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A Super-Resolution Parameter Estimation Algorithm for Multi-Dimensional NMR Spectroscopy

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A Super-Resolution Parameter Estimation Algorithm for Multi-Dimensional NMR Spectroscopy[1]

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ABSTRACT

In this paper, we will propose a super-resolution scheme for the parameter estimation of multi-dimensional (M-D) NMR spectroscopy. M-D NMR signals can be modeled as the summation of M-D damped sinusoids. The frequencies and the damping factors of M-D damped sinusoids play important roles in protein structure determination using M-D NMR spectroscopy. We will develop a super-resolution frequency and damping factor estimation algorithm–damped MUSIC (DMUSIC) algorithm. Since the DMUSIC algorithm makes full use of the rank-deficiency and the Hankel property of the data matrix composed of the M-D NMR data, compared with other NMR data analysis algorithms, it can resolve the spectrum using very few data points. The performance of the DMUSIC algorithm is demonstrated by computer simulations.

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INTRODUCTION

The spectral analysis of the NMR spectroscopy is very important in protein structure determination. At early stages of NMR spectroscopy analysis, the application of discrete Fourier transform (DFT) has made a great progress in this field. However, the frequency resolution of the DFT-based algorithms is limited by the short acquisition time of the NMR spectroscopy and measurement noise. Since NMR signals can be modeled as the summation of damped sinusoids, the model-based algorithms have been used in the parameter estimation of one-dimensional (1-D) and two-dimensional (2-D) NMR spectroscopy to improve the frequency resolution (3-19). Among them, the auto-regressive (AR) algorithm is one of the most commonly used algorithms in the analysis of 1-D NMR spectroscopy (8). The approach (15) based on the linear prediction (LP) can obtain better estimation of 2-D NMR data spectrum than the standard DFT algorithm can. Unfortunately, the existing model-based parameter estimation algorithms for 2-D NMR spectroscopy analysis are still sensitive to measurement noise, which limits their resolutions.

The super-resolution or the subspace methods (20,21) in signal processing can be applied to spectral analysis of NMR spectroscopy to alleviate the resolution problem. Multiple signal classification (MUSIC) algorithm (20) is one of the most effective and commonly used algorithms for 1-D stationary signals. The MUSIC algorithm can achieve the *Cramér-Rao* lower bound under some mild conditions. However, the NMR signal is nonstationary and usually multi-dimensional. Therefore, the traditional MUSIC algorithm is not applicable. The MUSIC analysis in (22) ignores the damping factors of signal, which is inappropriate for NMR spectroscopy. In this paper, we will develop a super-resolution algorithm for M-D NMR spectroscopy, which is called the M-D DMUSIC algorithm because of its similarity to the MUSIC algorithm.

MATHEMATICAL MODEL OF NMR SPECTROSCOPY

Before developing the DMUSIC algorithm for multi-dimensional NMR spectroscopy, we will briefly describe the mathematical model of M-D NMR spectroscopy here. Since multi-dimensional NMR spectroscopy is an extension of two-dimensional NMR spectroscopy and one-dimensional NMR spectroscopy is a special case of two-dimensional NMR spectroscopy,

we first briefly introduce the mathematical model of two-dimensional (2-D) NMR spectroscopy. The detailed description of 2-D NMR spectroscopy is given by (23,24).

A 2-D NMR signal in physical system can be expressed as a continuous hypercomplex form $X_h(t_1, t_2)$ as following

$$\begin{aligned} X_h(t_1,t_2) = \; & \textstyle\sum_{k=1}^{K} a_k \{\cos(\Omega_k^{(1)} t_1 + \theta_k^{(1)}) \cos(\Omega_k^{(2)} t_2 + \theta_k^{(2)}) \\ & + \imath \sin(\Omega_k^{(1)} t_1 + \theta_k^{(1)}) \cos(\Omega_k^{(2)} t_2 + \theta_k^{(2)}) \\ & + \jmath \cos(\Omega_k^{(1)} t_1 + \theta_k^{(1)}) \sin(\Omega_k^{(2)} t_2 + \theta_k^{(2)}) \\ & + \imath\jmath \sin(\Omega_k^{(1)} t_1 + \theta_k^{(1)}) \sin(\Omega_k^{(2)} t_2 + \theta_k^{(2)})\} e^{-t_1/T_k^{(1)} - t_2/T_k^{(2)}}, \end{aligned} \qquad [1]$$

where K is the model order, $\Omega_k^{(1)}$ and $\Omega_k^{(2)}$ denote the angular frequencies of the magnetization corresponding to t_1 and t_2 respectively, and $T_k^{(1)}$ and $T_k^{(2)}$ are the decay constants of the magnetization.

In our discussion, we employ the commonly used complex representation $X_c(t_1, t_2)$, that can be obtained by letting $\imath = \jmath$ and $\imath\jmath = -1$ in [1]:

$$X_c(t_1,t_2) = \sum_{k=1}^{K} c_k e^{(-\gamma_k^{(1)} + \jmath\Omega_k^{(1)})t_1 + (-\gamma_k^{(2)} + \jmath\Omega_k^{(2)})t_2}, \qquad [2]$$

where $c_k = a_k e^{\jmath(\theta_k^{(1)} + \theta_k^{(2)})}$, and $\gamma_k^{(1)} = 1/T_k^{(1)}$, $\gamma_k^{(2)} = 1/T_k^{(2)}$ which are called the decay rate.

If the continuous complex 2-D NMR signal is measured at uniform intervals, Δ_1 for t_1 and Δ_2 for t_2, a two-dimensional time-series data $\{x(n_1, n_2)\}$ will be obtained as

$$x(n_1,n_2) = \sum_{k=1}^{K} c_k e^{s_k^{(1)} n_1 + s_k^{(2)} n_2}, \qquad [3]$$

where $s_k^{(l)} = -\alpha_k^{(l)} + \jmath\omega_k^{(l)}$, and $\omega_k^{(l)} = \Omega_k^{(l)}\Delta_l$, $\alpha_k^{(l)} = \gamma_k^{(l)}\Delta_l$ for $l = 1,\ 2$ with $\alpha_k^{(l)}$ being called the damping factor. Without loss of generality, we suppose that $\mathbf{s}_k = (s_k^{(1)},\ s_k^{(2)})$ for $k = 1,\ 2, \cdots,\ K$ be distinct. If measurement error or noise $w(n_1, n_2)$ is considered, the

measured NMR data can be expressed as

$$y(n_1, n_2) = x(n_1, n_2) + w(n_1, n_2), \qquad [4]$$

for $n_i = 0,\ 1, \cdots,\ N_i - 1$ for $i = 1,\ 2$. In the above expression N_i's are acquisition time of each time domain. We will assume $N_1 = N_2 = N$ in our discussion.

If $N_2 = 1$ and in [3] and [4], the mathematical model of 2-D NMR signals is degenerated into that of one-dimensional (1-D) NMR spectroscopy, which can be rewritten as

$$y(n) = x(n) + w(n), \qquad [5]$$

where $w(n)$ denotes the measurement noise and $x(n)$ is as following

$$x(n) = \sum_{k=1}^{K} c_k e^{s_k n}, \qquad [6]$$

for $n = 0,\ 1, \cdots, N - 1$.

The mathematical model of 2-D NMR spectroscopy can be easily extended to that of L-dimensional NMR spectroscopy as following

$$y(\mathbf{n}) = x(\mathbf{n}) + w(\mathbf{n}) \qquad [7]$$

and

$$x(\mathbf{n}) = \sum_{k=1}^{K} c_k e^{\mathbf{s}_k \mathbf{n}^T}. \qquad [8]$$

for $\mathbf{n} \in \{0,\ 1, \cdots, N-1\}^L$. In the above expression, $\mathbf{n} = [n_1, \cdots, n_L]$ is a time index-vector and $\mathbf{s}_k = [s_k^{(1)}, \cdots, s_k^{(L)}]$ is a complex frequency vector. Similar to the two-dimensional case, $w(.)$ represents measurement noise and K denotes the model order.

To determine the protein structure by means of NMR spectroscopy, the complex frequencies $\mathbf{s}_k$ have to be estimated from the measured NMR data. Normally, we have to make sure $N \geq 2K$ in order to estimate the parameters of NMR spectroscopy.

1-D DMUSIC ALGORITHM

We first present the DMUSIC algorithm for one-dimensional NMR spectroscopy (1-D DMUSIC) for it has clear physical meaning.

To derive 1-D DMUSIC algorithm, we will set up an $(N-J)\times J$ *prediction matrix*:

$$\mathbf{A}=\begin{pmatrix} y(0) & y(1) & \cdots & y(J-1) \\ y(1) & y(2) & \cdots & y(J) \\ \vdots & \vdots & \vdots & \vdots \\ y(N-J-1) & y(N-J) & \cdots & y(N-1) \end{pmatrix}, \qquad [9]$$

where J has to be in between K and $N-K$. The prediction matrix to DMUSIC algorithm is as the correlation matrix to MUSIC algorithm (21). From equation [5] and [6], $\mathbf{A}$ can be written as

$$\mathbf{A}=\sum_{k=1}^{K} c_k \mathbf{r}_l(s_k)\mathbf{r}_r^T(s_k)+\mathbf{W}=\mathbf{S}_l\mathbf{C}\mathbf{S}_r^T+\mathbf{W}. \qquad [10]$$

In [10], $\mathbf{r}_r(s)$ and $\mathbf{S}_r$ are the *right signal vector* and the *right signal matrix*, respectively, that are defined as

$$\mathbf{r}_r(s_k)=\begin{pmatrix} 1 \\ e^{s_k} \\ \vdots \\ e^{(J-1)s_k} \end{pmatrix} \quad \text{and} \quad \mathbf{S}_r=[\mathbf{r}_r(s_1),\mathbf{r}_r(s_2),\cdots,\mathbf{r}_r(s_K)], \qquad [11]$$

respectively. The *left signal vector* $\mathbf{r}_l(s)$ and the *left signal matrix* $\mathbf{S}_l$ are similarly defined. $\mathbf{C}$ is a $K\times K$ diagonal matrix with $\text{diag}(\mathbf{C})=(c_1,\ c_2,\cdots,c_K)$. The *noise matrix* $\mathbf{W}$ is

given by

$$\mathbf{W} = \begin{pmatrix} w(0) & w(1) & \cdots & w(J-1) \\ w(1) & w(2) & \cdots & w(J) \\ \vdots & \vdots & \vdots & \vdots \\ w(N-J-1) & w(N-J) & \cdots & w(N-1) \end{pmatrix}. \quad [12]$$

If s_k's are distinct, then $\mathbf{r}_r(s_k)$ for $k = 1,\ 2, \cdots, K$ are linear independent, hence $\mathbf{S}_r$ is of full column rank, and so is $\mathbf{S}_l$. Since the rank of $\mathbf{C}$ is K, the rank of $\mathbf{A}$ is equal to K if there is no measurement noise. Now, assume that there is no noise. By means of singular value decomposition, $\mathbf{A}$ can be decomposed into the product of three matrices

$$\mathbf{A} = \mathbf{U}\mathbf{D}\mathbf{V}^H, \quad [13]$$

where $\mathbf{U}$ and $\mathbf{V}$ are unitary matrices, and $\mathbf{D}$ is a diagonal matrix with

$$\text{diag}(\mathbf{D}) = (\sigma_1,\ \sigma_2, \cdots \sigma_K,\ 0, \cdots,\ 0), \quad \sigma_1 \geq \sigma_2 \geq \cdots \geq \sigma_K. \quad [14]$$

According to [13],

$$\mathbf{A}\mathbf{V} = \mathbf{U}\mathbf{D} \quad [15]$$

Denote $\mathbf{v}_i$ the i-th column of $\mathbf{V}$. span$\{\mathbf{v}_1, \cdots,\ \mathbf{v}_K\}$ is called *signal subspace* for

$$\text{span}\{\mathbf{v}_1, \cdots,\ \mathbf{v}_K\} = \text{span}\{\mathbf{r}_r(s_1), \cdots,\ \mathbf{r}_r(s_K)\}, \quad [16]$$

where span{} is referred to as the subspace that is defined by the set of all linear combinations of the vectors.

From [14] and [15], we have the following *orthogonality relations*

$$\mathbf{A}\mathbf{V}_\mathbf{n} = \mathbf{0}, \quad \text{or} \quad \mathbf{A}\mathbf{v}_k = \mathbf{0} \quad \text{for } k = K+1, \cdots, L. \quad [17]$$

Table 1: Damped MUSIC algorithm

Step 1	Forming data matrix $\mathbf{A}$ using [9]
Step 2	Finding $\mathbf{V_n}$ by making SVD to $\mathbf{A}$
Step 3	Estimating s_k by find the peaks of [19]

where $\mathbf{V_n} = [\mathbf{v}_{K+1}, \cdots, \mathbf{v}_L]$. From [10], we have

$$\mathbf{S}_l \mathbf{C} \mathbf{S}_r^T \mathbf{v}_k = \mathbf{0} \quad \text{for } k = K+1, \cdots, L. \tag{18}$$

Since both $\mathbf{S}_l$, $\mathbf{S}_r$ and $\mathbf{C}$ are of full rank, $\mathbf{S}_r^T \mathbf{v_k} = \mathbf{0}$ for $k = K+1, \cdots, L$, i.e. $\mathbf{r}_r^T(s_n)\mathbf{v_k} = 0$ for $k = K+1, \cdots, L$ and $n = 1,\ 2, \cdots K$. Hence, $\mathbf{V_n}^T \mathbf{r}_r(s) = \mathbf{0}$ only when $s = s_1, \cdots, s_K$. Therefore, s_k can be obtained by finding s which makes $\| \mathbf{V_n}^T \mathbf{r}_r(s) \| = 0$.

When noise exists, the orthogonality relations [17] no longer hold. In this case, we can search for signal vectors that are most closely orthogonal to the noise subspaces. Hence, s_k can be obtained by finding the peak of the following MUSIC spectrum

$$P(s) = \frac{1}{\bar{\mathbf{r}}_r^H(s)(\sum_{k=K+1}^{J} \mathbf{v}_k^* \mathbf{v}_k^T)\bar{\mathbf{r}}_r(s)}, \tag{19}$$

where

$$\bar{\mathbf{r}}_r = \frac{\mathbf{r}_r}{\| \mathbf{r}_r \|} \tag{20}$$

The algorithm is summerized in Table 1.

The algorithm discussed above is called the damped MUSIC (DMUSIC) algorithm for it looks like the MUSIC algorithm. But, there are several crucial differences between DMUSIC algorithm and MUSIC algorithm in that DMUSIC algorithm is for parameter estimation of damped sinusoidal signals which are nonstationary. Since the correlation matrix is not available for nonstationary signals, the prediction matrix is used in DMUSIC algorithm. DMUSIC algorithm searchs on (α, ω) so that these two parameters can be estimated simultaneously.

M-D DMUSIC ALGORITHM

The DMUSIC algorithm for one-dimensional NMR spectroscopy developed in the previous section can be extended to the DMUSIC algorithm for multi-dimensional NMR spectroscopy (M-D DMUSIC).

To obtain a 2-D MUSIC algorithm for the two-dimensional NMR signals modeled in [3] and [4], we first generate an $(N-J+1)\times J$ matrix,

$$\mathbf{A}(n)=\begin{pmatrix} y(n,0) & y(n,1) & \cdots & y(n,J-1) \\ y(n,1) & y(n,2) & \cdots & y(n,J) \\ \vdots & \vdots & \vdots & \vdots \\ y(n,N-J) & y(n,N-J+1) & \cdots & y(n,N-1) \end{pmatrix}, \qquad [21]$$

for $n=1,\ 2,\cdots,\ N-1$. Using $\mathbf{A}(n)$, an $(N-J+1)^2\times J^2$ matrix is formed,

$$\mathbf{A}=\begin{pmatrix} \mathbf{A}(0) & \mathbf{A}(1) & \cdots & \mathbf{A}(J-1) \\ \mathbf{A}(1) & \mathbf{A}(2) & \cdots & \mathbf{A}(J) \\ \vdots & \vdots & \vdots & \vdots \\ \mathbf{A}(N-J-1) & \mathbf{A}(N-J) & \cdots & \mathbf{A}(N-1) \end{pmatrix}, \qquad [22]$$

where J must satisfy $K\le J\le N-K$. It is usually chosen to be $\lceil N/2\rceil$ to obtain the best performance.

Similar to the derivation of 1-D DMUSIC algorithm, we can prove that $\mathbf{s}_k$ can be obtained by finding the peaks of the following 2-D DMUSIC spectrum

$$P(\mathbf{s})=\frac{1}{\bar{\mathbf{r}}_r^H(\mathbf{s})\left(\sum_{k=K+1}^{J^2}\mathbf{v}_k^*\mathbf{v}_k^T\right)\bar{\mathbf{r}}_r(\mathbf{s})}, \qquad [23]$$

where $\mathbf{v}_k$ for $k=K+1,\cdots,J^2$ are the right sigular vectors of $\mathbf{A}$ corresponding to the

$J^2 - K$ smallest sigularvalues and

$$\mathbf{r}_r(\mathbf{s}_k) = \begin{pmatrix} 1 \\ e^{s_k^{(2)}} \\ \vdots \\ e^{(J-1)s_k^{(2)}} \\ e^{s_k^{(1)}} \\ e^{s_k^{(1)}+s_k^{(2)}} \\ \vdots \\ e^{s_k^{(1)}+(J-1)s_k^{(2)}} \\ \vdots \\ e^{(J-1)s_k^{(1)}} \\ e^{(J-1)s_k^{(1)}+s_k^{(2)}} \\ \vdots \\ e^{(J-1)s_k^{(1)}+(J-1)s_k^{(2)}} \end{pmatrix} \quad \text{and} \quad \bar{\mathbf{r}}_r = \frac{\mathbf{r}_r}{\| \mathbf{r}_r \|} \qquad [24]$$

In general, for multi-dimensional NMR spectroscopy, $(N - J + 1)^L \times J^L$ *data matrix* $\mathbf{A}$ is defined as

$$\mathbf{A} = \begin{pmatrix} \mathbf{A}(0) & \mathbf{A}(1) & \cdots & \mathbf{A}(J-1) \\ \mathbf{A}(1) & \mathbf{A}(2) & \cdots & \mathbf{A}(J) \\ \vdots & \vdots & \vdots & \vdots \\ \mathbf{A}(N-J-1) & \mathbf{A}(N-J) & \cdots & \mathbf{A}(N-1) \end{pmatrix}, \qquad [25]$$

where

$$\mathbf{A}(n_1,\cdots,n_l) = \begin{pmatrix} \mathbf{A}(n_1,\cdots,n_l,0) & \cdots & \mathbf{A}(n_1,\cdots,n_l,J-1) \\ \mathbf{A}(n_1,\cdots,n_l,1) & \cdots & \mathbf{A}(n_1,\cdots,n_l,J) \\ \vdots & \vdots & \vdots \\ \mathbf{A}(n_1,\cdots,n_l,N-J-1) & \cdots & \mathbf{A}(n_1,\cdots,n_l,N-1) \end{pmatrix}, \quad [26]$$

for $l = 1,\ 2,\cdots,L-2$, and

$$\mathbf{A}(n_1,\cdots,n_{L-1}) = \begin{pmatrix} y(n_1,\cdots,n_{L-1},0) & \cdots & y(n_1,\cdots,n_{L-1},J-1) \\ y(n_1,\cdots,n_{L-1},1) & \cdots & y(n_1,\cdots,n_{L-1},J) \\ \vdots & \vdots & \vdots \\ y(n_1,\cdots,n_{L-1},N-J) & \cdots & y(n_1,\cdots,n_{L-1},N-1) \end{pmatrix}. \quad [27]$$

The *right signal vector* corresponding to the data matrix $\mathbf{A}$ is defined as

$$\mathbf{r}(\mathbf{s}) = \begin{pmatrix} \mathbf{r}_{L-1}(\mathbf{s}) \\ e^{s_k^{(1)}}\mathbf{r}_{L-1}(\mathbf{s}) \\ \vdots \\ e^{(J-1)s_k^{(1)}}\mathbf{r}_{L-1}(\mathbf{s}) \end{pmatrix}. \quad [28]$$

where

$$\mathbf{r}_l(\mathbf{s}) = \begin{pmatrix} \mathbf{r}_l(\mathbf{s}) \\ e^{s_k^{(L-l+1)}}\mathbf{r}_{l-1}(\mathbf{s}) \\ \vdots \\ e^{(J-1)s_k^{(L-l+1)}}\mathbf{r}_{l-1}(\mathbf{s}) \end{pmatrix} \quad [29]$$

for $l = 2,\ 3, \cdots,\ L-1$, and

$$\mathbf{r}_1(\mathbf{s}) = \begin{pmatrix} 1 \\ e^{s_k^{(L)}} \\ \vdots \\ e^{(J-1)s_k^{(L)}} \end{pmatrix}. \qquad [30]$$

From the definition, $J^L \times 1$ vector $\mathbf{r}(\mathbf{s}_k)$ for $k = 1,\ 2, \cdots K$ are independent if $J \geq K$. Therefore, similar to 1-D DMUSIC algorithm, the frequency vector $\mathbf{s}$ can be estimated by finding the peaks of M-D DMUSIC spectrum

$$P(\mathbf{s}) = \frac{1}{\bar{\mathbf{r}}_r^H(\mathbf{s})(\sum_{k=K+1}^{J^L} \mathbf{v}_k^* \mathbf{v}_k^T)\bar{\mathbf{r}}_r(\mathbf{s})} \quad \text{and} \quad \bar{\mathbf{r}}_r = \frac{\mathbf{r}_r}{\| \mathbf{r}_r \|}, \qquad [31]$$

where vectors $\mathbf{v}_{K+1}, \cdots, \mathbf{v}_{J^L}$ are $J^L - K$ right singular vectors of $\mathbf{A}$ corresponding to the $J^L - K$ smallest sigular values.

SIMPLIFIED PEAKING SEARCH ALGORITHMS

To estimate the parameters of L-D NMR signals, we have to find the peak of L-D DMUSIC spectrum, which is a function of $2L$ variables: $\alpha^{(1)}, \cdots,\ \alpha^{(L)},\ \omega^{(1)}, \cdots,\ \omega^{(L)}$. To find the peak of the L-D DMUSIC spectrum, we have to calculate it in a fine lattice, which is a 2L-dimensional search.

Since the damping factors of NMR signals are normally very small (usually less than 0.3), the following simplified peak searching algorithm can be used to reduce the computation of the 2-D DMUSIC spectrum. For the convenience of our discussion, we rewrite $P(s^{(1)},\ s^{(2)})$ into $P(\alpha^{(1)},\ \alpha^{(2)};\ \omega^{(1)},\ \omega^{(2)})$. If the damping factors of signals are small, then the maxima of $P(\alpha^{(1)},\ \alpha^{(2)};\ \omega^{(1)},\ \omega^{(2)})$ will be near $\omega^{(1)}$-$\omega^{(2)}$ palne. Because $P(\alpha^{(1)},\ \alpha^{(2)};\ \omega^{(1)},\ \omega^{(2)})$ is convex around its maxima, $P(0,\ 0;\ \omega^{(1)},\ \omega^{(2)})$ is also convex around maxima. Hence, $P(0,\ 0;\ \omega^{(1)},\ \omega^{(2)})$ has maximum points $(\widehat{\omega}_k^{(1)},\ \widehat{\omega}_k^{(2)})$ for $k = 1,\ 2, \cdots,\ K$, which are near the peaks of $P(\alpha^{(1)},\ \alpha^{(2)};\ \omega^{(1)},\ \omega^{(2)})$. For each maximum $(\widehat{\omega}_k^{(1)},\ \widehat{\omega}_k^{(2)})$ of $P(0,\ 0;\ \omega^{(1)},\ \omega^{(2)})$, $(\widehat{\alpha}_k^{(1)},\ \widehat{\alpha}_k^{(2)})$ can be found to maximize $P(\alpha^{(1)},\ \alpha^{(2)};\ \widehat{\omega}_k^{(1)},\ \widehat{\omega}_k^{(2)})$ since $P(\alpha^{(1)},\ \alpha^{(2)};\ \widehat{\omega}_k^{(1)},\ \widehat{\omega}_k^{(2)})$

Table 2: 2-D Peak searching algorithm

Step 1	Find $(\widehat{\omega}_k^{(1)},\ \widehat{\omega}_k^{(2)})$ for $k = 1,\ 2, \cdots, K$ maximizing $P(0,\ 0;\ \omega^{(1)},\ \omega^{(2)})$
Step 2	Find $(\widehat{\alpha}_1^{(1)},\ \widehat{\alpha}_1^{(2)})$ maximizing $P(\alpha^{(1)},\ \alpha^{(2)};\ \widehat{\omega}_1^{(1)},\ \widehat{\omega}_1^{(2)})$
Step 3	Find $(\widehat{\widehat{\omega}}_1^{(1)},\ \widehat{\widehat{\omega}}_1^{(2)})$ around $(\widehat{\omega}_1^{(1)},\ \widehat{\omega}_1^{(2)})$ and maximizing $P(\widehat{\alpha}_1^{(1)},\ \widehat{\alpha}_1^{(2)},\ \omega^{(1)},\ \omega^{(2)})$
Step 4	Repeat Step 2, 3 until the estimation of $s_1^{(1)} = -\alpha_1^{(1)} + \jmath\omega_1^{(1)}$ $s_1^{(2)} = -\alpha_1^{(2)} + \jmath\omega_1^{(2)}$ attains certain precision
Step 5	Repeat Step 2, 3 and 4 for $k = 2,\ 3, \cdots, K$

is convex. Then, we can find $(\widehat{\widehat{\omega}}_k^{(1)},\ \widehat{\widehat{\omega}}_k^{(2)})$ around $(\widehat{\omega}_k^{(1)},\ \widehat{\omega}_k^{(2)})$ and maximizing $P(\widehat{\alpha}_k^{(1)},\ \widehat{\alpha}_k^{(2)},\ \omega^{(1)},\ \omega^{(2)})$. Repeating the above procedures, the paeks of $P(\alpha^{(1)},\ \alpha^{(2)};\ \omega^{(1)},\ \omega^{(2)})$ can be searched. The above searching procedures can be summerized in Table 2. The above simplified peak-searching algorithm reduces the peak-search of four-variable function to that of two-variable function. Hence, the computation is significantly reduced.

The parameter estimation of higher-dimensional NMR signals can be decomposed into the parameter estimation of lower-dimensional NMR signals to reduce the computation. Taking 3-D NMR signal $y(n_1, n_2, n_3)$ as an example, it is a 2-D NMR signal if n_3 is fixed. Hence, the frequency pairs corresponding to time index n_1 and n_2 can estimated by 2-D MUSIC algorithm. Similarly, the frequencies corresponding to n_3 can be estimated using 1-D DMUSIC algorithm. The three-dimensional complex frequency vector can be found by searching the peak of the 3-D DMUSIC spectrum near all the combinations of the frequency pairs corresponding to index n_1 and n_2 and the frequencies corresponding to index n_3. In this way, the parameter estimation of 3-D NMR signals is simplified into the parameter estimation of 2-D NMR signals and 1-D NMR signals. In fact, the parameter estimation of higher-dimensional NMR spectroscopy can always be decomposed into the parameter estimation of 2-D NMR spectroscopy and 1-D NMR spectroscopy in this way.

COMPUTER SIMULATION EXAMPLES

To illustrate the theoretical consistency, the 1-D, 2-D and 3-D DMUSIC algorithm are tested by four examples. In our simulation examples, the measurement noise $w(.)$ is complex

white Gaussian noise with variance σ^2. The SNR is the peak signal noise ratio defined as

$$SNR = 10log\frac{1}{2\sigma^2}. \quad [32]$$

Example 1:

The synthetic one-dimensional NMR spectroscopy are generated by

$$y(n) = e^{s_1 n} + e^{s_2 n} + w(n), \quad [33]$$

where $s_1 = -0.2 + \jmath 2\pi(0.42)$, $s_2 = -0.1 + \jmath 2\pi(0.42 + \Delta)$. The data length is $N = 24$, therefore we pick $J = 12$.

When SNR = 40dB, $\Delta = 0.1$. the 1-D DMUSIC spectrum is shown in Figure 1 (a) and the contour in Figure 1 (b). From the figures, the damping factors and frequencies of the signal can be easily estimated simultaneously by finding the peak on the spectrum. But if SNR = 40dB, $\Delta = 0$, i.e. two exponentially damped signals with the same frequency, the spectrum has just one peak (see Figure 1 (c) and (d)). Hence, the damping factors of the signals can not be correctly estimated under this condition. However, if SNR is increased to $60dB$, both the damping factors and the frequencies of the signals can be estimated again as demonstrated by Figure 1 (e) and (f).

Example 2:

In this example, a synthetic two-dimensional NMR signal is first generated using Equation [3] and [4]. The model order $K = 5$ and the frequency pairs are shown in Table 3. The data length is $N = 24$ and J is chosen to be 12 to obtain best performance.

When $SNR = 30dB$, the 2-D DMUSIC spectrum $P(\mathbf{s})$ and its contour using 2-D peak searching algorithm are shown in Figures 2 and 3. From the figures, we can see that $P(\mathbf{s})$ only has four peaks on $\omega_1 - \omega_2$ plane with $\alpha^{(1)} = \alpha^{(2)} = 0$, but five peaks are found by the simplified peak searching algorithm and the parameters can be estimated successfully as illustrated by Table 3.

When $SNR = 20dB$, the estimated parameters are in Table 3. From the table, we can see that the forth and fifth frequency pairs can not be successfully estimated because they are so close that our algorithm can not resolve them under $20dB$ noise.

Table 3: Estimated parameters of a synthetic 2-D NMR signal

	k	$\alpha_k^{(1)}$	$\omega_k^{(1)}$	$\alpha^{(2)_k}$	$\omega_k^{(2)}$
True values	1	-0.20	0.10π	-0.10	0.10π
	2	-0.00	0.30π	-0.00	0.10π
	3	-0.05	0.20π	-0.02	0.25π
	4	-0.02	0.05π	-0.02	0.30π
	5	-0.10	0.06π	-0.02	0.31π
Estimated values SNR=30dB	1	-0.21	0.10π	-0.11	0.10π
	2	-0.00	0.30π	-0.00	0.10π
	3	-0.05	0.20π	-0.02	0.25π
	4	-0.11	0.05π	-0.04	0.31π
	5	-0.09	0.07π	-0.01	0.31π
Estimated values SNR=20dB	1	-0.19	0.10π	-0.10	0.10π
	2	-0.00	0.30π	-0.00	0.10π
	3	-0.05	0.20π	-0.02	0.25π
	4	-1.00	0.64π	-0.00	0.31π
	5	-0.07	0.06π	-0.01	0.31π

Example 3:

This example demonstrates the application of 2-D DMUSIC algorithm in the parameter estimation of a real 2-D NMR signal. The measured 24 × 24 2-D NMR spectroscopy is obtained from the National Institution for Health. The DFT of the 24 × 24 NMR data that are zero padded to 512 × 512 points is shown in Figure 4. From Figure 4, we can not estimate the parameters of this NMR signal using DFT. The 2-D spectrum $P(0,0;\omega^{(1)},\omega^{(2)})$ and its contour are shown in Figure 5. From the figure, $P(0,0;\omega^{(1)},\omega^{(2)})$ have five peaks. The 2-D spectrum $P(\alpha^{(1)},\alpha^{(2)};\ 0.10\pi,-0.12\pi)$ and its contour are shown in Figure 6. Only repeating Step 2 and 3 in Table 2 twice, we can clearly estimate the frequencies and the damping factors of the signal which are listed in Table 4.

Example 4:

The three-dimensional synthetic NMR signal is generated by [7] and [8]. The model order is $K = 3$. The frequency vectors are shown in Table 5. The synthetic NMR signal is corrupted by measurement noise with $SNR = 15dB$. First, we estimate the complex frequency pairs corresponding to the first two indexes using simplified 2-D searching algorithm and the complex frequencies corresponding to the third index. Then, we get the right 3-D frequency vectors by finding if the 3-D DMUSIC spectrum is the maximum point at the

Table 4: Estimated parameters of a real 2-D NMR signal

k	$\alpha_k^{(1)}$	$\omega_k^{(1)}$	$\alpha^{(2)_k}$	$\omega_k^{(2)}$
1	0.06	0.04π	0.06	-0.02π
2	0.07	-0.56π	0.08	0.10π
3	0.07	-0.42π	0.09	0.40π
4	0.13	0.10π	0.09	-0.12π
5	0.21	0.12π	0.29	0.64π

all possible combinations of the complex frequency pairs and the complex frequencies. The estimated frequency vectors are shown in Table 5.

Table 5: Estimated parameters of a synthetic 3-D NMR signal

	k	$\alpha_k^{(1)}$	$\omega_k^{(1)}$	$\alpha^{(2)_k}$	$\omega_k^{(2)}$	$\alpha^{(3)_k}$	$\omega_k^{(3)}$
True values	1	0.040	-0.740π	0.140	-0.820π	0.100	-0.140π
	2	0.010	0.050π	0.190	-0.190π	0.170	0.310π
	3	0.140	0.290π	0.080	-0.720π	0.010	0.150π
Estimated values SNR=15dB	1	0.040	-0.740π	0.150	-0.815π	0.100	-0.140π
	2	0.010	0.050π	0.190	-0.190π	0.180	0.310π
	3	0.140	0.295π	0.080	-0.720π	0.020	0.145π

CONCLUSIONS

To determine protein structure using the NMR signals, the parameters of the NMR spectroscopy have to be estimated. This paper deals with the parameter estimation of multi-dimensional NMR signals. We propose a novel singular-value-decomposition based parameter estimation algorithm called M-D DMUSIC algorithm for it has super-resolution performance like MUSIC algorithm. We aslo discuss simplified peak-searching problem in order to reduce the computation of M-D DMUSIC algorithm. The performance of the M-D DMUSIC algorithm is tested by extensive computer simulations. The M-D DMUSIC algorithm proposed in this paper can obtain very closely-spaced frequency and damping factors by using only very few data points.

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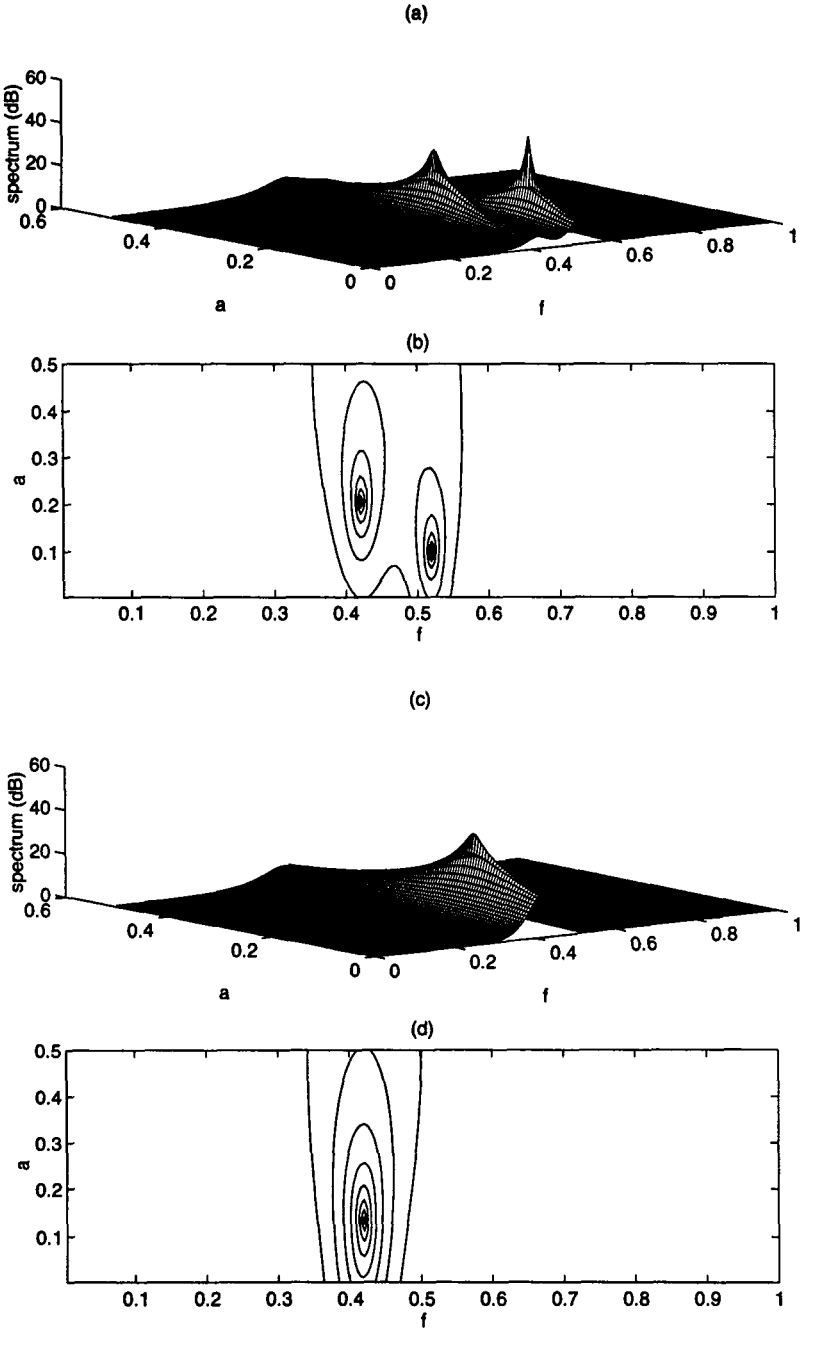
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spectrum (dB)
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40
20
0
0.6
0.4
0.2
0
a
0
0.2
0.4
0.6
0.8
1
f
(b)
0.5
0.4
0.3
0.2
0.1
a
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1
f
(c)
spectrum (dB)
60
40
20
0
0.6
0.4
0.2
0
a
0
0.2
0.4
0.6
0.8
1
f
(d)
0.5
0.4
0.3
0.2
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a
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1
f

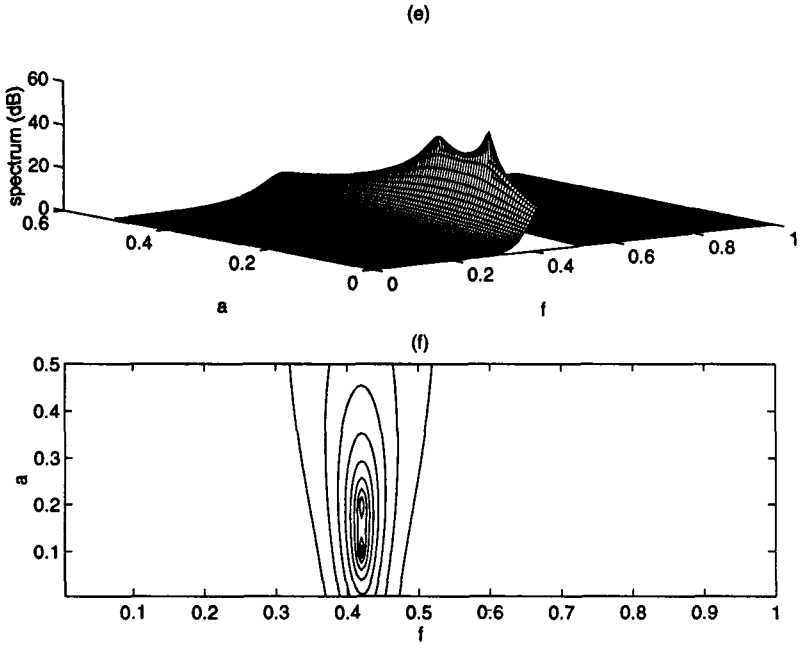

Figure 1: Spectrum and contour of DMUSIC algorithm (a) and (b) when $s_1 = -0.2 + \jmath 2\pi 0.42$, $s_2 = -0.1 + \jmath 2\pi 0.52$ and $SNR = 40dB$, (c) and (d) when $s_1 = -0.2 + \jmath 2\pi 0.42$, $s_2 = -0.1 + \jmath 2\pi 0.42$ and $SNR = 40dB$, (e) and (f) when $s_1 = -0.2 + \jmath 2\pi 0.42$, $s_2 = -0.1 + \jmath 2\pi 0.42$ and $SNR = 60dB$.

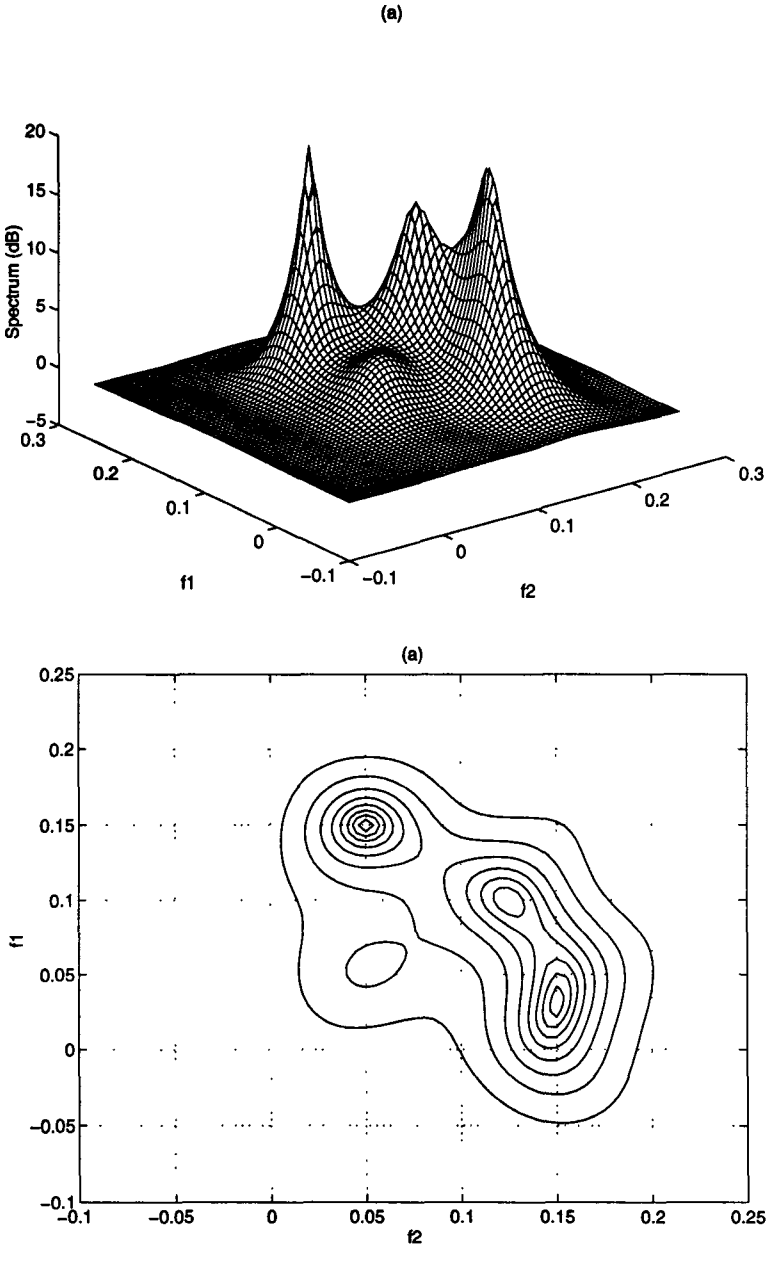

Figure 2: The spectrum $P(0,0;\ \omega^{(1)},\omega^{(2)})$ and its contour for a synthetic 2-D NMR signal using 2-D peak searching method when $SNR = 30dB$.

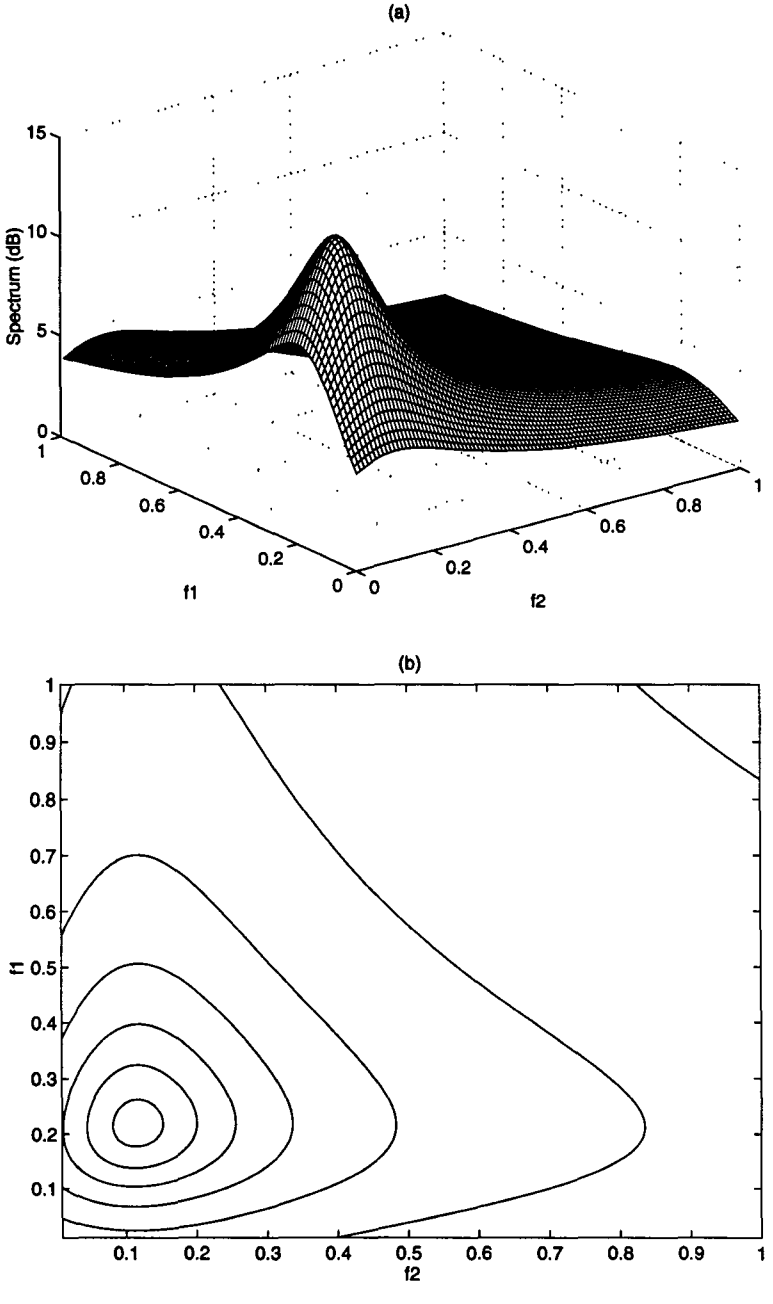

Figure 3: The spectrum $P(\alpha^{(1)}, \alpha^{(2)};\ 0.20\pi, 0.25\pi)$ and its contour for a synthetic 2-D NMR signal using 2-D peak searching method when $SNR = 30dB$.

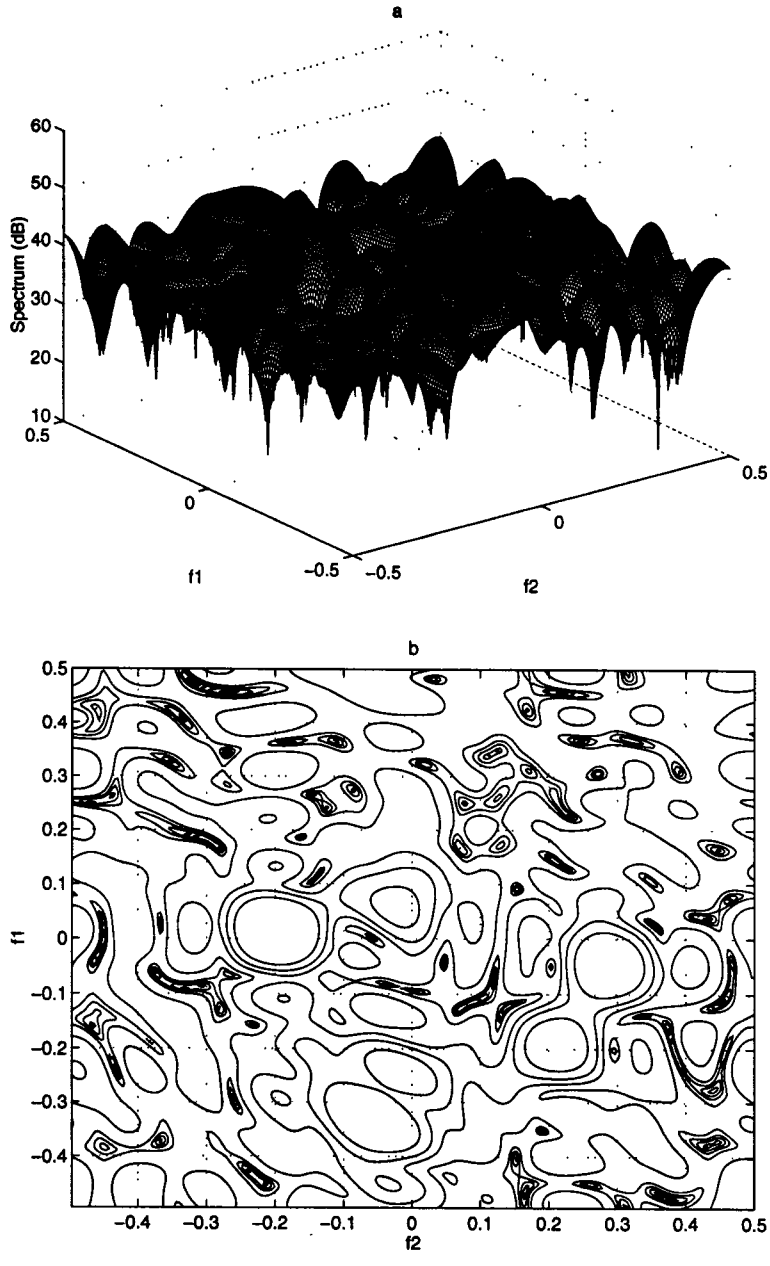

Figure 4: 2-D FFT of NMR data that are zero padded to 512×512, (a)Fourier spectrum (b)its contour plot.

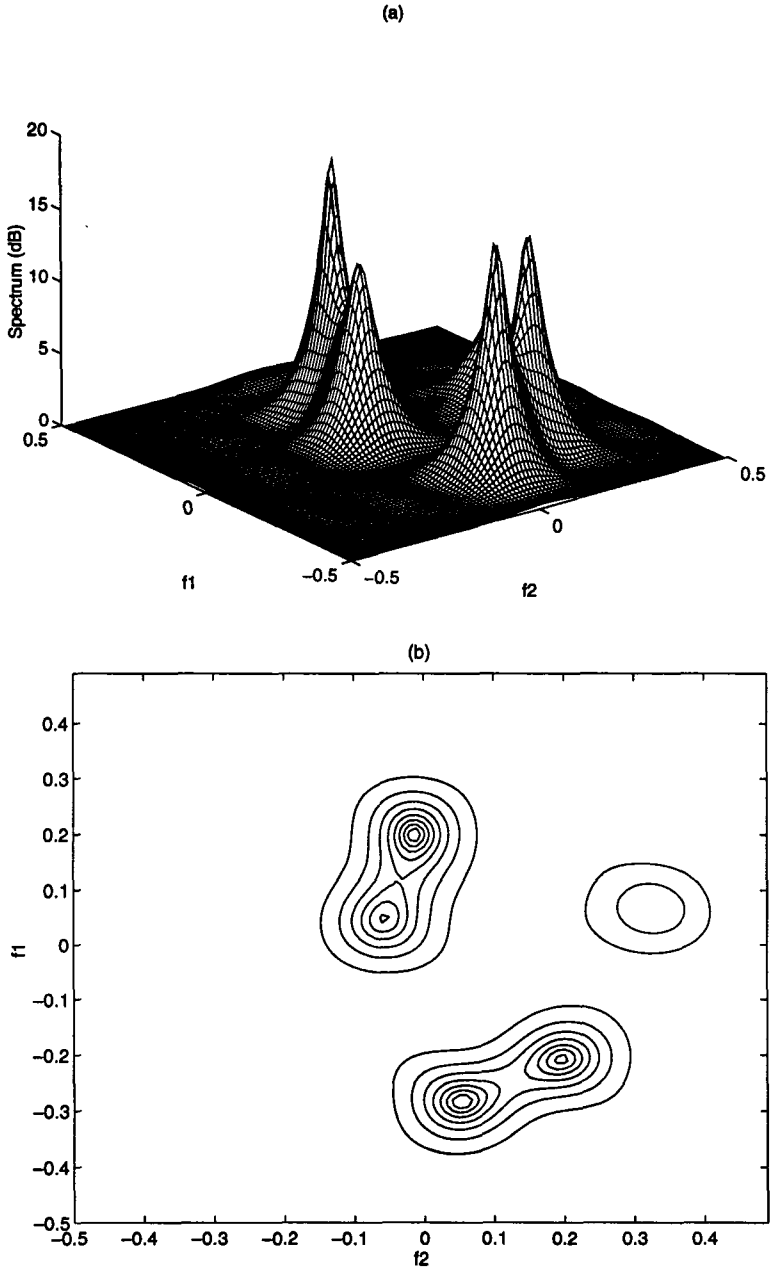

Figure 5: The spectrum $P(0,0;\ \omega^{(1)},\omega^{(2)})$ and its contour for a real 2-D NMR signal.

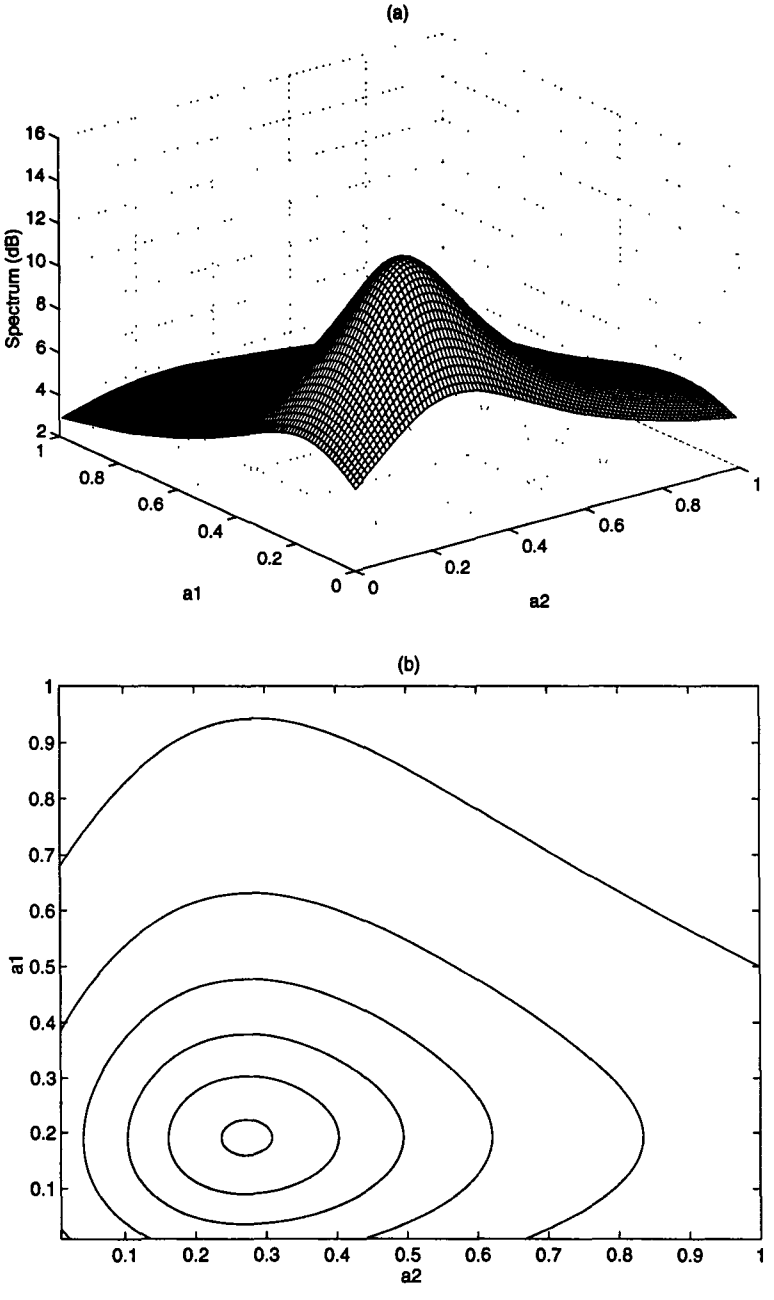

Figure 6: The spectrum $P(\alpha^{(1)}, \alpha^{(2)};\ 0.10\pi, -0.12\pi)$ and its contour for a real 2-D NMR signal.