and 6 of $\mathbf{X}$ have nonzero elements in column 2 and zero elements in columns 3 and 4. Both rows 2 and 5 of $\mathbf{X}$ and $\mathbf{C}'$ give

$$1 \cdot B_1^{(1)} = 0, \qquad [66]$$

and row 6 gives

$$1 \cdot B_1^{(2)} = 0. \qquad [67]$$

These two equations give the zero results [48] and [49]. This implies that the length of the phase cycle must be expanded to $L = 4$, with the known rows of the phase matrix given by

$$\mathbf{F}' = \begin{pmatrix} 0 & 0 & 0 & 0 \\ 0 & 1 & 2 & 3 \end{pmatrix}. \qquad [68]$$

The third row of $\mathbf{F}'$ is determined by considering the sets of simultaneous equations

$$\begin{pmatrix} 1 & 1 & 1 & 1 \\ 1 & -i & -1 & i \\ 1 & -1 & 1 & -1 \end{pmatrix} \vec{\mathbf{B}}^{(1)} = \begin{pmatrix} 0 \\ 0 \\ 0 \end{pmatrix} \qquad [69]$$

and

$$\begin{pmatrix} 1 & i & -1 & -i \\ 1 & 1 & 1 & 1 \\ 1 & -i & -1 & i \\ 1 & -1 & 1 & -1 \end{pmatrix} \vec{\mathbf{B}}^{(2)} = \begin{pmatrix} 0 \\ 0 \\ 0 \\ 0 \end{pmatrix}, \qquad [70]$$

which are obtained from Eq. [35] using rows 3, 7, and 8 and rows 9–12 of $\mathbf{X}$ and $\mathbf{C}'$, respectively. The solutions to Eqs. [69] and [70] are

$$\vec{\mathbf{B}}^{(1)} = \begin{pmatrix} 1 \\ -i \\ -1 \\ i \end{pmatrix} \quad \text{and} \quad \vec{\mathbf{B}}^{(2)} = \begin{pmatrix} 0 \\ 0 \\ 0 \\ 0 \end{pmatrix}. \qquad [71]$$

The zero result for $\vec{\mathbf{B}}^{(2)}$ implies that phase cycle expansion to $L = 16$ with the three known rows of the phase matrix given by

$$\mathbf{F}' = \begin{pmatrix} 0&0&0&0&0&0&0&0&0&0&0&0&0&0&0&0 \\ 0&0&0&0&1&1&1&1&2&2&2&2&3&3&3&3 \\ 0&1&2&3&0&1&2&3&0&1&2&3&0&1&2&3 \end{pmatrix},$$

is required. The halfcycle flag is set for this expansion because a twofold expansion may be sufficient.

All key phases have been determined, so the phases of the pulses may now be determined using Eqs. [29] and [30]. The results, including the receiver phase, are

$$\mathbf{f}' = \begin{pmatrix} 0&2&1&3&1&3&2&0&2&0&3&1&3&1&0&2 \\ 0&1&3&0&0&1&3&0&0&1&3&0&0&1&3&0 \\ 0&1&3&0&1&2&0&1&2&3&1&2&3&0&2&3 \\ 0&2&1&3&0&2&1&3&0&2&1&3&0&2&1&3 \end{pmatrix}, \qquad [72]$$

with consecutive rows corresponding to the phases of pulses 1, 2, 3, and the receiver. The phases $\mathbf{F}'$ computed from this $\mathbf{f}'$ using Eq. [26] satisfy the requirements in Eq. [27] and the phases in [72] are a valid phase cycle for the DQFCOSY sequence. The halfcycle

$$\mathbf{f}' = \begin{pmatrix} 0&2&1&3&2&0&3&1 \\ 0&1&0&1&0&1&0&1 \\ 0&1&1&2&2&3&3&0 \\ 0&2&0&2&0&2&0&2 \end{pmatrix} \qquad [73]$$

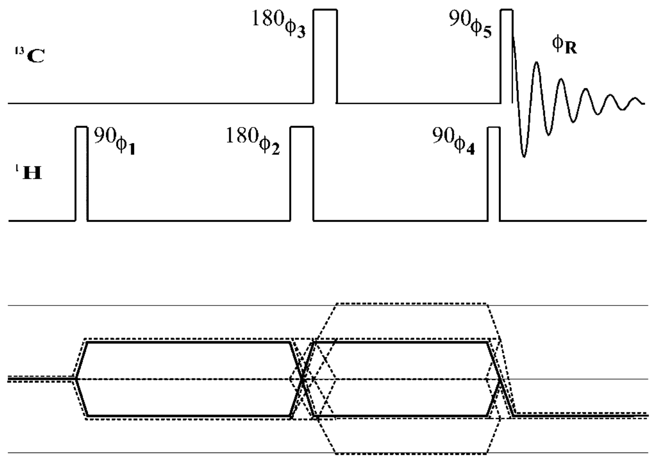

FIG. 3. Pulse sequence and coherence transfer pathways for INEPT. The solid trajectories are the selected pathways, and the dotted ones are to be blocked by the phase cycle.

does not give a set of phases $\mathbf{F}'$ which satisfies Eq. [27], hence the 16-step cycle [72] is the phase cycle of minimum length which will select the appropriate pathways and suppress signals which follow all other pathways including those opened up by imperfections in the first pulse. It should be noted that the second row of $\mathbf{f}'$ in [72], which corresponds to the phase of the second pulse in the sequence, is unusual in that it contains phases 0, 1, and 3 but not phase 2.

INEPT

The INEPT (insensitive nuclei enhanced by polarization transfer) pulse sequence (*10*) shown in Fig. 3 contains three proton pulses and two carbon pulses. Signals which traverse 2 of the 27 possible coherence transfer pathways are selectively accumulated and the signals from all other pathways are blocked as shown in Fig. 3. Since there are so many more pathways than in the two previous examples, the dimensions of the pathway, phase, collection, and transformation matrices are much larger so they are not given here. Application of the reduction algorithm in Table 1 to the pathway matrix $\mathbf{P}$ shows that there are five linearly independent phases: the receiver phase (see Eq. [31]) and four key phases. The solution process follows the methodology used in earlier examples, and, in the interest of brevity, only a brief sketch highlighting the important results are given here. One begins with $L = 1$ and $F'_{11} = 0$ since $C'_1 = 1$ and proceeds with phase cycle expansions in the determination of the elements of rows 2 and 3 of $\mathbf{F}'$, with the halfcycle flag set in the first expansion, but not the second. The four key rows of $\mathbf{F}'$ are

$$\mathbf{F}' = \begin{pmatrix} 0&0&0&0&0&0&0&0&0&0&0&0&0&0&0&0 \\ 0&0&0&0&2&2&2&2&1&1&1&1&3&3&3&3 \\ 0&1&2&3&0&1&2&3&0&1&2&3&0&1&2&3 \\ 1&2&3&0&3&0&1&2&3&0&1&2&1&2&3&0 \end{pmatrix}, \qquad [74]$$

and the pulses/receiver array

$$\mathbf{f}' = \begin{pmatrix} 1 & 3 & 1 & 3 & 3 & 1 & 3 & 1 & 1 & 3 & 1 & 3 & 3 & 1 & 3 & 1 \\ 0 & 1 & 2 & 3 & 2 & 3 & 0 & 1 & 1 & 2 & 3 & 0 & 3 & 0 & 1 & 2 \\ 3 & 3 & 0 & 0 & 3 & 3 & 0 & 0 & 0 & 0 & 1 & 1 & 0 & 0 & 1 & 1 \\ 3 & 1 & 0 & 2 & 1 & 3 & 2 & 0 & 1 & 3 & 2 & 0 & 3 & 1 & 0 & 2 \\ 0 & 2 & 1 & 3 & 0 & 2 & 1 & 3 & 0 & 2 & 1 & 3 & 0 & 2 & 1 & 3 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix} \qquad [75]$$

represents a valid 16-step phase cycle for INEPT. In [75], the consecutive rows of $\mathbf{f}'$ correspond to the phases of pulses 1, 2, 3, and 5, the receiver phase, and the phase of pulse 4 (which is arbitrarily set to zero).

The halfcycle flag was set for the first phase cycle expansion, and the 8-step pulse/receiver phase matrix

$$\mathbf{f}' = \begin{pmatrix} 1 & 3 & 1 & 3 & 3 & 1 & 3 & 1 \\ 0 & 1 & 2 & 3 & 2 & 3 & 0 & 1 \\ 3 & 3 & 0 & 0 & 3 & 3 & 0 & 0 \\ 3 & 1 & 0 & 2 & 1 & 3 & 2 & 0 \\ 0 & 2 & 1 & 3 & 0 & 2 & 1 & 3 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix} \qquad [76]$$

composed of the first eight columns of $\mathbf{f}'$ in Eq. [75] gives a phase array $\mathbf{F}'$ which satisfies the requirements of [27]. Therefore the 8-step cycle in [76] represents a phase cycle of minimum length for the INEPT sequence. It should be noted that the cycling of phase of pulse 3 in the 8- and 16-step cycles is rather unconventional since it does not involve phase 2. Only phases 0 and 3 are used for this pulse in [76] and only phases 0, 1, and 3 in [75].

The Bruker AM pulse program INEPT.AU (DISR94 release) uses a 16-step phase cycle, but the phase cycle actually accumulates signals from four pathways—the two pathways (1 2 0 1 3) and (3 2 0 3 3) selected here, and two extraneous pathways (1 0 0 3 3) and (3 0 0 1 3). The Varian Unity series pulse program `inept.c` (VNMR 6.1 version), with `focus = 'n'` and `normal = 'n'`, uses an unusual 4-step phase cycle, but it accumulates signals from six pathways—the four above plus the pathways (1 3 0 0 3) and (3 0 0 1 3). The undesired pathways in these implementations of INEPT are traversed if the second pulse (a ^{1}H 180 pulse) is imperfect and may lead to observable phase anomalies in the resultant carbon signals. These extraneous pathways are blocked with the 8-step phase cycle [76].

CONCLUSION

In this article, an algorithm for the construction of phase cycles of minimum length has been developed. The application of this algorithm to three representative and well-known pulse sequences has shown that the procedure generates valid phase cycles, some of which have shorter lengths than those used in conventional pulse programs. Furthermore, the phase cycles for the INEPT sequence constructed here block pathways which the longer phase cycles do not. A Windows 98 platform computer implementation of the phase cycle generation algorithm in C is available (*11*) so that robust phase cycles of minimum length can be produced with minimal effort.

We have restricted our attention here to pulse sequences which use only modulo 4 cycling of the phases of pulses and receiver. In principle, the ideas presented here can be extended to other moduli, and multiple quantum filters which require dividing the circle into more than four elements could be handled. However, since the minimum phase cycling required for multiple quantum filters is well-known, such extensions are not being pursued.

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